

280. A New Reaction of the Dichloroacetyl Group in Derivatives of Glucose.

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THE author has recently discovered that dichloroacetyl groups occupying positions 2, 3, 4, and 6 in α - and β -methylglucopyranosides may be quantitatively eliminated by the action of silver acetate suspended in aqueous acetone, whereas acetyl, benzoyl, *p*-toluenesulphonyl, or benzylidene groups are not removed from the molecule. Unfortunately, in certain instances, the well-known tendency of acyl groups of sugar derivatives to migrate, in alkaline media, towards position 6, appears to limit the application of this otherwise useful reaction which is also hindered by toluenesulphonyl groups. By the action of dichloroacetyl chloride on solutions of the appropriate starting materials below -10° , the following substances were prepared: (a) crystalline: 2:3-bisdichloroacetyl benzylidene α - and β -methylglucosides; 4-dichloroacetyl 2:3:6-triacetyl β -methylglucoside; 6-dichloroacetyl 2:3:4-tri-*p*-toluenesulphonyl β -methylglucoside; 6-dichloroacetyl 2:3-dibenzoyl 4-*p*-toluenesulphonyl α -methylglucoside; (b) amorphous: 4:6-bisdichloroacetyl 2:3-dibenzoyl α -methylglucoside; 6-dichloroacetyl 2:3:4-tribenzoyl α -methylglucoside.

The results obtained on treatment of the above substances with silver acetate are tabulated below. Diminished yields are due to acyl migration.

Derivatives of methyl glucoside.	Crude yield, %.	Pure yield, %.
2:3-Bisdichloroacetylbenzylidene- α -	—	96
2:3-Bisdichloroacetylbenzylidene- β -	—	97
4-Dichloroacetyl 2:3:6-triacetyl- β -	100	91
4:6-Bisdichloroacetyl 2:3-dibenzoyl- α -	96	63*
6-Dichloroacetyl 2:3:4-tribenzoyl- α -	87.4	42†
6-Dichloroacetyl 2:3:4-tri- <i>p</i> -toluenesulphonyl- β -	95	nil

* Isolated as crystalline diacetate.

† „ „ „ *p*-toluenesulphonate.

The case of 6-dichloroacetyl 2:3:4-tri-*p*-toluenesulphonyl β -methylglucoside is of interest. Although the dichloroacetyl group was completely eliminated, the product was not pure 2:3:4-tri-*p*-toluenesulphonyl β -methylglucoside, suggesting that migration and slight loss of toluenesulphonyl may have taken place.

In only one example investigated was the dichloroacetyl group completely resistant, *viz.*, in 6-dichloroacetyl 2:3-dibenzoyl 4-*p*-toluenesulphonyl α -methylglucoside, the starting material being recovered unchanged. This result cannot be attributed solely to the presence of the toluenesulphonyl group in position 4, since the same substituent in 2:3:4-tri-*p*-toluenesulphonyl β -methylglucoside caused no interference.

EXPERIMENTAL.

Introduction of the Dichloroacetyl Group.—The starting material was dissolved in 5 parts of dry pyridine, and, the temperature being kept below -10° , a solution of 1.5 parts per hydroxyl group of dichloroacetyl chloride in 2 vols. of dry benzene was added dropwise with stirring. The whole was kept in ice for 3 hours, and more benzene and water were then added. The product was obtained from the benzene solution, after appropriate washing, by evaporation in a vacuum and the addition of a little alcohol, from which the crystalline derivatives readily separated.

Elimination of Dichloroacetyl Group.—To a solution of the dichloroacetate in 25% aqueous acetone, were added solid silver nitrate and sodium acetate (each 25% excess over theory per chlorine atom). The whole was heated under reflux on the boiling water-bath for 3 hours, the solid matter removed by filtration, and the filtrate evaporated to dryness under reduced pressure. The product was obtained from the solid residue by extraction with boiling chloroform, and the solvent distilled off. Neither silver nitrate nor sodium acetate separately affected the dichloroacetyl groups.

Rotatory powers were determined in chloroform in a 2-dm. tube, unless otherwise stated.

