Cr^{+++} in chrome alum solution was found to react slowly with the dye. The green Cr^{+++} reacts more rapidly than the blue; increase of temperature hastens the reaction. At room temperature, 0.10 mg. of green Cr^{+++} gave after fifteen minutes a color equivalent to 0.0005 mg. of aluminum, after thirty minutes 0.001 mg. of aluminum, and after eighteen hours 0.008 mg. of aluminum. It is seen that Cr^{+++} is but a slight source of interference under the conditions. Complete elimination of this interference is indicated by an increase in *P*H dependent on the quantity of Cr^{+++} with, of course, a resultant decrease in over-all sensitivity of the test.

Under the present conditions, the aurin reaction with aluminum is extremely delicate. A faint pink is obtained with 0.0001 mg. of aluminum, so that the sensitivity is about twenty times that reported by Yoe and Hill under alkaline conditions. Besides the elimination of fading and of carbon dioxide evolution, turbidity in the presence of foreign ions such as that observed by Yoe and Hill is also obviated.

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Structure of the Chloraloses, Alpha and Beta-Glucochloraloses

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The literature regarding the structure of the chloral derivatives of glucose and of xylose was reviewed in the previous publications[1] of this series. The experimental data of these previous publications as well as the data presented below are summarized for glucose in Table I and for xylose in Table II.

Referring to Table I, the condensation of glucose with chloral under the specified conditions yields a crystalline mixture from which can be isolated dichloralglucose (A), dichloralglucose (C), and dichloralglucose (D). Boiling the mother liquor from this separation causes β-glucochloralose to separate. Neutralization or ether extraction of the mother liquor remaining after the separation of the β-glucochloralose yields α-glucochloralose. The condensation of β-glucochloralose with chloral yields dichloralglucose (A) and dichloralglucose (C). The condensation of α-glucochloralose with chloral yields dichloralglucose (E). A fifth dichloralglucose (B) is reported by Pictet and Reichel.[2]

Repeated methylations[1a] of β-glucochloralose introduced only three methyl groups to give trimethyl-β-glucochloralose. This indicated that

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[1] (a) Coles, Goodhue and Hixon, THIS JOURNAL, **51**, 519 (1929); (b) Goodhue, White and Hixon, *ibid.*, **52**, 3191 (1930).

[2] Pictet and Reichel, *Helv. Chim. Acta*, **6**, 621 (1923). The dichloralglucoses A and B were so designated by Pictet and Reichel. Further descriptions of dichloralglucoses A, C and D are given by Ross and Payne, THIS JOURNAL, **45**, 2363 (1923).

β-glucochloralose had only three free hydroxyl groups and since condensation with a molecule of chloral yielded dichloralglucoses with only one free hydroxyl group, it was concluded that the chloral group in β-glucochloralose was linked with the glucose molecule in a typical acetal linkage.

An attempt was made to determine the configuration of β-glucochloralose by removing the chlorines from the chloral group in trimethyl-β-glucochloralose, hydrolyzing the resulting acetaldehyde glucose derivatives, and characterizing the resulting trimethylglucose. In this investigation both trimethylglucose-dichloroacetaldehyde and trimethylglucose-monochloroacetaldehyde were prepared and hydrolyzed but it was not possible to characterize the resulting trimethylglucose. The 3,5,6-trimethylglucose was prepared and condensed with chloral but the resulting 3,5,6-trimethylglucochloralose was not identical with the trimethyl-β-glucochloralose. Difficulties in purification of both the trimethyl derivatives may indicate that isomers were present in each case which were lost in the repeated fractional crystallizations.

Condensation of 3-monomethylglucose with chloral yielded two 3-monomethyldichloralglucoses, one of which proved to be identical with the methyl derivative of dichloralglucose (A). The other 3-monomethyldichloralglucose is not identical with the methyl derivative of either dichloralglucose (C) or (D).

