precipitate was collected and recrystallized from petroleum ether (90–100°). The white, waxy crystals melted at 76–76.5°.[20] The ester also crystallized well from ethyl methyl ketone.

**Anilide of Tetratriacontanoic Acid.**—One gram of acid was mixed with 10 ml. of thionyl chloride, allowed to stand for thirty minutes and then heated under reflux for several minutes. Excess thionyl chloride was removed by distillation and the residue, dissolved in 60 ml. of petroleum ether, was added to 5 ml. of aniline. The mixture was stirred thoroughly and evaporated to dryness; the residue was triturated with cold, dilute hydrochloric acid and the crystals were separated by filtration. The product was recrystallized once from a small volume of ethyl methyl ketone and then twice from 100-ml. portions of petroleum ether (90–100°). The anilide, 1.05 g., melted at 110–110.5°. Francis[2] reported a melting point of 113–114°.

**Acknowledgment.**—We should like to acknowledge the continued interest and suggestions of Dr. Howard Gilbert of the Bureau of Aeronautics, Navy Department. Miss Eleanor Werble performed the microanalyses, and Mr. Herman Sanders aided in the preparation of certain intermediates.

## Summary

1. The preparation of hexacosanoic acid and tetratriacontanoic acid is described.

2. The same method has been applied to the synthesis of 1-cyclohexoxydotriacontane and 1-cyclohexoxyhexatriacontane.

3. A convenient synthesis of ethyl hydrogen hexadecanedicarboxylate has been developed. The method depends upon the selective solvent action of petroleum ether which has been shown to be a solvent of useful specificity.

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[20] Francis, King and Willis, ref. 2, have recorded the melting point of this ester as 75.4°.

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[CONTRIBUTION FROM THE WOOD CONVERSION LABORATORY OF THE UNIVERSITY OF IDAHO]

# The Constitution of Mesquite Gum. IV. 4-Methoxy-D-glucuronic Acid[1]

BY E. V. WHITE

A large number of the polysaccharides occurring in nature are known to contain uronic acid residues as an integral part of their molecular structure. The carboxyl group in such instances usually does not occur in the free state but rather is combined as a salt with metallic ions such as calcium, magnesium, and the like or as an ester with methyl alcohol. In general, the uronic acid possesses the glucose, mannose or galactose configuration and it has been considered to play an important role in the mechanism of plant synthesis. In a few instances polysaccharides have been reported to contain small percentages of ether type methoxyl and this grouping appears to be associated invariably with the uronic acid component. The observation is particularly interesting since it records the natural synthesis of an aliphatic ether linkage as contrasted with the usual aromatic, ester and acetal types. Unfortunately, however, the presence of this particular grouping[2] has been indicated hitherto only by analyses and no definite crystalline compounds or derivatives have been prepared to prove the actual existence of the group or to establish its exact location in any given polysaccharide.

The presence of ether methoxyl in mesquite gum was reported first by Anderson and co-workers[3a,b,c,d] who traced the group to the uronic acid component and, largely by a process of elimination, suggested the three position thereof as the most likely point of attachment. It has now been shown[4] that the uronic acid residues occupy terminal positions in the mesquite gum macromolecule and the present study was designed to locate definitely the position of the methyl ether linkage.

The well known reaction of polysaccharides with anhydrous acidic methyl alcohol solutions results in simultaneous esterification of the uronides and formation of the corresponding methyl glycosides and uronosides. In such reactions, whereas a single methyl group is substituted in the saccharides, two such groups are introduced into the uronic acid component. One of these is uronosidic or acetal in character while the second is of the ester type. In the present instance these two methyl groups together with the aliphatic ether group originally present furnish a trimethyl substituted uronic acid fission product which can be separated readily from the glycosidic fragments. Accordingly, mesquite gum which had been partially hydrolyzed to remove the labile arabinose fraction[5] was treated with methanolic hydrogen chloride and the resulting sirup extracted with anhydrous acetone. The extract was concentrated and then diluted with anhydrous ether to precipitate residual methyl galactoside. Evaporation of the mixed solvent and fractional

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[1] Presented in part at the Fall Meeting of the Technical Association of the Pulp and Paper Industry, Appleton, Wisconsin, September 3–5, 1947.

