base than a saturated analog, *e.g.*, piperidine. In fact it is much weaker. This apparent anomaly can again be attributed to the different states of hybridization of the two types of nitrogen, sp^2 in pyridine and sp^3 in piperidine.

The results in Table IV can also be used to estimate the heats of dissociation (ΔH) of the ions II or VII into water, or an alcohol, and NO^+ or NO_2^+, *i.e.*

$$\text{II} \longrightarrow \text{ROH} + NO^+$$
$$\text{VII} \longrightarrow \text{ROH} + NO_2^+ \qquad (7)$$

The heat of formation of NO_2^+ has been measured[15] but not that of NO^+; we calculated the latter by the MINDO method, using the experimental value (1.0619 Å[16]) for the bond length. The values are given in (8).

$$NO^+ = +197.96 \text{ kcal/mol}$$
$$NO_2^+ = 244.5 \text{ kcal/mol} \qquad (8)$$

Using these values together with the heats of formation in Table IV, and the heats of formation calculated previously[3b] for water, methanol, and ethanol, we arrive at the values of ΔH shown in the last column of Table IV.

It will be seen that the values of ΔH for II are negative, or small and positive, implying that II should dissociate very readily; this of course is the case, nitrous acid derivatives readily giving NO^+ with no evidence for the formation of stable protonated intermediates. The values of ΔH for VII are quite large and positive; the nitracidium ion is known as a stable species in solution, and dissociation to NO_2^+ occurs only under conditions where the resulting water is immediately protonated, this protonation helping to displace the equilibrium toward NO_2^+.

(15) H. F. Cordes and N. R. Fetter, *J. Phys. Chem.*, **62**, 1340 (1958).
(16) E. Meischer, *Can. J. Phys.*, **33**, 355 (1955).

Vinyl Ether Hydrolysis. Specific Acid Catalyzed Hydrolysis of 4-Methoxy-3-buten-2-one[1]

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Received January 9, 1969

Abstract: The hydrolysis of 4-methoxy-3-buten-2-one (**1**) to 3-ketobutanal in aqueous solution is specific acid catalyzed and is further characterized by $k_2(D_2O)/k_2(H_2O) = 2.08$ and $\Delta S^{\ddagger} = -26.0 \pm 1.7$ eu. These results are consonant with an A2 mechanism involving rate-determining hydrolysis of the conjugate acid of **1**.

The hydrolysis of vinyl ethers (eq 1) is general acid catalyzed and exhibits a deuterium solvent isotope

$$\text{R'OCH=CHR} + H_2O \xrightarrow{k_{HA}} \text{RCH}_2\text{CHO} + \text{R'OH} \qquad (1)$$

effect $k(D_2O)/k(H_2O) < 1$,[3-7] results in accord with a mechanism involving rate-determining proton transfer from the catalyst to the olefin. The present study is concerned with the hydrolysis of a substituted vinyl ether, 4-methoxy-3-buten-2-one (**1**), a reaction which

$$\underset{\mathbf{1}}{\text{CH}_3\text{OCH=CHCOCH}_3}$$

formally involves olefin hydration of an α,β-unsaturated ketone and which proceeds *via* a mechanism exhibiting specific acid catalysis only.

(1) This work was supported by a research grant (AM-11403) from the National Institute of Arthritis and Metabolic Diseases and by a training grant (5-Tl-GM-555) from the Division of Medical Sciences, U. S. Public Health Services, Bethesda, Maryland.
(2) To whom inquiries concerning this work should be directed.
(3) A. J. Kresge and J. Chiang, *J. Chem. Soc., B*, 53, 58 (1967).
(4) A. J. Kresge, D. S. Sagatys, and H. L. Chen, *J. Amer. Chem. Soc.*, **90**, 4174 (1968).
(5) T. H. Fife, *ibid.*, **87**, 1084 (1965).
(6) E. J. Stamhuis, W. Drenth, and H. van den Berg, *Rec. Trav. Chim. Pays-Bas*, **83**, 167 (1964).
(7) D. M. Jones and N. F. Wood, *J. Chem. Soc.*, 5400 (1964).

