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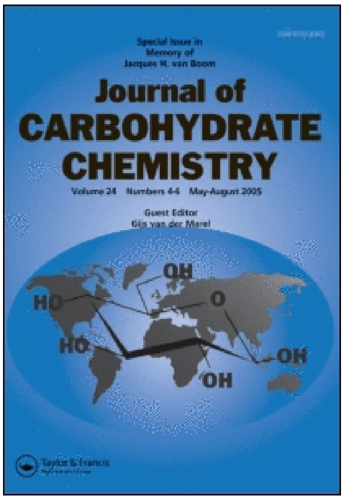

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COMMUNICATION

ESTIMATION OF THE ANOMERIC EFFECT OF THE CYANO GROUP

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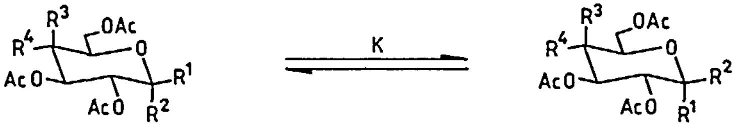
The anomeric effect[1,2] is a well established phenomenon among carbohydrate derivatives, and more generally among 2-substituted tetrahydropyrans. The generalized anomeric effect[1] refers to structural moieties R-X-C-Y (where X possesses one or two lone pairs of electrons, and Y is an atom or group of high electronegativity) in both open chain or cyclic molecules. Thus hydroxyacetonitrile prefers to exist in the *gauche* conformation,[3,4] and several 3-cyano-perhydro-1,2-oxazine derivatives prefer conformations in which the C-3--CN bond and the lone pair of the nitrogen are coplanar.[5] Investigation of conformational equilibria of all but one 2,6-anhydro-hexononitrile[6,7] (pentopyranosyl cyanides) left doubt relating to the anomeric effect of the cyano group, and raised the possibility of a stabilizing interaction between *1,3-diaxial* cyano and acetoxy groups.

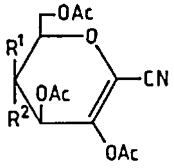
On investigating the reaction of (1R)2,3,4,6-tetra-*O*-acetyl-1-bromo-D-galactopyranosyl cyanide[8] (1) with equimolar tetrabutylammonium-bromide (Bu_4NBr) in refluxing carbon tetrachloride we observed with surprise that rather high proportions (~10%) of the (1S) anomer (2) were present in the reaction mixture. Similar observations were made with the analogous D-gluco compound (3). Monitoring the reactions by polarimetry showed that the rotation of the mixtures reached a constant



	R^1	R^2	R^3	R^4		
1	CN	Br	OAc	H	2	} *eq.(1)*
3	CN	Br	H	OAc	4	
5	H	Br	OAc	H	6	} *eq.(2)*
7	H	Br	H	OAc	8	
9	CN	H	OAc	H	10	} *eq.(3)*
11	CN	H	H	OAc	12	

Scheme

value after 15 minutes. The ^1H NMR spectrum of the mixture in the D-galacto case contained two new, clearly distinguishable resonances in addition to those of **1** at 5.62 ppm (d, 10.5 Hz) and 5.08 ppm (dd, 10.5 Hz and 3 Hz), and these were assigned as H-2 and H-3 of compound **2**. The ratio of integrals for H-3 in **1** and **2** was about 9:1. After washing out the Bu_4NBr with water, analysis of the residual syrup indicated the presence of one bromine (calculated for $C_{15}H_{19}BrNO_9$: N 3.21, Br 18.34; found N 3.20, Br 18.16). For the D-gluco compounds the ^1H NMR spectrum was not informative because the resonances of **3** and **4** were not separated. The ultimate proof of both configurations at C-1 and conformations came from the proton coupled ^{13}C spectra (Table I) which contained two resonances for the cyano groups. The significantly different couplings of these doublets indicate unequivocally that **2** and **4** are in the $^4C_1$ conformation and that the CN is in an *axial* position in both cases. After prolonged reaction times (1-2 h) the unsaturated compounds[9] **13** and **14** could be detected in the NMR spectra, but the ratio of **1** and **2** was practically the same as it was after 15 minutes.



