REACTION OF METHYL 6-DEOXY-3-O-*p*-TOLUENESULFONYL-α-D-GLUCOPYRANOSIDE IN ALKALINE MEDIUM*

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The preparation of methyl 6-deoxy-3-O-*p*-toluenesulfonyl-α-D-glucopyranoside (*I*) and its 2-O-benzoyl (*VII*), 4-O-benzoyl (*V*) and 2,4-di-O-benzoyl derivatives (*IV*) is described. Under the effect of sodium methoxide in methanol all the substances mentioned afford methyl 2,3-anhydro-6-deoxy-α-D-allopyranoside (*VI*). On the basis of comparison with analogous cases the highly specific formation of 2,3-anhydro derivative *VI* is attributed to the structure of transition states.

Peat and Wiggins[1] found that in the reaction of methyl 2,4,6-tri-O-acetyl-3-O-*p*-toluenesulfonyl-β-D-glucopyranoside with sodium methoxide a mixture of methyl 2,3-anhydro-β-D-allopyranoside, methyl 3,4-anhydro-β-D-allopyranoside, and methyl 3,6-anhydro-β-D-glucoside was formed, from which 2,3-anhydro derivative was isolated as the dominant product. As the 3,6-anhydro derivative[2,3] is formed from 2,3-anhydro derivative by a consecutive reaction, the statement of Newth[4] that methyl 3-O-*p*-toluenesulfonyl-β-D-glucopyranoside affords predominantly the 2,3-anhydro derivative from the two possible anhydro derivatives with oxirane ring may be considered as justified. The preferential formation of the 2,3-anhydro derivative is interpreted by Newth[4] by conformational analysis of the starting methyl 3-O-*p*-toluenesulfonyl-β-D-glucopyranoside. Later on Černý and coworkers[5] found that an analogous derivative with a fixed conformation, *i.e.* 1,6-anhydro-3-O-*p*-toluenesulfonyl-β-D-glucopyranose, affords in the reaction with sodium hydroxide a mixture of 1,6;3,4-dianhydro-β-D-allopyranose and 1,6;2,3-dianhydro-β-D-allopyranose, in which the 3,4-anhydro derivative predominates. The preferential formation of 3,4-anhydro derivative the authors[5] attribute to the inductive effect of the acetal grouping on the carbon atom 1; this effect decreases the nucleophilicity of the alkoxide ion in the position 2, *i.e.* in the intermediate leading to 1,6; 2,3-dianhydro derivative. We have found recently[6] that in the reaction of the conformationally mobile methyl 6-deoxy-

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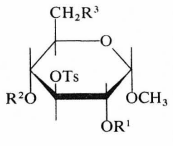
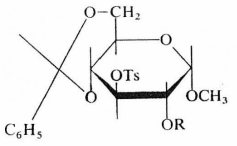
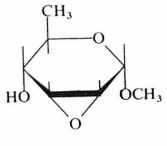
-3-O-*p*-toluenesulfonyl-β-D-glucopyranoside with a strong anion exchanger or with sodium methoxide a mixture of methyl 3,4-anhydro-6-deoxy-β-D-allopyranoside and methyl 2,3-anhydro-6-deoxy-β-D-allopyranoside is formed in which the 3,4-anhydro derivative strongly predominates. In order to specify more closely whether predominantly the steric or the inductive effects of the acetal grouping are responsible for the preferential formation of methyl 3,4-anhydro-6-deoxy-β-D-allopyranoside we have decided in this paper to find which of the anhydro derivatives is formed under the same conditions from the equally conformationally mobile methyl 6-deoxy--3-O-*p*-toluenesulfonyl-α-D-glucopyranoside (*I*). In this case the decrease in the nucleophilicity of the alkoxide ion in the position 2 should be essentially the same as in methyl 6-deoxy-3-O-*p*-toluenesulfonyl-β-D-glucopyranoside. From the comparison of the ratio in which 2,3-anhydro and 3,4-anhydro derivatives are formed from both anomers, it should follow which of the above mentioned effects predominates.







I, $R^1 = R^2 = R^3 = H$
III, $R^1 = R^2 = Bz$, $R^3 = Br$
IV, $R^1 = R^2 = Bz$, $R^3 = H$
V, $R^1 = R^3 = H$, $R^2 = Bz$
VII, $R^1 = Bz$, $R^2 = R^3 = H$
IX, $R^1 = R^2 = H$, $R^3 = OH$
X, $R^1 = R^2 = H$, $R^3 = OTs$
XI, $R^1 = Ts$, $R^2 = H$, $R^3 = OH$
XIII, $R^1 = R^2 = H$, $R^3 = I$
XIV, $R^1 = Bz$, $R^2 = H$, $R^3 = OH$
XV, $R^1 = Bz$, $R^2 = H$, $R^3 = OTs$

