THE METHYL 2-O-(BENZYLTHIO)CARBONYL DERIVATIVE AS A PRECURSOR TO PARTIAL ESTERS OF METHYL α-D-GLUCOPYRANOSIDE

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ABSTRACT

The utility of the thiocarbonyl group for blocking the C_2 hydroxyl in methyl glucosides has been demonstrated. Methyl 2-*O*-(benzylthio)carbonyl-α-D-glucopyranoside has been synthesized in good yield and its structure proved. Use of this 2-*O*-thiocarbonyl derivative in conjunction with acid-labile blocking groups has permitted the first syntheses of the following esters of methyl α-D-glucopyranoside: 3-*O*-benzoyl-, 3,4-di-*O*-benzoyl-, and 3,4,6-tri-*O*-benzoyl-, and the crystalline 2-*O*-(*p*-toluene)sulphonate derivative of each.

INTRODUCTION

In a previous communication (1) the synthesis of methyl 2,3-di-*O*-(benzylthio)-carbonyl-α- and -β-D-glucopyranosides and the use of these compounds for the synthesis of methyl 4,6-di-*O*-benzoyl-α- and -β-D-glucopyranosides were described. Thiocarbonate derivatives of carbohydrates are conveniently prepared, are stable to mild aqueous acid conditions, but are readily decomposed by oxidation with hydrogen peroxide in glacial acetic acid or by reduction with Raney nickel, conditions which do not generally disturb other ester groups. Thus, a (benzylthio)carbonyl derivative can be used in conjunction with acid-sensitive blocking groups to furnish several classes of partial ester derivatives of the methyl glucosides.

It has been found that crystalline methyl 4,6-*O*-benzylidene-2-*O*-(benzylthio)carbonyl-α-D-glucopyranoside (III), as seen in Fig. 1, can be isolated in 58% yield after treating

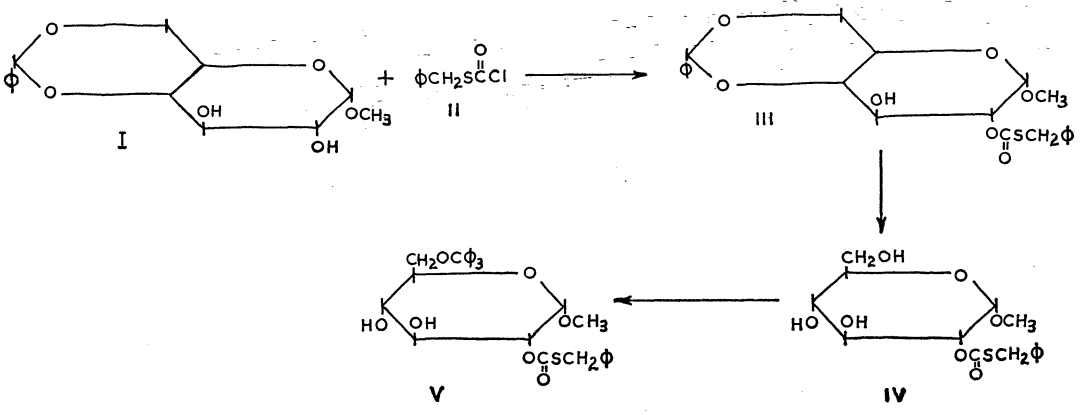

FIG. 1.

methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (I) with 1 mole of (benzylthio)carbonyl chloride (II) in pyridine solution. Removal of the benzylidene group by mild acid

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hydrolysis gave, in 98% yield, a crystalline product which was shown to be methyl 2-*O*-(benzylthio)carbonyl-α-D-glucopyranoside (IV). These compounds serve as useful intermediates in the synthesis of 3-, 3,4-di-, and 3,4,6-tri-*O*-substituted derivatives of methyl α-D-glucopyranoside in the following ways: (i) esterification of III followed by removal of the benzylidene and (benzylthio)carbonyl groups provides 3-*O*-substituted methyl glucosides, (ii) esterification of IV and subsequent removal of the (benzylthio)-carbonyl group gives 3,4,6-tri-*O*-substituted derivatives, and (iii) formation of the triphenylmethyl (trityl) ether of IV provides a compound (V) which is suitable for the formation of 3,4-di-*O*-substituted methyl glucosides. This is the first general synthetic route to each of these three classes of partial ester derivatives of methyl α-D-glucopyranoside.

