[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY AND THE RESEARCH DEPARTMENT, ATLAS POWDER COMPANY]

# Sugar Interconversion under Reducing Conditions. IV.[1] D,L-Glucitol[2]

BY M. L. WOLFROM, B. W. LEW,[3] R. A. HALES[4] AND R. MAX GOEPP, JR.[4]

Previous investigations[1,5] of the composition of a commercial product, designated product B and produced by the Atlas Powder Company by the alkaline electroreduction of D-glucose, have led to the isolation and identification of products predictable, by the enediolic mechanism of sugar interconversion, as arising from the 1,2- and 2,3-enediols of D-glucose. In a manufacturing plant operation, a small amount of a crystalline product was isolated which was further purified in the laboratory and has now been identified as D,L-glucitol. Such a formation of racemic glucitol would require the inversion of carbons three and four of the D-glucose chain. According to the enediolic mechanism of sugar interconversion by alkali, this would indicate that enolization had proceeded down the chain through the 3,4-enediol. Such an interpretation would also indicate that in addition to the D-mannitol, allitol, sorbitol and L-glucitol found so far, dulcitol, D-talitol and D-iditol may be present in this complex mixture. The amount of D,L-glucitol in the product is undoubtedly very small and was isolable through a manufacturing plant operation involving large quantities of materials. We therefore believe it probable that the bulk of the constituents of product B arise from the 1,2- and 2,3-enediols.

The above explanation for the formation of D,L-glucitol depends upon an original carbonyl group at carbon one as the source of enolization. Should dehydrogenation of a hexitol at the cathode surface be possible, a new carbonyl group could be formed at any of the original carbons, such as carbon five, and this could give rise either to a diastereoisomeric pair or, by 4,5-enolization, to two such pairs. Thus, inversion at carbon four might be achieved without a 3,4-enolization proceeding from carbon one.

The transformation of D-glucose into D,L-glucitol is a unique carbohydrate reaction. In order to identify the product as the racemate it was necessary to prepare a synthetic product of known structure. D,L-Glucitol has hitherto not been reported. Fischer and Stahel[6] synthesized L-glucitol by the reduction of sirupy D-gulose with sodium amalgam and obtained a crystalline product melting at *ca.* 75° and showing $[\alpha]^{20}$D *ca.* $-1.4°$ in saturated aqueous borax solution. Fischer and Stahel reported that these constants were in agreement (rotation of opposite sign) with those exhibited by their preparations of sorbitol. It is now known that sorbitol exhibits[7] $[\alpha]^{20}$D $-2°$ (*c* 10, water) and $[\alpha]^{20}$D $+ 6.5°$ (*c* 10, 2 parts of borax to 1 part of sorbitol). The melting point is difficult to raise to its maximum state but most preparations of good purity melt in the range 89–93°.[8] The preparations of Fischer and Stahel were therefore quite impure. A crystalline sample of L-glucitol of good purity (m.p. 89–91°, cor.; $[\alpha]^{29}$D $+2°$, *c* 3.6, water) was accordingly prepared from D-gulose (sirup) in our laboratory by the modern method of high pressure catalytic hydrogenation, a procedure greatly more advantageous than the sodium amalgam reduction available to Fischer and Stahel. Since the hexaacetate is by far the best characterizing derivative for sorbitol, the hexaacetate of the enantiomorph was synthesized and its constants established.

Having in hand the enantiomorphous forms of glucitol, D,L-glucitol was synthesized. This substance crystallized much more readily than either enantiomorph and melted higher (m. p. 136–138°). D,L-Glucitol hexaacetate likewise exhibited a higher melting point (117–118°) than the hexaacetate of either enantiomorph (m. p. 99–100°). Trimethylene-D,L-glucitol (m. p. 203–205°) was also synthesized but did not exhibit an enhanced melting point. The trimethylene derivative of sorbitol was first synthesized by Schulz and Tollens.[9] They recorded for this substance the constants: m. p. 206°, $[\alpha]^{20}$D $-30°$ (chloroform). Ness, Hann and Hudson[10] established the structure of the compound as 1,3:2,4:5,6-trimethylene-sorbitol for which they found the constants: m. p. 212–216°, $[\alpha]^{20}$D $-30.8°$ (chloroform). Lobry de Bruyn and Alberda van Ekenstein[11] had reduced D-sorbose (designated by them *l*-sorbose) with sodium amalgam and identified D-iditol (designated by them *l-iditol*) as the tribenzylidene derivative and L-glucitol as the trimethylene derivative (m. p. 203°, $[\alpha]$D $+30°$, *c* 0.4 in methanol).

