P.M.R. SPECTROSCOPY OF MONOMETHYL ETHERS OF D-GALACTOPYRANOSE AND ITS DERIVATIVES

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ABSTRACT

P.m.r. parameters (determined at 100 MHz for solutions in deuterium oxide) are presented for mono-*O*-methyl derivatives of D-galactopyranose (eight), methyl D-galactopyranoside (ten), and galactitol (four). The effects of methylation of a neighboring hydroxyl group and change in configuration of an adjacent hydroxyl or methoxyl group on the chemical shift of methoxyl and anomeric protons are discussed.

INTRODUCTION

Previous papers[1–4] have described investigations into the p.m.r. spectroscopy of methyl ethers of D-galactopyranose, the methyl D-galactopyranosides, and galactitol, the identification of methyl ethers of D-galactopyranose being one of the aims. Other workers have studied the p.m.r. spectra of solutions (in deuterium oxide and other solvents) of aldohexoses[5–15] and their methyl glycosides[13–21], and *O*-methyl derivatives of these compounds[10,19–24]. In particular, spectra of the monomethyl ethers[19] of D-glucose, D-galactose, and D-mannose (in deuterium oxide) and of certain *O*-methyl derivatives of D-glucopyranose [in *N*,*N*-dimethylformamide[20], chloroform-*d* (Ref. 21), and methyl sulfoxide-d_6 (Ref. 21)] were investigated in order to determine the effect of neighboring hydroxyl or methoxyl groups on the chemical shift of a methoxyl group.

P.m.r. spectra of aldohexoses[7–9] and their methyl ethers[10] have also been used in determining the composition of solutions of these compounds at equilibrium.

Methyl ethers of aldohexoses may be characterized either by comparison of the methoxyl-signal pattern produced in their p.m.r. spectra with those of authentic specimens[2,19], or by conversion of the aldohexose methyl ether into its per(deuteriomethyl)ated methyl glycopyranosides[1,2,24], glycopyranoses[2], or the derived alditol[2], and comparison of the p.m.r. spectrum of the relevant one of these compounds with that of the methyl tetra-*O*-methylglycopyranosides, tetra-*O*-methylglycopyranoses, or tetra-*O*-methylalditol, respectively.

The present paper discusses the p.m.r. spectra of the monomethyl ethers of

D-galactopyranose, methyl α- and β-D-galactopyranoside, and galactitol. Results obtained for the di- and tri-*O*-methyl derivatives of D-galactopyranose will be presented in subsequent articles; the p.m.r. parameters for the tetra-*O*-methyl derivatives have been given in an earlier communication[2]. Consequently, this series of papers constitutes a systematic study of the mono-, di-, tri-, and tetra-*O*-methyl derivatives of D-galactopyranose.

RESULTS AND DISCUSSION

P.m.r. parameters for α- and β-D-galactopyranose (**1** and **2**) and the following derivatives of D-galactopyranose are given in Table I: 2-*O*-methyl-α- and β-D-galactopyranose (**3** and **4**), 3-*O*-methyl-α- and β-D-galactopyranose (**5** and **6**), 4-*O*-methyl-α- and β-D-galactopyranose (**7** and **8**), and 6-*O*-methyl-α- and β-D-galactopyranose (**9** and **10**); methyl α- and β-D-galactopyranoside (**11** and **12**), methyl 2-*O*-methyl-α- and β-D-galactopyranoside (**13** and **14**), methyl 3-*O*-methyl-α- and β-D-galactopyranoside (**15** and **16**), methyl 4-*O*-methyl-α- and β-D-galactopyranoside (**17** and **18**), and methyl 6-*O*-methyl-α- and β-D-galactopyranoside (**19** and **20**); 2-*O*-methyl-D-galactitol (**21**), 3-*O*-methyl-D-galactitol (**22**), 4-*O* -methyl-D-galactitol (**23**), and 6-*O*-methyl-D-galactitol (**24**). The results in Table I have been so set out as to permit easy comparison of methoxyl (and anomeric) proton signals for the D-galactopyranoses (**1–10**) with those for the corresponding methyl D-galactopyranosides (**11–20**). The assignment of methoxyl signals in the p.m.r. spectra of **3–24** is relatively easy, as these compounds contain a maximum of two methoxyl groups each. For solutions in deuterium oxide, methoxyl-group signals showed negligible concentration-dependence.

