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SELECTIVE SULFONYLATION AND ACYLATION OF METHYL AND BENZYL GLYCOPYRANOSIDES OF D-XYLOSE AND D-GLUCOSE*†

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ABSTRACT

The relative reactivities of the hydroxyl groups of methyl α- and β-D-xylopyranosides in selective sulfonylation reactions with methanesulfonyl chloride in pyridine have been determined. For the α-anomer, the order of reactivity is O-2> O-4>O-3, and for the β-anomer O-4>O-3>O-2. Useful yields of mono- or di-substituted xylosides can be obtained from both anomers by suitable choice of reactant ratios and the structures of the major products have been established. Reports that the hydroxyl groups of benzyl α-D-xylopyranoside and benzyl α-D-glucopyranoside show orders of reactivity different from those of the corresponding methyl glycosides have been found to be erroneous. The correct structures of the major products formed by selective *p*-toluenesulfonylation of benzyl α-D-xylopyranoside and by selective methanesulfonylation and lauroylation of benzyl α-D-glucopyranoside have been established by synthetic routes.

INTRODUCTION

In previous parts of this series[1,2], we have described selective methanesulfonylation of some methyl hexosides. This paper describes the results obtained with methyl α- and β-D-xylopyranosides. From results so far reported, it is evident that the products obtained by selective sulfonylation with sulfonyl chlorides in pyridine are closely paralleled by the products of selective acylation with carboxylic acid chlorides in pyridine[3,4]. Selective esterification with carboxylic acid anhydrides in pyridine often results in different relative reactivities of hydroxyl groups[5–7] but, so far, very little work with the sulfonic acid anhydrides has been reported.

During the course of this work, two publications appeared which indicated that, in the benzyl glycosides of α-D-glucopyranose[8] and α-D-xylopyranose[9], the C-3 hydroxyl groups are the most reactive of the ring hydroxyl groups towards

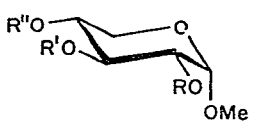
*Dedicated to Dr. Louis Long, Jr., in honor of his 70th birthday; under his guidance this program was initiated.

†Part III in a series of publications on the selective sulfonylation of carbohydrates. For Part II, see ref. 2.

esterification by lauroyl chloride–pyridine and *p*-toluenesulfonyl chloride–pyridine, respectively. This observation contrasts with the preferential reactivity of the C-2 hydroxyl group in the corresponding methyl glycosides. Such a difference between methyl and benzyl glycosides would have potential synthetic utility, but there seemed to be some doubt that this difference had been demonstrated. Both groups of investigators relied on negative periodate-oxidation results for their structural assignments and, as Sivakumaran and Jones[10] had shown that the C-2 hydroxyl group of benzyl α-D-xylopyranoside is the most reactive towards benzoyl chloride–pyridine, a reinvestigation of the foregoing esterifications of benzyl glycosides was clearly necessary.

DISCUSSION

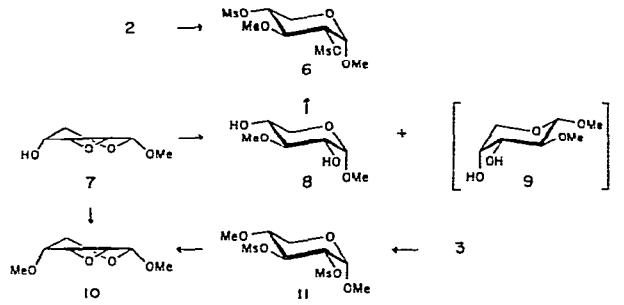
Fractional crystallization of the chloroform-soluble products obtained by treating methyl α-D-xylopyranoside with two equivalents of methanesulfonyl chloride gave, in addition to a small proportion of the known trimethanesulfonate **1**, a crystalline dimethanesulfonate in 55% yield. P.m.r. spectroscopy indicated that the free



1 R = R' = R" = Ms
2 R = R" = Ms, R' = H
3 R = R' = Ms, R" = H
4 R = Ms, R' = R" = H
5 R = Ms, R' = R" = Me

hydroxyl group was at C-3 and that the major product was thus methyl 2,4-di-*O*-methylsulfonyl-α-D-xylopyranoside (**2**). A small proportion of an isomeric, crystalline dimethanesulfonate was also isolated and was shown (by p.m.r. spectroscopy) to be the 2,3-dimethanesulfonate **3**. Chromatographic fractionation of the water-soluble products gave a little more **2** and a crystalline monomethanesulfonate. The latter was obtained in 35% yield from a monomolar methanesulfonylation and was shown to be the 2-*O*-methylsulfonyl derivative **4** by conversion into a mixture of methyl 2,3-anhydro-α-D-lyxopyranoside and methyl 3,4-anhydro-α-D-arabinopyranoside, as previously described for the characterization of methyl 2-*O*-*p*-tolylsulfonyl-α-D-xylopyranoside[11]. Methylation of **4** gave a crystalline dimethyl ether (**5**).

