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The Preparation of Crystalline 2-*O*-Methylsulfonyl-D-arabinose and Some of Its Derivatives

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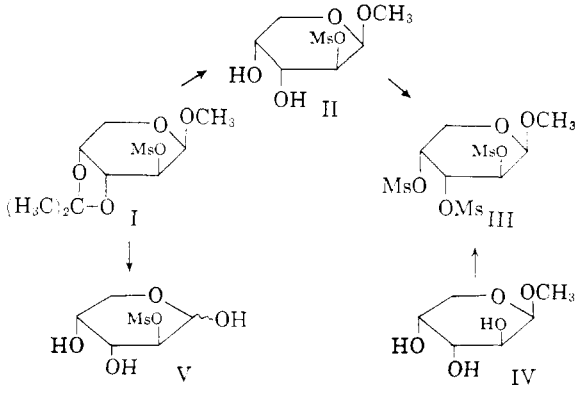
2-*O*-Methylsulfonyl-D-arabinose has been obtained through the hydrolysis of methyl 3,4-*O*-isopropylidene-2-*O*-methylsulfonyl-β-D-arabinoside, from the hydrogenolysis of benzyl 2-*O*-methylsulfonyl-β-D-arabinopyranoside and from the hydrolysis of 4-*O*-formyl-2-*O*-methylsulfonyl-D-arabinose. Its structure has been confirmed through conversion to the previously known 1,3,5-tri-*O*-benzoyl-2-*O*-methylsulfonyl-β-D-arabinose. Benzoylation of 2-*O*-methylsulfonyl-D-arabinose gives the two anomeric 1,3,4-tri-*O*-benzoyl-2-*O*-methylsulfonyl-D-arabinoses. The β-anomer was converted to 3,4-di-*O*-benzoyl-2-*O*-methylsulfonyl-β-D-arabinosyl bromide. With silver benzoate this halide afforded 1,3,4-tri-*O*-benzoyl-2-*O*-methylsulfonyl-α-D-arabinose; with methanol it gave methyl 3,4-di-*O*-benzoyl-2-*O*-methylsulfonyl-α-D-arabinoside. Various derivatives related to these substances have been synthesized and characterized.

Recent communications from this Laboratory have described 1,3,5-tri-*O*-benzoyl-2-*O*-methylsulfonyl-α-D-ribose[1] and 1,3,5-tri-*O*-benzoyl-2-*O*-methylsulfonyl-β-D-arabinose[2] while closely related compounds such as 2-*O*-*p*-tolylsulfonyl-D-xylose,[3] 2-*O*-methylsulfonyl-D-arabinose[3,4] and 4-*O*-formyl-2-*O*-methylsulfonyl-D-arabinose[5] have been reported by other workers. These 2-*O*-sulfonylaldose esters having actual or potential hydroxyl groups at C1 show marked lability toward sodium methoxide, giving readily that methyl glycoside of the epimeric sugar wherein the hydroxyl group at C2 is *trans* to the methoxyl group at C1.[1,2,5] Likewise, cautious treatment with aqueous alkali converts them directly to the epimeric sugar.[3] In order to study further the chemical behavior of this interesting class of sulfonyl esters we turned our attention to the preparation of 2-*O*-methylsulfonyl-D-arabinose.

Overend and Stacey[4] treated both methyl 3,4-*O*-isopropylidene-2-*O*-methylsulfonyl-β-D-arabinoside (I) and methyl 2-*O*-methylsulfonyl-β-D-arabinopyranoside (II) with boiling *N* sulfuric acid for four hours to obtain a crystalline product which they described as 2-*O*-methylsulfonyl-D-arabinose (V) solvated with one-half mole of water and one-half mole of alcohol. The substance reduced Fehling solution in the cold and mutarotated in 5:1 chloroform–ethanol. We have now repeated this hydrolysis, using methyl 3,4-*O*-isopropylidene-2-*O*-methylsulfonyl-β-D-arabinoside (I), and obtained a product with the same elementary analysis as that reported by Overend and Stacey.[4] Our substance reduced Fehling solution when heated, but its physical constants differed from those reported by the earlier authors. Moreover the substance did not mutarotate and consumed only one molar equivalent of sodium metaperiodate. Actually, as the periodate oxidation suggests, the material was the monohydrate of methyl 2-*O*-methylsulfonyl-β-D-arabinoside (II); further mesylation afforded methyl 2,3,4-tri-*O*-methylsulfonyl-β-D-arabinoside (III) identical with a sample prepared directly from methyl β-D-arabinopyranoside (IV). It may be noted, in passing, that sulfonyl esters having accessible neighboring hydroxyl groups normally give a positive Fehling test.[6]



Jones and Nicholson[3] hydrolyzed methyl-3,4-*O*-isopropylidene-2-*O*-methylsulfonyl-β-D-arabinoside (I) under more drastic conditions—boiling 2 *N* sulfuric acid for twenty-four hours. They obtained a sirup which was chromatographically homogeneous and rotated $[\alpha]^{24}D$ −85° in water (*c* 4.4). After the successful preparations of crystalline 2-*O*-methylsulfonyl-D-arabinose from other sources as described later in this paper, we repeated the procedure of Jones and Nicholson[3] and obtained, after seeding, 2-*O*-methylsulfonyl-D-arabinose (V) in 8% yield. It was apparent that the strong acid and high temperature employed in this procedure had caused extensive destruction of the sugar. It may be noted in passing that a sulfonyloxy group at C2 in an aldoside greatly stabilizes the glycoside.

