

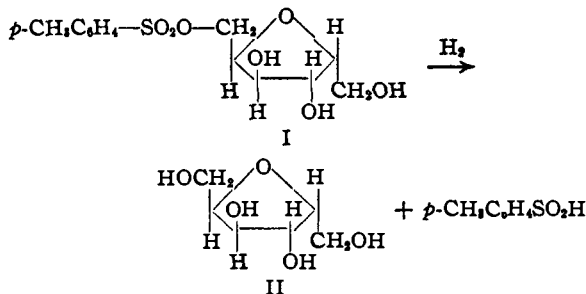
[CONTRIBUTION FROM THE ORGANIC CHEMICAL INSTITUTE OF THE HUNGARIAN UNIVERSITY "BOLYAI" AT CLUJ-KOLOZSVÁR, RUMANIA]

Alcohols of the Sugar Group. IV. 2,5-Anhydro-L-Iditol

By L. VARGHA, T. PUSKÁS AND E. NAGY

Experiments reported in Part III¹ of this series have resulted in the elucidation of the structure and configuration of a monotonuesulfonyl anhydrohexitol² which has been shown to represent the 1-*p*-toluenesulfonyl 2,5-anhydro-L-Iditol (I). However, we have been unable to prepare the 2,5-anhydro-L-Iditol from this derivative by hydrolysis, or from the 1,6-diiodo derivative in the usual manner. In the meantime Professor Freudenberg has kindly called our attention to one of his earlier experiments in which he succeeded in producing diacetone-glucose from its 3-*p*-toluenesulfonyl derivative by reductive scission with sodium amalgam.³ Since we have been interested in the elimination of the *p*-toluenesulfonyl group from its esters, we applied this method not only to (I) but also to the *p*-toluenesulfonyl esters of other polyhydric alcohols.

By treatment of (I) in dilute alcohol with sodium amalgam we obtained, beside the sodium salt of *p*-toluenesulfinic acid, a sirupy product, the acetate of which was separated into two fractions by distillation under diminished pressure. On saponification of the higher boiling fraction, a uniform, crystalline substance was obtained which proved to be the expected 2,5-anhydro-L-Iditol (II). The lower boiling fraction, probably a



dianhydrohexitol according to the analytical data, could not be brought to crystallization even after removal of its acetyl residues.

We also carried out, in a similar way, the reduction of the 6-*p*-toluenesulfonyl⁴ and 5,6-di-*p*-toluenesulfonyl 1,2-monoacetone-glucofuranose,⁵ respectively. From the former compound, beside a sirupy substance of unknown structure, crystalline 1,2-monoacetone-glucofuranose was obtained in about 40% yield, whereas the 5,6-di-*p*-toluenesulfonyl compound gave rise to 5-*p*-toluenesulfonyl 3,6-anhydro-1,2-monoacetone-glucos-

furanose⁶ and a small quantity of an unidentified product.

From these results it can be concluded that although the reductive cleavage of the *p*-toluenesulfonyl esters into alcohols and *p*-toluenesulfinic acid often can be carried out without difficulty, yet, simultaneously, as undesirable by-products, anhydro compounds may also form by splitting out of *p*-toluenesulfonic acid from the esters. The occurrence of the latter process cannot be avoided by carrying out the reduction in approximately neutral medium as by passing carbon dioxide gas through the solution. Under such experimental conditions 6-*p*-toluenesulfonyl 1,2-monoacetone-glucofuranose gave 5,6-anhydro-1,2-monoacetone-glucofuranose⁷ in surprisingly good yield (70%), while the 5,6-di-*p*-toluenesulfonyl 1,2-monoacetone-glucofuranose remained unchanged.

Experimental

Reduction of 1-*p*-Toluenesulfonyl 2,5-Anhydro-L-Iditol by Sodium Amalgam. 2,5-Anhydro-L-Iditol Tetraacetate and Dianhydro-hexitol Diacetate.—Ten grams of 1-*p*-toluenesulfonyl 2,5-anhydro-L-Iditol (I) in 160 cc. of 80% alcohol was stirred three days at 15° with 200 g. of 2% sodium amalgam. The solution was then neutralized with carbon dioxide, filtered from the precipitated sodium bicarbonate and evaporated to a residue which was extracted with 30 cc. of pyridine. From the aqueous solution of the insoluble part crystalline *p*-toluenesulfinic acid (m. p. 88°) was isolated by treatment with strong sulfuric acid. Concentration of the pyridine solution *in vacuo* yielded a thick sirup (4.6 g.) which was acetylated by treatment overnight with 20 cc. of acetic anhydride and 30 cc. of pyridine at room temperature. After removal of the pyridine *in vacuo* the residue was dissolved in chloroform, the solution treated with water, dried, then the solvent evaporated. The sirupy substance was submitted to fractionate distillation under 0.003 mm. pressure. The first fraction distilled at 108–124° bath temperature, the second one at 124–140°; yields, 1.8 and 3.3 g., respectively.