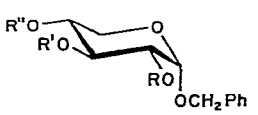
Confirmation of the structures of the dimethanesulfonates **2** and **3** was obtained as shown in Scheme I. Methylation of **2** and of **3** gave the crystalline monomethyl ethers **6** and **11**, respectively. Methyl 2,3-anhydro-α-D-ribopyranoside (**7**) was prepared in high yield from methyl 2-*O*-methylsulfonyl-α-D-arabinopyranoside[12] by treatment with sodium methoxide in methanol and *N*,*N*-dimethylformamide at 0°. In boiling methanolic sodium methoxide, **7** gave two compounds that were separated by column chromatography. The minor product was not characterized, but was presumed to be methyl 2-*O*-methyl-α-D-arabinopyranoside (**9**).



Methanesulfonylation of the major product gave the xylose derivative **6**, thus establishing (*a*) that the *ribo*-epoxide **7** opened mainly by attack at C-3 as expected, and (*b*) that the major product from the dimolar methanesulfonylation was the 2,4-dimethanesulfonate **2**. This structure was also proved independently by other workers[13]. Methylation of **7** gave a crystalline 4-*O*-methyl derivative **10**, and this epoxide was also obtained from the reaction of **11** with sodium methoxide, confirming that the minor dimethanesulfonate was the 2,3-isomer **3**.

The order of reactivity to sulfonylation of the hydroxyl groups in methyl α-D-xylopyranoside is 2>4>3, in qualitative agreement with the results of selective benzoylation of benzyl α-D-xylopyranoside[10], although much less 2,3-diester was formed in the sulfonylation. For benzoylation of methyl α-D-glucopyranoside, the order of reactivity is 6>2>3>4, and the low reactivity of the 4-hydroxyl group was attributed[4] to a skew interaction with the substituted hydroxymethyl group at C-5. When this group is replaced by hydrogen, as in methyl α-D-xylopyranoside, the hydroxyl group at C-4 becomes less sterically hindered[10] than that at C-3.

In view of the consistency of the results of methanesulfonylation and *p*-toluenesulfonylation[11] of methyl α-D-xylopyranoside with the benzoylation of benzyl α-D-xylopyranoside[10], a report that selective *p*-toluenesulfonylation of benzyl α-D-xylopyranoside gave predominantly the 3-sulfonate[9] was somewhat surprising. Treatment of benzyl α-D-xylopyranoside with 1.5 equivalents of *p*-toluenesulfonyl chloride gave crystalline mono- and di-*p*-toluenesulfonates, in 45 and 25% yields respectively, with physical constants in good agreement with those reported by Friedman *et al.*[9] In the p.m.r. spectrum of the monosulfonate, the signal for H-2 appeared as a doublet of doublets well downfield of H-3 and H-4, indicating that the sulfonyloxy group was at C-2 and that this compound is benzyl 2-*O*-*p*-tolylsulfonyl-α-D-xylopyranoside (**12**) and not the 3-sulfonate (**13**). This assignment was confirmed chemically, as hydrogenation of **12** over palladium black gave a crystalline mono-*O*-

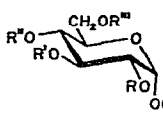


12 R = Ts, R' = R'' = H
13 R' = Ts, R = R'' = H
14 R = R'' = Ts, R' = H
15 R = R' = Ts, R'' = H

p-tolylsulfonyl-D-xylose identical with a sample of 2-*O*-*p*-tolylsulfonyl-D-xylose prepared by hydrolysis of methyl 3,5-*O*-isopropylidene-2-*O*-*p*-tolylsulfonyl-α-D-xylofuranoside[14]. In the p.m.r. spectrum of the di-*p*-toluenesulfonate, the signals for H-2, H-3, and H-4 appeared as a complex multiplet, but addition of trichloroacetyl isocyanate resulted in the appearance of a triplet downfield of H-1 that could be due only to H-3. The disulfonate was therefore benzyl 2,4-di-*O*-*p*-tolylsulfonyl-α-D-xylopyranose (**14**) and not the 2,3-isomer (**15**) as previously suggested.

Friedman and co-workers assigned structure **13** to their product on the basis of a lack of reaction with periodic acid. Clearly, caution must be exercised in interpreting such results, and it should be noted that Sivakumaran and Jones had previously observed that benzyl 2-*O*-benzoyl-α-D-xylopyranoside consumes periodate very slowly[10].

The subsequent publication of some results of selective lauroylation of methyl and benzyl-D-glucopyranosides gave cause for concern as it was reported that, in benzyl α-D-glucopyranoside, the most reactive of the ring hydroxyl groups is that[8] at C-3. However, structural assignments were again based on glycol-cleavage results and, in view of the foregoing findings, were considered to be suspect. Selective lauroylation of benzyl α-D-glucopyranoside was performed as described[8], except that 2.2 equivalents of lauroyl chloride were used to optimize the yield of diester. A crystalline dilaurate was obtained in 48% yield, having physical constants in good agreement with those previously reported for the major dilaurate, thought to be the 3,6-isomer **16**. In the p.m.r. spectrum of this compound (in pyridine-d_5), the signals for H-1 (doublet, $J_{1,2} \sim 3.5$ Hz) and H-2 (a doublet of doublets, $J_{2,3} \sim 10$ Hz) appeared



