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

# METHODS FOR ACCELERATION OF A TYPICAL DIELS-ALDER REACTION

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An addition reaction such as that of Diels and Alder, which occurs with a marked decrease in entropy is obviously favored by low temperature. However in many cases elevated temperatures are required in order to attain equilibrium within a reasonable time. It is apparent that conditions permitting reaction at moderate temperatures are desirable. In the present report it will be shown that these conditions include choice of reaction medium and inclusion of acidic catalysts. Our observations have partly been anticipated by Wassermann, *et al.* (1), who reported the catalytic effect of acids on the reaction between benzo-quinone and cyclopentadiene.

The reaction which we have chosen for study is the original one of Diels and Alder (2, 3). We chose the addition of dialkyl azodicarboxylate (I) to cyclopentadiene (II) because the diene and the adduct, 1,2-dicarboalkoxy-3,6-



endomethylene-1,2,3,6-tetrahydropyridazine (III) are colorless in the spectral range over which I is highly absorptive of light. Furthermore solutions of the colored ester follow Beer's Law closely. We were thus able to examine the kinetics of the reaction.

When benzene, dioxane, or petroleum ether (b.p.  $60-70^{\circ}$ ) is used as the medium the reaction between ester (I) and diene (II) can be described fully by equation (i). The over-all reaction appears to be second-order, first order in respect of either ester or diene. This is in agreement with the kinetic results obtained by other authors for the Diels-Alder reaction both in the gas phase and in solution (4). An example of extensive investigations using the dimethyl and the diethyl ester and cyclopentadiene in benzene is shown in Table I. The calculation of the specific rate constants in Table I adapted the usual second order rate expression:

$$k = \frac{1}{t} \left[ \frac{1}{a - x} - \frac{1}{a} \right] \quad \text{when } a = b \tag{ii}$$

or

$$k = \frac{2.303}{(a - b)t} \log \frac{b(a - x)}{a(b - x)} \quad \text{when } a \neq b$$
 (iii)

where a and b are the initial ester and diene concentrations and x the amount consumed in time t. In terms of the colorimeter readings equations (ii) and (iii) become:

$$k = \frac{1}{at} \left[ \frac{(R_s)_0}{(R_s)_t} - 1 \right] \quad \text{when } a = b \tag{iv}$$

or

$$k = \frac{2.303}{(a - b)t} \log \frac{(R_b)_0 \cdot (R_a)_t}{(R_a)_0 \cdot (R_b)_t} \quad \text{when } a \neq b \tag{v}$$

where  $(R_a)_0$  and  $(R_a)_t$  are the colorimeter readings initially and at time t. Since the diene is transparent the values for  $(R_b)_0$  and  $(R_b)_t$  are necessarily derived from  $(R_a)$  initially and at time t.

TABLE I

THE REACTION BETWEEN DIALKYL AZODICARBOXYLATES AND CYCLOPENTADIENE IN ANHYDROUS BENZENE

temp., °C.	I. R =	CONCENTRATION IN MOLE	k, IN LITERS.		
		Ester	Diene	MOLES '' MIN.	
23.5	Me	0.010	0.020	0.72	
23.5	${ m Me}$	.020	.020	.72	
23.5	$\mathbf{Me}$	.020	.040	.72	
23.5	Me	.040	.020	.72	
6.0	$\mathbf{Et}$	.020	.020	.036	
15.0	Et	.020	.020	.075	
15.0	$\mathbf{Et}$	.020	.040	.075	
15.0	$\mathbf{Et}$	.040	.020	.075	
19.0	$\mathbf{Et}$	.020	.020	.10	
28.0	$\mathbf{Et}$	.020	.020	.17	
28.0	$\mathbf{Et}$	.020	.040	.17	
28.0	$\mathbf{Et}$	.040	.020	.17	

It may be seen from the rate constants in Table I that the methyl ester reacts five to six times as fast with II in benzene than does the ethyl ester. Not included in Table I are the specific rate constants, each at but one concentration, for the reaction of dimethyl azodicarboxylate (I,  $R = CH_3$ —) with II in dioxane and petroleum ether. The constant in dioxane is 1.02 and that in petroleum ether, is 0.22 as compared with 0.72 liters.moles<sup>-1</sup>.min.<sup>-1</sup> for this reaction in benzene.

The specific rate constants at several temperatures for the reaction of the diethyl ester (I,  $R = C_2H_5$ ) with II in benzene give an average value of 12.3 kcal. per mole for the energy of activation when calculated by equation (vi):

$$\log k = \frac{-E}{2.303RT} + C$$
(vi).