P.m.r. spectra of monomethyl ethers of D-*galactopyranose.* — (*a*) *Assignment of methoxyl signals.* The 100-MHz p.m.r. parameters (see Table I) of the eight monomethyl ethers of D-galactopyranose (**3–10**) were obtained, for those for which one anomer could be crystallized, by comparing spectra recorded for solutions at 5° (immediately after dissolution of the sample in deuterium oxide) with those of the sample at 32° after equilibration for at least 10 h. The methoxyl signals due to the α and β anomers were then distinguished by noting the change in proportions of the two anomeric forms as indicated by the low-field, H-1 signals.

A similar study of the 60-MHz p.m.r. spectra of monomethyl ethers of D-galactose and two other aldohexoses had been made by Gros *et al.*[19]; at this frequency, it was not possible to distinguish between the 4-methoxyl signals of **7** and **8**, or between the 6-methoxyl signals of **9** and **10**. At 100 MHz, a difference in chemical shift for the 4-methoxyl groups in the anomers of 4-*O*-methyl-D-galactose, and for the 6-methoxyl groups in the anomers of 6-*O*-methyl-D-galactose, has now been observed (see Table I). The chemical shifts found for methoxyl groups in compounds **3–10** and **12** (determined at 100 MHz and 32°) are 0.02–0.06 p.p.m. upfield from those reported in Ref. 19 (at 60 MHz, 38°).

TABLE I

P.M.R. PARAMETERS[a] FOR D-GALACTOPYRANOSE AND ITS DERIVATIVES

Compound		*Position(s) of O-methyl substitution*	*H-1*		$J_{1,2}$[b]		*1-OMe*		*2-OMe*		*3-OMe*		*4-OMe*		*6-OMe*	
α	β		α	β	α	β	α	β	α	β	α	β	α	β	α	β
1[c],	**2**[c]		4.75	5.43	3.0	7.1										
3,	**4**	2	4.54	5.41	3.5	7.9			6.56	6.43						
5,	**6**	3	4.76	5.42	3.9	7.5					6.57	6.57				
7,	**8**[d]	4	4.79	5.48	3.8	7.6							6.51	6.495		
9,	**10**	6	4.77	5.44	3.2	7.5									6.63	6.62
11[e],	**12**[e]	1	5.17	5.705	3.2	7.0	6.61	6.445								
13,	**14**	1,2	4.95	5.67	3.75	7.7	6.60	6.44[f]	6.545	6.45[f]						
15,	**16**	1,3	5.16	5.68	4.0	7.5	6.63	6.44			6.58	6.57				
17,	**18**[g]	1,4	5.20	5.73	3.3	7.6	6.61	6.45					6.50	6.50		
19,	**20**	1,6	5.195	5.70	3.25	7.3	6.61[h]	6.44							6.62[h]	6.60
21		2							6.50							
22		3									6.52					
23		4											6.52			
24		6													6.61	

[a]Determined at 100 MHz for deuterium oxide solutions at 32°. Chemical shifts are relative to internal sodium 4,4-dimethyl-4-silapentanesulfonate (τ′ scale). [b]Observed spacings of the doublets (in Hz). [c]Compare with Refs. 9–11. [d]Compare with Ref. 19. [e]Compare with Refs. 16 and 18–20. [f]These assignments may have to be reversed. [g]Compare with Ref. 22. [h]These assignments may have to be reversed.

(b) *Chemical shifts of anomeric protons.* The effect of methylation at O-2 on the chemical shifts of the anomeric protons in D-galactopyranose is significant only for the α anomer (a decrease of 0.21 p.p.m.). Methylation at O-3, O-4, and O-6 has a negligible effect on the H-1 chemical shift of either anomer.

The changes in the observed spacings of the H-1 doublets indicate possible distortions of the *C1* (D) conformation of the D-galactopyranose on methylation at O-2, O-3, O-4, and O-6.

