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Action of Strong Acids on Acetylated Glycosides

VI. Transglycosidation of Galactosides *

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The previus papers in this series have dealt with the transglycosidation of acetylated glucosides. It would be of interest to know whether the results of these investigations could be applied to glycosides of other sugars. In this paper the investigation of some galactosides is reported.

β-Galactose pentaacetate, in a solution of sulfuric acid in acetic anhydride--acetic acid, was transformed into the equilibrium mixture of α- and β-acetates at a rate which was 2.5 times faster than the analogous reaction for β-glucose pentaacetate. When ethyl β-galactoside tetraacetate was dissolved in the same solvent and the optical rotation observed, it was found to change in a similar manner to that of ethyl β-glucoside tetraacetate [1] under the same conditions (Fig 1.) The maximum rotation in both cases corresponds to an accumulation of α-glycoside. This has been demonstrated by isolation of the α-galactoside from the reaction mixture when this showed maximum rotation. The rotation then decreased below the value calculated on the assumption that only α/β--galactose pentaacetate is formed by the acetolysis of the galactoside. From analogy with the glucosides one must assume that this depends upon the formation of some galactose heptaacetate, which, similar to other *al*-sugars, has a rather low optical rotation. When the α-galactoside was treated in the same way, the rotation decreased rapidly to the same value as that for the maximum mentioned above, and then the values coincided with those for the β-galactoside. *iso*-Propyl β-galactoside tetraacetate and β-chloroethyl β-galactoside tetraacetate have also been investigated. For the former the transglycosidation is faster and the percentage of heptaacetate in the final product higher than for the ethyl derivative. For the latter the transglycosidation is slower than the α/β-transformation of the acetate. Thus the analogy with the

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glucose derivatives is complete. From the rotations of the pure α- and β-derivatives the percentage of α-isomer in the equilibrium mixture can be calculated. The values for galactose pentaacetate and ethyl galactoside tetraacetate are 87 % and 82 % respectively, while the values for corresponding glucose derivatives are 89 % and 89 %.

The velocity constants for the α/β-transformation and acetolysis of the galactosides, compared with those for the corresponding glucose derivatives are given in Table 1. The velocity of the transformation of β-glucose pentaacetate to the equilibrium mixture is taken as unity.

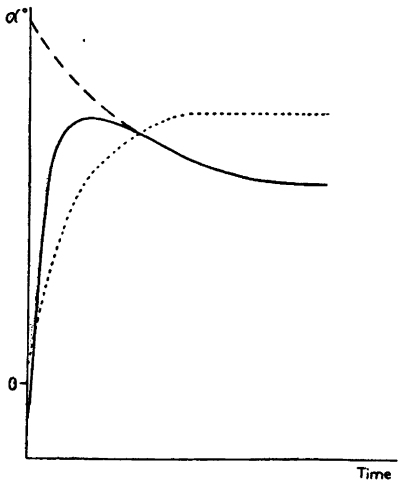

Fig. 1. Transglycosidation and acetolysis of the tetraacetates of α- and β-ethyl galactoside.

——— *Ethyl β-galactoside*
– – – – *Ethyl α-galactoside*
· · · · · · · · *β-Galactose pentaacetate*

From Table 1 it can be seen that the transglycosidation is faster for the galactose than for the glucose derivatives. The acetolysis is also faster. From this small amount of data, however, it is not possible to find any simple mathematical relationship between the different velocity constants.

Table 1. Relative velocity constants for transglycosidation and acetolysis of some acetylated galactose and glucose derivatives.*

	β-Pentaacetate	β-Ethyl		β-*iso*-Propyl		β-Chloroethyl
	$k_{\alpha/\beta\text{-transform.}}$	$k_{\text{trans-glyc.}}$	$k_{\text{aceto-lysis}}$	$k_{\text{trans-glyc.}}$	$k_{\text{aceto-lysis}}$	$k_{\text{transglyc.}}$
Galactose	2.5	31	0.35	71	0.15	0.7
Glucose	1	15	0.07	50	0.08	0.4
$\frac{k_{\text{galactose}}}{k_{\text{glucose}}}$	2.5	2.1	5	1.4	2	1.8

* The k-values are determined at different concentrations of sulfuric acid and hence not strictly comparable. See experimental part.

Ethyl α-galactoside tetraacetate was prepared by treating the β-galactoside with titanium tetrachloride. This reagent has been used chiefly for the transglycosidation of glucosides, but was, as expected, equally suitable for galactosides.

