and B-1146 showed the lowest specific rotations of all these dextrans, +214 to +215° and their triacetates showed the highest rotations, +218 to +219°. Periodate oxidation indicates that these dextrans have 5% or less of non-1,6-linkages and that, within the limitations of the method, these are of the 1,4-like type.

The dextrans from B-1254 and B-1299 and fraction L from B-742 constitute the third class of dextrans. Their specific rotations were +216 to +218° and those of their triacetates were +212 to +214°. Although these dextrans had 10% to 50% of non-1,6-linkages, they showed no detectable rotational dependence upon the content of these linkages. Periodate oxidation indicates these linkages to be 1,4-like, but this does not exclude the possibility of other types in small proportions. In fact, the rotational values of these three dextrans and of their triacetates, which were intermediate between those for the other two classes, suggest that small proportions of linkages, similar in influence to the 1,3-like, might be present.

The triacetates of dextrans having 50–80% 1,6-linkages decomposed at much lower temperatures than those from dextrans having higher proportions of these linkages. The behavior of the triacetate from the water-insoluble dextran B-523 was anomalous. These decomposition temperatures are believed to be indicative of the activation energies required to disrupt the forces of molecular aggregation.[19]

The observations reported here on the triacetates of nine bacterial dextrans of widely varying properties have established that differences in the dextrans manifested in values for periodate oxidation, specific rotation and intrinsic viscosity are due to fundamental structural characteristics which are carried through into the dextran triacetates.

Acknowledgment.—We wish to express our appreciation to Dr. Wm. C. Haynes of the Culture Collection Section of this Laboratory for assistance in production of the dextrans; to R. W. Jones for performing part of the experimental work; and to T. A. McGuire and C. H. Van Etten for the acetyl and formyl analyses, respectively.

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[19] W. O. Baker, C. S. Fuller and N. R. Pape, THIS JOURNAL, **64**, 776 (1942).

PEORIA, ILLINOIS

[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES, NATIONAL INSTITUTES OF HEALTH, PUBLIC HEALTH SERVICE, FEDERAL SECURITY AGENCY]

Derivatives of L-Xylose

BY ROBERT K. NESS AND HEWITT G. FLETCHER, JR.

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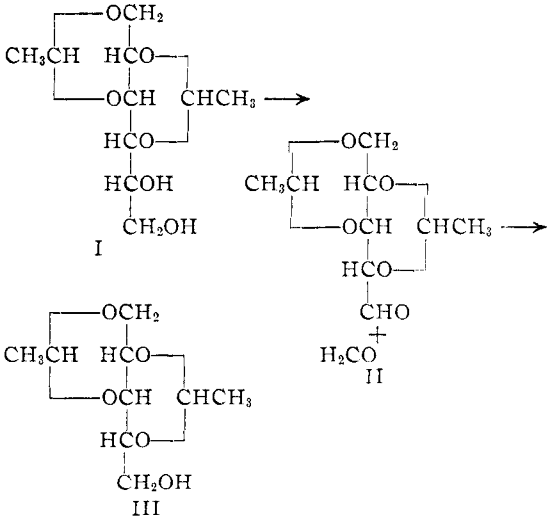
Improvements in the preparation of 1,3:2,4-diethylidene-D-glucitol and 2,4:3,5-diethylidene-L-xylose are described as well as various new derivatives of the latter. Crystalline 1,3:2,4-diethylidene-D-xylitol (= 2,4:3,5-diethylidene-L-xylitol) and some of its derivatives have also been prepared.

In the course of recent work, a quantity of 1,3:2,4-diethylidene-D-xylitol (III, synonym: 2,4:3,5-diethylidene-L-xylitol) was required as an intermediate. Since Hockett and Schaefer[1] have described the synthesis of 2,4:3,5-diethylidene-L-xylose (II) through 1,3:2,4-diethylidene-D-glucitol (I), this path of synthesis (I to III) was chosen.[1a]

The preparation of 1,3:2,4-diethylidene-D-glucitol, an important intermediate in the synthesis of L-xylose,[1] through the direct ethylidenation of D-glucitol has been studied by numerous authors.[1,2] By appropriate modification of the conditions of the reaction and through the use of ion-exchange resins we have raised the yield of crystalline 1,3:2,4-diethylidene-D-glucitol to 46%.



