Selective benzoylation of benzyl β-L-arabinopyranoside and benzyl α-D-xylopyranoside

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Benzoylation of benzyl β-L-arabinopyranoside with 2.2 molar equivalents of benzoyl chloride gave benzyl 2,3-di-*O*-benzoyl-β-L-arabinopyranoside (65–70%) and benzyl 2,3,4-tri-*O*-benzoyl-β-L-arabinopyranoside (10–15%). Benzyl α-D-xylopyranoside, under similar conditions, gave benzyl 2,4-di-*O*-benzoyl-α-D-xylopyranoside (45%), benzyl 2,3-di-*O*-benzoyl-α-D-xylopyranoside (27%), benzyl 2,3,4-tri-*O*-benzoyl-α-D-xylopyranoside (15%), and benzyl 2-*O*-benzoyl-α-D-xylopyranoside (9%). Several new derivatives of benzyl β-L-arabinopyranoside and benzyl α-D-xylopyranoside have been prepared. These benzoates lead to the ready preparation of 4-*O*-substituted L-arabinose and D-xylose derivatives. These results are compared with those obtained for the selective benzoylation of hexopyranosides.

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DISCUSSION

Selective benzoylation of the hydroxyl groups of the carbohydrates was the subject of a recent investigation (1, 2). The preferential benzoylation of primary hydroxyl groups has been recognized for some time (3–6). When benzoylation is carried beyond the esterification of the primary hydroxyl groups, selective reactivity of the secondary hydroxy groups is observed in some cases (1, 2, 7–10). We were mainly interested in the selective benzoylation of benzyl glycopyranosides, because the partially benzoylated derivatives that were obtained could be used in the synthesis of disaccharides. They have the advantage that the blocking groups can be removed readily by debenzoylation followed by catalytic hydrogenation to give the free disaccharide.[1] Accordingly, we have investigated the selective benzoylation of benzyl β-L-arabinopyranoside and benzyl α-D-xylopyranoside. Reaction of benzyl β-L-arabinopyranoside (1) with 2.2 molar equivalents of benzoyl chloride in the presence of dry pyridine at −30° gave a mixture of products. From this mixture, a syrupy tribenzoate and a crystalline dibenzoate were isolated by silica column chromatography in 10–15% and 65–70% yields, respectively. The tribenzoate was identical with benzyl 2,3,4-tri-*O*-benzoyl-β-L-arabinopyranoside (II) (identical infrared spectra, and optical rotation of the same sign and similar magnitude) synthesized directly from benzyl β-L-arabinopyranoside by using an excess of benzoyl chloride. The dibenzoate was shown to be benzyl 2,3-di-*O*-benzoyl-β-L-arabinopyranoside (III) in the following way. Treatment of the dibenzoate with methanesulfonyl chloride gave the *O*-methanesulfonyl derivative IV, which was debenzoylated by using catalytic amounts of sodium methoxide. The debenzoylated product V consumed 0.83 mole of sodium metaperiodate per mole; therefore, the methanesulfonyl group is attached to C-2 or C-4. A methanesulfonyl group at C-4 should be stable to sodium methoxide, whereas, if it is at C-2, this reagent should cause elimination to give an epoxide. Since no epoxide could be isolated by refluxing the methanesulfonyl dibenzoate with sodium methoxide, it is very likely that the methanesulfonyl group is attached to C-4. That this was the case was proved conclusively by refluxing IV with sodium benzoate in *N*,*N*-dimethylformamide, when benzyl 2,3,4-tri-*O*-benzoyl-α-D-xylopyranoside (VI) was formed as a result of the nucleophilic displacement (9, 12) at C-4. The tribenzoate was identified by mixture melting point with an authentic sample prepared directly from benzyl α-D-xylopyranoside (VII) and by comparison of infrared spectra. The formation of benzyl 2,3-di-*O*-benzoyl-β-L-arabinopyranoside, in which the hydroxyl group at C-4 is axial in the preferred conformation (III*b*),

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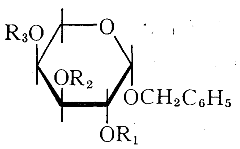
[1] No benzoyl migration was observed under the conditions (mercuric cyanide in nitromethane) used by Helferich (11) for the synthesis of disaccharides.



