c. Substituted triaryl phosphites were prepared using dimethylaniline in the case of phosphites with electron-donating groups, and triethylamine for phosphites with electron-withdrawing groups or *ortho* substitution.[1] The tris(*p*-methylphenyl) and tris(*p*-chlorophenyl) phosphites were prepared by the high-temperature method[23] of Walsh.

d. Trisubstituted (phosphite)copper(I) halide complexes were prepared[24] by mixing equimolar amounts of the appropriate phosphites and solid copper(I) halides in either pentane or benzene. The reaction was completed when all of the solid salts were dissolved. Correct copper analyses were obtained on all catalysts utilizing the method of Wilcocks and Belcher.[25] Infrared and nmr spectra were measured on several of the catalysts.

Analysis. The gas chromatographic analysis (glpc) were carried out on an F & M Model 720, dual-columned instrument utilizing thermal conductivity detectors. The column employed mainly for the ester separations was a 2 m × 0.64 cm copper tube filled with 10% *m*-bis(*m*-phenoxyphenoxy)benzene plus 10% Apiezon L on Chromosorb W (BPPB). Other columns utilized were: 5% polypropylene glycol adipate (PPGA) on Chromosorb W, 4 m × 0.64 cm, and 15% Carbowax 20M, 2 m × 0.64 cm. In all cases the analysis could be obtained at temperature less than 125°. Yields were determined utilizing internal standards and applying the appropriate response factors.

Catalytic Activity of Complexes. All solvents were passed through aluminum oxide and were degassed just before use: in addition, cyclohexene was distilled from sodium to remove peroxides and stored at −20°.

a. General Procedure for the Cyclohexene–Ethyl Diazoacetate Reaction. The catalyst (5.0 mmol, except when otherwise stated) was dissolved[8] in 20 ml of cyclohexene and placed in a constant temperature bath at 30.0 ± 0.1°. Ethyl diazoacetate (20 mmol) in 20 ml of cyclohexene was added from a constant dropping funnel at a rate of five drops/min. The nitrogen evolution began within 1–2 min and was formed in quantitative amounts. The solution was dark brown after *ca.* 1 ml of the diazoalkane solution had been added; 10–15 min after the addition was completed, a sample was removed and distilled without heating under 10^{-4} mm Hg. Final traces of volatile materials were removed by a final short heating period to 150–200°. The distilled solutions were then analyzed by glpc on the BPPB column at 125° or the PPGA column at 98°. The analysis of a second sample 3–6 hr after the completion of the addition of the diazoalkane showed no change in the product ratio, thus no isomerization of the products by the catalyst was observed. The yields of the cyclopropanes varied between 30 and 70%; the balance was mainly diethyl fumarate and maleate. The unsaturated esters were identified by comparison of the infrared spectra and glpc retention times with authentic materials. The cyclopropanes were identified by a comparison of the mixture melting points and infrared spectra of their acid derivatives with authentic material.[26] The substitution utilized in the Hammett study was *p*-CH$_3$O, *p*-CH$_3$, *m*-CH$_3$, *p*-H, *p*-Cl, and *p*-CH$_3$CO. The *ortho*-substituted derivatives were *o*-methyl- and *o*-*t*-butyl-*p*-methyl.

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(23) E. N. Walsh, *J. Am. Chem. Soc.*, **81**, 3023 (1959).

(24) (a) A. Arbuzov, *Ber.*, **38**, 1171 (1905); (b) Y. Nishizawa, *Bull. Chem. Soc. Japan*, **34**, 1170 (1961).

(25) I. M. Kolthoff and R. Belcher, "Volumetric Analysis," Vol. III, Interscience Publishers, New York, N. Y., 1957, pp 350–352.

(26) Authentic samples of the acid derivatives of **4** and **5** were kindly supplied by Professor H. Musso; H. Musso and U. Biethan, *Ber.*, **97**, 2282 (1964).

On the Mechanism of Acid-Catalyzed Enolization of Ketones[1]

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Contribution from the James Bryant Conant Laboratory, Harvard University, Cambridge, Massachusetts 02138. *Received August 9, 1968*

Abstract: The rate constants for the catalysis of the enolization of cyclohexanone and of the hydrolysis of 1-methoxycyclohexene by a number of general acids have been determined in water at 25°. The rate constants for ketonization of cyclohexanone enol have been calculated from those for enolization and the equilibrium constant for enolization. The rate constants for ketonization catalyzed by hydronium ion, carboxylic acids, and triethylenediammonium ion are approximately the same as the corresponding rate constants for hydrolysis of 1-methoxycyclohexene. Because the rate-determining step in the hydrolysis of enol ethers is known to be proton transfer to the β-carbon, this result shows that in the transition state of the rate-determining step of acid-catalyzed ketonization, proton transfer to carbon occurs with the bond between the enol oxygen and its hydrogen atom *substantially intact*. Consequently, acid-catalyzed enolization occurs by preequilibrium protonation of the carbonyl oxygen followed by rate-determining proton transfer from carbon to the general base. The approximate equality of rate constants does not hold for the conjugate acid of *p*-toluidine because the rates of enolization were measured by iodination, and *p*-toluidinium ion catalyzes iodination by a special mechanism: formation of the Schiff base salt of cyclohexanone and its enaminization.

The rate laws for the enolization of simple ketones in water contain the summation (ketone)Σk_a(HB) in which HB represents hydronium ion and other acids, such as carboxylic acids.[2] Several plausible mechanisms can be written to account for this acid catalysis; these mechanisms differ from one another in the extent to which the carbonyl oxygen is protonated in the transition state of the rate-determining step and also in the identity of the base that abstracts the proton from the α-carbon atom (see the Discussion for these mechanisms and for references to earlier work on this problem). This paper reports a study of the kinetics of the enoliza-

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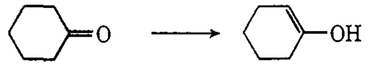
(1) This research was supported by a grant (GB 4848) from the National Science Foundation. Address inquiries to G. E. L.

(2) (a) R. P. Bell and O. M. Lidwell, *Proc. Roy. Soc.* (London), **A176**, 88 (1940); (b) R. P. Bell, G. R. Hillier, J. W. Mansfield, and D. G. Street, *J. Chem. Soc.*, *B*, 827 (1967).

tion of cyclohexanone (eq 1) catalyzed by general acids and general bases and of the kinetics of the acid-catalyzed hydrolysis of 1-methoxycyclohexene (eq 2).



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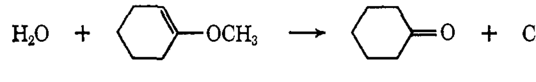

(2)

Through a comparison of the kinetics of the two reactions and a knowledge of the mechanism of the acid-catalyzed hydrolysis of the enol ether, we have been able to define more clearly the mechanism of acid-catalyzed enolization.

Experimental Section

Materials. Cyclohexanone was fractionally distilled under argon and stored at $-20°$ under argon.

1-Methoxycyclohexene was prepared from cyclohexanone and trimethyl orthoformate in methanol by the procedure of Lindsay and Reese,[3] with methanesulfonic acid rather than mesitylenesulfonic acid as the catalyst. Its proton magnetic resonance and infrared spectra were identical with the reported[3] spectra. Gas-liquid partition chromatography of the compound on a 10% diethylene glycol succinate column in a Research Specialties Co. Model 600 chromatograph showed one major peak and a very minor peak, the area of which was about 1-2% of the major peak. When the 1-methoxycyclohexene was stored at room temperature in the light an unidentified impurity that absorbed in the ultraviolet region below 250 mμ formed slowly over a period of a month. This decomposition was retarded by storing the compound at $-20°$ in the dark.

