Reactions of Conjugated Fatty Acids. III. Kinetics of the Diels-Alder Reaction[1]

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DIETHYLAZODICARBOXYLATE has been used as a dienophile in the Diels-Alder reaction with several dienes (1). This substance is particularly well suited for studying the kinetics of the diene reaction since it has an intense orange color with an adsorption maxima at 410 mμ (Figure 1). Solutions of diethylazodicarboxylate follow Beer's law closely. Hence the disappearance of the color as it forms colorless adducts with dienes can be used to study the kinetics of the reaction. Rodgman and Wright (6) have made an extensive kinetic study on the reaction between the dialkylazodicarboxylates and cyclopentadiene.

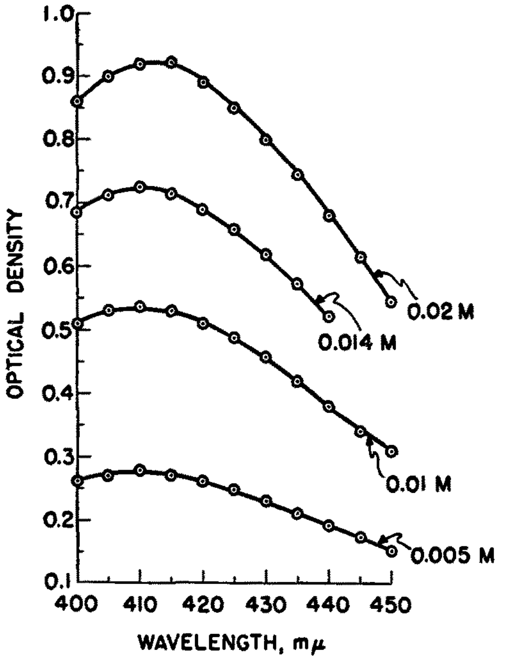
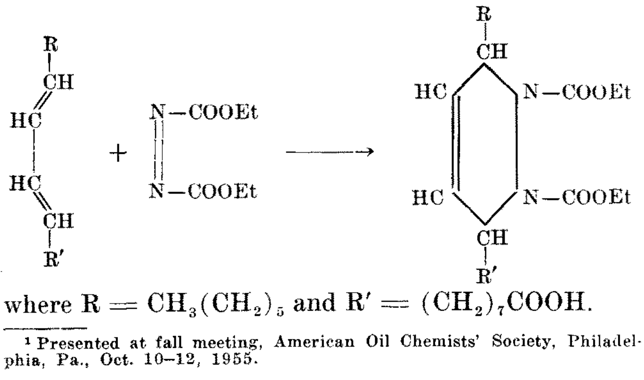


FIG. 1. Absorption curves of diethylazodicarboxylate in benzene at various concentrations.

During an investigation on the addition of various dienophiles to conjugated fatty acids, it seemed desirable to get some information on the velocity of the reaction in various solvents and with several catalysts. Diethylazodicarboxylate and *trans,trans*-9,11-octadecadienoic acid were chosen as reactants for this study. The reaction can be illustrated as follows:



where R = $CH_3(CH_2)_5$ and R' = $(CH_2)_7COOH$.

Experimental

Procedure. The reaction between *t,t*-9,11-octadecadienoic acid and diethylazodicarboxylate was followed by use of a Coleman universal spectrophotometer (model 14).[2] The tubes were carefully selected for uniform diameter to insure a snug fit in the cell carrier. Each tube was then balanced optically against a standard and marked so that it could be placed accurately in the spectrophotometer cell without rechecking against a standard. A Corning filter, No. 5113 (maximum transmission at 410 mμ), was used in the spectrophotometer. Linear plots of concentration *vs.* optical density were obtained for benzene solutions of diethylazodicarboxylate in the 0.001 to 0.02 molar range, as shown in Figure 2.

