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Studies on the Formation of Deoxy Sugars by Detosyloxylation with Lithium Aluminum Hydride*1

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The reduction of a number of tosylated, mesylated, sometimes further-benzoylated derivatives of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (I) with lithium aluminum hydride in tetrahydrofuran has been investigated; it has thus been found that methyl 4,6-*O*-benzylidene-2,3-di-*O*-tosyl-α-D-glucopyranoside (II) gave methyl 4,6-*O*-benzylidene-3-deoxy-α-D-*ribo*-hexopyranoside (III, major), methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*arabino*-hexopyranoside (IV, minor), and methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*ribo*-hexopyranoside (V, minor) as deoxy derivatives through two kinds of monotosyl derivatives (VIII and X), and that methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-tosyl-α-D-glucopyranoside (VII) and methyl 3-*O*-benzoyl-4,6-*O*-benzylidene-2-*O*-tosyl-α-D-glucopyranoside (IX) gave VIII and X respectively, as intermediates. 2-*O*-Methyl-3-*O*-tosyl (XI) and 2-deoxy-3-*O*-tosyl derivatives (XIII) gave detosylated derivatives, (XII) and (IV) respectively. These and other results suggest, for detosyloxylation, a mechanism through the formation of an alkoxy-aluminum hydride.

The reduction of a secondary sulfonyl ester group with lithium aluminum hydride (hereafter abbreviated to LAH) sometimes provides a facile method for the synthesis of deoxysugars; in recent years, this kind of reaction has been studied fairly extensively. In connection with other work in progress in our laboratory, it became desirable to investigate further the scope and the mechanism of this kind of reaction. This report will deal with the reduction, with LAH in boiling tetrahydrofuran, of secondary sulfonyl groups in methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (I).

In general, the reduction of a sulfonate of a secondary hydroxyl group with LAH causes desulfonylation, thus giving a corresponding secondary alcohol,[1] while a primary sulfonic ester is reduced to give a corresponding methyl group. In some cases,[2] however, a secondary sulfonyloxy group is eliminated to form a deoxy derivative, by the reduction with LAH, as in the usual case of a primary sulfonyloxy group.

Vis and Karrer[3] reported that the reduction of methyl 4,6-*O*-benzylidene-2,3-di-*O*-tosyl-α-D-glucopyranoside (II) with LAH in tetrahydrofuran caused both desulfonylation and desulfonyloxylation, thus giving a 3-deoxy sugar, namely, methyl 4,6-*O*-benzylidene-3-deoxy-α-D-*ribo*-hexopyranoside (III), apparently through a reaction intermediate epoxide, methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-allopyranoside (VI). However, the reduction[4] of VI with LAH in ether gave methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*ribo*-hexopyranoside (V), indicating that the epoxide (VI) may not be the intermediate.

On the other hand, Allerton and Overend[5] observed that the reduction of methyl 2-*O*-tosyl-β-L-arabinopyranoside with LAH in ether afforded two kinds of deoxy derivatives, namely, methyl 2-deoxy-β-L-*erythro*-pentopyranoside and methyl 3-deoxy-β-L-*erythro*-pentopyranoside, and methyl 2,3-anhydro-β-L-riboside, the last epoxy-compound being considered to be the intermediate for the formation of 2-deoxy- and 3-deoxy-pentosides.

As has been mentioned above, the behavior of a sulfonate group towards the reduction with this hydride is critically dependent upon its position in, and the stereochemistry of, the carbohydrate molecule.

Experimental Results

A number of tosylated, mesylated, sometimes

*1 Presented at the 22nd Annual meeting of the Chemical Society of Japan, Tokyo, April, 1969. (see Abstracts of the Meeting, Vol. 3, p. 1897).

1) R. S. Tipson, *Advan. Carbohydrate Chem.*, **8**, 164 (1953); D. H. Ball and F. W. Parrish, *ibid.*, **23**, 275 (1968).

2) See a recent example: M. Strandtman, C. Puchalski and J. Shavel, Jr., *J. Org. Chem.*, **33**, 4015 (1968).

3) E. Vis and P. Karrer, *Helv. Chim. Acta*, **37**, 378 (1954).

4) D. A. Prins, *J. Amer. Chem. Soc.*, **70**, 3955 (1948). The lack of any formation of 3-deoxy-hexoside was further confirmed by a) E. J. Hedgley, W. G. Overend and R. A. C. Rennie, *J. Chem. Soc.*, **1963**, 4701, and by b) A. C. Richardson, *Carbohyd. Res.*, **4**, 422 (1967).

5) R. Allerton and W. G. Overend, *J. Chem. Soc.*, **1954**, 3629.

further-benzoylated derivatives of 4,6-*O*-benzylidene-α-D-glucopyranoside were caused to react with LAH in tetrahydrofuran. At the beginning, the structure of the 3-deoxy derivative (III) obtained from II (see Chart 1) by the method of Vis and Karrer[3] was confirmed by NMR spectroscopy. Then, a derivative, in which one of the tosyloxy groups of II is replaced by a benzoyloxy group, namely, methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-tosyl-α-D-glucopyranoside (VII), was prepared and subjected to reduction with LAH for 20 hr. The separation of the resultant products by column chromatography with silica gel gave a mixture of deoxy products (A mixture, 73%) and a desulfonated product, methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (I, 6.3%), which was expected to be produced by the desulfonylation typical for secondary sulfonyloxy groups. The examination of the A mixture by NMR spectroscopy (see Experimental) suggested that it was composed of a 3-deoxy derivative (III, about 93%) and a 2-deoxy derivative, methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*ribo*-hexopyranoside (V, about 7%). When the reaction was pursued by thin-layer chromatography, it was found that the starting material (VII, R_f 0.95*2) disappeared rapidly and that, after 30 min, a product (R_f 0.8) became the main product; this was then gradually transformed to the above-mentioned three products constituting the A mixture, (III, V, and I). The intermediate proved to be methyl 4,6-*O*-benzylidene-3-*O*-tosyl-α-D-glucopyranoside (VIII); this pathway was supported by reducing VIII with LAH to give almost the same results as those obtained above.

