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Carbonyl Reactions. I. Kinetics and Mechanism of the Acid-catalyzed Aldol Condensation of Benzaldehyde and Acetophenone[1]

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The rate of the condensation of benzaldehyde and acetophenone to yield benzalacetophenone (chalcone) has been studied in acetic acid with sulfuric acid as catalyst. The rate was found to be proportional to the concentration of benzaldehyde, the concentration of acetophenone, and to Hammett's acidity function, h_0. The condensation between the enol of acetophenone and a protonated benzaldehyde is suggested as the rate-determining step. The usefulness of the Hammett acidity function in this medium is discussed.

Introduction

Carbonyl condensation reactions are of wide utility in synthetic organic chemistry. The base-catalyzed aldol condensation has been subjected to kinetic study[2] as has the Claisen-Schmidt condensation of benzaldehyde and acetophenone,[3] and the de-aldolization of diacetone alcohol.[4] Other examples of this general type of reaction which have been studied include the condensation of formaldehyde with malonic ester,[5] and the self-condensation of glyceraldehyde to hexoses.[6] However, the acid-catalyzed counterparts have received little attention. The self-condensation of acetone in the presence of hydrogen chloride has been briefly examined,[7] and the condensation of benzaldehyde with methyl ethyl ketone has been subjected to study by Gettler and Hammett[8] though no success was reported with the acid-catalyzed reaction. Since the structural course of condensation reactions involving unsymmetrical ketones is frequently dependent on the acidic or basic nature of the catalyst[9] it seemed of interest to examine these reactions in more detail. In the present study we have chosen to examine the kinetics of an acid-catalyzed reaction in which there is only one structural pathway possible to gain additional information concerning the rate laws for such reactions. The reaction between benzaldehyde and acetophenone satisfies this requirement, and has the further advantage that it has been investigated under basic conditions.[3] Both stereoisomers of the product have been prepared and characterized.[10]

Preliminary experiments indicated that the spectral differences of the three compounds, benzaldehyde, acetophenone and benzalacetophenone, were sufficient for satisfactory analysis. The reaction is quite slow, and hence a highly acidic medium was chosen, namely, acetic acid as solvent with sulfuric acid as catalyst. In this solvent yields as high as 95% of the theoretical may be obtained.

Experimental

Preparation of Materials.—Benzaldehyde (Eastman Kodak Co.) was washed with sodium carbonate, water, and dried. It was distilled at reduced pressure (56° (8 mm.)) under nitrogen into small ampules which were sealed directly. Prepared in this fashion the benzaldehyde remained colorless and showed no development of acid for a period of several months.

Acetophenone (Eastman Kodak Co.) was distilled twice under reduced pressure, with the center cut being retained each time, and this material was then fractionally frozen to constant spectrum and m.p. 19.6°.[11]

Sulfuric acid, 100%, was prepared by distilling fuming sulfuric acid into C.P. 95% sulfuric acid. This material,

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[1a] Union Carbide and Carbon Fellow, 1952–1953; U. S. Rubber Co. Fellow, 1953–1954.

[2] R. P. Bell, *J. Chem. Soc.*, 1637 (1937); K. F. Bonhoffer and W. D. Walters, *Z. physik. Chem.*, **181A**, 441 (1938).

[3] E. Coombs and D. P. Evans, *J. Chem. Soc.*, 1295 (1940); E. K. Nikitin, *J. Gen. Chem.*, **6**, 1278 (1936).

[4] C. C. French, THIS JOURNAL, **51**, 3215 (1929); G. M. Murphy, *ibid.*, **53**, 977 (1931); V. K. LaMer and M. L. Miller, *ibid.*, **57**, 2674 (1935).

[5] K. N. Welch, *J. Chem. Soc.*, 653 (1931).

[6] W. G. Berl and C. E. Feazel, THIS JOURNAL, **73**, 2054 (1951).

[7] O. L. Brady and J. Miller, *J. Chem. Soc.*, 1234 (1950).

[8] J. D. Gettler and L. P. Hammett, THIS JOURNAL, **65**, 1824 (1943).

[9] G. Harries and G. H. Muller, *Ber.*, **35**, 966 (1902); H. Haeussler and C. Brugger, *ibid.*, **77**, 152 (1944); see also ref. 7 and S. G. Powell and F. Hagemann, THIS JOURNAL, **66**, 372 (1944).

