products remained stable for several months if stored *in vacuo* under anhydrous conditions at 4°.

The following is an example of the procedure employed in other cases. After octaacetyl-β,β-trehalose had reacted with reagent I for 4 days at 25°, the reaction mixture was poured into an ice-cold solution of anhydrous glacial acetic acid[32] which contained a 50% excess of silver acetate required to react with all the bromine present. After one hour at 0° and 18 hours of shaking at 25°, the silver salts were removed by filtration and hydrogen sulfide and the acetic acid by distillation *in vacuo* with toluene (bath temperature, less than 50°). Crystalline material appeared spontaneously in the residue. After removal from the sirupy residue by ether and recrystallization from ethanol, it did not depress the melting point of pentaacetyl-β-D-glucopyranoside. When no further fractions of this glucose derivative could be separated, the sirupy residue, which constituted about 25% of the total product, was found to contain 9.4% bromine.

(c) **From the Reaction of Heptaacetyl-α-melibiosyl Bromide at 0°.**—In a total volume of 25 ml., a solution of 2.5 g. of heptaacetyl-α-melibiosyl bromide in dry, alcohol-free chloroform was treated at 0° with 7 ml. of acetyl bromide and 3 ml. of hydrogen bromide-in-acetic acid. After 48 hours of reaction, when the rotation had decreased from its initial value of +60.5 to +48.2°, the solution was made free of reagents as described for the octaacetyl-β,β-trehalose reaction mixture. The product was separated into crystalline and non-crystalline fractions. The former, after recrystallization from ethanol, was found to be octaacetyl-β-melibiose; m.p. 173–175°, $[\alpha]^{25}\text{D}$ +99.71° (*c* 1, chloroform), weight 0.6 g. The sirup was dried *in vacuo* to a frothy solid, weight 1.7 g., $[\alpha]^{25}\text{D}$ +25.1° (*c* 1, chloroform), bromine content, 4.1%.

(d) **From Dextran Triacetate.**—Ten grams of the triacetate of dextran from NRRL B-512 was treated with 115 ml. of each of hydrogen bromide-in-acetic acid and acetyl bromide at 25°. Approximately 4 hours was required for the solid to dissolve. The observed rotations were +16.8°, +13.0°, +12.6°, +12.1° and +12.0° at 4, 18, 24, 40 and 48 hours, respectively. Reagents were removed by distillation *in vacuo* with toluene under anhydrous conditions (solution temperature, 25° or less). The products were fractionated roughly by extraction with anhydrous solvents at room temperature, as shown in Table IV. Active bromine was replaced by acetoxyl groups by treatment with excess silver acetate in anhydrous glacial acetic acid at 25°. The products were obtained in high yield as low-melting glassy solids. Bromine of apparently intermediate activity was replaced when some of these products were treated again with excess silver acetate in glacial acetic acid. This treatment was carried out at 80° for 4 hours. No crystalline substance was obtained from any fraction.

PEORIA, ILLINOIS

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[32] W. C. Eichelberger and V. K. La Mer, THIS JOURNAL, **55**, 3633 (1933.)

[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY, UNIVERSITY OF CALIFORNIA, BERKELEY]

Derivatives of D-*manno*hexodialdose (6-*aldo*-D-Mannose)

BY CLINTON E. BALLOU[1] AND HERMANN O. L. FISCHER

RECEIVED MARCH 2, 1953

A crystalline substituted hexose dialdehyde with the D-*manno* configuration, 2,3-4,5-diisopropylidene-D-*manno*hexodialdose (II) has been obtained by the lead tetraacetate oxidation of 1,2-5,6-diisopropylidene-D-inositol. Deacetonation of II gave amorphous D-*manno*hexodialdose, characterized as the tetraethyl-1,2-3,4-mercaptal, while reduction of II gave 2,3-4,5-diisopropylidene-D-mannitol. Derivatives of the substituted dialdehyde prepared include the bisphenylhydrazone and the bis-*p*nitrophenylhydrazone.

