THE ACTION OF PERBENZOIC ACID ON GLUCAL AND ITS DERIVATIVES.

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M. Bergmann⁽¹⁾ has already observed that when the glucal derived from glucose was oxidised with perbenzoic acid in acetic acid ethyl ester, it was almost completely converted into mannose and thus he discovered a new way for the transformation of glucose into mannose, and such a conversion of sugar was previously regarded as being effected by intramolecular conversion in an aqueous alkali solution.⁽²⁾ The mechanism of the new transformation was explained by assuming a transitory formation of 1–2 anhydromannose from glucal, which will then be resolved by taking one molecule of water into the mannose.

The present writer has undertaken the experiment in order to study whether the conversion of glucal into mannose will take place not only in glucal but also in its derivatives, such as triacetyl glucal, and diacetyl pseudo-glucal or not, by oxidation with perbenzoic acid in a chloroform solution.

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(1) Bergmann & Schotte, *Ber.*, **54** (1921), 440.

(2) Lobry de Bruyn & van Ekenstein., *Rec. Trav. Chim.*, **14** (1895), 1010-1023.

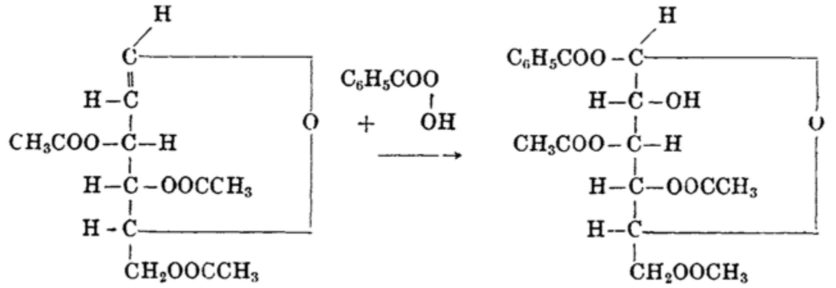
Glucal as Bergmann has stated, was oxidised instantly by perbenzoic acid, and converted into mannose. While, the oxidation of triacetyl glucal with perbenzoic acid was very slow, taking about four days, and diacetyl pseudo-glucal was noticed to undergo in oxidation with much difficulty.

In the latter case, contrary to our expectation, the addition of 1 mol of perbenzoic acid to the sugar will cause the formation of mono-benzoyl triacetyl compound (m.p. =141°—142°). The determination of the constitution of the addition compound established it as 1-benzoyl 2, 4, 6-triacetyl glucose (II), by the study of its chemical reactions (1) it yields neither hydrazone nor semicarbazide, (2) the benzoyl group in the molecule was very easily removed by treating with dilute alkali, (3) when the compound treated with phenyl-hydrazine and acetic acid at room temperature after being hydrolysed with N/5 barium hydroxide solution, gives almost quantitatively phenyl-glucosazone but no crystals of mannose-phenylhydrazone. For the confirmation of the structure, the substance was benzoylated and the product was identified with 1, 2-dibenzoyl 3, 4, 6-triacetyl glucose (m.p. =149°) prepared from 3, 4, 6-triacetyl glucose⁽¹⁾ with benzoyl chloride and pyridine, and their specific rotatory power shown in Table 1 was studied for comparison.

Table 1.

Glucose derivatives	$[\alpha]_D$
1-benzoyl 3, 4, 6-triacetyl glucose	+18.35° (in benzene)
1, 2-dibenzoyl 3, 4, 6-triacetyl glucose	−15.7° (in chloroform)
1-benzoyl 2, 3, 4, 6-tetra-acetyl-glucose	−24.43° (in chloroform)

Thus, in the conversion of 1-benzoyl triacetyl β-glucose from triacetyl glucal, the trans-addition of perbenzoic acid to the double bond of the



(I) Triacetyl glucal

(II) 1-Benzoyl 3, 4, 6-triacetyl β-glucose

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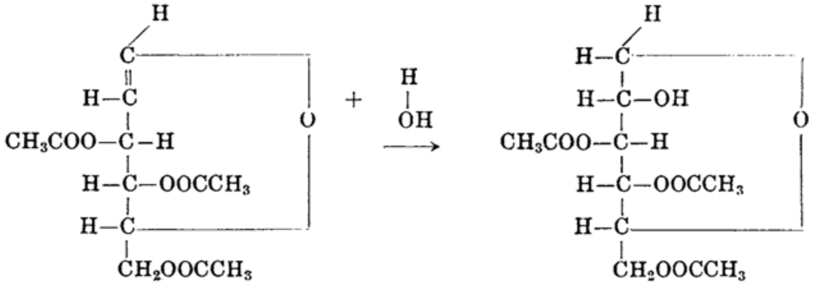
(1) P. Brigl, *Z. Physiol. Chem.*, **122** (1922), 245.

