out a part of this investigation. The reading of the manuscript by Dr. F. F. Blicke is deeply appreciated.

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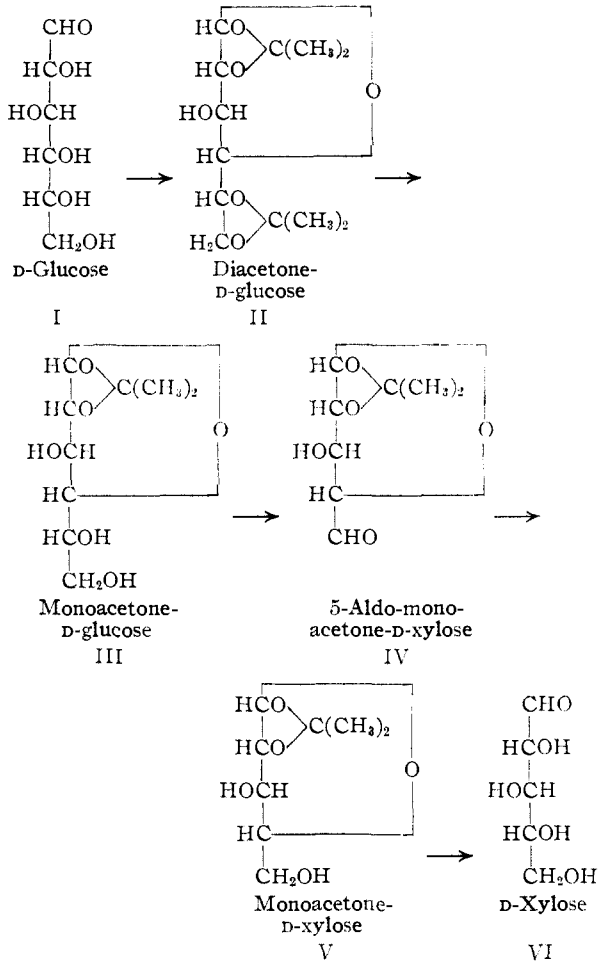
Preparation of 1-C^{14}-D-Xylose from 1-C^{14}-D-Glucose

BY JOHN C. SOWDEN

The development of methods for the isotopic labeling of sugars in the aldehydic carbon has supplied a valuable means of elucidating certain chemical and biochemical reactions that involve fragmentation of the sugar carbon chain. Either the nitromethane synthesis using C^{14}-nitromethane[1] or the cyanohydrin synthesis using C^{14}-cyanide,[2] which were first used to prepare 1-C^{14}-D-glucose and 1-C^{14}-D-mannose from D-arabinose, are generally applicable to the synthesis of aldehyde-labeled aldose sugars. In the pentose series, Rappoport and Hassid have described the preparation of 1-C^{14}-L-arabinose by application of the C^{14}-nitromethane synthesis to L-erythrose.[3]

Recently, 1-C^{14}-D-xylose has been employed in a study of the mechanism of fermentation of this aldopentose by *Lactobacillus pentosus*.[4] The preparation of aldehyde-labeled D-xylose by one of the two chain-lengthening synthetic methods would require as a starting material the tetrose sugar, D-threose. An alternate method, described herein, starts from 1-C^{14}-D-glucose and utilizes a sequence of reactions that eliminates carbon-6 from the glucose molecule and transforms the grouping at carbon-5 to a primary alcohol.

The well-known acetonation of D-glucose (I)[5] to 1,2;5,6-diisopropylidene-D-glucofuranose (diacetoneglucose) (II) and the controlled hydrolysis of the latter to 1,2-isopropylidene-D-glucofuranose,[6] (monoacetoneglucose) (III) have been improved recently[7] to provide excellent yields of III in solution.[8] The oxidative glycol cleavage of monoacetoneglucose leads to the substituted dialdehyde, 5-aldo-1,2-isopropylidene-D-xylofuranose (IV).[9] The reduction of the latter with hydrogen in the presence of Raney nickel produced the previously known[10] 1,2-isopropylidene-D-xylofuranose (V). Finally, mild acid hydrolysis of V removed the acetone substituent to give D-xylose (VI). The transformation of D-glucose to D-xylose by this reaction sequence has been accomplished, without the isolation of intermediates, in 55–60% yield.



The substituted dialdehyde, IV, is of interest in that its asymmetry is maintained only by virtue of the 1,2-ketal substituent. (Hydrolysis of the blocking acetone group would produce the *meso* compound, xylaric dialdehyde.) Similar preservation of asymmetry by substitution is a familiar and intrinsic feature of asymmetric glycerol chemistry.[11]

Experimental

1-C^{14}-D-glucose,[1] (630 ± 20 ct./min./mg.), was acetonated by the method of Bell[12] and the resulting diacetoneglucose hydrolyzed according to the directions of Coles, Goodhue and Hixon[13] to monoacetoneglucose. The latter, after recrystallization, was oxidized with aqueous sodium metaperiodate and the resulting 5-aldo-monoacetonexylose was reduced to monoacetonexylose as described below. The acetonated pentose was purified by distillation in a high vacuum and then hydrolyzed with dilute sulfuric acid to 1-C^{14}-D-xylose, m.p. 145–146°, $[\alpha]^{24}D$ 18.8° equil. in water (*c* 1.2). The isolation of the intermediates, especially monoacetoneglucose, leads to considerable losses and consequently the over-all yield of 1-C^{14}-D-xylose was only about 20%.