With respect to the state of oxidation, hexose dialdehydes may be placed between the hexoses and hexuronic acids. That they have biological significance as intermediates in such a transformation has not been shown by experiment. From a chemical standpoint, however, the dialdehydes offer a wide field for study, including that of their behavior in the classical reactions of carbohydrate chemistry.

Although the literature contains several references to straight chain dialdehydes derived by chemical means from carbohydrate substances, the investigation of this class of compounds has not been extended beyond the preparation of a few simple derivatives. Micheel[2] mentions the preparation of 2,3-4,5-tetraacetyl-*galacto*hexodialdose[3,4] by the catalytic reduction of tetraacetylgalactaric acid dichloride. Mrs. Gerda Dangschat in 1942 obtained 2,3,4,5-tetraacetyl-D,L-*iodo*hexodialdose (not crystallized) from tetraacetyl myoinositol.[5] The substance gave a crystalline bisphenylhydrazone, bis-*p*-nitrophenylhydrazone and bis-*p*-dinitrophenylhydrazone. From tetraacetyl alloinositol, Dangschat and Fischer prepared 2,3,4,5-tetraacetyl-*allo*-hexodialdose.[6] The latter gave a crystalline bisphenylhydrazone, bis-*p*-nitrophenylhydrazone and a dioxime. The pentose dialdehyde, 1,2-isopropylidene-D-*xylo*pentodialdose,[7] prepared from 1,2-isopropylidene-D-glucose, has been used as an intermediate in the synthesis of hexoses, hexuronic acids and cyclitols.[8] Fischer and Appel obtained 2,3-isopropylidene-D-*threo*tetrodialdose from 3,4-isopropylidene-D-mannitol,[9] and prepared, among other derivatives of this dialdehyde, the bisphenylhydrazone and tetraethyl acetal.

Through the kindness of Dr. A. B. Anderson, we have obtained quantities of pinitol from which D-inositol is readily prepared. This paper describes a simplified procedure for the acetonation of D- or L-

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[1] Public Health Service Research Fellow of the National Heart Institute.

[2] F. Micheel, "Chemie der Zucker und Polysaccharide," Akademische Verlagsgesellschaft, Leipzig, 1939, pp. 176–177.

[3] Uenzelmann, Dissertation, Gottingen (1931).

[4] Since a general system for the nomenclature of the sugar dialdehydes has not been devised, these substances have in the past been named as (a) polyhydroxy derivatives of aliphatic dialdehydes, (b) derivatives of saccharic acid dialdehydes, (c) 6-aldo-hexoses and 5-aldo-pentoses. In this paper the general name "dialdose" has been adopted, *i.e.*, hexodialdose, and the substances are treated as members of a distinct class rather than as derivatives of the hexoses.

[5] G. Dangschat, *Naturwissenschaften*, **30**, 146 (1942); *C. A.*, **37**, 3408 (1943).

[6] G. Dangschat and H. O. L. Fischer, *Naturwissenschaften*, **27**, 756 (1939).

[7] K. Iwadare, *Bull. Chem. Soc. Japan*, **16**, 40 (1941); *C. A.*, **35**, 4740 (1941).

[8] J. C. Sowden, THIS JOURNAL, **74**, 4377 (1952); J. M. Grosheintz and H. O. L. Fischer, *ibid.*, **70**, 1476, 1479 (1948).

