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A Convenient Synthesis of 1,2,4-Tri-*O*-acetyl-5-deoxy-5-[(*R*)- and (*S*)-ethylphosphino and phenylphosphino]-3-*O*-methyl-α,β-D-xylopyranoses and Their Phosphinothioyl Derivatives§

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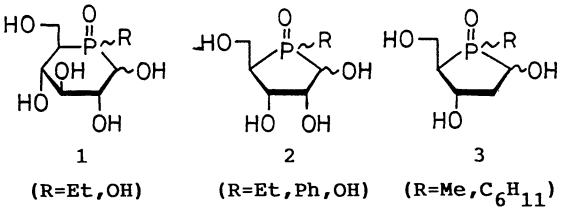
1,2,4-Tri-*O*-acetyl-5-deoxy-5-[(*R*)- and (*S*)-ethylphosphinyl]-3-*O*-methyl-α,β-D-xylopyranoses (**8a—d**) were prepared from 5-deoxy-5-[(*R*)- and (*S*)-(ethoxy)ethylphosphinyl]-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-xylofuranoses in two steps. Reduction of **8a—d** and their 5-(phenylphosphinyl) congeners with trichlorosilane-triethylamine in benzene smoothly afforded the corresponding title 5-deoxy-5-phosphino-D-xylopyranoses (**9a—d** and **14a—d**) without causing inversion of the ring-phosphorus atom. Treatment of **9a—d** and **14a—d** with sulfur in benzene efficiently provided the corresponding (phosphinothioyl)-in-ring D-xylopyranoses. Structural and conformational assignments of these newly obtained compounds were made on the basis of mass and NMR (^{1}H and ^{31}P) spectral data.

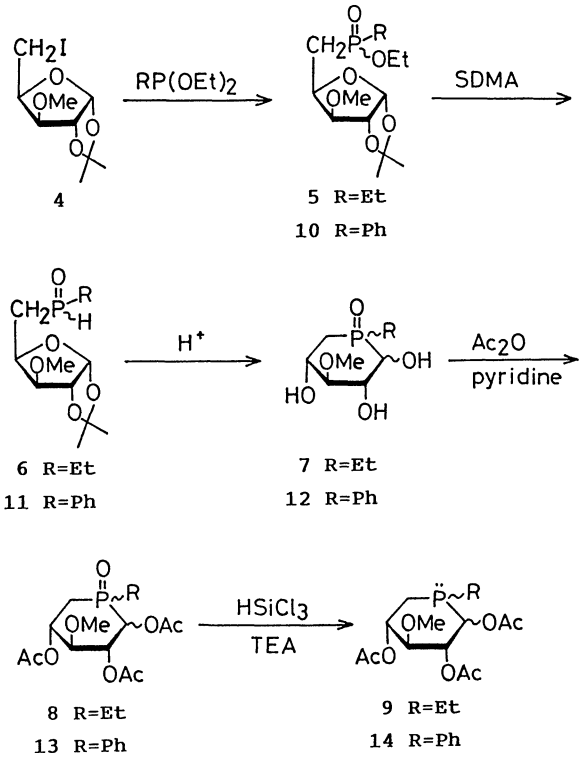
A large number of sugar analogues having a phosphorus atom in place of oxygen in the hemiacetal ring have been prepared in recent years:[1] e.g., D-glucopyranoses **1**,[2,3] D-ribofuranoses **2**,[4,5] and 2-deoxy-D-ribofuranoses **3**.[6] Such compounds are of interest from the viewpoint of their physicochemical properties and potential biological activity.[1b] All of these sugars contain a phosphinyl group in the ring and no analogues having a phosphino group have been reported so far.[7] We now describe a detailed study on a convenient synthesis of the first P-in-ring pyranose analogues having an ethyl- or phenyl-phosphinidene group in the hemiacetal ring by employing 3-*O*-methyl-D-xylopyranose as a model compound.[8] Hitherto unreported physicochemical properties, as well as biological activity, of this type of compounds are anticipated to be highly of interest. For example, with powdered sulfur these compounds are shown to be readily convertible into the corresponding 5-phosphinothioyl derivatives,[9] of which the P=S functional group is expected to play an important role in potential biological activity.[10]



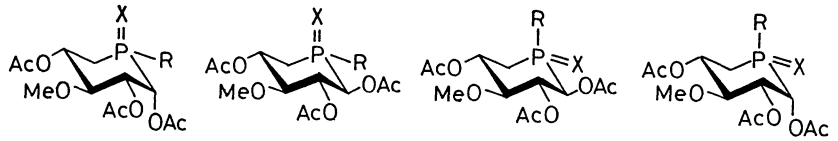
§ Although contrary to the very recently modified Chem. Abstr. nomenclature for some of these P-in-ring sugar analogues (e.g. [1*S*-(1α,2α,3α,4β,5α)]-1-ethyl-4-methoxy-2,3,5-phosphorinanetriol triacetate for **9a** and its 1-sulfide for **17a**), "5-deoxy-5-phosphino-D-xylopyranose" and its "5-phosphinothioyl" derivative will be used in this paper, because these have been permitted as comprehensible names in carbohydrate section.

Results and Discussion

Michaelis-Arbuzov reaction of 5-deoxy-5-iodo-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-xylofuranose[11] (**4**) with diethyl ethylphosphonite gave 5-deoxy-5-[(ethoxy)ethylphosphinyl] derivative[12] (**5**), which was now found separable into two diastereomers **5a** (colorless prisms, mp 70—71 °C) and **5b** (colorless syrup) by silica-gel chromatography (Scheme 1). These compounds are epimers with respect to the phosphorus atom but their assignment of (*R*)- or (*S*)-configuration



Scheme 1. Preparation of 5-deoxy-5-phosphino-D-xylopyranoses.