Glycolic acid, chloroacetic acid, imidazole, triethylenediamine (1,4-diazobicyclo[2.2.2]octane), and *p*-toluidine hydrochloride were recrystallized. Distilled water was used throughout.

Kinetic Measurements. The rates of enolization of cyclohexanone were determined by iodination of the enol and were followed spectrophotometrically by the decrease in the absorbance of the triiodide ion at 351 mμ.[4] The usual procedure was the following. Aliquots from stock solutions of buffer, iodine-iodide, and sodium perchlorate (sufficient to give an ionic strength of 0.25 *M*) were mixed in a 3-ml, Teflon-stoppered cuvette and equilibrated for at least 15 min in a 25° water bath. Reaction was initiated by the addition of an aliquot from an aqueous solution of cyclohexanone, which was prepared daily and maintained at 25°; the decrease in absorbance was followed with a Zeiss PMQ II spectrophotometer equipped with a cell holder thermostated at 25.0 ± 0.1°. The concentrations of cyclohexanone which were used varied from 0.02 to 0.2 *M*, and those of iodine plus triiodide ion varied from 2×10^{-5} to 8×10^{-5} *M*. With perchloric acid and the carboxylic acid buffers, the reaction mixtures contained 0.005-0.01 *M* potassium iodide. When the buffer was an amine, a higher concentration of iodide ion (0.1 *M* potassium iodide with imidazole, 0.1 *M* sodium iodide with triethylenediamine and *p*-toluidine) was used in order to shift the iodine-triiodide ion equilibrium toward triiodide ion and so retard the reaction of iodine with the amine.[5] Determinations of the rates of reaction of iodine with the buffers alone under the conditions which were used to measure the enolization showed that consumption of iodine by the amine buffers as well as the carboxylic acid buffers never accounted for more than 2% of the total rate in the presence of cyclohexanone. Each observed first-order rate constant (k_{obsd}) was calculated from the linear slope of the plot of absorbance at 351 mμ against time by use of the equation k_{obsd} = slope $\{[(\text{I}^-) + K_{\text{I}_3^-}]/(\text{I}^-)\}/\epsilon_{\text{I}_3^-}$-(cyclohexanone), where $[(\text{I}^-) + K_{\text{I}_3^-}]/(\text{I}^-)$ is the factor which accounts for the iodine-triiodide ion equilibrium ($K_{\text{I}_3^-} = (\text{I}^-)(\text{I}_2)/(\text{I}_3^-)$), and $\epsilon_{\text{I}_3^-}$ is the extinction coefficient of triiodide ion at 351 mμ.[4] The values of $K_{\text{I}_3^-}$ and $\epsilon_{\text{I}_3^-}$ under our conditions are 1.5×10^{-3} *M* and 26,000 M^{-1} cm^{-1}, respectively.[4] The fact that all the plots were linear from the time of the first reading (about 10 sec after the addition of cyclohexanone) until at least 90% of the iodine had reacted showed that the kinetics of iodine consumption were zero order. Also, variations in the initial concentration of iodine did not alter the rate of its disappearance. A number of determinations of the rates in the perchloric acid, glycolic acid, and amine buffers were carried out at one buffer concentration with several concentrations of cyclohexanone; in each case the rate of iodine disappearance was directly proportional to the concentration of the ketone.

The extinction coefficient of 1-methoxycyclohexene in 5×10^{-5} *N* NaOH at 230 mμ is 350 M^{-1} cm^{-1}, a value which is considerably larger than that of cyclohexanone (ϵ_{230} 0.88 M^{-1} cm^{-1}). Consequently, with the exception of experiments in *p*-toluidine buffers (see below), the rates of hydrolysis of the enol ether were measured spectrophotometrically by the decrease in absorbance at 230 mμ. The usual procedure was as follows. Aliquots from stock solutions of the buffer and of sodium perchlorate (sufficient to give a final ionic strength of 0.25 *M*) were mixed in a 3-ml, Teflon-stoppered cuvette with enough water to give a volume of 2.0 ml. The cuvette was equilibrated at 25° in a water bath for at least 15 min. Reaction was initiated by the addition of 1.0 ml from a stock solution of 0.005 *M* 1-methoxycyclohexene in 5×10^{-5} *M* NaOH, which was prepared daily and maintained at 25°, and the decrease in absorbance at 230 mμ was followed with the Zeiss spectrophotometer with the cell holder thermostated at 25.0 ± 1°, against a blank of the same composition as the reaction mixture except for the omission of the enol ether. The strong ultraviolet absorption of *p*-toluidine (in water $\lambda_{\max}$ 233 (ϵ 7600) and 286 (ϵ 1320))[6] completely prevented the use of the above spectrophotometric method for measurement of the hydrolysis in *p*-toluidine buffers. In these buffers the rates of hydrolysis were followed by use of a colorimetric test for cyclohexanone.[7] The procedure was as follows. A stoppered 10-ml volumetric flask which contained in a 6.0 ml volume *p*-toluidine hydrochloride buffer and sufficient sodium chloride to give a final ionic strength of 0.25 *M* in 10.0 ml was placed in a water bath at 25.0 ± 1° for at least 15 min; the reaction was started by the addition of 4.0 ml of 0.005 *M* 1-methoxycyclohexene at 25°. At various times 0.20-ml samples of the reaction mixture were mixed with 0.2 ml of 0.1 *N* KOH in 10% aqueous ethanol in order to stop the hydrolysis; after the entire reaction was over (about 2 hr) 0.2 ml of 1% *m*-dinitrobenzene in ethanol immediately followed by 0.2 ml of 5 *N* KOH were mixed with the samples. After 30 min at room temperature, the test solutions were diluted with 2.4 ml of 50% aqueous ethanol, and 30 min later the absorbance at 520 mμ was measured. A standard curve for the colorimetric test which was prepared with a solution of cyclohexanone in 0.1 *M* *p*-toluidine buffer, 50% hydrochloride, showed that the absorbance at 520 mμ was linearly dependent on the concentration of cyclohexanone up to at least 0.002 *M* in the original 0.2-ml sample.

A few determinations of the rate of hydrolysis of the enol ether in hydrochloric and acetic acid buffers were also made at 280 mμ, where cyclohexanone (ϵ_{280} 20.5) absorbs more strongly than 1-methoxycyclohexene (ϵ_{280} 3.8). However, the limited solubility of the enol ether in water (about 0.005 *M*) restricted the total change in absorbance to the inconveniently small value of 0.08. In addition, several kinetic runs were carried out in 80% aqueous acetonitrile, both at 280 mμ (with 0.016 *M* 1-methoxycyclohexene) and at 230 mμ.

The observed first-order rate constants for the hydrolysis of 1-methoxycyclohexene were calculated from semilogarithmic plots of $A_t - A_\infty$ (for measurements at 230 mμ) or $A_\infty - A_t$ (for measurements at 280 mμ and for *p*-toluidine buffers) against time, by use of the equation $k_{\text{obsd}} = 0.693/t_{1/2}$. Here A_t is the absorbance at time *t* and A_∞ is the absorbance upon completion of the reaction. These plots were in all cases linear for at least two half-times.

Many determinations of the rates of enolization of cyclohexanone and of hydrolysis of 1-methoxycyclohexene under a given set of conditions were carried out several times. The values of k_{obsd} from these duplicate determinations always agreed within ±5% of the average value.

