

Flash Photolysis of 10-Diazo-9(10*H*)-phenanthrenone in Aqueous Solution. Hydration of Fluorenylidene ketene and the Fluorene-9-carboxylic Acid Keto–Enol System

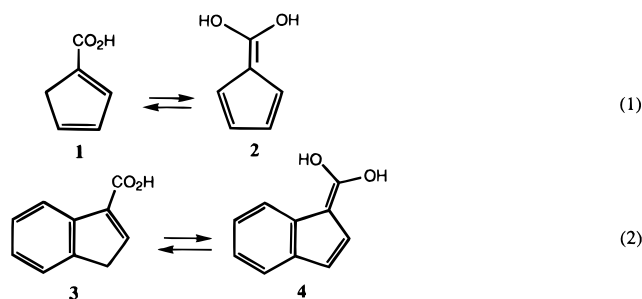
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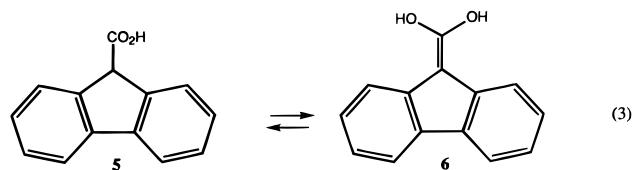
Received April 30, 1997[⊗]

Abstract: Flash photolysis of 10-diazo-9(10*H*)-phenanthrenone in aqueous solution was found to give two successively formed transient species and to produce fluorene-9-carboxylic acid as the major reaction product. These transients were identified, through solvent isotope effects and the form of acid–base catalysis, as fluorenylidene ketene, formed by photo-Wolff reaction of the diazophenanthrenone, and fluorene-9-carboxylic acid enol, formed by hydration of this ketene. Analysis of the rate profile of the enol ketonization reaction produced the first and second ionization constants for the enol ionizing as an oxygen acid, $pQ_a^E = 2.01$ and $pQ_a^{E'} = 9.61$, respectively. The rate of enolization of fluorene-9-carboxylic acid was also determined, by bromine scavenging, and that, coupled with a literature value of the acidity constant of this acid, allowed evaluation of the two keto–enol equilibrium constants ($pK_E = 9.67$ for interconverting un-ionized carboxylic acid and enol and $pK'_E = 8.24$ for interconverting singly ionized acid and enol), and it also allowed evaluation of the two carbon acid acidity constants ($pQ_a^K = 11.67$ for ionization of the un-ionized carboxylic acid as a carbon acid and $pQ_a^{K'} = 17.85$ for ionization of its carboxylate ion as a carbon acid). (All acidity constants are concentration quotients applicable at ionic strength 0.10 M.) These keto–enol equilibrium constants and acid dissociation constants are large because of the enol and enolate ion stabilizing effects of the cyclopentadienyl ring of the fluorenyl group; this ring also makes fluorenylidene ketene an unusually reactive substance.

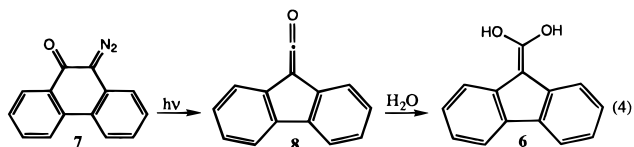
During the past 15 years there has been a remarkable development of methods for generating the enol isomers of simple aldehydes and ketones in solution, and as a result much is now known about the chemistry of these unstable substances.¹ Much less, however, is known about enols of carboxylic acids, undoubtedly because these substances are very much less stable than the already quite labile aldehyde and ketone enols. Most of the relatively little information that is available² has been obtained from systems in which the carboxylic acid enol is stabilized, either sterically^{3,4} or electronically.^{5–7} The cyclopentadienyldiene group has proved to be especially good at stabilizing carboxylic acid enols, and this effect has enabled studies of fulvenediol, **2**,⁵ the enol of cyclopentadienecarboxylic acid, **1**, eq 1, and its benzo analog **4**, the enol of indenecarboxylic



acid, **3**,^{5b,6b,d,7} eq 2. We have now completed this series by investigating the dibenzo analog **6**, which is the enol of fluorene-9-carboxylic acid, **5**, eq 3.



We generated the enol of fluorene-9-carboxylic acid by hydration of fluorenylidene ketene, **8**, obtained by photo-Wolff reaction of the diazoquinone 10-diazo-9(10*H*)-phenanthrenone, **7**, eq 4. We were able to measure rates of this hydration reaction



as well as rates of ketonization of the enol, and we consequently gained information about the chemistry of the ketene in addition to that of the enol.

(3) O'Neill, P.; Hegarty, A. F. *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.

(4) Frey, J.; Rappoport, Z. *J. Am. Chem. Soc.* **1995**, *117*, 1161–1162; **1996**, *118*, 5169–5181, 5182–5191.

(5) (a) Urwyler, B.; Wirz, J. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 790–792. (b) Almstead, J.-I. K.; Urwyler, B.; Wirz, J. *J. Am. Chem. Soc.* **1994**, *116*, 954–960.

(6) (a) Chiang, Y.; Kresge, A. J.; Pruszyński, P.; Schepp, N. P.; Wirz, J. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 792–794. (b) Andraos, J.; Chiang, Y.; Huang, C.-G.; Kresge, A. J.; Scaiano, J. C. *J. Am. Chem. Soc.* **1993**, *115*, 10605–10610. (c) Andraos, J.; Chiang, Y.; Kresge, A. J.; Pojarlieff, I. G.; Schepp, N. S.; Wirz, J. *J. Am. Chem. Soc.* **1994**, *116*, 73–81. (d) Andraos, J.; Kresge, A. J.; Popik, V. V. *J. Am. Chem. Soc.* **1994**, *116*, 961–967.

(7) Barra, M.; Fisher, T. A.; Cernigliaro, G. J.; Sinta, R.; Scaiano, J. C. *J. Am. Chem. Soc.* **1992**, *114*, 2630–2634.

[⊗] Abstract published in *Advance ACS Abstracts*, August 15, 1997.

(1) See, for example: *The Chemistry of Enols*; Rappoport, Z., Ed.; Wiley: New York, 1990.

(2) For a brief review: see Kresge, A. J. *Chem. Soc. Rev.* **1996**, *25*, 275–280.

Experimental Section

Materials. 10-Diazo-9(10*H*)-phenanthrenone was prepared by treating 9,10-phenanthrenequinone with (*p*-tolylsulfonyl)hydrazine.⁸ Other materials were the best available commercial grades.

Flash Photolysis. Flash photolysis experiments were done using two different systems: (1) a conventional apparatus with excitation flash produced by capacitor discharge through a pair of xenon flash lamps, 50 μ s pulse width,⁹ and (2) a KrF excimer laser system, $\lambda_{\text{exc}} = 248$ nm, 25 ns pulse width.^{6b} Substrate concentrations were *ca.* 10^{-5} M.