	8	9	17	13	14	18
R	Et	Et	Et	Ph	Ph	Ph
X	O	lone pair	S	O	lone pair	S

Chart 1. Structures of 1,2,4-tri-*O*-acetyl-5-deoxy-3-*O*-methyl-5-phosphino-D-xylopyranoses and their 5-phosphinyl and 5-phosphinothioyl derivatives.

Table 1. ^{1}H and ^{31}P NMR Parameters for P-in-Ring Sugars **8**, **9**, **13**, **14**, **17**, and **18** in $CDCl_3$

Compd	Chemical shift (δ)													
	H-1	H-2	H-3	H-4	He-5	Ha-5	AcO-1,2,4[a]			MeO-3	HC-P	H'C-P	Me-C-P (Ph(*o*, *m*, *p*))	^{31}P[b]
8a	5.73	5.52	3.59	5.36	2.54	1.95	2.17,	2.09,	2.05	3.48	1.79	1.79	1.21	39.3
8b	5.21	5.64	3.41	5.39	2.61	1.70	2.15,	2.09,	2.07	3.47	1.93	1.77	1.19	35.7
8c	5.63	5.05	3.43	4.81	2.61	2.04[c]	2.12,	2.11,	2.07	3.49	2.14[c]	1.78	1.34	34.8
8d	5.68	4.94	3.61	4.80	2.49	2.31	2.23,	2.12,	2.08	3.50	1.92	1.92	1.34	32.9
9a	5.73	5.12	3.53	5.05	2.04[c]	1.88	2.18,	2.09,	2.03	3.46	1.46	1.35	1.01	−38.1
9b	5.26	5.23	3.25	5.05	2.18	1.55	2.08,	2.05,	2.04	3.44	1.62	1.50	1.05	−39.5
9c	5.33	5.45	3.19	5.10	2.10	1.57	2.08,	2.05,	2.04	3.46	1.78	1.78	1.16	−38.9
9d	5.59	5.20	3.48	5.12	2.05	1.95[c]	2.13,	2.09,	2.04	3.47	1.71	1.71	1.16	−35.0
17a	5.66	5.73	3.56	5.46	2.46	2.22	2.20,	2.09,	2.03	3.46	1.85	1.83	1.17	39.0
17b	5.35	5.66	3.39	5.49	2.53	2.00	2.14,	2.09,	2.07	3.46	1.96	1.94	1.19	38.8
17c	5.58	5.16	3.41	4.86	2.67	2.08	2.11,	2.11,	2.06	3.48	2.15[c]	2.03	1.31	37.4
17d	5.61	5.06	3.58	4.87	2.55	2.31	2.24,	2.10,	2.06	3.49	2.07[c]	2.07[c]	1.34	39.3
14a	5.85	5.24	3.59	5.24	2.29	2.52	1.77,	2.14,	2.03	3.49	(7.35,	7.33,	7.33)	−35.5
14b	5.58	5.34	3.39	5.17	2.34	2.03	1.92,	2.08,	2.05	3.48	(7.52,	7.38,	7.39)	−41.5
14c	5.49	5.35	3.29	5.01	2.70	1.81	2.16,	2.09,	2.05	3.39	(7.64,	7.40,	7.31)	−35.0
14d	6.07	4.94	3.55	5.03	2.54	2.05	2.20,	2.11,	2.02	3.43	(7.52,	7.41,	7.29)	−31.9

	Coupling constant (Hz)															
	$J_{1,2}$	$J_{1,P}$	$J_{1,5e}$	$J_{2,3}$	$J_{2,P}$	$J_{3,4}$	$J_{4,5e}$	$J_{4,5a}$	$J_{4,P}$	$J_{5a,5e}$	$J_{5e,P}$	$J_{5a,P}$	P-Et				
													$^{2}J_{P,H}$	$^{2}J_{P,H'}$	$^{2}J_{H,H'}$	$^{3}J_{H,H}$	$^{3}J_{P,H}$
8a	2.9	10.2	1.8	9.1	3.8	8.6	4.3	10.8	6.6	14.3	17.5	6.3	11.9	11.9	—	7.8	18.1
8b	10.8	3.4	0	9.2	3.4	9.5	4.4	11.7	3.8	14.5	18.2	3.9	15.6	11.3	15.3	7.8	18.6
8c	10.7	11.9	0	9.0	2.9	9.5	4.3	11.7	4.2	15.2	15.7	c)	c)	5.7	15.4	7.7	17.5
8d	2.7	8.2	1.6	9.4	2.6	9.0	4.5	12.1	4.7	14.7	14.8	18.9	15.4	15.4	—	7.7	17.5
9a	2.5	9.6	2.0	10.0	2.5	9.6	3.5	12.2	3.5	12.3	c)	5.9	1.7	7.8	15.6	7.8	17.6
9b	10.8	5.3	0	9.1	3.6	9.4	3.7	12.4	3.3	12.4	7.1	6.9	3.1	3.2	15.6	7.8	15.5
9c	10.7	10.8	0	9.6	1.8	9.8	4.4	11.9	0.5	15.1	4.6	7.9	15.6	15.6	—	7.8	17.3
9d	3.0	11.7	1.4	9.6	0.5	9.3	4.0	12.0	0.5	15.0	3.5	c)	15.6	15.6	—	7.8	17.3
17a	2.7	6.9	2.0	9.8	2.0	9.3	4.2	11.4	4.7	13.3	15.2	9.1	11.4	11.4	15.2	7.6	21.2
17b	10.7	1.4	0	9.5	4.4	9.4	4.1	11.7	4.5	13.7	15.8	7.4	9.3	11.4	15.2	7.6	20.9
17c	10.8	8.0	0	9.3	2.9	9.7	4.2	12.3	2.8	14.8	14.9	15.6	c)	15.0	15.2	7.6	20.2
17d	2.9	5.6	2.0	9.8	0.5	9.4	4.4	12.2	1.9	14.8	13.5	16.2	c)	c)	c)	7.6	20.0
14a	2.2	8.9	1.7	10.0	3.3	9.7	3.8	12.2	2.9	12.0	6.0	4.8	d)				
14b	10.8	5.4	0	9.4	4.7	9.4	3.7	12.2	3.4	12.5	6.7	4.3	d)				
14c	11.0	18.2	0	9.3	2.5	9.7	4.0	11.7	0.5	15.4	4.6	9.6	d)				
14d	2.9	12.4	1.5	9.9	0	9.5	4.1	11.3	0.8	15.0	3.1	9.8	d)				

