

reported that by spraying sulfur dichloride into an atmosphere of ethylene he was able to obtain mustard gas of 93% purity after one distillation.

Summary.

1. The reaction between selenium monochloride and olefins is shown to take place in two stages.

2. By spraying the monochloride or its solution into an atmosphere of olefin the reaction may be stopped at the first stage. In this manner *bis*-(β -chloropropyl) selenide, *bis*-(β -chlorobutyl) selenide, and *bis*-(β -chloro-amy) selenide have been prepared, and their properties described.

3. By leading the olefin into selenium monochloride or its solution the above products are acted upon by the excess of the monochloride, being converted into *bis*-(β -chloropropyl) selenide dichloride, *bis*-(β -chlorobutyl) selenide and *bis*-(β -chloro-amy) selenide dichloride, respectively. This constitutes the second stage of the reaction.

4. The mechanism of the reaction between selenium monochloride and olefins is formulated, using the unsymmetrical structure for selenium monochloride. The quantitative results obtained in these syntheses is offered as evidence in favor of the unsymmetrical structure for selenium monochloride.

5. The same mechanism has been applied to explain the formation of mustard gas from ethylene and sulfur monochloride. The possibility of preparing mustard gas by spraying sulfur monochloride is again pointed out.

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CRYSTALLINE CHLORO-TETRA-ACETYL MANNOSE.

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A halogenated derivative of an acetylated sugar was first obtained by Colley¹ by the action of acetyl chloride on glucose in a sealed tube at room temperature. The author, however, succeeded only twice in crystallizing the syrupy chloro-tetra-acetyl glucose. As this derivative was found to be a valuable intermediate for preparing synthetic glucosides,² many chemists have studied different methods for preparing crystalline halogenated acetyl derivatives of sugars. Koenigs and Knorr³ prepared bromo-acetyl glucose in a crystalline condition by shaking glucose with acetyl bromide at ordinary temperature, the derivative separating from the

¹ Colley, *Ann. chim. phys.*, [4] 21, 367 (1870).

² Michael, *Am. Chem. J.*, 1, 305 (1879).

³ Koenigs and Knorr, *Ber.*, 34, 957 (1901).

concentrated, washed and dried ether solution. This method was successfully simplified by Moll van Charante,⁴ who found that shaking was not necessary.

More recent investigators successfully used the fully acetylated sugar as an intermediate. Von Arlt⁵ obtained crystalline chloro-acetyl glucose by the action of phosphorus pentachloride and aluminum chloride on a solution of penta-acetyl glucose in chloroform. Bodart⁶ prepared crystalline chloro-acetyl lactose by suspending lactose in acetic anhydride and passing hydrogen chloride into the mixture. Skraup and Koenig⁷ used Bodart's method on cellose, obtaining crystalline chloro-acetyl cellose. Fischer and Armstrong⁸ used dry hydrogen chloride, acetyl chloride and hydrobromic acid on the fully acetylated sugar under high pressure at room temperature, and obtained in this way crystalline chloro- and bromo-acetyl glucose, as well as crystalline chloro-acetyl galactose and chloro-acetyl maltose. Ryan and Mills⁹ prepared crystalline chloro-acetyl arabinose by the action of acetyl chloride on arabinose in an open vessel. Crystalline chloro-acetyl xylose was obtained by Ryan and Ebrill¹⁰ by treating xylose with acetyl chloride at 0°. The corresponding crystalline bromo-acetyl xylose has also been prepared¹¹ by the action of a concentrated solution of hydrobromic acid in acetic anhydride on xylose. E. Fischer and H. Fischer¹² have devised a method for preparing bromo-acetyl lactose by the action of a saturated solution of hydrobromic acid in glacial acetic acid on octa-acetyl lactose at room temperature, no sealing of the vessel being necessary. This method was recognized as one of the simplest ways to obtain the reactive bromo-acetyl derivatives of many sugars, and crystalline bromo-acetyl rhamnose was prepared.¹³ The procedure for the preparation of bromo-acetyl glucose¹⁴ was described in detail and the possibility of preparing the earlier reported α halogenated derivatives of the sugars according to any description of their preparation was denied, as all the described methods yielded the β halogenated derivatives of the sugars. These earlier reported α derivatives are also

⁴ Moll van Charante, *Rec. trav. chim.*, **21**, 42 (1902).

⁵ Von Arlt, *Monatsh.*, **22**, 144 (1901). See also Skraup and Kremann, *ibid.*, **22**, 373 (1901).

