

## Action of Strong Acids on Acetylated Glycosides

## IV. Investigation of Disaccharide Models

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In a previous paper in this series<sup>1</sup>, it was reported that the velocity of transglycosidation of alkyl glucosides decreases with increasing + I activity (electron attraction) of the alkyl group. In the disaccharides, gentiobiose and cellobiose, there are one and two oxygen atoms respectively on the carbon atoms in  $\beta$ -position to the glycosidic linkage, which will attract electrons and thus lower the reactivity. In order to investigate the possibility of transforming disaccharides, a number of acetylated glucosides of halogen and oxygen substituted alcohols have been investigated, using the methods outlined in the previous paper. Thus the velocity constants given in Table 1 are relative, the velocity constant for the transformation of  $\beta$ -glucose pentaacetate to the equilibrium mixture taken as unity.

Table 1. Transglycosidation and acetolysis of some substituted alkyl glucosides.

$\beta$ -Glucoside tetraacetate	$k_{\text{transglyc.}}$	$\alpha_{\text{max}}$	$k_{\text{acetolysis}}$	$\alpha_{\infty}$
— O · CH <sub>2</sub> · CH <sub>2</sub> · CH <sub>3</sub>	15	+ 5.13°	0.08	+ 2.71°
— O · CH <sub>2</sub> · CH <sub>2</sub> · CH <sub>2</sub> OH	2.5	4.66	0.06	2.95
— O · CH <sub>2</sub> · CH <sub>3</sub>	15	5.20	0.07	3.53
— O · CH <sub>2</sub> · CH <sub>2</sub> · OOC · CH <sub>3</sub>	0.85	3.99	0.025	2.55
— O · CH <sub>2</sub> · CH <sub>2</sub> · Cl	0.40	3.99	0.03	2.40
— O · CH(CH <sub>3</sub> ) <sub>2</sub>	50	5.50	0.08	1.25
— O · CH(CH <sub>2</sub> Cl) <sub>2</sub>	≈ 0.02	1.71	—	1.55

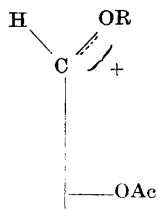
In all runs 0.500 g of glucoside were dissolved in 20 ml of a solution of sulfuric acid in acetic anhydride-acetic acid (10 : 3). The rotation was measured at 20.0° in 2 dm tubes. As the velocity constants differed by several powers of ten, the concentration of sulfuric acid was varied between 0.1 C and 1.5 C in the different runs in order to get a convenient velocity of the reaction studied. The final rotation for glucose pentaacetate in the parallel runs was + 4.90°.

When a hydroxyl group is introduced at the  $\gamma$ -carbon atom in propyl  $\beta$ -glucoside tetraacetate, the velocity of the transglycosidation decreases from 15 to 2.5. The hydroxyl group becomes acetylated, but this does not seem to complicate the kinetics. The velocity of the acetolysis also decreases, but to a much smaller extent.

An electron attracting group in the  $\beta$ -position has a still greater effect. This is demonstrated with the ethyl,  $\beta$ -acetoxyethyl and  $\beta$ -chloroethyl glucosides.

The 1,3-dichloropropyl(2-)  $\beta$ -glucoside tetraacetate reacts extremely slowly compared to the unsubstituted isopropyl glucoside. The velocity of transglycosidation is of the same magnitude as that of acetolysis, which is indicated by the low maximum. Consequently, no exact values can be calculated. The transglycosidation seems to be about 2500 times slower than that of the unsubstituted glucoside.

The final rotations of the substituted alkyl glucosides do not differ appreciably from those of the unsubstituted ones. This is rather unexpected. The low final rotation indicates a high percentage of glucose heptaacetate, but the yield of heptaacetate from the unsubstituted glucosides, however, increases with the velocity of transglycosidation. If this were also true for the unsubstituted glucosides, one would get very little glucose heptaacetate and consequently much higher values for the final rotation than those obtained. These results are difficult to interpret. According to the theory outlined in the preceding paper, transglycosidation and acetolysis have the same intermediate step — the cation



must assume that 'acetylation and acetolysis' of this cation, leading to glucose heptaacetate, is much more rapid for the substituted glucosides than for the unsubstituted ones.

From the above results, one may conclude that disaccharides of the gentio-biose type, analogous to the chloroethyl  $\beta$ -glucoside and the acetoxyethyl  $\beta$ -glucoside, could be transformed into the  $\alpha$ -derivates. (Helferich and Werner<sup>2</sup> have synthesized chloroethyl  $\alpha$ -glucoside from the  $\beta$ -glucoside with titanium tetrachloride as a catalyst.) The cellobiose type seems to be more difficult to transform. The reaction with a strong acid always involves some decomposition, and the transglycosidation would be so slow that most of the substance would probably be destroyed before any appreciable amounts of the  $\alpha$ -glucoside were formed.

#### EXPERIMENTAL

The experimental conditions were the same as in the preceding paper. The syntheses of the glucosides investigated, with the exception of 1,3-dichloropropyl (2-)  $\beta$ -glucoside tetraacetate, are described in an earlier communication<sup>3</sup>.