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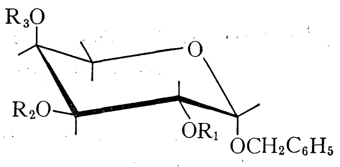


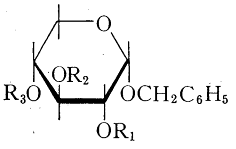
b

I $R_1 = R_2 = R_3 = H$
II $R_1 = R_2 = R_3 = C_6H_5CO$
III $R_1 = R_2 = C_6H_5CO$, $R_3 = H$
IV $R_1 = R_2 = C_6H_5CO$, $R_3 = CH_3SO_2$
V $R_1 = R_2 = H$, $R_3 = CH_3SO_2$
XII $R_1 = H$, $R_2,R_3 = (CH_3)_2C<$
XIII $R_1 = C_6H_5CO$, $R_2,R_3 = (CH_3)_2C<$
XIV $R_1 = C_6H_5CO$, $R_2 = R_3 = H$
XV $R_1 = C_6H_5CO$, $R_2 = R_3 = CH_3SO_2$
XIX $R_1 = R_2 = R_3 = CH_3SO_2$
XXII $R_1 = CH_3SO_2$, $R_2 = R_3 = C_6H_5CO$
XXIII $R_1 = R_3 = C_6H_5CO$, $R_2 = CH_3SO_2$
XXIV $R_1 = CH_3SO_2$,$R_2 = R_3 = H$

may be rationalized on the basis that the acylation of axial hydroxyl groups proceeds less rapidly than that of the equatorial hydroxyl groups (13). Methyl β-L-arabinopyranoside also gives the 2,3-dibenzoate in a high yield (14). It is interesting to note that methyl α-D-galactopyranoside (1), with an axial group at C-4, gives the 2,3,6-tribenzoate on selective tribenzoylation.

Reaction of benzyl α-D-xylopyranoside with 2.2 molar equivalents of benzoyl chloride in dry pyridine at −30° gave a mixture of four products. From the crude mixture, a crystalline tribenzoate (15%), a syrupy dibenzoate (45%), a crystalline dibenzoate (27%), and a crystalline monobenzoate (9%) were isolated by silica column chromatography. The yields reported are accurate to 5%. The tribenzoate was found to be identical (mixture melting point and infrared spectra) with benzyl 2,3,4-tri-*O*-benzoyl-α-D-xylopyranoside synthesized directly from benzyl α-D-xylopyranoside by using excess benzoyl chloride. The structure of the syrupy dibenzoate was proved by preparing the crystalline *O*-methanesulfonyl derivative, which was shown to be benzyl 2,4-di-*O*-benzoyl-3-*O*-methanesulfonyl-α-D-xylopyranoside (XI) by a five-step synthesis starting from benzyl β-L-arabinopyranoside. Benzyl 3,4-*O*-isopropylidene-β-L-arabinopyranoside (XII) prepared according to Ballou (15) gave crystalline benzyl 2-*O*-benzoyl-3,4-*O*-isopropylidene-β-L-arabinopyranoside (XIII) on treatment with benzoyl chloride in the presence of dry pyridine. Hydrolysis of XIII with *N* sulfuric acid yielded crystalline benzyl 2-*O*-benzoyl-β-L-arabinopyranoside (XIV). The slight possibility of benzoyl migration under these conditions was ruled out by condensing the resulting monobenzoate with acetone in the presence of anhydrous copper sulfate and sulfuric acid and reconstituting the *O*-isopropylidene derivative XIII in a 63% yield. Benzyl 2-*O*-benzoyl-β-L-arabinopyranoside was methanesulfonated in the usual manner, and crystalline benzyl 2-*O*-benzoyl-3,4-di-*O*-methanesulfonyl-β-L-arabinopyranoside (XV) was obtained. When XV was refluxed with sodium benzoate (1.2 molar equivalents), benzyl 2,4-di-*O*-benzoyl-3-*O*-methanesulfonyl-α-D-xylopyranoside (57%) was formed, with nucleophilic displacement at C-4. This product was found to be identical with the methanesulfonyl derivative derived from the syrupy xyloside dibenzoate (mixture melting point and infrared spectra). The above sequence of reactions unequivocally proves that the dibenzoate is benzyl 2,4-di-*O*-benzoyl-α-D-xylopyranoside (VIII).

The crystalline xyloside dibenzoate gave a crystalline methanesulfonyl derivative, which was shown to be benzyl 2,3-di-*O*-



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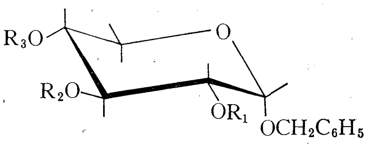

b

VI $R_1 = R_2 = R_3 = C_6H_5CO$
VII $R_1 = R_2 = R_3 = H$
VIII $R_1 = R_3 = C_6H_5CO, R_2 = H$
IX $R_1 = R_2 = C_6H_5CO, R_3 = H$
X $R_1 = C_6H_5CO, R_2 = R_3 = H$
XI $R_1 = R_3 = C_6H_5CO, R_2 = CH_3SO_2$
XVI $R_1 = R_2 = C_6H_5CO, R_3 = CH_3SO_2$
XVII $R_1 = R_2 = CH_3SO_2, R_3 = C_6H_5CO$
XVIII $R_1 = C_6H_5CO, R_2 = R_3 = CH_3SO_2$
XX $R_1 = R_3 = H, R_2 = C_6H_5CO$
XXI $R_1 = R_3 = CH_3SO_2, R_2 = C_6H_5CO$

