

Summary

1. D-Mannoheptulose has been obtained by the rearrangement of D- α -mannoheptose (D-manno-D-gala-heptose) in dilute barium hydroxide solution, and also in pyridine solution.

2. D-Mannoheptulose α -hexaacetate, α -acetobromo-D-mannoheptulose, α -methyl-D-mannoheptuloside, and pentaacetyl- α -methyl-D-mannoheptuloside have been described.

3. A comparison of the rotations of these mannoheptulose derivatives with the rotations of the corresponding derivatives of D-mannose indicates a pyranoid ring in the mannoheptulose compounds.

4. α -Methyl-D-mannoheptuloside is very readily formed and very readily hydrolyzed; this behavior has been shown not to be inconsistent with the ketopyranoside formulation.

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Relations between Rotatory Power and Structure in the Sugar Group. XXXIII. The Alpha and Beta Methyl Pyranosides of L-Fucose (L-Galactomethylose) and their Triacetates¹

BY R. C. HOCKETT, F. P. PHELPS AND C. S. HUDSON

In 1925 one of us² reported two independent calculations of the specific rotation of α -methyl-L-fucoside, based upon its relationship to α -methyl-D-galactoside and to α -L-fucose, respectively; the values so predicted were -188 and -190 . The deviation from the value (-122) that had been observed by Tadokoro and Nakamura³ was so great that the purity of their product appeared doubtful; its rotation indicated that it might be a mixture of α - and β -forms. We undertook the preparation of the pure forms and soon found that the α -isomer is purified readily by recrystallization; its specific rotation was observed to be -196.9 as the average value of eleven preparations. It was then sought to obtain the pure β -form from the mother liquors of the other; the fractionation proved to be very slow and difficult because the isomers form mixed crystals over a wide range of composition, but it was learned that the β -form is certainly dextrorotatory. In 1930 Votoček and Valentin⁴ reported the specific rotation of α -methyl-rhodeside (α -methyl-D-fucoside) as $+190$. We then re-investigated the purification of α -methyl-L-fucoside, confirmed our higher value and prepared the β -methyl-L-fucoside by fractional crystallization

from the mother liquors of the α -form, obtaining a product of specific rotation $+14$, which was not changed by further recrystallization of the substance. In 1932 Minsaas⁵ reported the values -197 and $+16$ for the specific rotations of the α - and β -methyl-L-fucosides, respectively, and Schlubach and Wagenitz⁶ found the value -14 for β -methyl-D-fucoside (prepared by synthesis from D-galactose) and -5.9 for its triacetate. It was then discovered⁷ that the β -L-fucoside forms a crystalline molecular compound with potassium acetate, but that the α -isomer does not, which enabled us to obtain the β -isomer readily in definite purity; its rotation confirmed the value $+14$. In 1937 Minsaas⁸ reported the preparation of the triacetates of α - and β -methyl-L-fucosides (α -form, m. p. 74° , $[\alpha]^{20D} -151$; β -form, m. p. 99° , $[\alpha]^{20D} +7.0$). We have prepared both of these substances and find for the α -form, m. p. 67 and $[\alpha]^{20D} -149.7$, and for the β -form, m. p. $96-97^\circ$ and $[\alpha]^{20D} +7.1$; by deacetylating them we have confirmed the purity of the original fucosides of rotations -197 and $+14$, respectively. It is evident that the value -197 which Minsaas found for the α -fucoside is substantially correct and that the α -methyl-D-fucoside (rhodeside) of Votoček ($+190$) was an impure preparation containing some of the β -isomer. Our data con-

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(2) Hudson, *ibid.*, **47**, 275 (1925).

(3) Tadokoro and Nakamura, *J. Biochem. (Japan)*, **2**, 461 (1923).

(4) Votoček and Valentin, *Coll. Czechoslov. Chem. Commun.*, **2**, 36 (1930).

(5) Minsaas, *Rec. trav. chim.*, **51**, 475 (1932).

(6) Schlubach and Wagenitz, *Ber.*, **65**, 304 (1932).

