SYNTHESIS OF *d*-TALOSE FROM *d*-GALACTOSE.

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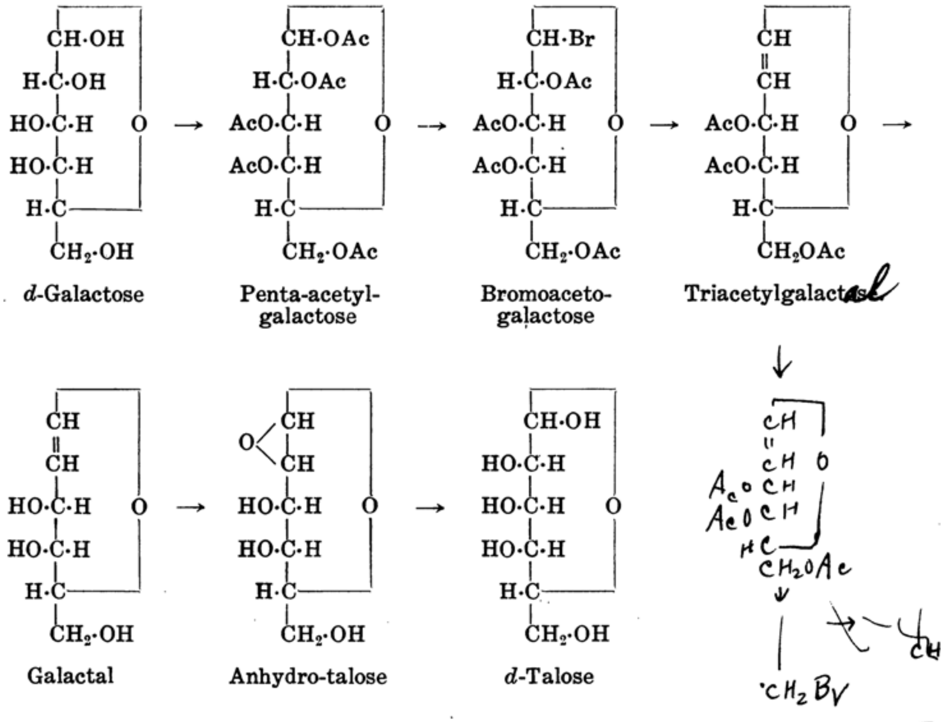
Whilst the research reported in this paper was in progress, Levene and his collaborator⁽¹⁾ published the results of an investigation of the same subject. Accordingly, the results already obtained, though somewhat imperfect, are published in their present form.

It has been shown by Bergmann and Schotte⁽²⁾ that *d*-glucose is converted into *d*-mannose by the action of perbenzoic acid on the glucal derived from the former. By a similar method, the present author prepared *d*-talose from *d*-galactose through galactal as shown in the following scheme:



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(1) *J. Biol. Chem.*, **93** (1931), 631.

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

Experimental.

Preparation of Penta-acetylgalactose and its Conversion into Acetobromogalactose.

Penta-acetylgalactose was first prepared by Erwig and König's method(1) by heating *d*-galactose with freshly distilled acetic anhydride and fused sodium acetate, and the acetate was then by Fischer and Armstrong's method(2) converted into acetobromogalactose by the action of hydrogen bromide in glacial acetic acid on it.

Preparation of Triacetylgalactal. Thirty grams of acetobromogalactose were mixed with 60 gr. of zinc dust and 300 c.c. of cold 50 per cent. aqueous acetic acid. The mixture was shaken for one hour and a half, and the zinc dust was filtered off. The colourless filtrate was diluted with water, and extracted several times with ether. The ethereal solution was washed with water, neutralised with a solution of sodium bicarbonate, and again washed with water. After being dried over anhydrous sodium sulphate, the ethereal solution was evaporated. The faint yellow viscid oil thus obtained was subjected to fractional distillation under a high vacuum of 0.3–0.4 mm., when a fraction boiling at 128.5–154°C. (principally 149–154°C.) was collected. On repeating the fractional distillation, an almost colourless syrup boiling at 128.5–140°C. (principally 138–140°C.) under 0.2–0.3 mm. passed over:

Anal.: Subst. = 3.125 mg. $CO_2 = 6.107$; $H_2O = 1.740$ mg.
Found: C = 53.30; H = 6.23%. Calc. for $C_{12}H_{16}O_7$: C = 52.94; H = 5.88%.

