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Anchimeric Assistance by Benzyloxy Groups and the Effect of Configuration on an Intramolecular Displacement Reaction of the Pentitols[1]

GARY R. GRAY,[2] FREDERICK C. HARTMAN,[3] AND ROBERT BARKER[4]

Department of Biochemistry, University of Tennessee, Memphis, Tennessee, and the Department of Biochemistry, The State University of Iowa, Iowa City, Iowa

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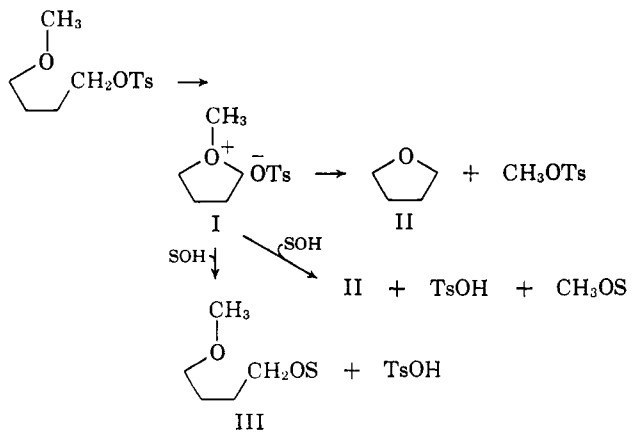
A 4-benzyloxy group renders powerful anchimeric assistance in the displacement of a 1-*p*-tolylsulfonyloxy group. The products are the corresponding tetrahydrofuran and benzyl tosylate. The rate of the reaction is greatest when the substituents on the tetrahydrofuran ring in the product are *trans*.

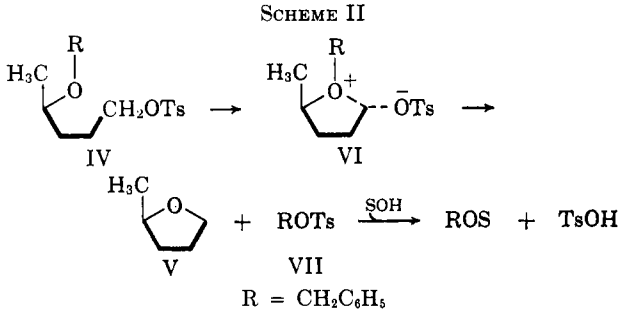
In the absence of a neighboring group capable of rendering anchimeric assistance alkyl *p*-tolylsulfonyl esters are reasonably stable under both acidic and alkaline conditions.[5] The presence of an alkoxyl group adjacent (β) to an ester function usually increases its stability[6] (by induction), although the presence of β-substituents in addition to the alkoxyl group tends to reverse the stabilizing effect[7] and it is probable that β-alkoxyl functions assist in solvolysis of arylsulfonic acid esters. The resultant of inductive and anchimeric forces is a net decrease in rate for β-alkoxyl solvolyses compared with those of unsubstituted esters.

The presence of a methoxyl group δ to an arylsulfonic acid ester increases the rate of ethanolysis of the ester by a factor of 20 at 75°[8] indicating a vigorous anchimeric assistance. The products of the displacement reaction point to the occurence of a cyclic oxonium ion intermediate (I) which can decompose in different ways[8] (Scheme I). From *n*-alkyl esters the only product is the corresponding acyclic derivative III. However, under similar conditions, 2-*o*-anisyl-2-methyl-1-propyl bromobenzenesulfonate gives a cyclic product exclusively. The cyclization appears to be due to a steric effect of the *gem*-methyl groups, since from 2-*o*-anisylethyl bromobenzenesulfonate only the acyclic solvolysis product is obtained.

SCHEME I



SCHEME II



We find that 4-*O*-benzyl-1-*O*-*p*-tolylsulfonylpentanediol (IV) in ethanol at 75° is rapidly decomposed to give 2-methyltetrahydrofuran (V), *p*-toluenesulfonic acid, and benzyl ethyl ether. When the reaction is followed by intermittent titration of the acid produced, the rate constant is found to increase with time (Figure 1). This finding is reasonable if acid production is the resultant of two first-order processes in which the rate constant of one step does not differ from that of the other step by more than a factor of 100.[9] Since all of the compounds studied (see below) evinced similar behavior, and since a good fit of the experimental data could be obtained in each case if the second step was assigned a value of 6.6×10^{-3} sec.$^{-1}$, we propose that the process involves the formation of an ion pair (VI) which collapses to give 2-methyltetrahydrofuran and benzyl *p*-toluenesulfonate (VII). Solvolysis of VII, $k = 6.6 \times 10^{-3}$ sec.$^{-1}$, then yields *p*-toluenesulfonic acid and benzyl ethyl ether (Scheme II). If the reaction is carried out in ethanol–water (3:2, v./v.), benzyl alcohol is obtained rather than benzyl ethyl ether. Under the conditions used (95% ethyl alcohol at 75°) benzyl *p*-toluenesulfonate[10] has $k = (1.0 \pm 0.4) \times 10^{-2}$ sec.$^{-1}$ and gives an 80% yield of benzyl ethyl ether.

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(2) Research Participant, National Science Foundation Undergraduate Research Participation Program, University of Tennessee, summer 1963.