---

[1] Previous communication in this series: M. L. Wolfrom, B. W. Lew and R. M. Goepp, Jr., THIS JOURNAL, **68**, 1443 (1946).

[2] In the present communication the term L-glucitol will be adopted for the hexitol obtainable by the reduction of either L-glucose or D-gulose. The term sorbitol will be considered as a trivial name for D-glucitol.

[3] Atlas Powder Company Research Associate of The Ohio State University Research Foundation.

[4] Research Department, Atlas Powder Company, Wilmington, Delaware. Dr. Goepp was killed in an airplane accident on October 3, 1946.

[5] M. L. Wolfrom, F. B. Moody and M. Konigsberg, THIS JOURNAL, **68**, 578 (1946).

[6] E. Fischer and R. Stahel, *Ber.*, **24**, 528, 2144 (1891).

[7] R. S. Rose, Jr., and R. M. Goepp, Jr., paper presented before the Division of Sugar Chemistry and Technology at the 97th Meeting of the American Chemical Society, Baltimore, Maryland, April, 1939.

[8] H. H. Strain, THIS JOURNAL, **56**, 1756 (1934).

[9] M. Schulz and B. Tollens, *Ann.*, **289**, 23 (1896).

[10] A. T. Ness, R. M. Hann and C. S. Hudson, THIS JOURNAL, **66**, 665 (1944).

[11] C. A. Lobry de Bruyn and W. Alberda van Ekenstein, *Rec. trav. chim.* **19**, 7 (1900).

## Experimental

**D,L-Glucitol (and its Hexaacetate) from Product B.**—In a plant electroreduction of D-glucose at *p*H 10–13 and below 30° (resultant material designated product B) a crystalline substance was isolated from the mother liquors resulting from the crystallization of D-mannitol. Some purification was effected by crystallization from dioxane–water; m. p. 135–137° (cor.), $[\alpha]^{20}\text{D}$ 0° (water).

*Anal.* Calcd. for $C_6H_{14}O_6$: C, 39.55; H, 7.75. Found: C, 40.28; H, 7.78. Calcd. for a hexitol on periodate oxidation (moles per mole of substance): oxidant consumed, 5; acid formed, 4; formaldehyde, 2. Found: 4.6, 3.9, 2.0, respectively.

A mixed melting point with the below-described synthetic D,L-glucitol (m. p. 135–137°, cor.) was 136–137° (cor.).

An acetate of the isolated hexitol was prepared; m. p. 117–118° (cor.) unchanged on admixture with the below-described D,L-sorbitol hexaacetate of m. p. 116–117° (cor.), $[\alpha]^{20}\text{D}$ 0° (*c*, 3.8, U. S. P. chloroform, 2-dm. tube, throughout the visible spectrum).

*Anal.* Calcd. for $C_6H_8O_6(COCH_3)_6$: C, 49.77; H, 6.03; $CH_3CO$, 13.81 cc. 0.1 *N* NaOH per 100 mg.; mol. wt., 434. Found: C, 49.98; H, 5.96; $CH_3CO$, 13.7 cc.; mol. wt. (Rast), 428.

The parent substance was regenerated from its acetate by saponification; m. p. 136–138° (cor.).

**L-Glucitol.**—A solution of 2.0 g. of D-gulose sirup, obtained by the reduction of crystalline D-gulono-γ-lactone with sodium amalgam, in 15 cc. of water was treated with a suspension of 1.5 g. of kieselguhr-supported nickel catalyst in 15 cc. of absolute ethanol and the mixture was treated for ten hours at 100° at an initial hydrogen pressure of 890 lb. per sq. in. The cooled, filtered solution was concentrated under reduced pressure to a sirup which crystallized slowly from dilute ethanol on concentration in a desiccator; m. p. 89–91° (cor.), $[\alpha]^{29}\text{D}$ + 1.7° (*c* 3.6, water).

*Anal.* Calcd. for $C_6H_{14}O_6$: C, 39.55; H, 7.75. Found: C, 39.39; H, 7.85.