[9] H. O. L. Fischer and H. Appel, *Helv. Chim. Acta*, **17**, 1574 (1934).

inositol,[10] and the oxidation of diisopropylidene-D-inositol by lead tetraacetate to give crystalline 2,3-4,5-diisopropylidene-D-*manno*hexodialdose. Deacetonation of this substance gave amorphous D-*manno*hexodialdose, characterized as the tetraethyl mercaptal. Diisopropylidene - D - *manno*hexodialdose formed a bisphenylhydrazone, a bis-*p*-nitrophenylhydrazone and was converted by reduction to the new 2,3-4,5-diisopropylidene-D-mannitol.[11]

This series of reactions is similar to that carried out by Dr. S. J. Angyal with L-inositol by which he confirmed the configuration of the latter.[12]

Experimental

Acetonation of D-Inositol (I).—D-Inositol, from demethylation of pinitol,[13] was acetonated by the procedure of Baer.[14] To a solution of fused zinc chloride (375 g.) in dry acetone (1500 ml.) was added finely ground D-inositol (80 g.). The mixture was shaken until solution of the inositol was almost complete (one to two days). This solution was then poured into a rapidly stirred mixture of ether (1500 ml.) and potassium carbonate (400 g.) dissolved in water (400 ml.), contained in a 4-liter erlenmeyer flask. The stirring was continued for 30 minutes, and the solid which collected on the wall of the flask was occasionally scraped loose. The solution was then filtered from the zinc and potassium salts, which were washed well with 1:1 ether–acetone. The filtrate was dried by stirring for 30 minutes with 500 g. of anhydrous potassium carbonate, and then filtered a second time. The dried solution was concentrated *in vacuo* to a solid mass of crystals. The solid was extracted with hot water (three 100-ml. portions) to remove the water-soluble diisopropylidene-D-inositol. The insoluble crystals of triisopropylidene-D-inositol were collected on a funnel and washed with hot water. The yield of the latter was 35 g., and the product melted at 213–214° following recrystallization from absolute ethanol. It showed $[\alpha]^{21}_{\mathrm{D}}$ −36.5 (*c* 2, chloroform). For triisopropylidene-L-inositol Angyal and MacDonald report m.p. 213–214°.[10]

Anal. Calcd. for $C_{15}H_{24}O_6$ (300.1): C, 60.0; H, 8.0. Found: C, 60.2; H, 8.2.

The combined water filtrate which contained the water soluble diisopropylidene-D-inositol was concentrated to dryness *in vacuo*. The crystalline residue obtained was extracted with hot benzene and, upon cooling, the benzene extract deposited crystals of diisopropylidene-D-inositol (45 g.), m.p. 145–150°. This was dissolved in twice the weight of boiling water, and the solution was allowed to cool at room temperature, during which the product separated as heavy needles. The crystallization was completed at 5° for two or three days. The filtered dried product weighed 35 g., melted at 149–151°, and had $[\alpha]^{20}_{\mathrm{D}}$ +4.8° (*c* 3, ethanol). For diisopropylidene-L-inositol Angyal and MacDonald report m.p. 153°.[10]

Anal. Calcd. for $C_{12}H_{20}O_6$ (260.1): C, 55.4; H, 7.7. Found: C, 55.1; H, 7.4.

Triisopropylidene-D-inositol (12 g.) was partially deacetonated according to Angyal,[10] and the diisopropylidene-D-inositol obtained purified as described above. The yield of the latter was 8 g., m.p. 149–151°. The material insoluble in benzene was extracted with hot ethyl acetate. When cooled, the ethyl acetate extract gave 1.1 g. of isopropylidene-D-inositol, m.p. 152–153°, $[\alpha]^{20}_{\mathrm{D}}$ +95.7° (*c* 2, water). As reported, isopropylidene-L-inositol melts at 157.5–158°.[10]

Anal. Calcd. for $C_9H_{16}O_6$ (220.1): C, 49.1; H, 7.2. Found: C, 48.7; H, 7.2.

