lowing evidence. Some of the azo compound was always present in the sample introduced at the beginning of a rate run, but the amount of this compound initially present was determined and subtracted from the amount detected during the run to obtain the quantity actually formed in the course of the run. Inasmuch as samples introduced into the thermostated reaction vessel and maintained in solution therein before addition of the acid catalyst for at least an hour (to reach temperature equilibrium) failed to show detectable increases in *p*-azotoluene concentration, the protective atmosphere must have been functioning satisfactorily, for samples similarly treated in the absence of the nitrogen stream oxidized very rapidly to *p*-azotoluene. Furthermore, since rapid air oxidation of *p*-hydrazotoluene is known to occur in the absence of acids, any air oxidation taking place during the rate runs should be substantially uncatalyzed, and therefore an appreciable incursion of such a reaction must have changed the kinetics from those observed. Finally one might suspect that the observed azo compound could have been the result of air oxidation occurring between removal of samples from the mixtures and analysis of them, for these samples were not protected from the air. However, experiments showed that samples stored for two hours or less in ice showed no appreciable gain in concentration of azo compound. Moreover, had the azo compound apparently formed during the runs in fact been formed during storage of samples for analysis, then the largest concentrations of azo compound should have been found in the samples withdrawn at the smallest conversions, for these samples contained the greatest amounts of available hydrazotoluene for air oxidation and in general were held in storage for the longest periods before analysis. Actually of course the concentrations of azo compound formed during the reaction was observed to increase continuously as the reaction progressed.

Because the observed rate constants from which E_a and ΔS^* are computed undoubtedly are composites of two or more true rate and equilibrium constants, it follows that the apparent E_a (or ΔH^*) and ΔS^* are also composite energy and entropy functions, respectively. Therefore, these apparent values cannot be used to draw valid conclusions about the mechanisms of the rearrangement, reduction and disproportionation steps of the reaction sequence.[20]

Acknowledgment.—The authors are grateful to Drs. J. P. Fugassi, D. S. McKinney, R. G. Parr and A. K. Colter of this Department for their interest in this work and for their constructive advice during the preparation of the manuscript.

[20] For further discussion of this point, see ref. 3e.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA]

Carbonyl Reactions. IV. The Kinetics of the Acid-catalyzed Reaction of Anisaldehyde with Methyl Ethyl Ketone[1]

BY DONALD S. NOYCE AND LLOYD R. SNYDER

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The rate of formation of 3-methyl-4-(*p*-anisyl)-3-buten-2-one in acetic acid from anisaldehyde and methyl ethyl ketone shows simple bimolecular kinetics when both reagents are present in low concentrations. With high concentrations of methyl ethyl ketone, the rate of reaction does not continue to increase as rapidly as is theoretically predicted. Two causes have been shown to be responsible for this behavior. There is formation of a reasonably stable reaction intermediate, which reacts either to regenerate the starting reagents or to lead to formation of the observed product. There is also a decrease in the activity coefficient of methyl ethyl ketone at higher concentrations. The rate sequence and sequence of intermediates is outlined.

Introduction

Of the numerous reactions which lead to the formation of new carbon to carbon bonds, the aldol condensation has been subjected to the most extensive study. Though the base-catalyzed reaction has received considerable attention from a kinetic viewpoint,[2] the acid-catalyzed counterpart has not been so extensively investigated. It was recently reported that the acid-catalyzed condensation of acetophenone and benzaldehyde could be suitably examined spectrophotometrically[3] and the rate law and general sequence of intermediates were determined.

In the case of the condensation of an aldehyde with an unsymmetrical ketone such as methyl ethyl ketone, there arise the possibilities of two alternative products. Specifically, it has been shown by Harries and Muller[4] that with basic catalysts, benzaldehyde and methyl ethyl ketone afford 1-phenyl-1-pentene-3-one (I), while with acid catalysts the product is 3-methyl-4-phenyl-3-buten-2-one (II). That this is general with respect to methyl *n*-alkyl ketones is demonstrated by the work of Bogert and Davidson,[5] and that it is general for aromatic aldehydes is demonstrated by the work of Woodruff and Conger.[6] In all of these cases the demonstration rests upon the formation of

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[1] Supported in part by the Office of Ordnance Research, Contract No. DA-04-200-ORD-171.