⁶ Bodart, *ibid.*, **22**, 1033 (1901); **23**, 1 (1902).

⁷ Skraup and Koenig, *ibid.*, **22**, 1033 (1901).

⁸ Fischer and Armstrong, *Ber.*, **34**, 2885 (1901).

⁹ Ryan and Mills, *J. Chem. Soc.*, **79**, 704 (1901).

¹⁰ Ryan and Ebrill, *Proc. Roy. Dublin Soc.*, **11**, 249 (1903-8). See also Hudson and Johnson, *THIS JOURNAL*, **37**, 2751 (1915).

¹¹ Dale, *THIS ibid.*, **37**, 2745 (1915). See also Hudson and Johnson, Ref. 10.

¹² E. Fischer and H. Fischer, *Ber.*, **43**, 2530 (1910).

¹³ Fischer and Oetker, *ibid.*, **46**, 4035 (1913). See also Fischer, Bergmann and Rabe, *ibid.*, **53**, 2370 (1920).

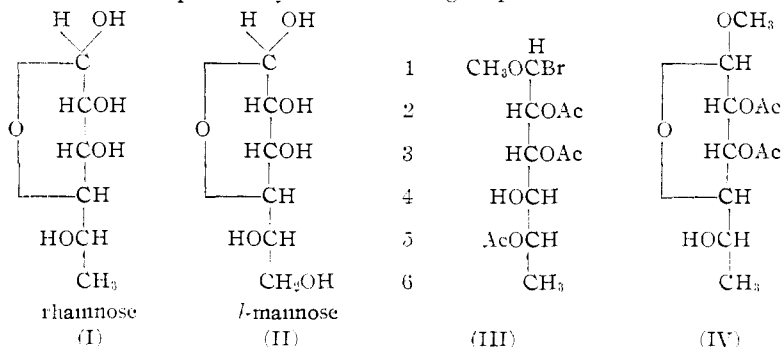
¹⁴ Fischer, *ibid.*, **44**, 1903 (1911).

given in several handbooks. Crystalline α - and β -chloro-tetra-acetyl fructose have, however, been prepared.¹⁵

This introductory study of the literature discloses that *mannose* is the only readily available sugar from which a crystalline halogenated acetyl derivative has not yet been prepared. Non-reducing sugars, as sucrose, need not be considered, as they do not contain a labile hydroxyl group easily replaceable by halogen. Fischer and Hirschberger¹⁶ in 1889 applied Colley's method to mannose by shaking this sugar with 5 parts of acetyl chloride, and obtained a syrupy chloro-tetra-acetyl mannose with properties analogous to those of the syrupy chloro-tetra-acetyl glucose of Colley. Later Fischer and Oetker¹⁷ succeeded in obtaining β -penta-acetyl mannose in a crystalline state by acetylating with certain precautions. They tried Fischer's bromination method on this crystalline compound, using a saturated solution of hydrobromic acid in glacial acetic acid but were not successful in crystallizing the syrupy bromo-acetyl mannose.

Theoretical Considerations.

By applying the method of von Arlt⁵ with some important modifications, fully described in the following pages, it has been possible to prepare crystalline chloro-tetra-acetyl mannose, and to open the way for the preparation of several derivatives of this sugar. The behavior of the halogenated tetra-acetyl derivative of mannose toward methyl alcohol and silver carbonate (reaction of Koenigs and Knorr) promises to be of special interest on account of the analogy in the structures of mannose and rhamnose. These two sugars differ only in that the methyl group in rhamnose is replaced by the CH_2OH group in mannose.



The interesting results obtained by Fischer, Bergmann and Rabe¹⁸ have

¹⁵ Brauns, *THIS JOURNAL*, **42**, 1846 (1920). See also Jaeger, *Verslag. Akad. Wetenschappen Amsterdam*, **29**, 150 (1920).

¹⁶ Fischer and Hirschberger, *Ber.*, **22**, 3224 (1889).

¹⁷ Fischer and Oetker, *Ref. 13*. See also Hudson and Dale, *THIS JOURNAL*, **37**, 1280 (1915).