The pH of each reaction mixture was measured at the end of the reaction at room temperature (21-23°) with a Radiometer 25 SE pH meter. The apparent p*K* values (pK_a') for the carboxylic acids used in Table I and Figure 2 are the averages of the values which

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[3] D. G. Lindsay and C. B. Reese, *Tetrahedron*, **21**, 1673 (1965).

[4] E. T. Harper and M. L. Bender, *J. Am. Chem. Soc.*, **87**, 5625 (1965).

[5] M. L. Bender and A. Williams, *ibid.*, **88**, 2502 (1966).

[6] G. Aulin-Erdtman and L. Hegbom, *Acta Chem. Scand.*, **11**, 1550 (1957).

[7] C. S. Corker, J. K. Norymberski, and R. Thow, *Biochem. J.*, **83**, 583 (1962).

were calculated from the pH values of the reaction mixtures and the acid-to-base ratios of the buffers in the reaction mixtures. Because the pK values of amines are very dependent upon temperature,[8] separate determinations of the apparent pK values of imidazolium, triethylenediammonium, and p-toluidinium ions were made by measuring the pH of partially neutralized solutions at 25° and at an ionic strength of 0.25 M (imidazole and p-toluidine) or 0.5 M (triethylenediamine), adjusted with sodium perchlorate.

Product Analysis. The product of the hydrolysis of 1-methoxycyclohexene was identified as cyclohexanone in several ways. (1) The ultraviolet spectra of the products from the hydrolysis at 25° of 0.0035 M enol ether in 5 × 10^{-4} N HCl and in 0.1 M sodium acetate buffer, 50% acid, both at 0.25 M ionic strength with sodium perchlorate, were identical with that of 0.0035 M cyclohexanone (λ_{max} 277) above 250 mμ. Below 250 mμ the absorbance of the product solution was greater than that of cyclohexanone (ϵ_{230} 8.5 for the product solution, ϵ_{230} 0.88 for cyclohexanone) due to the trace impurity described under Materials. (2) The yields of cyclohexanone upon hydrolysis of 1-methoxycyclohexene in the p-toluidine buffers were calculated from the end-point absorbances in the colorimetric test with the standard curve for cyclohexanone and were found to vary from 85 to 110%. (3) 1-Methoxycyclohexene (0.06 ml, 0.5 mmol) was stirred at room temperature with 10 ml of 0.1 M sodium acetate buffer, 50% acid–0.2 M sodium perchlorate for 1.5 hr. In this buffer, the half-time for hydrolysis is about 3 min. The reaction mixture was adjusted to pH 7.5 with 1 N NaOH and extracted with 10 ml of CCl_4. The same procedure was carried out with cyclohexanone and methanol (0.5 mmol of each) in place of the enol ether. The infrared spectra of the two CCl_4 extracts, taken after they have been dried over sodium sulfate, were identical. The yield of cyclohexanone, based on comparison of the absorbances at the carbonyl stretching frequency, was 94%. By the same method, it was shown that 1-methoxycyclohexene forms cyclohexanone in 100% yield upon hydrolysis in 2 × 10^{-3} N HCl–0.25 M $NaClO_4$.

Results

Enolization of Cyclohexanone. The rates of enolization of cyclohexanone were determined by trapping the enol through its reaction with iodine. The kinetic scheme for the process, in abbreviated form, is

$$\begin{gathered} C \xrightarrow{k} E \\ E + I_2 \xrightarrow{\text{fast}} CI + I^- \\ CI \xrightarrow{k'} EI \\ EI + I_2 \xrightarrow{\text{fast}} CI_2 + I^- \end{gathered} \qquad (3)$$

where C is cyclohexanone, E is the enol or enolate anion of cyclohexanone, CI is 2-iodocyclohexanone, EI is the enol or enolate anion of 2-iodocyclohexanone, and CI_2 is 2,2-diiodocyclohexanone. This scheme yields the following expression for the disappearance of iodine,[9] when, as is the case here, the concentration of ketone is much greater than that of iodine.

$$\frac{-d(I_2)}{dt} = k(C)\left(1 + \frac{k'}{k' - k} - \frac{k'e^{-k't}}{k' - k}\right) \qquad (4)$$

If the product k(C) is much larger than k'(CI), then rate of disappearance of iodine will be zero order and equal to the rate of enolization of cyclohexanone (k(C)); if k(C) is much smaller than k'(CI), then the rate of disappearance of iodine will be zero order and equal to twice the rate of enolization of cyclohexanone; and if k(C) and k'(CI) are approximately equal, then the rate of disappearance of iodine will not be zero order, but will increase with time according to eq 4. The fact that under our conditions the rates were zero order for at least 90% reaction excludes the last possibility as the predominant state during the iodination. In order to decide whether our rates of iodination are equal to or twice the rate of enolization of cyclohexanone, it is necessary to know the values of k' relative to k for acid and base catalysis as well as the ratio of the initial concentration of iodine to the concentration of cyclohexanone for each kinetic run. The values of k' relative to k can be estimated from data for acetones. The general acid catalyzed enolizations of iodoacetone and acetone occur at approximately the same rate;[10] general base catalysis of the enolization of bromoacetone (by water, acetate ion, and hydroxide ion) is 500–700 times more rapid than it is for acetone.[2] The ratio of the initial concentration of iodine to the cyclohexanone concentration in our rate measurements varied from 3 × 10^{-3} to 10^{-4}; whenever the ratio was greater than 4 × 10^{-4}, at least 90% of the enolization occurred by general acid catalysis. If it is assumed that the increase of 500–700 in the rate of general base catalyzed enolization also approximately holds for 2-iodocyclohexanone relative to cyclohexanone, it is easily calculated from this information that the rates of iodination which we have determined are approximately equal to, rather than twice, the rates of enolization of cyclohexanone. An exception to this conclusion is the catalysis of iodination by p-toluidinium ion, which is complicated in that it proceeds *via* the Schiff base salt of cyclohexanone (see Discussion). We do not have sufficient data to decide whether multiple iodination occurs with this catalyst.

On the basis of the extensive kinetic studies on the enolization of acetone[2a,5,11] we anticipated that for the enolization of cyclohexanone the general form of the dependence of k_{obsd} upon buffer concentration would be

$$\begin{aligned} k_{obsd} &= k_{+,0,-} + k_a(\text{acid}) + k_b(\text{base}) + k_{ab}(\text{acid})(\text{base}) \\ &= k_{+,0,-} + k_a(\text{acid}) + k_b r(\text{acid}) + k_{ab} r(\text{acid})^2 \end{aligned} \qquad (5)$$

where $k_{+,0,-}$ is the sum of the contributions due to catalysis by hydronium ion, water, and hydroxide ion, and r is the buffer ratio (base)/(acid). We found that, with the exception of the p-toluidine buffers, plots of k_{obsd} against the concentration of the buffer acid at each buffer ratio were linear.[12a] Consequently, under

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[8] J. T. Edsall and J. Wyman, "Biophysical Chemistry," Academic Press, New York, N. Y., 1958, p 452.

[9] In this discussion the term iodine refers to both iodinating species, I_2 and I_3^-.

[10] C. Rappe, *Acta Chem. Scand.*, **19**, 276 (1965).

[11] R. P. Bell and P. Jones, *J. Chem. Soc.*, 88 (1953).