Experimental Section

Reagents. Certified ACS grade inorganic salts were purchased from Fisher Scientific Co. Tap distilled water was redistilled through a Corning AG-1a still before use. 4-Methoxy-3-buten-2-one, bp 60° (6 mm) (lit.[8] 172°) was purchased from Aldrich Chemical Co., Inc. The pmr spectrum in $CDCl_3$ (TMS) showed singlets at δ 2.17 (CH_3CO), 3.72 (CH_3O), and doublets at 5.58 (OC=CH-) and 7.60 (OCH=C), J = 13 cps. Deuterium oxide, 99.8 atom % D, and DCl in D_2O were purchased from Diaprep, Inc. and from Ciba Corp.

Apparatus. Gilford Model 2000 and Beckman DBG spectrophotometers were used for the collection of rate data and for scanning reactions. Temperature was maintained in the cuvettes by circulating water of constant temperature from a Tamson T9 bath through thermospacers. pH was measured using a Radiometer PHM 22 pH meter with a PHA scale expander and a GK2021B combination electrode.

Kinetics. The course of the reaction of 4-methoxy-3-buten-2-one (**1**) was monitored at 250 mμ (ϵ 6.82 × 10^3) by following the loss of absorbance *vs.* time. All reactions were carried out in water at some specified temperature ±0.1° and at a calculated ionic strength of 1.0 *M* with KCl. The pH of each solution was determined before and after all runs and pH remained constant (±0.02 pH units) during all runs. Ⓢ cuvettes (3 ml) were filled to the stopper level with the appropriate HCl–KCl buffer or carboxylic acid–carboxylate salt buffer, capped, and allowed to come to thermal equilibrium. Reactions were started by adding a known amount of **1** in methanol *via* a micropipet to the appropriate solu-

(8) W. Franke, R. Kraft, D. Tietjen, and H. Weber, *Chem. Ber.*, **86**, 793 (1953).

Table I. Second-Order Constants and Arrhenius Activation Parameters[a] for the Reactions of 4-Methoxy-3-buten-2-one (**1**) in Dilute Acidic Solutions (μ = 1.0 *M* KCl)

Temp, °C	k_2, M^{-1} min^{-1}	No. of k_{obsd}	pH (pD) range	$k_2(D_2O)/k_2(H_2O)$	$\Delta H^{\pm}$, kcal/mol	$\Delta S^{\pm}$, eu
22 ± 0.1	28.0	3	3.33			
30 ± 0.1	43.5	12	1.95–2.97		10.1 ± 0.5	−26.0 ± 1.7
35 ± 0.1	62.0	3	3.28			
40 ± 0.1	78.0	3	3.46			
30 ± 0.1	90.5[b]	10	1.96–3.06	2.08		

[a] Calculated from $\Delta H^{\pm} = E_a - RT$; $\Delta F^{\pm} = -2.303RT \log (k_2h/kT)$; $\Delta S^{\pm} = (\Delta H^{\pm} - \Delta F^{\pm})/T$ for 25° using concentrations in *M* and time in sec. The uncertainties in $\Delta H^{\pm}$ and $\Delta S^{\pm}$ are the standard deviations (s) from the regression line of a plot of log k_2 *vs.* $1/T$ for which r = 0.998. [b] Solvent = D_2O.

tion in the cuvette. Reactions were carried out under pseudo-first-order conditions (concentration of **1** *ca.* 5×10^{-5} *M*) and pseudo-first-order rate constants were obtained by multiplying slopes of plots of log $((OD_i - OD_\infty)/(OD_t - OD_\infty))$ *vs.* time by 2.303. Reactions were monitored to completion and pseudo-first-order plots were nearly always linear to at least two half-lives. The activity of the hydrogen ion was determined with the glass electrode and pD was determined from pH +0.39 employing the equation of Fife and Bruice.[9]