II, R = Bz
VIII, R = H
XII, R = Ts

VI

Ts = p-$CH_3C_6H_4SO_2$, Bz = C_6H_5CO

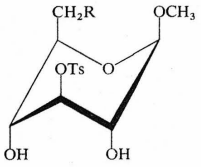
In the preparation of methyl 6-deoxy-3-O-*p*-toluenesulfonyl-α-D-glucopyranoside (*I*) we started from methyl 2-O-benzoyl-4,6-O-benzylidene-3-O-*p*-toluenesulfonyl--α-D-glucopyranoside[7] (*II*) and converted it to methyl 2,4-di-O-benzoyl-6-bromo-6--deoxy-3-O-*p*-toluenesulfonyl-α-D-glucopyranoside (*III*) on reaction with N-bromosuccinimide[8]. Although the same reaction took place in other *p*-toluenesulfonyl derivatives without complications[6], in this case the splitting of the benzylidene group was accompanied by partial bromination of the methyl group on the benzene nucleus;

pure *III* was obtained only by partial hydrogenation of the mixture on platinum. Hydrogenation of the bromo derivative *III* on Raney nickel in the presence of diethylamine yielded methyl 2,4-di-O-benzoyl-6-deoxy-3-O-*p*-toluenesulfonyl-α-D-glucopyranoside[9] (*IV*). We intended to debenzoylate the product *IV* to compound *I* with sodium methoxide in methanol. When a catalytic amount of sodium methoxide was used we obtained methyl 4-O-benzoyl-6-deoxy-3-O-*p*-toluenesulfonyl-α-D-glucopyranoside (*V*) in 62% yield (in addition to the unreacted *IV*), while when a larger amount of sodium methoxide was used we obtained (in addition to mono-O-benzoyl derivative *V*) methyl 2,3-anhydro-6-deoxy-α-D-allopyranoside (*VI*). However, in no case were we able to detect the presence of compound *I* even by thin-layer chromatography. The structure of mono-O-benzoyl derivative *V* followed both from the ^{1}H-NMR spectra and from the comparison with methyl 2-O-benzoyl-6-deoxy-3-O-*p*-toluenesulfonyl-α-D-glucopyranoside (*VII*), the preparation of which is described below. Anhydro derivative *VI* was identified by comparing its properties with those of an authentic sample prepared from methyl 2,3-anhydro-4,6-O-benzylidene-α-D-allopyranoside[10]. From the results of the reaction of di-O-benzoyl derivative *IV* with sodium methoxide it follows that the primary product of the reaction, *i.e.* 4-O-benzoyl derivative *V* is evidently converted more easily to anhydro derivative *VI* than it is debenzoylated to compound *I*. Then, of course, it could not be excluded that the specific formation of anhydro derivative *VI* from dibenzoyl derivative *IV* may be a consequence of the difference in the rate of reesterification of benzoyl group in the positions 2 and 4 of substance *IV*. Therefore, we selected another approach to the preparation of compound *I*. Substance *II* was debenzoylated with sodium methoxide to methyl 4,6-O-benzylidene-3-O-*p*-toluenesulfonyl-α-D-glucopyranoside[11] (*VIII*). In contrast to the recently published study[12] we worked at −15°C when a further conversion of substance *VIII* to methyl 2,3-anhydro-4,6-O-benzylidene-α-D-allopyranoside does not take place; thus we obtained compound *VIII* in a 87% yield (instead of the published[12] 52%), and that by mere crystallization instead of chromatography. Reacting substance *VIII* with hydrochloric acid in acetone we obtained a crystalline methyl 3-O-*p*-toluenesulfonyl-α-D-glucopyranoside (*IX*) which has been known[13] only in amorphous form until now. On partial tosylation of compound *IX* with 1·3-equivalents of *p*-toluenesulfonyl chloride in pyridine at 0°C we obtained a mixture of substances from which a small amount of a so far unidentified tri-O-*p*-toluenesulfonyl derivative, 22% of methyl 3,6-di-O-*p*-toluenesulfonyl-α-D-glucopyranoside (*X*), 5·5% of methyl 2,3-di-O-*p*-toluenesulfonyl-α-D-glucopyranoside (*XI*), and 58·5% of the starting *IX* were isolated. The structure of compound *X* followed from its conversion to compound *I*. Compound *XI* was identified by comparison of the product of its benzylidenation with authentic methyl 4,6-O-benzylidene-2,3-di-O-*p*-toluenesulfonyl-α-D-glucopyranoside[14] (*XII*). In the effort to increase the yield of 3,6-di-O-tosyl derivative *X* we carried out the partial tosylation of compound *IX* at room temperature; thus we did indeed obtain 37% of 3,6-di-O-tosyl deri-

