

# Solvent isotope effect on the hydroxide-ion-catalyzed hydration of ketenes in aqueous solution

J. Andraos, Y. Chiang, S.J. Eustace, A.J. Kresge, S.W. Paine, V.V. Popik, and K. Sung

**Abstract:** Five ketenes, phenyl(ethyl)ketene, phenyl(methylthio)ketene, diphenylketene, pentafluorophenylketene, and 1-naphthylketene, were generated flash photolytically and solvent isotope effects ( $\text{H}_2\text{O}$  vs.  $\text{D}_2\text{O}$ ) on their hydroxide-ion-catalyzed hydration in aqueous solution were determined. The values obtained are all weakly inverse and closely similar ( $k_{\text{H}_2\text{O}}/k_{\text{D}_2\text{O}} = 0.76\text{--}0.97$ ), as expected for these fast, hydroxide-ion-consuming reactions, known to proceed by nucleophilic attack of hydroxide on the ketene carbonyl group. The characteristic magnitude of these isotope effects should prove useful in identifying new examples of this reaction.

**Key words:** ketenes, flash photolysis, photo-Wolff reaction, solvent isotope effects on hydroxide ion consumption.

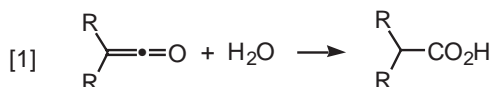
**Résumé :** Faisant appel à la photolyse éclair, on a généré cinq cétènes (phényl(éthyl)cétène, phényl(méthylthio)cétène, diphenylcétène, pentafluorophénylcétène et 1-naphthylcétène) et on a déterminé les effets isotopiques de solvant ( $\text{H}_2\text{O}$  vs.  $\text{D}_2\text{O}$ ) sur leur hydratation catalysée par l'ion hydroxyde, en solution aqueuse. Les valeurs obtenues sont toutes semblables, faibles et inverses ( $k_{\text{H}_2\text{O}}/k_{\text{D}_2\text{O}} = 0,76\text{--}0,97$ ) comme on peut s'y attendre pour ces réactions rapides utilisant l'ion hydroxyde qui se produisent par une attaque nucléophile de l'hydroxyde sur le groupe carbonyle du cétène. L'amplitude caractéristique de ces effets isotopiques devrait s'avérer utile dans l'identification de nouveaux exemples de cette réaction.

**Mots clés :** cétènes, photolyse éclair, réaction de photo-Wolff, effets isotopique du solvant sur la consommation de l'ion hydroxyde.

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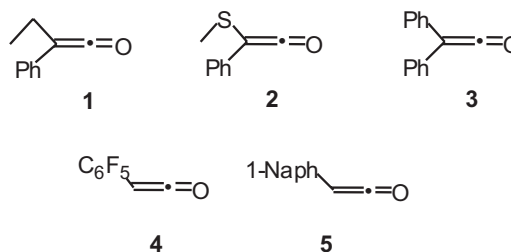
## Introduction

Solvent isotope effects on the hydration of ketenes to form carboxylic acids, eq. [1],

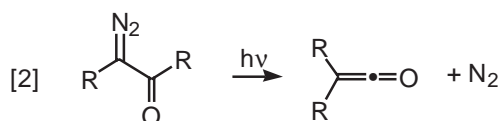


catalyzed by the hydronium ion, as well as on the uncatalyzed reaction, have proved to be useful in elucidating the mechanisms of these processes, and they have also served to help identify new examples (1). The same is not true of the hydroxide-ion-catalyzed reaction: we are aware of only one published determination of this isotope effect made prior to the present work, and that was done using a rather special substrate containing a second functional group that perturbed the isotope effect and gave it an atypical value (vide infra) (2).

In the present paper we provide five unperturbed examples of this isotope effect, determined using the monofunctional ketene substrates phenyl(ethyl)ketene, **1**, phenyl(methylthio)ketene, **2**, diphenylketene, **3**, pentafluorophenylketene, **4**, and 1-naphthylketene, **5**.



These ketenes were generated by photo-Wolff reactions, eq. [2],



of the corresponding diazo compounds,  $\alpha$ -diazobutyrophenone, **6**, *S*-methyl phenyldiazothioacetate, **7**, azibenzil, **8**, penta-

Received December 10, 1998.