This article describes the proof of structure of methyl 4,6-*O*-benzylidene-2-*O*-(benzylthio)carbonyl-α-D-glucopyranoside (III) and the syntheses of each of the above classes of partial esters as benzoates of methyl α-D-glucopyranoside; crystalline 2-*O*-(*p*-toluene)-sulphonates of each partially benzoated derivative were prepared.

DISCUSSION

Problems encountered in the use of previously reported blocking groups for the synthesis of partial esters of carbohydrates (namely the trifluoroacetate (2), the dichloroacetate (3), and the tosylate groups (4)) are largely overcome by making use of the thiocarbonate radical. The latter is stable under a wide range of conditions but is readily decomposed, when desired, by oxidative or reductive cleavage. It is now possible to synthesize a large number of previously inaccessible partial ester derivatives of the sugars.

There is ample evidence that the hydroxyl groups at C_2 and C_6 in methyl α-D-glucopyranoside are more reactive than those at C_3 and C_4 (5–7). Similarly, in methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (I) the hydroxyl at C_2 is more reactive in substitution reactions than that at C_3 (8–11). When I was treated with 1 mole of (benzylthio)-carbonyl chloride in pyridine solution, the 2-thiocarbonate derivative was isolated in 58% yield together with 10% of the disubstituted product, methyl 4,6-*O*-benzylidene-2,3-di-*O*-(benzylthio)carbonyl-α-D-glycopyranoside. These two products are readily separated by fractional crystallization from ethanol. Attempts to isolate another product from the mother liquors which might be the 3-thiocarbonate derivative were not successful. The 2-thiocarbonate gave a crystalline acetate, phenylcarbamate, and benzoate derivative.

In order to establish the position of substitution of the thiocarbonate group in III, use was made of its benzoate derivative, VI, Fig. 2, since removal of the thiocarbonate group would furnish one of the isomeric monobenzoate derivatives of I, both being well characterized (2). Attempts to remove the thiocarbonate group from VI by oxidation with hydrogen peroxide in glacial acetic acid resulted in loss of the benzylidene group. It was found, however, that the thiocarbonate radical is decomposed by treatment with Raney nickel in boiling ethanol. In order to accomplish this desulphurization, it was discovered that it is essential to shake the ethanol solution of VI with Raney nickel at room temperature for at least 24 hours prior to refluxing for 3 hours. Omission of this step resulted in the recovery of mostly starting material, in low yield, together with small amounts of other products which were difficult to separate from VI. Under the above conditions, a mixture of the isomeric monobenzoates was obtained containing 24% of the C_2 benzoate (VII) and 56% of the C_3 benzoate (VIII); in another experiment the yield of VIII was 71%. Both monobenzoates were characterized as their tosylates, IX and X. Replacement of the (benzylthio)carbonyl group in VIII yielded a product indistinguishable from that (VI)

