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Partial Esterification of 1,6-Anhydro-β-D-glucopyranose[1]

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The partial benzoylation and *p*-toluenesulfonylation of 1,6-anhydro-β-D-glucopyranose has been studied. The diesters and the monoesters at positions 2 and 4 have been prepared and their structure established by methylation.

A convenient pathway for introducing substituents into the sugar molecule is through the opening of sugar epoxides by various reagents. The rules governing the opening of epoxide rings have been firmly established, thus making it possible to predict the configuration of the products to be obtained. In the case of 1,6-anhydro-β-D-glucopyranose, four epoxides are possible, namely: 1,6:2,3-dianhydro-β-D-mannopyranose; 1,6:3,4-dianhydro-β-D-galactopyranose; 1,6:2,3- and 1,6:3,4-dianhydro-β-D-allopyranose. The rigidity and the conformation of these molecules are such that opening of the epoxide ring is stereoselective and will necessarily lead to the D-glucose configuration, in which all hydroxyls are in axial conformation. When attempts had been made in the past to synthesize 2-amino-2-deoxy-D-glucopyranose[4] or 2-*O*-methyl-D-glucopyranose[5] from derivatives not possessing the required rigidity, the yield of the desired compounds was low. With the use of the epoxides of 1,6-anhydro-β-D-glucopyranose, however, it would become possible to obtain derivatives of D-glucose selectively substituted at C-2, C-3, or C-4 with such radicals as $-NH_2$, $-OCH_3$, halogens, etc. Another possibility would be the labeling of the D-glucose molecule with O^{18} at any of these three positions.

The preparation of the epoxide derivatives of 1,6-anhydro-β-D-glucopyranose requires the synthesis of its *p*-tolylsulfonyl esters at C-2, C-3, and C-4. The purpose of the work presented in this paper was to study the synthesis of these *p*-tolylsulfonyl esters. The various benzoyl esters were also prepared, as possible intermediates for the selective introduction of the *p*-tolylsulfonyl groups.

Although total esterification of 1,6-anhydro-β-D-glucopyranose has been described previously by several authors, direct partial esterification has not been reported up to date. Partial etherification with benzyl groups has, however, been accomplished previously.[6]

From the conformation of the 1,6-anhydro-β-D-glucopyranose (XII) molecule, the hydroxyl at position 3 can be assumed to be less reactive then the two hydroxyls at C-2 and C-4. These two hydroxyls should be of equal reactivity, since they differ only slightly in their distances from the oxygen of the 1,6-anhydro bridge. As could be expected from these considerations, esterification of XII with two moles of *p*-toluenesulfonyl chloride or of benzoyl chloride, in pyridine solution, gave the 2,4-diesters XIII and XXVIII as major products; monoesters and triesters were, however, also obtained, as well as some starting material. The same products were obtained, but in different proportions, when the reaction was carried out with a single mole of either acid chloride: The amounts of the monoesters and of starting material were greater, while those of the di- and triesters were smaller. Separation of the various components of the reaction mixtures was accomplished by adsorption chromatography and by fractional crystallization. The low yields of purified monoesters were attributed to the complexity of the mixtures.

The positions of the *p*-tolylsulfonyl groups were determined by methylation procedure. The ditolylsulfonyl ester XIII was transformed into 3-*O*-methylglucose, proving the *p*-tolylsulfonyl groups to have been present at positions 2 and 4. By a similar sequence of reactions, 2-*O*-methylglucose, 3-*O*-methylglucose, 2,3-di-*O*-methylglucose and 3,4-di-*O*-methylglucose were prepared from the monotolylsulfonyl esters VII and XX. When sufficient amounts of the methylated derivatives of D-glucose were obtained, they were characterized by crystalline derivatives, otherwise by paper electrophoresis.

In the case of the dibenzoyl ester XXVIII, the benzoyl groups were shown to be located at positions 2 and 4 when the same product was obtained from the methylation of this ester and from the

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(2) Special Investigator of the Arthritis and Rheumatism Foundation.

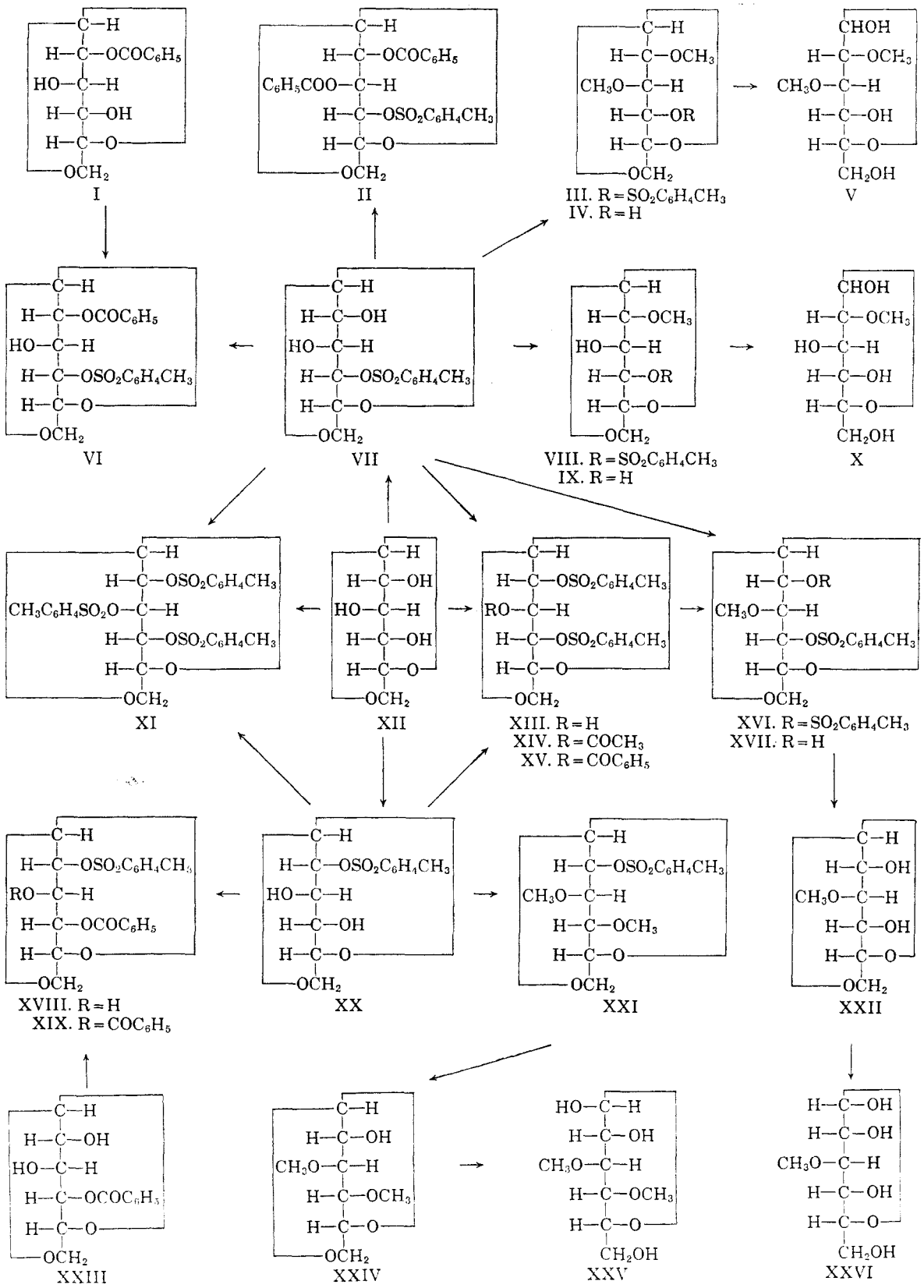
(3) Fulbright Fellow 1956–57.

