

Flash Photolytic Investigation of 4-Diazoisothiochroman-3-one in Aqueous Solution: Observation of a Short-Lived Carboxylic Acid Enol

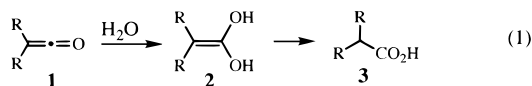
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Abstract: 4-Diazoisothiochroman-3-one was found to undergo a photo-Wolff reaction upon flash photolysis in aqueous solution, generating 1,3-dihydrobenzo[*c*]thiophen-1-ylideneketene, whose hydration produced a second, readily observable short-lived species. The latter, through the shape of its decay rate profile plus solvent isotope effects, was identified as the enol of 1,3-dihydrobenzo[*c*]thiophene-1-carboxylic acid. This behavior contrasts with that reported previously for the acyclic analogue of the presently studied system: flash photolysis of *S*-methyl phenyldiazothioacetate gives a photo-Wolff reaction as well, but the ketene so produced undergoes hydration 3 orders of magnitude more slowly than its cyclic counterpart; this makes ketene hydration in the acyclic system slower than enol ketonization, and that renders the acyclic enol a low-concentration, nonobservable intermediate. Analysis of the rate profile for ketonization of the presently examined cyclic enol provides enol acidity constants as well as rate constants for ketonization of enol and enolate species.

One of the reaction mechanisms for the hydration of ketenes, **1**, to carboxylic acid products, **3**, in aqueous solution involves enol, **2**, intermediates,¹ eq 1, and such intermediates have in



fact been observed in some sterically hindered systems² as well as in the hydration of cyclopentadienylideneketene and its mono- and dibenzo analogues,³ of phenylhydroxyketene,⁴ and of phenylcyanoketene.⁵ In each of these cases, some special structural feature stabilizes the enol, and that accelerates its formation while retarding its subsequent ketonization, thus rendering it directly observable. This, however, is not generally the situation: most ketenes hydrate more slowly than the resulting enols ketonize, and the enols cannot therefore be

(1) For a recent discussion, see: Tidwell, T. T. *Ketenes*; Wiley: New York, 1995; pp 576–587.

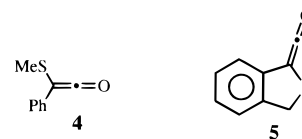
(2) Hegarty, A. F.; O'Neill, P. *J. Chem. Soc., Chem. Commun.* **1987**, 744–745. Allen, B. M.; Hegarty, A. F.; O'Neill, P.; Nguyen, M. T. *J. Chem. Soc., Perkin Trans. 2* **1992**, 927–934. Allen, B. M.; Hegarty, A. F.; O'Neill, P. *J. Chem. Soc., Perkin Trans. 2* **1997**, 2733–2736. Frey, J.; Rappoport, Z. *J. Am. Chem. Soc.* **1995**, *117*, 1161–1162; **1996**, *118*, 5169–5182, 5182–5191. Rappoport, Z.; Frey, J.; Sigalov, M.; Rochlin, E. *Pure Appl. Chem.* **1997**, *69*, 1933–1940.

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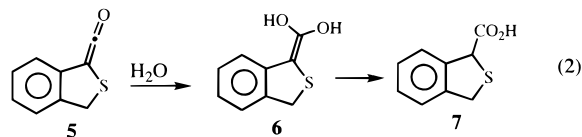
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observed directly. A case in point is phenyl(methylthio)ketene, **4**: no intermediate could be detected during the conversion of



this substance to its carboxylic acid hydration product.⁶

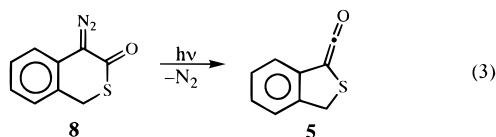
The cyclic analogue of phenyl(methylthio)ketene, 1,3-dihydrobenzo[*c*]thiophen-1-ylideneketene, **5**, on the other hand, behaves quite differently. We have found that hydration of this substance in aqueous solution produces a short-lived intermediate that we have identified as the enol, **6**, of 1,3-dihydrobenzo[*c*]thiophene-1-carboxylic acid, **7**, eq 2. We have also examined



the ketonization of this enol, and, by comparing rates of reaction in this system with those of its acyclic analogue, **4**, we have been able to propose a reason for the different behavior of these two seemingly quite similar systems.

