ethyl acetate saturated with water.[6] A band, yellow in both visible and ultraviolet light, moved off the column first. This portion was taken to dryness *in vacuo*, and the solid identified as quercetin. It showed R_f values of 0.08 in 15% acetic acid and 0.80 in butanol–acetic acid–water (40-10-50%, by volume), and no separation from authentic quercetin by mixed paper chromatography. Corresponding R_f values[7] reported for authentic quercetin are 0.07 and 0.78. The pentaacetate was prepared from the solid of the first eluate and recrystallized from ethyl acetate by adding pentane. Its m.p. was 195°, uncor. The recorded value for quercetin pentaacetate is 191–195°.[8]

The next band eluted from the magnesol with the ethyl acetate solution was a 15 mm. band, yellow in visible light, but brown under ultraviolet light. This portion was taken to dryness and dissolved in anhydrous acetone. The acetone solution was next rechromatographed on magnesol by the method described above until a sample of the eluate showed only one spot when analyzed by paper partition chromatography in 15% acetic acid and the butanol–acetic acid–water system, using basic lead acetate as a chromogenic spray.[7] This pigment spot had a R_f value of 0.46 in 15% acetic acid and 0.74 in the butanol–solvent system. These correspond to the values recorded for both isoquercitrin and quercimeritrin (quercetin-7-glucoside) in these solvents. A typical yield, at this point, of crude product was 200 mg. from 50 lb. of grapes.

The crude product was now recrystallized by dissolving it in 5 ml. of boiling water, then centrifuging, and discarding the residue. The supernatant liquor was allowed to cool to room temperature, made slightly acidic with acetic acid, and then placed in the refrigerator overnight. Crystallization occurred. The solution was next centrifuged, and the mother liquor discarded. The residue of brown-yellow crystals was washed with ice-water to remove the traces of acid and thus prevent possible subsequent hydrolysis. This recrystallization procedure was repeated eight times, each time more water being required, and finally yielded a light yellow powder. This product was dried *in vacuo* in the presence of phosphorus pentoxide at 80° for 3 hr.; yield 30 mg.

(6) C. H. Ice and S. H. Wender, *Anal. Chem.*, in press.

(7) T. B. Gage, C. D. Douglass and S. H. Wender, *ibid.*, **23**, 1582 (1951).

(8) A. G. Perkin and A. E. Everest, "The Natural Organic Colouring Matters," Longmans, Green and Co., London, 1918, p. 188.

Identification of the Isoquercitrin.—Hydrolysis of a portion of the yellow powder with 1% sulfuric acid solution produced glucose, identified by its osazone and R_f, and quercetin, identified by the method already described above for quercetin. At this point, the known possibilities were only isoquercitrin and quercimeritrin.

The ultraviolet absorption spectrum of the recrystallized pigment before hydrolysis, was identical with that obtained with authentic isoquercitrin.

The m.p. of the isoquercitrin isolated from the grapes was 232°, uncor. No lowering of the m.p. occurred when the isolated product was mixed with available authentic isoquercitrin (m.p. 233°, uncor.).

A sample of the isoquercitrin from grapes was methylated with dimethyl sulfate and potassium carbonate in acetone solution, according to the method of Shimokoriyama.[9] The resulting product was then hydrolyzed to yield 3′,4′,5,7-tetramethoxy-3-hydroxyflavone, which was recrystallized from benzene. The melting point was 193–195° (uncor.), which agrees with the literature value.[10] By this same series of reactions, quercimeritrin would have yielded 3,3′,4′,5-tetramethoxy-7-hydroxyflavone, which melts at 284–285°.[10] Thus, the quercetin glucoside from grapes has been identified as isoquercitrin.

The grapes used in this investigation were purchased from a local grocery store. Original labels on the un-opened crates indicated that they were California grapes, and of the type: Thompson white seedless, emperor or tokay.

Acknowledgments.—The authors express their appreciation to Dr. Carl D. Douglass, University of Arkansas Medical School, Little Rock, who, while at Oklahoma, made important experimental contributions on the preliminary studies of the flavonoids of grapes; to the Pharmacology Laboratory, Bureau of Agricultural and Industrial Chemistry, Albany, California, for the sample of authentic isoquericitrin and to Prof. T. R. Seshadri, Delhi, India, for the sample of authentic quercimeritrin.

(9) M. Shimokoriyama, *Acta Phytochim. (Japan)*, **15**, 63 (1949).

(10) G. F. Attree and A. G. Perkin, *J. Chem. Soc.*, 234 (1927).

NORMAN, OKLAHOMA

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

The Preparation of 1,6-Didesoxy-D-altritol, 1,6-Didesoxygalactitol and 1,6-Didesoxy-L-mannitol[1]

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Methyl α-D-altroside has been transformed by a series of reactions to 1-desoxy-D-altritol and 1,6-didesoxy-D-altritol. 1,6-Didesoxygalactitol has been prepared through the reductive desulfurization of L-fucose diethyl mercaptal, which can be obtained readily from the crude hydrolysis product of certain seaweeds. The reductive desulfurization of L-rhamnose diethyl mercaptal has produced 1,6-didesoxy-L-mannitol. Acetyl, methylene and benzylidene derivatives of these desoxyhexitols have been described.

