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SYNTHESIS OF 1,2,4-TRI-*O*-ACETYL-5-DEOXY-5-*C*-[(*R* AND *S*)-METHOXYPHOSPHINYL]-3-*O*-METHYL-α- AND -β-D-XYLOPYRANOSE, AND THEIR STRUCTURAL ANALYSIS BY 400-MHz, PROTON NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

HIROSHI YAMAMOTO, TADASHI HANAYA, SABURO INOKAWA*,
Department of Chemistry, Faculty of Science, Okayama University, Okayama 700 (Japan)

KUNIAKI SEO,
Department of Industrial Chemistry, Numazu Technical College, Numazu 410 (Japan)

MARGARET-ANN ARMOUR, AND TOM T. NAKASHIMA
Department of Chemistry, The University of Alberta, Edmonton, Alberta T6G 2G2 (Canada)
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ABSTRACT

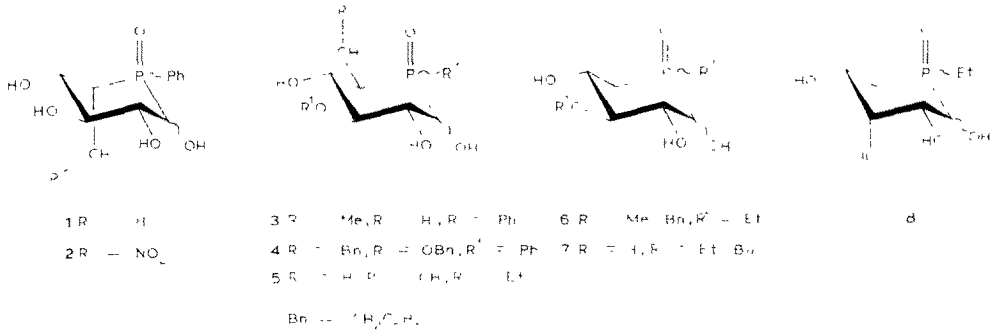
5-Deoxy-5-iodo-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-xylofuranose, prepared quantitatively from its 5-*O*-*p*-tolylsulfonyl precursor, readily gave the 5-*C*-(diethoxyphosphinyl) derivative. Treatment of this compound with sodium dihydrobis(2-methoxyethoxy)aluminate, followed by hydrogen peroxide, mineral acid, and hydrogen peroxide, yielded 5-deoxy-5-*C*-(hydroxyphosphinyl)-3-*O*-methyl-α,β-D-xylopyranoses in 65% overall yield. The structures of these sugar analogs were effectively established on the basis of the mass and 400-MHz, ^{1}H-n.m.r. spectra of the four title compounds, derived by treatment with diazomethane and then acetic anhydride in pyridine. 5-*C*-[(*S*)-(1-Acetoxyethenyl)phosphino]-1,2,4-tri-*O*-acetyl-5-deoxy-3-*O*-methyl-β-D-xylopyranose was also isolated and characterized.

INTRODUCTION

Sugar analogs having a phosphorus atom in the hemiacetal ring are interesting not only from the viewpoint of their physicochemical properties but also from that of their potential, biological activity. In an effort to prepare such hexopyranoses, we recently reported 5-deoxy-5-*C*-[(*R*,*S*)-phenylphosphinyl]-α,β-L-idopyranoses[1,2] (**1**,**2**) and the 5-*C*-phosphinyl-D-glucopyranoses[3–5] (**3**–**5**). As regards the pentopyranoses, 5-deoxy-5-*C*-phosphinyl-D-xylopyranoses[6,7] (**6** and **7**) and the D-ribopyranose[8] (**8**) had been prepared from the corresponding 5-deoxy-5-*C*-phosphinyl-D-pentofuranose precursors at an earlier stage of our investigation.

Instead of an alkyl- or aryl-phosphinyl group, as in **1**–**8**, the presence of a

*To whom correspondence should be addressed.