13 R^1= OAc R^2= H

14 R^1= H R^2= OAc

Table I

Characteristic ^{13}C NMR Data For The Anomers of Acetylated 1-Bromo-D-glycosyl Cyanides

Compound	δ_{CN}[a] (ppm)	$^3J_{H-2,CN}$ (Hz)
1	113.54	2.2
2	112.88	7.6
3	113.31	2.5
4	112.45	7.5

[a] 50.3 MHz for $CDCl_3$ solutions

Table II

Measured And Calculated Equilibrium Constants

Equilibrium	K_1[a]	K_2[10,11]	K_3[b]	ΔG_3[c]
1 ⇌ 2 (77°C)	0.104±0.003			
1 ⇌ 2 (40°C)	0.071±0.003	0.005	14.17	-1.65±0.02
3 ⇌ 4 (40°C)	0.152±0.005	0.005	30.4	-2.12±0.02

[a] Determined by gas chromatography

[b] $K_3 = K_1/K_2$

[c] $\Delta G = -RT\ln K$ (kcal/mol)

Because compounds **1-4** contain no *1,3-diaxial* interactions other than with H, estimations for the anomeric effect of the cyano group could be made. This was possible by comparing *equilibria (1)-(3)* (Scheme) from which it follows that $K_3 = K_1/K_2$.

K_2 was calculated from the anomeric effect of bromine,[10] and was accepted[11] for the corresponding equilibria of the acetobromo sugars 5-8. As this value refers to 40 °C equilibrations of **1** and **3** were carried out at this temperature and the ratios of anomers were determined by gas chromatography (Table II). In these experiments no unsaturated compounds (**13**, **14**) could be detected by NMR even after very long reaction times (one week).

From the calculated values of K_3, equilibrium compositions of 9:10 = 7:93 and 11:12 = 3:97 can be deduced. This resembles the equilibria of penta-*O*-acetyl-D-glycopyranoses where for the D-galacto configuration $\beta:\alpha$ = 21:79 and for the D-gluco case $\beta:\alpha$ = 12:88 was observed,[16] both in acetic acid-acetic anhydride (1:1 vol) solutions at 25 °C.

Taking into account the conformational energy (A_{CN}=0.2 kcal/mol[17] which was modified to 0.3 kcal/mol according to Franck's proposal[18]), the anomeric effect of the cyano group can be estimated as 1.95 kcal/mol in the 2,3,4,6-tetra-*O*-acetyl-D-galactopyranosyl cyanides and 2.42 kcal/mol in the corresponding D-gluco compounds. As the anomeric effect of bromine has been given as a lower limit, our estimations should also be considered this way. With the availability of a better value for K_2 the anomeric effect of the cyano group should be recalculated.

ACKNOWLEDGMENT

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REFERENCES and NOTES

1. A. J. Kirby, *The Anomeric Effect and Related Stereoelectronic Effects at Oxygen*, Springer Verlag, Berlin, 1983.
2. P. Deslongchamps, *Stereoelectronic Effects in Organic Chemistry*, Pergamon Press, Oxford, 1983.
3. G. Cazzoli, D. G. Lister, A. M. Mirri, *J. Chem. Soc., Faraday Trans. II*, 1973, 569.
4. G. L. Bendazzoli, F. Bernardi, P. Palmieri, *ibid.*, 579.
5. M. Riediker, W. Graf, *Helv. Chim. Acta*, 62, 2053 (1979).
6. P. Köll, A. Förtsch, *Carbohydr. Res.*, 171, 301 (1987).
7. L. Somsák, unpublished results.
8. L. Somsák, Gy. Batta, I. Farkas, *Carbohydr. Res.*, 124, 43 (1983).
9. L. Somsák, *ibid.*, 195, C1 (1989).
10. C. B. Anderson, D. T. Sepp, *J. Org. Chem.*, 32, 607 (1967).
11. K_2 is obviously very important. However, we were not able to locate a value for acetobromoglucose or galactose in the literature. As the anomeric effects for Cl in 2-chloro-4-methyl-tetrahydropyran in acetonitrile[10] and in acetochloroglucose in acetonitrile[12] are in good agreement (both of them being about 2 kcal/mol), and the polarity as

well as the chemical nature of solvent have an influence on the magnitude of the anomeric effect,[1,13] we think that the value for Br in neat 2-bromo-4-methyl-tetrahydropyran[10] can be regarded as an acceptable approximation for acetobromohexoses in carbon tetrachloride. This is also supported by the findings[14,15] that anomeric effects in 2-acetoxy-tetrahydropyrans and in peracetylated pyranoses do not differ from each other to a very high extent.

12. R. U. Lemieux, J. Hayami, *Can. J. Chem.*, 43, 2162 (1965).

13. J.-P. Praly, R. U. Lemieux, *ibid.*, 65, 213 (1987).

14. C. B. Anderson, D. T. Sepp, *Tetrahedron*, 39, 1707 (1968).

15. D. T. Sepp, C. B. Anderson, *ibid.*, 6873.

16. W. A. Bonner, *J. Am. Chem. Soc.*, 81, 1448 (1959).

17. E. L. Eliel, N. L. Allinger, S. J. Angyal, G. A. Morrison, *Conformational Analysis*, Interscience Publishers, New York, 1965. p. 44.

18. R. W. Franck, *Tetrahedron*, 39, 3251 (1983).