[2] R. P. Bell, *J. Chem. Soc.*, 1637 (1937); K. F. Bonhöffer and W. D. Walters, *Z. physik. Chem.*, **181A**, 441 (1938); E. Coombs and D. P. Evans, *J. Chem. Soc.*, 1295 (1940); 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).

[3] (a) D. S. Noyce and W. A. Pryor, *ibid.*, **77**, 1397 (1955); (b) D. S. Noyce, W. A. Pryor and A. H. Bottini, *ibid.*, **77**, 1402 (1955).

[4] G. Harries and G. H. Muller, *Ber.*, **35**, 966 (1902).

[5] M. T. Bogert and D. Davidson, THIS JOURNAL, **54**, 334 (1932).

[6] E. H. Woodruff and T. W. Conger, *ibid.*, **60**, 465 (1938).

distinct isomers, and the fact that one is readily oxidized by hypohalite to a substituted cinnamic acid. For the condensation of anisaldehyde with methyl ethyl ketone, Iwamoto has presented clear evidence for the structure of the two products,[7] 3-methyl-4-(*p*-methoxyphenyl)-3-buten-2-one (III) being formed with HCl as catalyst.

Gettler and Hammett[8] have investigated the kinetics of the base-catalyzed reaction of benzaldehyde and methyl ethyl ketone in dioxane–water as solvent, and have found that the condensation is first order in both methyl ethyl ketone (V) and benzaldehyde, and apparently of one-half order in sodium hydroxide. Earlier kinetic work on the base-catalyzed self-condensation of acetaldehyde[2] and acetone[2] which shows the first reaction to be first order in acetaldehyde and the latter reaction to be second order in acetone has been interpreted in terms of the enolization of the carbonyl component being slow with respect to the condensation step in the case of acetaldehyde and fast in the case of acetone. Thus Hammett's work[8] indicates that the rate of enolization is fast in the base-catalyzed condensation of benzaldehyde with methyl ethyl ketone. An attempt by Hammett to measure the rate of condensation in acid was unsuccessful.

It is the purpose of the present work to report the kinetics of the condensation of methyl ethyl ketone with a typical aromatic aldehyde in acid solution. The choice of anisaldehyde (VI) for the initial study is dictated by the rather significant difference in the absorption spectra of the two alternate condensation products (see below) and by the convenient rates observed in acetic acid solutions where the reaction proceeds smoothly to completion.

Experimental

Preparation and Purification of Materials.—C.P. acetic acid was analyzed for water content by Karl Fischer titration and adjusted to the desired value as described previously.[3a] Sulfuric acid, 100.0%, was prepared by the method of Kunzler[9] as previously described.[3a]

Methyl ethyl ketone (V) was purified by the procedure of Gettler and Hammett[8] and distilled through a packed column in an all-glass apparatus protected from moisture, and the center cut, b.p. 79.2–79.6°, was retained and sealed in glass ampules.

Anisaldehyde (VI) (Eastman white label) was washed with sodium bicarbonate, water, dried over magnesium sulfate, and distilled under nitrogen. A colorless product (b.p. 117° at 11 mm.) was retained and sealed under nitrogen in glass ampules. For periods up to six months there was no development of acid. The acid titer was less than 0.3%.

1-Anisyl-1-penten-3-one (IV) was prepared by the method of Iwamoto,[7] m.p. 61.3–61.9°.

3-Methyl-4-anisyl-3-buten-2-one (III) was prepared by the method of Woodruff and Conger,[6] melting after crystallization (with rather severe loss of material) at 28.0°.

3-Methyl-4-anisyl-4-acetoxybutan-2-one (VII).—This intermediate was prepared under conditions indicated by the kinetic evidence. One liter of acetic acid solution containing 0.280 mole (27.4 g.) of sulfuric acid, 10 g. of water, 2 moles (144 g.) of methyl ethyl ketone and 0.25 mole (34 g.) of anisaldehyde was prepared and allowed to react for two hours at 25.0°. At the end of this time, the reaction mixture was poured into excess ice and water, containing 0.56 mole (46 g.) of sodium acetate. Extraction of the total mixture with three 100-ml. portions of benzene was followed by washing the benzene extracts with 100 ml. of water. The benzene was removed *in vacuo* at room temperature. The residue was partially crystalline. Filtration at −10° afforded a pale yellow solid (1 g.) which on crystallization from pentane gave VII as colorless crystals, m.p. 84.1–85.1° (0.3 g.). In other preparations the yield of VII was as much as 10%.

