Isomaltose Synthesis Utilizing 2-Sulfonate Derivatives of D-Glucose[1]

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β-Isomaltose octaacetate was synthesized by a modified Koenigs–Knorr reaction between 3,4,6-tri-*O*-acetyl-2-*O*-(*p*-tolylsulfonyl)-β-D-glucosyl chloride (IVa) and 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose (IX) followed by reductive desulfonation and acetylation. At the same time desulfonation occurred with the formation, after acetylation, of β-gentiobiose octaacetate, presumably by an obscure participation reaction with the 2-sulfonate group. The halide IVa was obtained from D-glucose derivatives, unsubstituted at the C-2 position, formed by the Brigl phosphorus pentachloride reaction or by the Helferich ortho ester reaction. The chloride IVa was obtained in the β-D form by a succession of reactions involving Walden inversions at C-1 through the conversions: Cl(Br) → OAc by $Hg(OAc)_2$; OAc → SEt by EtSH–BF_3; SEt → Cl by Cl_2. No β-isomaltose octaacetate was obtained when the 2-(*p*-toluenesulfonate) group in the chloride IVa was replaced by the 2-(methylsulfonate) group but β-gentiobiose octaacetate was produced, after acetylation, by sulfonate participation. No α-D-(1→6) linkage was formed when the IVa + IX reaction was performed in acetonitrile solution under mercuric salt catalysis but a low yield of the β-D-(1→6) linkage was obtained.

The synthesis of disaccharides containing an α-D glycosidic linkage in the D-glucose structure has posed a difficult problem. Employment of a nonparticipating nitrate ester group on C-2 of D-glucose with a chlorine atom at C-1 in the β-D form led to the synthesis of the α-D-(1→6) or isomaltose interglycosidic linkage,[2,3] on reaction with 1,2,3,4-tetra-*O*-acetyl-β-D-glucose under definitive conditions. A smaller amount of the β-D-(1→6) linkage or gentiobiose was produced simultaneously. Some success toward the same objective was attained on employment of the trichloroacetate group at C-2 under somewhat analogous conditions.[4] The present work is concerned with a study of a sulfonate ester at C-2 on an appropriately substituted β-D-glucopyranosyl halide. It was considered that, if such a substituent were nonparticipating in a Koenigs–Knorr[5] type of condensation, then the halogen might be more reactive than with the highly deactivating nitrate group.

Brigl[6] had obtained 3,4,6-tri-*O*-acetyl-β-D-glucopyranosyl chloride and this had been sulfonated with *p*-toluenesulfonyl chloride by Reynolds,[7] but in the process the anomeric halogen had shifted to its usual α-D form. It then became our objective to convert this compound (Ia) into its anomeric form.

3,4,6-Tri-*O*-acetyl-2-*O*-(*p*-tolylsulfonyl)-α-D-glucosyl chloride (Ia) was converted (see Scheme I) into 1,3,4,6-tetra-*O*-acetyl-2-*O*-(*p*-tolylsulfonyl)-β-D-glucose (IIa) with mercuric acetate in acetic acid.[8] Reaction of IIa with ethanethiol in the presence of boron trifluoride[9] then led to the isolation, as an oil, of ethyl 3,4,6-tri-*O*-acetyl-2-*O*-(*p*-tolylsulfonyl)-1-thio-α-D-glucoside (IIIa) which on ethylthio replacement with chlorine[10] led to the desired 3,4,6-tri-*O*-acetyl-2-*O*-(*p*-tolylsulfonyl)-β-D-glucosyl chloride (IVa).

The chloride IVa was then subjected to methanolysis, as described previously for the analogous 2-nitrate, in the presence of freshly prepared silver perchlorate and silver carbonate, and, after reductive removal of the sulfonate group and acetylation, there was obtained methyl tetra-*O*-acetyl-α-D-glucopyranoside in a 72% over-all yield from the chloride.

A more direct route to a 3,4,6-tri-*O*-acetyl-α-D-glucosyl halide was reported by Helferich and Zirner[11] through a process involving the intermediate formation of a 1,2-orthoacetate. The 1,3,4,6-tetra-*O*-acetyl-α-D-glucopyranose (V) of Helferich and Zirner[11] could be *p*-toluenesulfonated at C-2 to produce VI which could then be transformed to the α-D-bromide VII and this could substitute for the Reynolds' halide Ia in the formation of the mixed ester IIa. Helferich and Zirner[11] also described a sirupy 3,4,6-tri-*O*-acetyl-2-*O*-(methylsulfonyl)-α-D-glucopyranosyl bromide (Ib) and from this an analogous series of 2-methanesulfonates (IIb, IIIb, and IVb) was obtained.

