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Hydration Reactivity of Persistent Conjugated Ketenes

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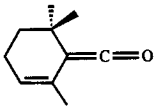
The acid, neutral, and base hydrations of the crowded alkenylketene **1** and the arylketenes *i*-PrCPh=C=O (**2**) and *t*-BuCPh=C=O (**3**) have been measured, together with solvent isotope effects and general acid catalysis of the hydration of **1**. The arylketenes **2** and **3** are the first for which acid-catalyzed hydration has been demonstrated. These ketenes show significantly lower reactivity than simple ketenes, and this is interpreted as the result of both steric and electronic factors operating in mechanisms involving rate-limiting proton transfer to carbon (the γ-carbon in **1**) for the acid-catalyzed reaction, while both the neutral and hydroxide-induced reactions involve rate-limiting nucleophilic attack in the plane of the ketene on the carbonyl carbon.

Mechanistic investigations of addition reactions of ketenes[1] and application of ketenes as synthetic intermediates[2] have been topics of active study in our laboratory,[3] as well as others.[4-8] The examination of ketenes bearing conjugating substituents (alkenyl, alkynyl, aryl) has been of particular recent interest.[4-7] These ketenes are valuable in synthesis because the conjugating substitutents contribute to the stability of the ketenes and provide useful additional functionality. As a guide to understanding the properties of these systems, we now have studied the hydrolytic stability of the vinylketene **1**[5,9] and the arylketenes **2**[10a] and **3**.[10c] These ketenes are rather persistent because of the bulky substituion and are therefore attractive for mechanistic study.



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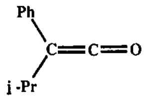

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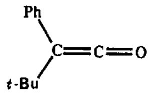

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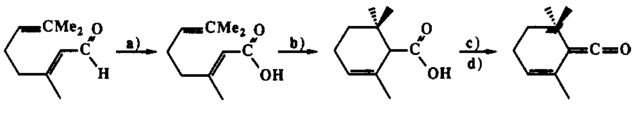
Results

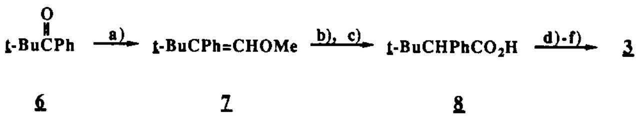
Reaction of α-citral with sodium chlorite/hydrogen peroxide followed by H_2SO_4 gave α-cyclogeranic acid (**5**) (Scheme I).[11,12] Conversion to the acid chloride and dehydrochlorination with triethylamine gave the ketene **1**, which could be stored for weeks at 0 °C.

Scheme I. Reagents and Conditions[a]



[a] (a) $NaClO_2$, H_2O_2. (b) H_2SO_4. (c) $(COCl)_2$. (d) Et_3N.

Scheme II[a]



$$\underset{\mathbf{6}}{t\text{-BuC}(=\text{O})\text{Ph}} \xrightarrow{\text{a)}} \underset{\mathbf{7}}{t\text{-BuCPh=CHOMe}} \xrightarrow{\text{b), c)}} \underset{\mathbf{8}}{t\text{-BuCHPhCO}_2\text{H}} \xrightarrow{\text{d)-f)}} \mathbf{3}$$

[a] (a) $Ph_3PCHOMe$. (b) HCO_2H, H_2O. (c) CrO_3, H^+. (d) $(COCl)_2$. (e) Br_2, P. (f) Zn.

Table I. Rates of Hydration of 1 in H_2O, 25 °C, μ = 0.1 (NaCl)

[HCl],[a] M	k_{obsd}, s^{-1}	[NaOH],[b] M	k_{obsd}, s^{-1}
0.0200	0.140	1.02×10^{-3}	5.60×10^{-4}
8.01×10^{-3}	7.29×10^{-2}	4.08×10^{-3}	1.32×10^{-3}
6.05×10^{-3}	4.95×10^{-2}	8.16×10^{-3}	1.62×10^{-3}
4.00×10^{-3}	3.70×10^{-2}	2.04×10^{-2}	3.63×10^{-3}
1.00×10^{-3}	9.01×10^{-3}	6.12×10^{-2}	8.08×10^{-3}
0.00 (H_2O)	2.97×10^{-4}	0.100[c]	1.30×10^{-2}
0.00 (D_2O)	1.28×10^{-4}	0.201[c]	2.41×10^{-2}
		0.301[c]	3.23×10^{-2}
		0.402[c]	4.07×10^{-2}
		0.502[c]	5.48×10^{-2}

[a] log $k_{obsd} = (6.72\ M^{-1}\ s^{-1})[HCl] + 9.16 \times 10^{-3}\ s^{-1}$. [b] log $k_{obsd} = (0.104\ M^{-1}\ s^{-1})[OH^-] + 1.34 \times 10^{-3}\ s^{-1}$. [c] No added NaCl, ionic strength varies.

