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^{1}H-NMR STUDIES ON (6R)- AND (6S)-DEUTERATED (1-6)-LINKED DISACCHARIDES : ASSIGNMENT OF THE PREFERRED ROTAMERS ABOUT C5-C6 BOND OF (1-6)-DISACCHARIDES IN SOLUTION

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Summary: Conformational properties of the C5-C6 bond in the α- and β(1-6)-linked disaccharides in solution were clarified based on the ^{1}H-NMR spectra of the (6R)- and (6S)-deuterated derivatives.

Conformational analysis of oligosaccharides in solution is important to understand their biological properties. ^{1}H- and ^{13}C-NMR spectroscopy have given a powerful method for the analysis and enabled to define the conformational properties of the (1-3) and (1-4)-linked di- or oligosaccharides to a considerable extent.[1-5] However, conformational preference of the (1-6) linkage of saccharides is rather difficult to be determined because they allow rotation about the C5-C6 bond (ω angle) next to the glycosidic linkage,[6,7] (Fig. 1). Although ^{1}H-NMR analysis based on the Karplus theory has been used for elucidating the preferred conformation about the C5-C6 bond[7-10] the difficulty to differentiate the two prochiral protons at C6, H6R and H6S, has remained the problem unsettled. Previously[11-13] we have developed the general synthetic method of sugars with a chirally deuterated hydroxymethyl group[11,12] and determined the preferred rotamers of the hydroxymethyl group of D-hexopyranoses in solution.[13] In this article, we wish to extend the method for the conformational analysis of α- and β(1-6)-D-diglucopyranosides 1-6 and di-gala-

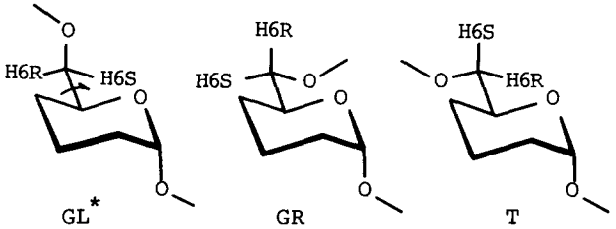
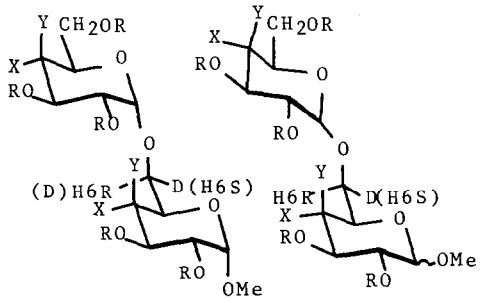


Fig. 1 Possible three rotamers about C5-C6 bond in (1-6) oligosaccharides.
* Relative position between C5-OR and C6-OR



α(1-6) : β(1-6) :

X=OR,Y=H ; 1-3 4-6

X=H,Y=OR ; 7-9 10-12

ctopyranosides 7-12.

The disaccharides chirally deuterated at C6 1-12 were prepared by use of the (6R)- and (6S)-(6-$^2H_1$)-D-glucose[11] or D-galactose derivatives[12] as the glycosyl acceptor and the corresponding D-glycosyl halides[14,15] as the donor. Halide ion catalyzed method[14] and Hanessian's method[15] were employed for syntheses of the α(1-6) disaccharides and the β(1-6) ones, respectively.

The results of the ^{1}H-NMR analysis shown in Fig. 2 and Table are summarized as follows.

1) The H6R and the H6S signals being clearly differentiated gave their chemical shifts and coupling constants.
2) The H6R proton signals of α(1-6) disaccharides 1-3 and 7-9 shifted at a lower field than the H6S signals, while the H6R signals of the β(1-6) disaccharides 4-6 and 10-12 shifted at a higher field the H6S signals.
3) The coupling constants, $J_{5,6R}$ and $J_{5,6S}$ determined the most favored conformations of the C5-C6 bond in 1-4 to be GL, 5-7 and 9-12 to be GR, and 8 to be T.

