stirred slurry, 300 ml. of ethyl ether was added and stirring continued for 15 min. The precipitate was collected by filtration, washed with water until the washings were neutral to litmus, and air-dried at 25–30°. The product, m.p. 162–164°, was obtained in 45.3% yield. After recrystallization from ethyl alcohol, it melted at 165–166°.

Anal. Calcd. for $C_{10}H_8N_2S$: N, 14.88; S, 17.03. Found: N, 14.42; S, 16.93.

α,3-Dimethylthiazolo[3,2-*a*]benzimidazole-2-methanol (XI).—To a stirred solution containing 46.1 g. (0.2 mole) of V in 500 ml. of ethyl alcohol was added dropwise at 65–70° a solution containing 7.6 g. (0.2 mole) of sodium borohydride in 200 ml. of ethyl alcohol over a 30-min. period. The stirred reaction mixture was heated at 75–80° for 2 hr. After cooling to 25°, the reaction mixture was added to 2000 g. of ice–water and stirred at 0–10° for 1 hr. The solid was collected by filtration, washed with water until the washings were neutral to litmus, and air-dried at 25–30°. The product, m.p. 222–228°, was obtained in 86.5% yield. After recrystallization from dimethylformamide, it melted at 227–228°.

Anal. Calcd. for $C_{12}H_{12}N_2OS$: N, 12.06; S, 13.80. Found: N, 12.06, S, 14.12.

2-Acetyl-3-methylthiazolo[3,2-*a*]benzimidazole Oxime (XII).—A stirred slurry containing 46.1 g. (0.2 mole) of V and 500 ml. of ethyl alcohol was heated to 75°. To the cooled stirred solution at 25° was added in one portion 16.4 g. (0.25 mole) of hydroxylamine hydrochloride in 50 ml. of water. A solution containing 17.4 g. (0.125 mole) of potassium carbonate in 60 ml. of water was added dropwise at 25–30° over a 15-min. period. The stirred reaction mixture was heated at 75–80° for 2.5 hr. After cooling to 5°, the precipitate was collected by filtration, washed with water until the washings were neutral to litmus, and air-dried at 25–30°. The product, m.p. 230–234° dec., was obtained in 77% yield. After recrystallization from ethyl alcohol, it melted at 246–247° dec.

Anal. Calcd. for $C_{12}H_{11}N_3OS$: N, 17.13; S, 13.07. Found: N, 16.95; S, 13.16.

3-Methylthiazolo[3,2-*a*]benzimidazole-2-carboxanilide (XIII).—To a stirred slurry containing 34.9 g. (0.15 mole) of IX, 14.1 g. (0.15 mole) of aniline, and 200 ml. of chlorobenzene, 6.9 g. (0.05 mole) of phosphorus trichloride was added dropwise at 80–90° over a 5-min. period. The stirred reaction mixture was heated at 120–130° for 6 hr. After cooling to 25°, 500 ml. of water containing 40 g. (0.25 mole) of 25% aqueous sodium hydroxide was added and stirring was continued for 1 hr. The precipitate was collected by filtration, washed with water until the wash water was neutral to litmus, and air-dried at 25–30°. The product, m.p. 232–233° dec., was obtained in 64.2% yield. The melting point remained unchanged after recrystallization from dimethylformamide.

Anal. Calcd. for $C_{17}H_{13}N_3OS$: N, 13.67. Found: N, 13.40.

Acknowledgment.—The writers wish to acknowledge their indebtedness to R. O. Zerbe for assistance rendered during the course of this investigation.

The 1,4-Anhydrohexitols. Synthesis and Periodate Oxidation[1]

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Received October 29, 1963

The 1,4-anhydrohexitols are prepared from the pentoses by application of the nitromethane synthesis followed by reduction and deamination. The rate of "overoxidation" of the 1,4-anhydrohexitols by sodium metaperiodate depends on the rearrangement of the initially formed trialdehyde to a rapidly oxidized form which absorbs at 272 mμ.

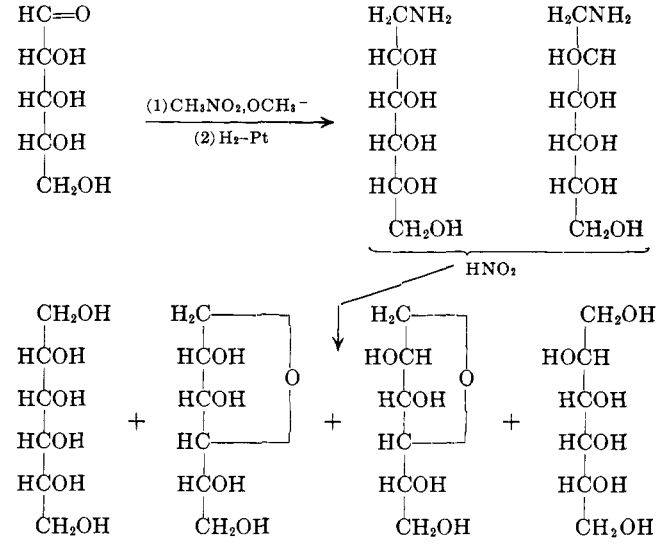
In connection with an investigation of the acid-catalyzed anhydrization of the alditols it was necessary to synthesize those 1,4-anhydrohexitols which are not described in the literature. Most methods of synthesis require the hexose, or a derivative thereof, as starting material and these are not all readily available.[2,3]