Enolization Rate Measurements. Rates of enolization of fluorene-9-carboxylic acid were determined by using bromine to scavenge the enol as it formed. Measurements were made in sodium hydroxide solutions using the absorbance of OBr⁻ at $\lambda = 330$ nm to monitor bromine concentration. Initial concentrations of the carboxylic acid substrate were 1.4×10^{-4} M and of bromine 1.7×10^{-4} M. The reaction is pseudo-first-order under these conditions, and the first-order rate law was obeyed accurately; observed rate constants were determined by least squares fitting of an exponential function.

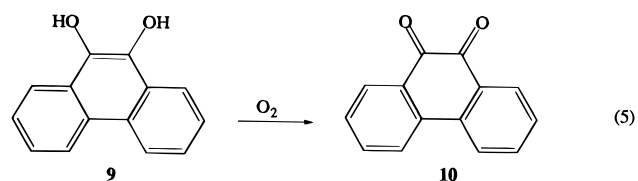
Further experimental details are available in the theses upon which part of this paper is based.¹⁰

Results

Stability of 10-Diazo-9(10*H*)-phenanthrenone. The UV spectrum of this substance in aqueous solution, which consists of bands at $\lambda_{\text{max}} = 245$ and 375 nm, showed no change over the acidity range used in the present work, $\text{pC}_{\text{H}^+} = 1-13$, and it was also invariant for periods of time longer than those taken to prepare solutions and subject them to flash photolysis. This shows that this substrate was stable under the flash photolytic conditions and that it underwent no thermal reaction before photolysis.

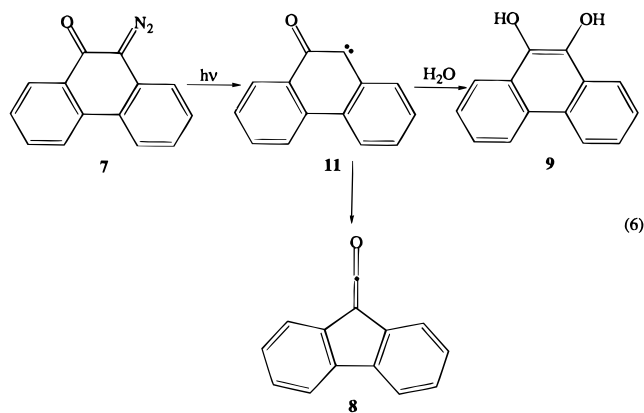
Product Study. HPLC analysis of aqueous solutions of 10-diazo-9(10*H*)-phenanthrenone at concentrations used for flash photolysis (10^{-5} M), which had been subjected to one flash from our conventional flash photolysis apparatus, showed two reaction products, formed in major and minor amounts, in addition to smaller quantities of unreacted starting material. Spiking with authentic samples identified the major product as fluorene-9-carboxylic acid, **5**, and the minor product as 9,10-phenanthrenequinone, **10**. In 0.001 M HClO₄ these products were formed in 80% and 15% yields, and in 0.002 M NaOH, in 53% and 20% yields.

Fluorene-9-carboxylic acid is the product expected from ketonization of the enol **6**, formed by photo-Wolff reaction of 10-diazo-9(10*H*)-phenanthrenone, **7**, and hydration of the resulting ketene **8** according to eq 4. It is likely that the minor product 9,10-phenanthrenequinone, **10**, was formed from 9,10-phenanthrenediol, **9**, which is known to oxidize readily to the quinone, eq 5.¹¹ The diol, in turn, was probably produced by conjugate



addition of water to the ketocarbene intermediate **11**, formed

by photodediazotization of the diazoquinone, eq 6, in competition



with Wolff rearrangement of this intermediate to fluorenylidene ketene, **8**; such addition of water to ketocarbenes is known to occur in aqueous solution.¹²

Further support for production of fluorene-9-carboxylic acid via hydration of fluorenylidene ketene and ketonization of the ensuing enol as the main process occurring upon flash photolysis of 10-diazo-9(10*H*)-phenanthrenone in aqueous solution is provided by the behavior of transient species observed during the flash photolysis experiments (*vide infra*).

Flash Photolysis. Irradiation of dilute (10^{-5} M) aqueous solutions of 10-diazo-9(10*H*)-phenanthrenone, with a pulse of light from either our conventional flash system or the laser apparatus operating at $\lambda_{\text{exc}} = 248$ nm, produced an intermediate bleaching of the substrate absorption bands at $\lambda_{\text{max}} = 245$ and 375 nm, followed by a growth and subsequent decay of absorbance in the region $\lambda = 305-320$ nm. The relative times required for these absorbance changes at $\lambda = 305-320$ nm depended strongly on the acid-base properties of the medium. When they were well separated in time, they were analyzed separately using a single-exponential form of the first-order rate law, to which they both conformed well, and when they occurred at comparable times, they were analyzed using a double-exponential expression, to which the data also conformed well.

Absorbance changes such as these were observed before in the flash photolysis of other diazoquinones in aqueous solution,^{5,6b,d} where they have been assigned to the occurrence of two consecutive reactions: (1) hydration of a ketene formed within the time of the light pulse by photo-Wolff reaction of the diazoquinone and (2) ketonization of the carboxylic acid enol generated by this ketene hydration. A similar assignment is made here; this is supported by the form of acid-base catalysis and the magnitude of solvent isotope effects shown by these absorbance changes (*vide infra*).

Ketene Hydration. Rates of the absorbance change attributed to hydration of fluorenylidene ketene were measured in aqueous solutions of perchloric acid, sodium hydroxide, and ammonium ion buffers, as well as in solutions with no added acid or base. The ionic strength of these solutions was maintained at 0.10 M through the addition of sodium perchlorate as required. The results are summarized in Tables S1-S4 in the Supporting Information.¹³

The measurements in ammonium ion buffers were done in series of solutions of constant buffer ratio but varying buffer concentration. Buffer catalytic coefficients were evaluated as

(12) (a) Chiang, Y.; Kresge, A. J.; Pruszyński, P.; Schepp, N. P.; Wirz, J. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1366-1368. (b) Chiang, Y.; Jefferson, E. A.; Popik, V. V. Unpublished work.

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

(8) Cava, M. P.; Litle, R. L.; Napier, D. R. *J. Am. Chem. Soc.* **1958**, *80*, 2257-2263. Sus, O.; Steppan, H.; Dietrich, R. *Justus Liebigs Ann. Chem.* **1958**, *617*, 20-25.

(9) Chiang, Y.; Hojatti, M.; Keefe, J. R.; Kresge, A. J.; Schepp, N. P.; Wirz, J. *J. Am. Chem. Soc.* **1987**, *109*, 4000-4009.

(10) Andraos, J. M.Sc. Thesis, University of Toronto, 1989; Ph.D. Thesis, University of Toronto, 1992.