[10] R. E. Lutz and R. H. Jordan, *ibid.*, **72**, 4090 (1950).

[11] L. A. Flexser, L. P. Hammett and A. Dingwall, *ibid.*, **57**, 2105 (1935).

which contained a slight excess of sulfur trioxide, was then titrated with 96% sulfuric acid by the method of Kunzler.[12] The final sulfuric acid had m.p. 10.4°.

Acetic Acid.—Glacial acetic acid was analyzed for water content by the Fischer method[13] and then adjusted to the desired value by the addition of water, or alternately of acetic anhydride. Contrary to statements in the literature,[13] it appears that the reaction of acetic anhydride with water in acetic acid is quite slow, and hence these samples were briefly heated to complete this reaction. Water concentration, which affects the acidity value of the solution, was controlled to an accuracy of ±0.5 g. per liter.

Isolation Experiment.[14]—A solution of benzaldehyde (10.6 g., 0.1 mole), acetophenone (12.0 g., 0.1 mole) and sulfuric acid (30.7 g., 0.3 mole) in 200 ml. of acetic acid was stirred at room temperature for two days. The solution was poured into water, the sulfuric acid neutralized with 6 *N* sodium hydroxide, and the products extracted with ether. The ether was washed with water, dried and distilled. There was obtained 19.8 g. (95%) of benzalacetophenone, b.p. 168–171° (3 mm.), m.p. 54–56°.

***cis* and *trans*-Benzalacetophenone.**—The isomeric benzalacetophenones were prepared by the procedure described by Lutz.[10] Preliminary studies indicated that the conversion of *cis*- to *trans*-benzalacetophenone proceeds more rapidly than the condensation reaction. Further, the equilibrium position is effectively 100% *trans* in acetic acid. Consequently the *trans*-benzalacetophenone is the only one of the isomers which enters into consideration here.

Symbols:

S = solvent; SH^+ = lyonium ion

( ) = moles/l. soln.; $(\ )_0$ = molarity at time zero

t = time in minutes

a_i = activity of ith species; f_i = activity coefficient of ith species, both referred to infinitely dilute aqueous soln.

tr^+ = transition complex

$k_u = \dfrac{\ln (\mathrm{lim})_0/(\mathrm{lim})_t}{t}$ = pseudo first-order rate constant, where (lim) is molarity of reactant present in limiting concn.

$k_1 = \dfrac{k_u}{(\mathrm{fl})}$ = second-order rate constant, where (fl) is concentration of flooded reactant

$D = \dfrac{\log (I_0/I)}{l} = \sum_i \epsilon_i(i)$ = Beer's law

l = light path length (1 cm. here); I_0, I = light intensity through blank soln. and through reaction soln.; ϵ_i = molar extinction coefficient of ith species

$H_0 = -\log (h_0) = -\log \dfrac{a_{H^+}f_B}{f_{BH^+}}$ = Hammett's acidity function, where B is an uncharged basic indicator

Typical Experimental Procedure.—A solution of benzaldehyde (2.856×10^{-3} *M*) in acetic acid, a solution of acetophenone (0.1178 *M*) and a solution of sulfuric acid (2.097 *M*) in acetic acid were prepared. The water content of the acetic acid was 10.7 g./l. Equal aliquots of each of these three solutions were mixed to initiate a kinetic run. A control solution containing equal aliquots of the acetophenone solution, the sulfuric acid solution and of acetic acid alone was prepared simultaneously. Spectral data from which rate constants were calculated are summarized in Table I.

The solutions prepared above were thermostated and at appropriate time intervals small aliquots were removed. The absorption of the reaction solution was determined relative to that of the control solution as blank, using a Beckmann D.U. spectrophotometer. From the relation

$$(trans\text{-chalcone}) = \frac{D - \epsilon_{C_6H_5CHO}(2.856 \times 10^{-3})}{\epsilon_{trans\text{-chalcone}} - \epsilon_{C_6H_5CHO}}$$

derived from Beer's law and the equation below, the concentration of *trans*-chalcone at time *t* was calculated. In general, five to ten values of (*trans*-chalcone) were obtained over a spectral region of some 50 mμ and were averaged.

