ATTEMPTED HYDROFORMYLATION
OF TRIACETYL-D-GLUCAL

by

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SUMMARY

Triacetyl-D-glucal, an unsaturated sugar has been prepared and submitted to the hydroformylation reaction, which is the addition of carbon monoxide and hydrogen to an unsaturated compound at high pressure and temperature. A cobalt catalyst is generally used, in this case, cobalt acetate tetrahydrate.

The mixture of products obtained was separated by column chromatography and distillation. The main products are probably triacetyl-D-deoxyglucose obtained by the addition of water to the starting material, 1,2-hydroglucal obtained by hydrogenation of the starting material, a small amount of the theoretical hydroformylation compound and varying amounts of the starting material.
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INTRODUCTION

Relatively few sugars containing a branched-carbon skeleton are known. Digitoxose and streptose are found in natural products. Isosaccharin and a series of heptoses derived from the cyanohydrin addition to fructose have been synthesized. Since digitoxose and streptose are both derived from medicinally important natural products (digitoxin and streptomycin), it is possible that synthetic branched-chain sugars could have some pharmaceutical value.

The method of synthesis used in this work is by means of the oxo, or hydroformylation reaction, using 3, 4, 6-triacetyl-D-glucal as the starting material:

![Chemical structure diagram]

The reaction might well be expected to yield two interesting new heptoses as represented by the above equation, both containing an anhydride ring, and a new aldehyde group. No heptoses of this type are known. Some 1, 2-dihydrotriacetyl-D-glucal might also arise by hydrogenation carried out in the presence of an equimolar amount of ethyl
orthoformate, thus momoethyl and diethyl acetals could also be formed, giving rise to further products.

The method of synthesis also affords an opportunity of studying hydroformylation, which has been applied to many unsaturated compounds, but not to a carbohydrate containing an ethylenic linkage. Such a reaction, requiring high temperature and pressure, is unusual in carbohydrate chemistry.

Triacetyl-D-glucal was subjected to the hydroformylation process and the products separated by chromatography and by distillation.

The structure of any branched chain sugars produced were to be studied by means of the following reactions:

1. deacetylation to the free sugar
2. oxidation to the lactone of the corresponding aldonic acid
3. reduction of the lactone to the lactone of an aliphatic acid, whose hydrazide could be prepared and compared to that of a known compound.
HISTORICAL INTRODUCTION

The "Oxo" Reaction

The addition of carbon monoxide and hydrogen to an olefinic bond, under the influence of a cobalt catalyst, is known as the "oxo" reaction.

\[
R - \text{C} = \text{C} - R' + \text{H}_2 + \text{CO} \xrightarrow{\text{Co}} R - \text{C} - \text{C} - R' + \text{CHO}
\]

The normal products are saturated aldehydes (I and II) containing one more carbon than the original olefin. Since the reaction can also be described as the addition of an atom of hydrogen and a formyl group to an olefinic bond, it is also known as hydroformylation. The term "oxo" is sometimes used to refer specifically to a two-stage process in which the aldehydes are reduced to alcohols. The reaction is carried out at 100° to 200°C., and at combined pressures of carbon monoxide and hydrogen of 100 to 200 atmospheres.

A related reaction is the older Fischer - Tropsch process (62) in which a mixture of carbon monoxide and hydrogen is hydrogenated at high temperature and pressure to form hydrocarbons. Oxygen containing compounds had been detected in the products (59), but were never investigated. The actual discovery of the "oxo" reaction is attributed to Roelen (52) (65). While attempting to extend the scope of the Fischer-
Tropsch process by the addition of olefins to the feed gas, Roelen produced aldehydes which were subsequently reduced to alcohols for industrial use. Alcohols have also been used as a starting material, to prepare alcohols containing one more carbon atom. In this instance the process is called homologation (43). Orchin and co-workers (43) found appreciable amounts of hydrocarbon in the final product when hydrogen and carbon monoxide were used in the ratio of two to one. However, aldehydes are the main products when carbon monoxide and hydrogen are used in equal quantities. Pino (48) has observed that increased yields of aldehydes may be obtained by the addition of ethyl orthoformate which will by acetal formation, prevent polymerization and reduction of these aldehydes.

The hydroformylation reaction has been applied to a variety of unsaturated compounds in which the double bonds are not conjugated, for example (1) (2) (43): olefins, allyl ethers, unsaturated esters, unsaturated alcohols, and some heterocyclic compounds. If the reaction is applied to a conjugated system, simple hydrogenation usually results (43), except in the case of $\alpha,\beta$-unsaturated esters.

When the main products of hydroformylation are aldehydes two isomeric forms are obtained, if no rearrangements occur during the reaction. Some simple generalizations were formulated by Keulmans (32) to assist in the prediction of the composition of the mixture:

1. straight chain olefins in general yield 60 - 40 percent straight chain aldehydes, and 40 - 60 percent branched
chain aldehydes.

2. addition to a tertiary carbon does not occur.

3. addition to a carbon adjacent to a tertiary carbon is hindered.

4. addition of a formyl group adjacent to a quaternary carbon does not occur.

5. addition is not hindered by an isolated tertiary carbon.

Further, Adkins (2) noted that where the starting material contained a terminal double bond, the formyl group was added to the unsubstituted carbon as shown by the following equation:

\[
\text{R - CH = CH}_2 \xrightarrow{\text{H}_2\text{CO}} \text{R - CH}_2\text{-CH}_2\text{-CHO}
\]

The rule was reversed where R was phenyl, or \(\alpha\)-naphthyl. Where R was a large group n-C\(_4\)H\(_9\), n-C\(_{16}\)H\(_{33}\), or (CH\(_2\))\(_8\)CO\(_2\)CH\(_3\), complex mixtures were produced which have been attributed to shifting of the double bond before hydroformylation, thus forming many products. Since the reaction mechanism is not fully understood, the structure of the products cannot usually be predicted with any accuracy.