The oxidation of 1,3:2,4-diethylidene-D-glucitol (I) to 2,4:3,5-diethylidene-L-xylose (II) has been carried out with lead tetraacetate in acetic acid–benzene[2a] and in aqueous acetic acid.[1] While the work of Hockett and Schaefer[1] in this respect was fully confirmed, the product appeared to contain substances poisoning the platinum catalyst used in the succeeding hydrogenation. As an alternative, sodium metaperiodate in aqueous solution was employed as an oxidant and this proved to be preferable to lead tetraacetate for this purpose. Not only is the weight of sodium metaperiodate required less than half that of the lead tetraacetate but the

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[1] R. C. Hockett and F. C. Schaefer, THIS JOURNAL, **69**, 849 (1947).

[1a] While this paper was in press E. J. Bourne, W. M. Corbett and M. Stacey [*J. Chem. Soc.*, 2810 (1952)] published a study of 2,4:3,5-diethylidene-L-xylose which confirms and extends some of the observations noted here.

[2] *Cf.* (a) H. Appel, *ibid.*, 425 (1935); (b) W. R. Sullivan, THIS JOURNAL, **67**, 837 (1945); (c) P. Bladon and L. N. Owen, *J. Chem. Soc.*, 591 (1950).

oxidant is stable, more readily available and leaves a final reaction mixture which is simpler to work up. Our yield of 2,4:3,5-diethylidene-L-xylose (87%) was practically identical with that of Hockett and Schaefer[1,3] (89%). A modification of this procedure in which the 2,4:3,5-diethylidene-L-xylose is not isolated but hydrolyzed directly doubtless offers the most convenient method for the preparation of small quantities of L-xylose.

Hockett and Schaefer[1] characterized 2,4:3,5-diethylidene-L-xylose (II) as its dimethone. We have repeated this preparation and obtained a substance having the same analysis and optical rotation but melting some forty degrees higher. Quite possibly the substance exists in dimorphic forms. By solution in ethanolic hydrogen chloride at 20° 2,4:3,5-diethylidene-L-xylose dimethone was readily converted into the corresponding anhydride. 2,4:3,5-Diethylidene-L-xylose was also characterized as its crystalline benzylphenylhydrazone.

Breddy and Jones[4] in 1945 found that the action of a mixture of benzaldehyde, methanol and hydrogen chloride upon D-xylose produces a dibenzylidene-D-xylose dimethyl acetal, very probably 2,4:3,5-dibenzylidene-D-xylose dimethyl acetal, in very high yield. Wise and Ratliff[5] extended this study and prepared the corresponding derivative of the L-xylose series. In the course of the present work the raceme was prepared.

Catalytic hydrogenation of 2,4:3,5-diethylidene-L-xylose (II) gave 2,4:3,5-diethylidene-L-xylitol (III) or, more properly, 1,3:2,4-diethylidene-D-xylitol. This crystalline substance was characterized as its benzoate, phenylcarbamate and tosylate; attempts to remove the ethylidene groups in the latter derivative led to loss of the tosyl residue.

Experimental[6]

1,3:2,4-Diethylidene-D-glucitol (I).—To a well-cooled and rapidly-stirred mixture of 50 g. of pure D-glucitol, 10 ml. of water and 50 ml. of paraldehyde there was slowly added 10 ml. of concentrated sulfuric acid. The reaction mixture was shaken at room temperature for 30 hours, combined with three similar runs, cooled and treated with a solution of 200 g. of barium hydroxide octahydrate in 2 l. of water. The residual acidity was removed with 50 g. of barium carbonate and then a suspension of 0.5 g. of bentonite (325 mesh) in 20 ml. of water was stirred in to facilitate coagulation of the precipitate. After 17 hours at 0° the precipitate was removed on a bed of Filter-Cel and the filtrate deionized by successive passage through columns of Duolite A-4[7] and Amberlite IR-120.[8] The solution was concentrated *in vacuo* (80° bath), and the resulting residue dissolved in 250 ml. of absolute ethanol and reconcentrated *in vacuo*. From 160 ml. of cold absolute alcohol there was obtained 31.7 g. of crude 1,3:2,4-diethylidene-D-glucitol melting at 186–203°. The mother liquor was concentrated *in vacuo* at 100°, dissolved in 300 ml. of 50% (v./v.) aqueous acetic acid and the solution held at 100° for 50 minutes. Solvent was then removed rapidly *in vacuo* at 80° and two 150-ml. batches of absolute alcohol were successively evaporated from the residue. Dissolved in 120 ml. of absolute alcohol and held at +5° overnight, the residue furnished 86.8 g. (total crude yield, 46%[9]) more of 1,3:2,4-diethylidene-D-glucitol, m.p. 187–202°. Successive recrystallization from 6 parts of 2:1 methanol–ether, 4 parts of 1:1 methanol–ether and 10 parts of absolute ethanol afforded pure 1,3:2,4-diethylidene-D-glucitol melting at 217–219° and rotating in water −11.8° (*c* 2.1). A melting point of 218–219°[10] and a rotation in water of $[\alpha]^{15}\text{D}$ −10.9° (*c* 5.5)[11] have been recorded for this substance.

