The Kinetics and Mechanism of Reactions of *cis*- and *trans*-Chalcones with Amines

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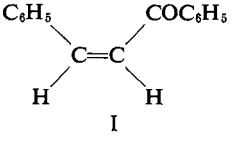
Abstract: The kinetics and mechanism of reactions of *cis*- and *trans*-chalcones with pyrrolidine in acetonitrile and heptane have been studied. The reaction of *trans*-chalcone has the following properties. (1) There is reversible formation of Michael adduct, with $K = 17$ and 80 M^{-1} in acetonitrile and heptane, respectively. (2) The reaction is faster in heptane than in acetonitrile, but in both solvents there is a second-order dependency on amine. (3) Pyrrolidine-*d* reacts twofold slower than nondeuterated amine. (4) The apparent activation parameters in acetonitrile are $\Delta H^{\ddagger} = 2.0$ kcal/mol and $\Delta S^{\ddagger} = -62$ eu. These results point to a cyclic concerted mechanism for Michael addition involving two amine molecules and the olefin. The behavior of the *cis*-chalcone reaction is quite different. (1) It is irreversible and first order in amine in both solvents. (2) The reaction is faster in acetonitrile than in heptane. (3) There is no isotope effect using pyrrolidine-*d*. (4) Tertiary amines weakly catalyze the isomerization of *cis* to *trans*. (5) The apparent activation parameters in acetonitrile are $\Delta H^{\ddagger} = 6.6$ kcal/mol and $\Delta S^{\ddagger} = -47$ eu. These results, along with a computer analysis of the rate data, show that *cis*-chalcone is not converted directly to Michael adduct, but is instead isomerized to *trans*-chalcone *via* a dipolar intermediate; the *trans*-olefin subsequently leads to Michael adduct.

The mechanism of visual reception involves a photochemical change of an organic pigment, a change that is readily reversed so that vision may continue.[2] The process is believed to occur as follows. 11-*cis*-Retinaldehyde (an unstable isomer of vitamin A aldehyde) complexes with a colorless visual protein to produce a red substance called rhodopsin. When rhodopsin is exposed to light, the complexed retinaldehyde isomerizes to the all-*trans* isomer. The new complex is colorless and unstable, so that the *trans*-retinaldehyde departs from the visual protein. Thus, the sole purpose of the light is to isomerize retinaldehyde and effect bleaching of rhodopsin. Somehow this sequence gives rise to a nerve impulse.

The organism reisomerizes the all-*trans* isomer back to 11-*cis* material in order that the supply of the latter not be exhausted. This interesting enzyme-catalyzed reaction prompted us to carry out a detailed mechanistic study of the amine-catalyzed *cis–trans* interconversion of chalcone (benzalacetophenone), an α,β-unsaturated carbonyl compound (I). Our hope was that the knowledge and experience gained with this very simple substrate would facilitate our subsequent examination of systems more closely allied with the visual process. Since the visual pigments of the retina are often found in lamellar micelles, it seemed appropriate to investigate the chalcone reactions using aprotic solvents.

Several other workers have investigated *cis–trans* isomerizations of activated carbon–carbon double bonds in aprotic solvents. For example, it was found that isomerization of maleate to fumarate is catalyzed by primary and secondary amines (but not by tertiary amines) and that the reaction is second order in amine.[3,4] Various mechanisms and intermediates have been proposed to explain these observations; one of the mechanisms involves conversion of maleate to a Michael adduct intermediate which then decomposes to fumarate.[5,6] The catalyzed isomerization of ethyl α-cyano-β-*o*-methoxyphenylacrylate in benzene requires, on the other hand, only one molecule of amine (primary, secondary, or tertiary).[5] This result is best explained by formation of a dipolar addition intermediate.[5]

In the present paper, we investigate both the pyrrolidine-catalyzed isomerization of *cis*-chalcone and the Michael addition of pyrrolidine to *trans*-chalcone in acetonitrile and heptane. We focus on questions such as whether *cis*-chalcone reacts by a polar or nonpolar mechanism, whether an enol is involved in the catalyzed isomerization, and whether *cis*-olefin forms a Michael adduct directly or *via trans* compound. Our mechanistic conclusions are based on kinetic order, isotope effects, solvent effects, sensitivity to tertiary amines, and activation parameters. It is found that the reactions of *cis*- and *trans*-chalcones with pyrrolidine have markedly different mechanisms.



