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^{13}C- AND ^{1}H-N.M.R. SPECTROSCOPY OF PERMETHYLATED GLUCO-, GALACTO-, AND MANNO-PYRANOSES AND THEIR 6-DEOXY ANALOGUES

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ABSTRACT

The ^{13}C- (25.16 MHz) and ^{1}H-n.m.r. (220, 300 MHz) spectra of permethylated mannopyranoses, their 6-deoxy analogues, and permethylated 6-deoxy-gluco- and -galacto-pyranoses have been analysed with the aid of specific trideuteriomethylation, heteronuclear spin-decoupling, and spectrum simulation. Comparison of spectral data for the aldohexose derivatives and their 6-deoxy analogues shows that the ring conformation is not significantly affected by the presence or absence of MeO-6; all compounds are present in the $^{4}C_{1}$ (D) or $^{1}C_{4}$ (L) conformation. Changes in orientation of the MeO groups have distinct effects on the chemical shifts of carbons and protons of the pyranoid rings and of the MeO groups. The possible origins of these effects are discussed.

INTRODUCTION

In our previous studies on the ^{13}C- and ^{1}H-n.m.r. spectra of fully methylated glucopyranoses[1] and galactopyranoses[2], it was shown that the spectral data for the carbons and protons of the sugar skeleton and the methoxyl groups are characteristic. This made possible the use of ^{13}C- and ^{1}H-n.m.r. spectroscopy for the determination of the positions of MeO groups in partially methylated monosaccharides. If the free hydroxyl functions of such a compound are converted into labelled (^{2}H, ^{13}C) MeO groups, the effect of variation in substituents at adjacent carbons on an MeO group is eliminated and chemical shifts can be compared accurately with reference data for permethylated compounds.

Differences between the chemical shifts of similar atoms in gluco- and galacto-pyranoses can be interpreted in terms of shielding and deshielding effects, arising from changes in substituent configurations. Change in anomeric configuration from β to α causes the ^{13}C resonances of C-1, C-2, C-3, C-5, MeO-1, and MeO-2 to shift upfield. The remaining carbon resonances are almost unaffected. Epimerization at C-4 from glucose (*eq* MeO-4) to galactose (*ax* MeO-4) introduces an upfield shift of the carbons C-2–C-5 and MeO-3, whereas the resonance position of MeO-4 is only slightly

influenced. An upfield shift of a particular skeleton carbon is accompanied by a downfield shift of the proton attached thereto and *vice versa*. However, the positions of the carbon and proton resonances of an MeO-group shift in the same direction on change in configuration.

We now report on the ^{13}C- and ^{1}H-n.m.r. spectra of permethylated manno-pyranoses and the 6-deoxy analogues of gl. -o-, galacto-, and manno-pyranose (D-quinovose, L-fucose, and L-rhamnose, respectively).

RESULTS

^{13}C-N.m.r. spectra

Comparison of the ^{13}C-n.m.r. spectra of permethylated α- and β-D-gluco-pyranose[1] (**1**, **2**) with those of 6-deoxy-α- and -β-D-glucopyranose (**3**, **4**) shows that substitution at C-6 causes a large upfield shift (~54 p.p.m.) for this carbon resonance and a smaller upfield shift (3.8 p.p.m.) for C-5 (Table I). The resonance of C-4 in **3** and **4** is shifted 5.8 p.p.m. downfield with respect to the corresponding glucose derivative, which is due to the smaller steric interaction between MeO-4 and the methyl group at C-5. The four MeO resonances of **3** and **4** nearly coincide with those of **1** and **2**, respectively (Table II). Similar increments in resonance positions are observed on changing from permethylated galactopyranose[2] (**5**, **6**) to permethylated fucopyranose (**7**, **8**). However, C-4 is shifted only ~3 p.p.m. downfield and C-5 ~3 p.p.m. upfield (Tables I and II). These opposite shifts for C-4 and C-5 were also found in the free sugars[3] and are in agreement with the results for aliphatic and alicyclic alcohols[4].