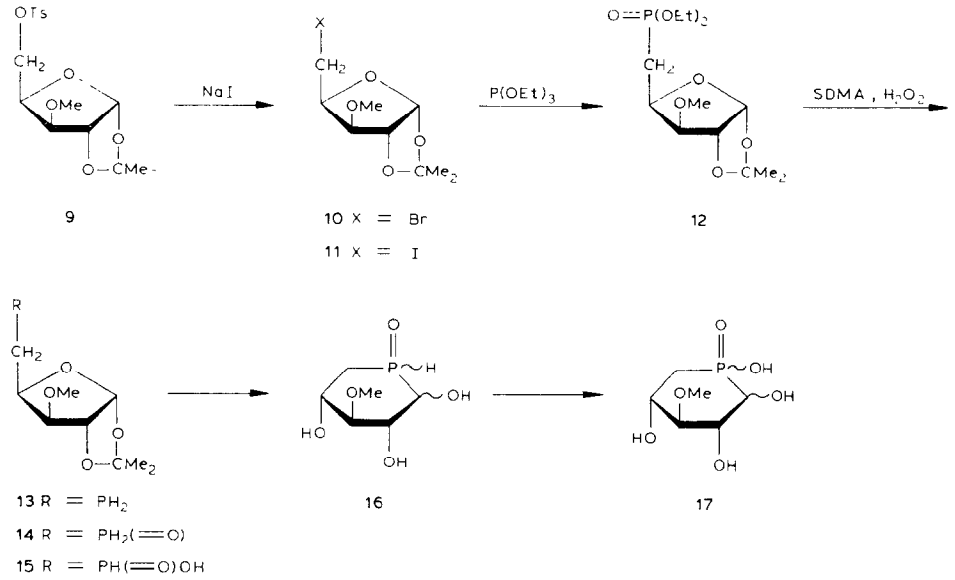


hydroxyphosphinyl group in the ring is also expected to be of high interest from various viewpoints. Only one such compound, **17**, has so far been reported, by Whistler and Wang[9], who prepared it, in ~10% overall yield, from 1,2-*O*-isopropylidene-3-*O*-methyl-5-*O*-*p*-tolylsulfonyl-α-D-xylofuranose (**9**) by the sequence **9**→**10**→**12**→**13**→**16**→**17**. Their structural assignments of compounds **16** and **17** were based mainly on elemental analyses and on insufficiently resolved, 60-MHz. ^{1}H-n.m.r. spectra. In order to establish an effective way of preparation, and characterization, of a series of such sugar analogs, we have reinvestigated the synthesis and properties of **17** as the initial part of our study on 5-deoxy-5-*C*-(hydroxyphosphinyl)pyranoses and 4-deoxy-4-*C*-(hydroxyphosphinyl)furanoses.

RESULTS AND DISCUSSION

On heating **9** with sodium iodide in acetone at 100° in a sealed tube, the hitherto unreported 5-deoxy-5-iodo-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-xylofuranose (**11**) was readily obtained in quantitative yield. The iodo compound **11** was used as our starting material, because of the simplicity of its preparation, and also its higher reactivity towards the nucleophile in the following step (compared with the bromo derivative **10**). Conversion of **11** into the phosphonate **12** was readily effected by heating with an excess of triethyl phosphite at 150°.

It had been reported[9] that compound **16** (m.p. 208–210°), obtained in 15% overall yield from **12** through ring enlargement of the 5-*C*-(phosphino)xylofuranose **13**, showed its H-1 signal as a pair of broad triplets, at δ 4.72, with $J_{1,P}$ 9, $J_{1,2}$ 2.5, and $J_{1,D}$ 2.0 Hz, in the ^{1}H-n.m.r. spectrum of a solution in D_2O. As we could not repeat the transformation of **12** into **16** *via* **13** by using lithium aluminum hydride[9] and then mineral acid, we attempted to reduce compound **12** to the phosphine oxide **14** with sodium dihydrobis(2-methoxyethoxy)aluminate (SDMA), which usually converts phosphinates and phosphonates into phosphine oxides under controlled conditions[1–5,10]. However, even by using a stoichiometric amount of SDMA, the phosphonate **12** was rapidly reduced to the phosphine **13**, which was found to be extremely sensitive to air-oxidation and technically difficult to handle. Therefore, instead of subjecting the product **13** to ring-enlargement by acid[9] to afford **16**, it



was immediately oxidized with one equivalent of hydrogen peroxide in 2-propanol, to give **14**. Although a small proportion of the further-oxidized product **15** was detected by t.l.c., the conversion proceeded satisfactorily. Being found also to be sensitive towards oxidation, compound **14** was, without isolation, refluxed with ethanolic 0.5M hydrochloric acid under nitrogen, affording the 5-deoxy-3-*O*-methyl-5-*C*-(phosphinyl)-α,β-D-xylopyranoses **16**.

Although its ^{1}H-n.m.r. spectrum in Me_2SO-d_6 was in conformity with structure **16**, our specimen was a white, hygroscopic, amorphous solid that did not crystallize from various solvents. No pure acetyl or benzoyl derivative of **16** was isolated after treatment with acetic anhydride or benzoyl chloride in pyridine; only a mixture of several, unseparated products were formed. This could partly be attributed to the facile phosphorus–phosphorus dimerization of **16**, analogous to the formation of tetraphenyldiphosphine monoxide [Ph_2P-P(=O)Ph_2] from diphenylphosphine oxide in the presence of acetic anhydride and pyridine at room temperature[11].

Compound **16** was, therefore, oxidized with hydrogen peroxide, to give the 5-deoxy-5-*C*-(hydroxyphosphinyl)xylopyranoses **17** in 65% overall yield (from **12**), which is far higher than the reported yield[9] (~10%). Although compound **17** had been reported[9] to have m.p. 192° after recrystallization from methanol–ether and to show its H-1 signals at an unusually high field (δ 2.93 and 2.80) in Me_2SO-d_6, recrystallization of our specimen from the same mixed solvent gave (with rather poor recovery) colorless needles of m.p. 95°, and its H-1 signal appeared at δ ~3.7, overlapping with other, ring-proton absorptions.