TABLE I

TYPICAL SPECTRA DATA FOR THE REACTANTS AND PRODUCT

λ(mμ)	Molar extinction coefficient of: $C_6H_5CHO^a$	$C_6H_5\overset{O}{\overset{\Vert}{C}}—CH_3{}^a$	*trans*-chalcone[a]	*trans*-chalcone[b]
300	....	315	22,000	21,500
310	106.2	144.0	22,000	22,700
320	41.0	60.2	20,700	20,500
330	25.7	33.3	16,100	14,300
340	16.2	16.0	10,000	8,090
350	9.75	...	5,530	3,880
360	4.38	...	2,900	1,790
370	1.62	...	1,400	806

Solvent: [a] HOAc + 0.60 *M* H_2O + 0.699 *M* H_2SO_4.
[b] HOAc + 0.60 *M* H_2O + 0.0699 *M* H_2SO_4.

The average deviation was of the order of 1% as in Table II. Using the relation

$$(C_6H_5CHO) = (C_6H_5CHO)_0 - (trans\text{-chalcone})$$

the concentration of the remaining benzaldehyde can be calculated, and from this k_u, the pseudo first-order rate constant. Data for a typical run are given in Table II, and represented in Fig. 1. For analysis at wave lengths near the maximum of chalcone, both the solution and the blank were diluted one to ten before spectrophotometric analysis. To convert these *D* values to (*trans*-chalcone) values the value of $\epsilon_{trans\text{-chalcone}}$ is required in 0.0699 *M* H_2SO_4. These data are given in Table I.

TABLE II

TYPICAL KINETIC RUN[a]

t (min.)	λ(mμ)[b]	(*trans*) × 10^{4c}	$(C_6H_5CHO) \times 10^{4d}$	$k_u \times 10^4$
0	.....	0	9.52	..
1460	330–400	1.90 ± 0.04	7.62	1.52
1740	350–400	2.30 ± .10	7.22	1.58
2520	320–400[e]	3.08 ± .05	6.44	1.56
2960	320–360[e]	3.46 ± .03	6.06	1.53
3020	360–400	3.60 ± .09	5.92	1.58
3980	355–400	4.49 ± .04	5.03	1.60
4390	360–400	4.80 ± .05	4.72	1.60
4440	320–365[e]	4.74 ± .05	4.78	1.56
5380	360–390	5.38 ± .03	4.14	1.55
5420	320–365[e]	5.52 ± .04	4.00	1.60
6810	330–370	6.28 ± .02	3.24	1.58
8480	330–370[e]	6.93 ± .07	2.49	1.58
9700	330–350[e]	7.48 ± .03	2.04	1.59

Av. $k_u = (1.57 \pm 0.02) \times 10^{-4}$ min.$^{-1}$
$k_1 = 4.00 \times 10^{-3}$ min.$^{-1}$ (moles/l.)$^{-1}$

[a] Solvent HOAc: $(C_6H_5CHO)_0 = 9.52 \times 10^{-4}$ *M*; $(C_6H_5\overset{O}{\overset{\Vert}{C}}—CH_3)_0 = 3.926 \times 10^{-2}$ *M*; $(H_2O) = 0.60$ *M*; $(H_2SO_4) = 0.699$ *M*; $T = 28.00 \pm 0.01°$. [b] Spectral region used to analyze for (*trans*-chalcone). [c] Average value and average deviation. [d] = $(C_6H_5CHO)_0$ − (*trans*-chalcone). [e] Solution and blank diluted one to ten to be read. Spectrum of *trans*-chalcone in 0.0699 *M* H_2SO_4 used to determine (*trans*-chalcone).

Trial analyses showed that the spectrophotometric determinations for chalcone were satisfactory with either reagent in excess (with acetophenone to 0.2 molar and with benzaldehyde to 0.03 molar). If the final concentration of the sulfuric acid was greater than 1.0 molar, dilution was to a final known volume, since there is a volume decrease of 2–3% on diluting the more concentrated sulfuric acid solutions. In general, reactions were followed past 50% reaction, with the exception of the very slowest runs, and there was in no case any apparent trend in the pseudo first-order rate constant.

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[12] J. E. Kunzler, *Anal. Chem.*, **25**, 93 (1953).