(4) W. N. Haworth, W. H. G. Lake, and S. Peat, *J. Chem. Soc.*, 271 (1939).

(5) W. H. G. Lake and S. Peat, *J. Chem. Soc.*, 1417 (1938).

(6) G. Zemplén, Z. Csürös, and S. Angyal, *Ber.*, **70**, 1848 (1937).

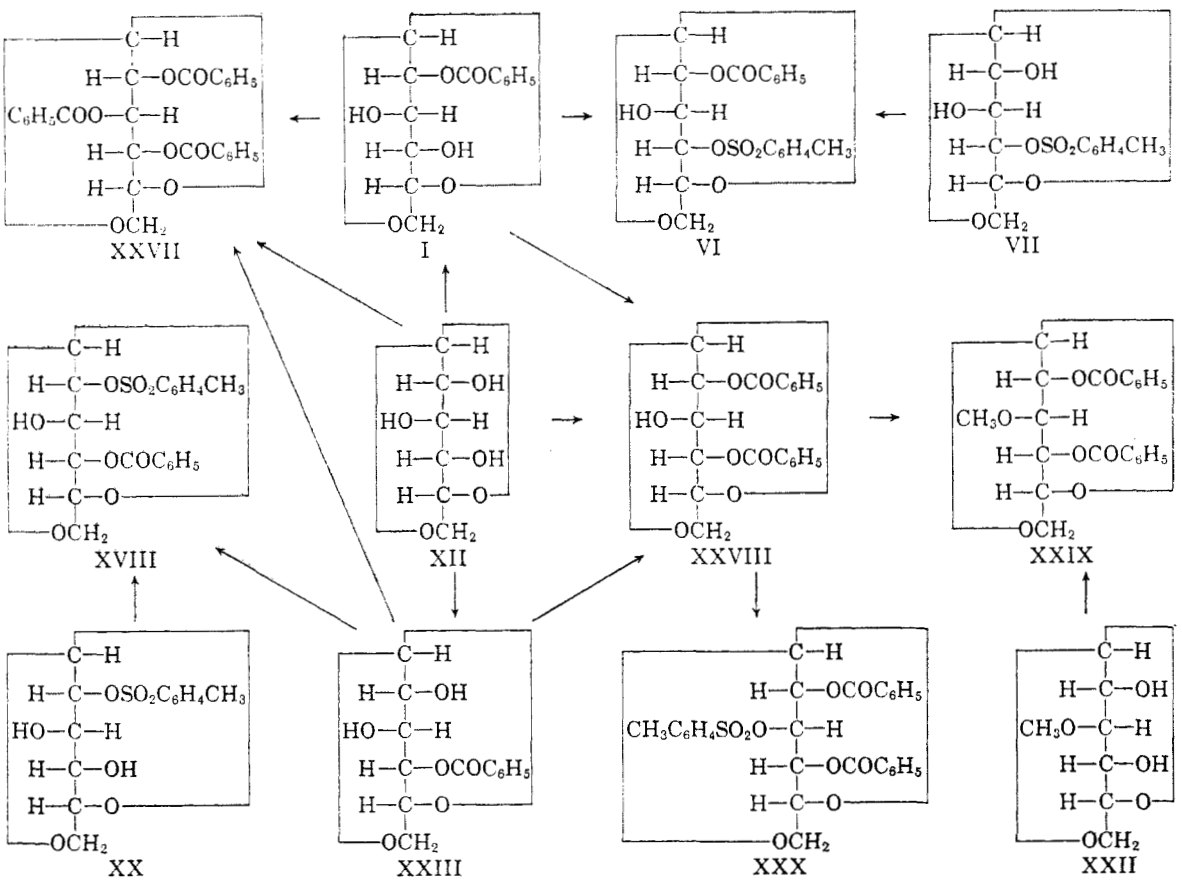
SCHEME 1



benzoylation of 1,6-anhydro-3-*O*-methyl-β-D-glucopyranose XXII.

The same 2-*O*-benzoyl-4-*O*-*p*-tolysulfonyl derivative VI was obtained by benzoylation of VII and by *p*-toluenesulfonylation of I. Similarly, the 4-*O*-benzoyl-2-*O*-*p*-tolylsulfonyl ester XVIII was pre-

SCHEME 2



pared either by benzoylation of XX or by *p*-toluenesulfonylation of XXIII.

The presence of one ester group in the molecule was found to make the two remaining free hydroxyl groups quite unreactive; much stronger conditions had to be used for the introduction in a monoester of a second or third group than for the direct preparation of the same di- or triesters from unchanged XII.

The preparation and structural determination of various esters of 1,6-anhydro-β-D-glucopyranose are summarized in schemes I and II.

EXPERIMENTAL

Melting points were taken on a hot stage, equipped with a microscope, and correspond to "corrected melting point". Rotations were determined in semimicro or micro (for amounts smaller than 3 mg.) tubes with lengths of 100 or 200 mm., using a polarimeter equipped with a Rudolph Photoelectric Attachment, Model 220; the chloroform used was A.R. grade and contained approximately 0.75% of ethanol.

Chromatograms were made with the flowing method on "Silica Gel Davison", from the Davison Co., Baltimore 3, Md. (grade 950; 60–200 mesh) used without pretreatment. When deactivation by contact with moist air occurred, reactivation was obtained by heating to 170–200° (Manufacturer's instructions). The sequence of eluants was hexane, benzene or chloroform, ether, ethyl acetate, acetone, and methanol individually or in binary mixtures. The proportion of weight of substance to be adsorbed to weight of adsorbent was 1 to 50–100; the proportion of weight of substance in g. to volume of fraction of eluant in ml. was 1 to 100. The ratio of diameter to length of the column was 1 to 20.

Evaporations were carried out *in vacuo*, with an outside bath temperature kept below 45°. Amounts of volatile solvent smaller than 20 ml. were evaporated by blowing dry nitrogen.

Unless otherwise mentioned, the esterification mixture, containing the carbohydrates and the resulting hydrochloric acid in pyridine solution, was extracted with a large amount of chloroform. The organic layer was washed successively three or four times with *2N* sulfuric acid, three times with saturated sodium bicarbonate, three times with water, and then dried over sodium sulfate. When an excess of acid chloride was present, this was destroyed by addition of a small amount of ice, and the solution was left standing for 0.5 hr. before extraction.

Paper electrophoreses were carried out according to Foster[7] on Whatman No. 3 paper, in borate buffer at *p*H 10, under cooling. A potential of 1500 v. was applied during 2 hr. The sugars were detected with aniline phthalate reagent.

Microanalyses by Dr. K. Ritter, Basel, and Dr. M. Manser, Zurich, Switzerland.