benzoyl-4-*O*-methanesulfonyl-α-D-xylopyranoside (XVI) in the following way. The product obtained by refluxing XVI with sodium benzoate in *N*,*N*-dimethylformamide gave, on debenzoylation, a crystalline compound which was identified as benzyl β-L-arabinopyranoside (mixture melting point and infrared spectra). An L-arabinose derivative can be obtained from a derivative of D-xylose only if there is inversion of configuration at C-4. This can occur only if the methanesulfonyl group is at C-4; therefore, the methanesulfonyl derivative is benzyl 2,3-di-*O*-benzoyl-4-*O*-methanesulfonyl-α-D-xylopyranoside. Hence the crystalline dibenzoate is benzyl 2,3-di-*O*-benzoyl-α-D-xylopyranoside (IX).

Benzyl 4-*O*-benzoyl-2,3-di-*O*-methanesulfonyl-α-D-xylopyranoside (XVII) was prepared from benzyl 2,3,4-tri-*O*-methanesulfonyl-β-L-arabinopyranoside (XIX) by the selective nucleophilic displacement (16) of the methanesulfonyl group at C-4, using sodium benzoate in *N*,*N*-dimethylformamide. Benzyl 4-*O*-benzoyl-2,3-di-*O*-methanesulfonyl-α-D-xylopyranoside differed from the di-*O*-methanesulfonyl derivative of the monobenzoate X in melting point, infrared spectrum, and optical rotation. Therefore, the monobenzoate cannot be benzyl 4-*O*-benzoyl-α-D-xylopyranoside. The monobenzoate gave a negative reaction to the sodium metaperiodate – potassium permanganate reagent (17); indeed, it consumed sodium metaperiodate very slowly. This would suggest the monobenzoate to be benzyl 3-*O*-benzoyl-α-D-xylopyranoside (XX). However, chemical evidence shows the monobenzoate to be benzyl 2-*O*-benzoyl-α-D-xylopyranoside. If it had been benzyl 3-*O*-benzoyl-α-D-xylopyranoside, the 2,4-di-*O*-methanesulfonyl derivative XXI would have given benzyl 3,4-di-*O*-benzoyl-2-*O*-methanesulfonyl-β-L-arabinopyranoside (XXII) on selective nucleophilic substitution with sodium benzoate. The product (XXIII) obtained, however, differed from benzyl 3,4-di-*O*-benzoyl-2-*O*-methanesulfonyl-β-L-arabinopyranoside (optical rotation and infrared spectra). The latter compound was synthesized from benzyl 2-*O*-methanesulfonyl-β-L-arabinopyranoside (19).

When methyl α-D-xylopyranoside was selectively dibenzoylated, the major product was methyl 2,4-di-*O*-benzoyl-α-D-xylopyranoside (14). Methyl α-D-glucopyranoside (1) gave methyl 2,3,6-tri-*O*-benzoyl-α-D-glucopyranoside as the major product and methyl 2,4,6-tri-*O*-benzoyl-α-D-glucopyranoside as the minor product on selective tribenzoylation. Selective dibenzoylation of benzyl α-D-xylopyranoside gave benzyl 2,4-di-*O*-benzoyl-α-D-xylopyranoside as the major product and benzyl 2,3-di-*O*-benzoyl-α-D-xylopyranoside as the minor product. This is to be expected from the arguments put forward by Williams and Richardson (1) to explain the preponderance of the 2,3,6-tribenzoate over the 2,4,6-tribenzoate in the benzoylation of methyl α-D-glucopyranoside. In benzyl α-D-xylopyranoside also, the hydroxyl group at C-2 is the most reactive, as can be seen from the relative amounts of the products obtained on selective dibenzoylation and also by the fact that monobenzoylation gives benzyl 2-*O*-benzoyl-α-D-xylopyranoside in a 58.8% yield. In benzyl 2-*O*-benzoyl-α-D-xylopyranoside, the hydroxyl group at C-3 has gauche interactions with a benzoyl and a hydroxyl group, whereas the hydroxyl group at C-4 is adjacent to a hydrogen atom and a hydroxyl group and is less sterically hindered. Thus the hydroxyl group at C-4 is benzoylated faster than the one at C-3, causing a preponderance of the 2,4-dibenzoate over the 2,3 isomer. No isomerization of benzyl 2,4-di-*O*-benzoyl-α-D-xylopyranoside to benzyl 2,3-di-*O*-benzoyl-α-D-xylopyranoside, or vice versa, takes place in pyridine solution saturated with pyridine hydrochloride at room temperature for 24 h. This rules out the possibility that benzoyl migration may occur and exercise thermodynamic control over the reaction products.

