The Formation of *d*-Erythrulose.

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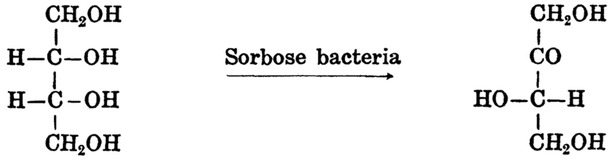
The syntheses of monoses were recently much investigated, and all the aldo- and keto-sugars of hexoses and pentoses, whose existence is supposed by theory, have already been prepared. As for tetroses, among the six theoretically possible forms, *d*-erythrulose has been the only sugar hitherto not synthetized. Its antipode, *l*-erythrulose, or *l*-2-keto-tetrose, was prepared by G. Bertrand(1) by oxidative fermentation of erythritol with sorbose bacteria (*bacterium xylinum*) about forty years ago, and its crystalline derivative was prepared by H. Müller, C. Montigel and T. Reichstein(2) in recent year. This biochemical method, however, is of course unavailable for the formation of *d*-form.



$$\begin{array}{c} CH_2OH \\ | \\ H-C-OH \\ | \\ H-C-OH \\ | \\ CH_2OH \end{array} \xrightarrow{\text{Sorbose bacteria}} \begin{array}{c} CH_2OH \\ | \\ CO \\ | \\ HO-C-H \\ | \\ CH_2OH \end{array}$$

Erythritol *l*-Erythrulose

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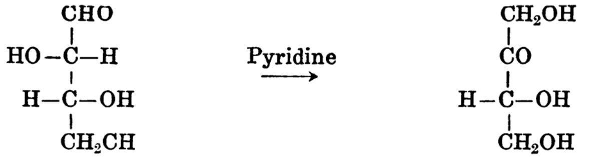
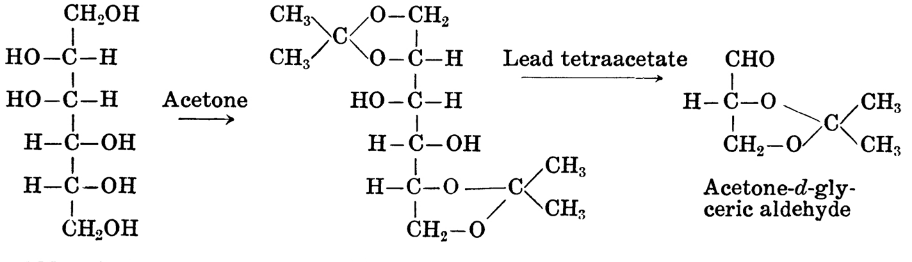
(1) G. Bertrand, *Compt. rend.*, **130** (1900), 1330. In this literature the sugar is written as *d*-erythrulose by old nomenclature, but it is quite clear from the reduction product that it should be *l*-form.

(2) H. Müller, C. Montigel, and T. Reichstein, *Helv. Chim. Acta*, **20** (1937), 1468.

In general, aldoses can be partly transformed to ketoses by heating them with organic bases such as pyridine or quinoline.(3) So *d*-threose was heated with pyridine at various temperatures in order to obtain *d*-erythrulose by epimerization. However, the mixture soon became quite dark, and *d*-erythrulose could not be obtained by this way.


d-Threose *d*-Erythrulose

So the method of R. Prince, K. Gätzi, and T. Reichstein(4) for preparing ketose by the addition of diazo-methane on the acetone derivative of glyconic acid chloride, which has one carbon atom less than the ketose to be obtained, was used successfully for this preparation of *d*-erythrulose. For this purpose, first of all, acetone-*d*-glyceric aldehyde is prepared from *d*-mannitol according to the method of H. O. L. Fischer and E. Baer.(5) That is, *d*-mannitol is shaken mechanically with acetone adding hydrochloric acid for condensing agent, then the mixture is neutralized with lead carbonate, and, after the removal of the solvent by distillation, 1,2,5,6-diacetone-*d*-mannitol is separated from triacetone-mannitol. The former is oxidized with lead tetraacetate, and thus acetone-*d*-glyceric aldehyde is obtained, the boiling points of which are 54° at 12 mm. and 63° at 20 mm.


