Mutarotational Equilibrium in Water of 3-*O*-Methyl-D-glucose and 3-*O*-Methyl-D-xylose

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In their extensive studies of pyranose-furanose equilibria of aldoses and deoxyaldoses,[1-4] Angyal and Pickles have observed that the proportion of furanose forms in aqueous solution of 3-deoxyglucose is much higher than that for glucose, for which the proportion of furanose forms is insignificant. They rationalize this fact by suggesting the presence of an unfavourable *cis* interaction between the C-3 hydroxyl group and the side-chain at C-4 in glucofuranose. Removal of this interaction by introducing a deoxy grouping at C-3 is thought to be responsible for the higher amount of furanose forms at equilibrium in aqueous solutions of 3-deoxyglucose.[4]

The relative stability of furanose forms of 3-substituted glucose and xylose derivatives as compared to the corresponding pyranose forms has interested us for some time. In previous investigations of the mobility of sugars on paper electrophoresis in germanate buffer [5] at pH about 10 and sulfonated benzeneboronic acid [6] at pH about 7, we found that 3-substituted glucose and xylose have mobilities higher than those observed for the parent sugars. The same effect was produced both on removal of O-3 (3-deoxyaldose) and on substitution at O-3. This effect is noticeable also for the (1→3)-linked disaccharides. Since other results strongly indicated that by far the greatest contribution to complex formation came from *cis*-1,2-hydroxyl groups in the furanose forms, we considered a possible connection between the high mobility on electrophoresis of the 3-substituted sugar and the proportion of α-D-furanose forms present. Some support for this surmise was found in studies of the composition of equilibrium mixtures obtained on methanolyses of aldoses and methylated aldoses subsequently published by Bishop and Cooper.[7]

However, if removal of O-3 and substitution at O-3 both should produce similar increases in furanose content at the mutarotational equilibrium of glucose, we find it difficult to reconcile this with the C-3 substituent/C-4 side-chain interaction suggested by Angyal and Pickles.[4]

Angyal and Pickles studied the mutarotational equilibria by means of NMR spectroscopy on solutions in deuterium oxide.[4] We have now examined the corresponding NMR spectra, in deuterium oxide, of equilibrated solutions of 3-*O*-methyl-D-glucose and 3-*O*-methyl-D-xylose. Spectral assignments were made as described by Angyal and Pickles.[2-4] The interfering DOH peak was moved by adding small amounts of acid or suppressed by pulsing techniques. D-Glucose and D-xylose were examined in the same manner. The proportions of furanose forms for these latter sugars were below the limits of detection. The results for the two 3-*O*-methylaldoses are given in Table 1 and in Fig. 1. The small differences in chemical shifts of H-1 in furanose forms and in β-D-pyranosides do not lend themselves to a high degree of accuracy in signal integrations. Clearly, however, alkylation at O-3 produces a significant increase in furanose content.

On the basis of these results we suggest that the observed increase in the amount of furanose forms of 3-deoxy-D-glucose, 3-*O*-methyl-D-glucose and 3-*O*-methyl-D-xylose as compared to glucose and xylose is not necessarily caused by an instability factor consisting in OH-3/C-4 side-chain interaction in the parent sugars. We would prefer to describe this phenomenon in terms of destabilization of the pyranose forms relatively to the furanose forms by altering the hydrogen bonding to water on removal or alkylation of O-3. A better understanding of this effect should, however, be desirable.

Table 1. Mutarotational equilibrium and first-order coupling constants of anomeric protons for 3-*O*-methyl-D-glucose, "3-deoxy-D-glucose", 3-*O*-methyl-D-xylose and parent sugars.