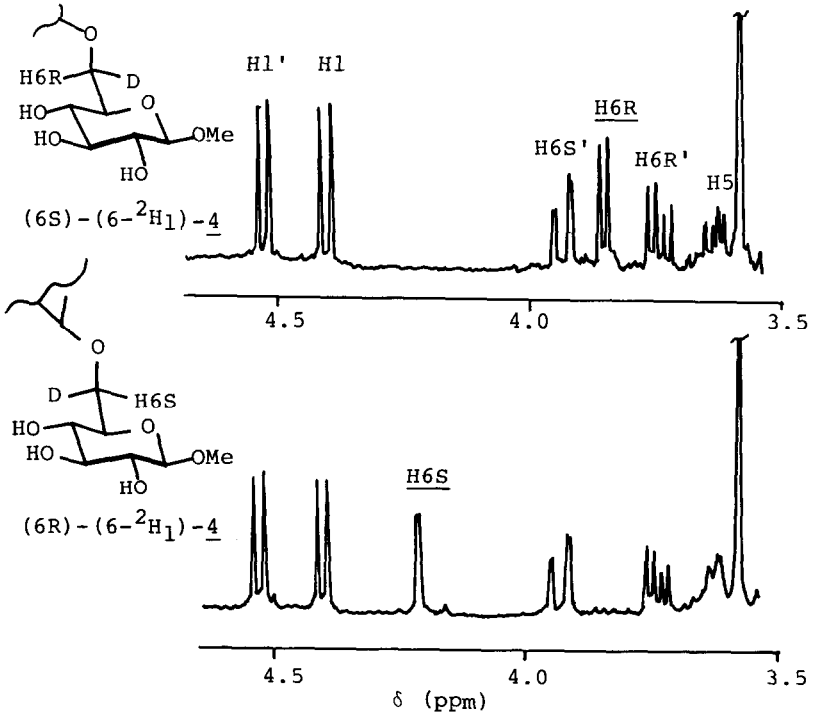


Fig. 2 400 MHz ^{1}H-NMR Spectra of (6R)- and (6S)-(6-$^2H_1$)-4.

The relative chemical shifts of the two protons, δH6R and δH6S in the (1-6) disaccharides 1-12 were found to change to reflect their anomeric configurations of the linkage. The change was independent of the species of the protecting groups, and even of the conformational changes about the C5-C6 bond. Thus, the rule will become useful not only for differentiating the two prochiral protons at C6 but also for elucidating the (1-6) likage conformations defined by the ϕ and ψ angles. The rotamer distributions in 1-4, 7, 8, and 10 showed similar trends to those found in their mono-saccharide derivatives.[13] Moreover, the GL preference in 1 and the GR preference in 7 well accorded with the results derived from the crystallographic analysis of the α(1-6) glycans, raffinose and plateose, respectively.[6] However, it should be noticed that the GL population of 1-3 decreased, whereas the GR population

Table

Compounds	R	Anom.[a]	Solv.	δ (ppm) H6R	δ (ppm) H6S	J (Hz)[b] H5,H6R	J (Hz)[b] H5,H6S	Populations%[c] GL	GR	T
α(1-6)-di-Glu.										
1	H	α	D_2O	4.01	3.73	4.3	1.8	70	29	1
2	Ac	α	$CDCl_3$	3.74	3.55	5.8	2.3	54	42	4
3	Bz	α	$CDCl_3$	4.01	3.68	6.4	2.0	50	50	0
β(1-6)-di-Glu.										
4	H	β	D_2O	3.87	4.23	5.7	2.0	56	41	3
5	Ac	β	$CDCl_3$	3.62	3.88	7.3	1.8	40	60	0
6	Bz	β	$CDCl_3$	3.85	4.08	8.2	1.9	31	69	0
α(1-6)-di-Gal.										
7	H	α	D_2O	~3.9	3.73	7.4	4.9	16	53	31
8	Ac	α	$CDCl_3$	3.72	3.41	6.2	6.2	28	29	43
9	Bz	α	$CDCl_3$	3.98	3.73	7.7	3.9	20	61	19
β(1-6)-di-Gal.										
10	H	β	D_2O	~3.9	~4.1	8.2	4.3	12	64	24
11	Ac	β	$CDCl_3$	3.63	3.82	7.7	3.7	21	62	17
12	Bz	β	$CDCl_3$	3.78	4.16	8.2	3.8	16	66	18

a) Anomeric Configuration b) J ± 0.2 Hz
c) The values were obtained with following equations,[18]

$$1.3\,GL + 2.7\,GR + 11.7\,T = J_{H5,H6S} \quad --(1)$$
$$1.3\,GL + 11.5\,GR + 5.8\,T = J_{H5,H6R} \quad --(2)$$
$$GL + GR + T = 1 \quad --(3)$$

increased as the increment of the bulkiness of the protecting groups. The change was much more significant for the β(1-6) disaccharides 4-6: the acetylated and the benzoylated derivatives 5 and 6 preferred the GR rotamer rather than the GL rotamer. This change strongly suggests that anomeric configurations of the likage would become an important factor for the conformations of the (1-6) disaccharide at a branch-point.

The small population of the T rotamer in 1-6 and the GL rotamer in 7-12 could be attributed to the unfavored interaction between the C6-OR and the C4-OR in a syn-diaxial relation, and the result confirmed the validity of the assumption made by Brisson et al.[8,9] Although Lemieux et al.[7] have concluded in their recent NMR and HSEA studies on oligosaccharides that the T rotamer would be the most favored conformation of the D-galactose moiety, the discrepancy of the result with ours in this paper could be attributed primarily to their ambiguous assignment of the two protons at C6.

In conclusion, we clarified the most favored conformation about the C5-C6 bond in α- and β(1-6)-D-di-glucopyranosides and di-galactopyranosides in solution on the bases of the ^{1}H-NMR spectra of their stereospecifically deuterated derivatives. We believe that the method and the result in this paper will become an useful tool for elucidating[16] and discussing the coformational properties of more complicated oligosaccharides like antennary glycans.[10]

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