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Experimental Section

Materials. *cis*-Chalcone was prepared by irradiating 10 g of *trans*-chalcone in 100 ml of acetonitrile for 6 hr with a 100-W General Electric mercury lamp. The solvent was removed and the residue shaken with 140 ml of heptane. The heptane was decanted from a small amount of oil, cooled to −23° for 2 hr, decanted from the resulting solid, and then stored 2 days in a freezer. The heptane was again separated from the crystals, condensed to 25 ml, and placed overnight in a freezer. This yielded 0.9 g of solid which was removed by filtration and dried, mp 43–45°. The *cis*-chalcone was crystallized repeatedly from methanol (−23°) or methanol–water to give 0.055 g of beautiful yellow crystals, mp 44–46° (lit.[7] mp 45–46°). The material was shown to be greater than 99% pure by

(1) National Defense Education Act Predoctoral Fellow.
(2) G. Wald in "Recent Progress in Photobiology," E. J. Bowen, Ed., Academic Press, Inc., New York, N. Y., 1965, p 333.
(3) K. Nozaki, *J. Am. Chem. Soc.*, 63, 2681 (1941).
(4) M. Davis and F. P. Evans, *Trans. Faraday Soc.*, 51, 1506 (1955).
(5) Z. Rappoport, C. Degani, and S. Patai, *J. Chem. Soc.*, 4513 (1963).
(6) S. Patai and Z. Rappoport in "The Chemistry of Alkenes," S. Patai, Ed., Interscience Publishers, New York, N. Y., 1964, pp 565–573.
(7) R. E. Lutz and R. H. Jordan, *J. Am. Chem. Soc.*, 72, 4090 (1950).

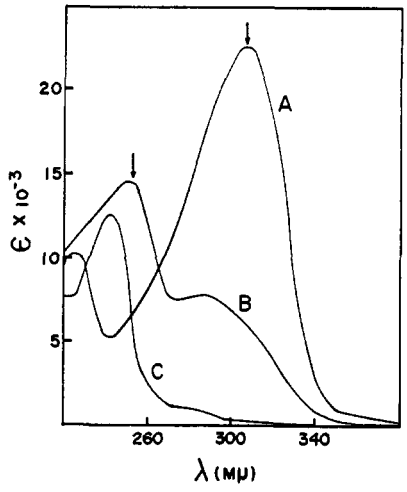


Figure 1. The spectra of *trans*-chalcone (A), *cis*-chalcone (B), and Michael adduct (C) in acetonitrile. The arrows indicate the two wavelengths used to follow the reactions in this solvent.

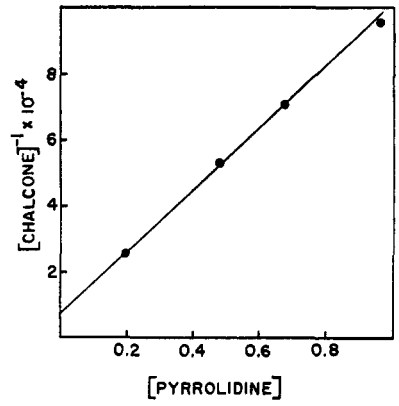


Figure 2. The data in this plot were obtained by adding *trans*-chalcone to several acetonitrile solutions of pyrrolidine, allowing Michael addition to proceed to equilibrium, and then determining the equilibrium chalcone concentrations. The equilibrium constant for Michael addition is derived from the slope of this plot (eq 2); $C_0 = 1.87 \times 10^{-4}$ *M*.

comparison of its extinction coefficient at 298 mμ with that reported.[7]

trans-Chalcone (Eastman) was crystallized twice from heptane. Both *cis*- and *trans*-chalcone and their solutions were protected from light at all times except during weighing.

The Michael adduct of chalcone and pyrrolidine was isolated as its hydrochloride salt by the following procedure. *trans*-Chalcone (3 g) and an excess of pyrrolidine were added to about 25 ml of heptane and kept at room temperature for several hours. The solvent and excess amine were removed, and the residue was dissolved in 100 ml of heptane. A gummy precipitate, which formed when hydrogen chloride was passed through the heptane, was separated by filtration. Several crystallizations from acetone–ethyl acetate yielded a white crystalline solid, mp 146–147°.

Anal. Calcd for $C_{19}H_{22}ONCl$: C, 72.25; H, 7.02; N, 4.44. Found: C, 71.79; H, 7.25; N, 4.38.

Pyrrolidine-*d* was prepared by adding 15 ml of pyrrolidine dropwise with stirring to 200 ml of 1.6 *M* butyllithium in hexane at 0° under nitrogen. The mixture was allowed to stand overnight at room temperature after which the solvent was removed under reduced pressure. Deuterium oxide (5.3 ml) was then added slowly to the solid residue under a nitrogen blanket. Distillation of the product from the wet solid gave 5 ml of a mixture of pyrrolidine-*d* and deuterium oxide. The latter was removed from the amine by distillation over barium oxide to yield 3 ml of pyrrolidine-*d*. Analysis by nmr showed a satisfactory isotopic purity.