1,6-Anhydro-β-D-glucopyranose (XII). A mixture of 165 g. of phenyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside[8] and 1 l. of 3.3*N* sodium hydroxide was refluxed for 20 hr. After cooling, the solution was passed first through a column of 5 l. of Dowex 50 (H^+ form) and then through a column of 5 l. of Amberlite IRA 400 (OH^- form). The columns were

(7) A. B. Foster, *Advances in Carbohydrate Chem.*, **12**, 81 (1957).

(8) G. H. Coleman, C. M. McCloskey, and R. Kirby, *Ind. Eng. Chem.*, **36**, 1040 (1944).

washed with water (about 10 l.) until the effluent gave a negative Molisch test. The solution was concentrated, then filtered through a double layer of Darco G-60 and Celite, and concentrated to a sirup. After addition of absolute ethanol, crystallization started, and was completed at 0°. Yield 52.0 g. (82%), m.p. 184–186°.

p-Toluenesulfonylation of 1,6-anhydro-β-D-glucopyranose (XII). To a solution of 7.0 g. of XII in 50 ml. of anhydrous pyridine was added gradually, over a period of 24 hr., a solution of 8.26 g. of *p*-toluenesulfonyl chloride (1.0 mole-equiv.) in a mixture of 30 ml. of anhydrous pyridine and 50 ml. of ethylene dichloride. This operation was carried out at 0° with stirring. After 5 hr. at 0°, the reaction mixture was kept overnight at room temperature. It was then extracted with chloroform, and after concentration 15.9 g. of sirup was obtained, which was dissolved in benzene and chromatographed on silicic acid. A mixture of benzene and ether (39:1) eluted 535 mg. (2%) of partially crystalline *1,6-anhydro-2,3,4-tri-O-p-tolylsulfonyl-β-D-glucopyranose* (XI), which, by crystallization from a mixture of acetone and ether, gave 341 mg. of needles, m.p. 102–105°, $[\alpha]_D^{25}$ −19 ± 1° (in chloroform, *c*, 0.88).[9]

Anal. Calcd. for $C_{27}H_{28}O_{11}S_3$: C, 51.91; H, 4.52; S, 15.40. Found: C, 51.82; H, 4.45; S, 15.55.

Mixtures of benzene and ether (9:1 and 4:1) eluted 6.3 g. (31%) of partially crystalline *1,6-anhydro-2,4-di-O-p-tolylsulfonyl-β-D-glucopyranose* (XIII). It was crystallized from a mixture of acetone and ether to give 3.15 g. of small prisms, m.p. 119–121°, $[\alpha]_D^{27}$ −44 ± 2° (in chloroform, *c*, 0.9).

Anal. Calcd. for $C_{20}H_{22}O_9S_2$: C, 51.05; H, 4.71; S, 13.63. Found: C, 51.03; H, 4.65; S, 13.73.

Crystallization of the mother liquors gave an additional crop of 0.69 g. of crystals, m.p. 116–120°.

Mixtures of benzene and ether (1:2 and 1:4), pure ether, and a mixture of ether and acetone (1:1) eluted two different monotosylates weighing a total of 3.9 g. (29%). The first of these (1.36 g.) was eluted by a mixture of benzene and ether (1:2) and, after being recrystallized twice from a mixture of acetone, ether, and pentane, consisted of 569 mg. (4%) of *1,6-anhydro-4-O-p-tolylsulfonyl-β-D-glucopyranose* (VII), needles of m.p. 125–127° and $[\alpha]_D^{26}$ − 53 ± 2° (in chloroform, *c*, 0.43).

Anal. Calcd. for $C_{13}H_{16}O_7S$: C, 49.36; H, 5.10; S, 10.14. Found: C, 49.30; H, 5.08; S, 10.04.

The second fraction weighed 2.56 g. and, after two recrystallizations from a mixture of acetone, ether, and pentane, gave 834 mg. (6%) of *1,6-anhydro-2-O-p-tolylsulfonyl-β-D-glucopyranose* (XX), thick prisms, m.p. 116–119°, $[\alpha]_D^{26}$ − 75 ± 2° (in chloroform, *c*, 0.58).

Anal. Calcd. for $C_{13}H_{16}O_7S$: C, 49.36; H, 5.10; S, 10.14. Found: C, 49.33; H, 5.39; S, 10.02.

By crystallization of the mother liquors another crop of 268 mg. (2%) of crystals was obtained, m.p. 114–118°.

In another experiment, the esterification was carried out with 2.1 mole-equiv. of *p*-toluenesulfonyl chloride, and the reaction mixture was kept at 0° for 5.5 hr. followed by 2 days at room temperature. The crude yield of XI was 7% (6% after crystallization), and that of the ditosylate XIII was 69% (55% crystals). The total yield of the monotosyl derivatives was 13.5%, from which 0.3% was isolated as crystalline VII and 1.5% as crystalline XX.

Acetylation of 100 mg. of XIII with acetic anhydride in pyridine solution, in the usual manner gave, after crystallization from a mixture of acetone, ether, and pentane, 81 mg. (74%) of *1,6-anhydro-3-O-acetyl-2,4-di-O-p-tolylsulfonyl-β-D-glucopyranose* (XIV) as needles, m.p. 164–165°, $[\alpha]_D^{25}$ − 42 ± 1° (in chloroform, *c*, 2.10).

Anal. Calcd. for $C_{22}H_{24}O_{10}S_2$: C, 51.56; H, 4.72. Found: C, 51.81; H, 4.77.

Benzoylation of 200 mg. of XIII with benzoyl chloride in pyridine solution, in the usual manner gave, after two crystallizations from a mixture of acetone, ether, and pentane, 219 mg. (90%) of *1,6-anhydro-3-O-benzoyl-2,4-di-O-p-tolylsulfonyl-β-D-glucopyranose* (XV). It was obtained as a mixture of two crystalline forms, small prisms, m.p. 154–156°, and long prismatic needles, m.p. 164–166°, $[\alpha]_D^{25}$ − 49 ± 1° (in chloroform, *c*, 2.17).

Anal. Calcd. for $C_{27}H_{26}O_{10}S_2$: C, 56.44; H, 4.56. Found: C, 56.33; H, 4.64.

1,6-Anhydro-3-O-methyl-2,4-di-O-p-tolylsulfonyl-β-D-glucopyranose (XVI). A mixture of 2.0 g. of XIII, 2 g. of silver oxide, and 40 ml. of methyl iodide was refluxed for 24 hr. with stirring, an additional 2 g. of silver oxide being added after the first 16 hr. After cooling overnight, the mixture was filtered on a double layer of Darco G-60 and Celite and the silver residue was washed exhaustively with hot acetone. After distillation of the solvents, 2.04 g. of partially crystalline material was obtained, which was recrystallized twice from a mixture of acetone and ether, to give 1.31 g. (63%) of hexagonal prisms, m.p. 113–115°, $[\alpha]_D^{24}$ − 42 ± 1° (in chloroform, *c*, 1.71).

Anal. Calcd. for $C_{21}H_{24}O_9S_2$: C, 52.06; H, 4.99; OCH_3, 6.40. Found: C, 52.04; H, 4.98; OCH_3, 6.57.

The mother liquors were purified by chromatography on silicic acid, and gave an additional 253 mg. (22%) of crystalline XVI, m.p. 112–115°.

