solution was treated with solid sodium carbonate to bring the pH to 7.9. After further buffering the solution by the addition of sodium bicarbonate (3.0 g.), benzoyl chloride (9.0 g., 0.064 mole) was added in small portions over a 60-hr. period at room temperature while stirring vigorously. During this period a pH of approximately 8 was maintained by the addition of sodium carbonate as needed.

The supernatant solution was decanted from the gummy solid which had formed. This gummy residue was washed with benzene, and the major portion of it which was soluble in warm water was recombined with the aqueous supernatant. After acidification to pH 3.5, the aqueous solution was extracted six times with 300-ml. volumes of ether. It was then readjusted to pH 6 and subjected to a continuous extraction with ethyl acetate.

The white, powdery, crystalline material (5.83 g., m.p. 171–175°) recovered was recrystallized three times from absolute ethanol and dried for 10 hr. at 100° (1 mm.) to yield XI, m.p. 179–181°; $[\alpha]^{22}D$ −58.9° (*c*, 1.5 in water); λ_{max}^{alc} 226 mμ (11,500); λ_{max}^{Nujol} 2.90 (sh., m), 3.00 (s), 6.13 (s), 6.53 (s) μ.

Anal. Calcd. for $C_{13}H_{17}O_5N$ (267.3): C, 58.42; H, 6.41; N, 5.24. Found: C, 58.59; H, 6.39; N, 5.60.

This compound reduced Fehling's solution and consumed 0.93 mole of periodate in two hours.

N-Benzoylmycosaminol (XII).—To a solution of N-benzoylmycosamine (5.25 g.) in water (330 ml.), prepared by heating at 60° and then quickly recooling to room temperature, a solution of sodium borohydride (1.82 g.) in water (45 ml.) was added with stirring over a 10-min. period. The reaction mixture was kept at room temperature for 5.5 hr., and the pH was then adjusted to 5 with 10% acetic acid. This solution was passed through a column (4 × 30 cm.) of MB-3 ion exchange resin.[18]

A large volume of water (5 l.) was used to elute the product from the column, and the resulting solution was brought to dryness *in vacuo*. Any boric acid remaining was removed from the residue by repeated addition and evaporation of absolute methanol. Crystallization of the residue (4.2 g.) from methanol–ether yielded XII, m.p. 125.5–127°; $[\alpha]^{24}D$ +39° (*c*, 1.5 in water).

Anal. Calcd. for $C_{13}H_{19}O_5N$ (269.3): C, 57.98; H, 7.11; N, 5.20. Found: C, 58.11; H, 7.16; N, 4.97.

β-Ethylthio-N-benzoylmycosaminide.—N-Benzoylmycosamine (300 mg., m.p. 176–179°) was dissolved in fuming hydrochloric acid (2 ml.) at 0°, and after the addition of ethanethiol (1.4 ml.), the reaction mixture was stirred vigorously at 0° for 16 hr. Lead carbonate was added until the supernatant was neutral. The solids were removed by filtration and washed with ethanol. Evaporation of the filtrate and washings gave a residue (*ca.* 350 mg.), the methanolic solution of which on chilling deposited crystals. These were recrystallized from methanol, 50 mg., m.p. 248–250° dec.; $[\alpha]^{23}D$ −57° (*c*, 0.7 in water).

Anal. Calcd. for $C_{15}H_{21}O_4NS$ (311.4): S, 10.30; N, 4.49. Found: S, 10.09; N, 4.42.

No other crystalline products could be isolated from the original mother liquor.

Isopropylthio-N-benzoylmycosaminide.—This compound was prepared from N-benzoylmycosamine (300 mg., m.p. 176–179°) and propanethiol-2 in the same way as described above for the ethyl thioglycoside. The crude partially crystalline product was recrystallized from methanol and then ethanol; 100 mg., m.p. 230.5–232°, $[\alpha]D$ −99° (*c*, 0.5 in methanol).

Anal. Calcd. for $C_{16}H_{23}O_4NS$ (325.4): C, 59.05; H, 7.12; S, 9.86. Found: C, 59.33; H, 7.35; S, 10.15.

Acknowedgment.—The authors are indebted to Mr. J. F. Alicino and his associates for the microanalyses, and to Dr. N. Coy and her associates for the spectral determinations reported in this paper.

(18) A mixed bed resin obtained from Rohm & Haas Co., Philadelphia, Pa.

The Mechanism of Cyclic Anhydride Formation from Mono-*O*-tolylsulfonyl Tetritols[1,2]

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Under mild basic conditions, displacement of a tolylsulfonate anion from a tolylsulfonyl ester having hydroxyl groups both α and γ to the ester function proceeds preferentially by direct attack of the γ hydroxyl group with formation of a tetrahydrofuran ring. That an epoxide, which could be formed by a displacement involving the α hydroxyl group, is not an intermediate in the formation of the tetrahydrofuran ring is demonstrated by the fact that 1,2-epoxy-4-butanol gives only 1,2,4 butanetriol upon treatment with dilute base. 2-*O*-Tolylsulfonyl-L-erythritol gives only L-threitol and 2-*O*-tolylsulfonyl-D-threitol gives only erythritol. The synthesis of a number of derivatives of the tetritols is described.