In the synthesis reported here, the pentoses, which are readily available, were used as starting materials and the following sequence of reactions was applied to them: pentose → 2-epimeric sodio *aci*-nitro alcohols[4] → 2-epimeric hexitylamines → 2-epimeric hexitols + 2-epimeric 1,4-anhydrohexitols.

The reactions were carried out on D-ribose, D-arabinose, D-lyxose, and D-xylose. In Scheme I the sequence is illustrated using D-ribose as an example.

Paper column chromatography[5] using butanone–water as solvent in all cases gave a fractionation of the products into at least three components. The fastest moving component was an impurity identified as a 1-deoxy-1-(methylnitrosoamino)pentitol.[6] The second and third fractions were the two epimeric 1,4-anhydro-

SCHEME I



hexitols, and the slowest moving component was a mixture of the two epimeric alditols. The 1,4-anhydroalditols from lyxose and xylose were not well-resolved on the column and were separated *via* the isopropylidene derivatives. In all cases one of the pair had *cis* hydroxyl groups in the tetrahydrofuran ring and, therefore, formed a diisopropylidene derivative, whereas the other, having *trans* hydroxyl groups in the ring, could form only a monoisopropylidene deriva-

(1) This investigation was supported in part by a grant from the Atlas Powder Co., Wilmington, Del., and in part by Public Health Service Research Grant GM 09021 from the National Institute of General Medical Sciences.

(2) L. F. Wiggins, *Advan. Carbohydrate Chem.*, **5**, 191 (1950).

(3) R. K. Ness, H. G. Fletcher, Jr., and C. S. Hudson, *J. Am. Chem. Soc.*, **73**, 3742 (1951).

(4) J. C. Sowden and H. O. L. Fischer, *ibid.*, **67**, 1713 (1945).

(5) LKB, Chro Max Column, Stockholm, Sweden.

(6) R. Barker, in preparation.

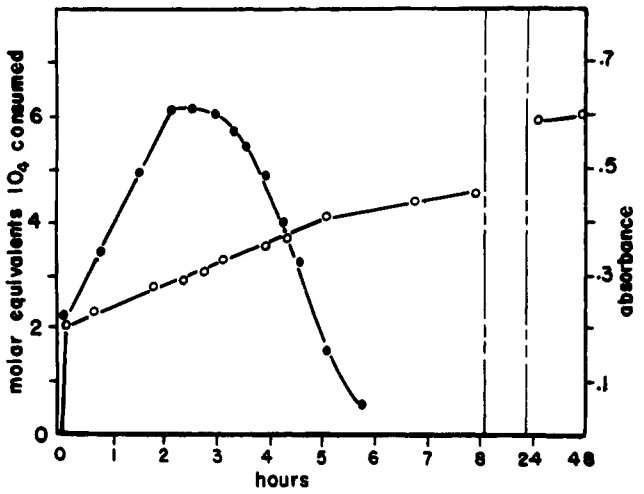


Fig. 1.—Uninterrupted oxidation of 1,4-anhydro-DL-allitol. Periodate consumption, 3 m*M* alditol and 20 m*M* sodium metaperiodate. Absorbance of a 25-fold dilution of the oxidation mixture.