The specific rate constant may then be expressed in the form

 $k = 1.41 \times 10^{8} e^{(-12,300/2.303 \text{ RT})}$ 

In contrast to the simple second-order kinetics for the reaction of dimethyl azodicarboxylate with cyclopentadiene in the inert media, benzene, dioxane and petroleum ether, the reaction in substrates containing active hydrogen seems to be more complex, the kinetics tending toward over-all first-order. For example the rate curves in benzene containing increasing amounts of methanol deviate continuously from the linearity expected for a true bimolecular reaction to that for a pseudo-unimolecular reaction until an over-all first order expression describes exactly the addition of ester to diene which takes place in pure methanol. It has previously been shown (5) that, contrary to the report of Diels and Wulff (6), this reaction in methanol gives the product, III, identical with



FIG. 1. THE EFFECT OF SOLVENTS ON THE RATE OF REACTION BETWEEN 0.020 molar CYCLOPENTADIENE AND DIMETHYL AZODICARBOXYLATE AT 23.5° (Procedure A).  $\bigcirc$  96% acetic acid;  $\bigcirc$  glacial acetic acid;  $\bigcirc$  chloroform;  $\bigcirc$  methanol;  $\bigcirc$  ethanol;  $\bigcirc$  acetone.

that obtained in the inert solvents. Media similar in behavior with that of methanol include ethanol, chloroform, glacial acetic acid, 96 % acetic acid, and acetone (Fig. 1). Each of these substances including chloroform (7) can be described as type S—H, where S is CH<sub>3</sub>O—, C<sub>2</sub>H<sub>5</sub>O—, etc. Furthermore these substances have a typical tendency toward hydrogen bonding, as expressed in equation (vii):

$$I + S - H \xrightarrow[k_2]{k_1} SH - N - COOR \qquad (vii)$$

$$I + S - H \xrightarrow[k_2]{k_2} M - COOR \qquad IV$$

whereas stronger acids would undergo reaction (viii):

$$I + HA \rightleftharpoons \underset{V}{AH \leftarrow N-COOR} \rightleftharpoons \begin{bmatrix} HN-COOR \\ \parallel \\ N-COOR \\ V \end{bmatrix}^{+} A^{-} \qquad (viii)$$

The early work of Diels and Wulff (6) discloses some information about equation (vii). They found that methanol and ethanol added slowly to dialkyl azodicarboxylates. The product, to which they assigned the structure VII, may be thought to form *via* IV, according to equation (ix):

$$IV \rightarrow \begin{array}{c} S \longrightarrow N \longrightarrow COOR \\ | \\ H \longrightarrow N \longrightarrow COOR \\ VII \end{array}$$
(ix)

However the rate of this reaction is about one-hundredth that of the formation of III from I and II in methanol or ethanol (Fig. 4), so VII cannot be an intermediate in this case. Indeed pure VII does not react with cyclopentadiene. The formation of VII may be considered to be alternative to that of III when diene (II) is absent, but it may be ignored when the diene is present. Actually the formation of III is so much more rapid in methanol or ethanol than in the inert solvents such as benzene that equation (i) cannot describe the reactions in alcohols adequately.

Inspection of Fig. 4 shows that initially a reaction must be occurring which is distinct from the formation of the Diels-Wulff addition product, VII. We assume that this initial reaction is (vii) which, in presence of alcohols and absence of diene, proceeds slowly by reaction (ix) to form VII. In presence of alcohols and diene, we assume that reaction (x) occurs rapidly compared with (vii). A steady state is thus established for formation of IV ( $k_1 < k_2$  and  $k_3$ )

$$IV + II \xrightarrow{k_3} III + SH$$
 (x)

$$Rate = \frac{k_1[Ester][Diene][CH_3OH]}{k_2/k_3 + [Diene]}$$
(xi)

and the rate equation has the form shown in equation (xi). When the kinetics of the reaction between dimethyl azodicarboxylate (I,  $R = CH_3$ —) and cyclopentadiene (II) are investigated in benzene containing low concentrations of methanol the reaction appears second order. However, variation in the concentration of the alcohol, if the concentration is sufficiently low, maintains the second order kinetics but the specific rate constants so obtained are proportional to the concentration of methanol as shown in Table II. This is explained by assuming that  $k_2/k_3 > [Diene]$  in equation (xi) for low concentrations of methanol in benzene.

If the concentration of the methanol in benzene is still further increased, the second-order plots obtained are no longer linear. In pure methanol, the rate can be expressed by equation (xii) which is derived from (xi) by letting  $k_1[MeOH] = k_m$ .

$$Rate = \frac{k_m [Ester][Diene]}{k_2 / k_3 + [Diene]}$$
(xii)

# TABLE II

The Reaction Between Dimethyl Azodicarboxylate (0.020 moles per liter) and Cyclopentadiene (0.020 moles per liter) in Benzene in the Presence of Methanol  $(23.5^{\circ})$ 

METHANOL (moles per liter)	k liters·moles <sup>-1</sup> ·min. <sup>-1</sup>	k/[MeOH] liters <sup>2</sup> ·moles <sup>-2</sup> ·min. <sup></sup>	
	0.72		
0.50	1.45	2.90	
1.00	2.81	2.81	
2.00	5.40	2.70	



Fig. 2. The Rate of Reaction Between Dimethyl Azodicarboxylate and Cyclopentadiene in Methanol at  $23.5^{\circ}$  (Procedure A).

- 0.020 molar diene, 0.067 molar ester
- 0.020 molar diene, 0.010 molar ester
- 0.040 molar diene, 0.020 molar ester
- 0.020 molar diene, 0.015 molar ester
- ⊖ 0.020 molar diene, 0.020 molar ester

On letting  $k_2/k_3 = K$ , integration gives

$$k_{m} = \frac{K}{t} \left[ \frac{1}{a-x} - \frac{1}{a} \right] + \frac{2.303}{t} \log \frac{a}{a-x} \quad \text{when } a = b \quad (xiii)$$

or

$$k_{m} = \frac{2.303}{t} \left[ \frac{K}{a-b} \log \frac{b(a-x)}{a(b-x)} + \log \frac{a}{a-x} \right] \quad \text{when } a \neq b \quad (xiv)$$



FIG. 3. THE RATE OF REACTION BETWEEN DIMETHYL AZODICARBOXYLATE AND CYCLO-PENTADIENE (0.020 mole/liter) IN METHANOL AT 23.5°. ESTER CONCENTRATIONS:  $\bigcirc$  0.025 molar;  $\bigcirc$  0.020 molar;  $\bigcirc$  0.015 molar;  $\bigcirc$  0.010 molar.