As **17** was expected to be a mixture of, at least, two anomers, unambiguous structural assignment was made by converting **17** into its 5-*C*-(methoxyphosphinyl) peracetates **18** (in 56% yield as a mixture of diastereoisomers) by treatment with

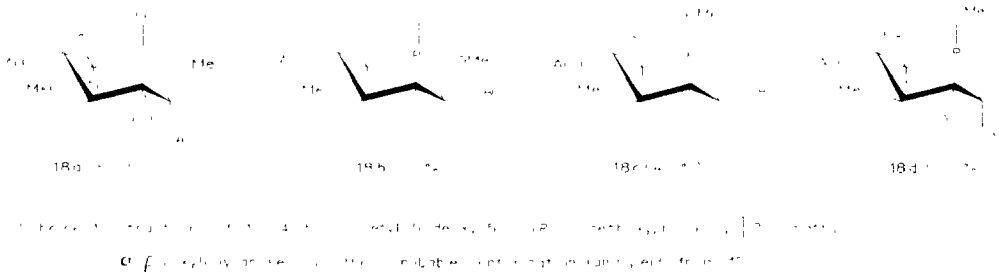


TABLE I

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

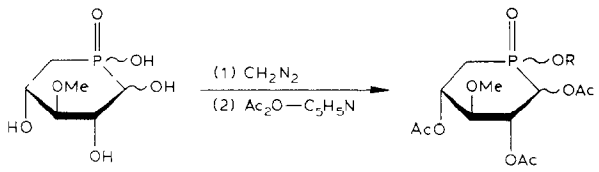
Compounds	*Chemical shifts (δ)*								
	H-1	*H-2*	*H-3*	*H-4*	*H-5e*	*H-5a*	*4cO-1,2,4[a]*	*MeO-3*	*MeO-P*
3[b]	5.60	5.78	3.58	5.52	1.06[c]	1.90	2.14, 2.05, 1.90	3.49	[d]
18a	5.60	5.41	3.62	5.24	2.43	2.13	2.22, 2.12, 2.09	3.51	3.73
18b	5.27	5.45	3.42	5.24	2.55	1.91	2.16, 2.10, 2.08	3.48	3.77
18c	5.44	5.22	3.36	4.98	2.52	1.92	2.14, 2.12, 2.09	3.51	3.94
18d	5.64	5.04	3.54	4.94	2.48	2.22	2.22, 2.12, 2.06	3.50	3.88
23	5.43	5.63	3.49	5.40	2.62	1.95	2.11, 2.09, 2.08	3.51	2.26[e] 6.08[f] 6.19[g]

	Coupling constants (Hz)[h]											
	$J_{1,2}$	$J_{1,P}$	$J_{1,5e}$	$J_{2,3}$	$J_{2,P}$	$J_{3,4}$	$J_{4,5e}$	$J_{4,5a}$	$J_{4,P}$	$J_{5a,5e}$	$J_{5e,P}$	$J_{5a,P}$	$^3J_{HP}$ (POMe)
3[b]	11.0	2.2	0.3[c]	9.6	2.8	9.8		12.0	2.7	7.0[i]	15.0[k]	3.5	[d]
18a	2.8	14.2	2.0	9.8	1.0	9.3	4.5	12.0	3.0	14.0	22.5 ~ 12[l]		11.0
18b	10.5	5.5	0	8.7	3.8	8.6	4.5	12.5	0.8	14.8	22.5	11.0	11.2
18c	10.8	3.6	0	9.6	2.1	9.6	4.5	12.0	2.0	14.8	23.6	10.0	10.5
18d	3.0	15.0	2.0	10.0	0	9.7	4.8	12.0	2.1	14.3	21.5 ~ 12[l]		10.5
23	10.8	1.6	0	9.2	2.6	9.5	4.4	12.0	3.2	14.4	20.0	5.3	[d]

[a]Acetoxyl assignments are interconvertible. [b]Ref. 4. [c]CH_2-5. [d]δ 7.75, 7.47, 7.56 (all m) due to P-C_6H_5. [e]P-C(OCOCH$_3$) CH_2. [f]P-C C-H(*E*) ($^3J_{HP}$ 29.8, $^3J_{H,H}$ 2.8 Hz). [g]P-C C-H(*Z*) ($^3J_{H,P}$ 10.2, $^3J_{H,H}$ 2.8 Hz). [h]*J* values confirmed by double resonance. [i]$J_{1,5a}$, $J_{5a,6}$. [k]$^2J_{6,P}$. [l]Approximate value, because of overlapping with acetoxyl signals.

diazomethane and then acetic anhydride–pyridine. [Preparation of other derivatives, such as the acetyl or *p*-bromophenacyl compounds (**19** and **20**) resulted in less satisfactory yields; *i.e.*, **19**: 20%, and **20**: 5%]. The crude **18** was separated (by column chromatography on silica gel, using ethyl acetate–hexane as the eluant) into five major fractions, which will be referred to as A, B, C, D, and E according to their decreasing R_F values.