[13] J. Mitchell, "Aquametry," Interscience Publishers, Inc., New York, N. Y., 1948.

[14] This experiment was carried out by Mr. Gordon Bixler.

Discussion

Order with Respect to Reactants.—Table III summarizes the data representing the change in concentration of both benzaldehyde and acetophenone. It is apparent that over a twenty-fold variation in the concentration of acetophenone as flooded reagent and a threefold variation in the concentration of benzaldehyde as flooded reagent the apparent second-order rate constant represents the data satisfactorily, and therefore the reaction depends upon each reagent to the first power.

TABLE III

SUMMARY OF KINETIC RUNS AT CONSTANT ACIDITY[a]

Run no.	$(C_6H_5CHO)_0$	$(C_6H_5\overset{\overset{O}{\|}}{C}-CH_3)_0$	k_1, min.$^{-1}$ (moles/l.)$^{-1}$ $\times 10^3$	n[b]
		$T = 28.00 \pm 0.01°$		
1	3.31×10^{-4}	0.1973	4.05	2
2	3.31×10^{-4}	.0986	4.12	2
3	3.867×10^{-4}	.08667	3.88	2
4	3.867×10^{-4}	.04320	4.04	2
5	9.52×10^{-4}	.03926	4.00	1
6	9.52×10^{-4}	.01963	4.08	1
7	9.52×10^{-4}	.009817	4.07	1
8	0.03433	1.443×10^{-4}	4.00	1
9	.01717	1.443×10^{-4}	4.08	1
10	.02107	2.076×10^{-4}	4.02	1
11	.01053	2.076×10^{-4}	3.88	1
	Av.		$(4.02 \pm 0.05) \times 10^{-3}$	
		$T = 40.80 \pm 0.01°$		
12	8.48×10^{-4}	0.0980	9.30	2
		$T = 51.10 \pm 0.01°$		
13	17.73×10^{-4}	0.0920	16.25	2
		$T = 21.90 \pm 0.01°$		
14	8.44×10^{-4}	0.0891	2.53	2

[a] Solvent HOAc + 0.699 M H_2SO_4 + 0.60 M H_2O.
[b] Number of runs averaged for the value listed.

This is also apparent from Fig. 1, where the usual graph for a first-order reaction indicates the condensation to be first order in benzaldehyde. Similar graphs showed this behavior for all the runs in Table III. The reaction is therefore conclusively first order in both reactants over the range studied.

Acidity Dependence.—Hammett has defined an acidity function H_0, for highly acidic solutions[15]

$$H_0 = -\log \frac{a_{H^+} f_B}{f_{BH^+}} = pK_A + \log \frac{(B)}{(BH^+)}$$

where $pK_A = -\log (a_{H^+} a_B / a_{BH^+})$, and B is any uncharged base. The significance of this function is that it can be shown to be a thermodynamic property of the solvent in aqueous acid and independent of B.[16]

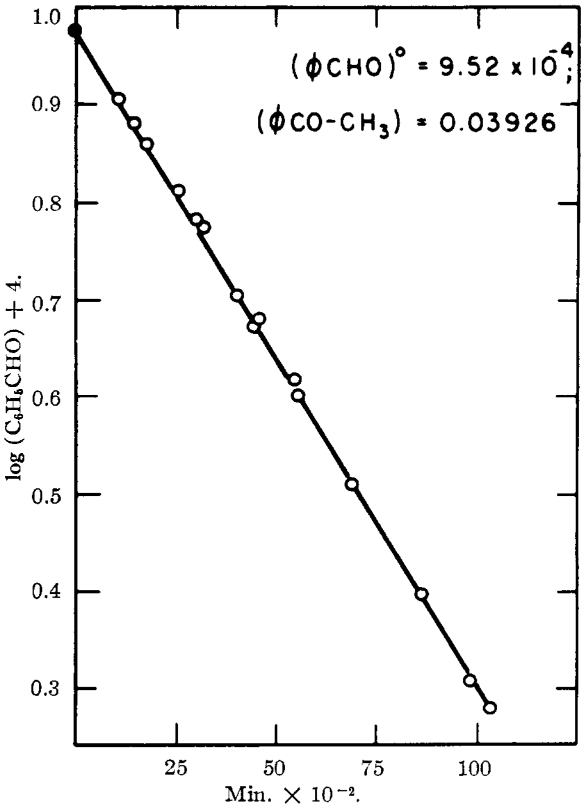

Fig. 1.—Typical kinetic run: solvent, HOAc + 0.60 M H_2O + 0.699 M H_2SO_4; T = 28.00°.