Spectrograde acetonitrile was distilled once over phosphorus pentoxide and once over anhydrous potassium carbonate. *n*-Heptane was distilled over lithium aluminum hydride. Pyrrolidine was distilled over barium oxide.

Kinetics. All reactions were followed by means of a Cary 14 spectrophotometer equipped with a thermostated cell compartment. The disappearance of *cis*-chalcone was followed at the isosbestic point of *trans*-chalcone and its pyrrolidine Michael adduct (252.6 mμ in acetonitrile and 249.6 mμ in heptane; see Figure 1). The appearance or disappearance of *trans*-chalcone was followed at the λ_{max} for *trans*-chalcone (306 mμ in acetonitrile and 298 mμ in heptane). Solutions of pyrrolidine were used the same day that they were prepared, although the same rate constants were obtained when we once used solutions that had stood for 3 days. The reactions were initiated by adding 25 or 50 μl of substrate solution to 3.00 ml of an amine solution which had been equilibrated at 25.0° in a cuvette placed within the Cary cell compartment. The amine was always present in large excess over the substrate so that pseudo-first-order kinetics were observed. The spectrophotometer beam did not catalyze any detectable reaction of the substrates.

Computer Analysis. All computer work was done at the Emory University Department of Statistics and Biometry on an RCA Spectra 70/55 digital computer. A nonlinear regression program[8] containing a mixed Marquardt–Hartley algorithm was used to estimate the kinetic parameters. A California Computer Products routine was used to plot two of the figures shown in the Discussion section.

Miscellaneous Experiments. There is no question that the system under consideration in this paper is well behaved. Isosbestic points are sharp. The value of the rate parameter k_2 (see Discussion) is the same whether equilibrium is approached starting with *cis*-chalcone, *trans*-chalcone, or with Michael adduct. Infrared and ultraviolet analyses showed no 1,2 addition of pyrrolidine to chalcone. These results do not exclude formation of trace amounts of 1,2 adduct, but such traces would be of no kinetic importance since *cis*-chalcone cannot isomerize by means of hemiaminal formation. An approximate rate constant, obtained by following the disappearance of the chalcone carbonyl stretching band using a Perkin-Elmer 257 infrared spectrophotometer, agreed well with the corresponding rate constant secured by ultraviolet spectrophotometry.

Results

The rate constants for the reaction of *trans*-chalcone (5×10^{-5} *M*) with excess pyrrolidine (0.05 to 0.5 *M*) in acetonitrile and heptane were determined by measuring the disappearance of olefin spectrophotometrically at wavelengths where Michael adduct does not absorb strongly (Figure 1). Michael addition to *trans*-chalcone has the following properties.

(1) The reaction is reversible. This was shown by the fact that the infinity absorbance depends on the amine concentration; the higher the amine concentration, the smaller the amount of chalcone at equilibrium and the smaller the value of the infinity absorbance. Moreover, the same infinity values and observed rate constants were obtained when we approached equilibrium from the side of the Michael adduct; in these experiments we added the hydrochloride salt of the Michael adduct to the amine solutions and followed the *appearance* of *trans*-chalcone (no *cis*-chalcone was observed). Equilibrium constants (*K* in eq 1) were evaluated from eq 2 by plotting C_{eq}^{-1} *vs.* [P] (Figure 2). C_{eq} and C_0 are the equilibrium and initial concentrations of chalcone and

$$\textit{trans}\text{-chalcone} + \text{pyrrolidine} \underset{}{\overset{K}{\rightleftharpoons}} \text{Michael adduct} \qquad (1)$$

P is pyrrolidine. The value of *K* is 17 M^{-1} in acetonitrile and roughly 80 M^{-1} in heptane.

$$1/C_{eq} = (1/C_0) + (K(\mathrm{P})/C_0) \qquad (2)$$

(8) We wish to thank Mr. B. A. Blumenstein for use of this program and for his generous help throughout the project.

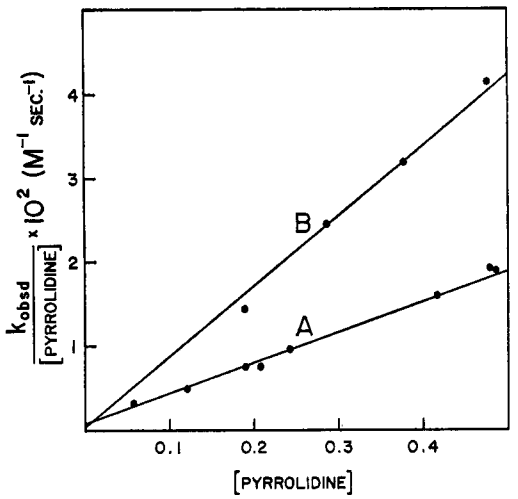


Figure 3. Plot of k_{obsd}/[pyrrolidine] *vs.* [pyrrolidine] for the reaction of *trans*-chalcone with pyrrolidine at 25.0° in acetonitrile (A) and heptane (B).