(c) *Chemical shifts of methoxyl-group protons.* As was noted earlier[3], there is a relatively large difference (of 0.13 p.p.m.) in chemical shift for the 2-methoxyl group in **3** as compared with that in **4**, the methoxyl signal for the β anomer (**4**) appearing at unusually low field. The same effect has been observed (*a*) for the 2-methoxyl group in α and β anomers of both 2-*O*-methyl-D-glucose and 2-*O*-methyl-D-mannose[19] (the 2-methoxyl group appearing 0.14 to 0.16 p.p.m. downfield for the β anomers, compared with the α anomers), and (*b*) when comparing the chemical shifts of the 3-methoxyl groups of 3-*O*-methyl-D-galactoses[19] with those of corresponding anomers of 3-*O*-methyl-D-glucose[19]—the change of the orientation of the neighboring 4-hydroxyl group from axial (in the galactose derivative) to equatorial (in the glucose derivative) produces a downfield shift (of 0.17 to 0.18 p.p.m.) of the 3-methoxyl signal for both anomers. This effect takes places for a change in configuration at C-4, as well as at C-1, showing that it is not peculiar to anomeric change. As may be noted in subsection (*c*) of the next section, an adjacent, equatorially attached methoxyl group/axially attached hydrogen atom causes a similar, but weaker, deshielding of methoxyl protons.

Anomeric change produces negligible differences in 3-, 4-, and 6-methoxyl chemical-shifts, as shown in the spectra of **5** and **6**, **7** and **8**, and **9** and **10**, respectively. The (primary) 6-methoxyl signals of **9** and **10** appear at higher field[3,18,21] than the methoxyl groups on C-2, C-3, and C-4 in compounds **3**–**8**.

The 4- and 6-methoxyl groups of 4-*O*-methyl-D-galactose and 6-*O*-methyl-D-galactose, respectively, absorb at approximately the same chemical shift as they do for 2,3,4,6-tetra-*O*-methyl-D-galactose[2].

P.m.r. spectra of monomethyl ethers of methyl D-*galactopyranoside.* — (a) *Assignment of methoxyl signals.* The p.m.r. spectra of compounds **11**–**20** showed no equilibration effect such as was observed for compounds **1**–**10**; for the anomerically pure methyl glycosides used (**11**–**14**, **16**, **19**, and **20**), a single low-field doublet (H-1) and either one (**11** and **12**) or two (**13**, **14**, **16**, **19**, and **20**) methoxyl signals appeared in their spectra.

P.m.r. parameters for **15** were deduced from a spectrum of a mixture of the methyl α- and β- glycosides (synthesized from **16**; see Experimental section). A mixture of methyl 4-*O*-methyl-α- and β-D-galactopyranoside, prepared by methyl glycosidation of 4-*O*-methyl-D-galactopyranose, was used to obtain a spectrum for (**17**+**18**).

Methoxyl assignments for compounds **15**–**20** were made by using the results obtained for compounds **5**–**12** and assuming that there would be a negligible effect on the 3-, 4-, and 6-methoxyl signals for these compounds by the introduction of a

glycosidic methyl group. There is some doubt about the assignments indicated in Table I for the 1- and 2-methoxyl signals of **14**, and the 1- and 6-methoxyl signals of **19**. In the spectra of **14** and **19**, these signals appear close to each other (with ~0.01 p.p.m. separation). Assignments for the spectrum of **14** were, nevertheless, made by comparison with the 1-methoxyl signal for methyl 2,3,4,6-tetra-*O*-methyl-β-D-galactopyranoside, and for that of **19**, by comparing the methoxyl chemical shifts with the 1-methoxyl signal for **11** and noting the relative positions of the 1- and 6-methoxyl signals for methyl 2,3,4,6-tetra-*O*-methyl-α-D-galactopyranoside.

(b) *Chemical shifts of anomeric protons.* The anomeric-proton signals for the methyl glycosides (**11–20**) appear, on the average, 0.41 p.p.m. (α anomers) and 0.26 p.p.m. (β anomers) upfield from the corresponding signals of the D-galactopyranoses (**1–10**). As found for compounds **1–10**, the effect of introducing an additional methyl group (into **11** and **12**) is significant only for methylation at O-2 in the α anomer (**13**), a decrease of 0.22 p.p.m. being observed (as compared with **11**). The anomeric-proton signals are affected only very slightly by methylation at O-3, O-4, and O-6.