Fraction C gave colorless needles of m.p. 194–195°, which clearly exhibited in the high-resolution mass spectrum, the molecular-ion peak at *m/z* 352, correspond-



17

18 R = Me
19 R = H
20 R = $CH_2COC_6H_4Br$-*p*

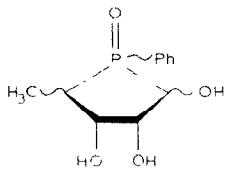
ing to $C_{13}H_{21}O_9P$, and this formula was supported by the elemental analysis. The precise structure of this compound was determined by comparing its 400-MHz, ^{1}H-n.m.r. spectrum with those[1,4,5] of the structurally similar analogs **1–5** (*cf.*, the parameters for **3** shown in Table I). The assignments of all signals were readily made by employing first-order analysis with the aid of a decoupling technique, and the results are summarized in Table I. The splitting patterns of the H-1 signal (doublet of doublets with $J_{1,2}$ 10.5 and $J_{1,P}$ 5.5 Hz) and the relatively low δ values of H-2 and H-4 (compared with those of **18c** and **d**; see later) led to the 5-deoxy-5-*C*-[(*R*)-methoxyphosphinyl]-β-D-xylopyranose structure **18b**, in the $^4C_1$(D) conformation, for product C.

The fastest-eluting fraction (A) afforded a single product as a colorless oil, the n.m.r. spectrum of which indicated the structure of 5-deoxy-5-*C*-[(*R*)-methoxyphosphinyl]-α-D-xylopyranose (**18a**) in the $^4C_1$(D) conformation. The α configuration was derived from the presence of the 1,5 W coupling ($J_{1,5e}$ 2.0 Hz) and the relatively low δ values of H-1 and H-5a, as well as the reversed magnitude of the values of $J_{1,2}$ (2.8) and $J_{1,P}$ (14.2 Hz), compared with those of the β anomer **18b**; such characteristic features had been utilized[1,4,5] for distinguishing between the anomers of the 5-deoxy-5-*C*-(phosphinyl)hexopyranoses **1–5**. The assignments of the signals of **18a** are recorded in Table I.

Fraction D also gave a single product as a colorless oil, which, by means of its high-resolution mass spectrum, was found to possess a molecular formula ($C_{13}H_{21}O_9P$) identical to that of **18b**. Although the splitting pattern in the n.m.r. spectrum of this product somewhat resembled that of **18b**, the upfield shift (0.2–0.5 p.p.m.) of the H-2 and H-4 signals, and the downfield shift (0.2 p.p.m.) of the H-1 and P-OMe signals accounted for the 5-*C*-[(*S*)-methoxyphosphinyl]-β-D-xylopyranose structure **18c**, presumably in the $^4C_1$(D) conformation; analogous shielding and deshielding by phosphinyl oxygen were observed for the 5-*C*-[(*R* and *S*)-phosphinyl] epimers[1,5] (**1–5**), and for 4-deoxy-4-[(*R* and *S*)-phenylphosphinyl]pentofuranoses[12] (**21**). Assignments for the n.m.r. signals of **18c** are recorded in Table I.

The slowest-moving fraction (E) mainly consisted of a colorless oil whose structure was shown by n.m.r. spectroscopy to be the α anomer (**18d**) of compound **18c**. The spectrum was completely consistent with this structure; see the assignments in Table I.

Besides these four diastereoisomers (**18a–d**) of the 5-deoxy-5-*C*-(methoxy-



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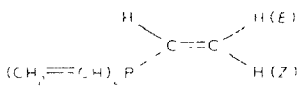

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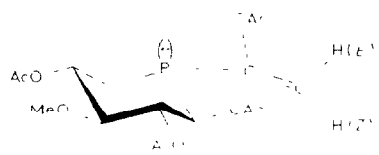
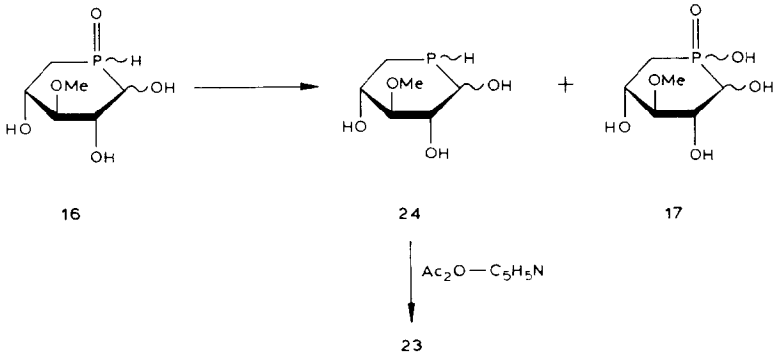