(3) U. S. Public Health Service Predoctoral Fellow, 1963–1964.

(4) Department of Biochemistry, State University of Iowa, Iowa City, Iowa, to whom inquiries regarding this article should be addressed.

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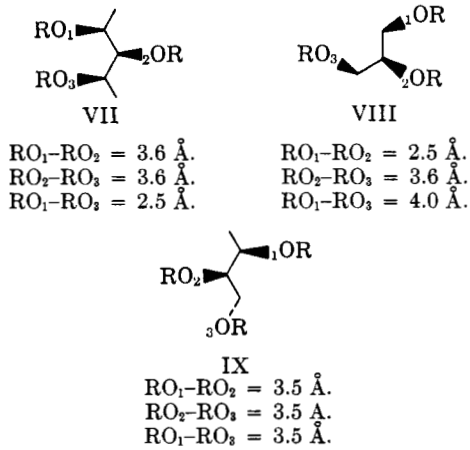
SCHEME III



The possibility that the increase in k_{obsd} with time might be due to catalysis by the acid being released was checked by carrying out the reaction in the presence of added toluenesulfonic acid. The rate of the process is approximately the same when 1 or 3 mole equiv. of acid is added (Figure 2).

The effect of substitution at the 2-, 3-, and 5-positions of the pentane was examined. The 1,5-di-*O*-*p*-tolylsulfonyl-2,3,4-tri-*O*-benzylpentitols were prepared from the corresponding pentitols by the following series of reactions: pentitol → 2,3,4-tri-*O*-acetyl-1,5-di-*O*-tritylpentitol → 2,3,4-tri-*O*-benzyl-1,5-di-*O*-tritylpentitol → 2,3,4-tri-*O*-benzylpentitol → 2,3,4-tri-*O*-benzyl-1,5-di-*O*-*p*-tolylsulfonylpentitol. The *ribo*, *xylo*, and D-*arabino* isomers were prepared and the rate of acid formation in 95% ethanol at 75° of each was measured (Figure 1).

That the products of the reaction were 1,4-anhydrides was proved by comparison to compounds having this structure which were synthesized in an unequivocal fashion.

The presence of bulky substituents does not necessarily effect the rate of the reaction since the *xylo* and *arabino* derivatives decompose at approximately the same rate as does the unsubstituted compound. The *ribo* derivative decomposes much more slowly. As inductive effects are probably the same for all the substituted compounds, it is probable that the marked decrease in rate in the *ribo* derivative is due to steric interactions between the substituent groups.

Differences between the activation energies for the cyclization of the various pentitol derivatives could be due to differences between the ground-state energies of the reactants, to the energies of the transition states, or to a combination of both factors. It has been proposed that, in the case of unsubstituted alditols, the *ribo* configuration is the most stable since when the carbon chain is arranged in a zigzag conformation the hydroxyl groups are farther apart than in the *xylo* or *arabino* isomers. The assumption that the zigzag conformation is the most stable implies that the steric interactions which have the most powerful effect reside in the carbon chain. However, if repulsions between substituents of the chain have the greatest effect, the zigzag arrangement would be an unstable one since it results in groups β to each other coming as close together as vicinal eclipsed groups. This point is illustrated in Scheme III where a three-carbon segment bearing OR groups is shown as it would be arranged in a zigzag chain (VII). The distance between 1- and 3-OR groups is 2.5 Å. The distance between adjacent eclipsed OR groups is also 2.5 Å. (VIII). In the case where R = benzyl, if it is assumed that there is a steric repulsion between groups, the latter conformer (VIII) will be more stable since one of the interactions is decreased relative to those in VII. It is apparent, however, that a third conformer in which a maximum separation of all OR groups is achieved will be more stable than either VII or VIII. Such a conformer is IX in which adjacent OR groups are *gauche*.

Although it is obviously incorrect to neglect steric interactions involving the carbon chain, if this is done and if the interactions of the substituents are minimal when the groups are *gauche*, the arrangements shown in Scheme IV (Xa, XIa, XIIa) are arrived at as the minimum energy conformers of the pentitols and their derivatives. The relative energies of these ground-state conformations cannot be evaluated. However, the resemblance of the ground state and the transition state decreases in the series *xylo*, *arabino*, *ribo*, and *lyxo* (compare the a and b structures in Scheme IV) predicting a similar decrease in cyclization rate with configuration.

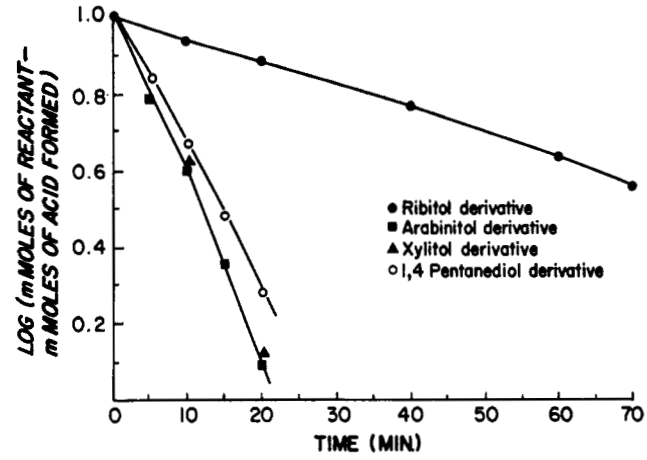


Figure 1.—The rate of acid release from 1-*p*-tolylsulfonyl-4-benzyloxypentanediol and the 1,5-di-*O*-*p*-tolylsulfonyl-2,3,4-tri-*O*-benzylpentitols in 95% aqueous ethyl alcohol at 75°. The rate of acid release from the ribitol and xylitol derivatives has been corrected (by a factor of 0.5) for the fact that the reactants are symmetrical.

