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SYNTHESIS AND N.M.R.-SPECTRAL ANALYSIS OF UNENRICHED AND [1-^{13}C]-ENRICHED 5-DEOXYPENTOSES AND 5-*O*-METHYLPENTOSES

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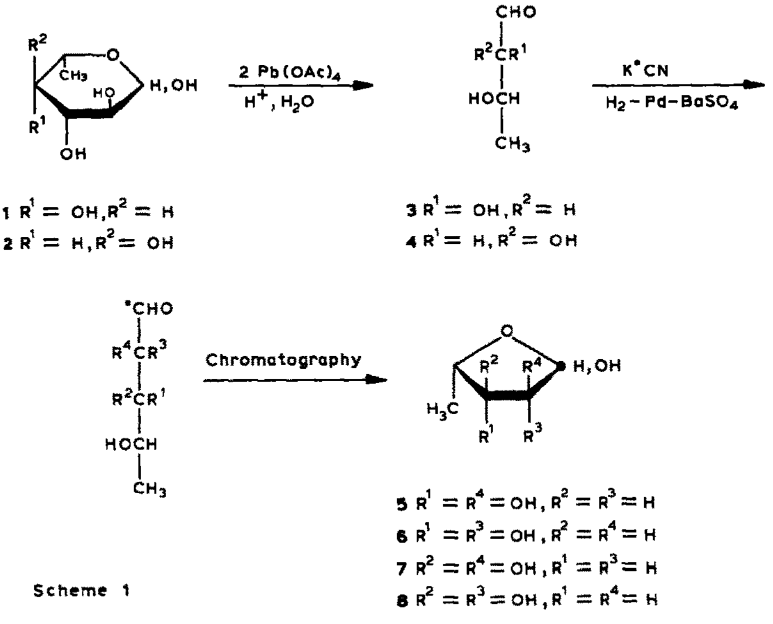
ABSTRACT

Chemical methods are described for preparing unenriched and [1-^{13}C]-enriched 5-deoxy- and 5-*O*-methyl-pentoses in the D or L configuration. The ^{1}H-n.m.r. spectra of these compounds have been interpreted, and the ^{13}C-n.m.r. spectra assigned with the aid of 2-D ^{13}C–^{1}H chemical-shift correlation spectroscopy. Tautomeric forms (furanoses, hydrate, and aldehyde) in solution in ^2H_2O have been quantified with the aid of [1-^{13}C]-enriched derivatives. Spectra of 5-deoxypentoses, 5-*O*-methylpentoses, and methyl pentofuranosides have been compared, in order to assess the effect of 5-*C*-deoxygenation and 5-*O*-methylation on chemical shifts and coupling constants (^{1}H–^{1}H, ^{13}C–^{1}H, and ^{13}C–^{13}C) and on the pentofuranose conformations.



1 $R^1 = OH, R^2 = H$
2 $R^1 = H, R^2 = OH$

3 $R^1 = OH, R^2 = H$
4 $R^1 = H, R^2 = OH$

5 $R^1 = R^4 = OH, R^2 = R^3 = H$
6 $R^1 = R^3 = OH, R^2 = R^4 = H$
7 $R^2 = R^4 = OH, R^1 = R^3 = H$
8 $R^2 = R^3 = OH, R^1 = R^4 = H$

Scheme 1

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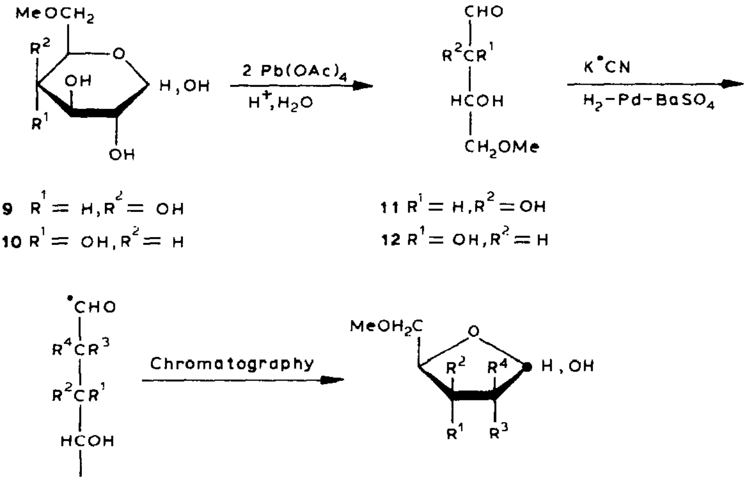
INTRODUCTION

Synthetic routes to stable-isotopically enriched carbohydrates[1a] are chosen to meet two important criteria, namely, that the isotope(s) be introduced near the end of the pathway and that reactions involving labeled compounds be reliable and of high yield. In contrast, preferred routes to unenriched sugars are often shorter and more elegant, and lower yields are acceptable. These features are illustrated in the routes to unenriched and [1-^{13}C]-enriched 5-*O*-methyl- and 5-deoxy-pentoses[1b] reported in this study; different routes had previously been reported for the preparation of 5-deoxy-L-arabinose[1c,d,e] and 5-deoxy-D-lyxose[1f]. We were interested in preparing these modified pentoses in order to study the effect of furanose structure on unidirectional rates of anomerization[2a,b,c].

The preparation of 5-substituted [1-^{13}C]pentoses involves the oxidation of appropriate hexoses with lead tetraacetate[3] in order to generate tetroses, followed by addition of one carbon atom by using [^{13}C]cyanide[4,5], and separation of the labeled C-2 epimers by chromatography[6,7] (see Schemes 1 and 2). In contrast, unenriched pentoses are prepared by selective protection of secondary hydroxyl groups of appropriate aldose precursors, tosylation of O-5, and displacement of tosyloxy by hydride or of tosyl by methoxide ion; molybdate epimerization[8] is used to improve the efficiency (see Schemes 3 and 4).

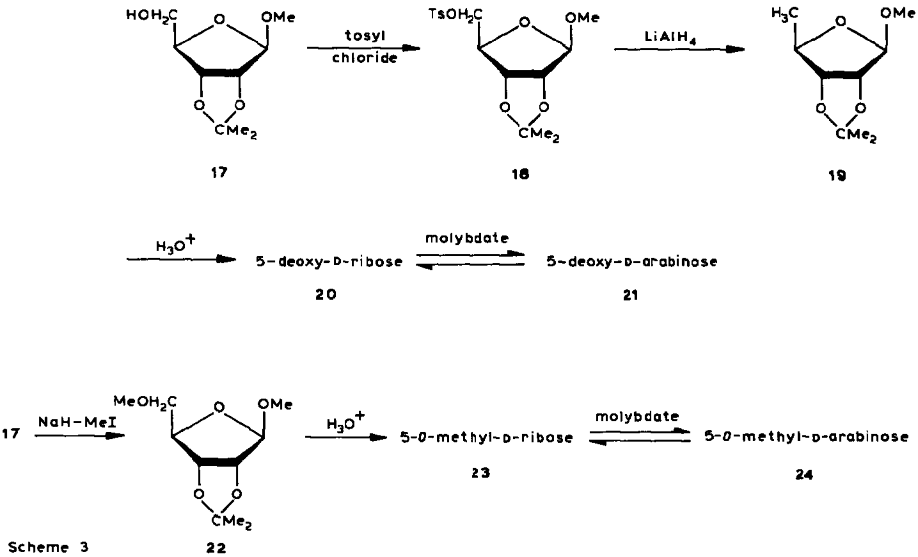


9 $R^1 = H, R^2 = OH$
10 $R^1 = OH, R^2 = H$

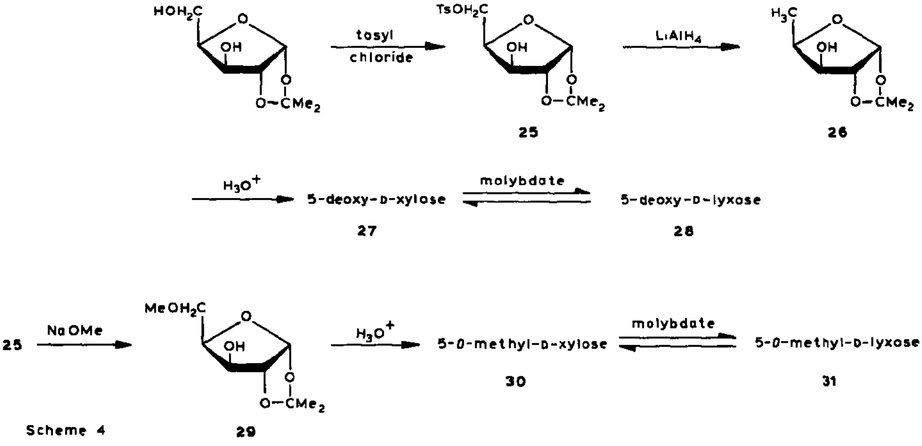
11 $R^1 = H, R^2 = OH$
12 $R^1 = OH, R^2 = H$