EXPERIMENTAL

Solutions were concentrated under reduced pressure below 50° unless otherwise stated. Melting points were determined on a Fisher–Johns apparatus and are uncorrected. Optical rotations were measured in chloroform solution (unless otherwise stated) at 22 ± 3° with a Bendix automatic polarimeter, type 143A. Infrared spectra were measured as a 5% (w/v) solution in chloroform or as a powder (0.8% w/w) dispersed in potassium bromide pellets, using a Beckman model IR5A spectrophotometer. Thin-layer chromatography was carried out on glass microplates (40 × 90 mm) coated with silica gel (Camag), using the following solvent systems (by volume): (*a*) methanol–benzene (1:9), (*b*) ethyl acetate – petrol (b.p. 30–60°) (1:4), and (*c*) ethyl acetate – petrol (b.p. 30–60°) (2:3). The spots were detected by spraying the chromatograms with a 5% (v/v) solution of sulfuric acid in ethanol and heating the plates at 120°. Column chromatography was carried out with Davison silica gel (grade 950, 60–200 mesh).

Selective Benzoylation of Benzyl β-L-Arabinopyranoside (1)

Benzyl β-L-arabinopyranoside (12.0 g, 0.05 mole) was stirred with dry pyridine at about −30° and benzoyl chloride (12.7 ml, 0.11 mole) was added dropwise during 90 min. The solution was cooled in ice water, stirred overnight, and then stirred at room temperature for 3 h. After the addition of water (2 ml), the reaction mixture was diluted with methylene chloride (200 ml) and washed successively with 3 *N* sulfuric acid, saturated aqueous sodium bicarbonate solution, and distilled water. The methylene chloride solution was dried over sodium sulfate and filtered. The filtrate was evaporated under reduced pressure to a syrup (22.0 g), which crystallized on standing. The crude product was shown by thin-layer chromatography in solvent *a* to be a mixture of four components in which benzyl 2,3-di-*O*-benzoyl-β-L-arabinopyranoside (III) predominated. A portion of the crude product (5.21 g) was fractionated on a silica column (71 × 4.5 cm) with 3:7 (v/v) ethyl acetate – petrol (b.p. 30–60°). The component (0.79 g) that was first eluted from the column and benzyl 2,3,4-tri-*O*-benzoyl-β-L-arabinopyranoside (II) had identical infrared spectra and similar optical rotations. The major component (3.46 g) eluted from the column was crystallized from ethyl acetate – petrol (b.p. 30–60°) as needles which melted at 122–123.5° and had $[\alpha]_{\mathrm{D}}$ +204° (*c*, 0.55). It was proved to be benzyl 2,3-di-*O*-benzoyl-β-L-arabinopyranoside.

Anal. Calcd. for $C_{26}H_{24}O_7$: C, 69.6; H, 5.4. Found for III: C, 69.5; H, 5.5.

Benzyl 2,3,4-Tri-O-benzoyl-β-L-arabinopyranoside (II) and Benzyl 2,3,4-Tri-O-benzoyl-α-D-xylopyranoside (VI)

Benzyl β-L-arabinopyranoside (3.0 g) was dissolved in dry pyridine (25 ml), and benzoyl chloride (5.8 ml) was added to the solution cooled in ice water. After the mixture was stirred overnight at room temperature, tribenzoate II was isolated in the usual way as a syrup (6.4 g, 91%) which had $[\alpha]_{\mathrm{D}}$ +277° (*c*, 1.0). Benzyl α-D-xylopyranoside (3.0 g) was benzoylated under similar conditions. After crystallization from methanol, benzyl 2,3,4-tri-*O*-benzoyl-α-D-xylopyranoside (VI) (6.2 g, 89%) melted at 127.5–130° and had $[\alpha]_{\mathrm{D}}$ +69° (*c*, 1.0).

Anal. Calcd. for $C_{33}H_{28}O_8$: C, 71.7; H, 5.1. Found for II: C, 71.2; H, 5.3. Found for VI: C, 71.9; H, 5.1.

Benzyl 2,3-Di-O-benzoyl-4-O-methanesulfonyl-β-L-arabinopyranoside (IV)

Benzyl 2,3-di-*O*-benzoyl-β-L-arabinopyranoside (3.7 g) (III) was dissolved in dry pyridine (41 ml) and treated with methanesulfonyl chloride (1.65 ml) in the usual manner. The methanesulfonyl derivative, obtained as a glass in a nearly quantitative yield, had $[\alpha]_{\mathrm{D}}$ +194° (*c*, 0.96).

Anal. Calcd. for $C_{27}H_{26}O_9S$: C, 61.6; H, 5.0; S, 6.1. Found: C, 61.3; H, 5.1; S, 6.5.