Our next task was to utilize the 3,4,6-tri-*O*-acetyl-2-*O*-(*p*-tolylsulfonyl)-β-D-glucosyl chloride (IVa) in an isomaltose synthesis similar to the one formerly reported[2] for the analogous 2-nitrate derivative. Accordingly IVa was treated (Scheme II) with 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose tetraacetate (IX) under prescribed conditions[2]; the reaction mixture was acetylated. Chromatographic investigations of the final mixture led to the isolation of β-gentiobiose octaacetate (XI) in a 6% yield based on the halide IVa. This cleavage of the 2-(*p*-toluenesulfonate) group was a surprising result and indicated that the 2-(*p*-toluenesulfonate) was not a nonparticipating group. We have no immediate explanation for this finding. A sirupy sulfur-containing zone, presumably X, was then reductively desulfonated with Raney nickel and hydrogen, and after further acetylation there was isolated a 9% yield of β-isomaltose octaacetate (XII). It is therefore concluded that the 2-(*p*-toluenesulfonate) is not so useful a group for isomaltose synthesis as is the 2-nitrate.

It was considered that the 2-(methanesulfonate) might be sterically advantageous over the 2-(*p*-toluenesulfonate) and accordingly the halide[11] IVb was employed in the reaction with 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose (IX). However, the reaction product

(1) Preliminary communication: Abstracts of Papers, 148th National Meeting of the American Chemical Society, Chicago, Ill., Sept. 1964, p. 24D.

(2) M. L. Wolfrom, A. O. Pittet, and I. C. Gillam, *Proc. Natl. Acad. Sci. U. S.*, **47**, 700 (1961).

(3) M. L. Wolfrom and D. R. Lineback, *Methods Carbohydrate Chem.*, **2**, 342 (1963).

(4) H. Bredereck, A. Wagner, D. Geissel, and H. Ott, *Ber.*, **95**, 3064 (1962).

(5) W. Koenigs and E. Knorr, *ibid.*, **34**, 957 (1901); W. L. Evans, D. D. Reynolds, and E. A. Talley, *Advan. Carbohydrate Chem.*, **6**, 27 (1951).

(6) P. Brigl, *Z. Physiol. Chem.*, **116**, 1 (1921).

(7) T. M. Reynolds, *J. Chem. Soc.*, 2626 (1931).

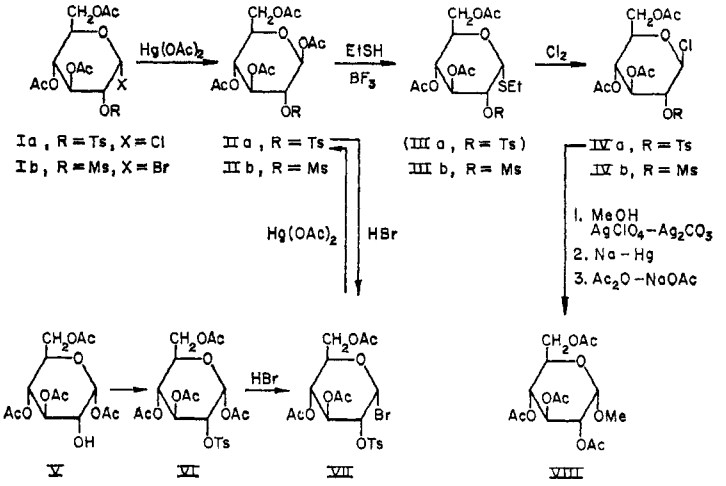
(8) B. Lindberg, *Acta Chem. Scand.*, **3**, 1355 (1949); L. Asp and B. Lindberg, *ibid.*, **5**, 340 (1951); **6**, 941 (1952).

(9) M. L. Wolfrom and T. E. Whiteley, *J. Org. Chem.*, **27**, 2109 (1962).

