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UPFIELD SHIFT OF CMR OF ANOMERIC CARBONS OF 1,1'-LINKED GLYCOPYRANOSYL GLYCOPYRANOSIDES

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Unusual upfield shifts are observed in CMR of anomeric carbons of α,α- and β,β-forms of 1,1'-linked D-glycopyranosyl D-glycopyranosides. On the contrary, α,β-forms of 1,1'-linked D-glycopyranosyl L-glycopyranosides show such upfield shifts. Possible cause of upfield shift is postulated in relation to the conformation of the glycoside linkage of 1,1'-linked glycopyranosyl glycopyranosides.

Trehalosamine and its analog are antibiotics having the structure of 1,1'-linked glycopyranosyl glycopyranoside.[1] Recently discovered apramycin and tunikamycin also possess 1,1'-linkage in their structures.[2] On the other hand, a variety of α-D-glycopyranosyl α-D-glycopyranoside have currently been synthesized for the development of trehalase inhibitors.[3] We now wish to communicate that inspection of CMR of trehalosamine and related 1,1'-linked glycopyranosyl glycopyranosides[4] enabled us to conclude that α-D-,α-D-, β-D-,β-D-, and α-D-,β-L-forms of 1,1'-linked glycopyranosyl glycopyranoside[5] may adopt a unique conformation to result unusual upfield shifts (-5.2 ppm, by average) of CMR of both anomeric carbons.[6]

Data in Table 1 show that the upfield shift of CMR of anomeric carbons observed in the case of α,α- and β,β-trehaloses[7] appears regardless of the constituents of 1,1'-linked D-glycopyranosyl D-glycopyranosides. Furthermore, data in Table 2 show that the upfield shift retains in the presence of protecting groups, strongly implying that the upfield shift does not arise from a special conformation set up by inter-unit hydrogen-bondings.[7]

Recently, Lemieux et al.[8] emphasized the significance of exo-anomeric effect, an inherent force orienting the aglyconic center to be synclinal to ring oxygen. In the case of 1,1'-linked glycopyranosyl glycopyranosides in the aforementioned forms, the forces possessed by both units may function to set the conformation of the glycoside linkage so that the dihedral angles of O5-C1-O-C1' and O5'-C1'-O-C1 are close to ±60° as illustrated in Fig. 1[9] wherein the gauche effect[10] works to shield CMR of both anomeric carbons. In the case of α-D-,β-D-, α-D,α-L-, and β-D-,β-L-forms, on the contrary, the disposition of ring oxygens is not favorable to such conformation; repulsive forces between polar C1-O5 and C1'-O5' bonds[11] rotate the dihedral angles away from ±60°. Data in Table 1 show that no significant upfield shift was indeed observed in the case of α-D-

Table 1 Chemical Shift of Anomeric Carbons of 1,1'-Linked Glycopyranosyl Glycopyranosides at 25.1 MHz in D_2O with ext. TMS.[1-4]

αDGlcp	αDGlcp	αDGlcp	αLGlcp	αDGalp	αDGalp
94.4[5] (-5.7)		101.5 (+1.4)		94.4 (-6.3)	
αDGlcp	βDGlcp	αDGlcp	βLGlcp	βDGalp	βDGalp
101.3 (+1.2)	104.0 (-0.2)	96.0 (-4.1)	98.4 (-5.8)	100.9 (-4.1)	
βDGlcp	βDGlcp	αDGlcp	αLFucp	αDManp	αDManp
100.3 (-3.9)		101.7 (+1.6)	101.9 (+1.3)	96.4 (-5.5)	
αDGlcp	αDGalp	αDGlcp	βLFucp	αDGlcp	αDManp
94.3 (-5.8)	94.5 (-6.2)	95.8 (-4.3)	98.6 (-6.2)	94.6[6] (-5.5)	96.1[6] (-5.8)
αDGlcp	αDGlcNp	αDGalp	αDGlcNp	αDManp	αDGlcNp
94.0 (-6.1)	94.8 (-6.4)	94.1 (-6.6)	94.8 (-6.4)	96.0 (-5.9)	95.5 (-5.7)
βDGlcp	αDGlcNp	βDGalp	αDGlcNp	βDManp	αDGlcNp
104.0 (-0.2)	102.1 (+0.9)	104.6 (-0.4)	102.1 (+0.9)	101.2 (-0.7)	101.6 (+0.4)
αDGlcp	βDGlcNp	αDGalp	βDGlcNp	αDManp	βDGlcNp
101.4 (+1.3)	105.0 (-0.3)	101.6 (+0.9)	104.8 (-0.5)	102.6 (+0.7)	104.2 (-1.1)
βDGlcp	βDGlcNp	βDGalp	βDGlcNp	βDManp	βDGlcNp
100.5 (-3.7)	101.4 (-3.9)	101.2 (-3.8)	101.4 (-3.9)	100.8 (-4.5)	97.9 (-4.3)

[1] Spectrum was determined by means of a JEOL-PS-100 instrument with a JEOL-EC-100 computer at 25°C (noise decoupled, pulse width 13 μs (45°), repetition 2 s, frequency range 5000 Hz, data points 8K).