Product Analysis. Hydrolysis of alkyl vinyl ethers gives alkanols and aldehydes (ketones).[3,5-7] Further, the reaction proceeds *via* oxygen–vinyl carbon bond cleavage.[10] Similarly, the hydrolysis of **1** gives methanol and 3-ketobutanal and the course of this reaction may be monitored *via* pmr spectrometry. In dilute DCl–D_2O solution, **1** exhibits singlets at δ 2.25 (CH_3CO), 2.55 (CH_3O), and doublets at 5.7 (OC=CH) and 6.57 (OCH=C), J = 13 cps.[11] As the reaction proceeds the signals at δ 2.55, 5.7, and 6.57 disappear and singlets at δ 3.37 (CH_3OD), 5.05, and 5.47 appear. The assignment of the methanol signal at δ 3.37 was verified using only methanol in an otherwise identical solvent system; the pmr signal appeared at δ 3.37. The signals at δ 5.05 and 5.47 correspond to a single proton and are tentatively assigned to the β-proton of 3-ketobutanal and its enol and their hydrates. Signals for hydrated and unhydrated aldehyde are absent. With regard to this finding acetaldehyde in D_2O exhibits two doublets (hydrated and unhydrated CH_3) and two quartets (hydrated and unhydrated CHO). On acidification with dilute DCl, the doublets merge into a single broad band and the two quartets from the aldehydic protons disappear.

The course of the reaction of **1** in aqueous acidic solution was scanned from 310 to 210 mμ. Only the disappearance of the 250-mμ peak (λ_{max}) with time was observed at the concentrations used in the kinetics experiments. An attempted scale-up of this reaction using 0.5 g of **1** in 1 ml of 1 *N* HCl resulted in the formation of insoluble needles of 1,3,5-triacetylbenzene, mp 162–163° (lit.[12] 162–163°), mixture melting point with authentic material, 162–163°. This result is in accord with the observations of Claisen[12] who reported that 3-ketobutanal is unstable and readily trimerizes spontaneously to 1,3,5-triacetylbenzene. The pmr spectrum of the product shows singlets at δ 2.74 and 8.78 and the uv spectrum shows a λ_{max} at 227 mμ (1 *N* HCl) (ϵ 6.5×10^4), identical with authentic material. Also, ir spectra are superimposable.

Results

In dilute acidic solution the hydrolysis of 4-methoxy-3-buten-2-one (**1**) in water, μ = 1.0 *M* (KCl), to give 3-ketobutanal is specific acid catalyzed and obeys the rate law given by eq 2. At constant pH pseudo-first-order conditions obtain and plots of k_{obsd} values *vs.* a_H values are linear with slope k_2 (Figure 1, Table I).

$$-d(\mathbf{1})/dt = k_{obsd}(\mathbf{1})$$

$$k_{obsd} = k_2 a_H \qquad (2)$$

Chloroacetic acid, formic acid, and acetic acid are not catalysts for this reaction. Thus hydrolytic rates in carboxylic acid buffers can be accounted for on the basis of the acidity of the solution alone (Table II). The hydrolytic reaction exhibits a deuterium solvent kinetic isotope effect $k_2(D_2O)/k_2(H_2O)$ = 2.08 (Figure 1, Table I) and is further characterized by an activation entropy of −26.0 ± 1.7 eu (Table I).

