

Synthesis of 2,4-Dideoxy-4-hydroxyphosphonoyl-D-erythro- and -L-threo-pentofuranoses

Tadashi Hanaya,^a Ayashi Noguchi,^a Margaret-Ann Armour,^b Alan M. Hogg^b and Hiroshi Yamamoto^{*,a}

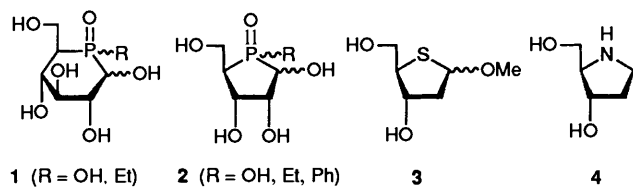
^a Department of Chemistry, Faculty of Science, Okayama University, Tsushima, Okayama 700, Japan

^b Department of Chemistry, The University of Alberta, Edmonton, Alberta, T6G 2G2, Canada

Treatment of 3,5, 6-trideoxy-1,2-*O*-isopropylidene-6-nitro- α -D-erythro-hex-5-enofuranose with dimethyl phosphonate in the presence of triethylamine, followed by catalytic hydrogenation and then deamination with nitrous acid, provided mainly a 2:1 mixture of 3,5-dideoxy-5-dimethoxyphosphinoyl-1,2-*O*-isopropylidene- α -D-ribo- and - β -L-lyxo-hexofuranose in 57% overall yield. This mixture was deacetonated, oxidized with sodium periodate, and then treated with acidic methanol to afford methyl 2,4-dideoxy-4-dimethoxyphosphinoyl- α,β -D-erythro-pentopyranosides (41% overall yield from the aforementioned phosphinoylfuranose) and -L-threo-pentopyranosides (17% overall yield). The major products were reduced with sodium dihydrobis-(2-methoxyethoxy)-aluminum, followed by hydrolysis with acid and then oxidation with hydrogen peroxide, to afford the title D-erythro compounds, whereas similar treatment of the minor pyranosides afforded the corresponding L-threo-pentofuranoses. These compounds were converted into the corresponding 1,3,5-tri-*O*-acetyl-5-methoxyphosphonoyl derivatives, whose structures and conformations [mostly ${}^3T_2(D)$ for one and ${}^2T_3(L)$ for the other] were established by spectroscopy.

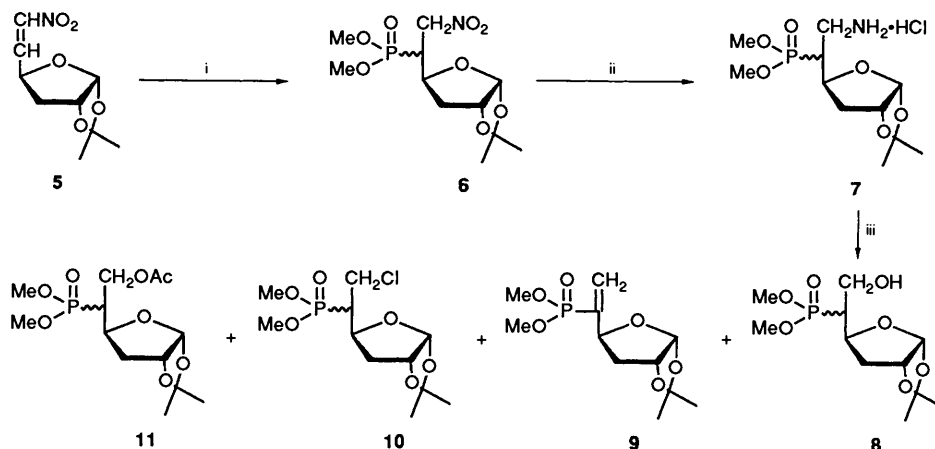
In view of the wide interest in their chemical and biochemical properties, various sugar analogues having a phosphorus atom in the hemiacetal ring¹ have been prepared in recent years: e.g., analogues of D-glucopyranose **1**²⁻⁴ and D-ribofuranose **2**.⁵⁻⁷ At the same time, other heteroatom-in-the-ring sugar analogues of the 2-deoxypentose type have drawn considerable interest from the viewpoint of their potential derivatization to nucleosides and nucleotides. For example, the preparation of methyl 2-deoxy-4-thio-D-erythro-pentofuranoside **3**⁸ and the isolation of 1,2,4-trideoxy-1,4-imino-D-erythro-pentitol **4**⁹ have been reported. We now describe our detailed study on the synthesis of hydroxyphosphonoyl-in-the-ring sugar analogues having a 2-deoxy-D-ribofuranose structure.¹⁰

An addition reaction of dimethyl phosphonate to 3,5,6-

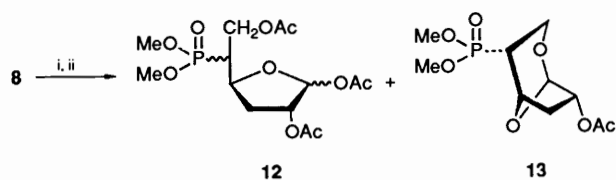


trideoxy-1,2-*O*-isopropylidene-6-nitro- α -D-erythro-hex-5-enofuranose **5**¹¹ proceeded smoothly at 25 °C in the presence of triethylamine (TEA) to give a 66:34 mixture of the α -D-ribo- and β -L-lyxo-hexofuranose **6** in 94% yield (Scheme 1); these two compounds remained inseparable even upon repeated chromatography. The exact assignment of the configuration of the major and minor products, respectively, to D-ribo and L-lyxo was possible only after these compounds had been converted into their methyl pentopyranosides **16** and **17** (see later). Hydrogenation of compound **6** in methanol in the presence of platinum(IV) oxide afforded compound **7** which, on deamination with nitrous acid, provided a 2:1 mixture of the 3,5-dideoxy-D-ribo- and -L-lyxo-hexofuranose **8** (in 61% yield from **6**), along with minor amounts of the dehydrated product **9** (12%), 6-chloro compounds **10** (8%), and 6-*O*-acetyl compounds **11** (7%) (Scheme 1). Compound **9** was derived from the chloride **10** by treatment with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), whereas compound **11** was converted into the corresponding alcohol **8** by treatment with sodium methoxide.

Attempted deacetonation of compound **8** by acid hydrolysis and then acetylation (for the purposes of confirmation of products) resulted in the formation of a considerable amount



Scheme 1 Reagents: i, HP(=O)(OMe)₂, TEA; ii, H₂, PtO₂, HCl; iii, NaNO₂, AcOH



Scheme 2 Reagents: i, H⁺; ii, Ac₂O, py

of a 1,6-anhydro-β-D-ribo-hexofuranose derivative **13** (25%) besides the desired triacetates **12** (60%) (Scheme 2). The structure of the bicycle **13** was established by ¹H NMR and mass spectrometry. The axial 6-H proton (6-H_{ax}), which is *trans*-diaxial to the 5-phosphinoyl group ($J_{6ax,P}$ 33.4 Hz), shows an NOE enhancement with the 2-H and 3-H_R protons (see Experimental section). The presence of long-range coupling between P-5 and 3-H_S ($J_{3S,P}$ 4.3 Hz) supports the *D-ribo* configuration of compound **13**.

Alternatively, compounds **8** were first treated with acetic anhydride-sulfuric acid at 25 °C for 4 h (to yield triacetates **12**) and then with sodium methoxide in methanol, thus giving the *D-erythro*-hexofuranoses **14** in 91% yield (Scheme 3). Periodate oxidation of triol **14** gave the (4*RS*)-3-*O*-formyl-*D-glycero*-pentopyranoses **15** which, upon treatment with methanol in the presence of an acidic ion-exchange resin followed by chromatographic separation, provided methyl 2,4-dideoxy-4-dimethoxyphosphinoyl-*α-D-erythro*-pentopyranoside (**16a**, 16% overall yield from **14**), its β-anomer **16b** (29%), the corresponding *α-L-threo*-pentopyranoside **17a** (15%), and its β-anomer **17b** (3.8%). Besides these four epimers, minor amounts of the following 3-*O*-methyl derivatives were also obtained unexpectedly: **18a** (2.2% from **14**), **18b** (4.8%), **19a** (6.3%), and **19b** (1.7%). Although these 3-*O*-methyl products appear to be formed as the result of an acid-catalysed β-elimination of formate from compound **15** and subsequent addition of MeOH to the Δ^{3,4}-pentose intermediate, the exact mechanism remains to be further studied.