23

phosphinyl)-D-xylopyranoses, a fifth product was obtained from Fraction B as colorless needles, m.p. 190–192°, which possessed the molecular formula $C_{15}H_{23}O_9P$ on the evidence of the high-resolution mass spectrum. The chemical shifts and the splitting patterns of this crystalline product closely resembled those of **18b**, but the spectrum differed from that of **18b** in the following respects: (*1*) the presence of a pair of AB-type doublets of doublets at δ 6.08 ($J_{H,P}$ 29.8 and $J_{H,H}$ 2.8 Hz) and 6.19 ($J_{H,P}$ 10.2 and $J_{H,H}$ 2.8 Hz), (*2*) the presence of an additional acetoxyl singlet at δ 2.26, and (*3*) the absence of the P-OMe doublet at δ 3.8. Taking into account the $^3J_{H,P}$ values commonly observed for a model such as trivinylphosphine (**22**), for which H(*E*) and H(*Z*) appear[13] as doublets of doublets at δ 5.64 ($J_{H,P}$ 30.2 Hz) and 5.51 ($J_{H,P}$ 13.6 Hz), respectively, the aforementioned n.m.r. data led to structure **23**, namely, 5-*C*-[(*S*)-(1-acetoxyethenyl)phosphino]-1,2,4-tri-*O*-acetyl-5-deoxy-3-*O*-methyl-β-D-xylopyranose in the $^4C_1$(D) conformation, for this crystalline product. The assignment of the configuration of the phosphino group in **23** was based on the generally observed feature[14] that $^2J_{H,P}$ is much larger when the coupled proton lies close to the orbital of the lone pair of P(III) compounds, and small when remote, see the $J_{1,P}$, $J_{5a,P}$ and $J_{5c,P}$ values in Table I.

It had been reported[1,4,5] that geminal, P–C–H coupling-constants for the 5-*C*-(phosphinyl)hexopyranoses **1**–**5** depend upon the approximate magnitude of the O=P–C-5–H dihedral angle, thus providing a quick method for assignment of the configuration of the ring-phosphorus atom and C-5; that is, small $J_{5,P}$ values (3–5 Hz) indicate the *anti* orientation of O=P–C-5–H, whereas large values ($J_{5,P}$ 15–22 Hz) are consistent with *gauche* coupling. The same feature, observed for the O=P–C-1–H dihedral angle, was used for distinguishing between the α and β anomers. As summarized in Table I, a similar angular-dependence of the $J_{1,P}$ and $J_{5,P}$ values upon the dihedral angles of O=P–C–H apparently exists in the case of the 5-*C*-(methoxyphosphinyl)xylopyranoses **18a**–**d** (except for the $J_{1,P}$ value of **18c**, which appears to be slightly smaller than anticipated for the *gauche* orientation). Thus, the utility of $^2J_{H,P}$ values, when coupled with careful analysis of the δ values of their H-1, H-2, H-4, and P-OMe signals, provides an effective way of assigning the configuration of the ring-phosphorus atom of 5-deoxy-5-*C*-(methoxyphosphinyl)xylopyranoses, as in the case of 5-*C*-(alkyl- or aryl-phosphinyl)hexopyranoses (**1**–**5**).

The yields of the four, theoretically possible, diastereoisomers of the 5-*C*-(methoxyphosphinyl)xylopyranoses **18a**–**d** are given in Scheme 1. It should be noted that the relatively low yield of each product from **12** can mainly be attributed to



Scheme 2 A reaction pathway for the formation of the 5-*C*-phosphino compound 23

inefficient methylation of **17** (dissolved in methanol) with ethereal diazomethane. Nevertheless, no particular preponderance seems to be apparent, during the formation of these D-xylopyranoses **18** from the precursor **13**, with regard to the configuration of C-1 and of the ring-P atom, because the ratio of the combined yields of the 5-*C*-[(*R*)-methoxyphosphinyl]pyranoses (**18a** and **b**) to the (*S*)-epimers (**18c** and **d**) is 46:41, while that of the α anomers (**18a**,**d**) to the β anomers (**18b**,**c**) is 49:39. This is in striking contrast to the markedly different preference in hemiacetal formation with regard to the configuration of C-5 and phosphorus[1-5].

Although an exact, mechanistic study remains to be conducted, the unusual formation of **23** as a minor product (2.7% overall yield from **12**) is most likely to have occurred through the pathway involving, to a small extent, the disproportionation reaction of **16** to form **17** and the 5-*C*-(phosphino)xylopyranose **24**, which would, in turn, produce **23** by an unusual acetylation, as shown in Scheme 2. A similar disproportionation reaction is known[15] for various primary and secondary phosphine oxides.

