

of our paper. For Expt. 17, Table I (see also No. 2, Table III), we find that the time intervals corresponding to values of a of 0.75, 0.99 and $(1 - 10^{-10})$ are 0.44, 1.44 and 7.3 minutes, respectively. For Expt. 5, Table III, the time required for y to reach a value of 0.99 y_s is 17 minutes when K and $[H_2O_2]_0$ are assumed to be 3.0×10^{-4} and 0.20, respectively. These new results do not affect any of the conclusions which we have already presented.

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**SYNTHESIS AND PROPERTIES OF 3-CHLORO-DIACETONE-
GLUCOSE**

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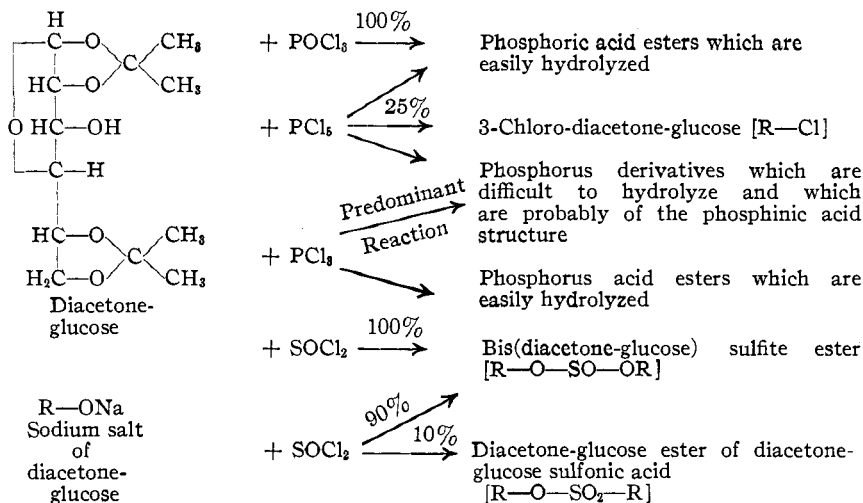
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The work of Freudenberg¹ and his students has emphasized the value of the diacetone hexoses in the preparation of definite mono-derivatives of the hexoses. The 3-chloro-diacetone-glucose was desired for the preparation of carbon-phosphorus and carbon-arsenic derivatives for biological purposes. It seemed probable that availability of this chlorine derivative would also make possible the synthesis of many other glucose derivatives not feasible from the diacetone-glucose itself.

The 3-chloro-diacetone-glucose has been obtained but its stability will preclude its use as a synthetic agent to any extent; however, in both the corresponding bromine and iodine derivatives the halogen atom should prove sufficiently labile for such work. Incidentally, the chlorination with phosphorus pentachloride has yielded phosphorus derivatives of diacetone-glucose not easily hydrolyzed, which are being further investigated.

The preparation of these derivatives depends upon the "non-acid nature" of hydrogen chloride in anhydrous petroleum ether. By operating in carefully purified petroleum ether over freshly ignited sodium carbonate, diacetone-glucose has been successfully treated with phosphorus pentachloride, trichloride, oxychloride and thionyl chloride, hydrogen chloride being evolved in all cases. The merest trace of moisture causes hydrolysis of the acetone groups from the glucose molecule with complete loss of the derivatives sought. The following chart shows the general course of the reactions, the 3-chloro-diacetone-glucose, the bis(diacetone-glucose) sulfite ester and the diacetone-glucose sulfonate of diacetone-glucose being the only products so far examined in detail.

¹ Freudenberg and students, *Ber.*, (a) 55, 929; (b) 3233, 3239 (1922); (c) 56, 1243; (d) 2119 (1923); (e) 58, 294; (f) 300 (1925).



The 3-chloro-diacetone-glucose has been prepared by the chlorination of diacetone-glucose with phosphorus pentachloride and by treating the sulfite ester of diacetone-glucose with the same reagent. The two methods of synthesis and the fact that hydrolysis with alcoholic sodium hydroxide yields 90% of the calculated amount of diacetone-glucose prove that the diacetone-glucose molecule has undergone no other change than the replacement of the hydroxy group by chlorine.

The chlorine atom in the 3-chloro-diacetone-glucose is extremely stable. It is not affected by 6 *N* aqueous sodium hydroxide at boiling temperatures and reacts only moderately rapidly with concd. alcoholic sodium hydroxide, yielding diacetone-glucose. The chlorine linkage is also stable to anhydrous hydrazine in the cold but reacts at higher temperatures apparently yielding a mixture of the primary hydrazino-diacetone-glucose and the unsymmetrical secondary hydrazine derivative in analogy with the reaction reported for hydrazine with diacetone galactose toluene-sulfonate.²

The bis(diacetone-glucose) ester of sulfurous acid has been prepared both by the action of thionyl chloride upon the free diacetone-glucose and upon its sodium salt. No chlorination takes place in either of these reactions. The sulfite ester is partially converted to 3-chloro-diacetone-glucose when heated with phosphorus pentachloride in anhydrous petroleum ether. The ester is saponified in the cold by ammonium hydroxide with quantitative yields of diacetone-glucose. Anhydrous hydrazine yielded no hydrazino-diacetone-glucose, diacetone-glucose being the only product obtained.