The rates of reaction involved in this study were rapid. We consequently used flash photolytic techniques, generating 1,3-dihydrobenzo[*c*]thiophen-1-ylideneketene by a photo-Wolff reaction with 4-diazoisothiochroman-3-one, **8**, as the photochemical substrate, eq 3.

(6) Jones, J., Jr.; Kresge, A. J. *J. Org. Chem.* **1992**, *57*, 6467–6469.



Experimental Section

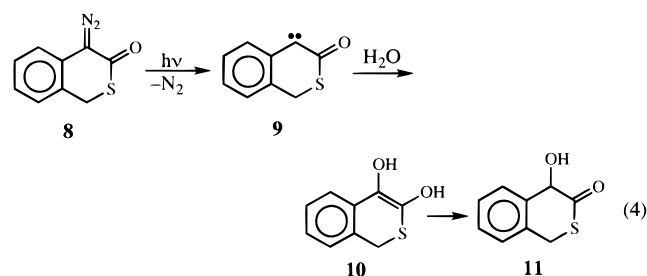
Materials. 4-Diazoisothiochroman-3-one was a sample whose preparation has already been described.⁷ 1,3-Dihydrobenzo[*c*]thiophene-1-carboxylic acid was obtained from this diazo compound by irradiating a 50 mg sample dissolved in 10 mL of water in a rayonet apparatus operating at $\lambda = 300$ nm. The solution was contained in a Pyrex tube, and irradiation was conducted for 30 min, during which time the solution turned from orange to colorless. The solvent was then removed under vacuum, leaving a quantitative yield of white needles: mp 114–115 °C; ¹H NMR (200 MHz, CDCl₃): δ /ppm = 9.84 (br s, 1H), 7.21–7.40 (m, 4H), 5.15 (d, $J = 3$ Hz, 1H), 4.53 (dd, $J = 3, 14$ Hz, 1H), 4.22 (d, $J = 14$ Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ /ppm = 177.37, 141.07, 137.53, 128.24, 127.17, 125.16, 124.86, 54.37, 39.08; MS (EI): $m/e = 180$ (10), 135 (100), 91 (30); HRMS: $m/e = 180.0245$ (calc), 180.0239 (found). The structure of this compound was determined by X-ray crystallography.⁸

All other materials were best available commercial grades.

Kinetics. Flash photolytic rate measurements were made using conventional (flash lamp) and laser ($\lambda = 248$ nm) systems that have already been described.^{3c,9} Substrate concentrations in the solutions used for kinetic measurements were of the order of 10^{-5} M, and the temperature of these solutions was controlled at 25.0 ± 0.05 °C. Reactions were monitored by following the rise and decay of enol absorbance at $\lambda = 320$ – 330 nm. Observed first-order rate constants were obtained by fitting of single exponential functions when the rates of absorbance rise and decay were sufficiently different and by fitting of double exponential functions when they were not.

Results

Product Identification. HPLC analysis showed that only one major product is formed by flash photolysis of 4-diazoisothiochroman-3-one in aqueous solution over the pH range examined in the present study, and spiking with an authentic sample indicated that this product is the same as the material that was obtained by preparative photolysis of this diazo compound. The high-resolution mass spectrum of this substance showed that it has the molecular formula C₉H₈O₂S, as expected for 1,3-dihydrobenzo[*c*]thiophene-1-carboxylic acid (7), but there is another substance with the same molecular formula that might have been formed by photolysis of this diazo compound. Photoinduced loss of nitrogen from 4-diazoisothiochroman-3-one, 8, would give the α -carbonylcarbene, 9, which could then undergo conjugative addition of water to provide enol 10, whose ketonization would produce 4-hydroxyisothiochroman-3-one, 11, eq 4. Such a sequence of events has recently been found to



occur upon flash photolysis of several other, similar α -diazo-carbonyl compounds.¹⁰ Since 4-hydroxyisothiochroman-3-one is an isomer of 1,3-dihydrobenzo[*c*]thiophene-1-carboxylic acid, these two substances cannot be distinguished by high-resolution mass spectroscopy, and their ¹H and ¹³C NMR spectra might be expected to be similar as well. We therefore established the structure of the present photolysis product by X-ray crystallography, which showed unequivocally that it is 1,3-dihydrobenzo[*c*]thiophene-1-carboxylic acid.⁸