TABLE I

^{13}C-N.M.R. DATA (25.16 MHz, ACETONITRILE-d_3); CHEMICAL SHIFTS (δ p.p.m.) OF THE SKELETON CARBONS IN PERMETHYLATED MONOSACCHARIDES

Permethyl derivative	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*
α-D-Glc*p*[a] (1)	98.16	82.58	84.28	80.61	70.98	72.41
α-D-Qui*p* (3)	98.10	82.85	84.04	86.54	67.16	18.17
α-D-Gal*p*[b] (5)	98.80	78.78	80.97	77.25	69.88	72.34
α-L-Fuc*p* (7)	98.79	78.58	81.25	80.05	66.83	16.75
α-D-Man*p* (9)	99.30	77.75	82.37	77.16	72.22	72.58
α-L-Rha*p* (11)	99.26	78.00	82.24	82.94	68.42	18.26
β-D-Glc*p*[a] (2)	105.00	84.58	87.21	80.48	75.38	72.36
β-D-Qui*p* (4)	104.84	84.85	87.02	86.14	71.57	18.08
β-D-Gal*p*[b] (6)	105.26	81.50	84.65	76.10	73.86	72.01
β-L-Fuc*p* (8)	105.22	81.33	85.07	79.13	70.88	16.88
β-D-Man*p* (10)	103.42	77.75	84.78	77.18	76.13	72.64
β-L-Rha*p* (12)	103.29	77.97	84.70	82.84	72.27	18.22

[a]See Ref. 1. [b]See Ref. 2.

TABLE II

^{13}C-N.M.R. DATA (25.16 MHz, ACETONITRILE-d_3); CHEMICAL SHIFTS (δ p.p.m.) OF THE MeO GROUPS IN PERMETHYLATED MONOSACCHARIDES

Permethyl derivative	*MeO-1*	*MeO-2*	*MeO-3*	*MeO-4*	*MeO-6*
α-D-Glc*p*[a] (1)	55.27	58.40	60.71	60.55	59.23
α-D-Qui*p* (3)	55.17	58.35	60.64	60.64	—
α-D-Gal*p*[b] (5)	55.30	58.52	58.11	61.31	59.19
α-L-Fuc*p* (7)	55.26	58.43	58.04	61.77	—
α-D-Man*p* (9)	55.12	59.11	57.50	60.55	59.18
α-L-Rha*p* (11)	55.05	59.11	57.43	60.73	—
β-D-Glc*p*[a] (2)	56.96	60.39	60.74	60.48	59.30
β-D-Qui*p* (4)	56.82	60.37	60.65	60.65	—
β-D-Gal*p*[b] (6)	56.82	60.64	58.27	61.26	59.21
β-L-Fuc*p* (8)	56.73	60.62	58.23	61.75	—
β-D-Man*p* (10)	57.17	61.26	57.36	60.64	59.29
β-L-Rha*p* (12)	56.99	61.22	57.26	60.76	—

[a]See Ref. 1. [b]See Ref. 2.

The resonances of C-1–C-6 of the α-D-mannopyranose derivative **9** were assigned by off-resonance ^{13}C-{^{1}H} spin-decoupling[1] (Table I). The chemical shifts of C-5 and C-6 differ only slightly, but, on off-resonance decoupling, C-5 appears as a doublet and C-6 as a triplet. The ^{13}C chemical shifts in the spectra of **9** and **11** show a similar relationship as those in **1** and **3**. The skeleton carbon resonances of the β-D-mannose derivative (**10**) could not be assigned by off-resonance spin-decoupling, because of the very similar ^{1}H chemical shifts in the solvent acetonitrile-d_3. The identification of these carbon resonances is based on the following premises. (*1*) On anomeric change from α to β (**9** → **10**), C-3 and C-5 become less shielded because the steric 1,3-diaxial interactions between MeO-1, H-3, and H-5 disappear; (*2*) δC-4 and δC-6 are independent of the anomeric configuration; (*3*) the shift increments for corresponding carbons in **10** and the β-L-rhamnose derivative (**12**) are identical to those observed for similar pairs of compounds (*e.g.*, **1**, **3**; **2**, **4**; and **9**, **11**). The ^{13}C resonances of the MeO groups of **9** and MeO-1 and MeO-2 of **10** have been assigned on the basis of the spectral data for permethylated mannopyranoses (**13**–**17**), selectively labelled with OCD_3 groups; specific trideuteriomethylation has no effect on the chemical shifts of OMe groups in the same molecule. The remaining MeO resonances of **10** could be identified by comparison with the spectral data for **9**, **12**, and methyl 2,3,4-tri-*O*-trideuteriomethyl-β-L-rhamnopyranoside (**18**). The spectrum of the latter compound shows an MeO signal at δ 57.02.