13 $R^2 = R^4 = OH, R^1 = R^3 = H$
14 $R^2 = R^3 = OH, R^1 = R^4 = H$
15 $R^1 = R^4 = OH, R^2 = R^3 = H$
16 $R^1 = R^3 = OH, R^2 = R^4 = H$

Scheme 2



Scheme 3



Scheme 4

Because the solution properties of the 5-*O*-methyl- and 5-deoxy-pentoses have not previously been reported*, we have recorded and interpreted the ^{1}H-(300 MHz) and ^{13}C-(75 MHz) n.m.r. spectra of these monosaccharides. ^{13}C-N.m.r. spectra have been unequivocally assigned with the aid of 2-D ^{13}C–^{1}H chemical-shift correlation spectroscopy. [1-^{13}C]-Enriched compounds were used to detect and quantify α-furanose, β-furanose, hydrate, and aldehyde forms in aqueous solution

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*The results of this study, which considerably extend those of a prior report[1b] on the ^{1}H-n.m.r. properties of the 5-*O*-methyl-D-pentoses, were presented at the 20th Midwest Regional ACS Meeting, Div. of Biochemistry–Medicinal Chemistry, Carbondale, IL, Nov. 1985, Abstr. No. 230.

by ^{13}C-n.m.r. spectroscopy. Finally, chemical shifts and coupling constants (^{1}H–^{1}H, ^{13}C–^{1}H, and ^{13}C–^{13}C) observed in these 5-*C*-substituted pentofuranoses are compared to each other and to those for methyl pentofuranosides, in order to evaluate the effect of exocyclic structure on pentofuranose n.m.r. parameters and conformation.

EXPERIMENTAL

Materials. D-Glucose, D-galactose, L-fucose, L-rhamnose, D-ribose, D-xylose, and palladium–barium sulfate (Pd–$BaSO_4$, 5%) were obtained from Sigma Chemical Company and used without purification. Potassium [^{13}C]cyanide ($K^{13}CN$, 99 atom-% of ^{13}C) was purchased from Cambridge Isotope Laboratories. Lead tetraacetate [$Pb(OAc)_4$] and lithium aluminum hydride (LAH) were obtained from Aldrich Chemical Company.

Anhydrous *N,N*-dimethylformamide (DMF) (Fisher) was distilled from CaH_2 and stored over 4A molecular sieves (Davison). Pyridine (Fisher) was predried over KOH, distilled from CaH_2, and stored over 4A molecular sieves. Anhydrous methanol (Mallinckrodt) was prepared from absolute methanol by storage over 3A molecular sieves; h.p.l.c.-grade dichloromethane (Aldrich) was dried similarly. Absolute diethyl ether (Fisher) was used without further purification.

Instrumentation. — The structure and purity of chemical intermediates (see Table I) and products were determined by ^{13}C- (75 MHz), or ^{1}H- (300 MHz) n.m.r. spectroscopy, or both, at ~25° with a Nicolet NT-300 FT-n.m.r. spectrometer equipped with quadrature-phase detection and a 293B pulse programmer. The observation of small coupling constants was improved by multiplying the corresponding f.i.d.s. by a double-exponential function (resolution enhancement) prior to Fourier transformation.

Resolution-enhanced, rapid-scan, cross-correlation ^{1}H-n.m.r. spectra at 600 MHz were obtained at the NMR Facility For Biomedical Studies, Department of Chemistry, Carnegie–Mellon University, Pittsburgh, PA, (facility partly supported by NIH Grant P41RR00292-19). Two-dimensional, ^{13}C–^{1}H chemical-shift correlation spectroscopy[2d] was conducted on the NT-300 n.m.r. spectrometer by using software supplied by GE N.m.r. Systems.

Mass spectra of peracetylated alditol acetate derivatives of the 5-*O*-methylpentoses and 5-deoxypentoses were obtained with a Dupont DP-102 GC-MS system operated in the positive-ion chemical ionization mode with isobutane and with a source temperature of 200°. The peracetylated alditol acetate derivatives were prepared as described by Blakeney *et al.*[9]. A gas–liquid chromatographic column (2 mm i.d. × 1.83 m) containing SP-2340 (3% on Chromosorb W-AW) was used, with a temperature program of 190–230° at 2°/min. The quasi-molecular ion $(M + 1)^+$ was used to characterize the products of all syntheses, occurring at *m/z* 305 and 335

TABLE I

^{13}C CHEMICAL-SHIFTS OF SOME CHEMICAL INTERMEDIATES

Compound	*Chemical shift (p.p.m.)*[a]
6-Deoxy-L-glucose (**2**)	93.6, 97.4, 77.1, 76.9, 76.6, 76.2, 74.3, 73.3, 69.0, 18.6
6-*O*-Methyl-D-galactose (**9**)	93.9, 97.9, 74.8, 74.3, 73.4, 73.2, 71.2, 70.7, 70.6, 70.1, 69.9, 60.0, 59.8
1,2-*O*-Isopropylidene-6-*O*-tosyl-α-D-glucofuranose (**33**)	145.9, 133.6, 130.9, 128.9, 112.7, 106.1, 86.2, 80.6, 75.4, 73.7, 68.2, 27.8, 27.2, 22.6
1,2-*O*-Isopropylidene-6-*O*-methyl-α-D-glucofuranose (**34**)	114.2, 106.3, 86.0, 81.5, 75.7, 75.2, 68.4, 60.3, 27.3, 26.8
6-*O*-Methyl-D-glucose (**10**)	93.6, 97.5, 77.3, 76.0, 75.7, 74.3, 73.1, 72.7, 72.6, 71.5, 71.4, 71.3, 60.2, 60.1
Methyl 2,3-*O*-isopropylidene-5-*O*-tosyl-β-D-ribofuranoside (**18**)	146.2, 133.8, 131.0, 129.0, 113.8, 110.5, 86.0, 84.7, 82.4, 70.4, 56.1, 27.4, 26.0, 22.7
Methyl 2,3-*O*-isopropylidene-5-deoxy-β-D-ribofuranoside (**19**)	113.0, 110.5, 86.8, 86.2, 84.1, 55.2, 27.5, 26.0, 22.0
1,2-*O*-Isopropylidene-5-*O*-tosyl-α-D-xylofuranose (**25**)	146.0, 133.7, 130.9, 128.9, 112.7, 106.1, 86.5, 79.2, 75.1, 69.1, 27.8, 27.4, 22.5
1,2-*O*-Isopropylidene-5-deoxy-α-D-xylofuranose (**26**)	112.4, 105.4, 86.6, 77.4, 77.0, 27.6, 27.2, 13.9
1,2-*O*-Isopropylidene-5-*O*-methyl-α-D-xylofuranose (**29**)	112.6, 105.9, 86.4, 79.2, 77.3, 71.9, 60.8, 27.8, 27.2
Methyl 2,3-*O*-isopropylidene-5-*O*-methyl-β-D-ribofuranoside (**22**)	113.0, 110.1, 86.0, 85.8, 82.9, 74.5, 59.8, 55.4, 27.3, 25.8

[a] Values are accurate to within ±0.1 p.p.m., and are referenced (external) to the anomeric carbon signal of β-D-[1-^{13}C]glucopyranose (97.4 p.p.m.). Compounds **2**, **9**, **10**, and **29** were analyzed in ^2H_2O, and the rest in C^2HCl_3.

for the deoxy and *O*-methyl series, respectively; these values increased by *m/z* 1 for the [1-^{13}C]-enriched compounds. For the 5-deoxypentoses and 5-*O*-methylpentoses, fragments at *m/z* M − 59 were uniformly observed, corresponding to the loss of a single OAc group from the structure. For the 5-*O*-methylpentoses, fragments at *m/z* M − 31 were also noted, corresponding to loss of the OCH_3 group; in the *arabino* and *xylo* isomers, an *m/z* M − 45 peak was also observed, corresponding to the loss of the terminal CH_2OCH_3 group.