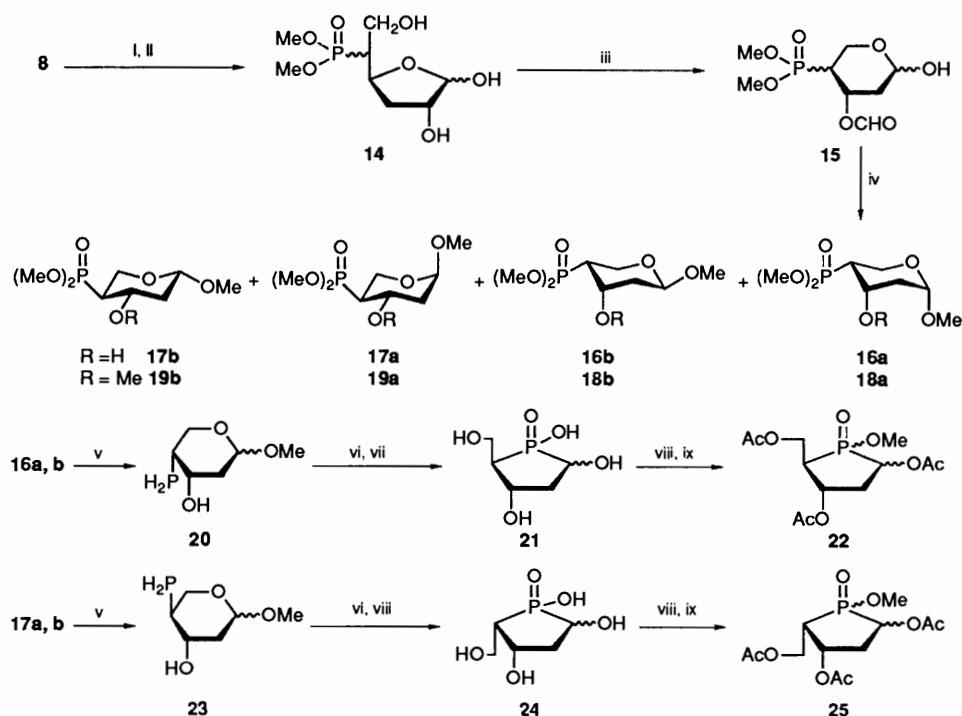
The structural and conformational assignments of these eight compounds (**16–19a, b**) were made on the basis of their NMR

data (see Experimental section). The presence of C-2-phosphorus coupling ($^3J_{2,P}$ 10–13 Hz) in the ¹³C NMR spectra and of equatorial 2-H (2-H_{eq})-phosphorus coupling ($J_{2eq,P}$ 4–6 Hz) in the ¹H NMR spectra indicates that all of these compounds have conformations in which the dimethoxyphosphinoyl group is equatorial. The smaller magnitude of the $J_{3,4}$ -values (2–3 Hz) in compounds **16** and **18** implies the *D-erythro* configuration with ⁴C₁(*D*) conformation. In contrast, the larger magnitude of $J_{3,4}$ (9–11 Hz) for compounds **17** and **19** supports the *L-threo* configuration with ¹C₄(*L*) conformation. The anomeric orientation at C-1 is readily perceived by the magnitude of $J_{1,2ax}$; namely, 3.4–4.3 Hz for **16–19a** (*α*-anomers) and 7.9–8.5 Hz for **16–19b** (*β*-anomers).

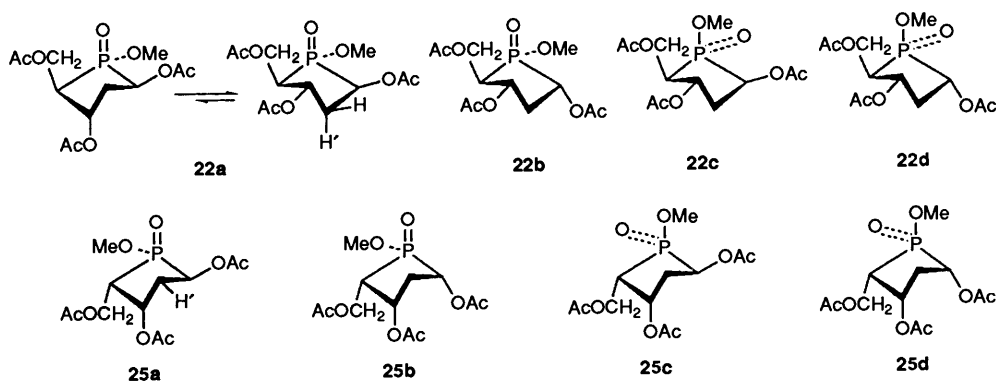
The major, *α,β-D-erythro* products **16a, b** were then reduced with sodium dihydrobis-(2-methoxyethoxy)aluminum (SDMA) to give the 4-phosphino derivative **20** which, by the action of hydrochloric acid in aq. propan-2-ol and then oxidation with hydrogen peroxide, afforded 2,4-dideoxy-4-hydroxyphosphinoyl-*D-erythro*-pentofuranoses **21** (Scheme 3).

As the separation and purification of compound **21** was extremely difficult, unambiguous structural assignment was made by its conversion into the 4-methoxyphosphonoyl triacetates **22** by treatment with acetic anhydride-pyridine and then ethereal diazomethane. After purification of the crude products by column chromatography on silica gel, the following four diastereoisomers were obtained, although some of the minor products were not completely separable (see Experimental section): 1,3,5-tri-*O*-acetyl-2,4-dideoxy-4-[(*R*)-methoxyphosphinoyl]-β-*D-erythro*-pentofuranose **22a** (6.1% overall yield from **16**), its *α*-anomer **22b** (3.9%), the corresponding 4-[(*S*)-methoxyphosphinoyl]-β-isomer **22c** (7.5%), and its *α*-isomer **22d** (5.2%).

Similar treatment of the minor, *α,β-L-threo* products **17a, b** afforded 2,4-dideoxy-4-hydroxyphosphinoyl-*L-threo*-pentofuranoses **24** via 5-phosphino compounds **23** (Scheme 3). Compound **24** was also converted into 4-methoxyphosphonoyl triacetates **25**: 1,3,5-tri-*O*-acetyl-2,4-dideoxy-4-[(*R*)-methoxyphosphinoyl]-*α-L-threo*-pentofuranose **25a** (11% from **17**), its β-anomer **25b** (5.4%), the corresponding 4-[(*S*)-



Scheme 3 Reagents: i, Ac₂O, H₂SO₄; ii, NaOMe; iii, NaIO₄; iv, MeOH, Amberlite (H⁺); v, SDMA; vi, H⁺; vii, H₂O; viii, Ac₂O, Py; ix, CH₂N₂



methoxyphosphonoyl]- α -isomer **25c** (4.8%), and its β -anomer **25d** (2.4%).

The molecular composition of compounds **22a-d** and **25a-d** was confirmed by their EI, high-resolution mass spectra, most of which gave the $(M + 1)$ ions at m/z 322 corresponding to $C_{12}H_{20}O_8P$. As the C-4 configuration of compounds **22a-d** (*D-erythro*) and **25a-d** (*L-threo*) is maintained during the transformation from substrates **16a, b** and **17a, b**, the favoured conformations of the furanoid ring, the anomeric orientation of C-1, and the orientation of the ring P=O group of these triacetates are established by analysis of their 500 MHz 1H NMR spectra; see Table 1 for the assignments of all signals.

Compounds **22b-d** have large $J_{2,P}$ -values (27–29 Hz) and small $J_{3,P}$ -values (5–6 Hz) and thus are considered to exist predominantly in the 3T_2 conformation. The relatively large $J_{2,3}$ - and $J_{3,4}$ -values (8–10 Hz) of these compounds further support the above conformation. In contrast, compounds **25a-d** have small $J_{2,P}$ -values (2–8 Hz) and large values for $J_{3,P}$ (25–32 Hz) and $J_{2,P}$ (26–32 Hz), therefore existing predominantly in the 2T_3 conformation; the relatively small $J_{2,3}$ -values (2–4 Hz) support this conformation. Compound **22a** has appreciably close $J_{2,P}$ (19 Hz) and $J_{3,P}$ (11 Hz)-values compared with those of its stereoisomers **22b-d**. This suggests an averaging between the interconverting 3T_2 and 2T_3 conformations with a slight tendency towards 3T_2 form (*ca.* 3:2), judging from the magnitudes of the corresponding J -values.