2,4:3,5-Diethylidene-L-xylose (II).—1,3:2,4-Diethylidene-D-glucitol (15 g.) was dissolved in 45 ml. of water, the solution cooled to 4° and treated with a hot solution of 13.8 g. (1.01 molar equivalents) of sodium metaperiodate in 30 ml. of water. After six minutes 100 ml. of anhydrous, peroxide-free dioxane was added and the mixture cooled in an ice-bath for 20 minutes. The fine white needles of sodium iodate (13.59 g.) were filtered off and the filtrate concentrated *in vacuo* (45° bath) to a sirup which was then dissolved in 75 ml. of anhydrous dioxane.[12] A small quantity (0.28 g.) of crystalline inorganic material was removed and the solution then concentrated *in vacuo* at 65° to a sirup which crystallized spontaneously when heated *in vacuo* at 85°. After further heating *in vacuo* for 30 minutes at 100° the crystalline product was dissolved in 40 ml. of boiling, peroxide-free *n*-butyl ether. The 2,4:3,5-diethylidene-L-xylose (11.24 g., 87%) which deposited at room temperature as elongated prisms melted at 152–160°. Sublimation at 110–125° and 0.03 mm. afforded, with little loss, material melting at 161–165° and rotating in water −13.2° (*c* 3) and in pure dioxane showing the much larger levorotation of −121° (*c* 1.2).

Hockett and Schaefer[1] reported a melting point of 162–163° and a rotation in water of −12.4° (*c* 2.9) for 2,4:3,5-diethylidene-L-xylose.

2,4:3,5-Diethylidene-L-xylose Benzylphenylhydrazone.—A solution of 250 mg. of benzylphenylhydrazine hydrochloride and 120 mg. of 2,4:3,5-diethylidene-L-xylose in 6 ml. of water, kept at room temperature for 1.5 hours, gave a fine, white crystalline precipitate which, recrystallized from 8 ml. of 60% ethanol, weighed 190 mg. (84%) and melted at 127–128°. Further recrystallization failed to change this value. The product showed a rotation in 95% alcohol of −127° (*c* 0.6).

Anal.[13] Calcd. for $C_{22}H_{26}O_4N_2$: C, 69.09; H, 6.85; N, 7.33. Found: C, 68.82; H, 6.76; N, 7.15.

2,4:3,5-Diethylidene-L-xylose Dimethone.—The 2,4:3,5-diethylidene-L-xylose (850 mg.) was added to a hot solution of 1.6 g. of dimethyldihydroresorcinol in 200 ml. of water. Precipitation of the product was rapid; after two minutes the mixture was cooled to +5°. Seven hours later the product was removed and recrystallized from 19 parts of 5:3 ethanol–water; 1.46 g. (75%), m.p. 233–239° (dec., heating at rate of 8°/min.). A second recrystallization gave large prisms of the same melting point and showing +41.0° in chloroform (*c* 1.2). Hockett and Schaefer[1] reported a melting point of 196–199° for this compound and a rotation of +40.3° in chloroform. The dimethone is soluble in 0.1 *N* sodium hydroxide and in alcoholic solution gives a positive ferric chloride test.

Anal. Calcd. for $C_{25}H_{36}O_8$: C, 64.63; H, 7.81. Found: C, 64.91; H, 7.85.