The couplings observed between H-1 and H-2 suggest that the *C1* (D) conformation is retained, with minor distortions of the ring, on methylation of the hydroxyl substituents, one at a time.

(c) *Chemical shifts of methoxyl-group protons.* The introduction of a glycosidic methyl group into compounds **3–10** was assumed to have a negligible effect on the 3-, 4-, and 6-methoxyl signals. The same assumption was made regarding the 2-methoxyl signals of **13** and **14**, as these signals appear at much the same chemical shifts as they do in the spectra of **3** and **4**, respectively.

The effect of a change in configuration at C-1 (α to β, from axially to equatorially attached OMe) is a downfield shift (0.10 p.p.m.) of the 2-methoxyl signal, the chemical shift of the 1-methoxyl group itself decreasing by 0.16 p.p.m. The 3-, 4-, and 6-methoxyl signals are not affected significantly by anomeric change.

Methylation at O-2, O-3, O-4, or O-6 has a negligible effect on the 1-methoxyl chemical-shift of either the methyl α- or β-glycosides (**13–20**).

P.m.r. spectra of monomethyl ethers of galactitol. — The p.m.r. spectrum of each of the mono-*O*-methyl-galactitols studied (**21–24**) shows one methoxyl signal only. No low-field signals corresponding to anomeric protons were observed, indicating completeness of reduction of the sugar in each preparation of the respective alditol. The (primary) 6-methoxyl signal (compound **24**) appears at highest field and at approximately the same chemical shift as it does in the spectra of compounds **9**, **10**, **19**, and **20**. The 2-, 3-, and 4-methoxyl groups absorb over a smaller range (τ′ 6.50–6.52) than for the D-galactopyranoses (**3–8**; τ′ 6.43–6.57) and methyl D-galactopyranosides (**13–18**; τ′ 6.45–6.58).

These spectra may, in certain cases*, be used to determine the position of

*The spectrum of 3-*O*-methyl-D,L-galactitol (obtained by Dr. L. D. Hayward, University of British Columbia) shows one unresolved methoxyl signal, which implies that 3- and 4-*O*-methyl-D-galactitol cannot be distinguished by this means.

TABLE II

P.M.R. PARAMETERS[a] FOR INTERMEDIATES USED IN THE SYNTHESIS OF MONOMETHYL ETHERS OF D-GALACTOPYRANOSE AND ITS DERIVATIVES

Compound	*Solvent*	*Galactose C-H protons*	*J*	*Methoxyl protons*[b]	*Substituent protons*[c]
25	$CDCl_3$[d]	H-1, 4.43; H-2, 5.37; H-3, 5.66; H-4, 5.73; other, 6.0–6.4	$J_{1,2}$ 5.0, $J_{2,3}$ 2.4; $J_{3,4}$ 7.8, $J_{4,5}$ 1.4		CMe_2: 8.46, 8.55, 8.655, 8.655 CMe_2: 8.45, 8.555, 8.64, 8.64
				C-6, 6.625	CMe_2: 8.47, 8.56, 8.67, 8.67
	D_2O	H-1, 4.40; other, 5.1–6.4	$J_{1,2}$ 5.0		
26[e]	$CDCl_3$	H-1, 4.49; H-2, 5.72; H-3, 5.41; H-4, 5.80; H-5, 6.10; other, 6.4–6.6	$J_{1,2}$ 5.0, $J_{2,3}$ 2.4, $J_{3,4}$ 7.8, $J_{4,5}$ 1.9		
27	$CDCl_3$	H-1,2,3,4, 4.5–5.1; H-5,6,6′, 5.87		C-1, 6.60	OAc: 7.87, 7.93, 7.965, 8.03
28	C_5D_5N	H-1, 4.93; other, 5.1–5.9	$J_{1,2}$ 3.0	C-1, 6.63	tosyl (aromatic), 2.02 (d, 2 H), 2.78 (d, 2 H), *J* 8.5; tosyl Me, 7.80; OH, 3.57
	$(CD_3)_2SO$	H-1, 5.39; other, 5.7–6.6	$J_{1,2}$ 2.0	C-1, 6.73	tosyl (aromatic), 2.17 (d, 2 H), 2.52 (d, 2 H) *J*, 8.2; tosyl Me, 7.53
29	$CDCl_3$	H-1, 5.275; other, 5.5-6.5	$J_{1,2}$ 3.7	C-1, 6.575	tosyl (aromatic), 2.15 (d, 2 H), 2.63 (d, 2 H), *J* 8.3; tosyl Me, 7.53; CMe_2, 8.57, 8.70
30	$CDCl_3$	H-1, 5.24; other, 5.6-6.6	$J_{1,2}$ 3.5	6.62, 6.495	tosyl (aromatic), 2.20 (d, 2 H), 2.70 (d, 2 H), *J* 8.5; tosyl Me, 7.53; CMe_2, 8.515, 8.69
31	$CDCl_3$	H-1, 5.20; other, 5.6-6.8	$J_{1,2}$ 3.5	6.61, 6.51	CMe_2, 8.48, 8.66; OH, 7.51
32	$CDCl_3$[f]	H-1, 5.83; other, 5.7-6.6	$J_{1,2}$ 7.5	C-1, 6.43	CMe_2, 8.48, 8.65; OH, 7.78
	D_2O	H-1, 5.68; other, 5.6-6.6	$J_{1,2}$ 8.0	C-1, 6.44	CMe_2, 8.48, 8.63
33	$CDCl_3$	5.7–7.0		C-1, 6.49	CMe_2, 8.535, 8.66; OH, 7.22; trityl, 2.4–2.9 (m)