Natta and Beati (40) have made a study of the kinetics of the production of methyl formyl stearate from methyl oleate by hydroformylation.

\[
\begin{align*}
\text{H - C - (CH\(_2\))\(_2\) - CH}_3 & \xrightarrow{\text{OHC - C - (CH\(_2\))\(_2\) - CH}_3} \text{H - C - (CH\(_2\))\(_2\) - CH}_3 \\
\text{H - C - (CH\(_2\))\(_7\)COMe} & \xrightarrow{\text{HOO - (CH\(_2\))\(_7\)COMe}} \text{HOC - C - (CH\(_2\))\(_7\)COMe}
\end{align*}
\]

and other isomers.
The reaction was found to be unimolecular at 100° to 150°C, and at pressures above 70 atmospheres. The reaction velocity was found to be solely dependent on the concentration of olefin, and did not vary between 70 and 210 atmospheres of combined carbon monoxide and hydrogen pressures, presumably because the gases were present in such excess that their concentrations were essentially constant. The following mechanism has been postulated (65):

\[
\begin{align*}
\text{C} = \text{C} + \text{CO} & \rightarrow \text{C} - \text{C} + \text{H}_2 \\
& \rightarrow \text{C} - \text{C} + \text{H}
\end{align*}
\]

Keulemans and Kwante (32) suggested a free radical mechanism in which \( \text{C}^\cdot \) and \( \text{H}^\cdot \) attack the double bond. Roelen (65) believed that the reaction mechanism involved the formation of a cobalt carbonyl. Subsequently, Adkins (1) and Orchin (67) both postulated that the reaction did not occur by heterogeneous catalysis, as the use of a solid catalyst suggested, but by homogeneous catalysis after the formation of dicobalt octacarbonyl during the reaction. Both workers were able to show independently that this compound was in fact a catalyst for the reaction. Orchin (67) proposed the following mechanism:

\[
\begin{align*}
2\text{Co} + 8\text{CO} & \Rightarrow [\text{Co(CO)}_4]^2 \\
[\text{Co(CO)}_4]^2 & \overset{\text{H}_2}{\Rightarrow} 2\text{Co(CO)}_3\text{COH} \\
4\text{Co(CO)}_3\text{COH} + 4\text{CH}_2 & = \text{CH}_2 \overset{\text{H}_2}{\Rightarrow} \frac{125 \text{ atm.}}{4\text{CH}_3\text{CH}_2\text{CHO} + [\text{Co(CO)}_3]^4}
\end{align*}
\]

Some support for a mechanism of the type above is afforded by studies of the reduction of alcohols to alkanes under hydroformylation conditions.
Wender and Orchin (43) have postulated a carbonium ion mechanism for the reduction involving cobalt carbynols, and have produced experimental evidence in its support.

The catalyst first used by Roelen (65) in hydroformylation was similar to the one used in the Fischer-Tropsch process, and probably consisted of 30 percent cobalt, two percent thorium oxide, and two percent magnesium oxide suspended on 66 percent kieselguhr. Catalysts of this type are called insoluble, or Fischer-Tropsch type catalysts and are used almost exclusively in industrial processes, many of which are patented (27).

Smith and co-workers (59) used a catalyst which was composed of cobalt oxide, manganese oxide and cupric oxide suspended on various unreducible carriers, for example, diatomite brick. Shexnalder (54) has used silica hydrogel impregnated with salts of cobalt, thorium and copper.

Finely divided cobalt suspended on kieselguhr, prepared by the reduction of cobalt oxide mixed with kieselguhr, may also be used as a catalyst (41) (53). Pino (48), Parker (46) and Natta (40)(42) have employed a variety of cobalt (II) salts: cobalt stearate, oleate napthenate, acetate, molybdate, oxide and iodide. The effectiveness of all these catalysts is probably due to the formation of dicobalt octacarbonyl during the reaction.

Adkins (1) has prepared crystalline dicobalt octacarbonyl from Raney cobalt and from Harshaw Chemicals Company Co 100 powder. Wender and Orchins (66)(67)(68) subsequently prepared dicobalt octacarbonyl, under conditions similar to those used in the oxo reaction, from a variety of cobalt salts. The reaction was performed in benzene, and the
preparations stored in solution was estimated to contain 0.21 grams of dicobalt octacarbonyl per millilitre.

A solution of dicobalt octacarbonyl may be analysed by means of the following reactions (43)(61):

\[
\begin{align*}
\left[\text{Co(CO)}_4\right]_2 + 2\text{I}_2 & \rightarrow 2\text{CoI}_2 + 4\text{CO} \quad 1.) \\
2\left[\text{Co(CO)}_4\right]^- + 3\text{I}_2 & \rightarrow 2\text{CoI}_2 + 8\text{CO} + 2\text{I}^- \quad 2.) \\
\text{Ni(o-phenanthroline)}_3\text{Cl}_2 + 2\text{Co(CO)}_4^- & \rightarrow \text{Ni(o-phenanthroline)}_3\left[\text{Co(CO)}_4\right]_2 + 2\text{Cl}^- \quad 3.)
\end{align*}
\]

Equations 1.) and 2.) are used to determine the total dicobalt octacarbonyl and the carbonyl anion. Equation 3.) gives the concentration of the anion alone, and thus, by difference, the concentration of dicobalt octacarbonyl may be determined.

It is useful to study the electron structure of dicobalt octacarbonyl in considering the mechanism of the oxo reaction (43). The outer orbitals of cobalt are 3d\(^7\), 4s\(^2\). By acquiring nine more electrons, cobalt may attain the structure of krypton. Since cobalt tetracarbonyl has been shown by cryoscopic studies to exist in dimeric form, and is paramagnetic, it must attain the rare gas structure by receiving two electrons from each of four carbon monoxide molecules, and by sharing a pair between the two cobalt atoms. The dimer may then dissociate in a cation and an anion, and the cation can react with Lewis bases, for example:

\[
\begin{align*}
3\left[\text{Co(CO)}_4\right]_2 + 12\text{C}_5\text{H}_5\text{N} & \rightarrow 2\text{Co(C}_5\text{H}_5\text{N})_6 + 3\text{Co(CO)}_4]_2 + 8\text{CO} \quad 4.) \\
2\text{Na} + \left[\text{Co(CO)}_4\right]_2 & \rightarrow 2\text{Na}\left[\text{Co(CO)}_4\right] \quad 5.) \\
\left[\text{Co(CO)}_4\right]_2 + \text{R} - \text{CH} = \text{CH}_2 & \rightarrow \text{R} - \text{CH} - \text{CH}_2 - \text{Co(CO)}_4^+ + \left[\text{Co(CO)}_4\right]^- \quad 6.)
\end{align*}
\]
The Glycals:

Two types of unsaturated sugars which should undergo hydroformylation are glycoseens and glycals (47e). The double bond may be found in other positions on the chain, though the 1,2 position is commonest in glycals.