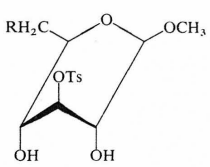
vative *X*, but in the reaction mixture a substantial amount of tri-O-tosyl derivative was also present, which can be separated from compound *X* only with difficulty. On reaction of compound *X* with sodium iodide in 2-butanone we obtained methyl 6-deoxy-6-iodo-3-O-*p*-toluenesulfonyl-α-D-glucopyranoside (*XIII*) from which derivative *I* was prepared by hydrogenation on Raney nickel in the presence of diethylamine. The structure of *I* was confirmed by benzoylation to 2,4-di-O-benzoyl derivative *IV*, which was identical with the product obtained in the above mentioned manner. When substance *I* is benzoylated with benzoyl chloride in pyridine the moment can be caught when 2-O-benzoyl derivative *VII* is present in the reaction mixture practically exclusively. This was isolated and identified by comparison with an authentic sample. The preparation of 2-O-benzoyl derivative was started from compound *II* which was first converted to methyl 2-O-benzoyl-3-O-*p*-toluenesulfonyl-α-D-glucopyranoside (*XIV*). On partial tosylation of compound *XIV* we obtained methyl 2-O-benzoyl-3,6-di-O-*p*-toluenesulfonyl-α-D-glucopyranoside (*XV*) in a satisfactory yield. It contained a very small amount of a compound with a higher R_F value. On reaction of substance *XV* with sodium iodide in 2-butanone and subsequent hydrogenation derivative *VII* was obtained.

Reaction of 3-O-tosyl derivative *I* with sodium methoxide in methanol gives 2,3-anhydro derivative *VI* almost exclusively. According to thin layer chromatography it was contaminated with a substance detectable with a reagent specific for oxirane derivatives[15]. According to gas chromatography the content of the minor product was about 1%, and its mass spectrum was almost identical with that of 2,3-anhydro derivative *VI*, with the exception of peak intensities. The same results were obtained in the reaction of 2-O-benzoyl-3-O-tosyl derivative *VII*.

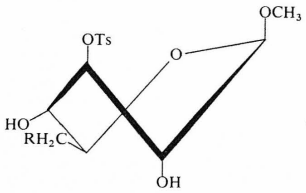
Hence, it can be stated that in contrast to methyl 6-deoxy-3-O-*p*-toluenesulfonyl-β-D-glucopyranoside the α-anomer *I* affords 2,3-anhydro derivative *VI* almost exclusively, while methyl 3,4-anhydro-6-deoxy-α-D-allopyranoside is formed in about a 1% yield only. Then, however, the inductive effect of the acetal grouping on the preferential formation of methyl 3,4-anhydro-6-deoxy-β-D-allopyranoside from methyl 6-deoxy-3-O-*p*-toluenesulfonyl-β-D-glucopyranoside is evidently small, in contrast to the situation in the conformationally rigid system of the 1,6-anhydro derivative, and the structures of the corresponding transition states will play the predominant role. The *a priori* requirement that the *p*-toluenesulfonyl group and the substituting hydroxyl group (or the anion derived from it) should be co-planar[16] in the transition state is fulfilled, in principle, in four transition states, corresponding to the chair conformer of compound *I*, or to its β-anomer (α-$^1C_4$(D) or β-$^1C_4$(D)), and to three boat conformers. However, the probability that the conformers represented by formulas β-$^1C_4$(D) and β-$^{0,3}B$(D), or α-$^1C_4$(D) and α-$^{0,3}B$(D), respectively, should participate in the reactions of both anomers of methyl 6-deoxy-3-O-*p*-toluenesulfonyl-D-glucopyranoside or methyl 3-O-*p*-toluenesulfonyl-β-D-glucopyranoside is small. If such transition states were to take a more important part



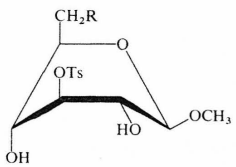
β-$^{1}C_{4}$ (D)



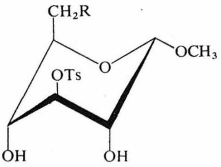
β-$^{0,3}B$ (D)



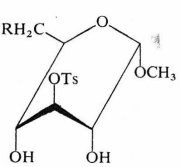
β-$B_{2,5}$ (D)



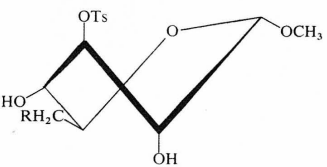
β-$B_{1,4}$ (D)



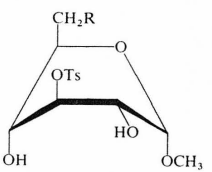
α-$^{1}C_{4}$ (D)



α-$^{0,3}B$ (D)



α-$B_{2,5}$ (D)



α-$B_{1,4}$ (D)

R = H, OH

in the reaction of methyl 6-deoxy-3-O-*p*-toluenesulfonyl-β-D-glucopyranoside and its hydroxymethyl analogue (despite the unfavourable synaxial interactions[4]), the variation in the substituent on the carbon atom 5 could be reflected in the differences in the total rate of formation of oxirane derivatives, but not in the observed differences in the ratio of epoxides formed, because the availability of the hydroxyl groups for the substitution of the *p*-toluenesulfonyloxy group remains the same in both substances. The practically selective formation of 2,3-anhydro derivative *VI* from *I* can also be only hardly reconciled with the idea that compound *I* reacts in a transition state corresponding to the conformer α-$^1C_4$(D) or α-$^{0,3}B$(D). Therefore, we assume that in all the above mentioned cases only the transition states come into play, that correspond to boat conformers β-$B_{2,5}$(D), β-$B_{1,4}$(D), α-$B_{2,5}$(D), and α-$B_{1,4}$(D).