a) The assignments of acetoxyl groups may have to be interchanged. b) Parameters for **13a—d**, δ=26.7, 24.3, 25.1, and 22.7, respectively, and for **18a—d**, δ=29.1, 30.8, 28.2, and 29.6, respectively. c) Approximate or uncertain because of overlapping with acetoxyl signals. d) Splitting patterns of the *P*-phenyl group are similar to those of **13a—d** and **18a—d** (see Ref. 9).

was not attained because of the insignificant differences in their ^{1}H NMR spectra.

The pure epimer **5a** was reduced with sodium dihydrobis(2-methoxyethoxy)aluminate (SDMA) to give the 5-(ethylphosphinyl) derivative **6**, which, on treatment with dilute hydrochloric acid, was converted to 5-deoxy-5-(ethylphosphinyl)-3-*O*-methyl-α,β-D-xylopyranoses (**7**). Acetylation of **7** gave triacetates **8**[13] which were separated by silica-gel chromatography into four diastereomers **8a** (mp 124—125 °C, 15% from **5a**), **8b** (mp 244—245 °C, 13%), **8c** (6%), and **8d** (4%) (see Chart 1). Structural assignments of these newly isolated triacetates **8a—d** were made by the analysis of their ^{1}H NMR spectra (see below). The same treatment of another epimer **5b** with SDMA, followed by acid hydrolysis and then acetylation, gave an almost the same ratio of a mixture of the triacetates: **8a** (14% from **5b**), **8b** (11%), **8c** (6%), and **8d** (5%). These results indicate that an epimerization took place at phosphorus atom during the reduction also with SDMA, although such an epimerization of acyclic secondary phosphine oxides by lithium aluminum hydride (LAH) reduction has been known.[14]

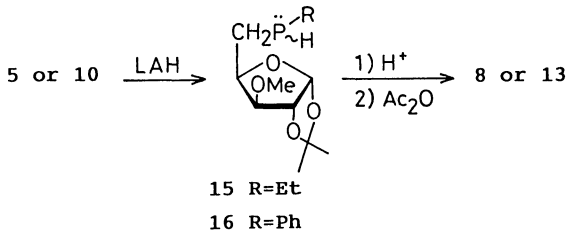
Reduction of **8a—d** with an appropriate reducing reagent was sought in order to obtain 5-(ethylphosphino) compounds **9**. After examination of various reagents, trichlorosilane[15,16] in boiling benzene in the presence of triethylamine (TEA) was found to give the best result (Scheme 1). Namely, a pure 5-[(*R*)-ethylphosphinyl]-α-D-xylopyranose **8a** furnished solely the deoxygenated 5-[(*S*)-ethylphosphino] derivative **9a** (colorless syrup, 70% yield) with retention of configuration of the ring-phosphorus atom. Similarly, 5-[(*S*)-*P*]-β-anomer **9b** (colorless syrup, 75%), 5-[(*R*)-*P*]-β-epimer **9c**, and 5-[(*R*)-*P*]-α-anomer **9d** were prepared from the corresponding 5-[(*R,S*)-ethylphosphinyl]-α,β-D-xylopyranoses **8b**, **8c**, and **8d**, respectively. It should be noticed that inversion of configuration of phosphorus atom has been generally observed upon reduction of cyclic tertiary phosphine oxides with $HSiCl_3$-TEA.[17]

Almost identical results were obtained when the 5-deoxy-5-(phenylphosphinyl)-D-xylopyranoses **13** [prepared from **4** via 5-(phenylphosphinyl) compounds **10**, **11**, and **12**, see Scheme 1][9] were subjected to the same procedures as those for 5-(ethylphosphinyl) compounds **8**. Namely, the four diastereomers **13a—d** were reduced with $HSiCl_3$-TEA, providing the corresponding 5-[(*R*)-phenylphosphino]-α-D-xylopyranose **14a** (syrup, 81% yield), 5-[(*R*)-*P*]-β-anomer **14b** (colorless prisms, mp 165—166 °C, 85% yield), 5-[(*S*)-*P*]-β-epimer **14c** (colorless prisms, mp 123—125 °C, 80%), 5-[(*S*)-*P*]-α-anomer **14d** (colorless needles, mp 143—145 °C, 75%), respectively, all with retention of the configuration of the ring-phosphorus. The configurations of **9a—d** and **14a—d**, all approximately in the $^4C_1$(D) conformation, were established by analysis of their high-resolution mass and ^{1}H (500 MHz) and ^{31}P (81 MHz) NMR spectra by taking into account the known parameters of structurally related compounds obtained before; e.g. **8** and **13**[9] (see below).