[2] It should be noted that the aliphatic methyl ether grouping has been found in the carbohydrate component of certain cardiac glycosides, notably, cymarose and digitalose. A review of these compounds is given by Elderfield, "Recent Advances in Carbohydrate Chemistry," Vol. I, Academic Press, Inc., New York, N. Y., 1945, p. 147.

[3] (a) Anderson, Sands and Sturgis, *Am. J. Pharm.*, **97**, 589 (1925); (b) Anderson and Sands, *Ind. Eng. Chem.*, **17**, 1257 (1925); (c) Anderson and Sands, THIS JOURNAL, **48**, 3172 (1926); (d) Anderson and Otis, *ibid.*, **52**, 4461 (1930).

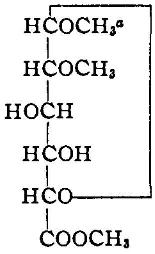
[4] White, *ibid.*, **68**, 272 (1946).

[5] White, *ibid*, **69**, 622 (1947).

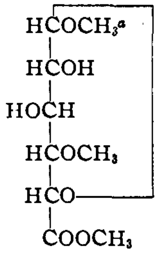
vacuum distillation of the sirup furnished the methyl ester of monomethyl-methyl-glucuronoside.

The ether type methoxyl group of this compound must obviously be located at either the second, third or fourth carbon atom since the uronoside ester contains the normal pyranose ring structure.[4] A decision as to the correct position was provided by the selective action of periodic acid which reacts in stoichiometric proportion with the compound. Since such reaction necessitates vicinal hydroxyl groups in the reacting substance, the presence of an ether grouping at the third carbon atom is untenable and the uronoside ester must be represented either by Formula I or Formula II.

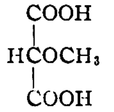
I



II



Ia

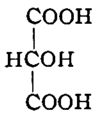


$COOH-HCOCH_3-COOH$

IIa

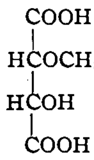
$COOH-COOH$

Ib



$COOH-HCOH-COOH$

IIb



$COOH-HCOCH_3-HCOH-COOH$

[a] The alpha form is represented although both alpha and beta forms are present in the uronoside ester sirup.

In the first example (I) treatment of the compound with periodic acid followed by bromine oxidation, acetal hydrolysis and re-oxidation according to the splendid methods of Jackson and Hudson[6] should provide eventually methoxymalonic acid (Ia) and hydroxymalonic acid (Ib), both of which are optically inactive. On the other hand, a similar treatment of the compound represented by Formula II should furnish oxalic acid (IIa) and a methoxy-*meso*-tartaric acid (IIb), the latter being optically active.

With these possibilities in mind the compound in quesion was subjected to a series of reactions employing one molecular equivalent of periodic acid and followed by oxidation with bromine in the presence of strontium carbonate. The product was isolated as both a crystalline and an amorphous strontium salt with identical analyses but different optical activity. Further reaction of this compound after quantitative removal of strontium as sulfate involved hydrolysis of the acetal grouping and bromine oxidation of the aldehyde thus formed. The resulting reaction product now contained two dibasic organic acids which were separated and identified. One of these was found to be oxalic acid and identified as the dimethyl ester. The second acid proved to be an optically active methoxy-*meso*-tartaric acid which was also isolated as the dimethyl ester and from which a crystalline diamide was prepared. Complete methylation of this ester furnished crystalline dimethoxy-*i*-dimethyl-succinate which was identified further as the crystalline diamide.

The above experiments seem to provide convincing proof that the methyl ester of monomethyl-glucuronoside isolated from mesquite gum possesses the structure represented by Formula II. The methyl ether linkage in this particular polysaccharide is thus located at the fourth carbon atom of the uronic acid component and its synthesis by natural agencies seems well established. It is interesting to note also that the position of ether linkage is characteristically that involved in the glycosidic linkage of glucose in the polysaccharides. This property is, of course, shared to some extent with the terminal hydroxyl grouping, while the remaining groups appear to be inactive.