glucal molecule was assumed to occur, but theoretically the cis-addition is possible in the reaction, by which a new isomeric substance should occur in the reaction product. As a matter of fact, an isomeric substance of m.p.$=168°$ was noticed to arise in the reaction product, but its physical and chemical properties were hardly to be determined owing to the meagreness of the sample.

In the meantime, a third new substance of the formula $C_{12}H_{18}O_8$, m.p.$=122°$, was isolated from the reaction product, which was supposed to be derived by the addition of H_2O to the triacetyl glucal, this differed in properties from the 2-desoxy glucose prepared by Bergmann⁽¹⁾ from glucal by treating with dilute acid when cold, and did not reduce Fehling's solution and form any oxide, semicarbazone or phenylhydrazone. As a consequence the constitutional formula (III) as 1-desoxy 3,4,6-triacetyl glucose was given for this compound.

(I)



(III)

Triacetyl glucal

1-Desoxy 3, 4, 6-triacetyl glucose

Experimental Part

Triacetyl Glucal.⁽²⁾ Twenty gr. of β-acetobromo glucose⁽³⁾ (m.p. 87°–88°) which were previously cooled to 0°C., were treated with 40 gr. of zinc powder in 200 c.c. of a 50% acetic acid solution. When all of the β-acetobromo glucose was dissolved, the zinc power was filtered and the filtrate was concentrated to a small volume under reduced pressure to remove acetic acid. The syrup was diluted with 100 c.c. of water, the sugar substance was extracted with ether, neutralized with sodium bicarbonate, washed with water, dried with calcium chloride, and the ether was distilled. The colourless syrup which remained in the flask was changed on standing to white crystals, the yield was about 11.8 gr. This was purified by recry-

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(1) *Ber.*, **55** (1922), 158.
(2) E. Fischer, *Ber.*, **47** (1914), 196.
(3) E. Fischer, *Ber.*, **49** (1916), 584.

stallization from absolute alcohol-petroleum ether solution m.p.$=54°-55°$, $[\alpha]^{10}_{D}=\frac{-1.03+0.06}{6.298\times 1}\times 100=-15.4°$ in absolute alcohol.

This substance decolourizes bromine water immediately, gives a dark green colour by pine shaving reaction, and reduces Fehling's solution when hot.

Glucal.⑴ This substance prepared from triacetyl glucal by following directions of Bergmann & Schotte, was slightly yellow-coloured and is very hygroscopic, melts at $60°-62°$, $[\alpha]^{9}_{D}=\frac{+0.25-0.45}{0.258\times 1}=-7.8°$ in aqueous solution.

Diacetyl Pseudo-glucal. Triacetyl glucal, m.p.$=54°-55°$, was converted by the method of Bergmann and Ludewig⑵ into a colourless syrup of diacetyl pseudo-glucal.

II. Oxidation of Glucal. A cold solution of 3.3 gr. of glucal dissolved in 30 c.c. of absolute methyl alcohol was added with vigorous agitation to an ice-cooled 280 c.c. of perbenzoic acid-chloroform solution (the amount of available oxygen in 1 c.c. of the solution corresponded to 3.40 c.c. of the $N/10$-$Na_2S_2O_3$ solution) which were prepared freshly by following the directions of J. Levy and R. Lagrave.⑶

Table 2.

Reaction temp.	Reaction time	C.c. of $\frac{N}{10}$ $Na_2S_2O_3$ required for 1 c.c. of the solution
0°	Soon after addition	3.07 c.c.
0°	0.5 h	1.70 ,,
0°	1.0 ,,	1.47 ,,
0°	2.0 ,,	1.47 ,,
9°	24.0 ,,	1.50 ,,

After the reaction was over, the product was treated with some distilled water to extract sugar compounds, and the aqueous solution was neutralized with calcium carbonate, evaporated up to a syrup under reduced pressure, 95% of alcohol was added to remove the salt remaining in the syrup, and

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(1) *Ber.*, **54** (1921) 440.

(2) *Ann.*, **434** (1923), 105.