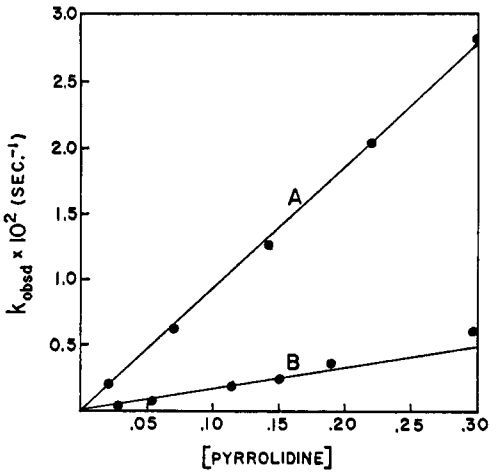


Figure 4. Plot of k_{obsd} *vs.* [pyrrolidine] for the reaction of *cis*-chalcone with pyrrolidine at 25.0° in acetonitrile (A) and heptane (B).

(2) The disappearance of *trans*-chalcone has a second-order dependency on amine concentration in both solvents, so that eq 3 may be presented as the simplest mechanism for reversible Michael addition (t-C, P, and MA represent *trans*-chalcone, pyrrolidine, and Michael adduct, respectively). A plot of k_{obsd}/[P] *vs.* [P] (Figure 3) is linear, which is consistent with

$$\text{t-C} + 2\text{P} \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \text{MA} + \text{P} \qquad (3)$$

eq 4 (the rate expression that describes eq 3). The k_{-2} term of eq 4 contributes little to k_{obsd}

$$k_{obsd} = k_2[\text{P}]^2 + k_{-2}[\text{P}] \qquad (4)$$

when the equilibrium constant favors adduct formation (as in heptane where $K = 80\ M^{-1}$) and when the amine concentration is close to unity. The third-order rate constants k_2, determined from the slopes of Figure 3, show that the Michael addition is twice as fast in heptane as in acetonitrile.

(3) The apparent activation parameters in acetonitrile, calculated from pseudo-first-order rate constants at 55, 45, 35, and 25°, are $\Delta H^{\ddagger} = 2.0$ kcal/mol and $\Delta S^{\ddagger} = -62$ eu.

(4) The k_H/k_D values using pyrrolidine-*d* (pyrrolidine deuterated at the nitrogen) are 1.92 and 1.80 in acetonitrile and heptane, respectively.

(5) In order to determine the effect of tertiary amines on Michael addition to *trans*-chalcone, we treated the substrate with an acetonitrile solution of pyrrolidine containing an equimolar amount of triethylamine. The observed rate constant decreased to 88% of that expected in the absence of tertiary amine. In a similar experiment using triethylenediamine (0.4 *M*) instead of triethylamine, a rate increase of 9% was observed.

The data on the reaction of *trans*-chalcone are summarized in Table I.

The reaction of *cis*-chalcone ($0.6–1.0 \times 10^{-4}$ *M*) with excess pyrrolidine (0.02–0.3 *M*) was followed at the isosbestic point of *trans*-chalcone and the Michael adduct. By monitoring the reaction in this manner it was possible to observe pseudo-first-order disappearance of *cis*-chalcone without complications arising from the presence of the equilibrium between Michael adduct and *trans*-chalcone (eq 1). The properties of the *cis*-chalcone reaction are as follows.

Table I. Properties of the *trans*-Chalcone to Michael Adduct Equilibrium Reaction at 25.0°

	Acetonitrile	Heptane
k_2,[a] M^{-2} sec^{-1}	3.64×10^{-2}	7.60×10^{-2}
K,[b] M^{-1}	17	80
k_H/k_D	1.92	1.80
$\Delta H^{\ddagger}$, kcal/mol	2.0	
$\Delta S^{\ddagger}$, eu	−62	

[a] Equation 3. [b] Equation 1.

(1) The reaction in both acetonitrile and heptane is first order in pyrrolidine (Figure 4), in contrast to the reaction of *trans*-olefin which is second order in amine. *cis*-Chalcone reacts 5.4 times faster in acetonitrile than in heptane.

