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Generation of the Enol of Methyl Mandelate by Flash Photolysis of Methyl Phenyldiazoacetate in Aqueous Solution and Study of Rates of Ketonization of This Enol in That Medium

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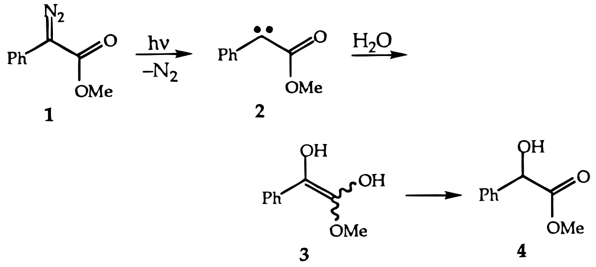
Flash photolysis of methyl phenyldiazoacetate in aqueous solution produced phenylcarbomethoxycarbene, whose hydration generated a short-lived transient species that was identified as the enol isomer of methyl mandelate. This assignment is supported by the shape of the rate profile for decay of the enol transient, through ketonization to its carbonyl isomer, as well as by solvent isotope effects and the form of acid−base catalysis of the ketonization reaction. Comparison of the present results with previously published information on the enol of mandelic acid shows some interesting and readily understandable similarities and differences.

Enols and enolate ions derived from carboxylic acid esters are essential intermediates in many chemical and biological reactions, and yet little direct information on their chemistry in aqueous solution is available. This is undoubtedly because the concentration of enol at equilibrium with its keto isomer is very low: interaction of the carbonyl group of esters with the adjacent ether oxygen atom stabilizes the keto form markedly, and that increases the free energy difference between keto and enol isomers by a substantial amount over what it is in the case of simple aldehydes and ketones,[1] where enol contents are already quite low.[2] For example, the keto−enol equilibrium constant for ethyl acetate, though not yet determined directly, has been reliably estimated as $\mathrm{p}K_\mathrm{E} = 19$;[3] this makes that equilibrium constant more than 10 orders of magnitude smaller than the constant for acetaldehyde or acetone, for which $\mathrm{p}K_\mathrm{E} = 6.23$[4] and 8.33,[5] respectively.

Enols can be stabilized by bulky substituents that block access to their β-carbon atoms, through whose protonation conversion of the enol to its keto tautomer must occur.[6] This technique has produced a number of remarkably stable enols of simple aldehydes and ketones,[7] and it has also been applied to enols of carboxylic acids,[8,9] esters,[8a,c,10] and amides.[11] Examination of less-stable enols has also been performed using fast reaction techniques, notably flash photolysis,[12] and we have employed such a method here.

We have found that flash photolytic dediazotization of methyl phenyldiazoacetate, **1**, in aqueous solution produces methyl mandelate, **4**, through the well-known O−H insertion reaction[13] of the α-carbonylcarbene, **2**, so generated, eq 1. This transformation is accompanied by the formation and decay of a short-lived transient intermediate which we have identified as the enol, **3**, of methyl mandelate.[14]



(1)

Experimental Section

Materials. Methyl phenyldiazoacatate was prepared by lead tetraacetate oxidation of the hydrazone of methyl benzoylformate.[15] Methyl *O*-acetylmandelate was prepared by acetylating methyl mandelate using acetyl chloride; its ^{1}H and ^{13}C NMR spectra were consistent with literature values.[16] All other materials were the best available commercial grades.

Kinetics. Rates of reaction were measured using conventional (flash lamp)[4] and laser ($\lambda = 248$ nm)[17] flash photolysis

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systems that have already been described. The temperature of all solutions upon which rate measurements were made was controlled at 25.0 ± 0.05 °C. Two successive reactions were observed. When the rates of these were sufficiently different, each reaction was monitored in separate experiments, and the data were analyzed by least-squares fitting of single-exponential functions. When the rates were too similar to allow such separation, both reactions were monitored in the same experiment, and the data were analyzed by least-squares fitting of double exponential functions.