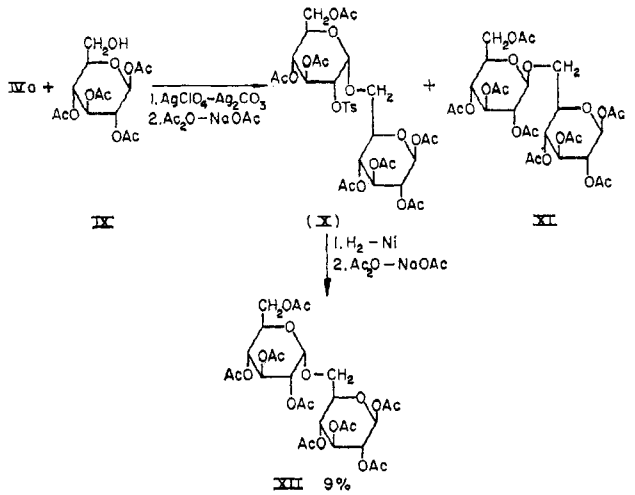
(10) M. L. Wolfrom and W. Groebke, *ibid.*, **28**, 2986 (1963).

(11) B. Helferich and J. Zirner, *Ber.*, **95**, 2604 (1962).

SCHEME I

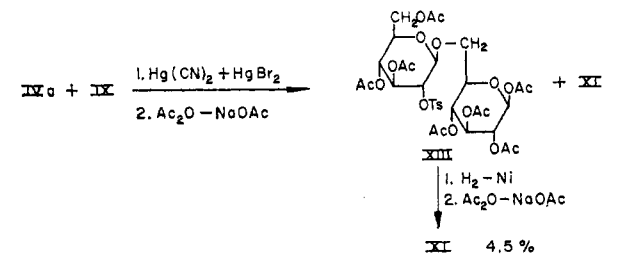


SCHEME II



was a complex mixture from which again there was isolated, by chromatographic techniques, β-gentiobiose octaacetate (after acetylation but without reduction) and in a 13% yield. No β-isomaltose octaacetate was isolated and we found it difficult to remove the methanesulfonate group by reductive methods.

Since there is evidence that the use of mercuric salts in a Koenigs–Knorr type of reaction may favor the synthesis of α-D linkages, the halide IVa was treated with the tetraacetate IX in an acetonitrile solution containing mercuric cyanide and mercuric bromide. There was isolated, by chromatographic methods, crystalline *O*-[3,4,6-tri-*O*-acetyl-2-*O*-(*p*-tolylsulfonyl)-β-D-glucosyl]-(1→6)-tetra-*O*-acetyl-β-D-glucopyranose (XIII) which on reductive desulfonation and acetylation produced β-gentiobiose octaacetate in 4.5% yield (based on the halide IVa). No isomaltose derivative was isolated.



Experimental Section

1,3,4,6-Tetra-*O*-acetyl-2-*O*-(*p*-tolylsulfonyl)-β-D-glucose (IIa).—3,4,6-Tri-*O*-acetyl-2-*O*-(*p*-tolylsulfonyl)-α-D-glucosyl chloride[7] (Ia, 2.0 g.) was added to 15 ml. of glacial acetic acid containing 1.8 g. of mercuric acetate and the mixture was heated at 70° for 20 hr. under stirring. The cooled solution was extracted with chloroform and the extract was washed successively with water, saturated aqueous sodium bicarbonate solution, and water. The crystalline residue obtained on solvent removal from the dried chloroform solution was recrystallized from methanol or ether, yield 1.6 g. (76%), m.p. 156–158°, $[\alpha]^{21}D$ +22° (*c* 1.2, chloroform).

Anal. Calcd. for $C_{21}H_{26}O_{12}S$: C, 50.19; H, 5.22; S, 6.38. Found: C, 50.07; H, 5.03; S, 6.43.

This substance was also synthesized from 3,4,6-tri-*O*-acetyl-2-*O*-(*p*-tolylsulfonyl)-α-D-glucosyl bromide (VII) described below. A mixture of 14 g. of VII, 12.6 g. of mercuric acetate, and 105 ml. of glacial acetic acid was heated at 60° for 24 hr. After cooling, 60 ml. of chloroform was added and the solution was washed successively with water, aqueous sodium bicarbonate solution, and water. Solvent removal from the dried chloroform layer yielded a crystalline solid which was recrystallized from ethanol, yield 13 g. (97%), m.p. and m.m.p. (with above product) 156–158°, $[\alpha]^{20}D$ +21° (*c* 1.0, chloroform).