[12] (a) In some cases the pH of a set of reaction mixtures at a constant buffer ratio varied slightly as the buffer concentration was changed. The difference between the lowest and highest pH value in a set was in no instance more than 0.05 pH units. In all these cases the pH value was low enough so that catalysis by hydronium ion predominated in the absence of the buffer. Consequently, the values of k_{obsd} were corrected for the small variations in hydrogen ion concentration by use of the equation, corrected $k_{obsd} = k_{obsd} + k_{H^+}(a'_{H^+} - a_{H^+})$, in which k_{H^+} is the rate constant for catalysis by hydronium ion calculated on the basis of the activity rather than the concentration of hydronium ion, a'_{H^+} is the largest hydrogen ion activity in the set, and a_{H^+} is the hydrogen ion activity of the reaction mixture for which k_{obsd} is being corrected. In no case did the correction amount to more than 6% of k_{obsd}. (b) Each value of $k_{+,0,-}$ which was used was that obtained from data for one of the other catalysts at the same pH value by extrapolation of the plot of k_{obsd} against buffer concentration to zero buffer concentration. $k_{+,0,-}$ varied from 10 to 0.07% of the corresponding k_{obsd}.

Table I. Rate Constants for Enolization of Cyclohexanone, at 25° and 0.25 M Ionic Strength[a]

Buffer	Buffer ratio, concn range, no. of concn[b]	pK_a'	$k_a \times 10^5$, M^{-1} min^{-1}	$k_b \times 10^5$, M^{-1} min^{-1}	k_{ab}, M^{-2} min^{-1}
Hydronium ion[c]	0.005–0.02, 3	−1.7	1380		
Sodium chloroacetate	9.3, 0.05–0.15, 5; 4.9, 0.05–0.125, 4; 3.1, 0.05–0.2, 4; 2, 0.05–0.2, 4	2.65	38	<1.5	
Triethylenediammonium[d] perchlorate	4, 0.076–0.226, 3; 2, 0.88–0.16, 3; 1, 0.07–0.2, 3; 0.5, 0.112–0.17, 2	3.38	40	9.3	
Sodium glycolate	3, 0.025–0.125, 5; 1, 0.025–0.2, 5; 0.49,[e] 0.025–0.2, 5	3.64	8.4	<0.5	
Sodium acetate	2, 0.025–0.125, 5; 1, 0.025–0.125, 5; 0.58, 0.025–0.125, 5; 0.33, 0.025–0.125, 5	4.56	1.5	2.35	
Sodium pivalate	1.7, 0.025–0.125, 5; 1.5, 0.025–0.125, 5; 1, 0.05–0.125, 4; 0.47, 0.025–0.125, 5; 0.33, 0.025–0.125, 5	4.90	2.2	3.7	
p-Toluidinium hydrochloride	1, 5×10^{-4}–0.0125, 10; 0.33, 0.0025–0.0125, 5; 0.11, 0.005–0.015, 5; 0.052,[f] 0.005–0.015, 5	5.19	150	130 ± 80	4.7[g]
Imidazolium perchlorate	1,[e] 0.0125–0.05, 4; 0.33,[e] 0.0125–0.05, 3; 0.11,[e] 0.0125–0.05, 3	7.15	<10	230	
Pyridine[h]		5.65		69.0	

[a] We estimate that the uncertainty in the value of each rate constant given in this table is ±15% or less of the given value, with the exception of those cases which are noted in the table. [b] The buffer ratio, (buffer base)/(buffer acid); the range of concentration of buffer ((base) + (acid)) within which values of k_{obsd} were determined; the number of different concentrations of buffer at this buffer ratio for which values of k_{obsd} were determined. [c] With perchloric acid; k_a is the average of the values for $k_{obsd}/(HClO_4)$. [d] Under these conditions the catalytic species are the mono- and dications. For this buffer the rates were measured at 0.5 M ionic strength, with $NaClO_4$. [e] All the determinations of k_{obsd} at this buffer ratio were carried out in duplicate. [f] The pH at this buffer ratio was kept constant by the addition of hydrochloric acid. [g] The average of the values from the four buffer ratios: 4.7, 4.5, 5.0, and 4.6. [h] From J. A. Feather and V. Gold, *J. Chem. Soc.*, 1752 (1965); at 25.0° and 0.1 M ionic strength.

our conditions the contribution of the k_{ab} term to k_{obsd} is negligible, and the slope of these plots is simply $k_a + k_b r$. For each buffer, the secondary plot of the slopes against r was linear and yielded the values of k_a(intercept) and k_b(slope). With the p-toluidine hydrochloride buffers, the plots of k_{obsd} against the concentration of p-toluidinium ion at each buffer ratio were concave; consequently with this catalyst the product term is significant. The data was treated by plotting ($k_{obsd} - k_{+,0,-}$)/(p-toluidinium ion) against (p-toluidine) for each buffer ratio.[12b] In accord with eq 5, the plots were linear: each slope equals k_{ab}, and the values of k_a and k_b were obtained from the dependence of the intercepts ($k_a + k_b r$) upon the buffer ratio. Table I presents the rate constants for general acid and general base catalyzed enolization of cyclohexanone. Our value for catalysis by hydronium ion is in good agreement with the value of 1.42×10^{-2} M^{-1} min^{-1} reported[13] for the same conditions.

Hydrolysis of 1-Methoxycyclohexene. The rates of hydrolysis of 1-methoxycyclohexene to methanol and cyclohexanone were determined spectrophotometrically at 230 mμ by the disappearance of the enol ether. A few determinations of rates in hydrochloric and acetic acid buffers were also based upon the appearance of cyclohexanone, which was measured spectrophotometrically at 280 mμ. Within experimental error, the same rate constants were obtained by the two methods (Table II). This fact shows that no intermediate accumulates to any significant extent during the course of the hydrolysis with these catalysts.

The hydrolysis of 1-methoxycyclohexene at each pH value was catalyzed by the buffer. Plots of k_{obsd} at each buffer ratio against the concentration of acid in the buffer were linear and parallel to each other.[12a] This result shows that the catalysis is by the acidic species in the buffer. Figure 1 illustrates the data for acetic acid. The slopes of such plots are the second-order rate constants for catalysis by the buffer acid (designated k_{-a}); these are given in Table III together with the conditions for the kinetic measurements.

Table II. Comparison of Rates Constants for Hydrolysis of 1-Methoxycyclohexene Measured at 230 and 280 mμ[a]

Catalyst	Wavelength	k_{obsd}, min^{-1}
0.1 M sodium acetate buffer, 50% base[b]	280	0.24
	230	0.23
4×10^{-4} N HCl[b]	280	1.22
	230	1.34
0.02 M sodium acetate buffer, 6% base[c]	280	0.076
	230	0.073
5×10^{-4} N HCl[c]	280	0.42
	230	0.43

[a] At 25.0 ± 0.1°. [b] Ionic strength 0.25 M, with $NaClO_4$. [c] In acetonitrile–water (v/v 2:8).

