in each case exclusively 2-bromopentane and 2-bromoheptane. If peroxide were present in any of the reactions, it would be in these for the reactants were well mixed with air in the shaking process. The fact that no color developed in the solution, however, indicates that there was no peroxide formed in these reactions.

Since this work was reported,[18] a similar addition of gaseous hydrogen bromide to form exclusively the primary bromide has been reported in the case of 4,4-dimethylpentene-1 by Whitmore and Homeyer.[19] Kharasch and co-workers[20] consider the 1-bromo-4,4-dimethylpentane obtained by Whitmore as the "abnormal" product and formed because of peroxide content. The 2-bromo-4,4-dimethylpentane is considered the "normal" product of the reaction and was obtained by Kharasch through the addition of hydrogen bromide in the absence of solvents and in the presence of antioxidants.

Linstead and Rydon[21] in an article appearing since this present material was reported give data which support the conclusions reached in this paper, namely, that the formation in organic solvents of the 1-bromo derivatives is not due to the effect of peroxide but rather to the type of solvent used. Hydrogen bromide added to allylacetic acid in hexane gave only the primary bromide, while in the absence of solvent the secondary bromide was obtained. These results are analogous to those obtained by Walker and Lumsden,[22] when undecylenic acid was treated with hydrogen bromide.

Summary

1. The primary olefins pentene-1 and heptene-1 have been prepared in a high degree of purity by two different methods and the physical constants of each measured.

2. The addition compound formed by saturating the olefin in an organic solvent with dry hydrogen bromide and allowing the reaction to take place under atmospheric pressure is exclusively the 1-bromo derivative.

3. The addition compound formed by the reaction of the olefin with aqueous hydrobromic acid is exclusively the 2-bromo derivative.

4. The difference in the products formed by the two methods is believed to be due primarily to the difference in the solvents and not to the presence of any peroxide in the olefin.

SOUTH HADLEY, MASS. RECEIVED NOVEMBER 27, 1933

(18) Organic Division, American Chemical Society, Chicago, September, 1933.

(19) Whitmore and Homeyer, THIS JOURNAL, **55**, 4555 (1933).

(20) Kharasch, Hannum and Gladstone, *ibid.*, **56**, 244 (1934).

(21) Linstead and Rydon, *Nature*, **132**, 643 (1933).

(22) Walker and Lumsden, *J. Chem. Soc.*, **29**, 1193 (1901).

[CONTRIBUTION FROM THE LABORATORY OF BIOLOGICAL CHEMISTRY, WASHINGTON UNIVERSITY MEDICAL SCHOOL]

Methylated Sugars. I. The Preparation of Tetramethylglucose[1]

BY EDWARD S. WEST AND RAYMOND F. HOLDEN

The preparation of tetramethylglucose by Haworth's procedure[2] requires much time, the yields are relatively small and the product is difficult to purify. The writers have introduced modifications by which it is now possible to obtain good yields of crystalline tetramethylglucose in eight to ten hours. This has been accomplished by changing radically both the methylation procedure and the method of hydrolyzing the tetramethylmethylglucoside.

Concentrated glucose or methylglucoside solution is methylated completely and quickly by treatment with a carbon tetrachloride solution of methyl sulfate and 60% sodium hydroxide solution. The tetramethylmethylglucoside either before or after isolation is hydrolyzed in 2 N hydrochloric acid by steam distillation.

The specific rotation of our rigorously purified tetramethylglucose was found to be $[\alpha]_D^{20}$ +81.3° in water, which is two degrees lower than the generally accepted value (83.3°) found in the literature.[3] Our value is believed to be the correct one. The rotation of the product of first crystallization from petroleum ether was not changed by four succeeding crystallizations from petroleum ether or followed by crystallization from either water or alcohol. Preparations of

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(1) Supported by a grant from the Rockefeller Foundation to Washington University for research in science. The material of this paper was presented in part at the meeting of the American Chemical Society, Denver, Colorado, August, 1932.

(2) Haworth, *J. Chem. Soc.*, **107**, 8 (1915); **113**, 188 (1918).