**L-Glucitol Hexaacetate.**—L-Glucitol was acetylated with acetic anhydride and pyridine and the product was recrystallized from acetone–water; m. p. 98–99° (cor.), $[\alpha]^{27}\text{D}$ − 10° (*c* 2.95, U. S. P. chloroform), six-sided prisms.

*Anal.* Calcd. for $C_{18}H_{26}O_{12}$: C, 49.77; H, 6.03. Found: C, 49.73; H, 6.04.

**Synthetic D,L-Glucitol.**—Equal amounts of the two enantiomorphous forms of glucitol were mixed, dissolved in water and crystallized by the addition of dioxane; m. p. 135–137° (cor.).

**Synthetic D,L-Glucitol Hexaacetate.**—Equal amounts of the two enantiomorphous forms of sorbitol hexaacetate were mixed and crystallized from acetone–water; m. p. 116–117° (cor.).

*Anal.* Calcd. for $C_{18}H_{26}O_{12}$: C, 49.77; H, 6.03. Found: C, 49.77; H, 5.90.

**Trimethylene-D,L-glucitol.**—An amount of 0.40 g. of D,L-glucitol was dissolved in 1.8 cc. of 40% aqueous formaldehyde and 1.6 g. of dry hydrogen chloride passed into the cooled (ice-salt) solution. The mixture was then heated to 90° over a period of forty-five minutes and maintained at that temperature for ten minutes. Fine needles separated on cooling; yield 0.31 g., m. p. 203–205° (cor.) unchanged on further crystallization from 95% ethanol.

*Anal.* Calcd. for $C_9H_{14}O_6$: C, 49.54; H, 6.47. Found: C, 49.53; H, 6.51.

## Summary

1. L-Glucitol and its hexaacetate have been prepared in pure, crystalline form.

2. D,L-Glucitol (its hexaacetate and trimethylene derivative) has been synthesized in crystalline form.

3. D,L-Glucitol has been identified as a product of the alkaline electroreduction of D-glucose.

COLUMBUS, OHIO
WILMINGTON, DELAWARE

RECEIVED JULY 15, 1946

---

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

# N-Methyl-L-glucosaminic Acid[1]

BY M. L. WOLFROM, ALVA THOMPSON[2] AND I. R. HOOPER[3]

The recent discovery that N-methyl-L-glucosamine[4] exists as a component of streptomycin calls attention to the fact that there is no satisfactory method for its preparation. Fischer and Leuchs[5] prepared D-glucosamine (isolated only as a derivative) by reduction of the lactone of D-glucosaminic acid. They synthesized the latter compound and its enantiomorph[6] by the addition of hydrogen cyanide to arabinosylamine with subsequent hydrolysis. E. Votoček and R. Lukeš[7] prepared N-methyl-D-glucosaminic acid by a somewhat similar procedure. They treated an aqueous solution of D-arabinose successively with methylamine and hydrogen cyanide over a period of three weeks. The resulting tar was then removed and the material in solution was hydrolyzed first with hydrochloric acid and then with barium hydroxide to produce, after acidification, an unspecified yield of the amino acid.

In this communication we wish to report the preparation in crystalline form of L-arabinosyl-N-methylamine and N-methyl-L-glucosaminic acid nitrile using anhydrous ethanol as a solvent. By this method, high yields of these intermediate compounds were readily obtained. Hydrolysis of the crystalline nitrile produced a good yield of the acid which was readily isolated in a high degree of purity. N-Methyl-L-glucosaminic acid nitrile was further characterized by the synthesis of its crystalline pentaacetate.

N-Methyl-L-glucosaminic acid nitrile is only the second nitrile in the sugar series to be isolated in the cyanohydrin reaction. Extension of the

---

[1] A preliminary report of this work has appeared in *Science*, **103**, 276 (1946).

[2] Research Foundation Associate of the Graduate School.

[3] Bristol Laboratories Research Associate of The Ohio State University Research Foundation (Project 224).

[4] F. A. Kuehl, Jr., E. H. Flynn, F. W. Holly, R. Mozingo and K. Folkers, THIS JOURNAL, **68**, 536 (1946).

[5] E. Fischer and H. Leuchs, *Ber.*, **36**, 24 (1903).

[6] E. Fischer and H. Leuchs, *ibid.*, **35**, 3787 (1902).

[7] E. Votoček and R. Lukeš, *Coll. Czechoslov. Chem. Commun.*, **7**, 424 (1935); *Chem. Listy*, **29**, 308 (1935).