In the case of glucose derivatives, both of these unsaturated sugars have been prepared from the intermediate 2,3,4,6-tetraacetyl-α-D-glucopyranosyl bromide commonly known as acetobromoglucose. The α-forms of the halogeno sugars are produced almost exclusively by most methods of synthesis, though Fischer (18) was able to produce the β-form by the action of dry hydrogen bromide on pentaacetyl-α-D-glucopyranose. Acetobromoglucose has been prepared from either α or β pentaacetyl-D-glucopyranose by the action of hydrogen bromide in acetic acid (12)(16) or directly from D-glucose by the action of hydrogen bromide in acetic anhydride (4). An early method of preparation was the addition of acetyl bromide to glucose (17)(50). Due to the lability of the halogen atom, acetobromoglucose is unstable unless very pure (4), and pentaacetyl-D-glucopyranose, and 2,3,4,6-tetraacetyl-D-glucopyranose are common side products of any reaction.

Fischer (18)(19)(21) prepared triacetyl-D-glucal by shaking acetobromoglucose with a mixture of zinc dust and fifty percent acetic acid. He was attempting to prepare a tetraacetyl derivative of sorbitol, but obtained instead an unsaturated compound which formed a dibromide and reduced Fehling's solution. Helferich and co-workers (26) have shortened the procedure for the preparation of triacetyl-D-glucal from glucose by not isolating the intermediate acetobromoglucose.

Fischer was not able to crystallize the deacetylated form but
proposed the following structure (21):

\[
\begin{align*}
\text{CHOH} \\
\text{HCOH} \\
\text{HCOH} \\
\text{H}_2\text{OCH} \\
\text{CH}_2\text{OH}
\end{align*}
\]

Subsequently Bergmann (5) obtained crystalline D-glucal by deacetylation of triacetyl-D-glucal with ammonia in anhydrous methanol. Stacey (44) and co-workers have used sodium alkoxides in anhydrous solution for deacetylation.

Fischer (21) reduced the non-crystalline deacetylation products with palladium sponge in acetic acid and obtained crystalline hydroglucal for which he proposed the following structure:

\[
\begin{align*}
\text{CH}_2\text{OH} \\
\text{CH} \\
\text{HOCH} \\
\text{HCOH} \quad 0 \\
\text{HC} \\
\text{CH}_2\text{OH}
\end{align*}
\]

The triacetate of the reduced compound was also prepared, but could not be crystallized, and was isolated as a syrup by high vacuum distillation (20). Deacetylation with aqueous barium hydroxide yielded the free hydroglucal in crystalline form.

Bergmann, Fischer and Schotte subsequently proposed a new structure for triacetyl D-glucal (22):
This structure was shown to be correct, by a series of reactions involving the double bond. An unstable dibromide and stable dichloride were prepared. Oxidation with ozone yielded triacetyl-D-arabonic acid and triacetyl arabinose. The only experimental observation incompatible with the new structure was the reduction of Fehling's solution by triacetyl-D-glucal, but Bergmann and Schotte (5) were able to show that, when pure, glycals do not have reducing properties. Finally, since the asymmetric centre at the first carbon is lost, epimeric pairs of aldoses should yield the same glycal, and it has been shown that D-mannal is identical with D-glucal.

The double bond of a free or acetylated glycal undergoes two important addition reactions (47b), besides the formation of dihalogen compounds. Firstly, a deoxy sugar is formed by treatment of a glycal with dilute sulphuric acid and barium carbonate (47b) (6) (38).

Secondly, a glycal is reacted with perbenzoic acid to form normal aldoses (5)(36)(37)(47b). D-Glucal yields mannose, but triacetyl D-glucal forms triacetyl D-galactose (36)(37). Similarly free D-galactal reacts to form
D-talose, while the acetylated form yields triacetyl D-galactose (36)(37). The suggestion has been made (36) that the third carbon is unsubstituted, the orientation of the free hydroxyl directs addition by formation of an oxide ring. Thus, unsubstituted glycals when reacted with perbenzoic acid form aldoses with the hydroxyl groups on carbons two and three on the same side of the ring.

A rearrangement of triacetyl-D-glucal was observed by Bergmann (10), who found that a new compound was formed by boiling triacetyl D-glucal with water for 15 minutes. The compound was named diacetylpseudo-glucal, and assigned the following structure:

\[\text{HCOH} \quad \text{HCOAc} \quad \text{H}_2 \text{OAc}\]

Hydrolysis of diacetylpseudoglucal with barium hydroxide yielded two more compounds (11) which were named isoglucal and protoglucal, and assigned structures:

\[\begin{array}{c}
\text{CH}_3 \\
\text{CHO} \\
\text{CH} \\
\text{CH}_2 \\
\text{H}
\end{array}\]

\[\begin{array}{c}
\text{CHO} \\
\text{CH} \\
\text{CH}_2 \\
\text{CH}_2
\end{array}\]

isoglucal

protoglucal
Ishell (28) has proposed a mechanism for the formation of pseudo-glucal from triacetyl D-glucal.

Isbell was unable to propose a carbonium ion mechanism for the formation of isoglucal and protoglucal on hydrolysis of diacetyl-pseudo-glucal.

**Deoxy and Anhydride Sugars**

A deoxy sugar is one in which a hydroxyl group has been replaced by a hydrogen, usually in the 2 or 6 position. Those found in nature most commonly contain a 6-deoxy group such as fucose, rhamnose and digitoxose (which is also a 2-deoxy sugar)(30)(47b). 2-Deoxyribose is an important constituent of some nucleic acids. 2-Deoxy sugars have been prepared from glycals as shown previously (6), by treatment with dilute sulphuric acid and barium carbonate.

Sugars containing a 1, 5 anhydride ring are usually classed as derivatives of polyhydric alcohols. Examples of naturally occurring ones are strycitol (1, 5-D-mannitan) and polygalitol (1, 5-D-sorbitan) (47b). 1, 2-Dihydro-D-glucal, obtained by hydrogenation of D-glucal is a 1, 5-anhydride compound.
Branched-Chain Sugars

Branched-chain sugars are very rare, and most of those known are of natural origin. Apiose (47f)(56) occurs in the glycoside apiin which is found in the leaves of parsley.

\[
\begin{align*}
\text{HOCH}_2 \\
\text{COH} - \text{CH(OH)} - \text{CHO} \\
\text{HOCH}_2
\end{align*}
\]

Apiose

Hamamelose (47c)(55) occurs in hamamelitanin found in the bark of the shrub *Hamamelis virginica*.

\[
\begin{align*}
\text{H}_2\text{COH} \\
\text{HOC} - \text{CHO} \\
\text{CHOH} \\
\text{CHOH} \\
\text{CH}_2\text{OH}
\end{align*}
\]

