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CHARACTERISATION OF METHYL DERIVATIVES OF D-GALACTOSE BY NMR SPECTROSCOPY

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Earlier communications described the NMR spectra in D_2O of a number of methyl ethers of D-galactopyranose[1] and of galactitol[2] with particular reference to chemical shifts of the methoxyl protons. The identification of the positions of substitution in a partially or fully methylated derivative of D-galactopyranose is now shown to be feasible by methyl glycosidation of the methylated compound, perdeuteriomethylation[3] of the product, and comparison of the methoxyl chemical shifts in the NMR spectrum run in benzene with those assigned for the methoxyl proton signals of methyl 2,3,4,6-tetra-O-methyl-α- and β-D-galactopyranosides (I and II, respectively). The procedure adopted resembles that employed by Gagnaire and Odier[4] for assignment of methoxyl proton signals in methylated D-glucopyranosides. We have found also that the 60 MHz NMR spectrum of 2,3,4,6-tetra-O-methyl-D-galactitol (≡ 1,3,4,5-tetra-O-methyl-L-galactitol) in either benzene or chloroform shows four separate methoxyl signals, the assignment of which is being made using suitable compounds (obtained from compounds IV to XI, below) containing CD_3 in place of CH_3.

The NMR spectra of I (Fig. 1) and II (Fig. 2) in benzene at 60 MHz, using TMS as internal standard, show five distinct methoxyl proton signals for both α- and β-anomers. NMR spectra in D_2O at 100 MHz (internal standard DSS, giving rise to the τ' scale[1]) showed five separate methoxyl signals for the α-glycoside I (τ' between 6.51 and 6.62) but only four for the β-glycoside II (τ' between 6.45 and 6.59). The assignments indicated in Figs. 1 and 2 were deduced and confirmed (apart from some uncertainty in identifying the C-2 and C-3 methoxyl signals of I) by comparing the methoxyl proton signals with those given by the following synthetic compounds, each compound being in effect fully methylated α- or β-D-galactopyranose

with partial replacement of CH_3 groups by CD_3: methyl 2,3,4,6-tetra-O-methyl-d_3-α-D-galactopyranoside (III), methyl 2-O-methyl-3,4,6-tri-O-methyl-d_3-α-D-galactopyranoside (IV), methyl 2,3-di-O-methyl-4,6-di-O-methyl-d_3-α-D-galactopyranoside (V), methyl 2,3,4-tri-O-methyl-6-O-methyl-d_3-α-D-galactopyranoside (VI), methyl 2,3,6-tri-O-methyl-4-O-methyl-d_3-α-D-galactopyranoside (VII), methyl 2-O-methyl-3,4,6-tri-O-methyl-d_3-β-D-galactopyranoside (VIII), methyl 2,3-di-O-methyl-4,6-di-O-methyl-d_3-β-D-galactopyranoside (IX), methyl 3,4-di-O-methyl-2,6-di-O-methyl-d_3-β-D-galactopyranoside (X) and methyl 2,4,6-tri-O-methyl-3-O-methyl-d_3-β-D-galactopyranoside (XI). Preparation of these compounds was effected by trideuteriomethylation of the free hydroxyl groups in corresponding partially methylated, anomerically pure methyl α- or β-D-galactopyranosides synthesised by adaptation of known procedures. All the above compounds behaved identically on thin-layer chromatography (silica gel; chloroform-methanol, 5:1 v/v).