2,4:3,5-Diethylidene-L-xylose Dimethone Anhydride.—2,4:3,5-Diethylidene-L-xylose dimethone (332.1 mg.) was dissolved in 95% ethanol, the solution diluted with ethanol to 15 ml. and then treated with 0.25 ml. of concentrated hydrochloric acid. After 70 hours at 20° the mixture had ceased to mutarotate; acid was removed by passage through

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(3) The by-product obtained by these authors when using glacial acetic acid–benzene as a solvent for the oxidation was not encountered.

(4) L. J. Breddy and J. K. N. Jones, *J. Chem. Soc.*, 738 (1945).

(5) L. E. Wise and E. K. Ratliff, *Anal. Chem.*, **19**, 694 (1947).

(6) Melting points are corrected for stem exposure. Unless otherwise specified rotations are specific rotations for the D-line of sodium at 20°; concentration is expressed in g. of substance per 100 ml. of solution.

(7) A Product of the Chemical Process Co., 801 Spring St., Redwood City, Calif.

(8) A product of the Resinous Products and Chemical Co., Washington Square, Philadelphia 5, Pa.

(9) Retreatment of the material remaining in the mother liquor with aqueous acetic acid as described, somewhat increased this total crude yield.

(10) K. Gätzi and T. Reichstein, *Helv. Chim. Acta*, **21**, 186 (1938).

(11) E. J. Bourne and L. F. Wiggins, *J. Chem. Soc.*, 1933 (1948). Hockett and Schaefer (ref. 1) report a rotation of 12.15° in water, an obvious misprint for −12.15°.

(12) In later experiments anhydrous methanol was found to be a satisfactory substitute for dioxane.

(13) Analytical determinations were carried out by the Institutes Microanalytical Laboratory under the direction of Dr. William C. Alford.

a column of Duolite A-4[7] and the solution concentrated *in vacuo* to a crystalline mass. Recrystallization from 25 ml. of ligroin (b.p. 90–100°) afforded 140 mg. (44%) of prisms melting at 207–209°. Further recrystallization from ligroin failed to change this value. The anhydride rotated −23.4° in chloroform (*c* 1.82), gave a negative test with alcoholic ferric chloride and was insoluble in 0.1 *N* sodium hydroxide.

Anal. Calcd. for $C_{25}H_{34}O_7$: C, 67.24; H, 7.67. Found: C, 67.35; H, 7.56.

2,4:3,5-Dibenzylidene-L-xylose Dimethyl Acetal and 2,4:3,5-Dibenzylidene-D,L-xylose Dimethyl Acetal.—When 2,4:3,5-diethylidene-L-xylose was dissolved in the mixture of methanol, benzaldehyde and hydrogen chloride described by Breddy and Jones[4] there was obtained, after 10 days at room temperature, crude 2,4:3,5-dibenzylidene-L-xylose dimethyl acetal. However, the yield was only 16% and the following two-stage procedure proved superior.

One gram of 2,4:3,5-diethylidene-L-xylose was hydrolyzed with boiling 0.2 *N* sulfuric acid in the manner described by Hockett and Schaefer.[1] After removal of acid with Duolite A-4[7] the solution was concentrated *in vacuo* and the resulting sirup dried by repeated distillation therefrom of absolute methanol. Dissolved in 10 ml. of the Breddy–Jones reagent[4] the clear colorless sirup gave, after 5 days, 0.97 g. (53%) of product melting at 206–210°. Recrystallization from 25 ml. of boiling methyl Cellosolve gave long flexible needles melting at 210–212°; further recrystallization failed to change this value. The 2,4:3,5-dibenzylidene-L-xylose dimethyl acetal showed in chloroform +6.6° (*c* 1.07). Wise and Ratliff[5] reported a melting point of 210–211° and $[\alpha]^{24}\text{D}$ +6.56° ($CHCl_3$) for this substance.

Equal amounts (233.2 mg.) of each of the enantiomorphs were dissolved in 10 ml. of boiling methyl Cellosolve. On cooling, 416.6 mg. of cotton-like needles melting at 212–217° was obtained. Recrystallization from methyl Cellosolve and from chloroform–pentane gave pure material melting at 214–216° and showing no rotation in chloroform (*c* 1.45). The melting point, higher than that of its components, shows the crystalline material to be a racemic compound.