Next, a positional isomer of VII, namely, methyl 3-*O*-benzoyl-4,6-*O*-benzylidene-2-*O*-tosyl-α-D- glucopyranoside (IX), was prepared and caused to react with LAH in the same manner. In this case, a 2-deoxy product, methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*arabino*-hexopyranoside (IV), was produced in a 29% yield, together with compound I (54%). The structure of IV was confirmed by its melting point and by its NMR spectrum. In this reaction, contrary to the case of VII, the deoxy sugar (IV) was produced in a low yield but was not contaminated by the formation of other deoxy sugars, as in the case of the A mixture. Here again the formation of an epoxy intermediate was not likely.

Hereupon, we made a further investigation of the above-mentioned Vis and Karrer's experiment, and a similar pursuit of the reaction and the identification technique described above was carried out. In a 40-hr reaction, the ditosylated starting material (II) was changed into a mixture of deoxy products (B mixture, 61%) and compound I (15%).

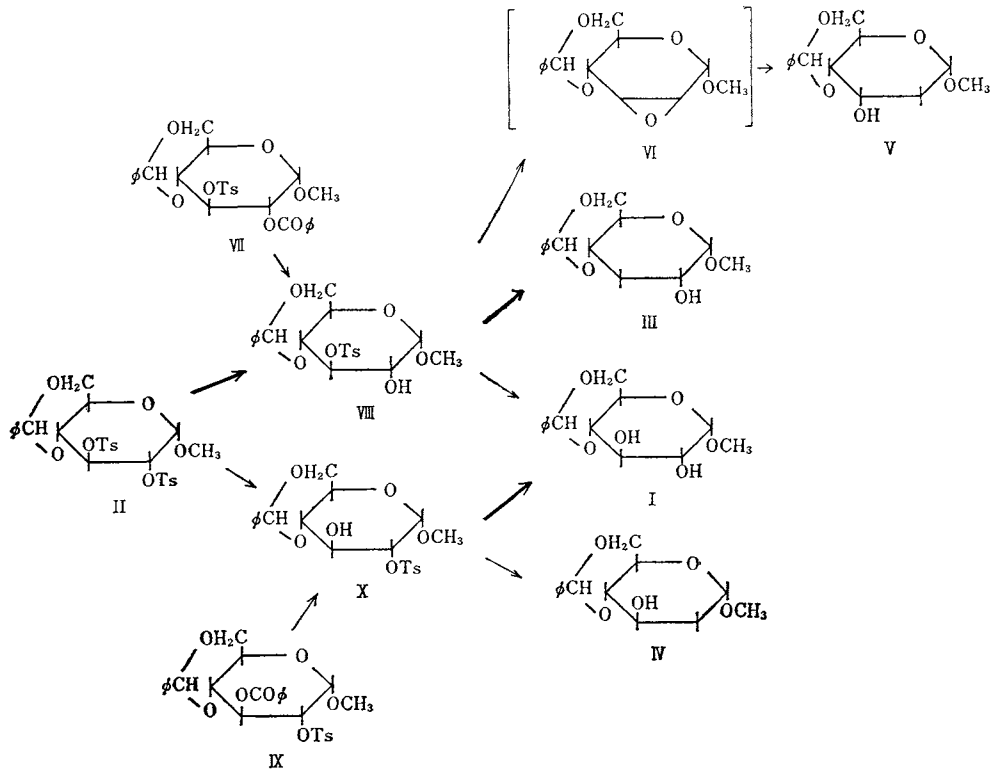


Chart 1

*2 See Experimental.

An inspection of the NMR spectrum of the B mixture (see Experimental) indicated that the mixture was composed of three components: a 3-deoxy derivative (III, ~75%), a 2-deoxy derivative (V, ~12%), and another 2-deoxy derivative (IV, ~12%); the former two were identical with the components of the A mixture, while the latter was identical with the compound obtained from IX. When the reaction was stopped after 3.5 hr, the formation of two monotosylated products, namely, methyl 4,6-*O*-benylidene-3-*O*-tosyl and 2-*O*-tosyl-α-D-glucopyranoside (VIII and X, respectively), was revealed. Thus, it necessarily follows that the reaction of the ditosylated compound (II) with LAH may involve reactions of two kinds of monotosylated compounds (VIII and X) with LAH. The overall reaction pathway from II is depicted in Chart 1, as are those from VII and IX.

We then went on to prepare several compounds bearing methanesulfonyl (mesyl) groups instead of tosyl groups, namely, methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-mesyl-[6] (XVII), 4,6-*O*-benzylidene-2,3-di-*O*-mesyl-[6,7] (XVIII), 4,6-*O*-benzylidene-2-*O*-mesyl-[6] (XIX), and 4,6-*O*-benzylidene-2-*O*-mesyl-3-*O*-tosyl-α-D-glucopyranoside (XX), and these compounds were caused to react with LAH under reaction conditions similar to those described above. It was found that, except for XX, the three compounds exclusively afforded the desulfonated compound I in high yields; on the contrary, XX gave a result analogous to that from VII. In conclusion, so far as this kind of reactions is concerned, a mesyloxy group acts similarly to that of a benzoyloxy group.