The ketene *i*-PrCPh=C=O (**2**)[10a] was prepared by Et_3N dehydrochlorination of the acid chloride of *i*-$PrCHPhCO_2H$.[10b] The ketene *t*-BuCPh=C=O (**3**)[10c] was obtained by reaction of *t*-BuCOPh with Ph_3P=CHOMe[10b] and further reaction as shown in Scheme II.

Rates of hydration of **1** in wholly aqueous media with added HCl and NaOH were measured by monitoring the disappearance of the UV absorption of **1**, and the derived rate constants are reported in Table I. The rates in HCl were correlated by the expression $k_{obsd} = (6.72\ M^{-1}\ s^{-1})[HCl] + 9.16 \times 10^{-3}\ s^{-1}$, while those in NaOH gave $k_{obsd} = (0.104\ M^{-1}\ s^{-1})[NaOH] + 1.34 \times 10^{-3}\ s^{-1}$. In both cases

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[1] (a) Allen, A. D.; Tidwell, T. T. *J. Am. Chem. Soc.* **1987**, *109*, 2774–2780. (b) Allen, A. D.; Kresge, A. J.; Schepp, N. P.; Tidwell, T. T. *Can. J. Chem.* **1987**, *65*, 1719–1723. (c) Kabir, S. H.; Seikaly, H. R.; Tidwell, T. T. *J. Am. Chem. Soc.* **1979**, *101*, 1059–1060.

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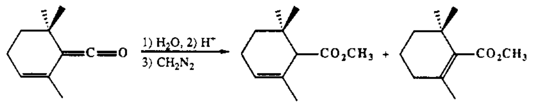
the standard deviation in the intercept exceeded the values found of the intercept and so could not be usefully compared to other rates in the absence of catalyst.

Hydration of 1 at a $[CH_3CO_2H]/[CH_3CO_2Na]$ buffer ratio of 0.975, pH = 4.63, $\mu = 0.1$ (NaCl), gave an expression $k_{obsd}(s^{-1}) = (0.000740\ M^{-1}\ s^{-1})[CH_3CO_2H] + 3.54 \times 10^{-4}\ s^{-1}$, while rates at $[HCO_2H]/[HCO_2Na] = 1.105$, pH = 3.56, $\mu = 0.1$ (NaCl), gave an expression $k_{obsd}\ (s^{-1}) = (0.0492\ M^{-1}\ s^{-1})[HCO_2H] + 2.25 \times 10^{-3}\ s^{-1}$. The derived values of k_{H^+} are 6.90 and 7.48 $M^{-1}\ s^{-1}$ for CH_3CO_2H and HCO_2H, respectively, as compared to the value of 6.72 $M^{-1}\ s^{-1}$ derived from the rates in HCl. The average of all three values is 7.03 $M^{-1}\ s^{-1}$.

Solvent isotope effects were measured separately on the same day for five HCl concentrations between 0.0200 and 0.00397 M and five DCl concentrations between 0.0206 and 0.00433 M. The expressions $k_{obsd} = (9.15\ M^{-1}s^{-1})[H^+] + (5.71 \pm 5.11) \times 10^{-3}\ s^{-1}$ and $k_{obsd} = (3.06\ M^{-1}\ s^{-1})[D^+] + (3.27 \pm 2.14) \times 10^{-3}\ s^{-1}$ lead to a value of $k_{H^+}/k_{D^+} = 2.99$. The rates without catalyst (Table I) lead to $k_{H_2O}/k_{D_2O} = 2.32$. The large uncertainties in the intercepts of the rate versus [HCl] or [DCl] plots preclude comparing their ratio to that measured directly.

Product studies on the hydration of 1 were carried out in 20% H_2O/80% acetonitrile under acidic (2×10^{-2} M HCl), neutral (pH 7 buffer), and basic (1×10^{-3} M NaOH) conditions. After completion, the reactions were acidified, the product acids were extracted into ether and esterified by diazomethane, and the resulting methyl esters **9** and **10** were analyzed by VPC. The product ratio **9**/**10** was 16/84, 95/5, and 92/8 in acidic, neutral, and basic solution, respectively.



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Solubility problems precluded carrying out these product studies under the highly aqueous conditions of the kinetic measurements, and the product ratio in acid was somewhat variable, apparently due to the occurrence of some uncatalyzed hydrolysis by adventitious water during handling leading to more of the unconjugated isomer. The acid **5** was unchanged after treatment under the conditions for acid-catalyzed hydration of **1**. Insufficient quantities of the conjugated acid **11** corresponding to **10** were available for examination of its stability under the reaction conditions.

