Tetrahedron Letters,Vol.27,No.48,pp 5877-5880,1986 0040-4039/86 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

PREPARATION OF 1,2-CIS-GLYCOSYL CYANIDES BY THE STEREOSELECTIVE REDUCTION OF ACETYLATED 1-BROMO-D-GLYCOSYL CYANIDES

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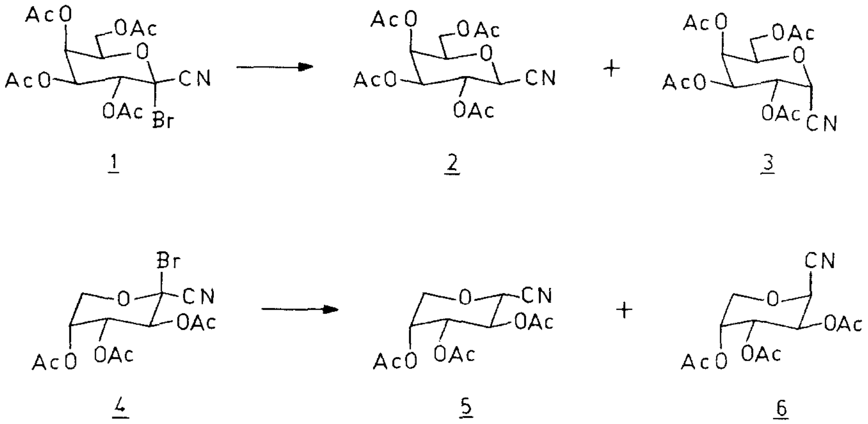
Abstract: Reductive dehalogenation of acetylated 1-bromo-D-glycosyl cyanides with tri-*n*-butyltin hydride favours the formation of 1,2-*trans*-glycosyl cyanides, while reactions with zinc-acetic acid, zinc-isopropanol, and sodium borohydride give 1,2-*cis*-glycosyl cyanides as the major product.

Glycosyl cyanides are important intermediates in the synthesis of C-nucleosides and their analogues.[1,2] Their methods of preparation have also been reviewed.[1,2]

Precursors protected with participating groups /mainly acetyl or benzoyl/ lead exclusively to 1,2-*trans*-glycosyl cyanides in the commonly applied nucleophilic substitution reactions. Using non-participating protecting groups /e.g. benzyl/ results in the formation of 1,2-*cis* derivatives, as well, but their separation from the epimeric compound is generally possible only with chromatographic methods.

Recently 1,2-*cis*-glycosyl cyanides have been prepared by dehydration of acetylated anhydro-heptonamides.[3] Acetylated C-glycosyl nitromethanes have been converted into glycosyl cyanides, and the method could be applied to 1,2-*cis* derivatives, too.[4]

Some years ago we reported on the reductive dehalogenation of the acetylated 1-bromo-D-glycosyl cyanides, to give epimeric mixtures of glycosyl cyanides.[5,6] A more detailed investigation of this reaction in the case of **1**



Scheme

Table - Reduction of acetylated 1-bromo-D-glycosyl cyanides

Method	Time	1		4	
	/min/	2:3[a]	Yield[b] /%/	5:6[a]	Yield[b] /%/
Zn/AcOH reflux	15	3:7	64	4:6	64
Zn/iPrOH reflux	20	4:6	78	4:6	66
nBu_3SnH/C_6H_6 AIBN, reflux	15	6:4	77	8:2	67
$NaBH_4$/DMF room temp.	10	4:6	64	4:6	67

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[a] Deduced from the ^1H n.m.r. spectra of the worked up rection mixtures

[b] Calculated for the syrupy residues obtained on working up the reaction mixtures

and 4[6,7] (Scheme, Table) showed the reduction proceeded stereoselectively with different reagents.

In the reactions with tri-*n*-butyltin hydride[8,9] compounds 2 and 5 were the major components formed. This is in accord with the experiences which show that glycosyl radicals react with high stereoselectivity in favour of the new substituent entering from the *axial* direction.[10-14] However, in our reactions the stereoselectivity was not so high possibly due to the capto-dative substitution[15,16] of the reaction centre. This may be cause the 1-cyano-glycosyl radical is more planar than pyramidal as in the glycosyl radicals,[17] which can result in a lower degree of stereoselectivity.

Opposite stereoselectivity was shown in the reductions with zinc dust[9] i. e. the 1,2-*cis*-glycosyl cyanides /3 and 6/ were formed as major products /Table/. Similar results were found with sodium borohydride. The understanding of these observations requires further investigations, which are in progress in our laboratory.

As the mixtures of the epimeric glycosyl cyanides /obtained after removal of solids from the reaction mixture and extracting the filtrate diluted with water by chloroform/ could easily be separated by fractionated crystallisation, the reductive dehalogenation of acetylated 1-bromo-D-glycosyl cyanides with zinc dust represents an alternative to the earlier methods of preparation of 1,2-*cis*-glycosyl cyanides. From ethanolic solutions the β-anomers 2[18] and 6 /m.p. 158 °C, $[\alpha]_D^{20}$ -180°/ crystallise first, and the mother liqour contains the α-anomers 3 /m.p. 92 °C, $[\alpha]_D^{20}$ +132°; ref[3]: m.p. 97 °C, $[\alpha]_D^{20}$ +120°/ and 5.[19] Compounds 2-6 are in the conformations depicted according to their ^{1}H n.m.r. spectra /200 MHz, C_6D_6, TMS internal standard/. Comparison of chemical shifts and $^3J_{H,H}$ coupling constants for H-1 /2 3.65 ppm, 10.2 Hz; 3 4.61 ppm, 5.7 Hz; 5 3.75 ppm, 7.3 Hz; 6 4.50 ppm, 5.3 Hz/ clearly indicates the given structures. Further proofs are the $^3J_{CN,H-2}$ heteronoclear coupling constants[7] and refs. therein /2 2.0 Hz; 3 7.6 Hz; 5 2.6 Hz; 6 7.3 Hz/.

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(Received in UK 16 July 1986)