If H_0 is to be independent of B, it is evident from the equation above that f_B/f_{BH^+} must be equal for all bases, B. This may be shown by considering two bases, B and C, compared in the same solution

$$\Delta pK = pK_B - pK_C = -\log \frac{(B)(CH^+)}{(BH^+)(C)} - \log \frac{f_B f_{CH^+}}{f_{BH^+} f_C}$$

If H_0 is a function of solvent and not B, the last term on the right is zero. Therefore, the observed ΔpK values are independent of solvent composition. For aqueous solutions, this is the case up to moderate concentrations.[16b] There are theoretical reasons for believing this should be the case. It is known[15] that ΔpK is a function of the type

$$\Delta pK = a + b/d$$

where a and b are constants and d is the dielectric constant. If d is near 80, as in water and aqueous acids, b/d is close to zero. The observed result, that ΔpK is a constant, then follows.

However, in carrying H_0 to solvents of low dielectric constant like acetic acid, new factors must be considered. The first is that f_B/f_{BH^+} may not be independent of B because of the low value of d in acetic acid.[17] Further, in aqeuous solution f_B/f_{BH^+} is defined to approach one as infinite dilution is approached. In acetic acid, f_B/f_{BH^+} is not necessarily unity at infinite dilution. In fact, this ratio is adjusted so H_0 has the same value in acetic acid and in water at constant ratio of $(B)/(BH^+)$ for a given indicator. Since $H_0 = pK_A + \log (B)/(BH^+)$, this can be accomplished by defining the observed

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[15] L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., New York, N. Y., 1940, pp. 264–268. References to original literature given there.

[16] (a) A. E. Remick, "Electronic Interpretations of Organic Chemistry," 2nd ed., John Wiley and Sons, New York, N. Y., 1949, p. 246; (b) B. Gutbezahl and E. Grunwald, THIS JOURNAL, **75**, 559, 565 (1953); (c) E. Grunwald and B. J. Berkowitz, *ibid.*, **73**, 4939 (1951); (d) E. Grunwald, *ibid.*, **73**, 4934 (1951); *J. Phys. Chem.*, **55**, 882 (1951); (e) S. Winstein, E. Grunwald and H. W. Jones, THIS JOURNAL, **73**, 2700 (1951); E. Grunwald and S. Winstein, *ibid.*, **70**, 846 (1948).

[17] d = 6.13 in acetic acid. See, for example, H. A. E. MacKenzie and E. R. S. Winter, *Trans. Faraday Soc.*, **44**, 162 (1948).

pK_A for a particular indicator (*p*-nitroaniline) in acetic acid as identical to its value in water,[18] and then basing the acetic acid H_0 scale on values obtained using this indicator. This adjusts the values of the activity coefficients to the same standard state in both solvents for this indicator, but it must be remembered it does not determine that f_B/f_{BH^+} is independent of B in the solvent for all indicators. In other words, H_0 may be a function of B in acetic acid.

Grunwald[16b] has attempted to separate the ratio f_B/f_{BH^+} into two terms, one depending on the solvent, and one on the base, B. The equation is

$$\log \frac{f_B}{f_{BH^+}} = m_B Y_0$$

where Y_0 is a function of solvent. Grunwald shows that h_0 is probably equal to a_{H^+} in aqueous acids up to moderate concentrations. In acetic acid, h_0 is proportional to a_{H^+} up to 2 or 3 molar sulfuric acid. This proportionality is all that is required if all the determinations are done in a single solvent. In this paper, the rate is shown proportional to h_0, and consequently to a_{H^+}, in the solvent acetic acid plus small amounts of water. The absolute value of the proportionality factor is immaterial.

