dinitrophenylhydrazone, melting at 162–163°. The quantity was not considered significant.

3,3′-Dibenzoyl-2,2′-di-(D-glyceraldehyde) Ether Dihydrate.—A solution of 50 cc. of glacial acetic acid containing 1 g. (0.0027 mole) of 2,5-monoanhydro-1,6-dibenzoylsorbitol and 1.8 g. (0.0041 mole) of lead tetraacetate was allowed to stand at room temperature for twenty-four hours. The mixture was then treated with hydrogen sulfide and the precipitate of lead sulfide was removed. The filtrate was aerated to remove hydrogen sulfide and was treated with 1 *N* potassium hydroxide solution until the first signs of permanent turbidity persisted upon shaking. The solution, still acid to litmus, was put away in the refrigerator. Long, colorless needles were deposited overnight. The crystals were filtered off, dissolved in a little ethyl alcohol, and precipitated by the careful addition of water to incipient turbidity. Two more recrystallizations from alcohol and water yielded colorless needles melting at 124–126° (cor.).

In another experiment the filtrate, after removal of lead sulfide, was concentrated *in vacuo* at 40° to a thin sirup. Water (40 cc.) was added followed by the careful addition of alcohol. Upon vigorous shaking the sirup disappeared and a colorless, crystalline product was deposited. Recrystallization was effected from a mixture of benzene and petroleum ether. Colorless, feathery needles, melting at 124–126°, which did not depress the melting point of the previous compound were obtained. The yield was 0.68 g. or 61%. No derivatives could be obtained with methone reagent, phenylhydrazine or 2,4-dinitrophenylhydrazine. Two per cent. solutions of the compound in ethyl alcohol, glacial acetic acid and chloroform exhibited no rotation. A molecular weight determination by freezing-point depression of benzene gave a value of 386 (calcd. 406). This measurement is sufficiently accurate to show that cleavage of the original substance into fragments did not occur.

Anal.[10] Calcd. for $C_{20}H_{22}O_9$: C, 59.11; H, 5.41. Found: C, 59.0, 59.2; H, 5.24, 5.09.

The rotations observed at all wave lengths utilized were within the range of experimental error.

TABLE I

DISPERSION OF 3,3′-DIBENZOYL-2,2′-DI-(D-GLYCERALDEHYDE) ETHER DIHYDRATE

0.1222 g. dissolved in 4 cc. of 95% ethyl alcohol in a 2-decimeter tube (equivalent to 3.055 g. in 100 cc.)

Temperature = 31.5°

	Red	Yellow	Green	Green	Green	Blue
Metal	Cd	Na	Cu	Hg	Cu	Cd
Wave length	6438	5890, 96	5700	5461	5105	4800
Reading	0.01	0.00	0.00	0.00	0.02	0.01

Rates of Oxidation.—The acetic acid was prepared exactly as that described by Hockett, Dienes and Ramsden.[6] The standardized conditions described by them were used for the rate determinations.

Summary

The preparation of a compound previously designated by Brigl and Grüner as 2,5-monoanhydro-1,6-dibenzoylmannitol has been repeated by their method of direct anhydridization of 1,6-dibenzoylmannitol. By debenzoylation of this product we have obtained also a monoanhydrohexitol. The behavior of these compounds when oxidized by lead tetraacetate shows that the 2,5-ring is present, but the observation that the resulting 3,3′-dibenzoyl-2,2′-di-(D-glyceraldehyde) ether dihydrate is optically inactive in three solvents and toward six wave lengths of light proves that a Walden inversion occurred during anhydridization and that the anhydrohexitol must be 2,5-monoanhydrosorbitol rather than 2,5-anhydromannitol.

CAMBRIDGE, MASSACHUSETTS

RECEIVED JANUARY 29, 1946

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[10] Analysis by Mrs. C. K. Fitz, M. I. T.

[CONTRIBUTION FROM THE SUGAR RESEARCH FOUNDATION LABORATORY AND FROM THE DEPARTMENT OF CHEMISTRY MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Hexitol Anhydrides.[1] The Preparation and Proof of Structure of 1,5,3,6-Dianhydromannitol (Neomannide). The Structure of Isomannide[2]

BY R. C. HOCKETT[3] AND ELIZABETH L. SHEFFIELD

In the preceding paper of this series, it was shown that Fauconnier's crystalline "isomannide" is either 1,5,3,6- or 1,4,3,6-dianhydromannitol. Since styracitol has recently been shown to be 1,5-monoanhydromannitol[4] we considered this substance to be a suitable starting material for synthesis of the 1,5,3,6-dianhydride by a method analogous to that introduced by Fischer and Zach[5] for the preparation of methyl 3,6-anhydro-D-glucopyranoside.