The solubilities of the arylketenes **2** and **3** in 100% H_2O were insufficient for rate studies, so 50% H_2O/CH_3CN was used for most of the experiments. Rate constants were monitored by observing the disappearance of the UV absorption at 254 nm and are reported in Tables II and III as a function of concentration of added HCl and NaOH.

Rate constants for *i*-PrCPh=C=O with added HCl gave upward curvature above 0.6 M HCl from a linear correlation when plotted against [HCl], but below this concentration gave $k_{obsd} = (0.120\ M^{-1}\ s^{-1})[HCl] + 0.0323\ s^{-1}$, $r = 0.964$. The mediocre correlation coefficient of this line reflects some apparently random scatter in the points.

Rate constants for *i*-PrCPh=C=O with added NaOH in 50% H_2O/CH_3CN gave a slightly curved correlation, $k_{obsd} = (58.4\ M^{-1}\ s^{-1})[NaOH] + 0.0405\ s^{-1}$, $r = 0.994$. The intercept of this line, 0.0405 s^{-1}, corresponds to k_{H_2O} and is in good agreement with the directly measured value of 0.0424 s^{-1}.

Table II. Rates of Hydration of *i*-PrCPh=C=O (2), 25 °C

50/50 v/v H_2O/CH_3CN		
[HCl],[a] M; k_{obsd}, s^{-1}	[NaOH],[b,c] M; k_{obsd}, s^{-1}	buffer; k_{obsd}, s^{-1}
1.185; 0.288	3.74×10^{-3}; 0.251	none;[c] 0.0424
1.033; 0.197	2.94×10^{-3}; 0.219	none; 0.0345
0.892; 0.151	2.13×10^{-3}; 0.170	none (D_2O); 0.0207
0.594; 0.113	1.36×10^{-3}; 0.124	pH 10.0;[f] 0.0404
0.592; 0.104	0.955×10^{-3}; 0.0877	pH 5.82;[g] 0.0397
0.490; 0.0830		pH 2.78;[h] 0.0394
0.474; 0.0880		
0.361; 0.0751		
0.296; 0.0618		
0.237; 0.0626		
0.120; 0.0514		

H_2O/CH_3CN:[d] $[H_2O]$, M; k_{obsd}, s^{-1}	H_2O/dioxane:[e] $[H_2O]$, M; k_{obsd}, s^{-1}
44.4; 0.289	44.4; 0.397
38.9; 0.180	33.3; 0.141
33.3; 0.0787	27.8; 0.0900
27.8; 0.0372	16.7; 0.0228
16.7; 0.0151	11.1; 0.0108
11.1; 0.00712	

[a] Rates below [HCl] = 0.6 M gave $k_{obsd} = (0.120\ M^{-1}\ s^{-1})[HCl] + 0.0323\ s^{-1}$, $r = 0.964$ (ionic strength not kept constant). [b] $k_{obsd} = 58.4[OH^-]\ M^{-1}\ s^{-1} + 0.0405\ s^{-1}$, $r = 0.994$. [c] $\mu = 0.05$, NaCl. [d] $\log k_{obsd} = (0.0481\ M^{-1}\ s^{-1})[H_2O] - 2.68\ s^{-1}$, $r = 0.996$. [e] $\log k_{obsd} = (0.0469\ M^{-1}\ s^{-1})[H_2O] - 2.43\ s^{-1}$, $r = 0.996$. [f] Buffer, 0.0102 M Et_3N/0.00985 M Et_3NHCl. [g] Buffer, CH_3CO_2H/CH_3CO_2Na. [h] Buffer, $CHCl_2CO_2H/CHCl_2CO_2Na$.

Table III. Rates of Hydration of *t*-BuCPh=C=O (3), 25 °C

50/50 v/v H_2O/CH_3CN		H_2O/CH_3CN:[d]
[HCl],[a] M; k_{obsd}, s^{-1}	[NaOH],[b,c] M; k_{obsd}, s^{-1}	$[H_2O]$, M; k_{obsd}, s^{-1}
0.390; 0.194	4.52×10^{-3}; 0.178	44.4; 0.103
0.312; 0.154	3.62×10^{-3}; 0.129	38.9; 0.0428
0.234; 0.116	2.72×10^{-3}; 0.0878	27.8; 0.00989
0.156; 0.0780	1.81×10^{-3}; 0.0390	11.1; 0.00149
0.0780; 0.0425	0.905×10^{-3}; 0.0116	
	none; 0.00997	

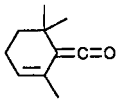
[a] $k_{obsd} = (0.488\ M^{-1}\ s^{-1})[HCl] + 0.00296\ s^{-1}$, $r = 1.000$ (ionic strength not kept constant). [b] $k_{obsd} = (46.7\ M^{-1}\ s^{-1})[NaOH] - 0.037\ s^{-1}$, $r = 0.996$. Point with no added NaOH not included. [c] $\mu = 0.05$, NaCl. [d] $\log k_{obsd} = (0.0547\ M^{-1}\ s^{-1})[H_2O] - 3.47\ s^{-1}$, $r = 0.996$.