(7) Watters, Hockett and Hudson, THIS JOURNAL, **56**, 2199 (1934).

(8) Minsaas, *Rec. trav. chim.*, **56**, 623 (1937). On p. 624 the rotations of β -methyl-L-fucoside and its triacetate are recorded as negative, obviously through a misprint because the context shows that the substances are dextrorotatory.

firm Minsaa's rotations except in the case of β -methyl-L-fucoside, for which his value (+16) appears to be about two degrees too large, due doubtless to the smallness of his observed reading (0.41°). The rotational data from our work are recorded in Table I. It is seen that the difference for the methyl fucosides (-37,600) agrees well with values found previously⁹ from five other pairs of methyl glycosides; the difference for the acetylated methyl fucosides (-45,150) is decidedly less than would be expected (about -53,500). In an accompanying article¹⁰ it is shown from the oxidation of these fucosides by periodic acid that they are pyranosides and that their alpha and beta classification, which has been made on the basis of their rotations, is correct from the standpoint of the configurations of carbon atom one.

TABLE I

THE ROTATIONS OF THE α - AND β -FORMS OF METHYL-L-FUCOPYRANOSIDE AND THEIR TRIACETATES

Substance	Mol. wt.	$[\alpha]^{20}_D$	$[M]_D$	Difference
α -Methyl-L-fucopyranoside	178	-197 ^a	-35070	-37600
β -Methyl-L-fucopyranoside	178	+14.2 ^a	+2530	
Triacetates of				
α -Methyl-L-fucopyranoside	288	-149.7 ^b	-43110	-45150
β -Methyl-L-fucopyranoside	288	+7.1 ^b	+2040	

^a In water. ^b In chloroform.

Experimental

Preparation of L-Fucose from Seaweed (Hockett and Hudson).¹¹—The seaweed (*Ascophyllum nodosum*) is cleaned by soaking it for several days in 3% hydrochloric acid, washing free of chlorides and drying on wire bot-tomed trays over a radiator until brittle; it is then broken into small pieces and stored.¹² A typical sample lost 12.6% moisture when dried at 110° to constant weight. A kilogram of air-dried seaweed (12.6% moisture) is hydrolyzed by boiling under reflux with 5 liters of 2% sulfuric acid for four hours. The cooled solution is filtered from insoluble material on a large porcelain filter, and the filtrate is neutralized to litmus with 110 g. of calcium carbonate (using a few drops of capryl alcohol to control foaming), followed by the addition of the necessary amount of calcium hydroxide. Seventy grams of decolorizing carbon is added and the mixture allowed to stand overnight. The solids are then removed by decantation and filtration, and the nearly colorless solution is concentrated *in vacuo* to about 2.5 liters, filtered from precipitated calcium sulfate, and further concentrated to 200 cc. Warm methyl alcohol (900 cc.) precipitates a granular material, which is filtered off and washed with three portions, 100 cc. each, of the same