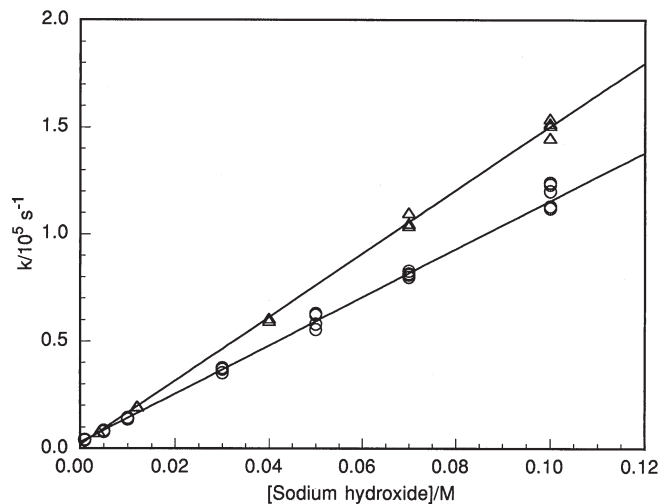
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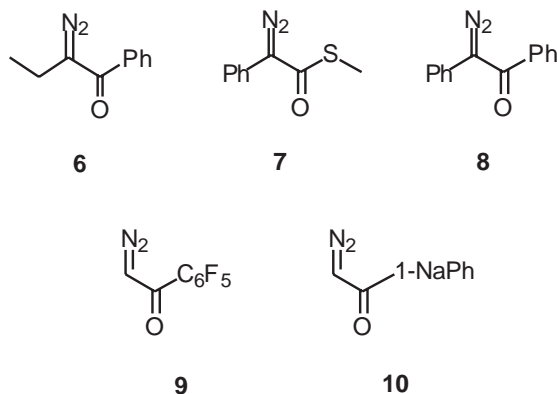
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**Fig. 1.** Relationship between sodium hydroxide concentration and observed first-order rate constants for the hydration of pentafluorophenylketene in aqueous solution at 25°C; O: H<sub>2</sub>O, Δ: D<sub>2</sub>O.



fluorobenzoyldiazomethane, **9**, and 1-naphthoyldiazomethane, **10**.



Because the reactions studied were fast, flash photolytic techniques were used to carry out rate measurements.

## Experimental section

### Materials

$\alpha$ -Diazobutyrophenone, **6**, was prepared by diazo group transfer from *p*-toluenesulfonyl azide to butyrophenone after the latter had been activated through introduction of an  $\alpha$ -formyl group (**3**). Formylation was effected using ethyl formate as the formyl source and sodium hydride as the basic catalyst. The diazo compound, a yellow oil, was purified by column chromatography on silica gel using 80% chloroform – 20% hexane as the eluent. Its spectral properties are as follows: <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>),  $\delta$ /ppm: 7.50 (m, 5H, Ar), 2.57 (q, *J* = 7.4 Hz, 2H, CH<sub>2</sub>), 1.20 (t, *J* = 7.4 Hz, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (50 MHz, CDCl<sub>3</sub>),  $\delta$ /ppm: 189.4 (C=O), 137.8 (Ar), 131.2 (Ar), 128.4 (Ar), 127.0 (Ar), 68.3 (C=N<sub>2</sub>), 17.0 (CH<sub>2</sub>), 11.3 (CH<sub>3</sub>); HRMS, M<sup>+</sup> for C<sub>10</sub>H<sub>10</sub>N<sub>2</sub>O, *m/e*, calcd.: 174.0793; found: 174.0792.

**Table 1.** Sodium hydroxide catalytic coefficients and solvent isotope effects on ketene hydration in aqueous solution at 25°C.<sup>a</sup>

Substrate	$k_{\text{HO}} / \text{M}^{-1} \text{s}^{-1}$	$k_{\text{HO}} / k_{\text{DO}}$
	$(6.05 \pm 0.06) \times 10^3$	$0.972 \pm 0.012$
	$(1.89 \pm 0.04) \times 10^4$	$0.928 \pm 0.026$
	$(4.64 \pm 0.14) \times 10^4$	$0.917 \pm 0.051$
	$(1.13 \pm 0.01) \times 10^6$	$0.759 \pm 0.009$
	$(1.18 \pm 0.05) \times 10^6$	$0.891 \pm 0.063$

<sup>a</sup>Ionic strength = 0.10 M.

Pentafluorobenzoyldiazomethane, **9**, has apparently been made before (4), but no details of its preparation nor of its spectral properties were given. It was synthesized here by treating pentafluorobenzoyl chloride with diazomethane. The product was a colorless crystalline solid, mp 45–46°C. Its spectral properties are as follows: IR (KBr),  $\nu/\text{cm}^{-1}$  = 2123 (N=N), 1650 (C=O); <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>),  $\delta$ /ppm: 5.71; <sup>13</sup>C NMR (50 MHz, CDCl<sub>3</sub>), <sup>19</sup>F decoupled, <sup>1</sup>H not decoupled)  $\delta$ /ppm: 176.8 (d, C=O), 144.3 (Ar), 142.7 (Ar), 137.6 (Ar), 113.3 (Ar), 60.1 (d, *J* = 204 Hz, C=N<sub>2</sub>).

*S*-Methyl phenyldiazothioacetate, **7**, was made by diazo transfer from *p*-toluenesulfonyl azide to *S*-methyl phenylthioacetate in the presence of 1,8-diazobicyclo[5.4.0]undec-7-ene and 4-(*N,N*-dimethylamino)pyridine (**5**), and *azibenzil* was prepared by mercuric oxide oxidation of benzil monohydrazone (**6**); 1-naphthoyldiazomethane was a sample that had been prepared before (7). All other materials were best available commercial grades.

