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TRANSFORMATION OF HEX-2-ENOPYRANOSYL TRICHLOROACETIMIDATES - A CORRECTION[1)]

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Summary: Contrary to previous results hex-2-enopyranosyl trichloroacetimidates do not rearrange to amino-branched glycals but give N-acylated hex-2-enopyranosyl amines.

Recently the [3.3]-sigmatropic rearrangement of allylic trichloroacetimidates[2)] could be worked out into a general procedure for the synthesis of R-C*-N-branched-chain amino sugars[3)]. This has been successfully confirmed by further studies with trichloroacetimidates of hex-2- and 3-enopyranosides as well as with sugar derivatives containing exocyclic allylic trichloroacetimidates[3,4)].

An extension of this approach to the 3-methyl-branched hex-2-enopyranosyl trichloroacetimidates should require particular interest. These could rearrange to yield amino-methyl-branched glycals which in turn comprise a reactive enol ether moiety and present attractive building units e.g. in N-iodosuccinimide glycosylation reactions[5)].

By mild saponification of the corresponding methyl glycoside[6)] 4-O-benzoyl-2,3,6-trideoxy-3-C-methyl-α/β-D-erythro-hex-2-enopyranose (3) was obtained. Treatment with sodium hydride and trichloroacetonitril at low temperature was anticipated to give the α- and β-trichloroacetimidates 4 which were reported to rearrange to the epimeric mixture of amino-branched chain glycals of ribo (5) and arabino configuration (6)[3)]. Further close inspection of this reaction revealed different results and demands a correction of the previous report[3)].

† Deceased

In a low temperature n.m.r. experiment by treatment of 3 with the reagents the immediate formation of four trichloroacetimidates could be observed (four C=NH signals at δ 8.3 - 8.5 of different intensity). These are presumably both the α- and β-pyranose species 4 as well as their α- and β-furanose isomers 2. On heating to room temperature the intensity of these imino proton signals rapidly approached zero which points to a fast rearrangement reaction.

Thus the preparative reaction at -40°C and further heating to room temperature resulted in a mixture which after chromatography gave two crystalline isomers 8α (57%) and 8β (23%). They do not show significant differences in the optical rotation which renders the application of Hudson's isorotation rule[7] for the assignment of anomers impossible, as previously demonstrated in other hex-2-enopyranosyl derivatives[8]. In ^{1}H n.m.r. the anomeric protons appear at similar shifts and each shows several small and one additional large J(1,NH) coupling[9].

Table

	Schmp. (°C)	$[\alpha]_D^{20}(CHCl_3)$	$\delta^{13}C$(C-1)	J(C-1,H)	$\delta^{13}C$(C-4)	δ^1H(1-H)
7α	97	-18.0	86.94	167.4	89.15	6.39 dddq [a]
7β	amorph	-29.2	88.24	167.1	88.82	6.47 dddq [b]
8α	149	+86.6	74.27	163.3	72.19	5.84 ddddq [c]
8β	144	+97.2	76.74	155.9	71.99	5.92 ddd [d]

a) J(1,NH) = 8.6, J(1,2) = 1.5, J(1,3-CH_3) = 1.5, J(1,4) = 1.5;

b) J(1,NH) = 8.7, J(1,2) = 1.3, J(1,3-CH_3) = 1.3, J(1,4) = 4.8;

c) J(1,NH) = 8.2, J(1,2) = 3.2, J(1,3-CH_3) = 1.5, J(1,4) = 1.6, J(1,5) = 0.3;