(11) Qesch, F.; Sparrow, A. J.; Platt, K. L. *J. Labelled Compd. Radiopharm.* **1980**, *17*, 93-100.

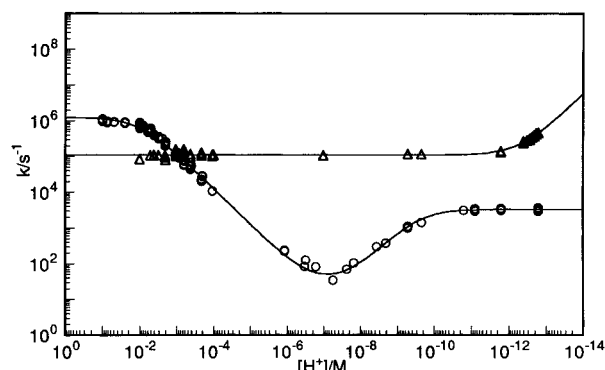


Figure 1. Rate profiles for the hydration of fluorenylidene ketene, Δ , and ketonization of the enol of fluorene-9-carboxylic acid, \circ , in aqueous solution at 25 °C.

slopes of buffer dilution plots, but buffer catalysis was weak, and, although it appeared that the reaction involved only the basic component of the buffer, the results were too uncertain to allow detailed analysis. This is the expected result, for bases are known to react with ketenes by direct nucleophilic attack on the ketene carbonyl carbon atom,¹⁴ with the direction of attack being in the ketene molecular plane:¹⁵ such attack in the case of fluorenylidene ketene will be hindered by steric interference from hydrogens in the peri positions of the benzene rings flanking the ketene group, and the buffer reaction will consequently be weak.

The intercepts of these ammonium ion buffer solution plots, on the other hand, were well defined, and they provide good estimates of rates of ketene hydration through solvent-related species in these solutions. They are displayed as triangles in Figure 1, and, together with rate constants measured in all of the other solutions, they provide the rate profile shown there. Hydrogen ion concentrations needed for this purpose were obtained by calculation using acidity constants from the literature and activity coefficients recommended by Bates.¹⁶

It may be seen that this ketene hydration consists of a wide region of uncatalyzed reaction, some, albeit weak, hydroxide ion catalysis, and no acid catalysis. Such behavior is typical of ketene hydrations, whose rate profiles commonly show large uncatalyzed regions and only weak acid and base catalysis.^{5,6b-d,17} Acid catalysis, moreover, is suppressed by aromatic substituents, such as the fluorenyl residue present here, and in such systems it can be detected only in concentrated acid solutions.^{17b,18}

The rate law that corresponds to this behavior is shown in eq 7, where k_o is the rate constant for the uncatalyzed reaction and k_{HO^-} is that for the hydroxide ion catalyzed process. Least

$$k_{\text{obs}} = k_o + k_{\text{HO}^-}[\text{HO}^-] \quad (7)$$

squares fitting of this expression gave $k_o = (1.07 \pm 0.02) \times 10^5 \text{ s}^{-1}$ and $k_{\text{HO}^-} = (3.47 \pm 0.10) \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$. Each one of

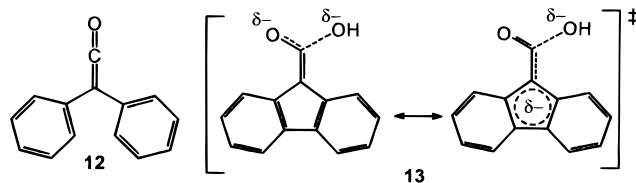
(14) Andraos, J.; Kresge, A. J. *J. Am. Chem. Soc.* **1992**, *114*, 5643–5646.

(15) Schiess, P.; Eberle, M.; Huys-Francotte, M.; Wirz, J. *Tetrahedron Lett.* **1984**, *25*, 2201–2204. Seikaly, H. R.; Tidwell, T. T. *Tetrahedron* **1986**, *42*, 2587–2613. Tidwell, T. T. *Acc. Chem. Res.* **1990**, *23*, 273–279.

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

(17) (a) Bothe, E.; Dessouki, A. M.; Schulte-Frohlinde, D. *J. Phys. Chem.* **1980**, *84*, 3270–3272. (b) Allen, A. D.; Kresge, A. J.; Schepp, N. P.; Tidwell, T. T. *Can. J. Chem.* **1987**, *65*, 1719–1723. (c) Allen, A. D.; Tidwell, T. T. *J. Am. Chem. Soc.* **1987**, *109*, 2774–2780. (d) Allen, A. D.; Stevenson, A.; Tidwell, T. T. *J. Org. Chem.* **1989**, *54*, 2843–2848. (e) Chiang, Y.; Kresge, A. J.; Popik, V. V. *J. Am. Chem. Soc.* **1995**, *117*, 9165–9171. Chiang, Y.; Guo, H.-X.; Kresge, A. J.; Tee, O. S. *J. Am. Chem. Soc.* **1996**, *118*, 3386–3391.

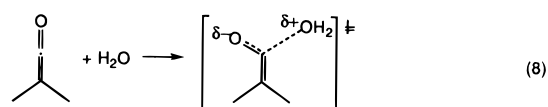
these rate constants is considerably greater than its counterpart for the hydration of the closely structurally related substance diphenylketene, **12**, for which $k_o = 2.75 \times 10^2 \text{ s}^{-1}$ and $k_{\text{HO}^-} = 6.11 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$.^{17b} This reactivity difference is a consequence of the cyclopentadienyl nature of the central ring in fluorenylidene ketene, which takes on aromatic character when it stabilizes the negative charge assumed by the substrate in the transition state of the reaction, **13**, as it undergoes nucleo-



philic attack by a water molecule or hydroxide ion. Another contributing factor is steric crowding of the benzene rings in diphenylketene, which forces these substituents out of coplanarity with the ketene group and reduces their ability to accept negative charge.