3,4,6-Tri-*O*-acetyl-2-*O*-(*p*-tolylsulfonyl)-β-D-glucosyl Chloride (IVa).—1,3,4,6-Tetra-*O*-acetyl-2-*O*-(*p*-tolylsulfonyl)-β-D-glucose (IIa, 16.0 g.) was suspended in a mixture of 50 ml. of ethanethiol and 50 ml. of boron trifluoride etherate and stirred at room temperature for 48 hr. At the end of this period, complete solution had occurred. The solution was poured into an excess of ice and water and extracted with chloroform. The extract was washed successively with water, saturated aqueous sodium bicarbonate solution, and water. The sirup obtained on solvent removal from the dried extract was chromatographed on alumina (Woelm, grade I) and the oily materials, small in amount, eluted with benzene and with benzene–chloroform (8:2 v./v.), were discarded. The eluates obtained on elution with benzene–chloroform (7:3) and with chloroform were combined and evaporated to give an oil. The resultant oil was dissolved in absolute ether and treated with decolorizing carbon. A yellow oil, considered to be ethyl 3,4,6-tri-*O*-acetyl-2-*O*-(*p*-tolylsulfonyl)-1-thio-α-D-glucoside (IIIa), was obtained on solvent removal, yield 10.8 g. (67.5%), $[\alpha]^{23}D$ +109.5° (*c* 1.7, chloroform).

An amount of 4.10 g. of the above oil (IIIa) was dissolved in 100 ml. of absolute ether and a stream of dried (sulfuric acid wash bottle) chlorine gas was passed in for 15 min. at −4.5°. The solution was stirred at 0° for 1 hr. A crystalline substance separated and was removed by filtration and recrystallized from chloroform–ether, yield 1.83 g., m.p. 142–146°. The ethereal mother liquor was washed successively with water, saturated aqueous sodium bicarbonate, and water and dried, and the solvent was removed under reduced pressure. The resultant crystalline residue was recrystallized from absolute ether, yield 120 mg., total yield 1.95 g. (50%). Further recrystallization from chloroform–ether gave pure material: m.p. 144–146°, depressed

to 105–113° on admixture with 3,4,6-tri-*O*-acetyl-2-*O*-(*p*-tolylsulfonyl)-α-D-glucosyl chloride (Ia) of m.p. 123–125°; $[\alpha]^{19}D$ +18° (*c* 1.12, chloroform).

Anal. Calcd. for $C_{19}H_{23}ClO_{10}S$: C, 47.65; H, 4.84; Cl, 7.40; S, 6.70. Found: C, 47.68; H, 5.10; Cl, 7.34; S, 6.87.

Dimorphism of 1,3,4,6-Tetra-*O*-acetyl-α-D-glucose (V).—This compound was prepared by the method of Helferich and Zirner,[11] who had noted that the substance crystallized as a mixture of needles and plates. In our hands these two forms were separable by recrystallization from ether and proper nucleation; they were interconvertible. The needles had m.p. 112–114°; $[\alpha]^{21}D$ +140 ± 1° (*c* 1.0, chloroform); X-ray powder diffraction data[12] 11.48 (s, 2), 7.69 (m), 5.34 (s, 1), 4.52 (w), 3.98 (m), 3.69 (w), 3.38 (vw). The plates had m.p. 99–101°; $[\alpha]^{21}D$ + 140 ± 1° (*c* 1.1, chloroform); X-ray powder diffraction data[12] 10.92 (m), 8.51 (vs, 1), 6.42 (vw), 5.44 (s, 2), 4.90 (m, 3.3), 4.68 (m, 3,3), 4.24 (w), 3.93 (m), 3.51 (w), 3.39 (w), 3.23 (w), 3.00 (w).

Anal. Calcd. for $C_{14}H_{20}O_{10}$: C, 48.28; H, 5.79. Found (needles): C, 48.56; H, 5.96. Found (plates): C, 48.46; H, 5.95.

1,3,4,6-Tetra-*O*-acetyl-2-*O*-(*p*-tolylsulfonyl)-α-D-glucose (VI).—To a solution of 2.1 g. of *p*-toluenesulfonyl chloride in 15 ml. of dry pyridine was added 2.1 g. of 1,3,4,6-tetra-*O*-acetyl-α-D-glucose (V) at 0°. The mixture was maintained at room temperature for 48 hr. and was then poured upon ice and extracted with chloroform and the extract was washed successively with cold water, cold saturated aqueous sodium bicarbonate solution, cold water, cold dilute hydrochloric acid, and water. The sirup obtained on solvent removal from the dried chloroform extract was crystallized as prisms from ether, yield 2.4 g. (71%), m.p. 124–126°. Pure material was obtained on further crystallization from ethanol, m.p. 125–127°, $[\alpha]^{21}D$ +83° (*c* 1.06, chloroform).

