62. *Some New Substituted Glucosides.*

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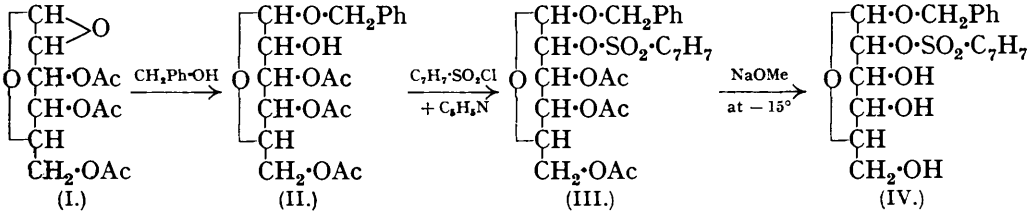
2-p-*Toluenesulphonyl* β-*methylglucoside*, 3 : 4 : 6-*triacetyl* β-*benzylglucoside* (II), 2-p-*toluenesulphonyl* 3 : 4 : 6-*triacetyl* β-*benzylglucoside* (III), and 2-p-*toluenesulphonyl* β-*benzylglucoside* (IV) have been prepared, the first by the regulated hydrolysis (cf. Helferich and Klein,

Annalen, 1927, **455**, 178) of 2-*p*-toluenesulphonyl 3 : 4 : 6-triacetyl β-methylglucoside (Reynolds, J., 1931, 2626) and the remainder from 1 : 2-anhydro-3 : 4 : 6-triacetyl glucose (I) (Brigl, *Z. physiol. Chem.*, 1922, **122**, 245; see also Hickinbottom, J., 1928, 3140) as shown below:



The reaction between 2-*p*-toluenesulphonyl 3 : 4 : 6-triacetyl β-methylglucoside (the most accessible of the glucosides described) and dimethylamine has also been examined, although it was realised that a complex mixture of substances might result (cf. Freudenberg and Hess, *Annalen*, 1926, **448**, 121; Ohle and Lichtenstein, *Ber.*, 1930, **63**, 2905). The process was carried out in methyl-alcoholic solution at 100° and a crystalline compound having the composition and properties of a β-*methylglycosidodimethylammonium* p-*toluenesulphonate* (V) was isolated. This substance yielded after hydrolysis an osazone (VI), which was separated,

by fractional crystallisation, from phenylhydrazine *p*-toluenesulphonate and another, as yet unidentified, compound (X), both of which were precipitated with it. The direction of the mutarotation of the osazone indicated that it was not a pentosazone (Levene and La Forge, *J. Biol. Chem.*, 1915, **20**, 429), the tetrosazones are optically inactive, and the nitrogen content was much greater than that of a hexosazone. The osazone was apparently, therefore, a dimethylamino-hexosephenylosazone (VI). The compound (X), which was obtained in only very small quantity, contained nitrogen and had the appearance and solubility of a phenylhydrazone or phenylhydrazide, but it markedly depressed the melting point of formaldehydephenylhydrazone.

It appears from this evidence that the dimethylamino-group of the β-methylglycosidodimethylammonium *p*-toluenesulphonate is not in the 2-position and that the action of dimethylamine on 2-*p*-toluenesulphonyl 3 : 4 : 6-triacetyl β-methylglucoside may be compared with that of ammonia on methylglucoside 2-chlorohydrin (Fischer, Bergmann, and Schotte, *Ber.*, 1920, **53**, 540), which yields a 3-amino-methylglycoside (Levene and Meyer, *J. Biol. Chem.*, 1923, **55**, 221; Freudenberg, Burkhard, and Braun, *Ber.*, 1926, **59**, 714). The *p*-toluenesulphonyl group may be removed from 2-*p*-toluenesulphonyl 3 : 4 : 6-triacetyl β-methylglucoside under conditions which do not affect 3-*p*-toluenesulphonyldiacetone glucose (Freudenberg and Ivers, *Ber.*, 1922, **55**, 929).

The method of isolation of 2-*p*-toluenesulphonyl 3 : 4 : 6-triacetyl α-glucosidyl chloride (Reynolds, *loc. cit.*) was modified in later preparations, and a substance having the composition and properties (cf. Meyer and Jacobson, "Lehrbuch der Organischen Chemie," 1920 ed., II, iii, 798; Fischer and Raske, *Ber.*, 1910, **43**, 1750) of a 2-p-*toluenesulphonyl* 3 : 4 : 6-*triacetylglucosidopyridinium* p-*toluenesulphonate* was isolated on one occasion in 1·5% yield from the mother-liquor.

