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THE ABSOLUTE CONFIGURATION OF dextro-1-DEUTERIOETHANOL¹

R. U. LEMIEUX² AND J. HOWARD³

Department of Chemistry, University of Ottawa, Ottawa, Ontario Received August 31, 1962

ABSTRACT

Reduction of 1,2-O-isopropylidene-3-O-benzyl-5-oxo- α -D-xylofuranose with lithium alumi-num deuteride followed by removal of the isopropylidene and benzyl groups provided 5-deuterio-D-xylose. Nuclear magnetic resonance examination of the 5-deuterio- β -D-xylopyranose tetraacetate showed the isomer with the 5-carbon in the R-configuration (deuterium equatorial) to be present in 30% excess. The substance was degraded to 1-deuterioethanol, which possessed a dextrorotation of the magnitude expected and which necessarily possessed the R-configuration. This result confirmed the prediction made by Brewster (Tetrahedron Letters, 20, 23 (1959)).

Recently, Althouse, Ueda, and Mosher (1) have reported on the reduction of 1-deuteriotrimethylacetaldehyde by actively fermenting yeast and have reviewed the results of the investigations by Westheimer, Vennesland, and their respective co-workers on the alcohol dehydrogenase catalyzed reduction of both acetaldehyde by monodeuterioreduced diphosphopyridine nucleotide (DPND) and of 1-deuterioacetaldehyde by unlabelled DPNH to form optically pure samples of 1-deuterioethanol. Furthermore, the various lines of conflicting reasoning applied by Vennesland, Streitweiser, Kaplan, Brewster, and their respective co-workers to predict the absolute configuration of optically active 1-deuterioethanol and other optically active primary alcohols rendered dissymmetric by monodeuteration of the 1-carbon are discussed. The speculations presented by Mosher and his collaborators (1) on the configurational relationship between the 1-deuterioneopentyl alcohol, obtained by reduction using actively fermenting yeast, and the 1-deuterioethanol prepared by the DPNH reduction of 1-deuterioacetaldehyde (2), overlook the fact that Lemieux and Giguere (3) found that, whereas the reduction of β -keto-*n*-caproic and β -keto-*n*-caprylic acids by actively fermenting yeast yielded the corresponding D- β -hydroxyacids, the similar reduction of β -ketobutyric acid gave L- β hydroxybutyric acid. Evidently, at least two mechanisms for the reduction of a carbonyl group are present in actively fermenting yeast and the procedure does not provide a reliable means for the establishment of configurational relationships. The purpose of this communication is to report an unequivocal proof for the absolute configuration of *dextro*-1-deuterioethanol.

The 3-O-benzyl derivative (II) of 1,2:5,6-di-O-isopropylidene- α -D-glucofuranose (I) was subjected to simultaneous preferential hydrolysis of the 5,6-O-isopropylidene group and periodate oxidation of the resulting 5,6-glycol by treatment in 90% aqueous acetic acid with 0.08 M periodic acid at room temperature for 25 minutes. The 1,2-O-isopropylidene-3-O-benzyl-5-oxo- α -D-xylofuranose (III) thus obtained was purified by distillation and reduced at room temperature in ether by slow addition (over 1 hour) of lithium aluminum deuteride in ether. The product (IV) was subjected to catalytic hydrogenolysis to remove the benzyl group and form 1,2-O-isopropylidene-5-deuterio- α -D-xylofuranose (V). Acid

¹Presented at the XXIXth Congrès de l'Association Canadienne-Française pour l'Avancement des Sciences, Ottawa, 1961.

²Present address: Department of Chemistry, University of Alberta, Edmonton, Alberta. ³National Research Council of Canada Postdoctoral Fellow 1959–61. Present address: Research Division, Rayonier Canada (B.C.) Limited, Vancouver, British Columbia.

