Summary

1. 2,3,4-Trimethoxyacetophenone has been condensed with *o*-, *m*- and *p*-nitrobenzaldehydes to the corresponding nitrochalcones.

2. Reduction of the *m*- and *p*-nitro derivatives gives the corresponding amino derivatives, whereas the *o*-nitro gives a trimethoxyphenylquinoline.

3. A similar condensation of 2-hydroxy-3,4-dimethoxyacetophenone with the nitrobenzaldehydes, gives first the aldols and then the chalcones.

4. When these hydroxynitrochalcones are acetylated, the acetyl derivatives converted into dibromides, and the latter subjected to the action of caustic alkali, the products are benzalcoumaranones and not flavones.

NEW YORK, N. Y. RECEIVED JULY 25, 1934

[CONTRIBUTION FROM THE LABORATORIES OF THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH, NEW YORK]

Reactions of Carbohydrates in Liquid Ammonia. II. Apparatus and Methods. Alkyl, Acyl and Certain Metallic and Non-metallic Derivatives of Diacetoneglucose

BY IRVING E. MUSKAT[1]

Since the publication of the preliminary paper on the reactions of carbohydrates in liquid ammonia,[2] the author has endeavored to develop and standardize the *modus operandi* of this process so that the method can be of general use. The apparatus used and the procedure followed have been modified and in the present paper these will be described.

At the time the preliminary paper was published, some previous work by L. Schmid[3] had been overlooked. Schmid and his collaborators tried liquid ammonia as a medium for the methylation of sugars and starch but failed. It is obvious from the work reported in the preliminary paper and here that the results differ markedly from those reported by Schmid and his co-workers.

Apparatus

The apparatus now used is shown in Fig. 1. It is so designed that it is easy to introduce either gaseous or liquid ammonia, solids or liquids, and carry on further reactions with the alkali metal salts of the carbohydrates without transferring them to other vessels. The tank used for the liquid ammonia is fully described by Johnson and Fernelius[4] and will not be described here. It is possible to obtain both gaseous and liquid ammonia from this tank. A is the reaction vessel, B is a ground glass top through which all materials are added, C is the inlet tube for gaseous ammonia and D is the outlet tube for the ammonia vapors or any gases which may be liberated during the reaction. E is a ground glass opening into which any one of three different parts—F, H or I—may be fitted. Attachment F is used to introduce the alkali metals or any solids used in the reaction (G is a glass rod used to push the substance down in case it sticks or cakes); attachment H to introduce liquids; and attachment I, shown in place, to introduce liquid ammonia or liquid ammonia solutions of the reagents. At the tip of I is attached a small test-tube J with a perforated bottom. In this test-tube the alkali metal is placed and the liquid ammonia allowed to drop over it, thus dissolving the metal to form a solution which drops down into the reaction vessel A.

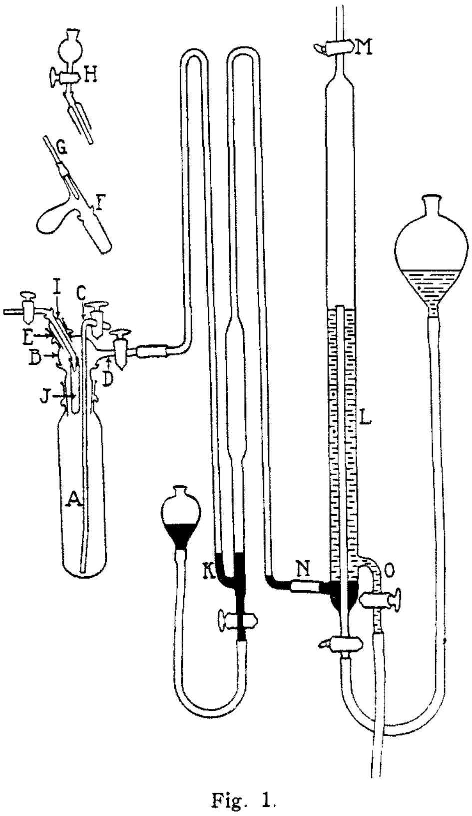


Fig. 1.