Preparation of the Samples

Methyl 2-*O*-benzoyl- and 3-*O*-benzoyl-4,6-*O*-benzylidene-α-D-glucopyranoside (XIV and XV respectively) were prepared from methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (I) by modifying the method of Jeanloz[6]; the yield of XIV was fairly well improved. The tosylation of XIV and XV was performed with tosyl chloride in pyridine, and the structural proofs of the products (VII and IX) were obtained from their NMR spectra. The debenzoylation of VII and IX were performed with sodium in methanol without the formation of any epoxy compounds to give methyl 4,6-*O*-benzylidene-3-*O*-tosyl- and 2-*O*-tosyl-α-D-glucopyranoside (VIII and X respectively). The methylation of VIII was performed by methyl iodide and silver oxide, thus giving methyl 4,6-*O*-benzylidene-2-*O*-methyl-3-*O*-tosyl-α-D-glucopyranoside (XI) in a high yield. The mesylation of I to methyl 4,6-*O*-benzylidene-2-*O*-mesyl-α-D-glucopyranoside (XIX) was performed by modifying the method of Jeanloz,[6] while XIX was tosylated to methyl 4,6-*O*-benzylidene-2-*O*-mesyl-3-*O*-tosyl-α-D-glucopyranoside (XX) in a good yield in a usual way. Methyl 4,6-*O*-benzylidene 2-deoxy-3-*O*-tosyl-α-D-*arabino*-hexopyranoside[8] (XIII) was prepared from methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*arabino*-hexopyranoside (IV), which had itself been prepared from methyl 3-*O*-benzoyl-4,6-*O*-benzylidene-2-*O*-tosyl-α-D-glucopyranoside (IX) by reduction with LAH. The identification and the differentiation of methyl 4,6-*O*-benzylidene-2- or 3-deoxy-α-D-hexopyranosides (III, IV, and V), which all have the same R_f value in thin-layer chromatography, were conveniently performed by an inspection of their NMR spectra, which differ in τ-values and in the splitting patterns of anomeric, *O*-methyl, and benzylic hydrogens.

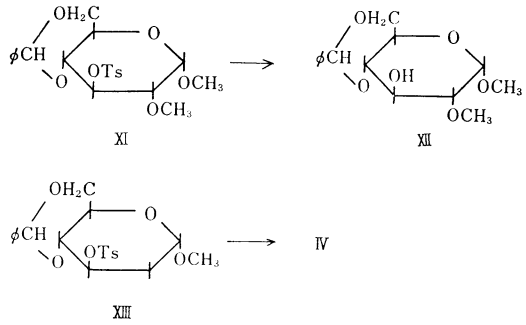


Chart 2

Discussion

In view of the above experimental results, it seems that any tosyl derivative desulfonyloxylated to a methylene-type deoxy compound by the action of LAH has a hydroxyl group, or a group easily changeable to a hydroxyl group by LAH, in the proximity of the secondary tosyloxy group in question. This suggests that the adjacent hydroxyl group may participate in this kind of reaction. To examine this point further, an *O*-methylated derivative (XI) of VIII was prepared and caused to react with LAH by the usual procedure; as expected, it has been found that this derivative was detosylated exclusively to give XII, while no trace of a detosyloxylated derivative was detected. Furthermore, a deoxy derivative of VIII, namely, methyl 4,6-*O*-benzylidene-2-deoxy-3-*O*-tosyl-α-D-*arabino*-hexopyranoside (XIII), was examined for this reaction; again, it has been found that no detosyloxylation, but rather detosylation, occurred to give IV. From these results, the important role of the adjacent

6) R. W. Jeanloz and D. A. Jeanloz, *J. Amer. Chem. Soc.*, **79**, 2579 (1957).

7) J. Honeyman and J. W. W. Morgan, *J. Chem. Soc.*, **1955**, 3660.

8) S. McNally and W. G. Overend, *J. Chem. Soc., C*, **1966**, 1978.

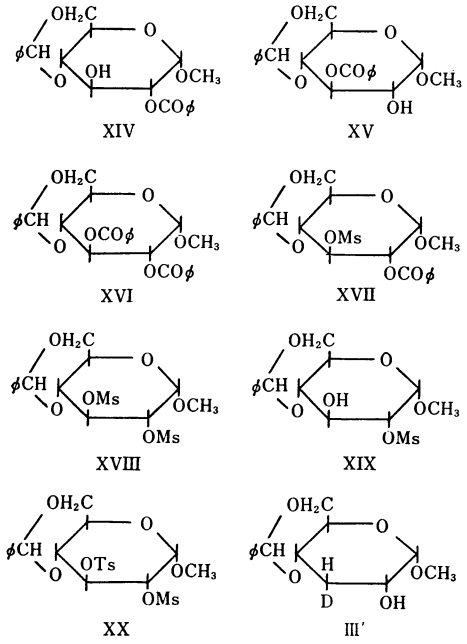
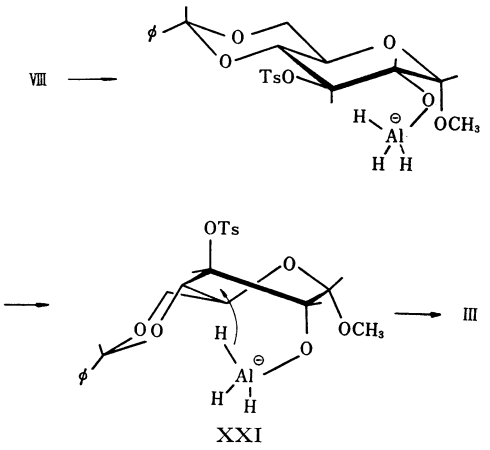


Chart 3. 4,6-*O*-Benzylidene derivatives used in this study other than those depicted in charts 1 and 2.

hydroxyl group in this kind of reaction became obvious. In this connection, Hedgley, Meresz, and Overend[9] found, in their synthesis of 5-deoxy-D-*xylo*-hexose, that 6-*O*-benzoyl-1,2-*O*-isopropylidene-5-*O*-tosyl-α-D-glucofuranose was converted mainly to 5-deoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranose by the reaction with LAH in ether (or in tetrahydrofuran); they therefore suggested that the product might be formed favourably through a *C*-3-alkoxy-aluminum hydride intermediate. A similar kind of mechanism of desulfonyloxylation would be very likely in our experiments, though the conversion of compound II, VII, or VIII to III requires a higher reaction temperature (in boiling tetrahydrofuran) and a small volume of tetrahydrofuran; when the reaction is performed in ether, ether-tetrahydrofuran, benzene-tetrahydrofuran, or dioxane, the reaction is very slow or the ratio of the yield of III to I becomes small, while when a larger volume of tetrahydrofuran than such described in the Experimental section is used, the ratio of the yield of III to I is considerably decreased. The mechanism shown in the following chart may be reasonable for the conversion of VIII to III.