In the continuation of our studies on the action of *Acetobacter suboxydans* on ω-desoxy sugar alcohols,[2] we have undertaken the synthesis of several 1,6-didesoxyhexitols that might serve either as substrates for that microörganism or as reference compounds for the subsequent identification of our products. The first of these substances, 1,6-didesoxy-L-glucitol (synonym, 1,6-didesoxy-D-gulitol), has already been described[3] as a sirup that could, however, be characterized through a crystalline tetraacetate, a dibenzylidene derivative and a monobenzylidene derivative.

In the D-altritol series we have now converted methyl α-D-altroside, with ethyl mercaptan and concentrated hydrochloric acid, directly to D-altrose diethyl mercaptal, whose reductive desulfurization has furnished 1-desoxy-D-altritol.[4] Trityla-

(1) Presented in part before the Division of Sugar Chemistry, Milwaukee Meeting of the American Chemical Society, March 31, 1952.

(2) For the biochemical oxidation of L-fucitol, see N. K. Richtmyer, L. C. Stewart and C. S. Hudson, THIS JOURNAL, **72**, 4934 (1950).

(3) E. Zissis, N. K. Richtmyer and C. S. Hudson, *ibid.*, **73**, 4714 (1951).

(4) The 6-desoxy-D-altritol has been described previously, ref. 2.

tion, acetylation, replacement of the trityloxy group by a bromine atom, and that in turn by a hydrogen atom, all by standard reactions, then yielded the crystalline tetraacetate of the desired 1,6-didesoxy-D-altritol. The deacetylated product, 1,6-didesoxy-D-altritol (synonym, 1,6-didesoxy-D-talitol), melted at 100–105°, showed $[\alpha]^{20}D$ −12.7° in water, and was characterized further through its crystalline dibenzylidene and monomethylene[5] derivatives. However, we were unsuccessful in our attempts to secure a dimethylene derivative for comparison with the substance described as "1,6-didesoxy-2,3,4,5-dimethylene-D-talitol" by Hann, Haskins and Hudson[6]; their compound was difficulty soluble in methanol, melted at 165–166°, and was reported to have a small rotation, $[\alpha]^{20}D$ +2.0° in chloroform. Our experiments have shown that our 1,6-didesoxy-D-altritol undoubtedly forms a dimethylene derivative, but it is too volatile to be isolated by the usual procedures. Meanwhile, Barker and Bourne[7] have stated that it was their belief that the parent "2,3,4,5-dimethylene-D-talitol" of Hann, Haskins and Hudson[6] was in reality the 2,4:3,5-dimethyleneallitol described by Wolfrom, Lew and Goepp.[8] The identity of the two substances has recently been confirmed by direct comparison of the samples in question,[9] and our results are in full agreement with those conclusions.

1,6-Didesoxygalactitol (a *meso* form) was prepared earlier in this Laboratory[10] through its 2,3,-4,5-diisopropylidene derivative, which, in turn, had been obtained through a series of reactions either from L-fucose *via* L-fucitol[10] or from D-galactose *via* galactitol.[10,11] We have now prepared 1,6-didesoxygalactitol through the reductive desulfurization of L-fucose diethyl mercaptal, the latter being obtainable directly from the sirupy hydrolysis products of suitable seaweeds without the necessity of first isolating the L-fucose. 1,6-Didesoxygalactitol has been characterized further by the preparation of a monobenzylidene derivative, a dibenzylidene derivative, and, in addition, an appreciably volatile dimethylene derivative.

During the course of our experiments still another method of making 1,6-didesoxygalactitol appeared from the discovery that 50% hydrobromic acid in acetic acid effected a remarkable conversion of the D-mannitol and D-glucitol configurations to that of galactitol.[12] Thus, hexaacetyl-D-mannitol and hexaacetyl-D-glucitol were converted to 1,6-dibromo - 1,6 - didesoxy - 2,3,4,5 - tetraacetylgalactitol, which could be isolated readily in 22–23% yields. Hydrogenation and deacetylation then produced 1,6-didesoxygalactitol.

Finally, 1,6-didesoxy-L-mannitol has been obtained through the reductive desulfurization of L-rhamnose diethyl mercaptal. The product has about the same melting point and magnitude of rotation (but of the opposite sign) as the enantiomorphous 1,6-didesoxy-D-mannitol described in an earlier communication from this Laboratory.[13] Our product has been characterized further through its tetraacetate and two dibenzylidene derivatives. In the D-series only one dibenzylidene derivative is known[13b]; however, two 2,3,4,5-dibenzylidenegalactitols have been reported,[14] each with its own set of 1,6-disubstituted derivatives, but in neither that series nor in ours has it been determined whether the isomerism is due to the position of the benzylidene residues or to the introduction of two new asymmetric centers by the condensation with benzaldehyde.

It may be of interest to compare the rotations of D-mannitol, D-altritol, and their mono- and didesoxy derivatives in water, in 5% aqueous ammonium molybdate, and in acidified molybdate solutions under the conditions adopted earlier in this Laboratory.[15] Although no attempt has yet been made to correlate these data, the values given in Table I may serve meanwhile for the additional characterization of the substances.

