CCCLXVI.—*The Effect of a 2-*p*-Toluenesulphonyl Group on the Reactivity of the Halogen Atom of a Glucosidyl Halide.*

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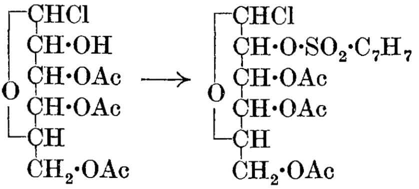
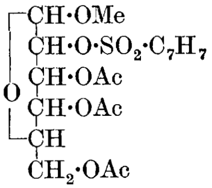
BY the action of *p*-toluenesulphonyl chloride and pyridine on 3 : 4 : 6-triacetyl β-glucosidyl chloride (I) (Brigl, *Z. physiol. Chem.*, 1921, **116**, 1) the author has obtained a glucosidyl chloride having the structure 2-p-*toluenesulphonyl* 3 : 4 : 6-*triacetyl* α-*glucosidyl chloride* (II). Its properties showed it to be a glucosidyl chloride and not a pyridinium salt, as might have been anticipated in view



(I.) (II.)



(III.)

of the formation of tetra-acetylglucosidopyridinium bromide from acetobromoglucose (Fischer and Raske, *Ber.*, 1910, **43**, 1750), and the behaviour of 3 : 4 : 6-triacetyl β-glucosidyl chloride towards trimethylamine (Micheel, *Ber.*, 1930, **63**, 386).

2-*p*-Toluenesulphonyl 3 : 4 : 6-triacetyl glucosidyl chloride differs from previously described glucosidyl halides, including 3-*p*-toluenesulphonyl triacetyl glucosidyl bromide (Freudenberg and Ivers, *Ber.*, 1922, **55**, 929), by virtue of the comparative inactivity of the chlorine atom. The rotation of a methyl-alcoholic solution remained almost constant for 14 days at 20—24°, and the compound was recovered unchanged after treatment similar to that which transformed the 3-*p*-toluenesulphonyl compound into the corresponding methylglucoside, namely, shaking a cold methyl-alcoholic solution of the substance with silver carbonate or silver oxide. It reacted, however, with methyl alcohol at higher temperatures, and the prolonged action of silver nitrate and pyridine in boiling methyl alcohol (Schlubach and Schröter, *Ber.*, 1928, **61**, 1216; Hickinbottom, J., 1929, 1676) yielded 2-p-*toluenesulphonyl* 3 : 4 : 6-*triacetyl methylglucoside* (III).

2-*p*-Toluenesulphonyl 3 : 4 : 6-triacetyl glucosidyl chloride was equally stable in the presence of pyridine in the cold, but it formed a pyridinium chloride at higher temperatures. In addition, all efforts to prepare the corresponding benzyl-, phenyl-, or nitrophenylglucoside, or to replace the chlorine atom by iodine, resulted in the recovery of the unchanged initial material.

The high specific rotation (+ 134·8°) of this substance and the direction of the change in rotation caused by glucoside formation ($[\alpha]_D^{16°}$ + 131·4° $\longrightarrow$ $[\alpha]_D^{17°}$ + 31·8°) indicated that it was an α-glucosidyl chloride. The rotation of an α-glucosidyl halide in a hydroxylic solvent falls steadily, whereas that of a β-glucosidyl halide rises to a maximum and then falls slowly to an equilibrium value (Schlubach, Stadler, and Wolf, *Ber.*, 1928, **61**, 287; Hickinbottom, *loc. cit.*). It has now been found that similar behaviour is displayed by α- and β-glucosidyl halides when dissolved in pyridine and, in this connexion, it may be noticed that 2-trichloroacetyl 3 : 4 : 6-triacetyl β-glucosidyl chloride (Brigl, *loc. cit.*) reacts with pyridine, forming a quaternary salt, although it does not react with trimethylamine (Micheel, *loc. cit.*). The mutarotation of 2-*p*-toluenesulphonyl 3 : 4 : 6-triacetyl α-glucosidyl chloride was followed in solution in pyridine at 100° and in boiling methyl alcohol, the reaction being very slow at lower temperatures. Under these somewhat drastic conditions the pyridine solution darkened slowly and the rapid fall in rotatory power appeared to indicate that some hydrolysis occurred in the methyl-alcoholic solution. It was obvious, however, that the substance was an α-glucosidyl chloride.

EXPERIMENTAL.