Canadian Journal of Chemistry. Volume 41 (1963)



hydrolysis of the latter compound gave 5-deuterio-D-xylose (VI), which was acetylated using sodium acetate and acetic anhydride to form 5-deuterio- β -D-xylopyranose tetraacetate (VII). The nuclear magnetic resonance signals produced by the hydrogen at the 5-carbon of this product, which is the mixture of diastereoisomers differing in the configuration of the 5-carbon depicted in Fig. 1B, are compared in Fig. 1 with those of the methylene group in undeuterated β -D-xylopyranose tetraacetate (Fig. 1A). Lemieux and his collaborators (4) have already made the assignment of the signals for the methylene

LEMIEUX AND HOWARD: dextro-1-DEUTERIOETHANOL

309

CANADIAN JOURNAL OF CHEMISTRY. VOL. 41, 1963





hydrogens in β -D-xylopyranose tetraacetate. In the case of the 5-deuterio derivatives (VII) the 5-hydrogen (either H_a or H_e) is coupled strongly only with the hydrogen at the 4-position. Therefore, the appearance of the two rough doublets (because of coupling with the deuterium atom) is in accord with expectation. Undoubtedly, the signal at low field, $\tau = 5.87$, with a spacing of 4.2 c.p.s. arose from the molecules in which the hydrogen is equatorial and the one at high field, $\tau = 6.46$, with a spacing of 8.1 c.p.s. arose from the molecules in which the hydrogen is axial (4). A comparison of the relative intensities of these two signals showed that the isomer which has the 5-hydrogen in axial orientation was 1.85 times more abundant than the other. Since the absolute configuration of β -D-xylopyranose tetraacetate is known to be that depicted in Fig. 1, the absolute configuration of the 5-carbon in the more abundant isomer of VII possesses, in terms of the Cahn–Ingold–Prelog designation (5), the R-configuration. Therefore, degradation of VII to 1-deuterioethanol by way of a sequence of reactions that does not disturb any of the four bonds of the 5-carbon would yield R-1-deuterioethanol (XVI) of about 30% optical purity. The degradation was accomplished as follows.

The tetraacetate (VII) was converted to tri-O-acetyl-5-deuterio- β -D-xylopyranosyl bromide (VIII) and this compound was reacted with *n*-butanol in the presence of silver

310

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LEMIEUX AND HOWARD: dextro-1-DEUTERIOETHANOL

carbonate and anhydrous calcium sulphate to give n-butyl tri-O-acetyl-5-deuterio-β-Dxylopyranoside (IX) (6). Deacetylation provided *n*-butyl 5-deuterio- β -D-xylopyranoside (X), which was oxidized with sodium periodate at pH 5 to 6. The resulting dialdehyde (XI) was reduced with sodium borohydride at pH about 8 to afford the diol (XII). On subjecting the ditosylate (XIII) of the diol to a treatment with a refluxing solution of sodium iodide in dry acetone for 3 hours, the 2-tosyloxy-1-deuterioethyl group of XIII was transformed to the 2-iodo-1-deuterioethyl group of XIV. Hydrogenolysis of the iodo compound using palladium-hydrogen in methanol containing an excess of diethylamine gave the *n*-butyl 1-deuterioethyl mixed acetal of O-tosyl glycolaldehyde (XV). This substance was heated under conditions for distillation with dry *n*-butanol containing p-toluenesulphonic acid. The 1-deuterioethanol in the distillate was isolated by fractional distillation using the Podbielniak semimicro, spinning-band column. Four successive, about 0.35-ml fractions were collected in the boiling point range expected for ethanol. Examination of these fractions by gas-liquid partition chromatography and nuclear magnetic resonance spectroscopy showed the first three fractions, which distilled at the same temperature, to be virtually pure 1-deuterioethanol. Although the n.m.r. spectra of the fractions indicated the presence of water, the amount certainly was no more than is present in the ethanol-water azeotropic mixture. Levy, Loewus, and Vennesland (ref. 2, footnote 12) have shown that the drying of optically active 1-deuterioethanol does not change the sign of rotation. Consequently, the samples were not dried before measuring their rotations at the D-line of sodium. The fact that the samples were the expected 1-deuterioethanol is clear from the spectra shown in Fig. 2. Spectrum A is for a commercial grade of anhydrous ethanol and spectrum B is for a sample of ethanolwater azeotropic mixture. Spectrum C is of the combined fractions of 1-deuterioethanol after their individual rotations and n.m.r. spectra had been measured. The essentially doublet character of the signal for the methyl group clearly requires the deuterium to be at the 1-position of the ethanol.





