On the Action of Phosphate upon Hexoses. IV.
Formation of Lactic Aldehyde side by side with Acetol.

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In the previous papers⁽¹⁾ of this series, it has been reported that when a mixture of glucose and a slightly acidic (pH 7-5) concentrated solution of potassium phosphate (about 40%) was distilled, acetol was

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(1) R. Nodzu and his co-workers, this Bulletin, **10** (1935), 122; 467; *Mem. Coll. Sci. Kyoto Imp. Univ.*, **20** (1937), 197.

found in the distillate, accompanied by small quantities of methylglyoxal, diacetyl and some indistinct substances, and that pyruvic acid was present in the distillation residue. From these facts, we have postulated that under these conditions glucose molecule may split into acetol and pyruvic acid, as well as into others.

In the present work, the same distillation experiment was repeated with a larger amount of the materials and the distillate was studied more thoroughly. Besides acetol and the other products described above, the presence of lactic aldehyde and of pyruvic acid was confirmed. At first sight, the appearance of lactic aldehyde side by side with acetol was somewhat surprising, since it has long been known⁽²⁾ that the former transforms very easily into the latter. It was found, however, that by the same distillation process, not only lactic aldehyde did convert almost completely into acetol, but the reverse process also took place and a small portion of the acetol changed into lactic aldehyde. Hence, at least in the solution of phosphate, both substances seem to be in a relation of desmotropic equilibrium:

$$\underset{\text{Acetol}}{CH_3COCH_2OH} \rightleftarrows \underset{\text{Lactic aldehyde}}{CH_3CHOHCHO}$$

shifting far on the left hand side. It is accordingly indecisive which of the two is the precursor in the postulated scheme of cleavage of glucose molecule:

$$\underset{\text{Glucose}}{C_6H_{12}O_6} \xrightarrow{-H_2O} \underset{\text{(Acetol or Lactic Aldehyde)}}{C_3H_6O_2} + \underset{\text{Pyruvic acid}}{CH_3COCOOH}$$

Experimental Part.

Glucose. The distillate⁽³⁾ (about 9 litres, about 5g. acetol) obtained from a mixture of 200g. glucose and 2 litres of 40% potassium phosphate solution (pH 5,2–5,6), was warmed on a boiling water bath for about half an hour with enough semicarbazide hydrochloride and sodium acetate to equal eight equivalents of the acetol content, was left to stand over night, and then filtered. The filtrate was evaporated⁽⁴⁾ to about 500 c.c. under a reduced pressure of carbon dioxide. After filtering off a yellowish white precipitate, the filtrate was concentrated further until an appreciable amount of precipitate reappeared and then filtered again. Repeating this process several times, four kinds of precipitates tabulated were obtained.

	m.p.	g.
I.	258°	0.7
II.	195°	4.8
III.	190°	2.35
IV.	239°	0.17

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(2) Nef (*Ann.*, **335** (1904), 247.) has suggested that "Das Acetol ist mit Oxyaceton identisch; der isomere r-Milchsäurealdehyd, r-$CH_3CHOHCHO$, existirt nicht, sondern geht in Acetol über." A. Wohl, *Ber.*, **41** (1908), 3599.

(3) The distillation, and the estimation of the iodine-consuming substances such as acetol in the distillate were carried out in the same ways as described in the previous papers. (R. Nodzu, *loc. cit.*)

(4) During the course of evaporation, some iodine-consuming substance which has no reducing power for Fehling solution, was distilled. This distillate presents an interesting subject for research.

On further meticulous fractional crystallization of these precipitates from hot water, the followings were isolated: From I, diacetyl-bis-semicarbazone (m.p. 279–280°) and methylglyoxal-bis-semicarbazone (m.p. 262–264°); from II and III, mainly acetol semicarbazone (m.p. 197–198°), and pyruvic acid semicarbazone (m.p. 212–213°) and diacetyl-mono-semicarbazone (m.p. 227–228°) in a small quantity; from IV, lactic aldehyde semicarbazone (m.p. 246–247°) and acetol semicarbazone. Besides these semicarbazones, hydrazodicarbonamide (m.p. 257-258°) was isolated from II, III, and IV. These semicarbazones were all identified by the mixed melting point determinations. Another similar experiment at pH 6.2–6.6 was made with similar results, as will be seen in Table 1 in which the former results are also cited.

Table 1.

No.	Glucose g.	K-phosphate mixture 40%		Distillate c.c.	Iodine consuming substance as acetol g.	Semicarbazones g.				
		pH.	c.c.			m.p. 278°	m.p. 261°	m.p. 245°	m.p. 211°	m.p. 197°
1	200	5.2–5.6	1000	9000	4.92	0.1	0.05	0.06	0.02	5.51
2	200	6.2–6.6	1000	9000	5.18	0.08	0.06	0.08	0.01	4.40

Acetol and Lactic aldehyde. Acetol (b.p. 53–54°/78mm.; semicarbazone m.p. 198–199°) was synthesized from monobromoacetone following A. Levene and A. Walti.⁽⁵⁾ Lactic aldehyde (m.p. 105–107°; semicarbazone m.p. 245–247°, Found N. 32.24 Calc. for $C_4H_9O_2N_3$: N. 32%; 2.4-dinitrophenylhydrazone m.p. 154–155°) was prepared by hydrolysis of monobromacetal, following R. Dwarzak and W. Prodinger.⁽⁶⁾ On treating with semicarbazide, the acetol gave only its semicarbazone and nothing of lactic aldehyde, and the lactic aldehyde also its semicarbazone only.

Thus it was confirmed that the acetol and the lactic aldehyde were free each from the other. The distillation of these substances with the phosphate solution and the analysis of distillates were carried out in the same ways as described in the case of glucose. The results of experiments are summerized in Tables 2 and 3.

Semicarbazones of methylglyoxal (m.p. 262–264°), lactic aldehyde (m.p. 246–247°) and acetol (m.p. 197–198°) in these tables, were respectively identified by the mixed melting point determination.

Table 2.

No.	Acetol g.	K-phosphate mixture 40%		Distillate c.c.	Iodine consuming substance as acetol g.	Semicarbazones g.		
		pH.	c.c.			m.p. 262°	m.p. 246°	m.p. 197°
1	1.0	5.2–5.6	100	1200	0.64	0.02	0.02	1.15
2	1.0	6.2–6.6	100	1200	0.68	0.03	0.02	1.25

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(5) A. Levene and A. Walti, *Organic Syntheses*, Vol. **10** (1930), 1.

(6) R. Dwarzak and W. Prodinger, *Monatsh*, **48** (1927), 252; **50** (1928), 459.

Table 3.

No.	Lactic aldehyde g.	K-phosphate mixture 40%		Distillate c.c.	Iodine consuming substance as acetol g.	Semicarbazones g.		
		pH.	c.c.			m.p. 262°	m.p. 246°	m.p. 197°
1	0.5	5.2–5.6	100	1500	0.43	Trace	0.1	0.35
2	0.5	5.2–5.6	100	1500	0.43	Trace	0.08	0.32
3	0.5	6.2–6.6	100	1500	0.4	Trace	0.1	0.4

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