Hamamelose

A branched-chain hexose containing two aldehyde groups occurs in streptomycin (47g).

\[
\begin{align*}
\text{CHO} \\
\text{CHOH} \\
\text{C(OH)} \text{CHO} \\
\text{CHOH} \\
\text{CH}_3
\end{align*}
\]

Streptose

Regna, Hochstein, Wagner and Woodward (51) have studied the structure of the sugar mycarose found in the antibiotic magnamycin. By degradation studies they have shown the new sugar to be a deoxy sugar branched at
A branched -chain sugar acid has been synthesized by the alkaline degradation of maltose. (33) Isosaccarinic acid is found among the products, and the lactone of this acid, isosaccharin, may be reduced to a non-crystalline branched-chain aldose: (17)

Schmidt and Weber-Molster (57) have prepared a series of branched-chain sugar acids by cyanohydrin addition to D-fructose, D-xyloketose and D-araboketose. In the case of the two acids produced by cyanohydrin addition to D-fructose the configurations were thoroughly studied.

Woods and Neish (72) have employed the branched-chain sugars obtained by cyanohydrin addition to D-fructose to prepare other branched-chain sugars. By periodate oxidation of the lactose of the seven carbon acid 4-C-hydroxymethyl-L-xyluronic acid was obtained. Reduction of the
lactone and aldehyde groups of this product with Raney nickel and sodium amalgam yielded 2-\text{C}-\text{hydroxymethyl-}\text{D-xylose}. Reduction of 4-\text{C}-\text{hydroxymethyl-}\text{L-xyluronic acid} with sodium borohydride yielded noncrystalline 4-\text{C}-\text{hydroxymethyl-}\text{D-arabinose}.

Stacey and co-workers (60) have synthesized a branched chain altrose derivative by the action of diethyl magnesium on methyl-2,3-anhydro-6-\text{O-benzylizene-\text{D-mannoside}}.

\[
\begin{align*}
\text{CH}_2\text{OH} & \quad \text{hydrolysis} \\
\text{H}_2\text{O} & \quad \text{magnesium}
\end{align*}
\]

3-\text{ethyl-}\text{D-altrose}

The structure of the branched chain sugar, apiose, has been elucidated by the following reactions (47f)(56):

\[
\begin{align*}
\text{H}_2\text{O}_2 & \quad \text{Ba(}\text{I}0\text{)}_2 & \quad \text{HI} \\
\text{HOCH}_2 & \quad \text{H}_3\text{C} & \quad \text{P}
\end{align*}
\]

3-\text{methyl butyric acid}

Similarly 1-\text{methyl valeric acid} was produced from hamamelose in 3.5 to 5 percent yield (56):
Kilian (33)(34) reduced isosaccharin, the lactone of isosaccharinic acid with hydriodic acid and red phosphorus to 1-methylvalerolactone in order to indicate the position of the hydroxymethyl group.
Preparation of 2, 3, 4, 6-Tetraacetyl-D-glucopyranosyl bromide

The preparation was done according to the method of Barczai-Martose (4) with no modifications, except that half quantities were used for convenience in handling the solutions. The product crystallized readily and 90g. (0.219 mole) of 2, 3, 4, 6-tetraacetyl-D-glucopyranosyl bromide was obtained from 50g. (0.28 mole) of D-glucose; yield 76%; m.p. 86-7°C. If the preparation was allowed to stand for one day in the presence of light and moisture, decomposition occurred as evidenced by a darkened color.

Preparation of 3, 4, 6-Triacetyl-D-glucal

The preparation was done according to the method of Fischer (20) with slight modification.

Acetobromoglucose (90g.; 0.22 mole) was dissolved in 900 ml. of 50% aqueous acetic acid. For convenience in handling, this solution was divided into two solutions of 450 ml. each. Zinc dust (90g.) was added to each batch, and both were shaken vigorously on a mechanical shaker for two or three hours. The zinc dust was removed by filtration, and the solutions recombined, and evaporated at 10-20 mm. pressure, and at 40°C, to about one third of the total volume. On cooling overnight in a refrigerator, the zinc salts crystallized. After filtration, the solution was extracted several times with ether, and the combined extracts, about 500 ml., were neutralized with sodium bicarbonate, washed with water, dried over anhydrous magnesium sulfate, and treated with decolorizing carbon. After filtration the solution was evaporated at 10-20 mm. pressure, and at 40°C, to a thick, colorless syrup which was inoculated with a seed crystal.
and placed in a refrigerator. The seed crystal was obtained from a previous batch which had crystallized spontaneously. In about seven days complete crystallization had occurred; yield 44.8 g (.165 mole; 67.2%).

After one recrystallization from 95% ethanol the product had the following constants; m.p. 54-55°C. (uncor.), \[ \alpha \frac{20}{D} = 19.5^\circ \text{(C.3.02, 95% ethanol),} \]
which decreased to \[ \alpha \frac{20}{D} = 13.2^\circ \text{(C.1.46, 95% ethanol).} \]
After three recrystallizations Fischer (20) reported a rotation of \(-13.02^\circ\), rising to \(-15.2^\circ\) on the seventh recrystallization. Danilov and Gakhokidze (16) reported a rotation of \[ \alpha \frac{18}{D} = -14.4^\circ \text{(25% alc.).} \]

On one occasion when the solution was allowed to stand in the cold after filtration of the zinc salts, 3, 4, 6-triacetyl-D-glucal crystallized. However, on concentration and extraction, more product was obtained, hence this was not considered to be a feasible method of isolating the product.

**Hydroformylation of 3, 4, 6-Triacetyl-D-Glucal**

3, 4, 6-Triacetyl-D-glucal was treated with carbon monoxide and hydrogen according to a modification of the procedure of Pino (48), Adkins and Kresk (1)(2), and Wender and co-workers (66).

**Reagents:**

Benzene was purified by treatment with several batches of sulphuric acid, followed by distillation over calcium chloride.

Cobalt (II) acetate tetrahydrate (Harshaw Chemicals Co acetate 101), supplied by the Harshaw Chemical Company of Cleveland, Ohio (25%), was used as catalyst after drying over phosphorous pentoxide.