In the case of substance *I*, the transition state leading to 3,4-anhydro derivative, *i.e.* the α-$B_{1,4}$(D) state, is apparently less advantageous. Both the interaction between synaxial substituents on the carbon atom 1 and 4, and that between the leaving *p*-toluenesulfonyloxy group and the methyl group (the former should increase during the formation of the anhydro derivative in consequence of the approaching of these groups) evidently apply in this transition state. In contrast to this, in the transition state leading to 2,3-anhydro derivative (α-$B_{2,5}$(D)) no such interaction occurs, which is evidently the cause of the selective formation of methyl 2,3-anhydro-6-deoxy-α-D--allopyranoside (*VI*).

In both methyl 6-deoxy-3-O-*p*-toluenesulfonyl-β-D-glucopyranoside and its 5--hydroxymethyl analogue, the same interaction between the leaving *p*-toluenesulfonyloxy group and the anomeric methoxyl group can apply in the transition state leading to the formation of 2,3-anhydro derivative (β-$B_{2,5}$(D)). In the transition state leading to the 3,4-anhydro derivative (β-$B_{1,4}$(D)), the stereopolar interaction between the leaving *p*-toluenesulfonyloxy group and the C_5 substituent (the methyl or the hydroxymethyl group, respectively) is important. For the 6-deoxy compound, the difference between the methyl group and the methoxyl group in the interactions mentioned evidently causes that the transition state leading to 3,4-anhydro derivative enters primarily into play during the reaction while, for the 5-hydroxymethyl derivative, the transition state leading to 2,3-anhydro derivative[4] predominates because the effect of the large polar hydroxymethyl group evidently prevails. A similar consideration can be applied even for the transition states corresponding to the conformers $^3S_1$(D) and $^0S_2$(D), which in view of the mutual positions of the *p*-toluenesulfonyloxy group and the vicinal hydroxyl group should be less favourable than the transition states corresponding to boat conformation.

EXPERIMENTAL

The melting points were determined on a Kofler block and they are not corrected. Optical rotations were measured on an instrument of the firm Opton at 20°C and a 0·5—1 concentration

in chloroform. Samples for analysis were dried at room temperature and 7–15 Pa pressure, unless stated otherwise. Thin-layer chromatography was carried out on silica gel G according to Stahl (Merck, Darmstadt), 10–40 μm, dimensions of the layer were 25 × 75 × 0·2–0·3 mm. Detection was carried out by spraying with a 1% cerium(IV) sulfate in 10% sulfuric acid and heating. For chromatography the following mixtures were employed: benzene–ethanol 100 : 5 (mixture A), benzene–ethanol 100 : 1 (mixture B), and benzene–ether 8 : 1 (mixture C). Column chromatographies were carried out on silica gel of the firm Lachema (Brno), 100–160 μm. The solvents were evaporated on a rotary evaporator under reduced pressure (water pump) and at a bath temperature not exceeding 50°C. For crystallization light petroleum of b.p. 45–60°C was used. The ^{1}H-NMR spectra were measured on a Varian XL-100-15 instrument, the IR spectra on a Perkin-Elmer 325 spectrophotometer. Under the "conventional work-up of the reaction mixture" a procedure is understood consisting in the dilution of the reaction mixture with chloroform, washing of the chloroform solution with cold 15% sulfuric acid until the aqueous layer becomes acid, then with water, 5% sodium hydrogen carbonate solution and again with water, then drying over magnesium sulfate and evaporation.

Methyl 2,4-Di-O-benzoyl-6-bromo-6-deoxy-3-O-*p*-toluenesulfonyl-α-D-glucopyranoside (*III*)

A mixture of 1·00 g (1·85 mmol) of benzylidene derivative[17] *II*, 625 mg of N-bromosuccinimide, 100 ml of tetrachloromethane, and 1·25 g of barium carbonate was refluxed for 45 minutes, then filtered and the filtrate washed 3 times with water, dried over magnesium sulfate and evaporated. The residue was purified by chromatography on a column of silica gel (40 g). Benzene eluted 771 mg of a chromatographically pure compound (in systems A and C); after double crystallization from ethanol–light petroleum 603 mg of a substance melting at 115–117°C were obtained, which after further crystallization from the same mixture remained unchanged, $[\alpha]_D$ +72·5 ± 2°; found: Br 17·48%, for methyl 2,4-di-O-benzoyl-3-O-(*p*-bromomethylbenzenesulfonyl)-6-deoxy-α-D-glucopyranoside calculated: 22·88% Br, for compound *III* 12·93% Br. A solution of this compound in 50 ml of methanol was stirred under hydrogen in the presence of PtO_2 and 600 mg of barium carbonate for 8 h. The mixture was filtered, the material on the filter washed with acetone and the combined filtrates were evaporated. The residue was extracted with acetone, the acetone extract evaporated and the residue (with an unchanged R_F value) was crystallized twice from ethanol–light petroleum. Yield, 480 mg (48%) of compound *III*, m.p. 122–124°C. For analysis the substance was crystallized twice more from the same mixture of solvents; m.p. 126–128°C, $[\alpha]_D$ +79·0°. For $C_{28}H_{27}BrO_9S$ (619·5) calculated: 54·29% C, 4·38% H, 12·90% Br, 5·17% S; found: 54·52% C, 4·31% H, 12·93% Br, 5·16% S.