Reduction of **13b, c** was also performed with hexachlorodisilane that has been reported[16,18] to result in inversion of phosphorus configuration of acyclic phosphine oxides and simple phospholane oxides. The products obtained from **13b** and **13c** after the treatment with this reagent turned out to be the corresponding **14b** and **14c**, respectively, with the complete retention of the ring-phosphorus configuration. These results of non-inversion of the ring-phosphorus could be explained in terms of an unfavorable conformation in the transition state for inversion that would require an expansion of the expected equatorial C(1)-P-C(5) bond angle to nearly 120° in order to effect an S_N2 type of hydride transfer at the apical-apical position.[16]

These 5-phosphino compounds **9** and **14** are stable at room temperature as long as they are kept as crystals or pure syrups (under nitrogen). In solution, however, they are rather unstable (particularly **9a—d**) and tend to be slowly oxidized to **8a—d** and **13a—d** in an open air; care to avoid oxygen should therefore be taken even on recrystallization. Four isomers of **9** (and **14**) have almost identical R_f values and therefore are inseparable by silica-gel column chromatography when a mixture of **8a—d** (and **13a—d**) is used as the starting material.

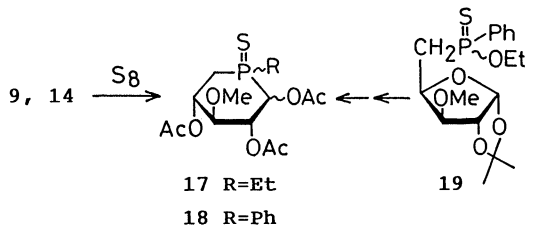
The present preparative scheme for **9** and **14** is expected to be readily applicable to the preparation of various, similar sugar analogues having ring-phosphino group.



Scheme 2. Attempted preparation of **9** and **14** via 5-deoxy-5-phosphinyl-D-xylofuranoses.

An alternative, shortcut preparative scheme was also sought to obtain 5-phosphino sugars **9** and **14** from D-xylofuranoses **5** and **10** via their 5-phosphino derivatives **15** and **16**, respectively, by using various reducing reagents (Scheme 2). Thus, phosphinate **5** was first reduced with LAH to give apparently 5-(ethylphosphino)-α-D-xylofuranose **15** (on the evidence of a higher R_f value of TLC than that of phospine oxide **6**, cf. Ref. 5). Attempts to derive **9a—d** directly from **15** even by carefully operating the usual method (i.e., acid hydrolysis and acetylation) gave the four diastereomers of the oxidized 5-(ethylphosphinyl) compounds **8a—d** after silica-gel

chromatography (but in a lower overall yield from **5** in comparison with the case of SDMA reduction described above). Likewise, 5-(phenylphosphino)-α-D-xylofuranose **16** prepared from **10** by LAH reduction (based on TLC) subsequently yielded only the oxidized 5-(phenylphosphinyl)-D-xylopyranoses **13a—d**. Use of other reagents such as phenylsilane of trichlorosilane for reduction of **5** and **10** also resulted in the formation of **8** and **13**, though these reducing reagents afforded the phosphine intermediates **15** and **16**. The main reason for failure in preparation of the phosphino compounds **9** and **14** directly from **5** and **10** is mostly ascribed to the extreme lability of the intermediates **15** and **16** towards oxygen during deprotection of their 1,2-*O*-isopropylidene group with hot ethanolic HCl to effect the ring-transposition.



Scheme 3. Preparation of 5-deoxy-5-phosphinothioyl-D-xylopyranoses.

A versatile reactivity of the 5-phosphino-D-xylopyranoses described above is demonstrated by a facile conversion of these compounds into the corresponding 5-phosphinothioyl derivatives (Scheme 3). Namely, the reactions of the 5-phosphino compounds **9a—d** and **14a—d** with powdered sulfur in boiling benzene under argon afforded the corresponding phosphine sulfides **17a—d** and **18a—d**, respectively (Chart 1). Yields of the products from **5** (in 5 steps without separation of intermediately formed **8a—d** and **9a—d**) were **17a** (3.6%), **17b** (3.2%), **17c** (1.9%), and **17d** (1.3%) after silica-gel column chromatography, whereas those from **10** were **18a** (6.5%), **18b** (6.9%), **18c** (3.6%), and **18d** (4.5%). The product ratios of these compounds resembled those of **8a—d** and **13a—d** from **5** and **10**, respectively, thus indicating that the reactions **9**→**17** and **14**→**18** all proceeded with retention of the configuration of the phosphorus atom of **9a—d** and **14a—d**. Structures and conformations of **17** and **18** were established by the analysis of their mass and NMR (^{1}H and ^{31}P) spectra (see below).

Compounds **18a—d** had been obtained[9] in 9.3% yield (in total) from the 5-[(ethoxy)phenylphosphinothioyl]-D-xylofuranose precursors **19** (prepared from **4** in 84%) (Scheme 3). In contrast, the present preparative scheme provide a 21.5% yield of the desired 5-phosphinothioyl compounds **18a—d** from **10**. Therefore, the above procedure via intermediates of phosphino-in-ring type is more suitable for an efficient synthesis of a wide variety of (phosphinothioyl)-in-ring sugar analogues that are considered to be of interest in view of potential biological activity.