The base-catalyzed displacement of *p*-tolylsulfonate anions from *p*-tolylsulfonyl esters by suitably situated hydroxyl groups in the same molecule leads to the formation of cyclic ethers. It has been demonstrated that tetrahydrofuran derivatives[3,5] as well as epoxides[3,4] can be formed directly and that 1,2-epoxides can undergo rearrangements to form tetrahydrofuran derivatives when a hydroxyl group is present at C-5 in a suitable steric position.[3,4]

The present study was designed to determine whether, in a system where there are free hydroxyl groups both α and γ to a tolylsulfonyl ester, the base-catalyzed displacement would preferentially involve the α hydroxyl group, and whether a 1,2-epoxide can undergo rearrangement with a C-4 hydroxyl group. To this end the 1- and 2-tolylsulfonyl esters of erythritol and threitol, and 2-*O*-*p*-tolylsulfonyl-1,2,4-butanetriol were prepared and their base catalyzed reactions studied.

1-*O*-Tolylsulfonyl-D-erythritol (I) was prepared by monotolylsulfonation followed by acid-catalyzed hydrolysis of 1,3-*O*-ethylidene-L-erythritol (II). The product contained approximately 35% of erythritol (III) as well as the desired monotolylsulfonyl ester, as could be demonstrated by paper chromatography. Attempts to purify it by paper column chromatography[6] gave a product which was contaminated by *p*-toluensulfonic acid and which, when attempts were made to isolate it from the column eluate, was largely decomposed to erythritol. The *p*-tolylsulfonyl ester component I which was present in the hydrolysate in ap-

(1) Taken in part from the M.S. thesis of F. C. Hartman, submitted to the Graduate Council of the University of Tennessee, September, 1962.

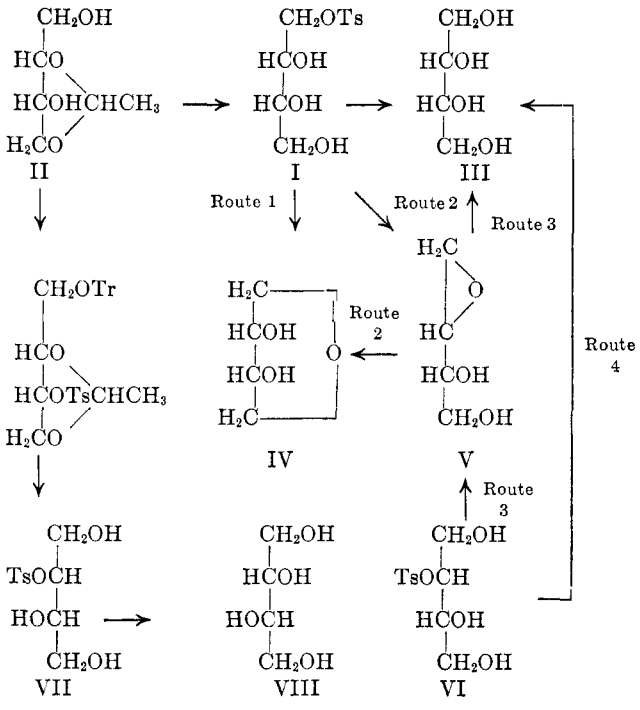
(2) Acknowledgment is made of support from the Atlas Powder Company, Wilmington, Del., and the Department of Health, Education, and Welfare, National Institutes of Health, Public Health Service, Bethesda 14, Md., (grant no. RG 9021).

(3) H. Ohle and H. Wilcke, *Ber.*, **71B**, 2316 (1938).

(4) L. von Vargha, *ibid.*, **68B**, 1377 (1935).

(5) L. F. Wiggins, *J. Chem. Soc.*, 1403 (1947).

(6) Chromax-column, LKB-Produkter, Stockholm, Sweden.



proximately 65% yield was demonstrated to yield only 1,4-anhydroerythritol (IV) on treatment with base in the following fashion. A sample was subjected to paper chromatography on a large sheet of Whatman I paper as if for two-dimensional chromatography. After development in the first direction the zone containing the separated components was sprayed with aqueous sodium hydroxide. When dry, the chromatogram was irrigated in the second direction and the spots developed. The *p*-tolylsulfonyl ester (R_f 0.46) had been quantitatively converted to a rapidly moving component identical in R_f (0.46) to IV. To demonstrate that the identity of R_f values obtained for the components before and after basic hydrolysis was fortuitous, samples of the crude tolylsulfonyl ester I were subjected to acidic hydrolysis before and after basic hydrolysis. After basic hydrolysis the acid treatment had no effect on the proportions of erythritol and the component with R_f 0.46. Acidic conditions, however, converted the *p*-tolylsulfonyl ester to erythritol which was the only polyol component present after 24 hr at 100° in 50% acetic acid. Basic hydrolysis of the crude 1-*O*-*p*-tolylsulfonyl-D-erythritol when carried out on a preparative scale gave a 60% yield of 1,4-anhydroerythritol (IV) characterized as the di-*O*-*p*-nitrobenzoate.

There are two possible routes for the formation of IV from 1-*O*-*p*-tolylsulfonyl-D-erythritol by a displacement reaction. The simplest is the direct displacement of the *p*-tolylsulfonate anion by the C-4 hydroxyl (route 1); the second involves the intermediate formation of 1,2-anhydro-D-erythritol (V) and its subsequent rearrangement to give the more stable tetrahydrofuran (route 2). If the latter mechanism is operative, then IV should be obtainable from 2-*O*-*p*-tolylsulfonyl-D-threitol (VI) which should give the same epoxide intermediate (V). Similarly 2-*O*-*p*-tolylsulfonyl-L-erythritol (VII) should give 1,2-anhydro-L-threitol which should rearrange to 1,4-anhydro-L-threitol.