Anal. Calcd. for $C_{21}H_{26}O_{12}S$: C, 50.19; H, 5.22; S, 6.38. Found: C, 50.16; H, 5.16; S, 6.36.

3,4,6-Tri-*O*-acetyl-2-*O*-(*p*-tolylsulfonyl)-α-D-glucosyl Bromide (VII).—To a solution of 500 mg. of 1,3,4,6-tetra-*O*-acetyl-2-*O*-(*p*-tolylsulfonyl)-α-D-glucose (VI) in 5 ml. of acetic anhydride was added, at 0°, 10 ml. of glacial acetic acid containing 40% hydrogen bromide. The solution was maintained at room temperature for 24 hr. and was then poured into iced water. The mixture was extracted with chloroform and the extract was washed successively with cold water, aqueous sodium bicarbonate solution, and water, dried, and concentrated to a sirup which was crystallized as plates from ether, yield 434 mg. (83%), m.p. 113–114°, $[\alpha]^{20}D$ +176° (*c* 1.19, chloroform).

Anal. Calcd. for $C_{19}H_{23}BrO_{10}S$: C, 43.60; H, 4.43; Br, 15.27. Found: C, 43.61; H, 4.34; Br, 15.38.

1,3,4,6-Tetra-*O*-acetyl-2-*O*-(*p*-tolylsulfonyl)-β-D-glucose (IIa) was treated as above and 3,4,6-tri-*O*-acetyl-2-*O*-(*p*-tolylsulfonyl)-α-D-glucosyl bromide was obtained in 80% yield.

Conversion of 3,4,6-Tri-*O*-acetyl-2-*O*-(*p*-tolylsulfonyl)-β-D-glucosyl Chloride (IVa) into Methyl Tetra-*O*-acetyl-α-D-glucopyranoside (VIII).—A mixture of 1.8 g. of pulverized Drierite,[13] 300 mg. of "active" silver carbonate,[3] 60 mg. of silver perchlorate,[14] and 20 ml. of absolute methanol was stirred for 10 min. after which 600 mg. of 3,4,6-tri-*O*-acetyl-2-*O*-(*p*-tolylsulfonyl)-β-D-glucosyl chloride (IV) was added. The mixture was stirred at room temperature for 20 hr. in the absence of light (foil-covered flask) and filtered. The filtrate was evaporated to a sirup which was dissolved in absolute ether, and the ethereal solution was treated with decolorizing carbon and again evaporated. The residue, which failed to crystallize but exhibited only one spot by thin layer chromatography, was dissolved in 20 ml. of 80% ethanol, and 4 g. of 2% sodium amalgam was added portionwise to the solution with stirring. After 20 hr., the alcoholic solution was separated from mercury by decantation, solid carbon dioxide was added, and the solution was evaporated to dryness under reduced pressure. The residue was extracted with absolute ethanol, the ethanol solution was filtered to remove inorganic salts, and the filtrate was evaporated to dryness under reduced pressure. To the residue was added 0.5 g. of anhydrous sodium acetate and 10 ml. of acetic anhydride. The mixture was heated at 140° for 1 hr. and was then poured onto ice. The mixture was extracted with chloroform and the chloroform extract was washed successively with water, saturated aqueous sodium bicarbonate solution, and water, dried, and evaporated to a sirup. The residue was crystallized and recrystallized from absolute ether–hexane, yield 334 mg. (72%), m.p. and m.m.p. 101–103°, $[\alpha]^{23}D$ +131° (*c* 1.0, chloroform). The product was thus identified as methyl tetra-*O*-acetyl-α-D-glucopyranoside.