The older formulas for β-glucochloralose indicated four free hydroxyl groups on the evidence of a tetraacetyl-β-glucochloralose reported by Hanriot.[3] Repeated efforts to duplicate Hanriot's result have yielded a mixture which could be separated into pentaacetyl-β-glucochloralose and triacetyl-β-glucochloralose. If pyridine and acetic anhydride are used as an acetylating agent only the triacetyl derivative is formed. Saponification of the pentaacetyl-β-glucochloralose with alkali yields the original β-glucochloralose. Although repeated methylation of β-glucochloralose has failed to introduce more than three methyl groups, the resulting trimethyl-β-glucochloralose will react to some extent with acetyl chloride in the presence of zinc chloride to give a sirup which has as yet resisted efforts at purification.

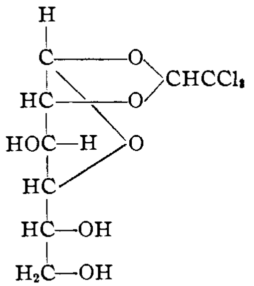
Acetylation of α-gluocchloralose yields two pentaacetyl derivatives. It was impossible to isolate a triacetyl derivative of the α-glucochloralose. The two pentaacetyl-α-glucochloraloses differ from the pentaacetyl-β-glucochloralose in their reaction with alkali, the former being completely decomposed under conditions which yield β-glucochloralose in the latter case.

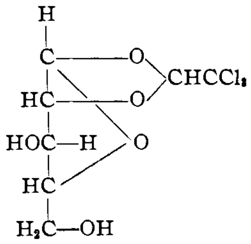
The structures of the chloral derivatives of xylose are related to the structure of the β-glucochloralose as indicated by the formation of chlo-

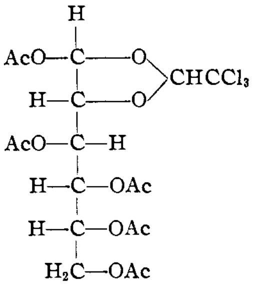
(3) Hanriot. *Ann. chim. phys.*, [8] **18**, 466 (1909); *Bull. soc. chim.*, [4] **5**, 819 (1909).

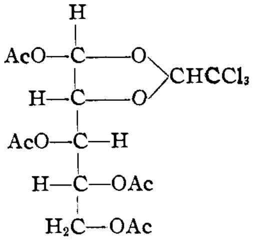
ralic acid by the oxidation of both β-xylochloralose and β-glucochloralose. Referring to Table II, β-xylochloralose is the only monochloral derivative of xylose so far reported. The β-xylochloralose can be condensed with another mole of chloral to yield dichloralxylose which can be neither acetylated nor methylated. Methylation converts β-xylochloralose to dimethyl-β-xylochloralose. Acetylation by means of acetic anhydride and pyridine yields only the diacetyl-β-xylochloralose, but the use of acetyl chloride in the presence of zinc chloride yields a tetraacetyl-β-xylochloralose.

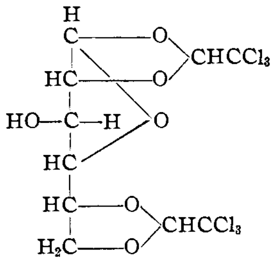
With the exception of the formation of the tetraacetyl-β-xylochloralose and the pentaacetyl derivatives of the glucochloraloses, the typical acetal linkage best explains the existence of the various chloral derivatives of these sugars. The best explanation for the formation of these acetylated derivatives seems to be by rupture of the oxide ring of the sugar molecule