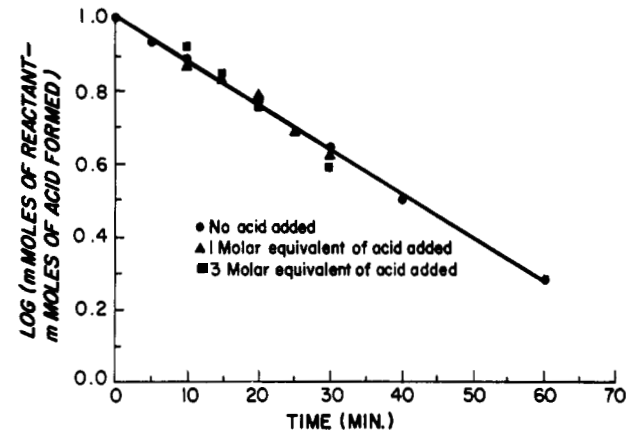
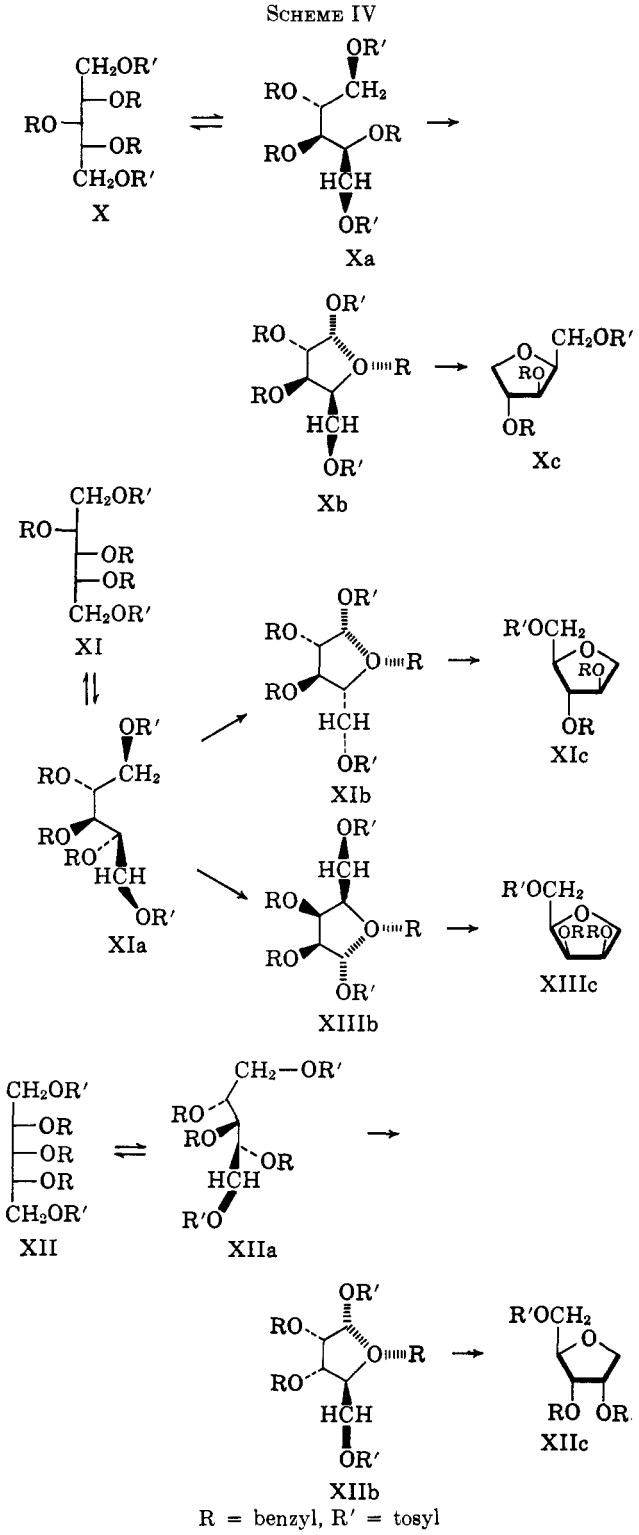


Figure 2.—The effect of added *p*-toluenesulfonic acid on the rate of acid release from 1,5-di-*O*-*p*-tolylsulfonyl-2,3,4-tri-*O*-benzylribitol in 95% aqueous ethyl alcohol at 75°.

SCHEME IV



The relative energies of the transition states can be inferred from the nonbonded interactions present in the products since the length of the newly forming bond is approximately the same in the onium ion intermediate as in the product and interactions involving the entering and leaving group are approximately the same in all cases. Referring to the b structures in Scheme IV it can be seen that the smallest interaction between nonbonded groups is present in XIb, and Xb and XIIb contain one *cis* interaction and XIIIb contains two. On this basis the rate of cyclization would be predicted to decrease in the series *arabino*, *xylo* and *ribo*, and *lyxo*.