34	$CDCl_3$	H-1, 5.89; other, 5.7–7.0	$J_{1,2}$ 8.0	6.45, 6.49	CMe_2, 8.525, 8.67; trityl, 2.4–2.9 (m)
35	$CDCl_3$	H-1,3,4,5, 5.5–6.2; H-2,6,6′, 4.7–5.5		C-1, 6.51	CMe_2, 8.43, 8.63
36	D_2O	H-1, 5.405; H-2, 4.80; H-3, 6.14; H-4,5, 6.1–6.5; H-6,6′, 5.4–5.7	$J_{1,2}$ 8.2, $J_{2,3}$ 9.8, $J_{3,4}$ 3.6	C-1, 6.455	
37[c]	$CDCl_3$	H-1, 5.67; H-2, 4.72; H-3, 6.625; H-4, 5.83; H-5, 6.23; H-6, 5.07; H-6′, 5.30	$J_{1,2}$ 8.2, $J_{2,3}$ 10.0, $J_{3,4}$ 3.5, $J_{4,5}$ 1.4, $J_{5,6}$ 6.5, $J_{5,6'}$ 5.0, $J_{6,6'}$ −12.1	6.475, 6.50	OH, 7.39
38[e]	$CDCl_3$	5.7–6.6		C-1, 6.41	C_6H_5CH, 2.4–2.7 (m); C_6H_5CH, 4.42; OH, 7.50
39[e]	$CDCl_3$	5.1–6.9		C-1, 6.45	C_6H_5CH and $C_6H_5CH_2$, 2.3–2.9 (m); C_6H_5CH, 4.54; $C_6H_5CH_AH_B$ (C-2): H_A, 5.04 (d); H_B, 5.29 (d); $J_{A,B}$ 10.9; $C_6HC_5H_2$ (C-3), 5.26
40	$CDCl_3$	H-1, 5.72; H-2,3, 5.1–5.5; H-4,6,6′, 5.9–6.7	$J_{1,2}$ 7.5	C-1, 6.44	$C_6H_5CH_2$, 2.6–2.8 (m); $C_6H_5CH_AH_B$ (C-2): H_A, 5.07 (d); H_B, 5.28 (d); $J_{A,B}$ 10.9; $C_6H_5CH_2$ (C-3), 5.28

[a]Determined at 60 MHz at 37°. Chemical shifts are relative to internal tetramethylsilane (τ scale) for chloroform-*d*, acetone-d_6, and pyridine-d_5 solutions; relative to sodium 4,4-dimethyl-4-silapentanesulfonate (τ' scale) for solutions in deuterium oxide. J = observed spacings (in Hz). [b]3-Proton singlets. [c]Singlets, unless otherwise stated; d = doublet, m = multiplet. [d]Compare Ref. 25. [e]Analyzed on a first-order basis, by using the expected multiplicities of the proton signals. [f]Compare Ref. 26. [g]Compare Ref. 32.

substitution in a mono-*O*-methyl derivative of D-galactopyranose (after suitable reduction).