TABLE I

ROTATIONS OF D-MANNITOL, D-ALTRITOL AND DERIVATIVES

Compound	$[\alpha]^{20}D$ in water	$[\alpha]^{20}D$ in 5% molybdate (*c* 0.40)	$[\alpha]^{20}D$ in excess acidified molybdate (*c ca.* 0.4)
D-Mannitol[a,b]	− 0.2°	+ 16°	+141°
1(= 6)-Desoxy-D-mannitol[a,b]	−12	+ 23	+151
1,6-Didesoxy-D-mannitol	−23	+347	+137
D-Altritol (= D-talitol)	+ 3[c]	+ 91[d]	+ 8[d]
1-Desoxy-D-altritol	+ 2	+ 15	− 78
6-Desoxy-D-altritol[e]	− 9	+113	− 43
1,6-Didesoxy-D-altritol	−13	+101	−139

[a] Reference 15. [b] N. K. Richtmyer and C. S. Hudson, THIS JOURNAL, **72**, 3880 (1950). [c] R. M. Hann, W. T. Haskins and C. S. Hudson, *ibid.*, **69**, 624 (1947). [d] The rotations in 5% molybdate (*c* 0.40) and in acidified molybdate (*c* 0.4) were obtained with portions of the original recrystallized D-altritol (= D-talitol) described in ref. *c*. [e] Reference 2.

Experimental

D-Altrose Diethyl Mercaptal.—To 50 g. of methyl α-D-altroside[16] dissolved in 50 ml. of concentrated hydrochloric

(5) According to the generalizations put forth by R. M. Hann and C. S. Hudson [THIS JOURNAL, **66**, 1909 (1944)], a 3,5-methylene-1,6-didesoxy-D-altritol structure would be favored for this derivative; however, to obtain a definitive proof of structure for these didesoxy compounds would seem to be difficult except by an independent synthesis in which the methylene group is introduced before one or both of the terminal groups are transformed to methyl groups.

(6) R. M. Hann, W. T. Haskins and C. S. Hudson, *ibid.*, **69**, 624 (1947).

(7) S. A. Barker and E. J. Bourne, *J. Chem. Soc.*, 905 (1952).

(8) M. L. Wolfrom, B. W. Lew and R. M. Goepp, Jr., THIS JOURNAL, **68**, 1443 (1946).

(9) C. S. Hudson, M. L. Wolfrom and T. Y. Shen, *ibid.*, **74**, 4456 (1952).

(10) A. T. Ness, R. M. Hann and C. S. Hudson, *ibid.*, **64**, 982 (1942).

(11) R. M. Hann, W. D. Maclay and C. S. Hudson, *ibid.*, **61**, 2432 (1939).

(12) P. Bladon, W. G. Overend, L. N. Owen and L. F. Wiggins, *J. Chem. Soc.*, 3000 (1950); see also P. Bladon, L. N. Owen, W. G. Overend and L. F. Wiggins, *Nature*, **164**, 567 (1949).

(13) W. T. Haskins, R. M. Hann and C. S. Hudson, (a) THIS JOURNAL, **65**, 67 (1943); (b) **65**, 1419 (1943).

(14) W. T. Haskins, R. M. Hann and C. S. Hudson, *ibid.*, **64**, 136, 137 (1942).

(15) N. K. Richtmyer and C. S. Hudson, *ibid.*, **73**, 2249 (1951).

(16) D. A. Rosenfeld, N. K. Richtmyer and C. S. Hudson, *ibid.*, **70**, 2201 (1948); N. K. Richtmyer and C. S. Hudson, *ibid.*, **63**, 1727 (1941).

acid was added 50 ml. of ethyl mercaptan and the mixture was shaken at room temperature for at least 5 hours in order to obtain the maximal yield of product. The mercaptal crystallized readily when the reaction mixture was chilled and diluted with ice-water. Filtered, washed with water, and dried, it weighed 52.1 g. (66%). The mercaptal was purified by two recrystallizations from water, forming needles at room temperature or elongated prisms when allowed to separate more slowly in an oven at 50°. The melting points of the two types of crystals were identical, being 103–106°. The prisms showed $[\alpha]^{20}D$ +4.4° in pyridine (*c* 1) and +12.3° in water (*c* 1).

Anal. Calcd. for $C_{10}H_{22}O_5S_2$: C, 41.93; H, 7.74; S, 22.39. Found: (prisms) C, 41.89; H, 7.82; S, 22.42.

1-Desoxy-D-altritol (= **6-Desoxy-D-talitol**).—The reductive desulfurization of 31.3 g. of D-altrose diethyl mercaptal with Raney nickel in the usual manner yielded a sirup that partially crystallized overnight. The mixture was dissolved in 60 ml. of hot absolute ethanol, the solution cooled, and ether added gradually until crystallization appeared to be complete; the product weighed 17.6 g. (97%). After two recrystallizations from ethanol and ether the short, flat prisms of 1-desoxy-D-altritol melted at 105–107° and showed $[\alpha]^{20}D$ +2.2° in water (*c* 1), +15.3° in 5% aqueous ammonium molybdate (*c* 0.40), and −77.6° in an acidified molybdate solution (*c* 0.40).