The fact that the *xylo* isomer cyclizes at approximately the same rate as the *arabino* isomer may be due to the fact that there is little increase in the nonbonded interactions in the transition state (Xb) compared to the ground state (Xa) or to an attraction between O-3 and C-5. The latter, as the positive end of a somewhat polarized sulfonic ester bond, would present little hindrance to the assumption of an eclipsed conformation with O-3.

As depicted in Scheme IV the *arabino* isomer might be expected to produce two products (XIc and XIIIc) arising from reactions at opposite ends of the asymmetric substrate (XI). No indication of the occurrence of any of the *lyxo* product (XIIIc) was obtained. The transition state (XIIIb) for the formation of XIIIc has all bulky groups *cis* and would be much more difficult to form than XIb in which all groups are *trans*. Therefore, the conversion of XI to XIc would be much more facile than its conversion to XIIIc.

In Table I are the calculated values of $k_{\text{cyclization}}$ for the compounds tested (*i.e.*, the rate of benzyl tosylate formation).

TABLE I
THE RATE OF BENZYL TOSYLATE FORMATION FROM 4-*O*-BENZYL TOSYL ESTERS[a]

Compd.	k_1, sec.$^{-1}$[b]
4-*O*-Benzyl-1-*O*-tosylpentanediol	1.7×10^{-3}
1,5-Di-*O*-tosyl-2,3,4-tri-*O*-benzylribitol[c]	2.2×10^{-4}
1,5-Di-*O*-tosyl-2,3,4-tri-*O*-benzyl-D-arabinitol	2.2×10^{-3}
1,5-Di-*O*-tosyl-2,3,4-tri-*O*-benzylxylitol[c]	2.2×10^{-3}

[a] Reaction in 95% ethanol at 75°. [b] Calculated values. [c] $k_{\text{calcd}} = 0.5k_{\text{obsd}}$, since substrate is symmetric.

Experimental

1,4-Pentanediol.—To an ice-cold solution of 100 g. of 1-pentanol-4-one[11] in 100 ml. of water was added dropwise during a 15-min. period a solution of 10 g. of sodium borohydride in 50 ml. of 0.02 *N* sodium hydroxide. The reaction mixture was left at room temperature for 24 hr. at which time the excess borohydride was decomposed by the dropwise addition of 0.5 ml. of glacial acetic acid. Sodium ions were removed from the solution by passing it through a column containing 250 ml. of IR120 (H^+) ion-exchange resin. The eluent was concentrated and the residual sirup was freed of boric acid by concentration from four 200-ml. portions of methanol. Distillation of the product at 15 mm. gave 2.6 g., b.p. 90–128°, of material which appeared by infrared spectroscopy to be contaminated with starting material and 71 g., b.p. 129–133°, of uncontaminated 1,4-pentanediol.

4-*O*-Benzyl-1,4-pentanediol.—To a solution of 10 g. of 1,4-pentanediol in 50 ml. of pyridine was added 30 g. of triphenylchloromethane. The reaction mixture was left at room temperature for 24 hr. at which time 5 ml. of water was added with vigorous stirring to hydrolyze the excess triphenylchloromethane followed by 200 ml. of methylene chloride. The solution was washed successively with two cold 500-ml. portions of water, 1 *N* sulfuric acid, saturated sodium bicarbonate, and water. The methylene chloride layer was dried over sodium sulfate, filtered, and concentrated. The sirupy 1-*O*-trityl-1,4-pentanediol (30 g.) thus obtained was converted to the 4-*O*-benzyl derivative by heating under reflux for 6 hr. in 300 ml. of benzene containing 23 g. of powdered potassium hydroxide and 25 ml. of benzyl chloride. The mixture was cooled and then filtered through a layer of Celite, and the filtrate was concentrated. Dibenzyl ether was removed by heating in an oil bath at 150° (1 mm.) for 3 hr., leaving 32 g. of product which could not be induced to crystallize. Twenty grams of this compound was converted to 4-*O*-benzyl-1,4-pentanediol by refluxing for 12 hr. in 200 ml. of dioxane containing 50 ml. of 1 *N* sulfuric acid. The solution was neutralized with 5 *N* sodium hydroxide and concentrated, and the residue

(11) Aldrich Chemical Co., Inc., Milwaukee 10, Wis.

was taken up in 200 ml. of methylene chloride. The methylene chloride solution was washed with two 100-ml. portions of water, dried over sodium sulfate, filtered, and concentrated. The residue (19 g.) was dissolved in 50 ml. of benzene and applied to a column containing 250 g. of Florisil[12] packed as a slurry in cyclohexane. Elution with 1.5 l. of benzene gave 11.3 g. (94%) of triphenylcarbinol, and elution with 1 l. of ether gave 7.0 g. (78%) of 4-*O*-benzyl-1,4-pentanediol as a sirup.

Anal. Calcd. for $C_{12}H_{18}O_2$ (194.3): C, 74.20; H, 9.34. Found: C, 73.10; H, 9.39.