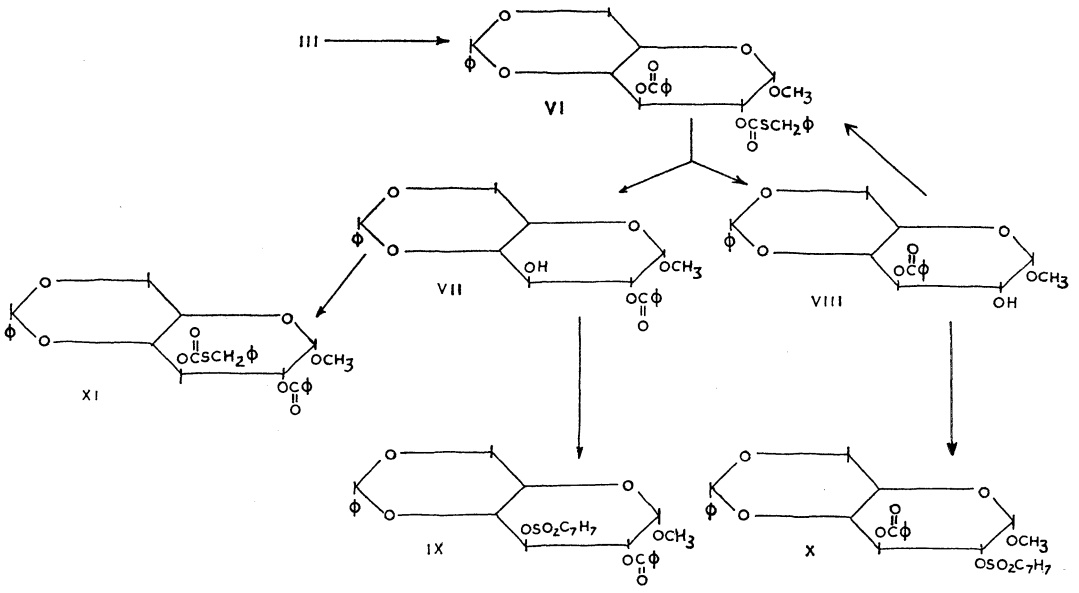

FIG. 2.

obtained by benzoylation of III. Since VIII and its tosylate (X) are well characterized as having the benzoyl group on C_3, the structure of VI must be as shown. Resubstitution of the (benzylthio)carbonyl group in VII yielded a product (XI) quite different from VI in melting point and specific rotation. The occurrence of VII as a product of Raney nickel desulphurization of VI must therefore have resulted from migration of the benzoyl group from the C_3 to the C_2 hydroxyl, possibly catalyzed by traces of alkali still present in the Raney nickel.

The migrations of ester groups in sugar derivatives are assumed to occur through orthoester intermediates (12) but factors which influence the direction of migration are not clearly understood. In derivatives of I there are reports of both C_3 to C_2 (2) and C_2 to C_3 (2, 13) migrations of ester groups; the present work provides another example of a C_3 to C_2 migration in these derivatives.

Benzoylation of IV gave a sirupy product XII, Fig. 3, which on treatment with hydro-

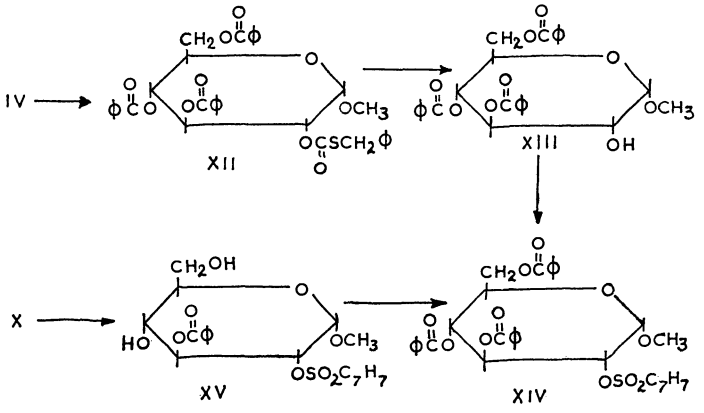

FIG. 3.

gen peroxide in glacial acetic acid gave 72% of the new crystalline tribenzoate of methyl α-D-glucopyranoside (XIII); this compound yielded a crystalline tosylate (XIV). The same tosylate was obtained from the known compound X by removal of the benzylidene group to give XV and benzoylation to yield methyl 3,4,6-tri-*O*-benzoyl-2-*O*-(*p*-toluene)-sulphonyl-α-D-glucopyranoside (XIV). Compound XIII was therefore proved to be methyl 3,4,6-tri-*O*-benzoyl-α-D-glucopyranoside.

The trityl derivative V of IV gave on benzoylation, XVI, Fig. 4. Detritylation to XVII followed by oxidative removal of the thiocarbonate group gave an amorphous solid,

