[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING OF THE UNIVERSITY OF CALIFORNIA]

Carbonyl Reactions. II. The Role of the Intermediate Ketol in the Kinetics of the Formation of Chalcone[1]

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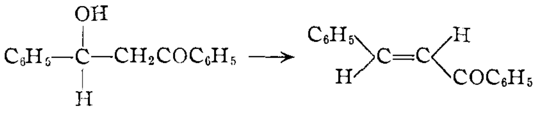
The ketol, 1,3-diphenyl-3-hydroxy-1-propanone has been shown to undergo competitive reactions in both acidic and basic media, and therefore to introduce complexities in the interpretation of the kinetics of the formation of chalcone from benzaldehyde and acetophenone. The reverse aldol reaction and the dehydration step are shown to be of comparable rates, and to be relatively fast with respect to the rate of the forward condensation step in dilute solution. The details of the mechanism of the acid-catalyzed aldol condensation are discussed.

Introduction

It recently has been shown[3] that the acid-catalyzed condensation of benzaldehyde and acetophenone to form chalcone (I) may be easily followed spectrophotometrically in acetic acid medium. The rate of the reaction was shown to depend upon the first power of the concentration of the benzaldehyde and the first power of the concentration of acetophenone, and upon the Hammett acidity function, h_0. It was concluded that the rate-determining step was the condensation step proper, and not a final dehydration. These conclusions on the acid-catalyzed reaction are similar to those drawn for the corresponding base-catalyzed reaction by Coombs and Evans,[4] who studied the formation of I in 90% ethanol solution with sodium hydroxide.

$$C_6H_5—CHO + C_6H_5—COCH_3 \longrightarrow$$



(1)

II I

To further verify these conclusions, we have examined the reactions of the intermediate ketol, 1,3-diphenyl-3-hydroxy-1-propanone (II), in both acidic and basic media. The ketol has been reported by Schopf and Thierfelder[5] and was prepared following their procedure. We find that the ketol is dimorphic, exhibiting melting points of 41–42° and 50–51°.

In acetic acid–sulfuric acid solutions, it quickly became apparent that II was undergoing competitive reactions, one leading to the formation of I, and the second resulting in reversion to benzaldehyde and acetophenone. Like results were obtained in 90% alcoholic sodium hydroxide solution, and it is the purpose of the present report to discuss the data on these reactions.

Experimental

1,3-Diphenyl-3-hydroxy-1-propanone (II).—The procedure of Schopf and Thierfelder[5] was followed. The initial product was obtained as an oil, and only after extensive manipulation was crystallization induced. From petroleum ether at −10°, small colorless needles (20% yield) were obtained, m.p. 41.5–42.5° (cor.).

Anal.[6] Calcd. for $C_{15}H_{14}O_2$: C, 79.61; H, 6.24. Found: C, 79.82; H, 6.35.

In a second preparation a similar yield of colorless granules, m.p. 49.7–50.7°, was obtained. When the lower melting sample was allowed to stand at 45° for three days, it slowly solidified, and then showed a m.p. of 49.5–50.5° (reported[5] 53–54°). There was no depression in m.p. on mixing the two higher melting samples. A sample of the higher melting material, when recrystallized, melted at 42.0–50.5°. On resolidification, it melted at 50.6–51.1°. Both samples showed essentially identical spectra (λ_{max} 280 mμ, ϵ_{max} 1030) in alcohol, and in standing in acetic acid–sulfuric acid mixtures, both showed the gradual appearance of the spectra of *trans*-chalcone.

Preparation of Solutions.—Acetic acid, benzaldehyde, acetophenone and *trans*-chalcone were prepared as described previously.[3] Ethanol (90%) was made up by volume.

Kinetic Measurements.—Measurements were carried out essentially as described previously.[3] Solutions of the ketol in appropriate solvents were diluted to a final known concentration of 10^{-3} to 10^{-5} molar. The appearance of I was then followed spectrophotometrically using a Beckman DU spectrophotometer.