2,3-4,5-Diisopropylidene-D-*manno*hexodialdose (II).—Diisopropylidene-D-inositol (2.0 g.) was suspended in dry thiophene-free benzene (50 ml.) and 1 mole equivalent of lead tetraacetate (3.5 g.) was added. The solid was triturated with a glass rod to ensure complete reaction. After 30 minutes the solution was tested for excess oxidant with starch–iodide paper. Small amounts of the inositol derivative were added to consume any excess that existed. After filtration from the lead salts, the benzene solution was concentrated *in vacuo* to give 1.95 g. of crystals. Recrystallization from dry benzene yielded pure 2,3-4,5-diisopropylidene-D-*manno*hexodialdose (1.7 g.) with m.p. 125–132°. The material is slowly soluble in water to give $[\alpha]^{20}_{\mathrm{D}}$ −4.5 (*c* 2), and in methanol $[\alpha]^{20}_{\mathrm{D}}$ −21.6° (*c* 2). It is easily soluble in chloroform (U.S.P.) and the initial rotation $[\alpha]^{20}_{\mathrm{D}}$ −131 (*c* 2) changed over two days to a constant value $[\alpha]^{21}_{\mathrm{D}}$ −85°. On storage in a closed vessel for several weeks, II decomposed to a sirup that smelled strongly of free acetone.

Anal. Calcd. for $C_{12}H_{18}O_6$ (258): C, 55.8; H, 7.0. Found: C, 56.1; H, 6.9.

Diisopropylidene-D-*manno*hexodialdose is apparently nonreducing to hot Fehling solution, although prior treatment with dilute acid to remove the acetone groups makes the substance strongly reducing. However, titration of the aldehyde groups in II by oxidation with alkaline iodine (0.02 *M* iodine in 0.2 *M* sodium bicarbonate–sodium carbonate buffer) gave an oxidation equivalent of 68.7 after two hours and 60.0 after four hours. The oxidation equivalent for structure II would be 258/4 or 64.5.

Cleavage of I by sodium metaperiodate proceeds with the uptake of one mole of periodate per mole of I. However, crystalline II was isolated only with difficulty and in a small yield. It was observed that exposure to water or alcohols decreased the tendency of II to crystallize, probably due to hydration or hemiacetal formation.

2,3-4,5-Diisopropylidene-D-*manno*hexodialdose Bisphenylhydrazone (III).—A sample of the crystalline dialdehyde II was refluxed in absolute ethanol for one hour with 3 mole equivalents of phenylhydrazine. The solution was left at 5° and crystallization of the bisphenylhydrazone occurred after a few weeks. It was recrystallized twice from methanol, after which the yellow fluffy needles melted at 159–162° with sintering at 155°.

Anal. Calcd. for $C_{24}H_{30}O_4N_4$ (438): N, 12.8. Found: N, 13.4.

2,3-4,5-Diisopropylidene-D-*manno*hexodialdose Bis-*p*-nitrophenylhydrazone (IV).—A solution of I (100 mg.) in water (10 ml.) was treated with 1 mole equivalent of sodium metaperiodate. After one hour, 2 moles of *p*-nitrophenylhydrazine dissolved in glacial acetic acid was added. The precipitate which formed immediately was collected by filtration, and recrystallized from absolute ethanol. The dark red granular crystals (100 mg.) melted at 214°, after sintering at 210°.

Anal. Calcd. for $C_{24}H_{28}O_8N_6$ (528.2): N, 15.9. Found: N, 15.8.

D-*Manno*hexodialdose Tetraethyl Mercaptal (V).—Diisopropylidene-D-*manno*hexodialdose (1.3 g.) dissolved in cold concd. hydrochloric acid (7.5 ml.), was shaken with ethyl mercaptan (5 ml.) in a closed flask. The contents of the flask solidified in about 30 seconds. After five minutes, ice-water (50 ml.) was added, the mixture was shaken, and the solid collected on a funnel. The solid was washed with cold water, then with petroleum ether. It weighed 1.3 g., 66% of the theoretical yield. The material was dissolved in 95% ethanol (5 ml. at 60°) and water was added to turbidity. The mercaptal crystallized as fine, white needles. The dried product weighed 1.2 g., melted at 109–111° and gave $[\alpha]^{21}_{\mathrm{D}}$ +26.9° (*c* 1.5, ethanol).

Anal. Calcd. for $C_{14}H_{30}O_4S_4$ (390.1): C, 43.2; H, 7.7; S, 32.8. Found: C, 43.9; H, 7.8; S, 32.9.