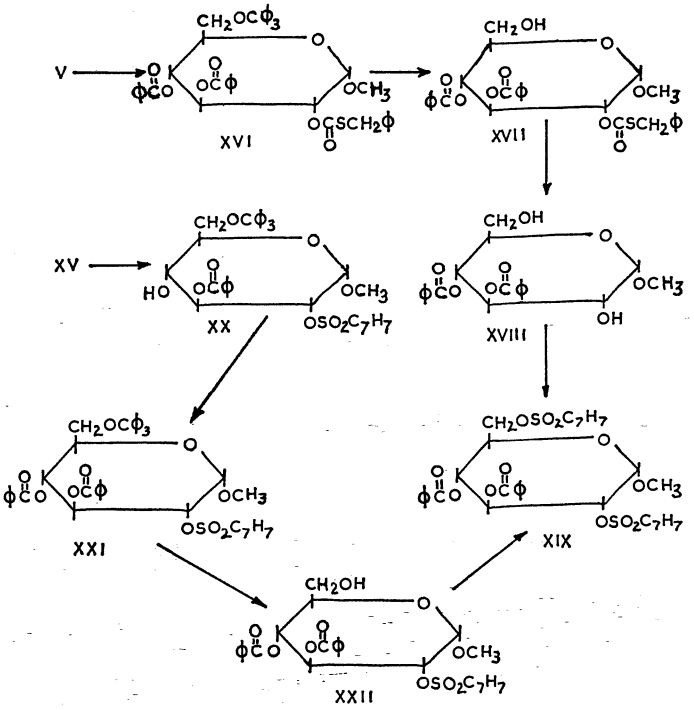

FIG. 4.

XVIII, which, however, gave a crystalline ditosylate derivative, XIX. To prove the structure of this compound, the known compound X was converted through three new crystalline products to an identical ditosylate dibenzoate derivative of methyl α-D-glucopyranoside. Contrary to the usual experience found in this laboratory with sugars having a free primary hydroxyl group, XV did not react with trityl chloride (1 mole) during 2 days at room temperature in pyridine solution. However, when the reaction mixture was warmed on the steam bath for 2 hours, a 93% yield of the crystalline trityl derivative XX was obtained. Benzoylation of the C_4 hydroxyl gave XXI, which was detritylated to give the crystalline 2-tosylate derivative of methyl 3,4-di-*O*-benzoyl-α-D-glucopyranoside. Tosylation of XXII gave a product indistinguishable from XIX obtained from XVIII. Thus, the structure of XVIII was also established.

Removal of the benzylidene group from the known 3-*O*-benzoyl derivative VIII furnished, in 70% yield, an hydroscopic amorphous solid, methyl 3-*O*-benzoyl-α-D-glucopyranoside. Its purity was established when the resynthesis of the benzylidene derivative, VIII, was accomplished in 93% yield.

These reactions confirm the assignment of structure to the monothiocarbonate derivative III as methyl 4,6-*O*-benzylidene-2-*O*-(benzylthio)carbonyl-α-D-glucopyranoside and to the compound IV, methyl 2-*O*-(benzylthio)carbonyl-α-D-glucopyranoside. Furthermore, the synthesis of the three new partial benzoate derivatives in good yield further demonstrates the use of the thiocarbonate group as a valuable blocking group for carbohydrate reactions.

EXPERIMENTAL[3]

Methyl 4,6-O-Benzylidene-2-O-(benzylthio)carbonyl-α-D-glucopyranoside (III)

Methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (I) was prepared by a standard method (14), as was (benzylthio)carbonyl chloride (15). To 15.0 g of I in 30 ml of anhydrous pyridine was added dropwise 9.0 ml of II during ½ hour, the solution being cooled with an ice bath. The mixture was kept an additional half hour at room temperature and was then poured into 300 ml of ice water. The sirupy product was extracted into 100 ml of chloroform, and the latter solution was extracted successively with 100 ml of *N* hydrochloric acid, *N* sodium hydroxide, and water. The chloroform layer was dried over magnesium sulphate. The sirup obtained by evaporation of the chloroform was dissolved in 150 ml of hot ethanol. When cooled to room temperature, this solution gave after 3 hours 3.1 g (10%) of methyl 4,6-*O*-benzylidene-2,3-di-*O*-(benzylthio)carbonyl-α-D-glucopyranoside (1), which was recrystallized from ethanol; there was thus obtained 2.7 g of product with m.p. 133–134°. The original ethanol solution was cooled overnight at −5° and furnished 14.4 g of product having m.p. 118–121°. After recrystallization from 1 liter of ligroin there was obtained 13.3 g (58%) of fine needles, m.p. 121–122°. The melting point was not changed after recrystallization from ethanol, and this product showed $[\alpha]_D^{22}$ +80.60° (*c* 2, $CHCl_3$). Anal. Calc. for $C_{22}H_{24}O_7S$: C, 61.06; H, 5.77; S, 7.37. Found: C, 61.21; H, 5.41; S, 7.45.