Results and Discussion

Base-catalyzed Condensation.—A spectrophotometric determination of the rate of condensation of benzaldehyde (0.05 *M*) and acetophenone (0.05 *M*) was carried out at 26.0° in 90% ethanol 0.02 *N* in sodium hydroxide. The bimolecular rate constant thus obtained, k_{obs}, 4.5×10^{-2} liter mole^{-1} min.$^{-1}$ is to be compared with a value for k of 5.5×10^{-2} liter mole^{-1} min.$^{-1}$ interpolated from the data of Coombs and Evans.[4]

Reactions of the Ketol II in Basic Media.—It quickly became apparent that II undergoes two rapid, competitive reactions in ethanolic sodium hydroxide solution, the first being the dehydration to form I, and the second being the reversal of the condensation to form benzaldehyde and acetophenone. From Table I it may be seen that at 310 mμ I is the only effectively absorbing species, while at 240 mμ the absorption due to benzaldehyde and acetophenone provides a measure of their concentration.

TABLE I

SELECTED SPECTRAL VALUES IN 95% ETHANOL

mμ	$\epsilon_{Benzaldehyde} \times 10^{-4}$	$\epsilon_{Acetophenone} \times 10^{-4}$	$\epsilon_{II} \times 10^{-4}$	$\epsilon_{I} \times 10^{-4}$
240	1.14	1.21	1.25	0.631
250	1.28	0.96	1.17	.552
260	0.444	.218	0.444	.764
280	0.142	.101	.103	1.38
300		.014		2.20
310		.0069	.010	2.40

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

[2] Union Carbide and Carbon Fellow, 1952-1953; U. S. Rubber Co. Fellow, 1953-1954.

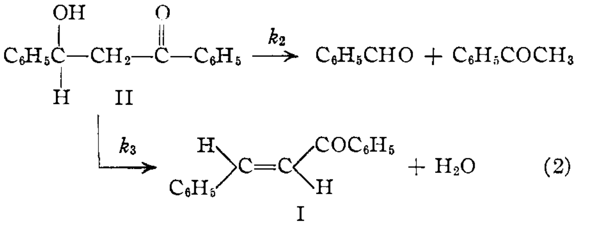
[3] D. S. Noyce and W. A. Pryor, THIS JOURNAL, **77**, 1397 (1955).

[4] E. Coombs and D. P. Evans, *J. Chem. Soc.*, 1295 (1940).

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

[6] Analysis by the Microanalytical Laboratory of the University of California.

Hence one can follow the rate of the two competitive reactions



$$C_6H_5CH(OH)-CH_2-CO-C_6H_5\ (II) \xrightarrow{k_2} C_6H_5CHO + C_6H_5COCH_3$$
$$II \xrightarrow{k_3} C_6H_5CH{=}CHCOC_6H_5\ (I) + H_2O \quad (2)$$

From the usual equations for parallel first-order reactions[7] where

$$k' = k_2 + k_3 \quad (3)$$

letting P represent the concentration of I at any time and R the concentration of benzaldehyde and acetophenone at any time, and K the concentration of II, then

$$P/R = k_3/k_2 \quad (4)$$

and

$$\frac{P_\infty}{K_0} = \frac{k_3}{k_2 + k_3} = \frac{k_3}{k'} \quad (5)$$

Further

$$\ln \frac{K_1}{K_2} = k'(t_2 - t_1) = \ln \frac{(R_\infty - R_1)}{(R_\infty - R_2)} = \ln \frac{(P_\infty - P_1)}{(P_\infty - P_2)} \quad (6)$$

From equation 6 it is apparent that k' may be obtained both from the appearance of I (measurement at 310 mμ) and from the appearance of benzaldehyde and acetophenone (measurement at 240 mμ). Table II shows the results of the kinetic measurements. It may be seen from comparison of run 1 with runs 2–5 that both reactions are essentially first order in stoichiometric sodium hydroxide. The ratio of k_2 to k_3 is determined by considering the ultimate formation of I(P_∞). It is also to be noted that the spectrophotometric material balance $((P_\infty + R_\infty)/K_0)$ is good, though the value of k' determined from the appearance of benzaldehyde and acetophenone is subject to a much greater uncertainty because of competing absorption at 240 mμ.