β-Isomaltose Octaacetate (XII) and β-Gentiobiose Octaacetate (XI) from 3,4,6-Tri-*O*-acetyl-2-*O*-(*p*-tolylsulfonyl)-β-D-glucosyl Chloride (IVa) and 1,2,3,4-Tetra-*O*-acetyl-β-D-glucopyranose (IX).—A mixture of 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose (IX,[15] 3.0 g.), 2 g. of silver carbonate,[3] 100 mg. of silver perchlorate,[14] 3 g. of pulverized Drierite,[13] and 80 ml. of chloroform (ethanol free) was stirred at room temperature for 10 min. after which 950 mg. of 3,4,6-tri-*O*-acetyl-2-*O*-(*p*-tolylsulfonyl)-β-D-glucosyl chloride (IVa) was added. The mixture was stirred at room temperature for 24 hr. in the absence of light, after which time the inorganic salts were removed by filtration and washed with chloroform. The combined filtrate and washings were evaporated to a sirup under reduced pressure, and the residue was acetylated with 30 ml. of acetic anhydride and 3 g. of anhydrous sodium acetate at 140° for 1 hr. The cooled reaction mixture was poured into an excess of iced water, stirred for 2 hr., and extracted with chloroform. The extract was washed successively with water, saturated aqueous sodium bicarbonate solution, and water, dried (magnesium sulfate), and evaporated to a sirup.

The above sirupy residue was dissolved in 20 ml. of benzene and the solution was added to the top of a 37 × 7.5 cm. column of Magnesol[16]–Celite (5:1 by wt.). The chromatogram was developed successively with 3 l. of *t*-butyl alcohol–benzene (1:99 v./v.) and 2 l. of *t*-butyl alcohol–benzene (5:95 v./v.). Extrusion and indication by the alkaline permanganate streak[16] located two zones (A and B) which were excised and eluted with acetone. The eluate from the faster moving zone A contained sulfur but failed to crystallize, yield 450 mg. The material was dissolved in 30 ml. of ethanol and treated at room temperature for 16 hr. with 27 p.s.i. of hydrogen and 5 g. of freshly prepared Raney nickel catalyst.[17] The catalyst was removed by filtration and washed with ethanol. The combined filtrate and washings were concentrated to a sulfur-free sirup which was acetylated at 140° for 1 hr. with 10 ml. of acetic anhydride and 0.5 g. of anhydrous sodium acetate. The cooled reaction mixture was poured into iced water and after 2 hr. the mixture was extracted with chloroform. The chloroform extract was washed successively with water, saturated aqueous sodium bicarbonate solution, and water, dried, and concentrated to a sirup. The sirup was crystallized from 2 ml. of ethanol, yielding 125 mg. (9.2%) of β-isomaltose octaacetate, m.p. 143–145°. Recrystallization from ethanol gave pure material, m.p. 144–146°, $[\alpha]^{21}D$ +95° (*c* 1.0, chloroform).

The eluate (350 mg.) from the slower moving zone B yielded crystalline material that was sulfur free and was identified as β-gentiobiose octaacetate, yield 80 mg. (6.1%), m.p. and m.m.p. 192–193°, $[\alpha]^{22}D$ −7.5° (*c* 1.07, chloroform), identical with authentic β-gentiobiose octaacetate by X-ray powder diffraction data[12] and comparative infrared spectra.

β-D-Glucopyranose pentaacetate was isolated from the column effluent, yield 1.8 g.

β-Gentiobiose Octaacetate (XI) from 3,4,6-Tri-*O*-acetyl-2-*O*-(*p*-tolylsulfonyl)-β-D-glucosyl Chloride (IVa) and 1,2,3,4-Tetra-*O*-acetyl-β-D-glucopyranose (IX) by Catalysis with Mercuric Salts. *O*-[3,4,6-Tri-*O*-acetyl-2-*O*-(*p*-tolylsulfonyl)-β-D-glucosyl]-(1→6)-tetra-*O*-acetyl-β-D-glucopyranose (XIII).—To a solution of 0.29 g. of mercuric cyanide, 0.37 g. of mercuric bromide, and 3.0 g. of 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose[15] (IX) in 30 ml. of acetonitrile (purified by treatment with solid sodium carbonate and distillation over phosphorus pentaoxide) was added 1.0 g. of 3,4,6-tri-*O*-acetyl-2-*O*-(*p*-tolylsulfonyl)-β-D-glucosyl chloride (IVa). The clear solution was stirred at room temperature (hood) for 24 hr. and then the solvent was removed

(12) Interplanar spacing, Å., Cu Kα radiation. Relative intensity, estimated visually: s, strong; m, medium; w, weak; v, very. Strongest lines are numbered (1, strongest); double numbers indicate approximately equal intensities.

(13) Anhydrous calcium sulfate as soluble anhydrite: W. A. Hammond Drierite Co., Xenia, Ohio.

