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AN EFFICIENT SYNTHESIS OF 1-CYANO-2,3-UNSATURATED SUGARS <u>VIA</u> THE REACTION OF GLYCALS WITH Et_2AlCN

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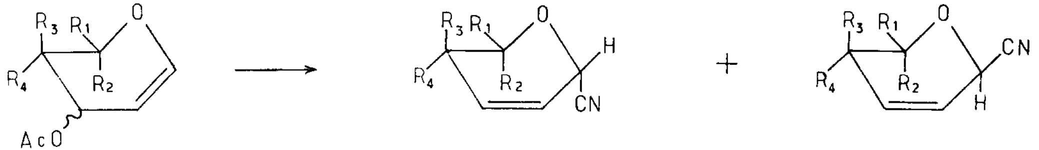
Abstract : The reaction of glycals 1a-d with Et_2AlCN in benzene at room temperature leads to formation of the corresponding 1-cyano-2,3-unsaturated sugars 2a-d and 3a-d in good to excellent yields.

Two recent reports [1] have demonstrated that the BF_3 etherate catalyzed reaction of glycals with trimethylsilyl cyanide leads to regioselective formation of C-1 substituted cyano sugars. Our attention has been directed towards the reaction of glycals with Et_2AlCN, an alternate source of "molecular" cyanide which is also a strong Lewis acid, in the expectation that the C-3 cyano substituted sugars may be formed [2].

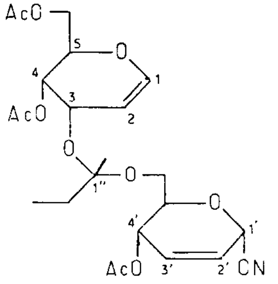
It was found however, that reaction of the glycals <u>1a</u>-d with Et_2AlCN (1.5-3.0 equiv.) in benzene at room temperature (1-4 hrs.) led once again to the exclusive formation of 1-cyano sugars. These reactions were remarkably clean producing the α- and



<u>2 a-d</u>

<u>3 a-d</u>

	R_1	R_2	R_3	R_4	
<u>1a</u>	H	CH_3	OAc	H	3α - OAc
<u>1b</u>	H	CH_3	H	OAc	3α - OAc
<u>1c</u>	CH_2OAc	H	H	OAc	3β - OAc
<u>1d</u>	H	H	H	OAc	3α - OAc



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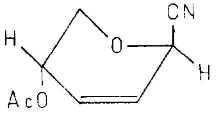

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β-cyano substituted products 2 and 3 in nearly equal proportions (2:3/60:40). The mixture of products 2a-3a, and 2b-3b derived from the di-O-acetyl derivatives of rhamnal 1a, and fucal 1b respectively were readily separated by flash chromatography on silica gel (EtOAc : Hexane/ 1:4)[3]. The combined yields on gram scale reactions were in the range 86-92%.

Compounds 2d and 3d were obtained as an inseparable mixture in 88% yield. The identification of each component was possible however by a detailed analysis of the ^{1}H (400 MHz) and ^{13}C NMR spectra for the mixture which showed that 3d exists in equilibrium with its pseudo diaxial conformer 4.

Cyano sugars 2c and 3c derived from triacetylglucal 1c were separable by flash chromatography on silica gel [3] ; however in this case the overall yield of the two products was lower (75 %) due to the concomitant formation of a chromatographically less polar dimeric product assigned the structure 5 [4]. Compound 5 apparently results from a reaction of the relatively exposed C-6 acetate carbonyl of 2c and Et_2AlCN, with transfer of Et^- rather than cyanide ion, followed by a reaction of the resulting hemi-ketal salt at C-3 of 1c.

Fraser Reid and Tulshian [5] have shown that reaction of 1c with Et_2AlCN at reflux leads to compounds 2c and 3c in markedly different proportions, the α-anomer 2c being highly favoured (2c:3c/> 9:1). In keeping with their observations we found that treatment of the β-anomer 3c under the same conditions results to a large extend in its anomerization to 2c. This temperature dependence of the anomeric distribution is a good indication that the reaction of glycals with Et_2AlCN occurs by an equilibrium process. However, not even minor amounts of the C-3 substituted cyano sugars were detectable in this and the above reactions.

In conclusion, although conditions have not as yet been found which favour formation of C-3 cyano substituted sugar from glycals, a new efficient and high yielding procedure has been developed for the preparation of synthetically important 1-cyano sugar derivatives.

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1) a) F.G. De Las Heras, A. San Felix, P. Fernandez-Resa, Tetrahedron, 39, 1617 (1983) ;
b) G. Grynkiewicz, J.N. BeMiller, Carbohyd. Res., 108, 229 (1982).

2) Reaction of both enones and conjugated iminium ions with Et_2AlCN is known to occur preferentially by 1,4-type addition, see : a) W. Nagata, M. Yoshika, Org. React., 25, 255 (1977) ; b) D.S. Grierson, M. Harris, H.-P. Husson, Tetrahedron, 39, 3683 (1983).

3) Physical (m.p., α_D, microanalysis) and spectral (MS, ^{1}H (400 MHz) and ^{13}C NMR) data were obtained for each product. The configuration at the anomeric center was determined from a measure of the $J13_{C(1)H(1)}$ coupling constants (to be reported at a later date).

4) 9 : ^{1}H NMR (400 MHz) : δ 6.70 (d, J = 6 Hz, H-1), 5.21 (dd, J = 6,5 Hz, H-2), 4.70 (t, J = 5 Hz, H-3), 1.77 (s, CH_3), 5.91 (dm, J = 10 Hz, H-2'), 5.75 (dt, J = 10, 2 Hz, H-3'), 5.11 (m, H-1') ; ^{13}C NMR : δ 149.3, 97.4 (C-1,2), 70.0 (C 3), 65.2 (C 1'), 123.3, 133.5 (C-2',3'), 98.42 (C 1").

5) D.B. Tulshian, B. Fraser-Reid, J. Org. Chem., 49, 518 (1984).

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