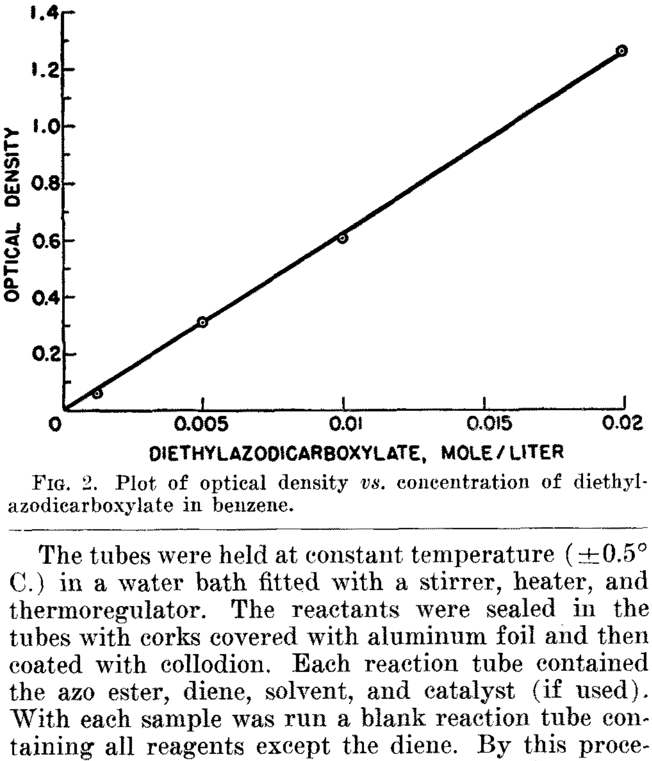


FIG. 2. Plot of optical density *vs.* concentration of diethylazodicarboxylate in benzene.

The tubes were held at constant temperature (±0.5° C.) in a water bath fitted with a stirrer, heater, and thermoregulator. The reactants were sealed in the tubes with corks covered with aluminum foil and then coated with collodion. Each reaction tube contained the azo ester, diene, solvent, and catalyst (if used). With each sample was run a blank reaction tube containing all reagents except the diene. By this procedure any reaction between the azo ester and the nondiene components could be detected. The colorimeter potentiometer was adjusted to zero with the solvent before readings were taken on the blank and the reaction tube. The data were plotted, and the order of the reaction was determined by the graphical method (2). The velocity constant, k, was obtained from the slope of line obtained by plotting 1/c against t (for second order reactions). The initial concentration of the reactants was 0.02 mole per liter. Catalysts, when used, were added in 0.02 molar amounts.

Preparation and isolation of the adduct in a variety of solvent systems has been carried out to establish that the desired adduct was formed. Solvents used were benzene, chloroform, 96% acetic acid, 70%

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[1] Presented at fall meeting, American Oil Chemists' Society, Philadelphia, Pa., Oct. 10–12, 1955.

[2] Mention of the names of firms or trade products does not imply that they are endorsed or recommended by the U. S. Department of Agriculture over other firms or similar products not mentioned.

acetonitrile, and 80% acetone. A typical analysis of the adduct is as follows:

calc. for $C_{24}H_{42}O_6N_2$; C, 63.4; H, 9.32; N, 6.16; N.E., 454.6; I.V., 55.8

found: C, 63.2; H, 9.05; N, 5.98; N.E., 462; I.V., 53.3

Reagents. *t,t*-9,11-Octadecadienoic acid, m.p. 52–53°C., was prepared by the dehydration of ricinelaidic acid (4). Diethylazodicarboxylate, b.p. 113°/15 mm., was prepared by reacting hydrazine hydrate and ethyl chlorocarbonate followed by nitric acid oxidation of the intermediate hydrazo compound (6). Alkali-conjugated soybean fatty acids were prepared by refluxing soybean fatty acids in ethylene glycol containing potassium hydroxide (3). Infrared spectra of the methyl ester of the conjugated product showed the presence of 45.1% of *cis,trans* conjugation and 1.9% of *trans,trans* conjugation.

The conjugated fatty acids prepared above were elaidinized in pentane-hexane containing a little iodine (5). Infrared spectra of the methyl ester of the elaidinized product showed the presence of 14.3% of *cis,trans* conjugation and 34.2% of *trans,trans* conjugation.

Solvents. Benzene was purified by distillation from sodium benzophenone. Chloroform, carbon tetrachloride, dimethyl formamide, and hexane were dried over magnesium sulfate and distilled. Acetic acid used was C.P. grade. Acetonitrile was purified by distillation, and the fraction boiling at 80–2°C. was collected. Acetone was the C.P. grade and was dried over Na_2CO_3 and distilled from potassium permanganate, b.p., 56°C.