[2] CMR of amines was determined at pD > 9.

[3] Data of chemical shift of anomeric carbon of anomeric methyl D-glucopyranosides, D-galactopyranosides, and D-mannopyranosides are quoted from TABLE 11.27 in Carbon-13 NMR Spectroscopy, by J.B.Stothers, Academic Press, New York and London, 1972. Data of other methyl glycosides are: Me αDFucp 100.6, Me βDFucp 104.8, Me αDGlcNp 101.2, and Me βDGlcNp 105.3.

[4] The average upfield shift is -5.2 ppm.

[5] α,α-Trehalose dihydrate (Wako Chemicals).

[6] E.Bar-Guilloux, J.Defaye, H.Driguez, and D.Robic, Carbohydr. Res., 45, 217 (1975).

glycopyranosyl α-L-glycopyranosides (Fig. 2).

Our findings will be of use for assigning the anomeric configuration of trehalose analog and antibiotics being 1,1'-linked glycopyranosyl glycopyranoside as well as understanding their conformational properties.

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Table 2 Chemical Shift of Anomeric Carbons of Protected 1,1'-Linked Glycopyranosyl Glycopyranosides at 25.1 MHz in $CDCl_3$ with TMS.[1-3]

αTBG	αTBG	αTBG'	αTBG'	αTBM	αTBM
94.4 (-3.7)		93.5 (-5.3)		93.3 (-5.7)	
αTBG	βTBG	αTBG'	βTBG'	αTCM	αTCM
99.4 (+1.3)	104.1 (-0.6)	99.7 (+0.9)	103.7 (-1.3)	93.4 (-5.4)	
βTBG	βTBG	αTBG	αTCG'		
99.3 (-5.4)		94.1 (-4.0)	93.4 (-5.1)		
αTBG	αADG	αTCG'	αTCG'	αTCM	αADG
93.7 (-4.2)	92.6 (-5.4)	93.5 (-5.0)	92.2 (-5.8)	93.7 (-4.2)	91.2 (-6.8)
βTBG	αADG	βTCG'	αADG	βTCM	αADG
102.0 (-2.7)	97.6 (-0.4)	102.2 (-2.7)	97.8 (-0.2)	102.6 (0.0)	99.2 (+1.2)
αTBG	βADG	αTCG	αADG	αTCM	βADG
100.0 (+1.9)	103.5 (0.0)	93.2 (-4.7)	92.4 (-5.6)	100.4 (+1.6)	102.2 (-1.3)
		αTCG	βADG	βTCM	βADG
		99.7 (+1.8)	103.5 (0.0)	97.2 (-5.4)	97.6 (-5.9)

[1] TBG = 2,3,4,6-Tetra-O-benzyl-D-glucopyranosyl
TBG'= 2,3,4,6-Tetra-O-benzyl-D-galactopyranosyl
TBM = 2,3,4,6-Tetra-O-benzyl-D-mannopyranosyl
TCG = 2,3,4,6-Tetra-O-p-chlorobenzyl-D-glucopyranosyl
TCG'= 2,3,4,6-Tetra-O-p-chlorobenzyl-D-galactopyranosyl
TCM = 2,3,4,6-Tetra-O-p-chlorobenzyl-D-mannopyranosyl
ADG = 3,4,6-Tri-O-acetyl-2-(2,4-dinitroanilino)-2-deoxy-D-glucopyranosyl

[2] Data of chemical shift of anomeric carbon of protected methyl glycosides are: Me αTBG 98.1, Me βTBG 104.7, Me αTBG' 98.8, Me βTBG' 105.0, Me αTBM 99.0, Me βTBM 102.7, Me αTCG 97.9, Me βTCG 104.6, Me αTCG' 98.5, Me βTCG' 104.9, Me αTCM 98.8, Me βTCM 102.6, Me αADG 98.0, and Me βADG 103.5

[3] The average upfield shift is -5.2 ppm.