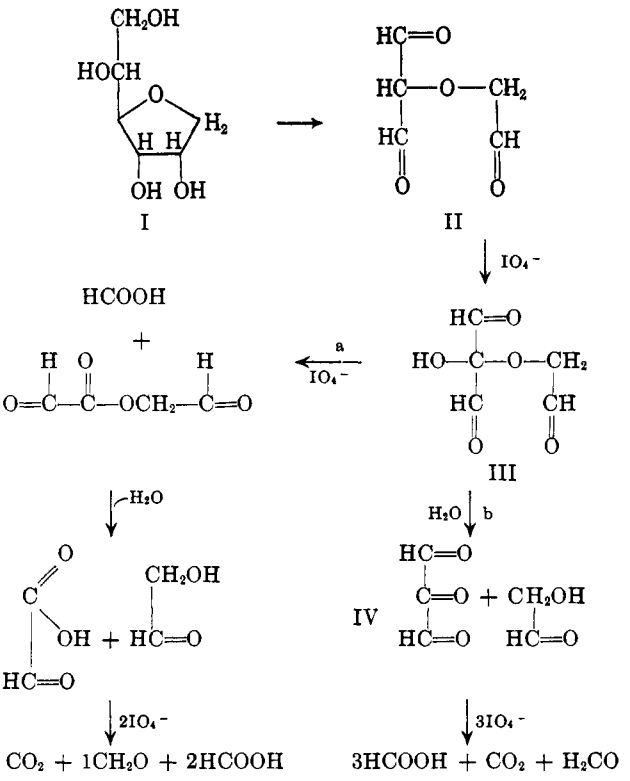
tive. The two types of isopropylidene derivatives can be separated readily by adsorption chromatography on Florisil.[7]

All of the 1,4-anhydrohexitols consumed 6 molar equivalents of periodate and gave 2 molar equivalents of formaldehyde and 3 molar equivalents of formic acid.[8] It was of interest to study the kinetics of the periodate reaction to ascertain whether configuration or internal hemiacetal formation of the intermediates affected the rate. To expedite this a more rapid spectrophotometric method of measuring periodate consumption was sought. The methods currently in the literature use very dilute solutions and give very low rates.[9] To this end the oxidation of D-mannitol was investigated. An excellent agreement between decrease in absorbance and molar equivalents of periodate consumed was obtained when the reaction was followed at 270 mμ. Using 3 ml. of 3.1 m*M* sodium metaperiodate and 1.0 μmole of mannitol, the oxidation was complete in 7 min., at which time 5.00 ± 0.02 molar equivalents of oxidant had been consumed.

When the same molar proportions of oxidant and 1,4-anhydroalditol were employed, the absorbance of the sample fell during the first 3 min. and then increased to a maximum at approximately 5 hr. and again decreased until a steady value was reached after 4 days. Total periodate consumption was then 6.05 molar equivalents.

The 1,4-anhydrohexitols (I) give rise, on consumption of 2 molar equivalents of periodate, to a "trialdehyde" (II). This compound has been postulated[8] to undergo oxidation to the mesoxaldehyde derivative (III) which undergoes further oxidation *via* pathways a or b[10] (Scheme II). The only component of this scheme which would be expected to have a strong absorption band at 270 mμ is the reductone (IV). Since it is unlikely that IV could occur in sufficient quantities to account for the observed absorbance early in the course of the oxidation (*cf.* Fig. 1), an attempt was

SCHEME II



made to elucidate the structure of the absorbing substance.

1,4-Anhydro-DL-allitol (I) was oxidized with sodium metaperiodate so that 2 molar equivalents of oxidant were consumed in 10 min. The dilute solution containing II and iodate was kept at room temperature and the amount of oxidizing material (iodate) and absorbance were assayed at intervals. No decrease in titer was observed over a period of 3 days, and no iodine[11,12] was formed. The absorbance increased steadily for a period of 24 hr. at which time it was stable at a value corresponding to a molar absorbance of 1.4×10^4 at 272 mμ. No other absorption maxima were observed. The rate of appearance of the absorbing substance is first order for approximately 90% of the reaction period, indicating that the reaction being observed probably involves only the rearrangement of the trialdehyde (II). Initial first-order kinetics are consistent also with an equilibrium in which the absorbing species predominates. The rearrangement is essentially instantaneous in neutral solution and is inhibited by acidic conditions. It procedes as shown in Fig. 2 in unbuffered iodate solution (pH 4–5). No alteration in the carbon skeleton of II occurs during the rearrangement, since reduction of II and its rearrangement product, followed by acetylation, yield the same material as analyzed by gas chromatography. The rearranged product behaves as a weak acid with a pK_a of 5.5, and when placed in basic solution it reacts with base in a nonstoichiometric fashion to yield a product, the molar extinction coefficient of which is 2.4×10^4 (λ_{max} 277 mμ).

When the rearranged product is treated with an excess of sodium metaperiodate, the optical density

(7) Floridin Co., Tallahassee, Fla.

(8) C. F. Huebner, S. R. Ames, and E. D. Bubl, *J. Am. Chem. Soc.*, **68**, 1621 (1946).

(9) J. S. Dixon and D. Lipkin, *Anal. Chem.*, **26**, 1092 (1954).

(10) M. Cantley, L. Hough, and A. P. Pittet, *J. Chem. Soc.*, 2527 (1963).

(11) T. G. Halsall, E. L. Hirst, and J. K. N. Jones, *ibid.*, 1427 (1947).