EXPERIMENTAL

Compounds **9–14** and **19** were synthesized by known methods, as indicated. P.m.r. parameters for the intermediate compounds (**25–34**) used in the synthesis of these compounds, as well as of those used for the preparation of **16** (namely, **35–37**) and **20** (namely, **38–40**) are listed in Table II.

6-O-*Methyl*-D-*galactose* (**9**+**10**). — Methylation of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose[27] (**25**) afforded 1,2:3,4-di-*O*-isopropylidene-6-*O*-methyl-α-D-galactopyranose[28] (**26**), which was hydrolyzed to 6-*O*-methyl-D-galactose[28] (**9**+**10**).

Methyl α-D-*galactopyranoside* (**11**). — Methyl 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranoside[29] (**27**) was deacetylated to give pure **11** (Ref. 30).

Methyl β-D-*galactopyranoside* (**12**). — Compound **12** (Refs. 31 and 32) was prepared[33] from 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide[34] by a Koenigs–Knorr reaction with methanol, followed by deacetylation. P.m.r. parameters of the intermediates obtained in this synthesis agreed with reported values[35,36].

Methyl 2-O-*methyl*-α-D-*galactopyranoside* (**13**). — Methyl 6-*O*-*p*-tolylsulfonyl-α-D-galactopyranoside[37] (**28**) was treated with acetone to yield methyl 3,4-*O*-isopropylidene-6-*O*-*p*-tolylsulfonyl-α-D-galactopyranoside[37] (**29**), which was methylated to give methyl 3,4-*O*-isopropylidene-2-*O*-methyl-6-*O*-*p*-tolylsulfonyl-α-D-galactopyranoside[37] (**30**). Reductive desulfonylation[38] with sodium amalgam in methanol afforded methyl 3,4-*O*-isopropylidene-2-*O*-methyl-α-D-galactopyranoside[37] (**31**). Mild hydrolysis of **31** with acid gave **13** (Ref. 37).

Methyl 2-O-*methyl*-β-D-*galactopyranoside* (**14**). — Methyl 3,4-*O*-isopropylidene-β-D-galactopyranoside[37] (**32**) was treated with chlorotriphenylmethane to produce methyl 3,4-*O*-isopropylidene-6-*O*-trityl-β-D-galactopyranoside[39] (**33**). Methylation of **33** with methyl iodide–silver oxide afforded methyl 3,4-*O*-isopropylidene-2-*O*-methyl-6-*O*-trityl-β-D-galactopyranoside[37] (**34**). Hydrolysis of **34** with 90% trifluoroacetic acid[40] removed the isopropylidene and trityl groups, yielding **14** (Ref. 37).

Methyl 3-O-*methyl*-β-D-*galactopyranoside* (**16**). — Compound **32** (5.1 g) was nitrated[41], to produce methyl 3,4-*O*-isopropylidene-β-D-galactopyranoside 2,6-dinitrate[42] (**35**); hydrolysis with 90% trifluoroacetic acid[40] afforded methyl β-D-galactopyranoside 2,6-dinitrate[42] (**36**, 3.86 g), which was methylated for 18 h with methyl iodide–silver oxide. The syrupy product was extracted with cold carbon tetrachloride, and the undissolved residue (which crystallized on addition of carbon tetrachloride) was remethylated. These steps were repeated three times, the carbon tetrachloride extracts being combined after each methylation. At this stage, approximately equal amounts of the mono- and di-*O*-methyl derivatives had formed, with only a trace of the starting material remaining [t.l.c. on silica gel, with 5:1 (v/v) chloroform–methanol]. This mixture was added to the carbon tetrachloride extracts,

and the components were separated on a column (180 × 30 mm) of silica gel (150 g) by using chloroform as the eluant. Methyl 3,4-di-*O*-methyl-β-D-galactopyranoside 2,6-dinitrate[42] was eluted first, and this was followed by methyl 3-*O*-methyl-β-D-galactopyranoside 2,6-dinitrate (**37**). Recrystallisation of the latter from aqueous methanol afforded **37** (1.21 g), m.p. 117°, $[\alpha]_D$ +12.6° (*c* 2.4, chloroform).