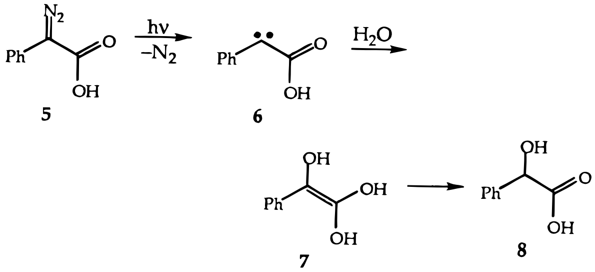
Product Analysis. Wholly aqueous solutions of methyl phenyldiazoacetate were photolyzed with 254 or 313 nm light from a low pressure mercury lamp for about 10 min until no absorption due to the diazo compound remained. Some of these solutions were then subjected directly to GC analysis; others were extracted with $CHCl_3$, and the extracts were subjected to GC-MS analysis; and still others were extracted with diethyl ether, the ether was removed, and the residues were subjected to ^1H NMR analysis.

Results

Product Analysis. GC analysis of reaction mixtures after complete photodecomposition of methyl phenyldiazoacetate in aqueous solution showed that only one product was formed throughout the acidity range used in the present work ($[H^+] = 0.1$ to 10^{-12} M), and comparison of MS and ^1H NMR spectra of this single product with those of an authentic sample identified this substance as methyl mandelate.

Transient Identification. Flash photolysis of methyl phenyldiazoacetate in weakly basic aqueous solution ($[NaOH] = 10^{-4}$ M) produced a transient absorbance with $\lambda_{max} \cong 275$ nm immediately after the laser pulse; this transient then decayed over a period of ca. 1 μs while another transient absorbance, with $\lambda_{max} \cong 310$ nm, grew in and then also decayed. The rate of decay at $\lambda = 275$ nm was the same as the rate of rise at $\lambda = 310$ nm, indicating that the 310 nm species is formed from the 275 nm species. The absorbance at $\lambda = 275$ nm did not change its wavelength with changes in the acidity of the medium, but the absorbance at $\lambda = 310$ shifted to $\lambda \cong 280$ in acidic solutions.

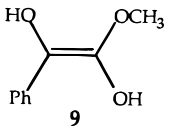
This is the behavior expected for photolysis of methyl phenyldiazoacetate, **1**, to phenylcarbomethoxycarbene, **2**, hydration of this carbene to methyl mandelate enol **3**, and ketonzation of the enol to methyl mandelate **4**, as shown in eq 1. The styrene-type chromophore of this enol can be expected to have a strong absorption band in the region about $\lambda = 280$ nm—β,β-dimethoxystyrene, for example, has $\lambda_{max} = 268$ nm[18]—and this band will shift to longer wavelengths as the enol is converted to enolate ion in basic solution.[19] The α-carbonylcarbene, on the other hand, having no acidic or basic groups, will have an acidity-independent absorption spectrum. These absorption changes, moreover, are similar to those produced by flash photolysis of phenyldiazoacetic acid, **5**, which were attributed to formation of phenylcarboxycarbene, **6**, hydration of that to mandelic acid enol, **7**, and ketonization of the enol to mandelic acid, **8**, eq 2.[20]



(2)

Further support for the assignment of the rise and decay of the $\lambda = 280/310$ nm transient absorbance to the formation and ketonization of the enol of methyl mandelate is provided by solvent isotope effects and the form of acid–base catalysis in buffer solutions (vide infra).

The enol of methyl mandelate can exist in two stereoisomeric forms, as (*Z*)-2-hydroxy-1-methoxy-2-phenylethenol, **9**, or (*E*)-2-hydroxy-1-methoxy-2-phenylethenol, **10**. The two isomers might be expected to ketonize at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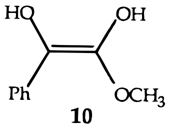
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different rates, and the fact that the ketonization rate data collected here confirmed well to a simple first-order rate law suggests that only one isomer was formed in the carbene hydration reaction. We have no information, however, that allows us to decide which isomer that is.

