Ketonization of the remarkably strongly acidic elongated enol generated by flash photolytic decarboxylation of *p*-benzoylphenylacetic acid in aqueous solution†

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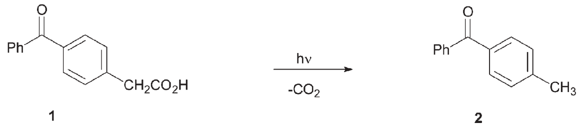
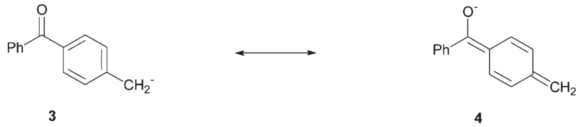
Photodecarboxylation of *p*-benzoylphenylacetic acid in aqueous solution produces the elongated enol 5, whose strength as an oxygen acid ($pQ_a^E = 7.67$) makes it more acidic than simple enol analogs by several orders of magnitude.

Photodecarboxylation of *p*-benzoylphenylacetic acid, **1**, is an efficient reaction that gives *p*-methylbenzophenone, **2**, as its product when carried out in aqueous solution, eqn (1).[1]



(1)

This product is formed through a carbanion intermediate whose negative charge is delocalized from methylene carbon, **3**, onto carbonyl oxygen, **4** eqn (2); product formation could therefore occur either by direct protonation of methylene carbon, eqn (3), or by protonation of carbonyl oxygen, eqn (4), to give an elongated enol, **5**, whose ketonization would afford the observed product. We have carried out this photodecarboxylation flash photolytically and have detected a short-lived transient species, which we have identified as enol **5**. This elongated enol has proved to be an unusually strongly acidic oxygen acid, several orders of magnitude more acidic than other simple enol analogs without the elongating cyclohexadienyl spacer.



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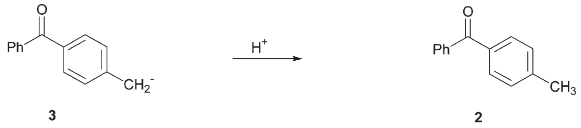

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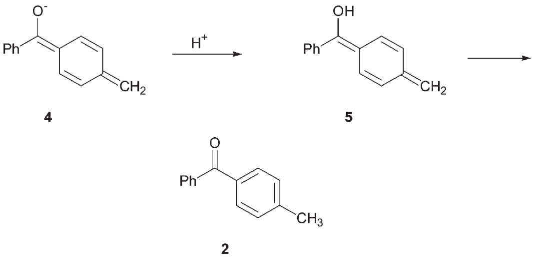

(4)

We found that flash photolyis of *p*-benzoylphenylacetic acid in aqueous solution, using either a conventional flash lamp (microsecond) system[2] or an eximer laser (nanosecond) system[3] operating at $\lambda_{exc} = 248$ nm, produces a transient species with broad absorbance centered at $\lambda = 370$ nm. Rates of decay of this transient were determined by monitoring the disappearance of this absorbance at $\lambda = 370$ nm and also at $\lambda = 320$ nm; identical results were obtained at the two wavelengths. Rate measurements were made in aqueous perchloric acid and sodium hydroxide solutions and also in acetic acid, biphosphate ion, and tris-(hydroxymethyl)-methaneammonium ion buffers using H_2O as the solvent; some measurements were made as well in perchloric acid, sodium hydroxide, and biphosphate ion solutions using D_2O as the solvent. The ionic strength of all solutions was kept constant at 0.10 M with sodium perchlorate as the inert electrolyte. The data so obtained conformed to the first-order rate law well, and observed first-order rate constants, k_{obs}, were obtained by least squares fitting of a single exponential function. The results are summarized in Tables S1–S3.[4,5]

The measurements in buffers were made in series of solutions of constant buffer ratio, and therefore constant hydronium ion concentration, but varying total buffer concentration. Buffer catalysis was strong, with observed rate constants within a given buffer solution series accurately proportional to buffer concentration; the data were therefore analyzed by least squares fitting of the linear buffer dilution expression shown as eqn (5). The zero-buffer concentration intercepts, k_{int},obtained in this way, plus the rate constants determined in perchloric acid and sodium hydroxide solutions, are displayed as the rate profiles shown in Fig. 1.