^{1}H and ^{31}P NMR Spectral Analysis of Tri-*O*-acetyl-5-deoxy-5-(ethylphosphino and phenylphosphino)-3-*O*-methyl-D-xylopyranoses (9a—d, 14a—d) and Their 5-Phosphinyl and 5-Phosphinothioyl Derivatives (8a—d, 13a—d, 17a—d, 18a—d). For the ^{1}H NMR structural assignments of the new products, the chemical shift of each proton signal and the dependence of various J values on the dihedral angles were carefully taken into consideration. ^{31}P NMR spectra of these compounds have now become available for the first time in this series of studies as representative examples of ring-phosphorus-containing pyranoses. The precise parameters obtained at 500 MHz (for ^{1}H) and 81 MHz (for ^{31}P) for these compounds are summarized in Table 1 for comparative study. Some characteristic features of **8**, **9**, **14**, and **17** are discussed here in detail in comparison with the previously known parameters (^{1}H NMR) of **13** and **18**.

1) The ^{1}H NMR data of the newly obtained 5-(ethylphosphinyl) and 5-(ethylphosphinothioyl) compounds **8a—d** and **17a—d** generally follow the characteristic features observed in the δ and J values for the 5-deoxy-5-(phenylphosphinyl and phenylphosphinothioyl)-D-xylopyranoses (**13**, **18**) which were shown to exist approximately in the $^4C_1$(D) conformation in $CDCl_3$ solution.[9] Namely, the axial orientation (*R*) of the ring P=O and P=S group in **8a,b** and **17a,b** is established by a downfield shift (0.5—0.7 ppm) of the H-2 and H-4 signals from those of **8c,d** and **17c,d** having equatorial P=O and P=S groups (see the δ values in Table 1). The α-orientation of C-1 is derived by considering the small magnitudes of $J_{1,2}$ (2.6—2.8 Hz) and $J_{1,5e}$ (1.6—2.0 Hz) of **8a,d** and **17a,d**, whereas the β-anomers **8b,c** and **17b,c** show large $J_{1,2}$ (10.7—10.8 Hz) and negligible $J_{1,5e}$. The proton signals of H-2 and H-4 of **17a** and **17b** appear at a slightly lower field (0.1—0.2 ppm) compared with those of **8a** and **8b**. The axial P=S group therefore apppears to exert a larger downfield shift on the signals of protons at the 1,3-diaxial positions in comparison with the same effect by the axial P=O group. In addition, the geminal $J_{H,P}$ values ($J_{1,P}$, $J_{5e,P}$, and $J_{5a,P}$) of 5-phosphinothioyl compounds **17a—d** and **18a—d** become slightly smaller than the corresponding 5-phosphinyl congeners **8a—d** and **13a—d**, respectively, particularly when the H-C-P=S dihedral angle is gauche. The anomalous upfield shifts observed for AcO-1 of **13a,b** and **18a,b** and the downfield shifts of Ha-5 signals of **13a,b** (both exerted apparently by the anisotropic effect of the *P*-phenyl ring) disappeared in the spectra of 5-(ethylphosphinyl and ethylphosphinothioyl)-D-xylopyranoses **8a,b** and **17a,b**, whose δ values for AcO-1 and Ha-5 are therefore considered to be interent ones in this type of compounds.

2) It is noteworthy that an appreciable upfield shift (ca. 0.2—0.5 ppm) is observed for signals of H-5

in the vicinity of a lone pair of electrons of ring-phosphorus in **9a—d** and **14a—d** compared with those close to P=O group in the corresponding 5-phosphinyl diastereomers **8a—d** and **13a—d**. A slight upfield shift is also observed for the signals of H-2 and H-4 of the epimers having axial *P*-lone pair (**9a** and **9b**) compared with those of the respective equatorial lone-pair epimers **9d** and **9c**), indicating that the axial lone pair exerts rather a slight shielding effect to the protons at 1,3-diaxial positions. Other parameters including *J* values of **9a—d** and **14a—d** are similar to those of the corresponding diastereomers of **8a—d** and **13a—d**, supporting the approximate $^4C_1$(D) conformation also for these 5-phosphino-D-xylopyranoses. Among **9a—d** and **14a—d**, only **9b** and **14b** show small $J_{1,P}$ values, which are in conformity of the generally observed anti-configuration[19] of the lone pair-P-C(1)-H group.

3) Although more examples of ^{31}P NMR data for phosphorus-containing sugars are anticipated to be accumulated, the parameters obtained in this study are believed to become important, standard values for ring-phosphorus-containing pyranoses. A few remarks for the present data are worth noting. For the phosphino compounds **9a—d** and **14a—d**, an upfield shift (1.6—6.0 ppm) of signals is generally observed in the spectra of β-anomers (**9b,c** and **14b,c**) compared with the corresponding α-anomers (**9a,d** and **14a,d**). Similarly, the signals of the epimers having axial lone pair (**9a,b** and **14a,b**) appear at slightly upfield (0.6—6.5 ppm) compared with the corresponding epimers having equatorial lone pair (**9d,c** and **14d,c**), although such a tendency has been reported in the case of conformationally fixed simple phenylphospholanes.[20] Similar features with respect to the direction of P=O and P=S group are observed for phosphinyl (**8**, **13**) and phosphinothioyl derivatives (**17**, **18**) but there exist a few exceptions (particularly for **17** and **18**).

These precise ^{1}H and ^{31}P NMR parameters obtained by the present study are thought to be of high value in determining the structures of other sugar analogues having phosphino, phosphinyl, and phosphinothioyl group in the ring.