In some instances, a third product, m.p. 42.5–44° and optically inactive, was obtained, which cocrystallized with III from ethanol. It was isolated by recrystallization of the mixture from ligroin, coming down last from that solvent. Its infrared spectrum and elemental analysis indicated that this compound was di(benzylthio)carbonyl, $(C_6H_5CH_2S)_2CO$, reported (16) previously as an oil. This same compound was sometimes encountered in low yield during the preparation of II from phosgene and benzylmercaptan, and can be distilled under high vacuum. Its formation during the synthesis of III can be attributed to a reaction of II with water, followed by loss of carbon dioxide to give benzylmercaptan, which reacts in turn with another mole of II. The use of strictly anhydrous pyridine was found to be essential for high yields of III. Anal. for di(benzylthio)carbonyl: Calc. for $C_{15}H_{14}OS_2$: C, 65.69; H, 5.12; S, 23.38. Found: C, 65.33; H, 5.23; S, 23.29.

Derivatives of III

The following derivatives of III were synthesized by standard procedures in pyridine solutions.

Methyl 3-O-Acetyl-4,6-O-benzylidene-2-O-(benzylthio)carbonyl-α-D-glucopyranoside

Yield: 59%; m.p. 135–136°; $[\alpha]_D^{22}$ +74.30° (*c* 2, $CHCl_3$). Anal. Calc. for $C_{24}H_{26}O_8S$: C, 60.75; H, 5.48; S, 6.74. Found: C, 59.61; H, 5.62; S, 6.99.

Methyl 4,6-O-Benzylidene-2-O-(benzylthio)carbonyl-3-O-phenylcarbamoyl-α-D-glucopyranoside

Yield: 84%; m.p. 120–121°; $[\alpha]_D^{22}$ +99.15° (*c* 2, $CHCl_3$). Anal. Calc. for $C_{29}H_{29}O_8NS$: C, 63.16; H, 5.26; S, 5.78; N, 2.54. Found: C, 63.68; H, 5.36; S, 5.78; N, 2.59.

Methyl 3-O-Benzoyl-4,6-O-benzylidene-2-O-(benzylthio)carbonyl-α-D-glucopyranoside (VI)

Yield: 87%; m.p. 138–139°; $[\alpha]_D^{25}$ +44.5° (*c* 2, $CHCl_3$). Anal. Calc. for $C_{29}H_{28}O_8S$: C, 64.92; H, 5.23; S, 5.97. Found: C, 64.87; H, 5.21; S, 6.08.

Methyl 2-O-(Benzylthio)carbonyl-α-D-glucopyranoside (IV)

To 1.0 g of III dissolved in 40 ml of acetone was added 12 ml of 0.2 *N* hydrochloric acid, and the solution was refluxed for 2 hours. After neutralization with excess barium carbonate and filtration, the solution was evaporated to dryness and the residue was extracted with several portions of warm ether, the insoluble barium chloride being removed by filtration. On cooling, the ether solution gave 0.78 g (98%) of product as large needles, m.p. 135–137°. After recrystallization from acetone – petroleum ether the product had m.p. 136–137° and $[\alpha]_D^{22}$ +112.2° (*c* 2, $CHCl_3$). Anal. Calc. for $C_{15}H_{20}O_7S$: S, 9.30. Found: S, 9.18.

Methyl 2-O-(Benzylthio)carbonyl-3,4,6-tri-O-phenylcarbamoyl-α-D-glucopyranoside

Compound IV was treated with phenyl isocyanate in pyridine solution by the usual procedure. The product had m.p. 192.5–193° and $[\alpha]_D^{22}$ +107.6° (*c* 2, $CHCl_3$). Anal. Calc. for $C_{36}H_{35}O_{10}N_3S$: C, 61.62; H, 4.99; N, 5.99; S, 4.57. Found: C, 60.95; H, 5.08; N, 6.01; S, 4.64.

Methyl 2-O-(Benzylthio)carbonyl-6-O-triphenylmethyl-α-D-glucopyranoside (V)

To 1.0 g of IV in 5 ml of anhydrous pyridine was added 0.81 g of triphenylmethyl chloride. The solution

[3]*Melting points are uncorrected. Solvents were removed in vacuo at 50°.*

stood for 2 days at room temperature, with protection from moisture, and was then poured into ice water. The product was extracted into chloroform and isolated in the usual way. The sirup obtained on evaporation of the chloroform turned to a glass on standing over phosphorus pentoxide, but failed to crystallize. It had $[\alpha]_D^{22}$ +46.7° (*c* 1, $CHCl_3$).