Acetone-*d*-glyceric aldehyde

d-Mannitol 1,2,5,6-Diacetone-*d*-mannitol

Acetone-*d*-glyceric aldehyde thus prepared is oxidized by potassium permangante in alkaline solution, and the potassium salt of acetone-*d*-glyceric acid is obtained in colourless crystalline powder. Its specific rotatory power is $[\alpha]^{15}_{D} = +23.7°$ ($c = 2.11$ in water). The potassium salt of acetone-*d*-glyceric acid is heated with thionyl chloride in ether solution and acetone-*d*-glyceric acid chloride is obtained. Freshly distilled chloride has specific rotatory power $[\alpha]^{15}_{D} = +14.9°$ ($c = 1.6$ in ether). Acetone-*d*-glyceric acid amide is prepared by pouring the chloride into ammonia

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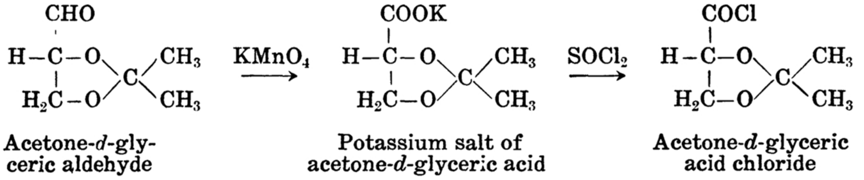
(3) S. Danilow, E. V. Danilowa, and P. Schantorowitsch, *Ber.*, **63** (1930), 2271; K. Iwadare and B. Kubota, *Sci. Papers Inst. Phys. Chem. Research* (Tokyo), **34** (1938), 183.

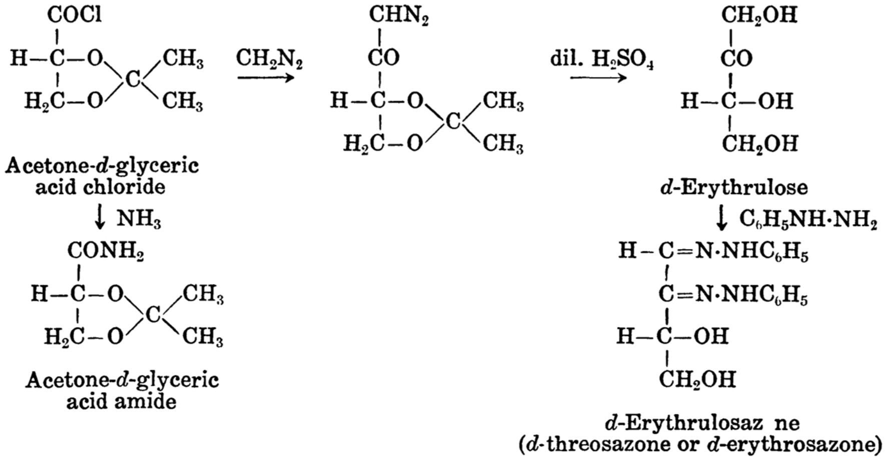
(4) K. Gätzi and T. Reichstein, *Helv. Chim. Acta*, **21** (1938), 186; R. Prince, Diss. Zürich, 1937.

(5) H. O. L. Fischer and E. Baer, *Helv. Chim. Acta*, **17** (1934), 622.

in ether solution. It melts at 72–73° and has specific rotatory power $[\alpha]^{16}_{D} = +39.1°$ $(c = 0.8$ in water).



Ether solution of acetone-*d*-glyceric acid chloride is slowly poured into diazo-methane solution in ether, cooled with freezing mixture. After a day's standing, the solution is evaporated, and the residual diazo-ketone is submitted to hydrolysis by heating with dilute sulphuric acid. *d*-Erythrulose thus obtained is distilled in vacuo. Colourless syrup with specific rotatory power $[\alpha]^{15}_{D} = -11 \pm 3°$ in dilute solution. This value is in good agreement with that of *l*-erythrulose $([\alpha]^{18}_{D} = +11.4° \pm 1°)$, which was reported by H. Müller, C. Montigel, and T. Reichstein.⁽²⁾ *d*-Erythrulose solution reduces Fehling's solution at once in the cold. Its osazone melts at 168°. (Found: N, 18.64. Calc. for $C_{16}H_{18}O_2N_4$: N, 18.72%). This melting point agrees with that of *d*-threosazone, which was prepared from *d*-threose by the author. So we may be able to say that *d*-erythrulose is now formed.



Experimental.