According to analytical data, the first fraction represents a dianhydro-hexitol diacetate. It is a clear sirup, easily soluble in organic solvents, but almost insoluble in water or petroleum ether; $[\alpha]_D^{20} +5.15^\circ$ in chloroform solution (*c*, 2.329).

Anal. Calcd. for C₁₀H₁₄O₆: C, 52.17; H, 6.13. Found: C, 52.14; H, 6.25.

The second fraction shows similar solubility behavior and, according to the analytical data, consists of 2,5-anhydro-L-Iditol tetraacetate; $[\alpha]_D^{20} -13.2^\circ$ in chloroform solution (*c*, 1.9556).

Anal. Calcd. for C₁₄H₂₀O₈: C, 50.60; H, 6.06. Found: C, 50.97; H, 6.52.

2,5-Anhydro-L-Iditol (II).—After addition of 11 g. of barium hydroxide dissolved in 130 cc. of water to the solution of 3.3 g. of 2,5-anhydro-L-Iditol tetraacetate in 20 cc. of alcohol, the mixture was shaken on the machine for twenty-four hours. Then the excess alkali was neutralized with carbon dioxide, the barium carbonate filtered off, and the soluted barium precipitated by the equiv-

(6) Ohle, Vargha and Erlbach, *ibid.*, **61**, 1211 (1928).

(7) Ohle and Vargha, *ibid.*, **63**, 2345 (1929).

(1) Vargha and Puskás, *Ber.*, **76**, 859 (1943).

(2) Vargha, *ibid.*, **68**, 1377 (1935).

(3) Freudenberg and Brauns, *ibid.*, **55**, 3288 (1922). We wish to thank Prof. Freudenberg for this information.

(4) Ohle and Spencker, *ibid.*, **59**, 1886 (1926).

(5) Ohle and Dickhauser, *ibid.*, **58**, 2593 (1925).

alent amount of sulfuric acid. After filtration the solution was concentrated *in vacuo*, the remaining sirup dissolved in a little absolute alcohol and the solution mixed with absolute ether to incipient turbidity. The substance crystallized at 0° in colorless prisms which were easily soluble in water; yield, 1.1 g., m. p. 111–113°; $[\alpha]^{20}_D +12.6^\circ$ in aqueous solution (*c*, 2.525).

Anal. Calcd. for $C_8H_{12}O_5$: C, 43.90; H, 7.37. Found: C, 43.94; H, 7.55.

Dianhydro-hexitol.—The solution of 1.8 g. of dianhydrohexitol diacetate in 12 cc. of alcohol was shaken for twenty-four hours with 7 g. of barium hydroxide in 80 cc. of water. After removal of the barium as described above and concentration of the solution *in vacuo*, there was obtained a sirup which was easily soluble in water and in alcohol; $[\alpha]^{20}_D +12.3^\circ$ in aqueous solution (*c*, 3.079).

Anal. Calcd. for $C_8H_{10}O_4$: C, 49.31; H, 6.80. Found: C, 49.63; H, 7.02.

Reduction of the 6-*p*-Toluenesulfonyl 1,2-Acetone-glucufuranose by Sodium Amalgam.—Two grams of the substance was stirred at 15° for twenty-four hours in 30 cc. of 80% alcohol with 25 g. of 2% sodium amalgam. After neutralization and removal of the barium as described above, the solution was concentrated *in vacuo* and the residue extracted with ethyl acetate. The insoluble portion proved to be the sodium salt of *p*-toluenesulfonic acid. From its aqueous solution the crystalline acid with m. p. 88° was isolated. From the concentrated ethyl acetate solution the 1,2-acetone-glucufuranose with m. p. 158° crystallized; yield, 0.5 g. After evaporation of the mother liquid an oily residue (0.6 g.) remained.