Reaction of Methyl 3-O-Benzoyl-4,6-O-benzylidene-2-O-(benzylthio)carbonyl-α-D-glucopyranoside with Raney Nickel

A solution of 5.4 g of VI in 500 ml of ethanol was treated with 8 g of Raney nickel (suspension in ethanol). The mixture was shaken for 24 hours at room temperature and then was refluxed for 3 hours. After filtering the hot solution, 100 ml of water was added. After concentrating this solution to 250 ml and cooling it at −25° for 3 hours, 2.2 g (56%) of product, m.p. 210–212°, was obtained. After recrystallization from acetone – petroleum ether the product had m.p. 216–217° and $[\alpha]_D^{25}$ +34.0° (*c* 1, $CHCl_3$). Reported for VIII: m.p. 217–218° and $[\alpha]_D^{19}$ +33.5° (*c* 2.6, $CHCl_3$).

Further concentration of the original solution gave two additional crops totaling 0.94 g, m.p. 160–163°. After recrystallization from acetone – petroleum ether this product had m.p. 166–168° and $[\alpha]_D^{25}$ +106° (*c* 2, $CHCl_3$). Reported (2) for VII, m.p. 165–166° and $[\alpha]_D^{15}$ +109.5° (*c* 2.1, $CHCl_3$). A mixed melting point with I (m.p. 163–164°) was depressed to 133–150°.

In a separate experiment, 50 mg of VI was shaken for 3 days at room temperature with 200 mg of Raney nickel prior to refluxing for 3 hours. Isolation as above gave, on cooling the ethanol solution, 26 mg (71%) of VIII, m.p. 217–218°.

Methyl 3-O-Benzoyl-4,6-O-benzylidene-2-O-(p-toluene)sulphonyl-α-D-glucopyranoside (X)

To 100 mg of VIII in 2 ml of anhydrous pyridine was added 58 mg of (*p*-toluene)sulphonyl chloride. After being left to stand overnight, the solution was poured into 50 ml of ice water. A solid product was obtained which was recovered by filtration and washed with water. It crystallized from ethanol, giving 125 mg (91%), m.p. 213–214° and $[\alpha]_D^{25}$ +52.4° (*c* 0.8, $CHCl_3$). Reported for X: m.p. 212–213°, $[\alpha]_D^{15}$ +51.6° (*c* 2.9, $CHCl_3$).

Methyl 2-O-Benzoyl-4,6-O-benzylidene-3-O-(p-toluene)sulphonyl-α-D-glucopyranoside (IX)

Compound VII (200 mg) was tosylated as described above except that 4 days' reaction time was required. The yield of IX was then 50%; the product, crystallized from ethanol, had m.p. 185–186° and $[\alpha]_D^{25}$ +78.9° (*c* 2.8, $CHCl_3$). Reported (2): m.p. 184–186° and $[\alpha]_D^{15}$ +83.8° (*c* 4.2, $CHCl_3$).

Resynthesis of VI from VIII

To 240 mg of VIII dissolved in 1 ml of anhydrous pyridine was added 140 mg of II. After 10 hours at room temperature, the product was isolated by the usual procedure. Evaporation of the chloroform gave a sirup which crystallized from ethanol, giving 220 mg (73%) after recrystallization from that solvent. This product had m.p. 138–139° and $[\alpha]_D^{25}$ +45.0° (*c* 2, $CHCl_3$). Found before: the same m.p. and $[\alpha]_D^{25}$ +44.5°. The melting point was not depressed after admixture with VI obtained by benzoylation of III.

Methyl 2-O-Benzoyl-4,6-O-benzylidene-3-O-(benzylthio)carbonyl-α-D-glucopyranoside (XI)

To 196 mg of VII in 1 ml of anhydrous pyridine was added 186 mg of II. The solution stood for 3 hours at room temperature (drying tube), and was then poured into 50 ml of ice water, giving a solid which was recovered by filtration. Two crystallizations from ethanol gave 130 mg (48%) of product as needles having m.p. 133–135° and $[\alpha]_D^{25}$ +107° (*c* 2, $CHCl_3$). Anal. Calc. for $C_{29}H_{28}O_8S$: C, 64.93; H, 5.23; S, 5.97. Found: C, 65.37; H, 5.43; S, 5.73.

Methyl 3,4,6-Tri-O-benzoyl-2-O-(benzylthio)carbonyl-α-D-glucopyranoside (XII)

To 0.5 g of IV in 5 ml anhydrous pyridine was added 1 ml of benzoyl chloride. Isolation in the usual way gave a sirup with $[\alpha]_D^{25}$ +28.0° (*c* 2, $CHCl_3$) which failed to crystallize.