16 R' = R''' = CO·$(CH_2)_{10}CH_3$, R = R'' = H
17 R = R''' = CO·$(CH_2)_{10}CH_3$, R' = R'' = H
18 R = R''' = CO·$(CH_2)_{10}CH_3$, R' = R'' = Me
19 R = R''' = H, R' = R'' = Me
20 R = R''' = Ms, R' = R'' = H
21 R = R''' = Ms, R' = R'' = Me

downfield of the remaining protons, strongly indicating that the diester is benzyl 2,6-di-*O*-lauroyl-α-D-glucopyranoside (**17**). Kuhn methylation of the dilaurate (conducted at low temperature to minimize acyl migrations) afforded a dimethyl ether (**18**) that did not crystallize but which was homogeneous by t.l.c. and p.m.r. spectroscopy. Catalytic deacylation gave a crystalline benzyl di-*O*-methyl-α-D-glucopyranoside (**19**) from which 3,4-di-*O*-methyl-D-glucose (identical with an authentic sample) was obtained by hydrogenolysis.

Selective methanesulfonylation of benzyl α-D-glucopyranoside with 2.2 equivalents of methanesulfonyl chloride gave a crystalline dimethanesulfonate in 60% yield. Kuhn methylation afforded a dimethyl ether, which was identified as benzyl 3,4-di-*O*-methyl-2,6-di-*O*-methylsulfonyl-α-D-glucopyranoside (**21**) as it was also formed by methanesulfonylation of **19**.

Acylation and sulfonylation of benzyl α-D-glucopyranoside with acid chlorides in pyridine therefore show similar selectivity, and are qualitatively analogous to previous results with methyl α-D-glucopyranoside[1,4,15,16].

Previous results for the selective methanesulfonylation of methyl β-D-glucopyranoside indicated only minor differences in reactivity between the ring hydroxyl groups, although the 4,6-dimethanesulfonate was the major product isolated[2]. By analogy with the α-series, it would be anticipated that, in the absence of a substituted hydroxymethyl group at C-5, the hydroxyl group at C-4 would exhibit an even greater reactivity. Dimolar methanesulfonylation of methyl β-D-xylopyranoside gave a mixture that was fractionated on silica gel. The trimethanesulfonate **22** was eluted

22 R = R' = R" = Ms
23 R = R' = H, R" = Ms
24 R = H, R' = R" = Ms
25 R = Me, R' = R" = Ms
26 R = Me, R' = R" = H

first, followed by a mixture of dimethanesulfonates, and then by a crystalline monomethanesulfonate. P.m.r. spectroscopy of the monoester and of its di[(trichloroacetyl)-carbamate] clearly showed this to be methyl 4-*O*-methylsulfonyl-β-D-xylopyranoside (**23**). This compound was obtained in 38% yield from a monomolar methanesulfonylation, and crystalline methyl 4-*O*-*p*-tolylsulfonyl-β-D-xylopyranoside has also been synthesized by selective sulfonylation[17].

As noted elsewhere[13], the mixture of dimethanesulfonates was difficult to resolve, but two further fractionations on silica gel afforded a pure sample of the major isomer in 44% yield. P.m.r. spectroscopy indicated this ester to be methyl 3,4-di-*O*-methylsulfonyl-β-D-xylopyranoside (**24**), and this assignment was confirmed chemically as follows. Methylation of **24** gave a crystalline monomethyl ether (**25**) identical with the compound formed by methanesulfonylation of methyl 2-*O*-methyl-β-D-xylopyranoside[18] (**26**). The order of reactivity to acid chlorides in pyridine of the hydroxyl groups in methyl β-D-xylopyranoside is therefore 4>3>2.

EXPERIMENTAL

General. — Solutions were concentrated under diminished pressure below 50°. Melting points were determined in glass capillaries with a Thomas–Hoover apparatus and optical rotations were measured with a Bendix Ericsson ETL-NPL automatic polarimeter. P.m.r. spectra were recorded at 100 MHz with a Varian HA-100 spectrometer operating in the frequency-sweep mode with tetramethylsilane ($\tau = 10.00$) as the internal reference. Infrared spectra were recorded with a Perkin–Elmer Model 137 Infracord spectrophotometer and were calibrated against the 1600 cm^{-1} band of polystyrene. Ascending t.l.c. was performed on Silica Gel G or Silica Gel GF and

developed plates were examined under u.v. light (where appropriate), and then sprayed successively with a 1% solution of 1-naphthol in ethanol and with sulfuric acid, and then heated. Column chromatography was performed on silica gel (70–325 mesh, ASTM; E. Merck AG, Darmstadt, Germany; distributed by Brinkmann Instruments, Inc.).

Dimolar methanesulfonylation of methyl α-D-xylopyranoside. — Methyl α-D-xylopyranoside (20 g) was treated with two equivalents (28 g) of methanesulfonyl chloride according to a general procedure[2]. Concentration of the reaction mixture afforded a syrup which was taken up in water (100 ml) and the solution was extracted with chloroform (4 × 25 ml) to give a crystalline mixture (28.8 g). T.l.c. (ethyl acetate) indicated a major product (B) together with small amounts of faster-moving (A) and slower-moving (C) compounds. Fractional recrystallization from ethyl acetate and from ethanol effected a separation of this mixture.

Compound A (4.5 g, 9.3%) had m.p. 131.5–132°, $[\alpha]_D^{21}$ +78.4° (*c* 1.0, acetone). Dick and Jones[19] reported m.p. 130.5–131.5° and $[\alpha]_D$ +80° (chloroform) for methyl 2,3,4-tri-*O*-methylsulfonyl-α-D-xylopyranoside (**1**).