Experimental

Melting points 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 [(*A*) 1:3 and (*B*) 1:1 AcOEt-hexane, (*C*) AcOEt, and (*D*) 19:1 AcOEt-EtOH]; components were detected by exposing the plates to UV light and/or by spraying them with 20% sulfuric acid-ethanol, with subsequent heating. Column chromatography was performed by Wako C-200 silica gel. The ^{1}H and ^{31}P NMR spectra were measured in $CDCl_3$ with Varian VXR-500 and VXR-200 instruments (500 MHz and 81 MHz, respectively; the CS-NMR Lab., Okayama Univ.) at 20 °C. Chemical shifts are reported as δ values relative to tetramethylsilane (internal standard for ^{1}H) and 85% phosphoric acid (external standard for ^{31}P). The assignments of all signals were made by employing a first-order analysis with the aid of decoupling technique and, if necessary, two-dimensional COSY measurements (for ^{1}H). The parameters were confirmed by computer-assisted simulation analysis. The mass spectra were taken on a Shimadzu LKB-9000 low-resolution or an A. E. I. MS 50 ultra-high resolution instrument and were given in terms of *m/z* (rel intensity) compared with the base peak.

5-Deoxy-5-[(*R*)- and (*S*)-(ethoxy)ethylphosphinyl]-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-xylofuranoses (5a,b). A mixture of **4**[11] (1.00 g, 3.18 mmol) and diethyl ethylphosphonite (2.80 g, 18.6 mmol) was heated at 140 °C for 6 h under argon and then concentrated in vacuo. The residue was dissolved in $CHCl_3$ and washed with water. The organic layer was dried (Na_2SO_4) and evaporated in vacuo. The residue was purified by column chromatography with 19:1 AcOEt-EtOH, giving a 1:1 (by ^{1}H NMR) mixture of **5a** and **5b** (5-[(*R*)-P] and [(*S*)-P] diastereomer, respectively). The mixture was separated by fractional recrystallization from AcOEt-hexane.

5a: Colorless prisms [371 mg (38%)], mp 70—71 °C (cf. Ref. 12, mp of a crystalline part 67.5—70 °C); R_f=0.12 (*C*); ^{1}H NMR δ=1.15 (3H, dt, J_{PCMe}=18.4, J_{Et}=7.7 Hz, P-C-CH_3), 1.31, 1.49 (3H each, 2s, CMe_2), 1.32 (3H, t, J_{Et}=7.0 Hz, PO-C-CH_3), 1.81 (2H, dq, J_{PCH}=14.2 Hz, PCH_2), 2.11 (2H, dd, $J_{5,P}$=14.1 and $J_{4,5}$=7.0 Hz, H_2-5), 3.43 (3H, s, MeO-3), 3.68 (1H, d, $J_{3,4}$=3.2 Hz, H-3), 4.06 (2H, dq, J_{POCH}=7.2 Hz, $POCH_2$), 4.53 (1H, qd, $J_{4,P}$=7.2 Hz, H-4), 4.57 (1H, d, $J_{1,2}$=3.9 Hz, H-2), 5.85 (1H, d, H-1).

5b: Colorless syrup [377 mg (38%)], R_f=0.12 (*C*); ^{1}H NMR δ=1.16 (3H, dt, J_{PCMe}=18.4, J_{Et}=7.8 Hz, P-C-CH_3), 1.31 (3H, t, J_{Et}=7.2 Hz, PO-C-CH_3), 1.32, 1.49 (3H each, 2s, CMe_2), 1.76 (2H, dq, J_{PCH}=13.7 Hz, PCH_2), 2.15 (1H, ddd, $J_{5,5'}$=15.1, $J_{5,P}$=13.9, $J_{4,5}$=7.1 Hz, H-5), 2.17 (1H, ddd, $J_{5',P}$=12.0, $J_{4,5'}$=6.8 Hz, H-5'), 3.43 (3H, s, MeO-3), 3.72 (1H, d, $J_{3,4}$=2.9 Hz, H-3), 4.08 (2H, dq, J_{POCH}=7.2 Hz, $POCH_2$), 4.47 (1H, qd, $J_{4,P}$=7.2 Hz, H-4), 4.58 (1H, d, $J_{1,2}$=3.9 Hz, H-2), 5.85 (1H, d, H-1).

1,2,4-Tri-*O*-acetyl-5-deoxy-5-[(*R*)- and (*S*)-ethylphosphinyl]-3-*O*-methyl-α,β-D-xylopyranoses (8a—d). To a solution of **5a** (100 mg, 0.325 mmol) in dry benzene (2 ml) was added, with stirring, a solution of SDMA (70% in toluene, 0.12 ml, 1.2 equiv), in small portions, at 5 °C under argon. The stirring was continued at this temp for 1 h. Then water (0.1 ml) was added at 0 °C and the mixture was stirred for 30 min. The precipitate was centrifuged and washed with several portions of benzene. The organic layers were combined and evaporated in vacuo, giving 5-deoxy-5-[(*R*)- and (*S*)-ethylphosphinyl]-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-xylofuranoses (**6**) as a colorless syrup: R_f=0.34 (*C*).

This was immediately dissolved in EtOH (3 ml) and 1 M hydrochloric acid (3 ml) (1 M=1 mol dm^{-3}). The mixture was degassed with argon and then stirred at 100 °C for 4 h. After cooling, the product was neutralized by adding enough Amberlite IRA-45. The resin was filtered off and washed with water and EtOH. The filtrate was evaporated in vacuo to give crude 5-deoxy-3-*O*-methyl-5-[(*R*)- and (*S*)-ethylphosphinyl]-α,β-D-xylopyranoses (**7**) as a colorless syrup: R_f<0.03 (*C*).

