

The α,β -hexenoic acid (m. p. 33–34°) gives with silver chlorate the *dl*-1,2-dihydroxycaproic acid (m. p. 108.5°) with 86% yield and with perbenzoic acid the *dl*-1,2-dihydroxycaproic acid (m. p. 99.5°) with 46% yield.

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STRUCTURE OF THE CHLORALOSSES. BETA-XYLOCHLORALOSE

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In a preceding paper¹ it has been shown that the available evidence indicates an acetal type of linkage for the union of chloral with glucose in β -glucochloralose rather than the carbon-carbon linkage depicted by the older formulas in the literature. The attempt to determine the configuration of the β -glucochloralose by means of methylation failed due to the resistance to hydrolysis of the partially dechlorinated trimethyl- β -glucochloralose.

In the literature² it has been shown that β -xylochloralose (formula III) yields chloralic acid (Formula II), which is identical with the acid obtained by oxidation of β -glucochloralose (Formula I), the formulas being used with the limitations of the preceding report.¹ The β -xylochloralose was accordingly drawn into these investigations in the hope that its greater range of solubility would make it possible completely to remove the chlorine, or on failure of this to hydrolyze the partially dechlorinated compound. Other than the chloralic acid,² the only definite derivative of β -xylochloralose reported in the literature is the dibenzoate.³

The β -xylochloralose was prepared according to the method of Hanriot. By further treatment with chloral hydrate and sulfuric acid, β -xylochloralose was converted to a crystalline dichloralxylose which could not be acetylated. This would indicate the absence of a free hydroxyl group in the dichloralxylose and could only be interpreted in terms of the acetal type of linkage as was the case with the conversion of β -glucochloralose to the dichloralglucoses. The possible structures for the dichloralxylose would accordingly be analogous to the corresponding acetone derivatives reported by Freudenberg and Svanberg.⁴ Experimental evidence indicates the existence of at least two isomeric dichloralxyloses.

Dimethyl β -xylochloralose was obtained by methylation of β -xylochloralose with dimethyl sulfate. Repeated methylations failed to increase the methoxy content above that for the di-derivative. Attempts to

¹ Coles, Goodhue and Hixon, *THIS JOURNAL*, 51, 519 (1929).

² Hanriot, *Compt. rend.*, 120, 153 (1895); 148, 487 (1909); *Bull. soc. chim.*, [4] 5, 819 (1909); *Ann. chim. phys.*, [8] 18, 466 (1909).

³ Hanriot, *ibid.*, [8] 18, 466 (1909).

⁴ Freudenberg and Svanberg, *Ber.*, 55, 3239 (1922).

acetylate the dimethyl- β -xylochloralose yielded a sirup whose chlorine analysis indicated slightly more acetylation than that required for mono-acetyl-dimethyl- β -xylochloralose. Acetylation of trimethyl- β -glucochloralose also gave a sirup whose chlorine analysis was within 1% of that calculated for the introduction of one acetyl group. These two compounds have not been obtained crystalline and are very difficult to distil, rendering further purification difficult.

The chlorines were partially removed from the dimethyl- β -xylochloralose by the use of sodium amalgam. It was not possible to obtain a preparation free from chlorine, and hydrolysis of the partially dechlorinated sirup introduced the same difficulties encountered with the corresponding glucose derivative. No attempt was made to isolate the intermediate dechlorinated compounds.

In working with the partially dechlorinated sirup, it was observed that alcoholic potassium hydroxide removed some of the chlorine. Hanriot and Kling⁵ in working with the chloraloses were able to remove one chlorine atom by alcoholic ammonia but stronger alkalies were discarded because of the decomposition of the sugar molecule. Using β -glucochloralose, it has been found that refluxing with alcoholic potassium hydroxide yields a sirup very easily hydrolyzed by acids. The intermediate compound does not reduce Fehling's solution to any extent. The glucosazone is easily obtained after the acid hydrolysis.

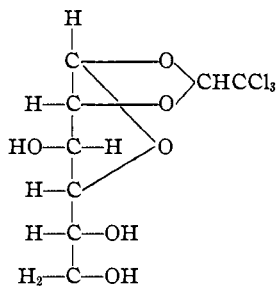
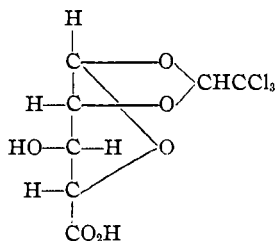
Acetylation of β -xylochloralose by means of pyridine and acetic anhydride yields a beautifully crystalline diacetyl- β -xylochloralose. As Hanriot² reports, acetylation by means of acetyl chloride and zinc chloride yields an indefinite sirup. Distillation of this sirup in a high vacuum is accompanied by some decomposition. Chlorine analyses indicate a degree of acetylation greater than that of the diacetyl derivative.