When V was oxidized with sodium metaperiodate, there was an initial rapid consumption of seven moles of oxidant (over a period of one hour) with liberation of four moles of formic acid, and a slow additional consumption of periodate for several hours. Lead tetraacetate oxidation of mercap-

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[10] S. J. Angyal and C. G. MacDonald, *J. Chem. Soc.*, 686 (1952).

[11] A following paper will describe the reaction of II with methanol and hydrogen chloride, by which a number of methyl glycosides have been obtained.

[12] Dr. S. J. Angyal, Personal Communication to H. O. L. F., dated October 29, 1951.

[13] Pinitol (100 g.) was refluxed with 47% hydriodic acid (250 ml.) for two hours in a hood using an air condenser. The hot solution was poured in boiling absolute ethanol (1600 ml.) and the D-inositol crystallized immediately. After completion of crystallization in the cold, the D-inositol was collected on a funnel, washed thoroughly with absolute ethanol, and dried *in vacuo* at 80°. Depending on the purity of the pinitol, the product obtained (85 g.) melted between 238 and 246°.

[14] E. Baer, "Biochemical Preparations," John Wiley and Sons, Inc., New York, N. Y., 1952, p. 31.

tals has indicated oxidation of the sulfur atoms.[15] The above results are consistent with a mechanism involving (1) the consumption of three moles of periodate to cleave the contiguous hydroxyl bearing carbon chain to give two moles of formic acid and two of glyoxal diethyl mercaptal, (2) the consumption of four moles of periodate to give two moles of glyoxal diethyl sulfoxide, (3) the spontaneous decomposition of the latter to give two moles of formic acid and two of formaldehyde diethyl sulfoxide and (4) slow oxidation of the latter to formaldehyde diethyl sulfone.

D-*Manno*hexodialdose (VI).—Diisopropylidene-D-*manno*-hexodialdose (5 g.) was heated at 100° for 40 minutes with 50% acetic acid (20 ml.) the solvent was removed by distillation, and the thick sirup obtained was dissolved in water (5 ml.). This solution was poured into absolute ethanol (50 ml.). The amorphous material that precipitated was collected and dried. It sintered at 150–160° and turned brown. The specific rotation at 20° was +47.7° (*c* 1, water).

Anal. Calcd. for $C_6H_{10}O_6$: C, 40.3; H, 5.6. Calcd. for $C_6H_{10}O_6 \cdot 0.5H_2O$: C, 38.5; H, 5.9. Found: C, 38.9; H, 5.9.

D-*Manno*hexodialdose was not fermented by a bakers yeast that fermented D-mannose readily.

2,3-4,5-Diisopropylidene-D-mannitol (VII).—A solution of I (1.0 g.) in water (25 ml.) was treated with 0.3 *M* sodium metaperiodate (15 ml.). After one hour most of the periodate had been consumed, and sodium borohydride (0.38 g.) was added to reduce the aldehyde groups. After one hour, the solution was extracted four times with chloroform (25 ml. each portion). The combined chloroform extract was washed once with water (10 ml.), then the organic layer was concentrated to a thick sirup which began to crystallize. It was recrystallized from benzene, to give 2,3-4,5-diisopropylidene-D-mannitol (0.7 g.) with m.p. 90–92°, and $[\alpha]^{19}_D$ +13.4° (*c* 3, chloroform).

Anal. Calcd. for $C_{12}H_{22}O_6$ (262): C, 55.0; H, 8.4. Found: C, 55.3; H, 8.4.

Deacetonation of VII was accomplished by refluxing 0.25 g. in 0.5 *N* hydrochloric acid for five minutes. After removal of the solvent by distillation, the D-mannitol was crystallized from a mixture of water and ethanol. It melted at 164–165°, and the m.p. was not depressed when the substance was mixed with authentic D-mannitol. The specific rotation, +29.4° (*c* 4.5), in the presence of two parts of sodium borate decahydrate, compares well with the literature value +28.6° (*c* 10) determined under similar conditions.