Kinetics, Perchloric Acid, and Buffer Solutions. Identification of this carboxylic acid as the product formed in the present flash photolysis experiments indicates that the process being examined is the photo-Wolff reaction shown in eq 3. The rise and subsequent decay of absorbance observed at $\lambda = 320$ – 330 nm may then be attributed to formation of the carboxylic acid enol, 6, by hydration of the ketene, 5, followed by consumption of the enol through ketonization to the carboxylic acid product, 7, eq 2: the styrene-type chromophore of this enol can be expected to provide an absorption band in this region,¹¹ whereas the carboxylic acid product does not absorb light at these wavelengths. This assignment is confirmed by isotope effects and the shape of rate profiles for the rise and decay of this absorbance (vide infra).

Rates of ketene hydration and enol ketonization were measured in perchloric acid solutions over the concentration range [HClO₄] = 0.0001–3 M. A number of different concentrations were used, and replicate measurements were made at most concentrations. The data so obtained are summarized in Tables S1 and S2.¹²

Some rate measurements were made in D₂O solutions of DClO₄ as well. The data are summarized in Tables S1 and S2.¹²

Rates of ketene hydration and enol ketonization were also measured in buffer solutions of formic and pivalic acid and *tert*-butylphosphonate monoanion. Series of solutions of constant buffer ratio and constant ionic strength (0.10 M) but varying buffer concentration were used. These data are summarized in Tables S3 and S4.¹²

Observed first-order rate constants for both ketene hydration and enol ketonization in each buffer solution series increased linearly with buffer concentration. The data were therefore analyzed in the form of buffer dilution plots, according to eq 5. Linear least-squares fitting of this expression produced buffer-

$$k_{\text{obs}} = k_0 + k_{\text{buff}} [\text{buffer}] \quad (5)$$

independent intercepts, k_0 , which, together with the data obtained in perchloric acid solutions, are displayed as the acidic and neutral portions of the rate profiles shown in Figure 1. Hydrogen ion concentrations of the buffer solutions needed to construct these rate profiles were obtained by calculation, using literature pK_a values of the buffer acids and activity coefficients recommended by Bates.¹³

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(11) Okuyama, T.; Kawao, S.; Fueno, T. *J. Org. Chem.* **1981**, *46*, 4372–4375.

(12) Supporting Information; see paragraph at the end of this paper regarding availability.

(13) Bates, R. G. *Determination of pH Theory and Practice*; Wiley: New York, 1973; p 49.

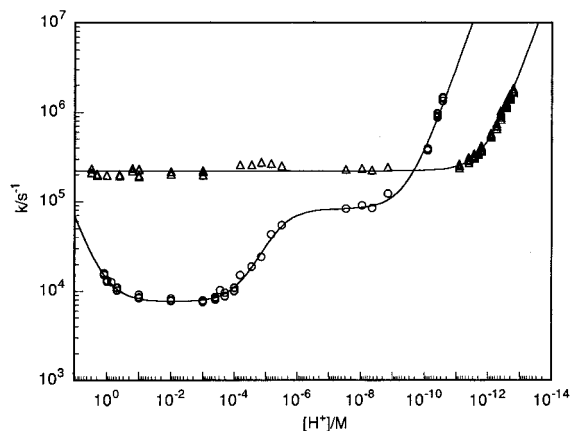


Figure 1. Rate profiles for the hydration of 1,3-dihydrobenzo[*c*]-thiophen-1-ylidene ketene (Δ) and the ketonization of 1,3-dihydrobenzo[*c*]-thiophen-1-carboxylic acid enol (\circ) in aqueous solution at 25 °C.

