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New Derivatives of 2,3,4,5-Dibenzylidene-D,L-xylitol and 2,4 : 3,5-Dimethylene-L-xylitol

BY ARTHUR T. NESS, RAYMOND M. HANN[1] AND C. S. HUDSON

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The long-known dibenzylidenexylitol has been proved to be 2,3,4,5-dibenzylidene-D,L-xylitol by converting it, through a series of reactions, to 1-desoxy-2,3,4,5-dibenzylidene-D,L-xylitol and then to 1-desoxy-2,4:3,5-dimethylene-D,L-xylitol of established structure. The transformation of 2,4:3,5-dimethylene-L-xylitol to 1-desoxy-2,4:3,5-dimethylene-L-xylitol has also been described.

In an earlier paper[2] from this Laboratory we have shown that the condensation product[3] of xylitol (a *meso* form) with acetone contains a primary hydroxyl group, and that the substance, therefore, has the structure 2,3,4,5-diisopropylidene-D,L-xylitol. Subsequently,[4] the condensation product of xylitol with formaldehyde was proved to be 2,4:3,5-dimethylene-D,L-xylitol. Similarly, we might expect that the condensation of xylitol with benzaldehyde—a reaction described first by Bertrand[5]—would lead to a dibenzylidene derivative that also contained a primary hydroxyl group. This assumption received strong support from the work of Wolfrom, Burke and Metcalf,[6] who reported that the dibenzylidenexylitol readily formed a triphenylmethyl ether. Furthermore, its *p*-toluenesulfonate reacted slowly with sodium iodide in acetonylacetone with the separation of a 66% yield of sodium *p*-toluenesulfonate after 40 hours at 100°.

We have found that the exchange reaction with sodium iodide can be effected quantitatively by heating the same mixture at 120° for 48 hours in the presence of sodium bicarbonate, which prevents decomposition and the formation of tar. The resulting iodo derivative, upon hydrogenation with Raney nickel as catalyst, formed a crystalline desoxydibenzylidenexylitol. Removal of the benzylidene groups by acid hydrolysis and reaction of the resulting sirupy desoxyxylitol with formaldehyde and concentrated hydrochloric acid then yielded the known 1-desoxy-2,4:3,5-dimethylene-D,L-xylitol.[4] Since the structure of the last-named compound has already been established definitively,[4] it follows that the sirupy desoxyxylitol must have been 1-desoxy-D,L-xylitol,[2] its immediate antecedent in this series of reactions was 1-desoxy-2,3,4,5-dibenzylidene-D,L-xylitol, and the original dibenzylidene compound was 2,3,4,5-dibenzylidene-D,L-xylitol. Some evidence that the benzylidene groups in this compound occupy the 2,4- and 3,5-positions, as do the methylene groups in the dimethylenexylitol series, may be derived from an experiment in which 2,4-benzylidenexylitol[7] (a *meso* form) was converted to the dibenzylidene compound by benzaldehyde and anhydrous zinc chloride. It seems improbable, though not impossible, that such a mild condensing agent would cause any migration of the original 2,4-benzylidene group to another position in the molecule.

The second series of xylitol derivatives described in the Experimental part of this paper begins with the 2,4:3,5-dimethylene-L-xylitol that is obtained from 1,3:2,4-dimethylene-D-glucitol by periodate oxidation to *aldehydo*-2,4:3,5-dimethylene-L-xylose and subsequent hydrogenation.[8] Now, by the customary reactions of tosylation, iodide exchange and hydrogenation we have eliminated the oxygen atom of the primary hydroxyl group and thus prepared 1-desoxy-2,4:3,5-dimethylene-L-xylitol. The enantiomorph, 1-desoxy-2,4:3,5-dimethylene-D-xylitol, will be described and a comparison of other derivatives of 1-desoxy-D-xylitol with those of the corresponding D,L-forms will be made in the accompanying paper by Zissis and Richtmyer.[9]

Experimental[10]

2,3,4,5-Dibenzylidene-D,L-xylitol (a) from Xylitol, Benzaldehyde and Sulfuric Acid.—An ice-cold solution of 10 g. of xylitol in 60 ml. of 50% sulfuric acid (w./w.) was agitated with 20 ml. of benzaldehyde until the mixture quickly set to a stiff magma. After standing overnight at 5°, the mixture was thinned with 100 ml. of cold water, immediately filtered, and the product washed successively with cold 5% aqueous sodium hydroxide, 50% ethanol and ether. The product, 22 g., was recrystallized from 50 parts of ethanol and yielded 18 g. (84%) of 2,3,4,5-dibenzylidene-D,L-xylitol as fine needles melting at 187–188° (cor.). Wolfrom and Kohn,[11] and Wolfrom, Burke and Metcalf[6] reported a melting point of 187.5–188° (cor.) for this acetal.[12] The substance is readily soluble in acetone and pyridine, moderately soluble in benzene and chloroform, and practically insoluble in hexane, ether, water and cold methanol and ethanol.