Kinetics: Carbene Hydration. Rates of hydration of phenylcarbomethoxycarbene were measured in aqueous sodium hydroxide solutions and in aqueous acetic acid, biphosphate ion, and ammonium ion buffers. For each kind of solution, a range of concentrations was employed and replicate measurements were made at each concentration; the ionic strength was maintained constant at 0.10 M. These data are summarized in Tables S1 and S2.[21]

The measurements in buffers were done in series of solutions of constant buffer ratio and constant ionic strength but varying buffer concentration. As Figure 1 illustrates, observed rate constants within a given series increase linearly with buffer concentration, and the data were therefore analyzed by least-squares fitting of the buffer dilution expression shown in eq 3. The zero-buffer-

$$k_{obs} = k_o + k_{buff}[\text{buffer}] \tag{3}$$

concentration intercepts, k_o, obtained in this way, together with the rate constants measured in sodium hydroxide solutions, are displayed as the upper rate profile of Figure 2. Hydronium ion concentrations of the buffer solutions needed to construct this profile were obtained by calculation using literature values of the buffer acidity constants and activity coefficients recommended by Bates.[22]

Kinetics: Enol Ketonization. Rates of ketonization of methyl mandelate enol were measured in aqueous perchloric acid and sodium hydroxide solutions and in formic acid, acetic acid, cacodylic acid, biphosphate ion,

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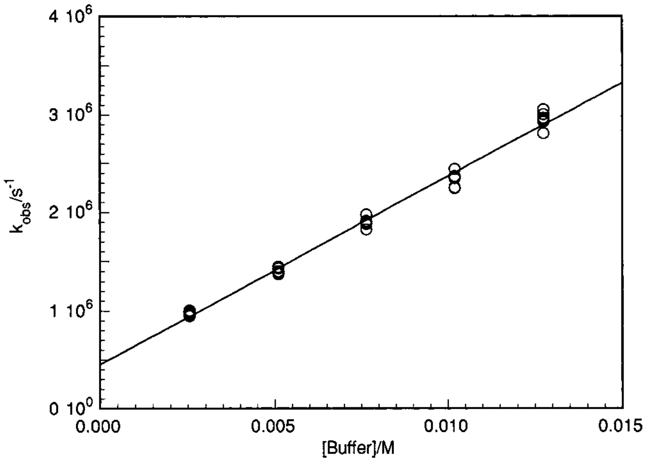

Figure 1. Relationship between buffer concentration and observed rate constants for the hydration of phenylcarbomethoxycarbene in aqueous acetic acid buffer solutions at 25 °C; $[CH_3CO_2H]/[CH_3CO_2^-] = 0.28$.

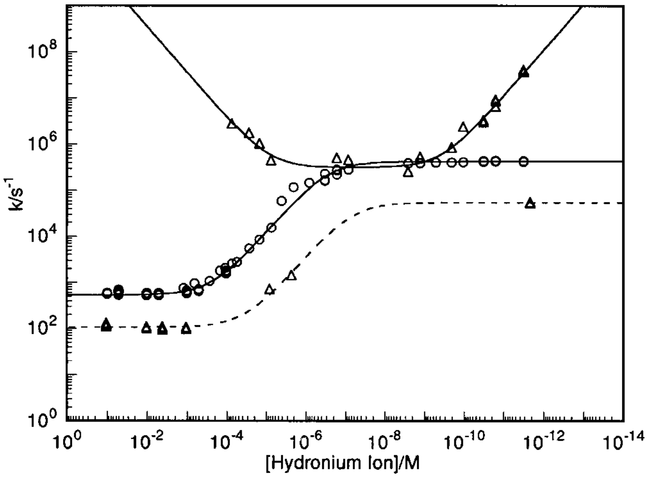

Figure 2. Rate profiles for the hydration of phenylcarbomethoxycarbene in H_2O solution (Δ, solid line) and the ketonization of methyl mandelate enol in H_2O (O, solid line) and D_2O (Δ, broken line) solution at 25 °C.

and ammonium ion buffers. Again, a range of concentrations was employed, replicate measurements were made, and ionic strength was maintained at 0.10 M. These data are summarized in Tables S3−S5.[21]

The rate measurements in buffers were performed in series of solutions of constant buffer ratio but varying buffer concentration, and, as Figure 3 shows, observed rate constants once again increase linearly with buffer concentration. These data were therefore also analyzed using eq 3. The zero-buffer-concentration intercepts, plus the rate constants measured in perchloric acid and sodium hydroxide solutions, are displayed as the middle rate profile shown in Figure 2.