The upper one of these rate profiles, showing an unchanged rate of reaction from $[H^+] = 3$ M down to $[H^+] = 10^{-9}$ M, refers to the absorbance rise attributed to enol formation through ketene hydration. Its shape is typical of profiles for ketene hydration, which commonly consist of long uncatalyzed portions representing simple nucleophilic addition of water to the ketene¹ with little or no acid catalysis.^{3a,e,4,14} The lower one of these rate profiles, on the other hand, shows a more complex behavior. It refers to the absorbance decay attributed to enol ketonization, and like rate profiles for other enol ketonizations is readily interpretable in terms of rate and equilibrium constants for the various species involved,¹⁵ as will be demonstrated later (vide infra). This rate profile assignment is also supported by solvent isotope effects. The near unity value of the effect on the upper profile, $k_H/k_D = 1.17 \pm 0.03$, is typical of uncatalyzed ketene hydration,^{3c,e,4,16} and is as expected for a nucleophilic process that involves no making or breaking of bonds to isotopically substituted hydrogen. The solvent isotope effect on the lower profile, on the other hand, is much stronger, $k_H/k_D = 4.66 \pm 0.15$ in the region about $H^+ = 10^{-2}$ M, but this is also as expected because enol ketonization occurs through rate-determining carbon protonation in a process that does involve making and breaking bonds to isotopically substituted hydrogen.¹⁵

Kinetics, Sodium Hydroxide Solutions. Figure 1 shows that rates of ketonization become faster in neutral and weakly basic solution and begin to approach those of ketene hydration at $[H^+] \cong 10^{-9}$ M. When the rates of two consecutive first-order reactions become similar, determination of both rate constants by least-squares fitting of a double exponential function becomes difficult or impossible.¹⁷ Assignment of the rate constants to the individual reaction steps becomes problematical as well, because the initial phase of the biphasic change no longer necessarily represents the first reaction.^{17b,18} We could not, in

Table 1. Summary of Rate and Equilibrium Constants^a

Process	Constant
	$k_o = 2.21 \times 10^5 \text{ s}^{-1}$
	$k_{HO^-} = 1.66 \times 10^7 \text{ M}^{-1} \text{ s}^{-1}$
	$k_{H^+} = 6.31 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$
	$k'_{H^+} = 1.60 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$
	$k'_o = 7.48 \times 10^4 \text{ s}^{-1}$
	$k''_o = 2 \times 10^8 \text{ s}^{-1b}$
	$Q_a^E = 4.74 \times 10^{-6} \text{ M}$ $pQ_a^E = 5.32$
	$Q_a^E = 2 \times 10^{-13} \text{ M}^b$ $pQ_a^E = 12.8^b$

^a Aqueous solution, 25 °C, ionic strength = 0.10 M. ^b Estimated value.

fact, in the present case obtain sensible results by double exponential fitting, with both rate constants as disposable parameters, throughout the region $[H^+] = 10^{-9} - 10^{-11}$ M.

In this region the initial absorbance rise became progressively weaker as the acidity decreased until at $[H^+] \cong 10^{-11}$ M it disappeared completely. An absorbance decay, however, still remained, and it could in fact be fitted well using a single-exponential function. This behavior suggests that the rate profiles cross in this region and ketonization of the enol becomes faster than hydration of the ketene. The enol then becomes a low concentration steady-state intermediate that can no longer be seen, and the simple first-order decay seen at $[H^+] < 10^{-11}$ M represents ketene hydration. This argument is supported by several additional lines of evidence (vide infra).

Rates of ketene hydration obtained by fitting of a single-exponential function were provided over the acidity range $[H^+] = 10^{-11} - 10^{-13}$ M by making measurements in sodium hydroxide solutions over the concentration range $[NaOH] = 0.002 - 0.1$ M. The ionic strength of these solutions was maintained at 0.10 M by adding sodium perchlorate as required. These data are summarized in Table S5¹² and are displayed as the basic portion of the ketene rate profile in Figure 1. Some measurements were also made in D₂O solutions of NaOD over the concentration range $[NaOD] = 0.01 - 0.08$ M; these data are also summarized in Table S5.¹²

This basic portion of the ketene rate profile shows catalysis by the hydroxide ion, as is commonly found for ketene hydration reactions.¹ It also shows that hydroxide-ion catalysis takes off from a background of uncatalyzed reaction that is still prominent at $[H^+] \cong 10^{-11}$ M and whose rate constant is the

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(18) Fersht, A. R.; Jencks, W. P. *J. Am. Chem. Soc.* **1970**, *92*, 5432-5442.

same as that determined in acidic and buffer solutions: $k = 2.2 \times 10^{-5} \text{ s}^{-1}$. This implies that uncatalyzed ketene hydration also occurs with this rate constant in the region, $[\text{H}^+] = 10^{-9} - 10^{-11} \text{ M}$, where sensible results could not be obtained by fitting of a double exponential function with no parameters fixed, and that suggests that this difficulty might be overcome by using a double exponential function with one rate constant fixed at $2.2 \times 10^{-5} \text{ s}^{-1}$. This proved to be the case, and rates of enol ketonization were obtained using this strategy over the concentration range $[\text{NaOH}] = 0.0002 - 0.0006 \text{ M}$. These data are summarized in Table S6.¹²

