Note

Proton magnetic resonance spectra of methyl ethers of disaccharides; chemical shifts of anomeric protons

D. E. MINNIKIN
Microbiological Chemistry Research Laboratory, School of Chemistry, The University, Newcastle upon Tyne, NE1 7RU (Great Britain)

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INTRODUCTION

Proton magnetic resonance (p.m.r.) spectroscopy has been used occasionally in recent years for the determination of anomeric configuration of naturally occurring glycosides. The stereochemistry of the inter-sugar linkages may be revealed by inspection of the coupling constants of the anomeric protons. A systematic study of model glycosides[1] was followed by a comprehensive p.m.r. investigation of the water-soluble glycosides from the mannolipids of Mycobacteria[2,3]. Other workers have occasionally employed p.m.r. spectroscopy to deacylation products of various glycolipids[4-6], and a further systematic study of free oligosaccharides has been made[7].

Examination of derivatives soluble in organic solvents would have the advantage over the use of aqueous solutions that solvent effects, for example benzene-induced shifts, could be explored. Acetyl derivatives have the disadvantage that anomeric protons may have chemical shifts in the same region of the spectrum as the ring –*CH*(OAc)– resonances. Methyl and trimethylsilyl ethers would be expected to be suitable for p.m.r. spectroscopy, since the signals due to anomeric protons should occupy a region of the spectrum free from other peaks. Systematic studies of trimethylsilyl ether derivatives in acetone-d_6[8] and carbon tetrachloride[9] have been made, and these derivatives were used in the assignment of anomeric configuration of glycosides derived from bacterial lipopolysaccharides[10-12]. A permethylated glycolipid from Streptomyces has been partially characterised by p.m.r. spectroscopy[13], but methyl ethers of oligosaccharides have not been systematically studied. This note reports details of the chemical shifts of the anomeric protons of the methyl ethers of some disaccharides.

EXPERIMENTAL

Disaccharides and D-glucose were methylated by the procedure of Brimacombe *et al.*[14], involving treatment with sodium hydride and iodomethane in *N*,*N*-dimethylformamide. The methylated derivatives were purified by preparative thin-layer chromatography (Merck Silica gel PF 254+366; hexane–acetone, 60:40). In two examples (maltose and cellobiose), both α- and β-glycosides were obtained, but usually the predominant β isomer was isolated, being easily separated from a trace of the α isomer.

P.m.r. spectra were taken on a Bruker HFX 90-MHz spectrometer for solutions in deuteriochloroform and benzene, using tetramethylsilane as internal standard.

RESULTS AND DISCUSSION

In considering the p.m.r. spectra of methyl ethers of disaccharides, it is necessary to distinguish between signals due to inter-sugar and methyl glycosidic, anomeric protons. Each methylated disaccharide (except trehalose) showed two separate signals due to anomeric protons (Figs. 1 and 2). The signal at higher field is assigned to the methyl glucosidic proton since it corresponds more closely to the signals due to the anomeric protons of methyl per-*O*-methyl-α- and β-D-glucosides. This assignment is confirmed for the methyl ethers of maltose and cellobiose by an investigation of the spectra of both methyl α- and β-glycoside derivatives.

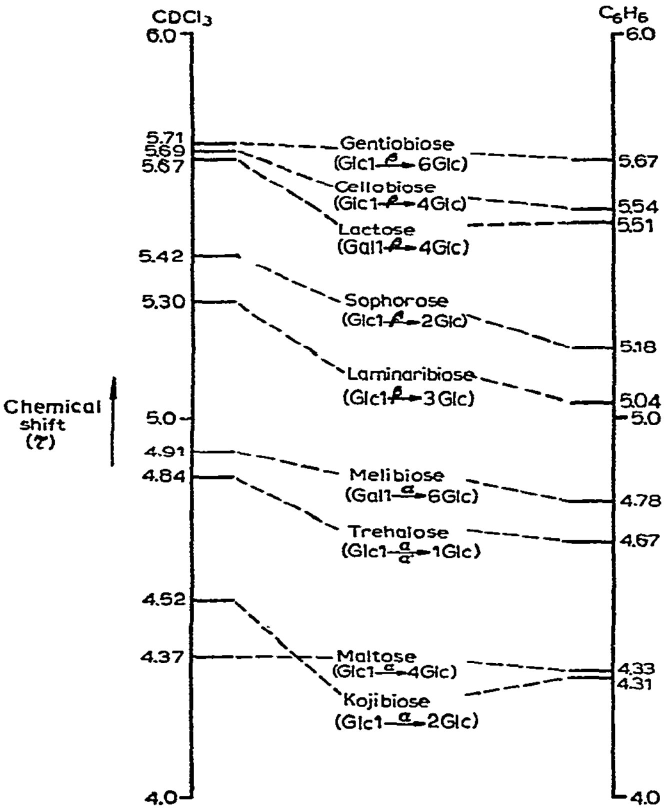

Fig. 1. Chemical shifts of the anomeric protons at the inter-sugar linkages of methylated disaccharides.