(14) H. Bredereck, A. Wagner, G. Faber, H. Ott, and J. Rauther, *Ber.*, **92**, 1135 (1959).

(15) A. Thompson, M. L. Wolfrom, and M. Inatome, *J. Am. Chem. Soc.* **77**, 3160 (1955).

(16) M. L. Wolfrom, R. M. de Lederkremer, and L. E. Anderson, *Anal. Chem.*, **35**, 1357 (1963).

(17) R. Mozingo, *Org. Syn.*, **21**, 15 (1941).

under reduced pressure below 30°. The residue was extracted with chloroform and the extract was washed five times with 1 *M* potassium bromide, dried (magnesium sulfate), and concentrated to a sirup. The residue was acetylated with 30 ml. of acetic anhydride and 3 g. of anhydrous sodium acetate at 140° for 1 hr. and the sirupy product was isolated as described above. The product was dissolved in 20 ml. of benzene and chromatographed on a column of Magnesol–Celite as described above. Two zones were located, excised, and eluted with acetone.

The eluate (206 mg.) from the slower moving band was crystallized and recrystallized from ethanol to give needles identified as β-gentiobiose octaacetate, yield 60 mg. (4.6%), m.p. and m.m.p. 192–193°.

The eluate (334 mg.) from the faster moving band was crystallized as needles from absolute ether, yield 160 mg. (12.2%). Recrystallization from chloroform–ether gave pure *O*-[3,4,6-tri-*O*-acetyl-2-*O*-(*p*-tolylsulfonyl)-β-D-glucosyl]-(1→6)-tetra-*O*-acetyl-β-D-glucopyranose, yield 93 mg. (5.64%), m.p. 139–141°, $[\alpha]^{21}D$ + 8° (*c* 1.0, chloroform).

Anal. Calcd. for $C_{33}H_{42}O_{20}S$: C, 50.12; H, 5.35; S, 4.06. Found: C, 49.82; H, 5.39; S, 4.13.

A 36-mg. portion of the above crystalline material was desulfurized with Raney nickel and hydrogen and acetylated with acetic anhydride and sodium acetate as described above and the product, isolated in the same manner, was crystallized and recrystallized from ethanol to give β-gentiobiose octaacetate, yield 24.2 mg. (78.3%), m.p. and m.m.p. 192–193°.

1,3,4,6-Tetra-*O*-acetyl-2-*O*-(methylsulfonyl)-β-D-glucose (IIb).—The sirupy 3,4,6-tri-*O*-acetyl-2-*O*-(methylsulfonyl)-α-D-glucosyl bromide (Ib), prepared from 33 g. of 1,3,4,6-tetra-*O*-acetyl-α-D-glucose according to Helferich and Zirner,[11] was treated with mercuric acetate in acetic acid as described above for the analogous *p*-toluenesulfonate except that the reaction was maintained at room temperature. The product was isolated in the same manner and was recrystallized as fine needles from chloroform–ethanol: yield 32.6 g.; m.p. 153.5–154.5° with sintering at 146–147°; $[\alpha]^{21}D$ +19° (*c* 1.05, chloroform); X-ray powder diffraction data[12] 9.30 (m), 8.36 (vs, 1), 6.03 (s), 5.40 (m), 5.12 (s), 4.66 (vs, 2), 4.39 (vs, 2), 4.10 (vs, 2), 3.77 (s), 3.40 (m), 3.14 (m).

Anal. Calcd. for $C_{15}H_{22}O_{12}S$: C, 42.25; H, 5.20; S, 7.52. Found: C, 42.69; H, 5.30; S, 7.59.

Ethyl Tri-*O*-acetyl-2-*O*-methylsulfonyl-1-thio-α-D-glucoside (IIIb).—This substance was synthesized from 26 g. of 1,3,4,6-tetra-*O*-acetyl-2-*O*-(methylsulfonyl-)β-D-glucose (IIb) as described above for the analogous *p*-toluenesulfonate by treatment with ethanethiol and boron trifluoride etherate except that the reaction mixture was maintained at room temperature for 24 hr. The sirupy product was isolated in the same manner and was chromatographed on 600 g. of alumina (Woelm, grade I). The eluate obtained on elution with 2 l. of benzene was discarded but that obtained on elution with 5 l. of chloroform was concentrated to small volume and was crystallized by the addition of ethanol, yield 4.2 g. (16%), m.p. 106–108°. Pure material was obtained on recrystallization from chloroform–ether: m.p. 112–113°; $[\alpha]^{25}D$ +168° (*c* 2.53, chloroform); X-ray powder diffraction data[12] 8.42 (m), 7.31 (s, 3), 6.05 (s, 2), 5.05 (w), 4.47 (s, 3), 4.27 (m), 3.79 (vs, 1), 3.40 (m), 3.29 (m), 2.78 (m), 2.36 (m).