Anal. Calcd. for $C_{21}H_{24}O_6$: C, 67.73; H, 6.50. Found: C, 67.63; H, 6.57.

1,3:2,4-Diethylidene-D-xylitol (III) (= 2,4:3,5-Diethylidene-L-xylitol).—To a solution of 6 g. of 2,4:3,5-diethylidene-L-xylose in 20 ml. of methanol was added 300 mg. of platinum oxide and the mixture hydrogenated at room temperature and pressure. When the reduction was complete, 100 ml. of water and 70 mg. of bentonite (325 mesh) were added and the whole concentrated *in vacuo* (80° bath) to dryness. The residue was extracted with 100 ml. of ethyl acetate, the extract filtered through carbon and then concentrated on the steam-bath to a volume of 15–20 ml. On cooling, 5.25 g. (87%) of compact prisms melting at 160–164° was obtained. Recrystallization from ethyl acetate or chloroform gave pure 1,3:2,4-diethylidene-D-xylitol melting at 164–165° and showing a rotation of −3.5° in water (*c* 1.02).

Anal. Calcd. for $C_9H_{16}O_5$: C, 52.93; H, 7.90. Found: C, 52.95; H, 7.63.

The substance is readily soluble in water, chloroform, glacial acetic acid, hot ethyl acetate and hot benzene; it is sparingly soluble in ether and practically insoluble in cold carbon tetrachloride and pentane.

5-Benzoyl-1,3:2,4-diethylidene-D-xylitol.—1,3:2,4-Diethylidene-D-xylitol (750 mg.) was benzoylated in the usual fashion with benzoyl chloride in pyridine. Crystallization was spontaneous when the reaction mixture was poured into ice-water. Recrystallized from 15 ml. of absolute alcohol, the product (960 mg., 85%) was obtained as stout prisms melting at 155–156° and showing a rotation in chloroform of −5.0° (*c* 1.08) and in dioxane of +0.1° (*c* 1.17).

Anal. Calcd. for $C_{16}H_{20}O_6$: C, 62.32; H, 6.54. Found: C, 62.60; H, 6.44.

1,3:2,4-Diethylidene-5-phenylcarbamyl-D-xylitol.—A mixture of 1.00 g. of 1,3:2,4-diethylidene-D-xylitol, 5 ml. of dry pyridine and 0.60 g. of freshly distilled phenyl isocyanate was heated on a steam-bath for 45 minutes and then concentrated *in vacuo* at 100° to a thick sirup which was dissolved in 25 ml. of hot ligroin (b.p. 90–100°). The crystals deposited were recrystallized from 25 ml. of acetone to give clusters of hexagonal plates: 1.06 g. (67%), m.p. 214–216°. Two further recrystallizations from acetone raised the melting point to 215–217°; the pure material showed a rotation of +15.7° in chloroform (*c* 0.97).

Anal. Calcd. for $C_{16}H_{21}O_6N$: C, 59.43; H, 6.55; N, 4.33. Found (sample dried *in vacuo* at 137°): C, 59.67; H, 6.40; N, 4.45.

1,3:2,4-Diethylidene-5-tosyl-D-xylitol.—1,3:2,4-Diethylidene-D-xylitol (16.19 g.) was tosylated in the usual manner with tosyl chloride in pyridine solution. When the reaction was complete the mixture was diluted with methylene dichloride and washed successively with cold water, cold 3 *N* sulfuric acid and saturated aqueous sodium bicarbonate. After drying with sodium sulfate, the solution was concentrated *in vacuo* (60° bath) and the residual sirup dissolved in a mixture of 60 ml. of absolute ethanol and 25 ml. of pentane. Upon seeding[14] and standing at +5° there was obtained 21.73 g. (76%) of prisms melting at 70–74°; recrystallization from ether–pentane and methyl Cellosolve gave material melting at 71–74° and showing $[\alpha]^{20}\text{D}$ ±0°, $[\alpha]^{20}_{4710}$ −2.2° and $[\alpha]^{20}_{\text{ca. }7500}$ +1.6° in chloroform (*c* 0.73).

Anal. Calcd. for $C_{16}H_{22}O_7S$: C, 53.62; H, 6.19; S, 8.95. Found: C, 53.76; H, 6.01; S, 8.89.

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[14] Seeds were initially obtained from a fraction which had been purified by chromatography on alumina.