An Anomalous Tischenko Reaction

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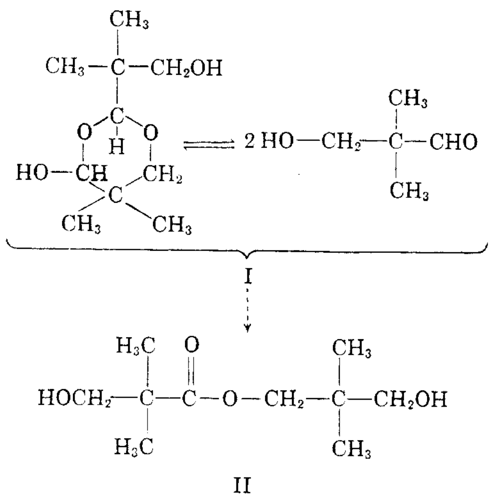
The self-condensation of aldehydes to yield esters has been known for some time. In studying the Cannizzaro reaction, Claisen[1] found that the use of sodium alkoxides with benzaldehyde gave benzyl benzoate. Tischenko[2] showed that aluminum alkoxides as catalysts gave still better results and that they worked as well with aliphatic aldehydes as with aromatic aldehydes. Villani and Nord[3] more recently have shown the effect of the basicity of the alkoxide on the type of product obtained. However, all usual Tischenko reactions require the use of a metal alkoxide and the complete absence of water. The latter requirement is due primarily to destruction of the catalyst by hydrolysis with the water.

It has now been found that hydroxypivalaldehyde (I), shown by Spath and Szilagyi[4] to exist as a monomer and a dimer, will undergo self-condensation to 3-hydroxy-2,2-dimethylpropyl 3-hydroxy-2,2-dimethylpropionate ester (II) in the absence of the usual catalysts and in the presence of water.



It has been found that heat is all that is required to bring about this condensation in good yield without a catalyst,[5] and that it is difficult to prevent the reaction from taking place if I is heated.

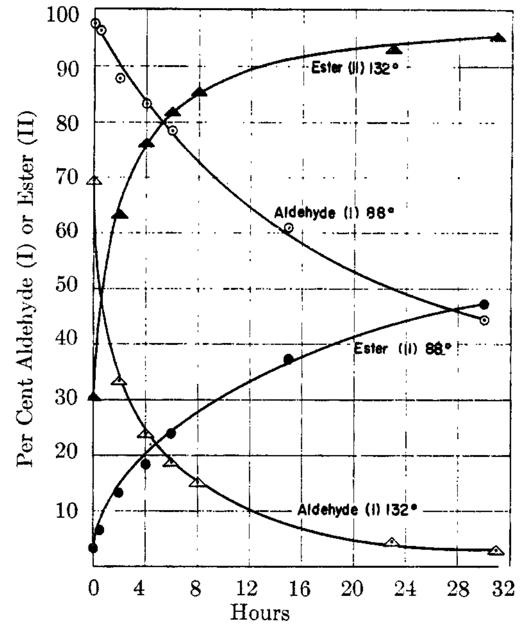


Fig. 1. Tischenko reaction of hydroxypivalaldehyde without catalyst. Aldehyde concentration versus time at 88°, ⊙; aldehyde concentration versus time at 132°, △; ester concentration versus time at 88°, ●; ester concentration versus time at 132°, ▲

The effect of temperature on the rate of condensation was determined by following the extent of the reaction at 88° and at 132°. Fig. 1 shows the effect of temperature on the concentrations of I and II with respect to time. Although the composition *versus* time curves are quite smooth, attempts at fitting first, second, or third order rate equations to the data were not successful. This probably results because with such high concentrations the composition of the system is continuously changing, giving in effect a continuously changing solvent and a changing activity coefficient. The half life of the aldehyde is approximately thirty hours at 88° and approximately forty-eight minutes at 132°. The condensation appears to take place equally well with carefully refined I or with I obtained in crude stripped form, as shown in Table I by the rate of formation of II at 95 and 98° with the lowest water ratio. Also, crude I has been converted in good yield to crude II merely by storing it at 60° or above.

It has been found also that as much as 10 to 20% of water does not have any appreciable effect on the reaction. Approximately an equal weight of water is necessary to prevent the reaction at up to 80° and approximately two parts of water by weight are necessary to prevent the reaction above 80°.

In order to determine the effect of water on inhibiting the selfcondensation, experiments were carried out using different weight ratios of water to I and to crude stripped I at several temperatures. The data from this experiment are given in Table I.

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(1) L. Claisen, *Ber.*, **20**, 646 (1887).

(2) V. E. Tischenko, *J. Russ. Phys. Chem. Soc.*, **38**, 355 (1906).

(3) F. J. Villani and F. F. Nord, *J. Am. Chem. Soc.*, **69**, 2605 (1947).

(4) E. Spath and I. V. Szilagyi, *Ber.*, **76B**, 949 (1943).

(5) M. S. Kharasch and M. Foy, *J. Am. Chem. Soc.*, **57**, 1510 (1935) found that peroxides must be present for the Cannizzaro reaction to take place; therefore, although no catalyst is used in this reaction being reported, it is possible that peroxides may have an effect.