2:3-Bisdichloroacetyl Benzylidene α -Methylglucoside (I).—10 G. of benzylidene α -methyl-

glucoside yielded 8.5 g. (50%) of long needles from alcohol, m. p. 120—122°, $[\alpha]_D^{18} + 57.6^\circ$ ($c = 5.642$) (Found: Cl, 27.1; OMe, 6.2. $C_{18}H_{18}O_8Cl_4$ requires Cl, 28.1; OMe, 6.16%). The substance is easily soluble in organic solvents except light petroleum and cold alcohol.

Elimination of dichloroacetyl. The crude product obtained from 1.000 g. of (I), when recrystallised from water, gave 0.560 g. (96%) of needles, m. p. 161°, undepressed after admixture with 4:6-benzylidene α -methylglucoside; $[\alpha]_D^{18} + 117.8^\circ$ ($l = 4$, $c = 5.642$). Mathers and Robertson (J., 1933, 696) quote $[\alpha]_D + 117.5^\circ$ for the latter substance.

2:3-Bisdichloroacetyl Benzylidene β -Methylglucoside (II).—3.7 G. of benzylidene β -methylglucoside yielded 2.5 g. (53%) of fine needles, from alcohol, m. p. 154—155°, $[\alpha]_D^{18} - 63.7^\circ$ ($c = 3.477$) (Found: Cl, 28.1. $C_{18}H_{18}O_8Cl_4$ requires Cl, 28.1%). Solubilities as for (I).

Elimination of dichloroacetyl. The crude product from 0.815 g. of (II), recrystallised from water, gave 0.463 g. (97.4%) of fine needles, m. p. 200°, undepressed after admixture with 4:6-benzylidene β -methylglucoside; $[\alpha]_D^{18} - 74.5^\circ$ in alcohol ($l = 4$, $c = 0.614$). Zervas (Ber., 1931, 64, 2289) gives $[\alpha]_D - 74.8^\circ$ for the latter substance.

4-Dichloroacetyl 2:3:6-Triacetyl β -Methylglucoside (III).—7.0 G. of triacetyl methylglucoside (Levene and Raymond, J. Biol. Chem., 1932, 97, 763) yielded 7.9 g. (80.9%) of prisms, m. p. 78—79.5° (from alcohol), $[\alpha]_D^{18} - 30.0^\circ$ ($c = 4.157$) (Found: C, 41.74; H, 4.65; Cl, 16.20; OMe, 7.10. $C_{15}H_{20}O_{10}Cl_2$ requires C, 41.76; H, 4.64; Cl, 16.47; OMe, 7.19%). Solubilities as for (I).

Elimination of dichloroacetyl. 2.670 G. of (III) gave 1.980 g. of crude product (theor. yield) which rapidly crystallised. Recrystallisation from dry ether gave 1.803 g. of needles, m. p. 112—115° (no depression with 2:3:6-triacetyl β -methylglucoside), $[\alpha]_D^{18} - 62^\circ$ ($c = 3.238$). Helferich and Bredereck (Ber., 1931, 64, 2411) and Levene and Raymond (*loc. cit.*) give respectively $[\alpha]_D - 64.9^\circ$ and -59° for the latter substance.

4:6-Bisdichloroacetyl 2:3-Dibenzoyl α -Methylglucoside (IV).—6.0 G. of 2:3-dibenzoyl α -methylglucoside (Mathers and Robertson, J., 1933, 1076; Bell, J., 1934, 1177) yielded an amorphous product; this was dissolved in ether, and light petroleum added to turbidity, a small amount of deeply coloured material being precipitated. The supernatant liquid gave, on evaporation, 6.3 g. (96%) of an almost colourless glass, $[\alpha]_D^{18} + 119.6^\circ$ ($c = 4.210$) (Found: OMe 5.06. $C_{25}H_{22}O_{10}Cl_4$ requires OMe 4.97%).

