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SOLVENT AND SECONDARY SUBSTRATE ISOTOPE EFFECTS ON THE ACID-CATALYZED KETONIZATION OF ACETOPHENONE ENOL IN AQUEOUS SOLUTION

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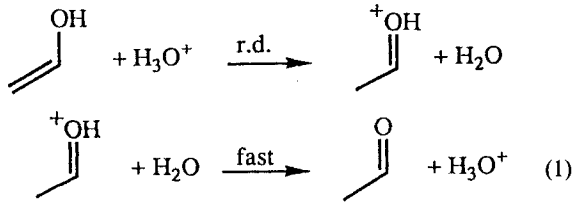
The enol of acetophenone was generated flash photolytically in aqueous solution by photosolvolysis of PhCBr=CH$_2$ and photohydration of PhC≡CH and PhC≡CD, and rates of its ketonization were measured in dilute perchloric acid solutions in H$_2$O and D$_2$O at 25 °C. The rate constants so obtained provide the solvent isotope effects, $k_{H^+}/k_{D^+} = 5{\cdot}02 \pm 0{\cdot}08$, and the secondary isotope effect for deuterium substitution at the β-position of the enol double bond, $(k_H/k_D)_\beta = 0{\cdot}999 \pm 0{\cdot}014$. Arguments are presented which show that these isotope effects requre a stepwise rather than a concerted mechanism for the ketonization reaction.

INTRODUCTION

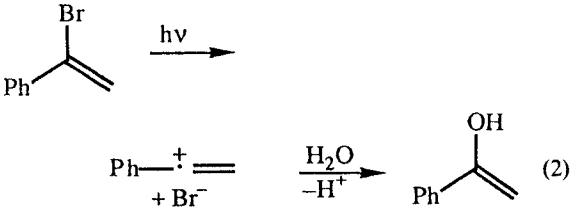
The ketonization of simple enols catalyzed by the hydronium ion is believed to occur by a stepwise mechanism involving rate-determining protonation of the enol at β-carbon followed by rapid proton loss from the hydroxyl group of the hydroxycarbocationic intermediate:[1]



(1)

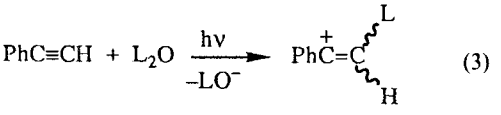
This mechanism is based in part on the magnitude of solvent isotope effects on the reaction, but that information has so far been lacking for the enol of the prototype aromatic ketone, acetophenone. We have therefore now determined k_{H^+}/k_{D^+} for the ketonizaton of acetophenone enol and, in the course of so doing, we have also evaluated secondary substrate isotope effects that are of mechanistic interest.

We generated the enol of acetophenone for this purpose flash photolytically in wholly aqueous solution using two different photochemical reactions: photosolvolysis of α-bromostyrene and photohydration of phenylacetylene. The first of these produces a vinyl cation[2] which gives the enol on hydration:[3]



(2)

and comparison of rates of ketonization in H$_2$O and D$_2$O solutions gave the hydronium-ion isotope effect, k_{H^+}/k_{D^+}. Photohydration of phenylacetylene also produces a vinyl cation, but this cation, unlike that obtained by photosolvolysis, contains a solvent-derived hydrogen in its methylene group because it is formed by protonation of acetylenic carbon:[4]



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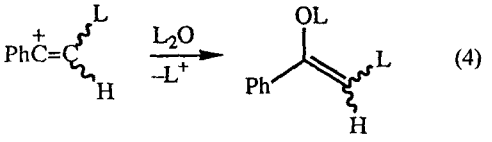
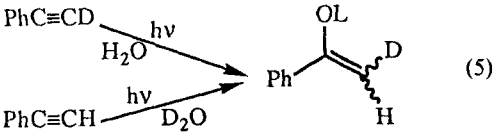
The enol produced by hydration of this cation therefore also contains a solvent-derived hydrogen in its methylene group:



(4)

Comparison of rates of ketonization of enols produced in this way in H_2O and D_2O then gives an isotope effect that includes a substrate β-deuterium effect, $(k_H/k_D)_\beta$, in addition to the hydronium-ion rate ratio, k_{H^+}/k_{D^+}.

We were able to remove this secondary effect, and to determine it as well, by working with phenylacetylene-d_1, PhC≡CD, in addition to the all-protio isotoplog, PhC≡CH. Because protonation of the triple bond is rate determining,[4a] photohydration of acetylenes introduces only one solvent-derived hydrogen into the enol obtained by this reaction. Photohydration of PhC≡CD in H_2O and PhC≡CH in D_2O then produce the same enol:



(5)

and comparison of rates of hydronium ion-catalyzed ketonization of this enol in these solvents consequently gives k_{H^+}/k_{D^+} free of any substrate secondary effects. The secondary effect can of course be evaluated by using PhC≡CH and PhC≡CD to generate enols in the same solvent: in H_2O this provides a comparison of PhC(OH)=CH_2 with PhC(OH)=CHD, and in D_2O a comparison of PhC(OH)=CHD with PhC(OH)=CD_2.