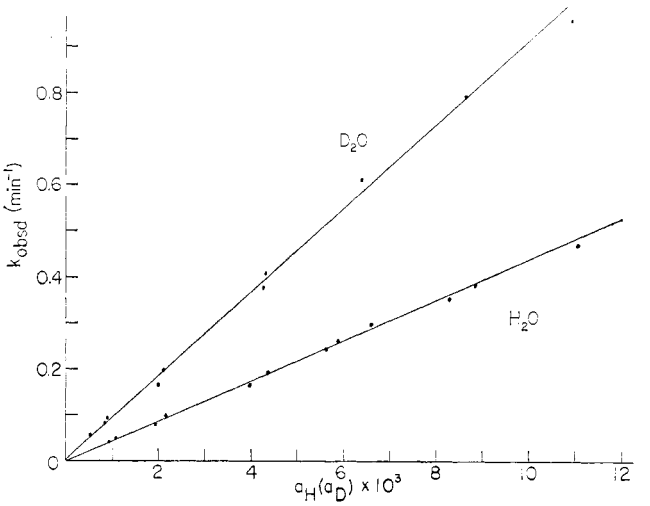


Figure 1. Plot of the pseudo-first-order rate constant, k_{obsd}, *vs.* the activity of the hydrogen ion (a_H) or the activity of the deuterium ion (a_D) for the reaction of 4-methoxy-3-buten-2-one in water (lower line) and in deuterium oxide (upper line), μ = 1.0 *M* (KCl), t = 30 ± 0.1°.

Table II. First-Order Rate Constants for the Hydrolysis of 4-Methoxy-3-buten-2-one (**1**) in Dilute Formate Buffer, HCO_2H/HCO_2^- = 4, t = 30°, μ = 1.0 *M* (KCl)

$[Buffer]_{total}$, *M*	pH	k_{obsd}, min^{-1} Exptl	k_{obsd}, min^{-1} Calcd (k_2a_H)
0.02	3.02	0.0424	0.0416
0.04	2.97	0.0468	0.0465
0.06	2.95	0.0486	0.0488
0.08	2.94	0.0500	0.0505
0.10	2.93	0.0510	0.0517

Discussion

The hydrolysis of an alkyl vinyl ether likely proceeds *via* rate-determining protonation of the olefin bond followed by rapid addition of water to give the hydrolytically labile hemiacetal,[3-7] a conclusion consonant

(9) T. H. Fife and T. C. Bruice, *J. Phys. Chem.*, **65**, 1079 (1961).
(10) L. A Kiprianova and A. F. Rekasheva, *Dokl. Akad. Nauk SSSR*, **142**, 589 (1962).
(11) The chemical shifts are reported relative to TMS and were determined from the chemical shift measured from *t*-butyl alcohol in D_2O and the chemical shift of *t*-butyl alcohol from TMS in $CDCl_3$.
(12) L. Claisen and N. Stylos, *Chem. Ber.*, **21**, 1144 (1888).

with the results that general acids catalyze hydrolysis and $k_2(D_2O)/k_2(H_2O) < 1$. In contrast, the hydrolysis of 4-methoxy-3-buten-2-one (**1**) is specific acid catalyzed only and exhibits an inverse deuterium solvent kinetic isotope effect, $k_2(D_2O)/k_2(H_2O) > 1$ (Tables I and II). Thus proton transfer is not rate determining in this reaction. Further, the hydrolyses of ethyl vinyl ether[3] and of 2-ethoxy-1-cyclopenten-1-carboxylic acid[5] are characterized by activation entropies of −11.1 and −14.5 eu, respectively; hydrolysis of **1** is characterized by an activation entropy of −26.0 eu. A less remarkable difference between the hydrolytic behavior of alkyl vinyl ethers and **1** is evident on examination of the relative reactivities of ethyl vinyl ether and **1**. In this connection Jones and Wood[7] have shown that the rates of hydrolysis of alkyl vinyl ethers are reasonably correlated by Taft's σ^* constants and that β-electron-withdrawing substituents in the vinyl group accelerate the rate of reaction. They also established that β-chlorovinyl ethyl ether undergoes hydrolysis *ca.* 660 times more slowly than ethyl vinyl ether and attributed the effect of the chloro group to "... unfavorable mesomeric forms involving the chlorine atom...."[13] An alternative interpretation of the results could be offered: β-alkyl substituents in the vinyl group decelerate the rate of hydrolysis *via* steric effects; the β-chloro substituent *via* inductive effects. The former interpretation requires that **1** undergo hydrolysis *via* carbon protonation more rapidly than ethyl vinyl ether; the latter is 3.7 times *more* reactive than **1**. This result raises the question of why **1** undergoes reaction more slowly by a mechanism different from C protonation when C protonation is favorable (*vide supra*, Jones and Wood). Acceptance of the alternative interpretation of the results of Jones and Wood, which is in accord with the relative reactivities of **1** and ethyl vinyl ether, circumvents the dilemma. Thus the electron-withdrawing aceto group of **1** might so diminish the basicity of the olefin that rate-determining C protonation is disfavored compared with protonation *via* an optional mechanism. Clearly the similarity between **1** and alkyl vinyl ethers ends with their structural resemblance.