Anal. Calcd. for $C_{19}H_{20}O_5$: C, 69.50; H, 6.14. Found: C, 69.47; H, 6.16.

(b) From Xylitol, Benzaldehyde and Zinc Chloride.—A mixture of 1.0 g. of xylitol, 10 ml. of benzaldehyde and 5 g. of powdered fused zinc chloride was shaken 24 hours and the turbid, viscous mass allowed to stand 3 more days at 25°. The mixture was dissolved in 100 ml. of ethanol, and water added (150 ml.) until the turbidity became permanent; after 3 hours at 0° the precipitate was collected on a filter.

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[1] Deceased, April 30, 1949.

[2] R. M. Hann, A. T. Ness and C. S. Hudson, THIS JOURNAL, 66, 73 (1944).

[3] R. S. Tipson and L. H. Cretcher, *J. Org. Chem.*, 8, 95 (1943).

[4] R. M. Hann, A. T. Ness and C. S. Hudson, THIS JOURNAL, 66, 670 (1944).

[5] G. Bertrand, *Bull. soc. chim. France*, [3] 5, 554 (1891).

[6] M. L. Wolfrom, W. J. Burke and E. A. Metcalf, THIS JOURNAL, 69, 1667 (1947).

[7] R. M. Hann, A. T. Ness and C. S. Hudson, *ibid.*, 68, 1769 (1946).

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

[9] E. Zissis and N. K. Richtmyer, *ibid.*, 75, 129 (1953).

[10] The experiments with 2,3,4,5-dibenzylidene-D,L-xylitol were performed during the period June, 1946, to January, 1947, and those with 2,4:3,5-dimethylene-L-xylitol during the period June to August, 1943.

[11] M. L. Wolfrom and E. J. Kohn, THIS JOURNAL, 64, 1739 (1942).

[12] G. Bertrand (ref. 5) and E. Fischer and R. Stahel [*Ber.*, 24, 528 (1891)] did not mention the melting point, while C. A. Lobry de Bruyn and W. Alberda van Ekenstein [*Rec. trav. chim.*, 18, 150 (1899)] and A. Ashida [*J. Agr. Chem. Soc. Japan*, 20, 264 (1944)] reported a lower melting point, 175°.

The product (1.7 g.) was recrystallized from 50 parts of ethanol and yielded 1.3 g. (60%) of 2,3,4,5-dibenzylidene-D,L-xylitol as fine needles melting at 187–188° (cor.).

(c) From 2,4-Benzylidenexylitol, Benzaldehyde and Zinc Chloride.—A mixture of 1.0 g. of 2,4-benzylidenexylitol,[7] 10 ml. of benzaldehyde and 5 g. of powdered fused zinc chloride was shaken for 24 hours, then allowed to stand 3 days at 25°; 0.7 g. (50%) of once-recrystallized 2,3,4,5-dibenzylidene-D,L-xylitol was obtained as described in the preceding experiment. The m.p. was 187–188° (cor.).

1-Acetyl-2,3,4,5-dibenzylidene-D,L-xylitol.—A mixture of 1.0 g. of 2,3,4,5-dibenzylidene-D,L-xylitol, 10 ml. of pyridine and 5 ml. of acetic anhydride was allowed to stand 48 hours at room temperature and the thick slurry of needles poured into 300 ml. of ice and water. The product (1.2 g.) could be recrystallized from 100 parts of ethanol or 30 parts of ethyl acetate to yield 1.0 g. (90%) of 1-acetyl-2,3,4,5-dibenzylidene-D,L-xylitol as balls of tiny needles melting at 174–175° (cor.). The compound is readily soluble in acetone and chloroform, moderately soluble in benzene, and practically insoluble in ether, hexane, glacial acetic acid, water and cold methanol and ethanol.

Anal. Calcd. for $C_{21}H_{22}O_6$: C, 68.09; H, 5.99; CH_3CO, 11.6. Found: C, 68.10; H, 6.26; CH_3CO, 11.6.