^{1}*H-N.m.r. spectra*

Chemical shifts and coupling constants of the skeleton protons. The 220-MHz ^{1}H-n.m.r. spectra of the mannose derivatives **9** and **10** and of the 6-deoxy sugars **3**, **4**, **7**, **8**, **11**, and **12** were recorded for solutions in acetonitrile-d_3. The spectra of **9** and **10** were also measured at 300 MHz (Table III). The coupling constants $J_{1,2}$, $J_{2,3}$, and

TABLE III

^{1}H-N.M.R. DATA (δ p.p.m., JHz, ACETONITRILE-d_3) OF THE SKELETON PROTONS OF PERMETHYLATED MONOSACCHARIDES

Permethyl derivative		*H-1*	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*H-6'*	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$
α-D-Glc*p*[a]	(1)	4.76	3.09	3.29	3.01	3.47	3.48	3.48	3.5	9.6	8.8	9.8	3.4	3.4	—[b]
α-D-Qui*p*	(3)	4.72	3.10	3.26	2.70	3.49	1.18		3.5	9.7	8.6	9.7	6.2		
α-D-Gal*p*[c]	(5)	4.78	3.42	3.44	3.64	3.76	3.48	3.42	~2.2	~11.0	~1.6	1.5	6.0	6.7	−9.7
α-L-Fuc*p*	(7)	4.72	3.41	3.41	3.43	3.76	1.14		~2.5	—[b]	~2.6	1.3	6.5		
α-D-Man*p*[f]	(9)	4.68	3.51	3.34	3.25	3.42	3.49	3.48	1.9	3.2	9.4	9.8	3.8	2.4	−10.5
α-L-Rha*p*	(11)	4.64	3.51	3.31	2.96	3.44	1.19		1.9	3.2	9.5	9.6	6.2		
β-D-Glc*p*[a]	(2)	4.12	2.83	3.09	3.01	3.24	3.47	3.54	7.8	8.9	9.0	9.6	4.9	2.1	−10.8
β-D-Qui*p*	(4)	4.10	2.84	3.05	2.72	3.21	1.21		7.6	9.2	8.8	9.4	6.2		
β-D-Gal*p*[c]	(6)	4.09	3.05	3.15	3.59	←	3.45–3.53[d]	→	7.5	9.7	3.0	0.8	—[d]	—[d]	—[d]
β-L-Fuc*p*	(8)	4.04	3.00	3.11	3.37	3.45	1.19		7.5	9.9	3.0	1.1	6.4		
β-D-Man*p*[f]	(10)	4.27	3.64	←	3.17–3.19[d]	→	3.50	3.55	0.9	2.7	—[d]	—[d]	~4.6	1.5	−10.7
β-L-Rha*p*	(12)	4.26	3.63	3.11	2.91	3.14	1.23		0.9	3.1	9.4	9.3	6.2		
β-D-Man*p*[e]	(10)	3.90	3.38	2.98	3.60	3.32	3.63	3.65	0.4	3.0	9.3	9.6	7.0	0.8	—[b]
α-L-Fuc*p*[e]	(7)	4.71	3.71	3.52	3.05	3.65	1.20		3.5	10.0	3.1	1.2	6.4		

[a]See Ref. 1. [b]Not observed. [c]See Ref. 2. [d]Complex multiplet. [e]Recorded in benzene-d_6. [f]Data from 300-MHz spectrum.