The presence of a small, long-range, W-coupling ($J_{1,4}$ 0.5 Hz) observed for species **22a, c** and **25b, d** indicates, respectively, the β -D- and β -L-configuration for 1-H of these compounds. The orientation of the ring P=O group was established by examination of the δ -values of 3-H for compounds **22a-d** and of 2-H for **25a-d**. Namely, a slight downfield shift of the 3-H signals was observed for compounds **22a** and **22b** compared with those of the respective anomers **22c** and **22d**, thus showing nearly a 1,3-diaxial proximity of the P=O group to 3-H in the case of isomers **22a** and **22b** [*i.e.*, both possess a 4-[(R_P)] configuration}. A similar downfield shift indicative of the same configuration of the ring phosphorus was observed for the 2-H signals of isomers **25a** and **25b** (in comparison with those of the corresponding diastereoisomers **25c** and **25d**).

The rest of the spectral data of compounds **22a-d** and **25a-d** are completely in conformity with the structures shown. It has often been rather difficult^{2,3,5} to determine the exact configurations of methoxyphosphonoyl sugar analogues compared with the case of the corresponding alkyl- or arylphosphonoyl congeners.^{1,4,6,7} Therefore, a complete set of the present data summarized in Table 1 is of high value in the structural analysis of related 2,4-dideoxy-4-phosphonoyl-pentofuranoses, some of which are currently being prepared.

Experimental

M.p.s were determined with a Yanagimoto MP-S3 instrument and are uncorrected. All reactions were monitored by TLC

(Merck silica gel 60F, 0.25 mm) with an appropriate solvent system [AcOEt (Solvent A); (19:1) AcOEt:EtOH (Solvent B); (19:1) $CHCl_3$ -MeOH (Solvent C); and (5:3:1) propan-2-ol-AcOEt-water (Solvent D)]; components were detected by spraying of the plates with 20% sulfuric acid-ethanol, with subsequent heating. Column chromatography was performed by Wako C-200 silica gel. The NMR spectra were measured in $CDCl_3$ with Varian VXR-500 (500 MHz for 1H , 126 MHz for ^{13}C) and VXR-200 (81 MHz for ^{31}P) instruments (the SC-NMR Lab., Okayama Univ.) at 21 °C, unless otherwise stated. Chemical shifts are reported as δ -values relative to tetramethylsilane (internal standard for 1H and ^{13}C) and 85% phosphoric acid (external standard for ^{31}P). J Values are given in Hz. The assignments of all signals were made by employing a first-order analysis with the aid of decoupling techniques and, if necessary, 2D COSY and NOEDS measurements. The mass spectra were taken on an A.E.I. MS 50 ultra-high-resolution instrument and were given in terms of m/z (relative intensity) compared with the base peak.

3,5,6-*Trideoxy-5-dimethoxyphosphinoyl-1,2-O-isopropylidene-6-nitro- α -D-ribo- and - β -L-lyxo-hexofuranose 6*.—TEA (0.60 cm³, 4.3 mmol) was added dropwise at 0 °C to a mixture of compound **5**¹¹ (3.00 g, 13.9 mmol) and dimethyl phosphonate (15.0 g, 136 mmol), and the mixture was stirred for 1 h at 25 °C. The excess of phosphonate was distilled off at ~40 °C (0.2 Torr). The residue was purified on a column of silica gel with AcOEt-hexane as eluent, giving an inseparable mixture of the *hexofuranoses 6* (*ribo:lyxo* 66:34) as a syrup (4.22 g, 94%), the ratio being determined by 1H and ^{31}P NMR spectroscopy [Found: C, 40.4; H, 6.1; N, 4.0%; ($M^+ - CH_3$), 310.0690. $C_{10}H_{20}NO_8P$ requires C, 40.62; H, 6.20; N, 4.31%; ($M - 15$), 310.0692]; R_f 0.37 (Solvent A); δ_H for *ribo-6* 1.30 and 1.50 (3 H, each, 2 \times s, CMe_2), 1.73 (1 H, ddd, $J_{3R,3S}$ 13.7, $J_{3R,4}$ 10.7, $J_{2,3R}$ 4.9, 3- H_R), 2.37 (1 H, dd, $J_{3S,4}$ 4.4, $J_{2,3S} \sim 0$, 3- H_S), 3.04 (1 H, ddt, $J_{5,P}$ 21.1, $J_{4,5}$ 8.2, $J_{5,6}$ 6.2, $J_{5,6}$ 6.0, 5-H), 3.77 and 3.78 [3 H each, 2 \times d, J_{POMe} 10.7 and 10.9, P(OMe)₂], 4.40 (1 H, dddd, $J_{4,P}$ 6.6, 4-H), 4.64 (1 H, td, $J_{6,6'}$ 14.6, $J_{6',P}$ 14.3, 6-H'), 4.73 (1 H, ddd, $J_{6,P}$ 16.0, 6-H), 4.74 (1 H, dd, $J_{1,2}$ 3.8, 2-H) and 5.76 (1 H, d, 1-H); δ_C for *ribo-6* 26.01 and 26.61 (CMe_2), 38.49 ($^3J_{3,P}$ 3.5, C-3), 39.84 ($^1J_{5,P}$ 141.2, C-5), 53.05 and 53.38 ($^2J_{C,P}$ 6.9 and 6.3, MeOP), 71.89 (C-6), 74.16 (C-4), 80.41 (C-2), 104.87 (C-1) and 111.53 (Me_2C); δ_P for *ribo-6* 25.0; δ_H for *lyxo-6* 1.30 and 1.49 (3 H each, 2 \times s, CMe_2), 2.07 (1 H, ddd, $J_{3R,3S}$ 13.5, $J_{3R,4}$ 10.9, $J_{2,3R}$ 4.8, 3- H_R), 2.17 (1 H, dd, $J_{3S,4}$ 4.6, $J_{2,3S} \sim 0$, 3- H_S), 3.33 (1 H, dddd, $J_{5,P}$ 23.1, $J_{5,6}$ 7.3, $J_{5,6}$ 5.9, $J_{4,5}$ 3.5, 5-H), 3.76 and 3.78 [3 H each, 2 d, J_{POMe} 10.8, P(OMe)₂], 4.52 (1 H, dddd, $J_{4,P}$ 16.3, 4-H), 4.60 (1 H, ddd, $J_{6,6'}$ 14.1, $J_{6',P}$ 10.6, 6-H'), 4.61 (1 H, ddd, $J_{6,P}$ 10.8, 6-H), 4.75 (1 H, dd, $J_{1,2}$ 3.6, 2-H) and 5.78 (1 H, d, 1-H); δ_C for *lyxo-6* 26.05 and 26.68 (Me_2C), 35.49 (C-3), 38.05 ($^1J_{5,P}$ 140.7, C-5), 52.73 and 53.33 ($^2J_{C,P}$ 6.4 and 6.3, MeOP), 71.70 (C-6), 74.81 (C-4), 80.33 (C-2), 105.20 (C-1) and 111.72 (Me_2C); δ_P for *lyxo-6* 24.4; m/z 310

Table 1 ^1H and ^{31}P NMR parameters for compounds **22a-d** and **25a-d** in CDCl_3

Compound	Chemical shifts (δ)								POMe	1-, 3-, and 5-OAc ^c	^{31}P
	1-H	2-H	2-H'	3-H	4-H	5-H	5-H'				
22a	5.07	2.45	2.13 ^b	5.28	2.39	4.39	4.28	3.87	2.16, 2.07, 2.07	56.5	
22b	5.03	2.73	1.95	5.13	2.44	4.35	4.35	3.83	2.13, 2.07, 2.06	55.2	
22c	5.12	2.42	2.18	5.20	2.50	4.31	4.22	3.79	2.12, 2.08, 2.07	54.0	
22d	4.82	2.69	2.05 ^b	4.98	2.59	4.33	4.24	3.88	2.17, 2.08, 2.07	52.2	
25a	4.66	2.14 ^b	2.60	5.52	2.59	4.34	4.21	3.91	2.18, 2.07, 2.04	54.3	
25b	4.93	2.24	2.49	5.38	2.55	4.36	4.26	3.79	2.10, 2.07, 2.06	60.5	
25c	5.15	1.96	2.62	5.48	2.52	4.37	4.32	3.83	2.12, 2.11, 2.05	54.9	
25d	4.96	2.14 ^b	2.51	5.31	2.41	4.43	4.38	3.88	2.14, 2.11, 2.05	60.5	