CANADIAN JOURNAL OF CHEMISTRY. VOL. 41, 1963

The optical rotations of the three fractions of 1-deuterioethanol were measured under conditions of replication whereby a solution which was expected to produce a rotation of -0.052° different from the commercial alcohol used as a blank actually gave a rotation of $-0.057 \pm 0.02^{\circ}$. The observed optical rotations of the first three 1-deuterioethanol fractions were found to be $+0.061^\circ$, $+0.066^\circ$, and $+0.069^\circ$, respectively. From the known (2) rotation of an optically pure sample of 1-deuterioethanol, the expected magnitude for the rotation was $\pm 0.066^{\circ}$. It is inconceivable that these fractions would contain an optically active compound other than the deuterioethanol. Nevertheless, should the distillate possess such a compound and it, rather than the deuterioethanol, was responsible for the optical rotation, the substance would have to be present in about the same trace quantity in each of the three fractions and be present in just sufficient quantity to produce the magnitude of rotation expected if all of the optical activity came from the deuterioethanol. This event is too unlikely to warrant consideration. It is therefore concluded that, as anticipated both by Brewster (7) and by van Eys and Kaplan (8), dextrorotatory 1-deuterioethanol has the R-configuration shown in XVI. Therefore, since the reduction of 1-deuterioacetaldehyde by DPNH leads to the formation of levorotatory s-1-deuterioethanol (2), it is now definite that the acetaldehyde accepts the hydride ion in the manner depicted in XVII.



Of the variety of reducing conditions studied for the reduction of the aldehyde (III) using a deuterated reducing agent, the conditions reported herein gave the largest extent of partial asymmetric synthesis. The effects of temperature and order of addition using lithium aluminum deuteride have already appeared in Table III of the paper recently published by Haubenstock and Eliel (9) and require no further comment. Of real interest is the fact that a solution of deuterated isobornylmagnesium bromide which rapidly (2 hours) reduced benzaldehyde (10) left the aldehyde III unchanged even after prolonged (3 days) reaction times. Other attempts to make the aldehyde enter into a Meerwein-Ponndorf-Verley type of reduction were unsuccessful. Most likely these results are due to ready enolization of the aldehyde and the consequent formation of an enolate which resists reduction. Schaffer and Isbell (11) have demonstrated that 1,2-Oisopropylidene-5-oxo- α -D-xylofuranose undergoes aldol condensation and we observed (paper chromatography) the formation of the *arabo*-configuration in the reduction of one of our preparations of the 3-O-benzyl derivative (III). Whatever the reason for the resistance to reduction by alkoxides, displayed by the aldehyde III, this property precluded our ability to prepare optically pure 1-deuterioethanol.

EXPERIMENTAL

The melting points were determined on a Leitz microstage and are uncorrected. Unless otherwise stated, the optical rotations were measured at room temperature to $0.01\pm0.01^{\circ}$. The nuclear magnetic resonance spectra were measured on high-resolution Varian Associates spectrometers operating at 60 Mc/s.

1,2:5,6-Di-O-isopropylidene- α -D-glucofuranose (I)

The compound was prepared under the conditions described by Mehltretter and co-workers (12) except that the glucose was ground to pass through a 100-mesh sieve and no temperature control was used. A study of the progress of the reaction showed that the yield passed through a maximum after about 45 minutes' reaction time. At this time, only 3% of the glucose remained undissolved and the yield of product, melting

LEMIEUX AND HOWARD: dextro-1-DEUTERIOETHANOL

at $93-104^{\circ}$ and giving pure product after one recrystallization from $80-100^{\circ}$ petroleum ether, was 80% based on the glucose which had reacted. Since these experiments were performed Recondo and Rinderknecht (13) reported the use of acetic acid to help solubilize the glucose and evolved a procedure which appears equivalent to the best conditions developed in this investigation.

1,2:5,6-Di-O-isopropylidene-3-O-benzyl- α -D-glucofuranose (II)

The procedure reported by Adams, Reeves, and Goebel (14) was followed and the product was distilled at $170-180^{\circ}$ and 0.1 mm pressure. The yield was 95%.