I. β-Glucochloralose


II. β-Xylochloralose


III. Pentaacetyl-β-glucochloralose


IV. Tetraacetyl-β-xylochloralose


V. Dichloralglucose (A)

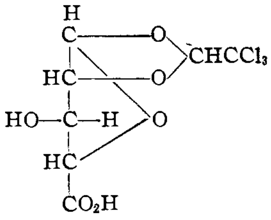
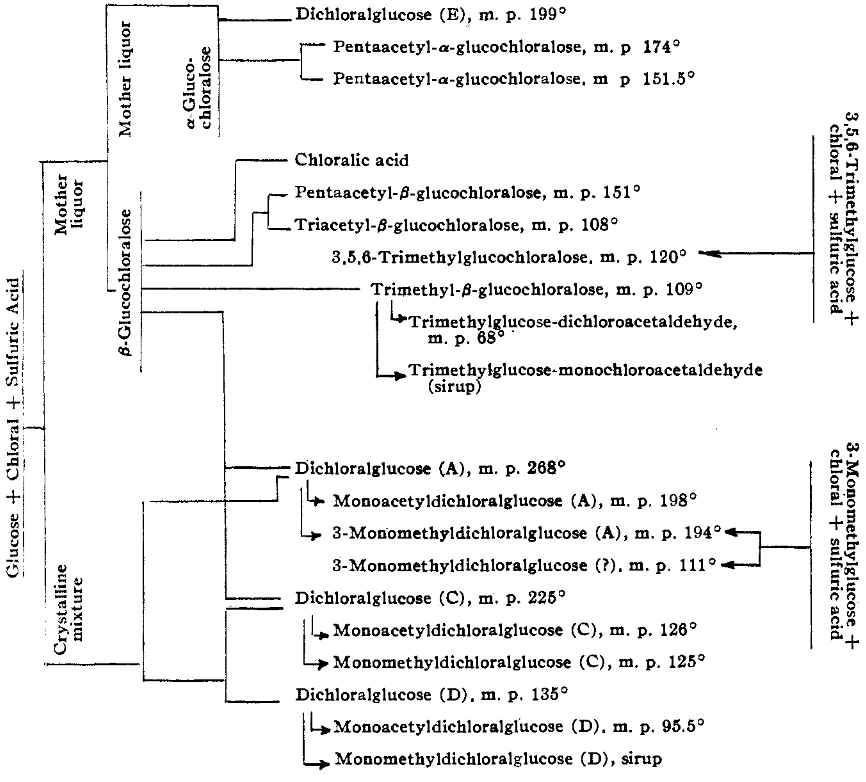

VI. Chloralic acid

TABLE I

DIAGRAM SHOWING THE INTERRELATION OF THE CHLORAL DERIVATIVES OF GLUCOSE



Dichloralglucose (B), m. p. 85°. Reported by Pictet and Reichel

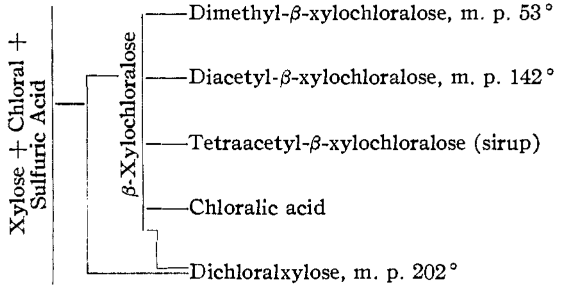
as indicated in Formulas III and IV. This explanation is supported by the following facts. (a) Mild acetylation yields the expected diacetyl-β-xylochloralose and the triacetyl-β-glucochloralose. The tetraacetyl and pentaacetyl derivatives appear to be formed only under the catalytic action of zinc chloride in the presence of acetyl chloride. (b) Repeated methylation gives only a dimethyl-β-xylochloralose and a trimethyl-β-glucochloralose. Although additional methyl groups cannot be introduced, acetyl chloride in the presence of zinc chloride causes some acetylation. (c) The three dichloralglucoses so far investigated give only a monomethyl and a monoacetyl derivative. The dichloralxylose cannot be methylated or acetylated.

The absence of reducing properties in β-xylochloralose and β-glucochloralose would indicate that the chloral group binds the first carbon of the sugars. The other chloral linkage is probably to the second carbon of the sugars since only five and six membered rings are known for this type of structure and the six membered ring is excluded by the fact that position three is free (synthesis of 3-monomethyldichloralglucose). If this conclusion is correct, then the lack of identity between 3,5,6-trimethylchloralglucose and trimethyl-β-glucochloralose must be explained as due to possible change in the position of the oxide ring of the glucose according to the method of synthesis. The lability of this ring has been indicated by the acetylation products.