TABLE II

RATE OF DEHYDRATION AND REVERSE ALDOL REACTIONS OF II IN 90% ETHANOL AT 26.0°

Run	K_0	$\frac{P_\infty + R_\infty}{K_0}$	$\frac{P_\infty}{K_0}$	λ, mμ	k', min.$^{-1}$	$k'(P_\infty/K_0) = k_3$, min.$^{-1}$	$k' - k_3 = k_2$, min.$^{-1}$
1[a]	8.30×10^{-5}	0.964	0.203	310	0.375	0.075	0.29
2[b]	3.69×10^{-3}	1.01	.206	310	.192	.040[c]	.152[d]
				240	.151	.031	.120
3[b]	3.80×10^{-3}	1.01	.214	310	.157	.034[c]	.123[d]
				240	.130	.028	.102
4[b]	1.96×10^{-2}	1.00	.223	310	.137	.031[c]	.106[d]
5[b]	3.83×10^{-3}	0.98	.211	310	.153	.032[c]	.121[d]
				240	.103	.022	.081

[a] (NaOH) = 0.02 *M*. [b] (NaOH) = 0.01 *M*. [c] Average $k_3 = 3.1 \pm 0.4 \times 10^{-2}$ min.$^{-1}$. [d] Average $k_2 = 1.15 \pm 0.16 \times 10^{-1}$ min.$^{-1}$.

These data show that in the base-catalyzed condensation of benzaldehyde and acetophenone, in dilute solutions, the carbon–carbon bond forming step is the rate-determining process, with dehydration being rapid.

Reactions of the Ketol in Acetic Acid Solutions.—In acetic acid solutions the sitution is more complex. From typical kinetic measurements carried out in acetic acid 0.7 molar in sulfuric acid and 0.6 molar in water, as illustrated in Fig. 1, there are competing reactions which must be considered. The ultimate production of *trans*-chalcone is only 76% under these conditions (determined spectrophotometrically). The ketol II is apparently suffering partial reversion to benzaldehyde and acetophenone. Further we conclude that II is first undergoing acid-catalyzed esterification, and that the ester is slowly losing the elements of acetic acid to give I, complicated by a concurrent loss of the elements of water from II. This reaction scheme is summarized in (7).

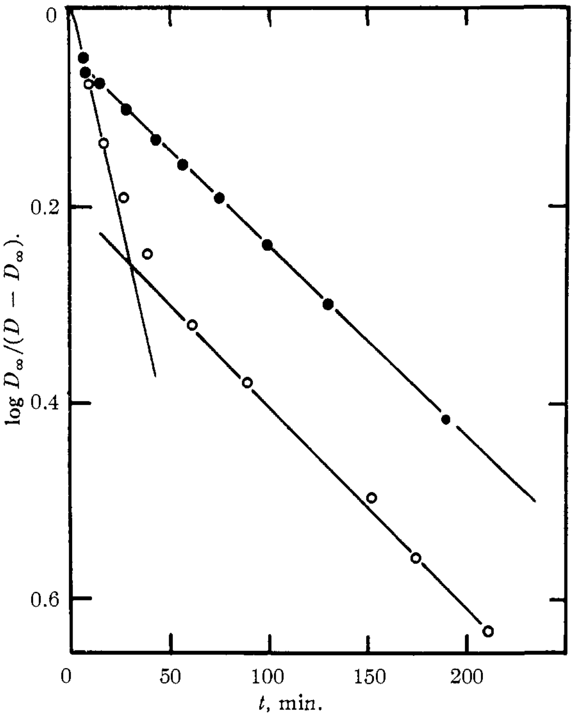
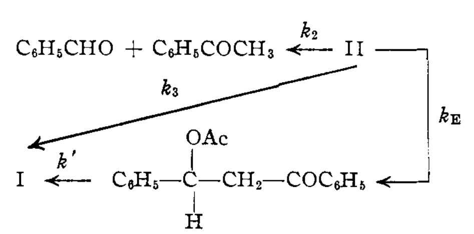


Fig. 1.—Typical kinetic results for the dehydration of the ketol in acetic acid: ●, anhydrous; ○, H_2O 0.6 molar.



$$C_6H_5CHO + C_6H_5COCH_3 \xleftarrow{k_2} II \xrightarrow{k_3} I; \quad II \xrightarrow{k_E} C_6H_5CH(OAc)-CH_2-COC_6H_5 \xrightarrow{k'} I \quad (7)$$

The absorption of acetic acid below 250 mμ precludes the determination of k_2, and with this complexity only approximate values may be assigned to the individual rate constants for all of the processes in (7). From the initial rate of formation of I, k_3 is determined as about 1.9×10^{-2} min.$^{-1}$. Since $k_E + k_3 = (76/24)k_2$ and approximately 50% of I arises from the ester, the ratios k_2:k_3:k_E are about 1:1:2.