In terms of colorimeter readings (R) these become

$$k_{m} = \frac{K}{at} \left[ \frac{(R_{a})_{o}}{(R_{a})_{t}} - 1 \right] + \frac{2.303}{t} \log \frac{(R_{a})_{o}}{(R_{a})_{t}} \quad \text{when } a = b \qquad (xv)$$

or

$$k_{m} = \frac{2.303}{t} \left[ \frac{K}{a-b} \log \frac{(R_{b})_{0} \cdot (R_{a})_{t}}{(R_{b})_{t} \cdot (R_{a})_{0}} + \log \frac{(R_{a})_{0}}{(R_{a})_{t}} \right] \quad \text{when } a \neq b \qquad (xvi)$$

The value of K has been determined experimentally as 0.0125 for the reaction of dimethyl azodicarboxylate (I) and cyclopentadiene (II) in methanol at 23.5° by constancy of  $k_m$  over a variety of values for a and b after attainment of a steady state depending on whether the reagents are put together according to procedure "A" or "B," which are described as follows: A. Ester and methanol are mixed and allowed to reach reaction temperature over a time period of eight to ten minutes. When the diene is added, the rate follows first order kinetics as shown in Fig. 2.

$$Rate = k [Ester]$$
(xvii)

B. Diene and methanol are mixed and allowed to reach reaction temperature and the ester is then added. It may be seen in Fig. 3 that equations (xv) and (xvi) are applicable and the observed rate is in agreement with equation (xii). The same agreement is observed when the ester is maintained at a concentration of 0.02 mole per liter, while the concentration of diene is varied from 0.02 to 0.04 mole per liter.



FIG. 4. THE REACTION BETWEEN DIALKYL AZODICARBOXYLATES (0.020 mole/liter) AND ANHYDROUS METHANOL (23.5°).  $\odot$  I, R = Me;  $\odot$  I, R = Et;  $\bigcirc$  I, R = Et, 0.020 molar in trifluoroacetic acid.

Interpretation of these behaviors is facilitated by observation of the rate of the slow reaction leading to the methanol-dimethyl azodicarboxylate addition compound (VII), described by Diels and Wulff (6). It has already been noted (Fig. 4) that two reactions must be occurring of which the latter slow one obviously represents formation of VII. If it is assumed that VII is formed *via* that reaction described by equation (ix) then the rapid reaction occurring during the first ten minutes may be ascribed to equation (vii).

If this information is applied to the reaction of ester I with diene II in methanol it is evident that mixing by procedure "A" will establish a steady state concentration of the coordination complex, IV. Since methanol is in excess, and equation (vii) represents a reaction which is slower than the over-all reaction of I and II giving III in methanol (although faster than I and II giving III in benzene) then (vii) will be rate controlling according to equation (xvii) and may be thought to be followed by the faster reaction expressed by equation (x). On the other hand the rate expected when reactants are mixed according to procedure "B" must involve the steady state of both (vii) and (x) and thus must be expressed by equation (xii).

We have found, in agreement with Wassermann's observations (1) on the reaction of benzoquinone and cyclopentadiene, that addition of dialkyl azodi-



FIG. 5. THE EFFECT OF VARIOUS ACIDS AND PYRIDINE ON THE REACTION BETWEEN DI-METHYL AZODICARBOXYLATE (0.020 mole/liter) AND CYCLOPENTADIENE (0.020 mole/liter) IN BENZENE AT 23.5°.  $\bullet$  0.020 molar in trifluoroacetic acid; ① 0.020 molar in benzoic acid; ① 0.020 molar in acetic acid;  $\bigcirc$  0.020 molar in pyridine;  $\bigcirc$  0.125 molar in pyridine; ---reaction in benzene alone.

carboxylates to this diene is profoundly affected by inclusion of acids. However our reaction seems to be more complex than that observed by Wassermann, in that acids accelerate reaction in benzene but decelerate it in alcoholic media.

We shall first consider the effect of acids in an inert solvent such as benzene. The extent to which the reaction is accelerated is directly related to the ionization constant of the acid (as it is measured in water). It seems reasonable to consider equation (viii) as operative. The product, V, of the reaction would then be expected to react with the diene (II) at a faster rate than does the ester (I) to form the adduct (III) according to equation (xviii). Furthermore this increase in rate should be proportional to the concentration of acid which is present.



$$II + V \rightarrow III + HA$$
 (xviii)

FIG. 6. THE EFFECT OF TRIFLUOROACETIC ACID ON THE REACTION BETWEEN 0.020 molar DIETHYL AZODICARBOXYLATE AND CYCLOPENTADIENE IN BENZENE (28.0°).  $\bigcirc$  0.020 molar in trifluoroacetic acid (TFA);  $\bigcirc$  0.015 molar in TFA;  $\bigcirc$  0.010 molar in TFA;  $\bigcirc$  0.005 molar in TFA;  $\bigcirc$ 