Rates of hydration of fluorenylidene ketene were also measured in D_2O solutions of perchloric acid and in D_2O solution with no added acid or base. These data summarized in Tables S1 and S3.¹³

The observed rate constants determined in D_2O solution showed no systematic variation with acidity. They were therefore simply averaged to give the result $(k_o)_{\text{D}_2\text{O}} = (7.92 \pm 0.12) \times 10^4 \text{ s}^{-1}$. Combination of this with its H_2O counterpart gives the isotope effect $k_{\text{H}_2\text{O}}/k_{\text{D}_2\text{O}} = 1.35 \pm 0.03$. The small magnitude of this isotope effect is again typical of ketene hydration reactions.^{6b,10,17b} It is also consistent with the nucleophilic nature of this process, which involves no breaking of isotopically substituted bonds but does include some weakening of the nonreacting bonds of the attacking water molecule as it takes on positive charge in the transition state of the process, eq 8.¹⁹



Enol Ketonization. Rates of the absorbance change attributed to ketonization of the enol of fluorene-9-carboxylic acid were measured in aqueous solutions of perchloric acid and sodium hydroxide. Measurements were also made in aqueous biphosphate ion and ammonium ion buffers using series of solutions of constant buffer ratio but varying buffer concentration. The ionic strength of all solutions was maintained at 0.10 M using sodium perchlorate as required. The results obtained are summarized in Tables S5–S7.¹³

The rate constants determined in perchloric acid and sodium hydroxide solutions, together with the intercepts of buffer dilution plots, are also displayed as the rate profile defined by circles in Figure 1. Hydrogen ion concentrations of the buffer solutions needed to construct this rate profile were again obtained by calculation using literature acidity constants and activity coefficients recommended by Bates.¹⁶

Figure 1 shows that in neutral and basic solution the ketene hydration and enol ketonization reactions were well separated

(18) (a) Allen, A. D.; Baigrie, L. M.; Gong, L.; Tidwell, T. T. *Can. J. Chem.* **1991**, *69*, 138–145. (b) Andraos, J.; Kresge, A. J.; Schepp, N. P. *Can. J. Chem.* **1995**, *73*, 539–543.

(19) Kresge, A. J.; More, O'Ferrall, R. A.; Powell, M. F. *In Isotopes in Organic Chemistry*; Buncl, E., Lee, C. C., Eds.; Elsevier: Amsterdam, 1987; Vol. 7, pp 177–273.

in time. Rate constants for the two reactions could therefore be calculated separately by analyzing the absorbance changes using single exponential functions. Since the chemistry requires ketene hydration to occur before enol ketonization and, if enol ketonization is to be seen, also to be the faster process, assignment of the absorbance changes and the rate constants derived from them to the respective reactions in these media was straightforward. In acidic solutions, however, rates of the two reactions became comparable, and the data had to be analyzed by fitting of double exponential functions. In such a situation, assignment of the rate constants is more difficult,²⁰ because the initial phase of the biphasic absorption change no longer necessarily represents the first reaction: this initial phase instead always corresponds to the faster reaction, regardless of whether that reaction occurs first or is second.

This difficulty was overcome in the present case by noting how the maximum concentration of enol formed in the overall process changed as the relative rates of the two reactions varied. The question is whether, as the reaction medium becomes more acidic, the rate of ketene hydration remains constant and that of enol ketonization continues to increase, eventually crossing the ketene rate at $[H^+] \cong 0.001$ M and becoming the faster process (as shown in Figure 1), or whether this crossing is avoided and the enol rate levels off at $[H^+] \cong 0.001$ M and the ketene rate begins to increase at this point. If the rate of enol ketonization crosses that of ketene hydration and then becomes progressively faster, the maximum concentration of enol intermediate will progressively drop. If, on the other hand, crossing is avoided and ketene hydration becomes progressively faster, then the maximum concentration of enol will rise. At the wavelengths employed for these rate measurements, the enol absorbed more strongly than either its ketene precursor or the carboxylic acid product, and the observed absorbance consequently first rose and then fell, with the maximum absorbance representing the maximum concentration of enol. We found that this maximum absorbance decreased with increasing acidity of the medium as the system passed through $[H^+] \cong 0.001$ M, and we were therefore able to conclude that the two rates did in fact cross, as indicated in Figure 1.

This assignment is supported by the fact that the alternative would have the ketene hydration reaction become acid catalyzed at $[H^+] \cong 0.001$ M and then, at about $[H^+] = 0.01$ M, have the acid catalysis become saturated. As was pointed out above, acid catalysis of ketene hydration is weak at best and is suppressed by aromatic substituents; for mesitylketene in aqueous perchloric acid, it does not become apparent until the acid concentration reaches 2 M.^{18b} It is difficult, moreover, to see why such catalysis should become saturated.

The assignment made, in addition, produces sensible rate and equilibrium constants that show reasonable isotope effects. These isotope effects are based upon further rate measurements made in D₂O solutions of perchloric acid. The results are summarized in Table S5¹³ and are displayed, along with the corresponding data for H₂O solutions, in Figure 2.

It may be seen that the rates in D₂O are slower than those in H₂O at all of the acid concentrations investigated, but that the difference is greater in the plateau regions above the bends in these profiles than in the diagonal regions below the bends. Bends in rate profiles such as these are commonly produced by ionization of acid or basic groups in the system,²¹ and similar bends in the rate profiles for ketonization of other carboxylic acid enols have been shown to be caused by acid ionization of

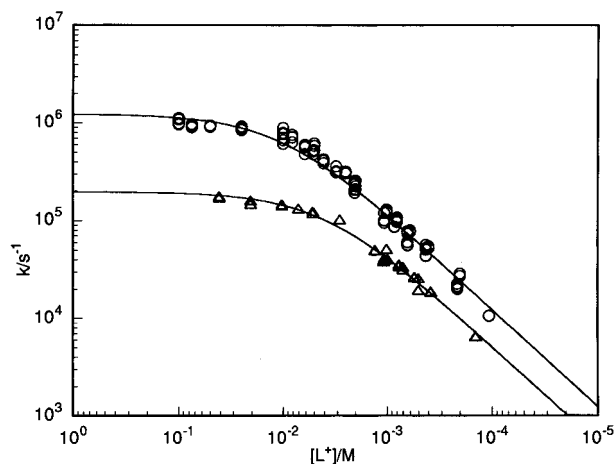
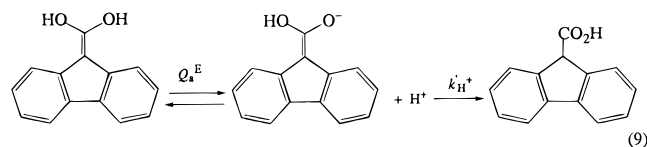


Figure 2. Comparison of rate profiles for the ketonization of fluorene-9-carboxylic acid enol in H₂O (O) and D₂O (Δ) solutions of perchloric acid at 25 °C.

the enol.^{5,6} The corresponding reaction scheme for the present case is shown in eq 9, where ketonization occurs by rate-



determining β -carbon protonation of the more reactive ionized, enolate-ion form. The horizontal regions of the rate profiles then represent reaction starting with un-ionized enol as the initial state, and the diagonal regions that with enolate ion as the initial state. Observed rate constants in the horizontal region are consequently equal to the enol ionization constant times the rate constant for the subsequent step, $k_{\text{obs}} = Q_a^E k'_{H^+}$, whereas those in the diagonal region are equal to the rate constant for the subsequent step alone, $k_{\text{obs}} = k'_{H^+}$. Observed isotope effects in the horizontal region will therefore consist of isotope effects on equilibrium constants times those on rate constants and will thus be greater than observed isotope effects in the diagonal region, which are on rate constants alone.