$J_{3,4}$ in **7** and $J_{3,4}$ and $J_{4,5}$ in **10** could not be determined accurately because H-2–H-4 of **7** and H-3–H-5 of **10** have apparently the same chemical shifts. However, for solutions in benzene-d_6, the spectra were better dispersed, which allowed the determination of all coupling constants. The differences in coupling constants, obtained for solutions in acetonitrile-d_3 and benzene-d_6, are due to solvation effects.

TABLE IV

^{1}H-N.M.R. DATA (100 MHz, ACETONITRILE-d_3); CHEMICAL SHIFTS (δ p.p.m.) OF THE MeO GROUPS IN PERMETHYLATED MONOSACCHARIDES

Permethyl derivative	*MeO-1*	*MeO-2*	*MeO-3*	*MeO-4*	*MeO-6*
α-D-Glc*p*[a] (1)	3.29	3.37	3.49	3.43	3.30
α-D-Qui*p* (3)	3.29	3.37	3.48	3.46	—
α-D-Gal*p*[b] (5)	3.28	3.35	3.39	3.43	3.30
α-L-Fuc*p* (7)	3.27	3.35	3.39	3.47	—
α-D-Man*p* (9)	3.28	3.37	3.36	3.40	3.30
α-L-Rha*p* (11)	3.28	3.37	3.35	3.43	—
β-D-Glc*p*[a] (2)	3.41	3.45	3.51	3.43	3.31
β-D-Qui*p* (4)	3.40	3.45	3.51	3.46	—
β-D-Gal*p*[b] (6)	3.39	3.43	3.40	3.42	3.30
β-L-Fuc*p* (8)	3.39	3.43	3.40	3.47	—
β-D-Man*p* (10)	3.38	3.44	3.37	3.39	3.31
β-L-Rha*p* (12)	3.38	3.44	3.36	3.42	—

[a]See Ref. 1. [b]See Ref. 2.

Chemical shifts of the MeO groups. The MeO signals of the α-D-mannose derivative **9** (Table IV) were identified by comparison of the spectra (100 MHz, acetonitrile-d_3) of the specifically trideuteriomethylated mannoses. For the β-anomer **10**, the signals were assigned by using the spectra of the mannose derivative **17**, permethylated β-L-rhamnose (**12**), and methyl 2,3,4-tri-*O*-trideuteriomethyl-β-L-rhamnoside (**18**). The latter compound shows one MeO singlet (δ 3.38).

The chemical shifts of the various MeO singlets of a permethylated aldohexopyranose and the corresponding 6-deoxy sugar derivative are almost identical, except for the MeO-4 resonances (Table IV). The latter show downfield shifts of 0.03–0.05 p.p.m. on change from CH_2OMe to CH_3 at C-5.

DISCUSSION

Configurational effects on the chemical shifts of ring carbons and protons

Changes in configuration of the permethylated aldohexopyranoses and 6-deoxyaldohexopyranoses introduce distinct alterations in the shielding of ring carbons (Table I) and the appended protons (Table III).

(*1*) Inversion of MeO from an equatorial to an axial position causes (*a*) a

shielding effect (6.4–7.0 p.p.m.) on the ring carbon to which it is bonded*, and a deshielding effect (0.6–0.8 p.p.m.) on the proton attached to that carbon; (*b*) a shielding effect on an adjacent ring carbon, and a deshielding effect on the proton attached to that carbon.

(*2*) A 1,3-diaxial interaction between a ring proton and an MeO group enhances the shielding (2.4–4.4 p.p.m.) of the carbon bearing that axial proton and diminishes the shielding (0.16–0.33 p.p.m.) of the axial proton itself.

(*3*) A vicinal gauche interaction between two MeO substituents has a shielding effect (2–3 p.p.m.) on the directly attached ring-carbons and a deshielding effect (0.2–0.4 p.p.m.) on the appended protons.

Explanations for the observed influences of substituent configuration on the chemical shifts of ring carbons and protons can be found in steric compression effects (Van der Waals effect), anisotropy effects (diamagnetic and electric), and also in small changes in bond angles with the accompanying changes in hybridisation state and bond lengths[5]. However, these effects cannot yet be treated quantitatively.