Crystalline 2-*O*-methanesulfonyl-D-arabinose was first obtained by us through the following sequence of reactions which also provide the best means of preparing this substance. Benzyl 3,4-*O*-isopropylidene-β-D-arabinoside[7] (VI) was converted to its methanesulfonate VII which was hydrolyzed to benzyl 2-*O*-methylsulfonyl-β-D-arabinopyranoside (VIII). Hydrogenolysis of this latter compound in the presence of palladium readily afforded 2-*O*-methylsulfonyl-D-arabinose (V) in high yield. On standing, the sirupy product crystallized and thereafter was purified easily by recrystallization from any of a variety of solvents. The form which

(1) R. K. Ness and H. G. Fletcher, Jr., THIS JOURNAL, **78**, 4710 (1956).

(2) R. K. Ness and H. G. Fletcher, Jr., *ibid.*, **80**, 2007 (1958).

(3) J. K. N. Jones and W. H. Nicholson, *J. Chem. Soc.*, 3050 (1955).

(4) W. G. Overend and M. Stacey, *ibid.*, 1235 (1949).

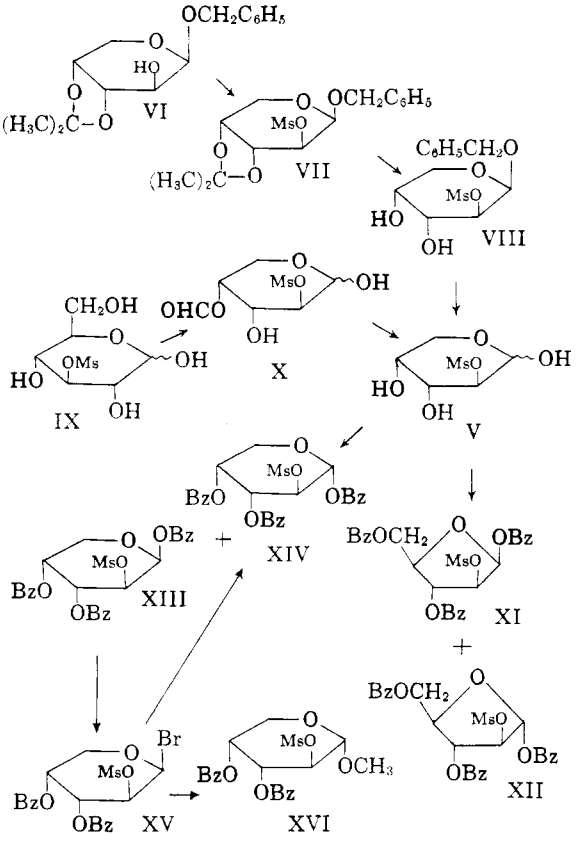
(5) D. C. C. Smith, *ibid.*, 2690 (1957).

(6) In general, the majority of halogen-free sulfonic acid esters which we have tested give a positive Beilstein test also.

(7) C. E. Ballou, THIS JOURNAL, **79**, 165 (1957).

we obtained was solvent free and rotated $[\alpha]^{20}D$ $-88.0°$ in water (c 1.35); quite evidently this is the substance that Jones and Nicholson[3] had in hand and, as mentioned above, repetition of their procedure, indeed, gave the same product, albeit in low yield.

While this work was in progress, Smith[5] described some reactions of 4-O-formyl-2-O-methylsulfonyl-D-arabinose (X). This substance, which had been prepared from 3-O-methylsulfonyl-D-glucose[8] (IX) through the action of one molar equivalent of sodium metaperiodate,[9] had been partially hydrolyzed by this author[9] to yield amorphous 2-O-methylsulfonyl-D-arabinose (V). Repetition of this procedure in our hands gave, after seeding, crystalline V, identical with that obtained from benzyl 2-O-methylsulfonyl-β-D-arabinopyranoside (VIII).



The structure of 2-O-methylsulfonyl-D-arabinose was further confirmed in another fashion. On treatment at 50° for about twelve hours with methanol containing 4% of hydrogen chloride it gave an amorphous mixture which was benzoylated and then treated with hydrogen bromide in glacial acetic acid. Condensation of the amorphous product with silver benzoate afforded two tri-O-benzoyl-2-O-methylsulfonyl-D-arabinoses. One of these proved to be identical with the 1,3,5-tri-O-benzoyl-2-O-methylsulfonyl-β-D-arabinose (XI) which has recently been described[2]; the other is most probably its anomer XII. It appears probable, therefore, that the treatment of 2-O-methylsulfonyl-D-arabinose (V) with methanolic hydrogen chloride affords considerable quantities of the methyl 2-O-methylsulfonyl-D-arabinofuranosides. Such a high temperature and high acid concentration normally convert unsubstituted aldoses almost quantitatively to the corresponding methyl glycopyranosides; the abnormal behavior of 2-O-methylsulfonyl-D-arabinose (V) in this respect may be assumed to arise from the influence of the mesyl group at C2.[10]

Benzoylation of 2-O-methylsulfonyl-D-arabinose (V) in pyridine at a low temperature led to the isolation of the two anomeric 1,3,4-tri-O-benzoyl-2-O-methylsulfonyl-D-arabinoses.[11] Treatment of the β (more levorotatory) isomer XIII with hydrogen bromide in glacial acetic acid afforded a crystalline halide; in view of the strong levorotation of this substance ($[\alpha]^{20}D$ $-351°$ in methylene chloride) it may tentatively be assigned structure XV, 3,4-di-O-benzoyl-2-O-methylsulfonyl-β-D-arabinosyl bromide. Treatment of the halide with silver benzoate gave XIV indicating that XIII and XIV are anomers.