$$k_{obs} = k_{int} + k_{buff}[\text{buffer}] \tag{5}$$

The shape of these rate profiles is characteristic of enol ketonization reactions, which are known to occur by rate-determining β-carbon hydronation of either the enol or its enolate ion by any available acid.[6] Because these profiles refer to solvent-related species, the available acids will be either the hydronium ion,

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† Electronic supplementary information (ESI) available: Tables S1–S3 of rate data. See http://dx.doi.org/10.1039/b506706e

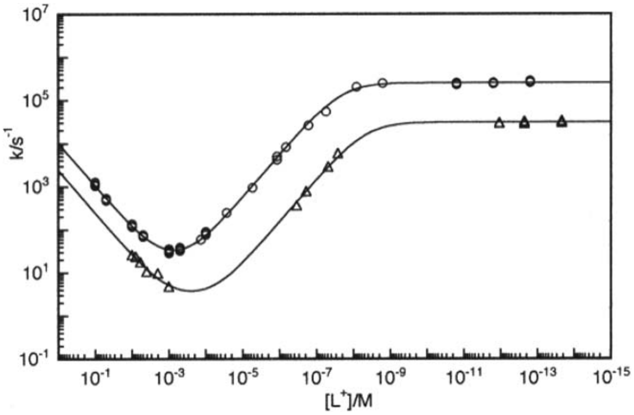
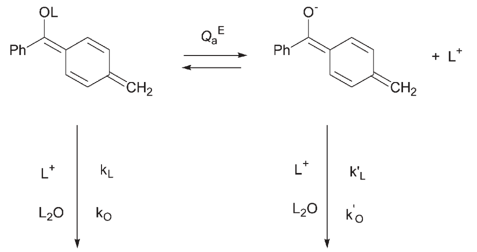


Fig. 1 Rate profiles for the ketonization of elongated enol **5** in H_2O (○) and D_2O (△) solutions.

written here as L^+,[7] or a solvent water molecule, L_2O, as shown in eqn (6). The acid-catalzyed, descending, diagonal portions at the high acidity end of these profiles then represent β-carbon hydronation of the enol by hydronium ion. These sections are followed by short "uncatalyzed" horizontal portions, which could be due either to β-carbon hydronation of enol by solvent water, or to ionization of the enol to enolate and hydronium ions followed by β-carbon hydronation of the enolate ion by hydronium ion. This latter process generates hydronium ions in its rapid pre-equilibrium ionization step and then uses them up in its rate-determining step, to give a reaction independent of hydronium ion concentration.



(6)

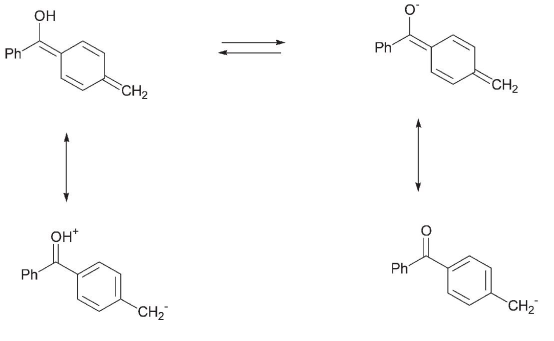
These short horizontal sections are followed by base-catalzyed, ascending, diagonal portions that can be assigned to ionization of enol to enolate ion followed by β-carbon hydronation of enolate by solvent water. This process produces hydronium ions in its rapid pre-equilibrium step but does not use them up in its rate-determining step, to give an overall reaction whose rate is inversely proportional to hydronium ion concentration and has the appearance of hydroxide ion catalysis. Finally, at sufficiently low acidity, the position of the enol–enolate equilibrium shifts over to the side of the enolate ion, and the process reduces to simple hydronation of enolate β-carbon by solvent water. This gives the final horizontal rate profile plateau.

The rate law that applies to this reaction scheme is shown as eqn (7), where k_{uc} is used to designate the process of uncertain mechanism represented by the central short horizontal sections of the rate profiles and the other rate and equilibrium constants are defined by eqn (6). Least squares fitting using this expression gave, for H_2O solutions: $k_H = (1.03 \pm 0.02) \times 10^4$ M^{-1} s^{-1}, $k_{uc} = (1.87 \pm 0.09) \times 10^1$ s^{-1}, $Q_a^E = (2.14 \pm 0.08) \times 10^{-8}$ M,[8] p$Q_a^E = 7.67 \pm 0.04$,[8] and $k'_o = (2.52 \pm 0.05) \times 10^5$ s^{-1}, plus results for D_2O solution which, when combined with their H_2O counterparts, gave the isotope effects: $k_H/k_D = 4.27 \pm 0.32$, $(k_{uc})_H/(k_{uc})_D = 7.27 \pm 1.50$, $(Q_a^E)_H/(Q_a^E)_D = 4.50 \pm 0.31$, and $(k'_o)_H/(k'_o)_D = 8.20 \pm 0.25$. The lines through the data shown in Fig. 1 were drawn using these results. It may be seen that the data fit the reaction scheme of eqn (6) very well and thus provide strong evidence that the process under observation is an enol ketonization reaction.