Some measurements were also made in D_2O solutions of NaOD over the concentration range $[\text{NaOD}] = 0.0002 - 0.001 \text{ M}$. Rates of enol ketonization were again calculated by fitting of a double exponential function with the ketene hydration rate constant fixed, this time using $k = 2.2 \times 10^5 \text{ s}^{-1}$ modified by the isotope effect on this rate constant, $k_{\text{H}}/k_{\text{D}} = 1.17$ (vide supra). These data are also summarized in Table S6.¹²

The rate law that applies to ketene hydration reactions showing an uncatalyzed reaction plus hydroxide-ion catalysis is shown in eq 6, and least-squares fitting of the data using this

$$k_{\text{obs}} = k_0 + k_{\text{HO}^-} [\text{HO}^-] \quad (6)$$

expression gave $k_0 = (2.21 \pm 0.02) \times 10^5 \text{ s}^{-1}$ for the uncatalyzed reaction and $k_{\text{HO}^-} = (1.66 \pm 0.02) \times 10^7 \text{ M}^{-1} \text{ s}^{-1}$ as the hydroxide-ion catalytic coefficient. These results are consistent with a relationship between k_0 and k_{HO^-} found for a group of 14 ketenes of various structure, eq 7.¹⁹ This relationship predicts $\log k_{\text{HO}^-} = 7.581 \pm 0.410$ for the present ketene, which

$$\log k_0 = -2.813 \pm 0.250 + (1.076 \pm 0.048) \log k_{\text{HO}^-} \quad (7)$$

is nicely consistent with the observed value, $\log k_{\text{HO}^-} = 7.220 \pm 0.006$, thus lending support to the assignment of this portion of the rate profile to the ketene hydration reaction.

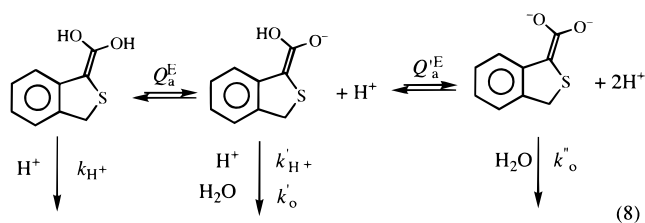
Further support for this assignment comes from the solvent isotope effect on the hydroxide-ion catalytic coefficient for ketene hydration provided by the measurements made in NaOD/ D_2O solutions. The near-unity value obtained, $k_{\text{HO}^-}/k_{\text{DO}^-} = 1.20 \pm 0.05$, is consistent with other near-unity values observed recently for a group of five ketenes.²⁰ The isotope effect on the other reaction, on the other hand, that observed in sodium hydroxide solutions and attributed to enol ketonization, is considerably stronger, $k_{\text{HO}^-}/k_{\text{DO}^-} = 2.07 \pm 0.07$, and is therefore not consistent with ketene hydration. As will be shown below, however, this isotope effect is wholly consistent with enol ketonization.

Discussion

Ketonization Rate Profile. The ketonization of enols is known to occur by rate-determining proton transfer, from whatever acid happens to be present, to the β -carbon atom of either the enol or the enolate ion.¹⁵ The mechanism for the present ketonization reaction, effected by solvent-related species in aqueous solution, may consequently be formulated as shown in eq 8; the hydronium ion, written here as H^+ , is the proton donor in acidic solutions, but that role will be taken over by solvent water when $[\text{H}^+]$ becomes too low for the hydronium ion to be effective.

(19) Andraos, J. Ph.D. Thesis, University of Toronto, 1992; pp 163–164.

(20) Andraos, J.; Chiang, Y.; Eustace, S. E.; Kresge, A. J.; Paine, S. W.; Popik, V. V.; Sung, K. *Can. J. Chem.* **1999**, *77*, 459–462.