Methanolysis of 3,4-di-O-benzoyl-2-O-methylsulfonyl-β-D-arabinosyl bromide (XV) gave a crystalline methyl 3,4-di-O-benzoyl-2-O-methylsulfonyl-D-arabinoside which was shown to be the α-anomer XVI in the following fashion. Methyl α-D-arabinopyranoside (XVII) was condensed with acetone to give the 3,4-O-isopropylidene derivative XVIII which was then converted to the 2-O-methanesulfonate XIX and hydrolyzed to methyl 2-O-methylsulfonyl-α-D-arabinopyranoside (XX). This substance, whose structure was confirmed through the fact that it consumed one mole of periodate, gave, on benzoylation, methyl 3,4-di-O-benzoyl-2-O-methylsulfonyl-α-D-arabinoside (XVI), identical with the product from the methanolysis of the bromide XV. That no change in anomeric configuration had taken place in going from methyl α-D-arabinopyranoside (XVII) to its 2-O-methylsulfonyl ester XX was shown through the mesylation of these two substances, the same methyl 2,3,4-tri-O-methylsulfonyl-α-D-arabinoside (XXI) being obtained from each. Although previously described by Overend and Stacey,[4] we report here the preparation and characterization of compounds XVIII to XXI since the physical constants which we have found for these substances differ markedly from those reported by the earlier authors.

The preparation and properties of methyl 3,4-O-isopropylidene-2-O-methylsulfonyl-β-D-arabinoside (I), methyl 2-O-methylsulfonyl-β-D-arabinopyranoside (II), methyl 2,3,5-tri-O-methylsulfonyl-α-D-arabinoside and methyl 2,3,4-tri-O-methylsulfonyl-β-D-arabinoside (III) are described, the last-named compound being prepared both from

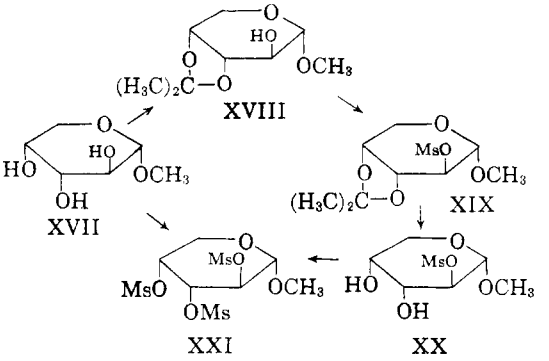
(8) B. Helferich, H. Dressler and R. Griebel, *J. prakt. Chem.*, **153**, 285 (1939).

(9) D. C. C. Smith, Ph.D. Thesis, Manchester, 1952. We are much indebted to Dr. Smith for providing us with details of his preparation of 4-O-formyl-2-O-methylsulfonyl-D-arabinose and of amorphous 2-O-methylsulfonyl-D-arabinose therefrom.

(10) Chromatography of the benzoylated mixture of methyl 2-O-methylsulfonyl-D-arabinosides obtained from 2-O-methylsulfonyl-D-arabinose failed to yield methyl 3,4-di-O-benzoyl-2-O-methylsulfonyl-β-D-arabinoside although this substance crystallizes with great ease.

(11) 2-O-Methylsulfonyl-D-arabinose was not observed to mutarotate in aqueous solution. Possibly the influence of the methanesulfonyl greatly slows mutarotation or, as the benzoylation data suggest, the substance may be a molecular compound of the two anomeric pyranose forms, having a composition close to the equilibrium mixture.

methyl β-D-arabinopyranoside (IV) and its 2-methanesulfonate II.



Further properties of 2-*O*-methylsulfonyl-D-arabinose are being investigated and will be described in a future paper.

Experimental[12]

Benzyl 2-*O*-Methylsulfonyl-β-D-arabinopyranoside (VIII).—Benzyl 3,4-*O*-isopropylidene-β-D-arabinoside (VI, 7.5 g.), prepared according to Ballou[7] was added with stirring to a mixture which had been made from 25 ml. of dry pyridine and 2.75 ml. of methanesulfonyl chloride precooled to 10°. After 2 hr. at room temperature the excess methanesulfonyl chloride was decomposed by the addition of a little water. An excess of water was then added and the product extracted with methylene chloride. The extract was washed successively with cold 3 *N* sulfuric acid and aqueous sodium bicarbonate; moisture was removed with sodium sulfate and the solvent evaporated *in vacuo*. The residual sirup (10 g.), diluted with 15 ml. of acetone and 150 ml. of *N* sulfuric acid, was refluxed for 3 hr., most of the acetone escaping in the process. The product, benzyl 2-*O*-methylsulfonyl-β-D-arabinoside (VIII), crystallized on cooling and was removed by filtration: 7.1 g. (84%). Recrystallized once from 3:1 methanol-water and then twice from water alone, the pure material melted at 129–130° and showed $[\alpha]^{20}D$ −189.5° in 5:1 chloroform–ethanol (*c* 3.2).

Anal. Calcd. for $C_{13}H_{18}O_7S$: C, 49.05; H, 5.70. Found: C, 48.88; H, 5.70,

A sample (447 mg.) of the product was found to consume 1.1 molar equivalents of sodium metaperiodate within 2 hr.; no further consumption of periodate was observed after 4.5 hr.