(3) Purdie and Irvine, *J. Chem. Soc.*, **85**, 1049 (1904); Haworth and Hirst, *ibid.*, **119**, 193 (1921); Gustus and Lewis, THIS JOURNAL, **49**, 1515 (1927).

tetramethylglucose by four modified procedures, after purification, gave identical rotations.

We are indebted to Dr. Elias Yanovsky of the Carbohydrate Division, Bureau of Chemistry and Soils, United State Department of Agriculture, for measuring the rotations of our preparation for both Na_D and Hg_{5461} light. The values found by him were $[\alpha]^{20}_{D}$ +81.18° (compared to our value of +81.3°) and $[\alpha]^{20}_{5461}$ +94.76°, giving a ratio $[\alpha]^{20}_{5893}/[\alpha]^{20}_{5461}$ of 0.856. Lowry and Richards[4] give $[\alpha]^{20}_{5461}$ 95.29° and calculate $[\alpha]^{20}_{D}$ +81°, assuming a dispersion ratio of 0.85. Using the ratio of Dr. Yanovsky's values, the calculated $[\alpha]^{20}_{D}$ of Lowry and Richards becomes +81.57°.

The new procedure should be applicable to other sugars and derivatives. The work is being continued.

The writers are indebted to Mr. A. J. Steiner for technical assistance.

Experimental

Apparatus.—The methylating apparatus consisted of a 2-liter Pyrex distilling flask fitted with a good cork through which passed a dropping tube and mechanical stirrer. The dropping tube was connected by rubber tubing to a 500-cc. reservoir flask and the rate of flow controlled by a screw clamp. The stirrer consisted of a 5 mm. monel rod formed into a 2.5 cm. flattened loop at the end. The stirrer was passed through a closely fitting 1 × 12.7 cm. brass bearing with packing nut at the lower end, the top of the bearing being countersunk to facilitate oiling with heavy engine oil.[5] The stirrer was driven by a Cenco motor. A water condenser was attached by cork to the side tube of the distilling flask and to a one-liter suction flask. A rubber tube carried fumes from the suction flask to a fume flue. The distilling flask was placed in a 4-liter water-bath. The entire apparatus was assembled in a hood.

α,β-Tetramethylmethylglucoside from Glucose.—Twenty-five grams of glucose and 15 cc. of water were placed in the methylating flask and the apparatus assembled. The water-bath temperature was raised to 55° and the glucose brought into solution with rapid stirring which was maintained throughout the process; 90 cc. of methyl sulfate in 125 cc. of carbon tetrachloride was then added quickly through the dropping tube. The clamp was closed and 400 cc. of 60% sodium hydroxide placed in the reservoir. The alkali was admitted to the flask at the rate of 1 drop in two seconds for five minutes, then 1 drop per second for five minutes, and then 3 drops per second until the distillation of carbon tetrachloride slackened or ceased, which was usually accomplished in twenty minutes, and after the addition of 70–90 cc. of alkali. The heat of reaction generally maintains the proper temperature of 50–55° throughout this stage and it is not necessary to heat the bath externally. The remainder of the alkali was added to the flask as quickly as possible and the bath temperature raised rapidly to and maintained at 70–75°; 160 cc. of methyl sulfate was placed in the reservoir and added 3–4 drops per second (slower if mixture foams seriously). After addition of all of the methyl sulfate the bath was heated to boiling for thirty minutes (stirring continued), after which the contents of the flask were cooled, diluted with sufficient water to dissolve most of the separated sodium sulfate, and extracted four times with 150-cc. portions of chloroform. The combined chloroform extracts were dried with sodium sulfate, filtered and the chloroform distilled off. The sirup distilled at 88–90° at 0.15 mm.,[6] yield about 25 g.

Anal. Calcd. for $C_{11}H_{22}O_6$: OCH_3, 61.97. Found (micro): 62.2. Rotation $[\alpha]^{31}_{D}$ +9.19°, $c = 4.19$. Another sample gave +12.29°. n^{20}_{D} 1.4445.

The optical rotation corresponds to 83–85% of β form.