This was dissolved in dry pyridine (2 ml) and acetic anhydride (1 ml) at 0 °C. The mixture was stirred at 20 °C

overnight, diluted with a small amount of cold water, and concentrated in vacuo. The residue was dissolved in $CHCl_3$ and washed with water, dried (Na_2SO_4), and evaporated in vacuo. The residue was chromatographed with 19:1 AcOEt-EtOH to give **8a—d**:[13] **8b** was separated from **8a** by recrystallization (several times); **8c** and **8d** were obtained as an inseparable mixture but their structures and yields were based on the ^1H NMR spectral data.

8a (5-[(*R*)-Ethylphosphinyl]-α-isomer): Colorless needles (17.7 mg, 15% overall yield from **5a**), mp 124—125 °C (from AcOEt-hexane); R_f=0.28 (*D*); ^1H and ^{31}P NMR, see Table 1; MS *m/z* 351 (M+1; 2), 319 (2), 291 (68), 264 (22), 249 (28), 235 (48), 207 (14), 189 (25), 177 (68), 129 (58), 87 (100).

Found: *m/z* 351.1212. Calcd for $C_{14}H_{24}O_8P$: M+1, 351.1209.

8b (5-[(*R*)-*P*]-β-Isomer): Colorless needles (14.9 mg, 13%); mp 244—245 °C (from AcOEt-hexane); R_f=0.28 (*D*), ^1H and ^{31}P NMR, see Table 1.

8c (5-[(*S*)-*P*]-β-Isomer): Colorless syrup (6.9 mg, 6%); R_f=0.22 (*D*); ^1H and ^{31}P NMR, see Table 1.

8d (5-[(*S*)-*P*]-α-Isomer): Colorless syrup (4.5 mg, 4%); R_f=0.22 (*D*); ^1H and ^{31}P NMR, see Table 1.

The same procedure described above was followed for the conversion of **5b** into **8a—d**: Thus, **5b** (122 mg, 0.396 mmol) gave **8a** (19.8 mg, 14% overall yield from **5b**), **8b** (15.4 mg, 11%), **8c** (8.6 mg, 6%), and **8d** (7.1 mg, 5%).

1,2,4-Tri-*O*-acetyl-5-deoxy-5-[(*R*)- and (*S*)-ethylphosphino]-3-*O*-methyl-α, β-D-xylopyranoses (9a—d). To a solution of **8a** (28 mg, 0.080 mmol) in dry benzene (1 ml) containing triethylamine (66 mg, 0.65 mmol) was added, with stirring, a solution of trichlorosilane (88 mg, 0.65 mmol) in dry benzene (0.3 ml) in small portions at 0 °C under argon. After 30 min, the mixture was refluxed for 2 h. Saturated aq $NaHCO_3$ (0.5 ml) was added at 0 °C. The precipitate was centrifuged and washed with benzene. The organic layer was dried (Na_2SO_4), and evaporated in vacuo. The residue was purified by column chromatography with AcOEt-hexane (1:3) as an eluant, giving **9a** (5-[(*S*)-ethylphosphino]-α-isomer) as a colorless syrup (18.6 mg, 70% yield): R_f=0.26 (*A*); ^1H and ^{31}P NMR, see Table 1; MS *m/z* 335 (M+1; 0.8), 292 (M−CH_2CO; 5), 275 (51), 263 (13), 249 (8), 233 (88), 221 (25), 201 (12), 191 (100), 173 (67), 161(35), 119 (20), 87 (31).

Found: *m/z* 292.1060. Calcd for $C_{12}H_{21}O_6P$: M−CH_2CO, 292.1076.

Care should be taken in the chromatographic purification, because **9a—d** tend to slowly revert to **8a—d** by oxidation with air in the column.

Similarly, **8b** was converted into **9b** (5-[(*S*)-*P*]-β-isomer) as a colorless syrup in 75% yield: R_f=0.26 (*A*); ^1H and ^{31}P NMR, see Table 1.

The 3:2 mixture of **8c** and **8d** gave an inseparable mixture (3:2) of **9c** (5-[(*R*)-*P*]-β-isomer) and **9d** (5-[(*R*)-*P*]-α-isomer) as a colorless syrup: R_f=0.26 (*A*); ^1H and ^{31}P NMR, see Table 1; MS *m/z* 334 (M^+; ca. 0), 291 (M−CH_3CO; 43), 264 (13), 249 (32), 235 (37), 221 (15), 207 (26), 189 (42), 177 (52), 163 (25), 129 (40), 87 (58), 43 (100).

Found: *m/z* 291.0986. Calcd for $C_{12}H_{20}O_6P$: M−CH_3CO, 291.0998.

1,2,4-Tri-*O*-acetyl-5-deoxy-3-*O*-methyl-5-[(*R*)- and (*S*)-phenylphosphino]-α,β-D-xylopyranoses (14a—d). A. Procedure by the Use of Trichlorosilane: The same procedures described above for **8** converted **13a—d**[9] into the corresponding phosphino compounds **14a—d**.

14a (5-[(*R*)-Phenylphosphino]-α-isomer): Colorless needles (81% yield from **13a**), mp 144—145 °C (from AcOEt-hexane); R_f=0.27 (*A*); ^1H and ^{31}P NMR, see Table 1.

14b (5-[(*R*)-*P*]-β-Isomer): Colorless needles (85% yield), mp 165—166 °C (from AcOEt-hexane); R_f=0.23 (*A*); ^1H and ^{31}P NMR, see Table 1; MS *m/z* 382 (M^+; 0.2), 340 (M−CH_2CO; 4), 323 (21), 282 (15), 281 (100), 239 (28), 221 (16), 209 (17), 207 (21), 167 (34), 125 (19).