A similar condition is encountered in acetylating β -glucochloralose. In the absence of zinc chloride, triacetyl- β -glucochloralose only is obtained. Refluxing with acetyl chloride and zinc chloride gives a mixture from which Hanriot² reports a tetra-acetyl- β -glucochloralose. Repeated fractional crystallization of this mixture yields the above triacetyl- β -glucochloralose, with a melting point (108°) which is almost identical with that reported by Hanriot for the tetra-derivative (106°). The analyses of the higher-melting compound (151°) correspond to a penta-acetyl- β -glucochloralose. Determinations of the acetyl groups by saponification are not possible, due to the above reported action of the alkali on the chlorines.

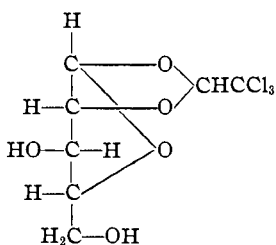
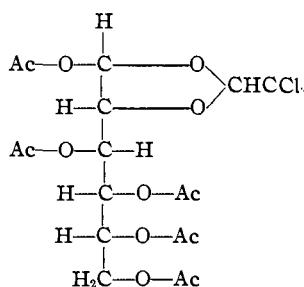
Repeated efforts have failed to give the tetra-acetyl- β -glucochloralose. The keto-enol isomerization postulated in the former paper¹ would not be necessary for the explanation of the tri- and penta-acetyl derivatives.

⁵ Hanriot and Kling, *Bull. soc. chim.*, [4] **11**, 207 (1912); *Compt. rend.*, **152**, 1398 (1911).

The triacetyl- β -glucochloralose would be formed by the acetylation of the free hydroxyl groups in the β -glucochloralose (Formula I). The penta-acetyl- β -glucochloralose could be explained as due to the rupture of the oxide ring, as shown in Formula IV.

I. β -Glucochloralose

II. Chloralic acid

III. β -XylochloraloseIV. Penta-acetyl- β -glucochloralose

Experimental Part

β -Xylochloralose was prepared according to the method of Hanriot. Attempts to isolate an α -xylochloralose in analogy with α -glucochloralose were unsuccessful. It was found that the β -xylochloralose could be crystallized from hot benzene and from hot water. The yield was low, 100 g. of xylose giving only 60 g. of β -xylochloralose. The oxidation of the β -xylochloralose to chloralic acid identical with that from β -glucochloralose was repeated for confirmation. β -Xylochloralose is optically inactive in chloroform.

Preparation of Dichloralxylose.—The method is essentially the same as that used by Ross and Payne for the preparation of dichloralglucose. Fifty grams of xylose was stirred into a mixture of 200 cc. of sulfuric acid and 100 g. of chloral hydrate which was cooled to 12–15° under the tap. The mixture is allowed to come to room temperature and is stirred with a mechanical stirrer for six hours. The compound forms a rubber-like layer at the surface of the solution; transferred to cold water it was broken up to give a granular solid of lavender color. More compound is precipitated when the sulfuric acid mixture is poured into one liter of cold water. Heating the sulfuric acid solution to boiling precipitates about 10 g. of β -xylochloralose, which was crystallized in the usual manner from benzene. The combined portions of dichloralxylose were warmed with dilute sodium hydroxide solution until the excess of chloral was decomposed; yield, 90 g. of crude product. After repeated recrystallization from acetic acid and alcohol the melting point remained constant at 202°. By treating β -xylochloralose as described above, the same crystalline dichloralxylose was obtained.

Anal. (Carius). Calcd. for $C_9H_9O_5Cl_6$: Cl, 52.08. Found: Cl, 52.15, 52.32.

The rotation in acetone (6.7 g. per 100 cc.) was $[\alpha]_D^{25} +25.2^\circ$.

Attempts to acetylate the compound with acetyl chloride and zinc chloride were without results. It is unchanged by dissolving in fuming nitric acid and allowing to stand for twenty-four hours. The compound is soluble in all common organic solvents.

Evaporation of the mother liquors used to recrystallize the above compound gave an oily sirup that will distil at 200° in a high vacuum to give a solid resin-like substance which softens at 100° . Analysis for chlorine is within 1% of that calculated for dichloralxylose. This is presumably an isomeric dichloralxylose.

Dimethyl- β -xylochloralose.—The method of preparation is essentially the same as that previously reported for the methylation of β -glucochloralose.¹ β -Xylochloralose is more soluble in dimethyl sulfate and is therefore more easily methylated. The product is sirupy, but is easily distilled at 135° under 2 mm. pressure. On long standing crystals form. They are oily and melt at about 53° . Attempts to introduce another methyl group by repeated treatment with dimethyl sulfate and by the silver oxide method of Purdie and Irvine⁶ were unsuccessful.

Anal. (Carius). Calcd. for $C_9H_{13}O_5Cl_3$: Cl, 34.60; MeO, 20.15. Found: Cl, 34.68, 34.70; MeO, 19.70, 19.65.

The rotation in chloroform (8.7 g. per 100 cc.) was $[\alpha]_D^{25} -41.08^\circ$.