1-Tosyl-2,3,4,5-dibenzylidene-D,L-xylitol.—To a cold solution of 10 g. of 2,3,4,5-dibenzylidene-D,L-xylitol in 50 ml. of pyridine was added a cold solution of 10 g. of *p*-toluenesulfonyl chloride in 25 ml. of pyridine. After standing 48 hours at room temperature, the mixture was poured into 800 ml. of ice and water and 15 g. of product recovered by filtration. Several recrystallizations from 10 parts of chloroform by the addition of 15 parts of ethanol furnished long, fine needles of 1-tosyl-2,3,4,5-dibenzylidene-D,L-xylitol. In a series of experiments, the melting point of the crude product was recorded as about 155–157° while that of the recrystallized material was about 146–147° (cor.). The 1-tosyl-2,3,4,5-dibenzylidene-D,L-xylitol described by Wolfrom, Burke and Metcalf,[6] after recrystallization from pyridine–ethanol, melted at 155–156°. The reason for this discrepancy in melting points is not known, but it may have been caused by a difference in the rates of heating of this somewhat unstable benzylidene compound. The substance is readily soluble in acetone, chloroform and pyridine, moderately soluble in benzene, and practically insoluble in ether, hexane, water and cold methanol and ethanol.

Anal. Calcd. for $C_{26}H_{26}O_7S$: C, 64.71; H, 5.43; S, 6.64. Found: C, 64.74; H, 5.41; S, 6.50.

1-Iodo-1-desoxy-2,3,4,5-dibenzylidene-D,L-xylitol.—In agreement with the experience of Wolfrom, Burke and Metcalf,[6] the replacement of the tosyloxy group in 1-tosyl-2,3,-4,5-dibenzylidene-D,L-xylitol by an iodine atom was not readily effected. After a mixture of 1.0 g. of the tosyl derivative, 1.0 g. of sodium iodide and 50 ml. of acetone had been heated in a pressure bottle 24 hours at 100°, 0.8 g. of unchanged tosyl derivative was recovered. However, a quantitative conversion was secured by heating a mixture of 1.5 g. of the tosylate, 1.5 g. of sodium iodide, 1.5 g. of sodium bicarbonate and 15 ml. of redistilled acetonylacetone at 120° for 48 hours. The amber-colored slurry was poured into 400 ml. of ice and water. The solid product (1.4 g.) was recrystallized from a mixture of 20 parts of pyridine and 30 parts of ethanol and yielded 1.2 g. of 1-iodo-1-desoxy-2,3,4,5-dibenzylidene-D,L-xylitol as small needles melting at 207–208° (cor.). The compound is soluble in acetone, benzene, chloroform and pyridine, and practically insoluble in ether, hexane, water and cold methanol and ethanol.

Anal. Calcd. for $C_{19}H_{19}O_4I$: C, 52.07; H, 4.37; I, 28.96. Found: C, 52.08; H, 4.36; I, 28.86.

1-Desoxy-2,3,4,5-dibenzylidene-D,L-xylitol.—To a suspension of 1.0 g. of 1-iodo-1-desoxy-2,3,4,5-dibenzylidene-D,L-xylitol in 100 ml. of methanol were added 2.5 ml. (1.1 molecular equivalents) of *N* aqueous sodium hydroxide and 2 g. of Raney nickel catalyst, and the mixture was agitated at 28° with hydrogen under a slight positive pressure for one hour, at which time the absorption of hydrogen had stopped at 76 ml. (theory, 56 ml.). The catalyst was removed by filtration and washed well with acetone, and the filtrate was evaporated to dryness. The residue was extracted with 75 ml. of hot absolute ethanol and the extract, on cooling, deposited 0.7 g. (quantitative) of fine needles. Recrystallization from 50 parts of ethanol afforded 0.6 g. of pure 1-desoxy-2,3,4,5-dibenzylidene-D,L-xylitol melting at 173–174° (cor.). The substance is soluble in acetone, benzene, chloroform and pyridine, and practically insoluble in ether, hexane, water and cold methanol and ethanol.

Anal. Calcd. for $C_{19}H_{20}O_4$: C, 73.06; H, 6.45. Found: C, 73.02; H, 6.47.