Anal. Calcd. for $C_6H_{14}O_5$: C, 43.36; H, 8.49. Found: C, 43.29; H, 8.34.

Monobenzylidene-1-desoxy-D-altritol.—The reaction between 0.5 g. of 1-desoxy-D-altritol in 1 ml. of concentrated hydrochloric acid and 0.37 ml. of benzaldehyde (1.2 molecular equivalents) at 0° overnight produced clusters of needles that were filtered, washed with water, dried, and recrystallized from chloroform by the addition of pentane. The product melted at 148–149° and had the composition of a monobenzylidene derivative of 1-desoxy-D-altritol. Its rotation in chloroform, determined with only a very small amount of material, was estimated as $[\alpha]^{20}D$ +8°.

Anal. Calcd. for $C_{13}H_{18}O_5$: C, 61.40; H, 7.13. Found: C, 61.24; H, 7.28.

Ditosyltribenzoyl-1-desoxy-D-altritol.—Attempts to obtain a 6-tosyl derivative by the monotosylation of 2 g. of 1-desoxy-D-altritol followed by benzoylation yielded only about 0.1 g. of a crystalline product. After three recrystallizations from a mixture of chloroform and pentane the small needles melted at 174–175° (dec.) and had the composition of a ditosyltribenzoyl derivative of 1-desoxy-D-altritol.

Anal. Calcd. for $C_{41}H_{38}O_{12}S_2$: C, 62.58; H, 4.87; S, 8.15. Found: C, 62.49; H, 4.78; S, 7.99.

1-Desoxy-6-trityl-D-altritol Ethanolate.—A solution containing 20 g. of 1-desoxy-D-altritol and 40 g. of triphenylchloromethane in 65 ml. of pyridine was allowed to stand at room temperature for 3 days. The mixture was then poured over cracked ice and the precipitated heavy gum extracted with chloroform. The extract was washed with cold dilute sulfuric acid, aqueous sodium bicarbonate, and water, dried with anhydrous calcium chloride, and concentrated *in vacuo* to a sirup. Solution of the sirup in hot absolute ethanol, followed by cooling and dilution with pentane, yielded 43.3 g. (79%) of crystalline product. The trityl compound was recrystallized twice from a mixture of chloroform, ethanol and pentane; it formed clusters of flat prisms melting at 69–79° and containing one molecule of ethanol of crystallization. The ethanolate showed $[\alpha]^{20}D$ +2.4° in chloroform (*c* 1).

Anal. Calcd. for $C_{25}H_{28}O_5 \cdot C_2H_5OH$: C, 71.34; H, 7.54; C_2H_5OH, 10.14. Found (sample dried 2 hours at 37° *in vacuo*): C, 71.00; H, 7.42; C_2H_5OH (by heating 4 hours, to constant weight, at 77° *in vacuo*), 9.86. Calcd. for $C_{25}H_{28}O_5$: C, 73.50; H, 6.91. Found (after loss of ethanol by heating): C, 73.44; H, 7.04.

1-Desoxy-2,3,4,5-tetraacetyl-6-trityl-D-altritol.—Acetylation of 9 g. of 1-desoxy-6-trityl-D-altritol ethanolate with acetic anhydride and pyridine in the usual manner furnished 10.3 g. (90%) of once-recrystallized product. After two additional recrystallizations from ethanol–pentane, the clustered prisms of the tetraacetate melted at 108–110° and showed $[\alpha]^{20}D$ +9.0° in chloroform (*c* 1).

Anal. Calcd. for $C_{33}H_{36}O_9$: C, 68.73; H, 6.29; CH_3CO, 29.86. Found: C, 69.02; H, 6.31; CH_3CO, 29.60.

1,6-Didesoxy-2,3,4,5-tetraacetyl-D-altritol (= **1,6-Didesoxy-2,3,4,5-tetraacetyl-D-talitol**).—A solution of 10 g. of 1-desoxy-2,3,4,5-tetraacetyl-6-trityl-D-altritol in 80 ml. of alcohol-free chloroform was added slowly to a mixture of 40 ml. of alcohol-free chloroform, 2.6 ml. of phosphorus tribromide and 1.3 ml. of bromine (equivalent to a 50% excess of PBr_5). After 3 hours at room temperature the mixture was poured on cracked ice and stirred well to decompose the phosphorus bromides. The chloroform layer was separated, washed successively with water, aqueous sodium bicarbonate, water, aqueous sodium thiosulfate, and water, then dried with sodium sulfate, and concentrated *in vacuo* until the characteristic hexagonal crystals of triphenylcarbinol began to separate. Pentane was added and a total of 3.9 g. of triphenylcarbinol, in several crops, was removed. The final filtrate was concentrated to a sirup that was dissolved in a small amount of methanol; on standing in the refrigerator the solution deposited about 0.3 g. of additional crystalline material that was identified by m.p. and analyses as methyl triphenylmethyl ether. Concentration of the mother liquor yielded 6.8 g. of sirup containing the desired 1-desoxy-2,3,4,5-tetraacetyl-6-bromo-6-desoxy-D-altritol. When efforts to crystallize this substance were unsuccessful, the sirup was dissolved in 50 ml. of methanol and hydrogenated at room temperature and atmospheric pressure in the presence of 6 g. of Raney nickel and 1.9 ml. of diethylamine. The reaction was complete within 2 hours. The consumption of hydrogen was only about one-half of the theoretical amount, indicating that the sirupy starting product was rather impure. This conclusion was borne out by the isolation of only 1.2 g. (22% based on the acetylated trityl derivative) of crystalline product from the hydrogenation reaction. The resulting 1,6-didesoxy-2,3,4,5-tetraacetyl-D-altritol was recrystallized twice from pentane, forming thick prisms with m.p. 63–65° and $[\alpha]^{20}D$ +43.8° in chloroform (*c* 1).