The first two steps of this proposed synthesis had already been carried out successfully by Zervas and Papadimitriou,[4] who obtained a crystalline 6-tosyl-2,3,4-tribenzoylstyracitol. The presence of the tosyl group in the six position is indicated not only by the numerous analogous cases where selective tosylation has been carried out upon substances containing both primary and secondary hydroxyl groups,[6] but likewise by

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[1] The previous paper of this series, THIS JOURNAL, **68**, 935 (1946).

[2] The material in this paper is taken from a thesis submitted to the Graduate School of the Massachusetts Institute of Technology in partial fulfillment of the requirements for the degree of Doctor of Philosophy by Elizabeth L. Sheffield in October, 1944. The paper was read before the Division of Sugar Chemistry and Technology at the New York meeting of the American Chemical Society in September, 1944.

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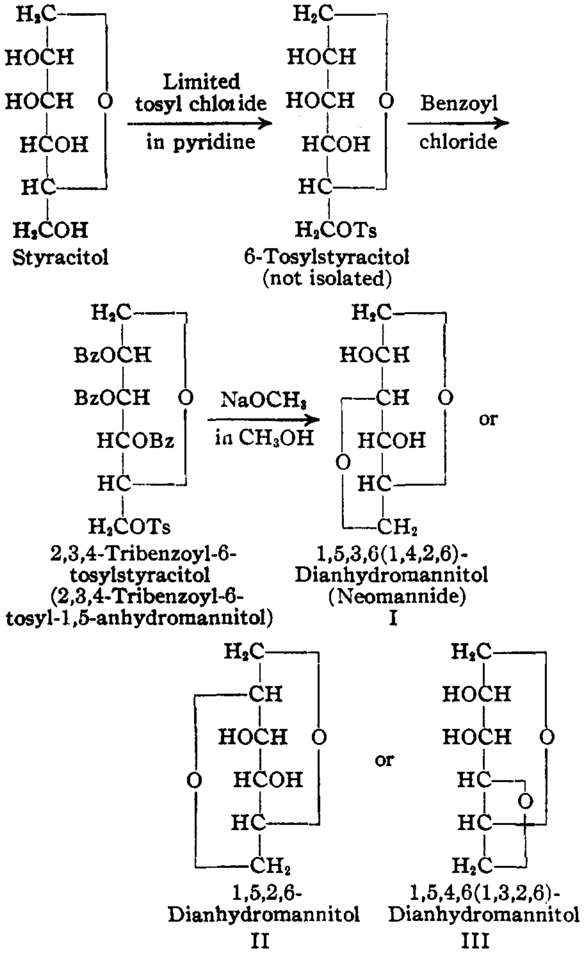
[4] Zervas and Papadimitriou, *Ber.*, **73**, 174 (1940); *cf.* Hockett and Conley, THIS JOURNAL, **66**, 464 (1944); *cf.* Richtmyer, Carr and Hudson, *ibid.*, **65**, 1477 (1943).

[5] Fischer and Zach, *Ber.*, **45**, 456, 2068 (1912); *cf.* Hockett, Nickerson and Reeder, THIS JOURNAL, **66**, 472 (1944).

[6] Compton, *ibid.*, **60**, 395 (1938); Hockett and Downing, *ibid.*, **64**, 2463 (1942); *cf.* Brigl and Grüner, *Ber.*, **65**, 641 (1932); also unpublished results.



the rate at which replacement of tosyloxy by iodide takes place.[4]

We were able to duplicate the preparation and obtain the substance described by these authors. On treating the compound with methanolic sodium methylate, we obtained a substance without benzoyl groups and corresponding in composition to a dianhydromannitol. It proved to be a new compound not identical with any of the known mannides.[1] We designate this compound as neomannide.

TABLE I

	M. p., °C.	[α]D (H$_2$O)	Author
β-Mannide	119	+94.05°	Siwolobow[a]
Isomannide	87	+90.9°	Hockett, *et al.*[b]
			Fauconnier[c]
Mannide	...	.....	Berthelot[d]
Neomannide	112.8–113.3 (cor.)	+ 6.4°	Hockett and Sheffield

[a] Siwolobow, *Ann.*, **233**, 368 (1886). [b] Reference 1. [c] Fauconnier, *Bull. soc. chim.*, (2) **41**, 119 (1884). [d] Berthelot, *Ann. chim.*, (3) **47**, 312 (1856).