(3) *Bull. soc. chim.*, **37** (1925), 1597.

filtered. When the filtrate was evaporated to a syrup in vacuo, about 3.5 gr. of the colourless syrup were obtained, which gave no Pinoff's reaction. The specific rotation of the syrup was as follows:

$$[\alpha]_D^8 = \frac{1.74-0.45}{0.4238\times 1}\times 100 = +30.4^\circ \text{ in aqueous solution.}$$

Mannose-phenylhydrazone was prepared in the usual way, melted at 195°–198°, $[\alpha]_D^8 = \frac{+0.36-0.15}{0.0802\times 1}\times 100 = +26.2^\circ$ in pyridine.

III. Action of Perbenzoic Acid on Triacetyl Glucal. A cold solution of 5.2 gr. of triacetyl glucal dissolved in 50 c.c. of chloroform was added drop by drop to an ice-cooled 140 c.c. of perbenzoic acid-chloroform solution (1 c.c. of the solution corresponding to 4.33 c.c. of the $\frac{N}{10}$ $Na_2S_2O_3$ solution). The progress of the reaction is shown in the following Table 3.

Table 3

Reaction temp.	Reaction time	C.c. of $\frac{1}{10}$ N-$Na_2S_2O_3$ to 1 c.c. of the solution	Blanc test. C.c. of $\frac{1}{10}$ N-$Na_2S_2O_3$ required to 1 c.c. of perbenzoic acid solution
0°	Soon after addition	3.40	4.33
,,	1.0 h ,, ,,	3.40	4.17
,,	2.0 h ,, ,,	3.20	4.33
,,	3.0 h ,, ,,	2.70	4.30
,,	4.0 h ,, ,,	2.65	4.33
9°	24.0 h ,, ,,	1.65	4.33
,,	48.0 h ,, ,,	1.20	4.15
,,	72.0 h ,, ,,	1.00	4.15
,,	96.0 h ,, ,,	0.90	4.15

After about four days, the theoretical amount of oxygen in the sugar solution having been consumed, the reaction product was neutralized with a sodium carbonate solution, washed with water, dried with anhydrous sodium sulphate, and concentrated to a small volume under diminished pressure to remove the chloroform and a colourless syrup was obtained, which changed to crystals on being left standing in an ice box, and weighed ca. 5 gr.

1-Benzoyl 3,4,6-Triacetyl Glucose. The crystals above mentioned were treated with absolute alcohol and 2.5 gr. of the glucose derivative were isolated from the solution. When recrystallized from hot absolute alcohol, it melts at 141°–142°, is soluble in ether and chloroform, slightly soluble in absolute alcohol, but insoluble in water.

The rotatory power in benzene solution shows $[\alpha]_D^8=+18.35°$ The analytical results are as follows:

Anal. Subst. $=0.1148$; $CO_2=0.2322$; $H_2O=0.0554$ gr. Found: $C=55.17$; $H=5.36\%$. Calc. for $C_{19}H_{22}O_{10}$: $C=55.6$; $H=5.3\%$.

Cryoscopy. Subst. $=0.2876$, glacial acetic acid $=15.1050$ gr.; depression $=0.179°$. Mol. wt., found: 414. Subst. $=0.4240$, glacial acetic acid $=15.9090$ gr.; depression $=0.249°$. Mol. wt., found: 417. Mol. wt., calc. for $C_{19}H_{22}O_{10}$: 410.

It reduces Fehling's solution when hot, oxidises Schiff's reagent, and gives the silver mirror with ammoniacal silver nitrate solution, but does not show any mutarotation. When the alcohol solution was heated with dilute alkali, the liberation of the benzoic acid ethyl ester was recognized by its characteristic odour.

The acyl value of the substance was estimated by an N/14 HCl solution after hydrolysing with N/5.32 barium hydroxide solution, and the results agree with the theoretical value for one benzoyl group and three acetyl groups in the molecule.

A. *Hydrolysis of 1-Benzoyl 3,4,6-Triacetyl Glucose.* 1.7 gr. of 1-benzoyl 3,4,6, triacetyl glucose were dissolved in hot alcohol, and 340 c.c. of N/5 barium hydroxide were added, and let stand at room temperature over night. After the solution was neutralized with 1–N sulphuric acid, filtered and concentrated to a small volume under diminished pressure, acidified with some 1–N sulphuric acid, and benzoic acid was extracted with ether. Benzoic acid isolated was found to melt at 122° and confirmed to be so by elementary analysis and study of chemical properties. The yield was 0.5 gr.