Rate constants for *i*-PrCPh=C=O in neutral H_2O/CH_3CN solutions of varying H_2O molarity gave a good correlation, $\log k_{obsd} = (0.0481\ M^{-1}\ s^{-1})[H_2O] - 2.68\ s^{-1}$, $r = 0.996$. Extrapolation of this line to 100% (55.5 M) H_2O gave $k_{H_2O} = 0.982\ s^{-1}$. A plot of k_{obsd} versus $[H_2O]^2$ was strongly curved.

For comparison with rate constants measured[7a,b] for hydration of $Me_2C=C=O$ and $Ph_2C=C=O$ in neutral H_2O/dioxane solutions of varying H_2O content, rate constants were also measured for *i*-PrCPh=C=O in a series of these solvents (Table II) and gave a good correlation, $\log k_{obsd} = (0.0469\ M^{-1}\ s^{-1})[H_2O] - 2.43\ s^{-1}$, $r = 0.996$. Extrapolation of this line to 100% (55.5 M) H_2O gave $k_{H_2O} = 1.48\ s^{-1}$. The average of the two extrapolated values of k_{H_2O} is 1.23 s^{-1}. A plot of k_{obsd} versus $[H_2O]^2$ for H_2O/dioxane solutions was strongly curved. Rate ratios $k_{obsd}^{dioxane}/k_{obsd}^{CH_3CN}$ for *i*-PrCPh=C=O varied from 1.37 to 2.42 for the same H_2O concentrations and equalled 1.51 for 50% H_2O.

Hydration of *i*-PrCPh=C=O at $[CH_3CO_2H]/[CH_3CO_2Na]$ and $[CHCl_2CO_2H]/[CHCl_2CO_2Na]$ buffer ratios of 1.0 in 50% H_2O/CH_3CN, $\mu = 0.05$ (NaCl), gave rate constants that were invariant with buffer concentration between 0.050 M and 0.0050 M in each case. The rate constants equalled $(0.0394 \pm 0.0010)\ s^{-1}$ with $CHCl_2CO_2H$ and $(0.0397 \pm 0.0011)\ s^{-1}$ with CH_3CO_2H. The measured

Table IV. Ketene Reactivities in H_2O and in H_2O/CH_3CN, 25 °C

ketene	solvent	k_{H^+}, $M^{-1}\ s^{-1}$	k_{H_2O}, s^{-1}	k_{OH^-}, $M^{-1}\ s^{-1}$	k_{OH^-}/k_{H_2O}	ref
$CH_2{=}C{=}O$	H_2O		44			8b
n-$BuCH{=}C{=}O$	H_2O	3.98×10^3	99.4	3.29×10^4	330	1b
t-$BuCH{=}C{=}O$	H_2O		37.9^a			1a
$Et_2C{=}C{=}O$	H_2O		8.26^a			1a
t-$Bu_2C{=}C{=}O$	H_2O	434	1.57×10^{-4}	–		1a
$PhCH{=}C{=}O$	H_2O	–	4.77×10^3	1.22×10^6	260	1b
$Ph_2C{=}C{=}O$	H_2O	–	275	6.11×10^4	220	1b
i-$PrCPh{=}C{=}O$	H_2O		1.23^b			c
	H_2O	7.03	2.97×10^{-4}	0.104	350	c
t-$BuCPh{=}C{=}O$	H_2O		0.370^a			c
t-$BuCH{=}C{=}O$	50% CH_3CN	135	0.0780			1a
$Et_2C{=}C{=}O$	50% CH_3CN	13.0	0.319		790^e	1a
i-$PrCPh{=}C{=}O$	50% CH_3CN	0.120	0.0424^d	58.4^d	1400	c
t-$BuCPh{=}C{=}O$	50% CH_3CN	0.488	0.00997^d	46.7^d	4700	c
t-$Bu_2C{=}C{=}O$	50% CH_3CN	3.6				1c

[a] Extrapolated from values measured in H_2O/CH_3CN mixtures. [b] Average of values extrapolated from 50% H_2O/CH_3CN and 50% H_2O/dioxane mixtures. [c] This work. [d] $\mu = 0.05$. [e] temperature 5.5 °C, see ref 1a.