With the above reservations as to the position of the oxide ring of the sugar, Formulas I and II are presented as the best working hypothesis at present for the configurations of β-glucochloralose and β-xylochloralose. Formulas III and IV would represent the corresponding pentaacetyl-β-glucochloralose and tetraacetyl-β-xylochloralose. Formula V would represent the configuration of dichloralglucose (A), the correctness of which is rendered fairly definite by the synthesis of the methyl derivative from 3-monomethylglucose. The configuration of chloralic acid, which if formed by the oxidation of both β-glucochloralose and β-xylochloralose, would be represented by Formula VI. The stereoisomerism of the chloral grouping would make possible a number of isomers of these structures.

TABLE II

DIAGRAM SHOWING INTERRELATION OF THE CHLORAL DERIVATIVES OF XYLOSE



Experimental Part

Separation and Purification of α-Glucochloralose.—This compound has been prepared in the past by evaporating the mother liquors from the β-glucochloralose procedure and then extracting the α-glucochloralose from these concentrated acid solutions with ether. This procedure is tedious and gives low yields since the α-glucochloralose is partially decomposed by acids.[2]

Observations of different preparations of β-glucochloralose indicate that a low temperature, particularly during the first ten hours, favors the production of α-glucochloralose. Neutralization of the mother liquors, after separation of β-glucochloralose, causes about 50 g. of α-glucochloralose to separate in an impure condition. The solution should not be made alkaline.

To purify the α-glucochloralose, the aqueous solution containing the impure precipitate was brought to boiling and filtered hot (some β-glucochloralose may precipitate here). The solution was allowed to stand overnight and the crystalline precipitate separated. Evaporation of the mother liquor to one-fourth its volume at 40° yields a little more precipitate. The combined precipitates were air dried, taken up in alcohol and filtered from any undissolved sodium sulfate. The clear alcohol solution was diluted with an equal volume of water, warmed on the hot plate until turbid, and cooled to 15° or lower. A product separated out in needle crystals and was recrystallized from 38% alcohol. It can be recrystallized from water and also from chloroform containing some alcohol. Alternate use of the solvents proved most successful, m. p. 187°; specific rotation (0.9 g. per 100 cc.) $[\alpha]^{28}_{D}$ −15.96°.

Condensation of α-Glucochloralose with Chloral.—By treating 25 g. of α-glucochloralose with concentrated sulfuric acid and chloral as described in the previous papers, then diluting with water, an insoluble mass of material was obtained. Repeated attempts were made to isolate the known dichlorals but were without success. Crystals were obtained from a carbon tetrachloride solution which were recrystallized from 57% alcohol. The constant melting point was 199°. The small amount available was analyzed for chlorine and considering the very small samples the results were reasonably accurate.

Anal. Calcd. for $C_{10}H_{10}O_6Cl_4$: Cl, 48.48. Found: Cl, 49.08, 48.07.

Condensation of 3-Methylglucose with Chloral.—About 30 g. of 3-methyldiacetoneglucose was treated with chloral according to the previously reported method for condensation. The reaction product was washed free from acid, filtered and air dried. It was then dissolved in alcohol and allowed to crystallize. All the crystals that could be obtained from this solution were combined and recrystallized several times from alcohol. They reached a constant melting point of 194°; specific rotation in chloroform (1.5 g. per 100 cc.) $[\alpha]^{30}_{D}$ −19.73°. This compound was identified as the methyl derivative of dichloralglucose (A). When no further precipitate of these crystals could be obtained from the alcoholic solution, the alcohol was diluted with water, the oily residue dissolved in carbon tetrachloride and precipitated by cautious addition of petroleum ether. After separation it was recrystallized from 76% alcohol. It formed very small needles which melted at 111°. These were very soluble in alcohol and chloroform, slightly soluble in petroleum ether. The yield of crystalline product was 16 to 20%; specific rotation in chloroform (1.26 g. per 100 cc.) $[\alpha]^{30}_{D}$ −10.8°.

Anal. Calcd. for $C_{11}H_{12}O_6Cl_6$: Cl, 47.27. Found: Cl, 47.29; 47.07.

The analysis indicates that this is also a methyldichloralglucose which may at present be designated as "3-monomethyldichloralglucose, m. p. 111°."