(2) The disappearance of *cis*-chalcone displays no pyrrolidine-*d* isotope effect in acetonitrile. Again, this is very different from the behavior of the *trans*-chalcone reactions.

(3) The apparent activation parameters in acetonitrile are $\Delta H^{\ddagger} = 6.6$ kcal/mol and $\Delta S^{\ddagger} = -47$ eu.

(4) Triethylenediamine catalyzes the isomerization of *cis*-chalcone in acetonitrile with a second-order rate constant which is 94 times smaller than that for the pyrrolidine reaction. The data are summarized in Table II.

Table II. Properties of the Reaction of *cis*-Chalcone with Pyrrolidine at 25.0°

	Acetonitrile	Heptane
k_1,[a] M^{-1} sec^{-1}	9.25×10^{-2}	1.70×10^{-2}
k_H/k_D	1.01	0.91
$\Delta H^{\ddagger}$, kcal/mol	6.6	
$\Delta S^{\ddagger}$, eu	−47	

[a] Equation 5.

Although the method used to follow the disappearance of *cis*-chalcone allows the determination of k_1

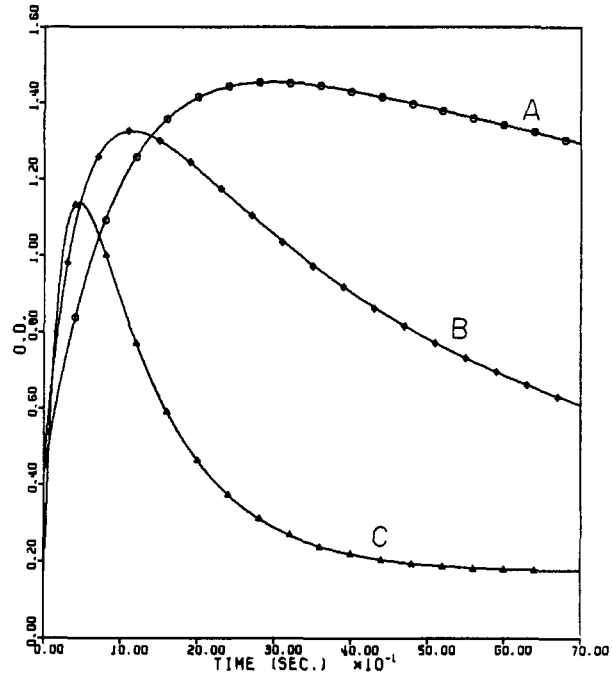


Figure 5. Computer plots of optical density *vs.* time for the reaction of *cis*-chalcone with pyrrolidine in acetonitrile at 25.0° followed at the absorbance maximum of *trans*-chalcone (306 mμ). The solid curves are theoretical lines calculated from eq 10; the points are experimental. The pyrrolidine concentrations are 0.122 *M* (A), 0.244 *M* (B), and 0.487 *M* (C). Excellent agreement between experiment and theory was also found at two higher concentrations of amine, but the curves are omitted to avoid cluttering.

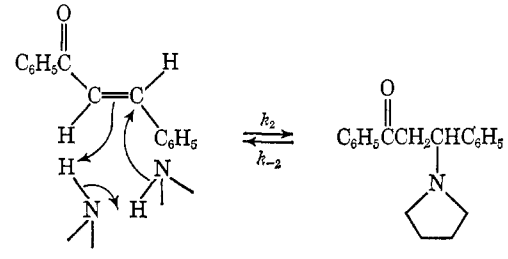
(eq 5), it precludes detailed observation of the reaction

$$\textit{cis}\text{-chalcone} \xrightarrow{k_1} [\textit{trans}\text{-chalcone} + \text{Michael adduct}] \quad (5)$$

product(s). In order to determine the fate of *cis*-chalcone, experiments were carried out in which the *cis* isomer was allowed to react in acetonitrile solutions of pyrrolidine while we monitored the system at the λ_{max} of the *trans* isomer. The beautiful optical density–time curves obtained in this manner (Figure 5) are analyzed with the aid of an RCA Spectra 70/55 computer in the next section.