The method of preparation of neomannide limits the possible structures to the three (I, II, III) shown in the equations, since the 1,5 ring preexisted and conditions were too mild to cause any shift. Since neomannide is not attacked by lead tetraacetate, structures II and III are eliminated and only the 1,5,3,6(1,4,2,6) remains (I).

The possibility of a Walden inversion at carbon three is very remote for the reasons discussed in an analogous case.[7] Therefore neomannide is 1,5,3,6-dianhydromannitol. This structure is consequently eliminated for isomannide, which is not identical with neomannide, and the only probable structure remaining for isomannide is 1,4,3,6-dianhydromannitol, which was selected as one of two possibilities in the preceding paper.[1]

Acknowledgment.—The authors wish to acknowledge the advice and counsel of Dr. R. Max Goepp, Jr., of the Atlas Powder Co. throughout this investigation.

Experimental

Styracitol.—This compound was prepared by the method of Maurer and Mahn[8] as modified by Hockett and Conley.[4] Our product melted at 153.1–154.3° (cor.).

6-Tosyl-2,3,4-tribenzoylstyracitol.—Styracitol (5 g., 0.031 mole) was suspended in 50 cc. of pyridine and tosyl chloride (5.8 g., 0.031 mole) was added. The mixture was shaken until solution was complete and left for one hour at room temperature. It was then cooled to −5° and benzoyl chloride (17.6 g., 0.11 mole) was added. The mixture was kept at 0° for two hours and then at room temperature for three hours. Ice water (100 cc.) was added and a sirup separated. The water was decanted and the sirup treated with ten 50-cc. portions of hot water containing a few drops of acetic acid. The crude product separated crystalline from a mixture of 100 cc. of reagent alcohol and 2 cc. of acetic acid. The yield was 8.5 g. or 47% of the theoretical quantity of crystals melting at 161.4–162.7°. Zervas and Papadimitriou[4] give 162°.

1,5,3,6-Dianhydromannitol (Neomannide).—Sodium (0.8 g., 0.034 mole) was dissolved in 200 cc. of dry methanol, by warming under reflux for five minutes and then cooling to room temperature. To the sodium methylate solution was added 20 g. (0.032 mole) of 6-tosyl-2,3,4-tribenzoylstyracitol. The mixture was boiled under reflux for two hours. The styracitol ester dissolved in the first fifteen minutes.

The mixture was cooled, neutralized to phenolphthalein with 10% sulfuric acid and filtered. The filtrate was evaporated dry under diminished pressure and the residue extracted with three 100-cc. portions of hot ethyl acetate. After 24 hours at 0° the combined extracts deposited crystals (0.7 g.). By concentrating to 50 cc. and cooling, a total of 2.9 g. or 63% of the theoretical yield of product was obtained. The melting point was initially 109.1–110.9° but rose to 112.8–113.3° (cor.) after two recrystallizations from 45–55-cc. portions of ethyl acetate. Further recrystallization was without effect on the melting point. The substance showed a specific rotation of +6.40° (*c*, 2.93 or 5.65; H$_2$O; 22°; D line of sodium).

Anal. Calcd. for $C_6H_{10}O_4$: C, 49.25; H, 6.87. Found: C, 49.00, 49.10; H, 6.94, 6.90.

Oxidation of Neomannide by Lead Tetraacetate.—The conditions described by Hockett, Dienes and Ramsden[9] were used, but no consumption of the oxidant occurred.

Summary

The preparation of a new dianhydromannitol,

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(7) Hockett, Conley, Yusem and Mason, THIS JOURNAL, **68**, 922 (1946).

(8) Maurer and Mahn, *Ber.*, **60**, 1316 (1927).

(9) Hockett, Dienes and Ramsden, THIS JOURNAL, **65**, 1474 (1943).

neomannide, is described and its structure determined as 1,5,3,6-dianhydromannitol. The observation that the latter is not identical with isomannide eliminates this structure and leaves only the 1,4,3,6-dianhydromannitol structure for isomannide.

CAMBRIDGE, MASSACHUSETTS

RECEIVED JANUARY 29, 1946

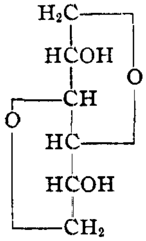
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, AND FROM THE RESEARCH DEPARTMENT, ATLAS POWDER COMPANY]

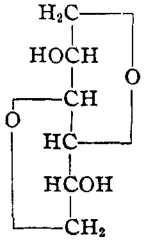
Hexitol Anhydrides.[1] 1,4,3,6-Dianhydro-L-iditol and the Structures of Isomannide and Isosorbide

BY HEWITT G. FLETCHER, JR.,[2] AND R. MAX GOEPP, JR.[2]

The ring structure of isomannide has recently been determined independently by the present authors with their collaborators[3] and by Wiggins[8] as 1,4,3,6. The closely analogous substance, isosorbide, was shown by Hockett, Fletcher, Sheffield and Goepp[4] to contain the same ring system. The present research provides independent and conclusive proof of the correctness of these structure assignments and has also resulted in the characterization of a new dianhydrohexitol, 1,4,3,6-dianhydro-L iditol.