Conformational change will be required to force one of the hydrogens of the metal hydride part of the intermediate to come close to carbon-3; the proximity of the hydrogen will be the driving force of the reaction. The backside attack of the metal hydride was supported by the result obtained



by means of lithium aluminum deuteride, which afforded methyl 3-deoxy-3-deuterio-4,6-*O*-benzylidene-α-D-allopyranoside (III').

In like manner, the formation of methyl 2-deoxy-β-L-*erythro*-pentopyranoside from methyl 2-*O*-tosyl-β-L-arabinopyranoside reported by Allerton and Overend[5] can be understood by the above-mentioned mechanism instead of that through an epoxy intermediate.

As for the mesyl derivatives (XVII, XVIII, and XIX), their desulfonylation may be ascribed to the fact that a mesyloxy group is more basic than a tosyloxy group and less functional as a leaving group in a transition state such as XXI.

Experimental

The NMR spectra were measured with a Varian A-60D spectrometer or a Japan Electron Optics 4H-100 spectrometer. Tetramethylsilane (τ 10.0) was used as the internal standard. The following abbreviations were used: p: proton, s: singlet, d: doublet, t: triplet, q: quartet, m: multiplet. Thin-layer chromatography (TLC) was carried out on microscope slides coated with silica gel, and the spots were visualized by spraying with 95% sulfuric acid and then heating at 110°C.

Methyl 2-*O*-Benzoyl-4,6-*O*-benzylidene-α-D-glucopyranoside (XIV) and Methyl 3-*O*-Benzoyl-4,6-*O*-benzylidene-α-D-glucopyranoside (XV). The method of Jeanloz and Jeanloz[6] was used; when the quantity of pyridine was increased about 20-fold, XIV was obtained in a higher yield as follows. To an ice-cold solution of I (5.0 g) in dry pyridine (100 m*l*) benzoyl chloride (2.1 m*l*) was gradually added; the mixture was allowed to stand under cooling for 4 hr and then at room temperature overnight. The reaction mixture was then treated as has been described in the literature[6] to give a crude syrup, which showed four spots on TLC (benzene-ethyl acetate 6 : 1): R_f 0.87 (XVI, a dibenzoylated derivative), 0.71 (XIV), 0.44 (XV), and 0.06 (I). The syrup was chromatographed on a silica-gel column (500 g, 4.7×54 cm) and then eluted with the same solvent system. After the first fraction (500 m*l*), the eluate was cut into 15-g portions. A dibenzoylated compound (XVI) was eluted between Nos. 12—20

9) E. J. Hedgley, O. Meresz and W. G. Overend, *J. Chem. Soc., C*, **1967**, 888.

(1.14 g, 13%); another, XIV, between Nos. 29—52 (3.47 g, 51%); a third, XV, between Nos. 110—154 (0.50 g, 7%). The starting material (I, 1.3 g, 26%) was eluted after the solvent had been changed to ethyl acetate. The dibenzoylated product (XVI) was recrystallized from benzene-*n*-hexane; mp 155°C (lit,[6] 154°C), $[\alpha]_D^{20}$ +97° (*c* 1, $CHCl_3$) (lit,[6] +94°); IR: 1725, 1275, 1095, 756, 707, 697 cm^{-1}.

Compound XIV was recrystallized from benzene-ether; mp 170—172°C (lit,[6] 169—170°C), $[\alpha]_D^{20}$ +112° (*c* 1, $CHCl_3$) (lit,[6] +111°); IR: 3450, 1735, 1270, 750, 713, 697 cm^{-1}; NMR (60 MHz, in pyridine-d_5): τ: 6.64 (3-p. s., OCH_3), 4.69 (1-p. d., H-1), 4.44 (1-p. q., H-2), 4.21 (1-p. s., benzylic); $J_{1,2}$ 3.5 Hz, $J_{2,3}$ 9.5 Hz.

Compound XV was recrystallized from benzene; mp 225—226°C (lit,[6] 219—220°), $[\alpha]_D^{20}$ +34° (*c* 1, $CHCl_3$) (lit,[6] +34°); IR: 3380, 1725, 1275, 750, 705, 695 cm^{-1}; NMR (60 MHz, in pyridine-d_5): τ: 6.62 (3-p. s., OCH_3), 4.89 (1-p. d., H-1), 4.23 (1-p. s., benzylic), 3.79 (1-p. t., H-3); $J_{1,2}$ 3.5 Hz, $J_{2,3}$—$J_{3,4}$ ~9.3 Hz.

Compound XIV was clearly differentiated from XV by comparing their NMR spectra. When $CDCl_3$ was used instead of pyridine-d_5, the separation of signals was indistinct.

Methyl 2-*O*-Benzoyl-4,6-*O*-benzylidene-3-*O*-tosyl-α-D-glucopyranoside (VII). Prepared by the usual method (yield 90%); mp 190°C (lit,[10] 188—189°C), $[\alpha]_D^{20}$ +89° (*c* 1, $CHCl_3$) (lit,[10] +88.5°); IR: 1730, 1600, 1365, 1270, 1175, 830, 750, 712 cm^{-1}; NMR (100 MHz, $CDCl_3$): τ: 7.87 (3-p. s., $TsCH_3$), 6.65 (3-p. s., OCH_3), 4.95—4.8 (2-p. m., H-1, H-2), 4.62 (1-p. s., benzylic), 4.58 (1-p. t., H-3); $J_{2,3}$—$J_{3,4}$ ~9.7 Hz.