2-*O*-Methylsulfonyl-D-arabinose (V) from Benzyl 2-*O*-Methylsulfonyl-β-D-arabinopyranoside (VIII).—Five grams of commercial palladium black was suspended in 150 ml. of absolute ethanol and saturated with hydrogen at room temperature and slightly elevated pressure. Benzyl 2-*O*-methylsulfonyl-β-D-arabinopyranoside (15 g.) was then added and the suspension shaken with hydrogen until absorption of the gas ceased (2 hr.). Removal of the catalyst and concentration *in vacuo* at 40° (bath) afforded a sirup which crystallized spontaneously. From a mixture of 25 ml. of warm ethanol and 10 ml. of pentane the product crystallized as needles (8.4 g.) melting at 113–114°. A second crop of 0.5 g. raised the total yield to 8.9 g. (83%). In another run a yield of 96% was obtained. Two recrystallizations from ethanol–pentane afforded pure 2-*O*-methylsulfonyl-D-arabinose melting at 118–119° and showing $[\alpha]^{20}D$ −80° (5:1 $CHCl_3$–EtOH, *c* 0.47), $[\alpha]^{20}D$ −87.0° (MeOH, *c* 0.5) and $[\alpha]^{20}D$ −88.0° (H_2O, *c* 1.35, no mutarotation in 2 days).

Anal. Calcd. for $C_6H_{12}O_7S$: C, 31.57; H, 5.30; S, 14.05. Found: C, 31.72; H, 5.36; S, 14.01.

The infrared spectrum of the pure ester showed no aromatic absorption. When chromatographed on paper for 20 hr. using a propanol–water system (89:28 v./v.) only one spot, pink in color, was observed after spraying with aniline hydrogen phthalate and heating. The substance is stable in anhydrous pyridine at room temperature, being recovered unchanged after two hours in solution in this solvent. It appears to be unaffected by Fehling solution at room temperature, but is rapidly oxidized by this reagent when heated.

2-*O*-Methylsulfonyl-D-arabinose (V) from 3-*O*-Methylsulfonyl-D-glucose (IX) *via* 4-*O*-Formyl-2-*O*-methylsulfonyl-D-arabinose (X).—The method employed by Smith[9] was used with minor modifications. A solution of 6.0 g. of 3-*O*-methylsulfonyl-D-glucose[8] in 10 ml. of water was cooled in ice and a solution of 9.8 g. of sodium metaperiodate in 60 ml. of water added at such a rate that the temperature of the reaction mixture was maintained below 15°. The solution was then stirred for an hour, sodium iodate precipitating during this period, and then decanted into a stirred mixture of 4 l. of ether and 300 g. of anhydrous magnesium sulfate. The resulting mixture was stirred for 30 min. and then filtered. Concentration of the filtrate afforded crystalline 4-*O*-formyl-2-*O*-methylsulfonyl-D-arabinose (1.9 g., 32%).[13]

This product was dissolved in a mixture of 1 ml. of concentrated hydrochloric acid and 60 ml. of water. The solution was heated on the steam-bath for 30 min., cooled and deionized by passage through a column of Duolite A-4. Concentration *in vacuo* gave a sirup which was dissolved in 10 ml. of absolute ethanol and filtered. Solvent was again removed *in vacuo* to give a thin sirup which on seeding and cooling afforded 1.2 g. (23%, based on 3-*O*-methylsulfonyl-D-glucose) of 2-*O*-methylsulfonyl-D-arabinose which rotated $[\alpha]^{20}D$ −87.7° in water (*c* 0.5) and melted at 118–119° either alone or in admixture with the product obtained from benzyl 2-*O*-methylsulfonyl-β-D-arabinopyranoside.

1,3,5-Tri-*O*-benzoyl-2-*O*-methylsulfonyl-β-D-arabinose (XI) and 1,3,5-Tri-*O*-benzoyl-2-*O*-methylsulfonyl-α-D-arabinose (XII) from 2-*O*-Methylsulfonyl-D-arabinose (V).—Two grams of 2-*O*-methylsulfonyl-D-arabinose was dissolved in 100 g. of 4% (w./w.) methanolic hydrogen chloride and the rotation of the resulting solution observed in an all-glass polarimeter tube held at 49.0 ± 0.5°. After dropping relatively sharply[14] the rotation rose after 700 min. to a constant value.[15] Dry silver carbonate (30 g.) was added and the reaction mixture stirred until neutral to litmus. After filtration, the clear, colorless solution was concentrated *in vacuo* to a sirup (2.2 g.) which was benzoylated in the usual manner with benzoyl chloride in pyridine. Excess reactants were removed to give a sirup which was dissolved in 10 ml. of glacial acetic acid. Hydrogen bromide in glacial acetic acid (32% w./w.) was added and the solution observed polarimetrically. After *ca.* 45 hr. the rotation had attained a maximum and the solution was then diluted with methylene chloride, extracted several times with cold water and once with cold aqueous sodium bicarbonate. Moisture was removed with sodium sulfate and the solution concentrated *in vacuo* to a volume of approximately 25 ml. Three grams of silver benzoate then was added and the suspension stirred for 3 hr. After filtration through a mixture of decolorizing carbon and Super-Cel the solution was concentrated to a sirup which was dissolved in 25 ml. of hot methanol to yield 0.63 g. of crystalline product melting at 154–155° after sintering at 148°. Mixed with 1,3,5-tri-*O*-benzoyl-2-*O*-methylsulfonyl-β-D-arabinose (XI), prepared as described by Ness and Fletcher,[2] it melted at 153.5–154° after sintering at 147°. The ester showed $[\alpha]^{20}D$ −43.0° in chloroform (*c* 1.14); Ness and Fletcher[2] reported $[\alpha]^{20}D$ −41.0° in chloroform (*c* 1.28).

Anal. Calcd. for $C_{27}H_{24}O_{10}S$: C, 59.99; H, 4.48. Found: C, 59.87; H, 4.64.