### Kinetics

Flash photolytic generation of ketenes was performed using a conventional flash lamp system (**8**) and an excimer laser system (**1b**), operating at  $\lambda$  = 248 nm; these have already been described. With both systems, reaction mixtures were thermostatted at  $25.0 \pm 0.05^\circ\text{C}$ . The ketene hydration reactions were followed by monitoring the decay of ketene absorbance at 250–270 nm for the phenyl-substituted substrates and at  $\lambda$  = 320–330 nm for the naphthyl derivative. All decays conformed well to the first-order rate law, and observed first-order rate constants were calculated by nonlinear least-squares fitting of exponential functions.

### Results

Rates of hydration of the ketenes examined here were measured in dilute solutions of sodium hydroxide using H<sub>2</sub>O and D<sub>2</sub>O as the solvent. In all cases, a range of sodium hydroxide concentrations, usually spanning a variation of at least an order of magnitude, was employed. The ionic strength of these solutions was maintained at 0.10 M by adding sodium perchlorate as required. The data so obtained

have been summarized, as supplementary material, in Table S1.<sup>2</sup>

As Fig. 1 illustrates, the observed first-order rate constants determined in this way are accurately proportional to sodium hydroxide concentration. Sodium hydroxide catalytic coefficients were therefore evaluated by linear least-squares analysis with proportional weighting, and solvent isotope effects were calculated as ratios of these catalytic coefficients. The results are listed in Table 1.

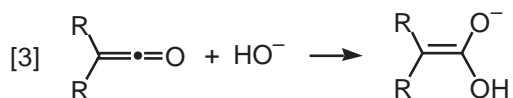
The sodium hydroxide catalytic coefficient for 1-naphthylketene in H<sub>2</sub>O determined here,  $1.18 \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$ , agrees well with that reported for this substrate before,  $1.25 \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$  (7). The present values for diphenylketene,  $4.64 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$ , and phenyl(methylthio)ketene,  $1.89 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$ , are also consistent with previous determinations,  $6.11 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$  (9) and  $3.09 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$  (5), respectively.

## Discussion

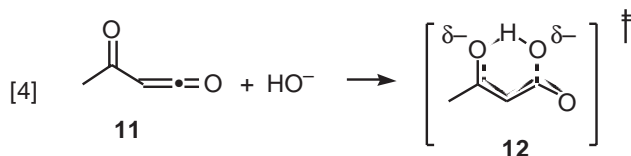
Each of the ketenes examined here reacts more rapidly in D<sub>2</sub>O than in H<sub>2</sub>O solutions of sodium hydroxide, and each consequently gives an inverse ( $k_{\text{H}}/k_{\text{D}} < 1$ ) isotope effect. This is the expected direction for solvent isotope effects on hydroxide-ion-consuming reactions such as these. That follows from a model proposed by Gold and Grist (10), in which the hydroxide ion in aqueous solution is strongly solvated by three water molecules whose solvating O—H bonds are looser than the O—H bonds of bulk water. When such a hydroxide ion is consumed by reaction with a substrate, the solvating water molecules are transformed into bulk solvent, and they consequently move from a more loosely bound state to a more tightly bound state, thus producing an inverse isotope effect. This phenomenon has now been extensively documented (11).

The maximum magnitude of the solvent isotope effect on consumption of a hydroxide ion has been estimated as  $k_{\text{H}_2\text{O}}/k_{\text{D}_2\text{O}} = 0.43$  (11a). The isotope effects observed here are much weaker than that, but they are on a rate process in whose transition state the hydroxide ion will be only partially consumed. The rates of the present reactions, moreover, are fast, and their transition states will consequently be especially reactant-like (12).

Another feature contributing to the weakness of the present isotope effects is the nucleophilic nature of the hydroxide ion plus ketene reaction (13): this generates negative charge on the ketene carbonyl oxygen atom, giving that atom alkoxide ion character, eq. [3]. Solvation of this charge, in much the same way as the hydroxide ion is solvated, then provides a normal component ( $k_{\text{H}}/k_{\text{D}} > 1$ ) to the solvent isotope effect, which offsets the inverse factor given by hydroxide ion desolvation.



The present inverse isotope effects are quite different from the value,  $k_{\text{H}_2\text{O}}/k_{\text{D}_2\text{O}} = 1.87$ , reported for the only previous example of a solvent isotope effect on a ketene plus hydroxide ion reaction (2). The substrate in that case was acetylketene, **11**, and it was argued then that the acetyl group assisted hydroxide ion attack, as evidenced by its strong rate acceleration, by allowing strong hydrogen bond formation between the hydroxyl group and the acetyl oxygen atom in the transition state of this reaction, **12**, eq. [4]:



strong hydrogen bond formation is known to produce sizeable isotope effects in the normal direction (14). The inverse nature of the presently determined isotope effects reinforces this explanation.

It would seem fair to conclude, therefore, that solvent isotope effects on the reaction of hydroxide ion with simple, monofunctional, short-lived ketenes will be weakly inverse. This characteristic magnitude should be useful in identifying this reaction.

## Acknowledgement

We are grateful to the Natural Sciences and Engineering Research Council of Canada for financial support of this research.

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<sup>2</sup>Table S1 may be purchased from: The Depository of Unpublished Data, Document Delivery, CISTI, National Research Council of Canada, Ottawa, ON K1A 0S2, Canada.

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