Tetrahedron Letters No.11, pp. 833-836, 1970. Pergamon Press. Printed in Great Britain.

ANOMERIC CONFIGURATION IN CARBOHYDRATES

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(Received in USA 24 October 1969; received in UK for publication 2 February 1970)

In carbohydrate chemistry, nmr spectroscopy is well established (1) as a powerful tool for elucidating conformational and configurational structures. But one problem has persisted. Since interacting protons are located in similar electron-density environments, carbohydrates and derivatives show complex low-field spectra. One method of improving the low field resolution is to operate the spectrometer at higher magnetic field (2); another method is to convert the carbohydrate to a derivative (3) that shifts the desired resonance peak away from the low field region. We report here a procedure for determining the anomeric configuration in carbohydrates. This procedure depends upon sufficient carbohydrate being available for conversion to a 6-deoxyhexose and also both anomers being available.

The preferred formation of the α-anomer of 1-substituted-D-glucopyranosides (and several other carbohydrates) is well known (4) and has been called the anomeric effect (4,5). This effect was explained by Edwards (6) in terms of a dipole interaction between the C-O bond in the ring and the anomeric substituent. On examination of models we were persuaded that this "anomeric effect" or dipole interaction would influence in a regular manner the electron-density environment around the C_6 position in glycopyranosides. When a C_5-hydroxylmethyl is converted to a C_5-CH_3, a 6-deoxyhexose, a three-proton doublet appears upfield and widely separated from other resonance peaks. When a series of 6-deoxypyranoside anomers were compared, the C_5-CH_3 peak for the α-anomer was located always at a higher field than the β-anomer (Table I). With a pure monosaccharide anomer the appearance on anomerization of another doublet, usually observed as a three-line pattern (two overlapping doublets), was sufficient to establish the anomeric configuration of the starting monosaccharide.

The utility of this observation was demonstrated when, in a study of the reaction of p-toluenesulfonyl (tosyl) chloride and methyl β-maltoside, we isolated and purified a di-O-tosyl

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TABLE I.

C_5-CH_3 resonance peak in anomeric 6-deoxypyranosides

Compound	Anomer α δ	Anomer α J, Hz	Anomer β δ	Anomer β J, Hz	Solvent[a]	Ref
6-Deoxy-L-mannose	1.60	6	1.65	6	P	b
Methyl 6-deoxy-L-mannoside	1.26	6	1.28	6	D	b
Methyl 2,3,4-tri-O-acetyl-6-deoxy-L-mannoside	1.20 1.17	6 6	1.28 1.24	6 6	C T	b b
6-Deoxy-D-galactose	1.19	7	1.22	7	D	b
Methyl 2,3,4-tri-O-acetyl-6-deoxy-D-galactoside	1.13 1.11	6 8	1.21 1.18	6 6	C T	b b
Methyl 6-deoxy-2,4-di-O-methyl-D-galactoside	1.29	6.1	1.36	6	C	c
Methyl 3-acetamido-2,3,6-trideoxy-D-arabino-hexopyranoside	1.28	6	1.34	6	C	d
4-O-acetyl of above compound	1.20	6	1.25	6	C	d
6-Deoxy-D-glucose	1.21	6.5	1.26	6	D	b
Methyl 6-deoxy-D-glucoside	1.24	6	1.26	6	D	b
Methyl 2,3,4-tri-O-acetyl-6-deoxy-D-glucoside	1.18 1.15	6 6	1.22 1.21	6 6	C T	b b
2-Methoxy-trans-5,6-dimethyltetrahydropyran	1.08	6.2	1.17	6.3	C	e
2-Methoxy-cis-5,6-dimethyltetrahydropyran	1.01	6.6	1.10	6.3	C	e
Methyl L-oleandroside	1.30	6	1.35	5.5	C	f
Di-O-acetyl-L-oleandroside	1.14	6	1.19	6	C	f
n-Butyl D-desoaminide	1.18	6.2	1.28	6.2	C	f
Chalcose	1.53	6	1.60	6	D	g
Desoamine	1.62	6.5	1.67	6.6	D	h
Ossamine·hydrochloride	1.1	---	1.2	---	D	i
Viosamine·hydrochloride	1.85	6.5	1.90	6.5	D	j

[a] P = pyridine, D = D_2O, C = $CDCl_3$, T = CCl_4.

Footnotes continued--

TABLE I. Footnotes continued--

[b] This study.