Experimental.

All solvents were pure and dry; all evaporations were carried out under diminished pressure.

2-p-*Toluenesulphonyl* 3 : 4 : 6-*Triacetyl* α-*Glucosidyl Chloride*.—A solution of *p*-toluenesulphonyl chloride (13·5 g.) and pyridine (17·5 c.c.) in $CHCl_3$ (20 c.c.) was added to a suspension of 3 : 4 : 6-triacetyl β-glucosidyl chloride (22 g.) in the same solvent (90 c.c.). After 48 hr. the

solvent was removed as far as possible at 35—40°, and the residue cooled and poured into ice-cold MeOH (80 c.c.; 75%) containing AcOH (10 c.c.); 2-*p*-toluenesulphonyl 3 : 4 : 6-triacetyl α-glucosidyl chloride crystallised and was collected after 1 hr. (20·4 g.; m. p. 120—121°).

2-p-*Toluenesulphonyl* 3 : 4 : 6-*Triacetyl Glucosidopyridinium* p-*Toluenesulphonate*.—3 : 4 : 6-Triacetyl β-glucosidyl chloride (52 g.) was treated in the manner described above. The MeOH–AcOH filtrate obtained after the removal of 2-*p*-toluenesulphonyl 3 : 4 : 6-triacetyl α-glucosidyl chloride (42 g.) was diluted with H_2O and extracted thrice with $CHCl_3$. The combined extracts were washed with dil. HCl (5%), Na_2CO_3 aq. (3%), and H_2O, dried over Na_2SO_4, and evaporated. The brown residue, which crystallised slowly (several days), was drained on tile; from the solid (m. p. about 118°), boiling CCl_4 extracted 2-*p*-toluenesulphonyl 3 : 4 : 6-triacetyl α-glucosidyl chloride (3·5 g.). The final residue (approx. 1·5 g.) was neutral to litmus, contained S, did not reduce Fehling's solution even after boiling with H_2O or hydrolysis with dil. acid, and resinified immediately when boiled with 20% NaOH aq., an alkaline vapour having an odour resembling that of NMe_3 being evolved. The substance yielded a ppt. of phenylhydrazine *p*-toluenesulphonate (*see below*) when shaken with cold aq. phenylhydrazine acetate; it was sol. in hot H_2O, EtOH, and glycerol, almost insol. in these solvents when cold, and insol. in all other solvents, including pyridine. After four recrystns. from H_2O (charcoal) it was obtained in colourless shining plates, m. p. 218—219° (after darkening; decomp. 222°) (Found: C, 53·7; H, 5·2; N, 1·9; S, 9·2. $C_{31}H_{35}O_{13}NS_2$ requires C, 53·7; H, 5·1; N, 2·0; S, 9·2%). In glycerol containing 10% by vol. of H_2O, $[\alpha]_D^{14°}$ + 29·0° (c = 0·424). There was no mutarotation.

2-p-*Toluenesulphonyl* β-*Methylglucoside*.—Solutions of 2-*p*-toluenesulphonyl 3 : 4 : 6-triacetyl β-methylglucoside (3·6 g.) in $CHCl_3$ (12·5 c.c.) and of NaOMe (9 c.c. of a solution of Na, 0·5 g., in MeOH, 25 c.c.) were mixed, and kept for 1·5 hr. at − 15° and then washed with dil. AcOH (4%); the aq. layer was extracted twice with $CHCl_3$. The combined $CHCl_3$ solutions were washed (H_2O), dried (Na_2SO_4), and evaporated, and the residual syrup treated with Et_2O–MeOH (2 : 1); the white cryst. solid obtained (1·2 g.), after two recrystns. from EtOAc, had m. p. 116—117°, $[\alpha]_D^{23°}$ − 44·4° in H_2O (c = 2·006) and $[\alpha]_D^{22°}$ − 40·3° in $CHCl_3$ (c = 1·363) (Found: C, 48·4; H, 5·7. $C_{14}H_{20}O_8S$ requires C, 48·3; H, 5·7%). The *glucoside* was insol. in Et_2O and light petroleum but readily sol. in warm EtOAc, H_2O, and the usual org. solvents.

