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# DETERMINATION OF THE ANOMERIC CONFIGURATION OF 1-CYANO-$\Delta^{2,3}$-UNSATURATED SUGARS FROM $J_{C(1)-H}$ COUPLING VALUES

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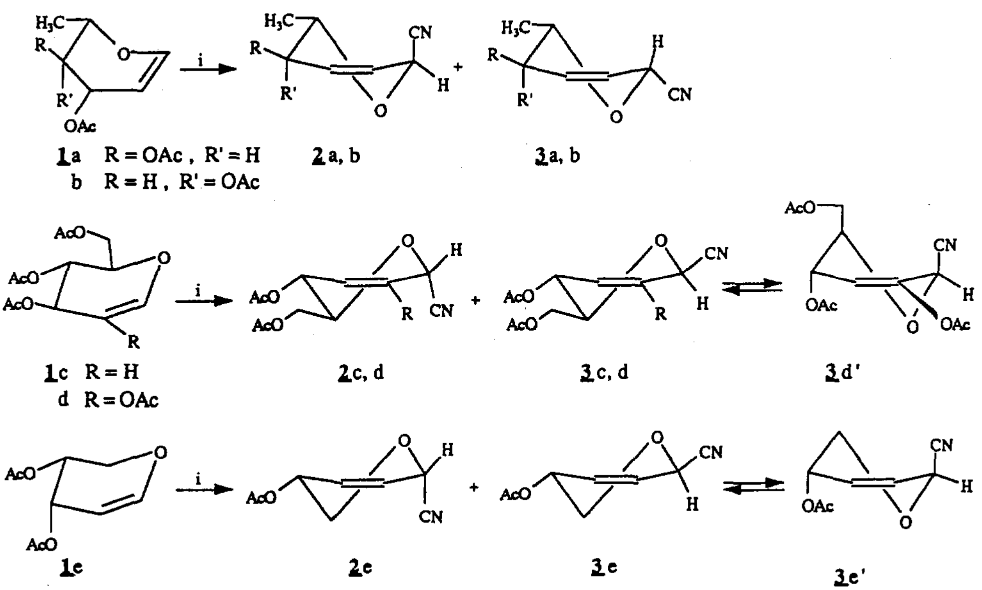
*Abstract :*

*Measurement of $J_{C(1)-H}$ coupling constants provides a direct means for assignment of the anomeric configuration of the 1-cyano-$\Delta^{2,3}$-unsaturated sugars 2a-e and 3a-e.*

1-Cyano sugars are valuable intermediates for the synthesis of C-nucleosides and other C-glycosyl compounds as the cyano group is readily convertible into a variety of functional groups.[1] Concerning 1-cyano-$\Delta^{2,3}$-unsaturated pyranose sugars, several new methods have appeared for their preparation,[2-5] including one from our laboratories involving the reaction of glycals 1 with diethylaluminium cyanide ($C_6H_6$, RT, 2-4 hrs. ; 75-90 % yields).[2] As mixtures of cyano sugars 2 and 3 are obtained in these reactions (scheme 1) it is important to have in hand a rapid and unambiguous method to determine the anomeric configuration of each product. Unfortunately, for compounds 3a, 3b, and 3e this could not be achieved by comparison of the vicinal $J_{1,2}$, allylic $J_{1,3}$ and homoallylic $J_{1,4}$ coupling constants[6] as the H-1 and H-4 absorptions were superimposed in their 400 MHz proton spectra. For this reason we decided to examine whether the anomeric configuration of the $\Delta^{2,3}$-unsaturated cyano sugars 2a-e and 3a-e could be determined from the $^1J_{C(1)-H}$ coupling constants. For saturated pyranose systems a difference of ~ 10 Hz is observed between the values for C(1)-Hax and C(1)-Heq with $^1J_{C(1)-Hax} < {}^1J_{C(1)-Heq}$.[7] This phenomenon is interpreted in terms of a $n \rightarrow \sigma^*$ interaction between a pair of non-bonded electrons in an orbital of $\pi$ symmetry on oxygen and the axial C(1)-H bond.[8,9] To our knowledge only one report has appeared concerning the extension of this technique to $\Delta^{2,3}$ unsaturated sugars, which, due to the conformational mobility of the systems studied, did not yield any meaningful information.[10]

Scheme I



1a R = OAc , R' = H
b R = H , R' = OAc

2a, b

3a, b

1c R = H
d R = OAc

2c, d

3c, d

3d'