Anal.[10] Calcd. for $C_{14}H_{18}O_4$: C, 67.1; H, 7.25; sapon. equiv., 250.4. Found: C, 67.1; H, 7.3; sapon. equiv., 250.

When subjected to the reaction conditions, this sample of the intermediate acetate gave a limiting yield of anisaldehyde and 3-adduct of 97% of the theoretical. The infrared spectrum showed a strong ester band at 1740 cm.$^{-1}$ and no hydroxyl band.

1-Anisyl-2-methyl-3-keto-1-butanol (VIII).—Five grams of the above intermediate acetate was dissolved in 300 ml. of 95% ethanol, and 1000 ml. of 30% sulfuric acid was added rapidly. The reaction solution was maintained at room temperature. After 35 minutes, the reaction mixture was extracted with benzene, and the combined benzene extracts washed with water. The benzene was removed at room temperature *in vacuo*, and there remained 3.5 g. of a somewhat discolored sirup, which by saponification equivalent and spectral analysis before and after reaction in 3 *M* sulfuric acid–acetic acid solution was shown to be 77% 1-anisyl-2-methyl-3-keto-1-butanol, 8% intermediate acetate and 4% III.

Analysis.—Table I presents values of the molar extinction coefficient of anisaldehyde, methyl ethyl ketone, III and IV at selected wave lengths.

TABLE I

SELECTED VALUES OF MOLAR EXTINCTION COEFFICIENT

	$\epsilon \times 10^{-3}$, solvent, acetic acid			
λ, mμ	Anisaldehyde (VI)	MEK (V)	III	IV
270	13.9	0.06	6.45	...
280	15.5	.04	11.5	7.30
290	13.9	.02	16.5	12.0
300	7.20	< .01	20.3	16.6
310	1.68	...	21.5	20.8
320	0.25	...	18.8	23.6
330	0.04	...	12.9	21.4
340	...	...	6.95	...

Spectral analysis for the total concentration of condensation product in reaction solutions containing only anisaldehyde, methyl ethyl ketone and III is seen to be possible in the region from 290 to 330 mμ with relatively high accuracy, because of the large absorption of III relative to the starting reagents. Furthermore, ϵ for III changes only slowly with wave length in this region, and no appreciable error in optical density will result from small uncertainties in wave length. Past 5% reaction, the ratio of the optical density of anisaldehyde to the optical density of III will be less than 0.08; therefore correction is made for it easily. The absorption due to methyl ethyl ketone will be negligible.

To simplify the initial kinetic treatment, all but a specified few reactions between V and VI have been carried out with methyl ethyl ketone in large excess (at least 80 times the initial concentration of anisaldehyde). This reduces the reaction to pseudo first-order conditions.

Typical Kinetic Results.—The results of a typical kinetic run are given in Table II.

In reactions in which the initial concentration of anisaldehyde was greater than 10^{-3} molar, samples were diluted 1:10 or 1:100 as necessary to keep the observed optical density within the range 0.2 to 1.0 as determined by means of a Beckman DU spectrophotometer. Symbols used: k' = limiting rate constant under pseudo unimolecular conditions; k^0 = apparent bimolecular rate constant derived from limiting slope; $k_1{}^0$ = true bimolecular rate constant for condensation step; $(A)_0$ = initial concentration of anisaldehyde; (III) = concentration of III.

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[7] K. Iwamoto, *Bull. Chem. Soc. Japan*, **2**, 51 (1927).

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

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

[10] Analysis by the Microanalytical Laboratory, University of California.

TABLE II

TYPICAL RATE DATA[a]

Time, sec. × 10^{-}	(III)/(A_0)	(A)/(A_0)[b]	$k_1 \times 10^5$[c]
1.47	0.022	0.978	
3.38	.065	.935	
5.22	.119	.881	
7.63	.196	.804	
9.90	.269	.731	
12.4	.384	.616	4.60
14.6	.406	.594	4.44
17.0	.471	.529	4.56
19.8	.536	.464	4.61
22.9	.600	.400	4.65
25.51	.655	.345	4.81
32.4	.756	.244	4.89
37.71	.811	.189	4.86

[a] Solvent acetic acid, 0.96% water; sulfuric acid = 0.400 *M;* initial methyl ethyl ketone concentration = 1.00 *M;* initial anisaldehyde concentration = 0.00828 *M;* temperature = 25.14°. [b] Apparent remaining fraction of anisaldehyde. [c] k_1 = pseudo first-order rate constant calculated from t = 9900 sec.; average $k_1 = 4.68 \pm 0.13 \times 10^{-5}$ sec.$^{-1}$.

