

changes from +69 to +45 in five hours, likewise indicates that the substance may be a delta lactone or a mixture of delta and gamma lactones; a reinvestigation of both the α - and β -L-fucohexonic lactones seems required. They possess the Class B configuration and experience has shown that the isolation of pure gamma lactones of this class requires careful control if the absence of delta lactones, crystalline free acids and their alkyl esters is to be assured.¹²

The optical behavior of D-gluco-D-ido-heptonic lactone appeared unique to Fischer¹³ when he discovered the substance. He reported that its initial specific rotation in water, twenty minutes after dissolving, was -80, which decreased and became nearly constant at -67.7 in twenty-four hours, but that "the mutarotation in this case is not caused by the partial transformation to acid, that occurs with many lactones, since the reaction of the solution remained neutral [*ganz neutral*] throughout the process." Philippe¹⁴ has confirmed this observation of Fischer, finding -82 for the rotation after three minutes, and -68 after six hours, the solution remaining neutral during the change. The cause of this unusual behavior remains hidden but its explanation appears to be required before it is possible to assign a rotatory value to this lactone.

(12) Nef, *Ann.*, **403**, 306 (1914); Isbell and Frush, ref. 3b.

(13) Fischer, *ibid.*, **270**, 64 (1892).

(14) Philippe, *Ann. chim. phys.*, **26**, 330 (1912).

During a conference at Princeton in January, 1939, the data here presented were discussed by Messrs. Walter Kauzmann and John Walter, Dr. Everett Gorin, Prof. H. Eyring, Prof. E. Pacsu and the author. The helpfulness of this conference to the author is gratefully acknowledged.

Summary

The aldonic gamma lactones are divided into two classes, in one of which the configurations are like the ribonic-arabonic pair of epimers (Class A) and in the other like the xyloxylic-lyxonic pair (Class B). Lactones of Class A show an epimeric difference of molecular rotation that is nearly constant. Lactones of Class B, for which the data are not nearly so numerous or dependable as for Class A, show an indication of constancy of epimeric difference with a value that is different from that found for Class A. It seems possible in the case of lactones of Class A to extend the qualitative lactone rule of rotation to a quantitative comparison of rotations, because the constancy of epimeric difference, and certain other comparisons, indicate that optical superposition and isorotation hold fairly closely for lactones of Class A. The unusual characters of the mutarotations of epirhammonic, β -L-fucohexonic and D-gluco-D-ido-heptonic lactones are discussed, and the rotations of six lactones, now unknown, are calculated.

WASHINGTON, D. C.

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[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF HEALTH, U. S. PUBLIC HEALTH SERVICE]

The Action of Triphenylchloromethane on α -Methyl-D-mannopyranoside¹

BY A. J. WATTERS,² R. C. HOCKETT AND C. S. HUDSON

Recent publications³ have pointed out that polyalcohols containing only secondary hydroxyl groups may be etherified directly by triphenylchloromethane (trityl chloride) in pyridine solution, just as many simple secondary alcohols are etherified.⁴ The preparation of a ditryl uridine

(1) Publication authorized by the Surgeon General, U. S. Public Health Service.

(2) Commonwealth Fellow, September, 1929-June, 1932.

(3) (a) Hockett and Hudson, *THIS JOURNAL*, **53**, 4456 (1931); (b) Hockett and Hudson, *ibid.*, **56**, 945 (1934); (c) Jackson, Hockett and Hudson, *ibid.*, **56**, 947 (1934).

(4) Helferich, Speidel and Toeldte, *Ber.*, **56**, 766 (1923); Josephson, *Ann.*, **493**, 175 (1932); Fairbourne and Cowdrey, *J. Chem. Soc.*, 129 (1929). We are also informed by Dr. N. M. Carter, Pacific Biological Station, Nanaimo, B. C., Canada, that α,α' -benzylidene glycerol forms a crystalline monotrityl ether; cf. Norris and Young, *THIS JOURNAL*, **52**, 754 (1930).

by Levene and Tipson⁵ provides an example, moreover, of the etherification of a coexistent primary and secondary group and further establishes the limitations of trityl chloride as an agent for analytical determination of the number of primary hydroxyls in compounds of unknown constitution.⁶ It remains unquestioned that the greater velocity with which this reagent attacks primary groups may be utilized advantageously in synthetic work.