Transformation of 1-Desoxy-2,3,4,5-dibenzylidene-D,L-xylitol to 1-Desoxy-2,4:3,5-dimethylene-D,L-xylitol.—A mixture of 3.7 g. of 1-desoxy-2,3,4,5-dibenzylidene-D,L-xylitol, 80 ml. of ethanol and 20 ml. of 5 *N* hydrochloric acid was refluxed 6 hours and then concentrated *in vacuo* to dryness. The residual sirupy 1-desoxy-D,L-xylitol[2] (1.5 g., 93%) was dissolved in a mixture of 5 ml. of 37% aqueous formaldehyde and 5 ml. of concentrated hydrochloric acid and the solution allowed to concentrate in an evacuated desiccator containing small beakers of sodium hydroxide pellets and concentrated sulfuric acid. After 5 days, the dry product (1.5 g., 83% from 1-desoxy-D,L-xylitol; m.p. 145–150°) was recrystallized from 20 parts of ethanol and yielded 0.7 g. of pure 1-desoxy-2,4:3,5-dimethylene-D,L-xylitol as needles melting at 155–156° (cor.); concentration of the ethanol filtrate to 10 ml. gave an additional 0.2 g. of pure product, making a total yield of 0.9 g. (51%). A mixed melting point with authentic 1-desoxy-2,4:3,5-dimethylene-D,L-xylitol[4] (m.p. 155–156°) showed no depression.

1-Benzoyl-2,4:3,5-dimethylene-L-xylitol.—A solution of 0.8 g. of 2,4:3,5-dimethylene-L-xylitol[8] and 0.65 ml. of benzoyl chloride in 20 ml. of pyridine was allowed to stand at room temperature for 3 days. The mixture was poured into ice-water and the separated crystalline product (1.2 g., m.p. 169–171°) was recrystallized from 40 parts of ethanol to yield 1.0 g. (80%) of fine needles. The 1-benzoyl-2,4:3,5-dimethylene-L-xylitol thus prepared melted at 170–171° and had a rotation $[\alpha]^{20}D$ −23.8° in chloroform (*c* 0.90). It was soluble in acetone, chloroform and hot methanol and ethanol, and practically insoluble in water and cold methanol and ethanol.

Anal. Calcd. for $C_{14}H_{16}O_6$: C, 59.99; H, 5.76; C_6H_5CO, 37.5. Found: C, 59.92; H, 5.86; C_6H_5CO, 37.5.

1-Tosyl-2,4:3,5-dimethylene-L-xylitol.—The tosylation of 1.0 g. of 2,4:3,5-dimethylene-L-xylitol for 3 days in the usual manner produced 1.9 g. of crude product melting at 144–146°. Recrystallization from 30 parts of ethanol produced rectangular plates of 1-tosyl-2,4:3,5-dimethylene-L-xylitol that weighed 1.7 g. (90%), melted at 146–147°, and had a rotation $[\alpha]^{20}D$ −2.7° in chloroform (*c* 1.0). The substance is soluble in acetone and chloroform, and practically insoluble in water and cold methanol and ethanol.

Anal. Calcd. for $C_{14}H_{18}O_7S$: C, 50.90; H, 5.49. Found: C, 51.04; H, 5.49.

1-Iodo-1-desoxy-2,4:3,5-dimethylene-L-xylitol.—A solution of 2.0 g. of 1-tosyl-2,4:3,5-dimethylene-L-xylitol and 2.0 g. of sodium iodide in 15 ml. of acetonylacetone was heated 24 hours at 120°. The reaction mixture was cooled, diluted with 200 ml. of ice-water, and kept at 5° for 2 days. The iodo derivative separated as prismatic needles melting at 165–167° and weighing 1.4 g. (81%). Recrystallization from 25 parts of ethanol yielded prismatic needles with m.p. 166–167° and $[\alpha]^{20}D$ −35.9° in chloroform (*c* 0.90). The product was soluble in acetone and chloroform, and practically insoluble in water and cold methanol and ethanol.

Anal. Calcd. for $C_7H_{11}O_4I$: C, 29.39; H, 3.88. Found: C, 29.34; H, 3.93.

1-Desoxy-2,4:3,5-dimethylene-L-xylitol.—A suspension of 1.4 g. of 1-iodo-1-desoxy-2,4:3,5-dimethylene-L-xylitol and 1 g. of Raney nickel catalyst in 5.5 ml. of *N* aqueous sodium hydroxide (10% excess) and 50 ml. of water was agitated at 31° under a slight positive pressure of hydrogen. The reaction appeared to be complete in 1 hour with the absorption of 113 ml. of hydrogen (theory, 122 ml.). The catalyst was removed by filtration and the filtrate concentrated *in vacuo* to dryness. The solid residue was extracted with 12 ml. of hot absolute ethanol, and the extract, on cooling, deposited 0.4 g. (50%) of the prismatic needles of 1-desoxy-2,4:3,5-dimethylene-L-xylitol melting at 154–155° and showing $[\alpha]^{20}D$ −33.1° in water (*c* 0.8). Neither melting point nor rotation was changed by further recrystallization from 15 parts of ethanol.