Tetramethylglucose.—The undried, filtered chloroform solution of α,β-tetramethylmethylglucoside (or the isolated sirup) obtained in the direct methylation of glucose above was placed in a 2–3-liter distilling flask with 400 cc. of 2 *N* hydrochloric acid and the chloroform distilled off. A vigorous current of steam was then passed through the solution for an hour, care being taken to maintain the volume of solution approximately constant by heating the flask. Five grams of Norit was added to the hot solution, which was then cooled and filtered. The filtrate was saturated with sodium sulfate and extracted four times with 150-cc. portions of chloroform. The combined chloroform extracts were dried with sodium sulfate, 1 g. of Norit added and filtered. Chloroform was distilled off as much as possible without vacuum and then in a boiling water-bath at the water pump. The sirup was treated with 40–50 cc. of petroleum ether (30–60°), and shaken for a short time whereupon it set to a mass of crystals. After cooling in an ice-bath for half an hour the crystals were filtered off, washed with a little cold petroleum ether, and dried over calcium chloride in a vacuum; yield 18–20 g.

The crude product as obtained above generally gave an $[\alpha]_D$ value of about +79°.[7] Recrystallization from petroleum ether containing 0.5% ether (100 cc. for 6–7 g. of compound) in a continuous extractor gave a product of $[\alpha]^{24}_{D}$ +80.4°, $c = 4$ in water, m. p. 90–93°. A second crystallization is seldom necessary. The rotation remained constant through five crystallizations from petroleum ether–ether. The rotation was unchanged after crystallization from either water or alcohol.

Anal. Calcd. for $C_{10}H_{20}O_6$: OCH_3, 52.54; C, 50.93; H, 8.54. Found: OCH_3, 52.39; C, 50.59; H, 8.59.

Tetramethyl-α-methylglucoside and Tetramethylglucose from α-Methylglucoside.—From 27 g. of α-methylglucoside methylated with $^4/_5$ the quantity of reagents used above, and in the same way, 27.7 g. of tetramethyl-α-methyl-

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[4] Lowry and Richards, *J. Chem. Soc.*, **127**, 1385 (1925).

[5] This metal stirrer permits much more vigorous stirring than the glass mercury seal apparatus commonly used. The long bearing lubricated with heavy oil is an effective vapor seal.

[6] We have used a 100 cc. distilling flask filled with glass wool and having a low side tube for this distillation. The distilling temperature is considerably lower when glass wool is used. Bumping is entirely eliminated.

[7] A drop of 15% ammonia was added to 25 cc. of the solution for equilibration and the rotation observed after one hour. Values checked with those obtained on solutions without ammonia and equilibrated for forty-eight hours.

glucoside, distilling at 89–92° (glass wool in flask) at 0.4 mm., were obtained; $[\alpha]^{27}_{D}$ +150.1°, c = 4.32 in H_2O. Moelwyn-Hughes[8] found +151.1° at 25°; n^{20}_{D} 1.4460. Purdie and Irvine found 1.4464 and Haworth 1.4454.

Twenty-seven grams of tetramethyl-α-methylglucoside obtained above was steam hydrolyzed in 2 *N* hydrochloric acid for three hours and worked up in the usual way; twenty grams of tetramethylglucose, $[\alpha]^{28}_{D}$ +80.0°, c = 4.26 in H_2O, was obtained. After one crystallization from petroleum ether–ether $[\alpha]_D$ 80.6°, which remained unchanged after five crystallizations from petroleum ether–ether. The chloroform solution of tetramethyl-α-methylglucoside may be used for hydrolysis without isolating the compound.

Products Formed during First Stage of the Direct Methylation of Glucose.—Nearly all of this material consisted of tri- and tetramethylmethylglucosides, as indicated by the methoxyl content of 55.67%.

Properties of Tetramethylglucose Prepared in Different Ways.—I. Prepared by hydrolysis of tetramethyl-α,β-methylglucoside with 2 *N* hydrochloric acid for two and one-half hours at 61°, followed by three hours at 90°. The product was crystallized five times and gave the following rotations (temp. 23–26°) and melting points (in parentheses), respectively: crude, $[\alpha]_D$ 77.80°; 78.76° (90–91°); 80.84° (93–94°); 80.56° (95–96°); 80.44° (96°); 80.48° (96°).