The work so far described, therefore, clearly demonstrates achievement of an efficient preparation of 5-deoxy-5-*C*-(hydroxyphosphinyl)-D-xylopyranoses, and also the effective use of 400-MHz, ^{1}H-n.m.r. spectroscopy for determining the configuration and conformation of 5-deoxy-5-*C*-(methoxyphosphinyl)pyranoses.

EXPERIMENTAL

General methods. — Melting points were measured with a Yanagimoto MP-S3 instrument and are uncorrected. Optical rotations were determined with a Nihonbunko DIP-4 polarimeter. Column chromatography was performed by using Merck Lobar silica gel. T.l.c. was conducted on plates precoated with silica gel (0.25 mm, Merck). All reactions were monitored by t.l.c., and the products were detected with sulfuric acid–ethanol, or cobalt(II) chloride–acetone, as the indicator. ^{1}H-N.m.r. spectra were recorded for solutions in $CDCl_3$ (unless stated otherwise) with a Hitachi–

Perkin–Elmer R-20A (60 MHz) or Bruker WH-400 cryospectrometer (400-MHz, for **18a–d** and **22**) at 27°. Chemical shifts are reported as δ values relative to tetramethylsilane (δ 0.0) as the internal standard. Spin decoupling was performed for each proton signal, to confirm the coupling constants. Mass spectra were recorded with an A.E.I. MS 50 ultra-high-resolution instrument, and are given in terms of *m/z* (relative intensity) compared with the base peak.

5-Deoxy-5-iodo-1,2-O-isopropylidene-3-O-methyl-α-D-xylofuranose (**11**). – A mixture of the 5-*p*-toluenesulfonate[9] **9** (9.71 g) and sodium iodide (12.0 g) dissolved in acetone (80 mL) was heated in a sealed tube for 10 h at 100°. The precipitate was filtered off, and the filtrate evaporated *in vacuo*. A solution of the residue in water was extracted with chloroform, and the extract was washed with water, dried (Na_2SO_4), and evaporated *in vacuo*, to give **11** (8.37 g, 98%) as a colorless syrup which was chromatographically pure and was used directly for the next step; R_f 0.8 (2:1 EtOAc–hexane); ^{1}H-n.m.r.: δ 1.31, 1.49 (2 s, 6 H, CMe_2), 3.27 (d, 2 H, $J_{4,5}$ 7.2 Hz, H_2-5), 3.48 (s, 3 H, OMe), 3.85 (d, 1 H, $J_{3,4}$ 3.3 Hz, H-3), 4.40 (dt, 1 H, H-4), 4.57 (d, 1 H, $J_{1,2}$ 3.9 Hz, H-2), and 5.92 (d, 1 H, H-1).

5-Deoxy-5-C-(diethoxyphosphinyl)-1,2-O-isopropylidene-3-O-methyl-α-D-xylofuranose (**12**). – A mixture of **11** (4.25 g) and triethyl phosphite (2.8 mL) was stirred under nitrogen at 150°; additional amounts (1.4 and 0.9 mL) of $P(OEt)_3$ were added after 3 and 6 h. After 10 h (total), the mixture was evaporated *in vacuo*, to remove the excess of phosphite and diethyl ethylphosphonate produced. The residue was dissolved in dichloromethane, and the solution was washed with water, dried (Na_2SO_4), and evaporated *in vacuo*, to give **12** (3.63 g, 83%) as a colorless syrup. The material was found by n.m.r. spectroscopy and t.l.c. to be pure, and thus it was used for the subsequent steps without purification: R_f 0.35 (3:1 EtOAc–hexane); ^{1}H-n.m.r.: δ 1.32 [t, 6 H, $J_{H,H}$ 6.9 Hz, P(O-C-CH_3)$_2$], 1.32, 1.47 (2 s, 6 H, CMe_2), 2.15 (dd, 1 H, $J_{5,P}$ 19.5, $J_{4,5}$ 1.0 Hz, H-5), 2.28 (dd, 1 H, $J_{5',P}$ 19.5, $J_{4,5'}$ 3.5 Hz, H-5'), 3.45 (s, 3 H, OMe), 3.71 (d, 1 H, $J_{3,4}$ 3.4, $J_{2,3}$ ~0 Hz, H-3), 4.11 [dq, 4 H, $^3J_{H,P}$ 7.2 Hz, P(OCH_2)$_2$], 4.4 (m, 1 H, H-4), 4.55 (d, 1 H, $J_{1,2}$ 3.9 Hz, H-2), and 5.82 (d, 1 H, H-1).

5-Deoxy-5-C-(hydroxyphosphinyl)-3-O-methyl-D-xylopyranose (**17**). – A solution of **12** (2.39 g) in dry benzene (10 mL) was degassed, and then bubbled with nitrogen. SDMA (70% in toluene, 4.0 mL) was slowly added at 0° under nitrogen, followed by stirring for 1 h at 5°. A small amount of cold water was added at 0°, to decompose the excess of SDMA, and the mixture was stirred for 30 min, and centrifuged to remove aluminum hydroxide; the precipitate was extracted with several portions of oxygen-free benzene. The organic layers were combined, washed twice with water (free from oxygen gas), dried (Na_2SO_4), and evaporated *in vacuo*, to give *5-deoxy-3-O-methyl-5-C-phosphino-D-xylofuranose* (**13**) as a colorless liquid; R_f 0.84 (3:1 EtOAc–hexane), 0.91 (5:3:1 *i*PrOH–EtOAc–H_2O).