1,6-Anhydro-3-O-methyl-β-D-glucopyranose (XXII). To a solution of 1.93 mg. of XVI in 160 ml. of 90% ethanol was gradually added 24 g. of 2.5% sodium amalgam. The reaction mixture was left at room temperature for 36 hr. with occasional shaking; it was then filtered and the residue was washed with hot 90% ethanol. Carbon dioxide was passed through the filtrate until a *p*H of 5 to 6 was attained. The salts were filtered off and extracted with hot acetone, and the solution concentrated to give a partially crystalline residue. This residue was extracted with chloroform, and the water-soluble material was deionized by passage through columns of Amberlite IRA 400 (OH^- form) and Dowex 50 (H^+ form). After concentration, 456 mg. of a sirup was obtained, which was purified by chromatography on silicic acid. Ether and ethyl acetate eluted 337 mg. of partially crystalline material. This was crystallized from a mixture of acetone, ether, and pentane to give 260 mg. (37%) of stout, hygroscopic prisms, m.p. 59–69°. After recrystallization at low temperature, pure XXII was obtained, m.p. 68–70° (with rapid heating from 55°), $[\alpha]_D^{28}$ −59 ± 1° (in methanol, *c*, 1.20).[12]

Anal. Calcd. for $C_7H_{12}O_5$: C, 47.72; H, 6.87; OCH_3, 17.62. Found: C, 47.84; H, 6.81; OCH_3, 17.45.

3-O-Methyl-α-D-glucopyranose (XXVI). A solution of 150 mg. of XXII in 10 ml. of 2*N* hydrochloric acid was heated on the water bath for 2 hr. An excess of solid silver carbonate was added and the salts were removed by filtration through a double layer of Darco G-60 and Celite, washing the residue exhaustively with hot absolute ethanol. After concentration of the filtrate, 167 mg. of sirup was obtained, which was crystallized from methanol to give 106 mg. (64%) of small needles, m.p. 162–167°. Two recrystallizations raised the m.p. to 165–168°. The product had a mutarotation from $[\alpha]_D^{23}$ +91 (after 10 min.) to +55 ± 2° (after 96 hr., in water, *c*, 1.05).[14]

Anal. Calcd. for $C_7H_{14}O_6$: C, 43.30; H, 7.27; OCH_3, 15.98. Found: C, 43.24; H, 7.28; OCH_3, 15.84.

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(9) Hann and Richtmyer[10] found a m.p. of 103–106° and 121°, $[\alpha]_D^{20}$ −20° (in chloroform, *c*, 4); Vis[11] reported a m.p. of 122–124°, $[\alpha]_D^{18}$ −33.4° (in chloroform, *c*, 1.177).

(10) Personal communication of Dr. N. Richtmyer.

(11) E. Vis, *Diss. Univ. Zurich*, 1956.

(12) Reeves[13] reported a m.p. of 65–66°, $[\alpha]_D$ −64.8° (in acetone, *c*, 5.9).

(13) R. E. Reeves, *J. Am. Chem. Soc.*, **71**, 2116 (1949).

(14) Vargha[15] reported a m.p. of 167–168° and $[\alpha]_D^{20}$ from +104.5 to +55.5° (in water, *c*, 1.11).

(15) L. v. Vargha, *Ber.*, **67**, 1223 (1934).

The product was further identified by paper electrophoresis in borate buffer at *p*H 10, where it migrated in a manner identical with authentic 3-*O*-methylglucose, the observed M_G values being: glucose, 1.00; 2-*O*-methylglucose, 0.31; 3-*O*-methylglucose, 0.90; compound XXVI, 0.91; 4-*O*-methylglucose, 0.27. The product was characterized by formation of 3-*O*-methyl-*N*-phenyl-D-glucosylamine. A solution of 117 mg. of XXXI and 0.6 ml. of redistilled aniline in 5 ml. of methanol was refluxed for 5 hr. under moisture protection. After standing overnight, the solution was concentrated and the last traces of aniline were removed by codistillation with methanol and toluene. The residual orange sirup was crystallized from a mixture of methanol, ether, and pentane to give 95 mg. (59%) of plates, m.p. 143–149°. Recrystallization raised the m.p. to 152–153°. The melting point was not depressed in admixture with authentic material. The compound showed a mutarotation of $[\alpha]_D^{28}$ −108° (after 10 min.) to −46 ± 2° (after 24 hr., at equilibrium; in methanol, *c*, 0.53).[16]

Anal. Calcd. for $C_{13}H_{19}O_5N$: C, 57.98; H, 7.11. Found: C, 57.89; H, 7.05.

1,6-Anhydro-2,4-di-O-benzoyl-3-O-methyl-β-D-glucopyranose (XXIX) *from* XXII. To a solution of 50 mg. of XXII in 0.5 ml. of anhydrous pyridine cooled at −20° was added 0.19 ml. of benzoyl chloride cooled at 0°. The resulting solution was kept for 2 days at −20°, 1 day at 0°, and then was extracted with chloroform to give a partially crystalline residue. After recrystallization from a mixture of acetone, ether, and pentane, 81 mg. (74%) of small prisms was obtained, m.p. 139–141°, $[\alpha]_D^{27}$ − 30 ± 2° (in chloroform, *c*, 1.29).[18] No depression in melting point was observed in admixture with XXIX prepared by methylation of XXVIII as described below.

Anal. Calcd. for $C_{21}H_{20}O_7$: C, 65.62; H, 5.24. Found: C, 65.55; H, 5.23.

p-Toluenesulfonylation of 1,6-anhydro-4-O-p-tolylsulfonyl-β-D-glucopyranose (VII). To a solution of 50 mg. of VII in 1 ml. of anhydrous pyridine was added 66 mg. (2.2 mole-equiv.) of *p*-toluenesulfonyl chloride, and the mixture was kept for 4 days at 55°. It was then extracted with chloroform to give 82 mg. of a sirup which was dissolved in benzene and chromatographed on silicic acid. A mixture of benzene and ether (19:1) eluted 8 mg. (8%) of partially crystalline material which, by crystallization from a mixture of acetone and ether, gave 4 mg. of XI, m.p. 103–109°. Mixtures of benzene and ether (7:1 and 3:1) eluted 48 mg. (73%) of XIII, which was crystallized from a mixture of acetone and ether to give 34 mg. of small prisms, m.p. 117–120°. The melting point was not depressed in admixture with XIII prepared from XII or from XX.

An attempt was made to carry out this reaction with 1.1 mole-equiv. of *p*-toluenesulfonyl chloride, keeping the mixture at room temperature overnight, but only starting material was recovered.

p-Toluenesulfonylation of 1,6-anhydro-2-O-p-tolylsulfonyl-β-D-glucopyranose (XX). The reaction was carried out on 50 mg. of XX, as described for VII, and gave 37 mg. (38%) of crude XI, and 17 mg. (23%) of recrystallized XIII, m.p. 115–119°. No depression in melting point was observed in admixture with XIII obtained from XII or from VII, as described above.

When the reaction was carried out with 1.1 mole-equiv. of reagent at room temperature overnight, only starting material was recovered.