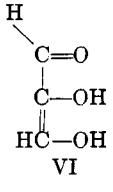
(12) H. G. Fletcher, Jr., H. W. Diehl, and R. K. Ness, *J. Am. Chem. Soc.*, **76**, 3029 (1954).

falls rapidly to a value corresponding to a molar extinction of 1.15 × 10^4. During the same interval (1 min.) 1 molar equivalent of periodate is consumed, and no formaldehyde, formic acid, or carbon dioxide is evolved. The subsequent uptake of periodate (3 molar equivalents) is slow and follows second-order kinetics as shown in Fig. 2. The appearance of formic acid and formaldehyde parallel the consumption of periodate. These findings are interpreted as indicating that, in the consumption of the last 3 moles of oxidant, the rate is limited by the consumption of the first of these 3 moles. The finding that the process is second order indicates that a hydrolysis does not limit the rate of the reaction since a hydrolysis would be expected to show first-order kinetics.[13]

The sequence of events outlined above is represented in Fig. 2.

The same series of events appears to occur in the uninterrupted oxidation of I. This hypothesis is borne out by the finding that the initial rate of increase in absorbance at 270 mμ in the uninterrupted oxidation (Fig. 1) is essentially the same as the rate of rearrangement of II to the absorbing substance (III) in the absence of oxidation. These rates would concur if III is instantaneously oxidized, and if the product of that oxidation (IV) also absorbs at 270 mμ and is itself much more slowly oxidized. The rate of destruction of the absorbing substance (IV) in the uninterrupted oxidation would reflect a balance between rate of formation and rate of breakdown and would be expected to appear lower than when only breakdown is being observed. The observed change in absorbance with time (Fig. 1) is as predicted by these considerations.

The structure of the rearranged product has not been elucidated. It is probable that it is a hemialdal or hemiacetal,[14] and it must contain a conjugated system to have ε 1.4 × 10^4 at 272 mμ. According to Evans and Gillam,[15] an acyclic α,β-unsaturated aldehyde substituted at both the α- and β-position should have λ_{max} 230 ± 5 mμ. However, triose reductone (VI) has been reported to have λ_{max} 266 mμ,[16] and a number of other endiols conjugated with carbonyls have absorptions



VI

in the range of 260–290 mμ with molar absorbancies of the order of 10^4 l. mole^{-1} cm.$^{-1}$.[17]

The very rapid oxidation of the absorbing material is reminiscent of the finding of Wolfrom and Bobbitt that cyclic 1,3-diketones oxidize considerably faster than do their acyclic counterparts.[18] It has been suggested by Bose, Foster, and Stephens[19] that a cyclic enol may be the reactive species in the oxidation of

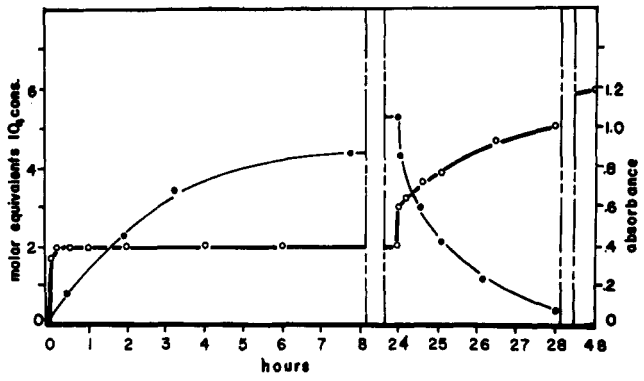
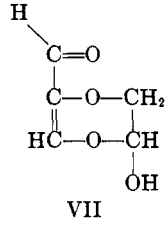


Fig. 2.—Interrupted oxidation of 1,4-anhydro-DL-allitol. Periodate consumption, 50 m*M* alditol and 2 molar equivalents of periodate at time 0; diluted to give 2 m*M* alditol after 30 min.; added 16 mmoles of periodate at 24 hr. Absorbance of a 50-fold dilution of the oxidation mixture.

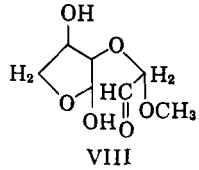
cyclic 1,3-diketones. A possible structure for the reactive species which is formed by the rearrangement of II based on the above considerations is VII which may oxidize rapidly to yield III or one of the many forms of III which would be present in aqueous solution.



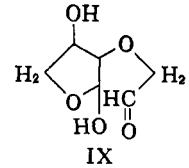
VII

It is also possible that to some extent the variations in rate of oxidation of active methylene compounds with pH which have been observed[20] are a function of the rate of formation of a rapidly oxidizeable form of the malondialdehyde derivative analogous to VII.