Benzyl 4-O-Methanesulfonyl-β-L-arabinopyranoside (V)

Benzyl 2,3-di-*O*-benzoyl-4-*O*-methanesulfonyl-β-L-arabinopyranoside (2.23 g) in dry methanol (50 ml) was treated with a catalytic amount of sodium methoxide. When debenzoylation was complete, the solution was deionized and concentrated to a crystalline mass. After recrystallization from ethanol, the product (0.72 g) melted at 131.5–133.5° and had $[\alpha]_{\mathrm{D}}$ +177° (*c*, 0.73). A further 0.47 g was recovered from the mother liquor.

Anal. Calcd. for $C_{13}H_{18}O_7S$: C, 49.0; H, 5.7; S, 10.1. Found: C, 49.0; H, 5.8; S, 10.0.

Reaction of Benzyl 2,3-Di-O-benzoyl-4-O-methanesulfonyl-β-L-arabinopyranoside with Sodium Benzoate

A solution of benzyl 2,3-di-*O*-benzoyl-4-*O*-methanesulfonyl-β-L-arabinopyranoside (0.89 g) in *N*,*N*-dimethylformamide (42 ml) containing sodium benzoate (2.45 g) was refluxed for about 8 h. The disappearance of the starting material was followed by thin-layer chromatography in solvent *c*. When the reaction mixture was cooled to room temperature, it solidified. It was stirred with hot acetone and filtered to remove sodium benzoate and sodium methanesulfate. The filtrate was concentrated under reduced pressure (bath temperature 60°) to a syrup, which was crystallized from methanol. The crystalline product (0.71 g, 75%) obtained by the displacement reaction was identical with an authentic sample of benzyl 2,3,4-tri-*O*-benzoyl-α-D-xylopyranoside (mixture melting point and infrared spectra).

Reaction of Benzyl 2,3-Di-O-benzoyl-4-O-methanesulfonyl-β-L-arabinopyranoside (IV) with Sodium Methoxide

Benzyl 2,3-di-*O*-benzoyl-4-*O*-methanesulfonyl-β-L-arabinopyranoside (0.21 g) was dissolved in dry methanol (5 ml), and sodium methoxide (0.023 g) was added. The mixture was refluxed on a steam bath for 18 h. A certain amount of decomposition took place during the above treatment. The solution was deionized and concentrated under reduced pressure, when the product crystallized. After recrystallization from ethanol, the product (0.025 g) melted at 129.5–131°. One more crystallization raised the melting point to 131.5–133.5°. This product and benzyl 4-*O*-methanesulfonyl-β-L-arabinopyranoside, obtained by the debenzoylation of V with catalytic amounts of sodium methoxide, were found to be identical (mixture melting point and infrared spectra). No anhydro sugar could be isolated from the reaction mixture.

Selective Benzoylation of Benzyl α-D-Xylopyranoside (VII)

Benzyl α-D-xylopyranoside (12.0 g) was benzoylated under the same conditions as described for the arabinose isomer, using 2.2 molar equivalents of benzoyl chloride. The syrupy product (23.6 g) isolated in the usual manner was shown to be a mixture of four components by thin-layer chromatography in solvent *b*. A portion of the crude product (10.4 g) was fractionated on a silica column with solvent *b*. The product (1.75 g) that was first eluted from the column was found to be identical with an authentic sample of benzyl 2,3,4-tri-*O*-benzoyl-α-D-xylopyranoside (mixture melting point and infrared spectra). The second component, which was shown to be benzyl 2,4-di-*O*-benzoyl-α-D-xylopyranoside (VIII) (4.44 g), was obtained as a syrup and had $[\alpha]_D$ +79° (*c*, 0.54).

Anal. Calcd. for $C_{26}H_{24}O_7$: C, 69.6; H, 5.4. Found for VIII: C, 69.6; H, 5.4.

Since the first two components were only partially separated, the column chromatography was repeated twice to obtain a complete separation of the two compounds. After benzyl 2,4-di-*O*-benzoyl-α-D-xylopyranoside had been eluted completely, solvent *c* was used to elute the third component (also a dibenzoate, 2.46 g, IX), which melted at 88–89° and had $[\alpha]_D$ +187° (*c*, 1.06).

Anal. Calcd. for dibenzoate: C, 69.6; H, 5.4. Found for IX: C, 69.4; H, 5.3.

The fourth component (X) was eluted from the column with 1:4 (v/v) petrol (b.p. 30–60°) – ethyl acetate. The product (0.69 g) was crystallized from chloroform – petrol (b.p. 30–60°) as needles which melted at 140–141.5° and had $[\alpha]_D$ +132° (*c*, 0.71). This compound was shown to be benzyl 2-*O*-benzoyl-α-D-xylopyranoside.

Anal. Calcd. for $C_{19}H_{20}O_6$: C, 66.3; H, 5.9. Found for X: C, 66.0; H, 6.1.