The rate profile of Figure 1 is readily understood in terms of this reaction scheme. The acid-catalyzed portion, at the highest acidities examined, represents ketonization through carbon protonation of un-ionized enol by H^+ . The uncatalyzed portion immediately following this has two possible interpretations, the first of which is carbon protonation of un-ionized enol by H_2O . That, however, as shown by the results obtained through least-squares fitting of this profile (vide infra), would give this process a rate constant, $k = (7.57 \times 10^3)/55.5 = 1.36 \times 10^2 \text{ M}^{-1} \text{ s}^{-1}$, not very much less than that for carbon protonation of un-ionized enol by the much stronger acid H^+ , $k = 6.31 \times 10^3 \text{ M}^{-1} \text{ s}^{-1}$. This is contrary to the behavior of other enols, whose carbon protonation obeys the Bronsted relation with many orders of magnitude separating rates of protonation by H_2O and H^+ .²¹ That leaves the second interpretation, which has this uncatalyzed portion of the rate profile occurring through ionization of enol to enolate monoanion followed by carbon protonation of that by H^+ ; in this sequence of steps, H^+ is produced in a prior equilibrium and is then used up in the rate-determining carbon-protonation step, giving an overall process whose rate is independent of $[\text{H}^+]$. Although the enolate ion is only a minor species in these solutions, it is nevertheless the reactive form: ketonization, being an electrophilic addition to a carbon–carbon double bond, is a process in which the much more electron-rich enolate ions are many orders of magnitude more reactive than the corresponding un-ionized enols.²¹

The diagonal region following this uncatalyzed portion also represents carbon protonation of the enolate monoanion but now by H_2O rather than by H^+ . Un-ionized enol is still the initial state of the process, and, because the H^+ produced by enol ionization is not used up in the rate-determining step, there is an overall inverse dependence of rate on $[\text{H}^+]$, giving an apparent hydroxide-ion catalysis. At still lower acidities, the position of the enol ionization equilibrium shifts over to the side of enolate monoanion. The advantage of converting a less reactive to a more reactive substrate form is consequently lost, and the apparent hydroxide-ion catalysis becomes saturated, giving way to simple carbon protonation of monoanion by H_2O , represented by a second uncatalyzed region. Eventually, however, at even lower acidities in what are now quite basic solutions, carbon protonation of the even more reactive enolate dianion takes over, and since H_2O is the only effective proton source in these solutions, this produces a second region of apparent hydroxide-ion catalysis.

The rate law that applies to this reaction scheme is shown in eq 9, with rate and equilibrium constants as defined by eq 8.²²

$$k_{\text{obs}} = k_{\text{H}^+} [\text{H}^+] + (k'_{\text{H}^+} [\text{H}^+] + k'_0) \left\{ \frac{Q_a^E}{Q_a^E + [\text{H}^+]} \right\} + k''_0 Q_a^E / [\text{H}^+] \quad (9)$$

(21) (a) Pruszyński, P.; Chiang, Y.; Kresge, A. J.; Schepp, N. P.; Walsh, P. A. *J. Phys. Chem.* **1986**, *90*, 3760–3766. (b) Chiang, Y.; Kresge, A. J.; Santaballa, J. A.; Wirz, J. *J. Am. Chem. Soc.* **1988**, *110*, 5506–5510.

(22) Rate and equilibrium constants of un-ionized enol are written with no superscript; those of the enolate monoanion with a single prime; and those of the enolate dianion, with a double prime.

Least-squares analysis of the data using this expression gave $k_{\text{H}^+} = (6.31 \pm 0.49) \times 10^3 \text{ M}^{-1} \text{ s}^{-1}$, $k'_{\text{H}^+} Q_a^{\text{E}} = (7.57 \pm 0.20) \times 10^3 \text{ s}^{-1}$, $k'_0 = (7.48 \pm 0.44) \times 10^4 \text{ s}^{-1}$, $Q_a^{\text{E}} = (4.74 \pm 0.57) \times 10^{-6} \text{ M}$, $pQ_a^{\text{E}} = 5.32 \pm 0.05$,²² and $k''_0 Q_a^{\text{E}} = (2.98 \pm 0.08) \times 10^{-5} \text{ M s}^{-1}$.