Methyl 3,4,6-Tri-O-benzoyl-α-D-glucopyranoside (XIII)

The product XII from above was dissolved in 10 ml of glacial acetic acid containing 1 ml of chloroform. Sodium acetate (150 mg) and 2 ml of 30% hydrogen peroxide were added and the solution was kept for 5 days at room temperature. The solution was then poured into 200 ml of ice water containing sufficient sodium bicarbonate to neutralize the acetic acid. The product was extracted into chloroform, and the latter was dried and evaporated, leaving a sirupy product which crystallized from ligroin. After recrystallization from ligroin there was obtained 391 mg (72%) of product as needles having m.p. 103–105° and $[\alpha]_D^{25}$ +75.5° (*c* 2, $CHCl_3$). Anal. Calc. for $C_{28}H_{26}O_9$: C, 66.40; H, 5.14. Found: C, 66.52; H, 5.09.

Methyl 3,4,6-Tri-O-benzoyl-2-O-(p-toluene)sulphonyl-α-D-glucopyranoside (XIV)

To 100 mg of XIII in 1 ml of pyridine was added 100 mg of (*p*-toluene)sulphonyl chloride. After being left to stand overnight, the solution was poured into 50 ml of ice water; a solid product was obtained which crystallized from ligroin. There was obtained after recrystallization from that solvent 103 mg (79%) of product having m.p. 158–159° and $[\alpha]_D^{25}$ +67.2° (*c* 2, $CHCl_3$). Anal. Calc. for $C_{35}H_{32}O_{11}S$: C, 63.64; H, 4.85; S, 4.85. Found: C, 63.50; H, 5.35; S, 4.91.

Methyl 3-O-Benzoyl-2-O-(p-toluene)sulphonyl-α-D-glucopyranoside (XV)

Compound X (125 mg) was treated as described before for the synthesis of IV. After two crystallizations from acetone – petroleum ether, the product (82 mg, 80%) was obtained as large needles having m.p. 192–193° and $[\alpha]_D^{25}$ +114° (*c* 2, acetone). Anal. Calc. for $C_{21}H_{24}O_9S$: C, 55.77; H, 5.32; S, 7.08. Found: C, 55.40; H, 5.66; S, 6.78.

Benzoylation of 15 mg of XV by the usual procedure gave 11 mg of product having $[\alpha]_D^{25}$ +66.5° (*c* 0.2, $CHCl_3$) and m.p. 157–158°. Admixture of this product with XIV synthesized from XIII did not depress the melting point.

Methyl 3,4-Di-O-benzoyl-2-O-(benzylthio)carbonyl-α-D-glucopyranoside (XVII)

One gram of IV was tritylated as described before and 1.2 ml of benzoyl chloride was added to the pyridine solution after 2 days. After a third day, the product was isolated by the usual procedure and was obtained as a glass having $[\alpha]_D^{25}$ +19° (*c* 2, $CHCl_3$). This product was dissolved in 6 ml of glacial acetic acid, and 1 ml of acetic acid saturated with hydrogen bromide was added, the solution being kept cool with an ice bath. The triphenylmethyl bromide (0.75 g) was recovered by filtration, and the solution was poured into 100 ml of ice water containing 1 g of sodium bicarbonate. The water was decanted from the sirup, and the latter was then dissolved in chloroform. After washing, drying, and evaporating the chloroform, there was obtained a sirup with $[\alpha]_D^{25}$ +13° (*c* 2, $CHCl_3$).

Methyl 3,4-Di-O-benzoyl-α-D-glucopyranoside (XVIII)

The product from the above reaction was dissolved in 10 ml of glacial acetic acid containing 3 ml of chloroform. Sodium acetate (275 mg) and 3 ml of hydrogen peroxide were added and the solution was kept for 4 days at room temperature. It was then poured into 200 ml of ice water containing sufficient sodium bicarbonate to neutralize the acetic acid. Evaporation of the chloroform left the product as a solid suspended in the water. This product was recovered by filtration and washed thoroughly with water. It could not be induced to crystallize. The yield was 0.69 g (59% based on IV) and the amorphous product had $[\alpha]_D^{25}$ +32° (*c* 0.5, acetone). Anal. Calc. for $C_{21}H_{22}O_8$: C, 62.68; H, 5.48. Found: C, 61.83; H, 5.61.