Some ketonization rate measurements were also made in D_2O solutions of perchloric acid, sodium hydroxide, and acetic acid buffers. These data are summarized in Tables S6−S8,[21] and the rate profile they provide is shown as the bottom curve of Figure 2.

Discussion

Carbene Hydration. The rate profile for hydration of phenylcarbomethoxyketene shown in Figure 2 indicates that this reaction is subject to catalysis by hydronium and hydroxide ions, and that there is also a region of no catalysis by solvent-related species. The detailed mechanisms of these reactions are at present unknown, but the data may nevertheless be analyzed using the general rate law given in eq 4.

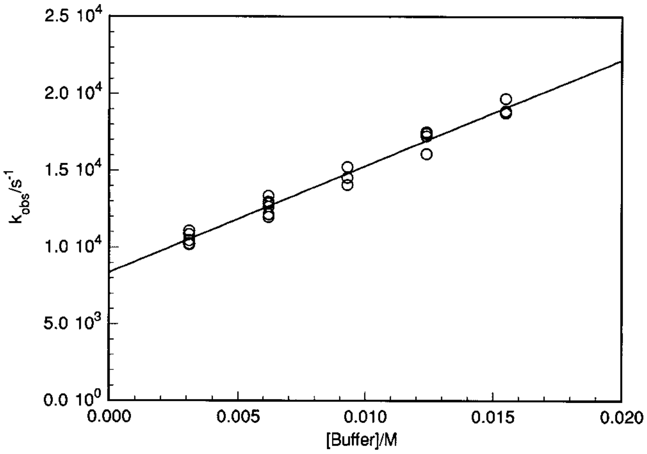

Figure 3. Relationship between buffer concentration and observed rate constants for the ketonization of methyl mandelate enol in aqueous acetic acid buffer solutions at 25 °C; $[CH_3CO_2H]/[CH_3CO_2^-] = 0.55$.

$$k_{obs} = k_{H^+}[H^+] + k_o + k_{HO^-}[HO^-] \tag{4}$$

Least-squares fitting of this expression gave $k_{H^+} = (3.53 \pm 0.60) \times 10^{10}$ M^{-1} s^{-1}, $k_o = (3.09 \pm 0.40) \times 10^5$ s^{-1}, and $k_{HO^-} = (6.64 \pm 0.32) \times 10^9$ M^{-1} s^{-1}.

These results are quite similar to those obtained for the closely analogous hydration of phenylcarboxycarbene,[20] shown in eq 2. The lifetime of the present carbene in the central "uncatalyzed" region of its hydration rate profile, $\tau = 3$ μs, is considerably longer than the ca. 1 ns lifetimes recently reported for other α-carbonylcarbenes.[23] Those lifetimes, however, refer to reactions performed in nonpolar organic solvents, unlike the wholly aqueous medium used here. The previous substrates were also different from the present carbene in that they lacked a phenyl substituent next to the carbenic center. Such a phenyl group might be expected to stabilize the carbene, and microsecond lifetimes have in fact been reported for phenylcarbomethoxycarbene and 2-naphthylcarbomethoxycarbene in organic solvents.[24]

Enol Ketonization: Rate Profile. The ketonization of enols is known to occur by rate-determining proton transfer from any available acid to the β-carbon atom of the enol or its enolate ion.[6] The present rate profile for ketonization of methyl mandelate enol by solvent-related species in aqueous solution, shown in Figure 2, may consequently be interpreted in terms of the reaction scheme of eq 5, in which water and the hydronium ion, written here as H^+, are the proton donors.