Reduction of Dimethyl- β -xylochloralose was carried out in a dilute alcoholic solution at 60° with sodium amalgam; 17 g. was treated in this manner for six days with 600 g. of 3% amalgam. The amalgam was added in small portions and the precipitate of sodium bicarbonate formed by passing in carbon dioxide was filtered off from time to time. At times the carbon dioxide was shut off and the mixture became strongly alkaline. Evaporation and extraction with ether gave 6–7 g. of a sirup boiling from 90 to 135° at 2 mm. pressure. The first fraction up to 115° gave an analysis for 5.5% chlorine. That calculated for one chlorine left in the molecule is 14.90. It reduced Fehling's solution on boiling.

The first fraction was hydrolyzed with 2 *N* hydrochloric acid and the aldehyde distilled out. Its water solution reduced Fehling's solution but the amount was too small to identify. An unsuccessful attempt was made to prepare a phenylhydrazine derivative of the sugar part of the molecule, the product forming a resin as does the methylglucose obtained from β -glucochloralose.

Action of Alkalies on Chloralose.—Seven grams of β -glucochloralose was refluxed for one-half hour with 50 cc. of alcoholic potassium hydroxide consisting of 25 cc. of a saturated solution of potassium hydroxide in 95% alcohol diluted with 25 cc. of alcohol. The alkali was partially neutralized and most of the alcohol evaporated under reduced pressure. Extraction with ether gave a compound that did not reduce Fehling's solution to any extent but which reduced very strongly after hydrolysis with dilute acid. An abundance of glucosazone separated after treatment with phenylhydrazine. The intermediate compound has not been obtained in a form suitable for analysis as yet.

Diacetyl- β -xylochloralose was prepared by dissolving 8 g. of β -xylochloralose in 50 cc. of pyridine and adding 20 cc. of acetic anhydride. The mixture was stoppered and kept at 60° for three hours. About an equal volume of water is added, which causes the acetylated product to crystallize. It is filtered, washed with warm water and decolorized in alcohol with charcoal. The compound crystallizes as beautiful leaflets and after three recrystallizations melts sharply at 142° ; yield, about 8 g.

Anal. (Carius). Calcd. for $C_{11}H_{13}O_7Cl_3$: Cl, 29.26. Found: Cl, 29.32, 29.43.

The rotation in chloroform (3.3 g. per 100 cc.) was $[\alpha]_D^{27} -7.61^\circ$.

⁶ Purdie and Irvine, *J. Chem. Soc.*, **83**, 1021 (1903); **85**, 1049 (1904).

Triacetyl- β -glucochloralose was prepared from β -glucochloralose by the method given in the preceding paragraph for diacetyl- β -xylochloralose. It can also be prepared by treating β -glucochloralose with acetyl chloride without the addition of zinc chloride. It crystallizes well from dilute alcohol and melts at 108°.

Anal. (Carius). Calcd. for $C_{14}H_{17}O_8Cl_3$: Cl, 24.42. Found: Cl, 24.52, 24.64.

The rotation in chloroform (5.47 g. per 100 cc.) was $[\alpha]_D^{27} +22.72^\circ$.

Penta-acetyl- β -glucochloralose.—Fifteen grams of β -glucochloralose was refluxed for two hours with 100 cc. of acetyl chloride and 1 g. of zinc chloride. After evaporation of the acetyl chloride the sirup was dissolved in chloroform and extracted repeatedly with water. The chloroform was evaporated under reduced pressure and one volume of absolute alcohol added to the sirup. After long standing crystals form. The time required to crystallize the compound is much shortened if the solution is seeded.

Anal. (Carius). Calcd. for $C_{18}H_{20}O_{12}Cl_5$: C, 40.25; H, 4.13; Cl, 19.82. Found: C, 40.14, 40.05; H, 4.02, 4.12; Cl, 19.89, 19.90.

The rotation in chloroform (12 g. per 100 cc.) was $[\alpha]_D^{27} +46.12^\circ$.

If more than three acetyl groups can be introduced into the β -glucochloralose molecule, it would seem probable that trimethyl- β -glucochloralose could be acetylated. Trimethyl- β -glucochloralose is very markedly changed by treatment with acetyl chloride and zinc chloride but the resulting compound is a sirup that is very difficult to distil and so far has not been obtained sufficiently pure to warrant analysis.

Summary

1. Dichloralxylose was prepared from xylose and from β -xylochloralose.
2. Dimethyl and diacetyl derivatives of β -xylochloralose are reported.
3. Triacetyl and penta-acetyl- β -glucochloralose are described. The tetra-acetyl- β -glucochloralose reported by Hanriot could not be obtained.
4. The reactions of β -xylochloralose, like those of β -glucochloralose, indicate an acetal linkage between the sugar and chloral molecules.
5. Chlorine may be removed from β -glucochloralose by the action of alcoholic potassium hydroxide without decomposition of the molecule. The glucose can then be regenerated by dilute acids and identified as the osazone. The intermediate compound has not been isolated sufficiently pure for analysis.

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