Results and Discussion

1. *Reaction in Anhydrous Solvents.* Kinetic data for the reaction between diethylazodicarboxylate and *t,t*-9,11-octadecadienoic acid in various solvents is shown in Table I. The reaction followed second-order kinetics, especially in nonpolar solvents, such as benzene and hexane. The addition of equimolar amounts of trifluoroacetic acid or trichloroacetic acid had a marked catalytic effect on the reaction in benzene and carbon tetrachloride. The reaction rate in benzene was more than doubled by the addition of acidic catalysts. Carbon tetrachloride quadrupled the rate attained in uncatalyzed runs. We cannot explain the failure of acidic catalysts to promote the reaction in hexane. However the use of strong acids, *e.g.*, trifluoroacetic acid, in nonpolar solvents altered the kinetics of the reaction slightly after considerable time so that the reaction was not quite second order (see Figure 3). The velocity constant of the diene reaction in benzene, hexane, and carbon tetrachloride was about the same when no catalysts were used. Acid catalysts in chloroform did not cause pronounced effects. The velocity constant in chloroform at 40°C. was about 7.8×10^{-3} and the reaction was second order, while k for the trifluoroacetic and trichloroacetic acid catalyzed reactions was 8.2×10^{-3} and the reaction was almost second order. Again, the presence of strong acids appeared to alter the kinetics of the reaction slightly. The failure of acids to promote the reaction in chloroform is not surprising since it has been shown by other workers (6) that the presence of strong acids in polar solvents, such as ethyl and methyl alcohol, reduces the rate of reaction below that in the solvent alone.

TABLE I

Reaction of Diethylazodicarboxylate and *t,t*-9-11-Octadecadienoic Acid in Anhydrous Solvents

Solvent	Catalyst	Rate constant,[a] k x 10^3		Activation energy, E
		40°C.	50°C.	
Chloroform	TFA[b]	8.2	14.1	10.8
Chloroform	TCA[c]	8.2	14.0	10.7
Chloroform	HOA[c]	6.7	......	......
Chloroform	......	7.8	10.8	6.6
Carbon tetrachloride	TFA[b]	9.4	15.7	10.0
Carbon tetrachloride	TCA[c]	8.5	11.9	6.7
Carbon tetrachloride	......	2.1	3.2	8.4
Benzene	TFA[b]	3.6	7.5	14.7
Benzene	TCA[c]	3.5	5.2	7.9
Benzene	......	1.4	2.3	9.9
Hexane	TFA[b]	1.7	......	......
Hexane	TCA[c]	1.8	......	......
Hexane	......	1.5	......	......
Acetonitrile	......	4.4	7.8	11.4
Acetic acid	......	11.9	22.0	12.3
Acetone	......	1.1	2.1	13.3
Dimethyl formamide	......	2.8	4.2	8.1

[a] Expressed in liters $mole^{-1}$ sec^{-1} calculated as second-order reactions

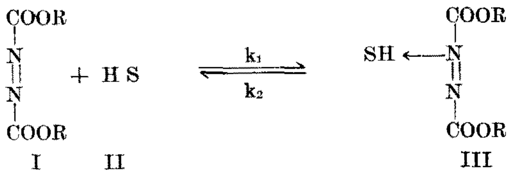
$$\left[k = \frac{1}{t} \frac{x}{a(a-x)} \right]$$

[b] Trifluoroacetic acid.

[c] Trichloroacetic acid.

In acetic acid the reaction was faster than in any other anhydrous solvent in this series.

Rodgman and Wright (6) found that, in polar solvents such as acetone, chloroform, and acetic acid, the over-all reaction between cyclopentadiene and azo esters followed first-order kinetics. This result seems to differ from our results in these solvents, but a closer look at the data appears to resolve the situation. Rodgman and Wright proposed that alkyldiazodicarboxylates react with proton donor solvents to form a complex, III:



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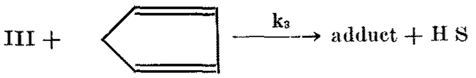
and that this material reacts with cyclopentadiene rapidly to form the final adduct:



They assumed further that k_1 is slow compared with k_2 and k_3 and hence k_1 is the rate determining step. Since II is in great excess the over-all reaction is pseudo first order. Our work deals with a diene compound that is less reactive than cyclopentadiene, and it is reasonable to expect k_3 in our reaction to be small compared with k_1 and k_2. Thus in the equation

$$\text{rate} = \frac{k_1\,[\text{ester}]\,[\text{diene}]\,[\text{H S}]}{k_2/k_3 + [\text{diene}]}$$

k_2/k_3 becomes very large compared to [diene] and letting k_1 [HS] $= k_m$, the equation reduces to

$$\text{rate} = \frac{k_m}{k_2/k_3}\,[\text{ester}]\,[\text{diene}].$$

This expression describes a second order reaction.