## Experimental Part

**Preparation of Monomethyl-methyl-glucuronoside Methyl Ester from Mesquite Gum.**—Two hundred grams of crude mesquite gum was dissolved in one liter of distilled water and filtered to remove extraneous material. The solution was then made 0.15 *N* with sulfuric acid and heated at 92° on a water-bath for thirty-six hours.[5] The hydrolyzate was dialyzed against water for two days to remove acid, arabinose, etc., filtered and concentrated at 50° to a thin sirup by evaporation. The concentrate, diluted with an equal volume of methyl alcohol, was added slowly to rapidly stirred anhydrous methanol. The flocculent precipitate was settled, filtered, washed with fresh alcohol and ether, and finally dried at 40° under reduced pressure; yield 78 g.

The above product was suspended in 500 cc. of methanol containing 7% anhydrous hydrogen chloride and heated under reflux for eighteen hours. The polysaccharide under these conditions dissolves rapidly with frequent swirling during the first half hour. The concentration of hydrogen chloride decreased steadily during the heating period and residual acidity was finally removed with silver carbonate. After filtering off silver salts the solution was evaporated to a sirup, taken up in 100 cc. of fresh acetone and 400 cc. of anhydrous ether added slowly with swirling. After a few hours the clear solution was siphoned off and the residue re-extracted using one-third quantities of the same solvents. The combined extracts were evaporated to a sirup which was distilled, b. p. 130° (0.2 mm.), under high vacuum; yield 15.2 g.; specific rotation +95° (25°, *c* 10, water).

*Anal.* Calcd. for $C_9H_{16}O_7$: $OCH_3$, 39.4. Found: $OCH_3$, 39.3.

Treatment of a sample, 1.0 g., with methyl alcoholic ammonia in the usual manner furnished an amide, recrystallized from methanol–acetone, m. p. 218°.

*Anal.* Calcd. for $C_8H_{15}O_6N$: $OCH_3$, 28.0; N, 6.34. Found: $OCH_3$, 27.8; N, 6.3.

**Preparation of the Strontium Salt of Oxidized Monomethyl-methyl-glucuronoside Methyl Ester.**—The above ester, 16.7 g., was dissolved in 300 cc. of water, treated with norite and filtered. To the filtrate was added one molecular equivalent plus 5% excess of periodic acid dissolved in 200-cc. of water. The solution was allowed to stand at room temperature for sixteen hours when an excess of strontium carbonate was carefully added with stirring. The precipitate of strontium salts was then re-

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

moved and washed with 100 cc. of water. The filtrate, 600 cc., was added in 200-cc. portions to three flasks each containing 5 cc. of bromine dissolved in 500 cc. of water and 50 g. of strontium carbonate. After eighteen hours in the dark, with occasional swirling especially during the first two hours, excess bromine was removed by aeration. Silver carbonate was added to remove bromine ion and after filtering, silver ion was removed as sulfide. The colorless, combined filtrates were distilled at 30° under reduced pressure to a thin sirup which was diluted with two volumes of 95% ethanol. The crystalline strontium salt of the acid separated overnight and was removed, washed with cold 65% ethanol, ethanol and ether, and dried; yield 13.3 g.; specific rotation −24° (25°, *c* 5, water).

*Anal.* Calcd. for $C_9H_{12}O_9Sr$: $OCH_3$, 26.5; Sr, 24.9. Found: $OCH_3$, 25.4; Sr, 24.0.

The filtrates upon evaporation to dryness gave a residue which did not crystallize but gave the same analysis as above: yield, 7.8 g.; specific rotation +13° (25°, *c* 5, water).

The former compound, which has not yet been recrystallized in pure form, is thought to be derived from the alpha form of the uronoside, with the latter representing a mixture of the alpha and beta modifications.