All the solvents used were pure and dry. The specific rotations employed in plotting mutarotation curves were calculated from the weight of glucosidyl halide initially present in the solution.

2-p-*Toluenesulphonyl* 3 : 4 : 6-*Triacetyl* α-*Glucosidyl Chloride* (II).—(1) A solution of *p*-toluenesulphonyl chloride (7·8 g.) and pyridine (10 c.c.) in chloroform (15 c.c.) was added to a suspension of 3 : 4 : 6-triacetyl β-glucosidyl chloride (12·5 g.) in chloroform (50 c.c.). After 48 hours, the solution was washed successively with dilute sulphuric acid (5%), potassium bicarbonate solution (3%), and water and dried over sodium sulphate, the chloroform removed, and the residue macerated with ether; the solid obtained crystallised from carbon tetrachloride in colourless platelets, m. p. 121—122°. Yield, 9·8 g. or 53% of the theoretical.

(2) 3 : 4 : 6-Triacetyl β-glucosidyl chloride (5 g.) was warmed gently with *p*-toluenesulphonyl chloride (3 g.) and pyridine (1·6 c.c.). After a few minutes a jelly-like mass was formed which solidified on standing and, after 24 hours, was ground with water. The product was washed with water, dried, and recrystallised. Yield, 3·3 g. or 45% of the theoretical.

A specimen which had been recrystallised three times from carbon tetrachloride had m. p. 122—123°, and $[\alpha]_D^{16\cdot5^\circ}$ + 134·8° in chloroform (c = 1·618) (Found : C, 47·6 ; H, 4·9 ; Cl, 7·5 ; S, 6·6. $C_{19}H_{23}O_{10}ClS$ requires C, 47·6 ; H, 4·8 ; Cl, 7·4 ; S, 6·7%). After being kept for 8 months in a corked tube, it had m. p. 116—118°, and $[\alpha]_D^{22^\circ}$ + 132·7° in chloroform (c = 1·628).

The substance was insoluble in light petroleum, almost insoluble in water and ether, and difficultly soluble in methyl and ethyl alcohols and cold carbon tetrachloride, but readily soluble in chloroform, benzene, ethyl acetate, acetone, and hot carbon tetrachloride. After boiling for a few minutes, an aqueous solution was acid to litmus, reduced Fehling's solution, and gave a precipitate of silver chloride with silver nitrate solution. A solution in pyridine slowly darkened at 100° and, after 3 hours, the addition of ether yielded an amorphous precipitate which became syrupy in air. This syrup probably consisted essentially of a pyridinium chloride, since it was readily soluble in cold water, giving a neutral solution which yielded an immediate precipitate of silver chloride with silver nitrate solution and did not reduce Fehling's solution.

The reaction between 3 : 4 : 6-triacetyl β-glucosidyl chloride (0·3024 g.), *p*-toluenesulphonyl chloride (0·178 g.), and pyridine (0·25 c.c.) in chloroform (to 20 c.c.) was followed polarimetrically, giving the following results :

Time (hours)	1·0	2·97	19·0	22·92	24·95	27·67	29·99	41·76	45·98	66·66	78·71	139·79	176·52
$[\alpha]_D^{17-18^\circ}$	+ 10·6°	16·9°	129·7°	144·9°	148·1°	150·1°	149·6°	+145·1°	142·9°	134·2°	127·2°	106·1°	98·3°

Mutarotation of 3 : 4 : 6-*Triacetyl* β-*Glucosidyl Chloride in Pyridine.*—The following results were obtained (l = 1, c = 1·518) :

Time (hours)	0·08	0·95	2·88	3·88	4·55	5·42	6·37	8·0	10·45	22·5	46·5
$[\alpha]_D^{16-18^\circ}$	+ 17·3°	45·5°	108·8°	125·3°	129·2°	134·0°	131·7°	+129·2°	122·0°	85·7°	56·0°

The mutarotation of 3 : 4 : 6-triacetyl β-glucosidyl chloride (0·3024 g.) in the presence of pyridine (0·25 c.c.) in chloroform (to 20 c.c.) was also observed (l = 2) :

Time (hours)	0·79	3·0	18·95	22·8	26·39	29·74	41·49	66·29	78·36	139·42	176·22
$[\alpha]_D^{16-18^\circ}$	+ 21·5°	28·8°	130·3°	149·9°	159·5°	162·8°	+164·0°	153·0°	149·2°	132·1°	123·8°