The rate law that applies to the reaction scheme of eq 9 is shown in eq 10. Least squares fitting of the data using this expression produced the results $Q_a^E = (9.96 \pm 3.30) \times 10^{-3} \text{ M}^{22}$ and $k'_{H^+} = (1.24 \pm 0.03) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$ for H₂O solution, plus D₂O values that gave the isotope effects $k'_{H^+}/k'_{D^+} = 2.38 \pm 0.08$ and $(Q_a^E)_{\text{H}_2\text{O}}/(Q_a^E)_{\text{D}_2\text{O}} = 2.65 \pm 0.21$. Both of these

$$k_{\text{obs}} = \frac{Q_a^E k'_{H^+} [H^+]}{Q_a^E + [H^+]} \quad (10)$$

isotope effects are reasonable values for the processes they represent. Isotope effects on rate-determining hydron transfer to carbon should be in the normal direction ($k_H/k_D > 1$), and those on hydron transfer from hydronium ion should be weaker than those involving other acids because, in addition to their normal primary component, they contain an inverse secondary contribution from the nonreacting bonds of H₃O⁺.¹⁹ The large value of the present rate constant, moreover, implies an unsymmetrical, reactant-like transition state, which will reduce the magnitude of this isotope effect still further.^{19,23} The isotope

(20) Bonneau, R.; Wirz, J.; Zuberbühler, A. D. *Pure Appl. Chem.* **1997**, 69, 979–992.

(21) Loudon, G. M. *J. Chem. Educ.* **1991**, 68, 973–984.

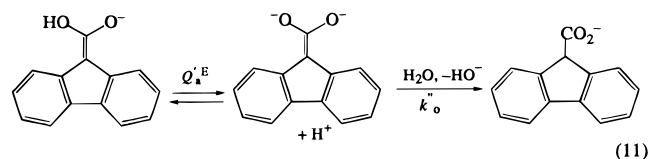
(22) This is a concentration dissociation constant applicable at ionic strength 0.10 M.

(23) Kresge, A. J.; Sagatys, D. S.; Chen, H.-L. *J. Am. Chem. Soc.* **1977**, 99, 7228–7233.

effect on Q_a^E is also consistent with expectation, inasmuch as oxygen acids are less ionized in D_2O than in H_2O and ratios in the vicinity of 3 are not uncommon.^{19,24}

In contrast to these reasonable isotope effects, the alternative assignment of ketene hydration and enol ketonization rate constants, that which avoids crossing of rates at $[H^+] \cong 0.001$ M, produces $(Q_a^E)_H/(Q_a^E)_D = 0.65$. We know of no example of an inverse solvent isotope effect on the ionization of an oxygen acid, and such a value is in fact difficult to rationalize on the basis of solvent isotope effect theory.¹⁹

The second bend in the rate profile for ketonization of fluorene-9-carboxylic acid enol seen in Figure 1 is similar to that shown by enols of other carboxylic acids, where it has been attributed to the second ionization of the enol.^{5,6c} The diagonal portion of slope 1 before this bend may then be assigned to ketonization via β -carbon protonation of the enolate dianion by a water molecule under conditions where the enolate monoanion is the initial state, eq 11. The overall rate of this reaction will



be inversely proportional to hydrogen ion concentration, producing an apparent hydroxide ion catalysis. This catalysis, however, will become saturated when the initial state of the reaction shifts to enolate dianion, and that will give rise to the horizontal portion of the rate profile that appears beyond the second bend.

The rate law that corresponds to this reaction scheme is shown as eq 12. When this expression plus the rate law for the acidic portion of the rate profile (eq 10) were used to analyze the data, it was found that a better fit could be obtained if an additional term, k'_o , was added to include an uncatalyzed reaction at the bottom of the profile near $[H^+] = 10^{-7}$ M.

$$k_{\text{obs}} = \frac{Q_a^E k''_o}{Q_a^E + [H^+]} \quad (12)$$

Least squares fitting of the entire expression gave $k'_{H^+} = (1.25 \pm 0.03) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k'_o = (2.98 \pm 0.47) \times 10^{-1} \text{ s}^{-1}$, $k''_o = (3.22 \pm 0.13) \times 10^{-3} \text{ s}^{-1}$, $Q_a^E = (9.87 \pm 0.53) \times 10^{-3}$ M ($pQ_a^E = 2.01 \pm 0.02$),²² and $Q_a^E = (2.46 \pm 0.29) \times 10^{-10}$ M ($pQ_a^E = 9.61 \pm 0.05$).^{22,25}

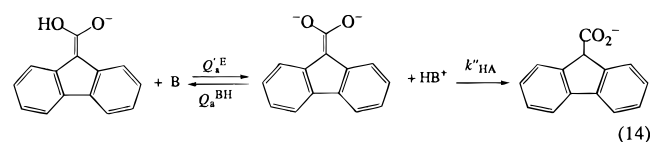
The uncatalyzed region at the bottom of the ketonization rate profile could represent β -carbon protonation of the enolate monoanion by a water molecule, or β -carbon protonation of the enolate dianion by hydrogen ion. The latter mechanism, however, appears unlikely because the rate law that would then apply to this region is $Q_a^E k''_{H^+}$, and the value of k''_{H^+} required by the data is the improbably high rate constant $k''_{H^+} = (1.21 \pm 0.245) \times 10^{11} \text{ M}^{-1} \text{ s}^{-1}$.

In contrast to the weak buffer catalysis found for the hydration of fluorenylidene ketene, buffer catalysis of the ketonization of fluorene-9-carboxylic acid enol was strong, and reliable values of buffer catalytic coefficients could be obtained. These were evaluated as slopes of buffer dilution plots, k_{cat} , and values of k_{cat} determined at several different buffer ratios were then separated into general acid, k_{HA} , and general base, k_{B} , components through the use of eq 13, where f_A is the fraction of buffer

$$k_{\text{cat}} = k_{\text{B}} + (k_{\text{HA}} - k_{\text{B}})f_A \quad (13)$$

present as acid. The data for $H_2PO_4^-/HPO_4^{2-}$ buffers showed both general acid and general base catalysis, in keeping with the fact that these buffers were used in a region where the rate profile showed both acid and base catalysis; least squares analysis gave $k_{\text{HA}} = (3.95 \pm 0.10) \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$ and $k_{\text{B}} = (6.15 \pm 1.05) \times 10^3 \text{ M}^{-1} \text{ s}^{-1}$. The data for NH_4^+/NH_3 buffers, on the other hand, showed only general base catalysis, again in keeping with the fact that these buffers were used in a more basic region of the rate profile where only base catalysis occurred; least squares analysis gave $k_{\text{HA}} = (1.49 \pm 2.07) \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$ and $k_{\text{B}} = (6.26 \pm 0.27) \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$.²⁶