Information on the kinetics and relative rates of reaction of diethylazodicarboxylate with *cis,trans* and *trans,trans* fatty acid isomers was obtained by investigating the reaction of the azo ester with alkali-conjugated soybean fatty acids before and after isomerization with iodine. In these experiments an

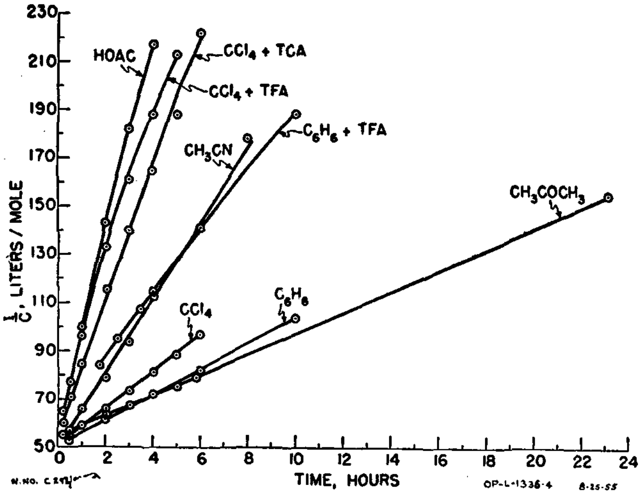


FIG. 3. Reaction of *t,t*-9,11-linoleic acid and diethylazodicarboxylate in various anhydrous solvents.

amount of azo ester equivalent to the total of all types of fatty acid present was used.

Infrared analysis showed that, before isomerization with iodine, the alkali-conjugated fatty acids contained predominately *cis,trans* isomers and about 2% of *trans,trans* isomers. Over a period of 32 hrs. the optical density of the mixture of azo ester and fatty acids changed by only 3%. This result indicates that, under the conditions used, the rate of reaction of azo ester with *cis,trans* conjugated fatty acids is negligible.

After isomerization of the alkali-conjugated fatty acids with iodine, infrared analysis showed that 34% of *trans,trans* isomers were present. Since azo ester and *trans,trans* conjugated fatty acid were not present in equimolar amounts, the specific reaction rate could not be obtained from a plot of 1/c *vs.* time. Instead the quantity

$$\log \frac{b\,(a-x)}{a\,(b-x)}$$

was plotted against time. In this expression a and b are the initial concentrations of *trans,trans* conjugated fatty acid and diethylazodicarboxylate, respectively, and x is the amount reacted at time t. As shown in Figure 4, a straight line was obtained, confirming second-order reaction kinetics. The specific reaction rate constant (k) corresponding to Figure 4 is 1.7×10^{-3} liter mole^{-1} sec^{-1} as compared with a value of 1.4×10^{-3} obtained for pure *trans,trans*-9,11-octadecadienoic acid. The agreement of these values for k is excellent since the slope of the line of Figure 4 is sensitive to errors in the value of a. The results suggest that the measurement of rate of reaction of diethylazodicarboxylate with conjugated fatty acids would be a useful method of analysis for determination of the amount of *trans,trans* isomers in the conjugated fatty acids.

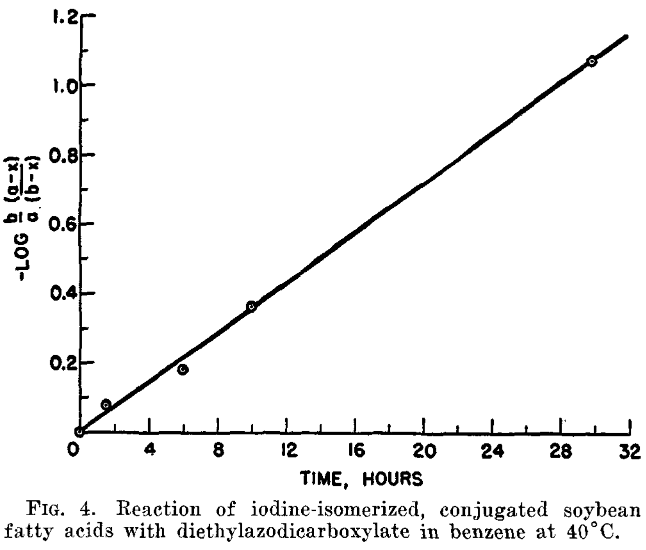


FIG. 4. Reaction of iodine-isomerized, conjugated soybean fatty acids with diethylazodicarboxylate in benzene at 40°C.