The rest of the apparatus and the general methods concerning the technique of working with liquid ammonia as

---

[1] National Research Fellow in Chemistry.

[2] Muskat, THIS JOURNAL, **56**, 693 (1934).

[3] L. Schmid and B. Becker, *Ber.*, **58**, 1966 (1925); Schmid Waschkau and Ludwig, *Monatsh.*, **49**, 107 (1928).

[4] Johnson and Fernelius, *J. Chem. Ed.*, **6**, 441 (1929).

developed by Kraus and Franklin are fully described by Johnson and Fernelius,[4] and this work should be consulted.

Before using, the apparatus is completely swept out with dry ammonia gas. A mixture of solid carbon dioxide and acetone contained in a clear Dewar cylinder is used to condense the ammonia in vessel A.

Preparation of the Alkali Metal Salts of Carbohydrates.—In the preliminary paper the various general methods for preparing the alkali metal salts of carbohydrates are given. In this paper are described the conditions under which any particular method should be used, and the technique best suited to each with the apparatus just described. Any of the alkali metals, lithium, sodium or potassium may be used. The lithium salts are most soluble in liquid ammonia and consequently it is advisable to use lithium when a larger number of hydrogen atoms are to be replaced with the metal. For most work, however, it is desirable to use potassium since the potassium salts of the carbohydrates are most reactive. The temperature at which the salts are formed is of considerable importance. As a general rule one equivalent of the alkali metal can be introduced readily at the temperature of solid carbon dioxide and acetone (app. −80°). However, if a number of equivalents of the alkali metal are to be introduced it is best to carry out the reaction at the boiling point of liquid ammonia (−33.4°).

The general methods for preparing the salts follow.

(1) A weighed quantity of the carbohydrate is placed in vessel A, and F with the proper quantity of the alkali metal cut up in small pieces, is attached at E. The reaction vessel is swept out with ammonia gas introduced at C. A Dewar cylinder containing the solid carbon dioxide and acetone cooling mixture is placed around A and sufficient ammonia to dissolve the carbohydrate is condensed in A. A stream of ammonia is allowed to bubble through the liquid ammonia solution during the reaction in order to keep it well stirred. The alkali metal is then dropped in, piece by piece, from F by revolving it around in the ground joint E. The formation of the salt is complete when all of the alkali metal has been added and the blue color has disappeared. This method can be used in those cases where a localized high concentration of the alkali metal is not objectionable, and where the reaction products do not cover the surface of the alkali metal and prevent it from reacting completely. When carbohydrates containing but one free hydroxyl group (such as acetone methylrhamnofuranoside) are used, this reaction takes place even at the temperature of the cooling bath (app. −80°). In the case of carbohydrates containing more than one free hydroxyl group and when all the hydrogen atoms attached to the hydroxyl groups are to be replaced with alkali metal, the cooling bath must be removed and the temperature of liquid ammonia allowed to come to its boiling point (−33.4°) in order to complete the reaction in a reasonable time.

(2) A weighed quantity of the carbohydrate is placed in vessel A, and I and J containing a proper quantity of the alkali metal are attached at E. A sufficient amount of ammonia is condensed in A and dry liquid ammonia is introduced through I. The liquid ammonia dissolves the alkali metal in J and the solution drops into the reaction mixture. A stream of ammonia is allowed to bubble through the liquid ammonia solution during the reaction in order to keep it well stirred. This method is used where the reaction products cover up the surface of the alkali metal. It is, as a rule, much easier and faster to prepare the salts in this manner, and in most of the work now being done this method is used except in those cases where it is necessary to use the alkali metal amide.

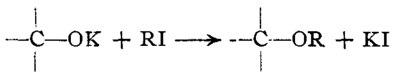
(3) A weighed quantity of the alkali metal is placed in A, and ammonia is condensed in A as described above for (1). The carbohydrate is introduced through F if it is a solid, or through H if it is a liquid. This method can be used where an excess of the alkali metal is not undesirable, that is, where all the hydrogen atoms attached to the hydroxyl groups are to be replaced.