1,2-O-Isopropylidene-3-O-benzyl-5-oxo-α-D-xylofuranose (III)

1,2:5,6-Di-O-isopropylidene-3-O-benzyl- α -D-glucofuranose, 30 g (0.086 *M*), was dissolved in 1 liter of glacial acetic acid. A solution of 21 g of periodic acid (H₅IO₆, 0.092 *M*) in 150 ml of water was added. After thorough mixing, the reaction was allowed to continue at 25°. After 25 minutes, the reaction was quenched by the addition of 60 g of sodium acetate dissolved in 2 liters of water. The aqueous solution was extracted using five 200-ml volumes of benzene, and the combined extracts were washed free of iodine with 0.1 *N* sodium thiosulphate solution. The yellowish oily residue, 20 g, which remained after the benzene was removed by distillation *in vacuo*, was dried by azeotropic distillation with benzene. The infrared spectrum showed weak carbonyl and very strong hydroxyl stretching vibrations and, consequently, the aldehyde was in the aldehydrol form. The oil was distilled in a high vacuum using a flask and condensing unit which had both been washed previously with concentrated nitric acid and distilled water to remove surface basicity in order to minimize the possibility for enolization. The faintly yellow viscous liquid, 16 g (67% yield), boiled at 140° at 0.15 mm pressure and its infrared spectrum showed no hydroxyl, but very strong carbonyl stretching vibrations. However, on exposure to moisture in the atmosphere the substance soon reverted to the aldehydrol form. The semicarbazone of the aldehyde was prepared, and melted at 170–173°. Anal. Calc. for C₁₆H₂₁N₅O₃: C, 57.29; H, 6.31%. Found: C, 57.71; H, 6.49%.

1,2-O-Isopropylidene-3-O-benzyl-5-deuterio- α -D-xylofuranose (IV)

Lithium aluminum deuteride (purchased from Metal Hydrides Inc., Beverly, Mass.), 0.923 g (0.022 *M*) (98% pure), was dissolved in 200 ml of ether (dried over lithium aluminum hydride) contained in a two-neck flask fitted with a condenser and calcium chloride tube, serum cap, and magnetic stirrer. As soon as the lithium aluminum deuteride had dissolved in the ether, 20-ml portions were slowly added, using a large hypōdermic syringe, to 1,2-O-isopropylidene-3-O-benzyl-5-oxo- α -D-xylofuranose (III), 21.7 g (0.078 *M*), dissolved in 500 ml of dry ether contained in a liter flask fitted with a magnetic stirrer, serum cap, condenser, and calcium chloride tube. The time taken for the addition of all the deuteride was 60 minutes. After allowing the reaction mixture to stand for a further 15 minutes, a small portion of the solution was added to water. A moderate evolution of gas indicated that a slight excess of lithium aluminum deuteride had been added. Water, 5 ml, was then added with stirring. The precipitate was removed by filtration with the aid of Celite and the ether was removed *in vacuo*. The clear colorless oil, 21 g (96% yield), which remained was dried by azeotropic distillation with benzene. The infrared spectrum indicated strong hydroxyl and C—D stretching vibrations but no signal characteristic of the carbonyl group. No purification was achieved as could be judged by infrared spectroscopy on distilling the substance at 160° and 0.1 mm pressure. The material, $[a]_D^{27} = -31.3^{\circ}$ (c, 6 in ethanol), resisted crystallization as did the 2,4-dinitrobenzoate ester.

1,2-O-Isopropylidene-5-deuterio- α -D-xylofuranose (V)

Substance IV, 21 g (0.075 M), was dissolved in 150 ml of absolute alcohol and hydrogenolyzed at room temperature and 4 atm pressure using a 10% palladium on charcoal catalyst (purchased from Engelhard Industries Inc., Newark 2, N.J.). The uptake of hydrogen was complete after 9 hours. The catalyst was removed by filtration and the filtrate was evaporated to a thick colorless syrup, 13.5 g (95% yield). The infrared spectrum showed that removal of the benzyl group was complete. The compound was characterized through its hydrolysis to 5-deuterio- α -D-xylose (VI) as described below.