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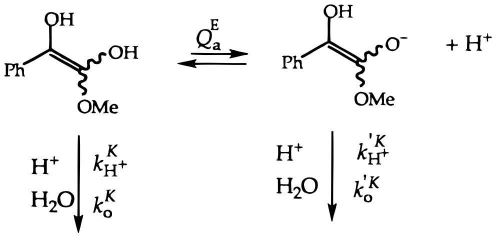

(5)

The present rate profile shows no acid catalysis. This means that carbon protonation of the un-ionized enol by H^+, with the rate constant $k_{H^+}^K$, takes place to a significant extent only at acidities greater than the most acidic solution examined, $[H^+] = 0.1$ M. In more acidic solutions, however, the flash photolytic substrate, methyl phenyldiazoacetate, undergoes rapid acid-catalyzed hydrolysis,[25] and the region above $[H^+] = 0.1$ M could therefore not be investigated.

The horizontal plateau at the high acidity end of the present profile has two possible interpretations: it could be due to carbon protonation of the un-ionized enol by H_2O, with rate constant k_o^K, or it could be caused by equilibrium ionization of the enol to enolate ion followed by carbon protonation of enolate by H^+, with rate constant $k_{H^+}^{'K}$. The latter process produces H^+ in its initial equilibrium, and then uses it up in the rate-determining step, to give an overall reaction whose rate is independent of $[H^+]$. Enolate ions, moreover, are many orders of magnitude more reactive than the corresponding enols,[26] and reaction via the enolate can be a favorable process even when the enolate concentration is quite low.

A choice between these two alternatives may be made on the basis of the fact that enol ketonization obeys the Brϕnsted relation, and the rate of reaction effected by proton transfer from an acid as strong as H^+ can be expected to be many orders of magnitude greater than that effected by proton transfer from an acid as weak as H_2O.[26] Assignment of the high acidity profile plateau to protonation of un-ionized enol by H_2O, however, coupled with the nonappearance of protonation of un-ionized enol by H^+ at acidities as high as $[H^+] = 0.1$ M, makes the rate of reaction effected by H^+ at least comparable to, if not less than, the rate of reaction effected by H_2O. This is contrary to expectation, and this molecular interpretation of this part of the rate profile may therefore be rejected; the alternative explanation—ionization of the enol followed by carbon protonation of enolate ion by H^+—may consequently be accepted.

This part of the rate profile is followed by a rising portion of slope $= +1$ that extends from $[H^+] \cong 10^{-4}$ M to $[H^+] \cong 10^{-7}$ M. This section may be attributed to ionization of the enol to enolate ion followed by carbon protonation of the ion by H_2O. Since the H^+ produced in the prior equilibrium is not used up in the rate-determining step, the overall reaction rate will be inversely proportional to $[H^+]$ or directly proportional to $[HO^-]$, for an apparent hydroxide ion catalysis.

Downward bends in rate profiles such as that seen here at $[H^+] \cong 10^{-7}$ M are commonly caused by a change in the state of ionization of acidic or basic groups in the substrate,[27] and the present bend may be attributed to ionization of the enolic hydroxyl group. At acidities lower than $[H^+] = 10^{-7}$ M, ionized enol is then the substrate form in the initial state of the ketonization reaction; the advantage of converting less reactive enol to more reactive enolization is consequently lost and the apparent hydroxide ion catalysis becomes saturated. This produces the plateau seen at the low acidity end of the rate profile, which represents simple carbon protonation of enolate ion by H_2O.

The rate law that applies to this reaction scheme is shown in eq 6,

$$k_{obs} = (k_{H^+}^{'K}\,[H^+] + k_o^{'K})\,\{Q_a^E/(Q_a^E + [H^+])\} \qquad (6)$$

whose rate and equilibrium constants are defined by eq 5. Least-squares fitting of this expression using the data obtained in H_2O solution gave $k_{H^+}^{'K} = (1.85 \pm 0.10) \times 10^9$ M^{-1} s^{-1}, $(k_o^{'K})_{H_2O} = (4.20 \pm 0.09)\ 10^5$ s^{-1}, and $Q_a^E = (2.83 \pm 0.12) \times 10^{-7}$ M, $pQ_a^E = 6.55 \pm 0.02$,[28] and similar treatment of the data obtained in D_2O solution gave $k_{D^+}^{'K} = (1.63 \pm 0.17) \times 10^9$ M^{-1} s^{-1}, $(k_o^{'K})_{D_2O} = (5.42 \pm 0.26) \times 10^4$ s^{-1}, and $(Q_a^E)_{D_2O} = (6.51 \pm 0.66) \times 10^{-8}$ M, $(pQ_a^E)_{D_2O} = 7.19 \pm 0.04$.[28]