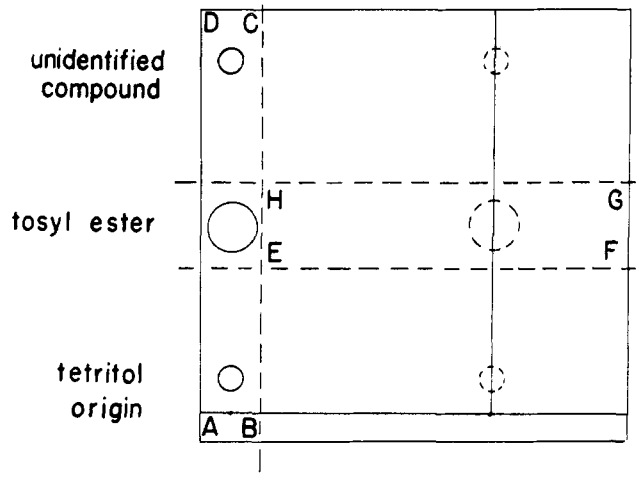


Fig. 1.—Chromatography of the acid hydrolysate of 2,4-*O*-ethylidene-3-*O*-tolylsulfonyl-1-*O*-trityl-D-erythritol; ABCD cut off and components detected; EFGH cut off and subjected to electrophoresis.

To test the above hypothesis 2-*O*-*p*-tolylsulfonyl-L-erythritol (VII) was prepared from 1,3-*O*-ethylidene-L-erythritol by tritylation and tolylsulfonylation followed by acid hydrolysis of the blocking groups. The product obtained was not pure; it contained erythritol, a component of R_t 0.41, which was demonstrated to be a tolylsulfonyl ester, and a component R_t 0.95 which was not identified. Utilizing the same technique as was applied to 1-*O*-tolylsulfonyl-D-erythritol the tolylsulfonyl ester present in this hydrolysis mixture was shown to give only a tetritol on basic hydrolysis. That this tetritol was, in fact, threitol (VIII) was demonstrated as follows: samples were chromatographed on a large sheet of Whatman 3-mm. paper. One spot was placed at the edge and another at the center of the paper on a line 2.5 in. from one side. After development of the chromatogram, a strip was cut from the side so as to contain the separated components of the sample applied to the side of the paper. This was sprayed with periodate–benzidine[7] to locate the separated zones. Using this guide a strip parallel to the solvent front was cut from the chromatogram so as to contain the tolylsulfonyl ester component. The strip was subjected to electrophoresis in arsenite buffer at pH 9.6.[8] This pH is sufficient to hydrolyze rapidly the *p*-tolylsulfonyl ester. A control containing III and VIII was applied. Threitol migrates twice as far from the point of application as does erythritol and no difficulty was experienced in determining that the tetritol obtained from 2-*O*-*p*-tolylsulfonyl-L-erythritol (VII) was threitol.

An analogous series of experiments was performed on 2-*O*-*p*-tolylsulfonyl-D-threitol (VI) which was shown to be quantitatively converted to erythritol (III).

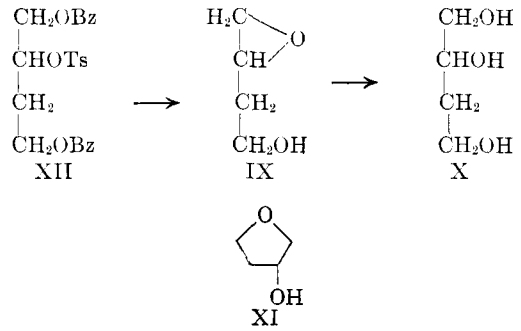
Since it is possible to rationalize the formation of a tetritol from its epimeric 2-tolylsulfonyl ester by a direct intermolecular reaction (SN2) of the latter with a hydroxyl ion, several attempts were made to obtain pure samples of the 2-tolylsulfonyl esters of both threitol and erythritol. It would be possible to discriminate between an initial intermolecular reaction

(7) M. Viscontini, D. Hoch, and P. Karrer, *Helv. Chim. Acta*, **38**, 642 (1955).

(8) J. L. Frahn and J. A. Mill, *Australian J. Chem.* **12**, 65 (1959).

and an initial intramolecular reaction leading to an epoxide by determining the product of the reaction of the ester with methoxide ion. If intramolecular reaction occurs first, *i.e.*, epoxide formation (route 3) the product would be a 1-*O*-methyltetritol; if intermolecular reaction occurs first (route 4) the product would be a 2-*O*-methyltetritol.

None of the approaches used gave a 2-tolylsulfonyl ester appreciably purer than that obtained from the hydrolysis reaction. For this reason the previously described[9] 1,2-epoxy-4-butanol (IX) was prepared and its base-catalyzed reactions were studied. Treatment of this epoxide under the conditions used for the hydrolysis of the tolylsulfonyl esters gave 1,2,4-butanetriol (X) as the only detectable product. No 3-hydroxytetrahydrofuran (XI) could be detected.



From this finding we conclude that a 1,2-epoxide cannot undergo a base-catalyzed rearrangement involving a hydroxyl group in the 4 position of the system with the formation of a tetrahydrofuran ring. In the base-catalyzed displacement of a tolylsulfonylate anion from a 1-*O*-tolylsulfonyltetritol the tetrahydrofuran ring must be formed by direct attack of the oxygen of the C-4 hydroxyl groups (route 1) on the carbon bearing the ester and not by attack of the C-2 hydroxyl group and subsequent rearrangement.