These general acid catalytic coefficients refer to direct β -carbon protonation of the enolate monoanion by the acid involved; *i.e.*, for $H_2PO_4^-$, $k_{\text{HA}} = k'_{\text{HA}}(H_2PO_4^-)$.²⁵ The general base catalytic coefficients, on the other hand, may be assigned to a reaction mechanism where the base involved first removes the remaining oxygen-bound proton from enolate monoanion in a rapidly established equilibrium, and the enolate dianion and general base conjugate acid thus produced then react by rate-determining proton transfer to β -carbon, eq 14. This leads



to the expression $k_{\text{B}} = Q_a^E k''_{\text{HA}}/Q_a^{BH}$, from which values of k''_{HA} , the rate constant for general acid, β -carbon protonation of the enolate dianion may be calculated. The results so obtained are $k''_{\text{HA}}(H_2PO_4^-) = (4.14 \pm 0.86) \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$ and $k''_{\text{HA}}(NH_4^+) = (1.30 \pm 0.16) \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$.²⁵

The pattern of values that these rate constants furnish provides support for the reaction schemes involved. The value of $k''_{\text{HA}}(H_2PO_4^-)$ is considerably greater than that of $k'_{\text{HA}}(H_2PO_4^-)$, consistent with the expected greater reactivity of the dianion to electrophilic reagents, and the value of $k''(H_2PO_4^-)$ is also greater than that of $k''(NH_4^+)$, consistent with the greater acid strength of $H_2PO_4^-$.

Further support for these reaction schemes comes from additional isotope effects determined in basic solutions. These isotope effects are based upon additional rate measurements made in D_2O solutions of sodium hydroxide, at the concentration $[NaOD] = 0.001$ M, and also in D_2O solutions of ammonium ion buffers at a single buffer ratio. The data so obtained are summarized in Tables S6 and S7.¹³

In these basic solutions, the deuterium analog of eq 12 applies. The average of the rate constants determined in sodium hydroxide solution plus the average intercept of the ammonium ion buffer dilution plot then provides values of k_{obs} at two different values of $[D^+]$, from which $(k''_o)_{D_2O} = (4.56 \pm 1.24) \times 10^2 \text{ s}^{-1}$ and $(Q_a^E)_{D_2O} = (7.37 \pm 1.43) \times 10^{-11}$ M, $p(Q_a^E)_{D_2O} = 10.13 \pm 0.08$,²² may be calculated. The slope of the buffer dilution plot leads to the additional result $k''_{\text{DA}}(ND_4^+) = (1.16 \pm 0.23) \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$. Calculation of these results used literature values of the solvent isotope effect on the autoprotolysis constant of water²⁷ and that on the acid ionization

(25) Primed symbols are used for reactions of the monoanion and doubly primed symbols for those of the dianion.

(26) These results refer to reactions beginning with enolate monoanion as the initial state; values of k_{cat} were corrected to account for small quantities of dianion present in some of the buffer solutions.

(27) Covington, A. K.; Robinson, R. A.; Bates, R. G. *J. Phys. Chem.* **1966**, *70*, 3820–3824. Gold, V.; Lowe, B. M. *J. Chem. Soc. A* **1967**, 936–943.

(24) Laughton, P. M.; Robertson, R. E. In *Solute-Solvent Interactions*; Coetzee, J. F., Ritchie, C. D., Eds.; Marcel Dekker: New York, 1969; Chapter 7.

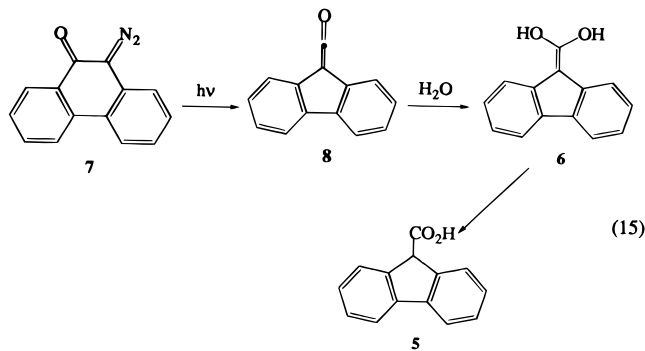
of ammonium ion.²⁸ Combination of these results with their H₂O counterparts gives the isotope effects (Q_a^E)_{H₂O}/(Q_a^E)_{D₂O} = 3.34 ± 0.76, (k''_o)_{H₂O}/(k''_o)_{D₂O} = 7.07 ± 1.94, and $k''_{HA}(\text{NH}_4^+)/k''_{HA}(\text{ND}_4^+) = 11.2 ± 2.6$.

These isotope effects agree well with values expected for the processes they represent. The effect on the second ionization of the enol is near 3, which is typical for the ionization of oxygen acids.²⁴ It is significant, moreover, that this isotope effect is stronger than that on the first ionization of the enol, (Q_a^E)_{H₂O}/(Q_a^E)_{D₂O} = 2.65, for isotope effects on the ionization of structurally similar acids generally increase with decreasing acid strength.²⁹ The two kinetic isotope effects are also as expected. They are both in the normal direction ($k_H/k_D > 1$), as they should be for rate-determining hydron transfer to carbon. They are also both quite large, which implies that they refer to reactions with central, fairly symmetrical transition states; application of Marcus theory relationships governing variation in the magnitude of isotope effects with transition state structure^{23,30} confirms this, suggesting that both of these isotope effects lie within 90% of their maximum possible value.

Enolization of Acid. Rates of enolization of fluorene-9-carboxylic acid were measured in aqueous sodium hydroxide solutions over the concentration range 0.02–0.10 M. The data are summarized in Table S8.¹³ Observed first-order rate constants were accurately proportional to hydroxide ion concentration, and linear least squares analysis gave the hydroxide ion catalytic coefficient, $k^E_{\text{HO}^-} = (2.88 ± 0.05) × 10^{-1} \text{ M}^{-1} \text{ s}^{-1}$.

Discussion

Reaction Scheme. We have found that flash photolysis of 10-diazo-9(10*H*)-phenanthrenone, **7**, in aqueous solution gives fluorene-9-carboxylic acid, **5**, as the major product via two transient intermediate species which we have identified as fluorenylidene ketene, **8**, and the enol of fluorene-9-carboxylic acid, **6**, eq 15. Identification of these intermediates is based upon a number of pieces of evidence.