(4) A weighed quantity of the alkali metal is placed in A, and a rusty iron nail or screw is suspended in A through E. Ammonia is condensed in A and the alkali metal reacts with the ammonia in the presence of the iron rust catalyst to form the amide. The completion of this reaction is evidenced by the disappearance of the blue color of the alkali metal in liquid ammonia. (The alkali metal amides are yellow in liquid ammonia solution.) The carbohydrate is introduced through F if it is a solid, or through H if it is a liquid. This method may be used where the alkali metal is harmful.

(5) A solution of either the alkali metal or its amide is prepared in A and a liquid ammonia solution of the carbohydrate is introduced through I. This can be accomplished easily by using two reaction vessels and preparing the ammonia solution of the alkali metal or its amide in one of them and the ammonia solution of the carbohydrate in the other. Then C of the vessel containing the carbohydrate solution is attached to I of the vessel containing the alkali metal or its amide. On closing the stopcock at D of the first vessel and cooling A of the second vessel, the solution will be forced by the difference of vapor pressure from the first to the second vessel. A stream of ammonia is allowed to bubble through the liquid ammonia solution in order to keep it well stirred during the reaction. Of course this reaction could be reversed and the solution of the alkali metal amide added to the solution of the carbohydrate.

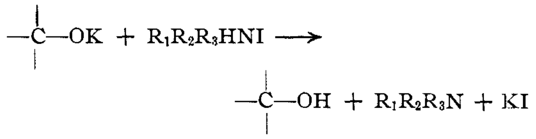
Reaction of the Alkali Metal Salts of Carbohydrates with the Substituting Reagent.—In the preliminary paper it was stated that when the material to be coupled with the alkali metal salt of the carbohydrates does not react with ammonia, then the coupling reaction could be carried out directly in the reaction mixture; if the coupling reagent does react with the ammonia, the ammonia is removed from the alkali metal salt of the carbohydrate and the reaction is carried out in an inert medium. In the early experimental work methyl iodide was used in the presence of liquid ammonia, and under the conditions outlined and for the particular carbohydrates methylated, gave good results. Further work has shown that methyl iodide as well as other alkyl halides vary to a considerable degree in their reactivity toward ammonia. Therefore, it is now considered desirable to remove the ammonia from the alkali metal salts before further reaction with alkyl and aryl halides as well as acyl halides.

In the case of alkylation the following concurrent reactions may take place

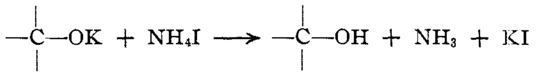
(1) 

$$-\overset{|}{\underset{|}{C}}-OK + RI \longrightarrow -\overset{|}{\underset{|}{C}}-OR + KI \quad (1)$$

$$NH_3 + RI \longrightarrow R_1R_2R_3R_4NI + NH_4I \ (R_1, R_2, R_3, R_4 \text{ may be alkyl groups or hydrogen}) \quad (2)$$

(3) 

$$-\overset{|}{\underset{|}{C}}-OK + R_1R_2R_3HNI \longrightarrow -\overset{|}{\underset{|}{C}}-OH + R_1R_2R_3N + KI \quad (3)$$

(4) 

$$-\overset{|}{\underset{|}{C}}-OK + NH_4I \longrightarrow -\overset{|}{\underset{|}{C}}-OH + NH_3 + KI \quad (4)$$

Equation (1) represents the formation of the desired substituted carbohydrate, $-\overset{|}{\underset{|}{C}}-OR$. Equation (2) represents the side reaction between the alkyl halide and ammonia to form ammonium salts. Equations (3) and (4) represent the effects of the ammonium salts on the alkali metal salt of the carbohydrate, thus preventing the formation of the desired compound, $-\overset{|}{\underset{|}{C}}-OR$.