Found: *m/z* 382.1205. Calcd for $C_{18}H_{23}O_7P$: M, 382.1182.

14c (5-[(*S*)-*P*]-β-Isomer): Colorless needles (80% yield), mp 123—125 °C (from AcOEt-hexane); R_f=0.23 (*A*); ^1H and ^{31}P NMR, see Table 1; MS 382 (M^+, 1), 340 (M−CH_2CO; 5), 323 (20), 281 (100), 239 (32), 221 (18), 209 (15), 207 (24), 167 (32), 125 (18).

Found: *m/z* 382.1181. Calcd for $C_{18}H_{23}O_7P$: M, 382.1182.

14d (5-[(*S*)-*P*]-α-Isomer): Colorless needles (75% yield), mp 143—145 °C (from AcOEt-hexane); R_f=0.27 (*A*); ^1H and ^{31}P NMR, see Table 1; MS *m/z* 383 (M+1; 2), 382 (M^+; 7), 340 (2), 323 (25), 281 (100), 239 (32), 221 (17), 209 (9), 167 (20), 125 (17).

Found: *m/z* 382.1183. Calcd for $C_{18}H_{23}O_7P$: M, 382.1182.

B. Procedure by the Use of Hexachlorodisilane: To a solution of **13b** (15 mg, 0.038 mmol) in dry benzene (2 ml), was added hexachlorodisilane (12 mg, 0.045 mmol) at 5 °C under argon. The mixture was refluxed for 2 h and saturated aq $NaHCO_3$ (0.5 ml) was slowly added at 5 °C to decompose excess hexachlorodisilane. The resulting precipitate was centrifuged and washed with benzene. The combined organic layer was dried (Na_2SO_4) and evaporated in vacuo. The residue was purified by column chromatography to give **14b** as colorless needles: 12 mg (83%).

With the same procedure described above, **13c** (15 mg) was converted into **14c** as colorless needles: 11 mg (76%).

1,2,4-Tri-*O*-acetyl-5-deoxy-5-[(*R*)- and (*S*)-ethylphosphinothioyl]-3-*O*-methyl-α,β-D-xylopyranoses (17a—d). A suspension of **9a—d** [prepared from **5** (890 mg, 2.89 mmol) in 4 steps] and element sulfur (176 mg, 5.50 mmol) in dry benzene (8 ml) was refluxed for 2 h under argon. After cooling, sulfur was filtered off and the filtrate was evaporated in vacuo. The residue was separated by column chromatography to give **17a—d**. Compounds **17c** and **17d** were obtained as an inseparable mixture but their structures and ratio were confirmed by ^1H NMR.

17a (5-[(*R*)-Ethylphosphinothioyl]-α-isomer): Colorless prisms (38 mg, 3.6% from **5**), mp 109—111 °C (from AcOEt-hexane); R_f=0.20 (*B*); ^1H and ^{31}P NMR, see Table 1; MS *m/z* 367 (M+1; 6), 366 (M^+; 32), 334 (10), 307 (27), 275 (60), 265 (19), 247 (8), 232 (100), 221 (18), 205 (21), 191 (81), 149 (14), 113 (14).

Found: *m/z* 366.0924. Calcd for $C_{14}H_{23}O_7PS$: M, 366.0903.

17b (5-[(*R*)-*P*]-β-Isomer): Colorless prisms (34 mg, 3.2% from **5**), mp 237—238 °C (from AcOEt-hexane); R_f=0.15 (*B*); ^1H and ^{31}P NMR, see Table 1; MS *m/z* 366 (M^+; 3), 334 (1), 307 (7), 274 (46), 265 (6), 233 (26), 232 (100), 205 (5), 190 (30), 175 (10).

Found: *m/z* 366.0890. Calcd for $C_{14}H_{23}O_7PS$: M, 366.0903.

17c (5-[(*S*)-*P*]-β-Isomer): Colorless syrup (20 mg, 1.9% from **5**); R_f=0.40 (*B*); ^1H and ^{31}P NMR, see Table 1; MS 367 (M+1; 3), 366 (M^+; 7), 306 (26), 263 (7), 247 (47), 246 (30), 211 (16), 205 (100), 204 (90), 188 (31), 177 (22), 155 (54), 113 (88).

Found: *m/z* 366.0903. Calcd for $C_{14}H_{23}O_7PS$: M,

366.0903.

17d (5-[(*S*)-*P*]-α-Isomer): Colorless syrup (14 mg, 1.3% from **5**); R_f=0.40 (*B*); ^{1}H and ^{31}P NMR, see Table 1.

1,2,4-Tri-*O*-acetyl-5-deoxy-3-*O*-methyl-5-[(*R*)- and (*S*)-phenylphosphinothioyl]-α,β-D-xylopyranoses[9] (**18a—d**). With the same procedures described above for **17**, a mixture of **13a—d** (195 mg) obtained from **10** (500 mg, 1.40 mmol) was converted into **18a** (38 mg, 6.5% from **10**, lit,[9] 1.8% from **19**), **18b** (40 mg, 6.9% from **10**, lit,[9] 1.8% from **19**), **18c** (21 mg, 3.6% from **10**, lit,[9] 2.3% from **19**), and **18d** (26 mg, 4.5% from **10**, lit,[9] 3.4% from **19**). ^{31}P NMR for **13a—d** and **18a—d**, see Table 1. Other physical data for these compounds, see Ref. 9.

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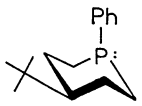
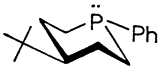


20a



20b