solvent. Further impurity is removed by adding 500 cc. of ether to the alcoholic filtrate and filtering again. The solution is now concentrated to a sirup of honey-like consistency, which is dissolved in absolute alcohol to a volume of about 200 cc. At this stage one may proceed to crystallize a portion of the fucose or to prepare the crystalline phenylhydrazone. To follow the first procedure, the 200-cc. solution is reconcentrated to a thick sirup (to reduce the water content), which is then dissolved in about 75 cc. of absolute alcohol and the solution seeded; the yield of crystalline fucose ranges from 13 to 25 g., and the remainder may be recovered from the mother liquor through the phenylhydrazone. To follow the second procedure, there is added to the 200 cc. of alcoholic solution 70 cc. of phenylhydrazine; fucose phenylhydrazone soon crystallizes and the mixture becomes solid. After standing overnight the hydrazone is filtered, washed thrice with absolute alcohol and dried at 50° (wt. 65 to 100 g., corresponding to 43-63 g. of fucose, which represents 5 to 7% of the dry seaweed). The fucose phenylhydrazone is readily converted to the sugar by heating 75 g. of it at 90° for one-half hour with 1800 cc. of water and 36 g. of benzaldehyde, with frequent stirring; an additional 10 g. of benzaldehyde is then added, and the heating and stirring are continued for fifteen minutes. The solution is cooled to 0° and the benzaldehyde hydrazone filtered off through a layer of decolorizing carbon; the filtrate is extracted three times with 100 cc. of chloroform (to remove benzoic acid and excess benzaldehyde) and concentrated to a sirup, which is dissolved in 50 cc. of hot absolute alcohol. Crystallization of fucose begins promptly and is allowed to continue overnight in a refrigerator. The yield of crystalline fucose, after filtration, washing with absolute alcohol and drying at 60° two hours, is about 40 g. The sugar is recrystallized (70% yield) by dissolving in 3 parts of water, concentrating to a sirup *in vacuo* and taking up with 3 volumes of absolute alcohol; the m. p. was 140-141° and the equilibrium $[\alpha]^{20}_D$ was -74.9. The rotation of L-fucose, after several recrystallizations to constancy, was $[\alpha]^{20}_D$ -76.0. The sugar may also be recrystallized from its solution in absolute methyl alcohol, prepared by refluxing the dry sugar with the solvent. The yield of crystalline fucose from 1 kg. of moisture-free cleaned seaweed through the phenylhydrazone procedure has ranged between 39 and 60 g.

The α - and β -Forms of Methyl-L-fucopyranoside. (a) (Experiments by Phelps).—The fucoside was obtained readily by refluxing 15 g. of fucose for six hours with methyl alcohol containing 1% hydrochloric acid, removing the acid as silver chloride, concentrating *in vacuo* to a sirup and crystallizing from ethyl acetate; yield 7.3 g. After one recrystallization from methyl alcohol and ethyl acetate the plate-like crystals showed $[\alpha]^{20}_D$ -197.0 in water. The mother liquor deposited material which proved to be mixed crystals of the α - and β -fucosides. The pure β -form is difficult to obtain from these mixed crystals, but by working with larger quantities and fractionating repeatedly it was finally obtained pure; it showed $[\alpha]^{20}_D$ +14.0 \pm 0.3 in water (c, 4). It crystallizes from methyl or ethyl alcohol and ethyl acetate as long slender almost thread-like needles, which are anhydrous;

(9) Dale and Hudson, *THIS JOURNAL*, **52**, 2534 (1930).

(10) Maclay, Hann and Hudson, *ibid.*, **61**, 1860 (1939).

(11) These directions follow in general, but with some modifications, those of E. P. Clark, *J. Biol. Chem.*, **54**, 65 (1922).

(12) Grinding the seaweed is not necessary; its dust seems to be harmful to some persons.

from water it forms rather long thick prismatic crystals, which are a monohydrate that is stable in air but which soon becomes anhydrous in a desiccator over lime, passing to a white powder.

(b) (Experiments by Hockett).— α -Methyl-L-fucoside, prepared by refluxing fucose with 1% hydrochloric acid in methanol for twelve hours and isolated as described above, was recrystallized from methanol-ethyl acetate to constant properties readily. The pure substance shows m. p. 154° (corr.) and $[\alpha]^{20}_D -197.1$ (*c*, 3.42; 4-dm. tube); a sample which was prepared by deacetylation of its purified triacetate (described below) showed the rotation -197.0 (*c*, 4.16; 4-dm. tube). Analyses for carbon, hydrogen and methoxyl gave the expected values (the substance has been analyzed by previous investigators). The mother liquor from the α -form was treated in absolute alcoholic solution with double the theoretical quantity of dried potassium acetate (CH_3COOK) dissolved in absolute alcohol; silky needles of the 1:1 molecular compound of the β -fucoside separated at once and they were recrystallized from hot absolute alcohol. The β -fucoside was obtained by preparing its triacetate from this molecular compound (as described below) and deacetylating the triacetate with barium methylate, the over-all yield of the two steps being nearly quantitative. The pure β -L-fucoside showed m. p. $121-123^\circ$ and $[\alpha]^{20}_D +14.2$ (*c*, 3.9; 4-dm. tube) in water.