Table I shows the experimental results for hydroformylation of triacetyl-D-glucal. The following is a description of run II, which exemplifies the procedure used.
Triacetyl-D-glucal (4.30g., 0.0158 mole), cobalt acetate tetrahydrate (0.25g. 0.0009 mole), ethyl orthoformate (0.034 mole) and 35 ml. of purified benzene were placed in the glass liner of a high pressure hydrogenator, leaving a void of 264 ml. in the bomb. Carbon monoxide was introduced to a pressure of 780 p.s.i., followed by hydrogen to a total pressure of 1570 p.s.i., both pressures measured at 17°C. The mechanical rocker was started and the temperature was raised to 100°C. over a period of two hours, and maintained for a total of seven hours. The maximum pressure observed was 1950 p.s.i. On cooling overnight to room temperature the pressure was 1530 p.s.i., corresponding to a drop of 40 p.s.i. (theor. 41.8 p.s.i.).

The gases were released, and the solution washed into a flask with benzene, filtered and evaporated at 10-20 mm. pressure and 40°C. to a syrup. The syrup was pale yellow in color and started to crystallize as soon as evaporation was complete, m.p. 43-45°C. (uncor.), yield 4.73g. The product reacted with 2, 4-dinitrophenylhydrazine.

**Chromatographic Separation of the Products of Hydroformylation**

The product obtained from the hydroformylation of triacetyl-D-glucal was chromatographically fractionated according to the procedure of Wolf from and co-workers (70).

Magnesol (2MgO.5SiO2) was dried overnight in an oven at 100 C., and mixed with celite (No. 532, Johns-Manville) (31), in a ratio of five to one by weight; by shaking the mixture in a large glass bottle with a tight fitting lid. The mixture was screened mechanically through a 200 mesh per inch screen, and stored in large brown bottles.
A tapered glass column (30 x 5.5 cm) was packed with 175 g. of the prepared adsorbent using a reduced pressure of 740 mm. The finished column was moistened with 50 ml. of benzene, followed immediately by 850 mg. of the hydroformylation product dissolved in 15 ml. of benzene. The chromatogram was developed with 350 ml. of benzene. The column was then extruded and air dried for 12 hours. A streak of 1% potassium permanganate in 2.5N NaOH located two zones; one 80 mm. broad, extending from the top of the column, and one 20 mm. broad, extending from 95 mm. to 115 mm. from the top of the column. The column was cut in segments, and the part of the column which had been sprayed was removed with a scalpel and discarded. Each zone was extracted with a volume of 500 ml. of chloroform, followed by further extraction with 500 ml. of acetone. From the upper zone 450 mg. of sugar was recovered, and from the lower zone 200 mg., making the total recovery 76%. The fractions from the upper and lower zones were each recrystallized, once from ether, twice from ethanol-water, and twice from ethyl acetate-petroleum ether (boiling range 40°-60°C.) to form colorless, needle-like crystals with constant melting points. The material from the upper zone reduced Fehling's solution in 15 seconds and had the following constants: m.p. 76.5°-78.5°C. (uncor.), $\left[ \alpha \right]_{D}^{24} + 100°(c 0.179, 95% \text{ ethanol}).$ The material from the lower zone did not reduce Fehling's solution or take up bromine and had the following constants: m.p. 51°-52°C. (uncor.) $\left[ \alpha \right]_{D}^{23.5} - 5.7°(c 1.34, 95% \text{ alc.}).$ A mixed melting point with triacetyl-D-glucal was 45°-49°C.

Infra-red analysis of the compound melting at 51°-52°C. appears in Figure 1 (p. 208).
Distillation of the Products of Hydroformylation

A portion (12.05g.) of the syrup from hydroformylation VII (see Table I) was distilled under high vacuum (0.05 mm.) yielding thick syrups which ranged in color from yellow to orange going from lower to higher boiling fractions. The residue remaining in the distillation flask was charred and polymerized. After standing in a vacuum desiccator over phosphorus pentoxide for periods ranging from eight hours for the lower boiling fractions, to two weeks for the higher boiling fractions, crystallization was complete. The crude products were recrystallized from ethanol (95%)-water and from ethyl acetate-petroleum ether to form colorless, needle-like crystals with constant melting points of 51°-52°C. and 112°-113°C. The crude yield of the compound melting at 51°-52°C. was 3.29g., and this fraction was found to be identical with that obtained chromatographically. The higher melting compound (7.60g.) rapidly reduced Fehling's solution, gave a negative bromine test, and the following rotations: \( \left[ \frac{\alpha}{D} \right]_D + 90.0^\circ (C 0.806, \text{CHCl}_3) \) and \( \left[ \frac{\alpha}{D} \right]_D + 115.0^\circ \) (alc., C 9.237).

Anal: Calcd. for \( \text{C}_{12}\text{H}_{18}\text{O}_6 \): C, 49.84; H, 6.28; \( \text{CH}_3\text{CO} \), 44.53 MW 290.

Found: C, 49.45; H, 6.28; \( \text{CH}_3\text{CO} \), 54.7. MW 344 (camphor), 351 (benzene), 274 (exaltone).
A summary of the separation of the products of hydroformylation by distillation and by chromatography is given in Table II.

**Analysis of the Products of Hydroformylation**

1. The molecular weights were determined cryoscopically using benzene.

2. Carbon, hydrogen and acetyl determinations were done by Weiler and Strauss (74), and by Manser (39).

3. Infra-red analysis was done by Dr. R. Wright (73).

**Deacetylation of Products Obtained from Hydroformylation of Triacetyl-D-Glucal.**

The products of hydroformylation which had been separated by distillation and by chromatography were deacetylated according to the method of Overend, Shofizadeh and Stacey (44), a modification of the Zemplin method (75).

A sample (0.4g.) of the sugar acetate melting at 51°-52°C. was dissolved in 4.2 ml. of anhydrous methanol to which freshly cut sodium metal (0.005g.) was added. The flask was sealed and allowed to stand at room temperature for 48 hours. The solution was treated with solid carbon dioxide, and on addition of acetone an inorganic precipitate, probably sodium acetate, appeared. The precipitate was removed by filtration and the remaining solution was evaporated under reduced pressure yielding a syrup (0° l0g., yield 50%). After standing in a vacuum desiccator over phosphorus pentoxide for one month no crystallization of the syrup occurred. No uptake of bromine by this syrup could be observed. An optical rotation was taken on the dried syrup, \[ \alpha_D^{20} + 12.0^\circ (C 0.584, \text{ water}) \].
Fischer (21) reported a rotation $\left[ \alpha_{D}^{20} \right] + 16.31^\circ$ (water) for crystalline hydroglucal.

A further sample (1.2g.) was dissolved in 7.5 ml. of anhydrous methanol to which freshly cut sodium metal was added. After 48 hours, the solution was treated with two ion exchange resins; Amberlite IR120 (23) and Duolite D5683 (14) and evaporated to dryness under reduced pressure to a syrup; yield 0.40 g., 62%.