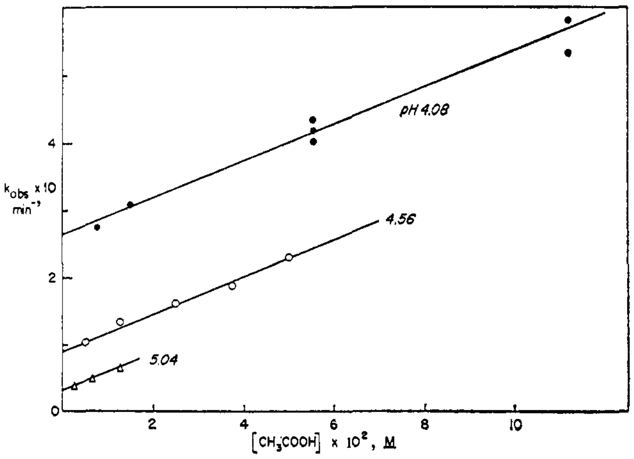

Figure 1. Catalysis of the hydrolysis of 1-methoxycyclohexene by sodium acetate buffers. The buffer ratios ((base)/(acid)) were: 0.33 (●), 1 (○), and 3 (▲).

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(13) A. J. Green, T. J. Kemp, J. S. Littler, and W. A. Waters, *J. Chem. Soc.*, 2722 (1964).

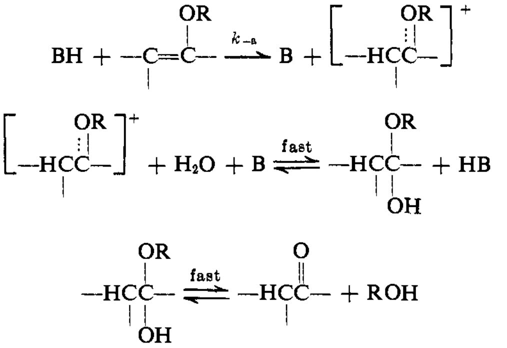
Table III. Rate Constants for the Hydrolysis of 1-Methoxycyclohexene, at 25° and 0.25 *M* Ionic Strength

Buffer	Buffer ratio, concn range, no. of concn[a]	k_{-a},[b] M^{-1} min^{-1}	$k_{-a,\text{ calcd}}$,[c] M^{-1} min^{-1}
H_3O^+ [d]	2.3-1 × 10^{-3}, 3	2810	3360
Sodium chloroacetate	19,[e] 0.05–0.15, 3; 9,[e] 0.05–0.15, 3	76, 75	93
Triethylenediammonium[f] perchlorate	7, 0.05–0.2, 4; 4, 0.05–0.2, 3; 2, 0.05–0.15, 3	12.0, 13.2, 13.0	98
Sodium glycolate	9,[e] 0.02–0.12, 5; 3, 0.02–0.12, 5; 1,[e] 0.02–0.12, 3	11.9, 10.2, 10.2	21
Sodium acetate	3, 0.01–0.05, 3; 1, 0.01–0.1, 5; 0.33, 0.01–0.15, 4	2.7, 2.8, 2.6	3.7
Sodium pivalate	3, 0.02–0.1, 5; 1, 0.01–0.06, 5; 0.33,[e] 0.01–0.05, 3	3.0, 3.6, 3.8	5.4
p-Toluidinium hydrochloride	1,[e] 0.025–0.1, 3	1.32	365

[a] See footnote *b* of Table I. [b] Each value is the slope of the plot of k_{obsd} against (buffer acid) at a single buffer ratio. [c] $k_{-a,\text{calcd}} = k_a/K_{\text{enol}}$ in which k_a is the catalytic constant of the same acid for enolization of cyclohexanone (Table I) and K_{enol} is the equilibrium constant for enolization of cyclohexanone at 25°, the value of which 4.1 × 10^{-6}.[28] See the Discussion. [d] With hydrochloric acid; k_a is the average of the values for k_{obsd}/(HCl). [e] All determinations of k_{obsd} at this buffer ratio were carried out in duplicate. [f] The catalytic species is the dication. For this buffer the rates were measured at 0.5 *M* ionic strength, with $NaClO_4$.

Discussion

Hydrolysis of Enol Ethers. A number of investigations of the mechanism of hydrolysis of enol ethers have recently been reported.[14–20] These have concluded that the initial and rate-determining step of the reaction is proton transfer from the catalyzing acid to the β-carbon, yielding an alkoxycarbonium ion which rapidly goes to the aldehyde or ketone by way of the hemiacetal or hemiketal (eq 6).[21] The salient evidence in support of this mechanism is the following. (1) The hydrolysis of enol ethers in aqueous solution is catalyzed by general acids, but not by bases.[15,17,19] (2) Hydrolysis of alkyl vinyl ethers in water enriched in oxygen-18 does not yield alcohols enriched in oxygen-18. Thus, the alkenyl oxygen (C=C···O) bond is the one that is cleaved.[22] (3) Reversible protonation of the β-carbon does not occur during hydrolysis. When ethyl vinyl ether was hydrolyzed with dilute acid in deuterium oxide, only one atom of deuterium was found in the product acetaldehyde.[19] Also, neither *cis-* nor *trans-β*-monoalkylvinyl alkyl ethers undergo geometrical isomerization concurrent with hydrolysis.[20] (4) The solvent deuterium isotope effects upon the rate of hydrolysis of enol ethers indicate that proton transfer is occurring in the rate-determining step of the reaction. The following ratios of the catalytic constants for H_3O^+ and D_3O^+ ($k_{H_3O^+}/k_{D_3O^+}$) in completely aqueous solution at 25–30° have been determined: 2-ethoxy-1-cyclopentenecarboxylic acid,[15] 2.85; 2-ethoxy-1-cyclopentenecarboxylate anion,[15] 2.42; 2-chloroethyl vinyl ether,[17] 2.5; and ethyl vinyl ether,[19] 2.95. In addition, the larger isotope effects expected for catalysis of hydrolysis by carboxylic acids have been found: for 2-ethoxy-1-cyclopentenecarboxylate anion,[15] $k_{CH_3COOH}/k_{CH_3COOD}$ is 4.5; and for ethyl vinyl ether,[19] k_{HCOOH}/k_{HCOOD} is 6.8. (5) The rates of hydronium ion catalyzed hydrolysis of a series of alkyl vinyl ethers ($CH_2{=}CHOR$) increase in the order of inductive electron donation by R,[14,16,17] and methyl isopropenyl ether undergoes hydrolysis 500 times more rapidly than ethyl vinyl ether.[17] These structure–reactivity correlations are those expected for a transition state with considerable alkoxycarbonium ion character, because it will be stabilized by inductive electron donation and also, in the case of the methyl isopropenyl ether, by hyperconjugation. In this regard, Salomaa, *et al.*,[17] have shown that there is a linear relationship between the values of log $k_{H_3O^+}$ for the hydrolysis of four enol ethers ($CH_2{=}CHR_2OR_1$) and the values of log $k_{H_3O^+}$ for the hydrolysis of the corresponding monoethyl acetals ($R_2C(OR_1)(H)OC_2H_5$) with ethoxy carbon cleavage. It is known[21] that the hydrolysis of the acetals proceeds by unimolecular decomposition of the protonated acetal to the alkoxycarbonium ion ($[R_2CH(\overset{+}{=}OR_1)\cdots OC_2H_5]^+$). (6) The entropies of activation for the hydronium ion catalyzed hydrolysis of a number of enol ethers fall in the range of −1 to −15 eu.[15,17,19] Entropies of activation are an ambiguous criterion upon which to make a decision about mechanism,[23] but there are reasons (see ref 15 and 19) to



$$BH + \text{—}C{=}\overset{OR}{C}\text{—} \xrightarrow{k_{-a}} B + \left[\text{—}HC\overset{OR}{C}\text{—}\right]^+$$

$$\left[\text{—}HC\overset{OR}{C}\text{—}\right]^+ + H_2O + B \overset{\text{fast}}{\rightleftharpoons} \text{—}HC\underset{OH}{\overset{OR}{C}}\text{—} + HB \qquad (6)$$

$$\text{—}HC\underset{OH}{\overset{OR}{C}}\text{—} \overset{\text{fast}}{\rightleftharpoons} \text{—}HC\overset{O}{\overset{\|}{C}}\text{—} + ROH$$

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(14) D. M. Jones and N. F. Wood, *ibid.*, 5400 (1964).