TABLE II

^{1}H CHEMICAL-SHIFTS FOR 5-DEOXY- AND 5-*O*-METHYL-PENTOFURANOSES IN ^2H_2O

Compound	*Chemical shift (p.p.m.)*[a]						
	H-1	*H-2*	*H-3*	*H-4*	*H-5*	*H-5'*	CH_3
5-Deoxy-α-L-arabinose	5.21	4.00	3.72	4.13			1.30
5-Deoxy-β-L-arabinose	5.24	4.04	obs	~3.82			~1.32
5-Deoxy-α-L-lyxose	5.22	4.11	4.06	4.36			1.20
5-Deoxy-β-L-lyxose	5.18	obs	obs	obs			1.26
5-Deoxy-α-L-ribose	5.35	4.16	3.82	4.13			1.24
5-Deoxy-β-L-ribose	5.18	4.01	3.98	4.02			1.32
5-Deoxy-α-L-xylose	5.39	~4.09	~4.09	4.38			1.18
5-Deoxy-β-L-xylose	5.12	4.04	4.00	4.32			1.28
5-*O*-Methyl-α-D-arabinose	5.23	4.02	3.93	4.17	3.68	3.57	3.41
5-*O*-Methyl-β-D-arabinose	5.28	4.07	4.00	3.89	3.67	obs	3.41
5-*O*-Methyl-α-D-lyxose	5.28	4.08	4.32	4.41	3.70	3.60	3.40
5-*O*-Methyl-β-D-lyxose	5.26	4.17	4.26	4.17	3.77	3.66	3.41
5-*O*-Methyl-α-D-ribose	5.36	4.09	obs	obs	3.65	3.52	3.39
5-*O*-Methyl-β-D-ribose	5.23	3.98	4.17	4.04	3.70	3.56	3.41
5-*O*-Methyl-α-D-xylose	5.40	4.07	4.29	4.37	3.65	3.53	3.37
5-*O*-Methyl-β-D-xylose	5.20	4.06	4.19	4.34	3.76	3.66	3.40

[a] Values are reported in p.p.m., are relative to external sodium 4,4-dimethyl-4-silapentane-1-sulfonate, and are accurate to within ±0.01 p.p.m. "Obs" denotes obscured resonances.

Detection, identification, and quantitation of aldoses. — Column-chromatographic assay of reducing sugars was performed with phenol–sulfuric acid[10]. The 5-deoxypentoses and 5-*O*-methylpentoses were quantified by hypoiodite oxidation[11].

In the synthesis of [1-^{13}C]-enriched compounds, two products (C-2 epimers) are generated that have distinctly different ^{1}H- and ^{13}C-n.m.r. spectra (see Tables II and IV). One compound in each pair was configurationally assigned by comparison of its ^{1}H- and ^{13}C-spectra with those obtained with the appropriate unenriched compound prepared from configurationally defined precursors by the alternative routes described in this study [5-deoxy-D-ribose (**20**), 5-*O*-methyl-D-ribose (**23**), 5-

TABLE III

^{1}H CHEMICAL SHIFTS FOR METHYL α-D-ARABINOFURANOSIDE, METHYL α-D-LYXOFURANOSIDE, AND METHYL 5-DEOXY-α-D-ARABINOFURANOSIDE IN ^2H_2O

Compound	*Chemical shift (p.p.m.)*[a]						
	H-1	*H-2*	*H-3*	*H-3'*	*H-4*	*H-5*	*H-5'*
Methyl α-D-arabinofuranoside[b]	4.91	4.04	3.93		4.02	3.80	3.69
Methyl α-D-lyxofuranoside[b]	4.95	4.11	4.32		4.24	3.81	3.73
Methyl 3-deoxy-α-D-arabinofuranoside	5.00	4.30	2.45	1.70	4.38	3.79	3.69

[a] Conditions are the same as those in Table II. [b] Data taken from ref. 21.

TABLE IV

^{13}C CHEMICAL-SHIFTS FOR 5-DEOXY- AND 5-*O*-METHYL-PENTOFURANOSES IN ^2H_2O

Compound	*Chemical shift (p.p.m.)*[a]					
	C-1	*C-2*	*C-3*	*C-4*	*C-5*	*CH_3*
5-Deoxy-α-L-arabinose	102.3	83.6	82.5	80.1	19.3	
5-Deoxy-β-L-arabinose	96.3	77.6	80.6	78.3	20.7	
5-Deoxy-α-L-lyxose	102.2	79.8	74.5[b]	78.1[b]	15.3	
5-Deoxy-β-L-lyxose	96.7	73.5	72.9[c]	78.0[c]	16.3	
5-Deoxy-α-L-ribose	97.3	72.0	76.4	79.6	19.4	
5-Deoxy-β-L-ribose	102.4	77.1	76.7	79.7	20.7	
5-Deoxy-α-L-xylose	96.9	78.0	78.0	76.7	15.2	
5-Deoxy-β-L-xylose	103.1	82.6	77.4	79.4	15.8	
5-*O*-Methyl-α-D-arabinose	102.8	82.9	77.7	83.0	73.5	60.13[d]
5-*O*-Methyl-β-D-arabinose	96.9	77.7	76.2	80.9	75.1	60.10[d]
5-*O*-Methyl-α-D-lyxose	101.3	77.6	71.8	78.7	71.6	59.0
5-*O*-Methyl-β-D-lyxose	96.0	72.0	70.7	78.9	72.5	59.0
5-*O*-Methyl-α-D-ribose	97.9	72.3	71.8	82.6	73.6	60.22
5-*O*-Methyl-β-D-ribose	102.8	76.7	72.4	82.0	75.2	60.19
5-*O*-Methyl-α-D-xylose	95.8	76.4	75.4	76.9	71.2	58.7
5-*O*-Methyl-β-D-xylose	102.1	80.8	75.3	80.0	71.8	58.7

[a] Chemical shifts are reported in p.p.m., are referenced (external) to the anomeric carbon of β-D-[1-^{13}C]-glucopyranose (97.4 p.p.m.), and are accurate to within ±0.1 p.p.m. [b,c,d] Assignments may have to be reversed.

deoxy-D-xylose (**27**), and 5-*O*-methyl-D-xylose (**30**)]. The assignment of furanose anomeric configuration for each compound was made by using the well established rule (see later) relating C-1 chemical shift to the relative orientation of O-1 and O-2, namely, furanose anomers having O-1 and O-2 *cis* give a C-1 signal upfield of the C-1 signal of the corresponding anomer having these atoms *trans*. Further support for the assignment of anomeric configuration derives from the magnitude of coupling between C-1 and C-2, which differs markedly and consistently between furanose anomers (see later).

Stability of aldoses. — Like other short-chain aldoses[5], the 4-deoxy- and 4-*O*-methyl-tetroses cannot cyclize, and therefore tend to undergo spontaneous dimerization–oligomerization which may be irreversible. Therefore, aqueous solutions of these compounds were not evaporated to syrups in the following syntheses, and long-term storage was avoided. The tetroses generated by lead tetraacetate oxidation were not isolated or quantitated, because of their instability, and were used directly in cyanide-condensation reactions to prepare the target pentoses.

Aqueous solutions of the 5-deoxy- and 5-*O*-methyl-pentoses were also not evaporated to syrups in the following syntheses, again to avoid oligomerization. After purification, these compounds were stored as dilute, neutral solutions (~0.1M) at 4°; over a period of three months under these conditions, no degradation was observed.