When the sodium salt of diacetone-glucose is treated with thionyl chloride at higher temperatures, small quantities of the isomeric diacetone-

² Freudenberg, Hixon and Doser, *Ber.*, **56**, 2124 (1923).

glucose-diacetone-glucose-sulfonate are produced in addition to the sulfite ester. The sulfonate is quite stable to alkaline saponification. It is distinguished from the isomeric sulfite ester by the fact that it yields hydrazino-diacetone-glucose when treated with anhydrous hydrazine according to the reaction of Freudenberg and Brauns^{1b} for diacetone-glucose-toluene-sulfonate.

Experimental Part

3-Chloro-diacetone-glucose.—A mixture of 150 cc. of petroleum ether³ (b. p., 60–70°), freshly ignited sodium carbonate and 4 g. of pure phosphorus pentachloride was introduced into a 3-necked flask fitted with a mercury-sealed stirrer. When the impurities of the phosphorus pentachloride had completely reacted with the sodium carbonate, 4 g. of dry diacetone-glucose was added and the mixture stirred until the reaction was completed (two to four hours). The petroleum ether solution was shaken with 5% sodium hydroxide solution until it remained neutral to methyl orange when allowed to stand in contact with water. Extreme care is necessary as to this detail, for quantities of phosphorus derivatives are formed which are difficult to remove and which apparently are slightly acid, causing hydrolysis of the acetone groups from the glucose molecule. The neutralized petroleum ether solution is dried, the solvent removed under reduced pressure, and the remaining colorless oil distilled in a high vacuum (0.05–0.005 mm.) produced by a Langmuir pump, the 3-chloro-diacetone-glucose coming over at 127°; yield, 25%.

Anal. Calcd. for $C_{12}H_{19}Cl$: C, 51.89; H, 6.85; Cl, 12.72. Found: C, 50.98; H, 7.20; Cl, 12.89.

The 3-chloro-diacetone-glucose can also be prepared by the action of phosphorus pentachloride upon the bis(diacetone-glucose) sulfite ester in anhydrous petroleum ether, neutralization and distillation being conducted as indicated above. This method has the advantage over the first method in that all reaction products other than the 3-chloro-diacetone-glucose are easily saponified and removed by the alkali so that no trouble due to phosphorus derivatives is encountered in the distillation.

The 3-chloro-diacetone-glucose has been allowed to stand in 6 *N* sodium hydroxide solution for 24 hours and has been refluxed for one-half hour without undergoing any saponification. Boiling, concd. sodium methylate in methyl alcohol causes moderately rapid saponification with recovery of about 90% of the calculated amount of diacetone-glucose. The formation of the 3-chloro-diacetone-glucose from the disulfite ester as well as from the free diacetone glucose, and the quantitative saponification of the chloro compound to the original diacetone-glucose, prove that the structure has undergone no other change than the replacement of the hydroxy group by chlorine.

In the chlorination of diacetone-glucose by phosphorus pentachloride,

³ The petroleum ether must be distilled over sodium and be free from unsaturated hydrocarbons for this reaction mixture.

about 75% of the diacetone-glucose is converted to a mixture of easily saponifiable and difficultly saponifiable phosphorus derivatives. The easily saponifiable linkage is probably composed entirely of phosphoric acid esters, for this type of linkage only is produced when phosphorus oxychloride is allowed to react with diacetone-glucose. The difficultly saponifiable phosphorus derivative seems to be a phosphinic acid, for this stable linkage predominates when diacetone-glucose is treated with phosphorus trichloride, the reaction probably being analogous to that studied by Boyd and Smith⁴ for triphenylcarbinol and phosphorus trichloride.

Bis(diacetone-glucose) Sulfite.—The diacetone-glucose was converted to the sodium salt in ethyl ether or in petroleum ether; b. p., 60–70°. A solution of thionyl chloride in the corresponding solvent was freed from acidic compounds by treatment with sodium chips and then was allowed to drop into this solution cooled to 0° until no further sodium chloride separated. The solution of sulfite was filtered off, treated with silver oxide or with a dilute solution of sodium carbonate to remove any excess of thionyl chloride and the solvent separated at room temperature under reduced pressure. The bis(diacetone-glucose) sulfite was obtained as a colorless oil, soluble in all inert, dry solvents. It decomposes when subjected to vacuum distillation. It is hydrolyzed by hydrazine and dilute alkali solutions. The stability of the sulfite is comparable with that of the aryl sulfites. The yield was quantitative.