Benzyl 2,4-Di-O-benzoyl-3-O-methanesulfonyl-α-D-xylopyranoside (XI) and Benzyl 2,3-Di-O-benzoyl-4-O-methanesulfonyl-α-D-xylopyranoside (XVI)

Benzyl 2,4-di-*O*-benzoyl-α-D-xylopyranoside (2.4 g) was treated with slightly more than 1 molar equivalent of methanesulfonyl chloride in dry pyridine solution. The product was isolated by pouring the reaction mixture into ice water. The precipitate was filtered off and crystallized from methanol to give XI (2.4 g, 85%), which had m.p. 160–161.5° and $[\alpha]_D$ +71° (*c*, 0.63). Benzyl 2,3-di-*O*-benzoyl-α-D-xylopyranoside (3.0 g) was methanesulfonylated under similar conditions. After crystallization from methanol, the product (2.9 g, 81%) had $[\alpha]_D$ +131° (*c*, 0.96). This product has two crystalline forms, one melting at 114.5–115.5° and the other at 104.5–106.5°. Both had identical infrared spectra.

Anal. Calcd. for $C_{27}H_{26}O_9S$: C, 61.6; H, 5.6; S, 6.1. Found for X: C, 61.6; H, 4.8; S, 6.1. Found for XVI: C, 61.6; H, 5.0; S, 6.2.

Reaction of Benzyl 2,3-Di-O-benzoyl-4-O-methanesulfonyl-α-D-xylopyranoside (XVI) with Sodium Benzoate and Debenzoylation of the Reaction Product

Sodium benzoate (1.44 g) was added to a solution of benzyl 2,3-di-*O*-benzoyl-4-*O*-methanesulfonyl-α-D-xylopyranoside (0.53 g) in *N*,*N*-dimethylformamide (25 ml), and the mixture was refluxed for 7 h. The disappearance of the starting material was followed by thin-layer chromatography in solvent *c*. The reaction mixture was shaken with acetone and filtered to remove sodium methanesulfonate and sodium benzoate. The filtrate was evaporated to give a syrup, which was dissolved in dry methanol (15 ml). Sodium methoxide (a catalytic amount) was added and the debenzoylation was followed by thin-layer chromatography in solvent *c*. After complete debenzoylation, the solution was deionized by passage through Rexyn 101 (H^+ form) and concentrated, when the debenzoylated product (0.16 g) crystallized. The product was recrystallized from ethanol and found to be identical with an authentic sample of benzyl β-L-arabinopyranoside (mixture melting point and infrared spectra).

Benzyl 3,4-O-Isopropylidene-β-L-arabinopyranoside (XII)

Benzyl 3,4-*O*-isopropylidene-β-L-arabinopyranoside was prepared essentially by the procedure of Ballou (7). In the final stage, instead of purifying the product by vacuum distillation, it was fractionated on a silica column with solvent *c*. The product (about a 75% yield) melted at 54–56° and had $[\alpha]_D$ +220° (*c*, 1.0 in ethanol). The literature (7) reports m.p. 55–58° and $[\alpha]_D$ −209° (*c*, 2 in ethanol) for the D isomer.

Benzyl 2-O-Benzoyl-3,4-O-ispropylidene-β-L-arabinopyranoside (XIII)

To a solution of benzyl 3,4-*O*-isopropylidene-β-L-arabinopyranoside (3.82 g) in dry pyridine (30 ml) cooled in ice water, benzoyl chloride (2.4 ml) was added gradually. The reaction mixture was then stirred overnight at room temperature. Water (2 ml) was added to destroy the excess benzoyl chloride. The mixture was diluted with methylene chloride (175 ml), washed successively with cold 3 *N* sulfuric acid, saturated aqueous sodium bicarbonate solution, and distilled water, and dried over sodium sulfate. The solution was filtered and the filtrate concentrated, when the benzoate derivative (4.90 g) crystallized. The product was recrystallized from acetone–water as needles which melted at 110.5–112° and had $[\alpha]_D$ +212° (*c*, 1.13).

Anal. Calcd. for $C_{22}H_{24}O_6$: C, 68.7; H, 6.3. Found: C, 68.5; H, 6.3.

Benzyl 2-O-Benzoyl-β-L-arabinopyranoside (XIV)

Benzyl 2-*O*-benzoyl-3,4-*O*-isopropylidene-β-L-arabinopyranoside (1.82 g) was dissolved in acetone (5 ml), and 1 *N* sulfuric acid (30 ml) was added. The mixture was refluxed on a steam bath for 1 h and then cooled; needle-shaped crystals (1.58 g) were deposited. These were recrystallized from chloroform – petrol (b.p. 30–60°). The recrystallized product melted at 131–132° and had $[\alpha]_D$ +176° (*c*, 0.5).

Anal. Calcd. for $C_{19}H_{20}O_6$: C, 66.3; H, 5.9. Found: C, 66.1; H, 5.8.