Kinetic measurements in anhydrous acetic acid–sulfuric acid mixtures are more easily interpreted.

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[7] A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," John Wiley and Sons, Inc., New York, N. Y., 1953. p. 147.

Here, the initial rapid reaction more nearly disappears, and the ultimate production of chalcone (P_∞) is essentially quantitative. Thus the observed rate constant, k'_3, 4.9 × 10^{-3} min.$^{-1}$, is that for the step involving elimination of the elements of acetic acid. The nature of the limiting rate in wet acetic acid is thus also established as being similarly the elimination of the elements of acetic acid from the ester of II. From these data, one may conclude that the rates of k_E, k_3 and k_2 are clearly of the same order of magnitude, with the rate of hydrolysis of the ester, k_H, being slow.

It may be seen from Table III that the rate of elimination (the limiting rate) is closely proportional to H_0, and appears to be the same process in wet and in anhydrous acetic acid. As can be seen from Fig. 1, the limiting rate is reached in about 4% of a half-life in anhydrous acetic acid, and in about 40% of a half-life in wet acetic acid. Table IV shows that the amount of benzaldehyde and acetophenone (R) produced by the reverse aldol reaction similarly increased from about 1–2% in anhydrous acetic acid to 24% in wet solvent.

Table III

Limiting Rates for the Formation of Chalcone from Ketol in Acetic Acid, Sulfuric Acid

Run	$K_0 \times 10^5$	$\frac{P_\infty}{K_0}$	$k \times 10^3$, min.$^{-1a}$	(H_2O)	(H_2SO_4)	H_0	log $k + H_0$^{b}
1	6.02	1.01	4.49	0.01	0.420	−2.43	−4.78
2	6.95	0.98	11.7	.01	.930	−2.92	−4.85
3	6.23	.93	4.85	.040	.419	−2.43	−4.75
4	5.47	.89	4.45	.054	.410	−2.39	−4.74
5	6.73	.83	4.65	.23	.535	−2.47	−4.80
6	6.29	.764	4.34	.60	.699	−2.47	−4.83
7	5.35	.767	4.78	.60	.699	−2.47	−4.79

^{a} $T = 26.0°$. ^{b} Average value of log $k + H_0 = -4.81 \pm 0.03$.

As was true in basic solution, the forward condensation step is very slow at the concentrations of the reactants regenerated through the reverse aldol step (k_2), and may thus be ignored in the kinetics starting with the ketol. The "induction periods" observed in Fig. 1 are interpreted as follows: in anhydrous solvent, evidently k_E is very rapid[8] and k_H very slow; practically all the ketol is esterified, and hence only 1–2% returns to reactants. Under these circumstances neither k_2 nor k_3 can compete effectively with k_E. Hence the limiting rate k_3' is very quickly reached. In contrast in the wet acetic acid medium, the initially high rate of formation of I signifies the competitive reactions mentioned earlier, followed eventually by a slower process, the acetate elimination.

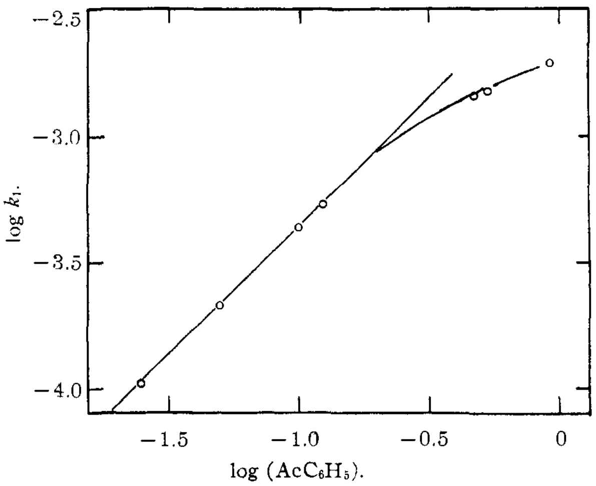

Fig. 2.—Limiting rate of formation of chalcone as a function of acetophenone concentration.