¹⁸ *Ref. 13*.

established the fact that the reaction of Koenigs and Knorr applied to crystalline bromo-tetra-acetyl rhamnose yields a mixture of 3 *different methyl tri-acetyl rhamnoses*, notwithstanding the results of several experiments which showed that crystalline bromo-tri-acetyl rhamnose is not a mixture but one chemical individual. This peculiar behavior can be explained only in the following way. First, addition of methyl alcohol takes place by breaking the oxygen ring, the available new valences being saturated by CH_3O and $(\text{O})\text{H}$ groups (III). This substance splits off hydrogen bromide in the 4-1 position, by which ordinary β methyl tri-acetyl rhamnose is formed (IV). At the same time the addition product undergoes intermolecular rearrangement by which the hydrogen of the hydroxyl group in the position changes place with the acetyl group in the third *or* the fifth position, which ultimately leads to the formation of two other methyl tri-acetyl rhamnoses, having their oxygen ring formation in the 1-3 *or* the 1-5 position. This explains the formation of the 3 methyl tri-acetyl rhamnoses. One of these three compounds loses only 2 acetyl groups on alkaline hydrolysis. The third acetyl group is removed only on acid hydrolysis, a peculiarity which is well explained by its formula, as the 1-3 position of the oxygen ring protects one acetyl group. This behavior of bromo-acetyl rhamnose differs from that of chloro- or bromo-tetra-acetyl *glucose* and *galactose* which yield only one derivative each, the β -methyl tetra-acetyl derivative, having the oxygen ring formation in the 1-4 position. This behavior, however, as will be reported in detail later, resembles that of the crystalline chloro-tetra-acetyl mannose, which also gives a mixture of various methyl tetra-acetyl mannoses, in spite of the fact that crystalline chloro-tetra-acetyl mannose is a pure substance, not a mixture.

Experimental Work.

Crystalline β -penta-acetyl mannose was obtained by acetylating β -mannose at 0° with acetic anhydride and zinc chloride.¹⁹ This penta-acetyl mannose was converted into chloro-tetra-acetyl mannose by applying, with certain modifications, the method which von Arlt⁵ used for preparing chloro-acetyl glucose. It is especially important that ether must not be used, and that the reaction product be freed as completely as possible from chloroform before petroleum ether is added.

Method of Preparation.—Fifteen g. of crystalline β -penta-acetyl mannose was dissolved in 30 cc. of dry chloroform in an Erlenmeyer flask with glass stopper, and 4 g. of dry (sublimed) aluminum chloride and 9 g. phosphorus pentachloride added. The mixture was slightly warmed on the steam-bath in order to keep the reaction going slowly, shaking not being necessary. After $\frac{1}{2}$ to 1 hour, in which nearly all of the aluminum chloride and phosphorus pentachloride had disappeared forming a greenish solution, the reaction product was cooled and thoroughly shaken in a separatory funnel with ice-

¹⁹ Hudson and Dale, Ref. 17.

water and pieces of ice. The watery solution was drawn off and the shaking with ice-water repeated thrice. The watery solution may be shaken again with chloroform, and the chloroform extract added to the main part before a new portion of ice-water is added. The chloroform solution was dried with anhydrous sodium sulfate, evaporated *in vacuo*, and the resulting solution heated on the steam-bath at moderate temperature with constant stirring until the chloroform was evaporated as completely as possible. The syrupy residue may be dried in a vacuum desiccator in order to remove traces of chloroform. The dry, colorless residue was stirred with a small amount of petroleum ether, and the sides and bottom of the crystallizing dish scratched. If crystallization does not occur, the petroleum ether may be poured off and replaced by a little fresh petroleum ether and the mixture cooled and stirred. After crystallization had started, the whole mass solidified and no difficulty was encountered in crystallizing subsequent preparations. For recrystallizing, the nearly pure product was reduced to a fine powder, boiled with 100 cc. of petroleum ether (b. p. 30–35°), and the boiling solution rapidly filtered through a folded filter into a beaker. This solution was kept separate, as it contained most of the impurities. The extraction was repeated 4 times with 200 cc. of petroleum ether. By evaporating the petroleum ether in the air (in the hood) beautiful, brilliant crystals were deposited. These were found to be pure chloro-tetra-acetyl mannose, as repeated fractional crystallization did not change the melting point or specific rotation. The yield was about 9 g., or 64% of the calculated amount.

Identification and Properties.—Combustion with lead chromate gave the following results.

Subs., 0.2412, 0.2427: CO₂, 0.4033, 0.4065; H₂O, 0.1136, 0.1167. Calc. for C₆H₇O-(C₂H₃O₂)₄Cl: C, 45.83; H, 5.22. Found: C, 45.61, 45.68; H, 5.27, 5.38.

A chlorine determination on the original substance gave the following data. Subs. 0.2196: AgCl (Carius), 0.0847. Calc. for C₆H₇O-(C₂H₃O₂)₄Cl: Cl, 9.67. Found: 9.54.