This has been found in fact. Fig. 5 shows that the acid strengths (based on ionization constants in water) for acetic, benzoic, and trifluoroacetic acids closely parallel the increase in rate of reaction over that for the addition of I ( $R = CH_3$ —) and II in benzene. Fig. 6 shows the increase in the rate of reaction between I ( $R = C_2H_5$ —) and II (compared with that in benzene alone) when the concentration of trifluoroacetic acid is increased from 0.005 to 0.020 moles

per liter. Similar results were obtained with this acid when the reaction between I ( $R = CH_3$ —) and II was investigated. Table III shows that the increase in the rate of ester-diene addition is directly proportional to the concentration of trichloroacetic acid.

Inspection of Fig. 6 shows that the rate of the acid-catalyzed reaction in benzene deviates to some extent from the second-order kinetics observed in benzene alone, and this deviation is greatest with the strongest acids. The behavior corresponds to that observed by Wassermann and his explanation seems to be applicable. Either the dimerization of the cyclopentadiene may be catalyzed by acids or the acids may be involved in a teleomerization, such as has actually been observed (8, 9).

The addition of dimethyl azodicarboxylate (I) to cyclopentadiene (II) in benzene is slightly inhibited by pyridine, although the retardation of the reaction is not extensive until the concentration of the pyridine is six-fold that of the

TABLE III THE TRICHLOROACETIC ACID CATALYZED REACTION OF DIETHYL ESTER (0.020 M./L.) AND CYCLOPENTADIENE (0.020 M./L.) IN ANHYDROUS BENZENE AT 28°

CONCENTRATION OF TRICHLOROACETIC ACID IN M./L.	INITIAL RATE	$\frac{\text{INITIAL RATE}}{\text{ACID CONCENTRATION}} \times 10^{-3}$		
0.005	11	2.20		
.010	20	2.00		
.015	28	1.81		
.020	41	2.05		
.030	64	2.13		

diene or ester (Fig. 5). The effect must be due to the free pyridine since it is not caused by pyridinium trifluoroacetate. The inhibition is probably caused by a competition between the coördinative nitrogen atoms in the azo-ester and pyridine. The coördinated species may be an unknown impurity or may be one of the reagents but in any circumstance the inhibition does not seem to be very significant.

The use of equations (viii) and (xviii) depends on the assumption that the catalysis by acid involves the ester (I) rather than the diene (II). This assumption was verified when trifluoroacetic acid was included with either dimethyl or diethyl azodicarboxylate and cyclopentadiene in reactions over a temperature range of  $15-28^{\circ}$ . Confirmatory results obtained with trichloroacetic acid and various diene-diethyl ester ratios are shown in Fig. 7. It is apparent that the acid is affecting the dienophile more than the diene. This conclusion is in agreement with that of Wassermann for the reaction of benzoquinone with cyclopentadiene (1).

In view of the marked acceleration by acids when azoester (I) and diene (II) react in benzene, it is surprising to find that trifluoroacetic acid retards the reaction in methanolic medium. Fig. 8 shows that the retardation is greatest with minimal amounts of acid. Although the rate is increased by addition of larger



FIG. 7. THE TRICHLOROACETIC ACID-CATALYZED REACTION BETWEEN DIETHYL AZODI-CARBOXYLATE AND CYCLOPENTADIENE IN BENZENE (28.0°).

0.020 molar ester, 0.020 molar diene, 0.030 molar acid.
0.020 molar ester, 0.020 molar diene, 0.020 molar acid.
0.020 molar ester, 0.030 molar diene, 0.020 molar acid.
0.020 molar ester, 0.040 molar diene, 0.020 molar acid.
0.030 molar ester, 0.020 molar diene, 0.020 molar acid.
0.030 molar ester, 0.030 molar diene, 0.020 molar acid.
0.030 molar ester, 0.030 molar diene, 0.020 molar acid.
0.030 molar ester, 0.020 molar diene, 0.020 molar acid.
0.030 molar ester, 0.030 molar diene, 0.020 molar acid.
0.040 molar ester, 0.020 molar diene, 0.020 molar acid.
0.020 molar ester, 0.020 molar diene, 0.020 molar acid.

amounts of acid it never reaches the value for reaction in methanol alone. This behavior of the acid probably does not involve its esterification in the methanolic medium, since Wassermann (10) has shown in his study of the acid-catalyzed benzoquinone-cyclopentadiene reaction in ethanol, that esterification is negligible at 25° over a period of three to four hours. Presumably the retardation involves the effect on the dienophile rather than the diene, because in absence of the diene the slow formation of the addition product, VII, of azo-ester and methanol also is retarded by acids (see Fig. 4).