EXPERIMENTAL

Materials. Phenylacetylene-d_1 was prepared by treating phenylacetylene with methyllithium and then decomposing the lithium acetylide so obtained with D_2O. It was purified by distillation and the ^1H NMR spectrum of the distillate showed its deuterium content at the labelled position to be greater than 99%. All other materials were of the best available commercial grades.

Kinetics. Acetophenone enol was generated in a conventional flash photolysis apparatus that has already been described,[5] and rates of ketonization were measured by monitoring the decrease of enol absorption at 270 nm. The temperature of the reaction mixtures was maintained at 25·0 ± 0·05 °C. The data obtained obeyed the first-order rate law well, and observed first-order rate constants were calculated by least-squares fitting to an exponential function.

RESULTS

Rates of ketonization of acetophenone enol were measured in H_2O and D_2O solutions of perchloric acid over the concentration range 0·010–0·10 M; the ionic strength of these solutions was maintained at 0·10 M with $NaClO_4$. Six series of measurements were made using the three enol precursors, PhCHBr=CH_2, PhC≡CH, and PhC≡CD, each in H_2O and in D_2O. In each case, the entire perchloric acid concentration range from 0·01 to 0·1 M was covered using 6–11 separate concentrations, and replicate determinations were made at each concentration; the number of separate determinations of k_{obs} in a set of measurements varied from 48 to 112. These data are summarized in supplementary tables which are available from the authors on request. measurements proved to be linear functions of perchloric acid concentration, and bimolecular hydronium-ion catalytic coefficients were evaluated by linear least-squares analysis. The results obtained are summarized in Table 1.

Two of the systems listed in Table 1 (1 and 3) produced the same enol, PhCH(OH)=CH_2, in the same solvent, H_2O, albeit from different precursours. The two catalytic coefficients obtained, $k_{H^+} = 1255 \pm 15$ and $1244 \pm 17\ l\,mol^{-1}\,s^{-1}$, are nicely consistent with one another, as expected, and their weighted average, $k^+ = 1250 \pm 11\ l\,mol^{-1}\,s^{-1}$, is in excellent agreement with a previous determination[6] of this rate constant, $k^+ = 1250 \pm 20\ l\,mol^{-1}\,s^{-1}$.

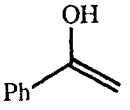
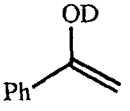
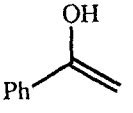
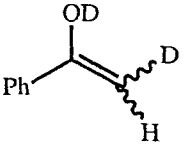
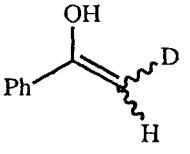
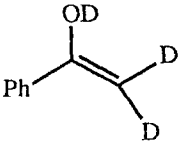
DISCUSSION

Solvent isotope effect

The measurements made here provide two separate determinations of the solvent isotope effect on the ketonization of acetophenone enol catalyzed by the hydronium ion: $k_{H^+}/k_{D^+} = 5·15 \pm 0·11$ based on enol obtained from the photosolvolysis of α-bromostyrene (Table 1, systems 1 and 2) and $k_{H^+}/k_{D^+} = 4·88 \pm 0·12$ based on enol obtained from the photohydration of phenylacetylene (Table 1, systems 5 and 4). These two values are consistent with one another; their weighted average is $k_{H^+}/k_{D^+} = 5·02 \pm 0·08$.

This is a large value for this kind of isotope effect,[7] and it consequently provides clear evidence that the ketonization of acetophenone enol occurs by rate-determining proton transfer from the hydronium ion to the enol. This, of course, is consistent with the stepwise mechanism of equation (1), but it is also consistent with a concerted mechanism in which proton transfer to the substrate and proton removal from its hydroxyl group

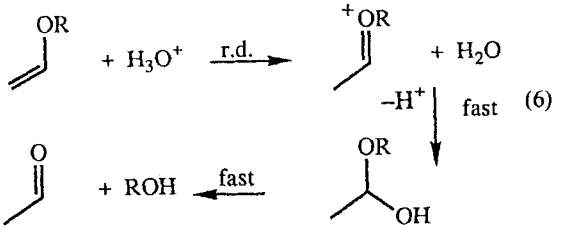
Table 1. Summary of hydronium-ion catalytic coefficients for the ketonization of acetophenone enol in aqueous perchloric acid solutions at 25 °C[a]