The present investigation was undertaken to

(5) Levene and Tipson, *J. Biol. Chem.*, **105**, 419 (1934).

(6) Cf. Josephson, *Ann.*, **472**, 230 (1929); **493**, 174 (1932); *Ber.*, **62**, 313 (1929); Karrer, Schwarzenbach and Schöpp, *Helv. Chim. Acta*, **16**, 302 (1933); Vargha, *Nature*, **131**, 363 (1933).

learn whether α -methyl-D-mannopyranoside when treated with trityl chloride in pyridine solution would form readily a monosubstituted product similar to that from free mannose⁷ or whether polysubstitution would occur as with β -methyl-D-xylopyranoside.^{8c} A crystalline monotrityl- α -methyl-D-mannopyranoside was isolated as the major product of reaction (R. C. H.), a coordination compound of this with calcium chloride was prepared (C. S. H.), and the position of the substituent group was shown by the following transformations (A. J. W.): α -methyl-D-mannopyranoside \rightarrow 6-trityl- α -methyl-D-mannopyranoside \rightarrow 6-trityl-2,3,4-triacetyl- α -methyl-D-mannopyranoside⁸ \rightarrow 2,3,4-triacetyl- α -methyl-D-mannopyranoside \rightarrow 6-methyl-D-mannose \rightarrow 6-methyl-D-glucosazone. The last had the same properties as the 6-methyl-D-glucosazone of Helferich and Becker,⁹ the structure of which was proved conclusively by these investigators.

Experimental

6-Trityl- α -methyl-D-mannopyranoside.—A mixture of 5 g. of dry powdered α -methyl-D-mannopyranoside and 10 g. of Eastman triphenylchloromethane in 50 cc. of dry pyridine was heated under reflux for three hours on a steam-bath; water was added to turbidity and the triphenylcarbinol which separated overnight was removed. The gum which was precipitated by pouring into ice water solidified; yield, 10 g. Well formed prisms crystallized from pyridine solution by adding water; they contained pyridine of crystallization which was partially eliminated by drying over caustic soda for two months; m. p., 101–102° (corr.); rotation¹⁰ in CHCl_3 , +23.45° (*c*, 1.47; 2-dm. tube). Its analysis corresponds fairly well to that of a monotrityl methylmannoside with one mole of pyridine.

Anal. Calcd. for $(\text{C}_6\text{H}_5)_3\text{C}(\text{C}_7\text{H}_{13}\text{O}_6) \cdot \text{C}_6\text{H}_5\text{N}$: trityl, 51.69. Found: trityl, 50.41, 50.66 (Valentin's¹¹ method).

6-Trityl- α -methyl-D-mannopyranoside Calcium Chloride.—To a solution of 10 g. of crude trityl- α -methyl-D-mannopyranoside in 45 cc. of absolute alcohol, was added a clear solution of 5 g. of $\text{CaCl}_2 + 2\text{H}_2\text{O}$ in 25 cc. of absolute alcohol. Clusters of needles appeared promptly; yield 11 g. Recrystallized from absolute alcohol, they showed a dextrorotation¹⁰ in methanol of +26.6° (*c*, 1.04; 2-dm. tube) and m. p. 110–112° (corr.) (rather unsharp). Water and most organic solvents, other than ethanol and methanol, separate the substance into its constituents by selective solution of either the organic or inorganic portion.

Anal. Calcd. for $(\text{C}_{26}\text{H}_{28}\text{O}_6)_2 \cdot \text{CaCl}_2 \cdot 2\frac{1}{2}\text{C}_2\text{H}_5\text{OH}$: Ca, 3.65; Cl, 6.46; $\text{C}_2\text{H}_5\text{OH}$, 10.48. Found: Ca, 3.53; Cl, 6.46, 6.44; $\text{C}_2\text{H}_5\text{OH}$, 10.36 (loss of wt. on heating).

(7) Helferich and Leete, *Ber.*, **62**, 1549 (1929).

(8) This substance has been described by Valentin, *Coll. Czechoslov. Chem. Commun.*, **6**, 354 (1934).

(9) Helferich and Becker, *Ann.*, **440**, 1 (1924).