Anal. Calcd. for $C_{14}H_{22}O_8$: C, 52.82; H, 6.97; CH_3CO, 54.1. Found: C, 52.97; H, 6.94; CH_3CO, 54.2.

1,6-Didesoxy-D-altritol (= **1,6-Didesoxy-D-talitol**).—Catalytic deacetylation of 3.5 g. of the preceding tetraacetate with sodium methoxide in the usual way yielded 1.5 g. (91%) of the crystalline didesoxyhexitol. It was recrystallized twice from ethanol by the addition of pentane, and formed flat, rectangular prisms melting at 100–105°. It showed $[\alpha]^{20}D$ −12.7° in water (*c* 2), +101° in 5% aqueous ammonium molybdate (*c* 0.40), and −139° in the acidified molybdate solution (*c* 0.32).

Anal. Calcd. for $C_6H_{14}O_4$: C, 47.99; H, 9.40. Found: C, 47.73; H, 9.28.

1,6-Didesoxy-2,3,4,5-dibenzylidene-D-altritol (= **1,6-Didesoxy-2,3,4,5-dibenzylidene-D-talitol**).—When 3 ml. of cold benzaldehyde was added to a solution of 0.9 g. of 1,6-didesoxy-D-altritol in 2 ml. of concentrated hydrochloric acid at 0°, the mixture solidified almost immediately. After 2 hours the product was filtered, washed with cold water and ethanol, and dried in the air. The 1.6 g. (82%) of product thus obtained was recrystallized twice from chloroform by the addition of pentane, and once from absolute ethanol. The needles of this dibenzylidene derivative melted at 153–155° and showed $[\alpha]^{20}D$ +59.5° in chloroform (*c* 1).

Anal. Calcd. for $C_{20}H_{22}O_4$: C, 73.59; H, 6.80. Found: C, 73.80; H, 6.98.

Monomethylene-1,6-didesoxy-D-altritol (= **Monomethylene-1,6-didesoxy-D-talitol**).[5]—A mixture of 0.2 g. of 1,6-didesoxy-D-altritol, 0.4 ml. of 37% formaldehyde and 0.4 ml. of concentrated hydrochloric acid was heated in a glass-stoppered flask for 20 minutes in an oven at 50°, and the product concentrated at room temperature in a vacuum desiccator over solid potassium hydroxide; the dry residue weighed 0.15 g. (75% of the original weight of the altritol). When 2.0 g. of 1,6-didesoxy-D-altritol was heated similarly with 6 ml. of formaldehyde and 4 ml. of hydrochloric acid for 2 hours at 50° and then concentrated, the residue weighed 0.5 g. (only 25% of the original weight of the altritol). The residues were recrystallized twice from ethanol by the addition of pentane, the product separating as needles with m.p. 126–127° and $[\alpha]^{20}D$ −10.1° in chloroform (*c* 0.7). It had the composition of a monomethylene derivative of 1,6-didesoxy-D-altritol. From the relative weights of the residues in these two experiments we must conclude, there-

fore, that the monomethylene derivative is formed first and is then converted, by the excess of reagents and by the longer heating, to a dimethylene derivative. The latter, however, must be readily volatile, even more so than the dimethylene-1,6-didesoxygalactitol described below, for in the present case the usual procedure of isolating the product by concentration of the aqueous solution left only the monomethylene derivative as the residual product.

L-Fucose Diethyl Mercaptal.—A solution of 30 g. of crystalline L-fucose in 60 ml. of concentrated hydrochloric acid was shaken with 30 ml. of ethyl mercaptan for 5 minutes. An ice-bath was used to moderate the vigorous reaction. The mercaptal crystallized quickly to a nearly solid mass. After standing for 2 hours in the ice-bath it was filtered, washed with cold water and ethanol, and dried at room temperature overnight. The crude product weighed 30.4 g. (62%). Recrystallization from 50 parts of water furnished long rods of L-fucose diethyl mercaptal with m.p. 167–168°; Votoček and Veselý[17] reported 167–168.5°. Two additional recrystallizations did not change the m.p., and the rotation, not previously reported, was $[\alpha]^{20}D$ −5.9° in pyridine (*c* 2).