Anal. Calcd. for $C_6H_{14}O_6$ (182): C, 39.5; H, 7.7. Found: C, 39.8; H, 7.8.

Acknowledgment.—The authors wish to express their gratitude to the Nutrition Foundation, Inc., for the generous support of this work.

BERKELEY, CALIFORNIA

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[15] C. Huebner, R. Pankratz and K. P. Link, THIS JOURNAL, **72**, 4811 (1950).

[CONTRIBUTION FROM THE NAVAL STORES RESEARCH DIVISION, SOUTHERN REGIONAL RESEARCH LABORATORY[1]]

Peroxides from Turpentine. II. Pinane Hydroperoxide[2]

BY G. S. FISHER, J. S. STINSON AND L. A. GOLDBLATT[3]

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The preparation of *cis-l*-pinane-2-hydroperoxide from β-pinene is described. The β-pinene was converted to *cis-l*-pinane by hydrogenation and fractional distillation of the product. The *cis-l*-pinane was oxidized at about 90° for 20 hours to give an oxidate containing about 50% of pinane hydroperoxide. The pure *cis-l*-pinane-2-hydroperoxide was isolated by a combination of distillation and precipitation of the sodium salt. Its structure was proved by reduction to the known *cis*-pinanol-2.

In the first paper of this series[4] it was reported that pinane could be oxidized with oxygen to give a hydroperoxide which is a very good polymerization catalyst, but the hydroperoxide was not isolated or identified. The purpose of the present paper is to describe the preparation of a pure pinane hydroperoxide and to present evidence that it is *cis-l*-pinane-2-hydroperoxide.

Since there are four stereoisomers of pinane there should also be four stereoisomers for each position isomer of pinane hydroperoxide. In order to minimize the problem of stereoisomerism, the pinane used in this investigation was prepared from *l*-β-pinene by hydrogenation under conditions which were expected to give the *cis* isomer. The crude pinane obtained after simple distillation to remove the catalyst had the properties indicated in Table I. These properties are in very good agreement with those reported by Lipp[5] for *cis*-pinane. He reported n^{20}_D 1.4624, d^{20}_4 0.8562 and $[\alpha]_D$ −18.9 for *cis-l*-pinane prepared from impure *l*-α-pinene and n^{20}_D 1.4624, d^{20}_4 0.8566 and $[\alpha]_D$ +23.08 for *cis-d*-pinane. Fractionation of this crude pinane through an efficient distillation column at 20 mm. yielded a series of fractions of substantially constant boiling point, refractive index and density, but whose optical rotation increased throughout the distillation. Properties of typical fractions from this distillation are also given in Table I. The nature of the low rotating impurity will be discussed further in connection with the oxidation studies.

TABLE I

PHYSICAL PROPERTIES OF β-PINENE AND DERIVED PINANES

	n^{20}_D	d^{20}_4	$[\alpha]_D$	Total distillate, %
β-Pinene	1.4787	0.8723	−21.3°	..
Crude pinane	1.4624	.8571	−22.7°	..
Fraction 16	1.4622	.8563	−21.6°	10
36	1.4624	.8567	−22.9°	40
47	1.4624	.8569	−23.2°	60
56	1.4626	.8565	−23.6°	78
63	1.4624	.8567	−23.8°	90

In order to determine whether this variation in optical rotation of the pinane would affect the op-

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[1] One of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, U. S. Department of Agriculture. Article not copyrighted.

[2] Presented in part before the Division of Organic Chemistry at the 122nd Meeting of the American Chemical Society, Atlantic City, N. J., September, 1952.

[3] Southern Regional Research Laboratory, New Orleans, Louisiana.

[4] G. S. Fisher, L. A. Goldblatt, I. Kniel and A. D. Snyder, *Ind. Eng. Chem.*, **43**, 671 (1951).

[5] A. Lipp, *Ber.*, **56**, 2096 (1923).