FIG. 8. THE EFFECT OF TRIFLUOROACETIC ACID ON 0.020 molar CYCLOPENTADIENE AND DIETHYL AZODICARBOXYLATE IN ANHYDROUS METHANOL AT 28.0° (Procedure A).  $\bigcirc$  No trifluoroacetic acid (TFA);  $\bigcirc$  0.020 molar TFA;  $\bigcirc$  0.004 molar TFA;  $\bigcirc$  0.002 molar TFA;  $\bigcirc$  0.002 molar TFA;  $\bigcirc$  0.002 molar TFA;  $\bigcirc$  0.002 molar TFA;  $\bigcirc$  0.004 mol

It was suggested earlier in this report that the rapid reaction which occurs within the first ten minutes after dimethyl azodicarboxylate and methanol are mixed is a coördination complex (IV) of the two. Alternatively one might consider addition to the carbonyl group in the ester. But ester interchange ought to occur under this circumstance if the dimethyl ester reacted in ethanol or the diethyl ester reacted in methanol. It has been shown previously that this interchange does not occur in the uncatalyzed system (5). It might be expected that such interchange would be accelerated by the presence of trifluoro- or trichloroacetic acid. However we still find no evidence for ester interchange during the period of time involved in the kinetic studies. When diethyl azodicarboxylate and cyclopentadiene are allowed to react completely in methanol containing trifluoroacetic acid the adduct (III) is identical with that obtained in ethanol; no contamination with the adduct (III) prepared from dimethyl azodicarboxylate can be detected. It thus appears that if a coördination complex exists then it must have the structure, IV.

A similar coördination complex has been postulated in (viii) for the intermediate in the acid catalysis of the Diels-Alder reaction of azo-ester (I) and diene (II) in benzene. It might be expected that the complex or ion-pair (V) would tend to dissociate more in the polar solvent, methanol, than in benzene.



If the resulting ion (VI) were degenerate as shown in VIII then the species might be expected to be less reactive toward addition of diene, with consequent retardation of the reaction.

Small amounts of acid ought to be able to accomplish the retardation if, as would be expected, the coördination with the strong trifluoroacetic acid predominated over the coördination with the weak acid, methanol. Larger amounts of trifluoroacetic acid should however depress the ionization,  $V \rightarrow VI$ , especially because of the anion population resulting from reaction of methanol with acid as shown in (xix).

$$CH_{3}OH + HA \rightarrow [CH_{3}OH_{2}]^{+} + A^{-}$$
(xix)

However it would not be expected that the depression of the ionization,  $VI \rightarrow V$ , would restore the rate to that observed in methanol alone. The concentration of V will be increased at the expense not only of VI but also of IV. Although a small amount of methanol is less effective than a small amount of trifluoroacetic acid in benzene medium, the converse seems to be true of methanol in its own environment. All rates in benzene with or without acid are slower than the rate of addition of I to II in methanol. If these coördination complexes (IV and V) exist, then the complex of azo-ester with methanol (IV) must be more reactive toward cyclopentadiene than the complex (V) involving trifluoroacetic acid. Depletion of the methanol-azo-ester complex (IV), because of appropriation by trifluoroacetic acid of the ester to form V, would therefore prevent the attainment of the rate observed in methanol above.

Although the foregoing explanations seem adequately to fit the observed facts,

a mechanism involving the geometric isomerism of dialkyl azodicarboxylates can also be formulated. This would seem to merit consideration because the reaction of cyclopentadiene and benzoquinone was not found by Wassermann (11-15) to be accelerated in ethanol over its rate in benzene, nor to exhibit first-order kinetics. Wassermann's dienophile could not exist in *cis-trans* forms.

Several analogies seem to recommend the inclusion of the geometric isomerism into the mechanism of the dialkyl azodicarboxylate-cyclopentadiene reaction.

	REACTION ORDER $I + II \rightarrow III$							
(a) Dimethyl Azodicarboxylate								
55.54	2nd							
51.64	2nd							
54.79	2nd							
54.64	2nd							
53.15	sl. less than 2nd							
45.77	sl. less than 2nd							
44.17	less than 2nd							
23.58	Exactly 1st							
25.45	Exactly 1st							
36.29	Exactly 1st							
34.81	Exactly 1st							
oxylate								
55.30	2nd							
55.14	sl. less than 2nd							
54.91	sl. less than 2nd							
54.76	sl. less than 2nd							
54.52	sl. less than 2nd							
24.03	sl. more than 1st							
23.88	sl. more than 1st							
23.88	sl. more than 1st							
23.88	sl. more than 1st							
23.88	sl. more than 1st							
	$E_{m} (405 m\mu) = 74.86D$ boxylate 55.54 51.64 54.79 54.64 53.15 45.77 44.17 23.58 25.45 36.29 34.81 boxylate 55.30 55.14 54.91 54.76 54.52 24.03 23.88 23.88 23.88 23.88 23.88							

TABLE IV Spectrophotometry of Dialkyl Azodicarboxylates

\* TFA indicates trifluoroacetic acid.

Firstly it is known (16) that maleic acid reacts faster in typical Diels-Alder reactions than fumaric acid. Secondly there is a close parallelism between the rates of reaction of the azo-ester (I) with cyclopentadiene (II) in various media (Fig. 1) and the rate of isomerization of the geoisomeric azobenzenes in these same media (17).

However we can find no further correlation with the phenomenon of geometric isomerism. Since neither *cis*- nor *trans*-azobenzene could be made to react with cyclopentadiene, we attempted to separate the dialkyl azodicarboxylates into their geoisomers but without success. Irradiation rich in the spectral region in

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which dimethyl azodicarboxylate displays an absorption peak (405 m $\mu$ ) fails to change the extinction at this peak or to alter the region of maximum transparency (330 m $\mu$ ).