Benzoylation of 1,6-anhydro-4-O-p-tolylsulfonyl-β-D-glucopyranose (VII). To a solution of 100 mg. of VII in 0.5 ml. of anhydrous pyridine at − 20° was added a cooled solution of 0.04 ml. of benzoyl chloride (1.2 mole- equiv.) in 1 ml. of anhydrous pyridine, and the reaction mixture was kept at − 20° for 24 hr. and at room temperature for 17 hr. The mixture was extracted with chloroform and the resulting sirup (120 mg.) was purified by chromatography on silicic acid. A mixture of benzene and ether (19:1) eluted 10 mg. (6%) of II (see below) which, after crystallization from a mixture of acetone, ether, and pentane, gave 3 mg. of needles, m.p. 163–165°. Mixtures of benzene and ether (9:1 and 4:1) eluted 95 mg. (72%) of sirupy *1,6-anhydro-2-O-benzoyl-4-O-p-tolylsulfonyl-β-D-glucopyranose* (VI) which only crystallized after several months in the cold room. After three recrystallizations from a mixture of acetone, ether, and pentane, 48 mg. of needles was obtained, m.p. 114–116°, $[\alpha]_D^{31}$ + 24 ± 2° (in chloroform, *c*, 0.98). No depression of the melting point was observed in admixture with VI obtained by *p*-toluenesulfonylation of I as described below.

Anal. Calcd. for $C_{20}H_{20}O_8S$: C, 57.14; H, 4.80. Found: C, 57.10; H, 4.78.

Elution with more polar solvents gave 17 mg. of a sirup which was not further investigated.

In another experiment the esterification was carried out with 1.6 mole-equiv. of benzoyl chloride and, after 3 days at − 20° and extraction, a sirup was obtained which could be crystallized directly from a mixture of acetone, ether, and pentane to give 71% of *1,6-anhydro-2,3-di-O-benzoyl-4-O-p-tolylsulfonyl-β-D-glucopyranose* (II), m.p. 163–165°, $[\alpha]_D^{27}$ + 34 ± 2° (in chloroform, *c*, 1.05).

Anal. Calcd. for $C_{27}H_{24}O_9S$: C, 61.82; H, 4.61. Found: C, 62.07; H, 4.60.

Benzoylation of 1,6-anhydro-2-O-p-tolylsulfonyl-β-D-glucopyranose (XX). Benzoylation was carried out on 100 mg. of XX as described for VII, with the exception that the mixture was kept at 0° instead of at room temperature. This gave 2 mg. of recrystallized XIX (see below), and 89 mg. (66%) of partially crystalline *1,6-anhydro-4-O-benzoyl-2-O-p-tolylsulfonyl-β-D-glucopyranose* XVIII which, after being recrystallized twice from a mixture of acetone, ether, and pentane, gave 57 mg. of rectangular plates, m.p. 162–164°, $[\alpha]_D^{25}$ − 92 ± 1° (in chloroform, *c*, 1.14). The melting point was not depressed in admixture with XVIII obtained by *p*-toluenesulfonylation of XXIII as described below.

Anal. Calcd. for $C_{20}H_{20}O_8S$: C, 57.14; H, 4.80. Found: C, 57.03; H, 4.85.

The recovery of starting material XX, m.p. 114–116°, was 23 mg.

When the benzoylation was carried out with 4 mole-equiv. of benzoyl chloride, keeping the reaction mixture at 0° overnight and extracting as described above, a sirup was obtained which crystallized spontaneously. This was recrystallized twice from a mixture of acetone, ether, and pentane to give 70% of *1,6-anhydro-3,4-di-O-benzoyl-2-O-p-tolylsulfonyl-β-D-glucopyranose* (XIX), small prismatic needles, m.p. 162–164°, $[\alpha]_D^{23}$ − 124 ± 1° (in chloroform, *c*, 1.31).

Anal. Calcd. for $C_{27}H_{24}O_9S$: C, 61.82; H, 4.61. Found: C, 62.04; H, 4.68.

Methylation of 1,6-anhydro-4-O-p-tolylsulfonyl-β-D-glucopyranose (VII). A mixture of 474 mg. of VII, 475 mg. of silver oxide, and 15 ml. of methyl iodide was refluxed with stirring for 3 days, with addition of another 475 mg. of silver oxide after the first 24 hr. It was then filtered, and the silver residue was washed exhaustively with hot acetone. After evaporation of the solvents, 559 mg. of a sirup was obtained, which was dissolved in benzene and chromatographed on silicic acid. Mixtures of benzene and ether (9:1 and 4:1) eluted 155 mg. of partially crystalline material which, after crystallization from a mixture of acetone, ether and pentane, gave 72 mg. (14%) of *1,6-anhydro-2,3-di-O-methyl-4-O-p-tolylsulfonyl-β-D-glucopyranose* (III), short needles, m.p. 74–77°, $[\alpha]_D^{22}$ − 45 ± 1° (in methanol, *c*, 0.92).

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(16) Irvine and Hogg[17] reported a m.p. of 154–155°, $[\alpha]_D^{20}$ −108.5° to −50.3° (in methanol, *c*, 0.636).

(17) J. C. Irvine and T. P. Hogg, *J. Chem. Soc.*, **105**, 1386 (1914).

(18) Bardolph and Coleman[19] reported a m.p. of 134–136°, $[\alpha]_D^{25}$ −36° (in chloroform, *c*, 1.44).

(19) M. P. Bardolph and G. H. Coleman, *J. Org. Chem.*, **15**, 169 (1950).

Anal. Calcd. for $C_{15}H_{20}O_7S$: C, 52.31; H, 5.85; S, 9.31: OCH_3, 18.02. Found: C, 52.36; H, 6.01; S, 8.99; OCH_3, 16.62.

Mixtures of benzene and ether (3:2 and 1:1) eluted 358 mg. of partially crystalline material which could not be further purified by repeated crystallizations, and which was again chromatographed on silicic acid. From mixtures of benzene and ether (5:1 and 1:1), 311 mg. of partially crystalline material was obtained which, after three recrystallizations from a mixture of acetone, ether, and pentane, gave 60 mg. (12%) of *1,6-anhydro-3-O-methyl-4-O-p-tolylsulfonyl-β-D-glucopyranose* (XVII), thin transparent plates, m.p. 111–113°, $[\alpha]_D^{25} - 33 \pm 1°$ (in methanol, *c*, 0.93).

Anal. Calcd. for $C_{14}H_{18}O_7S$: C, 50.90; H, 5.49; OCH_3, 9.39. Found: C, 50.84; H, 5.52; OCH_3, 9.20.

From the mother liquors of XVII (269 mg.) were obtained, after rechromatography, 28 mg. of III, 56 mg. of XVII, and 70 mg. of partially crystalline material which, after four recrystallizations from a mixture of acetone and ether, gave 18 mg. of *1,6-anhydro-2-O-methyl-4-O-p-tolylsulfonyl-β-D-glucopyranose* (VIII), small prisms, m.p. 110–113°, $[\alpha]_D^{26} - 54 \pm 3°$ (in methanol, *c*, 0.64).

Anal. Calcd. for $C_{14}H_{18}O_7S$: C, 50.90; H, 5.49. Found: C, 51.02; H, 5.50.

The structure of XVII was determined by its transformation into 1,6-anhydro-3-*O*-methyl-β-D-glucopyranose (XXII) and 3-*O*-methyl-D-glucose (XXVI), as described above. The resulting XXVI was identified by paper electrophoresis in borate buffer, *p*H 10. The observed M_G values were: glucose, 1.00; 2-*O*-methylglucose, 0.28; 3-*O*-methylglucose, 0.82; 4-*O*-methylglucose, 0.24; 2,3-di-*O*-methylglucose, 0.17; compound XXVI, 0.82.