1e

2e

3e

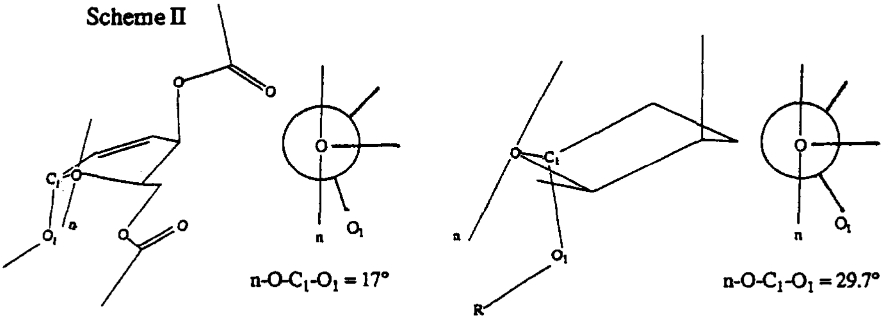
3e'

i : $Et_2AlCN$, $C_6H_6$, RT, 2-4 hrs.

Table I

| Product 2 | $^1J_{C(1)-H}$ | Product 3 | $^1J_{C(1)-H}$ | Δ J |
|---|---|---|---|---|
| 2 a | 160.0 | 3 a | 150.2 | 9.8 |
| b | 159.5 | b | 150.0 | 9.5 |
| c | 160.2 | c | 150.7 | 9.5 |
| d | 160.9 | d | 154.7 | 6.2 |
| e | 159.4 | e | 154.8 | 4.6 |

Scheme II



n-O-C$_1$-O$_1$ = 17°

n-O-C$_1$-O$_1$ = 29.7°

4

5

The $^1J_{C(1)-H}$ coupling values for our cyano sugars, determined from either proton coupled gated coupling or heteronuclear 2D J resolved (Hetero 2DJ) experiments[11], are presented in Table 1. Considering first the data for compounds 2a-c and 3a-c derived from the O-acetyl derivatives of L-rhamnal 1a, L-fucal 1b, and D-glucal 1c respectively, one sees that two distinct sets of values are obtained. In keeping with the trend mentioned in the preceeding paragraph the larger 160±0.9 Hz value observed for 2a-c is attributed to $J_{C(1)-Heq}$ and the smaller value of 150 ± 0.4 Hz to $J_{C(1)-Hax}$ in compounds 3a-c. The difference between these values $\Delta J=9.6$ Hz is very close to that observed for saturated pyranose systems indicating that the $n \rightarrow \sigma^*$ interaction is not diminished by the introduction of a $\Delta^{2,3}$-unsaturation into the molecule. In fact, in the half chair conformation of these sugars the p-type lone pair orbital on oxygen and the axial C-H bond are more rigourously aligned. This point is illustrated in Scheme 2 by comparison of the dihedral angle n-O-$C_1$-$O_1$, in compounds 4 and 5 whose X-ray crystal structures have been determined.[12] The nearly constant 9.6 Hz value observed for $\Delta J$ indicates that these epimeric pairs of cyano sugars are conformationally stable adopting the normally preferred L-$^5H_0$ and D-$^0H_5$ half chair conformations.[13] This was confirmed for compounds 2a,c and 3a,c by the observed 9.0 Hz coupling constant for $J_{H(4)-ax,\ H(5)-ax}$ in the proton spectra. Thus, the configuration at the anomeric center of cyano sugars 2a,b is designated to be L-β and for 2c it is D-α. Conversely the L-α and D-β configurations are assigned to the epimeric compounds 3a,b and 3c respectively.

In keeping with the above results it is apparent that compounds 2d and 2e also possess the D-α anomeric configuration ($J_{C(1)-H} \sim 160$ Hz). However, for compound 3d a value intermediate between the two established limits is observed confirming earlier reports that this molecule is conformationally mobile.[3,14] A major factor that contributes to this mobility is the release of $A^{1,2}$ allylic strain between the C-2 acetoxy and C-1 cyano groups in 3d'.

The 154.8 Hz coupling found for 3e similarly indicates that it is equilibrium with 3e'. This can be accounted for by the fact that there is no C-5 substituent in this molecule to "anchor" it in the $^0H_5$ conformation and 3e' is stabilized by the combined allylic [15] and anomeric effects.

In conclusion, based upon the results of this study, one should be able to routinely assign the anomeric configuration of 1-cyano-$\Delta^{2,3}$ unsaturated sugars from the $J_{C(1)-H}$ value.

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