#### 1,3-Dichloropropyl (2-) glucoside tetraacetate

A solution of acetobromoglucose (8.22 g) and mercuric acetate (3.03 g), in a mixture of absolute benzene (40 ml) and glycerol  $\alpha,\gamma$ -dichlorohydrin (20 g), was boiled on the steam bath for 15 minutes. After cooling, it was washed several times with water, dried

#### Typical runs

Table 2. *Transglycosidation of chloroethyl  $\beta$ -glucoside tetraacetate.*

*$\beta$ -Glucose pentaacetate and chloroethyl  $\beta$ -glucoside tetraacetate, 0.500 g of each, dissolved in 20 ml of 0.36 N sulfuric acid in acetic anhydride-acetic acid, 10 : 3.  $t = 20^\circ \text{C}$ . Rotations determined in 2 dm tubes. (The table gives only a part of the observed values.)*

Time min	$\beta$ -Glucose pentaacetate		Chloroethyl $\beta$ -glucoside tetraacetate	
	$\alpha_D$	$k$	$\alpha_D$	$k$
0	+ 0.37°		- 0.98°	
20	2.27	0.0120	- 0.06	0.0044
40	3.36	0.0119	+ 0.68	0.0044
60	4.02	0.0121	1.36	0.0046
80	4.42	0.0126	1.87	0.0046
100	4.60	0.0124	2.31	0.0046
226	4.86		3.60	0.0047
313			3.85	
370			3.99	
1440			3.64	
2880			3.25	
	Mean value	0.0121	Mean value	0.0046

Table 3. Acetolysis of acetoxyethyl  $\beta$ -glucoside tetraacetate.  $\beta$ -Glucose pentaacetate and acetoxyethyl  $\beta$ -glucoside tetraacetate, 0.500 g of each, dissolved in 20 ml of 1.65 *N* sulfuric acid in acetic anhydride-acetic acid, 10 : 3.  $t = 20^\circ \text{C}$ . Rotations determined in 2 dm tubes.

Time min	$\beta$ -Glucose pentaacetate		Acetoxyethyl $\beta$ -glucoside tetraacetate	
	$\alpha_D$	$k$	$\alpha_D$	$k$
0	+ 0.37°		- 1.04°	
10	4.53	0.092	+ 1.70	
20	5.00		2.81	
50			3.62	
60			3.64	
70			3.60 *	
80			3.56	0.0017
90			3.50	0.0022
100			3.46	0.0021
110			3.41	0.0022
120			3.35	0.0024
1374			2.55	
	Mean value	0.097	Mean value	0.0024

Table 4. Transglycosidation and acetolysis of 1,3-dichloropropyl (2-)  $\beta$ -glucoside tetraacetate.  $\beta$ -Glucose pentaacetate and 1,3-dichloropropyl (2-)  $\beta$ -glucoside tetraacetate, 0.500 g of each, dissolved in 20 ml of 1.65 *N* sulfuric acid in acetic anhydride-acetic acid, 10 : 3.  $t = 20^\circ \text{C}$ . Rotations determined in 2 dm tubes. (The table gives only a part of the observed values.)

Time min	$\beta$ -Glucose pentaacetate		1,3-Dichloropropyl (2-) $\beta$ -glucoside tetraacetate
	$\alpha_D$	$k$	$\alpha_D$
0	0.37°		- 0.68°
10	3.05	0.038	- 0.65
25	4.50		- 0.62
50	4.91		- 0.47
100	4.99		- 0.26
200			+ 0.08
1340			1.40
1570			1.50
2800			1.70
4205			1.71
7000			1.57
8500			1.55
	Mean value	0.039	

\* Chosen as initial value.

over calcium chloride and concentrated under reduced pressure. The oily residue was recrystallized from ethanol-water, 1:1. After three recrystallizations, the melting point was constant at 122–123° (uncorr.). Yield 1.3 g (14 %).  $[\alpha]_D^{20} - 10.8^\circ$  in chloroform ( $c = 2.5$ ). The melting point is identical and the yield, although very low, is somewhat better than that obtained by Coles, Dodds and Bergeim<sup>4</sup>, who synthesized the same substance by the method of Koenigs and Knorr. They did not determine the optical rotation.

#### SUMMARY

The transglycosidation and acetolysis of some halogen and oxygen substituted alkyl glucosides have been investigated in acetic anhydride-acetic acid solution. The substituents reduce the reactivity of the glucoside considerably. With one substituent on the  $\beta$ -carbon atom of the agluconic group (the gentiobiose type), transglycosidation is more rapid than acetolysis and the  $\alpha$ -glucoside accumulates in the reaction mixture. With substituents on two  $\beta$ -carbon atoms (the cellobiose type), both transglycosidation and acetolysis are very slow, and no appreciable accumulation of  $\alpha$ -glucoside can be observed.

1,3-Dichloropropyl (2-)  $\beta$ -glucoside tetraacetate has been<sup>1</sup> synthesized by the mercuric acetate method.

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