If the alkyl halide RX reacts with the alkali metal salt of the carbohydrate faster than it does with ammonia then the reaction as represented in equation (1) will predominate. If the reverse is true then the alkali metal salt of the carbohydrate will be ammonolyzed before it can react with the alkyl halide and the yield of the substituted sugar will be correspondingly low.

Therefore, as a general procedure where the reactivity of the alkali metal salts of the carbohydrates and of the substituting reagent is unknown, it is advisable to remove the ammonia after the formation of the salt and add the reagent in an inert medium.

It must be emphasized that the complete removal of the ammonia necessitates warming the salt under a good vacuum for about thirty minutes. Dry ether may be added and the ether removed by means of suction.

The alkali metal amides are sometimes formed during the reaction. With oxygen or moisture these amides may react with explosive violence. Consequently it is highly advisable to introduce dry nitrogen into the reaction vessel after all of the ammonia has been removed. The alkylating or acylating reagent may then be added directly to the alkali metal salt and heated or not, as may be required.

In the preparation of alkyl or aryl ethers it is of advantage to follow the course of the reaction by removing an aliquot portion of the reaction mixture, treating with water, and titrating the alkali formed by the hydrolysis of any unreacted alkali metal salt.

The Reaction of Acyl Esters of Carbohydrates with Alkali Metals and Alkali Metal Amides in Liquid Ammonia Solution.—Liquid ammonia, at its boiling point and at atmospheric pressure, dissolves the acetylated and benzoylated derivatives of any sugar compound in which the reducing group is suitably blocked (*i. e.*, the methylglycosides and 1,2-acetone compounds) *without removing the acyl groups.* If, however, the acyl group is attached to the aldehydic (or ketonic) carbon atom it is readily removed with the subsequent formation of aldehyde ammonia derivatives and amino sugars. At room temperature in a sealed tube (app. 8.5 atmospheres pressure), liquid ammonia removes all acyl groups from the sugars.

The acylmethylglycosides interact with the alkali metals and alkali metal amides in liquid ammonia solution, resulting in the elimination of the acyl groups and the formation of the alkali metal salts of the methylglycoside. The alkali metal reacts in the proportion of two atoms of the metal to each acyl group. Hydrogen is not liberated during the reaction. The precise mechanism of the reaction has not yet been ascertained. Alkali metal amides appear to react in a similar manner.

Oxidation in Liquid Ammonia Solution.—Carbohydrates containing potentially free aldehyde or ketone groups are readily oxidized with iodine in liquid ammonia solution. Iodine reacts with ammonia to form iodoamine, INH_2, which reacts as an oxidizing agent in a manner similar to hypochlorous acid. Iodine is exceedingly soluble even in ammonia vapors with the evolution of considerable heat. It has been found most convenient to place the carbohydrate, together with slightly more than the calculated weight of iodine, in the bottom of the reaction vessel A, and then to condense ammonia into A in the usual manner. Reaction occurs quite readily, the color of the iodine disappears and a greenish-white precipitate is formed. Carbohydrates containing potentially free aldehydic groups are oxidized to the corresponding acid amide. It is presumed that amidines are first formed and that these are then hydrolyzed to the acid amides.

Silver Salts of Carbohydrates.—The alkali metal salts of carbohydrates react with silver salts in liquid ammonia medium to give the corresponding silver salts of the carbohydrates. Thus, silver acetate, which is fairly soluble in liquid ammonia, reacts with the potassium salt of diacetoneglucose to give the corresponding silver salt of diacetoneglucose. The silver salt has not been isolated as such, but its presence was shown by the fact that it reacted with methyl iodide to give the methyl ether of diacetoneglucose. Of course, care was taken to remove any unreacted potassium salt by extracting a number of times with dry ether, in which the potassium salt is soluble. The silver salts should be used as soon as they have been prepared since they are quite unstable and decompose on standing.

Alkyl, Acyl and Certain Metallic and Nonmetallic Derivatives of Diacetoneglucose.—Diacetoneglucose reacts somewhat more slowly with the alkali metals than do the unsubstituted sugar derivatives. This is probably due to the steric effect of the two acetone groups. The monopotassium salt of diacetoneglucose is completely soluble in liquid ammonia and also in anhydrous ether. In the work described here a filtered ethereal solution of the potassium salt of diacetoneglucose was used.