Methyl 4,6-*O*-Benzylidene-3-*O*-tosyl-α-D-glucopyranoside (VIII). To a suspension of VII (594 mg) in dry methanol (60 m*l*) we added a piece of sodium metal; the mixture was then stirred at room temperature for several hours. If the suspension did not become clear, a little more of sodium was added and the mixture was treated as above. The resultant clear solution was neutralized with carbon dioxide and evaporated *in vacuo*. A chloroform solution of the residue was washed with water, dried over sodium sulfate, and evaporated to give a solid which contained a slight amount of an epoxy product (VI, R_f 0.55 on TLC) as a contaminant. Recrystallization from chloroform-*n*-hexane gave pure VIII; 398 mg (83%); R_f 0.30 (VII, R_f 0.72) by TLC (benzene-ethyl acetate 5 : 1); mp 164°C (lit,[7],*3 164°C), $[\alpha]_D^{22}$ +32° (*c* 1, $CHCl_3$) (lit,[7] +32.5°); NMR (60 MHz, $CDCl_3$): τ: 7.72 (3-p. s., $TsCH_3$), 6.55 (3-p. s., OCH_3), 5.18 (1-p. d., H-1), 5.10 (1-p. t., H-3), 4.67 (1-p. s., benzylic), 2.27 and 3.01 (4-proton AB quartet, *J* 8.3 Hz, Tosyl), ~2.65 (5-p., Ph.); $J_{1,2}$ 3.5 Hz, J_2,—$_3J_{3,4}$ ~9.5 Hz.

Methyl 4,6-*O*-Benzylidene-2-*O*-methyl-3-*O*-tosyl-α-D-glucopyranoside (XI). To a solution of VIII (586 mg) in dry acetone (6 m*l*) we added methyl iodide (1 m*l*), silver oxide (1.2 g), and freshly-prepared Drierite (1 g), after which the mixture was stirred overnight. The filtrate was evaporated, and the residue was dissolved in chloroform. The solution was then washed with water, dried over sodium sulfate, and evaporated. The residue was recrystallized from benzene-ethyl acetate (5 : 1), 591 mg (98%); mp 163—164°C, $[\alpha]_D^{20}$ +26° (*c* 1, $CHCl_3$); R_f 0.56 by TLC (benzene-ethyl acetate 5 : 1); IR: 2930, 1600, 1365, 1175, 1090, 975, 842, 750, 725, 700 cm^{-1}; NMR (60 MHz, $CDCl_3$): τ: 7.72 (3-p. s., $TsCH_3$), 6.63 (3-p. s., $O(2)CH_3$), 6.57 (3-p. s., $O(1)$-CH_3), 5.12 (1-p. d., H-1), 4.91 (1-p. t., H-3), 4.63 (1-p. s., benzylic), ~2.63 (5-p., Ph.), 2.27 and 2.99 (4-proton AB quartet, *J* 8.3 Hz, Tosyl); $J_{1,2}$ 3.5 Hz, $J_{2,3}$—$J_{3,4}$ ~9 Hz.

Found: C, 58.75; H, 5.75; S, 7.16%. Calcd for $C_{22}H_{26}O_8S$: C, 58.65; H, 5.82; S, 7.12%.

Methyl 4,6-*O*-Benzylidene-2-*O*-tosyl-α-D-glucopyranoside (X). Prepared from IX[10] in a manner similar to that described in VIII; yield 91%; mp 155°C (lit, 155°C,[7] 154°C[11]); $[\alpha]_D^{23}$ +63° (*c* 1, $CHCl_3$) (lit, +63.5°,[7] +62.9°[11]); NMR (60 MHz, $CDCl_3$): τ: 7.35 (1-p. broad singlet, disappeared on deuteration, OH), 7.58 (3-p. s., $TsCH_3$), 6.67 (3-p. s., OCH_3), 5.60 (1-p. q., H-2), 5.15 (1-p. d., H-1), 4.50 (1-p. s., benzylic); $J_{1,2}$ 3.2 Hz, $J_{2,3}$ 9.0 Hz.

Methyl 4,6-*O*-Benzylidene-2-*O*-mesyl-α-D-glucopyranoside (XIX). The method of Jeanloz and Jeanloz[6] was followed; when the quantity of pyridine was increased, a higher yield was obtained. To an ice-cold solution of I (2.82 g) in dry pyridine (56 m*l*), we added methanesulfonyl chloride (1.2 m*l*), after which the mixture was allowed to stand at 5°C overnight. A few drops of water were then added, and the solution was evaporated *in vacuo*. A chloroform solution of the resultant residue was washed successively with water, a potassium bisulfate solution, a saturated bicarbonate solution, and water again. After drying over sodium sulfate, the solution was evaporated to give a syrup; the syrup was chromatographed on a silica-gel column (250 g, 4.7×32 cm) and eluted with benzene-ethyl acetate (5 : 1). The dimesylated product (R_f 0.61 by TLC with the same solvent system; 0.81 g) was eluted from a portion between 700 and 800 m*l*, while XIX (R_f 0.47; 2.68 g, 74%) was eluted from a 850-m*l* portion with tailing. XIX was recrystallized from benzene-ethyl acetate (5 : 1); mp 134—135°C (lit, 135—136°C,[6] 132—133°C[7]), $[\alpha]_D^{20}$ +73° (*c* 1, $CHCl_3$) (lit, +73°,[6] +72°[7]); NMR (60 MHz, $CDCl_3$): τ: 5.54 (1-p. q., H-2), $J_{1,2}$ 3.5 Hz, $J_{2,3}$ 9.7 Hz, collapsed to a doublet when irradiated at H-1; 5.07 (1-p. d., H-1), 4.49 (1-p. s., benzylic).