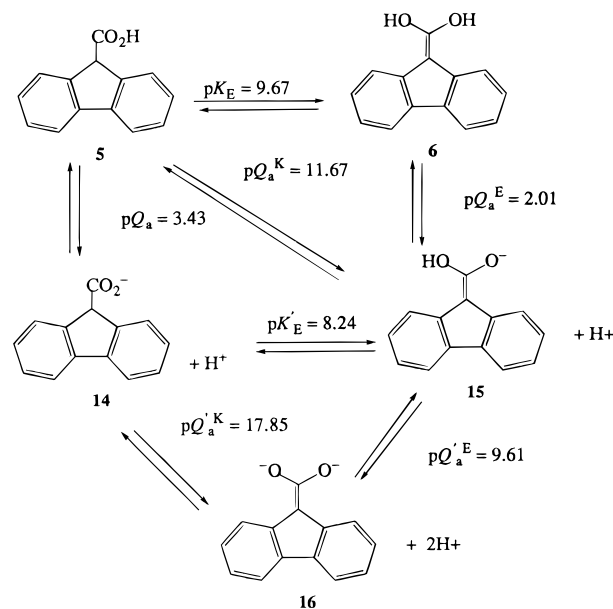
Conversion of the first transient into the second gives a rate profile typical of aromatic ketene hydration, *e.g.*, a long region of uncatalyzed reaction accompanied by weak hydroxide ion catalysis and no acid catalysis. The uncatalyzed reaction shows only a weak solvent isotope effect in the normal direction ($k_H/k_D > 1$), consistent with the fact that uncatalyzed ketene hydration involves nucleophilic attack by a water molecule with some weakening but no breaking of hydrogen–oxygen bonds. This intermediate also reacts only weakly with ammonium ion/

(28) Salomaa, P.; Schaleger, L. L.; Long, F. A. *J. Phys. Chem.* **1964**, *68*, 410–411.

(29) Bell, R. P. *The Proton in Chemistry*; Cornell University Press: Ithaca, NY, 1959; pp 187–189.

(30) Kresge, A. J. In *Isotope Effects on Enzyme-Catalyzed Reactions*; Cleland, W. W.; O'Leary, M. H.; Northrop, D. B., Eds.; University Park Press: Baltimore, MD, 1977; pp 37–63. Kresge, A. J. *J. Am. Chem. Soc.* **1980**, *102*, 7797–7798.

Scheme 1



ammonia buffers, again as expected from the nucleophilic nature of this reaction and the steric hindrance to such a process offered by the fluorenylidene group. The overall rates of these reactions are nevertheless high in comparison to other structurally related ketenes, again as expected because of the special ability of the fluorenylidene nucleus to stabilize the negative charge generated on the substrate by nucleophilic attack.

Disappearance of the second transient gives a rate profile different from the first, but one that is typical of enol ketonizations. In particular, it shows two bends, identified as first and second ionizations of fluorene-9-carboxylic acid enol by the fact that they produce sizable solvent isotope effects whose absolute as well as relative magnitudes are typical of oxygen acid ionization. Rate constants in various parts of this rate profile, assigned to ketonization of fluorene-9-carboxylic acid enol through rate-determining β -carbon protonation of the enolate mono- or dianion by either hydrogen ion or water, also show solvent isotope effects whose various magnitudes are completely consistent with isotope effect theory. Disappearance of this second transient is also strongly catalyzed by buffers, and analysis of the catalysis shows it to be of the general acid type; this again is typical of ketonization reactions and is wholly expected on the basis of their rate-determining proton-transfer nature.

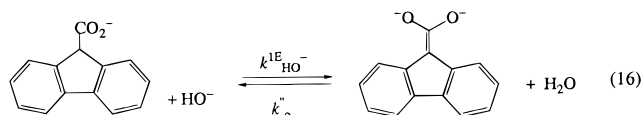
These arguments, elaborated in the preceding section where the experimental data upon which they are based are presented, leave little doubt that the transient species observed in these flash photolysis experiments are fluorenylidene ketene and fluorene-9-carboxylic acid enol.

Determination of Equilibrium Constants. The keto–enol system of a simple monofunctional carboxylic acid consists of five species, the un-ionized and ionized forms of the acid and the un-ionized, monoionized, and diionized forms of the enol, as illustrated in Scheme 1 for the present case. Some of the equilibrium constants connecting these various species have already been evaluated, from the ketonization rate profile and by measurement of the ionization constant of fluorene-9-carboxylic acid.³¹ The rest can be determined in the following way.

As eq 16 shows, fluorene-9-carboxylate ion and its enolate dianion are interconverted by reaction of the carboxylate ion

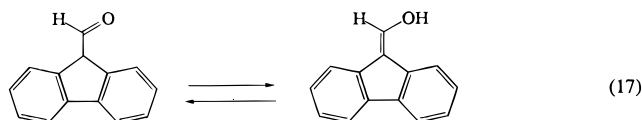
(31) Kresge, A. J.; Pojarlieff, I. G.; Rubinstein, E. M. *Can. J. Chem.* **1993**, *71*, 227–229.

with hydroxide ion and reaction of the enolate dianion with water. Rate constants for both of these reactions have been



determined here, and their ratio can therefore be used to provide a value of the equilibrium constant, Q_a^K for the overall process: $Q_a^K = (1.42 \pm 0.06) \times 10^{-18}$ M, $pQ_a^K = 17.85 \pm 0.02$.²² This equilibrium constant can then be used in conjunction with Q_a^E , evaluated from the ketonization rate profile, to calculate K'_E , which is the third member of the triangular cycle that makes up the lower part of Scheme 1. This gives $K'_E = (5.75 \pm 0.72) \times 10^{-9}$, $pK'_E = 8.24 \pm 0.06$. Knowledge of K'_E , together with Q_a^{31} and Q_a^E (rate profile) then allows evaluation of K_E as $K_E = (2.15 \pm 0.31) \times 10^{-10}$, $pK_E = 9.67 \pm 0.06$, and once all four legs of the upper square in Scheme 1 are known, the diagonal Q_a^K can be calculated as $Q_a^K = (2.13 \pm 0.32) \times 10^{-12}$ M, $pQ_a^K = 11.67 \pm 0.06$.²²

Comparison with Other Systems. The present results show the enol content of fluorene-9-carboxylic acid to be remarkably large for a carboxylic acid keto-enol system. The keto-enol equilibrium constant for acetic acid, the prototype carboxylic acid, has not been determined experimentally, but reliable estimates have recently been made by several different methods which give consistent results and put the value at $pK_E = 20$.³² This is 10 orders of magnitude less than the presently determined equilibrium constant, $pK_E = 9.67$. This large difference is of course due to the fact that the enolization of fluorene-9-carboxylic acid places a double bond exocyclic to a cyclopentadienyl ring, which creates fulvenoid resonance. A similar enol-content-enhancing effect has been found for simple aldehydes and ketones.³³ In the case of 9-formylfluorene, eq 17, for



example, the enol is actually the more stable isomer, and with $pK_E = -1.22$, the enol content in this system is 7 orders of magnitude greater than that of acetaldehyde ($pK_E = 6.23$).⁹

The enol of fluorene-9-carboxylic acid is also a remarkably strong acid. With $pQ_a^E = 2.01$, it is more acidic than most carboxylic acids, and it is in fact a stronger acid than the carboxylic acid group of its keto isomer, for which $pQ_a = 3.43$. A comparison with acetic acid enol is again instructive. The acidity of this enol has also not been measured experimentally, but $pQ_a^E = 7$ has recently been estimated for the enol of ethyl acetate,³⁴ and the fact that the acidities of the enols of methyl mandelate and mandelic acid are closely similar, $pQ_a^E = 6.45$ ^{12a} and 6.62 ,^{6a} respectively, suggests that $pQ_a^E = 7$ is a good estimate for acetic acid as well. The enol of fluorene-9-carboxylic acid is 5 orders of magnitude more acidic than this. The difference, of course, is due to the fact that the negative charge of the enolate ion produced upon ionization of the enol of fluorene-9-carboxylic acid can be delocalized into the five-membered ring, thus creating an aromatic cyclopentadienyl

(32) Guthrie, J. P. *Can. J. Chem.* **1993**, *71*, 2123–2128. Guthrie, J. P.; Liu, Z. *Can. J. Chem.* **1995**, *73*, 1395–1398.