The methyl ether of diacetoneglucose was prepared by allowing the potassium salt of diacetoneglucose to react either with methyl iodide or with freshly distilled (acid-free) dimethyl sulfate. In each case the yields were better than 95%. The dimethyl sulfate seemed to react faster than methyl iodide at the same temperature. The ethyl and *n*-propyl ethers were also prepared. It was observed that the yield of the alkyl ethers decreased with an increase in the size of the alkyl group. This is probably due to the steric hindrance of the two acetone groups as may be seen from a spacial model of the sugar.

Acetyldiacetoneglucose was prepared by treating the potassium salt with either acetyl chloride or acetic anhydride. The benzoyl and *p*-toluenesulfonyl esters were also prepared in a similar manner.

The potassium salt of diacetoneglucose reacts very rapidly with phosphorus trichloride, phosphorus oxychloride, arsenic trichloride, antimony trichloride, bismuth trichloride, mercuric chloride, *p*-tolyl mercuric chloride and sulfur monochloride to give the corresponding substituted derivatives. It is possible to replace the halogen atoms one at a time. Thus, the monodiacetoneglucose derivative of phosphorus trichloride was prepared as well as the completely substituted tridiacetoneglucose phosphite. All of these derivatives are exceedingly hygroscopic and very easily decomposed, and it was not possible, under the experimental conditions used, to isolate pure products in every case. In the case of the mercury derivatives it was difficult to separate completely (without decomposition) the inorganic salts from the mercury–sugar compound. Since the major purpose of this work was to demonstrate the scope of these varied reactions, no special effort was made to isolate these derivatives in pure form, although there is no doubt that this could be done.

The potassium salt of diacetoneglucose reacts with triphenylmethyl chloride but no definite conclusions were reached as to the nature of the product. Reaction takes place quite readily and a product was isolated which appeared from its analysis to be the triphenylmethyl derivative of diacetoneglucose. However, on treating with methyl alcohol the compound seemed to react to give triphenylmethylcarbinol and a sugar. Whether this means that the original compound was a mixture or whether it is easily broken down has not yet been ascertained.

An effort was made to prepare a disaccharide by allowing the potassium salt of diacetoneglucose to react with bromotetraacetylglucose. Although reaction occurred very readily, it was not possible to isolate a disaccharide from the reaction product. It seemed that the potassium salt reacted with the acetyl groups of the bromotetraacetylglucose. The reaction should be repeated with bromotetramethylglucose.

Experimental Part

The potassium salt of diacetoneglucose was prepared in liquid ammonia according to method (1) described above. After the ammonia was allowed to vaporize, dry ether was added to the reaction vessel and suction was applied until all of the ammonia was removed. The ethereal solution of the potassium salt was rapidly filtered under anhydrous conditions. Filtrates prepared in a similar manner were used in all the subsequent experiments.[5]

---

(5) Freudenberg and Hixon, *Ber.*, **56**, 2119 (1923).

Alkylations

3-Methyldiacetoneglucose.—The ethereal solution of the potassium salt of diacetoneglucose was refluxed with methyl iodide (dried over phosphorus pentoxide and distilled). After the reaction was complete (as shown by the fact that a sample of the reaction mixture dissolved in water gave a neutral solution) the excess methyl iodide was distilled off (and recovered) and the residue was extracted with dry ether. The ether was removed by vaporization and the residual oil was distilled under reduced pressure. A 97% yield of 3-methyldiacetoneglucose was obtained.

Anal. Calcd. for 3-methyldiacetoneglucose: OCH_3, 11.3; b. p. 105° (0.3 mm.); $[\alpha]^{20}_{\mathrm{D}}$ $-32.17°$ in alcohol; n^{17}_{D} 1.4518. Found: OCH_3, 11.17; b. p. 105° (0.3 mm.); $[\alpha]^{24}_{\mathrm{D}}$ $-34.2°$ (0.1214 g. in 10.00 cc. of absolute alcohol); n^{24}_{D} 1.4510.