Previous observations of the correlation of rate with acidity in essentially anhydrous acetic acid solutions have been somewhat limited. Paul[19] has correlated the data of Walker and Chadwick[20] on the acid-catalyzed decomposition of trioxane. The work of Conant also shows a correlation of the rate of acetylation of β-naphthol with acidity.[21]

On the other hand, the rate of bromination of *m*-nitroacetophenone (a reaction which has been classed as general acid-catalyzed in aqueous media) does not show any simple proportionality with H_0 in acetic acid solutions.[22] Hence it appears useful to ascribe those reactions following the H_0 function in acetic acid solution to the group of reactions which are specific oxonium ion catalyzed in aqueous solution.[23]

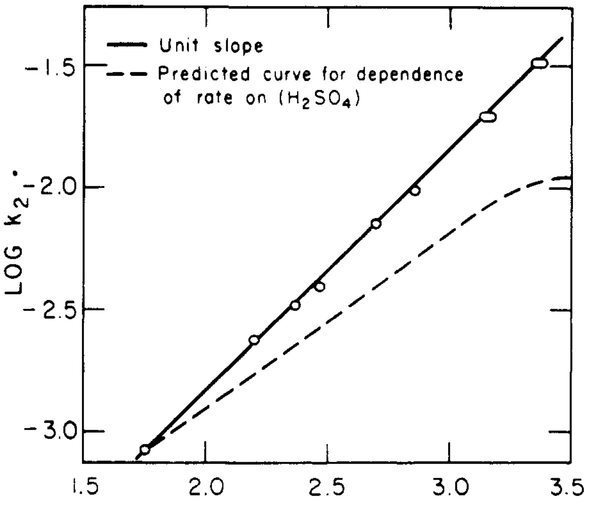

Fig. 2.—Acidity dependence.

The H_0 values used in this paper were taken from the work of Gold and Hawes[24a] for sulfuric acid concentrations less than 1 *M*. These authors determined H_0 at several water concentrations[25] including 0.000, 0.22 and 0.56 *M*. A graph of log(H_2SO_4) *versus* H_0 is a straight line, or very nearly so, and interpolation in the range studied is precise. The H_0 values of solutions greater than 1 *M* in sulfuric acid were taken from the work of Hall and Spengeman.[24b] These authors report H_0 in acetic acid that contains roughly 1–2 g. of water per liter as determined by freezing point. The solvent used here contains 4 g. of water per liter. The corrections for this difference, taken from the work of Gold and Hawes, would be less than 0.03 H_0 unit. This is not significant in view of the scatter in H_0 as reported by Hall and Spengeman. The accuracy of H_0 is probably ±0.05 unit below 1 *M* sulfuric acid, and ±0.1 unit above that. The internal consistency of Gold and Hawes' data is excellent, however, and in the lower range the error in the relative values of H_0 may be as low as ±0.01 unit. It is these relative values that are of interest.

Table IV gives values of k_1 as a function of sulfuric acid concentration. The table lists H_0 values, k_1, $k_1/(H_2SO_4)$, and $H_0 + \log k_1$. Whereas $H_0 + \log k_1$ is an excellent constant, $k_1/(H_2SO_4)$ varies by a factor of 3.

Figure 2 is a graph of log k_1 *versus* H_0. The experimental points fit a line of unit slope. The dashed line indicates the values predicted if k_1 were proportional to (H_2SO_4).

TABLE IV

RATE AS A FUNCTION OF CHANGING ACIDITY

$T = 28.0°$

Run	(H_2SO_4)	H_2O, g./l. in HOAc	H_0	k_1, min.$^{-1}$ M^{-1}	log $k_1 + H_0$	k_1/(H_2SO_4) × 10^3
1	0.1845	3.97	−1.75	8.25×10^{-4}	−4.83	4.53
2	.369	3.97	−2.21	2.39×10^{-3}	−4.83	6.50
3	.463	3.97	−2.37	3.31×10^{-3}	−4.85	7.15
4	.699	10.8	−2.47	4.00×10^{-3}	−4.87	5.71
5	.736	3.97	−2.69	7.02×10^{-3}	−4.84	9.55
6	.926	3.97	−2.86	9.71×10^{-3}	−4.87	10.45
7	1.678	3.97	−3.16	1.92×10^{-2}	−4.87	11.45
8	2.160	3.97	−3.38	3.35×10^{-2}	−4.86	15.52
				Av.	−4.85 ± 0.01	

Temperature Coefficients.—The variation of rate with temperature reported in Table III and presented in Fig. 3 permits the energy and entropy of activation to be calculated. From the usual equa-

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[18] L. P. Hammett and M. P. Paul, THIS JOURNAL, **56**, 827 (1934).