(33) Harcourt, M. P.; More, O'Ferrall, R. A. *J. Chem. Soc., Perkin Trans. 2* **1995**, 1415–1425.

(34) Amyes, T. L.; Richard, J. P. *J. Am. Chem. Soc.* **1996**, *118*, 3129–3141.

Table 1. Summary of Rate and Equilibrium Constants for the Fluorenylidene-ketene and Fluorene-9-carboxylic Acid Systems^a

Process	Constant
	$k_o = 1.07 \times 10^5 \text{ s}^{-1}$
	$k_{HO^-} = 3.47 \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$
	$k^E_{HO^-} = 2.88 \times 10^{-1} \text{ M}^{-1} \text{ s}^{-1}$
	$k^E_{H^+} = 1.25 \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$; $k^E_{H^+}/k^E_{D^+} = 2.38$
	$k^o_o = 3.0 \times 10^1 \text{ s}^{-1}$
	$k^o_o = 3.22 \times 10^3 \text{ s}^{-1}$; $(k^o_o)_{H_2O}/(k^o_o)_{D_2O} = 7.1$
	$k^E_{HA} = 1.49 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$
	$k^E_{HA} = 4.14 \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$
	$k^E_{HA} = 1.30 \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$
	$k^E_{HA}/k^E_{DA} = 11.2$
	$Q_a = 3.70 \times 10^{-4} \text{ M}$; $pQ_a = 3.43$
	$K_E = 2.15 \times 10^{-10}$; $pK_E = 9.67$
	$K'_E = 5.75 \times 10^{-9}$; $pK'_E = 8.24$
	$Q_a^E = 9.87 \times 10^{-3} \text{ M}$; $pQ_a^E = 2.01$
	$(Q_a^E)_{H_2O}/(Q_a^E)_{D_2O} = 2.65$
	$Q_a^E = 2.46 \times 10^{-10} \text{ M}$; $pQ_a^E = 9.61$
	$(Q_a^E)_{H_2O}/(Q_a^E)_{D_2O} = 3.34$
	$Q_a^K = 2.13 \times 10^{-12} \text{ M}$; $pQ_a^K = 11.67$
	$Q_a^K = 1.42 \times 10^{-18} \text{ M}$; $pQ_a^K = 17.85$

^a Aqueous solution, 25 °C, ionic strength 0.10 M.

Table 2. Comparison of Equilibrium Constants for Some Reactions of Carboxylic Acid Enols^a

Constant					
pK_E	9.7	9.3	8.4 ^d	7.2	15.4
pK'_E	8.2	6.6	5.0 ^d	6.5	-
pQ_a^E	2.0	1.9	1.3	1.0	6.6
pQ_a^E	9.6	8.3	8.7 ^d	8.7	-
pQ_a^K	11.7	11.2	9.7	8.2	22.0
pQ_a^K	17.9	15.2	13.7	15.2	-

^a Aqueous solution, 25 °C, ionic strength 0.10 M. ^b Reference 5b.

^c Reference 5a. ^d Revised value provided by Professor Wirz. ^e Reference 6c. ^f Reference 6a.

anion. This ability of the cyclopentadienyl group to stabilize a negative charge is aptly illustrated by the unusual carbon acidity of cyclopentadiene itself: $pK_a = 16$.³⁵

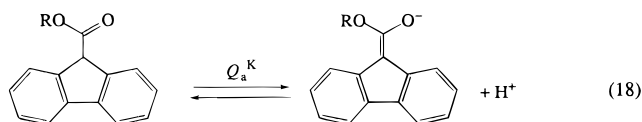
As the data summarized in Table 2 show, this ability of the cyclopentadienyl group to stabilize enols and enolate ions is apparent also in the indenecarboxylic acid system and in cyclopentadienecarboxylic acid itself. The effects, in fact, grow progressively stronger as the benzo groups are removed. This,

(35) Streitwieser, A.; Nebenzahl, L. L. *J. Am. Chem. Soc.* **1976**, *98*, 2188–2190.

of course, is to be expected, for benzo substitution will reduce the resonance energy of the cyclopentadienyl ring, as evidenced, for example, by the lower acidity of fluorene ($pK_a = 22.6$)³⁶ than that of indene ($pK_a = 20.1$).³⁶

The data of Table 2 also show that the combined effects of the phenyl and cyano groups in the enol of phenylcyanoacetic acid, **17**, are just about as effective in stabilizing enols and enolate ions as are the cyclopentadienyl groups in the enols of fluorene-9-carboxylic acid, indenecarboxylic acid, and cyclopentadienecarboxylic acid. The stabilization provided by the phenyl and hydroxyl groups in the enol of mandelic acid, **18**, however, is considerably less strong, which shows that a cyano group is much better than a hydroxyl group in enhancing enol content and increasing enol acidity.

It is interesting that the acidity of fluorene-9-carboxylic acid ionizing as a carbon acid, eq 18, $R = H$, $pQ_a^K = 11.67$, is practically the same as that of its methyl ester, eq 18, $R = Me$,



$pQ_a^K = 11.52$.³⁷ This, coupled with the expectation that

acidities of carboxylic acid and ester enols ionizing as oxygen acids might be similar as well, based upon the close similarity of Q_a^E for mandelic acid and methyl mandelate mentioned above, suggests, by virtue of the relationship $pQ_a^K = pK_E + pQ_a^E$, that enol contents of carboxylic acids and their esters might be similar also. Carboxylic acids could therefore serve as useful surrogates for esters in studies of enol chemistry; this would be especially advantageous in the case of investigations conducted in aqueous solution, where hydrolysis of the ester is often a troublesome competing reaction.³⁴

Acknowledgment. We are grateful to the Natural Sciences and Engineering Research Council of Canada and the United States National Institutes of Health for financial support of this research.

Supporting Information Available: Tables S1–S8 of rate data (15 pages). See any current masthead page for ordering and Internet access instructions.

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(36) Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456–463.

(37) Chiang, Y.; Jones, J., Jr.; Kresge, A. J. *J. Am. Chem. Soc.* **1994**, *116*, 8358–8359.