Addition of Bromine and Hydrogen. An excess of chloroform solution of bromine of known strength was added to a solution of the syrup in the same solvent and, after standing for a few minutes, potassium iodide solution and dilute sulphuric acid were added, and the liberated iodine was titrated with a N/10-sodium thiosulphate solution: 0.1120 gr. absorbed 0.0695 gr. of bromine. A solution of one gram of the syrup in absolute ether absorbed 90 c.c. of hydrogen at 0° and 760 mm. in the presence of platinum black.

$C_{12}H_{16}O_7$, with an ethylenic linking, requires 0.0660 gr. of bromine and 82 c.c. of hydrogen. From these facts, there can be little doubt that the syrup is triacetylgalactal.

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(1) *Ber.*, **22** (1889), 2207.
(2) *Ber.*, **35** (1902), 837.

Preparation of Galactal from Triacetylgalactal. From the analogy of glucose, the use of methyl alcoholic ammonia appears to be a suitable method of hydrolysing the acetylgalactal, because triacetylglucal is readily hydrolysed by the same reagent. As, however, the yield was unsatisfactory, the present author resorted to Zemplén's method.

A solution of triacetylgalactal (5 gr.) in chloroform (12.5 c.c.) was mixed with a solution of sodium (0.25 gr.) in absolute methyl alcohol (12.5 c.c.) at about –20°C., and the additive compound was hydrolysed by ice-cold water to ethyl acetate and galactal. After being neutralised with dilute hydrochloric acid, the aqueous layer was separated from the chloroform layer, shaken with animal charcoal, and filtered. The filtrate was evaporated to complete dryness under diminished pressure, when a colourless syrup was obtained. This syrup was freed from sodium chloride by dissolving it in cold absolute alcohol and filtering off any insoluble matter. In order to remove the last traces of sodium chloride, the operation was repeated several times. The syrup thus purified was still further purified by repeatedly dissolving it in cold absolute alcohol and precipitating it with absolute ether, when colourless needles were obtained in an almost quantitative yield, which melted at 95–100°C. with somewhat decomposition. The galactal thus obtained was to some extent hygroscopic, and still contained the traces of ash, which were very difficult to remove by recrystallisation. It readily decolorises bromine in a chloroform solution. For the next preparation, it was used without further purification.

Preparation of *d*-Talose from Galactal. For this purpose, perbenzoic acid was first prepared by a slight modification of Hibbert and Burt's method,(1) namely by carrying out each stage of reactions as rapidly as possible.(2) To a solution of 10 gr. of galactal in 120 c.c. of water, a solution of perbenzoic acid (12.6 gr.) in chloroform (70 c.c.) was added, and the mixture was cooled to about 0°C., stirred vigorously for an hour and left overnight in ice-cold water. The aqueous layer was separated from the chloroform layer, washed several times with ethyl acetate, and evaporated to a small bulk under diminished pressure.

An aliquot portion was treated with an excess of phenylhydrazine and warmed on a water-bath, when yellow crystals, melting at 184–185°C., were obtained, which were identified as galactosazone by the mixed melting point method.

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(1) *J. Amer. Chem. Soc.*, **47** (1925), 2240.

(2) When a chloroform solution of perbenzoic acid was kept in a dark place without being previously dried, no appreciable change was observed in the concentration, even after standing for one month and a half.

The remainder was evaporated to a syrupy consistency and a solution of 1.3 gr. of the syrup in 0.5 c.c. of water was then mixed with 0.78 gr. of phenylhydrazine. After standing for three hours, the pale yellow crystals were collected, washed with ether, and purified by dissolving them in absolute alcohol, and precipitating them with absolute ether. After being washed with ether, and dried over a vacuum desiccator, they melted with decomposition at 150–178°C. As the melting points of talose and galactose phenylhydrazones are 178°C. and 160–161°C., respectively, the product consisted presumably of a mixture of *d*-talose and *d*-galactose phenylhydrazones.

Preparation of the α-Methylphenylhydrazone. A solution of the syrup (1 gr.) in water (5 c.c.) was mixed with an absolute alcoholic solution of α-methylphenylhyrazine (0.9 gr.) and the mixture was warmed on a water-bath for a short time, when colourless needles were obtained, which were collected after standing for three hours. After being successfully washed with alcohol and with ether, the crystals (m.p. 160–164°C.) were recrystallised from 30 per cent. methyl alcohol, from which they separated in colourless crystals, melting at 181.5–182°C. A mixed melting point determination with an authentic galactose-α-methylphenylhydrazone (m.p. 189–190°C.) gave m.p. 176–177°C.

From these facts, it appears that the syrup consisted of galactose and talose.