**Proof of Structure of the Strontium Salt of Oxidized Monomethyl-methyl-glucuronoside Methyl Ester.**—Ten grams of either the crystalline or amorphous forms of the strontium salt was dissolved in 100 cc. of water and treated with the exact quantity of sulfuric acid dissolved in 100 cc. of ethanol to precipitate the strontium as sulfate. After several hours the precipitate was filtered off, washed with 50% ethanol and concentrated under reduced pressure (40–45° bath) to about 30 cc. The thin sirup was then diluted with ethanol, filtered free from residual strontium salt and re-evaporated. The sirup was diluted to 100 cc. with water and heated for two hours on a boiling water-bath to hydrolyze the acetal group. The hydrolyzate was then added to 500 cc. of distilled water containing 5 cc. of dissolved bromine. After forty-five hours in the dark excess bromine was removed by aeration and silver carbonate added to free the solution from bromine ion. Silver was then removed as sulfide and the clear solution evaporated to a thin sirup under reduced pressure. The sirup was extracted with ethanol, concentrated and re-extracted with ether to separate inorganic material. Excess solvent was then removed and the residue methylated by Purdie's method using methyl iodide and silver oxide. After complete methylation the silver residues were extracted with petroleum ether and upon removal of solvent the sirup was distilled fractionally under reduced pressure.

Fraction I, b. p. 62° (11 mm.), crystallized spontaneously and after recrystallization from light petroleum furnished dimethyl oxalate; m. p. 54°[7]; yield 2.4 g.

*Anal.* Calcd. for $C_4H_6O_4$: $OCH_3$, 52.5. Found: $OCH_3$, 52.1.

Fraction II, b. p. 78° (0.2 mm.), distilled as a colorless optically inactive liquid which crystallized completely upon standing, m. p. 68°[8] from ether; yield 4.6 g.

*Anal.* Calcd. for $C_8H_{14}O_6$: $OCH_3$, 60.2. Found: $OCH_3$, 60.2.

Treatment of a sample, 1.0 g., with methyl alcoholic ammonia in the usual manner furnished a crystalline compound upon removal of solvent. Recrystallization from methyl alcohol gave dimethoxy-*i*-succinic acid diamide; m. p. 256°.[9]

*Anal.* Calcd. for $C_6H_{12}O_4N_2$: $OCH_3$, 35.2. Found: $OCH_3$, 35.2.

Obviously, Fraction II must have been formed from a four-carbon dibasic acid in the above Purdie methylation. Accordingly, in a separate experiment a similar ether extract containing 4.0 g. dissolved material was treated with an excess of diazomethane in order to form the methyl esters of the dissolved organic acids. After removal of excess reactant and solvent the sirup was distilled under high vacuum. An optically active fraction was collected and redistilled, b. p. 87° (0.2 mm.); yield 2.2 g.; specific rotation +49° (25°, *c* 5, methanol).

*Anal.* Calcd. for $C_7H_{12}O_6$: $OCH_3$, 48.4. Found: $OCH_3$, 47.7.

Treatment of a sample, 0.5 g., with methyl alcoholic ammonia in the usual manner furnished the diamide of 3-hydroxy-2-methoxy-D-erythrosuccinic acid, recrystallized from acetone–methyl alcohol, m. p. 156°.

A similiar reaction using methyl alcoholic methylamine furnished 3-hydroxy-2-methoxy-D-erythrosuccinobismethyl amide; recrystallized from ethyl acetate, m. p. 135°[10]; specific rotation −10.5° (25°, *c*, 5, water).

Complete methylation of the ester by the Purdie method gave dimethoxy-*i*-dimethyl succinate which was identified as the above described diamide, m. p. 256°.[6]

## Summary

1. The uronic acid component of mesquite gum has been isolated as the monomethyl-methyl-glucuronoside methyl ester.

2. The structure of this compound is shown to be that derived from 4-methoxy-D-glucuronic acid.

3. The methyl ester grouping in mesquite gum is located at the fourth carbon atom of the glucuronic acid component.

MOSCOW, IDAHO RECEIVED AUGUST 16, 1947

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[7] Dumas and Peligot, *Ann. chim. phys.*, [2] **58**, 44 (1835).

[8] Patterson and Patterson, *J. Chem. Soc.*, **107**, 155 (1915).

[9] Haworth and Hirst, *ibid.*, **128**, 1965 (1926).

[10] Heslop, Salt and Smith, *ibid.*, 225, (1944).