Anal. Calcd. for $C_7H_{12}O_4$: C, 52.49; H, 7.55. Found: C, 52.43; H, 7.63.

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BETHESDA 14, MARYLAND

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Condensations by Sodium. XXXIII. The Effect of Alkali Metal Halides upon Amylsodium[1]

BY AVERY A. MORTON AND EDWARD F. CLUFF

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A previous paper[2] has shown that tertiary pentoxides which accelerate the reactions of amylsodium also accelerate the thermal dissociation of that reagent into radicals. The present paper describes the influence of alkali metal halides upon the stability of amylsodium. This study is important because amylsodium, as prepared from amyl chloride and sodium, contains a little more than an equal molal quantity of sodium chloride and probably derives some activity from association with that supposedly inert salt in view of evidence[3] that an alkali metal halide is essential for Alfin catalysis. The present work shows that these salts do indeed affect the decomposition of amylsodium and in proportion to the relative sizes of the component ions.

Commercial halide salts were used because some of the alkali metal fluorides are difficult to prepare in a Wurtz reaction, and because positive effects could be obtained with granular salts in spite of the fact that they are incorporated[3] in the aggregate with difficulty. Each dried salt was added to about a mole equivalent of amylsodium–sodium chloride, which had been prepared by the standard method[4] from amyl chloride and sodium at −10° and was ground in the high-speed stirring apparatus[5] at a specified r.p.m. for 1.5 hours. The mixture was next heated—usually to 50° for three hours—and was then carbonated on solid carbon dioxide in order to convert all organosodium compounds to sodium carboxylates. The caproic acid therefrom represented amylsodium. The water-soluble carboxylic acids, as explained in the earlier paper,[2] came from a dimetalation of pentene which in turn had come either from a small amount of disproportionation during the preparation of amylsodium or, if in large amount, from pyrolysis of amylsodium. Decane also formed in about 7% yield during the preparation of amylsodium but in excess of that amount was a consequence of pyrolysis. Some higher boiling material proved to be a mixture of diamyl ketone, triamylcarbinol and a hexadecene. These products were formed only when lithium bromide was used and were therefore nicely accounted for by the assumption that ion interchange took place—equation 1—and that during carbonation the lithium caproate

$$C_5H_{11}Na + LiBr \longrightarrow C_5H_{11}Li + NaBr \quad (1)$$

as lithium salts may do,[6] acted in a cascade of reactions, equation 2, to give the ketone and tertiary carbinol. Dehydration

$$C_5H_{11}Li + CO_2 \xrightarrow{(1)} C_5H_{11}CO_2Li \xrightarrow{(2)} (C_5H_{11})_2CO \xrightarrow{(3)} (C_5H_{11})_3COLi \quad (2)$$

of the latter during distillation would give a hexadecene.

All results are listed in Table I. The first three experiments are controls to establish the range of yields of amylsodium without pyrolysis. That they are a little higher than the 80% reported[5] earlier can be credited to small improvements in the technique and probably more to the better grade of amyl chloride[7] regularly used. The next two show the yields after three hours at 50° with no halide salt added. Experiments 6–14, inclusive, are arranged primarily in the order of decreasing amount of amylsodium, as represented by caproic acid, and, secondarily, in increasing amount of water-soluble acids, but all changes are small and for decane are nil.

Decisive effects are evident in experiments 15–19 where sodium iodide and lithium bromide were used. Sodium iodide caused a small drop in amylsodium in no. 15 and a sizable one in no. 16, accompanied by a considerable gain in the water-soluble acid. The next two experiments with the same salt but at higher temperatures were aimed at increasing the percentage of decane—supposedly an unusual product[8] of pyrolysis—and did so to a limited extent in no. 18. Lithium bromide, in no. 19, caused a greater drop in amylsodium than did sodium iodide and was responsible also for the ketone, carbinol and hexadecene mentioned before.

Potassium fluoride in 20–21 acted differently from the preceding salts in that a gain in water-soluble acid took place without a significant loss of amylsodium. Indeed totals of 91 and 94%, respectively, of organosodium compounds based on the amyl chloride originally used were obtained. These quantities were higher than in the controls and suggested that some hidden or less stable amyl-

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(1) The authors are indebted to the Synthetic Rubber Division, Reconstruction Finance Corporation, for financial support of this work.

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