Methyl 2,4-Di-O-benzoyl-6-deoxy-3-O-*p*-toluenesulfonyl-α-D-glucopyranoside (*IV*)

a) A mixture of 420 mg (0·68 mmol) of bromo derivative *III*, 20 ml of methanol, 0·1 ml of diethylamine and about 5 ml of Raney nickel was stirred under hydrogen for 45 minutes; according to thin-layer chromatography (in system C) all bromo derivative *III* had reacted after this period. The mixture was filtered, the material on the filter was washed with acetone and the combined filtrates were neutralized with 0·1M hydrochloric acid to Tashiro and filtered with charcoal and the filtrate evaporated. The residue was dissolved in 20 ml of chloroform and the solution was washed with water, dried over magnesium sulfate and evaporated. After crystallization of the residue from a mixture of ethyl acetate and light petroleum 273 mg (75%) of deoxy derivative *IV* were obtained, m.p. 138–140°C (change of modification at about 105°C), $[\alpha]_D$ +79 ± ± 1°. Literature[9] gives m.p. 140–141°C, $[\alpha]_D$ +69°. For the preparation of a larger amount

of deoxy derivative *IV* the product of the reaction of benzylidene derivative *II* with N-bromosuccinimide (m.p. 115–117°C) was employed directly instead of bromo derivative *III*; the yield was about 50%, calculated per starting benzylidene derivative *II*.

b) Benzoyl chloride (0·1 ml) was added to a solution of 32 mg of the hydrate of 3-O-tosyl derivative *I* in 3 ml of pyridine at 0°C and the mixture was allowed to stand at this temperature. According to thin layer chromatography (in system A) the mixture still contained some mono-O-benzoyl derivative *VII* after 48 hours. Therefore an additional 0·1 ml of benzoyl chloride was added and the mixture allowed to stand at room temperature for another 24 h, when it contained di-O-benzoyl derivative *IV* exclusively. The mixture was decomposed with water, diluted with chloroform and worked up in the conventional manner. After evaporation of the chloroform extract and decolorization of the residue (dissolved in ethyl acetate) with charcoal and filtration the yield was 52 mg of di-O-benzoyl derivative *IV* (100%), which after crystallization from a mixture of ethyl acetate and light petroleum had m.p. 139–140°C and $[\alpha]_D$ +79·2°. The IR spectrum of the product obtained by both procedures was identical.

Reaction of Methyl 2,4-Di-O-benzoyl-6-deoxy-3-O-*p*-toluenesulfonyl-α-D-glucopyranoside (*IV*) with Sodium Methoxide

a) Three drops of 0·9M sodium methoxide in methanol were added to a solution of 850 mg (1·575 mmol) of dibenzoyl derivative *IV* in 80 ml of methanol, kept at 0°C, and the mixture was allowed to stand at room temperature for 48 hours. According to thin-layer chromatography in system B the reaction mixture then contained in addition to the starting material (R_F about 0·8) monobenzoyl derivative *V* (R_F about 0·65) as the main product. Its pH was about 7; therefore 3 drops of the same sodium methoxide were added, the mixture allowed to stand for 24 hours and then evaporated. Water (10 ml) was then added and again evaporated in order to eliminate methyl benzoate. The residue was chromatographed on a column of silica gel (20 g) with benzene and benzene–ether 4 : 1 mixture. Two substances were obtained. The first one (175 mg) contained according to thin-layer chromatography predominantly dibenzoyl derivative in addition to 2 to 3 substances of R_F values higher than the R_F value of monobenzoyl derivative *V*; when crystallized from ethyl acetate–light petroleum mixture 107 mg (12·6%) of dibenzoyl derivative *IV* were obtained. The second substance from chromatography (426 mg, 62%) was pure monobenzoyl derivative *V*, which was crystallized from a mixture of ethyl acetate and light petroleum for analysis; m.p. 148–149°C, $[\alpha_D] + 27°$. For $C_{21}H_{24}O_8S$ (436·5) calculated: 57·78% C, 5·54% H, 7·37% S; found: 58·00% C, 5·74% H, 7·87% S. IR spectrum ($CHCl_3$): 3 565 cm^{-1} (OH), 1735 cm^{-1} (benzoate). ^{1}H-NMR data: (δ, $CDCl_3$): 1·19 (3 H, d, $J_{5,6}$ = 6·2, CH_3—CH), 2·18 (3 H, s, CH_3—C_6H_4), 3·48 (3 H, s, CH_3—O), 3·92 (1 H, dq, $J_{5,6}$ = 6·2, $J_{4,5}$ = 9·5, H-5), ≈3·8 (1 H, um, H-2), 4·81 (1 H, d, $J_{1,2}$ = 3·5, H-1), 4·85–5·20 (2 H, um, H-3, H-4), 6·8–8·0 (9 H, m, arom. H).