The structure of VIII was determined by its transformation into 1,6-anhydro-2-*O*-methyl-β-D-glucopyranose (IX) and 2-*O*-methyl-D-glucose (X), prepared in a similar manner as XXVI. The resulting X was identified by paper electrophoresis in borate buffer at *p*H 10. Its M_G was 0.28.

1,6-Anhydro-2,3-di-O-methyl-β-D-glucopyranose (IV). To a solution of 100 mg. of III in 10 ml. of 90% methanol was added 2.4 g. of 2.5% sodium amalgam, and the mixture was shaken for 24 hr. at room temperature, then left standing for 5 days. After filtering and washing of the mercury residue with hot 90% methanol, the solution was concentrated to a small volume and deionized by passage through columns of Amberlite IRA 400 (OH^- form) and Dowex 50 (H^+ form). The eluate was evaporated to dryness and 36 mg. (62%) of IV was obtained as a rather volatile sirup.[20] This was further purified by chromatography on silicic acid from which it was eluted by mixtures of benzene and ether and by pure ether. The purified compound had $[\alpha]_D^{25} - 82 \pm 2°$ (in chloroform, *c*, 0.97).

Anal. Calcd. for $C_8H_{14}O_6$: C, 50.52; H, 7.42. Found: C, 50.56; H, 7.55.

2,3-Di-O-methyl-D-glucose (V) *and 2,3-di-O-methyl-1,4,5,6-tetra-O-p-phenylazobenzoyl-D-glucitol.* A solution of 28 mg. of IV in 24 ml. of 2*N* hydrochloric acid was heated for 2 hr. on a water bath. The solution was then evaporated, the last traces of acid being removed by codistillation with ethanol and toluene. A quantitative yield of V was obtained as a sirup which was identified by paper electrophoresis in borate buffer, *p*H 10, where it migrated in a manner identical with authentic 2,3-di-*O*-methylglucose.[21]

It was further characterized by reduction to the corresponding glucitol and preparation of its tetra-*O*-*p*-phenylazobenzoyl derivative. The reduction was carried out by treating 13 mg. of V in 0.5 ml. of water at 0° with a cold solution of 10 mg. of sodium borohydride in 1 ml. of water. The solution was kept for 4.5 hr. at room temperature and was then acidified with 10% acetic acid. The sodium ions were removed by passage through a column of Dowex 50 (H^+ form), and the borate ions by distillation in the presence of methanol. After evaporation, 15 mg. (100%) of 2,3-di-*O*-methylglucitol was obtained as a sirup, which was *p*-phenylazobenzoylated directly, according to the method described by Boissonnas.[22] The sirup was dissolved in 8 ml. of anhydrous pyridine and treated with 87 mg. (5 mole-equiv.) of *p*-phenylazobenzoyl chloride in a sealed tube. The mixture was heated for 13 hr. at 36° and for 9 hr. at 100°. After decomposition of the excess of acid chloride with water, the solution was concentrated and the orange residue was taken up in chloroform. The azoic acid was removed by washing with 1% hydrochloric acid and filtering through a 0.5-cm. layer of alumina of Brockmann activity III. The chloroform layer was separated and washed twice with 1% hydrochloric acid and twice with water. After evaporation of the solvents and drying, 68 mg. of an orange solid was obtained which was dried overnight over phosphorus pentoxide, then purified by chromatography on a column of alumina of Brockmann activity III. Elution with 100 ml. of alcohol-free chloroform gave 41 mg. (63%) of orange material which was crystallized from a mixture of benzene and pentane to give 21 mg. of impure crystals from which, after two recrystallizations, 9 mg. of crystalline 2,3-di-*O*-methyl - 1,4,5,6 - tetra - *O* - *p* - phenylazobenzoyl - D-glucitol was obtained, m.p. 176–178°, $[\alpha]_D^{21} +102 \pm 2°$ (in benzene, *c*, 0.58).[23] No depression of the melting point was observed in admixture with authentic material.

A wide orange band, corresponding to partially azoylated material, remained on the alumina column. This was eluted with 100 ml. of C.P. chloroform, giving 12 mg. of residue which was treated with another 87 mg. of *p*-phenylazobenzoyl chloride, and heated at 100° for 19 hr. An additional crop of 9 mg. of recrystallized tetra-*O*-*p*-phenylazobenzoyl derivative was obtained.

1,6-Anhydro-3,4-di-O-methyl-2-O-p-tolylsulfonyl-β-D-glucopyranose (XXI). The methylation of 800 mg. of XX was carried out in a similar manner as the methylation of VII. After purification by chromatography and recrystallization from a mixture of acetone, ether, and pentane, 755 mg. (87%) of small prismatic needles was obtained, m.p. 105–107°, $[\alpha]_D^{22} -38 \pm 10$ (in methanol, *c* 0.92).

Anal. Calcd. for $C_{15}H_{20}O_7S$: C, 52.31; H, 5.85; S, 9.31; OCH_3, 18.02. Found: C, 52.33; H, 5.96; S, 10.01; OCH_3, 17.46.

1,6-Anhydro-3,4-di-O-methyl-β-D-glucopyranose (XXIV). A solution of 210 mg. of XXI was treated as described for the preparation of IV. The residual sirup was purified by chromatography on silicic acid to give 78 mg. (67%) of XXIV as a volatile sirup,[20] $[\alpha]_D^{24} -44 \pm 2°$ (in methanol, *c*, 1.36).

3,4-Di-O-methyl-β-D-glucopyranose (XXV). A solution of 32 mg. of XXIV in 3.2 ml. of 2*N* hydrochloric acid was heated for 2 hr. on a water bath. It was then concentrated *in vacuo* and the last traces of acid were removed by codistillation with ethanol and toluene. The residual sirup weighing 34 mg. (97%) was recrystallized three times from a mixture of methanol and ethyl acetate to give 10 mg. (34%) of XXV, small prisms, m.p. 114–118°. The compound showed mutarotation in methanol from $[\alpha]_D^{23} +33°$ (after 6 min.) to $[\alpha]_D^{23} + 92 \pm 3°$ (after 48 hr. at equilibrium; *c*, 0.70), but no mutarotation in water $[\alpha]_D^{25} +75 \pm 2°$ (after 10 min. and 24 hr.; *c*, 0.95).[24] The compound was shown by elemental analysis to crystallize with 1 mole of methanol.

Anal. Calcd. for $C_8H_{16}O_6 \cdot CH_3OH$: C, 44.99; H, 8.39. Found: C, 44.65; H, 8.43.

(20) The product was very volatile in water solution under a stream of dry nitrogen.

(21) J. C. Irvine and J. P. Scott, *J. Chem. Soc.*, 103, 575 (1913).

(22) R. Boissonnas, *Helv. Chim. Acta*, 30, 1689 (1947).

(23) Boissonnas[22] reported a m.p. of 181°, $[\alpha]_D^{15} +104°$ (in benzene, *c*, 0.71).

(24) Bell and Greville[25] reported a m.p. of 110–113° and various mutarotations, with end values of +77° in water and of +92° in methanol.

(25) D. J. Bell and G. D. Greville, *J. Chem. Soc.*, 1902 (1950).

In paper electrophoresis in borate buffer, *p*H 10, compound XXV migrated in a way identical with authentic 3,4-di-*O*-methylglucose, the observed M_G values being 0.32.