5-Deoxy-L-*[1-^{13}C]-xylose* (**5**) *and -lyxose* (**6**) *(Scheme 1)*. — L-Fucose (**1**; 4.9 g, 30 mmol) was dissolved in the minimal volume of H_2O (~2 mL), and $Pb(OAc)_4$ (31.5 g, 71 mmol) dissolved in 450 mL of glacial acetic acid was added with stirring. After 40 min at room temperature, anhydrous oxalic acid (11.1 g, 123 mmol) was added, the lead oxalate precipitate was removed by suction filtration through Celite, and the filtrate was evaporated at 30° *in vacuo* to a syrup. The oxidation product, 4-deoxy-2,3-di-*O*-formyl-L-threose, was dissolved in 100 mL of 0.1% (v/v) H_2SO_4, and after 6 h at 37°, the acidic solution containing **3** was treated batchwise with Dowex-50 X-8 (HCO_3^-) ion-exchange resin to adjust the pH to ~5.5. $K^{13}CN$ was added, and the resulting C-2-epimeric [1-^{13}C]cyanohydrins were hydrogenated with H_2 and Pd–$BaSO_4$ at pH 1.7, as described previously for the preparation of labeled trioses and tetroses[1a,5]. After reduction, the catalyst was removed by suction filtration, and the mixture containing [1-^{13}C]-enriched **5** and **6** was treated batchwise, and separately, with excess of Dowex-50 X-8 (H^+) and Dowex-1 X-8 (HCO_3^-) resin. The solution was concentrated to ~30 mL at 30° *in vacuo*, and the mixture was chromatographed on a column (2.5 × 100 cm) of Dowex-50 X-8 (Ca^{2+}) resin (200–400 mesh)[6,7], using H_2O as the eluant (1 mL/min). Fractions (18 mL) were collected; **5** (1.1 g) was eluted in fractions 63–73, and **6** (1.3 g) in fractions 154–174. The overall yield (**5** + **6**) from **1** was 60%. G.l.c.–mass-spectral analyses of the peracetylated alditol derivatives from **5** and **6** gave the expected $(M + 1)^+$ ion at *m/z* 306.

5-Deoxy-L-*[1-^{13}C]-ribose* (**7**) *and -arabinose* (**8**) *(Scheme 1)*. — Rhamnose (4.1 g, 25 mmol) and sodium molybdate[8] (0.88 g, 4.3 mmol) were dissolved in distilled water (250 mL), and the solution was kept for 3 h at 95° (oil bath). The resulting solution [containing L-rhamnose (~40%) and 6-deoxy-L-glucose (**2**; ~60%)] was cooled, treated batchwise with an excess of Dowex-1 X-8 (HCO_3^-) resin, and evaporated *in vacuo* at 30° to a syrup. The syrup was dissolved in H_2O (5 mL) and the mixture was chromatographed on a column (15 × 100 cm) of Dowex-50 X-8 (Ca^{2+}) resin (200–400 mesh)[6,7], using H_2O as the eluant (1 mL/min). Fractions (18 mL) were collected; 6-deoxy-L-glucose (**2**; 2.4 g; see Table I) was eluted in fractions 360–393, followed by L-rhamnose (1.5 g) in fractions 399–490.

Lead tetraacetate oxidation of **2** was conducted as described for **1**, generating 4-deoxy-2,3-di-*O*-formyl-L-erythrose. Hydrolysis of the formic ester groups, [^{13}C]cyanide addition–cyanohydrin reduction, and purification were performed as described for the preparation of **5** and **6**; during chromatography[6,7], **8** (0.8 g) was eluted first (fractions 41–47), followed by **7** (0.6 g; fractions 109–120). The overall yield (**7** + **8**) from L-rhamnose was 40%. G.l.c.–mass-spectral analyses of the peracetylated alditol derivatives from **7** and **8** gave the expected $(M + 1)^+$ ion at *m/z* 306.

5-O-Methyl-D-*[1-^{13}C]-xylose* (**14**) *and -lyxose* (**13**) *(Scheme 2)*. — D-Galactose (9.0 g, 50 mmol) was converted into 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (10.9 g, 44 mmol) as described previously[12], and the latter (10.5 g, 40.3 mmol) was methylated at O-6 with methyl iodide and sodium hydride[13] to give

1,2:3,4-di-*O*-isopropylidene-6-*O*-methyl-α-D-galactopyranose (9.9 g, 36.1 mmol). Subsequent hydrolysis of the ketal groups with 1% (v/v) H_2SO_4 for 3 h at 100° generated 6-*O*-methyl-D-galactose (**9**; 6.5 g, 33.5 mmol; see Table I) in an overall yield from D-galactose of 60%.

Compound **9** (6.5 g, 33.5 mmol) was treated with lead tetraacetate as described for the preparation of **5** and **6**, generating 2,3-di-*O*-formyl-4-*O*-methyl-D-threose; this was converted into the enriched pentoses with $K^{13}CN$ as described for **5** and **6**; during chromatography[6,7], **14** (1.4 g, 8.4 mmol) was eluted first (fractions 50–65), followed by **13** (1.9 g, 11.7 mmol) in fractions 155–185. The overall yield (**13** + **14**) from **9** was 60%. Mass-spectral analyses of the peracetylated alditol derivatives from **13** and **14** gave the expected $(M + 1)^+$ ion at *m/z* 336.

*5-O-Methyl-*D*-[1-^{13}C]-ribose* (**16**) *and -arabinose* (**15**) *(Scheme 2)*. — To a solution of 1,2-*O*-isopropylidene-α-D-glucofuranose (11.0 g, 50 mmol)[14] in dry pyridine (55 mL) in a sealed flask at −5° (NaCl–ice bath) was added, with stirring, a cold solution (~5°) of *p*-toluenesulfonyl chloride (10.4 g, 55 mmol) in CH_2Cl_2 (20 mL) from a dropping funnel at such a rate as to maintain the temperature of the reaction mixture below 0°. After the addition, the mixture was maintained for 1 h at 0°, allowed to warm to room temperature, and stirred overnight. Water (0.5 mL) was added and stirring was continued for 30 min. The mixture was poured into ice-cold distilled water (150 mL), and extracted with $CHCl_3$ (3 × 20 mL). The extracts were combined, dried ($MgSO_4$), and evaporated *in vacuo* at 30° to a syrup. The product, 1,2-*O*-isopropylidene-6-*O*-tosyl-α-D-glucofuranose (**33**; see Table I), crystallized from $CHCl_3$ (yield, 13.1 g, 70%).

The tosyl group of **33** was displaced by adding 4.6M $NaOCH_3$ (10.4 mL) to a solution of **33** (6.0 g, 16 mmol) in dry MeOH (10 mL). The reaction was monitored by t.l.c. (silica gel), using ethyl acetate as the solvent (reactant R_F, 0.60; product R_F, 0.56), and was complete in 4 h. The solution was treated separately, and batchwise, with an excess of Dowex-1 X-8 (HCO_3^-) and Dowex-50 X-8 (H^+) resins at 4°, and evaporated to a syrup at 30° *in vacuo*, to give 1,2-*O*-isopropylidene-6-*O*-methyl-α-D-glucofuranose (**34**; see Table I; yield, 2.8 g, 75%). Hydrolysis of **34** (2.5 g, 10.7 mmol) with 0.05M H_2SO_4 (25 mL) for 8 h at 56° afforded **10** (see Table I) in 75% yield (1.6 g).

Compound **10** (2.0 g, 10.3 mmol) was treated with lead tetraacetate as described for the preparation of **5** and **6**, generating 4-*O*-methyl-D-erythrose (**12**). Compound **12** was converted into the [1-^{13}C]pentoses with $K^{13}CN$, as described for **5** and **6**; during chromatography[6,7], **15** (0.5, 3.2 g, 1 mmol) was eluted first (fractions 48–60), followed by **16** (0.5 g, 3.2 mmol) in fractions 118–134. The overall yield (**15** + **16**) from **10** was 60%. G.l.c.–mass-spectral analyses of the peracetylated alditol derivatives from **15** and **16** gave the expected $(M + 1)^+$ ion at *m/z* 336.