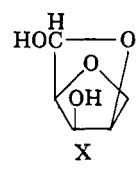
The rate of the uninterrupted periodate oxidation of 1,4-anhydroalditols can be used to determine whether the hydroxyls in the tetrahydrofuran ring are *cis* or *trans* to each other when sufficiently dilute solutions are used.[21] The oxidation of *cis* hydroxyls is essentially instantaneous and the oxidation of *trans* hydroxyls requires approximately 5 hr. when solutions 2 m*M* with respect to glycol and 16 m*M* with respect to periodate are used. That the difference in rates is not due to internal hemiacetal formation is shown by comparison with the rates of oxidation of 1,4-anhydroerythritol and 1,4-anhydro-DL-threitol which contain, respectively, *cis* and *trans* glycol structures in a tetrahydrofuran ring as the only oxidizable groups. In contrast to the findings by Criegee,[22] that methyl D-mannofuranoside is oxidized by lead tetraacetate preferentially at the *cis*-ring hydroxyls,



VIII



IX



X

(13) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1961, p. 11.
(14) R. D. Guthrie, *Advan. Carbohydrate Chem.*, **16**, 105 (1961).
(15) L. K. Evans and A. E. Gillam, *J. Chem. Soc.*, 565 (1943).
(16) H. V. Euler, H. Hasselquist, and G. Hanshoff, *Arkiv Kemi*, **6**, 471 (1953).
(17) E. F. Hartree, *J. Am. Chem. Soc.*, **73**, 6244 (1953).
(18) M. L. Wolfrom and J. M. Bobbitt, *ibid.*, **78**, 2489 (1956).
(19) J. L. Bose, A. B. Foster, and R. W. Stephens, *J. Chem. Soc.*, 3314 (1959).
(20) M. Cantley and L. Hough, *ibid.*, 2711 (1963), and earlier papers by the latter author.
(21) H. Klosterman and F. Smith, *J. Am. Chem. Soc.*, **74**, 5336 (1952).
(22) R. Criegee, *Ann.*, **495**, 211 (1932).

with the formation of a cyclic hemiacetal (VIII) which impedes further oxidation, no indication of a difference in the rate of consumption of the first 2 molar equivalents of periodate was observed in the oxidation of the 1,4-anhydrides of mannitol, allitol, gulitol, or talitol. It is, therefore, unlikely that structures such as IX or X occur to an appreciable extent during the oxidation.

In all cases the R_f of the 1,4-anhydro alditol having a *trans* glycol grouping in the tetrahydrofuran ring was slightly higher than that of its epimer having a *cis* glycol.

Experimental[23]

(1) **1,4-Anhydro-D-allitol and 1,4-Anhydro-D-altritol. A. Mixed Sodio-*aci*-nitro Alcohols from D-Ribose.**[4]—To a solution of 50 g. of D-ribose in 250 ml. of dry methanol and 250 ml. of nitromethane at room temperature was added during 30 min. 250 ml. of dry methanol containing 10 g. of sodium. The heavy precipitate which formed was collected after 2 hr. and thoroughly washed with dry methanol to remove nitromethane and ribose,[24] and then with ether. After drying *in vacuo* it weighed 52 g.

B. Mixed 1-amino-1-deoxy-D-allitol and D-altritol.—The mixed sodio-*aci*-nitro alditols from A (52 g.) in 500 ml. of 25% aqueous acetic acid were hydrogenated over platinum oxide (1 g.) in a Parr[25] pressure reaction apparatus at pressures between 10 and 30 lb. Hydrogen uptake was measured by decrease in pressure and ceased after 18 hr. when approximately 15 l. (3 molar equiv.) had been consumed. After removal of the catalyst by filtration, the solution was concentrated to a sirup which was redissolved in water and percolated through a column containing 350 ml. of IR 120[26] cation-exchange resin in the H^+ form. The column was washed with water until the eluate was no longer acidic,[27] and then eluted with approximately 6% aqueous ammonia slowly so that the reaction between the eluent and the resin did not cause the column to overheat. The first 300 ml. of basic eluate was collected and concentrated to give 56 g. of amber sirup. The product gave one zone on paper chromatography in butanone–water (100:8 v./v.), R_f 0.1, which reacted with ninhydrin and periodate–benzidine sprays.[28]

C. Mixed 1,4-Anhydro-D-allitol, 1,4-Anhydro-D-altritol, Allitol, and D-Altritol (D-Talitol) and Their Separation.—To a solution of 56 g. of mixed 1-amino-1-deoxy alditols from B in 250 ml. of 25% aqueous acetic acid was added 20 g. of sodium nitrite in small batches during 30 min. The temperature rose to 40° and nitrogen was evolved rapidly. After 18 hr. the reaction mixture was boiled for 1 hr. and then concentrated to yield 80 g. of a pale yellow sirup. This sirup was dissolved in 200 ml. of water and passed over columns containing 500 ml. of IR 120 (H^+) and 500 ml. of IR 45 in the free base form. The neutral eluate was concentrated and dried at 0.1 mm. overnight to yield a thick yellow sirup weighing 26 g. Paper chromatography in butanone–water showed that the sirup contained at least four components. The fastest moving (R_f 0.4) was shown to be 1-deoxy-1-(methyl nitrosoamino)-D-ribitol which was present in small amounts (*ca.* 5%). The next two zones which constituted more than 50% of the mixture had R_f values of 0.17 and 0.11. The fourth zone did not move from the point of application.