(15) T. H. Fife, *J. Am. Chem. Soc.*, **87**, 1084 (1965).

(16) A. Ledwith and H. J. Woods, *J. Chem. Soc., B*, 753 (1966). The mechanism proposed by these authors differs slightly from the one given in the text, but see a criticism of their reasoning in B. Capon, M. J. Perkins, and C. W. Rees, "Organic Reaction Mechanisms, 1966," John Wiley and Sons, Ltd., London, 1967, p 330.

(17) P. Salomaa, A. Kankaanperä, and M. Lajunen, *Acta Chem. Scand.*, 20, 1790 (1966).

(18) P. Salomaa and A. Kankaanperä, *ibid.*, 20, 1802 (1966).

(19) A. J. Kresge and Y. Chiang, *J. Chem. Soc., B*, 53, 58 (1967).

(20) T. Okuyama, T. Fueno, H. Nakatsuji, and J. Furukawa, *J. Am. Chem. Soc.*, **89**, 5826 (1967).

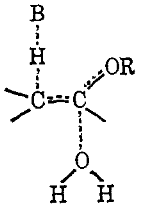
(21) By analogy with the mechanism for acetal hydrolysis (E. H. Cordes, *Progr. Phys. Org. Chem.*, **4**, 1 (1967)), the second step in this sequence almost certainly proceeds by unassisted attack of water upon the alkoxycarbonium ion. The third step is known to be catalyzed by both general acids and general bases (R. P. Bell, *Advan. Phys. Org. Chem.*, **4**, 1 (1966)).

(22) L. A. Kiprianora and A. F. Rekasheva, *Dokl. Akad. Nauk SSSR*, **142**, 589 (1962); *Chem. Abstr.*, **56**, 15346*f* (1962).

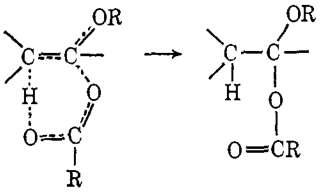
(23) L. L. Schaleger and F. A. Long, *Advan. Phys. Org. Chem.*, **1**, 1 (1963).

anticipate entropy values in this range for the proposed mechanism.

Although we make use of the above mechanism in our discussion of the mechanism of acid-catalyzed enolization of ketones, in our opinion the evidence does not rigorously exclude a transition state for the hydrolysis of enol ethers in which some slight bond formation between the α-carbon and water occurs simultaneously with the protonation of the β-carbon.



The kinetics of the hydrolysis of 1-methoxycyclohexene show that its behavior is typical of an enol ether. The rate constant for catalysis by hydronium ion (2810 M^{-1} min^{-1}) is between that determined for methyl isopropenyl ether (58,000 M^{-1} min^{-1}) and ethyl vinyl ether (112 M^{-1} min^{-1}) under the same conditions.[17] The Brønsted plot of the catalytic constants (Figure 2) resembles that for ethyl vinyl ether:[19] in each case the slope of the line described by the carboxylic acids is about 0.7 and the rate constant for hydronium ion falls considerably below this line. A special mechanism that can be imagined for the catalysis by the carboxylic acids which would explain the negative deviation of hydronium ion from the Brønsted plot is a cyclic one in which the carbonyl oxygen of the acid is forming a covalent bond with the α-carbon as the hydroxyl oxygen donates its proton to the β-carbon (eq 7).



(7)

The initial product of this reaction would be the acylal. *p*-Toluidinium ion and triethylenediammonium ion are acids which cannot participate in such a cyclic mechanism, and yet the catalytic constants for these acids in the hydrolysis of 1-methoxycyclohexene do not deviate by more than a factor of 1.5 from the Brønsted plot described by the carboxylic acids (Figure 2). Consequently, the cyclic mechanism appears unlikely. In this regard, our finding that the rate of disappearance of 1-methoxycyclohexene equals the rate of formation of cyclohexanone with acetic acid catalysis (Table II) cannot be used as evidence against the intermediacy of the acylal, since kinetic studies in the literature suggest that under our conditions the acylal would hydrolyze much more rapidly than it is formed.[24]

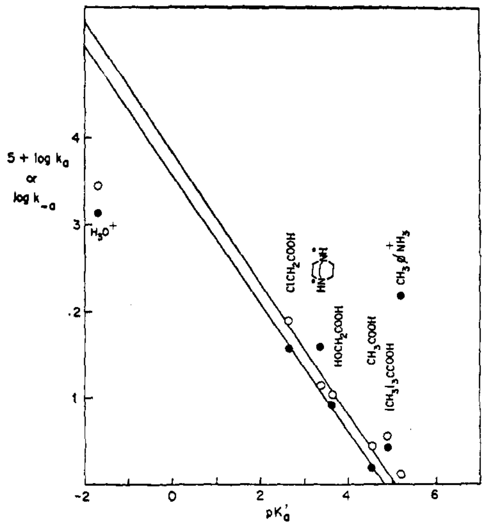
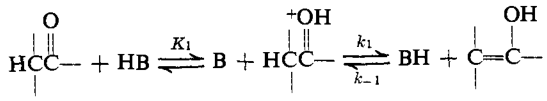
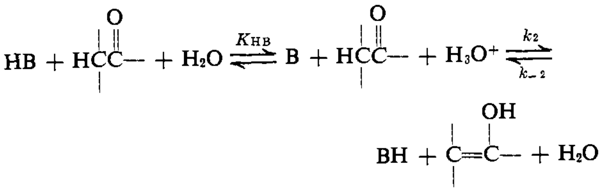


Figure 2. Brønsted plots for acid-catalyzed enolization of cyclohexanone (5 + log k_a, ●) and acid-catalyzed hydrolysis of 1-methoxycyclohexene (log k_{-a}, ○). The data is that given in Tables I and III. The lines are drawn through the points for chloroacetic, glycolic, and acetic acids. No statistical corrections have been made. The slope of the lines is 0.74.