4-*O*-Benzyl-1-*O*-*p*-tolylsulfonyl-1,4-pentanediol.—To a solution of 3 g. of 4-*O*-benzyl-1,4-pentanediol in 10 ml. of pyridine was added 5 g. of *p*-toluenesulfonyl chloride. After leaving the reaction mixture at room temperature for 8 hr., ice was added and the product was taken up in methylene chloride. The solution was extracted with 1 *N* sulfuric acid, saturated sodium bicarbonate, and water, then dried over sodium sulfate. Removal of the solvent gave 4.8 g. (94%) of a sirup which could not be crystallized.

Action of Sodium Iodide on 4-*O*-Benzyl-1-*O*-*p*-tolylsulfonyl-1,4-pentanediol.—A solution of 4-*O*-benzyl-1-*O*-*p*-tolylsulfonyl-1,4-pentanediol (2.0 g.) in 2.5 ml. of acetone containing 3.0 g. of sodium iodide was refluxed for 2 hr. The solution was then cooled to 0°; the sodium *p*-toluenesulfonate (1.02 g., 92%) was removed by filtration and characterized by infrared spectroscopy.

1,5-Di-*O*-trityl-2,3,4-tri-*O*-acetyl-D-arabinitol.—To a solution of 20 g. of D-arabinitol in 200 ml. of pyridine was added 73.7 g. of triphenylchloromethane. The reaction mixture was left at room temperature for 24 hr., after which 80 ml. of acetic anhydride was added. After a further 12 hr. at room temperature ice was added to the reaction mixture, and 1 hr. later 300 ml. of methylene chloride was added. The methylene chloride solution was washed twice with cold water, 1 *N* sulfuric acid, saturated sodium bicarbonate, and water, dried over sodium sulfate, and concentrated to a sirup which deposited crystals from solution in isopropyl ether: yield 75 g. (75%), m.p. 141–143°. After three recrystallizations from the same solvent the melting point was raised to 146–147°; $[\alpha]^{25}D$ −3.3° (*c* 2.13, dimethyl sulfoxide).

Anal. Calcd. for $C_{49}H_{46}O_8$ (762.9): C, 77.14; H, 6.08. Found: C, 77.33; H, 6.17.

1,5-Di-*O*-trityl-2,3,4-tri-*O*-benzyl-D-arabinitol.—To 200 ml. of benzene was added 48.5 g. of 1,5-di-*O*-trityl-2,3,4-tri-*O*-acetyl-D-arabinitol, 40 g. of anhydrous powdered potassium hydroxide, and 15 ml. of benzyl chloride. The suspension was refluxed with constant stirring. Three additional 40-g. portions of potassium hydroxide and two 15-ml. portions of benzyl chloride were added at 15-min. intervals. After 24 hr. the reaction mixture was filtered through Celite, the solids were washed thoroughly with benzene, and the filtrate was concentrated to a sirup, which, from an acetone–ethanol mixture (1:1), yielded 42 g. (72%) of crystals, m.p.143–146°. After three recrystallizations from the same solvents the melting point was raised to 146–147°; $[\alpha]^{25}D$ −5.1° (*c* 1.95, toluene).

Anal. Calcd. for $C_{64}H_{58}O_5$ (907.2): C, 84.71; H, 6.49. Found: C, 84.74; H, 6.49.

2,3,4-Tri-*O*-benzyl-D-arabinitol.—To a solution of 40 g. of 2,3,4-tri-*O*-benzyl-1,5-di-*O*-trityl-D-arbinitol in 800 ml. of dioxane was added 200 ml. of 0.1 *N* hydrochloric acid. The solution was refluxed for 24 hr., neutralized with 20 ml. of 1 *N* sodium hydroxide, and concentrated. The resulting crystalline mass was concentrated twice from 100-ml. portions of dioxane to remove water and then extracted with a total of 400 ml. of methylene chloride. The methylene chloride solution was dried over sodium sulfate, filtered, and concentrated. The residue was dissolved in 100 ml. of benzene and passed over a column containing 300 g. of Florisil packed as a slurry in cyclohexane. The column was eluted with 800 ml. of benzene, and the eluate was concentrated to give 23 g. (100%) of triphenylcarbinol. The column was eluted with ethyl acetate and the eluate (800 ml.) was concentrated leaving a crystalline mass, which when recrystallized from isopropyl ether gave 9 g. (47%) of material, m.p. 75–77°. After three recrystallizations from isopropyl ether the material melted at 76–77° and had $[\alpha]^{25}D$ −14.6° (*c* 2.9, dimethyl sulfoxide).

Anal. Calcd. for $C_{26}H_{30}O_5$ (422.5): C, 73.91; H, 7.16. Found: C, 74.56; H, 7.22.

2,3,4-Tri-*O*-benzyl-1,5-di-*O*-*p*-tolylsulfonyl-D-arabinitol.—To a solution of 8.6 g. of 2,3,4-tri-*O*-benzyl-D-arabinitol in 100 ml. of methylene chloride was added 13 ml. of pyridine and 15.5 g. of *p*-toluenesulfonyl chloride. After the reaction mixture had remained at room temperature for 24 hr., ice was added to destroy the excess reagent. The solution was washed successively with 1 *N* sulfuric acid, saturated sodium bicarbonate, and water, dried over sodium sulfate, and concentrated to a residue which yielded 11.5 g. (82%) of crystals, m.p. 97–99°, from 30 ml. of benzene–isopropyl ether (1:1). Two recrystallizations from the same solvents did not alter the melting point and the compound had $[\alpha]^{25}D \pm 0.2°$ (*c* 2.1, dimethyl sulfoxide).