[c] E. Akita, K. Maeda, and H. Umezawa, J. Antibiot. (Tokyo) Ser. A. 17, 200 (1964).

[d] H. H. Baer, K. Čapek, and M. C. Cook, Can. J. Chem. 47, 89 (1969).

[e] D. T. Sepp and C. B. Anderson, Tetrahedron 24, 6873 (1968). Anomeric designation in carbohydrate nomenclature. These authors did not differentiate the methyl resonance peaks; the assignment is ours.

[f] W. D. Celmer and D. C. Hobbs, Carbohyd. Res. 1, 137 (1965).

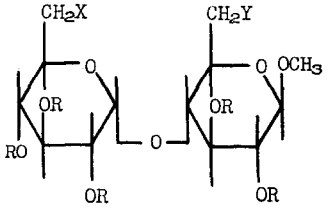
[g] P. W. K. Woo, H. W. Dion, and L. F. Johnson, J. Amer. Chem. Soc. 84, 1066 (1962). δ-values estimated from figure.

[h] P. W. K. Woo, H. W. Dion, L. Durham, and H. S. Mosher, Tetrahedron Lett. 735 (1962). δ-Values estimated from figure.

[i] C. L. Stevens, G. E. Gutowski, C. P. Bryant, R. P. Glinski, O. E. Edwards, and G. M. Sharma, Tetrahedron Lett. 1181 (1969). These authors did not assign any anomeric configuration to the methyl doublets; the assignment is ours.

[j] C. L. Stevens, P. Blumbergs, F. A. Daniker, D. H. Otterbach, and K. G. Taylor, J. Org. Chem. 31, 2822 (1966). Reference was external TMS.

derivative and two mono-O-tosyl derivatives. Displacement of the tosyl group with iodide ion produced the corresponding methyl deoxyiodo-β-maltosides, which on catalytic hydrogenolysis were converted to the methyl deoxy-β-maltosides. Proton spectra of these deoxymaltosides permitted the assignment of each methyl doublet to a specific position (Table II). Proof of structural assignments (and thus methyl assignments) was obtained chemically when crystalline II (R = Ac, X = OTs, Y = H) on treatment with aqueous sodium hydroxide gave methyl 3',6'-anhydro-β-maltoside as a chromatographically homogenous sirup. Quantitative periodate oxidation of this sirup found one α-glycol group.



I R = Ac, X = H, Y = H

II R = Ac, X = OAc, Y = H

III R = Ac, X = H, Y = OAc

Since methods (7) are established for transforming a primary hydroxyl to a 6-deoxyiodo- and 6-deoxyhexose, this new procedure for determining anomeric configuration is practical.

TABLE II.

Methyl resonance peaks of maltosides

Compound[a]	Peak[b] 6 ∫	6 J, Hz	6' ∫	6' J, Hz	mp, °C
I	1.16	6.2	1.39	6.0	186-187
II	---	---	1.39	6.0	120-121
III	1.15	6.0	---	---	176-177

[a] Satisfactory analyses were obtained for crystalline compounds.

[b] $CDCl_3$ with TMS internal reference, 100 MHz.

REFERENCES

1. L. D. Hall, Advan. Carbohyd. Chem. 19, 51 (1964); G. E. McCasland, Advan. Carbohyd. Chem. 20, 11 (1965).

2. N. S. Bhacca and D. Horton, J. Amer. Chem. Soc. 89, 5993 (1967); Chem. Commun., 867 (1967); N. S. Bhacca, D. Horton, and H. Paulsen, J. Org. Chem. 33, 2484 (1968).

3. R. H. Bell, D. Horton, and D. W. Williams, Abstr. Pap., Amer. Chem. Soc. 155, 4C (1968).

4. R. U. Lemieux, Molecular Rearrangements, P. DeMayo, ed., Interscience Publishers, New York, 1964, pp. 733-743.

5. Recently the disfavoring of conformations with parallel unshared electron pairs on non-adjacent atoms has been called "rabbit ear effect" by R. D. Hutchins, L. D. Kopp, and E. L. Eliel, J. Amer. Chem. Soc. 90, 7174 (1968).

6. J. T. Edwards, Chem. Ind. (London), 1102 (1955); E. L. Eliel and C. A. Giza, J. Org. Chem. 33, 3754 (1968).

7. S. Hanessian, Advan. Carbohyd. Chem. 21, 149 (1966).