Discussion

A mechanism which is consistent with our observations regarding the reaction of *trans*-chalcone with pyrrolidine is shown in eq 6. The substrate reacts with

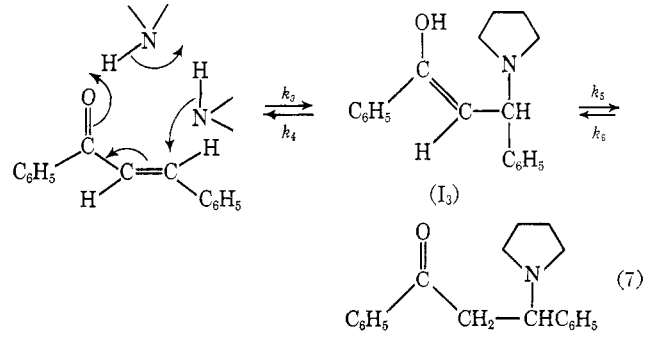


(6)

two molecules of amine through a cyclic, six-membered transition state that leads directly to Michael adduct. The reactive entity is probably an amine dimer (since a termolecular reaction is unlikely), although it is not possible to prove this from kinetic data. The mechanism (eq 6), which precludes charge formation in the transition state, has been previously proposed for addition of amines to ketenes[9,10] and to *p*-tolyl vinyl sulfone[11] in aprotic solvents. Equation 6 is consistent with the observed kinetics ($k_{obsd} = k_2[P]^2 + k_{-2}[P]$), with the pyrrolidine-*d* isotope effect of nearly two in both acetonitrile and heptane, and with the large negative entropy of activation. A general base mechanism, however, would also be consistent with these results. If the latter mechanism were operative, then the reaction should be faster in acetonitrile (dielectric constant = 37.5) than in heptane (dielectric constant = 1.9) because such a process entails charge formation. The twofold greater reactivity of *trans*-chalcone in heptane relative to acetonitrile therefore supports the cyclic concerted mechanism, eq 6.[12]

Triethylenediamine (0.40 *M*) increases the reaction rate of *trans*-chalcone with pyrrolidine (0.41 *M*) by 9% in acetonitrile. Since pyrrolidine is a stronger base than triethylenediamine in acetonitrile by 1.3 pK_a units,[13] the 9% increase may represent meaningful catalysis, although the acceleration is small enough to be simply a "medium effect." It has been claimed that tertiary amine catalysis of amine addition reactions in aprotic solvents constitutes evidence for a general base mechanism and evidence against a cyclic concerted process.[14] In our opinion this is not the case; unhindered tertiary amines may act as proton-transfer agents in cyclic five-membered transition states (much like eq 6 except that the tertiary amine accepts and delivers a *single* proton). Such a process would be sensitive to steric effects and accounts for the observed absence of catalysis by large amounts of triethylamine. In any event, the distinction between a general base catalysis and a cyclic concerted process is a subtle one. Charge formation in the cyclic mechanism occurs to the extent that the process is not completely concerted, and the degree of concertedness in eq 6 depends on the particular time scale one wishes to deal with. Thus, general base catalysis and the fully concerted mechanism (eq 6) are merely two extremes. In aprotic solvents, Michael addition to *trans*-chalcone resembles the latter extreme.

An alternative mechanism for addition of pyrrolidine to *trans*-chalcone which cannot be excluded from our data is shown in eq 7. The substrate reacts with two amine molecules through a cyclic, eight-membered

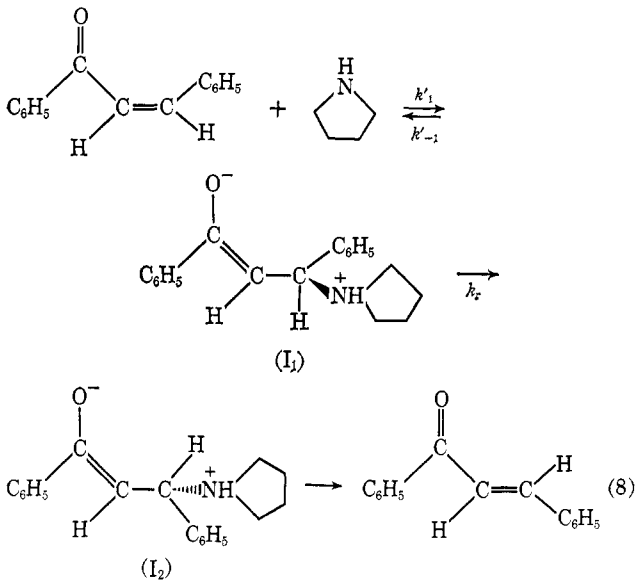


(7)

(9) P. J. Lillford and D. P. N. Satchell, *J. Chem. Soc.*, *B*, 360 (1967).
(10) P. J. Lillford and D. P. N. Satchell, *ibid.*, 54 (1968).
(11) S. T. McDowell and C. J. M. Stirling, *ibid.*, 343 (1967).
(12) Comparison of the reactions in heptane and acetonitrile is complicated by the possibility of a change in mechanism and by the fact that the amine dimer concentration in the two solvents is undoubtedly different.
(13) J. F. Coetzee and G. R. Padmanabhan, *J. Am. Chem. Soc.*, **87**, 5005 (1965).
(14) H. Anderson, C. Su, and J. W. Watson, *ibid.*, **91**, 482 (1969). This subject is discussed in more detail in a forthcoming article.

transition state to form a steady-state intermediate, an enol, which can undergo either reversal to starting material or else proton transfer to Michael adduct. Equation 7 is indistinguishable from eq 6 with $k_2 = k_3k_5/(k_4 + k_5)$ and $k_{-2} = k_4k_6/(k_4 + k_5)$. More will be said about the possibility of an enol intermediate later in this discussion.