The influence of MeO-6 on the chemical shift of ring atoms

The replacement of MeO-6 by a proton has a pronounced influence on the chemical shifts of atoms in positions 4, 5, and 6, which results from differences in electric field and inductive effects between the CH_2OMe and the CH_3 group. Upfield shifts are found for C-5, C-6, H-4, and H-6, whereas downfield shifts are observed for C-4 (Table V); the influence on δH-5 is smaller and less regular than in the pertrimethylsilyl (Me_3Si) derivatives[7]. The chemical shifts of the more remote ring atoms (positions 1, 2, and 3) are hardly affected.

Conformation of the pyranose rings

Calculation[1] of the dihedral angles between the ring protons in the permethylated glucopyranoses shows that these compounds are present in the $^4C_1$(D) conformation, which is in accordance with the conformation determined[6] for the per-Me_3Si derivatives. Comparison of the coupling constants of the permethyl derivatives **3**–**12**, presented in Table III with those of the corresponding Me_3Si derivatives[6,7] allows the conclusion that the former compounds also occur in the $^4C_1$(D) and $^1C_4$(L) conformation. The close similarity between the coupling constants $J_{1,2}$, $J_{2,3}$, $J_{3,4}$, and $J_{4,5}$ of a permethylated aldohexopyranose and its 6-deoxy analogue demonstrates that the conformation of the ring is not significantly affected by the presence or absence of the MeO-6 group.

Configurational effects on the ^{13}C and ^1H chemical shifts of the MeO groups

The position of the ^{13}C resonance of MeO-1 depends considerably on its orientation (anomeric effect) and is almost independent of the configuration of MeO-2.

*Exception: epimerization from glucose to galactose is associated with shifts for C-4 of 3.4–4.4 p.p.m., probably as a result of the different rotational preferences of the C-5 substituent in these sugars[6].

TABLE V

OBSERVED DIFFERENCES[a] IN CHEMICAL SHIFTS (p.p.m.) OF SKELETON CARBONS AND PROTONS BETWEEN PERMETHYLATED ALDOHEXOPYRANOSES AND 6-DEOXYALDOHEXOPYRANOSES

Configuration	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*H-1*	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*
α-D-Glc*p*	−0.06	+0.27	−0.24	+5.93	−3.82	−54.24	−0.04	+0.01	−0.03	−0.31	+0.02	−2.3
β-D-Glc*p*	−0.16	+0.27	−0.19	+5.66	−3.81	−54.28	−0.02	+0.01	−0.04	−0.29	−0.03	−2.3
α-D-Gal*p*	−0.01	−0.20	+0.28	+2.80	−3.05	−55.59	−0.06	−0.01	−0.03	−0.21	0.00	−2.3
β-D-Gal*p*	−0.04	−0.17	+0.42	+3.03	−2.98	−55.13	−0.05	−0.05	−0.04	−0.22	—[b]	−2.3
α-D-Man*p*	−0.04	+0.25	−0.13	+5.78	−3.80	−54.32	−0.04	0.00	−0.03	−0.29	+0.02	−2.3
β-D-Man*p*	−0.13	+0.22	−0.08	+5.66	−3.86	−54.42	−0.01	−0.01	−0.07	−0.27	−0.04	−2.3

[a]A positive value implies a decreased shielding of the atom in the 6-deoxy sugar with respect to the parent aldohexopyranose. [b]Cannot be calculated.

MeO-2(*ax*) in **9–12** and MeO-4(*ax*) in **5–8** resonate 0.7–1.1 p.p.m. downfield from the corresponding, equatorially oriented substituents in **1–4**, respectively. Apparently, the steric orientation of these MeO groups as such has only a small influence on their ^{13}C chemical shift.