Methyl 3,4-Di-O-benzoyl-2,6-di-O-(p-toluene)sulphonyl-α-D-glucopyranoside (XIX)

To 60 mg of XVIII in 1 ml of anhydrous pyridine was added 200 mg of (*p*-toluene)sulphonyl chloride. After 3 days the solution was poured into 50 ml of ice water; a solid product was obtained, which was recovered by filtration. After two crystallizations from ligroin, there was obtained 51 mg of product (48%) as needles which had m.p. 189–190° and $[\alpha]_D^{25}$ +25.9° (*c* 1, $CHCl_3$). Anal. Calc. for $C_{35}H_{34}O_{12}S_2$: C, 59.16; H, 4.78; S, 9.02. Found: C, 60.29; H, 5.06; S, 9.41.

Methyl 3-O-Benzoyl-2-O-(p-toluene)sulphonyl-6-O-trityl-α-D-glucopyranoside (XX)

To 300 mg of XV in 5 ml anhydrous pyridine was added 240 mg of triphenylmethyl chloride. While being protected with a drying tube, the solution was warmed on the steam bath for 2 hours, after which it was poured into ice water. The solid product thus obtained was recovered by filtration and crystallized from ethanol, giving 429 mg (93%), m.p. 174–176°. Recrystallization from ligroin did not change the melting point of the product, which had $[\alpha]_D^{25}$ +90.0° (*c* 2, $CHCl_3$). Anal. Calc. for $C_{40}H_{38}O_9S$: C, 69.16; H, 5.48; S, 4.61. Found: C, 69.39; H, 5.37; S, 4.64.

Methyl 3,4-Di-O-benzoyl-2-O-(p-toluene)sulphonyl-6-O-trityl-α-D-glucopyranoside (XXI)

To 330 mg of XX in 3 ml of anhydrous pyridine was added 120 mg of benzoyl chloride and this solution was heated for 1 hour on the steam bath (drying tube). The addition of ice water (50 ml) gave a solid product, which was crystallized from ethanol and then ligroin; there was thus obtained 210 mg (61%) of product in a low-melting crystalline form (m.p. 89–91°). Recrystallization from ligroin gave large needles, m.p. 179–181° and $[\alpha]_D^{25}$ +38.0° (*c* 1, $CHCl_3$). Anal. Calc. for $C_{47}H_{42}O_{10}S$: C, 70.67; H, 5.27; S, 4.01. Found: C, 70.56; H, 5.25; S, 4.30.

Methyl 3,4-Di-O-benzoyl-2-O-(p-toluene)sulphonyl-α-D-glucopyranoside (XXII)

Compound XXI (140 mg) was detritylated as previously described; there was obtained 50 mg (52%) of product which was crystallized twice as fine needles from ligroin. The product had m.p. 70–72° and $[\alpha]_D^{25}$ +18.0° (*c* 0.5, $CHCl_3$). Anal. Calc. for $C_{28}H_{28}O_{10}S$: C, 60.43; H, 5.04; S, 5.76. Found: C, 60.80; H, 5.07. For an unexplained reason, sulphur analyses were high, 6.7 and 7.1

This product (24 mg) was tosylated as previously described, giving 16 mg of product, which after two crystallizations from ligroin had m.p. 190–192°. The m.p. was not depressed after admixture with XIX obtained from tosylation of XVIII.

Methyl 3-O-Benzoyl-α-D-glucopyranoside

This compound was synthesized from 0.5 g of VIII by a method previously described. The product was obtained as an amorphous solid having $[\alpha]_D^{25}$ +169° (*c* 2, $CHCl_3$). Anal. Calc. for $C_{14}H_{18}O_7$: C, 56.37; H, 6.04. Found: C, 55.71; H, 6.34.

To 100 mg of this product dissolved in 1 ml of benzaldehyde was added 100 mg of anhydrous zinc chloride. After the mixture was shaken for 3 hours, it was treated with ice water and petroleum ether; the product

was thus obtained as a solid, which was recovered by filtration and crystallized twice from ethanol. There was obtained 120 mg (93%) of product having m.p. 216–217° and $[\alpha]_D^{25}$ +34.0° (*c* 1, $CHCl_3$). The melting point was not depressed after admixture with VIII.

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