This separation also was accomplished on a Chro Max[5] paper column (size 4). When 8 ml. of an aqueous solution containing 4.3 g. of the mixture was applied to a dry column, the column was eluted with 60 ml. of butanone followed by butanone–water (100:8 v./v.), and 25-ml. fractions of the eluate were collected, the fast moving components (214 mg.) was found in tubes 70–120. Fractions 161–255 contained 954 mg. of material which was crystallized and recrystallized from isopropyl alcohol and had m.p. 106.5–107.5° and $[\alpha]_D$ +13.9 (*c* 3.7, water). The compound was identified as 1,4-anhydro-D-altritol on the basis of (i) the consumption of 6 molar equiv. of periodate, (ii) the slow rate of consumption of the second mole of oxidant, (iii) higher R_f on paper chromatography, and (iv) the transformation to a monoisopropylidene derivative which consumed 1 molar equiv. of periodate.

Anal. Calcd. for $C_6H_{12}O_5$ (164.16): C, 43.90; H, 7.37. Found: C, 44.11; H, 7.45.

Fractions 285–420 contained 1.20 g. of material which was crystallized from ethyl alcohol to give m.p. 83–85°, $[\alpha]^{25}D$ +46.1 (*c* 5.5, water). The compound has an infrared spectrum essentially identical with that of the known 1,4-anhydro-DL-allitol,[29] and the spectra of the acetates taken as smears of the pure compounds are identical.

Anal. Calcd. for $C_6H_{12}O_5$ (164.16): C, 43.90; H, 7.37. Found: C, 44.05; H, 7.54.

The column then was washed with water. The eluate contained 1.6 g. of material which by electrophoresis in 0.2 *M* arsenite buffer pH 9.6[30] appeared to consist of equal parts of allitol and talitol.

(2) **1,4-Anhydro-D-iditol and 1,4-Anhydro-D-gulitol. A. B.**[31]—D-Xylose (50 g.) was dissolved in 35 ml. of water with warming. To this solution was added 500 ml. of an equivolume mixture of methanol and nitromethane and then a solution of 10 g. of sodium in 500 ml. of methanol slowly with constant, vigorous stirring. The precipitate was collected after 8 hr. by centrifugation in the cold and washed with several small volumes of ice-cold methanol. The washed precipitate was dissolved in 250 ml. of 50% aqueous acetic acid and hydrogenated over platinum oxide. The product which was isolated as described for the ribose derivatives weighed 36 g.

C.—The 1-amino-1-deoxyalditols (36 g.) were deaminated and the product was purified as described under 1 C.

Paper column chromatography of 7.6 g. of the product gave three fractions. The first fraction representing 6% of the mixture was an *N*-nitroso compound.[6] The second fraction representing 60% of the mixture was itself a mixture of 1,4-anhydro-D-iditol and 1,4-anhydro-D-gulitol in approximately equal amounts. The third fraction, representing 30% of the mixture, contained the alditols, iditol and glucitol, and was obtained by eluting the column with water.

D. Separation of 1,4-Anhydro-D-iditol and 1,4-Anhydro-D-gulitol *via* Their Isopropylidene Derivatives.—The mixture of 1,4-anhydro-D-glucitol and 1,4-anhydro-D-iditol (4.0 g.) was dissolved in 200 ml. of dry acetone containing 0.5 ml. of concentrated sulfuric acid. After 24 hr. the solution was passed over a column containing 50 ml. of IR 45 which had been washed previously with acetone. The neutral eluate was concentrated to give 5.3 g. (97%) of a sirup. An ethereal solution of this sirup was passed over a column containing 70 g. of Florisil[7]; the column was eluted with 500 ml. of dry ether and then with 500 ml. of methanol.

The ether eluate contained 2.3 g. of material which deposited crystals from solution in ether–petroleum ether (b.p. 60–90°); the melting point after two recrystallizations from the same solvent was 83–83.5°, $[\alpha]_D$ +30.4 (*c* 3.34, toluene). This is the diisopropylidene derivative of 1,4-anhydro-D-gulitol.