TABLE I

EFFECT OF WATER ON CONDENSATION OF HYDROXYPIVALALDEHYDE

Temp.	Wt. Ratio, H_2O/ Compd. I	Time, hr.	% Concentration	
			I	II
60	1.0	0	50.9	2.6
		1.0	—	—
		3.0	51.8	2.1
		5.0	50.5	4.0
60	2.0	0	32.3	—
		1.0	32.4	3.3
		3.0	36.1	0.6
		5.0	32.7	0.3
60	4.0	0	19.8	1.2
		1.0	19.6	0.1
		3.0	—	—
		5.0	20.2	0.9
80	1.0	0	50.6	—
		1.0	57.5	1.7
		3.0	56.6	3.7
		5.0	49.6	7.6
		7.8	49.3	9.8
80	2.0	0	31.2	0.7
		1.0	31.7	1.3
		3.0	32.7	—
		5.0	32.4	0.9
80	4.0	0	18.9	1.7
		1.0	19.6	0.5
		3.0	19.3	0.3
		5.0	19.6	1.6
95	1.0	0	49.2	2.7
		1.0	49.4	2.6
		3.0	48.0	8.4
		5.0	47.7	5.5
		7.5	46.2	5.8
95	2.0	0	—	0.9
		1.0	34.6	1.0
		3.0	28.4	5.5
		5.0	28.6	—
		8.0	34.3	3.2
95	4.0	0	19.9	0.8
		1.0	19.1	0.6
		3.0	19.2	1.9
		5.0	19.3	1.5
98	1.0[a]	1.0	65.0	4.2
		2.0	65.0	7.3
		3.0	64.6	7.7
		8.0	61.0	12.1
98	2.0[a]	1.0	36.0	2.5
		2.1	35.8	2.3
		3.0	34.4	2.9
98	4.0[a]	1.0	19.8	0.9
		2.0	18.9	0.4
		3.0	18.9	1.2

[a] Crude I (see Experimental).

These data show that at 60° within the weight ratio range of 1:1 to 4:1 the variations in aldehyde and ester contents with time are within the limits of analytical error. At 80° and above, the equal weight ratio does not completely inhibit the condensation, but the 2:1 and 4:1 ratios practically completely inhibit the condensation.

EXPERIMENTAL

Preparation of hydroxypivalaldehyde (I). The aldehyde was made by the alkaline condensation of formaldehyde with isobutyraldehyde according to the method of Hagemeyer.[6] For the material described as stripped crude product, the organic phase of the reaction mixture was separated and washed thoroughly with water to remove the potassium carbonate and other salts. It was then stripped at reduced pressure, with water added, up to a 95° base temperature to remove excess isobutyraldehyde; 470 g. of mixture [188 g. (92% yield) of I, 13 g. of II, and 269 g. of water] remained. Refined I was made by fractionation of the crude product. The fraction boiling at 88–95° (30 mm.) was recrystallized from water and then from a 1:1 benzene-ligroin mixture and dried. This method gave a solid, m.p. 90–92° (lit.[4] m.p. 96–97° for pure I) which contained 3.3% of the Tischenko ester II as determined by a modified saponification analysis method (see below).

The 2,4-dinitrophenylhydrazone melted at 187–188° (lit.[4] m.p. 191–192°). As the 2,4-dinitrophenylhydrazone of isobutyraldehyde melted at 183–185° (lit.[7] m.p. 185–187°) and a mixture of the two melted at 181–183°, the infrared spectrum of each was obtained; because the two spectra were different, it was concluded that the two derivatives were different.

Procedure used for analyses and in following the extent of the reactions. The general procedure used for each temperature and each water to aldehyde ratio was to mix the solid aldehyde and water and to heat the mixture rapidly to the desired temperature with vigorous stirring. The aldehyde was completely in solution in all cases before a temperature of 60° was attained. The samples for the analyses were obtained during the runs by pipetting aliquots into two weighing bottles. These were used, one for the aldehyde (by the usual hydroxylamine hydrochloride method[8]) and the other for the ester (by adding the exact amount of hydroxylamine theoretically required to react with all of the aldehyde); the ester was then determined by the usual saponification method.[9] The standard deviations for analyzing I and II in these mixtures are 0.89 and 0.82 respectively.

Compound I used for the rate studies at 88° and 132° was the distilled, recrystallized product which contained 3.3% of II. The samples were obtained and analyzed as indicated in the preceding paragraph.

3-Hydroxy-2,2-dimethylpropyl 3-hydroxy-2,2-dimethylpropionate (II). The crude ester (obtained in 94.2% yield) from the 132° Tischenko reaction titrated as 93.9% II. This material was recrystallized three times from 9:1 heptane-acetone, and once from pentane giving a white solid, b.p. 124–128° (with dec.) (1–2 mm.), m.p. 48–51°. This melting point was not depressed by the addition of a sample of the ester made by the esterification of neopentyl glycol with hydroxypivalic acid, and the infrared spectra for the two samples were identical. (The ester prepared by Franke and Kohn[10] melted at 51°.)

Anal. Calcd. for $C_{10}H_{20}O_4$: C, 58.82; H, 9.80. Found: C, 58.84; H, 9.83.

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[6] H. J. Hagemeyer, Jr., U. S. Patent **2,811,562** (1957).

[7] W. A. Mosher and C. L. Kehr, *J. Am. Chem. Soc.*, **75**, 3175 (1953).

[8] I. M. Kolthoff and V. A. Stenger, *Volumetric Analysis*, Vol. II, 2nd Ed., Interscience Publishers, Inc., New York, 1947, p. 222.

[9] I. M. Kolthoff and V. A. Stenger, *Volumetric Analysis*, Vol. II, 2nd Ed., Interscience Publishers, Inc., New York, 1947, p. 235.

[10] A. Franke and M. Kohn, *Monatsh.*, **25**, 865 (1904).