Product **13** was immediately dissolved in 2-propanol (8 mL), and 12% hydrogen peroxide (1.8 mL, 0.86 equiv.) was slowly added, with stirring under nitrogen, at 5°, until **13** disappeared (t.l.c.), thus affording mostly *the 5-phosphinyl derivative* (**14**),

which was contaminated with a small proportion of *the 5-(hydroxyphosphinyl) derivative* (**15**); R_F 0.57 and 0.23, respectively (5:3:1 *i*PrOH–EtOAc–H_2O).

To this solution was added oxygen-free, 0.5M hydrochloric acid (10 mL). The mixture was refluxed under nitrogen for 4 h at 100° (bath), cooled, and the acid neutralized by passing the mixture through a column of (weakly basic) Amberlite IR-45 ion-exchange resin, which was then eluted with water (200 mL). The eluate was filtered, and the filtrate evaporated *in vacuo*, to give *5-deoxy-3-O-methyl-5-C-phosphinyl-D-xylopyranoses* (**16**) as a white, amorphous solid; R_F 0.51, 0.43, and 0.35 (5:3:1 *i*PrOH–EtOAc–H_2O); ^{1}H-n.m.r. (Me_2SO-d_6): δ 1.7–2.2 (m, 2 H, H-5,5′), 3.0–3.9 (m, 3 H, H-2,3,4), 3.53 (s, 3 H, MeO-3), 3.9–4.3 (m, 1 H, H-1), 5.36 (s, 3 H, OH-1,2,4, D_2O exchangeable), and 10.90 (bs, 0.5 H, half-proton of PH).

A solution of **16** in 2:3 2-propanol–water (10 mL) was stirred with a large excess (~5–6 equiv.) of 30% hydrogen peroxide for 1 day at 20°, and the mixture was evaporated *in vacuo*, to give **17** (1.02 g, 65% overall yield from **12**) as a white solid that gave colorless needles on crystallization from methanol–ether; m.p. 95°; R_F 0.05 (5:3:1 *i*PrOH–EtOAc–H_2O); ^{1}H-n.m.r. (Me_2SO-d_6): δ 1.5–2.1 (m, 2 H, H-5,5′), 3.0–4.5 (m, 4 H, H-1,2,3,4), 3.50 (s, 3 H, OMe), and 5.8–6.5 (m, 4 H, HO-1,2,4, POH, D_2O-exchangeable).

1,2,4-Tri-O-acetyl-5-deoxy-5-C-[(R,S)-methoxyphosphinyl]-3-O-methyl-α,β-D-xylopyranoses (**18a–d**) *and 5-C-[(S)-(1-acetoxy)ethenylphosphino]-1,2,4-tri-O-acetyl-5-deoxy-3-O-methyl-β-D-xylopyranose* (**23**). — To a solution of **17** (1.02 g) in dry methanol (10 mL) was added an excess of ethereal diazomethane at 0°, with stirring; when the mixture became turbid, it was evaporated *in vacuo*, the residue dissolved in dry methanol, and repeatedly treated with cold, ethereal diazomethane. After being stirred for 30 min, the mixture was evaporated *in vacuo*, and the residue was treated with acetic anhydride (15 mL) in dry pyridine (15 mL) in the usual way[1–5], to give crude mixture **18** as an amber syrup (940 mg, 56% from **12**).

By chromatography on a column of silica gel with 1:1 EtOAc–hexane, which was gradually changed to EtOAc, as the eluant, the crude product was separated into five fractions A, B, C, D, and E [according to their decreasing R_F values (EtOAc)].

Fraction A (R_F 0.50) gave *5-C-[(R)-methoxyphosphinyl]-α-D-xylopyranose* (**18a**) as a colorless syrup (169 mg; 6.5% from **12**); $[\alpha]_D^{27}$ +27.0° (*c* 1.99, $CHCl_3$); for 400-MHz, ^{1}H-n.m.r. data, see Table I.

Fraction B (R_F 0.46) gave **23** as colorless prisms (75 mg; 2.7% from **12**); m.p. 189–190° (after recrystallization from EtOAc–hexane), $[\alpha]_D^{27}$ −10.0° (*c* 1.14, $CHCl_3$); for 400-MHz, ^{1}H-n.m.r. data, see Table I; high-resolution, e.i. mass spectrum: *m/z* (relative intensity) 378 (0.51, M^+), 364 (2.4), 336 (17), 322 (14), 280 (20), 263 (27), 262 (40), 221 (100), 220 (77), 217 (35), 203 (16), 178 (43), 87 (42), and 71 (64).