Similarly 1.18 g. of the sugar acetate melting at 112°-113°C. was deacetylated and taken to a syrup; yield 0.40 g., 65%.
A Infra red spectrum of triacetyl-D-glucal.
B " " " " Compound A, m.p. 51-52 °C.
C " " " " compound C, m.p. 112-113 °C.
D " " " " compound A, deacetylated.
E " " " " compound C, deacetylated.

Figure I
<table>
<thead>
<tr>
<th></th>
<th>Triacetyl-D-glucal</th>
<th>Cobalt Acetate$\cdot$4H$_2$O</th>
<th>Vol. of benzene</th>
<th>ethyl orthoformate</th>
<th>initial combined gas pressure (p.s.i.)</th>
<th>maximum pressure (p.s.i.)</th>
<th>maximum temperature</th>
<th>time for reaction</th>
<th>pressure drop (p.s.i.)</th>
<th>theoretical drop (p.s.i.)</th>
<th>product</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>0.83g.</td>
<td>0.0030mol.</td>
<td>35ml.</td>
<td>5.0ml.</td>
<td>0.034mol.</td>
<td>1500</td>
<td>1720</td>
<td>110°C.</td>
<td>1hr. at 100-110°C.</td>
<td>55</td>
<td>8.07</td>
</tr>
<tr>
<td>II</td>
<td>4.30g.</td>
<td>0.0158mol.</td>
<td>35ml.</td>
<td>1.0ml.</td>
<td>0.0081mol</td>
<td>1570</td>
<td>1950</td>
<td>105°C.</td>
<td>6hrs. at 100-105°C.</td>
<td>40</td>
<td>41.8</td>
</tr>
<tr>
<td>III</td>
<td>12.85g.</td>
<td>0.0472mol.</td>
<td>45ml.</td>
<td>3.0ml.</td>
<td>0.018mol.</td>
<td>1545</td>
<td>2240</td>
<td>150°C.</td>
<td>5hrs. at 90-100°C.</td>
<td>130</td>
<td>121</td>
</tr>
<tr>
<td>IV</td>
<td>6.80g.</td>
<td>0.0250mol.</td>
<td>45ml.</td>
<td>8.0ml.</td>
<td>0.043mol.</td>
<td>1490</td>
<td>1910</td>
<td>112°C.</td>
<td>9hrs. at 110-112°C.</td>
<td>50</td>
<td>69.2</td>
</tr>
<tr>
<td></td>
<td>Triacetyl-D-glucal</td>
<td>Cobalt Acetate .4H2O</td>
<td>Vol. of benzene</td>
<td>ethyl orthoformate</td>
<td>initial combined gas pressure (p.s.i.)</td>
<td>maximum pressure (p.s.i.)</td>
<td>maximum temperature</td>
<td>time for reaction</td>
<td>pressure drop (p.s.i.)</td>
<td>theoretical drop (p.s.i.)</td>
<td>product</td>
</tr>
<tr>
<td>----------</td>
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<td>----------------------------------------</td>
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<td>---------------------</td>
<td>-------------------</td>
<td>------------------------</td>
<td>---------------------------</td>
<td>--------------------------</td>
</tr>
<tr>
<td>V</td>
<td>6.32 g. 0.0232mol.</td>
<td>0.33 g.</td>
<td>35 ml.</td>
<td>8.0 ml.</td>
<td>0.048 mol.</td>
<td>1600</td>
<td>2010</td>
<td>100°C.</td>
<td>5 hrs. at 100-110°C.</td>
<td>80</td>
<td>59.4</td>
</tr>
<tr>
<td>VI</td>
<td>6.43 g. 0.0235mol.</td>
<td>0.35 g.</td>
<td>35 ml.</td>
<td>8.0 ml.</td>
<td>0.048 mol.</td>
<td>1550</td>
<td>2100</td>
<td>125°C.</td>
<td>6 hrs. at 100-125°C.</td>
<td>leak in bomb.</td>
<td>65.0</td>
</tr>
<tr>
<td>VII</td>
<td>20.1 g. 0.0738mol.</td>
<td>1.08 g.</td>
<td>55 ml.</td>
<td>13.2 ml.</td>
<td>0.081 mol.</td>
<td>1550</td>
<td>2000</td>
<td>115°C.</td>
<td>6 hrs. at 100-115°C.</td>
<td>2</td>
<td>153</td>
</tr>
</tbody>
</table>

1. Assuming hydroformylation occurs.

2. Due to mechanical difficulties, it was necessary to introduce and expel, and reintroduce gases in starting reaction. The solution appeared to have undergone a change before reaction.

3. Temperatures not constant in some runs due to poor thermostatic control.
<table>
<thead>
<tr>
<th>reaction</th>
<th>method of separation</th>
<th>products obtained</th>
<th>composition of mixture</th>
</tr>
</thead>
<tbody>
<tr>
<td>III</td>
<td>chromatography</td>
<td>a. crystals m.p.76.5-78.5°C.</td>
<td>a. 57.3%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>b. crystals m.p.51-52°C.</td>
<td>b. 16.8%</td>
</tr>
<tr>
<td>IV</td>
<td>chromatography</td>
<td>a. crystals m.p.51-52°C.</td>
<td>a. 58.0%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>b. syrup</td>
<td>b. 10.0%</td>
</tr>
<tr>
<td>V</td>
<td>chromatography</td>
<td>a. crystals m.p.51-52°C.</td>
<td>a. 63.0%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>b. syrup</td>
<td>b. 8.6%</td>
</tr>
<tr>
<td>VI</td>
<td>distillation</td>
<td>a.</td>
<td>a. 78.0%</td>
</tr>
<tr>
<td>VII</td>
<td>distillation</td>
<td>a. crystals m.p.51-52°C.</td>
<td>a. 25.6%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>b. crystals m.p.112-113°C.</td>
<td>b. 49.0%</td>
</tr>
</tbody>
</table>
DISCUSSION

In the preparation of the starting material, triacetyl-D-glucal, from acetobromoglucose according to the methods of Barczai-Martose (4) and Fischer (20), it was observed that acetobromoglucose is very unstable, and that the best overall yields are obtained if acetobromoglucose is converted to triacetyl-D-glucal immediately. In fact, by the method of Helferich and co-workers (26), acetobromoglucose need not actually be isolated. Crude triacetyl-D-glucal, or material which has been recrystallized only once, tends to darken and polymerize in the presence of light, moisture and traces of acid, and will in fact form a brittle, black material after standing for some weeks in the presence of light and air. After three recrystallizations triacetyl-D-glucal is quite stable and may be stored in ordinary sample bottles at room temperature for some weeks. If stored in the cold, the material is of course much more stable.