Anal. Calcd. for $C_{40}H_{42}O_9S_2$ (730.9): C, 65.73; H, 5.79; S, 8.77. Found: C, 65.62; H, 5.90; S, 8.93.

1,5-Di-*O*-trityl-2,3,4-tri-*O*-acetylxylitol was prepared as described for 1,5-di-*O*-trityl-2,3,4-tri-*O*-acetyl-D-arabinitol. Crystallization of the product from ethyl acetate–ethanol (5:3) gave 76% of material, m.p. 198–201°.

Anal. Calcd. for $C_{49}H_{46}O_8$ (762.9): C, 77.14; H, 6.08. Found: C, 76.79; H, 5.96.

1,5-Di-*O*-trityl-2,3,4-tri-*O*-benzylxylitol was prepared as described for 1,5-di-*O*-trityl-2,3,4-tri-*O*-benzyl-D-arabinitol, to yield crystals (84%) which when, recrystallized from acetone–ethanol (1:1), melted at 144–145°.

Anal. Calcd. for $C_{64}H_{58}O_5$ (907.2): C, 84.71; H, 6.49. Found: C, 84.52; H, 6.42.

2,3,4-Tri-*O*-benzylxylitol was prepared as described for 2,3,4-tri-*O*-benzyl-D-arabinitol and was obtained as a sirup in 88% yield which was not further characterized.

1,5-Di-*O*-tolylsulfonyl-2,3,4-tri-*O*-benzylxylitol.—This compound was prepared in the same manner as that described for the corresponding tosyl derivative of 2,3,4-tri-*O*-benzyl-D-arabinitol and was obtained as a sirup.

2,3,4-Tri-*O*-acetyl-1,5-di-*O*-tritylribitol was prepared as described for 1,5-di-*O*-trityl-2,3,4-tri-*O*-acetyl-D-arabinitol to yield a sirup which crystallized from methylene chloride–ethanol (1:1) to yield crystals (76%), m.p. 119–122°.

Anal. Calcd. for $C_{49}H_{46}O_8$ (762.90): C, 77.14; H, 6.08. Found: C, 76.81; H, 6.14.

1,5-Di-*O*-trityl-2,3,4-tri-*O*-benzylribitol was prepared as described for 1,5-di-*O*-trityl-2,3,4-tri-*O*-benzyl-D-arabinitol to yield a sirup which was not characterized.

2,3,4-Tri-*O*-benzylribitol was prepared as described for 2,3,4-tri-*O*-benzyl-D-arabinitol, using 75 g. of 1,5-di-*O*-trityl-2,3,4-tri-*O*-benzylribitol except that prior to chromatography on 1.4 kg. of Florisil the semicrystalline mixture containing the product and triphenylcarbinol was extracted with 200 ml. of cyclohexane in which only the product was completely soluble. In this way 22 g. of triphenylcarbinol was removed. The Florisil column was eluted with 10 l. of benzene to give 33 g. of a mixture of triphenylcarbinol and dibenzyl ether and then with 5 l. of ethyl ether to give 22.2 g. of 2,3,4-tri-*O*-benzylribitol as a clear sirup which could not be crystallized.

1,5-Di-*O*-*p*-tolylsulfonyl-2,3,4-tri-*O*-benzylribitol.—To a solution of 11.5 g. of 2,3,4-tri-*O*-benzylribitol in 50 ml. of pyridine was added 25 g. of *p*-toluenesulfonyl chloride. After the reaction mixture had remained at room temperature for 12 hr. the excess *p*-toluenesulfonyl chloride was hydrolyzed by the addition of a few chips of ice. Methylene chloride (100 ml.) was added and the solution was washed successively with two cold 300-ml. portions of each of the following: water, 1 *N* sulfuric acid, saturated sodium bicarbonate, and water. The methylene chloride layer was dried over sodium sulfate, filtered, and concentrated, leaving 18 g. of sirup from which 13.6 g. (68%) of crystals, m.p. 93–95.5°, were obtained from 100 ml. of benzene–cyclohexane (1:3).

Anal. Calcd. for $C_{40}H_{42}O_9S_2$ (730.9): C, 65.73; H, 5.79; S, 8.77. Found: C, 65.76; H, 5.86; S, 8.68.

1,4-Anhydro-5-*O*-trityl-DL-xylitol.—To a solution of 2 g. of 1,4-anhydro-DL-xylitol in 20 ml. of pyridine was added 5 g. of triphenylchloromethane. The reaction was allowed to proceed for 48 hr. at room temperature at which time 100 ml. of methylene chloride was added, and the solution was washed as described previously. From the resulting sirup was obtained 4.8 g. (86%) of crystals, m.p. 131–134°, by crystallization from 100 ml. of benzene–cyclohexane (1:2). Three recrystallizations from the same solvent raised the melting point to 135–137°.