L-Fucose and L-Fucose Diethyl Mercaptal from Seaweed.—For the preparation of L-fucose we used seaweed, presumed to be *Ascophyllum nodosum*, and followed the procedure for hydrolysis, neutralization, and precipitation of salts by methanol described by Hockett, Phelps and Hudson.[18] At that point the remaining ionizable material was removed by passage of the aqueous solution through columns of Amberlite IR-120 and Duolite A-4 ion-exchange resins. Concentration of the deionized solution to a thick sirup, followed by solution in hot absolute ethanol, cooling, and seeding, produced crystalline L-fucose. The yields averaged about 25 g. of crude sugar from each kg. of air-dried seaweed, but the product, at least from the first batch of seaweed, contained also appreciable amounts of D-mannitol and other organic material. The crude product, therefore, was converted without further purification to L-fucose diethyl mercaptal as described above. Additional mercaptal could usually be obtained by a similar treatment of the mother liquors from the crude L-fucose, or the original concentrated L-fucose sirups themselves could be treated directly with concentrated hydrochloric acid and ethyl mercaptan without the necessity of any intermediate crystallization of L-fucose. Our yields averaged about 20 g. of recrystallized L-fucose diethyl mercaptal from each kg. of seaweed. It seems obvious that batches of seaweed richer in L-fucose would have given higher yields, but we were unsuccessful even by following the original directions of Hockett, Phelps and Hudson[18] to obtain from our several lots of seaweed the yields of L-fucose reported by them.

If it were desirable, the L-fucose diethyl mercaptal could undoubtedly be converted to pure L-fucose by the action of mercuric chloride and cadmium carbonate as was described for the preparation of D-altrose from its dibenzyl mercaptal,[19] a procedure adapted in turn from that of Wolfrom[20] for acetylated mercaptals.

1,6-Didesoxygalactitol from L-Fucose Diethyl Mercaptal.—The reductive desulfurization of 20 g. of L-fucose diethyl mercaptal with Raney nickel yielded 7.6 g. (68%) of once-recrystallized 1,6-didesoxygalactitol of m.p. 181–183°. A mixture of our product with that prepared earlier in this Laboratory by Ness, Hann and Hudson[10] from L-fucitol also melted at 181–183°. They reported m.p. 183–184° for their product, and the values 185° and 179–180° have also been reported.[12] 1,6-Didesoxygalactitol in large amounts is recrystallized conveniently from water as long prisms and in small amounts from absolute ethanol plus ether. Our product had no observable rotation in water (*c* 6, *l* 4).

1,6-Didesoxy-2,3,4,5-tetraacetylgalactitol.—The acetylation of 1,6-didesoxygalactitol with acetic anhydride and fused sodium acetate yielded the tetraacetate, which crystallized from chloroform by the addition of pentane as plates with m.p. 186–187° and no observable rotation in chloroform (*c* 1, *l* 4). The previously reported m.p. of this tetraacetate from other sources was 182–184°.[12]

Anal. Calcd. for $C_{14}H_{22}O_8$: C, 52.82; H, 6.97; CH_3CO, 54.1. Found: C, 53.01; H, 6.82; CH_3CO, 54.0.

The Mono- and Dibenzylidene-1,6-didesoxygalactitols.—Two grams of 1,6-didesoxygalactitol was dissolved in 20 ml. of warm, concentrated hydrochloric acid, cooled in an ice-bath to room temperature, and 5 ml. of benzaldehyde quickly added. The product crystallized when left overnight in the refrigerator, and was then filtered, washed with water, alcohol and ether; it weighed 3 g. Recrystallization from hot absolute ethanol produced 0.6 g. of needles that, after further recrystallization, melted at 111–112°, had no observable optical activity in chloroform, and had the composition of a **1,6-didesoxy-2,3,4,5-dibenzylidenegalactitol**.

Anal. Calcd. for $C_{20}H_{22}O_4$: C, 73.60; H, 6.79. Found: C, 73.83; H, 6.84.

The filtrate from the 0.6 g. of dibenzylidene compound was concentrated to a dry residue. Extraction with chloroform, concentration, and the addition of pentane yielded 0.3 g. of needles of a second compound; further recrystallization, first from 50% ethanol and then from water, was sufficient to purify the substance, which then melted at 103–104° and had the composition of a **monobenzylidene-1,6-didesoxygalactitol**.

Anal. Calcd. for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.36; H, 7.71.

1,6-Didesoxy-2,3,4,5-dimethylenegalactitol.—A solution of 3 g. of 1,6-didesoxygalactitol in 6 ml. of concentrated hydrochloric acid and 6 ml. of 37% formaldehyde was heated for 2 hours at 50°. Upon cooling the solution to room temperature the dimethylene derivative began to crystallize in fairly large prisms. To hasten the crystallization and to remove the solvents the mixture was left for 2 days in an evacuated desiccator over solid potassium hydroxide. The residue weighed only 1.5 g. (43%), and the compound was found to be appreciably volatile even in the air at room temperature. The dimethylene derivative was recrystallized twice from aqueous alcohol, forming prisms of m.p. 40–42°.