b) A mixture of 870 mg (1·61 mmol) of dibenzoyl derivative *IV*, 80 ml of methanol and 8 drops of 0·9M sodium methoxide in methanol was allowed to stand at room temperature for 48 hours; according to thin-layer chromatography the mixture contained monobenzoyl derivative *V* as the main product, then traces of the starting dibenzoyl derivative *IV* and anhydro derivative *VI* (positive detection with the reagent for substances containing an oxirane ring). Further 0·25 ml of sodium methoxide were added to the mixture, which was worked up as under *a*) after 22 hours' standing. Chromatography of the residue on a column of silica gel (30 g) with benzene–ethanol 100 : 2–3 mixture gave 366 mg (52·3%) of chromatographically pure monobenzoyl derivative *V* and 80 mg (31%) of anhydro derivative *VI*, which was sublimated at 50–60°C and 2 Pa; m.p. 97–100°C, $[\alpha]_D$ +168°; its IR spectrum was identical with that of an authentic sample[10], m.p. 100–101°C, $[\alpha]_D$ +168°.

Methyl 4,6-O-Benzylidene-3-O-*p*-toluenesulfonyl-α-D-glucopyranoside (*VIII*)

Sodium methoxide in methanol (1M; 10 ml) was added to a solution of 2·63 g (4·87 mmol) of 2-O--benzoyl derivative *II* in 150 ml of chloroform, cooled in a bath with solid carbon dioxide in methanol, and the mixture was allowed to stand at −15°C for 6 hours. According to thin-layer chromatography (in system C) the mixture contained after this time tosyl derivative *VIII* only, while methyl 2,3-anhydro-4,6-O-benzylidene-α-D-allopyranoside was not present even in traces. The mixture was neutralized by the introduction of carbon dioxide, 50 ml of water were added, the mixture shaken, and the aqueous layer was again extracted with chloroform. The combined chloroform extracts were combined and evaporated. Water (30 ml) was added to the residue, and evaporated in order to eliminate methyl benzoate, and the residue (2·12 g, 100%), m.p. 163−166°C, was crystallized from ethanol–light petroleum. M.p. 166−167°C, $[\alpha]_D$ +34·5°, yield 87%. Literature[11,12] gives m.p. 164°C, $[\alpha]_D$ +32·5°.

Methyl 3-O-*p*-Toluenesulfonyl-α-D-glucopyranoside (*IX*)

A mixture of 1·51 g (3·46 mmol) of benzylidene derivative *VIII*, 50 ml of acetone, and 2·5 ml of conc. hydrochloric acid, was allowed to stand at room temperature overnight. After neutralization with barium carbonate, filtration and evaporation the residue was purified by chromatography on a 20 g column of silica gel. Benzene–ethanol eluted 1·19 g (99%) of chromatographically pure derivative *IX* (in systems A and B). For analysis substance *IX* was crystallized from ethanol–-light petroleum mixture, m.p. 137−138°C, $[\alpha]_D$ +140°. For $C_{14}H_{20}O_8S$ (348·4) calculated: 48·27% C, 5·78% H, 9·20% S; found: 48·28% C, 5·78% H, 9·01% S. Literature[13] describes compound *IX* as a syrup, $[\alpha]_D$ +106°.

Partial Tosylation of Methyl 3-O-*p*-Toluenesulfonyl-α-D-glucopyranoside (*IX*)

a) A solution of 1·150 g (6 mmol) of *p*-toluenesulfonyl chloride in 10 ml of pyridine was added to a solution of 1·58 g (4·54 mmol) of 3-O-tosyl derivative *IX* in 15 ml pyridine, cooled in a mixture of solid carbon dioxide and methanol. The mixture was allowed to stand at 0°C for 4 days, then decomposed with water and worked up in the conventional manner. Yield, 790 mg of syrup which according to thin-layer chromatography in system B contained three substances of R_F 0·65, 0·58 and 0·46. Chromatography of this mixture on a column of silica gel (70 g) with benzene–ethanol 100 : 1−2 gave 10 mg of pure substance of R_F 0·65, 40 mg of its mixture with 3,6-di-O-tosyl derivative *X* (R_F 0·58), 496 mg (22%) of 3,6-di-O-tosyl derivative *X* and 124 mg (5·5%) of 2,3-di-O-tosyl derivative *XI*. The aqueous fractions from the original mixture were extracted repeatedly with chloroform, the extracts were washed with water, dried over magnesium sulfate and evaporated. According to thin-layer chromatography the syrupy residue contained predominantly the unreacted derivative *IX* in addition to small amount of di-O-tosyl derivatives *X* and *XI*. After its chromatographic purification 920 mg (58·5%) of the starting material were recovered.

b) Tosylation of 920 mg (2·65 mmol) of 3-O-tosyl derivative in 10 ml of pyridine with 670 mg (3·5 mmol) of *p*-toluenesulfonyl chloride in 10 ml of pyridine at room temperature for 68 hours and working up as under *a*) gave 250 mg of pure derivative of R_F 0·65, 536 mg of its mixture with 3,6-di-O-tosyl derivative *X*, 490 mg (37%) of pure 3,6-di-O-tosyl derivative *X*, and 56 mg (4·2%) of 2,3-di-O-tosyl derivative *XI*.