Enol Ketonization: Isotope Effects. These results provide isotope effects that offer good support for the molecular interpretation of the rate profile given above. Primary isotope effects are known to vary in magnitude with transition state structure, passing through a maximum value for symmetrical transition states in which the atom in flight is half-transferred, and falling off from this maximum for reactant-like and product-like transition states.[29] Because carbon protonation of the enolate ion by H^+ is such a fast process—its rate constant, $k_{H^+}^{'K} = 1.85 \times 10^9$ M^{-1} s^{-1}, shows it to be a nearly diffusion-controlled process—it can be expected to have a very reactant-like transition state[30] and consequently to give only a weak isotope effect. The value provided by the present data, $k_{H^+}^{'K}/k_{D^+}^{'K} = 1.14 \pm 0.13$ is entirely consistent with this expectation; the present result is also similar to $k_{H^+}^{'K}/k_{D^+}^{'K} = 1.00 \pm 0.21$ determined for the carbon protonation of isobutyrophenone enolate ion by H^+,[31] which is also a very fast reaction with $k_{H^+}^{'K} = 3.0 \times 10^8$ M^{-1} s^{-1}.[26] The process identified as carbon protonation of the enolate ion by H_2O, on the other hand, is a much slower reaction with $k_o^{'K} = 4.20 \times 10^5$ s^{-1}, and its isotope effect is correspondingly stronger: $(k_o^{'K})_{H_2O}/(k_o^{'K})_{D_2O} = 7.74 \pm 0.40$. This isotope effect is also augmented by the fact that proton transfer from H_2O produces a hydroxide ion, and that provides a secondary isotope effect component in the normal direction, $k_H/k_D > 1$,[32] in addition to the primary isotope effect. The

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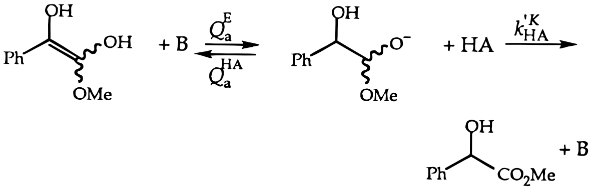
present result is also consistent with $(k_o'^K)_{H_2O}/(k_o'^K)_{D_2O} = 6.9$ determined for the same reaction of the closely related mandelic acid enol.[20]

The ionization of oxygen acids, such as the present enol, gives solvent isotope effects in the normal direction, and the value obtained from the present results $(Q_a^E)_{H_2O}/(Q_a^E)_{D_2O} = 4.34 \pm 0.48$, is of the magnitude expected for an acid with the strength of the present enol.[33] This value also agrees well with $(Q_a^E)_{H_2O}/(Q_a^E)_{D_2O} = 4.5$ determined for the ionization of mandelic acid enol.[20]

Enol Ketonization: Buffer Catalysis. Further support for the molecular interpretation of the ketonization rate profile given above comes from the form of acid–base catalysis in buffer solutions. The slopes, k_{buff}, of the buffer dilution expression of eq 3 used to analyze the buffer rate data, may be separated into their general acid, k_{HA}, and general base, k_B, components with the aid of eq 7, in which f_A is the fraction of buffer present in the acid form in a given buffer solution series. Least-squares fitting of this expression showed general base catalysis in formic acid, acetic acid, and cacodylic acid buffers and general acid catalysis in biphosphate ion and ammonium ion buffers.

$$k_{buff} = k_B + (k_{HA} - k_B) f_A \qquad (7)$$

The buffer-catalyzed component of the present enol ketonization reaction may be formulated as shown in eq 8. Its rate-determining step, being a proton transfer from catalyzing acid to substrate, will show general acid catalysis. In solutions where the substrate exists as un-ionized enol, however, the prior conversion of enol to enolate will transform the general acid catalysis of the rate-determining step into overall general base catalysis. The measurements in formic, acetic, and cacodyoic acid buffers were done in solutions where the enol was largely in its un-ionized form, and the data therefore showed general base catalysis, whereas the measurements in biphosphate and ammonium ion buffers were done in solutions where the enol was largely ionized, and these data consequently showed general acid catalysis.