5-Deuterio- α -D-xylose (VI)

The deuterioisopropylidene xylose (V), 13.5 g (0.071 *M*), was dissolved in 100 ml of 0.1 *N* sulphuric acid and the solution was heated on a steam bath for 45 minutes. After this time, the optical rotation was constant. The hot solution was neutralized with aqueous 0.1 *N* barium hydroxide and, after cooling, the barium sulphate was removed by filtration with the aid of Celite. The filtrate was evaporated *in vacuo* and the residue was dried by azeotropic distillation with benzene and ethanol. The colorless clear syrup after seeding with a small amount of undeuterated D-xylose and treatment with a little absolute ethanol crystallized completely within an hour. The dried crystals, 10.4 g (97% yield), melted at 142-143°. Pure α -D-xylose melts at 145°. A sample was chromatographed on paper using an ethyl acetate – pyridine – benzene – water (5:3:1:3) solvent system. Only one spot for xylose ($R_f = 0.36$) was detected using aniline phthalate as the spray reagent.

Tetra-O-acetyl-5-deuterio-β-D-xylopyranose (VII) (15)

The deuterated xylose (VI), 10.4 g (0.069 M), and 12 g of fused sodium acetate were mixed and cautiously heated, with efficient stirring, with 50 ml of acetic anhydride. The temperature of the initial reaction was

kept below 100° by cooling but after the initial strong liberation of heat had subsided, the mixture was kept at 100° for a period of 30 minutes, cooled, and poured into 200 ml of stirred water. Within a short time, the oil that separated began to crystallize and after 1 hour the mixture was cooled to 5° and the colorless product, 11 g (55% yield), melting at 122–125°, was collected by filtration. The filtrate was extracted with two 50-ml volumes of benzene and the combined extracts were washed with saturated sodium bicarbonate solution. Evaporation provided 8.4 g of a brown syrup which only partially crystallized. This material was retained and combined with the same syrups obtained in three subsequent acetylations of deuterated xylose. The mixture of α - and β -D-xylose tetraacetates, 26 g, was then deacetylated in 250 ml of anhydrous methanol made alkaline with a methanolic solution of potassium methoxide. The methanol was then evaporated to leave 14 g of syrupy deuterated xylose, which was immediately reacetylated using fused sodium acetate and acetic anhydride in the manner described above. The overall yield of tetra-O-acetyl-5-deuterio- β -D-xylopyranose (VII) was 78%.

The n.m.r. spectrum of the purified substance is shown in Fig. 1. Integration of the signals for the hydrogens on the 5-carbon, doublets centered at $\tau = 5.87$ (spacing 4.2 c.p.s.) and $\tau = 6.46$ (spacing 8.1 c.p.s.), showed the latter (high-field) signal to have an intensity 1.85 times that of the low-field signal.

Tri-O-acetyl-5-deuterio- α -D-xylopyranosyl Bromide (VIII)

The dry deuterated β -D-xylose tetraacetate (VII), 10.5 g (0.033 *M*), was dissolved in 100 ml of dry, ethanolfree chloroform. A 34-ml amount of 32% hydrobromic acid in acetic acid which contained 4 ml of acetic anhydride was then added to the chloroform solution at 10°. After 45 minutes, the optical rotation had become constant and the mixture was plunged into 300 ml of ice water contained in a separatory funnel. After thorough washing, first with ice water and then with saturated sodium bicarbonate solution at 0°, the chloroform solution was dried over sodium sulphate. The total time taken for washings was approximately 20 minutes. After filtration, the chloroform was evaporated *in vacuo* at a temperature not exceeding 50° to reduce the volume to 50 ml. This solution was used directly to prepare the butyl xyloside (IX) as described below. In a control experiment, removal of the chloroform gave a 91% yield of colorless crystalline product (VIII) melting in the range 95–100°. Pure tri-O-acetyl- α -D-xylopyranosyl bromide melts at 102° (16).

n-Butyl Tri-O-acetyl-5-deuterio- β -D-xylopyranoside (IX)

Hori (6) prepared this compound in 43% yield from the bromide VIII. The yield was improved to 53%-by maintaining anhydrous conditions throughout the addition over a period of 4 hours of the bromide (VIII), dissolved in chloroform (see above), to a slurry of silver carbonate in *n*-butanol containing anhydrous calcium sulphate. The reaction and work-up conditions were otherwise similar to those reported by Hori (6). The yield was 9.5 g of a syrup which crystallized spontaneously and gave only a faint Fehling test. Recrystallization from 3 parts of methanol-water (2:1) gave 6 g of crystalline product (IX) melting at 95–99°. The overall yield from the tetraacetate (VII) was 53%.