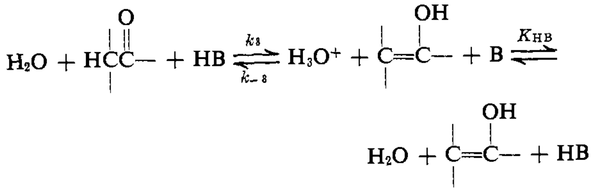
Acid-Catalyzed Enolization of Ketones. Substitution of tritium or deuterium for hydrogen at the α-carbon of ketones causes a marked decrease in the rates of general acid catalyzed enolization, and the magnitudes of these isotope effects ($k_{C-H}/k_{C-T} \approx 10$, $k_{C-H}/k_{C-D} \approx 5$) clearly show that the rate-determining step for general acid catalyzed enolization includes breaking of the carbon-hydrogen bond.[25] Three mechanisms which can account for the general acid terms found in the rate laws for the enolization of many ketones in water and which involve proton transfer from the α-carbon in the rate-determining step are



$$\mathrm{H\overset{|}{\underset{|}{C}}\overset{O}{\overset{\|}{C}}{-}} + \mathrm{HB} \overset{K_1}{\rightleftharpoons} \mathrm{B} + \mathrm{H\overset{|}{\underset{|}{C}}\overset{^{+}OH}{\overset{\|}{C}}{-}} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{BH} + \mathrm{\underset{|}{\overset{|}{C}}{=}\overset{OH}{\overset{|}{C}}{-}} \qquad (8)$$



$$\mathrm{HB} + \mathrm{H\overset{|}{\underset{|}{C}}\overset{O}{\overset{\|}{C}}{-}} + \mathrm{H_2O} \overset{K_{HB}}{\rightleftharpoons} \mathrm{B} + \mathrm{H\overset{|}{\underset{|}{C}}\overset{O}{\overset{\|}{C}}{-}} + \mathrm{H_3O^+} \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}}$$
$$\mathrm{BH} + \mathrm{\underset{|}{\overset{|}{C}}{=}\overset{OH}{\overset{|}{C}}{-}} + \mathrm{H_2O} \qquad (9)$$



$$\mathrm{H_2O} + \mathrm{H\overset{|}{\underset{|}{C}}\overset{O}{\overset{\|}{C}}{-}} + \mathrm{HB} \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} \mathrm{H_3O^+} + \mathrm{\underset{|}{\overset{|}{C}}{=}\overset{OH}{\overset{|}{C}}{-}} + \mathrm{B} \overset{K_{HB}}{\rightleftharpoons}$$
$$\mathrm{H_2O} + \mathrm{\underset{|}{\overset{|}{C}}{=}\overset{OH}{\overset{|}{C}}{-}} + \mathrm{HB} \qquad (10)$$

In mechanism 8 protonation of the carbonyl oxygen is followed by rate-determining proton transfer from the α-carbon to the general base. In mechanisms 9 and 10 proton transfer from the α-carbon to a general base or water is concerted with proton transfer to the carbonyl group from hydronium ion or a general acid,

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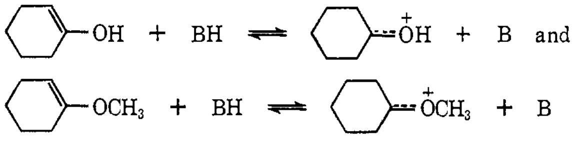
[24] The rate constant for the hydrolysis of α-methoxyethyl acetate, $CH_3OCH(CH_3)OC(=O)CH_3$, in water at 5° under neutral and acidic conditions is given by the expression $k_{obsd} = 0.16$ min^{-1} + 77.5 M^{-1} min^{-1} (H_3O^+) (P. Salomaa, *Acta Chem. Scand.*, **19**, 1263 (1965)). The expression for k_{obsd}[19] for the hydrolysis of ethyl vinyl ether in acetic acid buffers at 26.7° is k_{obsd} = 127 M^{-1} min^{-1} (H_3O^+) + 0.107 M^{-1} min^{-1} (CH_3COOH), and from the temperature dependence[19] of $k_{H_3O^+}$ these constants will be about $^1/_7$ as large at 5°. The hydrolysis of acylals does not appear to be catalyzed by general acids (T. Fife, *J. Am. Chem. Soc.*, **87**, 271 (1965)).

[25] C. G. Swain, E. C. Stivers, J. F. Reuwer, Jr., and L. J. Schaad, *ibid.*, **80**, 5885 (1958).

respectively. Swain, *et al.*,[25-27] have concluded that the correct mechanism is mechanism 8. Their conclusion is based upon an interpretation of the isotope effects upon the rates of enolization of acetone and α-phenylisocaprophenone which occur with various catalysts when deuterium or tritium are substituted for the α-hydrogen atom(s) of the ketones and also when the solvent is deuterium oxide. The following arguments, based upon the data in our present study, provide evidence of a different type in support of mechanism 8.

We have tentatively concluded that the initial and rate-determining step in the hydrolysis of enol ethers is proton transfer to the β-carbon of the enol ether. This transfer is identical with the initial and rate-determining step of ketonization according to mechanism 8 except for the substitution of an alkyl group for the hydroxyl hydrogen atom of the enol; it differs from the rate-determining steps of mechanisms 9 and 10 in which there is partial proton transfer from the enol oxygen. Consequently, if mechanism 8 is the predominant pathway for enolization, the rate of ketonization of the enol (rate constant k_{-1}) should not differ significantly from the rate of hydrolysis of the analogous enol ether (rate constant k_{-a}) in which the alkyl group is one with the same effect upon the basicity of the β-carbon as hydrogen. However, if mechanism 9 or 10 were the predominant pathway for enolization, then the free energy of activation for ketonization of the enol by mechanism 8 and so for hydrolysis of the analogous anol ether would be greater than the free energy of activation for ketonization by mechanism 9 or 10. in this case the rate of hydrolysis of the enol ether would be less than the rate of ketonization of the enol by mechanism 9 (rate constant $k_{-2}(H_2O)$) or mechanism 10 (rate constant $k_{-3}K_{HB}$, where K_{HB} is the dissociation constant of the general acid).

Regardless of which mechanism is correct, the rate of general acid catalysis of ketonization as expressed by the second-order rate constants given above is equal to the second-order rate constant for general acid catalysis of enolization of the ketone ($k_a = k_1K_1$, k_2K_{HB}, and $k_3(H_2O)$, in terms of mechanisms 8, 9, and 10, respectively) divided by the equilibrium constant for enol formation (K_{enol}). The value of K_{enol} for cyclohexanone at 25° has recently been accurately determined[28] and is 4.1×10^{-6}. The calculated rate constants for general acid catalyzed ketonization of cyclohexanone enol ($k_{-a,calcd}$) are given in Table III. The values of $k_{-a,calcd}$ for hydronium ion and the carboxylic acids are 1.2 to 2 times larger than the values for the corresponding rate constants for hydrolysis of 1-methoxycyclohexene (k_{-a}); for triethylenediammonium ion the difference between these constants is somewhat larger ($k_{-a,calcd}/k_{-a} = 6.5$); and the value of $k_{-a,calcd}$ for *p*-toluidinium ion is much larger than that of k_{-a} ($k_{-a,calcd}/k_{-a} = 280$). Thus, except for the case of *p*-toluidinium ion (see below), the rate constants for ketonization of cyclohexanone enol are *remarkably* similar to those for the hydrolysis of 1-methoxycyclohexene. This agreement is strong evidence for a mechanism of ketonization in which the bond between the enol oxygen and its hydrogen atom remains substantially intact during the protonation at carbon (mechanism 8), provided the agreement is not the fortuitous result of a marked increase in reactivity upon substitution of methyl for hydrogen. Several comparisons of pK values in the literature (Table IV), in fact, suggest that the equilibrium constants for the reactions



should be about equal and so that the free energies of activation for the proton transfers should be about the same. For all these cases it is probable that the acid-weakening inductive effect of the methyl group is counterbalanced by an acid-strengthening effect due to poorer solvation of the methyl cation.[29,30]

Table IV. Effect of Methyl Substitution upon pK_a

Acid	pK_a	Ref
$C_6H_5\overset{\overset{OH\ +}{\vdots}}{C}\cdots OH$	−7.38	29
$C_6H_5\overset{\overset{OH\ +}{\vdots}}{C}\cdots OCH_3$	−7.78	29
$C_6H_5\overset{+}{O}H_2$	−6.74	30
$C_6H_5\overset{+}{O}H(CH_3)$	−6.54	30