3 : 4 : 6-*Triacetyl* β-*Benzylglucoside* (II).—A solution of 1 : 2-anhydro-3 : 4 : 6-triacetyl glucose (7·5 g.) in $CH_2Ph{\cdot}OH$ (30 c.c.) was heated (boiling water-bath) for 12 hr., the alcohol then removed (2 mm. press.; bath temp. 100°), and the residue treated with aq. MeOH (approx. 70%). The sticky product crystallised from MeOH (80%) (charcoal) in colourless needles (4·5 g.), m. p. 113—114°. A specimen recryst. twice from MeOH (100%) had m. p. 115—116°, $[\alpha]_D^{24°}$ − 27·5° in $CHCl_3$ (c = 1·334) and $[\alpha]_D^{22°}$ − 15° in EtOH (c = 1·334) [Found: C, 57·3; H, 6·2; $CO{\cdot}CH_3$, 32·5. $C_{13}H_{15}O_6(CO{\cdot}CH_3)_3$ requires C, 57·6; H, 6·1; $CO{\cdot}CH_3$, 32·6%]. The *glucoside* was almost insol. in Et_2O, light petroleum, and cold H_2O, sol. in C_6H_6, EtOH, and hot H_2O, and very readily sol. in $CHCl_3$, acetone, and EtOAc. Acetylation with Ac_2O and pyridine yielded tetra-acetyl β-benzylglucoside, m. p. 95—97°, identified by comparison with a specimen prepared from acetobromoglucose (Fischer and Helferich, *Annalen*, 1911, **383**, 68).

2-p-*Toluenesulphonyl* 3 : 4 : 6-*Triacetyl* β-*Benzylglucoside* (III).—(1) Solutions of 3 : 4 : 6-triacetyl β-benzylglucoside (2·2 g.) in $CHCl_3$ (7 c.c.) and of *p*-toluenesulphonyl chloride (1·1 g.) and pyridine (1·5 c.c.) in $CHCl_3$ (4 c.c.) were mixed and, after 48 hr., washed successively with dil. H_2SO_4 (5%), $KHCO_3$ aq. (3%), and H_2O, and dried over Na_2SO_4; the $CHCl_3$ was removed, and the residue treated with Et_2O and light petroleum, yielding a white solid which crystallised from MeOH in fine needles (1·5 g.), m. p. 104°.

(2) 3 : 4 : 6-Triacetyl β-benzylglucoside (1 g.) was warmed with *p*-toluenesulphonyl chloride (0·46 g.) and pyridine (0·25 c.c.). The jelly-like product slowly solidified and, after 20 hr., was ground with H_2O, dried, and recrystallised as above. Yield, 0·8 g.

A specimen recryst. twice from MeOH had m. p. 105—106° and $[\alpha]_D^{24°}$ − 7·0 in $CHCl_3$ (c = 1·564) (Found: C, 56·7; H, 5·7. $C_{26}H_{30}O_{11}S$ requires C, 56·7; H, 5·5%). The *substance* was practically insol. in light petroleum and H_2O, difficultly sol. in Et_2O and cold EtOH, and readily sol. in hot EtOH and other org. solvents.

2-p-*Toluenesulphonyl* β-*Benzylglucoside* (IV).—Solutions of 2-*p*-toluenesulphonyl 3 : 4 : 6-triacetyl β-benzylglucoside (1·2 g.) in $CHCl_3$ (3 c.c.) and of NaOMe (3 c.c. of a solution of Na, 0·5 g., in MeOH, 25 c.c.) were mixed at − 15° and, after 1·5 hr., washed with a little dil. AcOH (3%) and with H_2O, dried over Na_2SO_4, and evaporated: the residue (0·8 g.) crystallised; m. p. 125—127°. After two recrystns. from EtOH the *glucoside* formed colourless platelets, m. p. 127—128°, $[\alpha]_D^{24°}$ − 34·3° in $CHCl_3$ (c = 1·252) (Found: C, 56·4; H, 5·7. $C_{20}H_{24}O_8S$

requires C, 56·6; H, 5·7%). It was insol. in light petroleum, slightly sol. in C_6H_6, Et_2O, H_2O, and cold EtOH, and readily sol. in hot EtOH and other solvents.