Anal. Calc. for $C_9H_{18}O_{11}S_3$: C, 27.13; H, 4.55; S, 24.14. Found: C, 27.50; H, 4.67; S, 24.0.

Compound B (21.6 g, 55%) had m.p. 159–159.5°, $[\alpha]_D^{21}$ +92° (*c* 1.5, acetone); p.m.r. data (acetone-d_6): τ 4.52 (doublet, J ~5.5 Hz, OH-3), 5.11 (doublet, $J_{1,2}$ ~3.5 Hz, H-1), 5.31–5.66 (2-proton multiplet, H-4, H-2), 6.00 (1-proton multiplet, simplifying to a triplet on addition of D_2O, $J_{2,3} \approx J_{3,4}$ ~9 Hz, H-3), 6.07–6.49 (2-proton multiplet, H-5,5′), 6.57 (3-proton singlet, OMe), 6.80, 6.82 (3-proton singlets, 2 OSO_2Me). These data indicate that this compound is the 2,4-dimethanesulfonate **2**.

Anal. Calc. for $C_8H_{16}O_9S_2$: C, 30.00; H, 5.03; S, 20.02. Found: C, 30.25; H, 5.03; S, 19.90.

Compound C (1.2 g, 3.0% after recrystallization from 1-propanol) had m.p. 138–139°, $[\alpha]_D^{21}$ +62° (*c* 1.5, acetone); p.m.r. data (acetone-d_6): τ 5.03 (doublet, $J_{1,2}$ ~3.5 Hz, H-1), 5.16 (quartet, $J_{2,3}$ ~10 Hz, $J_{3,4}$ ~8.5 Hz, H-3), 5.43 (quartet, H-2), 5.80–6.50 (3-proton multiplet, H-4,5,5′), 6.53 (3-proton singlet, OMe), 6.74, 6.77 (3-proton singlets, 2 OSO_2Me). These data indicate that this compound is the 2,3-dimethanesulfonate **3**.

Anal. Calc. for $C_8H_{16}O_9S_2$: C, 30.00; H, 5.03; S, 20.02. Found: C, 30.16; H, 4.94; S, 20.15.

Concentration of the aqueous layer gave a syrup (3 g) that was fractionated on silica gel (300 g) with ethyl acetate as eluant. An additional amount (0.7 g) of compound B was obtained, together with a crystalline methyl mono-*O*-methylsulfonyl-α-D-xylopyranoside. Recrystallization from 1-propanol gave 1.3 g (4.4%)*, m.p. 108–109°, $[\alpha]_D^{25}$ +113.5° (*c* 1.0, acetone); p.m.r. data (acetone-d_6, hydroxyl protons

*This compound was obtained in 35% yield from a monomolar methanesulfonylation of methyl α-D-xylopyranoside.

exchanged with D_2O): τ 5.19 (doublet, $J_{1,2}$ ~4 Hz, H-1), 5.72 (quartet, $J_{2,3}$ ~9 Hz, H-2), 6.08–6.54 (4-proton multiplet, H-3,4,5,5'), 6.60 (3-proton singlet, OMe), 6.82 (3-proton singlet, OSO_2Me). These data indicate that this compound is the 2-methanesulfonate **4**.

Anal. Calc. for $C_7H_{14}O_7S$: C, 34.71; H, 5.83; S, 13.24. Found: C, 35.08; H, 5.83; S, 13.27.

A solution of **4** (0.61 g) in *N,N*-dimethylformamide (6 ml) and methanol (3 ml) containing sodium methoxide (from 0.24 g of sodium) was kept for 24 h at 0°. Solvent was evaporated off and the residue was extracted with boiling benzene. Concentration of the extracts gave a syrup containing two components (t.l.c. in 4:1 benzene–ether), which were separated by chromatography on silica gel (25 g) using the foregoing solvent. The faster-migrating product (0.13 g) crystallized; after recrystallization from isopropyl ether, it had m.p. 64–66°, $[\alpha]_D^{25}$ +110° (*c* 0.68, water). Buchanan and Fletcher[11] gave m.p. 62–63°, $[\alpha]_D$ +111° (*c* 0.88, water) for methyl 2,3-anhydro-α-D-lyxopyranoside. The slower-moving product (0.01 g), after recrystallization from isopropyl ether, had m.p. 95–96°, the same as that reported for methyl 3,4-anhydro-α-D-arabinopyranoside[11].

Methyl 3,4-di-O-methyl-2-O-methylsulfonyl-α-D-xylopyranoside (**5**). — To a solution of **4** (1.0 g) in *N,N*-dimethylformamide (15 ml) at 0° were added methyl iodide (3 ml) and silver oxide (3 g). The suspension was stirred for 1 h at 0° and then for 5 h at room temperature. Solvent was removed by evaporation, the residue was extracted with chloroform and the extracts were dried ($MgSO_4$). Concentration afforded a syrup that crystallized. Recrystallization from 1-propanol gave pure material (0.66 g, 60%), m.p. 84–85°, $[\alpha]_D^{25}$ +101° (*c* 1.0, chloroform).