2. *Reaction in Aqueous Solvents.* The addition of water to those solvent systems where a homogeneous solution can be maintained causes a marked increase in the rate of reaction as shown in Table II. For example, in anhydrous acetonitrile the reaction was of second order with a velocity constant of 4.4×10^{-3}. In 90% aqueous acetonitrile the rate is quadrupled, and in 70% acetonitrile the rate is more than eight times as fast as in the anhydrous solvent. The rate appears to increase as we go to 50% aqueous solutions; however, when water is used in quantities greater than 30%, reactants are difficult to dissolve at the beginning of the run. The addition of water does not appear to alter the kinetics of the reaction since a straight line was obtained in the plot of time *vs.* 1/c in all acetonitrile runs (see Figure 5). A similar effect on the velocity constant was noted when the acetic acid-water solvent system was studied. The effect of water is more pronounced at lower concentrations in acetic acid, and a 3½-fold increase in velocity is noted at the 4% water level. Less than a twofold increase was obtained in acetonitrile at this level. However compatibility problems appear sooner in the acetic acid-water system, and difficulty is encountered in this system when 90% acetic acid is used as a solvent.

In a nonpolar solvent, such as benzene, no significant increase in reaction rate is observed when the solvent is saturated with water (approximately 0.02%).

3. *Energy Relationships.* The activation energy, E, for many of the reactions studied in anhydrous solvents is shown in Table I. In benzene and carbon tetrachloride E is lowest in the system catalyzed by trichloroacetic acid; intermediate values were ob-

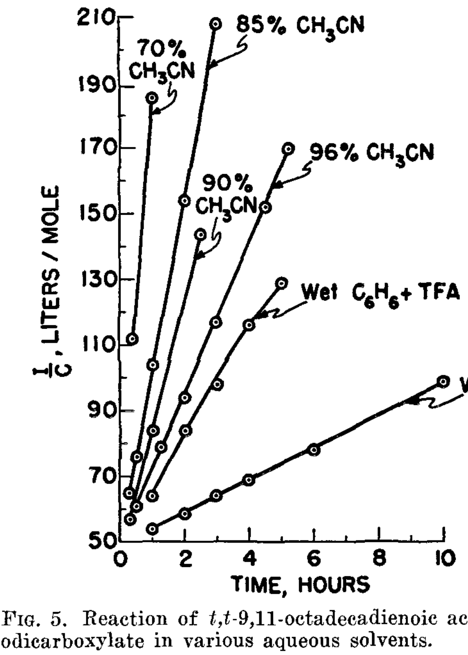


FIG. 5. Reaction of *t,t*-9,11-octadecadienoic acid and diethylazodicarboxylate in various aqueous solvents.

TABLE II

Reaction of Diethylazodicarboxylate and *t,t*,-9-11-Octadecadienoic Acid in Aqueous Solvents

Solvent	Catalyst	Rate constant,[a] $k \times 10^3$		Activation energy E
		40°C.	50°C.	
99.98% Benzene	TFA[b]	3.3	......	......
99.98% Benzene	TCA[c]	2.9	......	......
99.98% Benzene	......	1.4	......	......
96% Acetic acid	......	42.5	50.1	3.2
96% Acetonitrile	......	6.4	......	......
90% Acetonitrile	......	8.7	15.9	12.1
85% Acetonitrile	......	14.4	......	......
80% Acetonitrile	......	18.3	33.8	12.3
75% Acetonitrile	......	21.2	......	......
70% Acetonitrile	......	41.1	50.9	4.3
65% Acetonitrile[d]	......	42.2	......	......
50% Acetonitrile[d]	......	100.5	......	......
99.6% Acetone	......	1.4	......	......
90% Acetone	......	3.5	6.3	11.8
80% Acetone	......	10.9	14.3	5.4

[a] Expressed in liters $\text{mole}^{-1}\ \text{sec}^{-1}$ calculated as second-order reactions

$$\left[k = \frac{1}{t}\ \frac{x}{a(a-x)}\right]$$

[b] Trifluoroacetic acid.