Compound	Coupling constants (Hz)																	
	$J_{1,2}$	$J_{1,2'}$	$J_{1,4}$	$J_{1,P}$	$J_{2,3}$	$J_{2,P}$	$J_{2,2'}$	$J_{2',3}$	$J_{2',P}$	$J_{3,4}$	$J_{3,P}$	$J_{4,5}$	$J_{4,5'}$	$J_{4,P}$	$J_{5,P}$	$J_{5',P}$	$J_{5,5'}$	$^3J_{\text{POMe}}$
22a	5.0	7.2	0.5	4.9	5.3	19.0	14.3	7.1	c	7.4	10.6	7.0	7.8	16.3	9.9	13.8	11.7	11.2
22b	5.1	7.2	0	7.0	6.9	28.7	14.2	7.9	7.0	8.0	5.9	7.3	7.3	17.0	12.7	12.7		10.9
22c	3.3	4.9	0.5	5.8	5.6	27.1	14.4	9.6	7.4	8.4	5.3	7.4	7.9	16.4	16.4	8.8	11.3	10.8
22d	5.0	8.8	0	8.8	6.5	28.1	14.0	8.5	c	9.3	5.3	7.2	7.6	15.8	15.8	8.8	11.4	10.9
25a	10.9	8.6	0	4.9	3.4	c	14.4	2.6	31.7	5.0	30.7	9.5	6.0	18.4	9.2	4.9	11.3	11.2
25b	6.9	1.6	0.5	2.8	3.4	2.4	16.1	2.3	26.6	5.0	32.2	8.6	6.6	17.5	11.1	5.2	11.2	11.0
25c	8.8	7.8	0	5.8	4.3	8.3	14.4	4.2	25.7	5.0	25.4	7.8	8.3	15.9	8.7	13.1	11.3	10.8
25d	7.8	2.1	0.5	2.7	3.6	c	15.5	3.4	26.2	5.1	29.5	6.6	8.2	16.4	7.8	8.6	11.4	10.8

^a Acetoxy assignments may have to be interchanged. ^b Chemical shifts were confirmed by 2D COSY experiments in spite of the presence of overlapping acetoxy signals. ^c Values are uncertain because of overlap with acetoxy signals.

($\text{M}^+ - \text{CH}_3$, 61%), 268 (100), 250 (19), 221 (15), 210 (10), 203 (25), 191 (6.6), 165 (15), 149 (47), 137 (57) and 109 (45).

3,5-Dideoxy-5-dimethoxyphosphinoyl-1,2-O-isopropylidene- α -D-ribo- and - β -L-lyxo-hexofuranose 8, 6-Chloro-6-deoxy Derivatives 10, 6-O-Acetyl Derivatives 11, and 3,5,6-Trideoxy-5-dimethoxyphosphinoyl-1,2-O-isopropylidene- α -D-erythro-hex-5-enofuranose 9.—Compounds **6** (3.78 g, 11.6 mmol) dissolved in a mixture of methanol (100 cm^3) and 2 mol dm^{-3} hydrochloric acid (5.80 cm^3 , 11.6 mmol) were hydrogenolysed in the presence of platinum(IV) oxide (670 mg, 2.95 mol) at 25 °C under an atmospheric pressure of H_2 . After 16 h, the catalyst was filtered off, and the filtrate was evaporated under reduced pressure to give the 6-aminohexofuranose hydrochloride derivative **7** as a syrup; R_f 0.39 (Solvent D).

To a stirred solution of the amine **7** in water (35 cm^3) at 0 °C were added acetic acid (3.0 cm^3 , 52.4 mmol) and then sodium nitrite (4.60 g, 66.7 mmol). After 2 h, the mixture was extracted twice with CHCl_3 . The combined organic layers were washed successively with aq. NaHCO_3 and water, dried (Na_2SO_4), and evaporated under reduced pressure. The residue was separated by column chromatography, giving three fractions, A–C.

Fraction A [R_f 0.42 (Solvent B)] gave a syrup (680 mg) which consisted of the *hexenofuranose 9* (12% from **6**) [Found: ($\text{M}^+ - \text{CH}_3$), 263.0686. $\text{C}_{10}\text{H}_{16}\text{O}_6\text{P}$ requires ($\text{M} - 15$), 263.0685] and the *chloride 10* (8%, *ribo:lyxo* ~ 3:1) [Found: ($\text{M}^+ - \text{CH}_3$), 301.0423 and 299.0447. $\text{C}_{10}\text{H}_{17}\text{ClO}_6\text{P}$ requires ($\text{M} - 15$), 301.0422 and 299.0451], the relative amounts of products **9** and **10** being determined by the intensity ratio of their 1-H signals; δ_{H} for **9** 1.32 and 1.52 (3 H each, 2 \times s, CMe_2), 1.74 (1 H, ddd, $J_{3R,3S}$ 13.5, $J_{3R,4}$ 10.9, $J_{2,3R}$ 4.7, 3- H_R), 2.39 (1 H, dd, $J_{3S,4}$ 4.5, $J_{2,3S}$ ~ 0, 3- H_S), 3.73 [6 H, d, J_{POMe} 10.9, $\text{P}(\text{OMe})_2$], 4.76 (1 H, dd, $J_{1,2}$ 3.6, 2-H), 4.79 (1 H, tdt, $J_{4,P}$ 9.2, $J_{4,6(E)} = J_{4,6(Z)}$ 1.5, 4-H), 5.88 (1 H, d, 1-H), 6.12 [1 H, dt, $J_{6(Z),P}$ 22.6, $J_{6(Z),6(E)}$ 1.6, 6-H(Z)] and 6.19 [1 H, dt, $J_{6(E),P}$ 45.9, 6-H(E)]; δ_{P} for **9** 18.0; m/z 263 ($\text{M}^+ - \text{CH}_3$, 48%), 221 (100), 203 (32), 191 (7), 175 (15), 163 (47), 137 (29) and 109 (22); δ_{H} for *ribo-10* 1.29 and 1.51 (3 H each, 2 \times s, CMe_2), 1.89 (1 H, ddd, $J_{3R,3S}$ 13.6, $J_{3R,4}$ 11.0, $J_{2,3R}$ 4.7, 3- H_R), 2.26 (1 H, dd, $J_{3S,4}$ 4.3, $J_{2,3S}$ ~ 0, 3- H_S), 2.42 (1 H, ddt, $J_{5,P}$ 22.0,

$J_{4,5}$ 8.0, $J_{5,6}$ 4.8, $J_{5,6}$ 4.1, 5-H), 3.75 and 3.79 [3 H each, 2 \times d, J_{POMe} 10.9 and 10.7, $\text{P}(\text{OMe})_2$], 3.87 (1 H, td, $J_{6,6'}$ 11.5, $J_{6',P}$ 10.5, 6-H'), 3.95 (1 H, ddd, $J_{6,P}$ 24.9, 6-H), 4.57 (1 H, dtd, $J_{4,P}$ 8.9, 4-H), 4.74 (1 H, dd, $J_{1,2}$ 3.6, 2-H) and 5.78 (1 H, d, 1-H); δ_{P} for *ribo-10* 26.6; δ_{P} for *lyxo-10* 25.7; m/z 301 ($\text{M}^+ - \text{CH}_3$, 10%), 299 ($\text{M}^+ - \text{CH}_3$, 28), 257 (55) and 239 (14).