Methyl 4,6-*O*-Benzylidene-2-*O*-mesyl-3-*O*-tosyl-α-D-glucopyranoside (XX). Prepared from XIX (5.08 g) by the usual method; yield 6.62 g (91%); mp 194—195°C, $[\alpha]_D^{20}$ +11° (*c* 1, $CHCl_3$), R_f 0.73 by TLC (benzene-ethyl acetate 5 : 1); IR: 1600, 1365, 1320, 1175, 1095, 1050, 985, 747, 720, 700 cm^{-1}; NMR (60 MHz, $CDCl_3$): τ: 7.76 (3-p. s., $TsCH_3$), 6.87 (3-p. s., SO_2CH_3), 6.50 (3-p. s., OCH_3), 5.40 (1-p. q., H-2), 4.95 (1-p. d., H-1), 4.80 (1-p. t., H-3), 4.71 (1-p. s., benzylic), 2.8—2.5 (5-p. m., Ph), 3.07 and 2.33 (4-p. AB quartet, Ts); $J_{1,2}$ 3.5 Hz, $J_{2,3}$ 9.7 Hz, $J_{3,4}$ ~9.3 Hz.

Found: C, 51.31; H, 5.13; S, 12.65%. Calcd for $C_{22}H_{26}O_{10}S$: C, 51.35; H, 5.09; S, 12.46%.

Methyl 4,6-*O*-Benzylidene-2-deoxy-α-D-*ribo*-hexopyranoside (V). Prepared from methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-allopyranoside[12] (VI) as has

10) E. J. Bourne, A. J. Huggard and J. C. Tatlow, *J. Chem. Soc.*, **1953**, 735.

*3 Honeyman and Morgan[7] made VIII and X by different routes.

11) K. S. Ennor and J. Honeyman, *J. Chem. Soc.*, **1958**, 2586.

12) "Methods in Carbohyd. Chem.", Vol. 1, Academic Press, New York (1962) p. 107.

been described by Richardson[4b]; mp 129—131°C (lit,[4b] 127—129°C), $[\alpha]_D^{20}$ +140° (*c* 1, $CHCl_3$) (lit,[4b] +140°); R_f 0.72 (VI: R_f 0.82) by TLC (benzene-ethyl acetate 1 : 2).

NMR (60 MHz, $CDCl_3$): τ: 8.3—7.6 (2-p. m., H-2, H-2'), 6.98 (1-p. d., disappeared on deuteration, OH), 6.61 (3-p. s., OCH_3), 5.23 (1-p. q., J 3.3 and 1.5 Hz, H-1), 4.38 (1-p. s., benzylic).

Methyl 4,6-*O*-Benzylidene-2-deoxy-3-*O*-tosyl-α-D-*arabino*-hexopyranoside (XIII). Prepared in the usual way from IV; mp 97°C (lit,[8] 95°C), $[\alpha]_D^{24}$ +46° (*c* 1, $CHCl_3$).

Treatment of Methyl 4,6-*O*-Benzylidene-2,3-di-*O*-tosyl-α-D-glucopyranoside (II) with Lithium Aluminum Hydride for 40 hr. The method of Vis and Karrer[3] was followed essentially. Lithium aluminum hydride (1.13 g) was refluxed in dry tetrahydrofuran (THF, 13 m*l*) for 2 hr, and then well-dried II (3.12 g) was added to the mixture. After refluxing for 40 hr, the reaction mixture was cooled and shaken with ethyl acetate (3 m*l*) for a while. Ether (400 m*l*) and an aqueous solution (150 m*l*) of Rochelle salt (15 g) were added under shaking. The aqueous layer was separated and extracted with ether (100 m*l*×5). The ethereal extract was dried over potassium carbonate and evaporated to give a solid (1.3 g), which was then chromatographed on a silica-gel column (150 g, 3.3×35 cm) with benzene-ethyl acetate (1 : 2). A mixture (0.2 g) of the starting material (II) and an unidentified substance (R_f 0.90 and 0.85 respectively, as determined by TLC with the same solvent system) was eluted in a portion between 200—250 m*l*; then a mixture of the products (the B mixture, all having the same R_f-value of 0.72) was eluted in a portion between 330—460 m*l*; 0.86 g; 61%; mp 168—173°C, $[\alpha]_D^{24}$ +128° (*c* 1, $CHCl_3$). Finally I was eluted in a portion between 820—1200 m*l*; 0.23 g (15%); mp 163—164°C (lit,[12] 163—164°C), $[\alpha]_D^{25}$ +109° (*c* 1, $CHCl_3$) (lit,[12] +110°), R_f 0.3 (the same value as that of the authentic I sample).

The fractional crystallization of the B mixture from ethyl acetate and petroleum ether gave pure III; mp 186°C (lit, 186.5—187.5°C,[3] 190—192°C[13]), $[\alpha]_D^{24}$ +126° (*c* 1, $CHCl_3$) (lit, +126.9°,[3] +116°[13]).

NMR (100 MHz, $CDCl_3$): τ: 8.16 (1-p. q., H_{ax}-3, $J_{3e,3a}$—$J_{2,3a}$—$J_{3a,4}$ ~11 Hz), 7.75 (1-proton doublet of triplets, H_{eq}-3; $J_{3e,3a}$ 11.0 Hz, $J_{2,3e}$—$J_{3e,4}$ ~4.5 Hz), 6.55 (3-p. s., OCH_3), 5.33 (1-p. d., $J_{1,2}$ 3.2 Hz, H-1), 4.49 (1-p. s., benzylic), 2.75—2.4 (5-p. m., Ph.). The results confirm the structure of III.

A comparison of the NMR spectrum of the intact A mixture with those of the standard substances (III, IV, and V) showed that the mixture was composed of three components: III (~75%), V (~12%), and another substance (IV, ~12%), the last of which has the same NMR pattern as the substance produced by the action of LAH on methyl 3-*O*-benzoyl-4,6-*O*-benzylidene-2-*O*-tosyl-α-D-glucopyranoside (IX), which will be described later. NMR (here, τ-values are indicated in the order of III (main), V, and IV): τ 6.55, 6.61, 6.68 (each singlet, OCH_3); τ 5.33 (d.), 5.24 (q.), 5.25 (q.)(H-1); τ 4.49, 4.38, 4.46 (each singlet, benzylic).