*5-Deoxy-*D*-ribose* (**20**) *and -arabinose* (**21**) *(Scheme 3)*. — The route reported here for the preparation of **20** is modified from that described by Horton and Liav[15a]. Methyl 2,3-*O*-isopropylidene-β-D-ribofuranoside[15b] (**17**; 6.2 g, 30 mmol) was dissolved in dry pyridine (30 mL) in a cooled (ice-bath) flask and a solution of *p*-toluenesulfonyl chloride (6.4 g, 33.8 mmol) in dry CH_2Cl_2 (4.5 mL) was added during 10 min from a dropping funnel. The mixture was kept overnight at room temperature, poured into ice-cold distilled water (175 mL), and extracted with $CHCl_3$ (3 × 20 mL). The extracts were combined, dried ($MgSO_4$), and evaporated to dryness *in vacuo* at 30°, to give **18** (see Table I; yield, 9.1 g, 85%). A solution of methyl 2,3-*O*-isopropylidene-5-*O*-tosyl-β-D-ribofuranoside (**18**; 5.3 g, 15 mmol) in benzene (12 mL) and ether (150 mL) was added from a dropping funnel to LAH (1.9 g, 49.5 mmol) suspended in dry diethyl ether (150 mL) under reflux. After 18 h, ethyl acetate (9.0 mL) and distilled water (4.5 mL) were slowly added to decompose the excess of hydride. The mixture was filtered with suction, and the solids washed with diethyl ether. The filtrate and washings were combined, and evaporated to a syrup at 30° *in vacuo* (yield, 1.9 g, 67%). The product, methyl 2,3-*O*-isopropylidene-5-deoxy-β-D-ribofuranoside (**19**; see Table I; 1.9 g, 10 mmol), was dissolved in 0.1% (v/v) H_2SO_4 (140 mL), and the solution was refluxed for 3 h to effect deprotection. After cooling, the solution was treated batchwise with Dowex-1 X-8 (HCO_3^-), to adjust the pH to ~5.5, and the solution containing **20** was concentrated to ~20 mL at 30° *in vacuo* (yield, 0.9 g, 68%).

Molybdate epimerization[8] was used to generate an equilibrium mixture of **20** (41%) and its C-2 epimer, 5-deoxy-D-arabinose **21** (59%), which were separated by chromatography on a column (2.5 × 100 cm) of Dowex-50 X-8 (Ca^{2+}) resin (200–400 mesh)[6,7]. The elution profile was the same as that obtained for the [^{13}C]-enriched compounds **7** and **8**. G.l.c.–mass-spectral analyses of the peracetylated alditol derivatives from **20** and **21** gave the expected $(M + 1)^+$ ion at *m/z* 305.

5-O-Methyl-D-ribose (**23**) *and -arabinose* (**24**) *(Scheme 3).* — Methyl 2,3-*O*-isopropylidene-β-D-ribofuranoside (**17**; 3.0 g, 14.8 mmol)[15b] was dissolved in *N,N*-dimethylformamide (180 mL) at 5°, and NaH (3 g, 125 mmol) was added batchwise. The suspension was stirred until complete dissolution of the hydride had occurred (~1 h). Methyl iodide (13.6 mL, 220 mmol) was added, and the mixture was kept overnight at room temperature. The excess of hydride was decomposed by careful addition of absolute methanol (70 mL), and the solution was evaporated to dryness at 30° *in vacuo*. The resulting syrup was dissolved in distilled water (50 mL), and the mixture extracted with $CHCl_3$ (3 × 30 mL). The extracts were combined, dried ($MgSO_4$), and evaporated to a syrup at 30° *in vacuo* to give **22** (see Table I; yield, 2.9 g, 90%). Deprotection of **22** as described for **19** gave **23** (yield, 1.5 g, 68%).

Molybdate epimerization[8] gave an equilibrium mixture of **23** (~50%) and 5-*O*-methyl-D-arabinose (**24**; ~50%), which was purified by chromatography on Dowex-50 X-8 (Ca^{2+}) resin (200–400 mesh)[6,7]. The elution profile was the same as that obtained for the [^{13}C]-enriched compounds **15** and **16**. G.l.c.–mass-spectral analyses of the peracetylated alditol derivatives from **23** and **24** gave the expected $(M + 1)^+$ ion at *m/z* 335.

5-Deoxy-D-xylose (**27**) *and -lyxose* (**28**) *(Scheme 4).* — A solution of 1,2-*O*-isopropylidene-5-*O*-tosyl-α-D-xylofuranose (**25**; see Table I; 1.7 g, 5.0 mmol)[12] in $CHCl_3$ (4 mL) and ether (50 mL) was added from a dropping funnel to LAH (0.63

g, 16 mmol) suspended in diethyl ether (50 mL) under reflux. Refluxing was continued for 18 h, and the product, 1,2-*O*-isopropylidene-5-deoxy-α-D-xylofuranose (**26**; see Table I), was converted into 5-deoxy-D-xylose (**27**) as described for the preparation of **20** (yield, 0.3 g, 40%).

Molybdate epimerization[8] was used to generate 5-deoxy-D-lyxose **28** (55%) from **27** (45%), and the aldoses were separated as described for compounds **5** and **6**. G.l.c.–mass-spectral analyses of the peracetylated alditol derivatives from **27** and **28** gave the expected $(M + 1)^+$ ion at *m/z* 305.

5-O-Methyl-D-xylose (**30**) *and -lyxose* (**31**) *(Scheme 4)*. — 1,2-*O*-Isopropylidene-5-*O*-tosyl-α-D-xylofuranose (**25**; Table I; 2.4 g, 7 mmol)[12] was treated with 4.6M $NaOCH_3$ (4.6 mL, 21 mmol) in a Teflon-lined vial, and the mixture was heated for 4 h at 100° (oil bath). After cooling, distilled water (1 mL) was added, and the mixture was extracted with $CHCl_3$ (3 × 20 mL). The extracts were combined, dried ($MgSO_4$), and evaporated at 30° *in vacuo*; crystallization of 1,2-*O*-isopropylidene-5-*O*-methyl-α-D-xylofuranose (**29**; Table I) occurred readily upon concentration (yield, 1.0 g, 70%).

Compound **29** (1.0 g, 4.9 mmol) was deprotected as described for **19**, generating 5-*O*-methyl-D-xylose (**30**; 0.7 g; yield, 90%). Molybdate epimerization[8] of **30** generated an equilibrium mixture of **30** (42%) and 5-*O*-methyl-D-lyxose (**31**; 58%), which were separated by chromatography[6,7] as described for **13** and **14**. G.l.c.–mass-spectral analyses of the peracetylated alditol derivatives from **30** and **31** gave the expected $(M + 1)^+$ ion at *m/z* 335.

RESULTS AND DISCUSSION

Chemical methods for preparing the 5-deoxypentoses and 5-*O*-methylpentoses, with and without [^{13}C]-enrichment at C-1, are described herein. Several of these 5-substituted pentoses (unenriched) had not previously been prepared; the routes used for the synthesis of unenriched and enriched pentoses are distinct, and reflect the general criteria already described for preparing natural, and stable-isotopically enriched, compounds. Such glycol-cleavage reagents as periodate and lead tetraacetate are used to generate chiral precursors for the preparation of stable-isotopically enriched pentoses. Cleavage of the 6-substituted hexoses **1, 2, 9,** and **10** with $Pb(OAc)_4$ gives **3, 4, 11,** and **12**, respectively. Treatment of these 4-substituted tetroses with [^{13}C]cyanide, followed by reduction with Pd–$BaSO_4$ and chromatography, gives 5-substituted [1-^{13}C]pentoses in good yield. The tetroses **3** and **4** can be prepared in the D configuration starting from D-fucose and 6-deoxy-D-glucose, respectively, permitting access to the 5-deoxy-D-[1-^{13}C]pentoses*.