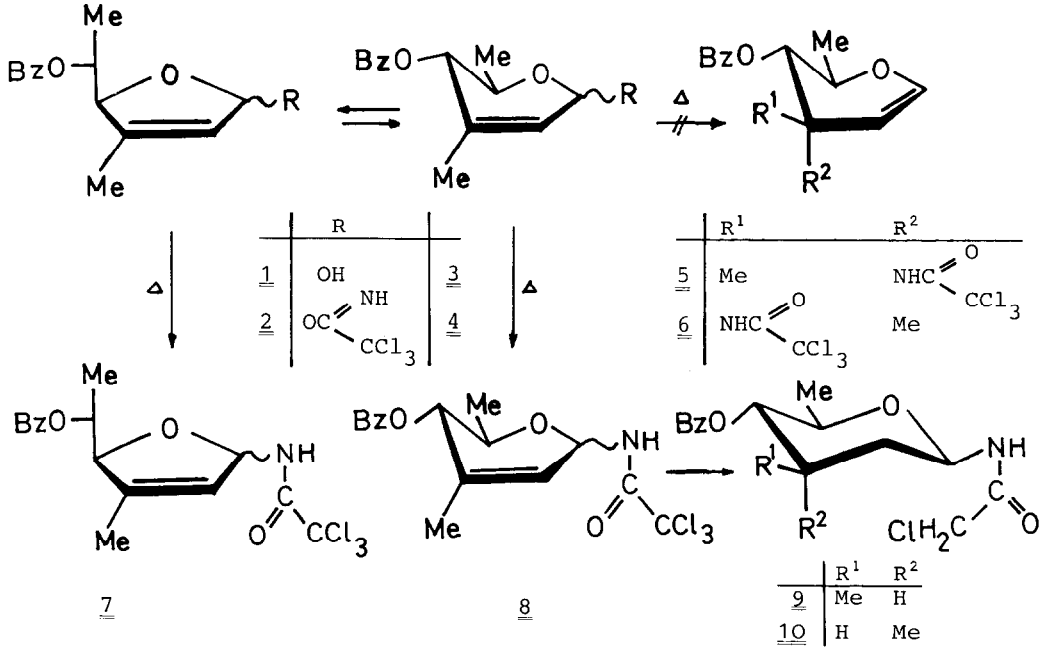
d) J(1,NH) = 9.2, J(1,2) = 1.9, J(1,4) = 3.0 Hz.

On account of these findings both the anomeric N-trichloroacetyl-4-O-benzoyl-2,3,6-trideoxy-3-C-methyl-α- (8α) and β-D-erythro-hex-2-enopyranosyl amines (8β) were obtained. The assignment of anomers is substantiated by carbon n.m.r. where 8α shows an almost 8 Hz larger J(C-1,H) coupling than 8β[10]. Further proof is provided by hydrogenolysis of the β anomer 8β which results

in a mixture of (3R)- and (3S)-N-monochloroacetyl-4-O-benzoyl-2,3,6-trideoxy-3-C-methyl-β-D-erythro-hexopyranosyl amine [9 and 10, 72%, 9 : 10 = 5 : 2; 9 : 1-H δ = 5.32 ddd, J(1,NH) = 8.8, J(1,2a) = 10.9, J(1,2e) = 2.2 Hz].

When in contrast the same reaction is performed at -15°C with subsequent warming to room temperature a mixture of four isomers is obtained which were chromatographically separated (silica gel, CH_2Cl_2) and eluted as follows: 8β (16%), 7β (17%), 8α (25%), and 7α (30%). Again the assignment of the crystalline N-trichloroacetyl-5-O-benzoyl-2,3,6-trideoxy-3-C-methyl-α- (7α) and the amorphous β-D-erythro-hex-2-enofuranosyl amines (7β) cannot be based on the optical rotation or ^1H n.m.r. data but is supported by the considerable downfield shift of the C-4 carbons (Tab.). The carbon shifts of C-1 are consistent with the furanose structure, and because the J(C-1,H) coupling is virtually identical as could be expected from the almost planar system the anomeric assignment is tentative. Unfortunately both hex-2-enofuranosyl amines are labile and degraded in hydrogenation experiments.

These results lead to a tentative interpretation of the reaction course. Obviously depending on the exact conditions there can occur a preceding isomerisation of the hex-2-enopyranose 3 into the furanose isomer 1 under benzoate migration, probable mediated by sodium hydride.



7 8

Thus subsequent formation of all anomeric trichloroacetimidates 2 and 4 could be demonstrated, whereas a careful search including trapping conditions for an anticipated intermediate occurrence of glycals 5 and 6 did not meet with success. Under mild thermal conditions (below or maximal room temperature) cleavage of the imidates gives ion pairs of a glycosyl cation and an ambident trichloroacetimidate/trichloroacetamide anion. There preferred recombination may be understood following Pearson's concept of a favourable interaction between the allylic oxocarbenium cation (hard acid) and the amide (hard base) which leads exclusively to the observed glycosyl amines 7 and 8 and no [3.3]-sigmatropic rearrangement products.

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