Fraction B [R_f 0.31 (Solvent B)] gave 6-O-acetyl compounds **11** (*ribo:lyxo* 2:1) as a syrup (275 mg, 7%) [Found: ($\text{M} + 1$)⁺, 339.1224. $\text{C}_{13}\text{H}_{24}\text{O}_8\text{P}$ requires ($\text{M} + 1$), 339.1209]; δ_{H} for *ribo-11* 1.31 and 1.50 (3 H each, 2 \times s, CMe_2), 1.87 (1 H, ddd, $J_{3R,3S}$ 13.5, $J_{3R,4}$ 11.0, $J_{2,3R}$ 4.8, 3- H_R), 2.05 (3 H, s, 6-OAc), 2.24 (1 H, dd, $J_{3S,4}$ 4.2, $J_{2,3S}$ ~ 0, 3- H_S), 2.38 (1 H, ddt, $J_{5,P}$ 21.7, $J_{4,5}$ 7.1, $J_{5,6'}$ 5.2, $J_{5,6}$ 4.9, 5-H), 3.75 and 3.77 [3 H each, 2 \times d, J_{POMe} 10.9, $\text{P}(\text{OMe})_2$], 4.39 (1 H, ddd, $J_{6',P}$ 13.9, $J_{6,6'}$ 11.5, 6-H'), 4.43 (1 H, ddd, $J_{6,P}$ 19.6, 6-H), 4.47 (1 H, tdd, $J_{4,P}$ 10.0, 4-H), 4.73 (1 H, dd, $J_{1,2}$ 3.6, 2-H) and 5.78 (1 H, d, 1-H); δ_{P} for *ribo-11* 27.3; δ_{H} for *lyxo-11* 1.31 and 1.50 (3 H each, 2 \times s, CMe_2), 2.13–2.15 (2 H, m, 3- $\text{H}_{R,S}$), 2.55 (1 H, ddd, $J_{5,P}$ 22.2, $J_{5,6'}$ 7.6, $J_{5,6}$ 5.0, $J_{4,5}$ 3.9, 5-H), 3.74 and 3.76 [3 H each, 2 \times d, J_{POMe} 10.8, $\text{P}(\text{OMe})_2$], 4.28 (1 H, td, $J_{6,6'} = J_{6',P} = 11.3$, 6-H'), 4.40 (1 H, m, 6-H), 4.53 (1 H, dddd, $J_{4,P}$ 18.4, $J_{3R,4}$ 9.0, $J_{3S,4}$ 7.0, 4-H), 4.73 (1 H, dd, $J_{2,3R}$ 4.8, $J_{1,2}$ 3.7, $J_{2,3S}$ ~ 0, 2-H) and 5.82 (1 H, d, 1-H); δ_{P} for *lyxo-11* 26.7; m/z 339 ($\text{M}^+ + 1$, 18%), 323 (100), 281 (90), 263 (11), 239 (53), 221 (54), 203 (31), 191 (14), 179 (12), 137 (64), and 109 (31).

Fraction C [R_f 0.20 (Solvent B)] gave a 2:1 mixture of the *hexenofuranoses 8* as a syrup (2.11 g, 61%) [Found: C, 45.0; H, 7.4%; ($\text{M} + 1$)⁺, 297.1108. $\text{C}_{11}\text{H}_{21}\text{O}_7\text{P}$ requires C, 44.60; H, 7.14%; ($\text{M} + 1$), 297.1103]; δ_{H} for *ribo-8* 1.31 and 1.51 (3 H each, 2 \times s, CMe_2), 1.73 (1 H, ddd, $J_{3R,3S}$ 13.7, $J_{3R,4}$ 10.8, $J_{2,3R}$ 4.8, 3- H_R), 2.20 (1 H, ddt, $J_{5,P}$ 20.3, $J_{4,5}$ 9.0, $J_{5,6}$ 5.7, $J_{5,6'}$ 5.5, 5-H), 2.30 (1H, br s, OH), 2.34 (1 H, dd, $J_{3S,4}$ 4.3, $J_{2,3S}$ ~ 0, 3- H_S), 3.76 and 3.78 [3 H each, 2 \times d, J_{POMe} 10.8 and 10.9, $\text{P}(\text{OMe})_2$], 3.98 (1 H, ddd, $J_{6',P}$ 17.2, $J_{6,6'}$ 11.7, 6-H'), 4.00 (1 H, ddd, $J_{6,P}$ 15.8, 6-H), 4.40 (1 H, dddd, $J_{4,P}$ 6.1, 4-H), 4.73 (1 H, dd, $J_{1,2}$ 3.6, 2-H) and 5.79 (1 H, d, 1-H); δ_{P} for *ribo-8* 28.7; δ_{H} for *lyxo-8* 1.31 and 1.51 (3 H each, 2 \times s, CMe_2), 1.92 (1 H, ddd, $J_{3R,3S}$ 13.6, $J_{3R,4}$ 11.1, $J_{2,3R}$ 4.7, 3- H_R), 2.20 (1 H, dd, $J_{3S,4}$ 4.8, $J_{2,3S}$ ~ 0, 3- H_S), 2.30 (1H, br s, OH) 2.46 (1 H, dq, $J_{5,P}$ 21.4, $J_{4,5}$ 5.7, $J_{5,6}$ 5.6, $J_{5,6'}$ 5.0, 5-H), 3.77 and 3.79 [3 H each, 2 \times d, J_{POMe} 11.1 and 11.0,

$P(OMe)_2$], 3.90 (1 H, ddd, $J_{6',P}$ 18.2, $J_{6,6'}$ 11.7, 6-H'), 3.92 (1 H, ddd, $J_{6,P}$ 15.3, 6-H), 4.55 (1 H, tt, $J_{4,P}$ 10.1, 4-H), 4.75 (1 H, dd, $J_{1,2}$ 3.7, 2-H) and 5.82 (1 H, d, 1-H); δ_P for *lyxo*-**8** 29.0; m/z 297 ($M^+ + 1$, 2.6%), 281 (85), 239 (100), 221 (25), 209 (17), 191 (23), 179 (17), 153 (32), 137 (29) and 109 (27).

Dehydrochlorination of Compound 10.—To a solution of compound **10** (350 mg, 1.11 mmol) and the hexenofuranose **9** (460 mg) in dry CH_2Cl_2 (10 cm^3) at 0 °C was added DBU (0.20 cm^3 , 1.3 mmol). The mixture was stirred for 2 h at 25 °C, and then concentrated under reduced pressure. The residue was purified by column chromatography to give the hexenofuranose **9** (745 mg, 92%) as a syrup.

Deacetylation of 6-Acetate 11.—To a solution of the acetate **11** (120 mg, 0.355 mmol) in abs. methanol (1.0 cm^3) at 0 °C was added a 25% methanolic solution of NaOMe (0.010 cm^3 , 0.044 mmol), and the mixture was stirred for 30 min before being neutralized with Amberlite IR-120 (H^+). The resin was filtered off and washed with MeOH. The combined filtrate and washings were evaporated under reduced pressure. The residue was purified by column chromatography to give compounds **8** (*ribo:lyxo* 2:1) (96.0 mg, 91%).

Acid Hydrolysis and Acetylation of Compounds 8.—Compounds **8** (55 mg, 0.19 mmol) were dissolved in a mixture of propan-2-ol (0.2 cm^3) and 0.25 mol dm^{-3} hydrochloric acid (1.8 cm^3), and the mixture was then refluxed for 2 h. The reactants were neutralized with Amberlite IRA-45. The resin was filtered off and the filtrate was evaporated under reduced pressure. The residue was acetylated with acetic anhydride (0.5 cm^3) and dry pyridine (1.0 cm^3), worked up, and separated by column chromatography into two fractions.

The faster eluting fraction [R_f 0.34 (Solvent B)] gave (5*RS*)-1,2,6-tri-*O*-acetyl-3,5-dideoxy-5-dimethoxyphosphinoyl- α - β -D-erythro-hexofuranoses **12** as a syrup (44 mg, 60%); δ_H for the predominant component (presumably 1,2,6-tri-*O*-acetyl-3,5-dideoxy-5-dimethoxyphosphinoyl- β -D-ribo-hexofuranose) 2.05, 2.07 and 2.08 (3 H each, 3 \times s, AcO), 2.26 (1 H, dd, $J_{3R,3S}$ 14.5, $J_{3S,4}$ 6.1, 3- H_S), 2.32 (1 H, ddd, $J_{3R,4}$ 9.7, $J_{2,3R}$ 4.4, 3- H_R), 2.33 (1 H, ddt, $J_{5,P}$ 21.8, $J_{4,5}$ 9.7, $J_{5,6} = J_{5,6'}$ = 4.8, 5-H), 3.77 [6 H, d, J_{POMe} 10.9, $P(OMe)_2$], 4.35–4.42 (2 H, m, 6- H_2), 4.70 (1 H, tt, $J_{4,P}$ 6.4, 4-H), 5.15 (1 H, dd, $J_{1,2}$ 0.8, 2-H) and 6.12 (1 H, d, 1-H).