An ethereal solution of 3.2 g. (0.025 mole) of dimethyl sulfate (freshly distilled and free of acid) was added to a filtered ethereal solution of potassium diacetoneglucose (7.5 g.—0.025 mole). Reaction occurred in a few minutes and a white precipitate settled out. Both the ether solution and the solid when shaken with water gave a neutral solution. The solid was collected on a filter, washed with dry ether, dried and analyzed. It proved to be the monopotassium salt of monomethyl sulfate. The ether was removed from the ethereal filtrate by means of suction, and the residual oil was distilled under reduced pressure. A 96.5% yield of 3-methyldiacetoneglucose identical in every respect with the methyl ether described above was isolated.

The above reaction was repeated using a large excess of dimethyl sulfate. The same methyl ether of diacetoneglucose was isolated with approximately the same yield.

3-Ethyldiacetoneglucose.—The ethyl ether was prepared from ethyl iodide or bromide and the potassium salt of diacetoneglucose in ether solution precisely as described above for the corresponding methyl ether. A 90% yield of the ethyl ether was isolated.

Anal. Calcd. for 3-ethyldiacetoneglucose: C, 58.29; H, 8.4; OC_2H_5, 15.6. Found: C, 58.03; H, 8.8; OC_2H_5, 15.2; b. p. 115° (0.8 mm.); $[\alpha]^{24}_{\mathrm{D}}$ $-25.75°$ (0.0990 g. in 10.00 cc. of acetone), $-30.33°$ (0.1368 g. in 10.00 cc. of chloroform), $-31.40°$ (0.1242 g. in 10.00 cc. of methyl alcohol); n^{27}_{D} 1.4461.

3-*n*-Propyldiacetoneglucose.—An ethereal solution of the potassium salt of diacetoneglucose was refluxed with anhydrous *n*-propyl iodide in a manner similar to that described above for the corresponding methyl ether. Only a 30% yield of the *n*-propyl ether was isolated. *n*-Propyl bromide gave a similar result.

Anal. Calcd. for 3-propyldiacetoneglucose: C, 59.56; H, 8.6; OC_3H_7, 19.5. Found: C, 59.49; H, 8.9; OC_3H_7, 18.4; b. p. 120° (1 mm.); $[\alpha]^{24}_{\mathrm{D}}$ $-29.2°$ (0.2225 g. in 10.00 cc. of chloroform); n^{30}_{D} 1.4455.

Acylations

3-Acetyldiacetoneglucose.—An ethereal solution containing 2 g. (0.025 mole) of acetyl chloride (freshly distilled) was added to an ethereal solution containing 7.5 g. (0.025 mole) of potassium diacetoneglucose. An immediate reaction occurred and a white precipitate (KCl) was formed. The reaction mixture was filtered and the precipitate washed with ether. The combined ether filtrates were washed with dilute alkali, then with water, and dried over anhydrous sodium sulfate. The solvent was removed by vaporization and the residual colorless oil was crystallized from 50% methyl alcohol. A 96% yield of acetyldiacetoneglucose was isolated.

Anal. Calcd. for 3-acetyldiacetoneglucose: C, 55.59; H, 7.3; m. p. 62°; $[\alpha]^{22}_{\mathrm{D}}$ $-31.5°$ in alcohol; $-31°$ in chloroform. Found: C, 55.84; H, 7.1; m. p. 62°; $[\alpha]^{24}_{\mathrm{D}}$ $-38.5°$ (0.1300 g. in 10.00 cc. of chloroform), $-35.4°$ (0.1553 g. in 10.00 cc. of methyl alcohol).

Similar results were obtained by using acetic anhydride in place of acetyl chloride in the above reaction.

3-Benzoyldiacetoneglucose.—The benzoyl ester was prepared from benzoyl chloride and the potassium salt of diacetoneglucose in ether solution exactly as described above for the corresponding acetyl ester. A 95% yield of the benzoyl ester was isolated.