Crystalline *n*-butyl 5-deuterio- β -D-xylopyranoside (X) was obtained in quantitative yield by deacetylation in dry methanol using sodium methoxide as catalyst in the usual manner. After one recrystallization from ethyl acetate and petroleum ether, the compound melted at 89–90°. Hori (6) reported the substance (X) to melt at 90–91°.

Periodate Oxidation of n-Butyl 5-Deuterio-B-D-xylopyranoside (X) to the Ditosylate XIII

The deuterated butyl xyloside (X), 10.3 g ($0.0475 \ M$), was dissolved in 210 ml of water containing 5 g of sodium acetate and 25.8 g of sodium metaperiodate ($0.12 \ M$) added over a 5-minute period to the stirred solution, kept at room temperature in a water bath. After approximately 15 minutes, the optical rotation was constant. The solution was filtered and extracted nine times using 50-ml portions of ethyl acetate. The combined extracts were dried over sodium sulphate and evaporated *in vacuo* to give 9.1 g of the syrupy hydrated dialdehyde XI. The infrared spectrum of the material showed strong absorptions in the hydroxyl, carbonyl, and C—D stretching regions.

The hydrated dialdehyde XI, 9.1 g, was dissolved in 100 ml of water, and 4 g of sodium borohydride in approximately 0.25-g portions was added over a period of 15 minutes to the stirred solution, which was kept at 0°. During the reduction the pH was kept at approximately 8.0 by the addition of glacial acetic acid. After 1 hour, the excess sodium borohydride was destroyed by the addition of glacial acetic acid to maintain a pH of 7. The solution was then extracted using six 60-ml portions of ethyl acetate and the combined extracts were dried over sodium sulphate. Filtration and solvent removal left 7.0 g of an oil which was distilled to give 5.4 g (64% yield) of clear colorless oil which boiled at 110° and 0.1 mm pressure. The n.m.r. spectrum of this compound in heavy water showed a triplet of 6 c.p.s. spacing at 5.25τ . The spectrum showed two bands, one in the region 8.0 to 6.5τ due to the hydrogens of the methylene groups attached to oxygen and the other in the region 8.2 to 9.3τ due to the propyl group of the *n*-butyl group. The relative intensities of these bands was 1:1, as expected for the monodeuterio derivative. The specific rotation of the undeuterated compound was too small to measure in water but was -11.7° in ethyl acetate (c = 4).

The deuterated diol XII, 5.3 g $(0.03 \ M)$, was dissolved in 80 ml of dry pyridine. Tosyl chloride, 35 g $(0.183 \ M)$, was dissolved in 80 ml of ethanol-free, dry chloroform. The two solutions were mixed at 0° and kept at this temperature for 1 hour. The reaction mixture was allowed to stand at room temperature for 3 hours and 8 ml of water was added with cooling. After 30 minutes, 200 ml of chloroform was added and the

LEMIEUX AND HOWARD: dextro-1-DEUTERIOETHANOL

solution was extracted successively using two 400-ml portions of ice-cold water, one 400-ml portion of 2 N hydrochloric acid at 0°, and one 50-ml portion of a saturated solution of sodium bicarbonate. The chloroform solution was then dried over magnesium sulphate, filtered, and evaporated *in vacuo* to a 14.5 g syrupy residue of the deuterated ditosylate XIII. The n.m.r. spectrum in carbon tetrachloride showed the presence of two tosyl groups per butyl group and a triplet of 5 c.p.s. spacing at 5.43 τ . The hydrogens of the methylene groups attached to oxygen produced their signals in a wide band ranging from 5.7 to 6.9 τ . The intensity of this band relative both to the signals for aromatic hydrogens and the signals of the hydrogens in the propyl group showed the deuterated compound (XIII) to possess one hydrogen less than the undeuterated normal substance prepared in the same way but from normal p-xylose. The compound (XIII) showed absorption in the region of the infrared, 2200 cm⁻¹, characteristic of the C—D bond stretch. The signal was not present in the absence of the deuteration.