The pure substances of R_F 0·65, *X* and *XI* were dissolved in acetone, filtered with charcoal, the acetone solutions evaporated and the residue dried in a vacuum. The substance of R_F 0·65

had $[\alpha]_D$ +49 ± 2°; for methyl tri-O-*p*-toluenesulfonyl-α-D-glucopyranoside $C_{28}H_{32}O_{12}S_3$ (656·7) calculated: 14·65% S; found: 14·39% S. 3,6-Di-O-tosyl derivative *X* had $[\alpha]_D$ +95 ± 3°. For $C_{21}H_{26}O_{10}S_2$ (502·6) calculated: 50·20% C, 5·14% H, 12·78% S; found: 50·30% C, 5·47% H, 13·08% S.

2,3-Di-O-tosyl derivative *XI* had $[\alpha]_D$ +62°. For $C_{21}H_{26}O_{10}S_2$ (502·6) calculated: 50·20% C, 5·14% H, 12·78% S; found: 49·8% C, 5·44% H, 13·07% S.

Benzylidenation of Di-O-tosyl Derivative *XI*

A mixture of 118 mg of di-O-tosyl derivative *XI*, 3 ml of benzaldehyde and 270 mg of molten zinc dichloride was shaken at room temperature for 30 h, then poured into 30 ml of saturated aqueous sodium hydrogen carbonate solution and the excess benzaldehyde was eliminated by steam distillation. The mixture was extracted with three 25 ml portions of chloroform, filtered with charcoal and evaporated. After crystallization from ethanol 104 mg (75%) of benzylidene derivative *XII* with m.p. 155°C (at 145—147°C the substance melted and resolidified) and $[\alpha]_D$ +13·3° were obtained, the IR spectrum of which was identical with that of an authentic specimen[18]. For benzylidene derivative *XI* reference[14] gives m.p. 148—149°C, $[\alpha]_D$ +13°, reference[18] gives m.p. 132, 147 and 157°C, $[\alpha]_D$ +13·8°.

Methyl 6-Deoxy-6-iodo-3-O-*p*-toluenesulfonyl-α-D-glucopyranoside (*XIII*)

A mixture of 283 mg (0·56 mmol) of 3,6-di-O-tosyl derivative *X*, 345 mg of sodium iodide and 23 ml of 2-butanone was refluxed and the reaction course followed by thin-layer chromatography (mixture B). After 4 h only iodo derivative *XIII* was present in the mixture. This was evaporated and the residue treated with 25 ml of chloroform. The mixture was shaken with water, 1% sodium thiosulfate solution, 1% sodium hydrogen carbonate solution and water. The washed chloroform extract was dried over magnesium sulfate, filtered and evaporated. The residue crystallized after addition of 2 drops of water. After recrystallization from ether by the addition of one drop of water 246 mg (92%) of the hydrate of iodo derivative *XIII* were obtained, m. 66—71°C, which was recrystallized for analysis from the same solvent. M.p. 68—71°C, $[\alpha]_D$ +115 ± 2°. For $C_{14}H_{19}IO_7S.H_2O$ (476·3) calculated: 35·30% C, 4·44% H, 6·73% S, 26·65% I; found: 35·29% C, 4·25% H, 7·14% S, 26·09% I.

Methyl 6-Deoxy-3-O-*p*-toluenesulfonyl-α-D-glucopyranoside (*I*)

A mixture of 227 mg (0·47 mmol) of the hydrate of compound *XIII*, 40 ml of methanol, 3 ml of Raney nickel and 5 drops of diethylamine was stirred under hydrogen for 4 h; according to thin-layer chromatography in mixture B all iodo derivative had reacted. The mixture was filtered, the catalyst washed with methanol, the combined filtrates neutralized to Tashiro with dilute hydrochloric acid and evaporated. Chloroform (25 ml) was aded to the residue and the solution washed with three 10 ml portions of water; the dried ($MgSO_4$) chloroform extract was evaporated and the residue dissolved in acetone, filtered with charcoal, evaporated and the residue treated with 2 drops of water in order to induce crystallization. After recrystallization from a mixture of ether and light petroleum and several drops of water 123 mg (74%) of hydrate of *I* were obtained, m.p. 48—51°C, which on further crystallization from the same mixture remained unchanged; $[\alpha]_D$ +136 ± 2°. For $C_{14}H_{20}O_7.H_2O$ (350·4) calculated: 47·99% C, 6·33% H, 9·15% S; found: 47·93% C, 6·36% H, 8·80% S.

Methyl 2-O-Benzoyl-3-O-*p*-toluenesulfonyl-α-D-glucopyranoside (*XIV*)

Concentrated hydrochloric acid (1·7 ml) was added to a solution of 1·00 g (1·85 mmol) of substance *II* in 20 ml of acetone and the mixture was allowed to stand overnight. After neutralization with barium carbonate, filtering and evaporation, the residue was treated with moist ether which brought the product to crystallization. Yield 735 mg (85%) of the hydrate of compound *XIV* which melted at 68–71°C after recrystallization, $[\alpha]_D$ +196°. For $C_{21}H_{26}O_{10}S$ (470·5) calculated: 53·61% C, 5·57% H, 6·80% S; found: 53·83% C, 5·65% H, 6·58% S.