The structure of XXV was determined by its transformation into 3,4-di-*O*-methylphenylglucosazone. To a solution of 21 mg. of XXV in 0.25 ml. of water was added 0.3 ml. of a mixture of equal parts of phenylhydrazine, glacial acetic acid, and water, and the resulting solution was heated for 30 min. on the water bath. It was then evaporated, and the gummy orange residue was dissolved in the minimum amount of methanol. Upon addition of a few drops of water and cooling in an ice bath, 18 mg. (81%) of crystals was obtained, m.p. 103–120°. A 10-mg. portion of this crude material was purified by chromatography on silicic acid, and 7 mg. of partially crystalline material was eluted by mixtures of chloroform and ether (3:2 and 1:1) by pure ether, and by mixtures of ether and ethyl acetate (4:1 and 1:1). Crystallization from a mixture of methanol and ether gave 4.5 mg. of small prisms, m.p. 126–128°.[26]

Anal. Calcd. for $C_{20}H_{26}O_4N_4$: C, 62.16; H, 6.78. Found: C, 61.93; H, 6.68.

Benzoylation of 1,6-anhydro-β-D-glucopyranose (XII). To a solution of 1.5 g. of XII in 3 ml. of anhydrous pyridine cooled at 0° was added 1.06 ml. (0.97 mole-equiv.) of cooled benzoyl chloride. The solution was left at 0° overnight and extracted with chloroform. After concentration, 2.02 g. of sirup was obtained which was dissolved in benzene and chromatographed on silicic acid. A mixture of benzene and ether (9:1) eluted 229 mg. (5%) of *1,6-anhydro-2,3,4-tri-O-benzoyl-β-D-glucopyranose* (XXVII). After crystallization from a mixture of acetone and ether 152 mg. (3.5%) of small prisms was obtained, m.p. 202–203°; $[\alpha]_D^{25}$ −36 ± 1° (in chloroform, *c*, 1.14). No depression of the melting point was observed in admixture with authentic material.[27]

Mixtures of benzene and ether (5:1, then 3:1) eluted 797 mg. (23%) of *1,6-anhydro-2,4-di-O-benzoyl-β-D-glucopyranose* (XXVIII). It was crystallized from a mixture of acetone and ether to give 465 mg. (17%) of small prisms, m.p. 136–138°; $[\alpha]_D^{23}$ −34 ± 1° (in chloroform, *c*, 0.80).

Anal. Calcd. for $C_{20}H_{18}O_7$: C, 64.86; H, 4.90. Found: C, 64.71; H, 4.92.

Pure ether eluted two fractions of monobenzoates weighing 771 mg. (31%). The first fraction, 180 mg. (7.1%) of *1,6-anhydro-4-O-benzoyl-β-D-glucopyranose* (XXIII), was obtained by crystallization from a mixture of acetone, ether, and pentane. The small prismatic needles had a m.p. of 123–126° and $[\alpha]_D^{23}$ − 87 ± 2° (in chloroform, *c*, 1.04), $[\alpha]_D^{19}$ −85 ± 1° (in methanol, *c*, 0.93).

Anal. Calcd. for $C_{13}H_{14}O_6$: C, 58.64; H, 5.30. Found: C, 58.65; H, 5.39.

The material from the second fraction was crystallized from ethyl acetate to give 198 mg. (8.1%) of *1,6-anhydro-2-O-benzoyl-β-D-glucopyranose* (I), fine needles, m.p. 162–164°; $[\alpha]_D^{22}$ + 28 ± 1° (in methanol, *c*, 1.08).

Anal. Calcd. for $C_{13}H_{14}O_6$: C, 58.64; H, 5.30. Found: C, 58.54; H, 5.46.

When the same reaction was carried out with 1.03 mole-equiv. of benzoyl chloride for 18 hr. at −20°, the following amounts of recrystallized benzoyl derivatives were obtained: 1% of XXVII; 4.5% of XXVIII; 1% of XXIII, and 15% of I. In another experiment, benzoylation of XII was carried out with 1.1 mole-equiv. of benzoic anhydride at 50–53° for 24 hr. The yield of crude XXVII was 3%, and that of crude XXVIII, 21%. Also isolated were 4% of recrystallized XXIII, and 8% of recrystallized I.

1,6-Anhydro-2-O-benzoyl-4-O-p-tolylsulfonyl-β-D-glucopyranose (VI) *from* I. To a solution of 18 mg. of I in 0.7 ml. of anhydrous pyridine, cooled at 0°, was added a cooled solution of 32 mg. (2.5 mole-equiv.) of *p*-toluenesulfonyl chloride in 1 ml. of anhydrous pyridine. The solution was kept at 0° for 20 hr., and at room temperature for 1 week. It was then extracted with chloroform and, after concentration, 27 mg. of yellow sirup was obtained, which was dissolved in benzene and chromatographed on silicic acid. Mixtures of benzene and ether (9:1, then 5:1) eluted 13 mg. (46%) of crystalline material. Two crystallizations from a mixture of acetone, ether, and pentane gave 6.5 mg. (23%) of small, prismatic needles, m.p. 114–116°. No depression of the melting point was observed by admixture with VI obtained by benzoylation of VII as described above.

Further elution with mixtures of benzene and ether (1:1), pure ether, then ether and acetone (1:1) gave 6.5 mg. (36%) of the starting material I.

An attempt was made to carry out the esterification with only 1.1 mole-equiv. of *p*-toluenesulfonyl chloride, keeping the reaction mixture at 0° for 3 hr. and at room temperature for 6 days, but only starting material (90%) was obtained.

1,6-Anhydro-4-O-benzoyl-2-O-p-tolylsulfonyl-β-D-glucopyranose (XVIII). To a solution of 20 mg. of XXIII in 0.5 ml. of anhydrous pyridine, cooled at 0°, was added a cooled solution of 32 mg. (2.2 mole-equiv.) of *p*-toluenesulfonyl chloride in 1 ml. of anhydrous pyridine. The solution was kept at 0° overnight, at room temperature for one week, and was then extracted with chloroform. The residual sirup (28 mg.) was dissolved in benzene and chromatographed on silicic acid. Mixtures of benzene and ether (9:1, then 5:1) eluted 15 mg. (47%) of partly crystalline material. After crystallization from a mixture of acetone and ether, 8.5 mg. (27%) of short prismatic needles was obtained, m.p. 163–165°. No depression in melting point was observed in admixture with XVIII obtained by benzoylation of XX, as described above.

Further elution with mixtures of benzene and ether, pure ether, then ether and acetone gave 6 mg. (30%) of the starting material XXIII.

When the esterification was carried out with 1.1 mole-equiv. of *p*-toluenesulfonyl chloride, keeping the reaction mixture at 0° for 3 hr. then at room temperature for 3 days, only starting material was recovered.