System	Enol precursor	Solvent	Enol	k_{L^+} (l mol^{-1} s^{-1})
1	PhCHBr=CH$_2$	H$_2$O		1255 ± 15
2	PhCHBr=CH$_2$	D$_2$O		243·5 ± 4.4
3	PhC≡CH	H$_2$O		1244 ± 17
4	PhC≡CH	D$_2$O		260·8 ± 4·9
5	PhC≡CD	H$_2$O		1272 ± 20
6	PhC≡CD	D$_2$O		252.7 ± 3.5

[a] Ionic strength = 0·10 M (NaClO$_4$).

occur in a single reaction step. Such a concerted mechanism has in fact recently been advocated for the ketonization of simple enols.[8]

The arguments recently advanced for the concerted mechanism are based on differences in reaction characteristics between enol ketonization and the hydrolysis of corresponding enol ethers. The hydrolysis of enol ethers is like the ketonization of simple enols in that it too occurs by rate-determining proton transfer to β-carbon:



(6)

but in this case this proton transfer cannot be concerted with proton removal from hydroxylic oxygen for enol ethers have no hydroxyl groups. Solvent isotope effects on enol ketonization by the concerted mechanism should therefore be greater than those on enol ether hydrolysis because the second proton transfer in the ketonization reaction will contribute an additional component to the isotope effect.

Solvent isotope effects on enol ketonization do tend to be greater than those on the hydrolysis of corresponding enol ethers, and the present system provides no exception: the value $k_{H^+}/k_{D^+} = 5{\cdot}0$ determined here is *ca* 20% greater than $k_{H^+}/k_{D^+} = 4{\cdot}1$ obtained for the hydrolysis of the methyl ether of acetophenone enol.[7] This difference, however, can be accommodated within the stepwise mechanism for ketonization, inasmuch as the enol hydroxyl group is taking on positive charge during this reaction and that can be expected to make an additional, positive, i.e. $k_H/k_D > 1$, contribution to the isotope effect. This contribution can be estimated as $l^{-\alpha}$,[9] where l ($= 0{\cdot}69$) is the isotopic fractionation factor for the hydronium ion and α is the Brønsted exponent. The Brønsted exponent for the ketonization of acetophenone enol is $\alpha = 0{\cdot}5$,[3b] and that gives $(0{\cdot}69)^{-0{\cdot}5} = 1{\cdot}20$ as the additional contribution. This brings the expected isotope effect for ketonization of acetophenone enol by the stepwise mechanism up to $k_{H^+}/k_{D^+} = 4{\cdot}9$, which is in good agreement with the experimentally determined value, $k_{H^+}/k_{D^+} = 5{\cdot}0$. Ketonization by the concerted mechanism would presumably make the isotope effect even greater than this predicted value, and the present result therefore supports the stepwide rather than the concerted pathway.

Secondary isotope effects

The rate constants measured here lead to two separate determinations of the effect of a single β-deuterium substitution on the rate of ketonization of acetophenone enol, that given by comparison of PhC(OH)=CH_2 and PhC(OH)=CHD (Table 1, weighted average of systems 1 and 3 and system 5): $(k_H/k_D)_\beta = 0{\cdot}982 \pm 0{\cdot}018$, and that given by comparison of PhC(OD)=CHD and PhC(OD)=CD_2 (Table 1, systems 4 and 6): $(k_H/k_D)_\beta = 1{\cdot}032 \pm 0{\cdot}024$. These isotope effects are not significantly different from one another; their weighted average is $(k_H/k_D)_\beta = 0{\cdot}999 \pm 0{\cdot}014$. Isotopic substitution at the β-position thus has no effect on the rate of ketonization of acetophenone enol.

This is similar to the result obtained for hydrolysis of the ethyl ether of acetaldehyde enol, $(k_H/k_D)_\beta = 1{\cdot}002 \pm 0{\cdot}004$.[10] The absence of an isotope effect there was attributed to a cancellation of two expected effects: (1) a normal ($k_H/k_D > 1$) isotope effect, produced by hyperconjugative interaction of β-hydrogen with the positive charge being delivered to the substrate by protonation at carbon in the transition state of this reaction, and (2) an inverse ($k_H/k_D < 1$) isotope effect, produced by the $sp^2 \rightarrow sp^3$ hybridization change taking place at the β-position. A similar explanation should apply to the present ketonization reaction, and that implies that the enol in the present case is also taking on positive charge as it undergoes reaction. This can be so only if ketonization occurs by the stepwise rather than the concerted mechanism, because in the concerted process the positive charge being transferred to the substrate by protonation at carbon is at the same time being removed by proton departure from hydroxyl oxygen. The secondary β-deuterium isotope effect on ketonization of acetophenone enol therefore also supports a stepwise mechanism for this process.

ACKNOWLEDGEMENTS

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