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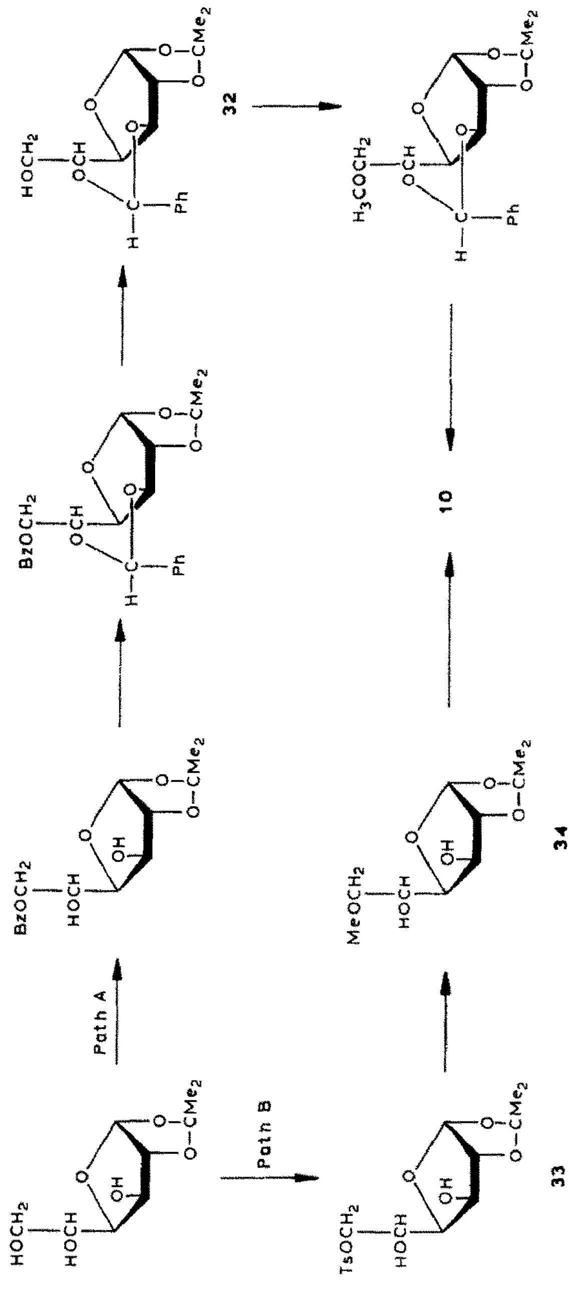
*D-Fucose is commercially available (Sigma); 6-deoxy-D-glucose can be prepared from **33** by LAH reduction.


HOCH2
HOCH
OH
O
O—CMe2
Path A
Path B
BzOCH2
TsOCH2
MeOCH2
H3COCH2
OCH
H—C—Ph
32
33
34
10

Scheme 5

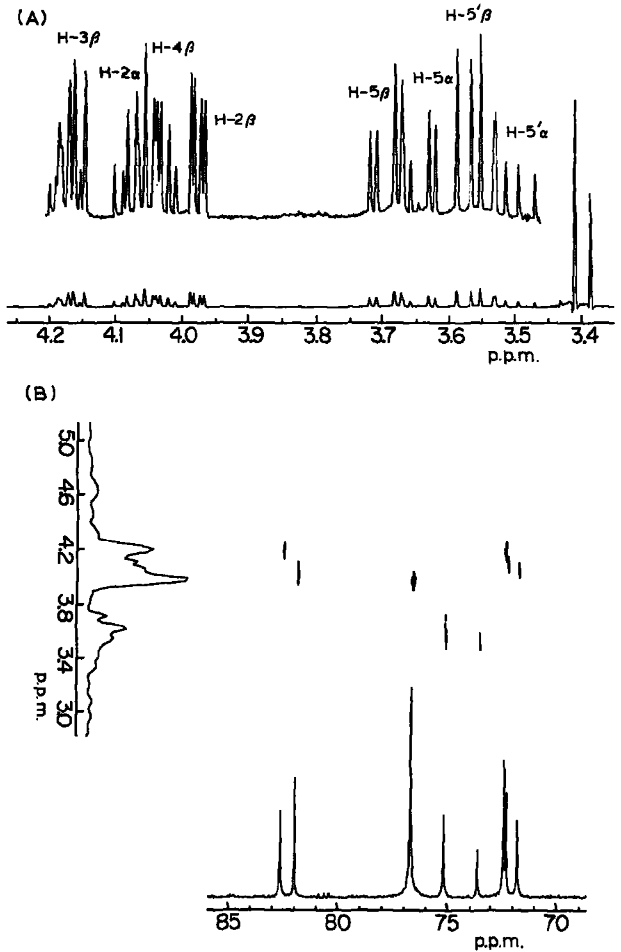


Fig. 1. (A) The nonanomeric region of the 300-MHz, ^{1}H-n.m.r. spectrum of 5-*O*-methyl-D-ribose (**23**) in ^2H_2O, showing signal assignments. (B) The 2-D ^{13}C–^1H shift-correlation map for 5-*O*-methyl-D-ribose; the assignments in (A) and the cross-peaks in (B) permit a complete assignment of the ^{13}C-n.m.r. spectrum (see Table IV).

In principle, glycol scission of L-rhamnose (6-deoxy-L-mannose) should yield **4**. However, Perlin and Brice[16] showed that the reaction consumes ~2.6 molar equivalents of $Pb(OAc)_4$ and yields both triose and tetrose, which are difficult to separate. This problem is alleviated by epimerizing L-rhamnose to **2** with sodium molybdate[8,17]; **2** yields **4** almost exclusively upon treatment with lead tetraacetate.

The preparation of 6-*O*-methyl-D-glucose **10** that is here described is shorter and more reliable than a recently reported method[18a], and gives comparable yields. The latter method (see Scheme 5, Path A) utilizes several protection–deprotection reactions to produce **32**. Our approach is essentially that used by Capon and Walker[18b] (Scheme 5, Path B), and involves the selective tosylation of O-6 of 1,2-*O*-

isopropylidene-α-D-glucofuranose. The reaction with one molar equivalent of tosyl chloride occurs in good yield at −5°, and **33** is readily crystallized. Subsequent displacement with methoxide ion gives **34**. It is noteworthy that the same reaction with methyl 6-*O*-tosyl-α-D-glucopyranoside gives the 3,6-anhydride almost exclusively[18c].

Proton chemical-shifts. — ^{1}H-Chemical shifts of the α- and β-furanose forms of 5-deoxy- and 5-*O*-methyl-pentoses are given in Table II. These data reveal that structure at C-5 can have a significant effect on the spectra of compounds having similar configurations and conformations (see later for a discussion of conformation). For example, the ^{1}H-n.m.r. spectrum of 5-*O*-methyl-D-ribose (see Fig. 1A) is essentially first-order at 300 MHz, whereas that of 5-deoxy-D-ribose is complex (see Fig. 2) due to chemical-shift changes at sites relatively remote from the site of substitution. The spectrum of the latter at 600 MHz (see Fig. 2) can, however, be deciphered.

Considering ring protons in a given configuration, the conversion of a C-5 fragment from $-CH_2OCH_3$ into $-CH_3$ results in upfield shifts (0.01–0.08 p.p.m.) in the signals of H-1 and H-4, and essentially no change in the chemical shift of H-2 (δ_{H-2}). Somewhat surprisingly, the H-3 signal is shifted upfield by 0.19–0.26 p.p.m. for compounds having H-3 and C-5 *cis*, as well as for those with these atoms *trans*. This fact suggests that a "through-bond" mechanism is responsible for the exocyclic effects on δ_{H-3}, although this may not be the sole mechanism. The conversion of methyl α-D-arabinofuranoside or methyl α-D-lyxofuranoside into methyl 3-deoxy-α-D-arabinofuranoside does not significantly affect the chemical shifts of the C-5 protons (see Table III); that is, the effect of C-3 deoxygenation on C-5 proton

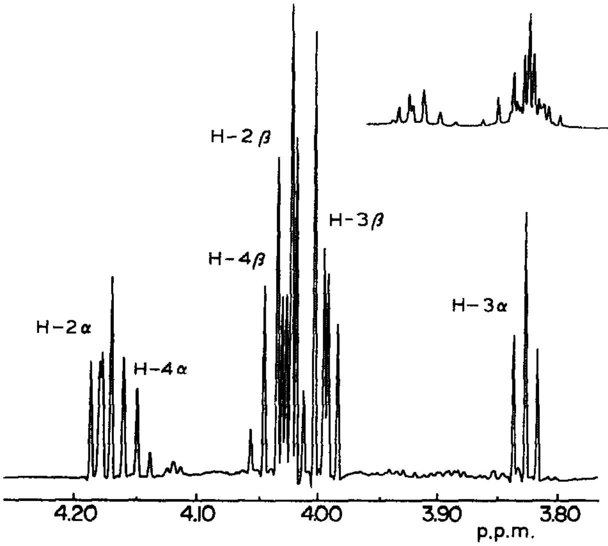


Fig. 2. The 600-MHz, ^{1}H-n.m.r. spectrum (H-2–H-4-region) of 5-deoxy-D-ribose (**20**) in ^2H_2O, showing signal assignments. The inset shows the same spectrum obtained at 300 MHz.

chemical shifts is negligible. From these facts, we concluded that the presence of O-5 in the exocyclic, hydroxymethyl fragment significantly alters the distribution at remote sites within the furanose ring, causing notable changes in chemical shieldings. This effect may result not only from substituent electronegativity differences, but also from the stereoelectronic *gauche* effect[19,20] that, in part, governs the favored torsions in O–C–C–O fragments. In other words, it is conceivable that stable geometries resulting from specific, oxygen lone-pair orbital-alignments may influence electron density in nearby bonds.

