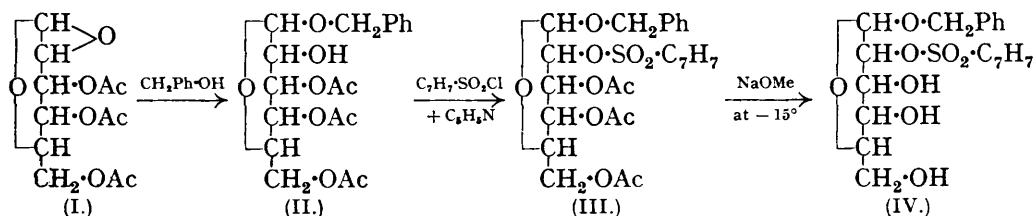


62. *Some New Substituted Glucosides.*

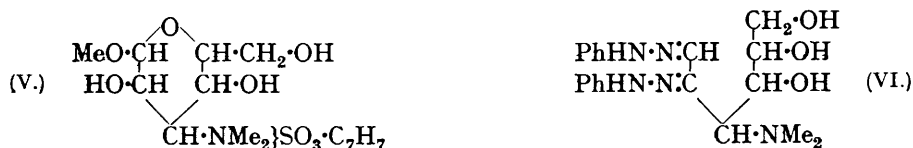
By (MISS) THELMA M. REYNOLDS.

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*-toluenesulphonyl-diacetone 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 H₂O and extracted thrice with CHCl₃. The combined extracts were washed with dil. HCl (5%), Na₂CO₃ aq. (3%), and H₂O, dried over Na₂SO₄, and evaporated. The brown residue, which crystallised slowly (several days), was drained on tile; from the solid (m. p. about 118°), boiling CCl₄ 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 H₂O or hydrolysis with dil. acid, and resinified immediately when boiled with 20% NaOH aq., an alkaline vapour having an odour resembling that of NMe₃ 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 H₂O, EtOH, and glycerol, almost insol. in these solvents when cold, and insol. in all other solvents, including pyridine. After four recrystns. from H₂O (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. C₃₁H₃₅O₁₃NS₂ requires C, 53.7; H, 5.1; N, 2.0; S, 9.2%). In glycerol containing 10% by vol. of H₂O, $[\alpha]_D^{25} + 29.0^\circ$ ($c = 0.424$). There was no mutarotation.

2-*p*-Toluenesulphonyl β -Methylglucoside.—Solutions of 2-*p*-toluenesulphonyl 3 : 4 : 6-triacetyl β -methylglucoside (3.6 g.) in CHCl₃ (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 CHCl₃. The combined CHCl₃ solutions were washed (H₂O), dried (Na₂SO₄), and evaporated, and the residual syrup treated with Et₂O–MeOH (2 : 1); the white cryst. solid obtained (1.2 g.), after two recrystns. from EtOAc, had m. p. 116–117°, $[\alpha]_D^{25} - 44.4^\circ$ in H₂O ($c = 2.006$) and $[\alpha]_D^{25} - 40.3^\circ$ in CHCl₃ ($c = 1.363$) (Found: C, 48.4; H, 5.7. C₁₄H₂₀O₈S requires C, 48.3; H, 5.7%). The glucoside was insol. in Et₂O and light petroleum but readily sol. in warm EtOAc, H₂O, 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 CH₂Ph–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°, $[\alpha]_D^{25} - 27.5^\circ$ in CHCl₃ ($c = 1.334$) and $[\alpha]_D^{25} - 15^\circ$ in EtOH ($c = 1.334$) [Found: C, 57.3; H, 6.2; CO·CH₃, 32.5. C₁₃H₁₅O₆(CO·CH₃)₃ requires C, 57.6; H, 6.1; CO·CH₃, 32.6%]. The glucoside was almost insol. in Et₂O, light petroleum, and cold H₂O, sol. in C₆H₆, EtOH, and hot H₂O, and very readily sol. in CHCl₃, acetone, and EtOAc. Acetylation with Ac₂O 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 CHCl₃ (7 c.c.) and of *p*-toluenesulphonyl chloride (1.1 g.) and pyridine (1.5 c.c.) in CHCl₃ (4 c.c.) were mixed and, after 48 hr., washed successively with dil. H₂SO₄ (5%), KHCO₃ aq. (3%), and H₂O, and dried over Na₂SO₄; the CHCl₃ was removed, and the residue treated with Et₂O 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 H₂O, dried, and recrystallised as above. Yield, 0.8 g.

A specimen recryst. twice from MeOH had m. p. 105–106° and $[\alpha]_D^{25} - 7.0$ in CHCl₃ ($c = 1.564$) (Found: C, 56.7; H, 5.7. C₂₆H₃₀O₁₁S requires C, 56.7; H, 5.5%). The substance was practically insol. in light petroleum and H₂O, difficultly sol. in Et₂O 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 CHCl₃ (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 H₂O, dried over Na₂SO₄, 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°, $[\alpha]_D^{25} - 34.3^\circ$ in CHCl₃ ($c = 1.252$) (Found: C, 56.4; H, 5.7. C₂₀H₂₄O₈S

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. $80-81^\circ$. 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. $78-81^\circ$, $70-72^\circ$ (after drying in vac.), $73-77^\circ$ (after 3 hr. in vac.), $68-70^\circ$ (after 24 hr. in vac.), and $68-69^\circ$ 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. $68-69^\circ$ and $[\alpha]_D^{18} - 105.7^\circ$ 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 $\alpha_D - 4.12^\circ$ ($l = 0.5$); after 3 hr. the rotation was $\alpha_D - 1.44^\circ$, and after 4 hr. $\alpha_D - 1.38^\circ$.

(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. $168-170^\circ$. 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. $115-117^\circ$ (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. $117-119^\circ$ (F). (C) and (D) were combined and recrystallised from $EtOH$ and H_2O (1 : 1), yielding almost colourless plates (X), m. p. $163-164^\circ$ (decomp. 205°) (Found: N, 22.4. $C_7H_8N_2$ requires N, 23.3%); mixed m. p. with formaldehydephenylhydrazone, $145-150^\circ$. (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 $130-132^\circ$, 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) $- 0.09^\circ \rightarrow \alpha_D$ (final) $+ 0.02^\circ$ ($l = 0.5$), corresponding to $\alpha_D - 0.31^\circ \rightarrow \alpha_D + 0.07^\circ$ for 0.1 g. dissolved in 5 c.c. of pyridine- $EtOH$. A specimen of glucosephenylosazone which had $\alpha_D - 0.23^\circ \rightarrow \alpha_D - 0.11^\circ$ for the concn. used above, corresponding to $\alpha_D - 0.79^\circ \rightarrow \alpha_D - 0.32^\circ$ for 0.1 g. in 5 c.c. of solvent, had $\alpha_D - 0.69^\circ \rightarrow \alpha_D - 0.31^\circ$ for 0.1 g. in 5 c.c. (Levene and La Forge, *J. Biol. Chem.*, 1915, 20, 429, give $\alpha_D - 0.62^\circ \rightarrow \alpha_D - 0.35^\circ$).

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