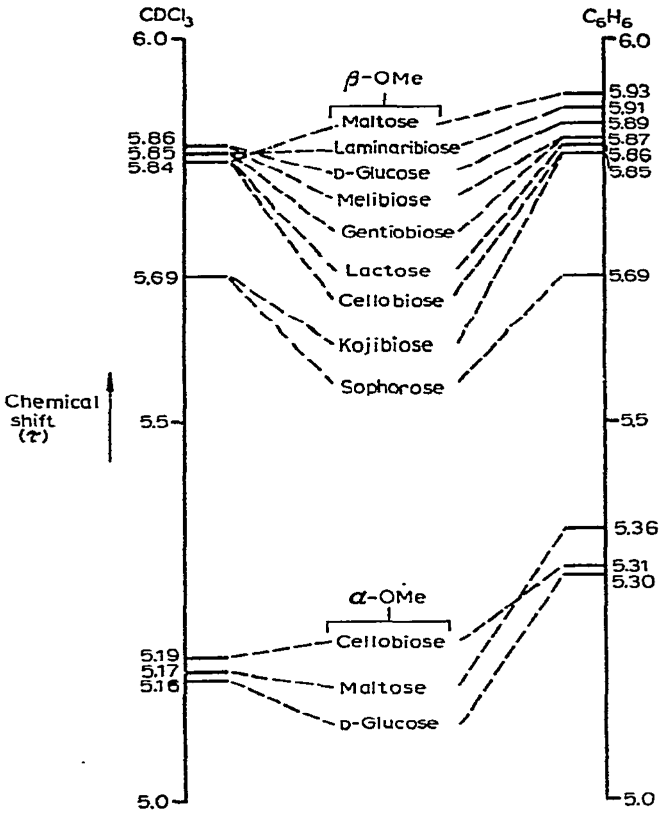

Fig. 2. Chemical shifts of the methyl D-glucosidic, anomeric protons of methylated disaccharides and D-glucose.

The p.m.r. chemical shifts of the anomeric protons at the inter-sugar linkages of a selection of methylated disaccharides are represented in Fig. 1. It is notable that, whereas the chemical shifts of the anomeric protons of the inter-sugar α-linkages (doublet, J 3.5 Hz) are concentrated in the region τ 4.3–5.0, those of the corresponding β-linkages (doublet, J 7.0 Hz) are up-field in the region τ 5.0–6.0. The spectra of trimethylsilyl ethers of disaccharides in carbon tetrachloride[9] show similar relationships but the separation of the anomeric proton signals of α- and β-linkages is not as great.

The chemical shifts of the methyl glucosidic, anomeric protons of the methylated disaccharides and D-glucose are shown in Fig. 2. As was found with the inter-sugar linkages, the α-anomeric protons show signals (doublet, J 3.5 Hz) in a region (τ 5.0–5.5) distinct from that (τ 5.5–6.0) occupied by signals (doublet, J 7.0 Hz) due to β-anomeric protons.

Change of solvent from deuteriochloroform to benzene enables signals due to anomeric protons at inter-sugar linkages to be distinguished from those of the methyl glycosidic group; the former are shifted down-field and the latter up-field. The numerical value of the shift induced by change of solvent varies with the position of the inter-sugar linkage and may have diagnostic value. Sophorose is notable in that the signal for the methyl glycosidic, anomeric protons does not shift on change of solvent; this is in contrast to the behaviour of kojibiose, the other (1→2)-linked disaccharide, which shows a shift in the same direction as the other disaccharides. Significant solvent effects have been observed in the p.m.r. spectra of acetylated monosaccharides[15], but this work has not been extended to disaccharides.

The chemical shifts of the anomeric protons at the inter-sugar linkages of methyl α-glycosides of maltose and cellobiose were found at τ 4.32 and 5.73 (in deuteriochloroform) and at τ 4.23 and 5.49 (in benzene), respectively. On comparison with the values shown in Fig. 1 for the methyl β-D-glycosides, it is apparent that the chemical shift of the anomeric protons at the inter-sugar linkages is sensitive to the sterochemistry of the methyl glycosidic group, at least in the two examples studied.

In the spectra of the methylated disaccharides considered in this study, the signals due to methyl glucosidic, anomeric protons were always encountered at higher field than those due to inter-sugar linkage protons. The results outlined above, however, indicate that this might not be a general rule. For example, methyl α-sophoroside and laminaribioside methyl ethers might be expected to have their signals due to both anomeric protons in the same region of the spectrum.

The results presented here illustrate the potential of the p.m.r. spectroscopic method for determination of the stereochemistry, and even position, of inter-sugar linkages of oligosaccharides as their permethyl ethers. Recent reports on the characterisation of the methoxyl p.m.r. signals of glucose[16] and galactose[17] methyl ethers suggest that a close study of the methoxyl resonances of methylated oligosaccharides would also be of value.

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