Results and Discussion

Role of Anisaldehyde.—With methyl ethyl ketone in large excess ("flooded"), the role of anisaldehyde in the rate law is initially most easily investigated. Correlation of rate data, with integrated rate expressions corresponding to various simple dependencies is possible only on the assumption of first-order dependence, and is not free from complicating features. Table II shows that an initial induction period is observed which is followed by asymptotic approach to a limiting rate constant. Furthermore, and most substantiating of a basic first-order dependence, the pseudo first-order rate constants, k', calculated from the limiting slopes are independent of initial anisaldehyde concentration at a *given* methyl ethyl ketone concentration. Table III gives results obtained in this manner.

$$k' = 2.303[\log\,(\text{anisaldehyde})_1 - \log\,(\text{anisaldehyde})_2]/t_2 - t_1$$

TABLE III

DEPENDENCY OF RATE UPON ANISALDEHYDE CONCENTRATION[a]

$(\text{MEK})_0$	$(\text{Anisaldehyde})_0$	Limiting k'
1.50	0.0114	2.14×10^{-5} sec.$^{-1}$
1.50	.0256	2.08×10^{-5} sec.$^{-1}$
1.00	.0121	1.72
1.00	.0248	1.69

[a] Solvent, acetic acid; sulfuric acid, 0.280 *M;* water, *about* 1%, but constant in all runs; T = 25.00°.

Role of Methyl Ethyl Ketone.—Variation of the flooded reactant concentration (methyl ethyl ketone) causes a non-proportional variation in the limiting pseudo first-order rate constant k' at high concentrations of methyl ethyl ketone as shown in Table IV. It is seen that the values of k^0 (the bimolecular rate constant from the limiting slopes) becomes reasonably constant for methyl ethyl ketone concentrations of 0.3 molar or less. For these reactions, the initial induction period noted at higher concentrations of methyl ethyl ketone vanishes.

TABLE IV

DEPENDENCY OF RATE UPON METHYL ETHYL KETONE CONCENTRATION[a]

MEK concn. m./l.	VI, init. concn., m./l. × 10^4	$k' \times 10^5$, sec.$^{-1}$	$k'/(\text{MEK}) \times 10^5$ l. m.$^{-1}$ sec.$^{-1}$ = $k^0 \times 10^5$[b]	$k_1^0 \times 10^5$, l. m.$^{-1}$ sec.$^{-1}$[c]
1.00	82.8	5.03	5.03	11.4
1.00	82.8	5.03	5.03	11.4
0.686	81.8	4.00	5.87	12.2
.686	78.5	4.17	6.08	12.8
.300	39.6	2.41	8.03	15.0
.300	39.8	2.44	8.13	15.2
.150	19.8	1.28	8.53	15.0
.150	19.8	1.22	8.13	14.4
.0854	3.16	0.694	8.13	13.9
.0854	3.16	.689	8.07	13.6
.0427	3.16	.356	8.33	14.2
.0427	3.16	.342	8.00	13.6
.02135	3.16	.183	8.57	14.7
.02135	3.16	.186	8.72	14.4
.0136	132	...	7.97	13.6
.0136	132		7.94	13.6
.00923	89.2		8.44	14.2
.00923	89.2		8.28	13.9
.00443	44.3		8.61	14.4
.00443	44.3		8.44	14.2

[a] Solvent, acetic acid; sulfuric acid concentration, 0.400 *M;* water content, 0.96%; temperature, 25.14°. [b] Average $k^0 = (8.27 \pm 0.22) \times 10^{-5}$ l. m.$^{-1}$ sec.$^{-1}$, for concentrations of methyl ethyl ketone 0.300 molar or less. [c] k'

$$= [k_1^0(\text{MEK}) + k_2 + k_3]/2 - \sqrt{([k_1^0(\text{MEK}) + k_2 + k_3{}^{1/2})^2 - k_1^0(\text{MEK})k_3}$$

Average $k_1^0 = 14.2 \pm 0.2 \times 10^{-5}$ l. m.$^{-1}$ sec.$^{-1}$ for concentrations of methyl ethyl ketone 0.300 molar or less.