A comparison of the spectra of 5-*O*-methylpentofuranoses with those of the methyl pentofuranosides[21] revealed that the H-1 signals shift upfield (0.35 ±0.03 p.p.m.) upon glycosidation; the C-5 protons behave similarly, shifting upfield by 0.09 ±0.04 p.p.m. when O-5 is methylated. Glycosidation shifts the H-4 signal upfield by 0.15 ±0.02 p.p.m. for the α anomers only, where O-1 and H-4 are *cis*. A "through-space" mechanism could account for the latter structural dependence.

Carbon chemical shifts. — The assignments of ^{13}C chemical shifts for the 5-deoxy- and 5-*O*-methyl-pentofuranoses are given in Table IV. Assignments for C-1 are based on the well established relationship[21,22] between $\delta_{C\text{-}1}$ and the relative orientation of O-1 and O-2. The remaining assignments were made by 2-D ^{13}C–^{1}H shift-correlation spectroscopy[2d] (see Fig. 1B); the assignments of C-3, C-4, and C-5 in the 5-*O*-methyl series were made solely from 2-D shift-correlation maps. Assignments for C-2 were confirmed by observation of one-bond, ^{13}C–^{13}C couplings in the ^{13}C spectra of [1-^{13}C]-enriched compounds, and C-5 signals of the 5-deoxypentoses were assigned from their characteristic, upfield position in the spectra.

Conversion of the pentofuranose C-5 fragment from $-CH_2OCH_3$ into $-CH_3$ causes considerable deshielding and shielding of C-3 and C-4, respectively. Smaller effects are observed on $\delta_{C\text{-}1}$ and $\delta_{C\text{-}2}$, and the largest effect occurs, as expected, at C-5. It is clear that, with respect to remote sites, the C-3–H-3 pentofuranose-ring

TABLE V

PROPORTIONS OF FORMS[a] IN AQUEOUS SOLUTIONS OF 5-DEOXY- AND 5-*O*-METHYL-PENTOSES AT 25° IN $^{2}H_2O$

Compound	*Percent in solution*			
	α-Furanose	*β-Furanose*	*Hydrate*	*Aldehyde*
5-Deoxy-L-arabinose	63.2	36.0	0.6	0.2
5-Deoxy-L-lyxose	78.0	20.3	1.5	0.2
5-Deoxy-L-ribose	31.8	67.2	0.8	0.1
5-Deoxy-L-xylose	54.0	42.9	2.7	0.4
5-*O*-Methyl-D-arabinose	60.0	37.4	2.5	0.2
5-*O*-Methyl-D-lyxose	71.7	24.9	3.1	0.3
5-*O*-Methyl-D-ribose	34.5	64.6	0.8	0.1
5-*O*-Methyl-D-xylose	54.5	41.4	3.9	0.2

[a] Values for α-furanose, β-furanose, and hydrate are accurate to within ±1%. Error in the values for the aldehyde form may be ±50%.

TABLE VI

SOME N.M.R.-SPECTRAL PARAMETERS[a] FOR THE HYDRATE FORMS OF THE 5-DEOXY- AND 5-*O*-METHYL-PENTOSES IN ^2H_2O

Compound	δ_{C-1}	δ_{H-1}	$^3J_{H-1,H-2}$
5-Deoxy-L-arabinose hydrate	91.8	5.01	6.6
5-Deoxy-L-lyxose hydrate	91.2	5.14	3.3
5-Deoxy-L-ribose hydrate	91.7		
5-Deoxy-L-xylose hydrate	91.5	5.01	6.5
5-*O*-Methyl-D-arabinose hydrate	91.0		
5-*O*-Methyl-D-lyxose hydrate	90.1	5.17	2.4
5-*O*-Methyl-D-ribose hydrate	91.0		
5-*O*-Methyl-D-xylose hydrate	90.0	5.02	6.1

[a]Conditions are the same as those for corresponding entries in Tables II, IV, and VII. No entry denotes values that were not determined.

fragment is most affected by C-5 deoxygenation. An alternating and corresponding shielding–deshielding–shielding pattern is observed for the C-4–C-3–H-3 ring-fragment that indicates a significant alteration in the electron distribution in this fragment of the molecule.

Tautomeric forms in aqueous solution. — With the aid of [1-^{13}C]-enriched compounds, the proportions of tautomeric forms of the 5-deoxy- and 5-*O*-methyl-pentoses in aqueous solution were determined by ^{13}C-n.m.r. spectroscopy (see Table V). The relative proportions of furanose anomers in both sets of structures are similar to those observed previously for the corresponding D-pentose 5-phosphates[2b,23]. The structure of the exocyclic fragment, therefore, does not appear to alter the relative stabilities of pentofuranose anomers.

The linear hydrate (1,1-*gem*-diol) forms have characteristic C-1 chemical-shifts of ~91 p.p.m. (see Table VI) and comprise 0.6–3.9 mol-% of the tautomeric mixture (see Table V). Aldehyde forms have C-1 chemical shifts of ~207 p.p.m.[2a,b,c], and are present in least abundance. Observation of the carbonyl form permits measurement of ring-opening and -closing rate-constants in these compounds by ^{13}C-n.m.r. spectroscopy[2a,b,c] and an evaluation of the effect of exocyclic structure on furanose anomerization.

Coupling constants and conformation. — Coupling constants (^{1}H–^{1}H, ^{13}C–^{1}H, and ^{13}C–^{13}C) for the 5-deoxy- and 5-*O*-methyl-pentofuranoses are listed in Tables VII and VIII. Spin couplings (^{1}H–^{1}H) are similar for both sets of configurationally related compounds, indicating that the conformation is conserved (these couplings are also similar to corresponding values for the methyl pentofuranosides[21]). In the *xylo* and *lyxo* series, however, notable differences in $^3J_{H-3,H-4}$ are found; the larger coupling in the 5-*O*-methyl series suggests a decrease in dihedral angle between H-3 and H-4, causing a minor change in the *quasi*-equatorial orientation of C-5. This conclusion is made with reservation, as electronegative substituents and their relative orientation are known to affect "Karplus" curves for HC–CH fragments[24].

TABLE VII

^{1}H-^{1}H COUPLING CONSTANTS[a] IN 5-DEOXY- AND 5-*O*-METHYL-PENTOFURANOSES IN ^2H_2O

Compound	*Coupled nuclei*					
	1,2	*2,3*	*3,4*	*4,5*	*4,5'*	*5,5'*
5-Deoxy-α-L-arabinose	2.7	5.0	7.0	6.4		
5-Deoxy-β-L-arabinose	4.8	7.7	obs	~6.0		
5-Deoxy-α-L-lyxose	4.7	4.6	2.7	6.4		
5-Deoxy-β-L-lyxose	5.1	obs	obs	6.4		
5-Deoxy-α-L-ribose	4.3	5.5	5.7	6.4		
5-Deoxy-β-L-ribose	1.7	4.6	6.5	6.0		
5-Deoxy-α-L-xylose	3.9	obs	4.1	6.6		
5-Deoxy-β-L-xylose	1.7	1.8	4.3	6.6		
5-*O*-Methyl-α-D-arabinose	2.7	4.6	6.5	3.0	6.7	−11.1
5-*O*-Methyl-β-D-arabinose	4.5	7.4	7.3	3.1	7.0	−11.0
5-*O*-Methyl-α-D-lyxose	4.4	~4.5	~4.3	3.8	7.5	−10.8
5-*O*-Methyl-β-D-lyxose	5.0	~4.8	4.3	3.8	~7.7	~−10.8
5-*O*-Methyl-α-D-ribose	4.0	5.7	obs	3.0	5.7	−11.1
5-*O*-Methyl-β-D-ribose	1.6	4.7	6.8	3.0	6.9	−11.1
5-*O*-Methyl-α-D-xylose	4.3	4.5	5.4	3.3	6.9	−10.9
5-*O*-Methyl-β-D-xylose	1.4	2.2	4.8	3.8	~8.0	−10.8

[a] Values are reported in Hz, and are accurate to within ±0.1 Hz. "Obs" denotes obscured resonances.