Methylation of Dichloralglucose (C), m. p. 225°.—The methylation was carried out according to the method previously reported for the methylation of β-glucochloralose.[1a] The chloroform was evaporated after extraction and the residue digested with several portions of petroleum ether. Long monoclinic crystals formed and were filtered from the solution. Three more crystallizations gave a constant melting product, m. p. 125°; specific rotation in chloroform (3.9 g. per 100 cc.) $[\alpha]^{27}_{D}$ −26.97°. This compound may be designated as monomethyldichloralglucose (C).

Anal. Calcd. for $C_{11}H_{12}O_6Cl_6$: Cl, 47.2. Found: Cl, 47.08, 47.47.

Acetylation of α-Glucochloralose.—After refluxing 5 g. of α-glucochloralose with 35 cc. of acetyl chloride and a small amount of freshly fused zinc chloride for an hour, the excess acetyl chloride was distilled off. The residue was poured into water, the insoluble portion was washed until free from acid, filtered and recrystallized from alcohol. A mixture, 2 g., resulted which was separated as follows. The solid was dissolved in slightly more than the least amount of boiling alcohol necessary for solution and cooled to 30° without disturbing the container. Long needles crystallized out; the liquid was carefully poured off and irregular four-sided platelets appeared as from a supersaturated solution. A certain degree of separation was achieved by washing the mixture with ether at room temperature, but this was not as sharp as the separation from the alcohol solution noted above. The needles recrystallized well from alcohol. They were more soluble in ether than the platelets; they were also soluble in petroleum ether, m. p. 174°; specific rotation in chloroform (1.4 g. per 100 cc.) $[\alpha]_D^{30}$ −11.5°.

Anal. Calcd. for $C_{18}H_{23}O_{12}Cl_3$: Cl, 19.80. Found: Cl, 19.83.

The platelets crystallized from alcohol and came out most readily when the solution was seeded. Large crystals were obtained if the crystallization was slow. They melted at 151.5°; soluble in chloroform, slightly soluble in ether, and in petroleum ether, insoluble in water; specific rotation in chloroform (1.6 g. per 100 cc.) $[\alpha]_D^{30}$ +66.2°.

Anal. Calcd. for $C_{18}H_{23}O_{12}Cl_3$: Cl, 19.80. Found: Cl, 19.91, 19.94.

Saponification of the Pentaacetyl Derivatives.—Pentaacetyl-β-glucochloralose was saponified with 15% potassium hydroxide in methyl alcohol at room temperature for twenty minutes. The mixture was poured into water and neutralized with sulfuric acid. β-Glucochloralose separated out at once; it was recrystallized and identified by melting point. Pentaacetyl-α-glucochloralose was saponified under the same conditions but it was not possible to isolate any definite organic product.

Acetylation of β-Xylochloralose.—β-Xylochloralose was acetylated by essentially the same method as that described above for β-glucochloralose. A sirup was obtained which analyzed for tetraacetylxylochloralose.

Anal. Calcd. for $C_{15}H_{19}O_{10}Cl_3$: Cl, 23.5. Found: Cl, 23.1, 23.3.

Acetylation of Dichloralglucose (D), m. p. 135°.—A mixture of 15 g. of dichloralglucose (D), m. p. 135°, with 25 cc. of pyridine and 40 cc. of acetic anhydride was left for forty-eight hours on a sand-bath (about 70°). The mixture was then poured into water and the insoluble oil washed free of acid. The oil was taken up in alcohol, decolorized with charcoal. Needles slowly crystallized upon concentration of the alcohol. Crystallization from petroleum ether was also possible, m. p. 95.5°; optically inactive in chloroform.

Anal. Calcd. for $C_{12}H_{12}O_7Cl_3$: Cl, 44.24. Found: Cl, 43.92, 44.06.

Summary

The synthesis of 3-monomethyldichloralglucose (A), m. p. 194°, is reported from dichloralglucose (A) and from 3-monomethylglucose.

Condensation of α-glucochloralose with chloral yielded dichloralglucose (E). This is the fifth dichloral glucose derivative to be reported.

Two pentaacetyl-α-glucochloraloses are reported.

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