(8)

It follows from the reaction scheme of eq 8 that the general base, k_B^K, and general acid, k'^K_{HA}, catalytic coefficients are related through the acid ionization constant of the enol, and the acid ionization constant of the buffer acid, as shown in eq 9.

$$k_B^K = k'^K_{HA} Q_a^E / Q_a^{HA} \qquad (9)$$

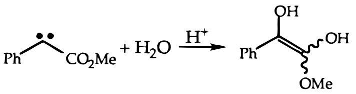
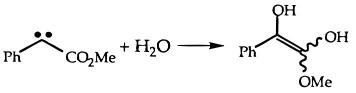
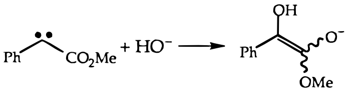
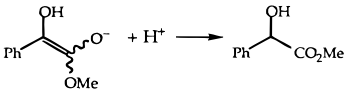
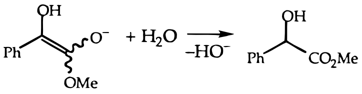
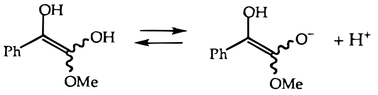
Since these acid ionization constants are known, the general base catalytic coefficients may be converted into general acid values. The results, summarized in Table 1, show a trend of generally decreasing values with decreasing acid strength of the catalyst, as expected. Although the catalysts are of mixed charge type, they nevertheless give a reasonable Brϕnsted correlation with $\alpha = 0.35 \pm 0.08$. The low value of this exponent is consistent with the great speed of these reactions and their consequently expected early transition states.[30]

Table 1. General Acid Catalytic Coefficients for the Ketonization of Methyl Mandelate Enolate Ion[a]

acid	pK_a	$k'^K_{HA}/10^7$ M^{-1} s^{-1}
HCO_2H	3.75	9.22
CH_3CO_2H	4.76	11.3
$(CH_3)_2AsO_2H$	6.27	9.33
$H_2PO_4^-$	7.20	2.50
NH_4^+	9.25	0.281

[a] Aqueous solution, 25 °C, ionic strength = 0.10 M.

Table 2. Summary of Rate and Equilibrium Constants[a]

Process	Constant
	$k_{H^+} = 3.53 \times 10^{10}$ M^{-1} s^{-1}
	$k_o = 3.09 \times 10^5$ M^{-1} s^{-1}
	$k_{HO^-} = 6.64 \times 10^9$ M^{-1} s^{-1}
	$k'^K_{H^+} = 1.85 \times 10^9$ M^{-1} s^{-1}
	$k_o'^K = 4.20 \times 10^5$ s^{-1}
	$Q_a^E = 2.83 \times 10^{-7}$ M
	$pQ_a^E = 6.55$

[a] Aqueous solution, 25 °C, ionic strength = 0.10 M.

Treatment of the data obtained in D_2O solutions of acetic acid in the manner described above for H_2O solutions, using the appropriate acidity constants for the enol and acetic acid[34] in D_2O, gave a catalytic coefficient, which when combined with its H_2O counterpart, produced the isotope effect $k'^K_{HA}/k'^K_{DA} = 3.02 \pm 0.47$. This is a rather weak isotope effect, though not as weak as that on carbon protonation of the enolate ion by H^+ described above. This difference, of course, is consistent with the fact that the acetic acid-catalyzed reaction, though fast, is nevertheless, not as fast as that promoted by H^+, and it should consequently have a less reactant-like and more symmetrical transition state and thus show a stronger isotope effect.