Comparison of the structures of isosorbide and isomannide shows that they are identical save for the configuration of the second carbon atom. Partial oxidation of isosorbide would produce 1,4,3,6-dianhydro-D-fructose, 1,4,3,6-dianhydro-L-sorbose or 1,4,3,6-dianhydro-D-*threo*-2,5-diketohexitol. Isomannide, because of its end-to-end symmetry would yield only the first and the third of these compounds. Subsequent reduction of 1,4,3,6-dianhydro-D-fructose would presumably give rise to a mixture of isomannide and isosorbide; reduction of 1,4,3,6-dianhydro-L-sorbose would lead to isosorbide and 1,4,3,6-dianhydro-L-iditol, while reduction of 1,4,3,6-dianhydro-D-*threo*-2,5-diketohexitol would result in the formation of a mixture of all three dianhydro-hexitols.


1,4,3,6-Dianhydro-D-sorbitol (isosorbide)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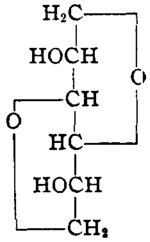
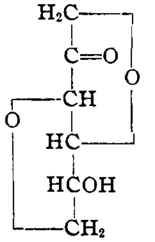
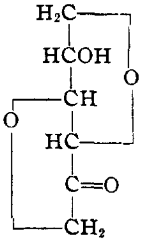
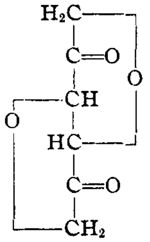

1,4,3,6-Dianhydro-L-iditol (isoidide)


1,4,3,6-Dianhydro-D-fructose


1,4,3,6-Dianhydro-L-sorbose


1,4,3,6-Dianhydro-D-*threo*-2,5-diketohexitol

The dehydrogenating properties of the catalysts usually employed for hydrogenation are well known. With this fact in mind a suspension of Raney nickel in molten isosorbide was heated at 140° *in vacuo* (2 mm.) for a brief period. Subsequent treatment of the mixture of sirup and catalyst at 190 to 200° under a pressure of 3750 pounds per square inch of hydrogen was, indeed, found to produce an amorphous mixture which, unlike isosorbide, could not be induced to crystallize. Complete benzoylation of this sirup and fractional crystallization of the resulting mixture gave a well-defined crystalline substance having the analysis of a dianhydrohexitol dibenzoate. It proved to be unlike the dibenzoate of either isosorbide or isomannide and apparently one or both of two changes had taken place during the treatment of isosorbide. Either isomerization had altered the ring structure of the isosorbide to a form more stable under the rather drastic conditions of the experiment, or inversion of one or more of the hydroxyl groups, as pictured above, had taken place. The latter hypothesis indicated that the crude isomerizate might contain, along with unchanged or reformed isosorbide, isomannide and the new hexide 1,4,3,6-dianhydro-L-iditol. Actually, chromatography of the crude isomerizate in another laboratory demonstrated the presence of three compounds.[5]

It is obvious that if this isomerization involves simply inversion of the hydroxyl groups in isosorbide, a similar isomerizate, containing the same new dianhydrohexitol, should be obtained by a similar treatment of isomannide. A parallel hydrogenation of isomannide was therefore run and yielded a sirupy mixture from which the new

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(1) The previous paper of this series, THIS JOURNAL, 68, 937 (1946). See also Fletcher and Goepp, *ibid.*, 67, 1042 (1945).

(2) Present addresses: Hewitt G. Fletcher, Jr., Division of Chemistry, National Institute of Health, Bethesda 14, Md.; R. Max Goepp, Jr., Research Department, Atlas Powder Company, Wilmington 99, Del.

(3) Hockett, Fletcher, Sheffield, Goepp and Soltzberg, THIS JOURNAL, 68, 930 (1946); Hockett and Sheffield, *ibid.*, 68, 937 (1946); Wiggins, *J. Chem. Soc.*, 4 (1945).

(4) Hockett, Fletcher, Sheffield and Goepp, THIS JOURNAL, 68, 927 (1946).

(5) Lew, Wolfrom and Goepp, *ibid.*, 67, 1865 (1945).