EXPERIMENTAL

Ethyl β-galactoside tetraacetate

Ethyl β-galactoside tetraacetate, which is described in the literature [2], was prepared here by the mercuric acetate method. A solution of galactose bromide tetraacetate (8.22 g) and mercuric acetate (3.03 g) in a mixture of absolute benzene (40 ml) and ethanol (16 ml) was boiled on the steam bath for 15 minutes. After cooling it was washed several times with water, dried over calcium chloride and concentrated under reduced pressure. The oily residue was dissolved in hot ethanol-water, 1 : 1, and on cooling somewhat sticky crystals were obtained, which were recrystallized from the same solvent. Yield 5.3 g (72 %) M. p. 86—87°*.

iso-Propyl β-galactoside tetraacetate

iso-Propyl β-galactoside tetraacetate was prepared by the same method as the β-ethyl galactoside and in a yield of 80 %. It was recrystallized from light petroleum. M. p. 58 $-59°$ $[\alpha]_D^{20} -9°$ (Chloroform, C = 2).

$C_9H_{14}O_6$ $(OCCH_3)_4$ (390.4). Calc. Acetyl 44.1 Found Acetyl 44.5

β-Chloroethyl β-galactoside tetraacetate

β-Chloroethyl β-galactoside tetraacetate was prepared by the same method as the ethyl β-galactoside and recrystallized from ethanol. Yield, 54 %. M. p. 115—116° $[\alpha]_D^{20} -5°$ (Chloroform, C = 2). Coles, Dodds and Bergeim [3] report the melting point as 117° but give no value for the optical rotation.

Ethyl α-galactoside tetraacetate

With titanium tetrachloride: A solution of ethyl β-galactoside tetraacetate (3 g) and titanium tetrachloride (1.5 g) in absolute chloroform (90 ml) was boiled on the steam bath for 45 minutes. When cold, the mixture was washed with ice water, dried over calcium chloride and concentrated under reduced pressure. The residue was recrystallized from light petroleum. Two recrystallizations yielded the pure substance. Yield, 2.0 g (67 %) M. p. 85—86° $[\alpha]_D^{20} + 136°$ (Chloroform, C = 2).

$C_8H_{12}O_6$ $(OCCH_3)_4$ (376.4) Calc. Acetyl 45.7 Found 45.8.

With sulfuric acid: Ethyl β-galactoside tetraacetate (2 g) was dissolved in a mixture of sulfuric acid (0.02 ml), acetic anhydride (8 ml) and acetic acid (2 ml). The optical rotation of the solution was observed, and when this showed maximum value the mixture was poured into ice water (150 ml) containing sodium acetate (1 g). A white

* All melting points uncorrected.

precipitate was slowly formed. This was filtered off and recrystallized from ethanol-water, 1 : 1. Yield, 1.1 g (55 %) M. p. 84—86°, alone or on admixture with the ethyl α-galactoside tetraacetate described above.

Typical run

The experimental conditions for the kinetic determinations were the same as in the preceding papers (Compare Part III[1]) For the transglycosidation and the acetolysis runs sulfuric acid of concentration 0.03 C and 0.5 C respectively was used. For the transglycosidation of β-chloroethyl β-galactoside however, the concentration of sulfuric acid was 0.4 C. The solvent was a mixture of acetic anhydride-acetic acid, 10 : 3.

Table 2. Transglycosidation of iso-propyl β-galactoside tetraacetate. β-Galactose pentaacetate and iso-propyl β-galactoside tetraacetate, 0.5 g of each, dissolved in 20 ml of 0.031 C sulfuric acid in acetic anhydride-acetic acid, 10 : 3. t = 20° Rotations determined in 2 dm tubes. (The table gives only a part of the observed values.)

Time min.	β-Galactose pentaacetate		*iso*-Propyl β-galactoside tetraacetate	
	α_D	k	α_D	k
0	+ 1.42		— 0.14	
4	1.46	0.00250	+ 2.42	0.0625
8	1.54	237	3.87	630
12	1.59	209	4.68	632
16	1.64	200	5.18	656
20	1.74	220	5.40	644
30	1.94	233	5.66	
40	2.06	215	5.70_{max}	
∞	5.17			
	Mean value 0.0022		Mean value 0.063	

SUMMARY

The transglycosidation of some galactosides with sulfuric acid and titanium tetrachloride has been investigated. The reaction is somewhat faster than that of the corresponding glucosides but otherwise perfectly analogous.

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