The slower eluting fraction [R_f 0.25 (Solvent B)] gave 2-*O*-acetyl-1,6-anhydro-3,5-dideoxy-5-dimethoxyphosphinoyl- β -D-ribo-hexofuranose **13** as a syrup (13 mg, 25%) [Found: C, 43.2; H, 6.45%; M^+ , 280.0723. $C_{10}H_{17}O_7P$ requires C, 42.86; H, 6.11%; M , 280.0712]; δ_H 1.77 (1 H, br dd, $J_{5,P}$ 19.9, $J_{5,6ax}$ 5.0, $J_{5,6eq}$ 1.0, $J_{4,5}$ 0.5, 5-H), 2.07 (3 H, s, AcO), 2.15 (1 H, dddd, $J_{3R,3S}$ 14.2, $J_{3S,4}$ 6.9, $J_{3S,P}$ 4.3, $J_{2,3S}$ 3.0, 3- H_S), 2.35 (1 H, br dd, $J_{2,3R}$ 7.3, $J_{3R,4}$ 0.5, 3- H_R), 3.78 and 3.88 [3 H each, 2 d, J_{POMe} 10.8, $P(OMe)_2$], 4.02 (1 H, ddd, $J_{6ax,P}$ 33.4, $J_{6ax,6eq}$ 12.8, 6- H_{ax}), 4.14 (1 H, br t, $J_{6eq,P}$ 13.4, 6- H_{eq}), 5.08 (1 H, br t, $J_{4,P}$ 7.3, 4-H), 5.30 (1 H, br s, $J_{1,2}$ 0.5, 1-H) and 5.37 (1 H, br dd, 2-H); NOESD experiment [observed NOEs (%) by irradiation of 6- H_{ax}]: 5-H 14, 3- H_R 5.2, 2-H 11; δ_P 28.2; m/z 280 (M^+ , 4.4%), 238 (99), 221 (4.6), 209 (72), 192 (15), 179 (32), 163 (36), 137 (86), and 110 (100).

(5*RS*)-3,5-Dideoxy-5-dimethoxyphosphinoyl- α - β -D-erythro-hexofuranose **14.**—Conc. sulfuric acid (0.20 cm^3) was added to a solution of compound **8** (860 mg, 2.90 mmol) in acetic anhydride (10 cm^3) at 0 °C. The mixture was stirred at 25 °C for 4 h, diluted with $CHCl_3$, and washed successively with cold aq. $NaHCO_3$ and water. The organic layer was dried (Na_2SO_4), and evaporated under reduced pressure to give 1,2,6-tri-*O*-acetyl derivative **12** (1.08 g) as a syrup.

To a cold solution of the above compound **12** in abs. MeOH (10 cm^3) was added a 25% methanolic solution of NaOMe (0.40 cm^3 , 1.7 mmol), and the mixture was stirred at 0 °C for 1 h before being neutralized with Amberlite IR-120 (H^+) ion-exchange resin. The resin was filtered off and washed with MeOH. The filtrate was evaporated under reduced pressure to give the hexofuranose **14** (675 mg, 91%) as a syrup; R_f 0.55 (Solvent D); δ_H (60 MHz) 2.00–2.35 (3 H, m, 3- H_2 and 5-H), 3.25–3.60 (3 H, m, 1-, 2-, and 6-OH, D_2O -exchangeable), 3.78 [6 H, d, J_{POMe} 11.0, $P(OMe)_2$], 3.90–4.85 (4 H, m, 2-, 4-H, and 6- H_2) and 5.28 (1 H, br s, 1-H).

Methyl 2,4-Dideoxy-4-dimethoxyphosphinoyl- α -D-erythro-pentopyranoside 16a, the β -Anomer 16b, the α -L-threo-Pentopyranoside 17a, the β -Anomer 17b, Methyl 2,4-Dideoxy-4-dimethoxyphosphinoyl-3-O-methyl- α -D-erythro-pentopyranoside 18a, the β -Anomer 18b, the α -L-threo-Pentopyranoside 19a and the β -Anomer 19b.—Sodium periodate (750 mg, 3.51 mmol) was added to a solution of triol **14** (675 mg, 2.63 mmol) in water (5.0 cm^3) at 0 °C. The solution was then stirred at 25 °C for 4 h and triturated with ethanol (50 cm^3). The precipitate was filtered off, and the filtrate was evaporated under reduced pressure. The residue was extracted with $CHCl_3$, dried (Na_2SO_4), and evaporated under reduced pressure to give (4*RS*)-2,4-dideoxy-4-dimethoxyphosphinoyl-3-*O*-formyl- α , β -D-glycero-pentopyranoses **15** as a syrup; R_f 0.63 (Solvent D); δ_H (60 MHz) 1.80–2.50 (3 H, m, 2- H_2 and 4-H), 3.32 (1 H, br s, OH, D_2O -exchangeable), 3.74 and 3.76 [3 H each, 2 \times d, J_{POMe} 10.8, $P(OMe)_2$], 3.70–4.30 (3 H, m, 1-H and 5- H_2), 4.75–5.25 (1 H, m, 3-H), and 8.08 (1 H, br s, 3-OCHO).

A solution of formate **15** and Amberlite IR-120 (H^+) (7 cm^3) in abs. methanol (15 cm^3) was refluxed for 8 h. The mixture was evaporated under reduced pressure to give a pale yellow syrup, which was separated by column chromatography with a gradient eluent of $CHCl_3 \rightarrow$ (19:1) $CHCl_3$ -MeOH into four fractions, A–D.

Fraction A [R_f 0.40 (Solvent C)] gave a mixture (110 mg) of the 3-*O*-methyl-D-erythro-pentopyranosides **18a, b** and the 3-*O*-methyl-L-threo-pentopyranosides **19a, b** as a syrup (see later).

Fraction B [R_f 0.34 (Solvent C)] gave the α -D-erythro-pentopyranoside **16a** as needles (98.2 mg, 16% from **14**), m.p. 106–107 °C (from AcOEt-hexane) [Found: C, 40.1; H, 7.3%; ($M + 1$)⁺, 241.0832. $C_8H_{17}O_6P$ requires C, 40.00; H, 7.13%; ($M + 1$), 241.0841]; δ_H 1.82 (1 H, dt, $J_{2ax,2eq}$ 14.5, $J_{1,2ax} = J_{2ax,3} = 3.5$, 2- H_{ax}), 1.99 (1 H, dddd, $J_{2eq,P}$ 6.4, $J_{2eq,3}$ 3.0, $J_{1,2eq}$ 1.4, 2- H_{eq}), 2.32 (1 H, dddd, $J_{4,P}$ 21.7, $J_{4,5ax}$ 12.0, $J_{4,5eq}$ 4.6, $J_{3,4}$ 2.3, 4-H), 3.37 (3 H, s, 1-OMe), 3.70 (1 H, br s, HO), 3.73 (1 H, m, 5- H_{eq}), 3.74, 3.75 [3 H each, 2 \times d, J_{POMe} 10.8 and 11.0, $P(OMe)_2$], 4.10 (1 H, td, $J_{5ax,P}$ 11.7, 5- H_{ax}), 4.31 (1 H, dq, $J_{3,P}$ 6.6, $J_{1,3}$ 2.0, 3-H) and 4.76 (1 H, dt, 1-H); δ_C 35.48 ($^3J_{2,P}$ 11.4, C-2), 40.18 ($^1J_{4,P}$ 142.0, C-4), 52.46 ($^2J_{C,P}$ 7.0, MeOP), 52.84 ($^2J_{C,P}$ 6.5, MeOP), 53.77 ($^2J_{5,P}$ 3.9, C-5), 55.50 (1-OMe), 62.95 ($^2J_{3,P}$ 6.7, C-3) and 98.19 (C-1); δ_P 28.0; m/z 241 ($M^+ + 1$, 0.2%), 225 (0.4), 208 (24), 191 (40), 180 (11), 154 (38), 149 (30), 137 (100), and 109 (32).