Anal. Calcd. for $C_{24}H_{24}O_4$ (376.5): C, 76.57; H, 6.42. Found: C, 76.80; H, 6.70.

1,4-Anhydro-2,3-di-*O*-benzyl-5-*O*-trityl-DL-xylitol.—A solution of 3.8 g. of 1,4-anhydro-5-*O*-trityl-DL-xylitol in 100 ml. of benzene containing 20 g. of powdered potassium hydroxide and 6 ml. of

(12) Floridin Co., Tallahassee, Fla.

benzyl chloride was refluxed for 5 hr., filtered through Celite, and concentrated. The dibenzyl ether was removed by distillation under reduced pressure and the residual sirup was dissolved in 20 ml. of benzene. The product crystallized after the addition of 60 ml. of cyclohexane, 5.6 g. (75%) of crystals, m.p. 134–138°, being obtained. After two recrystallizations from the same solvent, the compound melted at 140–142°.

Anal. Calcd. for $C_{38}H_{36}O_4$ (556.7): C, 81.98; H, 6.53. Found: C, 81.88; H, 6.64.

1,4-Anhydro-2,3-di-*O*-benzyl-5-*O*-*p*-tolylsulfonyl-DL-xylitol.—To a slurry of 4.5 g. of 1,4-anhyro-2,3-di-*O*-benzyl-5-*O*-trityl-DL-xylitol in 200 ml. of refluxing 95% ethanol was added tetrahydrofuran until an homogeneous solution was obtained. Concentrated sulfuric acid (5 ml.) and water (until slightly turbid) was added, and the solution was refluxed for 16 hr. The solution was then neutralized with 5 *N* NaOH and the tetrahydrofuran and ethanol were evaporated off, leaving an aqueous slurry which was extracted with methylene chloride. The methylene chloride extracts were concentrated, and the residue was dissolved in 25 ml. of benzene and applied to a column of 80 g. of Florisil slurried in cyclohexane. Elution with 1 l. of benzene gave 2.0 g. (95%) of triphenylcarbinol, and elution with 1 l. of ethyl acetate gave 2.5 g. (96%) of 1,4-anhydro-2,3-di-*O*-benzyl-DL-xylitol. A portion of this compound (1.8 g.) was converted to the 5-*O*-*p*-tolylsulfonyl derivative, which was crystallized from 30 ml. of ethanol to give 1.9 g. (70%) of crystals, m.p. 108–110°. After three recrystallizations from alcohol the material melted at 114–116°.

Anal. Calcd. for $C_{26}H_{28}O_6S$ (468.57): C, 66.64; H, 5.95; S, 6.84. Found: C, 66.63; H, 6.16; S, 6.40.

1,4-Anhydro-2,3-di-*O*-benzyl-5-*O*-*p*-tolylsulfonyl-DL-ribitol.—This compound was synthesized from 1,4-anhydro-DL-ribitol *via* the same series of reactions described in the preparation of the corresponding 1,4-anhydro-DL-xylitol derivative. The material was crystallized from ethanol and melted at 75–77°.

Anal. Calcd. for $C_{26}H_{28}O_6S$ (468.57): C, 66.64; H, 5.95; S, 6.84. Found: C, 66.59; H, 6.19; S, 6.71.

1,4-Anhydro-2,3-di-*O*-benzyl-5-*O*-*p*-tolylsulfonyl-L-arabinitol was prepared *via* the same series of reactions described for the synthesis of 1,4-anhydro-5-*O*-*p*-tolylsulfonyl-DL-ribitol. The product had the same infrared spectrum and melting point as the enantiomer obtained by refluxing 2,3,4-tri-*O*-benzyl-1,5-di-*O*-*p*-tolylsulfonyl-D-arabinitol in ethanol and had $[\alpha]^{25}D$ −23.8° (*c* 4.0, acetone).

1,4-Anhydro-5-*O*-*p*-tolylsulfonyl-D-arabinitol.—Palladium chloride (3 g. of 10% palladium chloride on charcoal) in 30 ml. of ethyl acetate was hydrogenated at room temperature and atmospheric pressure for 30 min. at which time it was filtered and thoroughly washed with ethyl acetate to remove hydrogen chloride. The catalyst was then rehydrogenated in 30 ml. of ethyl acetate and 1.00 g. of 1,4-anhydro-2,3-di-*O*-benzyl-5-*O*-*p*-tolylsulfonyl-D-arabinitol was added. After 30 min. the hydrogenation was complete. The catalyst was removed by filtration through Celite and the filtrate was concentrated to give 0.53 g. (86%) of crystals, which were recrystallized from benzene to yield 0.49 g. (80%) of crystals, m.p. 107–108°, $[\alpha]^{24}D$ +32.5° (*c* 4.0, acetone). The compound consumed 1 mole equiv. of periodate.

Anal. Calcd. for $C_{12}H_{16}O_6S$ (288.33): C, 49.99; H, 5.59; S, 11.12. Found: C, 50.06; H, 5.41; S, 10.95.