Selectivity of Product III Formation.—Determination of the spectra of reaction solutions after several half-lives revealed that the observed optical density in the region of 290 to 330 mμ was precisely as expected, showing after 71 hours under the conditions of the reaction in Table II 96 ± 1% of III. Less than 2% of 1-anisyl-1-pentene-3-one (IV) is formed under these conditions. It is to be noted that Gettler and Hammett[8] found that the base-catalyzed reaction of benzaldehyde and methyl ethyl ketone is likewise free from side reactions, particularly the condensation of 1-phenyl-1-pentene-3-one with a second mole of benzaldehyde when the ketone concentration exceeds that of the aldehyde.

The data in Table IV show that the calculated apparent bimolecular rate constant k^0 remains satisfactory up to concentrations of methyl ethyl ketone of about 0.3 *M*, but declines at concentrations above this point. It is to be noted that the induction period observed at the higher concentrations vanished at the lower concentrations. Hence for these latter reactions, the reaction kinetics become simple second order, exhibiting first-order dependence upon both the concentration of anisaldehyde and of methyl ethyl ketone.

The form of the k' dependence upon the concentration of methyl ethyl ketone (when MEK is "flooded") and the observation of the induction period make it likely that the reaction mechanism may be satisfactorily expressed by (1) or (2)

$$A \xrightarrow{k_a} B \xrightarrow{k_b} C \qquad (1)$$

$$A \underset{k_1}{\overset{k_2}{\rightleftarrows}} B \xrightarrow{k_3} C \qquad (2)$$

A superficial comparison of theory with experimental data is sufficient to eliminate equation 1 as a possible mechanistic description of the kinetic behavior noted in the condensation of anisaldehyde with methyl ethyl ketone, since at times large with respect to the half-life of the reaction the limiting first-order rate constant k' should approach either k_a or k_b, whichever is the slower. Equation 2 is a much more satisfactory representation.[10]

Kinetic Behavior of the Intermediate.—Isolation of 3-methyl-4-anisyl-4-acetoxybutan-2-one (VII) under conditions indicated by solution of the differential equations for case 2 indicated a major role for this compound in the kinetic scheme proposed. The intermediate acetate has been observed to react under the conditions used for the study of the condensation reaction to give the condensation product III and anisaldehyde. It is possible to carry out analysis for both processes by determination of the absorptivity at both 290 and 330 mμ. Table V gives typical data for such analysis of the behavior of the intermediate acetate; Table VI summarizes rate constants.

TABLE V

RATE DATA FOR DECOMPOSITION OF INTERMEDIATE ACETATE VII[a]

Time, sec. $\times 10^{-3}$	Anisaldehyde, concn. $\times 10^3$	III, concn. $\times 10^3$	$\frac{(III)}{(VI)}$	$\frac{\left[\frac{-\ln (VII)}{(VII)_0}\right]}{t} \times 10^4$
0.795	1.00	1.27	1.27	1.264
1.26	1.15	1.90	1.26	1.19
2.09	2.32	2.92	1.26	1.19
2.67	2.83	3.70	1.31	1.22
3.24	3.41	4.29	1.26	1.24
3.74	3.72	4.86	1.31	1.21
4.28	4.20	5.39	1.28	1.21
5.15	4.99	6.20	1.24	1.27
5.76	5.38	6.52	1.21	1.21
7.13	6.11	7.70	1.26	1.22
8.57	6.81	8.52	1.25	1.22
10.01	7.40	9.32	1.26	1.21
12.5	8.18	10.3	1.24	1.21
17.0	8.83	11.7	1.33	1.16
20.6	9.25	12.3	1.33	1.15
		Average	1.27 ± 0.03	1.21 ± 0.02

[a] Solvent, acetic acid; sulfuric acid 0.280 *M*; water content, 1%; temperature, 25.15°; initial concentration of VII, 0.0238 *M*. In a duplicate run (concentration of VII, 0.00695 *M*) the average ratio of III to VI was 1.30 ± 0.03 and the rate constant was $1.23 \pm 0.02 \times 10^{-4}$ sec.$^{-1}$.