For the isolation of talose, the syrup was treated as follows: Five grams of the syrup were dissolved in water (25 c.c.) and an absolute alcoholic solution of the calculated quantity of α-methylphenylhydrazine was mixed. The mixture was allowed to stand overnight in the dark, when colourless needles of α-methylphenylhydrazone separated, which were collected, washed with absolute alcohol, and dried in a vacuum desiccator. The crystals (I) have a melting point of 165–166°C. This was recrystallised from 30 per cent. methyl alcohol, from which it separated in the crystals (II) melting at 177–178°C. Crystals (II) were again recrystallised from 30 per cent. methyl alcohol, from which they separated in colourless crystals (III) melting at 181–181.5°C. The yield was 2 gr. The mother liquor from crystals (I) was concentrated to a small bulk on a water-bath, when the crystals (IV) separated, which, after being diluted with water, were collected. The crystals were washed with the least possible quantity of absolute alcohol and ether, and then dried in a vacuum, when they melted at 152–153°C. The crystals were recrystallised twice from 30 per cent. methyl alcohol, from which they separated in the crystals (V) melting at 153–153.5°C.

Talose-α-methylphenylhydrazone was thus separated from galactose-α-methylphenylhydrazone by taking advantage of the great solubility of the former in methyl alcohol.

Crystals (III) and (V) were analysed with the following results:—

(1) Analysis of Crystals (III): 3.029 Mg. of the air-dried substance lost 0.123 mg. on heating at 105–106°C. under diminished pressure. Found: $H_2O = 4.07\%$. Calc. for $C_{13}H_{20}O_5N_2$, H_2O : $H_2O = 5.96\%$.

Anhydrous substance = 2.906; $CO_2 = 5.809$; $H_2O = 1.693$ mg. And subst. = 3.830 mg.; $N_2 = 0.321$ c.c. at 14.5°C. and 761.7 mm. Found: C = 54.52; H = 6.52; N = 9.97%. Calc. for $C_{13}H_{20}O_5N_2$: C = 54.90; H = 7.04; N = 9.86%.

(2) Analysis of Crystals (V): This substance contained no water of crystallisation. Subst. = 3.235; $CO_2 = 6.516$; $H_2O = 2.075$ mg. And subst. = 3.320 mg.; $N_2 = 0.276$ c.c. at 15°C. and 761.8 mm. Found: C = 54.93; H = 7.01; N = 9.88%. Calc. for $C_{13}H_{20}O_5N_2$: C = 54.90; H = 7.04; N = 9.86%.

Decomposition of the α-Methylphenylhydrazone (m.p. 181–181.5°C.) **with Benzaldehyde.** The α-methylphenylhydrazone (0.5 gr.) was mixed with a solution of benzaldehyde (0.6 gr.) in 50 per cent. alcohol (11 c.c.) and the mixture was heated on a water-bath for about two hours, when an oily product separated, which, on cooling, solidified to a pale yellow mass. After being allowed to stand overnight, it was collected, washed with alcohol and dried. The crystals thus obtained melted at 104–105°C., and this melting point was not altered on admixture with an authentic specimen of benzaldehyde-α-methylphenylhydrazone. The filtrate from the benzaldehyde-α-methylphenylhydrazone was diluted with water and most of the alcohol was removed by evaporation. After being extracted with ether, the aqueous residue was evaporated and dissolved in hot alcohol, which, on cooling, separated as colourless crystals. This was washed with 80 per cent. alcohol, when it melted at 164–165.5°C. and produced no depression of the melting point on admixture with an authentic specimen of *d*-galactose. Its specific rotation was $[\alpha]_D^{19} = +78.8°$ (in water).

The Decomposion of the α-Methylphenylhydrazone (m.p. 153–153.5°C.) **with Benzaldehyde.** The decomposition of the α-methylphenylhydrazone (0.3 gr.) with a solution of benzaldehyde (0.6 gr.) in alcohol (6 c.c.) and the treatment of the filtrate from benzaldehyde-α-methylphenylhydrazone were carried out similarly as in the case of the above fraction. The aqueous solution was evaporated to a small bulk, decolorised with animal charcoal, and again evaporated to dryness, when a colourless mass was obtained, which was recrystallised from water. The specific rotation of the crystals in water was $[\alpha]_D^{17} = +14.8°$.

Owing to the lack of the available substance, no determination of the melting point was made with certainty.

In conclusion, the author wishes to express his hearty thanks to Professor Hiroshi Nomura, under whose guidance this investigation was carried out.

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