Calc. for $C_{15}H_{23}O_9P$: mol. wt., 378.1080. Found: mol. wt., 378.1051.

Fraction C (R_F 0.39) gave *5-C-[(R)-methoxyphosphinyl]-β-D-xylopyranose* (**18b**) as colorless needles (74 mg; 2.7% from **12**); m.p. 194–195° (from EtOAc–hexane), $[\alpha]_D^{27}$ −17.4° (*c* 0.78, $CHCl_3$); for 400-MHz, ^{1}H-n.m.r. data, see Table I;

high-resolution, e.i. mass spectrum: *m/z* 352 (5.1, M^+), 309 (3), 293 (68), 251 (26), 250 (15), 208 (24), 191 (21), 188 (66), 177 (13), 151 (13), 145 (21), 130 (54), 129 (29), 87 (100), 85 (71), and 71 (54).

Anal. Calc. for $C_{13}H_{21}O_9P$: C, 44.32; H, 6.01; mol. wt., 352.0923. Found: C, 44.68; H, 6.09; mol. wt., 352.0919.

Fraction D (R_f 0.36) gave *5*-C-[(S)-*methoxyphosphinyl*]-*β*-D-*xylopyranose* (**18c**) as a colorless syrup (128 mg; 4.9% from **12**); $[\alpha]_D^{27}$ −0.14 (*c* 2.89, $CHCl_3$); for 400-MHz, ^{1}H-n.m.r. data, see Table I; high-resolution, e.i. mass spectrum, *m/z* 352 (1.04, M^+), 293 (56), 251 (21), 250 (26), 209 (21), 20 (21), 191 (23), 190 (26), 188 (71), 179 (14), 177 (11), 151 (16), 145 (24), 130 (45), 129 (38), 87 (100), 85 (75), and 71 (63).

Calc. for $C_{13}H_{21}O_9P$: mol. wt., 352.0923. Found: mol. wt., 352.0919.

Fraction E (R_f 0.32) gave *5*-C-[(S)-*methoxyphosphinyl*]-*γ*-D-*xylopyranose* (**18d**) as a pale-yellow syrup (84 mg; 3.3% from **12**); $[\alpha]_D^{27}$ +6.2° (*c* 0.84, $CHCl_3$); for 400-MHz, ^{1}H-n.m.r. data, see Table I.

1,2,4-Tri-O-*acetyl*-*5-deoxy*-*5*-C-(*hydroxyphosphinyl*)-*3*-O-*methyl*-*α,β*-D-*xylopyranoses* (**19**). — To a solution of **17** (51 mg) in dry pyridine (2 mL) was added, at 0°, acetic anhydride (1 mL), and the mixture was stirred overnight at room temperature. A small amount of water was added, most of the pyridine was evaporated *in vacuo*, the residue was dissolved in chloroform, and the solution was washed with brine, dried (Na_2SO_4), and evaporated *in vacuo*, to give **19** as a colorless solid (23 mg, 28%), which afforded colorless needles on recrystallization from chloroform–hexane: m.p. 120–122°; R_f 0.0–0.14 (EtOAc); ^{1}H-n.m.r.: δ 1.9–2.5 (m, 11 H, OAc-1,2,4, H-5,5′), 3.4–3.6 (m, 1 H, H-3), 3.50 (s, 3 H, OMe), and 5.0–5.8 (m, 3 H, H-1,2,4).

1,2,4-Tri-O-*acetyl*-*5*-C-[(R,S)-(p-*bromophenacyloxy*)*phosphinyl*]-*5-deoxy*-*3*-O-*methyl*-*α,β*-D-*xylopyranoses* (**20**). — To a solution of **17** (146 mg) in methanol (5 mL) containing a trace of phenolphthalein was slowly added enough 5% aqueous sodium hydroxide to give pH 9 (faint red), and then 0.5M HCl (two drops) was added. The mixture was evaporated *in vacuo*, to remove water, and to a solution of the residue in dry DMF (3 mL) was added *p*-bromophenacyl bromide (191 mg), the mixture was stirred overnight at 40–45°, evaporated *in vacuo*, and the residue stirred with a mixture of pyridine (5 mL) and acetic anhydride (3 mL) overnight at room temperature, followed by the same processing as for **19**, to give a brown syrup (284 mg), which was separated by preparative t.l.c., using 3:1 EtOAc–hexane as the eluant. The band having R_f 0.3–0.4 (EtOAc) was collected, and eluted with EtOH, to give crude **20** as a yellow syrup (19 mg, 5%): ^{1}H-n.m.r.: δ 1.9–2.5 (m, 11 H, OAc-1,2,4, H-5,5′), 3.4–3.6 (m, 1 H, 3.55 (s, 3 H, OMe), 4.9–5.9 (m, 5 H, H-1,2,4, P-OCH_3), and 7.5–7.8 (m, 4 H, C_6H_4Br).

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