Benzoylation of 1,6-anhydro-2-O-benzoyl-β-D-glucopyranose (I). To a solution of 20 mg. of I in 0.5 ml. of anhydrous pyridine was added 0.1 ml. of a solution containing 0.01 ml. of benzoyl chloride (1.1 mole-equiv.) in anhydrous pyridine, both solutions being previously cooled to − 20°. The reaction mixture was left at 0° for 24 hr. and at room temperature overnight, and then extracted with chloroform. The residual sirup (32 mg.) was dissolved in benzene and chromatographed on silicic acid. A mixture of benzene and ether (9:1) eluted 3 mg. (8%) of partially crystalline *1,6-anhydro-2,3,4-tri-O-benzoyl-β-D-glucopyranose* (XXVII), which was crystallized from a mixture of acetone and ether to give 2 mg. of small prisms melting at 201–203°. No depression of the melting point was observed in admixture with authentic XXVII. Mixtures of benzene and ether (9:1, 4:1, 2:1, and 1:1) eluted 17 mg. (60%) of *1,6-anhydro-2,4-di-O-benzoyl-β-D-glucopyranose* XXVIII. After two recrystallizations from a mixture of acetone, ether, and pentane, 6 mg. of small prisms was obtained, m.p. 136–137°. No depression of the melting point was observed by admixture with the dibenzoate XXVIII obtained in the benzoylation of XII, nor with that obtained by benzoylation of XXIII. Elution of the column with a mixture of benzene and ether (1:1), with pure ether, and with a mixture of ether and acetone (1:1) gave 5 mg. (25%) of the starting material I.

When the esterification was carried out with 1.1 mole-equiv. of benzoyl chloride, keeping the reaction mixture at −20° for 3 days and at room temperature for 2 days, no tribenzoate was obtained. The crude yield of dibenzoate was 27% and the recovery of starting material was 70%.

Benzoylation of 1,6-anhydro-4-O-benzoyl-β-D-glucopyranose (XXIII). Benzoylation of 20 mg. of XXIII with 1.6 mole-

(26) Bell and Greville[25] reported a m.p. of 126–127°.

(27) Wood and Fletcher[28] reported a m.p. of 202–203° and $[\alpha]_D^{20}$ −36.4° (in chloroform, *c*, 1.37).

(28) H. B. Wood, Jr., and H. G. Fletcher, Jr., *J. Am. Chem. Soc.*, 78, 207 (1956).

equiv. of benzoyl chloride in the conditions described for I gave 18 mg. (51%) of crystalline XXVII, m.p. 203–204°, and 7 mg. (25%) of XXVIII, m.p. 135–137°.

When the benzoylation was carried out with 1.1 mole-equiv. of benzoyl chloride, keeping the reaction mixture at −20° for 3 days followed by 24 hr. at 0°, no tribenzoate was obtained, and only 16% of impure dibenzoate. The starting material XXIII was recovered to the extent of 81%.

1,6-Anhydro-2,4-di-O-benzoyl-3-O-p-tolylsulfonyl-β-D-glucopyranose (XXX). A mixture of the cooled solutions of 92 mg. of XXVIII and 143 mg. of *p*-toluenesulfonyl chloride (3 mole-equiv.), each in 1 ml. of anhydrous pyridine, was kept at 0° for 2 hr. and at room temperature overnight. It was then extracted with chloroform and gave 108 mg. of sirup which was dissolved in benzene and chromatographed on silicic acid. A mixture of benzene and ether (19:1) eluted 32 mg. of sirup which, by crystallization from a mixture of acetone, ether, and pentane, gave 15 mg. (11%) of long, slender needles, m.p. 125–127°.

Anal. Calcd. for $C_{27}H_{24}O_9S$: C, 61.82; H, 4.61; S, 6.11. Found: C, 61.68; H, 4.45; S, 6.09.

Mixtures of benzene and ether (9:1, 4:1 and 1:1) eluted 67 mg. of starting material.

1,6-Anhydro-2,4-di-O-benzoyl-3-O-methyl-β-D-glucopyranose (XXIX) *from* XXVIII. A mixture of 50 mg. of XXVIII, 50 mg. of silver oxide, and 3 ml. of methyl iodide was stirred for 1 day at room temperature under moisture protection. After addition of another 50-mg. portion of silver oxide, the mixture was stirred for 9 hr. longer. It was then filtered through a double layer of Darco G-60 and Celite, and the silver residue was washed exhaustively with hot acetone. After concentration of the filtrate 57 mg. of sirup was obtained. It was recrystallized twice from a mixture of acetone, ether, and pentane to give 29 mg. (56%) of XXIX, thick prisms, m.p. 137–140°, $[\alpha]_D^{24}$ − 30 ± 1° (in chloroform, *c*, 1.50). No depression of the melting point was observed in admixture with a sample of XXIX prepared by benzoylation of XXII as described above.

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[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY, PURDUE UNIVERSITY]

6,6′-Diglycose Anhydrides[1]

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5,6-Anhydro-1,2-*O*-isopropylidene-D-glucose reacts in the melted state with either 1,2-*O*-isopropylidene-D-glucose or 1,2:3,4-di-*O*-isopropylidene-D-galactose to produce in good yield the 6,6′-anhydrides. Addition of an alkaline catalyst increases reaction with secondary hydroxyls and consequently also increases the polymerization. Both diglycose anhydrides are obtained amorphous but the 6,6′-di-D-glucose anhydride octaacetate is obtained crystalline.

Sugar derivatives with 5,6-anhydro rings have proved useful in many synthetic reactions. The sugar derivative most extensively investigated is 5,6-anhydro-1,2-*O*-isopropylidene-D-glucofuranose whose reactivity is intensively examined in the work of Ohle.[2] In general, the derivative reacts with compounds containing an active hydrogen, with opening of the oxirane ring between the oxygen and carbon C-6. Consequently, the D-glucose configuration is predominantly retained and substitution occurs on carbon C-6. Addition reactions under anhydrous conditions are base-catalyzed by such reagents as pyridine and sodium ethoxide. Under certain basic conditions ring opening occurs to a small extent between the oxygen and carbon C-5 with derivatization and inversion of carbon C-5. Consequently, there is obtained a small amount of product with the L-idose configuration.

In this work attention was given to the use of 5,6-anhydro-1,2-*O*-isopropylidene-D-glucofuranose to derivatize corn amylose and to react with a second sugar derivative to create a 6,6′-diglycose anhydride. First attempts to react the 5,6-anhydro sugar with corn amylose led to self polymerization of the anhydride and to some degradation of the amylose with little evident substitution of the amylose. Hence, most of the effort was directed toward the reaction of the anhydro sugar with another sugar derivative.

When 5,6-anhydro-1,2-*O*-isopropylidene-D-glucofuranose is melted with 1,2-*O*-isopropylidene-D-glucofuranose, there occurs an extensive opening of the oxirane ring and combination of the two sugars with the formation of intermolecular anhydrides. The predominant product is the 1,2:1′,2′-di-*O*-isopropylidene-6,6′-di-D-glucofuranose anhydride which hydrolyzes to 6,6′-di-D-glucose anhydride. This compound is isolated in the amorphous condition but is readily converted to the crystalline octaacetate. Paper chromatographic analysis of the hydrolyzed products from the melt reaction suggests the presence of small amounts of polymer and possibly of 3,6′- and 5,6′-di-D-glucose anhydrides. Predominance of the 6,6′-anhydro linkage is evidence that the primary alcohol groups of the second sugar are more reactive than the secondary hydroxyls. Reaction with secondary hydroxyl

(1) Journal Paper No. 1724 of the Purdue Agricultural Experiment Station, Lafayette, Ind. Presented before the Division of Carbohydrate Chemistry at the 138th Meeting of the American Chemical Society at New York, N. Y., September 1960.

(2) See the review by S. Peat, *Adv. Carbohydrate Chem.*, 2, 37 (1946).