Although no direct evidence was obtained, it is probable that the base-catalyzed hydrolysis of the 2-*O*-*p*-tolylsulfonyltetritols proceeds by two steps, the first step being the formation of an epoxide and the second the opening of this epoxide by a hydroxyl ion to give a tetritol. This is deduced from the finding that 1,2 epoxy-4-butanol (IX) could be obtained in very good yield from 1,4-di-*O*-benzoyl-2-*O*-*p*-tolylsulfonyl-1,2,4-butanetriol (XII) by treatment of a methanol solution of the latter with sodium methylate. The two situations are clearly analogous.

Experimental[10]

4,6-*O*-Ethylidene-D-glucose.—4,6-*O*-Ethylidene-D-glucose was prepared by the method of Barker and MacDonald,[11] modified to facilitate the synthesis of larger quantities. A mixture of 900 g. of D-glucose and 810 ml. of paraldehyde containing 6 ml. of concentrated sulfuric acid was ground in a ball mill at room temperature for 72 hr. The reaction mixture was washed into a 3-l. erlenmeyer flask using approximately 1 l. of methanol and then neutralized with 1 *N* ethanolic potassium hydroxide (300 ml.). The slurry was heated to boiling while maintaining the pH at approximately 6.0 by the addition of 1 *N* ethanolic potassium hydroxide and the slightly turbid solution was filtered with suction through a layer of Celite. On standing for 6 hr. the filtrate deposited 720 g. of crystals, m.p. 178–181°, identical with that reported.[11] The filtrate was concentrated at 50° to a thick sirup which was taken up in 500 ml. of ethanol. After keeping the solution at 4° for 12 hr., 361 g. of the same material, m.p. 179–181°, was obtained; total yield 1081 g. (87%).

2,4-*O*-Ethylidene-1-*O*-*p*-tolylsulfonyl-D-erythritol.—To a well stirred solution of 1,3-*O*-ethylidene-L-erythritol[11] (40 g.) in 80 ml. pyridine at 0° was added 60 g. of *p*-toluenesulfonyl chloride in 50 ml. of dry pyridine so as to maintain a temperature of 0°. After 8 hr. at 0°, ice was added and then methylene chloride. The methylene chloride solution was extracted successively with ice-cold 1 *N* sulfuric acid, saturated sodium bicarbonate and water, dried over sodium sulfate, and concentrated to give 79 g. (95%) of a sirup.

A sample of this sirup was converted in 90% yield to 2,4-*O*-ethylidene-3-*O*-*p*-nitrobenzoyl-1-*O*-*p*-tolylsulfonyl-D-erythritol by treatment with an excess of *p*-nitrobenzoyl chloride in methylene chloride–pyridine solution. The product after three crystallizations from ethyl alcohol had m.p. 126–127° and $[\alpha]^{24}D$ −86.3° (*c* 4.0, chloroform).

Anal. Calcd. for $C_{20}H_{21}NO_9S$ (451.4): C, 53.21; H, 4.68. Found: C, 53.02; H, 4.79.

1-*O*-*p*-Tolylsulfonyl-D-erythritol.—A solution of 50 g. of 2,4-*O*-ethylidene-1-*O*-*p*-tolylsulfonyl-D-erythritol in 500 ml. of 50% aqueous acetic acid was boiled gently and the distillate collected and tested at intervals for the presence of acetaldehyde. Boiling was continued until there was no acetaldehyde in the distillate. Concentration of the solution gave 45.2 g. of sirup which was shown by paper chromatography to be approximately 35% erythritol R_f 0.09, and 65% of a material R_f 0.46 which was demonstrated to be a *p*-tolylsulfonyl ester as described in the introduction to this report. It was readily hydrolyzed by acid to to give erythritol.

1,4-Anhydroerythritol.—A solution of 35 g. of the impure 1-*O*-*p*-tolylsulfonyl-D-erythritol in 100 ml. of water was passed through a column of 175 ml. of IR 45 (OH^-),[12] and the resin was washed with water until the eluent gave a negative test with periodate–benzidine.[7] Concentration of the eluent gave 14 g. of sirup which was distilled *in vacuo* at 0.3 mm. The fraction (8.8 g., 52%) which distilled at 94–98° was chromatographically identical to 1,4-anhydroerythritol, R_f 0.46, and was characterized as the di-*O*-*p*-nitrobenzoyl derivative[13] which was obtained in a 90% yield; m.p. 173–174°.

Anal. Calcd. for $C_{18}H_{15}N_2O_9$ (402.3): C, 53.73; H, 3.51. Found: C, 53.78; H, 3.43.

The residue from the distillation was dissolved in 25 ml. of ethanol, decolorized with charcoal, filtered through Celite, concentrated to 10 ml., and seeded with erythritol. After keeping the solution overnight at 4°, 2.8 g. (15%) of erythritol was deposited, which was characterized by melting point, mixed melting point, and infrared spectrum.

It was demonstrated by two-dimensional chromatography of the acid hydrolysate of 2,4-*O*-ethylidene-1-*O*-*p*-tolylsulfonyl-D-erythritol that 1-*O*-*p*-tolylsulfonyl-D-erythritol gives only 1,4-anhydroerythritol on basic hydrolysis. (See preceding text.)