Since Q_a^{E} has now been determined, a value of k'_{H^+} may be extracted from the product $k'_{\text{H}^+} Q_a^{\text{E}}$; the result, $k'_{\text{H}^+} = (1.60 \pm 0.20) \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$, shows that carbon protonation of the enolate monoanion is a very fast, almost but not quite, diffusion-controlled process. It would therefore be expected to have an early, reactant-like transition state,²⁴ and, because such a transition state is quite unsymmetrical, to show only a weak isotope effect.²⁵ The observed effect of $k_{\text{H}}/k_{\text{D}} = 4.66 \pm 0.15$ on the product $k'_{\text{H}^+} Q_a^{\text{E}}$ may therefore be ascribed mainly to the equilibrium isotope effect on Q_a^{E} , which in similar systems has been found to lie in the region $Q_{\text{H}}/Q_{\text{D}} = 3\text{--}4$.^{3c,4b}

The other product of two constants obtained by analysis of the ketonization rate profile, $k''_0 Q_a^{\text{E}}$, cannot be so readily separated into its constituent parts, because saturation of the second apparent hydroxide-ion catalysis was not achieved and Q_a^{E} was consequently not determined. An estimate of this acidity constant may nevertheless be made using the average difference between first and second ionization constants of carboxylic acid enols for the few systems where both of these constants have been measured: $(pQ_a^{\text{E}} - pQ_a^{\text{E}}) \cong 7.5$.²⁶ That plus the value $pQ_a^{\text{E}} = 5.3$ determined here then leads to $pQ_a^{\text{E}} = 12.8$, and this coupled with $k''_0 Q_a^{\text{E}} = 3 \times 10^{-5} \text{ M s}^{-1}$ gives $k''_0 = 2 \times 10^8 \text{ s}^{-1}$.

This result shows that carbon protonation of the enolate dianion by water is a fast but certainly not diffusion-controlled process: a diffusion-controlled protonation by solvent water should be governed by the time required for a water molecule to rotate into a proton-transferring position, i.e. by the rotational correlation time of water, which corresponds to a rate constant of $k \cong 10^{11} \text{ s}^{-1}$.²⁷ This reaction is therefore a chemically activated process, and as such it should show a primary isotope effect, although probably a rather weak one because the reaction is nevertheless quite fast. It was noted above that the solvent isotope effect on enolization in this region of the rate profile treated as a hydroxide-ion catalyzed process is $k_{\text{HO}^-}/k_{\text{DO}^-} = 2.07$; this may be converted into an isotope effect on the product $k''_0 Q_a^{\text{E}}$ through multiplication by the solvent isotope effect on the self-ionization of water²⁸ to give $(k''_0 Q_a^{\text{E}})_{\text{H}_2\text{O}}/(k''_0 Q_a^{\text{E}})_{\text{D}_2\text{O}} = 15.2$. Solvent isotope effects on the ionization of normal acids are known to increase with decreasing acid strength,²⁹ and that on an oxygen acid as weak as the present enolate monoanion might lie in the range $(Q_a^{\text{E}})_{\text{H}_2\text{O}}/(Q_a^{\text{E}})_{\text{D}_2\text{O}} = 5\text{--}6$.³⁰ This leaves $(k''_0)_{\text{H}_2\text{O}}/(k''_0)_{\text{D}_2\text{O}} = 2.5\text{--}3.0$, a result wholly consistent with the weak value anticipated by the rapidity of this reaction.

(23) This is a concentration quotient applicable at ionic strength = 0.10 M.

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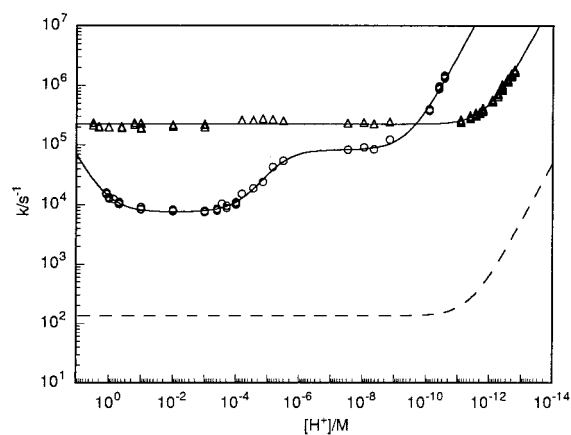
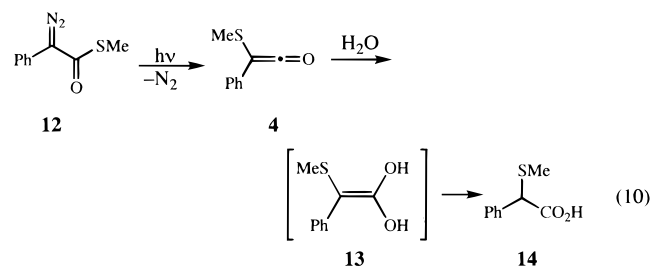