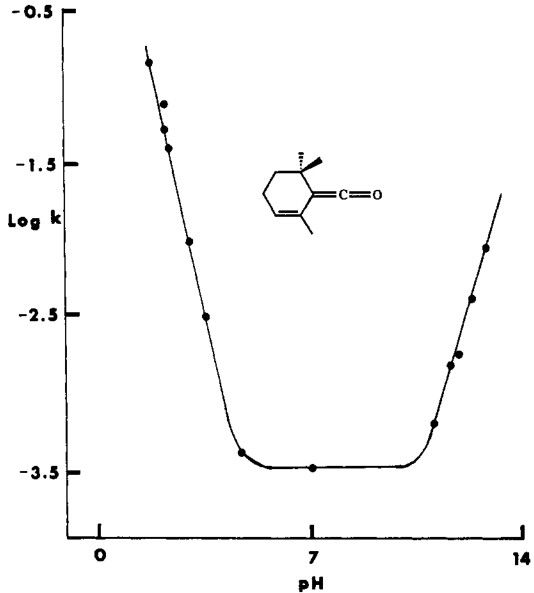


Figure 1. pH–rate profile for hydration of 1 in H_2O, 25 °C.

pH value of 5.82 ± 0.01 for the CH_3CO_2H buffers was used, but as the measured pH of the $CHCl_2CO_2H$ buffers varied from 2.54 to 2.85, the calculated pH of 2.78 based on the reported[13] pK_a of $CHCl_2CO_2H$ in this solvent was assumed to apply to these solutions. The reactions are not acid catalyzed in this pH region so the failure to observe general acid catalysis is expected.

A solvent isotope effect $k(H_2O)/k(D_2O)$ for hydration of i-$PrCPh{=}C{=}O$ in 50/50 v/v H_2O/CH_3CN without added NaCl equalled 1.67 (Table II).

Reaction of i-$PrCPh{=}C{=}O$ with H_2O gave i-$PrCHPhCO_2H$ (8) as the only observed product.

The reaction of t-$BuCPh{=}C{=}O$ in 50% H_2O/CH_3CN with HCl in the range 0.08–0.38 M (Table III) gave a good linear correlation, $k_{obsd} = (0.488\ M^{-1}\ s^{-1})[HCl] + 0.002\,96\ s^{-1}$, $r = 1.000$. Rates with added NaOH ($\mu = 0.05$) gave a slightly curved correlation, $k_{obsd} = (46.7\ M^{-1}\ s^{-1})[NaOH] - 0.037\ s^{-1}$, $r = 0.996$. The intercepts of both of these correspond to neutral rate constants significantly less than that observed in the absence of added catalysts, $0.009\,97\ s^{-1}$.

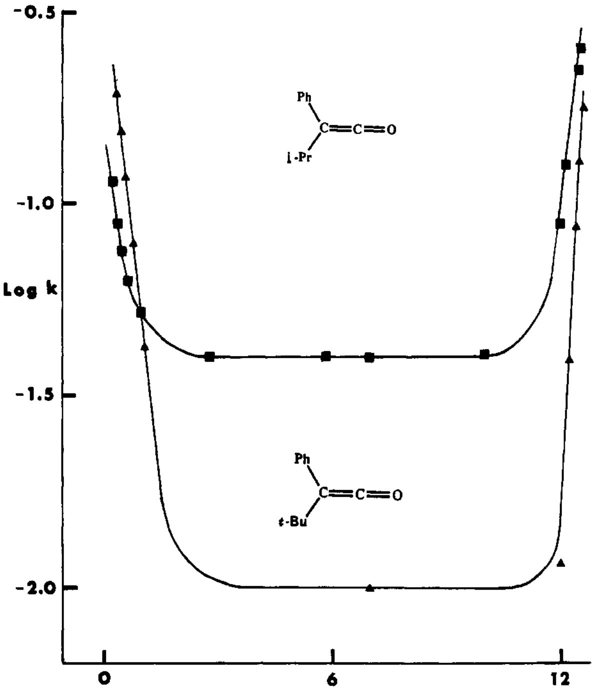


Figure 2. pH–rate profiles for hydration of i-$PrCPh{=}C{=}O$ (2) and t-$BuCPh{=}C{=}O$ (3) in 50% (v/v) H_2O/CH_3CN, 25 °C.

Rate constants for t-$BuCPh{=}C{=}O$ in neutral H_2O/CH_3CN solutions of varying H_2O molarity gave a good correlation, $\log k_{obsd} = (0.0547\ M^{-1}\ s^{-1})[H_2O] - 3.47\ s^{-1}$, $r = 0.998$. Extrapolation of this line to 100% H_2O gives $k_{H_2O} = 0.370\ s^{-1}$.