It should be noted that the magnitude of k_3' is similar to the measured rate of the condensation.[3] Therefore at high initial concentrations of benzaldehyde and acetophenone deviations from the simple linear dependencies should be observed.

The Rate of the Condensation Reaction at High Concentrations of Acetophenone.—Analysis of kinetic measurements made as described previously[3] with high concentrations of acetophenone showed that the rate of the formation of *trans*-chalcone was initially low and increased markedly during the early portions of the reaction. Table IV illustrates this situation.

Table IV

Condensation Reaction Showing Initial Induction Period

H_2SO_4 = 0.699 M; $C_6H_5COCH_3$ = 0.2583 M; C_6H_5CHO 1.95 × 10^{-2} M; H_2O = 0.60 M, T 26.0°.

t(min.)	$P \times 10^2$	$C_6H_5CHO \times 10^2$ apparent	$k_1 \times 10^4$ apparent
0	..	(1.95)	..
116	0.09	1.86	4.52
209	.19	1.76	4.98
278	.28	1.67	5.57
336	.35	1.60	5.83
555	.64	1.31	7.00
1421	1.30	0.65	7.72

k_1 (from limiting slope) = 8.5 × 10^{-4} min.$^{-1}$

The induction period thus observed accords well with the rate of elimination of the acetate ester of II, and thus represents the approach to a steady state concentration of this ester. The limiting rate, effectively reached after 20% reaction, gives a value for the rate constant for the over-all reaction $k_1 = 3.20 \times 10^{-3}$ l. mole^{-1} min.$^{-1}$ or log $k_1 + H_0 = -4.97$. The value of this latter constant is to be

Table V

The Rate of Formation of *trans*-Chalcone at High Concentrations of Acetophenone

H_2SO_4 = 0.420 M; H_2O = 0.0; T = 26.0°.

Run	CH_3CO-C_6H_5	C_6H_5CHO	$k_{lim} \times 10^4$, min.$^{-1}$	$k_{lim} \times 10^3$, l. mole^{-1} min.$^{-1}$
1	0.952	1.975 × 10^{-2}	19.8	2.08
2	.540	1.975 × 10^{-2}	15.2	2.82
3	.476	1.975 × 10^{-2}	14.3	3.06
4	.1237	1.975 × 10^{-2}	5.38	4.35^a
5	.0990	1.975 × 10^{-3}	4.34	4.38^a
6	.0495	1.975 × 10^{-3}	2.12	4.28^a
7	.0248	9.88 × 10^{-4}	1.05	4.24^a

^{a} Average k_1 = 4.31 ± 0.05 × 10^{-3} l. mole^{-1} min.$^{-1}$.

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(8) Perhaps the increased rate of esterification in the anhydrous medium is a result of a very small amount of Ac^+ (acetylium ion)[9] being generated in the medium as the last amounts of water are removed from the solvent.

(9) H. Burton and P. F. G. Praill, *J. Chem. Soc.*, 1203 (1950).

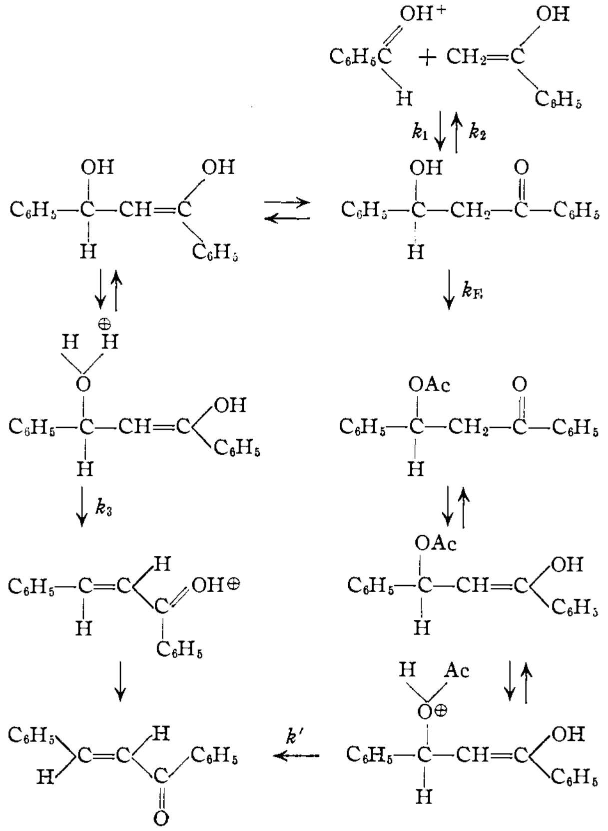
compared with an extrapolated value from the data reported earlier[3] of −4.97.