Anal. Calcd. for 3-benzoyldiacetoneglucose: C, 62.60; H, 6.6; m. p. 63–64° (sinters at 60°); $[\alpha]^{18}_{\mathrm{D}}$ $-49.7°$ in alcohol. Found: C, 62.38; H, 6.7; m. p. 64° (sharp); $[\alpha]^{24}_{\mathrm{D}}$ $-50.2°$ (0.1040 g. in 10.00 cc. of absolute alcohol).

3-*p*-Toluenesulfonyldiacetoneglucose.—An ethereal solution of *p*-toluenesulfonyl chloride (4.8 g., 0.025 mole) was added to an ethereal solution of potassium diacetoneglucose (7.5 g., 0.025 mole) and the product was worked up in a manner similar to that described above for the corresponding acetyl ester. A 96.5% yield of the purified (from 90% methyl alcohol) *p*-toluenesulfonyl ester was isolated.

Anal. Calcd. for 3-*p*-toluenesulfonyldiacetoneglucose: C, 55.04; H, 6.3; S, 7.72; m. p. 120°; $[\alpha]^{20}_{\mathrm{D}}$ $-68.6°$ in chloroform. Found: C, 55.26; H, 6.3; S, 7.56; m. p. 120°; $[\alpha]^{24}_{\mathrm{D}}$ $-70.4°$ (0.1427 g. in 10.00 cc. of chloroform).

Introduction of Phosphorus

Monodiacetoneglucose Phosphite.—An ethereal solution of freshly distilled phosphorus trichloride (3.4 g., 0.025 mole) was added to an ethereal solution of potassium diacetoneglucose (7.5 g., 0.025 mole). Reaction occurred at once and a white precipitate settled out. The reaction mixture was filtered quickly under anhydrous conditions and the precipitate was washed with dry ether. The ether was removed from the combined filtrates by means of vaporization, and the residual oil was allowed to stand overnight under a high vacuum. Even though precautions were taken to avoid hydrolysis of the phosphorus derivative, some hydrolysis occurred as shown by the following analysis (R = diacetoneglucose residue).

Anal. Calcd. for $RO\text{-}PCl_2$: C, 40.00; H, 5.3; P, 8.58; Cl, 19.63. For RO-PCl(OH): C, 42.02; H, 5.9; P, 9.04; Cl, 10.34. Found: C, 42.72; H, 6.2; P, 8.57; Cl, 9.83.

The above product was then hydrolyzed with 75% alcohol and the alcohol was removed by vaporization under high vacuum. A glassy residue remained which was free of halogen, and was soluble in ethyl and methyl alcohol but insoluble in the other organic solvents.

Anal. Calcd. for monodiacetoneglucose phosphite, $RO\text{-}P(OH)_2$: C, 44.41; H, 6.5; P, 9.56. Found: C, 44.25; H, 6.4; P, 8.76.

Tridiacetoneglucose Phosphite.—The above preparation was repeated except that one-third as much phosphorus trichloride was used (1.1 g., 0.008 mole). The ether was removed from the ethereal filtrate by means of suction and the residual oil was allowed to stand overnight under high vacuum. An amorphous solid remained which was free of halogen and very hygroscopic.

Anal. Tridiacetoneglucose phosphite: C, 53.42; H, 7.1; P, 3.83. Found: C, 52.90; H, 7.4; P, 3.90; m. p. app. 60°; $[\alpha]^{27}_{D}$ $-19°$ (0.0980 g. in 10.00 cc. of chloroform).

Monodiacetoneglucose Phosphate.—An ethereal solution containing 3.8 g. (0.025 mole) of phosphorus oxychloride (freshly distilled) was added to an ether solution containing 7.5 g. (0.025 mole) of potassium diacetoneglucose. Reaction occurred immediately and a white precipitate was formed. The reaction product was filtered and the ether removed from the filtrate by means of vaporization under reduced pressure. The residual oil was hydrolyzed with water, and the aqueous solution was neutralized with ammonium hydroxide. Barium hydroxide was then added and the barium salt of the phosphate of diacetoneglucose was isolated in the usual manner. The barium salt was identical with that prepared from diacetoneglucose and phosphorus oxychloride in pyridine solution.