Subsequent to the radioactive preparation, experiments with non-radioactive D-glucose have led to the improved procedure described below. The directions of Mehltretter, *et al.*,[7] for the production of monoacetoneglucose in solution were employed and the isolation of all intermediate products was eliminated with a consequent increase in yield to 55–60% of D-xylose from D-glucose. The main loss in the fol-

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lowing procedure seems to arise in the cleavage of monoacetoneglucose to 5-aldo-monoacetonexylose and the reduction of the latter to monoacetonexylose.

To a suspension of 5 g. of powdered D-glucose in 100 ml. of acetone at 0° there was added, dropwise, 4 ml. of sulfuric acid. The mixture was stirred in a closed flask (magnetic stirrer) for four hours at room temperature and then filtered from 140 mg. of unreacted D-glucose. The filtrate was made just alkaline by the addition, with shaking, of a 50% sodium hydroxide solution at 15–20° and filtered from the resulting sodium sulfate. After thorough washing of the salt cake with acetone, the combined filtrates were concentrated at reduced pressure, water was added and the concentration repeated to a volume of 50–75 ml. The solution was adjusted to *p*H 2.0 with concentrated hydrochloric acid and maintained at 40° with stirring for four hours. Following adjustment of the *p*H to 8–8.5 with sodium hydroxide, the solution was extracted with an equal volume (100–125 ml.) of benzene to remove unchanged diacetoneglucose. After addition of methyl red indicator, the aqueous layer was stirred with portions of powdered sodium metaperiodate while the *p*H was kept near that of the methyl red endpoint by the dropwise addition of aqueous sodium hydroxide. When 7.3 g. of sodium metaperiodate had been added, starch-iodide paper indicated the presence of excess oxidant and the latter was destroyed by the addition of a few drops of glycerol. The solution was concentrated at reduced pressure, absolute ethanol added and the concentration repeated, and the sirupy residue, after addition of anhydrous sodium sulfate, was extracted with five 40-ml. portions of chloroform. Concentration of the extract at reduced pressure produced 5 g. of the crude acetonated dialdehyde. This was shaken, in 65 ml. of 95% ethanol, with hydrogen in the presence of 5 g. of Raney nickel for 90 hours at room temperature and atmospheric pressure. Following filtration and concentration, the residual monoacetonexylose was hydrolyzed by heating for one hour at 100° with 100 ml. of 0.1 *N* sulfuric acid. Acid was removed from the solution by ion-exchange, and concentration then yielded a residue of crystalline D-xylose. After grinding with cold 95% ethanol and filtration, there was obtained 2.35 g. (58%) of D-xylose, m.p. 144–147° and $[\alpha]^{25}D$ 19.1° equil. in water (*c* 9). These values agree well with the reported constants of pure D-xylose.

The rate of reduction of 5-aldo-monoacetonexylose with hydrogen and Raney nickel at room temperature and atmospheric pressure varies considerably with successive preparations of catalyst and acetonated dialdehyde. Absorption of hydrogen is complete in from 15 to 90 hours. In one experiment the reduction was carried out in a rocking autoclave at 75° and 1500 p.s.i. of hydrogen during four hours but no improvement in the yield (57%) of D-xylose was observed.

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α-Bromocitraconic Anhydride and α-Bromomesaconic Acid[1]

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Early attempts to prepare α-bromocitraconic anhydride and α-bromomesaconic acid were hampered by failure to appreciate fully the catalyzed *cis–trans* interconversion of ethylenic compounds, failure to understand the steric course of addition and elimination, and lack of suitable solvents for the purification of the products or intermediates. For example, Fittig found it necessary to crystallize DL-*threo*-α,β-dibromomethylsuccinic acid from water[3] in which it is 57% soluble at 13°, whereas nitromethane affords better than 81% recovery on recrystallization. Indeed this solvent appears to be an excellent crystallizing medium for many saturated as well as unsaturated α,β-dicarboxylic acids and anhydrides.

While the mechanism of the addition reaction is not a simple one,[4] in the present instance the picture of *trans*-halogen addition suggested by Roberts and Kimball[5] is satisfactory.

The elimination of halogen or hydrogen halide from a molecule may be pictured as essentially the reverse of addition,[6] the over-all result usually being *trans*-elimination. The present preparative procedures were designed in conformity with these generalizations.

The addition of bromine to the less stable *cis*-isomer is attended by danger of isomerization to the more stable *trans* form. Either acid (HBr) or radical (Br·) catalyzed isomerization may occur,[7] and therefore great care must be exercised to prevent formation of hydrogen bromide while appreciable citraconic acid is still present and to exclude light in order to minimize the dissociation of bromine into atoms.

Previous study[8] had shown that the addition of a few drops of bromine to a chloroform–ether solution of citraconic acid in sunlight afforded a 68% yield of mesaconic acid after only a few minutes; and while the desired addition could be accomplished in the dark, several weeks were required for its completion. In the present study, iodine, as predicted by other work,[9,10] proved to be an effective catalyst, the reaction reaching completion overnight in complete darkness. The yield of the desired dibromo acid could not be raised above 62%, since citraconic acid is not very soluble in chloroform at room temperature and the ether required to effect a homogeneous reaction mixture reacted with the bromine to produce some hydrogen bromide, which in turn effected some isomerization. Excess bromine did not affect the yield, but when the reaction was run in chloroform *alone*, heated to 50° to dissolve the citraconic acid, only insoluble mesaconic acid was obtained. The increase in temperature apparently was sufficient to provide energy for the formation of free halogen atoms which then catalyzed isomerization.

The preparation of α-bromomesaconic acid has been reported previously: once without procedural information[11] and once in considerable detail.[12] Significantly, the latter report includes a crude yield without melting point and a melting point of a pure sample without yield. It is stated simply that the compound was difficult to purify. Several attempts were made to repeat this work, and in no case was a yield of more than 13% of pure

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