Anal. Calcd. for $C_{24}H_{33}O_{13}S$: S, 5.66. Found: 5.59.

The sulfite ester can also be prepared by treating the free diacetone-glucose with thionyl chloride as outlined for the treatment with phosphorus pentachloride. No chlorination takes place when thionyl chloride is used.

Diacetone-glucose-diacetone-glucosulfonate.—Some of the isomeric sulfonate ester as well as the sulfite ester is obtained when the reaction described above is carried out at the boiling point of petroleum ether (70–90°). The petroleum ether solution is neutralized with sodium carbonate and treated as indicated for the ester, the sulfite being removed by saponification. An oil was obtained which yielded a small amount of hydrazino-diacetone-glucose (m. p., 98°) when treated with dry hydrazine, thus distinguishing it from the isomeric sulfite ester.

Anal. Calcd. for $C_{24}H_{33}O_{13}S$: S, 5.66. Found: 5.78.

Reaction of Diacetone-glucose-toluenesulfonate with Grignard's Reagent.—No reaction took place when 2.07 g. of diacetone-glucose-toluenesulfonate was treated with 3 g. of bromobenzene and 0.5 g. of magnesium in ethyl ether for eight hours at room temperature. When the reaction was tried in boiling toluene instead of ether, *p*-tolylphenyl-sulfone was isolated. This behavior of the sulfonate ester is characteristic of the "aryl" compounds⁵ and substantiates other reactions which indicate "negative" properties for the third carbon atom in diacetone glucose. Physical data covering this point will be presented in the near future.

Summary

1. The synthesis of 3-chloro-diacetone-glucose is reported by the action of phosphorus pentachloride upon both diacetone-glucose and its sulfite ester. Proof of structure is based upon the two methods of prep-

⁴ Boyd and Smith, *J. Chem. Soc.*, 125, 1477 (1924).

⁵ Gilman and Beaber, *THIS JOURNAL*, 47, 578, 2047 (1925). Acknowledgment is made to N. J. Beaber for carrying out this reaction.

aration and upon saponification of the 3-chloro-diacetone-glucose to diacetone-glucose.

2. The neutral sulfite ester of diacetone-glucose is produced when thionyl chloride reacts with either diacetone-glucose or its sodium-salt at 0–20°. At higher temperatures, a mixture of the sulfite ester and the isomeric diacetone-glucose-sulfonate ester is produced.

3. The stability of the chlorine in the 3-chloro-diacetone-glucose, the stability of the sulfonate esters and the reaction of diacetone-glucose-toluenesulfonate with Grignard's reagent, all indicate "negative" properties for the third carbon atom in diacetone-glucose.

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NICKEL CARBONYL, CARBON MONOXIDE AND GRIGNARD REAGENTS¹

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It is well known that carbon dioxide reacts with Grignard reagents forming first the magnesium complexes that yield carboxylic acids on hydrolysis;² after prolonged treatment of the first product with excess of Grignard reagent the complex of tertiary alcohols is obtained.³

On the other hand, carbon monoxide does not ordinarily react with Grignard reagents. It is the purpose of this paper to show how we have succeeded in making carbon monoxide and Grignard reagents react freely when they are activated by a small amount of nickel carbonyl, yielding a series of compounds somewhat similar to the carbon dioxide series.

Some attempts have previously been made to prepare aldehydes and secondary alcohols from carbon monoxide. Zelinski⁴ reported the formation of aldehydes and ketones by the action of nickel carbonyl on propylmagnesium iodide. Vinay⁵ reported the formation of tertiary alcohols by the direct action of carbon monoxide on Grignard reagents of the types R_2CHMgX and R_3CMgX . Grignard, in a general address,⁶ makes a brief reference to the way in which the reaction with carbon monoxide might be expected to proceed and refers to some unpublished work of

¹ A part of a thesis presented by W. L. Gilliland in partial fulfillment of the requirements for the degree of Doctor of Philosophy, at the Massachusetts Institute of Technology.

² Grignard, *Ann. chim. phys.*, [7] **24**, 433 (1901). Gilman and Parker, *This Journal*, **46**, 2816 (1924).

³ Grignard, *Compt. rend.*, **138**, 152 (1904).

⁴ Zelinski, *J. Russ. Phys.-Chem. Soc.*, **36**, 339 (1904).

⁵ Vinay, *Thesis*, Geneva, 1913.

⁶ Grignard, *Bull. soc. chim.*, [4] **13**, XX (1913).