The reduction was also carried out by simultaneous introduction of carbon dioxide gas. In this case a colorless substance was isolated which showed, after recrystal-

lization from benzene, all the properties of the 5,6-anhydro-1,2-acetone-glucufuranose; yield, 70%, m. p. 132°. The crystals had $[\alpha]^{20}_D -26.4^\circ$ in aqueous solution (*c*, 3.025).

Reduction of the 5,6-Di-*p*-toluenesulfonyl 1,2-Acetone-glucufuranose by Sodium Amalgam.—The reduction was carried out as described above. From the concentrated ethyl acetate extract a colorless substance was isolated which proved to be identical with 5-*p*-toluenesulfonyl 3,6-anhydro-1,2-acetone-glucufuranose; m. p. alone and also in admixture with an authentic sample 133°. The ethyl acetate mother liquor contained a small quantity of an oily product. When the reduction was carried out in the presence of carbon dioxide gas the starting material was recovered almost quantitatively.

Summary

The reductive cleavage of several *p*-toluenesulfonyl polyhydric alcohols by sodium amalgam has been investigated under various experimental conditions.

It has been found that the reaction, in consequence of reduction, often yields the corresponding polyhydric alcohols and *p*-toluenesulfonic acid, but simultaneously, as products of a competitive reaction, anhydro compounds may also form by splitting out of *p*-toluenesulfonic acid.

By treatment of 1-*p*-toluenesulfonyl 2,5-anhydro-L-idoitol with sodium amalgam 2,5-anhydro-L-idoitol in crystalline state has been prepared.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF KANSAS]

Addition Compounds of Sulfur Dioxide with Three Isomeric Lutidines¹

BY HENRY A. HOFFMAN AND CALVIN A. VANDERWERF

The interesting results obtained in a recent study² of the sulfur dioxide-pyridine and the three sulfur dioxide-picoline systems suggested the present investigation, which comprises temperature-composition equilibria studies of the three systems consisting of sulfur dioxide with each of the bases, 2,6-lutidine, 2,3-lutidine and 2,4-lutidine.

Experimental³

Purification of Materials.—Dry sulfur dioxide was obtained by passing commercial grade⁴ gas through a train consisting of one tower containing saturated barium chloride solution, a tower containing calcium chloride granules, and finally two towers containing phosphoric anhydride. The rate of flow was controlled carefully and a slow stream of sulfur dioxide was allowed to pass through the train for an hour before the required amount was collected in a special freezing point cell⁵ which was cooled in a Dry Ice-bath and attached to a drying tube containing

phosphoric anhydride. The freezing point of sulfur dioxide collected in this manner was -74.0° .⁶

Purification of 2,6-lutidine⁷ was accomplished through the crystalline urea-2,6-lutidine complex reported by Reithof.⁸ The crystals of the complex were washed first with cold water, then with alcohol, and finally steam distilled. The portion of distillate boiling constantly at 95.6° under a pressure of 739 mm. was made alkaline with sodium hydroxide pellets and the lutidine layer separated and dried over three separate portions of sodium hydroxide pellets. Distillation of the dried product through a Todd column into a receiver protected from the atmosphere by means of a drying tube containing potassium hydroxide yielded 2,6-lutidine which boiled at 143.7° at 741 mm. and gave a freezing point (from cooling curve) of -5.9° .¹⁰

The 2,3-lutidine was purified through a previously unreported urea-2,3-lutidine complex which melted at 119.8–121.7°. The crystalline complex was washed with cold water, then with alcohol, and dried. Fusion of the

(6) Dry sulfur dioxide prepared according to the method of Hoffman and VanderWerk (ref. 2) gave essentially the same results as the tank product described above despite the slight difference noted in the freezing point.

(7) All three lutidines used were obtained from the Reilly Tar and Chemical Company.

(8) U. S. Patent 2,295,606, September 15, 1942.

(9) Lidstone, *J. Chem. Soc.*, 241 (1940), reported the value 144.4° at 760 mm.

(10) In exact agreement with the value reported by Coulson and Jones, *J. Soc. Chem. Ind. (London)*, 68, 169 (1946).

(1) Abstracted from a thesis presented by Henry A. Hoffman to the Graduate Faculty of the University of Kansas in partial fulfillment of the requirements for the degree of Master of Arts.

(2) K. R. Hoffman and VanderWerk, *THIS JOURNAL*, 68, 997 (1946).

(3) All boiling points are corrected.

(4) Furnished by the Ohio Chemical and Mfg. Co., Cleveland, Ohio.

(5) Davidson, Sisler and Stoenner, *THIS JOURNAL*, 66, 779 (1944).