The experimental procedure for hydroformylation was taken from that of Adkins and Kresk (1,2), and Wender and Levine (66), using cobalt acetate tetrahydrate as suggested by Pino (48). In this work pressures of 100 to 150 atmospheres of the gas mixture were employed and temperatures from 100 to 150° C, as it was thought that temperatures above 150° C would favor decomposition of the sugar and reduction of any aldehyde formed to an alcohol. Natta (40) has employed pressures of 70 to 210 atmospheres in the hydroformylation of methyl oleate, and Parker (46) has employed tem-
temperatures as high as $210^\circ \text{C}$ in the hydroformylation of various alkenes. Pressures as high as 300 atmospheres are found in some industrial processes.

Pressures greatly in excess of 2000 p.s.i. were avoided because the bomb had not been used at more than 1800 p.s.i. and $100^\circ \text{C}$ for some years, and although it was subsequently tested to 4500 p.s.i. in the cold, the maximum safe pressure at $100^\circ \text{C}$ was unknown.

The time for the reaction was chosen arbitrarily because no pressure drop could be observed at the maximum temperature and pressure. Since carbon monoxide and hydrogen form an extremely non-ideal gas mixture, it could not be determined whether or not the maximum theoretical pressure, calculated on the basis of the pressure of the gases originally introduced, was ever attained at the maximum temperature. As a consequence, the bomb had to be completely cooled before any pressure drop could be measured.

It is possible that most of the reaction occurs instantaneously because no pressure drops were observed at the maximum temperature and pressure. This suggestion is supported by the following observation. On introducing the gases, carbon monoxide was always added first, followed by hydrogen, in order to lessen the possibility of hydrogenation. A slight drop in the pressure of the carbon monoxide was always observed immediately after it had been introduced. It was originally supposed that this drop was due to a small leak in a valve, however, on one occasion when the carbon monoxide had been introduced, and had subsequently
to be expelled because of mechanical difficulties, the solution was observed to have taken on a yellow color and bubbles could be observed. According to Adkins and Kresk the starting pressure is that observed after both gases have been introduced, and the mixture rocked for one minute. In this work the total gas pressure observed was always slightly less than the total pressures of the gases originally introduced. Obviously the experimentally observed pressure drop could therefore be less than the true one. The accuracy of this observation was further impaired by the fact that the gauge scale was marked in divisions of 10 p.s.i.

It can be seen from Table 1 that the experimental pressure drop was in some cases greater and in some cases less than the theoretical pressure drop. Run 111 is of particular interest because the observed pressure drop was 130 p.s.i., as compared to the experimental theoretical drop of 121 p.s.i. A compound was found in the products of this run which was not isolated in any other case. The discrepancy between the two may perhaps be explained by the error introduced by the gauge, and by the amount of gas taken up by the catalyst. It may be significant that in Run 111, a high concentration of sugar was employed, and a temperature of 150° C was reached during the reaction.

The catalyst selected, cobalt acetate tetrahydrate, had been used by several other workers (67, 48) in the hydroformylation of olefinic compounds. It was supplied as a sample by the Harshaw Chemicals Co. of Cleveland, Ohio (25).

The chromatographic separation of the products was carried out according to the method of Wolfrom and co-workers (69, 70). Columns of
the type designed for extrusion chromatography were packed with the dry celite and magnesol mixed in a one to five ratio. It was found that the smaller columns could be packed with the dry adsorbent quite readily, but the largest size 5.5 x 30 cm. were more difficult to pack because the packing tended to form channels and cracks. Wet packing was found to be more reliable for the size of column. The packing to be placed in the column was stirred vigorously with sufficient benzene to make a mixture which could be poured easily into the column. If the mixture was too thick, air bubbles were entrapped, and if too thin the time required to pack the column was greatly increased. The solvent was removed from the packing using slightly reduced water pressure of 720-740 mm.

The products of hydroformylation were separated on the column using benzene as a developer. The column was extruded and the separated products isolated by extraction of the adsorbent with chloroform and acetone. Removal of the solvent yielded syrupy products which were purified by several recrystallizations. The results of chromatographic separation of several runs are shown in Table II.

In the separation of the products of hydroformylation by high vacuum distillation, no exceptional amount of decomposition took place during most of the distillation. The material remaining in the flask was charred, however, because of the very high bath temperature required to raise the vapor temperature to 150° C. The syrups distilled, especially the latter fractions, were so thick that no condenser was used in most cases, and if the equipment necessitated the use of a condenser, it was
filled with hot water and wrapped in aluminum foil. The syrups obtained by distillation of the products of hydroformylations VI and VII (see Table II) crystallized slowly and after several recrystallizations yielded compounds having melting points of 51° - 52° C. and 112° - 113° C.

The analysis of the acetylated compound melting at 51° - 52° C. \([\alpha]_{D}^{23.5} = 7.19° \text{ (c 1.05, alc.)}\) agrees closely with that of either triacetyl-D-glucal or 1,2-dihydro-3,4,6-triacetyl-D-glucal (Found: C, 52.81%; H, 6.05%; CH₃CO, 47.27%. Theor. for C₁₂H₁₈O₇: C, 52.54%; H, 6.62%; CH₃CO 47.09%. Theor. for C₁₂H₁₆O₇, C, 52.94%; H, 5.94%; CH₃CO, 47.42%). Fischer (14) has prepared 1,2-dihydro-3,4,6-triacetyl-D-glucal in non-crystalline form by the reduction of triacetyl-D-glucal with palladium sponge in acetic acid, followed by distillation of the product. A rotation of +33.93° - 35.55° alc. was reported for this product. No constants for the crystalline compound have been found elsewhere in the literature. Although the infra-red analysis of the compound melting at 51° - 52° C. shows the presence of a double bond by absorption at 1600 cm⁻¹ (see Figure 1 p. 25), the uptake of bromine by this compound is very slight. Moreover a small depression of melting point is obtained when this compound is mixed with triacetyl-D-glucal. The rotation of crystalline hydroglucal obtained by Fischer (14) was +16.31°, while that of the deacetylated syrup obtained in this work was +12°. Therefore the crystalline material obtained must be a mixture of triacetyl-D-glucal and 1,2-dihydro-3,4,6-triacetyl-D-glucal, having a greater proportion of the hydrogenated product. The similarity of the two compounds might render further separation difficult.
The analysis of the acetylated compound melting at 112°-113°C. is as follows: C, 49.76%; H, 5.62%; CH₃CO, 46.9%. The theoretical analysis of triacetyldeoxylglucose is: C, 49.64%; H, 6.26%; CH₃CO, 44.51%. The melting point of the fully acetylated derivative of the compound obtained in this work is 93-94°C, compared to 91°C reported by Stacey and co-workers (44) for tetraacetyl-α-D-2-deoxyglucose.