Since the hydrolysis of **1** is not kinetically characteristic of the hydrolysis of vinyl ethers it is instructive to consider the hydrolysis of **1** in terms of the hydration of an α,β-unsaturated ketone. The hydration of mesityl oxide and crotonaldehyde[14] as well as the hydration of 4-(*p*-nitrophenyl)-3-buten-2-one and 4-phenyl-3-buten-2-one[15,16] are postulated to proceed *via* preequilibrium protonation of the α,β-unsaturated ketone (aldehyde) followed by rapid 1,4 addition of water to the olefin to give the β-hydroxy enol which *via* slow proton transfer to the α-methylene carbon from a proton source is converted to the β-hydroxy ketone (aldehyde). The conclusions are supported by $k(D_2O)/k(H_2O) < 1$ and by the result that polyprotic acids are more reactive than monoprotic acids, suggesting that general acid catalysis obtains.

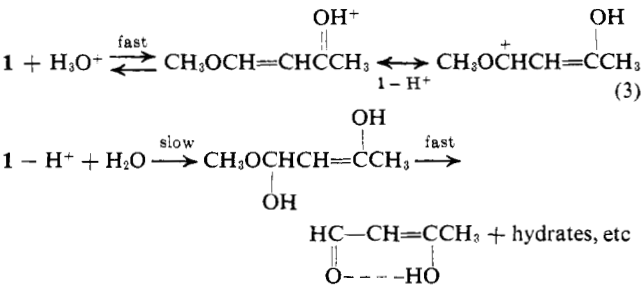
(13) The mesomeric effect cited by Jones and Wood is sometimes invoked to rationalize the decreased reactivity of aryl and vinyl halides toward nucleophilic displacement reactions.

(14) R. P. Bell, J. Preston, and R. B. Whitney, *J. Chem. Soc.*, 1166 (1962).

(15) The dehydrations of the alcohols were actually studied and the principle of microscopic reversibility is invoked in discussing the hydration reaction

(16) D. S. Noyce and W. L. Reed, *J. Amer. Chem. Soc.*, **80**, 5539 (1958).

The mechanism of Noyce and Reed[16] is applicable to the hydration of **1** provided a change in the rate-determining step occurs. Thus preequilibrium protonation of **1** followed by rate-determining reaction of $1H^+$ with water to give products provides a mechanism in accord with the data (eq 3): the reaction is



specific acid catalyzed only and the rate of reaction is dependent on the concentration of the conjugate acid of **1**; the reaction proceeds faster in deuterium oxide than in water since the concentration of **1**-D^+ is predictably greater than the concentration of **1**-H^+;[17] the reaction is attended by an activation entropy of −26 eu in accord with a transition state involving tightly bound water. In this latter connection the hydration of crotonaldehyde and β,β-dimethylacrolein are attended by activation entropies of −23 eu.[18] Also, the hydration of these compounds follows the stoichiometric acid concentration in dilute acidic solution rather than H_0.