The original mother liquor was concentrated to a sirup, dissolved in ether and adsorbed on a column (22 × 178 mm.) of neutralized, activated alumina. Elution with ethyl acetate afforded 0.54 g. (11%) of crystalline material melting at 130–135°. Two recrystallizations from absolute ethanol gave pure 1,3,5-tri-*O*-benzoyl-2-*O*-methylsulfonyl-α-D-ara-

(12) All melting points are corrected.

(13) In one run a sample of this material was recrystallized from ethyl acetate–methanol and found to melt at 142–144°. Smith[9] reported the same m.p. He also found $[\alpha]^{25}D$ −78.2° (10 min.) → −82.2° (35 min. and final value, *c* 4.27 in water) and reported C, 32.9; H, 4.6; S, 12.2. Calcd. for $C_7H_{12}O_8S$: C, 32.80; H, 4.72; S, 12.51.

(14) A run halted at this minimum and worked up as described here yielded only amorphous materials.

(15) Actually this point represented the beginning of a very broad peak in the mutarotation curve; eventually the rotation began to decrease slowly. A run worked up somewhat beyond the broad peak (2800 min.) yielded crystalline 1,3,5-tri-*O*-benzoyl-2-*O*-methylsulfonyl-β-D-arabinose, however.

binose (XII) melting at 135–136° and rotating $[\alpha]^{20}D$ +64.5° in chloroform (*c* 0.42).

Anal. Calcd. for $C_{27}H_{24}O_{10}S$: C, 59.99; H, 4.48. Found: C, 59.88; H, 4.66.

Further elution of the alumina gave 0.28 g. of the β-isomer, raising the total yield of this product to 19%.

1,3,4-Tri-*O*-benzoyl-2-*O*-methylsulfonyl-β-D-arabinose (XIII) and 1,3,4-Tri-*O*-benzoyl-2-*O*-methylsulfonyl-α-D-arabinose (XIV).—A mixture of 20 ml. of dry pyridine and 3.28 ml. of benzoyl chloride was cooled to 0° and 2.0 g. of 2-*O*-methylsulfonyl-D-arabinose added. The resulting solution was kept at 0° for 2 hr. and then at +5° overnight. A few drops of water then was added and, after being held for 15 min. at room temperature, the mixture was diluted with more water and extracted with methylene chloride. The combined extracts were washed successively with cold 1 *N* sulfuric acid, aqueous sodium bicarbonate and water. Moisture was removed with sodium sulfate, the solution filtered through a bed of decolorizing carbon and concentrated *in vacuo* (40° bath) to a sirup. From its solution in 20 ml. of methanol this material yielded 3.2 g. of crystalline product melting at 165–180°. Recrystallization from ethyl acetate–pentane afforded 1.8 g. of pure **1,3,4-tri-*O*-benzoyl-2-*O*-methylsulfonyl-β-D-arabinose** (XIII), melting at 196–197°, and rotating $[\alpha]^{20}D$ −238° in chloroform (*c* 0.91).

Anal. Calcd. for $C_{27}H_{24}O_{10}S$: C, 59.99; H, 4.48. Found: C, 59.84; H, 4.64.

The methanolic mother liquor from the above preparation was concentrated to dryness and heated with 10 ml. of methanol. A portion which did not dissolve (0.27 g., m.p. 193–194°) was filtered off; on cooling, the filtrate deposited 1.0 g. of crystalline material. This was warmed with 6 ml. of methanol, an insoluble fraction (0.30 g., m.p. 196–197°) removed, and the filtrate cooled to yield 0.6 g. (13%) of crystalline material melting at 121–122°. A fraction (0.5 g.) having the same m.p. also was obtained on concentration of the original mother liquor. Further recrystallization from methanol failed to change this value. The pure **1,3,4-tri-*O*-benzoyl-2-*O*-methylsulfonyl-α-D-arabinose (XIV)** showed $[\alpha]^{20}D$ −127° in chloroform (*c* 0.92).

Anal. Calcd. for $C_{27}H_{24}O_{10}S$: C, 59.99; H, 4.48. Found: C, 59.81; H, 4.65.

3,4-Di-*O*-benzoyl-2-*O*-methylsulfonyl-β-D-arabinosyl Bromide (XV) from 1,3,4-Tri-*O*-benzoyl-2-*O*-methylsulfonyl-β-D-arabinose (XIII).—To a solution of 0.5 g. of 1,3,4-tri-*O*-benzoyl-2-*O*-methylsulfonyl-β-D-arabinose in a mixture of 6.0 ml. of methylene chloride and 3 ml. of glacial acetic acid was added 1 ml. of glacial acetic acid–hydrogen bromide (32% HBr, w./w.) and the rotation of the resulting solution observed in an all-glass, 1-dm. polarimeter tube at 20°. The observed rotation, −10.17° (after 1 min.), rose to a maximum of −8.55° (6 min.) and then fell to a final, constant value of −14.50° (110 min.). The clear, slightly yellow solution was diluted with 30 ml. of methylene chloride and extracted successively with ice-cold water and cold aqueous sodium bicarbonate. After drying with sodium sulfate the solution was filtered through a thin layer of decolorizing carbon and concentrated *in vacuo* to a sirup. From its solution in a mixture of 6 ml. of ether and 4 ml. of pentane at −5° this material deposited 0.40 g. (87%) of crystalline product melting at 130–131°. A single recrystallization from ether gave the pure halide melting at 130.5–131.2° and rotating $[\alpha]^{20}D$ −351° in methylene chloride (*c* 0.70).

Anal. Calcd. for $C_{20}H_{19}O_8BrS$: C, 48.10; H, 3.84; Br, 16.01. Found: C, 48.17; H, 4.08; Br, 15.75.