Treatment of II with Lithium Aluminum Hydride for 3.5 hr. Compound II (1.45 g) was caused to react with LAH in the same manner as has been described above, except that the time of reaction was 3.5 hr. The ethereal extracts thus obtained were evaporated to give a solid (0.85 g). On TLC (benzene-ether 5 : 1), the solid showed the presence of four components: the starting material (II, major, R_f 0.71), X (minor, R_f 0.51), a monotosylated (?) compound (minor, R_f 0.26), and III (major, R_f 0.28). The monotosylated compound had the same R_f-value and the same color-change as methyl 4,6-*O*-benzylidene-3-*O*-tosyl-α-D-glucopyranoside (VIII) when sprayed with sulfuric acid. The attempted isolation of VIII by preparative TLC[14] was, however, unsuccessful because of the concomitance of the 3-deoxy derivative (III). Another minor substance (R_f 0.51) was separated by preparative TLC[14] to give methyl 4,6-*O*-benzylidene-2-*O*-tosyl-α-D-glucopyranoside (X, 0.04 g, mp 154°C, $[\alpha]_D^{23}$ +63°). The identity was confirmed by the IR and NMR patterns.

Treatment of Methyl 2-*O*-Benzoyl-4,6-*O*-benzylidene-3-*O*-tosyl-α-D-glucopyranoside (VII) with Lithium Aluminum Hydride for 20 hr. Lithium aluminum hydride (1.04 g) was refluxed in dry THF (12 m*l*) for 2 hr; well-dried VII (3.04 g) was then added, and the mixture was refluxed for 20 hr. A crude solid (1.4 g) was obtained by the procedure described for the corresponding reaction of II. Column chromatography with silica gel (140 g) and benzene-ethyl acetate (1 : 2) gave a monotosylated product (VIII, R_f 0.8) in a fraction between 210—240 m*l* (0.09 g (3.7%), mp 163°C, $[\alpha]_D^{23}$ +33° (*c* 1, $CHCl_3$)), which showed IR and NMR patterns identical with those of authentic VIII. A mixture of deoxy derivatives (the A mixture, R_f 0.72) was eluted in a portion between 270—350 m*l* (1.09 g (73%); mp 180—184°C, $[\alpha]_D^{24}$ +121° (*c* 1, $CHCl_3$)), and compound I (R_f 0.3) in a portion between 550—850 m*l* (0.10 g (6.3%); mp 163—164°C, $[\alpha]_D^{25}$ +110° (*c* 1, $CHCl_3$)).

The fractional crystallization of the A mixture from ethyl acetate and petroleum ether gave pure III; mp 187°C, $[\alpha]_D^{24}$ +126°. A comparison of the NMR pattern of the intact A mixture with those of III and V in respect to *O*-methyl, anomeric, and benzylic hydrogens indicated that the mixture consisted of two components: III (~93%) and a 2-deoxy derivative (V, ~7%).

Treatment of VII with Lithium Aluminum Hydride for 30 min. A mixture of VII (206 mg) and LAH (78 mg) in dry THF (4 m*l*) was refluxed as has been described above. When the reaction was pursued by TLC (benzene-ethyl acetate 1 : 2), it was found that the starting material (R_f 0.95) disappeared fairly rapidly and that after 30 min of the reaction only the debenzoylated product (VIII, R_f 0.8) could be detected, the deoxy products (R_f 0.72) being then produced gradually. When the reaction was stopped after 30 min, the usual isolation procedure gave VIII (145 mg, 87%); mp 165°C, $[\alpha]_D^{22}$ +33° (*c* 1, $CHCl_3$). Its IR and NMR spectra were identical with those of an authentic sample.

Treatment of Methyl 2-*O*-Benzoyl-4,6-*O*-benzylidene-3-*O*-tosyl-α-D-glucopyranoside (VII) with Lithium Aluminum Deuteride. Formation of Methyl 3-Deoxy-3-deuterio-4,6-*O*-benzylidene-α-D-allopyranoside (III'). Lithium aluminum deuteride (0.46 g) was refluxed in dry THF (6 m*l*) for 2 hr, well-

13) D. A. Prins, *Helv. Chim. Acta*, **29**, 1 (1946).

14) D. Horton and T. Tsuchiya, *Carbohyd. Res.*, **5**, 426 (1967).

dried VII (1.49 g) was added, and then the mixture was refluxed for 20 hr. The reaction product was purified by a usual procedure. The crude product (0.73 g) obtained from the ethereal extract was chromatographed on a silica-gel column (100 g) with benzene-ethyl acetate (1 : 2). The monotosylated product (VIII), a mixture of deoxy derivatives and compound I were obtained in yields of 0.03 g (3%), 0.57 g (78%), and 0.05 g (6%) respectively. The recrystallization of the mixture of deoxy derivatives from ethyl acetate-petroleum ether gave pure III′; mp 186°C, $[\alpha]_D^{22}$ +125° (*c* 1, $CHCl_3$); NMR (60 MHz, $CDCl_3$): τ: 7.8—7.65 (1-proton broad singlet, H_{eq}-3); no signals corresponding to H_{ax}-3 were observed. The other signals were quite identical with those of III.

Treatment of Methyl 4,6-*O*-Benzylidene-3-*O*-tosyl-α-D-glucopyranoside (VIII) with Lithium Aluminum Hydride. A mixture of VIII (0.72 g) and LAH (0.27 g) in dry THF (2.8 m*l*) was refluxed for 20 hr. The extraction of the resultant products by a usual method was followed by column chromatography with silica gel and benzene-ethyl acetate (1 : 2) to give a mixture of deoxy derivatives (0.31 g, 71%; mp 180—183°C) and compound I (0.07 g, 15%). A comparison of the NMR spectrum of the former mixture with that of above-mentioned A mixture indicated that the former mixture consisted of III (major) and the 2-deoxy derivative (V, minor).