The n-Butyl 1-Deuterioethyl Acetal of O-Tosylglycolaldehyde (XV)

The deuterated ditosylate (XIII), 14.4 g (0.02 M), was dissolved in a solution of 20 g of dry sodium iodide in 400 ml of dry acetone. On standing at room temperature overnight, 3.8 g of sodium p-toluenesulphonate precipitated. The filtrate was kept at a reflux temperature for $1\frac{1}{2}$ hours and a further 2.2 g of the salt precipitated. The total amount, 6.0 g, corresponds to the replacement of 1.04 tosyloxy groups per mole of XIII. The reaction mixture was then filtered and evaporated at 35° in vacuo to a salt cake. Water, 100 ml, was added and the mixture was extracted with three 50-ml portions of ether. The combined ethereal extracts were washed first with a solution of sodium thiosulphate and then with water. After drying over magnesium sulphate, the solvent was removed in vacuo to leave 12.2 g of colorless product (XIV). The substance was dissolved in 50 ml of dry methanol which contained 5 ml of diethylamine and 1.5 g of 10% palladium on charcoal. The solution was hydrogenolyzed at an initial pressure of 3 atm. The hydrogen uptake (1 mole per mole of XIV) was complete after 30 minutes. The catalyst was removed by filtration and the filtrate was evaporated to a semisolid mass, which was dissolved in 100 ml of water, and the mixture was extracted with two 100-ml portions of ether. After drying over magnesium sulphate, the ether was removed in vacuo to leave 8.2 g of a colorless oil (XV). Although the n.m.r. spectrum of this product was not determined, that of the ethyl n-butyl acetal of O-tosylglycolaldehyde prepared in the same manner from D-xylose was in complete agreement with the structure expected for the compound.

dextro-1-Deuterioethanol (XVI)

The 1-deuterioethyl *n*-butyl acetal of *O*-tosylglycolaldehyde (XV), 8.0 g (0.025 *M*), and 1.36 g of *p*-toluenesulphonic acid were dissolved in 70 ml of pure dry *n*-butanol contained in a 100-ml flask which was fitted with a take-off condenser and a dropping funnel containing *n*-butanol. The *n*-butanol was dried by fractional distillation and was found to be devoid of optical activity when examined in a 2-dm tube. The flask was immersed in an oil bath which was maintained at 140°. Slow distillation resulted and 26 ml of distillate boiling in the range 100–114° was collected over a period of $5\frac{1}{2}$ hours. Gas-liquid partition chromatography on an Apiezon column at 68° indicated that the distillate contained only ethanol and *n*-butanol. A second 4-ml fraction of distillate, which boiled over at 114°, was collected over a period of 1 hour. Analysis of this fraction showed only *n*-butanol to be present. The main fraction was then fractionally distilled using a Podbielniak, semimicro, spinning-band column under conditions which had previously been found to effect a sharp separation of ethanol from *n*-butanol. Three successive fractions were collected of 0.35-, 0.39-, and 0.36-ml volumes, respectively, boiling in the range 77–78° (uncorrected). A fourth fraction, 0.55 ml, boiled at 76–85° and was found by gas-liquid partition chromatography to contain a very small amount of *n*-butanol. However, the first three fractions appeared pure and represent a 74% yield.