Actually the similarity between the azobenzenes and the dialkyl azodicarboxylates is not so great as first seems apparent. Although Hartley found (7) that liquid or dissolved *cis*-azobenzene was more absorptive at 440 m $\mu$  than the *trans* isomer in similar states, this difference in absorption was also characteristic of the solid states. On the other hand the dimethyl and diethyl azodicarboxylates are colored in the liquid or dissolved state but are colorless as solids.

The spectral absorption of the dialkyl azodicarboxylates in various solvents is also unlike that found by Hartley for solutions of azobenzenes. The values of absorption maxima for the dimethyl and diethyl esters in the several solvents are shown in Table IV. It may be seen that those media in which  $E_m$  is high (44-55) are the ones in which the Diels-Alder reaction (I + II  $\rightarrow$  III) proceeds slowly by a second-order mechanism. The lower  $E_m$  (23-36) is observed for those solvents in which the addition of ester I to cyclopentadiene (II) takes place rapidly according to first-order kinetics. While these effects must involve the azo linkage there is no indication that they involve the geoisomerism of that linkage. Indeed the evidence precludes the specific participation of geoisomers since the Diels-Alder reaction is slowest in those media in which a high absorption might indicate preponderance of *cis*-isomer. On the other hand the low absorption in methanol, ethanol, chloroform, and acetone may well indicate the extent to which the dimethyl ester has coördinated with these media to form intermediates of type IV.

We are not now able to interpret dipole moment studies with diethyl azodicarboxylate in terms of the geometric isomerism. Calculation of the moment of the pure liquid by the method of Onsager (18) gave a value of  $\mu = 3.45$ D. The same ester in benzene solution gave  $\mu = 0.71$ D by Kumler's modification of the extrapolation method of Debye (19). It may be noted that the moment in benzene is much lower than that for ethyl maleate ( $\mu = 2.51$ D) or ethyl fumarate ( $\mu = 2.23$ D) as well as that for *cis*-azobenzene ( $\mu = 3.00$ D), whereas the moment for the pure liquid is higher than any of these values.

The foregoing attempts to correlate the kinetic behavior of the cyclopentadiene-azo ester addition with the possible geometric isomerism have thus indicated that this isomerism is not significantly involved in the measurements that we have made. It would be unwise to exclude the idea, but the present data seem to be adequately explicable on the basis of the coördination mechanism which we have presented.

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### EXPERIMENTAL

Apparatus for kinetic study. The reaction between dialkyl azodicarboxylates and cyclopentadiene was investigated colorimetrically using a Klett-Summerson photoelectric colorimeter equipped with a No. 42 (blue) filter. The cell employed for the reaction mixture is illustrated in Fig. 9. This Pyrex cell measured  $4.0 \times 2.0 \times 8.0$  cm.<sup>3</sup> and was equipped with an aluminum cover through which were inserted a cooling "finger," a thermometer, and a small stirrer driven by a type 240 "electrorotor" (3-6 volts input, Rex Motors Ltd., Knowsley House, Bolton, England). Water from a constant temperature bath was pumped through the finger in order to maintain temperature constancy of  $\pm 0.2^{\circ}$ . The color intensity was observed through the 2.0 cm. dimension of the cell.

Calibration of the colorimeter. It was found that a benzene solution of the azo-esters showed constant light absorption during several hours, but a methanolic or ethanolic solu-



FIG. 9. APPARATUS FOR KINETIC STUDIES. A, aluminum cover; B, stirrer; C, cell; D, light path; E, metal clamp; F, F', rubber shock absorbers; G, motor; H, motor shaft; K, 4.0 cm. dimension.

tion gave readings which decreased with time. Standardization of the two solvent types therefore differed.

For benzene the colorimeter was calibrated by readings taken after successive dilutions of a solution of the ester initially 0.040 *molar*. A typical calibration is shown by line A, Fig. 10.

The colorimeter was calibrated for methanolic solutions by readings taken 30 or 60 seconds after mixing the azoester with the solvent. Line B, Fig. 10, represents readings taken after 30 seconds, and line C the readings taken after 60 seconds. The deviation from Beer's law was not great.

*Reagents. 1. The diene.* The cyclopentadiene was freshly prepared a few minutes before each experiment by distillation from dicyclopentadiene through a 40-cm. fractionating column, b.p. 41.0° (760 mm.).

2. The dienophiles. (a) Dimethyl hydrazodicarboxylate was first prepared by a modification of known methods (22, 23). To a chilled suspension of 130 g. (1.0 mole) of hydrazine sulfate

in 125 ml. of water was added a chilled solution of 112 g. (2.0 moles) of potassium hydroxide in 75 ml. of water during 30 minutes. This suspension was filtered, after dilution to 500 ml. with ethanol, to increase the precipitation of potassium sulfate. The latter was washed with 150 ml. of ethanol.

The aqueous ethanolic solution was stirred at  $10-20^{\circ}$  while 189 g. (2.0 moles) of methyl chloroformate was added slowly. When half of the ester had been added, a solution of 106 g. (1.0 mole) of sodium carbonate in 500 ml. of water was then introduced simultaneously.



FIG. 10. CALIBRATION CURVES

After 30 minutes subsequent to the addition the solution was evaporated *in vacuo*. The remaining solid was washed with absolute ethanol. Vacuum evaporation of the ethanolic solution followed by re-extraction of the residue with absolute ethanol removed most of the sodium and hydrazinium chlorides. Final vacuum evaporation of the ethanol left 101 g. (70%) of dimethyl hydrazodicarboxylate, m.p. 129.5-130.5°.