Treatment of Methyl 4,6-*O*-Benzylidene-2-*O*-methyl-3-*O*-tosyl-α-D-glucopyranoside (XI) with Lithium Aluminum Hydride. A mixture of XI (591 mg) and LAH (260 mg) in dry THF (3.1 m*l*) was refluxed for 40 hr, and the product was extracted as before. A crude solid (293 mg) thus obtained was passed through a short column of silica gel with benzene-ethyl acetate (1 : 2), and the product (XII) was recrystallized from the same solvent; 244 mg (63%); mp 170°C (lit, 166°C,[15] 168°C[10]), $[\alpha]_D^{22}$ +95° (*c* 1, $CHCl_3$) (lit, +95.4°[15] ($CHCl_3$), +74.5°[10] (ethanol)); NMR (60 MHz, $CDCl_3$) τ: 7.1 (1-p., disappeared on deuteration, OH), 6.57 (3-p. s., OCH_3), 6.49 (3-p. s., OCH_3), 5.13 (1-p. d., $J_{1,2}$ 3.5 Hz), 4.48 (1-p. s., benzylic).

Found: C, 60.40; H, 6.71%. Calcd for $C_{15}H_{20}O_6$: C, 60.80; H, 6.80%.

Treatment of Methyl 3-*O*-Benzoyl-4,6-*O*-benzylidene-2-*O*-tosyl-α-D-glucopyranoside[10] (IX) with Lithium Aluminum Hydride. A mixture of IX (1.10 g) and LAH (0.36 g) in dry THF (4 m*l*) was refluxed for 20 hr, and the resulting products were extracted by a usual procedure. The crude product (0.52 g) was chromatographed on silica gel (50 g) with benzene-ethyl acetate (1 : 2). Methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*arabino*-hexopyranoside (IV) was eluted in a portion between 70—90 m*l* (R_f 0.72 by TLC with the same solvent mixture); 0.16 g (29%); mp 150—151°C (lit, 151—152°C,[16] 149—150°C[17]), $[\alpha]_D^{23}$ +95° (*c* 1, $CHCl_3$) (lit, +90°[16] (acetone), +83.8°[17] (ethanol)). Compound I was eluted in a portion between 150—270 m*l* (R_f 0.3, 0.31 g, 54%); mp 163—164°C, $[\alpha]_D^{24}$ +110° (*c* 1, $CHCl_3$).

NMR of IV (100 MHz, $CDCl_3$): τ: 8.23 (1-proton quartet of doublets, H_{ax}-2), 7.83 (1-proton quartet of small doublets, H_{eq}-2), 7.25 (1-proton broad singlet, disappeared on deuteration, OH), 6.69 (3-p. s., OCH_3), 6.58 (1-p. t., J~9.5 Hz, H-4), 6.28 (2-p. m., H-6, 6′?), 5.90 (1-p. m., H-3?), 5.77 (1-p. m., H-5?), 5.24 (1-proton doublet of small doublets, H-1), 4.47 (1-p. s., benzylic), 2.8—2.45 (5-p. m., Ph); $J_{1,2a}$ 3.6 Hz, $J_{1,2e}$~1.2Hz, $J_{2a,2e}$ 13 Hz, $J_{2a,3}$ 11Hz, $J_{2e,3}$ 5.5 Hz; irradiation at H-1 collapsed H_{ax}-2 to a quartet (J, 13 Hz and 11 Hz) and H_{eq}-2 to a quartet (J, 13 Hz and 5.5 Hz); irradiation at H_{ax}-2 collapsed H-1 to a singlet in appearance, and irradiation at H_{eq}-2 collapsed H-1 to a sharp doublet (J, 3.6 Hz). These values showed a fairly good agreement with those measured at 60 MHz by Coxon.[17]

Treatment of Methyl 4,6-*O*-Benzylidene-2,3-di-*O*-mesyl-α-D-glucopyranoside[6] (XVIII) with Lithium Aluminum Hydride. A mixture of XVIII (3.08 g) and LAH (1.17 g) in dry THF (12 m*l*) was refluxed for 20 hr, and then the product was extracted by a usual procedure. However, in this case, purification by column chromatography was not necessary. The crude product (1.9 g; R_f 0.3 by TLC with benzene-ethyl acetate 1 : 2) contained only a trace of the deoxy product (R_f 0.72). Recrystallization from chloroform-ether gave I (1.80 g, 91%); mp 163—164°C.

Treatment of Methyl 2-*O*-Benzoyl-4,6-*O*-benzylidene-3-*O*-mesyl-α-D-glucopyranoside[6] (XVII) with Lithium Aluminum Hydride. A mixture of XVII (2.93 g) and LAH (1.11 g) in dry THF (12 m*l*) was refluxed for 20 hr and then treated as above. The crude product (1.7 g), which was not contaminated by any deoxy product, was recrystallized from chloroform-ether to give I (1.16 g, 90%); mp 163—164°C.

Treatment of Methyl 4,6-*O*-Benzylidene-2-*O*-mesyl-3-*O*-tosyl-α-D-glucopyranoside (XX) with Lithium Aluminum Hydride. A mixture of XX (1.40 g) and LAH (0.47 g) in dry THF (6 m*l*) was refluxed for 20 hr, and then the reaction mixture was treated by a usual procedure. The crude product (0.70 g) obtained from the ethereal extract was chromatographed on silica gel (100 g) with benzene-ethyl acetate (1 : 2). At first, unidentified substances (0.08 g; TLC with benzene-ethyl acetate 5 : 1, R_f 0.59 and 0.49) were eluted, and then deoxy derivatives (R_f 0.72) were eluted, 0.43 g (59%); mp 172—175°C. Finally I was eluted (0.13 g (17%)). The deoxy derivatives were proved by a study of the NMR spectrum to be a mixture of the 3-deoxy compound (III, ~80%) and the 2-deoxy compound (V, ~20%).

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17) B. Coxon, *Tetrahedron* **21**, 3481 (1965).