1,3,4-Tri-*O*-benzoyl-2-*O*-methylsulfonyl-α-D-arabinose (XIV) from 3,4-Di-*O*-benzoyl-2-*O*-methylsulfonyl-β-D-arabinosyl Bromide (XV).—To a solution of 0.37 g. of 3,4-di-*O*-benzoyl-2-*O*-methylsulfonyl-β-D-arabinosyl bromide in 15 ml. of methylene chloride was added 2.0 g. of silver benzoate and the resulting suspension stirred for 2 hr. After filtration through a bed of decolorizing carbon the solution was concentrated to a sirup which was dissolved in warm methanol to give 0.265 g. (66%) of crystalline product melting at 121–122°. Recrystallization from methanol failed to change this value. A mixed melting point with 1,3,4-tri-*O*-benzoyl-2-*O*-methylsulfonyl-α-D-arabinose, prepared by the benzoylation of 2-*O*-methylsulfonyl-D-arabinose, was undepressed.

Methyl 3,4-Di-*O*-benzoyl-2-*O*-methylsulfonyl-α-D-arabinoside (XVI) from 3,4-Di-*O*-benzoyl-2-*O*-methylsulfonyl-β-D-arabinosyl Bromide (XV).—3,4-Di-*O*-benzoyl-2-*O*-methylsulfonyl-β-D-arabinosyl bromide (295 mg.) was dissolved in 10 ml. of dioxane and the solution diluted with 90 ml. of methanol. After 22 hr. at 20° the reaction mixture had ceased to mutarotate. It was then concentrated *in vacuo* to a crystalline mass which was redissolved in 50 ml. of methanol and reconcentrated to a volume of *ca.* 25 ml. On cooling, 250 mg. (94%) of product melting at 168–169° was obtained. Recrystallization from a mixture of 6 ml. of ethanol and 6 ml. of pentane afforded pure methyl 3,4-di-*O*-benzoyl-2-*O*-methylsulfonyl-α-D-arabinoside as flat rods melting at 169.5–170.2° and rotating $[\alpha]^{20}D$ −167.3° in chloroform (*c* 0.50). Mixed with the corresponding product, obtained through the benzoylation of methyl 2-*O*-methylsulfonyl-α-D-arabinopyranoside as described later in this paper, the material melted at 169–170°.

Anal. Calcd. for $C_{21}H_{22}O_9S$: C, 55.99; H, 4.92. Found: C, 56.13; H, 4.82.

Methyl 3,4-*O*-Isopropylidene-α-D-arabinoside (XVIII).—Methyl α-D-arabinopyranoside[16] (6 g.) was mixed with 300 ml. of dry acetone, 18 g. of anhydrous cupric sulfate and 0.3 ml. of concentrated sulfuric acid and shaken for 19 hr. After filtration through a bed of Super-Cel the clear, pale, yellowish-green solution was neutralized by stirring with 100 g. of anhydrous potassium carbonate for 2 hr. Refiltered, the solution was concentrated *in vacuo* to a sirup which was diluted with 50 ml. of ethyl ether. Unreacted methyl α-D-arabinopyranoside (0.25 g., m.p. 129–130°) was removed and the solution reconcentrated to a sirup. From 15 ml. of hot isopropyl ether 4.5 g. (60%) of methyl 3,4-*O*-isopropylidene-α-D-arabinoside, melting at 68–72°, was obtained. Three recrystallizations from isopropyl ether afforded pure material melting at 73–74° and rotating $[\alpha]^{20}D$ −43.0° in water (*c* 0.6).

Anal. Calcd. for $C_9H_{16}O_5$: C, 52.93; H, 7.90. Found: C, 52.99; H, 7.83.

Methyl 3,4-*O*-Isopropylidene-2-*O*-methylsulfonyl-α-D-arabinoside (XIX).—One gram of methyl 3,4-*O*-isopropylidene-α-D-arabinoside was added to a cold solution of 0.3 ml. of methanesulfonyl chloride in 2 ml. of dry pyridine. The mixture was held at 5° for 15 min., at room temperature for 2 hr. and then diluted with water. The product was extracted with methylene chloride, washed successively with cold 1 *N* sulfuric acid and aqueous sodium bicarbonate and dried with sodium sulfate. The solution was then concentrated *in vacuo* to a semi-crystalline mass which, from its solution in 6 ml. of warm alcohol, gave, on cooling, 1.11 g. (80%) of product melting at 144–145°. Further recrystallization from ethanol failed to change this value. The pure methyl 3,4-*O*-isopropylidene-2-*O*-methylsulfonyl-α-D-arabinoside rotated $[\alpha]^{20}D$ −33.1° in chloroform (*c* 0.54).

Anal. Calcd. for $C_{10}H_{18}O_7S$: C, 42.54; H, 6.43. Found: C, 42.41; H, 6.28.

Methyl 2-*O*-Methylsulfonyl-α-D-arabinopyranoside (XX).—Methyl 3,4-*O*-isopropylidene-2-*O*-methylsulfonyl-α-D-arabinoside (700 mg.) was added to a mixture of 50 ml. of *N* sulfuric acid and 2 ml. of acetone and the solution refluxed for 2 hr. The cooled solution was then neutralized to litmus with barium carbonate, filtered through a layer of Super-Cel and concentrated *in vacuo* to a semi-crystalline mass. The crude product was dissolved in a hot mixture of 10 ml. of alcohol and 2 ml. of water and the solution concentrated to a volume of *ca.* 5 ml. Two crops of needle-shaped crystals (450 mg., 75%) were obtained; recrystallization from a mixture of 4 ml. of ethanol and 4 ml. of pentane afforded with little loss pure methyl 2-*O*-methylsulfonyl-α-D-arabinopy-