Glucosazone. The acidic solution separated from benzoic acid was neutralized with dilute barium hydroxide solution, filtered off the barium sulphate and the filtrate evaporated to a small volume under reduced pressure. Then a mixture of phenylhydrazine and acetic acid, was added to the syrup and heated, and the osazone of m.p. 206° was obtained. The analysis of the substance gave $N=15.52\%$, theory for $C_{18}H_{22}O_4N_4$, $N=15.64\%$.

B. *1-Benzoyl 2,3,4,6-Tetra-acetyl Glucose.* 1.4 gr. of acetic acid anhydride was added to a solution of 0.7 gr. of 1-benzoyl 3,4,6-triacetyl glucose in 2.1 gr. of pyridine, the mixture was poured into ice water, whereon white crystals (ca. 0.7 gr.) were precipitated, and the substance purified from hot absolute alcohol solution, melts at 145°–146°.

This substance is soluble in chloroform, acetone, benzene, ether, slightly soluble in alcohol, petroleum ether, but insoluble in water.

Rotatory power in chloroform: $[\alpha]_D^4 = \frac{-0.45-0.12}{0.2158 \times 1} \times 100 = -26.43°$.

Anal. Subst. $= 0.1081$; $CO_2 = 0.2192$; $H_2O = 0.0538$ gr. Found: $C = 55.30$; $H = 5.53\%$.

Calc. for $C_{21}H_{24}O_{11}$: $C = 55{\cdot}8$; $H = 5.3\%$.

Molecular weight by Rast's method shows 444, theory 452 for $C_{21}H_{24}O_{11}$.

C. *1,2-Dibenzoyl 3,4,6-Triacetyl Glucose.* 1.0 gr. of benzoyl chloride was added to a solution of 0.6 gr. of 1-benzoyl 3,4,6 triacetyl glucose dissolved in 2.5 gr. of pyridine, and the mixture was left to stand at room temperature for one day, and then poured into ice water, whereon an oily substance was obtained, which solidified gradually. It was dissolved in chloroform, treated with sodium bicarbonate solution, washed with water, dried with anhydrous sodium sulphate, and the chloroform distilled off. The benzoyl acetyl glucose thus obtained, was purified in white crystals having a melting-point of 149°. It is soluble in chloroform, acetone, ether; slightly soluble in alcohol, petroleum ether; but insoluble in water.

$[\alpha]_D^5 = \frac{-0.20-0.12}{0.2031 \times 1} \times 100 = -15.7°$ (in chloroform)

Anal. Subst. $= 0.1069$; $CO_2 = 0.2364$; $H_2O = 0.0509$ gr. Found: $C = 60.31$; $H = 5.27\%$.
Calc. for $C_{26}H_{26}O_{11}$: $C = 60{\cdot}7$; $H = 5.06\%$.

The molecular weight by Rast's method being 506, agrees with the calculated value, 514 for $C_{26}H_{26}O_{11}$

For the preparation of 1, 2-dibenzoyl 3, 4, 6-triacetyl glucose, 1, 2-anhydro 3, 4, 6-triacetyl glucose (m. p. $= 56° - 57°$, $[\alpha]_D^{20} = +106.8°$ in benzene) prepared by the method by Brigl⁽¹⁾ was used; 2 gr. of the substance dissolved in 100 c.c. of water at room temperature and dried in a vacuum desiccator to a syrup to form 3, 4, 6-triacetyl glucose,⁽²⁾ which dissolved in 3.0 gr. of pyridine, and 1.5 gr. of benzoyl chloride were added, and the mixture was left to stand for two days, then poured into ice water, whereon an oily substance was obtained, separated, and dissolved in chloroform, treated with sodium bicarbonate solution, washed with water and dried with anhydrous sodium sulphate. By distilling off the chloroform, there were

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(1) Loc. cit.

(2) P. Brigl., loc. cit.

obtained white crystals of a melting-point of 149°. The properties of the substance agree well with those of 1, 2-dibenzoyl 3, 4, 6-triacetyl glucose.

$$[\alpha]_D^8 = \frac{-0{\cdot}12 - 0{\cdot}13}{0{\cdot}1402 \times 1} \times 100 = -17{\cdot}8^\circ \text{ (in chloroform)}$$

Anal. Subst.=0·1011; CO_2=0.2239; H_2O=0.0478 gr. Found: C=60.40; H=5.25%. Calc. for $C_{26}H_{26}O_{11}$: C=60.7; H=5.06%.