Change of anomeric configuration from $\beta \rightarrow \alpha$ results in an upfield ^{13}C shift of 2.0–2.2 p.p.m. for MeO-2(*eq* or *ax*). Similarly, MeO-3(*eq*) shows an upfield-shift increment of ~2.5 p.p.m. in **5–8** and of ~3.3 p.p.m. in **9–12** with respect to MeO-3(*eq*) in **1–4**. In conclusion, the positions of the carbon resonances of MeO-2 and MeO-3 depend strongly on the steric orientation of the substituents at adjacent skeleton carbons. Probably this also holds for MeO-4, but permethylated allopyranose has not yet been investigated. The ^{13}C chemical shift of MeO-6 is not influenced by anomeric or epimeric changes.

Similar trends are observed for the chemical shifts of the MeO groups in the ^{1}H-n.m.r. spectra (*cf.* Frasca *et al.*[8] and Rathbone *et al.*[9] for partially methylated monosaccharides). The ^{1}H chemical shifts of MeO-2 and MeO-4 are independent of their steric orientation.

The dependence of the ^{13}C and ^{1}H chemical shifts of the various MeO groups in compounds **1–12** on their own configuration as well as on the configurations of neighbouring substituents (MeO, CH_2OMe, CH_3) is summarized in Table VI. The ^{13}C and ^{1}H resonances of an MeO group (*eq* or *ax*), situated between two equatorially oriented substituents, appear at lower field than those of an MeO group (*eq* or *ax*, respectively) flanked by one equatorial and one axial substituent. The ranges found for equatorial MeO groups are in agreement with the data of Dorman and Roberts for partially methylated inositols[3]. The differences in chemical shift may result from particular preferences in the rotational conformations of the (neighbouring) substituents. Because of the adjacent polar bonds present in these structures, the contributions of different staggered rotamers to the mixture of conformational isomers will be dependent on the number of gauche interactions present in each rotamer[10,11]. However, the equal signs of the shift increments observed for ^{1}H and ^{13}C of an MeO group cannot be explained from the steric compression effect only, because this effect will cause downfield shifts for ^{1}H resonances and upfield shifts for ^{13}C resonances[12]. Therefore, it is proposed that the downfield, steric compression shift of the protons is more than offset by electric field and anisotropy effects arising from the neighbouring C–O–C fragments.

The ^{13}C and ^{1}H shift increments for MeO-1 between corresponding α- and β-glycosides arise from two important contributions. (*1*) An axial MeO-1 group (α-glycoside) experiences a larger steric compression effect than an equatorial MeO-1 group (β-glycoside), resulting in an upfield ^{13}C chemical shift and a downfield ^{1}H chemical shift. This does not hold for MeO groups in other ring positions, because the steric perturbation of the ring on an axially oriented group is more than balanced by the steric perturbation of neighbouring substituents on an equatorially oriented group (Table VI). (*2*) MeO-1(*eq*) and MeO-1(*ax*) have different orientations with respect to the lone-pair electrons of the ring oxygen. The electric field of these electron pairs has

a larger shielding effect on the protons of MeO-1(*ax*) than on those of MeO-1(*eq*), whereas the difference in shielding effect for the carbons is only relatively small. As a net result of the interactions mentioned under (*1*) and (*2*), the carbon and protons of MeO-1(*ax*) resonate upfield from the corresponding atoms of MeO-1(*eq*).

TABLE VI

CHEMICAL-SHIFT RANGES OF AXIAL AND EQUATORIAL MeO GROUPS AS A FUNCTION OF THE CONFIGURATION OF ADJACENT SUBSTITUENTS

Configuration[a]		δ ^{13}C (*p.p.m.*)	δ ^{1}H (*p.p.m.*)
eq EQ	*eq*	60.37–60.76	3.39–3.51
ax EQ	*eq*	57.26–58.52	3.35–3.40
eq AX	*eq*	61.22–61.77	3.42–3.47
ax AX	*eq*	59.11	3.37
eq MeO-1 (EQ)	—	56.73–56.96	3.39–3.41
ax MeO-1 (EQ)	—	56.99–57.17	3.38
eq MeO-1 (AX)	—	55.17–55.30	3.27–3.29
ax MeO-1 (AX)	—	55.05–55.12	3.28
— MeO-6	—	59.18–59.30	3.30–3.31

[a]The configuration of the considered MeO group (EQuatorial or AXial) is placed between the configurations of the adjacent ring substituents.