(16) H. G. Fletcher, Jr., and C. S. Hudson [THIS JOURNAL, **72**, 4173 (1950)] pointed out that the preparation of this compound through the action of methanolic hydrogen chloride on D-arabinose is exceedingly laborious and unsatisfactory and described an improved preparation involving 2,3,4-tri-*O*-acetyl-β-D-arabinosyl bromide. However, we are now of the opinion that the preparation of relatively large quantities of methyl α-D-arabinopyranoside is best carried out through the following sequence: D-arabinose → mixed anomeric D-arabinopyranose tetrabenzoates → 2,3,4-tri-*O*-benzoyl-β-D-arabinosyl bromide → methyl α-D-arabinopyranoside tribenzoate → methyl α-D-arabinopyranoside. In this sequence the halide is not isolated but allowed to react directly with methanol in the absence of an acid acceptor. The benzoylation of D-arabinose has been described by H. G. Fletcher, Jr., and C. S. Hudson [THIS JOURNAL, **69**, 1145 (1947)].

ranoside melting at 115–116° and rotating $[\alpha]^{20}D$ −12.2° in methanol (*c* 0.43). The ester reduces warm Fehling solution. A sample was found to consume 1.00 molar equivalents of sodium metaperiodate in 1 hr., no further consumption being observed after 4 hr.

Anal. Calcd. for $C_7H_{14}O_7S$: C, 34.71; H, 5.82. Found: C, 34.95; H, 5.96.

Methyl 3,4-Di-*O*-benzoyl-2-*O*-methylsulfonyl-α-D-arabinoside (XVI) from Methyl 2-*O*-Methylsulfonyl-α-D-arabinopyranoside (XX).—To a solution of 0.21 ml. of benzoyl chloride in 2.0 ml. of dry pyridine, cooled to 5°, was added 200 mg. of methyl 2-*O*-methylsulfonyl-α-D-arabinopyranoside. After 15 min. at 5° and 3 hr. at room temperature the excess benzoyl chloride was destroyed by the addition of water. The product crystallized directly: 440 mg., m.p. 154–158°. Recrystallized from a mixture of 10 ml. of hot absolute ethanol and 7 ml. of hexane it was obtained as needles (340 mg., 91%) melting at 169.5–170° and rotating $[\alpha]^{20}D$ −167.5° in chloroform (*c* 0.64).

Anal. Calcd. for $C_{21}H_{22}O_9S$: C, 55.99; H, 4.92. Found: C, 56.09; H, 5.12.

Methyl 2,3,4-Tri-*O*-methylsulfonyl-α-D-arabinoside (XXI). (a) **From Methyl α-D-Arabinopyranoside (XVII).**—Methyl α-D-arabinopyranoside[16] (400 mg.) was added to a cooled mixture of 4 ml. of dry pyridine and 0.6 ml. of methanesulfonyl chloride. After 30 min. in the cold the reaction mixture was left at room temperature overnight and then worked up in the usual fashion to give a sirup which, from ethyl acetate–hexane, afforded 960 mg. (99%) of crystalline product melting at 190.5–191°, a value unaltered after further recrystallization from methanol. The pure ester rotated $[\alpha]^{20}D$ −30.4° in chloroform (*c* 0.40).

Anal. Calcd. for $C_9H_{18}O_{11}S_3$: C, 27.13; H, 4.55. Found: C, 27.19; H, 4.66.

(b) **From Methyl 2-*O*-Methylsulfonyl-α-D-arabinopyranoside (XX).**—Methyl 2-*O*-methylsulfonyl-α-D-arabinopyranoside (100 mg.) was mesylated in the usual manner, the product crystallizing spontaneously when the pyridine solution was diluted with water. Recrystallization from a mixture of 10 ml. of hot ethyl acetate and 10 ml. of pentane afforded 120 mg. (73%) of pure product melting at 190–191° either alone or in admixture with the product obtained in (a) above.

Methyl 3,4-*O*-Isopropylidene-2-*O*-methylsulfonyl-β-D-arabinopyranoside (I).—Methyl 3,4-*O*-isopropylidene-β-D-arabinoside was obtained as a distilled sirup following the procedure which Honeyman[17] used for the enantiomorph. In chloroform (*c* 1.67) it rotated $[\alpha]^{20}D$ −201°; Overend and Stacey[4] reported $[\alpha]^{18.5}D$ −197.6° (*c* 0.344, $CHCl_3$) for this substance while Honeyman[17] found $[\alpha]^{20}D$ +199.1° (*c* 3.3, $CHCl_3$) for the enantiomorph. Other rotatory values have been reported by Mukherjee and Todd[18] and by Jones and Nicholson.[3] A solution of 21.85 g. of methyl 3,4-*O*-isopropylidene-β-D-arabinoside in anhydrous pyridine (total volume 100 ml.) was cooled and treated with 10 ml. of methanesulfonyl chloride. After standing at 40° overnight the reaction mixture was cooled and diluted with water, the product crystallizing spontaneously: 28.4 g. (94%). Recrystallized from absolute alcohol, the product was obtained as clear, stubby needles melting at 138–139° and showing $[\alpha]^{20}D$ −187° in chloroform (*c* 1.10). A second recrystallization from the same solvent failed to change these values. Overend and Stacey[4] reported for methyl 3,4-*O*-isopropylidene-2-*O*-methylsulfonyl-β-D-arabinoside m.p. 136.5–137.5 and $[\alpha]^{24}D$ −333° ($CHCl_3$, *c* 0.045); Jones and Nicholson[3] found m.p. 140–141° and $[\alpha]^{24}D$ −185° ($CHCl_3$, *c* 1.0).