Behavior of 1,5-Di-*O*-*p*-tolylsulfonyl-2,3,4-tri-*O*-benzylribitol in Refluxing Ethanol.—A solution of 1 g. (1.37 mmoles) of the di-*p*-tolylsulfonyl ester in 50 ml. of 95% ethanol was refluxed for 24 hr. Titration with 1 *N* sodium hydroxide demonstrated the presence of 1.35 mequiv. of acid. The solution was concentrated and the residue was taken up in 25 ml. of methylene chloride. The methylene chloride solution was extracted with water, dried over sodium sulfate, filtered, and concentrated to give a sirup which when dissolved in 10 ml. of ethanol deposited 0.52 g. (81%) of crystals, m.p. 75–77°, whose infrared spectrum was identical with that of 1,4-anhydro-2,3-di-*O*-benzyl-5-*O*-*p*-tolylsulfonyl-DL-ribitol prepared from 1,4-anhydro-DL-ribitol.

Behavior of 1,5-Di-*O*-*p*-tolylsulfonyl-2,3,4-tri-*O*-benzylxylitol in Refluxing Ethanol.—This compound was refluxed with 95% ethanol for 24 hr., and the decomposition product was isolated in the manner described for the corresponding ribitol derivative. The infrared spectrum and melting point of the crystalline material, which was obtained in 85% yield, were identical with those 2,3-di-*O*-benzyl-5-*O*-*p*-tolylsulfonyl-1,4-anhyro-DL-xylitol which was synthesized from 1,4-anhydro-DL-xylitol.

Behavior of 1,5-Di-*O*-*p*-tolylsulfonyl-2,3,4-tri-*O*-benzyl-D-arabinitol in Aqueous Ethanol.—To a mixture of 10 ml. of water and 50 ml. of ethanol was added 2.25 g. of 1,5-di-*O*-*p*-tolylsulfonyl-2,3,4-tri-*O*-benzyl-D-arabinitol, and the resulting solution was refluxed 24 hr. The solution was then neutralized with sodium hydroxide and extracted with three 50-ml. portions of methylene chloride. The methylene chloride extract was dried over sodium sulfate and concentrated to a crystalline mass, which when recrystallized from ether–petroleum ether (b.p. 60–68°) yielded 1.1 g. (76%) of crystals, m.p. 73–74°. The melting point was raised to 74–75° by two recrystallizations from ether–petroleum ether and the material had $[\alpha]^{25}D$ +23.6° (*c* 4.0, acetone). This compound had the same infrared spectrum, melting point, and magnitude of rotation as 1,4-anhydro-2,3-di-*O*-benzyl-5-*O*-*p*-tolylsulfonyl-L-arabinitol {m.p. 73–74, $[\alpha]^{25}D$ −23.8 (*c* 4.0, acetone)}.

Anal. Calcd. for $C_{26}H_{28}O_6S$ (468.5): C, 66.65; H, 6.02; S, 6.84. Found: C, 66.37; H, 5.82; S, 6.65.

Behavior of the 1,4-Anhydro-2,3-di-*O*-benzyl-5-*O*-*p*-tolylsulfonylpentitols in Refluxing Ethanol.—These compounds could be quantitatively recovered after refluxing in 95% ethanol for 48 hr.

Behavior of 4-*O*-Benzyl-1-*O*-*p*-tolylsulfonyl-1,4-pentanediol in Refluxing 95% Ethanol.—A solution of the *p*-tolylsulfonyl ester (1.1 g.) in 50 ml. of 95% ethanol was refluxed for 24 hr. and was then concentrated. The residue was dissolved in 25 ml. of methylene chloride and the resulting solution was washed with saturated aqueous sodium bicarbonate and water. The methylene chloride solution was then dried over sodium sulfate, filtered, and concentrated to give a residue (425 mg., 92%), whose infrared spectrum was identical with that of an authentic sample of benzyl ethyl ether. Also, the material could not be separated from benzyl ethyl ether by gas chromatography on Chromosorb W coated with Apiezon L at 150°.

Behavior of 4-*O*-Benzyl-1-*O*-*p*-tolylsulfonyl-1,4-pentanediol in Refluxing 60% Ethanol.—This experiment was performed in the same manner as the preceding experiment with the exception that 60% ethanol was used instead of 95% ethanol. The product obtained was shown by infrared spectroscopy and gas chromatography to be benzyl alcohol.

Behavior of Benzyl *p*-Toluenesulfonate in Refluxing 95% Ethanol.—To accurately weighed samples of benzyl *p*-toluenesulfonate (approximately 100 mg.) in flasks warmed to 50° was added approximately 20 ml. of boiling 95% ethanol and the solutions were heated on a hot plate. Dissolution of the sample and return to reflux took place in 10 sec. The samples were refluxed for varying lengths of time and then cooled in an ice–calcium chloride bath (−20°) and titrated rapidly with 0.035 *N* sodium hydroxide. The infinity (1 hr.) titer indicated that 1 mole of acid was released per 265 g. of ester (theory, 262). Benzyl ethyl ether was isolated in 80% yield and identified by infrared spectroscopy and gas chromatography.

Determination of the Kinetics of the Benzyloxy-Induced Intramolecular *p*-Tolylsulfonyloxy Displacement Reaction.—To 20 ml. of refluxing solvent was added 6.84 mmoles of the compound under investigation. At appropriate time intervals 2-ml. aliquots were removed and cooled in an ice bath. Water (5 ml.) was added to the aliquot, and it was then titrated to the phenolphthalein end point with 0.0100 *N* sodium hydroxide.