Comparison of the structure of **1** with that of an α,β-unsaturated ketone, *e.g.*, mesityl oxide, reveals that **1** has an additional capability for stabilizing positive charge *via* the β-methoxyl group. This likely accounts for the greater reactivity of **1**, by *ca.* 10^4 or more, compared with other α,β-unsaturated ketones. The reason for an apparent change in rate-determining step for the hydration of **1** *vs.* mesityl oxide[14] and certain 4-(*para*-substituted phenyl)-3-buten-2-ones,[16] assuming the proposed mechanisms are correct, may be due to the fact that **1**-H^+ (eq 3) can undergo rate-determining reaction with water to give the labile hemiacetal which rapidly undergoes hydrolysis to give products:[19] the protonated α,β-unsaturated ketones, upon addition of water, must undergo protonation at the α-carbon atom, a process known to be slow,[3,14,16] to give stable products.[20] Perhaps the best available model for comparison with **1** is 4-(*p*-methoxyphenyl)-3-buten-2-one[15] for which Noyce and Reed[16] suggest that hydration occurs *via* rapid specific acid catalyzed protonation of the ketone to give a stabilized carbonium ion which then undergoes hydration in a slow step to give product. This mechanism is essentially that of eq 3. However, recognition of the structural difference between **1**, a vinyl ether, and the β-aryl ketone leads to a quandary: vinyl ether hydrolysis is general acid catalyzed,[3-7] the hydrolysis of **1** is specific acid catalyzed. Arguments centered on the possibility that Brønsted $\alpha \rightarrow 1$ are negated by the finding that $k_{D_2O}/k_{H_2O} = 2.08$. Also, Kresge[3] reported that for ethyl vinyl ether hydrolysis α is *ca.* 0.5. It remains a possibility that **1** is less basic

(17) C. A. Bunton and V. J. Shiner, Jr., *ibid.*, **83**, 3207 (1961).

(18) S. Winstein and H. L. Lucas, *ibid.*, **59**, 1461 (1937).

(19) E. H. Cordes, *Progr. Phys. Org. Chem.*, **4**, 1 (1967), and references therein.

(20) We are grateful to Dr. A. J. Kresge for suggesting this plausible explanation for the changes in rate-determining steps.

than alkyl vinyl ethers owing to the presence of the carbonyl group and that as a result the critical transition state is reached when proton transfer to the olefin is complete; the mechanism of hydrolysis is then the same as for vinyl ethers with the provision that proton transfer be complete.

The mechanism of eq 3 satisfies the data. Further experimentation is required in order to accommodate the proton-transfer reactions of **1** within the framework of what is known of the mechanisms of vinyl ether hydrolysis and the hydrations of α,β-unsaturated ketones.

Interactant Structure and Complex Stability for Complexes of Theophylline with Cinnamate Esters and Related Compounds in Aqueous Solution[1]

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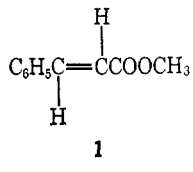
Abstract: Complex stability was evaluated by means of the spectral, solubility, and kinetic techniques for interactions between many esters and related compounds with theophylline and its anion. Stability constants were determined in aqueous solution at 25.0° and ionic strength 0.30 *M*. A plot of standard unitary free energy change for complex formation (for complexes of neutral interactants) against estimated planar area of the smaller interactant gives a rough but reasonable linear correlation over two orders of magnitude range in stability constant. A simple model of the complex formation process is consistent with this observation. It is suggested that these 1–1 complexes have a plane-to-plane orientation, that the solvent is important in determining complex stability, and that the complex structures probably do not involve maximum π-orbital overlap, but do permit extensive local dipole and induced dipole interactions.

It is not yet possible to make general statements about the stability of organic complexes in solution, though numerous limited correlations of complex stability with interactant properties have been described.[2] In an earlier paper[3] we reported stability constants for complex formation between methyl *trans*-cinnamate (**1**) (the *substrate*, or interactant whose property is measured in the solution) with numerous



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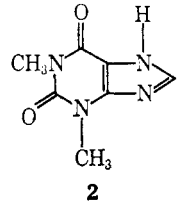

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heterocyclic *ligands* (the second interactant, whose concentration is the independent variable). The present paper describes studies on many substrates chosen as systematic variants of the methyl *trans*-cinnamate structure. Theophylline (**2**) or its anion (theophyllinate) was the ligand in most of these studies. Comparative studies by more than one technique were employed when possible to aid in detecting multiple equilibria and higher stoichiometries.[4]