Anal. Calc. for $C_9H_{18}O_7S$: C, 39.99; H, 6.71; S, 11.86. Found: C, 40.11; H, 6.81; S, 11.75.

Methyl 3-O-methyl-2,4-di-O-methylsulfonyl-α-D-xylopyranoside (**6**). — A. *From* **2**. To a solution of **2** (2.5 g) in *N,N*-dimethylformamide (40 ml) at 0° was added methyl iodide (8 ml) and silver oxide (8 g). The suspension was stirred for 24 h at room temperature after which time, t.l.c. (ether) indicated the absence of **2** and the formation of two products. The reaction mixture was worked up as before and the resultant syrup (2.0 g) was fractionated on a silica gel (200 g) with ether as eluant.

Fraction 1 (0.57 g) did not crystallize and was not fully characterized. The p.m.r. spectrum indicated this product to be methyl 3,4-anhydro-2-*O*-methylsulfonyl-β-L-arabinopyranoside.

Fraction 2 (0.27 g) was a mixture of the two products.

Fraction 3 (0.60 g) crystallized and after recrystallization from ethanol, had m.p. 105°, $[\alpha]_D^{25}$ +88° (*c* 1.6, chloroform).

Anal. Calc for $C_9H_{18}O_9S_2$: C, 32.33; H, 5.43; S, 19.18. Found: C, 32.60; H, 5.53; S, 18.92.

B. *From methyl 2-O-methylsulfonyl-α-D-arabinopyranoside.* To a solution of methyl 2-*O*-methylsulfonyl-α-D-arabinopyranoside[12] (1.0 g) in *N,N*-dimethylformamide (10 ml) at 0° was added a solution of sodium methoxide (1 g) in methanol

(5 ml). The solution was kept for 70 h at 0° after which time t.l.c. (ether) indicated the absence of starting material. Solvents were removed by evaporation, xylene was added, and the solution concentrated to a syrup. This was partitioned between ether and water and the ether layer was dried ($MgSO_4$). Concentration afforded a syrup that crystallized, and recrystallization from isopropyl ether gave methyl 2,3-anhydro-α-D-ribopyranoside (**7**) (0.58 g, 96%), m.p. 83–84°, $[\alpha]_D^{24}$ +160° (*c* 0.8, chloroform); lit.[20] m.p. 84–86°, $[\alpha]_D^{24}$ +164.5° (chloroform).

A solution of **7** (0.10 g) and sodium methoxide (0.70 g) in methanol (5 ml) was boiled for 24 h under reflux. Methanol was removed by evaporation and the residue was extracted with acetone. Concentration of the extracts afforded a syrup (0.12 g) that contained two components (t.l.c. in methyl acetate). The preponderant and faster moving of these was isolated by chromatography on a column of silica gel (30 g) with methyl acetate as eluant. The homogeneous product (0.07 g) did not crystallize and had $[\alpha]_D^{22}$ +131° (*c* 3.6, chloroform).

A portion (0.04 g) of the syrup was treated with methanesulfonyl chloride (0.1 ml) in pyridine (0.5 ml) for 18 h at room temperature. The residue obtained after removal of pyridine by evaporation was partitioned between chloroform and water. Concentration of the dried ($MgSO_4$) chloroform extract gave a crystalline product (0.04 g) which, after recrystallization from ethanol, had m.p. 103–104°, not depressed by admixture with the compound obtained in *A* (namely, **6**); $[\alpha]_D^{22}$ +88° (*c* 1.7, chloroform). The infrared and p.m.r. spectra of the two compounds were also identical. The preponderant product from the ring opening of **7** with methoxide ion is therefore methyl 3-*O*-methyl-α-D-xylopyranoside (**8**). The other product, presumably **9**, was not fully characterized.

*Methyl 4-*O*-methyl-2,3-di-*O*-methylsulfonyl-α-*D*-xylopyranoside* (**11**). — Methylation of **3** (0.90 g), by the same procedure described for the methylation of **2**, gave the crystalline methyl ether **11**, which was recrystallized from ethanol, yield 0.71 g (76%), m.p. 168–170°, $[\alpha]_D^{26}$ +75° (*c* 1.2, chloroform).

Anal. Calc. for $C_9H_{18}O_9S_2$: C, 32.33; H, 5.43; S, 19.18. Found: C, 32.30; H, 5.34; S, 19.08.

*Methyl 2,3-anhydro-4-*O*-methyl-α-*D*-ribopyranoside* (**10**). — A. *From* **7**. A mixture of **7** (0.17 g), silver oxide (1 g) and methyl iodide (5 ml) was boiled for 24 h under reflux. Silver salts were then removed by filtration and the filtrate was evaporated to a syrup that crystallized. Recrystallization from isopropyl ether gave **10** (0.11 g, 61%), m.p. 37–38°, $[\alpha]_D^{25}$ +128° (*c* 2.5, chloroform).

Anal. Calc. for $C_7H_{12}O_4$: C, 52.49; H, 7.55. Found: C, 52.30; H, 7.83.