(10) All rotations referred to in this paper are specific rotations of sodium light at 20°.

(11) Valentin, *Coll. Czechoslov. Chem. Commun.*, **3**, 499 (1931).

6-Trityl-2,3,4-triacetyl- α -methyl-D-mannopyranoside.—Pure trityl- α -methyl-D-mannopyranoside, 17.2 g., was added slowly to a chilled mixture of 80 cc. of acetic anhydride with 80 cc. of dry pyridine. After four days in a refrigerator, the sirup was poured into ice water and it crystallized overnight; yield 19.5 g. The thin, lustrous, hexagonal plates, recrystallized from 95% alcohol, rotated¹⁰ +44.33° in CHCl_3 (*c*, 1.24; 2-dm. tube) and showed m. p. 130° (corr.).

Anal. Calcd. for $\text{C}_{32}\text{H}_{34}\text{O}_8$: C, 68.29; H, 6.09; methoxyl, 5.5; acetyl, 22.94; trityl, 43.24. Found: C, 68.24, 68.07; H, 6.08, 6.13; methoxyl,¹² 5.3, 5.3; acetyl,¹³ 23.01, 22.90; trityl,¹¹ 42.97.

2,3,4-Triacetyl- α -methyl-D-mannopyranoside.—Pure 6-trityl-2,3,4-triacetyl- α -methyl-D-mannopyranoside (2 g.) was dissolved in 15 cc. of glacial acetic acid, cooled, and 1 cc. of saturated hydrogen bromide in glacial acetic acid added slowly with stirring. The triphenylbromomethane which separated at once was filtered on a hardened paper and washed with glacial acetic acid; the filtrate was poured into 400 cc. of ice water. The precipitated triacetate, extracted with chloroform and recovered by concentration *in vacuo* at 30°, was eventually crystallized from ether by addition of petroleum ether; yield 0.72 g. The fine glistening needles, after recrystallization in the same manner, rotated¹⁰ +55.54° in CHCl_3 (*c*, 1.14; 2-dm. tube) and showed m. p. 98° (corr.).

Anal. Calcd. for $\text{C}_{13}\text{H}_{20}\text{O}_8$: C, 48.75; H, 6.25; methoxyl, 9.7; acetyl, 40.31. Found: C, 48.76, 48.75; H, 6.10, 6.25; methoxyl, 9.8, 9.8; acetyl, 40.24, 40.00.

6-Methyl-2,3,4-triacetyl- α -methyl-D-mannopyranoside.—Five grams of the pure triacetate was methylated by refluxing five successive times with 30 cc. of pure methyl iodide and 12 g. of silver oxide for six hours. A methoxyl value of 18.7% was then attained (theoret., 18.56%). Efforts to crystallize the sirup from alcohol, ether and petroleum ether were unsuccessful.

Hydrolysis of 6-Methyl-2,3,4-triacetyl- α -methyl-D-mannopyranoside.—The sirup (4.1 g.) was deacetylated and hydrolyzed to the reducing sugar in one operation by refluxing with 50 cc. of 2% hydrochloric acid on a steam-bath until the saccharimeter readings became constant, after ninety minutes. After removal of chloride with silver carbonate and of silver with hydrogen sulfide the filtrate was concentrated *in vacuo* to constant weight with an oil pump. After further drying *in vacuo* over "anhydron," the methoxyl content was close to the theoretical. Rotation,¹⁰ +15.3° in CHCl_3 (*c*, 1.13; 2-dm. tube).

Anal. Calcd. for $(\text{C}_6\text{H}_{11}\text{O}_5)\text{OCH}_3$: methoxyl, 15.9. Found: methoxyl, 15.4.

6-Monomethyl-glucosazone.—The 6-methylmannose sirup remaining weighed about 1 g. When heated with phenylhydrazine in dilute acetic acid solution, the osazone separated in ninety minutes. Recrystallized from cold pyridine by adding water, 0.3 g. of substance was obtained of m. p. 172° (corr.) and rotating -68.6° in absolute alcohol (*c*, 0.5; 1-dm. tube) twenty minutes after solution began; after forty-eight hours, -48.0° . Helferich and Becker⁹ give m. p. 177°, initial rotation -70.3° and final rotation -46.9° for 6-monomethyl-glucosazone.