II. As in I except hydrolyzed in 2 *N* hydrochloric acid by steam distillation. Crude, 79.44°; 80.51° (90–93°); 80.64° (97°); 80.40° (98°); 80.48° (98°); 80.41° (98°).

III. Tetramethyl-α-methylglucoside was hydrolyzed in 8% hydrochloric acid according to Purdie and Irvine:[3] crude, 79.88°; 79.79° (80–85°); 79.76° (83–86°); 80.06° (84–87°); 80.55° (87°); 80.46°.

IV. As in III except hydrolyzed by steam distillation: crude, 80.53°; 80.40° (94–96°); 80.41° (98°); 80.54° (98°); 80.52° (99°); 80.44° (99°).

It will be noted that steam hydrolysis gave a purer product than the procedure of Purdie and Irvine and the crude product from steam hydrolysis of tetramethylmethylglucoside was apparently pure without recrystallization.

Effect of Temperature upon the Rotation of Tetramethylglucose.—The rotation of pure tetramethylglucose was found to be 84.29° (c = 4.28) at 5°, 80.41° (c = 4.08) at 24°, and 78.22° (c = 4.28) at 37°, the solutions being equilibrated for two weeks at each temperature without the addition of a catalyst. The equation $[\alpha]_D = 85 - 0.1846\ t$, expresses the relation between specific rotation and temperature between 5 and 37°.

Effect of Solvent upon the Rotation of Tetramethylglucose.—Solutions of the pure compound in benzene, ethyl alcohol, methyl alcohol and chloroform were equilibrated for ten days and their rotations observed. The results were: benzene, 86.57° (t 24°, c = 4.86); ethyl alcohol, 81.3° (t 24°, c = 4.35); methyl alcohol, 82.91° (t 25°, c = 4.87); chloroform, 85.42 (t 24°, c = 3.98).

Summary

A simplified method for the preparation of tetramethylmethylglucoside and tetramethylglucose is presented. The method should be of general application to the simple sugars. Evidence is presented that the generally accepted specific rotation of pure tetramethylglucose is in error. Various data relative to the properties of tetramethylmethylglucoside and tetramethylglucose are given.

ST. LOUIS, MO. RECEIVED DECEMBER 11, 1933

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[8] Moelwyn-Hughes, *Trans. Faraday Soc.*, **25**, 81 (1929).

Crystalline Compounds of *d*-Xylose and of *l*-Arabinose with Calcium Chloride

BY J. K. DALE

In an earlier work[1] the author reported the preparation and properties of two isomeric crystalline compounds of *d*-mannose with calcium chloride. One of these compounds, exhibiting a very unusual course of mutarotation, was believed to be a compound of calcium chloride with a new form of mannose. The preparation of calcium chloride compounds with other sugars has been undertaken with a view to comparing their mutarotation curves and specific rotations with that of the sugar component. In the meantime other investigators have reported crystalline double compounds of sugars with calcium chloride. Isbell[2] has described a gulose-calcium chloride compound, Hann and Hudson[3] one of galactose and calcium chloride, while Austin and Walsh[4] have prepared a crystalline compound, α-*l*-arabinose·$CaCl_2$·$4H_2O$. The rotational data on only one of these compounds can be compared with that of the crystalline sugar component since gulose and α-arabinose have not been crystallized; the galactose-calcium chloride gives a mutarotation curve similar to that of α-*d*-galactose.

The xylose calcium chloride compound and

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(1) Dale, THIS JOURNAL, **51**, 2788 (1929).

(2) Isbell, *Bureau Standards J. Res.*, **5**, 741 (1930).

(3) Paper presented before the Division of Organic Chemistry at the Chicago meeting of the American Chemical Society, September, 1933.

(4) The author has independently prepared the compound α-*l*-arabinose. $CaCl_2$·$4H_2O$ described in the succeeding paper by Austin and Walsh. In general, the original observations of these authors on this compound are confirmed.