B. *From* **11**. To a solution of **11** (0.50 g) in chloroform (6 ml) at 0° was added 2.7M sodium methoxide in methanol (3 ml), and the solution was left for 4 days at room temperature. The reaction mixture was partitioned between chloroform and water, and the chloroform layer was washed with water, and dried ($MgSO_4$). Evaporation afforded a crystalline mixture of **11** and an epoxide. Extraction of the solid with ether–hexane followed by evaporation of solvent gave a crystalline product that was recrystallized from isopropyl ether; yield 0.05 g (31%), m.p. 37–38°, $[\alpha]_D^{22}$ +126°

(*c* 1.0, chloroform). A mixture m.p. with the *ribo*-epoxide **10** was not depressed, and the i.r. and p.m.r. spectra of the two products were identical.

Monomolar p-*toluenesulfonylation of benzyl* α-D-*xylopyranoside.* — To a solution of benzyl α-D-xylopyranoside (2.4 g, 0.01 mole) in anhydrous pyridine (20 ml), cooled to −20°, was added *p*-toluenesulfonyl chloride (2.86 g, 0.015 mole). The reaction mixture was kept for 24 h at −20°, pyridine hydrochloride was removed by filtration, and the filtrate was stored for 48 h at room temperature. Concentration afforded a syrup that was partitioned between chloroform and water, and the chloroform layer was washed with dilute sulfuric acid and with water, and then dried ($MgSO_4$). The syrup obtained after evaporation of chloroform contained two major components (t.l.c. in ether) and these were isolated by chromatography on a column of silica gel (300 g) with ethyl acetate as eluant. The faster moving (and minor) component was a benzyl di-*O*-*p*-tolylsulfonyl-α-D-xylopyranoside which was recrystallized from chloroform–hexane; yield 1.5 g (25%), m.p. 135–136°, $[\alpha]_D^{25}$ +85° (*c* 0.9, chloroform); p.m.r. data (chloroform-*d*); τ 2.14–2.90 (13-proton multiplet, aromatic protons), 5.15 (doublet, $J_{1,2}$ ~3.5 Hz, H-1), 5.52 (center of an AB quartet, benzylic $-CH_2-$), 5.46–6.08 (3-proton multiplet, H-2,3,4), 6.20–6.40 (2-proton multiplet, H-5,5′), 7.40–7.70 (7 protons, 2 Ar-Me, OH). Addition of trichloroacetyl isocyanate resulted in the following (partial) spectrum: τ 4.61 (triplet, $J_{2,3} \approx J_{3,4} \approx 9.5$ Hz, H-3), 5.07 (doublet, $J_{1,2}$ ~3.5 Hz, H-1), 5.21–5.65 (4-proton multiplet, H-2,4, benzylic $-CH_2-$), 6.01–6.28 (2-proton multiplet, H-5,5′).

These data indicate that this compound is benzyl 2,4-di-*O*-*p*-tolylsulfonyl-α-D-xylopyranoside (**14**).

The major component was a benzyl mono-*O*-*p*-tolylsulfonyl-α-D-xylopyranoside, which was recrystallized from chloroform–hexane; yield 1.8 g (45%), m.p. 115–116°, $[\alpha]_D^{25}$ +130° (*c* 0.9, chloroform), in good agreement with physical constants reported by Friedman *et al.* for a benzyl mono-*O*-*p*-tolylsulfonyl-α-D-xylopyranoside[9]. P.m.r. data (chloroform-*d*): τ 2.16–2.96 (9-proton multiplet, aromatic protons), 5.18 (doublet, $J_{1,2}$ ~3.5 Hz, H-1), 5.50 (center of an AB quartet, benzylic $-CH_2-$), 5.70 (quartet, $J_{2,3}$ ~9 Hz, H-2), 5.88–6.60 (4-proton multiplet, H-3,4,5,5′), 6.94 (broad peak, 2 OH), 7.59 (3-proton singlet, Ar-Me).

These data indicate that this ester is the 2-*p*-toluenesulfonate **12**.

2-O-p-*Tolylsulfonyl*-D-*xylose.* — A solution of **12** (0.70 g) in ethanol (50 ml) was hydrogenated over palladium black (0.30 g) at room temperature and 50 lb. in^{-2} in a Parr hydrogenation apparatus. T.l.c. (ethyl acetate) indicated complete reaction after 8 h; the catalyst was removed by filtration and the filtrate was concentrated to a syrup that crystallized. Recrystallization from chloroform gave 0.40 g (74%), m.p. 146–147°, $[\alpha]_D^{25}$ +14° (*c* 1.8, water). Jones and Nicholson[21] reported m.p. 148°, $[\alpha]_D$ +14° (*c* 0.5, water) for 2-*O*-*p*-tolylsulfonyl-α-D-xylopyranose. A mixture m.p. with a sample prepared by hydrolysis of methyl 3,5-*O*-isopropylidene-2-*O*-*p*-tolylsulfonyl-α-D-xylofuranoside[14] was not depressed.