Anal. Calcd. for $C_{15}H_{24}O_{10}S_2$: C, 42.05; H, 5.65; S, 14.97. Found: C, 42.53; H, 5.84; S, 14.48.

3,4,6-Tri-*O*-acetyl-2-*O*-(methylsulfonyl)-β-D-glucosyl Chloride (IVb).—Ethyl 3,4,6-tri-*O*-acetyl-2-*O*-(methylsulfonyl)-1-thio-α-D-glucoside (IIIb, 1.58 g.) was dissolved in 20 ml. of chloroform and 20 ml. of absolute ether and a stream of dried (sulfuric acid wash bottle) chlorine was passed in for 15 min. at 0° whereupon a crystalline precipitate appeared. The stream of chlorine gas was maintained for a further 20 min. The precipitate was filtered and washed with absolute ether, yield 1.27 g. (86%). Recrystallization from absolute ether gave pure material: m.p. 144–146°; $[\alpha]^{18}D$ +14° (*c* 1, chloroform); X-ray powder diffraction data[12] 8.99 (m), 7.60 (s, 2), 6.81 (w), 6.10 (w), 5.12 (m), 4.80 (w), 4.29 (vs, 1), 3.84 (w), 3.61 (s, 3), 3.32 (w).

Anal. Calcd. for $C_{13}H_{19}ClO_{10}S$: C, 38.76; H, 4.75; Cl, 8.80; S, 7.96. Found: C, 39.01; H, 4.91; Cl, 8.98; S, 7.99.

β-Gentiobiose Octaacetate from 3,4,6-Tri-*O*-acetyl-2-*O*-(methylsulfonyl)-β-D-glucosyl Chloride (IVb) and 1,2,3,4-Tetra-*O*-acetyl-β-D-glucopyranose (IX).—3,4,6-Tri-*O*-acetyl-2-*O*-(methylsulfonyl)-β-D-glucosyl chloride (IVb, 1 g.) was brought into reaction with 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose (IX) as described above for the analogous *p*-toluenesulfonate except that the solvent was a mixture of 60 ml. of tetrahydrofuran and 40 ml. of anhydrous ether and the reaction time was 88 hr. The resultant reaction mixture was isolated as a sirup in the same manner and was dissolved in 20 ml. of benzene, and the solution was added to the top of a 25 × 7.5 cm. column of Magnesol[16]–Celite (5:1 by wt.). The chromatogram was developed successively with 2 l. each of *t*-butyl alcohol–benzene (3:97, 5:95 7:93, and 10:90 v./v.). Extrusion and indication by the alkaline permanganate streak[16] located a zone 8–17 cm. from the column top. The column was sectioned into three equal parts and each was eluted with acetone. The eluates from the column development and from each of the acetone elutions were isolated by solvent removal and rechromatographed on silica gel thin layer plates using benzene–ethyl acetate (6:4 v./v.) as developer with indication by anthrone–sulfuric acid. The zone materials so obtained were acetylated with acetic anhydride and anhydrous sodium acetate at 140° and rechromatographed as above on silica gel. In this manner there was obtained β-gentiobiose octaacetate, yield 220 mg. (13%), identified by melting point and mixture melting point (193–194°), $[\alpha]^{21}D$ −5° (*c* 2.1, chloroform), and comparative infrared spectra

The zone materials containing sulfur were combined and the sirup obtained on solvent removal was dissolved in 80% methanol and 20 g. of 2% sodium amalgam was added to the solution in small portions with stirring and cooling. After 20 hr. the solution was separated from the mercury by filtration and the filtrate was evaporated to dryness under reduced pressure. The residue was acetylated for 1 hr. at 140° with 30 ml. of acetic anhydride and 2 g. of anhydrous sodium acetate. The product obtained on pouring the cooled reaction mixture into water was chromatographed on Magnesol–Celite as described above for the analogous reaction with the 2-(*p*-toluenesulfonate), but the fractions obtained were not all sulfur free and none of them crystallized.

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