In addition to this data on cyclohexanone and its methyl enol ether, there are constants in the literature that allow a similar but incomplete analysis for the acid-catalyzed enolization of acetone. At 25° the rate constant for general acid catalysis of the enolization of acetone by hydronium ion is $1.6 \times 10^{-3}\ M^{-1}\ \text{min}^{-1}$;[2a] and K_{enol} is known to be less than 10^{-6},[28] so that the rate constant for hydronium ion catalyzed ketonization has a value greater than $1.6 \times 10^{3}\ M^{-1}\ \text{min}^{-1}$. The rate constant for hydronium ion catalyzed hydrolysis of methyl isopropenyl ether is $5.8 \times 10^{4}\ M^{-1}\ \text{min}^{-1}$ at 25°.[17]

Further support for mechanism 8 is the fact that the values of α, the slopes of the Brønsted plots for the carboxylic acids, are the same for the ketonization of cyclohexanone enol[31] and the hydrolysis of 1-methoxycyclohexene (Figure 2). If mechanism 9 were predominant, the α value for general acid catalysis of the hydrolysis of the enol ether would be expected to be considerably larger than that for ketonization of the enol. This is so because the enol ether is less basic than the transition state in mechanism 9 which, due to partial proton transfer from the enol oxygen to

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[26] C. G. Swain, A. J. Di Milo, and J. P. Cordner, *J. Am. Chem. Soc.*, 80, 5983 (1958).

[27] C. G. Swain and A. S. Rosenberg, *ibid.*, 83, 2154 (1961).

[28] R. P. Bell and P. W. Smith, *J. Chem. Soc., B*, 241 (1966).

[29] E. M. Arnett, *Progr. Phys. Org. Chem.*, **1**, 223 (1963).

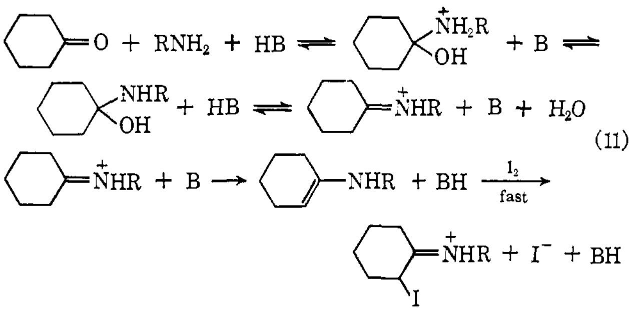
[30] (a) E. M. Arnett and C. Y. Wu, *J. Am. Chem. Soc.*, **82**, 5660 (1960); (b) A. J. Kresge and L. E. Hakka, *ibid.*, **88**, 3868 (1966).

[31] The value of α for the ketonization of cyclohexanone enol equals the value for α for the enolization of cyclohexanone since $\log k_a = -\alpha pK_a + \text{constant} = \log k_{-a,calcd} + \log K_{enol}$.

water, has a basicity between that of the enol and enol anion. The less basic the carbon to which a proton is transferred, the more complete should be the transfer in the transition state and so the larger should be the Brønsted coefficient for general acid catalysis.[32,33] A similar argument cannot be used to exclude mechanism 10 because mechanism 10 is, in the direction of ketonization, general base catalysis of proton transfer from the enol oxygen with protonation at carbon always by hydronium ion. There does not seem to be any reasonable way to predict on the basis of the α value from the Brønsted relationship ($\log k_{-3}K_{\mathrm{HB}} = -\alpha \mathrm{p}K_{\mathrm{HB}} +$ constant) for mechanism 10 what the α value for general acid catalysis of the hydrolysis of 1-methoxycyclohexene should be.

Several other aspects of the data for the acid-catalyzed enolization of cyclohexanone deserve comment.

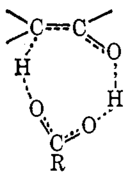
(1) The rate constant for catalysis by *p*-toluidinium ion is 250 times larger than that predicted for an acid of its strength by the Brønsted plot for carboxylic acid catalysts (Figure 2) and also is 280 times larger than the rate constant predicted from the catalytic constant for *p*-toluidinium ion in the hydrolysis of 1-methoxycyclohexene and the equilibrium constant for enolization (predicted $k_{\mathrm{a}} = K_{\mathrm{enol}}k_{-\mathrm{a}}$). The rate law for *p*-toluidinium buffers is unusual in that it contains a very large product (k_{ab}) term which does not exist with the other buffers. This enhanced catalysis of iodination is almost certainly due to formation of the protonated Schiff base which undergoes rapid general base catalyzed enaminization (eq 11). The mechanism for the formation of the protonated Schiff base in eq 11 is based on the finding of Cordes and Jencks that the formation of the protonated Schiff base from aniline and *p*-chlorobenzaldehyde proceeds *via* the intermediacy of the carbinolamine and that the formation and dehydration of the carbinolamine is catalyzed by general acids.[34] It is evident from eq 11 that the kinetic expression for general acid catalysis of the formation of the Schiff base from *p*-toluidine and cyclohexanone is not experimentally distinguishable from the kinetic expression for general base catalysis of enaminization of a small amount of protonated Schiff base in equilibrium with *p*-toluidine and cyclohexanone. Consequently, our present data do not allow a certain decision as to whether Schiff base formation or enaminization is the rate-determining step in the catalysis of iodination by the *p*-toluidine buffers. Bender and Williams[5] have reported results similar to ours for the catalysis of the iodination of acetone by *p*-toluidine buffers and, together with Hine, *et al.*,[35] have considered this mechanism in detail.



(11)

R is *p*-methylphenyl and HB is H_3O^+ or *p*-toluidinium ion

(2) A special cyclic mechanism that can be written for catalysis of enolization by carboxylic acids is



Strong evidence against its occurrence is the fact that triethylenediammonium ion, which cannot undergo the cyclic mechanism or form a Schiff base salt, is three times *more*, rather than markedly less, effective an acid catalyst than a carboxylic acid of the same p*K* (Figure 2).

(3) Pivalic acid is about three times more active as a catalyst for both the enolization of cyclohexanone and the hydrolysis of 1-methoxycyclohexene than is predicted from the Brønsted plots for the other carboxylic acids (Figure 2). This finding contrasts with that for the enolization of acetone in which the rate constant for catalysis by pivalic acid falls exactly on the Brønsted plot described by other carboxylic acid catalysts.[2a] A likely explanation for the positive deviations found here is that the transition states are stabilized to some extent by hydrophobic bonding between the *t*-butyl and cyclohexyl residues. Bell, *et al.*, have proposed the same explanation to account for deviations of a similar magnitude in the halogenation of bromoacetylacetone and benzoylacetone catalyzed by carboxylate anions with large hydrophobic side chains.[36]

Acknowledgment. G. E. L. is grateful to Professors W. P. Jencks and F. H. Westheimer for stimulating comments.

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[32] J. E. Leffler, *Science*, **117**, 340 (1953).

[33] R. P. Bell and J. E. Crooks, *Proc. Roy. Soc.* (London), **A286**, 285 (1965).

[34] E. H. Cordes and W. P. Jencks, *J. Am. Chem. Soc.*, **84**, 832 (1962).

[35] J. Hine, J. Mulders, J. G. Houston, and J. P. Idoux, *J. Org. Chem.*, **32**, 2205 (1967), and references therein.

[36] R. P. Bell, E. Gelles, and E. Möller, *Proc. Roy. Soc.* (London), **A198**, 308 (1949).