2,4-*O*-Ethylidene-1-*O*-trityl-D-erythritol.—To a solution of 5 g. of 1,3-*O*-ethylidene-L-erythritol in 50 ml. of dry pyridine was added 9.75 g. of triphenylchloromethane, and after the reaction had remained at room temperature for 24 hr., the excess triphenylchloromethane was hydrolyzed by adding a few chips of ice. The reaction mixture was concentrated to a sirup which was taken up in 100 ml. of methylene chloride, and the solution was washed in the usual manner and concentrated to give 13 g. of a sirup which was dissolved in 100 ml. of hot cyclohexane. On cooling the solution, 11.5 g. (88%) of crystals, m.p. 136.5–137.5°, was deposited. Three recrystallizations from cyclohexane raised the m.p. to 142–143° which was unchanged by additional recrystallizations. $[\alpha]^{24}D$ +35.7° (*c* 4.0, chloroform).

Anal. Calcd. for $C_{25}H_{26}O_4$ (390.5): C, 76.88; H, 6.71. Found: C, 77.03; H, 6.82.

2,4-*O*-Ethylidene-3-*O*-*p*-tolylsulfonyl-1-*O*-trityl-D-erythritol.—A solution of 5 g. of *p*-toluenesulfonylchloride in 10 ml. of dry pyridine was added to an ice-cold solution of 8 g. of 2,4-*O*-

(9) H. B. Henbest and B. Nichols, *J. Chem. Soc.*, **4608** (1957).

(10) Melting points are corrected. Analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn. Evaporations were performed at water-aspirator pressure. Descending paper chromatography was carried out on Whatman 31 paper using butanone–water (92:8 vol./vol.). Periodate–benzidine[7] sprays were used to locate the spots on the developed chromatograms.

(11) R. Baker and D. L. MacDonald, *J. Am. Chem. Soc.*, **82**, 2301 (1960).

(12) Rohm & Haas Co., Philadelphia, Pa.

(13) H. Klosterman and F. Smith, *J. Am. Chem. Soc.*, **74**, 5336 (1952).

ethylidene-1-*O*-trityl-D-erythritol in 25 ml. of dry pyridine. After standing for 48 hr. at room temperature, the reaction was washed in the usual manner. Crystallization was effected by dissolving the product in 20 ml. of methylene chloride, adding 100 ml. of ethyl alcohol, and boiling off the methylene chloride; 10.2 g. (95%) of crystals, m.p. 169–171°, was obtained. Four further recrystallizations from the same solvent raised the m.p. to 179.5–181°, which was unchanged by additional recrystallization. $[\alpha]^{24}D$ −36.2° (*c* 4.0, chloroform).

Anal. Calcd. for $C_{32}H_{32}O_6S$ (544.6): C, 70.57; H, 5.92. Found: C, 70.50; H, 5.77.

2-*O*-*p*-Tolylsulfonyl-L-erythritol.—2,4-*O*-Ethylidene-3-*O*-tolylsulfonyl-1-*O*-trityl-D-erythritol (3 g.) was refluxed with 200 ml. of 75% aqueous acetic acid for 3 hr.; the solution was concentrated at 40°, and the residue was dried over sodium hydroxide at 0.1 mm. pressure for 24 hr. The residue was extracted at room temperature with three 50-ml. portions of water, and the extracts were concentrated at 40° to give 1.5 g. of a sirup which was shown by chromatography to contain three components: a tetritol, R_f 0.09; the presumed 2-*O*-*p*-tolylsulfonyl-L-erythritol, R_f 0.41; and an unidentified component, R_f 0.95.

Basic Hydrolysis of the Presumed 2-*O*-*p*-Tolylsulfonyl-L-erythritol.—The mixture from the acid hydrolysis of 2,4-*O*-ethylidene-3-*O*-*p*-tolylsulfonyl-D-erythritol was subjected to two-dimensional chromatography. After development in one direction, the dried chromatogram was sprayed with 0.01 *N* sodium hydroxide in the zone containing the separated components of the mixture, redried, and developed in the second direction. By this method it was demonstrated that the 2-*O*-*p*-tolylsulfonyl-L-erythritol (R_f 0.41) gave only a tetritol (R_f 0.09) on basic hydrolysis.

The tetritol from the basic hydrolysis of 2-*O*-*p*-tolylsulfonyl-L-erythritol was demonstrated to be threitol by the following method (Fig. 1). Samples of the mixed tolylsulfonyl esters were applied to the center and one side of one edge of a 46 × 57 cm. sheet of Whatman 3-mm. paper, and the paper was developed with water-saturated butanone. The strip that contained the separated components of the sample which had been applied at the side of the paper was cut off, and the components were made visible with periodate–benzidine sprays.[7] The position of 2-*O*-*p*-tolylsulfonyl-L-erythritol in the center of the paper was determined using the strip which had been sprayed, and a 10-cm. strip containing it was cut out perpendicular to the direction of solvent flow. A standard sample containing erythritol, D-threitol, 1,4-anhydroerythritol, and 1,4-anhydro-D-threitol was applied near one edge in the same region as the 2-*O*-*p*-tolylsulfonyl compound, and the strip was dampened with 0.2 *M* arsenite buffer, pH 9.6,[8] and subjected to electrophoresis for 2 hr. at 1500 v. and 25 ma. The tolylsulfonyl compound was rapidly hydrolyzed at this pH. After drying the paper for 15 min. at 80°, the spots were located with periodate–benzidine.[7]

Under these conditions the migration of the various compounds is as follows: 1,4-anhydro-D-threitol, 0 cm./hr.; threitol, 2.3 cm./hr.; 1,4 anhydroerythritol, 4.6 cm./hr.; and erythritol, 1.3 cm./hr.