Anal. Calcd. for $C_{12}H_{20}O_5$ (244.29): C, 59.00; H, 8.25. Found: C, 58.86; H, 8.38.

1,4-Anhydro-D-gulitol.—The diisopropylidene derivative (1.4 g.) was hydrolyzed by heating at 100° in 50% aqueous acetic acid for 2 hr. After removal of the solvent and repeated concentration from water to remove acid, a neutral sirup was obtained which showed a strong absorption at 5.8 μ which was interpreted and indicated the presence of a considerable proportion of an acetate in the material. Saponification, followed by removal of the cations on IR120 (H^+) and removal of the water, gave a sirup which deposited 600 mg. of crystals from solution in 100 ml. of ethyl acetate. Recrystallization from ethyl acetate gave a material with m.p. 109–110° and $[\alpha]^{25}D$ +9° (*c* 8.6, water). Montgomery and Wiggins reported m.p. 113° and $[\alpha]_D$ −7.5 for the L isomer (3,6-anhydro-D-glucitol).

(23) Melting points are corrected. Evaporations were performed at water aspirator pressure on a rotary evaporator. Descending paper chromatography was carried out on Whatman 31 paper at room temperature. This paper gives similar separations to Whatman 1 but is twice as fast.

(24) Removal of nitromethane is essential to avoid the later formation of 1-deoxy-1-(methylnitrosoamino)pentitols.[5]

(25) Parr Instrument Co. Moline, Ill., U. S. A.

(26) Rohm and Haas Co., Phildelphia 5, Pa.

(27) Concentration of this eluate gave 2.7 g. of a sirup which was slightly reducing.

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

(29) R. Barker, K. O. Lloyd, R. R. Thompson, and J. C. Sowden, in preparation.

(30) J. L. Frahn and J. A. Mills, *Australian J. Chem.*, **12**, 65 (1959).

(31) Letters indicate the steps in the synthesis corresponding to the designation given under 1,4-anhydro-D-allitol and 1,4-anhydro-D-altritol.

1,4-Anhydro-D-iditol.—The material eluted from Florisil with methanol (2.13 g.) was hydrolyzed in aqueous acetic acid and then in aqueous base. After deionization, 1.6 g. of material was obtained which was crystallized twice from isopropyl alcohol to give 800 mg. of material with m.p. 94–95°, $[\alpha]^{25}D$ +17.9° (*c* 3.5, water). Le Maistre[32] has reported m.p. 95–96° and $[\alpha]^{25}D$ −17.7° for the L compound.

Anal. Calcd. for $C_6H_{12}O_5$ (164.16): C, 43.90; H, 7.37. Found: C, 44.00; H, 7.60.

1,4-Anhydro-D-galactitol and 1,4-Anhydro-D-talitol.—These were prepared from D-lyxose and isolated as described for the products from D-xylose. 1,4-Anhydro-D-galactitol had m.p. 95–96°, $[\alpha]^{25}D$ −18° (*c* 2, water), and an infrared spectrum identical with that of an authentic sample.[3]

2,3:5,6-Diisopropylidene-1,4-anhydro-D-talitol was shown to have an infrared spectrum in chloroform identical with that of the known racemic compound,[29] melted at 45°, and had $[\alpha]^{26}D$ −19.4° (*c* 2.9, toluene).

Anal. Calcd. for $C_{12}H_{20}O_5$ (244.29): C, 59.00; H, 8.25. Found: C, 59.31; H, 8.46.

Hydrolysis of the isopropylidene derivative gave a sirup which has not crystallized in more than a year and which has not given a crystalline acetate, benzoate, or *p*-nitrobenzoate. The sirup shows only one component on chromatography in a variety of solvents and has $[\alpha]D$ −57.8° (*c* 2.2, water).

Periodate Oxidations.—All oxidations were carried out in unbuffered sodium metaperiodate at room temperature (22–25°). Utilization of oxidant was followed by titration of iodine released from a suitable aliquot on addition of 5 ml. each of 2 *N* sulfuric acid and 20% aqueous potassium iodide with either 0.1 *N* or 0.01 *N* thiosulfate. The possibility of iodine consumption by the products of the oxidation was checked by the addition of a standard iodine solution, sulfuric acid, and iodide to a sample of the oxidation mixture and titration of the iodine present with standard thiosulfate. No consumption of iodine was observed.

Formaldehyde was determined with chromotropic acid by an adaptation of the method of Frisell, Meech, and Mackenzie.[33] Formic acid was determined by addition of an excess of ethylene glycol to an aliquot of the reaction mixture and titration with 0.01 *N* sodium hydroxide to the methyl orange end point, after 30 min.