More extensive data determined in anhydrous acetic acid are presented in Table V. At higher concentrations of acetophenone the value of the pseudo unimolecular rate constant k_{lim} does not increase as rapidly as would be predicted, as shown in Fig. 2. At the higher concentrations of acetophenone, the rate of the condensation approaches the rate of the elimination, k_3'.

Conclusions Regarding the Mechanism of the Forward Condensation Reaction.—Because of the complexity of the steps succeeding the actual bond-forming reaction, where even the observed rate of appearance of chalcone from the ketol in acid is a function of several competing reactions, it is not feasible to determine all of the rate constants from the present data.

However it may be concluded that the rate of the dehydration of the ketol is faster than the rate of the loss of acetic acid from the ketol acetate. This result is probably due to the greater basicity of the alcohol as compared to the ester.

One may present a fairly detailed picture of the pathway(s) by which chalcone arises under the conditions investigated. Such a reaction scheme is outlined below. Under the differing experimental conditions investigated, the value of the bimolecular rate constant determined is not exactly the same in both the anhydrous and the wet acetic acid media, at the same H_0. This difference is presumably due to the difference in the branching ratio of the different possible reactions of the intermediate ketol. It is also attractive to suggest that the elimination step takes place through the intermediate enol. The rate of enolization is of the appropriate order of magnitude for this to be feasible.



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[CONTRIBUTION FROM THE RESEARCH LABORATORY, GENERAL ELECTRIC COMPANY]

Kinetics of the Polymerization of a Cyclic Dimethylsiloxane[1]

BY W. T. GRUBB AND ROBERT C. OSTHOFF

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Cyclic dimethylsiloxanes are converted into high polymers by the action of potassium hydroxide at elevated temperatures. The kinetics of this process has been studied using the monomer, octamethylcyclotetrasiloxane (I). Precipitation and distillation analysis of this system at small conversions reveals that I and high polymer make up at least 90% of the material present. Because of this, the well known theories of polymer–solvent systems have been applied. In particular, the vapor pressure above the polymerizing system is a convenient measure of the extent of reaction. The kinetics have been measured by continuously monitoring the vapor pressure above the polymerizing solution. The reaction proceeds at a rate which is first order in the volume fraction of I in the solution attaining an equilibrium at about 94% polymer. A reversion reaction of the polymer takes place at a rate proportional to the volume fraction of polymer present. The rate law based on these concepts is in excellent agreement with the experimental kinetics. The apparent activation energy of the over-all polymerization is found to be 19.6 kcal. The rate of the polymerization is proportional to the square root of the potassium hydroxide concentration.

Many cyclic siloxanes undergo reaction in the presence of acidic or basic catalysts to form high molecular weight siloxane polymers. For example, dimethylsiloxane polymers may be formed from low molecular weight octamethylcyclotetrasiloxane (I) by the action of potassium hydroxide or other alkali metal hydroxides at elevated temperatures.[2] Some qualitative features of this reaction have been investigated previously,[3] and a mechanism involving the formation of intermediate alkali metal silanolates was proposed, but no exact kinetic data were obtained. It was therefore the purpose of the present investigation to develop a suitable experimental method for measuring the kinetics of polymerization of I under carefully controlled conditions and to investigate the effects of temperature and other conditions upon the reaction

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(1) Presented at the 126th meeting of the American Chemical Society, New York, N. Y., September, 1954.

(2) J. F. Hyde, U. S. Patent 2,490,357 (December 6, 1949).

(3) D. T. Hurd, R. C. Osthoff and M. L. Corrin, THIS JOURNAL, **76**, 249 (1954).