2,4-*O*-Ethylidene-D-threose.—A solution of 40 g. of 4,6-*O*-ethylidene-D-galactose[14] was oxidized with sodium metaperiodate as previously described for 4,6-*O*-ethylidene-D-glucose.[11] The product was extracted from the dried reaction residue with four 300-ml. portions of hot acetone. The volume of the acetone solution was reduced to 100 ml. and 100 ml. of ether was added causing the deposition of 26 g. (89%) of crystals, m.p. 162–164°. After four recrystallizations from acetone, the material (23.8 g.) melted at 172–173°. The m.p. was unchanged by further recrystallizations. $[\alpha]^{24}D$ −10.7° (*c* 4.0, water). The compound had no absorption in the carbonyl region of the infrared and is therefore probably a dimer similar to that reported by Schaffer for 2,4-*O*-ethylidene-D-erythrose.[15]

Anal. Calcd. for $C_6H_{10}O_4$ (146.1): C, 49.31; H, 6.90. Found: C, 49.35; H, 6.80.

1,3-*O*-Ethylidene-L-threitol.—A solution of 1.0 g. of sodium borohydride in 50 ml. of 0.1 *N* sodium hydroxide was added dropwise during a 30-min. period to a well stirred solution of 20 g. of 2,4-*O*-ethylidene-D-threose in 100 ml. of water, the temperature being maintained below 20° with an ice bath. The solution was kept for 24 hr. at room temperature, neutralized with glacial acetic acid, concentrated to 50 ml., and passed through a column containing 100 ml. of IRA 400 (OH^-).[12] The eluent was neutralized with 1 *N* sulfuric acid and concentrated at 50°, and the residue was dried overnight at 0.1 mm. and extracted with three 200-ml. portions of hot acetone. Concentration of the extracts gave 18 g. (90%) of a thick, slightly yellow sirup which could not be induced to crystallize.

2,4-*O*-Ethylidene-1-*O*-*p*-tolylsulfonyl-D-threitol.—To an ice-cold solution of 14 g. of 1,3-*O*-ethylidene-L-threitol in 50 ml. of dry pyridine was added a solution of 19 g. of *p*-toluenesulfonyl chloride in 20 ml. of dry pyridine, and the reaction was left at 4° for 12 hr. The reaction mixture was then concentrated to a sirup which was dissolved in 200 ml. of methylene chloride, and the solution was washed in the usual manner. The methylene chloride layer was dried over sodium sulfate, filtered, and concentrated to give 24.2 g. (85%) of a sirup which could not be crystallized. A crystalline 3,5-dinitrobenzoate was obtained, (87% from the sirup) which after two recrystallizations from ethyl alcohol melted at 118–120°. $[\alpha]^{24}D$ −36.0 (*c* 4.0, chloroform).

Anal. Calcd. for $C_{20}H_{21}N_2O_{11}S$ (497.4): C, 48.29; H, 4.25. Found: C, 48.41; H, 4.22.

1-*O*-*p*-Tolylsulfonyl-D-threitol.—The acid-catalyzed hydrolysis of 2,4-*O*-ethylidene-1-*O*-*p*-tolylsulfonyl-D-threitol (20 g.) was carried out in the same manner as described for 2,4-*O*-ethylidene-1-*O*-*p*-tolylsulfonyl-D-erythritol and gave 18 g. (99%) of sirup, which was shown by chromatography to be approximately 10% threitol, R_f 0.09, and 90% 1-*O*-*p*-tolylsulfonyl-D-threitol, R_f 0.46.

1,4-Anhydro-D-threitol.—A solution of 18 g. of 1-*O*-*p*-tolylsulfonyl-D-threitol in 50 ml. of water was passed over a column containing 100 ml. of IR 45 (OH^-),[12] and the resin was washed with water until the eluent gave a negative test with periodate–benzidine.[7] Concentration of the eluent gave 6.2 g. of sirup which on vacuum distillation at 0.03 mm. gave 4.1 g. (60%) of chromatographically pure 1,4-anhydro-D-threitol, R_f 0.46, which gave a 90% yield of the di-*O*-*p*-nitrobenzoyl derivative. After three recrystallizations from acetone the derivative had m.p. 191–192° and $[\alpha]^{24}D$ −115.0° (*c* 4.0, chloroform). Klosterman and Smith reported the m.p. of 1,4-anhydro-L-threitol di-*p*-nitrobenzoate as 191–192°.[13]

Anal. Calcd. for $C_{18}H_{14}N_2O_9$ (402.3): C, 53.73; H, 3.51. Found: C, 53.53; H, 3.61.

The residue from the distillation was dissolved in 10 ml. of isopropyl alcohol, decolorized with charcoal, filtered through Celite, and seeded with D-threitol. By storing at 4° overnight, 0.9 g. (11%) of D-threitol was obtained which was characterized by m.p., and infrared spectrum.

It was demonstrated by two-dimensional chromatography and chromatography followed by electrophoresis that the component designated above as 1-*O*-*p*-tolylsulfonyl-D-threitol gives only 1,4-anhydrothreitol on treatment with alkali and that the tetritol present in the acid-hydrolysis product from 2,4-*O*-ethylidene-1-*O*-*p*-tolylsulfonyl-D-threitol is threitol.