A modification of Diels' method (24) was used to oxidize the hydrazo- to the azo-ester, since Rabjohn's method (22) was found to give a contaminated product which gave anomalous kinetic results unless it was rigorously and wastefully purified. To a solution of 40 g. (0.27 mole) of dimethyl hydrazodicarboxylate in 80 ml. (1.29 mole) of nitric acid (sp. gr. 1.41) was added 75 ml. of chloroform. The mixture was chilled to  $-5^{\circ}$  and 25 ml. (0.40 mole) of 98-99% nitric acid was added dropwise during 17 minutes with vigorous stirring. After 150 minutes' subsequent stirring the chloroform layer was separated and the acid layer was washed four times with 20-ml. portions of chloroform. The combined chloroform solution was extracted four times with 25-ml. portions of water and then diluted with 100 ml. of diethyl ether. After drying with calcium chloride the solution was distilled giving 24.6 g. (63%) dimethyl azodicarboxylate, b.p. 95.0-96.5° (9.5 mm.).

(b) Diethyl hydrazodicarboxylate, m.p. 131.5–132.3° was prepared in 80% yield by a modification of the methods of Rabjohn (22) and Ingold and Weaver (23) as described for the dimethyl ester. Since the diethyl hydrazodicarboxylate is quite insoluble in cold aqueous ethanol the product could be obtained by filtration without the evaporation and ethanol extraction employed in the case of the dimethyl ester.

The procedure employed for the conversion of the hydrazo- to the azo-ester was that of Rabjohn (22). The diethyl azodicarboxylate was obtained in 81% yield, b.p.  $110.5-112.0^{\circ}$  (11 mm.). This material was extracted with dilute sodium carbonate (3%), then with water and redistilled in 3-g. lots prior to each series of rate studies to ensure freedom from acidic contaminants. The product had b.p.  $111.0-111.5^{\circ}$  (11 mm.),  $d^{20}$  1.1073,  $n_{2}^{20}$  1.42225.

Solvents. Methanol and ethanol were rendered pure and anhydrous by preparation under nitrogen according to the method of Lund and Bjerrum (25). The benzene, dioxane, and petroleum ether used in the experiments were freed from aliphatic unsaturated, hydroxylic, and peroxidic impurities and were distilled under nitrogen from sodium benzophenone.

Catalysts. The trifluoroacetic acid (Minnesota Mining and Mfg. Co.) was distilled, b.p. 71-72° (755 mm.). Trichloroacetic acid was crystallized from anhydrous benzene, m.p. 56.5-57.0°. Benzoic acid was crystallized from water, m.p. 122.0-122.3°. Acetic acid was purified by a known method (26), b.p. 118.2° (758 mm.). Pyridine was refluxed over barium oxide and distilled, b.p. 115.3° (758 mm.).

*Procedure.* The colorimeter potentiometer was adjusted to zero with respect to the solvent at the reaction temperature. The solvent together with ester and diene was quickly adjusted to a volume of 50 ml. and returned to the colorimeter after mixing for 15 seconds. The initial reading was made one minute after the reagents were mixed. The ester concentration was maintained initially between 0.040 and 0.010 *molar* in order to utilize the sensitive range of the colorimeter.

The kinetic results indicated in the various figures are in general the average curves for at least two determinations. The results were reproducible to within 1% and in the majority of cases almost superposable curves were obtained on successive runs.

#### DIETHYL AZODICARBOXYLATE AND CYCLOPENTADIENE

(i) In anhydrous benzene with added (a) trifluoroacetic acid. To a solution of 1.12 g. (0.0064 mole) of diethyl azodicarboxylate and 0.365 g. (0.0032 mole) of trifluoroacetic acid in 5 ml. of benzene was added 0.42 g. (0.0064 mole) of freshly prepared cyclopentadiene. The reaction mixture at 5° became colorless in 12 minutes. Removal of the solvent and acid *in vacuo* gave 1.49 g. (97%) of 1,2-dicarboethoxy-3,6-endomethylene-1,2,3,6-tetrahydropyridazine. Distillation at 1.5 mm. gave 1.02 g. of colorless oil, b.p. 138.0-139.0° (1.5 mm.),  $n^{20}$  1.4818,  $d^{20}$  1.1332. Bromination of 1.01 g. (0.0042 mole) of this material in 5 ml. of chloroform with 0.67 g. (0.0042 mole) of bromine in 5 ml. of chloroform at 0° gave 1.37 g. (80%) of 4,5-dibromo-1,2-dicarboethoxy-3,6-endomethylenepiperidazine, m.p. 66.0-66.5°.

The properties and yields of the pyridazine and its dibromo derivative were comparable with those obtained when the reaction was carried out with no added trifluoroacetic acid.

(b) *Trichloroacetic acid*. The reaction between 1.74 g. (0.01 mole) of the diethyl ester, 0.67 g. (0.01 mole) of cyclopentadiene, and 0.80 g. (0.005 mole) of trichloroacetic acid in 25 ml. of benzene at 5° gave 2.35 g. (97%) of the pyridazine. Bromination gave a comparable yield of the dibromopiperidazine, m.p. 66.5-67.0°.