Anal. Calc. for $C_8H_{14}N_2O_{10}$: C, 32.2; H, 4.7; N, 9.4; OCH_3, 20.8. Found: C, 32.5; H, 4.9; N, 9.3; OCH_3, 20.5.

A 30% solution of sodium hydroxide (10 ml) was saturated with hydrogen sulfide, and added to a solution of **40** (0.9 g) in ethanol (20 ml), and the mixture was boiled for 0.5 h under reflux[42]. Evaporation of the resulting mixture yielded a syrup which was treated with methanol, the suspension filtered, and the filtrate evaporated to afford crude **16**. Purification by column chromatography on silica gel with 5:1 chloroform–methanol yielded **16** (0.6 g) as a colorless, hygroscopic syrup[30], $[\alpha]_D$ +30.6° (*c* 2.1, water).

Hydrolysis of **16** afforded syrupy 3-*O*-methyl-D-galactose[30,43] (**5**+**6**), a portion of which was reduced to 3-*O*-methyl-D-galactitol. Recrystallization from ethanol afforded pure **22**, m.p. 156–7°, $[\alpha]_D$ −17.7° (*c* 1.98, water).

Anal. Calc. for $C_7H_{16}O_6$: C, 42.9; H, 8.2. Found: C, 42.9; H, 8.2.

Treatment of **16** with 2% methanolic hydrogen chloride gave a mixture of **15** and **16** which was used to obtain the p.m.r. parameters for the α-D-glycoside **15**.

Methyl glycosidation of 4-O-methyl-D-galactose. — Methyl glycosidation of 4-*O*-methyl-D-galactose (**7**+**8**) with 2% methanolic hydrogen chloride yielded a mixture of methyl 4-*O*-methyl-α- and β-D-galactopyranoside (~80% of **17**, and 20% of **18**) which was used to obtain their p.m.r. parameters.

Methyl 6-O-methyl-α-D-galactopyranoside (**19**). — 6-*O*-Methyl-D-galactose (**9**+**10**) was treated with methanolic hydrogen chloride, to give a mixture of the methyl glycosides (mostly **19**, plus some **20**). By fractional recrystallization from methanol, it was possible to obtain the pure α-D-glycoside **19** (Ref. 44).

Methyl 6-O-methyl-β-D-galactopyranoside (**20**). — Methyl 4,6-*O*-benzylidene-β-D-galactopyranoside[45] (**38**) was treated with benzyl chloride to give methyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-galactopyranoside[46] (**39**). Hydrolysis of **39** with 90% trifluoroacetic acid[40] (30 min at room temp.) yielded methyl 2,3-di-*O*-benzyl-β-D-galactopyranoside[46] (**40**). Three methylations of **40** with methyl iodide–silver oxide afforded a mixture of methyl 2,3-di-*O*-benzyl-6-*O*-methyl-β-D-galactopyranoside (major component) and methyl 2,3-di-*O*-benzyl-4,6-di-*O*-methyl-β-D-galactopyranoside[46]. The mixture was dissolved in ethanol and reductively debenzylated[47] with hydrogen at 60 lb. in.$^{-2}$ in the presence of 10% palladium-on-charcoal for 20 h at room temp., to produce a mixture of methyl 6-*O*-methyl-β-D-galactopyranoside (**20**) and methyl 4,6-di-*O*-methyl-β-D-galactopyranoside. Compound **20** was separated by dissolving the mixture in water and extracting the dimethyl ether into chloroform. Methyl 6-*O*-methyl-β-D-galactopyranoside [48] remained in the aqueous layer.

General. — Hydrolysis of methyl glycosides was performed in the usual way

by use of 0.5M sulfuric acid. Galactitol methyl ethers were prepared by reduction[49] of the appropriate *O*-methyl derivatives of D-galactopyranose with sodium borohydride.

P.m.r. spectra (see Table I) were recorded at 100 MHz and 32° with a Varian Associates HA-100 spectrometer for 5–10% solutions in deuterium oxide. Sodium 4,4-dimethyl-4-silapentanesulfonate was used as the internal standard (τ' scale). P.m.r. spectra of the intermediates (see Table II) were recorded at 60 MHz and 37° with a Varian Associates A-60 spectrometer.

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