The change in substituent at C-5 from CH_2OMe to CH_3 introduces small downfield incremental shifts in the ^{13}C and ^{1}H resonances of MeO-4 [for MeO-4(*eq*): 0.09–0.18 p.p.m. (^{13}C) and 0.03 p.p.m. (^{1}H); for MeO-4(*ax*): 0.46–0.49 p.p.m. (^{13}C) and 0.04–0.05 p.p.m. (^{1}H)]. Also, these shifts can reasonably be interpreted in terms of electric field and steric effects.

EXPERIMENTAL

Monosaccharide derivatives were permethylated according to the method of Kuhn[13], using MeI or CD_3I (99% D, Merck) as appropriate. Separation of anomers was effected by t.l.c. on silica gel G (Merck), using hexane–acetone (3:2), detection with u.v. light after spraying with 1% of morin in methanol, and extraction from the silica gel with chloroform. D-Mannose yielded only a few % of the β pyranoid form on methylation, as well as on methyl glycosidation (methanol–M HCl, 24 h, 85°). Methylation of D-galactose or of L-fucose yielded mainly the furanoid forms; formation of the pyranoid forms was favoured by methyl glycosidation before permethylation.

^{1}H-N.m.r. data for intermediate compounds in the syntheses of the specifically trideuteriomethylated mannoses **13–17** and the rhamnose derivative **18** were determined at 60 MHz and 25°. Chemical shifts (δ) are given relative to internal Me_4Si: s, singlet, d, doublet.

Deuteriomethyl derivatives. — Permethylated D-mannopyranose was hydrolysed (0.25M H_2SO_4, 100°, 16 h), the neutralised ($BaCO_3$) hydrolysate was dried, and the product was methylated with CD_3I to give trideuteriomethyl 2,3,4,6-tetra-*O*-methyl-α-D-mannopyranoside (**13**).

Likewise, methyl 2,3,4-tri-*O*-methyl-α-D-mannopyranoside[14] (b.p. 160°/0.02 mmHg) [n.m.r. data ($CDCl_3$): δ 4.85 (d, $J_{1,2}$ ~1.5 Hz, H-1), 3.42 (s, MeO-1), 3.54 (s, MeO-2,3), 3.59 (s, MeO-4), 2.80 (s, OH), other protons 3.5–3.9] was methylated to give methyl 2,3,4-tri-*O*-methyl-6-*O*-trideuteriomethyl-α-D-mannopyranoside (**14**), and methyl 2,3-di-*O*-methyl-α-D-mannopyranoside[15] [n.m.r. data ($CDCl_3$): δ 4.88 (d, J 1.5 Hz, H-1), 3.46 (s, MeO-1), 3.54 (s, MeO-2,3), 3.71 (s, OH), other protons 3.5–4.2] was converted into methyl 2,3-di-*O*-methyl-4,6-di-*O*-trideuteriomethyl-α-D-mannopyranoside (**15**).

2-*O*-Methyl-D-mannose dibenzyl dithioacetal[16] {m.p. 118°, $[\alpha]_D^{21}$ +34° (*c* 1, chloroform)} was dissolved in methanol and boiled with $HgCl_2$ under reflux[17]. The resulting anomeric mixture of methyl 2-*O*-methyl-D-mannopyranosides was trideuteriomethylated, yielding methyl 2-*O*-methyl-3,4,6-tri-*O*-trideuteriomethyl-α- (**16**) and -β-D-mannopyranoside (**17**).

L-Rhamnose was treated with methanolic hydrogen chloride, neutralised, and methylated with CD_3I to give methyl 2,3,4-tri-*O*-trideuteriomethyl-β-L-rhamnopyranoside (**18**), which was purified by t.l.c.