Anal. Calcd. for $C_8H_{14}O_4$: C, 55.16; H, 8.10. Found: C, 55.16; H, 8.22.

L-Rhamnose Diethyl Mercaptal.—The reaction between 67 g. of L-rhamnose in 67 ml. of concentrated hydrochloric acid and 100 ml. of ethyl mercaptan according to the original procedure of Fischer[21] evolved considerable heat and it was necessary to cool the flask occasionally in an ice-bath during 5 minutes of shaking. The product crystallized readily, and was filtered and washed with cold water to yield 71.8 g. (65%) of air-dried mercaptal. Fischer reported the m.p. as 135–137°, but included neither rotation nor analysis data. A portion of our product was recrystallized several times from 10 parts of water forming elongated plates with m.p. 137–138° and $[\alpha]^{20}D$ +4.6° in pyridine (*c* 4).[22]

Anal. Calcd. for $C_{10}H_{22}O_4S_2$: C, 44.41; H, 8.20; S, 23.71. Found: C, 44.59; H, 8.12; S, 23.83.

1,6-Didesoxy-L-mannitol.—Reductive desulfurization of 20 g. of L-rhamnose diethyl mercaptal by the usual procedure gave 9.3 g. (85%) of 1,6-didesoxy-L-mannitol. The product separated from alcohol in clusters of needles, or as fairly large prisms when the solution was allowed to stand at 60° in an oven. The m.p. 145–146° and $[\alpha]^{20}D$ +22.8° in water (*c* 1) are in accord with the m.p. 147–148° and rotations −22.5° and −21.4° for the enantiomorphous 1,6-didesoxy-D-mannitol reported earlier from this Laboratory.[13] A mixture of the two substances melted at 140–142°. The new L enantiomorph showed $[\alpha]^{20}D$ −347° in 5% aqueous ammonium molybdate (*c* 0.40) and −137° in the acidified molybdate solution (*c* 0.40).

Anal. Calcd. for $C_6H_{14}O_4$: C, 47.99; H, 9.40. Found: C, 47.97; H, 9.44.

1,6-Didesoxy-2,3,4,5-tetraacetyl-L-mannitol.—The reaction of 3 g. of 1,6-didesoxy-L-mannitol with acetic anhydride and fused sodium acetate yielded 5 g. (79%) of crude tetraacetate. After several recrystallizations from 30% ethanol the prismatic crystals melted at 66–68° and showed $[\alpha]^{20}D$ −50.4° in chloroform (*c* 1).

(17) E. Votoček and F. Veselý, *Ber.*, **47**, 1515 (1914).

(18) R. C. Hockett, F. P. Phelps and C. S. Hudson, THIS JOURNAL, **61**, 1658 (1939).

(19) N. K. Richtmyer and C. S. Hudson, *ibid.*, **57**, 1716 (1935).

(20) M. L. Wolfrom, *ibid.*, **51**, 2188 (1929).

(21) E. Fischer, *Ber.*, **27**, 673 (1894).

(22) NOTE ADDED JULY 3, 1952.—H. Zinner [*Chem. Ber.*, **84**, 780 (1951)] has reported for L-rhamnose diethyl mercaptal the m.p. 136.5–137° and rotation $[\alpha]^{18}D$ −10.5° in methanol (*c* 4.94). We have confirmed his rotation, finding $[\alpha]^{20}D$ −10.4° in methanol (*c* 5.4).

Anal. Calcd. for $C_{14}H_{22}O_8$: C, 52.82; H, 6.97; CH_3CO, 54.1. Found: C, 53.06; H, 6.82; CH_3CO, 54.3.

The Two 1,6-Didesoxy-2,3,4,5-dibenzylidene-L-mannitols.—A mixture of 3 g. of 1,6-didesoxy-L-mannitol, 12 ml. of concentrated hydrochloric acid and 10 ml. of benzaldehyde was kept at 0° for 2 days. The solution was neutralized with aqueous ammonia and extracted with chloroform. The residue obtained upon concentration of the chloroform extract was dissolved in absolute ethanol and overnight in the refrigerator the solution deposited 0.7 g. of thick needles. After 4 recrystallizations from a mixture of chloroform and pentane the product, of m.p. 159–160° and $[\alpha]^{20}D$ −47.5° in chloroform (*c* 1), was identified as the 1,6-didesoxy-2,3,4,5-dibenzylidene-L-mannitol that is enantiomorphous with the D form, of m.p. 159–160° and $[\alpha]^{20}D$ +49.5°, reported earlier from this Laboratory.[13b]

The ethanolic mother liquor from the 0.7 g. of thick needles was concentrated to a sirup that was dissolved in ether, diluted with pentane, and chilled to −10°. Additional crystalline material was obtained and by fractional crystallization from chloroform and pentane it could be separated to yield more of the levorotatory dibenzylidene compound described above and a second, lower-melting, dextrorotatory benzylidene compound. The latter crystallized as white prisms, melted at 131–134°, showed $[\alpha]^{20}D$ +12.3° in chloroform (*c* 0.2), and also had the composition of a 1,6-didesoxy-2,3,4,5-dibenzylidene-L-mannitol. Upon hydrolysis by heating with 80% acetic acid for 2 hours on the steam-bath the original 1,6-didesoxy-L-mannitol was recovered.