Aldose	Molar ratios and H-1 coupling constants ($Y_{1,2}$) α-Pyranose	β-Pyranose	α-Furanose	β-Furanose
D-Glucose [a,b]	0.38[a] (3.5 Hz)	0.62[a] (7.5 Hz)	Nil	Nil
3-*O*-Methyl-D-glucose [b]	0.39 (3.0 Hz)	0.47 (7.7 Hz)	low	0.14 (<1 Hz)
3-Deoxy-D-*ribo*-hexose [a]	0.25 (3.5 Hz)	0.55 (7.8 Hz)	0.05 (3.9 Hz)	0.15 (<1 Hz)
D-Xylose [b]	0.31 (3.2 Hz)	0.69 (7.5 Hz)	Nil	Nil
3-*O*-Methyl-D-xylose [b]	0.38 (3.3 Hz)	0.44 (7.5 Hz)	–	0.18 (2.2 Hz)

[a] Refs. 3 and 4; temperature 31 °C. [b] Present investigation; temperature 30±2 °C. Error in signal integration ±5 %.

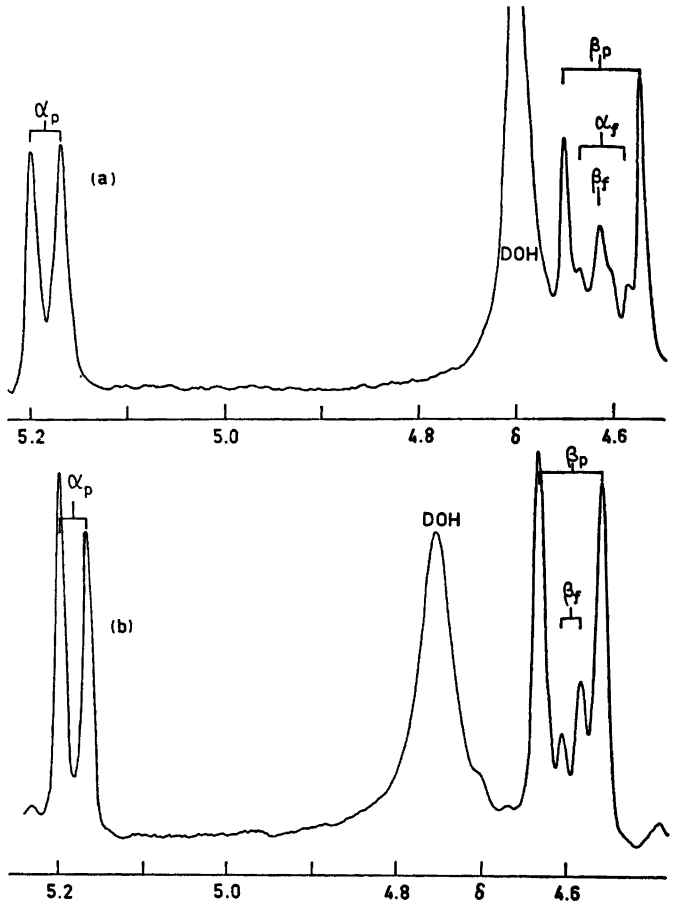

Fig. 1. 100 MHz NMR spectra showing anomeric protons only of 3-*O*-methyl-D-glucose (a) and 3-*O*-methyl-D-xylose (b).

Experimental. The spectra were recorded on a Varian XL-100, spectrometer, at 100 MHz. Deuterium oxide was used as solvent throughout, and the concentrations were 10 – 20 %. The sugars were dissolved in D_2O and their spectra recorded immediately upon dissolution and, after several days, at equilibrium. The DOH signals were suppressed by repeated concentrations and additions of fresh D_2O. Whenever required, the DOH signals were moved by adding small amounts of acid. The DOH signals were also supressed using a two-pulse techniqe (Fourier-transform spectrometry). Spectral assignments were made as described by Angyal and Pickles. Commercial samples of D-glucose and D-xylose were used. Crystalline samples of 3-*O*-methyl-D-glucose and 3-*O*-methyl-D-xylose were available in this Department; their physical constants agreed with those in the literature values.

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