TABLE VIII

^{13}C–^{13}C AND ^{13}C–^{1}H COUPLING CONSTANTS[a] IN 5-DEOXY- AND 5-*O*-METHYL-PENTOFURANOSES IN ^2H_2O

Compound	*Coupled nuclei*			
	C-1,C-2	*C-1,C-3*	*C-1,C-5*	*C-1,H-1*
5-Deoxy-α-L-arabinose	46.6	4.5		171.2
5-Deoxy-β-L-arabinose	43.5	3.1		173.2
5-Deoxy-α-L-lyxose	46.6	br		170.5
5-Deoxy-β-L-lyxose	42.6	br		173.8
5-Deoxy-α-L-ribose	41.9	2.3	1.9	172.6
5-Deoxy-β-L-ribose	46.4			172.0
5-Deoxy-α-L-xylose	41.7	br	2.1	172.4
5-Deoxy-β-L-xylose	45.3	2.2		170.7
5-*O*-Methyl-α-D-arabinose	46.4	4.2	br	171.4
5-*O*-Methyl-β-D-arabinose	43.7	3.1		173.6
5-*O*-Methyl-α-D-lyxose	46.6	2.2	2.2	171.3
5-*O*-Methyl-β-D-lyxose	43.0			174.2
5-*O*-Methyl-α-D-ribose	42.5	2.3	2.0	172.7
5-*O*-Methyl-β-D-ribose	46.1	3.3		172.9
5-*O*-Methyl-α-D-xylose	42.5	2.2		173.0
5-*O*-Methyl-β-D-xylose	45.5	2.8	2.5	171.8

[a] Values are reported in Hz, and are accurate to within ±0.1 Hz. No entry means that coupling was not observed. No coupling was observed between C-1 and C-4 in the spectra of these compounds. "Br" denotes broadened signals.

TABLE IX

ROTAMER DISTRIBUTION[a] ABOUT THE C-4–C-5 BOND IN 5-*O*-METHYL-D-PENTOSES, DETERMINED FROM $^3J_{H-4,H-5}$ IN TABLE VII.

Configuration of compound	*Rotamer*		
	P_{gg}	P_{gt}	P_{tg}
α-*arabino*	0.29 (0.42)	0.55 (0.49)	0.16 (0.10)
β-*arabino*	0.25 (0.38)	0.58 (0.51)	0.17 (0.10)
α-*lyxo*	0.13 (0.30)	0.63 (0.53)	0.24 (0.17)
β-*lyxo*	0.11 (0.28)	0.65 (0.55)	0.24 (0.17)
α-*ribo*	0.40 (0.51)	0.44 (0.38)	0.16 (0.11)
β-*ribo*	0.27 (0.40)	0.57 (0.51)	0.16 (0.09)
α-*xylo*	0.24 (0.38)	0.57 (0.49)	0.19 (0.13)
β-*xylo*	0.07 (0.25)	0.68 (0.59)	0.24 (0.16)

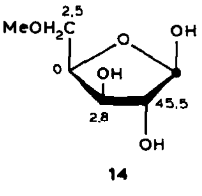
[a] Distribution of rotamers was calculated as described previously for the methyl pentofuranosides[20]. The two values for each entry represent results from two treatments of $^3J_{H-4,H-5}$ as described previously[20].

To examine the orientation of the C-4–C-5 bond in the 5-*O*-methylpentofuranoses, the stereochemical assignments of the C-5 protons were made with reasonable confidence by comparison to the methyl pentofuranosides, in which the more shielded C-5 proton has been found[20] to be H-5(*R*). Using methods described earlier[20], rotamer distributions were calculated (see Table IX). A comparison of these results with those reported for the methyl pentofuranosides[20] shows that 5-*O*-methylation does not significantly affect the orientation of the exocyclic hydroxymethyl group.

The value of $^3J_{H-1,H-2}$ for hydrates (see Table VI) varies from 2 to 7 Hz, depending on the configuration. The *arabino* and *xylo* forms have larger $^3J_{H-1,H-2}$ values than the *ribo* and *lyxo* forms, possibly due to the *trans* relation of O-2 and O-3 in the former, which permits the C-1–C-2 bond to assume an orientation where H-1 and H-2 are nearly antiperiplanar[21] and 1,3-OH interactions are avoided. Hydrates having the *ribo* and *lyxo* configurations orient H-1 and H-2 *gauche*, in order to minimize 1,2-OH and 1,3-OH interactions[21]

The magnitude of $^1J_{C-1,C-2}$ for furanoses is sensitive to anomeric configuration, as suggested previously from limited data[21,23]. Rings having O-1 and O-2 *trans* yield larger couplings (46.2 ±0.5 Hz) than those having O-1 and O-2 *cis* (42.7 ±0.7 Hz; see Table VIII). These couplings should, therefore, be useful in determining anomeric configuration in furanose systems. On the other hand, $^1J_{C-1,H-1}$ is relatively insensitive to the configuration at C-1; anomers having *cis*-O-1–O-2 give slightly larger couplings (173.2 ±0.6 Hz) than those having *trans*-O-1–O-2 (171.5 ±0.8 Hz).

Couplings between C-1 and C-3 are observed for furanoses[21], whereas C-1–C-4 couplings are very small, or nonexistent, for all furanoses studied to date, regardless of configuration (see Table VIII). The magnitude of these intra-ring couplings is determined by two coupling-pathways[25] (*e.g.*, for $J_{C-1,C-3}$, C-1–C-2–C-3 and C-1–



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(*β*-furanose)

O-4–C-4–C-3), and their interpretation is not possible until the coupling signs of each pathway have been established. Three-bond coupling between C-1 and C-5 varies between 1.9 and 2.5 Hz, and was not observed in all structures; these values suggest a dihedral angle of 130–140° between these nuclei[26], consistent with a *quasi*-equatorial orientation of C-5.

SUMMARY

This study has demonstrated that ^{1}H and ^{13}C chemical shifts for pentofuranose rings depend on the structure of the C-5 exocyclic moiety, even for nuclei rather remote from the site of substitution. In the two series of 5-substituted derivatives examined, however, exocyclic structure does not affect tautomeric distribution and the conformation in aqueous solution.

The results of this investigation are summarized as follows. (*a*) Chemical methods have been described for preparing 5-deoxy- and 5-*O*-methyl-pentoses with or without [^{13}C]-enrichment at C-1, and in either the D or the L configuration. (*b*) Spectra (^{1}H- and ^{13}C-n.m.r.) have been interpreted, the latter with the use of 2-D ^{13}C–^{1}H chemical-shift correlation spectroscopy. (*c*) With respect to remote nuclei, the conversion of the exocyclic C-5 fragment of a pentofuranose ring from –CH_2OCH_3 into –CH_3 affects the chemical shifts of H-3, C-3, and C-4 most significantly; the effect appears to be primarily "through-bond", and suggests that *gauche* effects involving O-4 and O-5 may, in part, be responsible for altering the electron distribution in nearby bonds. (*d*) The conformations of configurationally related 5-*O*-methylpentofuranoses, 5-deoxypentofuranoses, and methyl pentofuranosides are similar. (*e*) The orientations of the C-4–C-5 bond in 5-*O*-methylpentofuranoses are similar to those in the configurationally related methyl pentofuranosides. (*f*) The value of $^1J_{C\text{-}1,C\text{-}2}$ is sensitive to furanose anomeric configuration, and should be a useful tool for structure elucidation in these systems. (*g*) In addition to furanose forms, aqueous solutions of 5-*O*-methyl- and 5-deoxy-pentoses contain measurable amounts of hydrate and aldehyde forms. The detection of the carbonyl form permits studies of furanose anomerization by saturation-transfer n.m.r. spectroscopy[2a,b,c].

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