(ii) In anhydrous methanol with trifluoroacetic acid. Diethyl azodicarboxylate, 3.58 g. (0.02 mole), 1.32 g. (0.02 mole) of cyclopentadiene, and 2.28 g. (0.02 mole) of trifluoroacetic acid in 50 ml. of methanol gave 4.68 g. (95%) of the pyridazine. Distillation gave 3.25 g., b.p. 124.0-125.0° (0.75 mm.), m.p. -19.5° to -18.8°. Bromination gave an 86% yield of the dibromopiperidazine, m.p. 66.0-66.5°.

Anal. Calc'd for C<sub>11</sub>H<sub>16</sub>N<sub>2</sub>O<sub>4</sub>: N, 11.7. Found: N, 11.6.

The composition of the analogous dimethyl ester (m.p.  $83.7-84.1^{\circ}$ ) is calculated as N, 13.2. Since no crystallization occurs in the product, and the analysis and other properties (Table V) conform closely with those of the diethyl ester, we believe that any ester interchange, if it has occurred, is too slight to affect the kinetic results of this research. The analysis and physical properties would also indicate that very little methyl ester (N, 12.6) was formed by ester interchange.

Dielectric constant determinations. Measurements were made on a type 3A dielectric constant meter (Yellow Springs Instrument Co., Yellow Springs, Ohio) at 20° using a sample

 TABLE V

 The Preparation of 1,2-Dicarboethoxy-3,6-endomethylene-1,2,3,6-tetra

HYDROPYRIDAZINE								
ESTER,		CATALYST	VIELD	B.P. 4T	20	-20	4, 5-I	Dibromide
DIENE moles/liter	MEDIA	moles/liter	%	0.75 мм., °С.	<i>n</i> _D	d <sub>20</sub>	Yield, %	м.р., °С.
0.01	Diethyl ether	nil	92	123.4-124.5	1.4819	1.1332	81	66.4-67.0
.01	Methanol	nil	90	123.6 - 124.5	1.4820	1.1330	80	66.8-67.3
.02	Methanol	TFA <sup>a</sup> (0.02)	92	124.0 - 125.0	1.4818	1.1333	86	66.5-67.1
.0064	Benzene	nil	95	138.0-139.0	1.4819	1.1332	81	66.3-67.0
.01	Benzene	$TCA^{b}$ (0.01)	95	124.2 - 125.2			60	66.4-67.2
.0064	Benzene	TFA (0.0032)	97	138.0-139.0	1.4818	1.1332	80	66.0-66.5

" TFA denotes trifluoroacetic acid. " TCA denotes trichloroacetic acid. " 1.5 mm.

#### TABLE VI

### PREPARATION OF 1,2-DICARBOMETHOXY-3,6-ENDOMETHYLENE-1,2,3,6-TETRAHYDROPYRID-AZINE IN VARIOUS SOLVENTS

SOLVENT	CRUDE M.P., °C.	CRYST. M.P., °C.	YIELD, %		
			Crude	Pure	
Methanol	82.6-83.8	83.5-84.0	97	92	
Ethanol	82.2 - 84.0	83.3-84.0	94	89	
Chloroform	81.9-82.8	83.8-84.2	93	89	
Acetone	82.8-83.8	83.3-84.0	96	90	
Benzene	82.5-83.8	83.8-84.1	98	91	
Acetic acid	81.9-83.3	83.5-84.2	96	90	
Dioxane	82.5-83.5	83.4-84.0	94	90	

of ester, b.p. 111-111.5° (11 mm.),  $d_4^{20}$  1.1073,  $n_p^{20}$  1.42225. The dielectric constant for this liquid was 9.12.

Solutions containing 0.5034 g. of ester with 4.4645 g., 8.8600 g., and 13.255 g. of benzene were compared with benzene  $(d_4^{2^0} 0.8781, \epsilon 2.26)$ . These solutions with densities 0.8929, 0.8860, and 0.8835 showed dielectric constants of 2.85, 2.52, and 2.49. A similar comparison with pure ethanol  $(d_4^{2^0} 0.7924, \epsilon 25.90)$  was made with solutions containing 0.5006 g. of ester in 4.0631 g., 8.0081 g., and 11.953 g. of ethanol. These solutions with densities of 0.9119, 0.8509, and 0.8300 showed dielectric constants of 21.80, 23.62, and 24.85.

Spectroscopic studies. Measurements were made with a model D.U. Beckman spectrophotometer in a 1.0-cm. cell with slit width about 0.6 mm. at 22° using 0.01336 molar solutions of dimethyl azodicarboxylate and 0.01324 molar solutions of the diethyl ester. The pure liquids were too opaque for measurement in a 0.5-mm. cell. 1,2-Dicarbomethoxy-3,6-endomethylene-1,2,3,6-tetrahydropyridazine. When 0.73 g. (0.005 mole) of dimethyl azodicarboxylate and 0.35 g. (0.0053 mole) of cyclopentadiene in 15 ml. of solvent were allowed to react until the system was colorless, the products, crystallized from acetonitrile, were obtained in yields and purity as shown in Table VI.

Anal. Calc'd for C<sub>9</sub>H<sub>12</sub>N<sub>2</sub>O<sub>4</sub>: C, 50.94; H, 5.70.

Found: C, 50.74; H, 5.82.

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