The Preparation of Trialdehyde from 1,4-Anhydro-DL-allitol.—To an ice-cold solution of 492 mg. (3 mmoles) of 1,4-anhydro-DL-allitol in 50 ml. of water was added 11.5 ml. (6.1 mmoles) of 0.53 *M* sodium metaperiodate. After 0.5 hr. at room temperature, the reaction was essentially complete and the volume was made up to 1500 ml. with water. If this dilution was not made, iodine was produced in the reaction mixture in about 1 hr. No iodine was observed in the diluted solution even after 5 days at 25°. The dilute solution was used to follow the increase in absorbancy and to follow the oxidation of the absorbant compound. Absorbancy was measured in a Zeiss PM II spectrophotometer using 0.2-ml aliquots of the diluted reaction mixture diluted with 5.0 ml. of water.

When the absorbancy had reached a maximum value (24 hr.), 10 ml. of 0.53 *M* sodium metaperiodate was added to 500 ml. of the solution. The consumption of oxidant and the appearance of acid and formaldehyde were followed as outlined above.

Immediately after dilution to 1.5 l., a 500-ml. aliquot was treated with 1 g. of sodium borohydride. After standing overnight, the excess hydride was destroyed with acetic acid and the solution was concentrated to a small volume. After deionizing, the residue was acetylated in pyridine. Examination of the product by vapor phase chromatography using Dow–Corning high vacuum grease on Chromosorb W at 220° showed one component with a retention time greater than that for arabitol pentaacetate.

A second 500-ml. aliquot was similarly treated when the absorbancy had reached a maximum value. The same yield of the same acetate was obtained.

(32) J. W. Le Maistre, private communication.

(33) W. R. Frisell, L. A. Meech, and C. G. Mackenzie, *J. Biol. Chem.*, **207**, 709 (1954).

The Route of Cyclic Anhydride Formation from Mono-*O*-tolylsulfonyl Glycols[1]

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In the intramolecular displacement of *p*-tolylsulfonate anions by an oxide ion it is shown that a tolylsulfonyl ester on a primary hydroxyl function is displaced by oxide ions derived from hydroxyl groups in the following order of reactivity: primary γ-OH > secondary γ-OH = secondary α-OH > primary δ-OH. A tolylsulfonyl ester on a secondary hydroxyl function is displaced most readily by an oxide ion derived from a primary α-OH; reactions with competing oxide ions derived from primary γ-hydroxyls and secondary α-hydroxyls have not been observed.

It previously has been shown[2] that, under basic conditions in a system containing a primary hydroxyl group γ to a *p*-tolylsulfonyl ester function and a secondary hydroxyl group α to the function, intramolecular *p*-tolylsulfonate anion displacement proceeds preferentially by attack of the oxide ion in the γ-position.

The purpose of the present investigation was to elucidate the route of base-catalyzed tolylsulfonate anion displacement in each of the following three situations involving unbranched glycols: (1) primary hydroxyl group α and γ to the ester, (2) a primary hydroxyl δ and a secondary hydroxyl α to the ester, and (3) secondary hydroxyl groups α and δ to the ester.

To examine the first two situations, the products formed when the 2- and 1-*O*-*p*-tolylsulfonyl esters of L-1,2,5-pentanetriol (I)[3] were treated with alkali were investigated.

1,5-Di-*O*-benzoyl-2-*O*-*p*-tolylsulfonyl-L-1,2,5-pentanetriol (II) was prepared from L-glutamic acid by the following series of reactions: L-glutamic acid → L-α-hydroxyglutaric acid → dimethyl L-α-hydroxyglutarate → methyl L-α-hydroxyglutarolactonate → L-1,2,5-pentanetriol (I) → 1,5-di-*O*-benzoyl-L-1,2,5-pentanetriol → II.

Treatment of II with aqueous sodium hydroxide gave tetrahydrofurfuryl alcohol, $[\alpha]^{24}D$ +14.9 ± 0.3° (*c* 5.0, nitromethane), as the only isolable product. Kenyon, *et al.*,[4] reported $[\alpha]^{20}_{5893}$ −17.5° (*c* 5.0, nitromethane) for the levorotatory enantiomer. Since Gagnaire and Butt[5] found that the tetrahydrofurfuryl alcohol having a positive rotation is the L isomer, it is

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(2) F. C. Hartman and R. Barker, *J. Org. Chem.*, **28**, 1004 (1963).

(3) H. Katsura, *Nippon Kagaku Zasshi*, **77**, 1789 (1956); *Chem. Abstr.*, **53**, 5126 (1959).

(4) M. P. Balfe, M. Irwin, and J. Kenyon, *J. Chem. Soc.*, 313 (1951).

(5) D. Gagnaire and A. Butt, *Bull. soc. chim. France*, 312 (1961).