Figure 2. Comparison of rate profiles for the hydration of 1,3-dihydrobenzo[*c*]thiophen-1-ylideneketene (Δ) and the ketonization of 1,3-dihydrobenzo[*c*]thiophen-1-carboxylic acid enol (\circ) with the rate profile for hydration of phenyl(methylthio)ketene (broken line) in aqueous solution at 25 °C.

The generally good agreement of results obtained by these various analyses with expected values provides strong support for the essential correctness of the interpretations made.

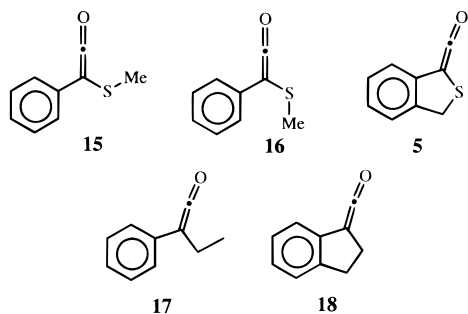
Comparison with Acyclic Analog. The present results thus show quite clearly that an enol intermediate is formed in the hydration of 1,3-dihydrobenzo[*c*]thiophen-1-ylideneketene and that ketonization of this enol to 2,3-dihydrobenzo[*c*]thiophene-1-carboxylic acid, eq 2, is slower than its formation over most of the aqueous solution pH range examined; the enol intermediate is consequently readily observable. This stands in striking contrast to the behavior of the corresponding acyclic system. Phenyl(methylthio)ketene, **4**, when generated by the photo-Wolff reaction of *S*-methyl phenyldiazothioacetate, **12**, was found to undergo hydration to α -(methylthio)phenylacetic acid, **14**, with a typical rate profile showing uncatalyzed and hydroxide-ion catalyzed portions; this implied formation of an enol intermediate, **13**, and yet no intermediate could be detected.⁶



This remarkable difference may be traced to a much greater reactivity of the cyclic over the acyclic ketene. Figure 2 compares the presently determined rate profiles for ketene hydration (Δ) and enol ketonization (\circ) in the cyclic system with the rate profile for hydration of the acyclic ketene (broken line). It may be clearly seen that the acyclic ketene is much less reactive (by a factor of 1700 for uncatalyzed hydration) than its cyclic analogue and that this difference makes the ketonization reaction considerably faster than hydration of the acyclic ketene but slower than hydration of its cyclic analogue.

It is likely that steric effects are the cause of this difference in ketene reactivity. Nucleophilic additions to ketenes, such as uncatalyzed and hydroxide-ion catalyzed hydrations, are known to occur by attack of the nucleophile on the ketene carbonyl atom in the ketene plane, and large substituents attached to the ketene functional group in that plane consequently slow these

reactions markedly.^{1,31} The present acyclic ketene, to eliminate interference between its methyl group and the benzene ring, is likely to exist in the *s*-cis, **15**, rather than the *s*-trans, **16**, conformation. In-plane attack will consequently be hindered on both sides of the ketene, by the methyl group on the sulfur side



and by an ortho hydrogen on the benzene side. In the cyclic ketene, **5**, on the other hand, hindrance on the sulfur side will be relieved, because the methylene group replacing methyl is tied back to the benzene ring. A similar relief of steric hindrance

is provided by a comparison of rates of hydration of phenyl-ethylketene, **17**, and its cyclic counterpart, 1-indenylideneketene, **18**, where the uncatalyzed reaction of the cyclic ketene is 190 times faster than that of the acyclic substrate.^{20,32}

This steric effect will of course have little influence on rates of ketonization of the enols formed from these ketenes, because the proton effecting ketonization is delivered in a plane perpendicular to that used in ketene hydration; this puts it out of the way of the groups interfering with the hydration reaction. It is likely, therefore, that the reactivity of the acyclic enol **13** will be similar to that of its cyclic analogue **6**, and that makes its decay faster than its formation and gives it the nature of a low-concentration "invisible" intermediate.

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Supporting Information Available: Tables of rate data (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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