The optical rotations of the above three fractions were measured separately in a 1-dm tube at the D-line of sodium. The fields were matched by one investigator and the readings were taken by someone else. This was done 10 times for each fraction, once with the tube pointing in one direction and once with the tube pointing in the opposite direction in order to be sure that there was no contribution to rotation arising from the glass windows. The investigators then changed positions and repeated the operation. The zero point was taken as the average reading obtained using the tube filled with pure synthetic ethanol. This reading coincided with the air blank. In this way, a minimum of 20 readings was made on each of the fractions and the blanks without the observer knowing the readings of the polarimeter. Thus, the results were kept as free as possible from subjective error. In no single reading (in over 100 readings) was the sign of rotation determined for a sample of 1-deuterioethanol not found to be positive relative to the blank. The averages of the rotations observed for the three fractions were $+0.061^{\circ}$, $+0.066^{\circ}$, and $+0.069^{\circ}$, respectively. In taking these averages, the root mean square deviations were calculated in order to exclude some of the readings. The n.m.r. spectra of the fractions indicated that the samples contained less water than is present in the ethanolwater azeotrope. The three fractions were combined to obtain the n.m.r. spectrum of 1-deuterioethanol shown in Fig. 2. These spectra were taken with a Varian A60 spectrometer and show beyond doubt that the sample represents virtually pure 1-deuterioethanol. The only impurities evident in this sample are a trace of n-butanol and about 6% water. Most of the water present was undoubtedly introduced during several transfers of the 1-deuterioethanol which were made before the spectrum was taken. On the basis of the known observed rotation of optically pure 1-deuterioethanol (2), $\pm 0.22 \pm 0.02^{\circ}$, and the fact that the sample prepared in this work could be expected to be 30% pure, the rotation of the sample should be $\pm 0.066^{\circ}$. The

CANADIAN JOURNAL OF CHEMISTRY. VOL. 41, 1963

observed rotation of a 0.25% solution of β -D-xylopyranose tetraacetate in ethanol would be expected to be -0.052° . When the rotation was measured, using the procedure described above to measure the rotation of the samples of 1-deuterioethanol, a value of -0.057 ± 0.02 was obtained. Thus, there can be no doubt that dextro-1-deuterioethanol was prepared.

ACKNOWLEDGMENTS

This research was supported by the National Research Council of Canada through a grant-in-aid for research to R. U. L. The n.m.r. spectra were measured by Mrs. A. Westland (U. of O.) and R. Swindlehurst (U. of A.) and the microanalyses were made by Miss E. Busk.

REFERENCES

- V. E. ALTHOUSE, K. UEDA, and H. S. MOSHER. J. Am. Chem. Soc. 82, 5938 (1960).
 H. R. LEVY, F. A. LOEWUS, and B. VENNESLAND. J. Am. Chem. Soc. 79, 2949 (1957).
 R. U. LEMIEUX and J. GIGUERE. Can. J. Chem. 29, 678 (1951).
 R. U. LEMIEUX, R. K. KULLING, H. J. BERNSTEIN, and W. G. SCHNEIDER. J. Am. Chem. Soc. 80 R. O. LEMIEUX, R. R. R. R. R. B. R. S. CAHN, C. K. INGOLD, and V. PRELOG. Experientia, **12**, 81 (1956).
 R. HORI. Yakugaku Zasshi, **78**, 523 (1958); Chem. Abstr. **52**, 17118 (1958).
 M. D. Tatrabedron Letters **20**, 23 (1959).
- 5.
- 6.

- R. HORI. Yakugaku Zasshi, 78, 523 (1958); Chem. Abstr. 52, 17118 (1958).
 J. H. BREWSTER. Tetrahedron Letters, 20, 23 (1959).
 J. van Eys and N. O. KAPLAN. J. Am. Chem. Soc. 79, 2782 (1957).
 H. HAUBENSTOCK and E. L. ELIEL. J. Am. Chem. Soc. 84, 2363 (1962).
 A. STREITWIESER, JR., J. R. WOLFE, JR., and W. D. SCHAEFFER. Tetrahedron, 6, 338 (1959).
 R. SCHAFFER and H. S. ISBELL. J. Am. Chem. Soc. 80, 756 (1958).
 C. L. MEHLTRETTER, B. H. ALEXANDER, R. L. MELLIES, and C. E. RIST. J. Am. Chem. Soc. 73, 2424 (1951) (1951).
- E. RECONDO and H. RINDERKNECHT. Helv. Chim. Acta, 43, 1653 (1960).
 M. H. ADAMS, R. E. REEVES, and W. F. GOEBEL. J. Biol. Chem. 140, 653 (1941).
 H. APPEL. J. Chem. Soc. 425 (1935).
 J. K. DALE. J. Am. Chem. Soc. 37, 2745 (1915).