The α - and β -Forms of Triacetyl-methyl-L-fucopyranoside.—Two grams of the pure α -fucoside was acetylated by heating for thirty minutes on the steam-bath with 12 cc. of acetic anhydride and 6 cc. of pyridine, followed by isolation according to standard procedure; yield 85%. The substance was recrystallized from hot water; a further recrystallization from aqueous methyl alcohol did not change its rotation, which was $[\alpha]^{20}_D -149.1$ (*c*, 0.9) in chloroform (Phelps). The pure α -fucoside was also

acetylated by heating with 5 parts of acetic anhydride and one-quarter part of fused sodium acetate; the triacetate was isolated by standard procedure and recrystallized from absolute alcohol, as brilliant plates, which gave the correct analyses (previously reported by Minsaas) for methoxyl, acetyl, carbon and hydrogen, melted at 67° and showed $[\alpha]^{20}_D -149.7$ (*c*, 1.8) in chloroform (Hockett). The β -methyl-L-fucoside triacetate was prepared by heating 5 g. of its pure potassium acetate compound for one hour on the steam-bath with 20 cc. of acetic anhydride, and isolating the substance through standard procedure (yield, quantitative); by recrystallization from absolute alcohol, from which it separates in clear tablets, it is readily brought to constant properties, m. p. $96-97^\circ$ and $[\alpha]^{20}_D +7.1$ (*c*, 4.5; 4-dm. tube) in chloroform (Hockett). Its analysis showed the correct values for carbon, hydrogen, methoxyl and acetyl, confirming Minsaas' reported analysis for the substance.

Summary

The α - and β -methylpyranosides of L-fucose (L-galacto-methylose) and their triacetates, previously reported by Minsaas, have been reprepared and their purity carefully controlled. The results confirm Minsaas' rotations except in the case of β -methyl-L-fucoside, the rotation of which is found to be $+14.2$ instead of $+16.0$. Some modifications of E. P. Clark's directions for preparing crystalline fucose from seaweed are presented. The difference of rotations of the glycosides shows the normal value; the difference for their triacetates is decidedly lower than would be expected.

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The Cleavage of the Carbon Chains of Some Methyl Aldohexamethylo-pyranosides by Oxidation with Periodic Acid¹

BY W. DAYTON MACLAY, RAYMOND M. HANN AND C. S. HUDSON

Jackson and Hudson² have described the crystalline dialdehyde (III) that results from the oxidation of α -methyl-L-mannomethylo-pyranoside³ (I) with periodic acid. We have now obtained this same dialdehyde by the similar oxidation of α -methyl-L-galactomethylo-pyranoside (II), and by oxidation of this dialdehyde with bromine water in the presence of strontium carbonate have ob-

tained the crystalline strontium salt of the corresponding dibasic acid (IV). In like manner it has been found that the periodic acid oxidation of α -methyl-D-glucomethylo-pyranoside (V) yields the crystalline enantiomorphous dialdehyde (VI), from which in turn has been prepared the crystalline strontium salt of the corresponding dibasic acid (VII), the enantiomorph of (IV). The hydrolysis of the dibasic acid formed from the strontium salt (IV) yields L-lactic acid⁴ in optical

(1) Publication authorized by the Surgeon General, U. S. Public Health Service.

(2) Jackson and Hudson, *THIS JOURNAL*, **59**, 994 (1937).

(3) We use the nomenclature for methyl pentoses that was suggested by Votoček: L-mannomethylose = L-rhamnose, L-galactomethylose = L-fucose, D-glucomethylose = D-isorhamnose (syn. D-epirhamnose). The D and L symbols refer throughout to configuration.

(4) In the case of the optically active lactic acids and their zinc salts the L-lactic acid is dextrorotatory and its zinc L-lactate levorotatory, while the D-lactic acid is levorotatory and its zinc D-lactate

dextrorotatory. D-Lactic acid has the configuration $\text{CH}_3-\overset{\text{H}}{\underset{\text{OH}}{\text{C}}}-\text{COOH}$.