Fraction C [R_f 0.29 (Solvent C)] gave a syrup (121 mg) which consisted of the L-threo-pentopyranosides **17a** (15% from **14**) and **17b** (3.8%), the relative amounts being determined from the integral ratio of their 1-H and 1-OMe signals [Found: ($M + 1$)⁺, 241.0848. $C_8H_{18}O_6P$ requires ($M + 1$), 241.0841]; δ_H for **17a** 1.58 (1 H, ddd, $J_{2ax,2eq}$ 13.3, $J_{2ax,3}$ 10.9, $J_{1,2ax}$ 3.6, 2- H_{ax}), 2.13 (1 H, dddd, $J_{4,P}$ 16.1, $J_{3,4}$ 10.7, $J_{4,5ax}$ 9.5, $J_{4,5eq}$ 7.5, 4-H), 2.14 (1 H, dtd, $J_{2eq,P}$ 5.9, $J_{2eq,3}$ 4.9, $J_{1,2eq}$ 1.5, 2- H_{eq}), 3.31 (3 H, s, 1-OMe), 3.70–3.73 (2 H, m, 5- H_2), 3.77 and 3.79 [3 H each, 2 \times d, J_{POMe} 10.9, $P(OMe)_2$], 3.93 (1 H, br s, HO), 4.21 (1 H, tdd, $J_{3,P}$ 8.2, 3-H) and 4.80 (1 H, dt, $J_{1,5eq}$ 2.2, 1-H); δ_C for **17a** 37.84 ($^3J_{2,P}$ 13.3, C-2), 42.57 ($^1J_{4,P}$ 136.3, C-4), 52.67

($^2J_{C,P}$ 8.2, MeOP), 52.80 ($^2J_{C,P}$ 7.7, MeOP), 54.89 (1-OMe), 56.58 ($^2J_{5,P}$ ~ 0 , C-5), 62.49 ($^2J_{3,P}$ 6.3, C-3) and 99.98 (C-1); δ_P for **17a** 28.8; δ_H for **17b** 1.55 (1 H, ddd, $J_{2eq,2ax}$ 13.1, $J_{2ax,3}$ 9.2, $J_{1,2ax}$ 7.9, 2- H_{ax}), 2.13 (1 H, dtd, $J_{4,P}$ 16.5, $J_{3,4}$ 9.5, $J_{4,5ax}$ 8.9, $J_{4,5eq}$ 4.3, 4-H), 2.28 (1 H, dtd, $J_{2eq,3}$ 4.5, $J_{2eq,P}$ 4.3, $J_{1,2eq}$ 2.4, 2- H_{eq}), 3.07 (1 H, br s, HO), 3.45 (3 H, s, 1-OMe), 3.52 (1 H, ddd, $J_{5eq,5ax}$ 12.3, $J_{5ax,P}$ 4.4, 5- H_{ax}), 3.77 and 3.79 [3 H, each, 2 \times d, J_{POMe} 11.0, 10.8, P(OMe) $_2$], 4.05 (1 H, tdd, $J_{3,P}$ 7.0, 3-H), 4.12 (1 H, ddd, $J_{5eq,P}$ 10.6, 5- H_{eq}) and 4.40 (1 H, dd, 1-H); δ_P for **17b** 28.9; m/z 241 ($M^+ + 1$, 0.1%), 208 (13), 191 (26), 180 (13), 154 (54), 137 (100) and 109 (29).

Fraction D [R_f 0.24 (Solvent C)] gave the β -D-erythro-pentopyranoside **16b** as needles (184 mg, 29% from **14**), m.p. 101–102 °C (from AcOEt–hexane) [Found: C, 40.2; H, 7.3%; ($M + 1$) $^+$, 241.0837. $C_8H_{17}O_6P$ requires C, 40.00; H, 7.13%; ($M + 1$), 241.0841]; δ_H 1.61 (1 H, ddd, $J_{2ax,2eq}$ 13.5, $J_{1,2ax}$ 8.2, $J_{2ax,3}$ 2.8, 2- H_{ax}), 2.04 (1 H, dtd, $J_{2eq,3} = J_{2eq,P} = 4.8$, $J_{1,2eq}$ 2.5, 2- H_{eq}), 2.31 (1 H, dddd, $J_{4,P}$ 21.0, $J_{4,5ax}$ 10.0, $J_{4,5eq}$ 4.4, $J_{3,4}$ 2.8, 4-H), 3.44 (1 H, s, 1-OMe), 3.75 (1 H, br s, HO), 3.76 [6 H, d, J_{POMe} 10.9, P(OMe) $_2$], 3.96 (1 H, dddd, $J_{5ax,5eq}$ 11.7, $J_{5eq,P}$ 7.9, $J_{3,5eq}$ 0.8, 5- H_{eq}), 4.02 (1 H, ddd, $J_{5ax,P}$ 3.5, 5- H_{ax}), 4.43 (1 H, dddd, $J_{3,P}$ 11.6, 3-H) and 4.74 (1 H, dd, 1-H); δ_C 37.74 ($^3J_{2,P}$ 10.4, C-2), 39.67 ($^1J_{4,P}$ 137.2, C-4), 52.71 ($^2J_{C,P}$ 7.0, MeOP), 52.89 ($^2J_{C,P}$ 6.2, MeOP), 56.22 (1-OMe), 59.47 ($^2J_{5,P}$ 3.1, C-5), 64.15 ($^2J_{3,P}$ 5.4, C-3) and 99.10 (C-1); δ_P 29.3; m/z 241 ($M^+ + 1$, 0.5%), 208 (17), 191 (17), 154 (30), 149 (41), 137 (100) and 109 (30).

Fraction A (110 mg) was rechromatographed with a gradient eluent of AcOEt \rightarrow (19:1) AcOEt–EtOH into three fractions, A $_1$ –A $_3$.

Fraction A $_1$ [R_f 0.42 (Solvent B)] gave the α -L-threo-pentopyranoside **19a** as a syrup (41.9 mg, 6.3% from **14**) [Found: C, 42.3; H, 7.75%; ($M + 1$) $^+$, 255.0983. $C_9H_{19}O_6P$ requires C, 42.52; H, 7.53%; ($M + 1$), 255.0998]; δ_H 1.47 (1 H, ddd, $J_{2ax,2eq}$ 12.7, $J_{2ax,3}$ 10.8, $J_{1,2ax}$ 3.4, 2- H_{ax}), 2.18 (1 H, dtd, $J_{4,P}$ 16.6, $J_{4,5ax}$ 11.0, $J_{3,4}$ 10.1, $J_{4,5eq}$ 5.9, 4-H), 2.26 (1 H, ddd, $J_{2eq,P}$ 5.8, $J_{2eq,3}$ 4.5, $J_{1,2eq}$ 2.0, 2- H_{eq}), 3.31 (3 H, s, 1-OMe), 3.38 (3 H, s, 3-OMe), 3.73 and 3.75 [3 H each, 2 \times d, J_{POMe} 11.0 and 10.8, P(OMe) $_2$], 3.80–3.84 [2 H, m, 5- H_2], 3.87 (1 H, tdd, $J_{3,P}$ 8.1, 3-H) and 4.80 (1 H, dt, $J_{1,5eq}$ 2.3, 1-H); δ_C 34.97 ($^3J_{2,P}$ 11.5, C-2), 41.31 ($^1J_{4,P}$ 139.4, C-4), 51.92 ($^2J_{C,P}$ 6.9, MeOP), 52.83 ($^2J_{C,P}$ 6.2, MeOP), 54.78 and 55.99 (1- and 3-OMe), 57.90 ($^2J_{5,P}$ ~ 0 , C-5), 72.20 ($^2J_{3,P}$ 6.4, C-3) and 98.80 (C-1); δ_P 28.5; FAB m/z 255 ($M^+ + 1$, 25%), 237 (223), 191 (100), 185 (19) and 93 (32).