The molecular weight by Rast's method gave 507, ($C_{26}H_{26}O_{11}$=514).

1-Desoxy 3, 4, 6-Triacetyl Glucose. The filtrate separated from the crystals of 1-benzoyl 3, 4, 6-triacetyl glucose was poured drop by drop into ice water, whereon a white substance (A) was precipitated, weighing ca. 10 gr., on this being filtered, and the filtrate was concentrated to a syrup under reduced pressure at ordinary temperature, a white semi-solid substance (B) was yielded (ca. 0.6 gr.); this was filtered, and the final filtrate again concentrated to a slightly yellow-coloured syrup. This residue was changed to crystals on being left standing in a ice box, the yield being about 1.4 gr. By recrystallisation from hot 94% alcohol, it melted at 122°. It is soluble in hot ethyl alcohol, acetic acid and water, slightly soluble in benzene and ether, but it does not reduce Fehling's solution before and after treatment with dilute sulphuric acid, and does not oxidise Schiff's reagent. Nor does this substance give silver mirror with ammoniacal silver nitrate, nor change with dilute alkali solution.

Rotatory power in chloroform: $[\alpha]_D^7 = \frac{+0.30 - 0.12}{2.06 \times 1} \times 100 = +8.7^\circ$

The dried substance gave the following analytical results:

Anal. Subst.=0.1158; CO_2=0.2112; H_2O=0.0686 gr. Found: C=49.74; H=6.58%. Calc. for $C_{12}H_{18}O_8$: C=49.7; H=6.2%.

Molecular weight by cryoscopic method in glacial acetic acid shows 283 ($C_{12}H_{18}O_8$=290).

Acetyl value was estimated and the results agreed with the triacetyl in the molecule.

The precipitate (A) was found to consist of a mixture of 0.7 gr. 1-benzoyl 3, 4, 6-triacetyl glucose and 0.3 gr. of 1-desoxy 3, 4, 6-triacetyl glucose.

The Isomer of 1-Benzoyl 3, 4, 6-Triacetyl Glucose. The semi-solid substance (B) was obtained in white crystals (ca. 0.15 gr.) m.p.=168° from an absolute alcohol solution. It reduces Fehling's solution when hot, and it's alcohol solution changes into yellow when heated with dilute alkali. The substance dried on a porcelain tile gave the following analytical results:

Anal. Subst. = 0.1036; $CO_2 = 0.2094$; $H_2O = 0.0565$ gr. Found: C = 55.13; H = 6.06%. Calc. for $C_{19}H_{22}O_{10}$: C = 55.6; H = 5.3%.

The molecular weight by Rast's method gave 401.

From the analytical results and also the chemical properties, it was ascertained to be an isomer of 1-benzoyl 3, 4, 6-triacetyl glucose.

Acetyl Sugar. From the filtrate separated from 1-desoxy 3, 4, 6-triacetyl glucose, 0.4 gr. of the syrup were obtained, which gradually changed to needle crystals. This substance is soluble in alcohol, ether and water, but insoluble in petroleum ether. It reduces Fehling's solution when hot.

$$[\alpha]_D^9 = \frac{+1.07-0.14}{0.2106 \times 1} \times 100 = +44.15^\circ \quad \text{(in chloroform)}$$

IV. Action of Perbenzoic Acid on Diacetyl Pseudo-glucal. A cold solution of 7.5 gr. of diacetyl pseudo-glucal dissolved in 50 c.c. of chloroform were added to an ice-cooled solution of 220 c.c. of perbenzoic acid-chloroform (the amount of active oxygen in 1 c.c. of the solution corresponded to 3.80 c.c. of the N/10 $Na_2S_2O_3$ solution). The progress of reaction was very slow, as shown in the following Table 4, and almost all of the substance remained unchanged.

Table 4.

Reaction temp.	Reaction time	Number of c.c. of $\frac{N}{10}$ $Na_2S_2O_3$ solution required for 1 c.c. of the solution
0°	Soon after addition	3.14
0°	0.5 h ,, ,,	3.14
0°	3.5 h ,, ,,	3.06
8°	24.0 h ,, ,,	2.85
8°	48.0 h ,, ,,	2.85
9°	72.0 h ,, ,,	2.90

In conclusion, the present writer wishes to express his hearty thanks to Prof. S. Komatsu for his masterly guidance and also to Prof. Nodzu for his invaluable advice.

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