Dimolar lauroylation of benzyl α-D-*glucopyranoside.* — A solution of lauroyl chloride (1.1 ml, 4.5 mmoles) in dichloromethane (5 ml) was added slowly (during

20 min) to a solution of benzyl α-D-glucopyranoside (0.54 g, 2 mmoles) and the solution was kept for 17 h at room temperature. Solvents were removed by evaporation and the major product was isolated by chromatography on a column of silica gel (100 g) with ether as eluent. After crystallization from aqueous ethanol, a yield of 0.61 g (48%) of a benzyl di-*O*-lauroyl-glucoside was obtained, m.p. 47.5–49.5°, $[\alpha]_D^{29}$ +70° (*c* 1.0, chloroform), +97° (*c* 1.0, pyridine): lit.[8] m.p. 44–46°, $[\alpha]_D^{20}$ +92.6° (*c* 1.0, pyridine), p.m.r. data (pyridine-d_5): τ 4.49 (doublet, $J_{1,2}$ ~3.5 Hz, H-1), 4.64 (quartet, $J_{2,3}$ ~10 Hz, H-2). The remaining ring protons, the C-6 protons, and the benzylic protons gave overlapping multiplets between τ 4.90 and 6.10. These data indicate that the dilaurate is the 2,6-isomer **17**.

Confirmation of the stereochemistry of **17**. — To a solution of **17** (0.40 g) in *N*,*N*-dimethylformamide (10 ml) at −10° were added methyl iodide (2 ml) and silver oxide (2 g). The suspension was stirred for 2 h at −10° and then for 2 days at room temperature. Concentration of the filtered mixture gave a syrup from which the major product (0.25 g) was isolated by chromatography on a column of silica gel (250 g) with ether–hexane (1:3) as eluant. The dimethyl ether **18** did not crystallize but was homogeneous by t.l.c. and p.m.r. spectroscopy. A portion (0.17 g) was dissolved in 0.1% sodium methoxide in methanol at room temperature. Deacylation was complete after 15 h (t.l.c. in ether); the solution was neutralized by stirring with Dowex-50W × 8 ion-exchange resin, concentrated, and fractionated on silica gel (20 g) with ether as eluant. Methyl laurate was eluted first; fractions containing the product were combined and concentrated to a syrup that crystallized (0.06 g). Recrystallization from ether–hexane afforded benzyl di-*O*-methyl-α-D-glucopyranoside (**19**), m.p. 75–76°, $[\alpha]_D^{26}$ +160° (*c* 0.5, chloroform).

Anal. Calc. for $C_{15}H_{22}O_6$: C, 60.39; H, 7.43. Found: C, 60.41; H, 7.56.

A solution of **19** (0.08 g) in ethanol (10 ml) was hydrogenated over palladium black (10 mg) in a Parr hydrogenation apparatus. T.l.c. (ethyl acetate) indicated complete reaction after 20 h; catalyst was removed by filtration and the filtrate was concentrated to a syrup, which crystallized from ethyl acetate. Recrystallization from the same solvent gave fine needles (0.03 g), m.p. 115.5–119°, not depressed by admixture with authentic 3,4-di-*O*-methyl-D-glucose.

Dimolar methanesulfonylation of benzyl α-D-*glucopyranoside*. — Benzyl α-D-glucopyranoside (0.54 g, 2 mmoles) was treated with methanesulfonyl chloride (0.34 ml, 4.4 mmoles) in dry pyridine (5 ml) by the procedure described previously[2]. The major product was isolated by chromatography on silica gel (50 g) with ether as eluent. The dimethanesulfonate **20** crystallized from chloroform and, after recrystallization from ethanol, gave a yield of 0.51 g (60%), m.p. 131.5–132.5°, $[\alpha]_D^{27}$ +116° (*c* 0.75, chloroform).

Anal. Calc. for $C_{15}H_{22}O_{10}S_2$: C, 42.25; H, 5.20; S, 15.04. Found: C, 42.39; H, 5.39; S, 14.81.

*Benzyl 3,4-di-*O*-methyl-2,6-di-*O*-methylsulfonyl-*α*-D-glucopyranoside*(**21**). — A. *From* **20**. To a solution of **20** (0.213 g, 0.5 mmole) in *N*,*N*-dimethylformamide (5 ml)

were added methyl iodide (1 ml) and silver oxide (1 g), and the suspension was stirred at room temperature in a foil-covered flask. T.l.c. (ethyl acetate) indicated complete methylation after 3 h, whereupon the suspension was filtered and the filtrate concentrated. The residue was extracted with chloroform and the extracts were evaporated to a syrup that crystallized. Recrystallization from ethanol gave **21** as needles (0.20 g, 87%), m.p. 163–164.5°, $[\alpha]_D^{27}$ +118° (*c* 0.95, chloroform).

Anal. Calc. for $C_{17}H_{26}O_{10}S_2$: C, 44.92; H, 5.77; S, 14.11. Found: C, 45.12; H, 5.90; S, 13.86.

B. *From* **19**. To a solution of **19** (30 mg, 0.1 mmole) in pyridine (1 ml) was added methanesulfonyl chloride (0.025 ml, 3.3 mmoles). T.l.c. (ethyl acetate) indicated rapid sulfonylation and, after 1 h at room temperature, pyridine was removed by evaporation and the product was purified by chromatography on a column of silica gel (20 g) with ethyl acetate as eluant. Recrystallization from ethanol afforded needles (30 mg), m.p. 163–164°, not depressed by admixture with the product obtained in *A*.

Dimolar methanesulfonylation of methyl β-D-xylopyranoside. — Methyl β-D-xylopyranoside (10 g) was treated with two equivalents of methanesulfonyl chloride (14 g) as previously described[2]. The resultant mixture was fractionated on a column of silica gel (600 g) with ethyl acetate as eluant, giving a partial separation of the four components indicated by t.l.c. (ethyl acetate).