(12) Clark, *J. Assoc. Off. Agr. Chem.*, **15**, 136 (1932).

(13) Kunz and Hudson, *This Journal*, **48**, 1932 (1926).

Summary

The direct action of triphenylchloromethane upon α -methyl-D-mannopyranoside in pyridine, yields 6-trityl- α -methyl-D-mannopyranoside, which is described. This substance forms a crystalline addition compound with calcium

chloride. The position of the trityl group was proved by conversion of the trityl methyl-mannopyranoside through a series of reactions to 6-monomethyl-glucosazone. The intermediate compounds are described.

WASHINGTON, D. C.

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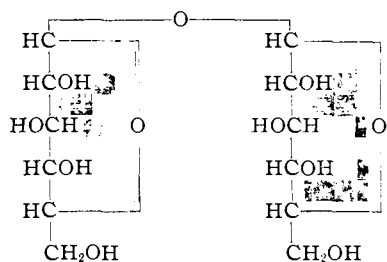
[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF HEALTH, U. S. PUBLIC HEALTH SERVICE]

The Periodic Acid Oxidation of α,α -Trehalose¹

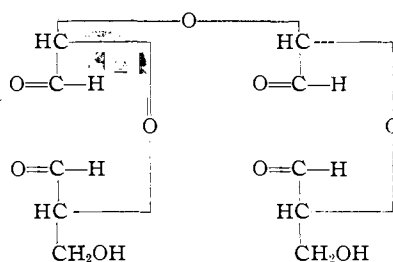
BY ERNEST L. JACKSON AND C. S. HUDSON

The two glucose components of the molecule of naturally occurring trehalose ($[\alpha]^{20}_D + 197^\circ$ in water) are now generally recognized from methyl-

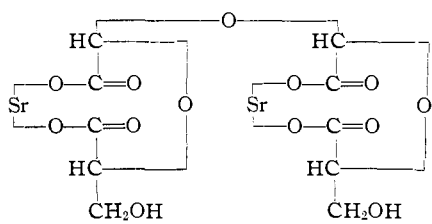
Trehalose (I) should be oxidized by periodic acid in the same manner as the methyl-D-aldohexopyranosides⁴ to produce the tetraaldehyde (II).



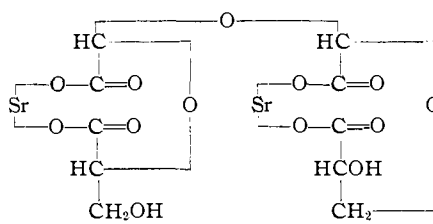
(I)
 α,α -Trehalose



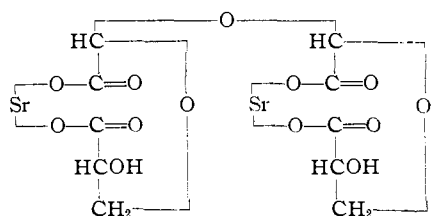
(II)
D',D'-Oxy-bis-(D-hydroxymethylidiglycolic aldehyde)⁵



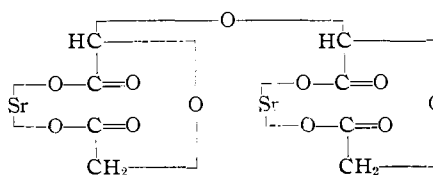
(III)
Di-strontium D',D'-oxy-bis-(D-hydroxymethylidiglycolate)



(IV)



(V)



(VI)

tion results to have the pyranoside structure² and from rotatory considerations the alpha, alpha configuration³ for carbon atoms 1 and 1'.

(1) Publication authorized by the Surgeon General, U. S. Public Health Service.

(2) Schlubach and Maurer, *Ber.*, **58**, 1178 (1925); cf. Bredereck, *ibid.*, **63**, 959 (1930).

(3) Hudson, *THIS JOURNAL*, **38**, 1586 (1916).

Oxidation of α,α -trehalose with periodic acid in aqueous solution has yielded a sirupy product, presumably the tetraaldehyde (II), which upon oxidation with bromine water kept neutral with

(4) Jackson and Hudson, *ibid.*, **59**, 994 (1937).

(5) The tetraaldehyde is named according to the plan previously adopted.⁴