Bergmann (6) reported triacetyl-2-deoxyglucose as an intermediate in the production of 2-deoxy-D-glucose from triacetyl-D-glucal, but did not crystallize the acetylated deoxy sugar.

The product obtained by deacetylation of the compound melting at 112°-113°C was a syrup, which could not be shown by paper chromatography to consist of more than one component. The rotation of this syrup was +5.95° as compared to +46.59° obtained by Bergmann (6), for the crystalline compound.

The presence of a compound containing a free hydroxyl is indicated by the reduction of Fehling's solutions, and infra red absorption at 3500 cm⁻¹. It is probable that compound melting at 112°-113°C is a mixture consisting of triacetyl-D-deoxyglucose contaminated with compounds of higher acetyl value.

The analysis of the compound melting at 76.5°-78.5°C agrees most closely with the theoretical analysis of the diethylacetal compound which should be produced by hydroformylation and subsequent reaction with ethylorthoformate. Found (ave.) C, 55.67%; H, 7.14%; CH₃CO, 34.0%; M.W. 356. Theor. for C₁₇H₂₈O₈: C, 54.39%; H, 7.48%; CH₃CO, 34.3%; M.W. 376.
Unfortunately such a small amount of this compound was obtained in pure form that further work could not be done to study the structure of the compound.

A number of experimental factors must be considered in attempting to determine why hydroformylation did not occur to any appreciable extent, except perhaps in Run III, Table II (p. 28). The first to be considered is the catalyst. Cobalt acetate tetrahydrate is not itself a catalyst for hydrogenation, but cobalt hydrocarbonyl, formed from dicobalt octacarbonyl in the presence of hydrogen will act as a hydrogenation catalyst.

\[
\left[\text{Co}(	ext{CO})_4\right]_2 + \text{H}_2 \rightleftharpoons 2 \text{HCo(CO)}_4
\]

Since considerable hydrogenation occurred in every hydroformylation, it may be assumed that the required hydroformylation catalyst, dicobalt octacarbonyl, does form under the reaction conditions employed. Unused cobalt acetate tetrahydrate remained in the reaction mixture, hence a sufficient amount was used.

The second factor to be considered is the effect of temperature. From consideration of Tables I and II, it would appear that there is a critical temperature between 125° C. and 150° C., at which hydroformylation occurs, even though the amount of the desired product formed is small even when a temperature of 150° C. is attained (see III, Table I). No work has been found in the literature comparing the reaction temperature required to hydrogenate an olefinic bond under the influence of a cobalt catalyst,
and the temperature required to hydroformylate the same bond, using the same catalyst. The absence of any studies on this subject is probably because the production of hydrogenated material, under experimental conditions similar to those used in this study, has been considered to be insignificant by other workers.

Hydrogenation is thermodynamically favored over hydroformylation but it has been found that (43) hydrogenation of an olefinic linkage only begins to compete with hydroformylation when the double bond of the system is conjugated to another unsaturated system. Adkin's observation of a number of compounds containing conjugated systems which failed to undergo hydroformylation, substantiates this generalization. Triacetyl-D-glucal contains no conjugated system, hence there must be some other reason why hydrogenation is favored and hydroformylation is hindered. It may be that the formation of an unknown intermediate is sterically hindered by the ring form of the compound, or by the steric effect of fully substituted hydroxyls.

The formation of triacetyl-2-deoxy-D-glucose normally occurs by treatment of triacetyl-D-glucal with dilute sulphuric acid, thus effecting the addition of water across the double bond. In considering, as a specific case Run VII (Table II), it is seen that 64 percent of the product is triacetyl-2-deoxy-D-glucose. The amount of water present in the catalyst is 0.024 moles; and the amount of sugar present is 0.0738 moles. The amount of water present in the gases must, therefore, be of considerable importance. Moreover, the amount of cobalt hydrocarbonyl formed must be able to exert a catalytic effect in the addition of water to the double bond. Though this
compound is only detected in Run VII (Table II), it was doubtless present in varying amounts in the products of each hydroformylation. Its isolation may have been prevented in chromatographic separation by the presence of numerous decomposition products. Since the distillation of run VI (Table II) was not as complete as that of run VII (Table II), the deoxy sugar probably remained in the undistilled residue.

Some suggestions regarding future hydroformylations of triacetyl-D-glucal may be made. First, to inhibit the formation of hydroglucal, a greater proportion of carbon monoxide might be employed. No studies were found in the literature where a partial pressure of carbon monoxide greater than that of hydrogen was used, probably for reasons of economy, since, as discussed previously, the amount of hydrogenated product found by other workers is usually insignificant anyway.

Second, to prevent the formation of triacetyl-2-deoxy-glucose, the water must be removed from the system. One means of producing anhydrous conditions would be by the addition of a non-reactive desiccant whose hydrate is stable at 150° C., for example magnesium sulphate. The desiccant could be added to the reaction mixture, the bomb charged, and rocked for two or three hours before heating is started. A second method of removing water from the system, would be to dry the gases before charging the bomb. Obviously, the mechanical difficulties involved in such a procedure, when pressures of 100 to 150 atmospheres are employed, are enormous.

A series of reactions might be done using more carbon monoxide,
and a desiccant, at 125° to 150° C., and at 2000 to 2500 p.s.i. The products could be most rapidly separated by distillation. The crude fractions so obtained could be further purified by chromatographic separation, and recrystallization. An interesting point in considering the reaction mechanism would be to determine what changes have taken place in the reaction mixture immediately after the addition of carbon monoxide.

When suitable conditions for hydroformylation are found the structure of the sugar produced could be determined by the following series of reactions: deacetylation to the free sugar, oxidation to the lactone of the aldonic acid and reduction to the lactone of an aliphatic acid, the hydrazide of which could be compared to that of a known compound.

Though the seven carbon sugar was found in only one run, it is hoped that this work will remove some of the difficulties in future attempts to hydroformylate triacetyl-D-glucal, and will be an addition to the existing knowledge of the oxo reaction.
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