Anal. Calcd. for $C_{20}H_{22}O_4$: C, 73.59; H, 6.80. Found (159–160° isomer): C, 73.52; H, 6.87; (131–134° isomer) C, 73.54; H, 6.87.

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BETHESDA, MARYLAND

[CONTRIBUTION FROM THE RADIOCHEMISTRY LABORATORY, DEPARTMENT OF CHEMISTRY, WASHINGTON UNIVERSITY]

6-C^{14}-D-Glucose and 6-C^{14}-D-Glucuronolactone[1]

BY JOHN C. SOWDEN

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6-C^{14}-D-Glucose has been prepared from D-glucose through the following successive intermediates: 1,2-isopropylidene-D-glucofuranose, 5-aldo-1,2-isopropylidene-D-xylofuranose, 6-C^{14}-1,2-isopropylidene-D-glucofuranuronic acid and 6-C^{14}-1,2-isopropylidene-D-glucofuranurono-γ-lactone. The isotopic carbon was introduced through a cyanohydrin condensation between NaC^{14}N and 5-aldo-1,2-isopropylidene-D-xylofuranose. The radiochemical yield of 6-C^{14}-D-glucose from NaC^{14}N was aproximately 10% while, as an alternative product, 6-C^{14}-D-glucuronolactone could be obtained in a radiochemical yield of approximately 18%.

Since their introduction a few years ago, C^{14}-labeled sugars have found extensive application for studies of chemical and, especially, biochemical reaction mechanisms. In the aldose sugar series, biosynthetic labeling has made available uniformly-labeled D-glucose[2] and D-galactose[3] as well as C_3,C_4-labeled D-glucose.[4] General synthetic methods applicable to C_1-labeling include the nitromethane[5] and cyanohydrin[6] syntheses. In addition, C_1-labeled D-xylose also may be obtained from C_1-labeled D-glucose by degradation.[7] No general synthetic method is available for the preparation of sugars with specific labeling in other than C_1.

The preparation of 6-C^{14}-D-glucose was of interest for the study of certain chemical and biochemical reactions involving scission of the D-glucose carbon chain. In addition 6-C^{14}-D-glucuronic acid should prove of value in elucidating the biochemistry of this physiologically important substance. The present synthesis, leading to both the labeled sugar and uronic acid, is unique for the glucose structure.

The reaction sequence employed is shown in the accompanying reaction scheme. The terminal carbon of D-glucose first is removed as formaldehyde by the cleavage of 1,2-isopropylidene-D-glucofuranose with sodium metaperiodate.[7,8] Introduction of the radioactive label then is accomplished by condensation of the resulting 5-aldo-1,2-isopropylidene-D-xylofuranose (I) with NaC^{14}N to give, after hydrolysis, a mixture of acetonated 6-C^{14}-L-iduronic acid and 6-C^{14}-D-glucuronic acid (II). The latter can be isolated by crystallization in about 20% yield based on the cyanide.

The use of excess 5-aldo-1,2-isopropylidene-D-xylofuranose in the cyanohydrin condensation to increase the radiochemical yield based on NaC^{14}N is limited by the following practical considerations: The sirupy dialdehyde, I, retains tenaciously a portion of the formaldehyde arising in the periodate cleavage and thus, with a large excess of dialdehyde, the yield of labeled uronic acids may be lowered seriously by the accompanying formation of labeled glycolic acid. Moreover, in the alkaline hydrolysis that follows the cyanohydrin condensation, appreciable amounts of unreacted dialdehyde give rise to troublesome quantities of sugar destruction products.

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(2) L. G. Livingston and G. Medes, *J. Gen. Physiol.*, **31**, 75 (1947); S. Aronoff, A. Benson, W. Z. Hassid and M. Calvin, *Science*, **105**, 644 (1947); E. W. Putman, W. Z. Hassid, G. Krotkov and H. A. Barker, *J. Biol. Chem.*, **173**, 785 (1948).

(3) E. W. Putman and W. Z. Hassid, Abstracts Papers Am. Chem. Soc., 119, 7Q (1951).

(4) A. K. Solomon, B. Vennesland, F. W. Klemperer, J. M. Buchanan and A. B. Hastings, *J. Biol. Chem.*, **140**, 171 (1941); H. G. Wood, N. Lifson and V. Lorber, *ibid.*, **159**, 475 (1945); D. B. Zilversmit, I. L. Chaikoff, D. D. Feller and E. J. Masoro, *ibid.*, **176**, 389 (1948).

(5) J. C. Sowden, *Science*, **109**, 229 (1949); *J. Biol. Chem.*, **180**, 55 (1949).

(6) D. E. Koshland, Jr., and F. H. Westheimer, THIS JOURNAL, **71**, 1139 (1949); **72**, 3383 (1950).

(7) J. C. Sowden, *ibid.*, **73**, 5496 (1951).

(8) K. Iwadare, *Bull. Chem. Soc. Japan*, **16**, 40 (1941).