Elimination of dichloroacetyl. 5.0 G. of (IV) yielded, after the crude product had been boiled in ether with norit, 3.10 g. (96%) of a pale yellow glass having the composition of a dibenzoyl methylhexoside, $[\alpha]_D^{18} + 153.3^\circ$. Bell (*loc. cit.*) found that 2:3-dibenzoyl α -methylglucoside had $[\alpha]_D + 165^\circ$, and that, on acetylation, it yields at least 90% as the crystalline diacetate. The product described above was acetylated, and a crystalline diacetate obtained in 96% yield. This was impure, and careful fractional crystallisation yielded pure 2:3-dibenzoyl 4:6-diacetyl α -methylglucoside, m. p. 124—126°, $[\alpha]_D^{18} + 140.6^\circ$ (Bell, *loc. cit.*), in amount corresponding to only 63% of the initial material. The residue (composition of dibenzoyl diacetyl methylhexoside) had $[\alpha]_D^{18} + 110^\circ$. Isomerisation had obviously occurred.

6-Dichloroacetyl 2:3:4-Tribenzoyl α -Methylglucoside (V).—1.5 G. of 2:3:4-tribenzoyl α -methylglucoside (Helferich and Becker, Annalen, 1924, 440, 1) yielded 1.6 g. (87.4%) of a rather insoluble brown glass which could not be crystallised; $[\alpha]_D^{18} + 45.3^\circ$ ($c = 3.100$) (Found: Cl, 11.1. $C_{30}H_{26}O_{10}Cl_2$ requires Cl, 11.5%).

Elimination of dichloroacetyl. 0.9 G. of (V) yielded (after treatment with norit in ether) 0.6 g. of a colourless glass, $[\alpha]_D^{18} + 45.4^\circ$ (2:3:4-tribenzoyl α -methylglucoside has $[\alpha]_D + 54.8^\circ$; Bell, *loc. cit.*). Since isomerisation had apparently occurred, as with (IV), the material was converted into the toluenesulphonyl derivative, under conditions normally giving a 90% yield of 6-toluenesulphonyl tribenzoyl α -methylglucoside. An impure crystalline product was obtained, and on fractional crystallisation it gave 0.300 g. of pure 6-toluenesulphonyl tribenzoyl α -methylglucoside (38% yield), identified by m. p., mixed m. p., and $[\alpha]_D$.

2:3:4-Tri-*p*-toluenesulphonyl β -Methylglucoside (VI).—This was obtained from 2:3:4-tritoluenesulphonyl β -methylglucoside-6-nitrate (Oldham and Rutherford, J. Amer. Chem. Soc., 1932, 54, 366) by reduction with zinc and iron in acetic acid; it is extremely insoluble, but crystallises readily in small needles, m. p. 188—189°, from glacial acetic acid; $[\alpha]_D^{18} - 40.6^\circ$ ($l = 4$, $c = 1.407$) (Found: S, 14.3. $C_{28}H_{32}O_{12}S_3$ requires S, 14.6%).

6-Dichloroacetyl 2:3:4-Tri-*p*-toluenesulphonyl β -Methylglucoside (VII).—0.50 G. of (VI) yielded 0.55 g. (94%) of fine needles (from equal parts of acetone and alcohol), m. p. 169—171°, $[\alpha]_D^{18} - 19.4^\circ$ ($c = 3.570$) (Found: S, 12.4; Cl, 10.0. $C_{30}H_{32}O_{13}S_3Cl_2$ requires S, 12.5; Cl, 9.3%).

Elimination of dichloroacetyl. The product, although free from chlorine, and crystalline, was not identical with (VI). It crystallised from acetic acid, in prisms, m. p. 164° not raised by

crystallisation from a number of solvents; $[\alpha]_D^{18} - 33.9^\circ$ (Found : C, 50.49; H, 5.33; S, 10.7. $C_{28}H_{32}O_{12}S_3$ requires C, 51.2; H, 4.9; S, 14.6%).

6-Dichloroacetyl 2 : 3-Dibenzoyl 4-*p*-Toluenesulphonyl α -Methylglucoside (VIII).—2.5 G. of 2 : 3-dibenzoyl 4-toluene-*p*-sulphonyl α -methylglucoside (Bell, *loc. cit.*) yielded 1.7 g. (56%) of lustrous, elongated prisms (from alcohol-acetone), m. p. 140—142°; $[\alpha]_D^{16} + 100.4^\circ$ ($c = 4.773$) (Found : C, 53.8; H, 4.47. $C_{30}H_{28}O_{11}S_2Cl_2$ requires C, 53.9; H, 4.19%).

Elimination of dichloroacetyl could not be effected in this instance : the starting material was recovered (pure) in 91% yield.

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