N.m.r. spectroscopy. — ^{1}H-N.m.r. spectra of solutions (5–20%) of the monosaccharide derivatives in acetonitrile-d_3 or benzene-d_6 were recorded on Varian HA-100 (Organic Chemical Institute T.N.O., Utrecht), HR-220 (T.N.O. Central Laboratories, Delft), or HA-300 spectrometers (Laboratory of n.m.r. spectroscopy, University of Ghent, Belgium). The instruments were operated in the field-sweep mode at a probe temperature of ~25°. Chemical shifts are given relative to that of internal Me_4Si on the δ-scale with an accuracy of 0.005 p.p.m. The accuracy of the coupling constants is ~0.1 Hz. The initial ^{1}H-n.m.r. parameters of the skeleton protons, obtained from first-order subspectral analysis, were refined by calculation of theoretical spectra in an interactive, iterative procedure with the spin-simulation program SIMEQ[18]. In these calculations, the spin system of an aldohexopyranose was treated as a seven-spin system ABCDEFG, and that of a 6-deoxyaldohexopyranose as an eight-spin system X_3ABCDE (CH_3, H-1–H-5). All vicinal coupling constants were taken as positive, and the geminal coupling constant $J_{6,6'}$ was taken as negative[19].

Proton-noise decoupled ^{13}C-n.m.r. spectra of the sugar derivatives were recorded at 25.16 MHz on a Varian XL-100-15 FT spectrometer, operating in the deuterio-lock mode at ~30°. Chemical shifts are given relative to that of internal Me_4Si (δ-scale) with an accuracy of 0.04 p.p.m. Assignments of the resonances of the skeleton carbons of **9** was performed by ^{13}C-{^{1}H} off-resonance spin-decoupling[1].

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REFERENCES

1 J. HAVERKAMP, J. P. C. M. VAN DONGEN, AND J. F. G. VLIEGENTHART, *Tetrahedron*, 29 (1973) 3431.
2 J. HAVERKAMP, J. P. C. M. VAN DONGEN, AND J. F. G. VLIEGENTHART, *Carbohyd. Res.*, 33 (1974) 319.
3 D. E. DORMAN AND J. D. ROBERTS, *J. Amer. Chem. Soc.*, 92 (1970) 1351, 1355.
4 J. B. STOTHERS, *Carbon-13 NMR Spectroscopy*, Academic Press, New York, 1972, p. 464.
5 A. S. PERLIN, B. CASU, AND H. J. KOCH, *Can. J. Chem.*, 48 (1970) 2596.
6 D. G. STREEFKERK, M. J. A. DE BIE, AND J. F. G. VLIEGENTHART, *Tetrahedron*, 29 (1973) 833.
7 D. G. STREEFKERK, M. J. A. DE BIE, AND J. F. G. VLIEGENTHART, *Carbohyd. Res.*, 38 (1974) 47.
8 A. R. FRASCA, I. O. MASTRONARDI, AND E. G. GROS, *Anales Asoc. Quim. Arg.*, 59 (1971) 87.
9 E. B. RATHBONE AND A. M. STEPHEN, *Carbohyd. Res.*, 23 (1972) 275.
10 S. WOLFE, *Accounts Chem. Res.*, 5 (1972) 102.
11 E. L. ELIEL, N. L. ALLINGER, S. J. ANGYAL, AND G. A. MORRISON, *Conformational Analysis*, Wiley–Interscience, New York, 1965, p. 36.
12 Ref. 4, p. 116.
13 R. KUHN, H. TRISCHMANN, AND I. LÖW, *Angew. Chem.*, 67 (1955) 32.
14 W. N. HAWORTH, E. L. HIRST, F. ISHERWOOD, AND J. K. N. JONES, *J. Chem. Soc.*, (1939) 1878.
15 G. O. ASPINALL AND G. ZWEIFEL, *J. Chem. Soc.*, (1957) 2271.
16 E. PACSU AND S. M. TRISTER, *J. Amer. Chem. Soc.*, 63 (1941) 925.
17 E. PACSU AND N. TICHARICH, *Ber.*, 62 (1929) 3008.
18 C. W. F. KORT AND P. J. VAN DER HAAK, University of Amsterdam, personal communication.
19 L. D. HALL AND J. F. MANVILLE, *Carbohyd. Res.*, 4 (1967) 271.