2,4-*O*-Ethylidene-1-*O*-trityl-D-threitol.—1,3-*O*-Ethylidene-L-threitol (3 g.) was treated with triphenylchloromethane (5.7 g.) in the same manner as described for 1,3-*O*-ethylidene-L-erythritol. Crystallization of the product from ether–petroleum ether (b.p. 30–60°) gave 5.5 g. (71%) of crystals, m.p. 118–120°. Three recrystallizations raised the m.p. to 128–129°, which was unchanged by additional recrystallization. $[\alpha]^{24}D$ −40.0° (*c* 0.6. chloroform).

Anal. Calcd. for $C_{25}H_{26}O_4$ (390.5): C, 76.88; H, 6.72. Found: C, 76.82; H, 6.92.

2,4-*O*-Ethylidene-3-*O*-*p*-tolylsulfonyl-1-*O*-trityl-D-threitol was prepared in the same manner as the corresponding erythritol derivative by treating 5 g. of 2,4-*O*-ethylidene-1-*O*-trityl-D-threitol with 3 g. of *p*-toluenesulfonyl chloride. Crystallization of the product from 100 ml. of isopropyl alcohol gave 5 g. (73%) of crystals, m.p. 141–144°, which after three recrystallizations from isopropyl alcohol melted at 144–145°. The melting point was unchanged by additional recrystallization. $[\alpha]^{24}D$ −39.7° (*c* 4.0, chloroform).

Anal. Calcd. for $C_{32}H_{32}O_6S$ (544.6): C, 70.57; H, 5.92. Found: C, 70.34; H, 6.07.

2-*O*-*p*-Tolylsulfonyl-D-threitol.—Acid hydrolysis of 2,4-*O*-ethylidene-3-*O*-*p*-tolylsulfonyl-1-*O*-trityl-D-threitol (3 g.), performed in the same manner as for the corresponding erythritol derivative, gave 1.4 g. of a sirup which was shown by chromatography to contain three components: a tetritol, R_f 0.09;

(14) D. H. Ball and J. K. N. Jones, *J. Chem. Soc.*, 905 (1958). The procedure was modified by the use of ethanolic potassium hydroxide in the place of ethanolic ammonia.

(15) R. Schaffer, *J. Am. Chem. Soc.* **81**, 2838 (1960).

2-*O*-*p*-tolylsulfonyl-D-threitol, R_f 0.41; and an unidentified component, R_f 0.95.

Basic Hydrolysis of the Presumed 2-*O*-*p*-Tolylsulfonyl-D-threitol.—Chromatography and electrophoresis of 2-*O*-*p*-tolylsulfonyl-D-threitol, performed in the same manner as for 2-*O*-*p*-tolylsulfonyl-L-erythritol, showed that basic hydrolysis of 2-*O*-*p*-tolylsulfonyl-D-threitol gave only erythritol.

1,4-Di-*O*-benzoyl-1,2,4-butanetriol.—A well stirred solution of 15 g. of 1,2,4-butanetriol[16] in 100 ml. of dry pyridine was cooled to −10° in a Dry-Ice bath, and 31.5 ml. of benzoyl chloride in 50 ml. of dry pyridine was added so as to maintain the temperature of the reaction mixture below 15°. When the addition was complete the reaction mixture was left at room temperature for 4 hr. and then concentrated to a sirup. The sirup was dissolved in methylene chloride and this solution washed in the usual fashion. After removal of the solvent, a sirup (45 g.) was obtained which crystallized spontaneously. After four recrystallizations from isopropyl ether the material (42 g.) melted at 70–71°.

Anal. Calcd. for $C_{18}H_{18}O_5$ (314.3): C, 68.78; H, 5.77. Found: C, 68.93; H, 5.82.

1,4-Di-*O*-benzoyl-2-*O*-*p*-tolylsulfonyl-1,2,4-butanetriol.—To a solution of 1,4-di-*O*-benzoylbutanetriol (42 g.) in 100 ml. of dry pyridine was added a solution of 30 g. of *p*-toluenesulfonyl chloride in 100 ml. of dry pyridine. The reaction was worked up after 8 hr. at room temperature to give 55 g. of a sirup which deposited 46.5 g. (73%) of crystals, m.p. 106–109°, from solution in 1.5 l. of ethanol. Three recrystallizations from ethanol raised the m.p. to 118–119.5°.

Anal. Calcd. for $C_{25}H_{24}O_7S$ (468.5): C, 64.09; H, 5.16. Found: C, 64.17; H, 5.26.

Basic Hydrolysis of 1,4-Di-*O*-benzoyl-2-*O*-*p*-tolylsulfonyl-1,2,4-butanetriol.—A solution of 10 g. of 1,4-di-*O*-benzoyl-2-*O*-*p*-tolylsulfonylbutanetriol in 100 ml. of 1 *N* sodium hydroxide was refluxed for 12 hr. concentrated to 50 ml., and passed through columns containing 100 ml. of IR 120 (H^+) and 200 ml. of IR 45(OH^-). The eluent was concentrated to give 2.27 g. (97.5%) of 1,2,4-butanetriol. A sample of this material was converted to the tri-*p*-nitrobenzoate in 84% yield.