Anal. Calcd. for $C_{10}H_{18}O_7S$: C, 42.54; H, 6.43; MeO, 10.99. Found: C, 42.17; H, 6.25; MeO, 11.00.

Methyl 2-*O*-Methylsulfonyl-β-D-arabinopyranoside (II).—The procedure which Overend and Stacey[4] employed to hydrolyze methyl 3,4-*O*-isopropylidene-2-*O*-methylsulfonyl-β-D-arabinoside to 2-*O*-methylsulfonyl-D-arabinose was used with minor modifications.

Methyl 3,4-*O*-isopropylidene-2-*O*-methylsulfonyl-β-D-arabinoside (5 g.), prepared as described above, was dissolved in a mixture of 25 ml. of acetone and 150 ml. of *N* sulfuric acid. The solution was refluxed for 4 hr., cooled, neutralized with barium carbonate, passed through a small column of Duolite A-4 and concentrated to a sirup. The latter was dissolved in 50 ml. of alcohol, the solution filtered through a little decolorizing carbon and reconcentrated *in vacuo* to a sirup. The product was crystallized from its solution in a mixture of 5 ml. of alcohol and 4 ml. of water at −5°: 3.4 g. (74%), m.p. 68–70°, $[\alpha]^{20}D$ −162° (5:1 $CHCl_3$-EtOH, *c* 3.20). Recrystallized from aqueous alcohol the methyl 2-*O*-methylsulfonyl-β-D-arabinopyranoside hydrate melted at 69–70° and showed $[\alpha]^{20}D$ −162° in 5:1 chloroform–ethanol (*c* 3.04, no mutarotation in 60 min.). In chloroform (*c* 0.79) a rotation of $[\alpha]^{20}D$ −153° was found. The pure material reduces hot Fehling solution. A sample was found to consume 0.966 molar equivalent of sodium metaperiodate after 3 hr. and 1.11 molar equivalents after 22.5 hr. at room temperature.

Anal. Calcd. for $C_7H_{14}O_7S \cdot H_2O$: C, 32.30; H, 6.20; MeO, 11.92; H_2O, 6.92. Found: C, 32.39; H, 6.09; MeO, 11.78; loss of weight *in vacuo* at 57°, 7.23.

2-*O*-Methylsulfonyl-D-arabinose (V) from Methyl 3,4-*O*-Isopropylidene-2-*O*-methylsulfonyl-β-D-arabinoside (I).—Methyl 3,4-*O*-isopropylidene-2-*O*-methylsulfonyl-β-D-arabinoside (2.2 g.) was hydrolyzed with boiling 2 *N* sulfuric acid as described by Jones and Nicholson.[3] The turbid, brown, odorous solution was neutralized with barium carbonate, filtered through a layer of Super-Cel and concentrated *in vacuo* to a sirup (0.75 g.). Dissolved in 2 ml. of absolute ethanol, this product yielded 0.151 mg. (8.5%) of crystalline 2-*O*-methylsulfonyl-D-arabinose melting at 118–119°. Recrystallization from ethanol–pentane gave, with little loss, pure material melting at 118.5–119° either alone or in admixture with a sample of 2-*O*-methylsulfonyl-D-arabinose prepared through the hydrogenolysis of benzyl 2-*O*-methylsulfonyl-β-D-arabinopyranoside. The sample made here showed $[\alpha]^{20}D$ −88.0° in water (*c* 0.45); its infrared spectrum (Nujol mull) was indistinguishable from that of a sample prepared from benzyl 2-*O*-methylsulfonyl-β-D-arabinopyranoside.

Methyl 2,3,4-Tri-*O*-methylsulfonyl-β-D-arabinoside (III). (a) **From Methyl β-D-Arabinopyranoside (IV).**—Methyl β-D-arabinopyranoside (1 g.) was added to a cooled mixture of 15 ml. of dry pyridine and 2.4 ml. of methanesulfonyl chloride. The reaction mixture was worked up in the usual fashion to give a sirup which crystallized on the addition of ethanol: 1.87 g. (77%). Recrystallization from ethanol gave pure material melting at 128–128.5° and rotating $[\alpha]^{20}D$ −143° in chloroform (*c* 1.1).

Anal. Calcd. for $C_9H_{18}O_{11}S_3$: C, 27.13; H, 4.55. Found: C, 27.15; H, 4.71.

(b) **From Methyl 2-*O*-Methylsulfonyl-β-D-arabinopyranoside (II).**—Methyl 2-*O*-methylsulfonyl-β-D-arabinopyranoside (200 mg.) was mesylated in the conventional fashion with methanesulfonyl chloride in pyridine to give a sirup which from alcoholic solution yielded 250 mg. (76%) of crystalline material melting at 129–129.5°. Recrystallization from ethanol failed to change this value. The pure product rotated $[\alpha]^{20}D$ −145° in chloroform (*c* 1.1); mixed with the product from (a) above it melted at 128–129°.

Methyl 2,3,5-Tri-*O*-methylsulfonyl-α-D-arabinoside.—Methyl α-D-arabinofuranoside (100 mg., prepared from its tribenzoate[2]) was added to a cold mixture of 0.3 ml. of dry pyridine and 0.52 ml. of methanesulfonyl chloride. The reaction mixture was worked up in the usual manner to yield 190 mg. (76%) of methyl 2,3,5-tri-*O*-methylsulfonyl-α-D-arabinoside, m.p. 86–87°. Recrystallization from absolute ethanol failed to change this melting point; the pure material showed $[\alpha]^{20}D$ +72.8° in chloroform (*c* 0.35).

Anal. Calcd. for $C_9H_{18}O_{11}S_3$: C, 27.13; H, 4.55. Found: C, 27.28; H, 4.96.

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