The results obtained by following the reaction of *cis*-chalcone with pyrrolidine at the isosbestic point for *trans*-chalcone and Michael adduct are best explained by an ionic intermediate (eq 8). (It will be proven later that *cis*-chalcone reacts to give only *trans*-chalcone.) The mechanism (eq 8) is similar to that proposed for the isomerization of ethyl α-cyano-β-*o*-methoxyphenylacrylate.[5] The observed solvent effect (Table II), the absence of a pyrrolidine-*d* isotope effect, the catalysis by tertiary amines, the large negative entropy of activation, and the kinetics ($k_{obsd} = k_1[P]$, where $k_1 = k'_1k_r/(k'_{-1} + k_r)$) are all consistent with eq 8.

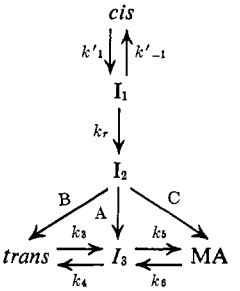


(8)

The fact that the reaction of *trans*-chalcone is an over-all third-order reaction while that of *cis*-chalcone is second order may be due to steric acceleration. *trans*-Chalcone prefers a cyclic transition state, which avoids charge separation, over the ionic intermediate that would form if the reaction were first order in amine. This requires the presence of an additional factor in the reaction of *cis*-chalcone that either favors an ionic mechanism or else inhibits a cyclic transition state. Such a factor could be the substantial steric crowding present in the *cis* isomer. Strain caused by the bulky *cis* groups can be relieved during formation of a dipolar intermediate (eq 8) to a greater extent than in the cyclic concerted mechanism.

In order to identify the primary reaction product of *cis*-chalcone, it was necessary to monitor the reaction at the absorbance maximum of *trans*-chalcone (Figure 1). The resulting absorbance–time curves are shown in Figure 5. There are three pathways available to intermediate I_2 of eq 8. These are summarized in eq 9. Path A involves proton transfer to the enolate oxygen to form enol intermediate I_3. Path B involves elimination of pyrrolidine to give *trans* isomer (as detailed in eq 8). Path C involves a proton transfer to the α-carbon of the incipient carbonyl to form Michael adduct directly.

It must be emphasized that we have no evidence demanding the involvement of enol intermediate I_3 in the conversion of *trans*-chalcone to Michael adduct. That is to say, we do not know whether eq 6 or eq 7 is correct. Since *cis*-chalcone could *a priori* be converted into either *trans*-chalcone, enol, or Michael adduct, we included I_3 in eq 9 to be as general as possible.



(9)

Figure 5 shows how the absorbance at the λ_{max} of *trans*-chalcone changes as a function of time during the *cis*-chalcone reaction. The absorbance increases at first because *cis* is converted into highly absorbing *trans;* the absorbance then decreases as equilibrium between *trans* and the nonabsorbing Michael adduct is established. Equation 10, which is based on the general mechanistic scheme of eq 9, describes the process quantitatively. This equation was derived by assuming path A and by making the steady-state assumption for the three intermediates of eq 9. We hope that the complexity of eq 10 will not discourage the reader. Simple qualitative arguments are often preferable to "deceptively authoritative numerical analyses,"[15] and indeed many of the important mechanistic conclusions in this paper are based on simple comparisons (pyrrolidine *vs.* pyrrolidine-*d*, acetonitrile *vs.* heptane, etc.). Equation 10, however, is necessary to prove the fact that *cis*-chalcone is converted entirely into *trans*-chalcone rather than into enol or Michael adduct.

$$OD = (\epsilon_{trans})[cis]_0\left[\frac{k_{-2}}{k_2[P] + k_{-2}} + \frac{k_{-2} - k_1\delta}{k_1 - k_2[P] - k_{-2}}e^{-k_1[P]t} + \frac{k_1k_2\delta[P] + k_1k_{-2}(\delta - 1)}{(k_2[P] + k_{-2})(k_1 - k_2[P] - k_{-2})}e^{-(k_2[P]^2 + k_{-2}[P])t}\right] + (\epsilon_{cis})[cis]_0e^{-k_1[P]t} \quad (10)$$

The symbols OD, [P], and t of eq 10 refer to the optical density, pyrrolidine concentration, and time, respectively. The rate constants k_1, k_2, and k_{-2} are those given in eq 5 and 6. (The three rate parameters may be complex quantities as was discussed previously in connection with eq 7 and 8.) Equation 10 is valid whether or not interconversion of *trans*-chalcone and Michael adduct proceeds by means of an enol intermediate.