Discussion

The hydration rate constants for 1–3 are summarized in Table IV, together with comparative data for other ketenes, and pH–rate profiles for 1–3 are shown in Figures 1 and 2. These pH–rate profiles closely resemble those we have previously observed for t-$BuCH{=}C{=}O$ and $Et_2C{=}C{=}O$ (both in 50% H_2O/CH_3CN)[1a] and n-$BuCH{=}C{=}O$ (in H_2O).[1b] These are the only three ketenes for which acid-, water-, and base-induced reactions have all been demonstrated before, although the reactivity of $CH_2{=}C{=}O$, $Me_2C{=}C{=}O$, t-$Bu_2C{=}C{=}O$, $PhCH{=}C{=}O$, and $Ph_2C{=}C{=}O$ could be observed in certain ranges of the pH scale, but not others, because of excessively high

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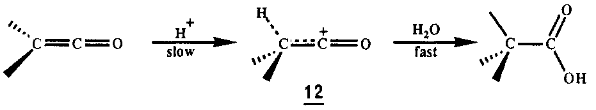
[13] Bunton, C. A.; Davoudazedeh, F.; Watts, W. E. *J. Am. Chem. Soc.* **1981**, *103*, 3855–3858.

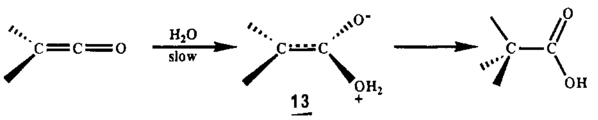
or low reactivity. We have interpreted the reactions of all of these ketenes as proceeding through the mechanisms of eq 1–3, with transition states **12**–**14**, respectively (the bonds to the incoming nucleophile in **13** and **14** would be only partly formed).[1]

Acid



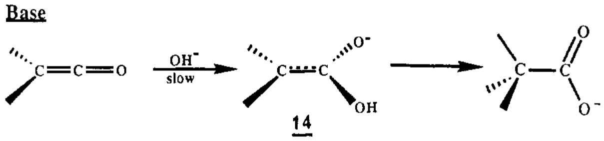
(1)

Neutral



(2)

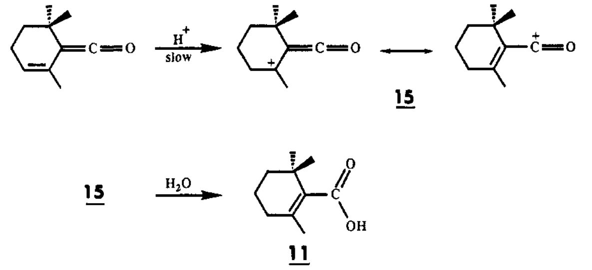
Base



(3)

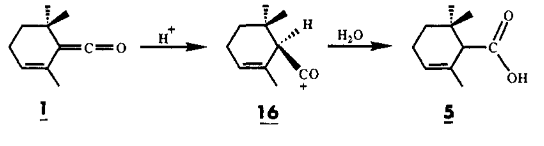
The evidence for these mechanistic proposals included the effects of structure upon reactivity and solvent isotope effects and, in the case of *t*-Bu$_2$C=C=O, the observation of general acid catalysis.[1c] The resemblance of the pH rate profiles as well as other evidence discussed below indicates that **1**–**3** also react by the pathways shown in eq 1–3.

In the case of **1**, the solvent isotope effect k_{H^+}/k_{D^+} of 2.99 in the acid-catalyzed hydrolysis is diagnostic of rate-limiting proton transfer to carbon and is comparable to values found for other ketenes.[1a,c] The observation of general acid catalysis in the hydration of this ketene is also definitive evidence for rate-limiting proton transfer to carbon, as discussed for the hydration of alkenes in general.[14] Reaction of **1** in acid gives, after diazomethane treatment, the methyl esters of the acids **5** and **11**, with an 84/16 preference for the conjugated isomer **11**. This result indicates that protonation occurs predominantly on the γ-carbon to give the conjugated cation **15** (eq 4).



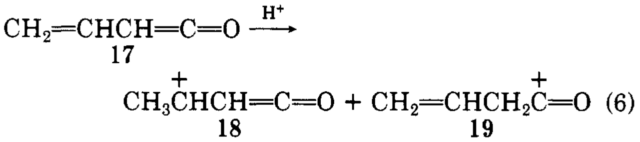
(4)

The formation of 16% of the ester of the nonconjugated acid **5** probably does *not* indicate that some protonation in acid occurs at C$_\alpha$ of **1** to give the cation **16** and then **5** (eq 5). A more plausible explanation is that some uncatalyzed hydration of **1** forming **5** occurs during the handling of **1**. Thus the amount of the ester of **5** observed increased with the age of the sample of **1**, implicating adventitious uncatalyzed hydrolysis.