Experimental Section

Materials. Methyl *trans*-cinnamate, *trans*-cinnamic acid, theophylline, and imidazole have been described earlier.[3] Ethyl *trans*-cinnamate (Eastman) was distilled; bp 122–123° (5–6 mm) (lit.[5] 128–133° (6 mm); 138–140° (10 mm)). Isopropyl *trans*-cinnamate (K & K) was distilled; bp 107° (1–2 mm) (lit.[6] 107.5–108° (2 mm)). *p*-Nitrophenyl *trans*-cinnamate was recrystallized from ethanol–water; mp 145–146.5° (lit.[7,8] 146°, 146.5–147.5°). *N*-*trans*-Cinnamoylimidazole was prepared by the method of Schonbaum, *et al.*,[9] mp 133° (lit.[9] 133–133.5°). *trans*-Cinnamaldehyde (Eastman) was shaken with 10% sodium carbonate solution, washed with water, dried over magnesium sulfate, and then distilled; bp 93–94° (1–2 mm) (lit.[10] 98–100° (3–4 mm)). *trans*-Benzalacetone (Eastman) was recrystallized twice from Skellysolve B; mp 40–41.5° (lit.[11] 41–42°). *p*-Methoxyphenyl *trans*-cinnamate was prepared from cinnamoyl chloride and *p*-methoxyphenol and recrystallized from 95% ethanol; mp 97.5–98.5°. *Anal.* Calcd for $C_{16}H_{14}O_3$: C, 75.57; H, 5.55. Found: C, 75.66; H, 5.49. *trans*-Cinnamyl acetate (J. T. Baker Chemical Co.) was distilled; bp 111–112° (2 mm) (lit.[12] 111–112° (2 mm)). Phenacyl acetate (East-

(1) Part IV in the series "Modification of Reaction Rates by Complex Formation." For part III see P. A. Kramer and K. A. Connors, *J. Amer. Chem. Soc.*, **91**, 2600 (1969).

(2) (a) G. Briegleb, "Elektronen-Donator-Acceptor Komplexe," Springer-Verlag, Berlin, 1961, Chapter IX; L. J. Andrews and R. M. Keefer, "Molecular Complexes in Organic Chemistry," Holden-Day, Inc., San Francisco, Calif., 1964, Chapter IV; J. Rose, "Molecular Complexes," Pergamon Press, Oxford, 1967, Chapter 5; (b) T. Higuchi and K. A. Connors, *Advan. Anal. Chem. Instr.*, **4**, 117 (1965).

(3) J. A. Mollica, Jr., and K. A. Connors, *J. Amer. Chem. Soc.*, **89**, 308 (1967).

(4) K. A. Connors and J. A. Mollica, Jr., *J. Pharm. Sci.*, **55**, 772 (1966)

(5) C. S. Marvel and W. B. King, *Org. Syn.*, **9**, 38 (1929); V. F. Kucherov, B. G. Kovalev, I. I. Nazarova, and L. A. Yanovskaya, *Izv. Akad. Nauk SSSR, Otdel. Khim. Nauk*, 1512 (1960); *Chem. Abstr.*, **55**, 1420c (1961).

(6) W. J. Svirbely, W. M. Eareckson, III, K. Matsuda, H. B. Pickard, I. S. Solet, and W. B. Tuemmler, *J. Amer. Chem. Soc.*, **71**, 507 (1949).

(7) R. Anschütz, *Ber.*, **60**, 1322 (1927).

(8) M. L. Bender, G. R. Schonbaum, and B. Zerner, *J. Amer. Chem. Soc.*, **84**, 2540 (1962).

(9) G. R. Schonbaum, B. Zerner, and M. L. Bender, *J. Biol. Chem.*, **236**, 2930 (1961); this sample was kindly provided by Mr. W. H. Hong.

(10) H. C. Brown and B. C. Subba Rao, *J. Amer. Chem. Soc.*, **80**, 5377 (1958).

(11) A. L. Wilds, L. W. Beck, W. J. Close, C. Djerassi, J. A. Johnson, Jr., T. L. Johnson, and C. H. Shunk, *ibid.*, **69**, 1985 (1947).