[19] M. A. Paul, *ibid.*, **72**, 3813 (1950).

[20] J. F. Walker and A. F. Chadwick, *Ind. Eng. Chem.*, **39**, 974 (1947).

[21] N. F. Hall and J. B. Conant, THIS JOURNAL, **49**, 3047 (1927); J. B. Conant and G. B. Bramann, *ibid.*, **50**, 2305 (1928). Conant determined the rate of acetylation in the presence of several acids and buffers. In every case, the points lie on a single straight line of unit slope when log *k* is plotted *versus* $p\text{H}^{(\text{HOAc})}$. Hall[19b] has shown from unpublished data of Conant's that

$$H_0 = 2 + p\text{H}^{(\text{HOAc})}$$

[22] M. A. Paul and L. P. Hammett, THIS JOURNAL, **58**, 2182 (1936).

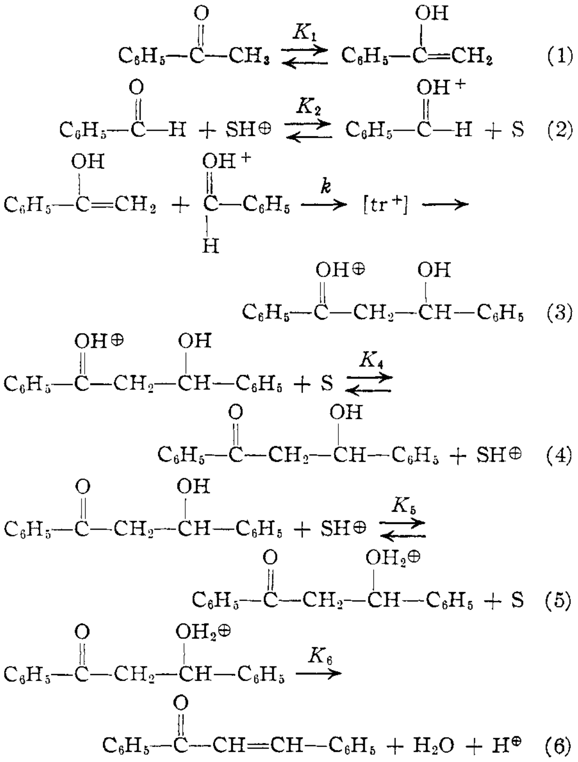
[23] Roberts has suggested the name lyonium ion activity control, or LIAC, for rates proportional to a_{H^+} in non-aqueous solutions.

[24] (a) V. Gold and B. W. V. Hawes, *J. Chem. Soc.*, 2102 (1951); (b) N. F. Hall and W. F. Spengeman, THIS JOURNAL, **62**, 2489 (1940).

[25] The HOAc solvent itself contained an additional 1 gram of water per liter as estimated from its freezing point.

tions[26] $\Delta H^{\ddagger}$ is 11.6 ± 0.1 kcal., and taking the value of k_0 as k_1/h_0 sec.$^{-1}M^{-2}$ the entropy of activation may be calculated to be -35 e.u.

Rate-determining Step.—A reasonable reaction sequence may be presented which is consistent with the data thus far reported.



$$C_6H_5-\overset{O}{\overset{\|}{C}}-CH_3 \overset{K_1}{\rightleftarrows} C_6H_5-\overset{OH}{\overset{|}{C}}=CH_2 \qquad (1)$$

$$C_6H_5-\overset{O}{\overset{\|}{C}}-H + SH^{\oplus} \overset{K_2}{\rightleftarrows} C_6H_5-\overset{OH^+}{\overset{\|}{C}}-H + S \qquad (2)$$

$$C_6H_5-\overset{OH}{\overset{|}{C}}=CH_2 + \underset{\underset{H}{|}}{\overset{OH^+}{\overset{\|}{C}}}-C_6H_5 \xrightarrow{k} [tr^+] \longrightarrow C_6H_5-\overset{OH^{\oplus}}{\overset{\|}{C}}-CH_2-\overset{OH}{\overset{|}{C}H}-C_6H_5 \qquad (3)$$