(5)

In agreement with the solution-phase results, the protonation of vinylketene (**17**) has been studied by ab initio (6-31G*//3-21G) calculations, and γ-protonation forming **18** is favored over α-protonation giving **19** by 15.8 kcal/mol (eq 6).[15]



$$\underset{\mathbf{17}}{\mathrm{CH_2{=}CHCH{=}C{=}O}} \xrightarrow{H^+} \underset{\mathbf{18}}{\mathrm{CH_3CH\overset{+}{C}H{=}C{=}O}} + \underset{\mathbf{19}}{\mathrm{CH_2{=}CHCH_2\overset{+}{C}{=}O}} \quad (6)$$

1,3-Dienes such as isoprene protonate at C$_1$[16] to give an allylic cation analogous to that proposed for **1** (eq 4). Not only is the positive charge in **16** not conjugated with the carbon–carbon double bond but this vinyl group is expected to retard protonation at C$_\alpha$, just as phenyl groups retard protonation at the phenyl-substituted carbon of PhCH=CHOCH$_3$, by an average factor of 690 for the *E* and *Z* isomers relative to CH$_2$=CHOCH$_3$.[17]

The value of k_{H^+} for **1** is 570 times less than that of *n*-BuCH=C=O, whereas *t*-Bu$_2$C=C=O is only 9 times less reactive than *n*-BuCH=C=O (Table IV). This modest rate-retarding effect in *t*-Bu$_2$C=C=O relative to *n*-BuCH=C=O (and to *t*-BuCH=C=O and Et$_2$C=C=O, Table IV) was attributed to steric repulsion in the transition state of the solvent and the proton donor, as well as increasing mutual repulsion of the *ter*-butyl groups.[1a] These effects are not expected to be any greater in protonation of **1** than in *t*-Bu$_2$C=C=O, so the additional rate retardation is evidently due to the vinyl group, which slows protonation at C$_\alpha$ so that protonation at C$_\gamma$ is observed.

The acid-catalyzed reactivities of *i*-PrCPh=C=O (**2**) and *t*-BuCPh=C=O (**3**) can be calculated, by using *t*-Bu$_2$C=C=O as a reference (Table IV), to exceed that of **1** by factors of 2 and 8, respectively. General acid catalysis was not observed for **2**, presumably because of the facile H$_2$O reaction for this compound. Rate ratios k_{H^+}/k_{H_2O} of 2.4 × 10^4, 2.8, and 49 are observed for **1**, **2**, and **3**, respectively (Table IV). The variation in these ratios results from the operation of a combination of factors, but enhancement of k_{H_2O} by effective stabilization by the phenyl of the enolate-like transition state **13** from **2** and **3** is apparently significant.

Even though the k_{H^+} values for hydration of **2** and **3** are small in comparison to those for alkylketenes, these are still the only arylketenes for which k_{H^+} has been measured. For Ph$_2$C=C=O[1b] and PhCH=C=O,[1b,8a] no catalysis in H$_2$O could be detected for HClO$_4$ up 0.10 M. These ketenes are highly reactive in H$_2$O, and because of the phenyl retarding effect on protonation, rather high acid concentrations will evidently be required to detect acid catalysis in these substrates.

Interestingly, HClO$_4$ was reported to *inhibit* the hydrolysis of Ph$_2$C=C=O in dioxane containing 2.2 M H$_2$O.[7a] It was stated,[7a] "We interpret our results as indicating that hydrogen ions catalyze the addition of water to diphenylketene feebly (or not at all), but that added HClO$_4$ reduces the spontaneous rate of addition by engaging water molecules, and altering their state of aggregation...."[7a] No indication of any inhibition of hydration of ketenes by added acids has been observed in any of our work, including CH$_2$=C=O with HCl in 5.56 M H$_2$O.[1a] However,

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[14] Nowlan, V. J.; Tidwell, T. T. *Acc. Chem. Res.* **1977**, *10*, 252–258.

[15] Leung-Toung, R.; Peterson, M. R.; Tidwell, T. T.; Csizmadia, I. G. *THEOCHEM* (*J. Mol. Struct.*) **1989**, *183*, 319–330.

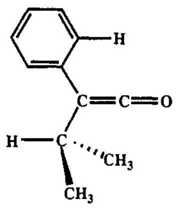
[16] Chwang, W. K.; Knittel, P.; Koshy, K. M.; Tidwell, T. T. *J. Am. Chem. Soc.* **1977**, *99*, 3395–3401.

[17] Chiang, Y.; Kresge, A. J.; Young, C. I. *Can. J. Chem.* **1978**, *56*, 461–464.

in 2.2 M H_2O a reduction in H_2O activity on addition of $HClO_4$ as proposed[7a] may occur.