Fraction A $_2$ [R_f 0.36 (Solvent B)] gave a syrup (43.6 mg) which consisted of the β -anomers **18b** (4.8% from **14**) and **19b** (1.7%), the relative amounts being determined from the integral ratio of their 1-H and 1-, 3-OMe signals; δ_H for **18b** 1.53 (1 H, ddd, $J_{2ax,2eq}$ 13.7, $J_{1,2ax}$ 7.9, $J_{2ax,3}$ 3.2, 2- H_{ax}), 2.24 (1 H, dtd, $J_{2eq,3} = J_{2eq,P} = 4.9$, $J_{1,2eq}$ 2.7, 2- H_{eq}), 2.35 (1 H, dddd, $J_{4,P}$ 20.6, $J_{4,5ax}$ 10.0, $J_{4,5eq}$ 4.2, $J_{3,4}$ 3.0, 4-H), 3.43 and 3.44 [3 H, each, 2 \times s, 1- and 3-OMe], 3.72 and 3.75 [3 H each, 2 \times d, J_{POMe} 10.9, P(OMe) $_2$], 3.90–3.99 (3 H, m, 3-H and 5- H_2) and 4.64 (1 H, dd, 1-H); δ_P for **18b** 28.5; δ_H for **19b** 1.39 (1 H, ddd, $J_{2ax,2eq}$ 12.9, $J_{2ax,3}$ 10.1, $J_{1,2ax}$ 8.5, 2- H_{ax}), 2.13 (1 H, dtd, $J_{4,P}$ 18.0, $J_{4,5ax}$ 10.3, $J_{3,4}$ 9.5, $J_{4,5eq}$ 4.5, 4-H), 2.37 (1 H, dtd, $J_{2eq,3} = J_{2eq,P} = 4.8$, $J_{1,2eq}$ 2.6, 2- H_{eq}), 3.46 and 3.47 (3 H each, 2 \times s, 1- and 3-OMe), 3.52 (1 H, ddd, $J_{5ax,5eq}$ 12.3, $J_{5ax,P}$ 3.8, 5- H_{ax}), 3.68 (1 H, tdd, $J_{3,P}$ 8.5, 3-H), 3.73 and 3.75 [3 H each, 2 \times d, J_{POMe} 11.0 and 10.8, P(OMe) $_2$], 4.17 (1 H, ddd, $J_{5eq,P}$ 7.6, 5- H_{eq}) and 4.30 (1 H, dd, 1-H); δ_P for **19b** 28.7.

Fraction A $_3$ [R_f 0.27 (Solvent B)] gave the pyranoside **18a** as a syrup (14.8 mg, 2.2% from **14**); δ_H 1.68 (1 H, dt, $J_{2ax,2eq}$ 14.8, $J_{1,2ax}$ 4.3, $J_{2ax,3}$ 3.7, 2- H_{ax}), 2.18 (1 H, dddd, $J_{2eq,P}$ 5.8, $J_{2eq,3}$ 3.6, $J_{1,2eq}$ 2.0, 2- H_{eq}), 2.39 (1 H, dtd, $J_{4,P}$ 21.3, $J_{4,5ax}$ 10.7, $J_{4,5eq}$ 4.2, $J_{3,4}$ 3.1, 4-H), 3.36 (3 H, s, 1-OMe), 3.42 (3 H, s, 3-OMe), 3.58 (1 H, ddd, $J_{5eq,5ax}$ 11.3, $J_{5eq,P}$ 5.9, 5- H_{eq}), 3.71 and 3.75 [3 H

each, 2 \times d, J_{POMe} 10.9 and 10.8, P(OMe) $_2$], 3.84 (1 H, dqd, $J_{3,P}$ 9.1, $J_{1,3}$ 1.0, 3-H), 4.16 (1 H, td, $J_{5ax,P}$ 2.4, 5- H_{ax}) and 4.62 (1 H, ddd, 1-H); δ_P 28.4.

1,3,5-Tri-O-acetyl-2,4-dideoxy-4-[(R and S)-methoxyphosphonoyl]- α,β -D-erythro-pentofuranose **22a-d**.—To a stirred solution of compounds **16a, b** (200 mg, 0.822 mmol) in dry benzene (3 cm 3) at 5 °C was added a solution of SDMA (3.4 mol dm $^{-3}$ in toluene; 0.90 cm 3 , 3.1 mmol) in dry benzene (1 cm 3) in small portions under argon. The mixture was stirred at this temperature for 30 min. Water (0.5 cm 3) was added and the mixture was stirred for a further 30 min. The precipitate was centrifuged and, after removal of the supernatant, extracted with several portions of benzene. The organic layers were combined, and evaporated under reduced pressure to give the 4-phosphino derivative **20** as a syrup; R_f 0.50 (Solvent C).

The above syrup was immediately treated at 90 °C with propan-2-ol (1.5 cm 3) and 0.5 mol dm $^{-3}$ hydrochloric acid (3 cm 3) for 1 h under argon. After cooling, the reactants were neutralized with Amberlite IRA-45. The resin was filtered off and washed with water, and the filtrate was evaporated under reduced pressure. The residue was dissolved in water (1.5 cm 3), treated, at 25 °C, with 30% aq. hydrogen peroxide (0.3 cm 3) for 10 h, and concentrated under reduced pressure to give crude 2,4-dideoxy-4-hydroxyphosphonoyl- α,β -D-erythro-pentofuranoses **21** as a syrup; R_f 0.15–0.10 (Solvent D).

This product was acetylated with acetic anhydride (0.5 cm 3) in dry pyridine (1.5 cm 3) for 1 d at 25 °C and the mixture was then concentrated under reduced pressure. The residue was passed through a column of Amberlite IR-120 (15 cm 3) and the eluent was concentrated under reduced pressure. The residue was dissolved in dry CH $_2$ Cl $_2$ (1 cm 3) and methylated with ethereal diazomethane, at 0 °C. The solvent was evaporated off under reduced pressure and the residue was separated by column chromatography with a gradient eluent of (3:1) AcOEt–hexane \rightarrow AcOEt, into two fractions, A and B.

Fraction A [R_f 0.45 (Solvent A)] gave a syrup (26.4 mg) which consisted of the 4-[(R)-methoxyphosphonoyl]- β -D-erythro-pentofuranose **22a** (6.1% from **16**) and the corresponding α -isomer **22b** (3.9%), the relative amounts being determined from the integral ratio of their 1-H and MeOP signals [Found: ($M^+ - CH_2CO$), 280.0713. $C_{10}H_{17}O_7P$ requires ($M - 42$), 280.0712]; 1H and ^{31}P NMR data, see Table 1; m/z 280 ($M^+ - CH_2CO$, 2.9%), 238 (100), 178 (10) and 150 (22).

Fraction B [R_f 0.42 (Solvent A)] gave a syrup (33.6 mg) which consisted of the 4-[(S)-methoxyphosphonoyl]- β -isomer **22c** (7.5% from **16**) and its corresponding α -isomer **22d** (5.2%) [Found: C, 45.1; H, 6.2%; ($M + 1$) $^+$, 323.0893. $C_{12}H_{19}O_8P$ requires C, 44.73; H, 5.94%; ($M + 1$), 323.0896]; 1H and ^{31}P NMR data, see Table 1; m/z 323 ($M^+ + 1$, 2.5%), 280 (17), 238 (100), 220 (22), 209 (30), 178 (39), 150 (56) and 123 (25).

1,3,5-Tri-O-acetyl-2,4-dideoxy-4-[(R and S)-methoxyphosphonoyl]- α,β -L-threo-pentofuranoses **25a-d**.—The procedures similar to those for the preparation of compounds **22** from substrates **16** were employed. Thus, compounds **17a, b** (111 mg, 0.456 mmol) were converted into the diastereoisomeric pentofuranoses **25** via intermediates **23** and **24**. The crude product **25** was separated by column chromatography into three fractions, A–C.

Fraction A [R_f 0.39 (Solvent A)] gave the 4-[(R)-methoxyphosphonoyl]- α -L-threo-pentofuranose **25a** (16.6 mg, 11% from **17**) as a syrup [Found: C, 45.0; H, 6.15%; ($M^+ - CH_2CO$), 280.0711. $C_{12}H_{19}O_8P$ requires C, 44.73; H, 5.94%; ($M - 42$), 280.0712]; 1H and ^{31}P NMR data, see Table 1; m/z 280 ($M^+ - CH_2CO$, 6.3%), 238 (100), 220 (18), 178 (15) and 150 (25).

Fraction B [R_f 0.36 (Solvent A)] gave a syrup (10.5 mg) which consisted of the 4-[(S)-methoxyphosphonoyl]- α -isomer

25c (4.8% from **17**) and its β -isomer **25d** (2.4%); ^1H and ^{31}P NMR data, see Table 1.

Fraction C [R_f 0.31 (Solvent A)] gave the 4-[(R)-methoxyphosphonyl]- β -isomer **25b** (8.0 mg, 5.4% from **17**) as a syrup [Found: ($M + 1$) $^+$, 323.0890. $\text{C}_{12}\text{H}_{20}\text{O}_8\text{P}$ requires ($M + 1$), 323.0896]; ^1H and ^{31}P NMR data, see Table 1; m/z 323 ($M^+ + 1$, 0.2%), 280 (5.3), 238 (100), 220 (8.5), 209 (10), 178 (16) and 150 (24).

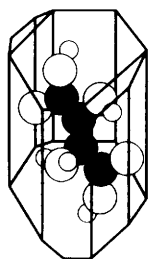
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