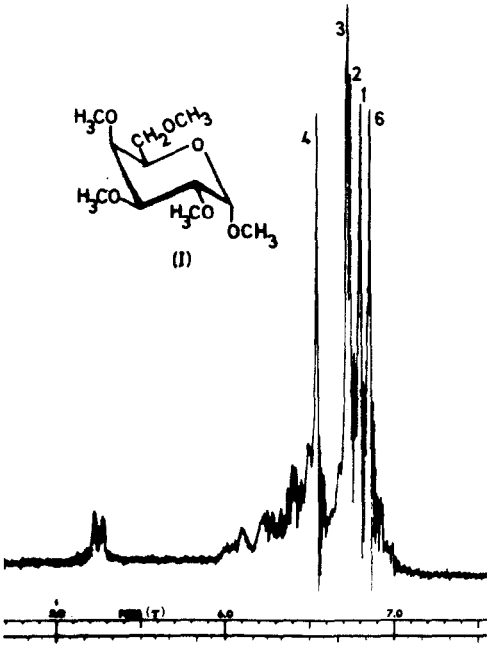

Figure 1

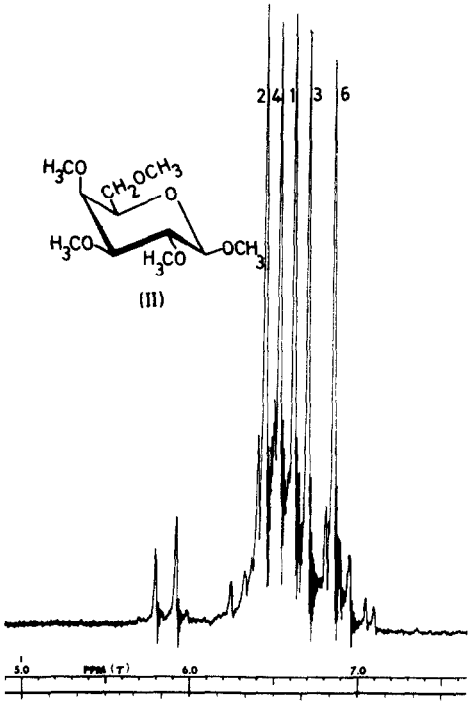

Figure 2

Fig. 1. 60 MHz NMR spectrum of I in benzene at 27°C.

Fig. 2. 60 MHz NMR spectrum of II in benzene at 27°C.

It is apparent from the chemical shifts given in Table I that signals arising from methoxyl groups at C-6, C-4 and C-3 substituted in the methyl-D-galactopyranoside structures are not much affected by anomeric change. On the contrary the C-2 methoxyl signal lies 0.25 ppm upfield in the spectrum of the α-glycoside (C-1 methoxyl axial) compared with that of the β-glycoside (C-1 methoxyl equatorial). A similar effect (with a change in shift of 0.24 ppm) has been observed in the D-glucose series.[4] For NMR spectra in D_2O, the difference in chemical shift of the methoxyl groups in the α and β forms of 2-O-methyl-D-galactopyranose was reported earlier[1] to be 0.13 ppm (shifted in the same direction), and we have recently observed[5] a corresponding difference in shift for the C-2 methoxyl signals of the methyl 2-O-methyl-α- and β-D-galactopyranosides.

TABLE I

Chemical shifts obtained from 60 MHz NMR spectra of compounds I - XI in benzene at 27°

Compound	Position(s) of OCH_3 group(s)	Position(s) of OCD_3 group(s)	Chemical shifts (τ scale) of methoxyl proton signals at carbon(s)				
			1	2	3	4	6
I	1α,2,3,4,6	-	6.76	6.70	6.69	6.52	6.82
II	1β,2,3,4,6	-	6.61	6.45	6.69	6.53	6.84
III	1α	2,3,4,6	6.76				
IV	1α,2	3,4,6	6.76	6.70			
V	1α,2,3	4,6	6.76	6.70	6.69		
VI	1α,2,3,4	6	6.76	6.70	6.69	6.52	
VII	1α,2,3,6	4	6.76	6.70	6.69		6.82
VIII	1β,2	3,4,6	6.61	6.45			
IX	1β,2,3	4,6	6.61	6.45	6.69		
X	1β,3,4	2,6	6.61		6.69	6.53	
XI	1β,2,4,6	3	6.61	6.45		6.53	6.84

The chemical shift of the anomeric methoxyl group in the fully methylated D-galactopyranoses changes from τ6.76 to τ6.61 when the configuration is changed from α (compound I) to β (compound II), a difference of 0.15 ppm. In the corresponding methylated D-glucopyranoses, the difference in chemical shift was found to be 0.14 ppm in the same direction.[4] A similar downfield shift of 0.16 ppm is found in the NMR spectra of methyl α-D-galactopyranoside (OMe, τ6.61) and methyl β-D-galactopyranoside (OMe, τ6.45) run in D_2O.[5]

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