TABLE VI

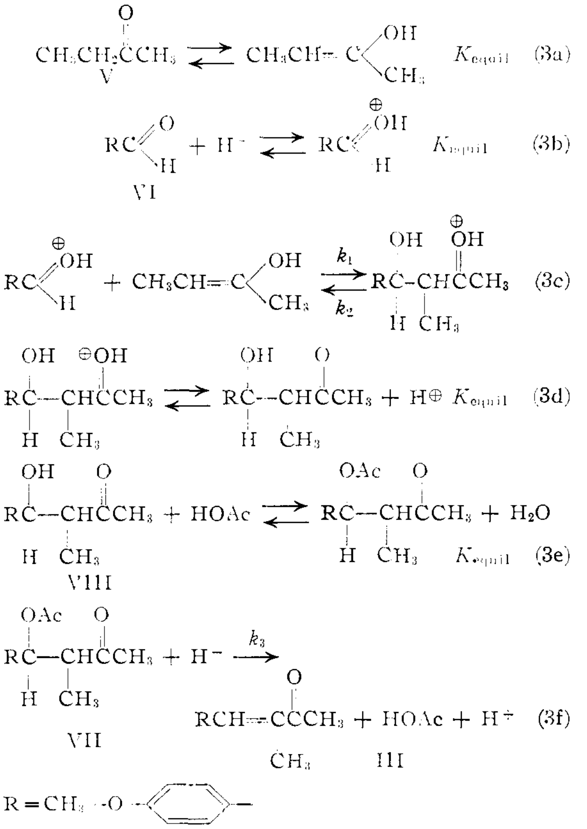
RATE OF DECOMPOSITION OF INTERMEDIATE ACETATE VII[a]

$(VII)_0$, *M*	$k_2 \times 10^5$, sec.$^{-1}$	$k_3 \times 10^5$, sec.$^{-1}$	k_3/k_2
7.38×10^{-3}	7.92	11.33	1.44
8.40×10^{-3}	7.78	11.22	1.45
8.78	7.61	10.94	1.44

[a] Solvent, acetic acid; (H_2O) = 0.96%; (H_2SO_4) = 0.400 *M*; *T* = 25.15°.

The constant ratio of the concentration of anisaldehyde and III under a given set of reaction conditions indicates competitive decomposition of the intermediate acetate by two parallel paths, k_2 and k_3.

This mechanism is adequate to describe the kinetic behavior of the system, but other descriptions, involving further equilibria, are not excluded, and are somewhat more attractive on general chemical grounds. More explicitly the best description may be that given by equations 3a-f.



In equation 3d a rapid equilibrium involving the ester and the alcohol would maintain a constant ratio of alcohol to ester during the reaction, inasmuch as the activities of acetic acid and water do not change appreciably during the course of the reaction. From the data of Table VI it is possible to calculate the values for the rate constant k_1^0 for each condensation run assuming the relation between k', k_2 and k_3 in the equation in footnote to Table IV. The calculated values for k_1 are included in Table IV.

The decrease in k_1^0 with increasing methyl ethyl ketone concentration is seen to be less, when calculated on this basis, than the decrease in the

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[10] Solution of the differential equations for equation 2 leads to the equation

$$\frac{(A_0) - C}{(A_0)} = \left[\frac{a+b}{2b}\right] e^{-(a-b)t} - \left[\frac{a-b}{2b}\right] e^{-(a+b)t}$$

where $a = (k_1 + k_2 + k_3)/2$ and $b = (a^2 - 2k_1k_3)^{1/2}$. As t becomes large, a limiting rate is obtained, $k = a - b$. Note that k' is now a non-simple function of the concentration of methyl ethyl ketone. A family of curves may be plotted of log k' *vs.* log (MEK) for various ratios of k_3/k_2, and from such a plot the ratio k_3/k_2 may be evaluated from the data. It is possible in this fashion to obtain approximate values for k_1, k_2 and k_3.

values of k_0 calculated previously. This apparent deviation of k_1^0 from the constant value 14.2 ± 2 × 10^{-5} l. m.$^{-1}$ sec.$^{-1}$ at higher methyl ethyl ketone concentrations is most easily attributed to a failure of the Henry's law activity of methyl ethyl ketone in this region; that is, the activity of a 1 *M* methyl ethyl ketone solution may be only eight times the activity of a 0.1 *M* methyl ethyl ketone solution. The direct measurement of k_1 for comparison purposes was deemed desirable in that it would check this type of hypothesis relative to discrepancies in some other of the steps in the over-all reaction.