Preparation of Benzyl-2-O-benzoyl-3,4-O-isopropylidene-β-L-arabinopyranoside from Benzyl 2-O-Benzoyl-β-L-arabinopyranoside

To a solution of benzyl 2-*O*-benzoyl-β-L-arabinopyranoside (0.46 g) in acetone (25 ml), anhydrous copper sulfate (1.50 g) and sulfuric acid (one drop) were added. The mixture was stirred for 20 h at room temperature and then carefully neutralized with a few drops of concentrated ammonium hydroxide solution. The solution was filtered and, when the filtrate was concentrated, the product (0.49 g) crystallized. It was recrystallized from acetone–water to give the pure compound (0.32 g). This was identical with the product obtained by the benzoylation of benzyl 3,4-*O*-isopropylidene-β-L-arabinopyranoside (mixture melting point and infrared spectra).

Benzyl 2-O-Benzoyl-3,4-di-O-methanesulfonyl-β-L-arabinopyranoside (XV)

To a solution of benzyl 2-*O*-benzoyl-β-L-arabinopyranoside (1.07 g) in dry pyridine (15 ml), methanesulfonyl chloride (0.75 ml) was added gradually. The solution was stirred for 1 h, with cooling in ice water, and for 2 h at room temperature. Water (2 ml) was added to destroy the excess methanesulfonyl chloride and the reaction mixture was poured into a mixture of ice and water. The precipitated methanesulfonyl derivative was allowed to stand at 0° for 4 h, removed by filtration, and washed well with ice-cold water. The dried product (1.40 g) was crystallized from chloroform – petrol (b.p. 30–60°) as needles which melted at 119.5–120° and had $[\alpha]_D$ +219° (*c*, 1.0).

Anal. Calcd. for $C_{21}H_{24}O_{10}S_2$: C, 50.4; H, 4.8; S, 12.8. Found: C, 50.3; H, 4.9; S, 12.7.

Reaction of Benzyl 2-O-Benzoyl-3,4-di-O-methanesulfonyl-β-L-arabinopyranoside with Sodium Benzoate

Benzyl 2-*O*-benzoyl-3,4-di-*O*-methanesulfonyl-β-L-arabinopyranoside (0.98 g) was dissolved in *N*,*N*-dimethylformamide (16 ml), sodium benzoate (0.34 g) was added to the solution, and the mixture was refluxed for 135 min. The dark-brown solution was cooled and filtered to remove sodium methanesulfonate. The filtrate was concentrated under reduced pressure (bath temperature 60°) to remove *N*,*N*-dimethylformamide. The resulting syrup was readily crystallized from methanol as fluffy needles (0.59 g). This compound was identical with the methanesulfonyl derivative of benzyl 2,4-di-*O*-benzoyl-α-D-xylopyranoside obtained in about a 45% yield by the selective benzoylation of benzyl α-D-xylopyranoside (mixture melting point and infrared spectra).

Benzyl 2,3,4-Tri-O-methanesulfonyl-β-L-arabinopyranoside (XIX)

Benzyl β-L-arabinopyranoside (3.00 g) in ice-cold dry pyridine (50 ml) was treated with methanesulfonyl chloride (7.5 ml). The solution was cooled in ice water and stirred for 1 h, after which the stirring was continued for 2 h at room temperature. The excess methanesulfonyl chloride was destroyed with water and the product was isolated in the usual manner as a glass (11.9 g) having $[\alpha]_D$ +158° (*c*, 1.15).

Anal. Calcd. for $C_{15}H_{22}O_{11}S_3$: C, 38.0; H, 4.7; S, 20.3. Found: C, 38.1; H, 4.7; S, 19.4.

Reaction of Benzyl 2,3,4-Tri-O-methanesulfonyl-β-L-arabinopyranoside with Sodium Benzoate (Benzyl 4-O-Benzoyl-2,3-di-O-methanesulfonyl-α-D-xylopyranoside (XVII))

Benzyl 2,3,4-tri-*O*-methanesulfonyl-β-L-arabinopyranoside (4.94 g) was dissolved in *N*,*N*-dimethylformamide (50 ml), sodium benzoate (2.45 g) was added to the solution, and the mixture was refluxed for 4½ h. The dark reaction mixture was concentrated to a syrup, which was stirred with chloroform and filtered. The filtrate was shaken with ice water and the chloroform solution was dried over sodium sulfate. When the solution was concentrated, the product crystallized. After recrystallization from methanol, the product (2.12 g) melted at 157.5–159° and had $[\alpha]_D$ +23.4° (*c*, 1.74).

Anal. Calcd. for $C_{21}H_{24}O_{10}S_2$: C, 50.4; H, 4.8; S, 12.8. Found: C, 50.2; H, 4.9; S, 12.7.

Benzyl 2-O-Benzoyl-3,4-di-O-methanesulfonyl-α-D-xylopyranoside (XVIII)

Benzyl 2-*O*-benzoyl-α-D-xylopyranoside (0.28 g) in dry pyridine (15 ml) was treated with methanesulfonyl chloride (0.2 ml) in the usual manner. After the excess methanesulfonyl chloride was destroyed, the reaction mixture was poured into ice water. The precipitated methanesulfonyl derivative was allowed to stand at 0° for 5 h, removed by filtration, and dried. The product (0.36 g) was crystallized from methanol. The crystals melted at 162–163° and had $[\alpha]_D$ +150.5° (*c*, 1.05).