Methyl 2-O-Benzoyl-3,6-di-O-*p*-toluenesulfonyl-α-D-glucopyranoside (*XV*)

p-Toluenesulfonyl chloride (800 mg, 4·2 mmol, 1·2 equivalents per anhydrous product) was added to a solution of 827 mg (1·76 mmol) of the hydrate of compound *XIV* in 15 ml of pyridine at 0°C and the mixture was allowed to stand at 0°C for 18 hours. The mixture was worked up in the conventional manner and the residue chromatographed on a silica gel column (80 g) with benzene and benzene–ethanol 200 : 1 mixture. Thus 965 mg (90%) of a syrup were eluted containing, according to thin-layer chromatography (in mixture A), traces of a ausbstance with a higher R_F value than that of compound *XV* (0·35), $[\alpha]_D$ +155°; for $C_{28}H_{30}O_{11}S_2$ (606·6) calculated: 10·57% S; found: 10·31% S.

Methyl 6-Deoxy-2-O-benzoyl-3-O-*p*-toluenesulfonyl-α-D-glucopyranoside (*VII*)

a) A mixture of 590 mg (0·97 mmol) of compound *XV*, 720 mg of sodium iodide and 25 ml of 2-butanone was refluxed for 3 hours, then filtered, the solvent evaporated and the residue dissolved in 100 ml of chloroform. The chloroform solution was washed with water, 1% sodium thiosulfate, 5% sodium hydrogen carbonate and water, dried over magnesium sulfate, filtered and evaporated. The residue was dissolved in ether, decolorized with charcoal and worked up. Yield 431 mg of a syrup with $[\alpha]_D$ +161°. According to thin-layer chromatography in mixture C it contains traces of a substance of R_F value slightly lower than that of the iodo derivative (about 0·5). A part of this product (358 mg) was stirred under hydrogen with 30 ml of methanol, 6 drops of diethylamine and 3 ml of Raney nickel for 1 h. The catalyst was filtered off, washed with methanol and the combined filtrates were evaporated. The residue was dissolved in chloroform (30 ml), the solution washed with three 10 ml portions of water, dried over magnesium sulfate and evaporated. The residue (255 mg) was chromatographically pure in system C; after crystallization from ethanol, under addition of a small amount of water, 230 mg of compound *VII* were obtained in the form of its hydrate, m.p. 59–61°C, $[\alpha]_D$ +191·5°. In another experiment compound *VII* crystallized out in anhydrous form from ethyl acetate–light petroleum, m.p. 99–100°C $[\alpha]_D$ +196° after drying at 50°C and 15 Pa. For $C_{21}H_{24}O_8S$ (436·5) calculated: 57·78% C, 5·54% H, 7·37% S; found: 57·87% C, 5·67% H, 7·35% S. When anhydrous compound *VII* was crystallized from ethanol containing minute amounts of water its hydrate was obtained again.

b) Benzoyl chloride (0·1 ml) was added to a solution of 40 mg (0·120 mmol) of compound *I* in 4 ml of pyridine at 0°C, the mixture was allowed to stand at 0°C for 2 h, and worked up in the usual manner. The syrupy product was purified on a silica gel column (25 g) with benzene that eluted 50 mg (95%) of chromatographically pure compound *VII* (in system A). After crystallization from ethanol, under addition of a drop of water, 47 mg of hydrate of m.p. 56–58°C and $[\alpha]_D$ +193° were obtained; when dried at 50°C and 15 Pa for 12 hours a product melting at 95°C was obtained. The IR spectra of the dried substances obtained by procedures *a*) and *b*) were identical.

Reaction of Compound *I* or *VII* with Sodium Methoxide in Methanol

a) A solution of 265 mg (0·80 mmol) of compound *I* in 12 ml of methanol and 4 ml of 0·9N sodium methoxide was allowed to stand at room temperature for 1·5 h. The mixture was neutralized with carbon dioxide gas and evaporated. The residue was triturated with ether, the solid part was filtered off and the filtrate evaporated. The residue, containing according to thin-layer chromatography in mixture A anhydro derivative *VI* (R_F about 0·35) and a small amount of a compound of R_F about 0·37 (detectable with the reagent for oxirane derivatives[15]), afforded on sublimation at 50—60°C and 2 Pa 111 mg (97%) of compound *VI*, m.p. 97—99°C, $[\alpha]_D$ +156°. According to gas chromatography (Varian aerograph 2100 with a Hewlett-Packard integrator 3380 A, column dimensions 900 × 2 mm, 10% Versamide 900 on Chromosorb N-AW, gas flow 20 ml He/min, temperature 200°C) substance *VI* contained about 1% of an admixture which gave the same mass spectrum as compound *VI* (on an LKB 9000 instrument).

b) In the same manner 210 mg (0·48 mmol) of compound *VII* gave 68 mg (89%) of anhydro derivative *VI* which had the same properties as compound *VI* obtained in the preceding experiment.

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