Acetone-*d*-glyceric aldehyde. Three hundred grams of *d*-mannitol were mechanically shaken with 6 kg. of acetone and 150 c.c. of concentrated hydrochloric acid for about four hours, excess of lead carbonate or potassium carbonate was added, and the mixture was stirred mechanically. After neutralization, it was filtered, and acetone was removed by distillation. The residual crystalline mass was dissolved in 200 c.c. of alcohol and poured into 2 or 3 litres of water with stirring. The mixture was filtered and evaporated in vacuo, and the residue was dissolved in water. It was again filtered and evaporated. Thus about 100 g. of crude diacetone-mannitol was obtained. It was dissolved in 5 *l*. of petroleum benzine and filtered as soon as the solution was cooled to room temperature. Yield, about 25 g.

Thirty grams of diacetone-*d*-mannitol was dissolved in 1 litre of benzene, and 50 g. of lead tetraacetate was added. After an hour it was filtered and neutralized with diazo-methane, and the greater part of the solvent was removed by distillation. Then it was fractionally distilled at diminished pressure. Acetone-*d*-glyceric aldehyde distilled at 54° at 12 mm., and 63° at 20 mm. Yield, 13 g.

Potassium salt of acetone-*d*-glyceric acid. Ten grams of aldehyde were dissolved in 600 c.c. of water and the solution of 6.5 g. of potassium hydroxide and 10 g. of potassium permanganate in 600 c.c. of water was added drop by drop to it, the mixture being stirred vigorously. After two hours it was filtered, and the filtrate was neutralized with dilute sulphuric acid and evaporated in vacuo to dryness. It was dissolved in absolute alcohol, filtered from inorganic salt, again evaporated to thin syrup, and ether was added to it. Precipitated potassium salt was filtered and recrystallized from alcohol. Its specific rotatory power is $[\alpha]_D^{15} = +23.7°$ ($c = 2.11$ in water). (Found: K, 21.63. Calc. for $C_6H_9O_4K$: K, 21.23%).

Acetone-*d*-glyceric acid chloride. Five grams of potassium salt was suspended in 40 c.c. of ether and 3 g. of thionyl chloride added. The mixture was boiled on a water bath for two hours and filtered. From the filtrate ether and the most of thionyl chloride were removed by distillation, and the residue was fractionally distilled at diminished pressure. The chloride distilled at 61° at 15 mm. It is a clear colourless liquid, with $[\alpha]_D^{15} = +14.9°$ ($c = 1.6$ in ether). Yield, 1 g.

Acetone-*d*-glyceric acid amide. To an excess of etherial solution of ammonia, 0.3 g. of chloride was added. It was then filtered from ammonium chloride and evaporated to syrup. The latter was dissolved in benzene, and soon crystallized. Recrystallized from benzene its melting point was 72–73°. $[\alpha]_D^{16} = +39.1°$ ($c = 0.8$ in water). (Found: N, 9.78. Calc. for $C_6H_{11}O_3N$: N, 9.65%).

***d*-Erythrulose.** One gram of acetone-*d*-glyceric acid chloride was dissolved in 150 c.c. of absolute ether and poured into 1.5 g. diazo-methane dissolved in 60 c.c. of ether, cooling with freezing mixture. After a day's standing, the solution was filtered and evaporated, and the yellow syrup of diazo-ketone was hydrolysed by heating with 100 c.c. of 1% sulphuric acid on the water bath for two hours. Then it was neutralized with freshly precipitated barium carbonate and filtered with active charcoal. The filtrate was evaporated in vacuo to syrup and *d*-erythrulose distilled at 68° at 0.01 mm., the temperature of the bath being 100–105°. Its specific rotatory power was $[\alpha]_D^{15} = -11° \pm 3°$.

***d*-Erythrulosazone.** *d*-Erythrulose was dissolved in water and heated with excess of phenylhydrazine and acetic acid for three hours. The separated oily substance was crystallized from alcohol. Melting point, 168° (Found: N, 18.64. Calc. for $C_{16}H_{18}O_2N_4$: N, 18.72%).

Summary.

(1) *d*-Erythrulose was formed by the hydrolysis of diazo-ketone which was obtained by condensing diazo-methane with acetone-*d*-glyceric acid chloride.

(2) Potassium salt of acetone-*d*-glyceric acid ($[\alpha]_D^{15} = +23.7°$), acetone-*d*-glyceric acid chloride ($[\alpha]_D^{15} = +14.9°$) and acetone-*d*-glyceric acid amide ($[\alpha]_D^{16} = +39.1°$) were obtained.

In conclusion the author wishes to express his hearty thanks to Prof. B. Kubota for his kind advice for this experiment.

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