Tridiacetoneglucose Phosphate.—The above preparation was repeated except that one-third as much (1.2 g., 0.008 mole) phosphorus oxychloride was used. The ether was removed from the ethereal solution by means of vaporization under reduced pressure and the residual solid was allowed to stand overnight under high vacuum.

Anal. Calcd. for tridiacetoneglucose phosphate: C, 52.39; H, 7.0; P, 3.75. Found: C, 52.34; H, 7.3; P, 3.00; m. p. app. 55°; $[\alpha]^{28}_{D}$ -44.4 (0.1385 g. in 10.00 cc. of chloroform).

Introduction of Arsenic

Tridiacetoneglucose Arsenite.—An ethereal solution of freshly distilled arsenic trichloride (1.5 g., 0.008 mole) was added to an ether solution of potassium diacetoneglucose (7.5 g., 0.025 mole). Reaction occurred at once and a white precipitate settled out. The reaction mixture was filtered quickly under strictly anhydrous conditions. Unless moisture is very rigidly excluded, the clear ethereal filtrate becomes cloudy with the separation of arsenous oxide. The ether was removed by means of vaporization under reduced pressure. A white solid remained which was allowed to stand overnight under high vacuum.

Anal. Calcd. for tridiacetoneglucose arsenite: C, 50.67; H, 6.7; As, 8.79. Found: C, 51.44; H, 7.3; As, 8.20.

Introduction of Sulfur

Bidiacetoneglucose Sulfide, RO—S—S—OR (R = diacetoneglucose residue).—An ethereal solution containing 1.7 g. (0.0125 mole) of sulfur monochloride (S_2Cl_2) was added to an ethereal solution of potassium diacetoneglucose (7.5 g., 0.025 mole). Reaction occurred fairly rapidly and the color changed from yellow to lavender in a short time. After standing for some hours the color of the solution changed to a reddish-brown. The reaction mixture was filtered and the filtrate was concentrated to a small volume by vaporization under reduced pressure. The solid which crystallized from the solution was collected on a filter and analyzed. The above structure is assigned provisionally pending further investigation.

Anal. Calcd. for bidiacetoneglucose sulfide: C, 49.45; H, 6.6; S, 11.00. Found: C, 49.71; H, 7.0; S, 10.38.

Introduction of Mercury, Antimony and Bismuth.—Mercuric chloride and *p*-tolylmercuric chloride were added to an ether solution of potassium diacetoneglucose. Reaction took place rapidly in each case. However, considerable difficulty was experienced in isolating the pure mercury derivatives free from inorganic salts.

Antimony trichloride reacts with potassium diacetoneglucose in a manner similar to that described above for arsenic trichloride. No effort was made to isolate a pure product.

Bismuth trichloride is but slightly soluble in dry ether and consequently it reacted very much slower with the ethereal solution of potassium diacetoneglucose. The reaction was complete after shaking for forty-eight hours.

It should be emphasized that the instability of these metallic and non-metallic derivatives of diacetoneglucose and the difficulties occasioned in their purification could be avoided largely by using derivatives of sugars which do not offer the same degree of steric hindrance and possess different solubilities.

Summary

1. A modified apparatus for working with carbohydrates in liquid ammonia solution is described. The apparatus is so designed that it is easy to introduce either gaseous or liquid ammonia, solids or liquids, and carry on further reactions with the alkali metal salts of the carbohydrates without transferring them to other vessels.

2. The general methods for preparing the alkali metal salts of carbohydrates and their further reaction with various substituting reagents are outlined.

3. The oxidation of carbohydrates in liquid ammonia solution is described.

4. The preparation of alkyl, acyl and certain metallic and non-metallic derivatives of diacetoneglucose is given.

PITTSBURGH, PA. RECEIVED JULY 25, 1934