Anal. Calcd. for $C_{21}H_{24}O_{10}S_2$: C, 50.4; H, 4.8; S, 12.8. Found: C, 50.3; H, 4.8; S, 12.7.

Periodate Oxidation of Benzyl 4-O-Methanesulfonyl-β-L-arabinopyranoside

Benzyl 4-*O*-methanesulfonyl-β-L-arabinopyranoside (6.995 mg) was dissolved in and diluted to 5 ml with 0.015 *M* sodium metaperiodate solution. The consumption of periodate was followed spectrophotometrically (18). A blank solution containing the same concentration of benzyl 4-*O*-methanesulfonyl-β-L-arabinopyranoside showed little absorption at 222.5 mμ. The amounts of periodate consumed at various time intervals at room temperature were: 0.03 (4 h), 0.31 (18 h), 0.62 (30 h), 0.67 (42 h), 0.80 (66 h), and 0.85 mole (75 h).

Periodate Oxidation of Benzyl 2-O-Benzoyl-α-D-xylopyranoside

The periodate uptake was less than 0.2 mole per mole of benzyl 2-*O*-benzoyl-α-D-xylopyranoside at the end of 36 h when the pyranoside was treated with sodium metaperiodate in 1:4 (v/v) acetone–water. The periodate consumption was determined iodometrically with the usual phosphate buffer solution. The spectrophotometric method was not used since benzyl 2-*O*-benzoyl-α-D-xylopyranoside absorbed considerably at 222.5 mμ.

Selective Monobenzoylation of Benzyl α-D-Xylopyranoside

Benzyl α-D-xylopyranoside (4.00 g) in dry pyridine (50 ml) was benzoylated at −30° with 1.1 molar equivalents of benzoyl chloride. After the reaction mixture was kept at 0° for 20 h and at room temperature for 2 h, the crude crystalline benzyl 2-*O*-benzoyl-α-D-xylopyranoside (4.83 g) was isolated in the usual manner. Recrystallization from chloroform–petrol (b.p. 30–60°) gave pure benzyl 2-*O*-benzoyl-α-D-xylopyranoside (3.37 g, 58.8%). This was found to be identical (mixture melting point and infrared spectra) with the monobenzoate X isolated in the selective dibenzoylation experiment.

Benzyl 3,4-Di-O-benzoyl-2-O-methanesulfonyl-β-L-arabinopyranoside

Benzyl 2-*O*-methanesulfonyl-β-L-arabinopyranoside (XXIV) prepared by the procedure described for the D isomer (19) melted at 127–128° and had $[\alpha]_D$ +190° (*c*, 0.42). The literature reports m.p. 129–130° (corrected) and $[\alpha]_D$ −189.5° (*c*, 3.2 in chloroform–ethanol (5:1 v/v)) for the D isomer. A solution of XXIV (0.80 g) in dry pyridine (15 ml) was treated with slightly more than 2 equivalents of benzoyl chloride, and the product (1.20 g) was isolated in the usual manner. After crystallization from chloroform–petrol, it melted at 98–99° and had $[\alpha]_D$ +298° (*c*, 1.12).

Anal. Calcd. for $C_{27}H_{26}O_9S$: C, 61.6; H, 5.0; S, 6.1. Found for XXII: C, 61.9; H, 5.1; S, 6.1.

Reaction of Benzyl 2-O-Benzoyl-3,4-di-O-methanesulfonyl-α-D-xylopyranoside with Sodium Benzoate

A solution of benzyl 2-*O*-benzoyl-3,4-di-*O*-methanesulfonyl-α-D-xylopyranoside (1.90 g) in *N*,*N*-dimethylformamide (50 ml) containing sodium benzoate (0.85 g) was heated at 160° for 3 h. The dark-brown solution was diluted with chloroform and filtered to remove sodium benzoate and sodium methanesulfonate. The solution was decolorized and concentrated to a syrup. Fractional crystallization from chloroform–petrol gave the unreacted starting material (identified by mixture melting point with the pure sample and by comparison of infrared spectra) contaminated with small amounts of the reaction product. After the removal of the starting material, the mother liquor contained mainly the reaction product. It was purified on a silica column with solvent *c*. The crystals obtained by triturating the syrup (0.83 g) with petrol (b.p. 30–60°) melted at 98–99° and had $[\alpha]_D$ +226° (*c*, 0.58).

Anal. Calcd. for $C_{27}H_{26}O_9S$: C, 61.6; H, 5.0; S, 6.1. Found for XXIII: C, 61.5; H, 5.0; S, 5.9.

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