Mutarotation of 2-*Trichloroacetyl* 3 : 4 : 6-*Triacetyl* β-*Glucosidyl Chloride in Pyridine.*—The following results were obtained for l = 0·5, c = 1·526 :

Time (hours)	0·08	0·78	3·42	4·58	5·62	7·0
$[\alpha]_{\mathrm{D}}^{17-18^\circ}$	−10·5°	−6·6°	+30·1°	70·8°	80·0°	100·9°

Time (hours)	8·05	10·55	22·55	26·55	29·85	46·18
$[\alpha]_{\mathrm{D}}^{17-18^\circ}$	+110·0°	115·1°	118·6°	111·6°	104·8°	81·4°

The addition of ether to this solution then yielded an amorphous precipitate which had the properties of a pyridinium chloride.

Mutarotation of α'-*Acetobromoglucose in Pyridine.*—The following results were obtained for $l = 1$, $c = 2·42$:

Time (hours)	0·07	0·65	5·0	7·3	10·1
$[\alpha]_{\mathrm{D}}^{20^\circ}$	+202·2°	193·1°	144·3°	115·0°	71·5°

After 22 hours the solution was too dark in colour to permit further readings to be obtained.

Mutarotation of 2-p-*Toluenesulphonyl* 3 : 4 : 6-*Triacetyl* α-*Glucosidyl Chloride.*—(a) *In pyridine.* The following results were obtained :

(1) $l = 1$, $c = 1·564$. $[\alpha]_{\mathrm{D}}^{17^\circ}$ + 136·8°, remained constant for 5 days.

(2) $l = 0·5$, $c = 1·558$. $[\alpha]_{\mathrm{D}}^{35^\circ}$ + 134·9°, remained constant for 24 hours.

(3) The solution was immersed in a boiling water-bath, samples being withdrawn at intervals for observation ($c = 1·530$) :

Time (hours)	—	1	2	3
$[\alpha]_{\mathrm{D}}$	+134·1°	128·1°	120·2°	113·7°
l	1	1	0·5	0·5

The solution darkened slowly and after 4 hours it was impossible to obtain accurate readings.

(b) *In methyl alcohol.* The following results were obtained :

(1) $l = 2$, $c = 1·008$.

Time (days)	—	6·3	12·0	13·3	59·2	73
$[\alpha]_{\mathrm{D}}^{20-24^\circ}$	+130·0°	127·1°	125·6°	125·6°	59·6°	58·7°

(2) $l = 1$, $c = 1·492$. $[\alpha]_{\mathrm{D}}^{35^\circ}$ + 129·9°, remained constant for 24 hours.

(3) The solution was heated under reflux, samples being withdrawn at intervals for observation ($l = 1$, $c = 1·542$) :

Time (hours)	—	1	3·25	6·25	9·0	11·0
$[\alpha]_{\mathrm{D}}$	+132·0°	132·0°	121·1°	101·8°	59·6°	20·2°

(4) A methyl-alcoholic solution of (II) whose rotation ($[\alpha]_{\mathrm{D}}^{16^\circ}$ + 131·4°, $l = 1$, $c = 1·256$) had remained constant for 4 days was refluxed for $3\frac{1}{2}$ hours with the equivalent quantities of silver nitrate and pyridine, also dissolved in methyl alcohol. The filtered solution, which was made up to 20 c.c. with methyl alcohol, gave $[\alpha]_{\mathrm{D}}^{17^\circ}$ + 31·8° ($l = 2$). The reaction was then complete.

2-p-*Toluenesulphonyl* 3 : 4 : 6-*Triacetyl* β-*Methylglucoside* (III).—

2-*p*-Toluenesulphonyl 3 : 4 : 6-triacetyl α-glucosidyl chloride (5 g.) was dissolved in warm methyl alcohol (100 c.c.) and mixed with silver nitrate (1·8 g.) and pyridine (0·85 c.c.) in methyl alcohol (100 c.c.). The precipitation of silver chloride commenced immediately and was complete after 8 hours' refluxing. The solution was filtered with the addition of a little charcoal and concentrated to about 30 c.c. The *glucoside* crystallised in white needles, m. p. 156—157°. Yield, 3 g. or 60% of the theoretical. After two recrystallisations from alcohol a specimen had m. p. 157—157·5°, and $[\alpha]_D^{24°}$ + 3·4° in chloroform ($c = 2·015$) (Found: C, 50·6; H, 5·7. $C_{20}H_{26}O_{11}S$ requires C, 50·6; H, 5·5%).

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