Compound A (1.4 g, 5.8%), after recrystallization from ethanol had m.p. 141–142°, $[\alpha]_D^{25}$ −26° (*c* 1.4, acetone). The p.m.r. spectrum was indicative of the trimethanesulfonate **22**.

Anal. Calc. for $C_9H_{18}O_{11}S_3$: C, 27.13; H, 4.55; S, 24.14. Found: C, 27,08; H, 4.42; S, 24.20.

Compounds B and C (14.1 g) were obtained as a crystalline mixture of dimethanesulfonates.

Compound D (1.5 g, 10%), after recrystallization from ethanol had m.p. 121°, $[\alpha]_D$ −60° (*c* 0.9, acetone); p.m.r. data (acetone-d_6, hydroxyl protons exchanged with D_2O): τ 5.64 (1-proton multiplet, H-4), 5.79 (doublet, $J_{1,2}$ ~7.5 Hz, H-1), 5.98 (quartet, H-5), 6.38 (triplet, $J_{2,3} \approx J_{3,4}$ ~7.5 Hz, H-3), 6.52–6.72 (5-proton multiplet; H-2,5′, OMe), 6.82 (3-proton singlet, OSO_2Me). Addition of trichloroacetyl isocyanate resulted in a spectrum having the following features: τ −0.87, −0.76 (singlets, 2 carbamate NH), 4.70 (triplet, $J_{2,3} \approx J_{3,4}$ ~9 Hz, H-3), 5.13 (quartet, $J_{1,2}$ ~7.5 Hz, H-2), 5.10–5.45 (multiplet, H-4), 5.40 (doublet, H-1), 5.82, 6.24 (1-proton quartets, AB part of an ABX system, J_{AB} ~12 Hz, H-5,5′) 6.54 (3-proton singlet, OMe), 6.80 (3-proton singlet, OSO_2Me). Assignments were confirmed by double-resonance experiments. These results indicate that compound D is methyl 4-*O*-methylsulfonyl-β-D-xylopyranoside (**23**).*

Anal. Calc. for $C_7H_{14}O_7S$: C, 34.71; H, 5.83; S, 13.24. Found: C, 34.56; H, 5.87; S, 12.95.

*This compound was obtained in 38% yield from a monomolar methanesulfonylation of methyl β-D-xylopyranoside.

Compound B, the major product of the reaction, was separated with difficulty from the minor isomer C by two further fractionations on columns of silica gel by using ethyl acetate and ether as eluents. Recrystallization from ethanol gave pure B; yield 8.5 g, (44%), m.p. 162–163°, $[\alpha]_D^{25}$ −16° (*c* 0.8, acetone); p.m.r. data (acetone-d_6, hydroxyl protons exchanged with D_2O): τ 5.20–5.52 (2-proton multiplet, H-3,4), 5.65 (doublet, $J_{1,2}$ ~7.5 Hz, H-1), 5.76–5.98 (1-proton multiplet, H-5), 6.24–6.55 (2-proton multiplet, H-2,5′), 6.51 (3-proton singlet, OMe), 6.75, 6.79 (3-proton singlets, 2 OSO_2Me). Ring proton assignments were confirmed by spin-decoupling experiments. These results indicate that compound B is the 3,4-dimethanesulfonate **24**.

Anal. Calc. for $C_8H_{16}O_9S_2$: C, 30.00; H, 5.03; S, 20.02. Found: C, 30.05; H, 5.00; S, 20.15.

The minor dimethanesulfonate was not characterized.

Methyl 2-O-methyl-3,4-di-O-methylsulfonyl-β-D-xylopyranoside (**25**). — A. *From methyl 2-O-methyl-β-D-xylopyranoside* (**26**). To a solution of methyl 2-*O*-methyl-β-D-xylopyranoside[18] (**26**) (89 mg, 0.5 mmole) in pyridine (2 ml) was added methanesulfonyl chloride (0.1 ml, 1.3 mmoles). T.l.c. (ethyl acetate) indicated a slow mesylation, complete after ~1 day at room temperature. Concentration afforded a syrup which was chromatographed on a column of silica gel (45 g) with ethyl acetate as eluant. The dimethanesulfonate **25** crystallized from ethanol (143 mg, 86%) and, after recrystallization, had m.p. 97–98°, $[\alpha]_D^{25}$ −31° (*c* 0.8, acetone).

Anal. Calc. for $C_9H_{18}O_9S_2$: C, 32.33; H, 5.43; S, 19.18. Found: C, 32.31; H, 5.42; S, 18.88.

B. *From* **24**. To a solution of **24** (1 g) in *N*,*N*-dimethylformamide (15 ml) at 0° was added methyl iodide (3 ml) and silver oxide (3 g). The mixture was stirred for 4 h at 0° and for 20 h at room temperature, after which time, t.l.c. (ether) indicated complete methylation. Solvents were removed by evaporation and the residue was extracted with chloroform. Concentration of the extracts afforded a syrup that was purified by chromatography on a column of silica gel (100 g) with 3:1 ether–isopropyl ether as eluant. The product crystallized (0.60 g, 60%) and, after recrystallization from ethanol, had m.p. 96–97.5°, not depressed by admixture with the product obtained in *A*. The p.m.r. spectra of the two products were identical.

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