Direct Measurement of the Rate of the Condensation Step, k_1.—If the first 10% of the initial condensation reaction be considered, it is seen that the amount of the intermediate acetate decomposing to condensation product is small relative to the amount of intermediate formed, and it is easily corrected for; this is especially true of the condensation product formed since it may be independently measured and equated to concentration of the intermediate for purposes of calculating k_1. Due to the small changes in the value of the extinction coefficient, which occur during the first 10% reaction, it is not possible by this method to get highly precise rate constants from direct spectral measurement. Nevertheless, by using blank solutions of appropriate absorption it was possible to obtain satisfactory values by a differential technique. These are summarized in Table VII, and are to be compared with the corresponding values of Table IV which were indirectly calculated from the equation in footnote *c*.

TABLE VII

RATE OF INITIAL CONDENSATION STEP[a]

MEK, *M*	Anisaldehyde, *M*	$k_1^0 \times 10^5$, l. mole^{-1} sec.$^{-1}$
0.997	0.0560	12.1
.997	.0560	11.9
.997	.0560	12.1
.596	.0336	14.0
.498	.0338	14.1
.498	.0338	14.3
.387	.0262	14.3
.386	.0262	14.8

[a] Solvent, acetic acid; (H_2O) = 0.96%; (H_2SO_4) = 0.400 *M*; *T* = 25.15°.

It is concluded that equations 3a–3f involving the rate constants k_1, k_2 and k_3 adequately describe the condensation reaction of methyl ethyl ketone with anisaldehyde in the solution used, if the activity of methyl ethyl ketone in the more concentrated solutions is taken into account. The values of the rate constants involved in 0.400 molar solution of sulfuric acid and acetic acid containing 0.96% water are

$$k_1^0 = 14.2 \pm 0.2 \times 10^{-5} \text{ l. mole}^{-1} \text{ sec.}^{-1}$$
$$k_2 = 7.77 \pm 0.1 \times 10^{-5} \text{ sec.}^{-1}$$
$$k_3 = 11.17 \pm 0.15 \times 10^{-5} \text{ sec.}^{-1}$$

Behavior of the Intermediate Alcohol.—Isolation of the alcohol derived from the intermediate acetate would permit the classification of the ester–alcohol equilibrium as either fast or slow relative to the other reaction processes. The alcohol was isolated in an impure form. The possibility of the intermediate acetate being slowly converted to the intermediate alcohol has been previously mentioned. Having both the ester and the alcohol the relative rate of the equilibration could now be determined. If the equilibrium be fast, the apparent rate constant for the production of anisaldehyde (k_2) and condensation products (k_3) from either intermediate acetate or alcohol should be the same under similar conditions. If the esterification of the alcohol is slow, that is, rate determining, the intermediate alcohol should revert rapidly in reaction solutions to an equilibrium mixture of anisaldehyde, methyl ethyl ketone and intermediate alcohol. It should then react further in the same manner as an equivalent solution containing only anisaldehyde and methyl ethyl ketone initially. Table VIII shows the results of a kinetic investigation of the reaction of the intermediate alcohol. The reaction is cleanly first order, as was the reaction of the acetate.

TABLE VIII[a]

RATE OF REACTION OF INTERMEDIATE ALCOHOL VIII

(VIII) concn.	k_2, sec.$^{-1}$	k_3, sec.$^{-1}$
0.00424 *M*	8.50 × 10^{-5}	11.9 × 10^{-5}

[a] Solvent, acetic acid; (H_2O) = 0.96%; (H_2SO_4) = 0.400 *M*; *T* = 25.15°.

The results given in Table VIII are to be compared with those presented in Table VI. It is to be seen that the rates are essentially identical and certainly to be contrasted with the rate of formation of condensation product from a mixture of 0.00424 molar methyl ethyl ketone and anisaldehyde ($k' = 3 \times 10^{-7}$ sec.$^{-1}$). It is concluded, then, that the equilibrium between VII and VIII is rapid or non-rate determining.

Summary and Extension of the Mechanism of the Over-all Condensation Reaction.—The over-all mechanism may be set forth in some detail. The fact that the isolated intermediate acetate, when submitted to reaction conditions, gives kinetic data correlatable with the over-all reaction data precludes the possibility of appreciable amounts of any other intermediate being formed during the course of the condensation reaction. Since it has been found that methyl ethyl ketone brominates instantaneously under the reaction conditions, the enol will be present in equilibrium concentration and is thus a very attractive reaction intermediate. All these facts support equations 3a–3f as outlining a reasonable reaction sequence for the condensation.

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