The quantitative estimation of acetyl was combined with the quantitative estimation of chlorine by the following method. 0.6000 g. of finely powdered substance was saponified by shaking with 181.3 cc. of 0.1 *N* sodium hydroxide solution for 7 hours at 0° and titrating with 0.1 *N* sulfuric acid and phenolphthalein. For neutralization 99.1 cc. of 0.1 *N* sulfuric acid was required; hence 82.2 cc. of 0.1 *N* sodium hydroxide had been neutralized. An excess of silver nitrate solution was added to the warm neutral solution and the precipitate filtered on a weighed Gooch crucible. 0.2340 g. of silver chloride, equivalent to 9.65% of the chlorine in the substance, was obtained. The 0.2340 g. of silver chloride had been formed from an amount of hydrochloric acid corresponding to 16.3 cc. of 0.1 *N* hydrochloric acid; hence in 0.6000 g. of substance 82.2–65.3=65.9 cc. of 0.1 *N* solution, or 65.9% acetic acid, was found. In a similar experiment, 9.61% of chlorine and 65.9% of acetic acid were found. The theoretical quantities for chloro-tetra-acetyl mannose are 9.67% of chlorine and 65.5% of acetic acid.

For identifying the preparation as a mannose derivative, the liquids resulting from these estimations were concentrated and filtered, and a concentrated solution of 0.7 g. of phenylhydrazine in dil. acetic acid was added. After standing for a short time, the separated hydrazone was filtered off and washed with ice-water, alcohol and ether. The yield was 0.6 g. of pure mannose phenylhydrazone, identified by its melting point. Since no particular precautions were taken for obtaining quantitative results, it may be mentioned that 0.9 g. of mannose phenylhydrazone is the theoretical amount obtainable from 1.2 g. of chloro-tetra-acetyl mannose. A small amount of crystalline mannose, identified by its melting point and specific rotation, was also obtained by boiling chloro-tetra-acetyl mannose for 5 hours under a reflux condenser with 0.1 *N* sulfuric acid, precipitating the sulfuric acid and hydrochloric acid with barium hydroxide and silver

acetate, and extracting the concentrated filtrate with absolute alcohol. Crystalline mannose separated on evaporating the alcohol in a vacuum desiccator.

The molecular weight of chloro-tetra-acetyl mannose was determined by the lowering of the freezing point of benzene. In three experiments, 3.8664, 6.6319 and 8.2938 g. of substance per 100 g. of benzene gave the respective depressions 0.523° , 0.890° and 1.090° , from which the values 370, 372 and 380 are obtained for the molecular weight in comparison with the theoretical value 367.

The specific rotation was measured in chloroform solution. 1.1497 g. of once recrystallized chloro-tetra-acetyl mannose was made up to 25 cc. with U. S. P. chloroform. The rotation, measured in a 2dcm. tube at 20° with sodium light, was 8.18 circular degrees to the right; hence $[\alpha]_{\text{D}}^{20} = +88.9$. After a second recrystallization from petroleum ether, 1.4038 g. of substance made up to 25 cc. with chloroform produced a rotation in a 2dcm. tube of 10.068 circular degrees to the right; hence $[\alpha]_{\text{D}}^{20} = 89.64$. After a third recrystallization from petroleum ether, 1.0358 g. of substance made up to 25 cc. with chloroform produced a rotation in a 2dcm. tube of 7.416 circular degrees to the right; hence $[\alpha]_{\text{D}}^{20} = +89.50$, which is taken as the specific rotation of the pure substance. Chloro-tetra-acetyl mannose is a stable substance, as it was kept in a desiccator during the hot summer months without decomposition. The melting point is 81° . It is colorless and odorless, has a bitter taste and is very soluble in the usual solvents other than water and petroleum ether.

Summary.

Chloro-tetra-acetyl mannose, hitherto known only in the form of a syrup, has been obtained in crystalline form.

The behavior of the crystalline substance toward methyl alcohol and silver carbonate (reaction of Koenigs and Knorr) is analogous to that of bromo-tri-acetyl rhamnose. This is well accounted for by their structural formulas given in this paper.

In the case of chloro-tetra-acetyl mannose, this reaction leads to various methyl tetra-acetyl derivatives and in this respect chloro-tetra-acetyl mannose differs from the corresponding derivatives of glucose and galactose, which yield only one methyl tetra-acetyl derivative.

This difference in behavior may lead to a more detailed knowledge of the arrangement of the constituent parts of their molecules.

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