$$k_{obs} = k_L[L^+] + k_{uc} + k'_o Q_a^E/(Q_a^E + [L^+]) \qquad (7)$$

Further support for assignment of the rate profiles of Fig. 1 to enol ketonzation comes from the isotope effects obtained by comparing results determined in H_2O with those made in D_2O. The rate constants k_L and k'_o refer to rate-determining substrate hydronation, and isotope effects on these quantities can therefore be expected to contain primary isotope effect components in the normal direction ($k_H/k_D > 1$) of appreciable magnitude. These isotope effects, however, will also contain secondary components, with that on k_L in the inverse direction ($k_H/k_D < 1$) and that on k'_o in the normal direction ($k_H/k_D > 1$).[9] This will make the isotope effect on k'_o considerably greater than that on k_L, which is nicely consistent with our observation: $(k'_o)_H/(k'_o)_D = 8.2$ and $k_H/k_D = 4.3$. The isotope effect on Q_a^E is also consistent with this quantity being the acidity constant of an enol ionizing as an oxygen acid. Such equilibrium isotope effects lie in the normal direction and generally fall in the range 3–5;[10] that, of course agrees well with the observed value $(Q_a^E)_H/(Q_a^E)_D = 4.5$.

The present results show the elongated enol **5**, with p$Q_a^E = 7.67$, to have an unusually strongly acidic hydroxyl group: simple enols ionizing as oxygen acids usually have acidity constants in the range p$Q_a^E = 10$–11.[6] An especially apt comparison of the present system can be made with the enol of acetophenone, **6**, which lacks the elongating cyclohexadienyl spacer of enol **5**: acetophenone enol has p$Q_a^E = 10.40$,[11] nearly three pK units weaker than the acidity constant of enol **5**. This striking difference is a result of the fact that ionization of elongated enol **5** creates an anion whose negative charge can be delocalized from enolate oxygen onto methylene carbon, eqn (8); this converts a cyclohexadienyl moiety into a benzene ring and thus benefits from a gain in benzene resonance energy. A similar shift of negative charge density is of course possible in the unionized enol, but that involves generation of charge and is consequently not as energetically advantageous. The anion is consequently stabilized more than the unionized enol, and that reduces the energy gap between enol and enolate ion making the enol a stronger acid than it would otherwise be.



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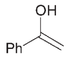

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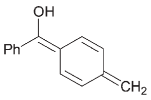

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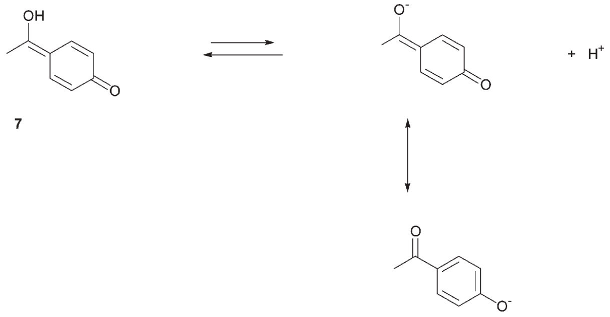
A similar argument may be made justifying the enhanced acidity of enol **7**, eqn (9), for which the estimate pK_a = −8 has been made.[12] In this case, however, the effect is much stronger than for enol **5**, because the oxygen atom onto which negative charge is delocalized is a much better negative charge acceptor than is a methylene group.



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Notes and references

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4 See supporting information†.
5 In perchloric acid solutions the absorbance from the transient species of interest here diminished as the acid concentration increased, consistent with decarboxylation occurring through the carboxylate ion form of the substrate, and HPLC analysis showed the formation of other (uninvestigated) products. These interferences could be diminished somewhat by using deoxygenated solutions and accumulating data from several replicate flash photolysis shots.
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