$$C_6H_5-\overset{OH^{\oplus}}{\overset{\|}{C}}-CH_2-\overset{OH}{\overset{|}{C}H}-C_6H_5 + S \overset{K_4}{\rightleftarrows} C_6H_5-\overset{O}{\overset{\|}{C}}-CH_2-\overset{OH}{\overset{|}{C}H}-C_6H_5 + SH^{\oplus} \qquad (4)$$

$$C_6H_5-\overset{O}{\overset{\|}{C}}-CH_2-\overset{OH}{\overset{|}{C}H}-C_6H_5 + SH^{\oplus} \overset{K_5}{\rightleftarrows} C_6H_5-\overset{O}{\overset{\|}{C}}-CH_2-\overset{OH_2^{\oplus}}{\overset{|}{C}H}-C_6H_5 + S \qquad (5)$$

$$C_6H_5-\overset{O}{\overset{\|}{C}}-CH_2-\overset{OH_2^{\oplus}}{\overset{|}{C}H}-C_6H_5 \xrightarrow{K_6} C_6H_5-\overset{O}{\overset{\|}{C}}-CH=CH-C_6H_5 + H_2O + H^{\oplus} \qquad (6)$$

Of the steps which will be consistent with bimolecular kinetics equation 3, representing the condensation step, and equation 6, representing the dehydration to final product, come to particular attention as possible rate-determining steps.[27]

Distinction between these two steps is necessarily subtle. Qualitatively, equation 3 is more attractive, since only in rare instances have intermediate hydroxyketones been isolated in reactions involving aromatic aldehydes. The reaction of *p*-nitrobenzaldehyde with acetone is reported[28] to give 4-*p*-nitrophenyl-4-hydroxy-2-butanone under carefully controlled conditions, and treatment of a mixture of benzaldehyde and acetophenone with hydrogen chloride leads to the formation of the β-chloroketone.[29]

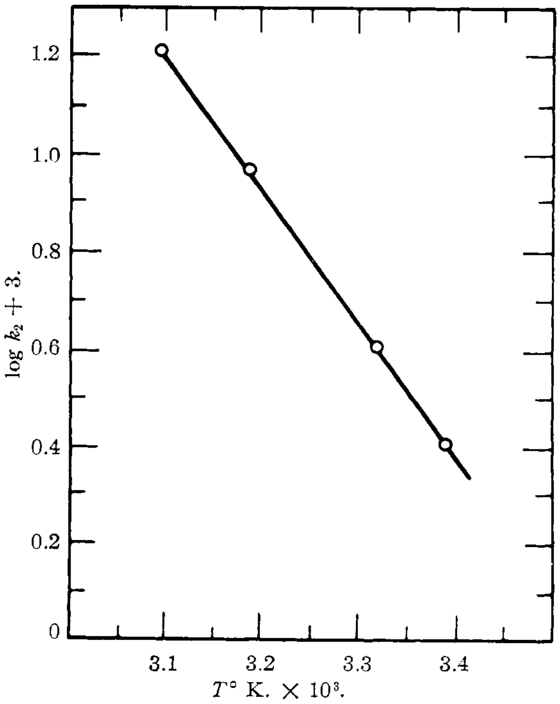


Fig. 3.—Temperature dependence.

The intermediate hydroxyketone which is involved in the present sequence has been prepared indirectly,[30] and its reactions are to be the subject of a succeeding report. The results to be reported do in fact substantiate equation 3 as representing the rate-determining process in dilute solution, but show that under other conditions this need not be true.

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[26] A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," John Wiley and Sons, Inc., New York, N. Y., 1953, p. 97.

[27] These equations require that the enolization of acetophenone be rapid relative to the condensation reaction. This is true; for example, in 46% aqueous sulfuric acid, H_0 is about -2.7,[15] and the enolization has a half-life of 0.23 hour at 25°. Run 5, in Table IV, with acetophenone = 9.106×10^{-4} M and benzaldehyde = 0.03167 M, had a half-life of 51.5 hours at 28°, or 63.2 hours at 25°.

[28] A. Baeyer and P. Becker, *Ber.*, **16**, 1968 (1883).

[29] L. Claisen and A. Claparede, *ibid.*, **14**, 2463 (1881).

[30] C. Schopf and K. Thierfelder, *Ann.*, **518**, 127 (1935).