[c] Trichloroacetic acid.

[d] Reactants not completely dissolved at the start of the reaction.

tained with no acidic catalyst, and the highest E value resulted when trifluoroacetic acid was used. The Arrhenius equation

$$k = Ae^{-E/RT}$$

shows that changes are occurring in both the non-exponential factor A and the activation energy, E. With trifluoroacetic acid in benzene a high activation energy is more than counterbalanced by a low steric factor (large value of A) since the reaction rate is fastest in this system. In chloroform the activation energy is about the same in the acidic systems studied and considerably higher than in the uncatalyzed run. Since the rate of the reaction is about equal in all chloroform runs, the acid-catalyzed reactions must involve less specific intermediates.

The activation energy for the reactions run in aqueous solvents is shown in Table II. In aqueous solvents and in the anhydrous polar solvents activation energy is of the same order (12–13 kc/mole) until an equimolar concentration of water and solvent is approached. At this point the activation energy of the reaction in the solvent water systems studied (acetone, acetic acid, and acetonitrile) falls to 3 to 5 kc/mole. One can assume that several reactions are competing in aqueous solvents to give the over-all rate constant

(A) Ester + solvent $\rightleftharpoons$ solvated ester

(B) Solvent + water $\rightleftharpoons$ hydrated solvent
Ester + hydrated solvent $\rightleftharpoons$ solvated hydrated ester

(C) Ester + diene $\xrightarrow{k_1}$ adduct

(D) Diene + solvated ester $\xrightarrow{k_2}$ adduct + solvent

(E) Diene + solvated hydrated ester $\xrightarrow{k_3}$ adduct + solvent + water

where $k_3 > k_2 > k_1$ but smaller than the rate constants for the solvating reactions A and B. When no water is present, we have rate-determining reactions C and D competing and leading to the adduct. As a quantity of water is added, reaction E starts. Since it is a faster reaction than C or D, it increases the over-all reaction rate constant. As more water is added, the over-all rate constant continues to increase. In aqueous acetonitrile the increase in k was almost proportional to the amount of water added as is shown in Table III. As the molar ratio of water to solvent approaches unity, reaction D contributes little to the over-all rate constant because most of the solvent is hydrated with water according to reaction B. If the amount of water added exceeds the one-to-one ratio to solvent, we can propose another reaction in which water is available to react with the azo ester

TABLE III

The Reaction Between Diethylazodicarboxylate and *t,t*-9,11-Octadecadienoic Acid in Acetronitrile in the Presence of Water (40°C.)

Water, moles/liter	$k \times 10^3$ liter $\text{mole}^{-1}\ \text{sec}^{-1}$	k/Water liters^2 $\text{moles}^{-2}\ \text{sec}^{-2}$
2.22	6.4	2.81
5.55	8.7	1.57
8.32	14.4	1.73
11.1	18.3	1.65
13.9	21.2	1.52
16.6	41.1	2.46
27.8	100	3.59

(F) Water + ester $\rightleftharpoons$ hydrated ester

(G) Hydrated ester + diene $\xrightarrow{k_4}$ adduct + water

where $k_4 > k_3$. Evidence for F and G is shown in Table III where water in amounts of 16 to 17 moles/liter starts to exceed the moles of acetonitrile present. Consequently water would be available for the formation of the hydrated ester. Perhaps this reaction is responsible for the lower activation energy in 80% acetone, 70% acetonitrile, and 96% acetic acid.

Summary

The kinetics of a Diels-Alder-type reaction between diethylazodicarboxylate and *t,t*-9,11-octadecadienoic acid has been studied in various solvent systems and with acidic catalysts. The rate of the reaction was found to vary as follows: a) the reaction rate is faster in polar solvents than in nonpolar solvents; b) addition of acidic catalysts to nonpolar solvents increases the rate of the reaction, and acidic catalysts appear to have no effect on the rate of reaction in polar solvents; c) when compatibility can be maintained, addition of water to polar solvent systems appears to increase the reaction rate in proportion to the amount of water added.

The reaction follows second-order or pseudo second-order kinetics. Probably it is more complex than the over-all reaction kinetics indicate. Certain reactions were studied at two temperatures, and information on activation energy of the reaction has been obtained.

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