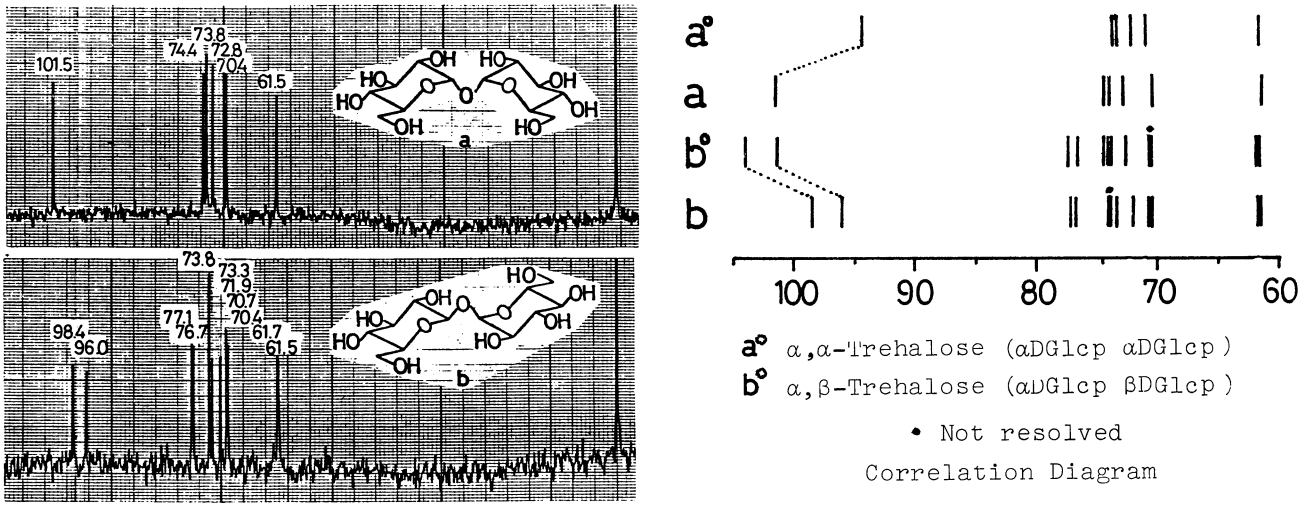

Fig. 2 CMR Spectra of αDGlcp αLGlcp (a) and αDGlcp βLGlcp (b) (25.1 MHz, D_2O, TMS)

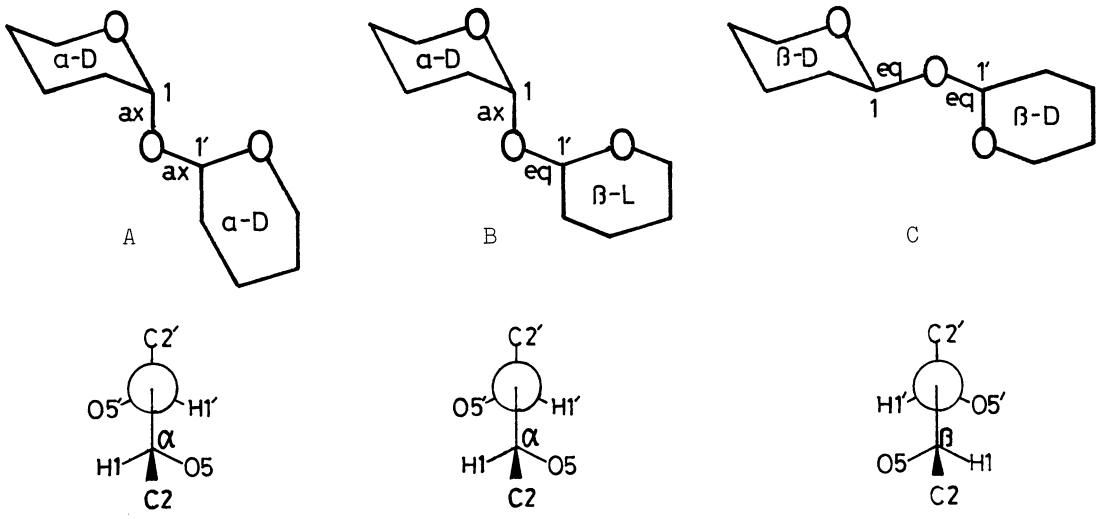

Fig. 1 Preferred Conformation of 1,1'-Linked Glycopyranosyl Glycopyranoside with Dihedral Angles of O5-C1-O-C1' and O5'-C1'-O-C1 close to +60°(A and B) and -60°(C)

References and Footnotes

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5) It is self-evident that α-L-,α-L-, β-L-,β-L-, and α-L-,β-D-forms are magnetically equivalent to enantiometric α-D-,α-D-, β-D-,β-D-, and α-D-,β-L-forms, respectivvely.

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