1,2-Epoxy-4-butanol.—To an ice-cold solution of 10 g. of 1,4-di-*O*-benzoyl-2-*O*-*p*-tolylsulfonylbutanetriol in 75 ml. of dry chloroform was added 50 ml. of dry methanol and 10 ml. of freshly prepared 3.5 *N* sodium methoxide. After remaining 8 hr. at 10° the reaction mixture was neutralized by the addition of Dry Ice and concentrated to dryness at 25°. The residue was taken up in 100 ml. of chloroform, and the solution was filtered to remove the sodium *p*-toluenesulfonate (4.4 g.). The filtrate was concentrated, and the residue was taken up in 30 ml. of cyclohexane and applied to a Florisil[17] column prepared by packing a 55 × 4 cm. tube with a slurry of 70 g. of Florisil (100/200 mesh) in cyclohexane. Elution with 1 l. of cyclohexane gave 5.4 g. (93%) of methyl benzoate; elution with 500 ml. of benzene gave 0.3 g. of an unidentified compound; elution with 1 l. of ether gave 1.4 g. (74%) of 1,2-epoxy-4-butanol.

Anal. Calcd. for $C_4H_8O_2$ (88.0): C, 54.54; H, 9.09; epoxy (C_2H_4O), 50.00. Found: C, 54.52; H, 8.98; epoxy (C_2H_4O), 50.00.

The Action of Alkali on 1,2-Epoxy-4-butanol.—A solution of 1 g. of 1,2-epoxy-4-butanol in 20 ml. of 1 *N* sodium hydroxide was heated for 30 min. at 60° and passed through a column containing 30 ml. of IR 120(H^+).[12] The eluent was concentrated to give 1.18 g. (98%) of 1,2,4-butanetriol, which was converted to the tri-*p*-nitrobenzoate in 80% yield.

1,2,4-Tri-*O*-*p*-nitrobenzoylbutanetriol.—Prepared in the usual fashion (in 82% yield) from 1,2,4-butanetriol, was crystallized from acetone–ethanol (1:1) and melted at 101–102°.

Anal. Calcd. for $C_{25}H_{19}N_3O_{12}$ (553.4): C, 54.25; H, 3.46. Found: C, 54.10; H, 3.58.

(16) General Aniline and Film Corporation, New York 14, N. Y.

(17) Floridin Co., Tallahassee, Fla.

Nucleophilic Displacement Reactions of Halogenated Cyclobutenes[1]

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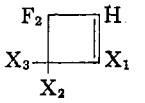
The nucleophilic displacement reactions of 3,3,4,4-tetrafluorocyclobutene (I), 1-chloro-3,3,4,4-tetrafluorocyclobutene (II), 1,4-dichloro-3,3,4-trifluorocyclobutene (III), and 1,4,4-trichloro-3,3-difluorocyclobutene (IVa) were carried out with ethanolic potassium hydroxide. I yielded 3-ethoxy-3,4,4-trifluorocyclobutene and 3,3-diethoxy-4,4-difluorocyclobutene (allylic substitution without rearrangement). II and III both gave identical rearranged products, 1-fluoro-2-chloro-3-ethoxy-4,4-difluorocyclobutene, and IVa yielded 1-chloro-3,3-difluoro-4,4-diethoxycyclobutene (allylic substitution).

Recent investigations concerning nucleophilic displacement reactions of halogenated cyclobutenes have shown that these cyclobutenes readily undergo reaction with nucleophilic reagents with and without rearrangement. In most studies,[2–6] the cyclobutenes possessed highly activated double bonds or groups attached thereon capable of stabilizing a charge. For this work, a series of halogenated cyclobutenes, namely 3,3,4,4-tetrafluoro-, 1-chloro-3,3,4,4-tetrafluoro-, 1,4-dichloro-3,3,4-trifluoro-, and 1,4,4-trichloro-3,3-difluorocyclobutene (I–IVa, respectively), were selected that contained neither highly activated double bonds nor charge stabilizing groups in a vinylic position.



I. $X_1 = H, X_2 = X_3 = F$
II. $X_1 = Cl, X_2 = X_3 = F$
III. $X_1 = X_2 = Cl, X_3 = F$
IVa. $X_1 = X_2 = X_3 = Cl$

These compounds were found to undergo interesting nucleophilic displacement reactions which include allylic rearrangement. The present paper describes this work, and specifically, the displacement reactions of I–IVa with ethanolic potassium hydroxide.

Discussion

The reactivity of the allylic halogens in the cyclobutenes I through IVa is demonstrated in their respective reactions with potassium hydroxide in ethanol. An exothermic reaction took place between I and one equivalent of the basic reagent with the immediate precipitation of potassium fluoride. The organic product isolated was a colorless liquid to which is assigned the structure 3-ethoxy-3,4,4-trifluorocyclobutene (V), resulting from direct displacement of

(1) This paper represents part of a thesis submitted by L. H. Wilson to the Graduate School, University of Colorado, in partial fulfillment of the requirements for the Ph.D. degree, June, 1961.

(2) J. D. Park, C. Snow, and J. R. Lacher, *J. Am. Chem. Soc.*, **73**, 2342 (1951).

(3) F. J. Lorenzi, Ph.D. thesis, University of Colorado, 1948.

(4) S. Cohen, Ph.D. thesis, University of Colorado, 1959.

(5) Y. Kitahara, M. C. Caserio, F. Scardiglia, and J. D. Roberts, *J. Am. Chem. Soc.*, **82**, 3106 (1960).

(6) E. F. Jenny and J. Drury, *ibid.*, **82**, 3111 (1960).