We now direct attention to δ of eq 10. This parameter (representing partitioning of I_2 to *trans*-chalcone) must have a value of between zero and unity. If it is assumed that only one of the three pathways of eq 9 can be important, then the value of δ depends upon the

(15) R. Hoffmann and R. B. Woodward, *Accounts Chem. Res.*, **1**, 17 (1968).

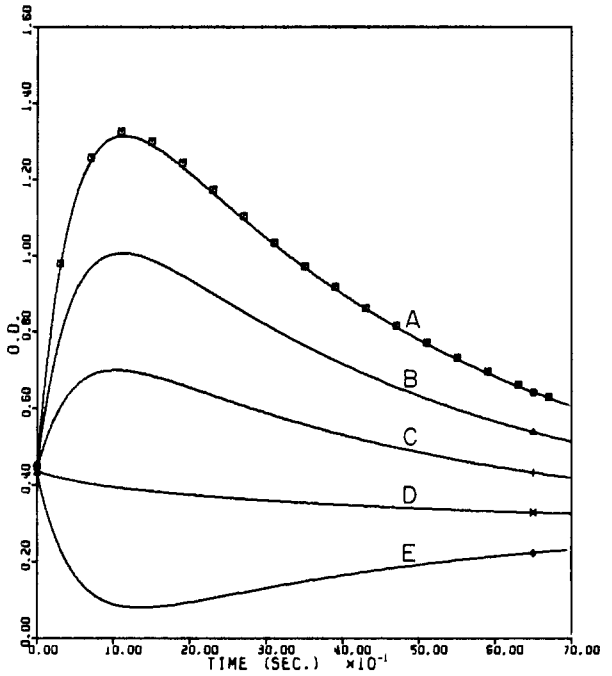


Figure 6. Computer plots of absorbance *vs.* time calculated from eq 10 for [pyrroline] = 0.244 *M* and δ = 1.00 (A), 0.75 (B), 0.50 (C), 0.25 (D), and 0.00 (E). The points (□) are experimental data for [pyrrolidine] = 0.244 *M*. λ = 306 mμ.

fate of I_2 in the following manner:[16] path A, $0 < \delta < 1$; path B, $\delta = 1$; path C, $\delta = 0$.

The parameters of eq 10 were estimated by means of a nonlinear regression program using the data shown in Figure 5 (plus additional data which were omitted from Figure 5 for the sake of clarity). The solid curves of Figure 5, which are theoretical lines drawn by the computer, are in excellent agreement with the experimental points. The value of δ is found to be 1.02, 1.01, and 0.98 for 0.122, 0.244, and 0.487 *M* pyrrolidine, respectively, thus establishing path B as the correct reaction mechanism.

Since eq 10 is complicated and multiparametered, it is necessary to show that the excellent agreement between experiment and theory (Figure 5) is meaningful. We present Figure 6 for this purpose. Figure 6 vividly demonstrates the sensitivity of the absorbance readings to the value of δ. The computer has graphed absorbance values as a function of δ, where δ varies from 0.0 to 1.0 in 0.25 increments while the other parameters of eq 10 remain fixed. Clearly path B (corresponding to $\delta = 1$) is the predominant reaction mode of *cis*-chalcone.

The primary reaction of *cis*-chalcone with pyrrolidine in chalcone in acetonitrile is, therefore, an isomerization to *trans*-chalcone; all Michael adduct obtained from addition of *cis*-chalcone to the amine solutions is really derived from *trans* material. Since path A of eq 9 can be eliminated, there is no need to postulate an enol intermediate, and the over-all mechanism is best represented as eq 11. The conversion of *cis*-chalcone to

$$\textit{cis}\text{-chalcone} \longrightarrow \textit{trans}\text{-chalcone} \rightleftharpoons \text{Michael adduct} \quad (11)$$

trans-chalcone, it will be recalled, proceeds through a dipolar intermediate (eq 8), and the conversion of *trans*-chalcone to Michael adduct proceeds through a cyclic concerted mechanism (eq 6).

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(16) This can be shown by letting δ equal 1 and 0 and observing that eq 10 simplifies to equations that can be derived for paths B and C, respectively. If $0 < \delta < 1$, then eq 10 does not simplify and it applies to path A since this is the path for which it was derived.