Comparison with Other Systems. It was pointed out above that hydronium-ion catalysis of the ketonization of the presently examined enol could not be detected because its diazo compound precursor is not stable in

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[33] Laughton, P. M.; Robertson, R. E. In *Solute–Solvent Interactions*; Coetzee, J. F., Ritchie, C. D., Eds.; M. Dekker: New York, 1969; Chapter 7.

[34] Gary, R.; Bates, R. G.; Robinson, R. A. *J Phys. Chem.* **1965**, *69*, 2750–2753. Gold, V.; Lowe, B. M. *J. Chem. Soc. (A)* **1968**, 1923–1932.

sufficiently acidic solutions. An upper limit for the hydronium-ion catalytic coefficient may nevertheless be estimated on the basis of the reasonable assumption that an acid-catalyzed reaction 10% above the “uncatalyzed” plateau at the high acidity end of the rate profile shown in Figure 2 would have been detected. The result, $k_{H^+} < 5 \times 10^2$ M^{-1} s^{-1}, makes this reaction at least 20 times slower than the hydronium-ion-catalyzed ketonization of the enol of mandelic acid, for which $k_{H^+} = 9.0 \times 10^3$ M^{-1} s^{-1}.[20] The present enol may, of course, be regarded as the monomethyl ether of the enol of mandelic acid, and this difference in k_{H^+} is therefore consistent with the decrease in reactivity, by 1 or 2 orders of magnitude, generally found in going from enols of simple aldehydes and ketones to their methyl enol ethers.[6]

This difference between enols and methyl enol ethers has been attributed to the better ability of an OH group to effect conjugative stabilization of an adjacent positive charge, such as that being generated on the substrate in the rate-determining step of these reactions, which in both cases involves protonation of the enolic double bond. This is evidenced, for example, by the stronger value of the σ^+ substituent constant for OH, $\sigma^+ = -0.92$,[35] than that for OCH_3, $\sigma^+ = -0.78$.[36] It is significant, therefore, that this difference in reactivity is reversed when the enol becomes ionized and the comparison changes to one between protonation of a double bond bearing OH and O^- groups on one hand and OCH_3 and O^- groups on the other hand: the former situation is represented by ketonization of mandelic acid enolate ion, for which $k'_{H^+} = 8.6 \times 10^8$ M^{-1} s^{-1} and $k'_o = 1.7 \times 10^5$ s^{-1},[20] and the latter situation is represented by the methyl mandelate enolate ion, for which the now somewhat greater rate constants are $k'_{H^+} = 18.5 \times 10^8$ M^{-1} s^{-1} and $k'_o = 4.2 \times 10^5$ s^{-1}. In these enolate ion reactions, of course, the partial positive charge being transferred to the substrate in the rate-determining step is neutralized by the full negative charge already there, and the better positive-charge-stabilizing ability of OH does not come into play. In situations such as this involving net negative charge, the relevant substituent property would seem rather to be the electron-withdrawing inductive or field effect, which is stronger for OH than for OCH_3, as judged by $F = 0.33$ for OH and $F = 0.29$ for OCH_3.[37] The enolate ion initial state of these negative-charge-destroying reactions is consequently stabilized more in the mandelic acid system than in the methyl mandelate system, making the former less reactive than the latter.

This difference between OH and OCH_3 substituent effects is also apparent in the difference between the acidity constants of mandelic acid and methyl mandelate enols ionizing as oxygen acids: $pQ_a^E = 6.39$ for mandelic acid enol[20] and $pQ_a^E = 6.55$ for methyl mandelate enol. These ionizations are negative-charge-generating reactions, and the greater ability of OH to stabilize such a charge makes mandelic acid enol the stronger acid.

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Supporting Information Available: Tables S1−S8 of rate data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(35) Clementi, S.; Linda, P. *J. Chem. Soc., Perkin Trans. 2* **1973**, 1887−1888.

(36) Brown, H. C.; Okamoto, Y. *J. Am. Chem. Soc.* **1958**, *80*, 4979−4987.

(37) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165−195.