Methylglycosidodimethylammonium p-*Toluenesulphonate* (V).—2-*p*-Toluenesulphonyl 3 : 4 : 6-triacetyl β-methylglucoside (8 g.), suspended in MeOH (20 c.c.) containing $NHMe_2$ (approx. 10 g.), was heated at 100° for 18 hr.; the solvent was then evaporated, and the acetodimethylamide removed (2 mm. press.; bath temp. up to 90°). The residual brown syrup was dissolved in MeOH, and the solution partly decolorised with charcoal and evaporated to a syrup, which crystallised after some weeks in the first prepn. but after 2—3 days when seeded. The semi-cryst. product was drained on tile, and the colourless needles obtained were recrystallised from acetone. Yield, 2·2 g.; m. p. 80—81°. The *substance* reduced Fehling's solution after hydrolysis with dil. HCl and was readily sol. in all solvents excepting Et_2O, light petroleum, C_6H_6, and cold acetone. Successive recrystns. from acetone gave material, m. p. 78—81°, 70—72° (after drying in vac.), 73—77° (after 3 hr. in vac.), 68—70° (after 24 hr. in vac.), and 68—69° after softening at 67° (after 48 hr. in vac.). The last value was const. for specimens which had been dried in vac. over P_2O_5, but the m. p.'s of air-dried specimens or of specimens which were left in the air after drying in vac. were higher. The specimen analysed was dried as above and had m. p. 68—69° and $[\alpha]_D^{18°}$ − 105·7° in MeOH (c = 1·372) (Found: C, 46·5; H, 7·0; N, 3·4; H_2O, 4·5. $C_{16}H_{27}O_8NS,H_2O$ requires C, 46·7; H, 7·1; N, 3·4; H_2O, 4·4%). The last mol. of H_2O was removed at 130°.

Dimethylaminohexosephenylosazone (VI).—(1) Methylglycosidodimethylammonium *p*-toluenesulphonate (0·44 g.) was dissolved in 0·5*N*-HCl (10 c.c.) and heated (boiling water-bath) for 4 hr. The initial rotation was α_D − 4·12° (l = 0·5); after 3 hr. the rotation was α_D − 1·44°, and after 4 hr. α_D − 1·38°.

(2) A solution of methylglycosidodimethylammonium *p*-toluenesulphonate (0·85 g.) in 0·5*N*-HCl (15 c.c.) was heated (boiling water-bath) for 3 hr., cooled, and mixed with NaOAc (0·8 g.) and $NHPh{\cdot}NH_2$ (0·25 c.c.). The ppt. of phenylhydrazine *p*-toluenesulphonate (m. p. 168—170°. Found: N, 10·1. Calc. for $C_{13}H_{16}O_3N_2S$: N, 10·0%) was removed after 0·5 hr., and $NHPh{\cdot}NH_2$ (2 c.c.) and AcOH (1·5 c.c.) were added to the filtrate, which was heated (boiling water-bath) for 1 hr. A light orange ppt. formed, and further material separated when the solution was cooled and diluted with H_2O (3 vols.). The product was dissolved in hot EtOH; addition of hot H_2O (2 vols.) caused separation of tar, so a little charcoal was added before filtration. An orange solid (A) [m. p. about 147° (indef.)] separated from the filtrate. After addition of H_2O (3 vols.), yellow needles formed, m. p. 115—117° (B). The material on the filter was extracted with hot EtOH, and H_2O (1 vol.) was added to the solution, giving slightly coloured plates, m. p. 161° (C). (A) was fractionated as above, giving plates, m. p. 162° (D), a yellow solid, m. p. 145° (approx.) (E), and another yellow solid, m. p. 117—119° (F). (C) and (D) were combined and recrystallised from EtOH and H_2O (1 : 1), yielding almost colourless plates (X), m. p. 163—164° (decomp. 205°) (Found: N, 22·4. $C_7H_8N_2$ requires N, 23·3%); mixed m. p. with formaldehydephenylhydrazone, 145—150°. (B) and (F) were combined and dissolved in EtOH; hot H_2O (2 vols.) was added, producing a slight cloudiness, which was removed by filtration; the light orange-yellow needles which crystallised from the filtrate contracted at 120°, melted at 130—132°, and decomposed at 188° (Found: N, 18·5. $C_{20}H_{27}O_3N_5$ requires N, 18·2%). 3·88 Mg. were dissolved in pyridine–EtOH (2 : 3) (0·65 c.c.). This solution gave α_D (initial) − 0·09° ⟶ α_D (final) + 0·02° (l = 0·5), corresponding to α_D − 0·31° ⟶ α_D + 0·07° for 0·1 g. dissolved in 5 c.c. of pyridine–EtOH. A specimen of glucosephenylosazone which had α_D − 0·23° ⟶ α_D − 0·11° for the concn. used above, corresponding to α_D − 0·79° ⟶ α_D − 0·32° for 0·1 g. in 5 c.c. of solvent, had α_D − 0·69° ⟶ α_D − 0·31° for 0·1 g. in 5 c.c. (Levene and La Forge, *J. Biol. Chem.*, 1915, **20**, 429, give α_D − 0·62° ⟶ α_D − 0·35°).

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