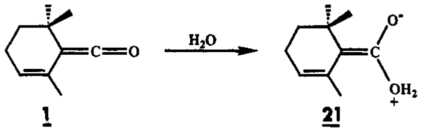
The neutral hydrations of 1 and 2 display solvent isotope effects $k(H_2O)/k(D_2O)$ of 2.32 and 1.67, respectively, and these values are typical of those found for other ketenes[1a,b] and other carbonyl group hydrations.[18] These isotope effects significantly greater than 1 have been interpreted[18] as indicating involvement of a second molecule of water acting as a general base in the rate-limiting step, and this may be the case here as well.

As seen in the data in Table IV, **1**–**3** have very low values of k_{H_2O} compared to less crowded ketenes. Thus, t-BuCPh=C=O is 1.4 × 10^4 times less reactive than PhCH=C=O. This effect is not due to an electronic effect of the *tert*-butyl substituent, as t-BuCH=C=O and CH_2=C=O have very similar values of k_{H_2O}. The value of k_{H_2O} for i-PrCPh=C=O is only 3.3 times more than for t-BuCPh=C=O, and the low reactivities of both these ketenes may be attributed to a steric barrier to attack in the plane of the ketene by water, which must approach from either the side of the phenyl or the side of the alkyl group. As illustrated in **20**, the isopropyl ketene adopts a conformation with a planar phenyl group that is strongly hindered to attack from either side. This distinctive pattern where a single bulky group causes little barrier to water attack but two such groups give rise to large rate retardations was pointed out by us before[1a,b] and convincingly argues against proposals[7] that water attack involves a concerted addition to the carbon–carbon double bond with attack perpendicular to the ketene plane.



20

Water attack on **1** is a factor of 4 × 10^3 slower than on i-PrCPh=C=O and only a factor of 2 greater than hydration of t-Bu_2C=C=O (Table IV). Thus the steric barrier to attack on **1** is very large, perhaps partly due to the rigidity of this cyclic structure. Furthermore, there is little evidence for any stabilization of a transition state with the character of **21** by the additional double bond in hydration of **1** (eq 7), in contrast to the large accelerations caused by phenyl groups. Subsequent protonation at C_α leading to the unconjugated acid **5** is normal for dienolate ions.[19]



(7)

There is general acceptance that hydroxide attack on ketenes occurs by in-plane attack on the carbonyl carbon (eq 3). As seen in Table IV, values of k_{OH^-}/k_{H_2O} for ketenes are in the range 220–4700, and the relative constancy of this ratio strongly argues for a similarity in mechanism for the neutral and hydroxide reactions, namely, the pathways shown in eq 2 and 3. All of **1**–**3** are quite unreactive relative to unhindered ketenes toward hydroxide, and the arguments presented above for the origin of this behavior in the case of the water reaction apply to the hydroxide reaction as well.

As noted above, it has been necessary to measure the reactivity of many ketenes in mixed solvents because of their high reactivity in pure water. In order to compare ketene reactivities, the extrapolation of rate constants in mixed solvents to estimate rate constants for 100% aqueous solutions is necessary.

Ketenes for which rate data are available in both mixed solvents and 100% water are CH_2=C=O[8b] and Ph_2C=C=O.[1b,7] Both of these ketenes also show an increase in rate with increasing water concentration.

We have used plots of log k_{obsd} versus $[H_2O]$ for extrapolations to 100% aqueous solutions.[1a] This empirical method bears some resemblance to the plotting of log k versus the solvent polarity parameter Y in the Grunwald–Winstein linear free energy treatment.[20] Rate constants extrapolated from our plots are however only crude approximations.

In the case of Ph_2C=C=O, the experimental data for the variation in hydration rate as a function of water concentration is available only up to 19.4 M H_2O (35%), and a plot of log k versus $[H_2O]$ is visibly curved.[21] Even using only the data for the highest three water concentrations from 11.1 to 19.4 M, the extrapolated value of k_{H_2O} in 100% H_2O from the correlation log k_{obsd} = (0.0527 M^{-1} s^{-1})$[H_2O]$ + 0.052 s^{-1} is 948 s^{-1}, as compared to the measured value[1b] of 275 s^{-1}. However, we believe this estimate within a factor of 3.5 is encouraging and suggests that estimates made from data at high water content with linear correlations may give useful estimates of k_{H_2O} in 100% H_2O.

We note in passing that plots of k_{obsd} versus various powers of the water concentration have been used to infer the molecularity of the reaction in the $[H_2O]$.[7] We believe this procedure is of dubious validity, as it neglects the effect of water concentration on the solvent polarity. Studies[8a] of the effect of aryl substituents on the hydration rates of phenylketenes show that this reaction has a polar transition state, and we believe the major cause of the increase in ketene hydration rates with increase in the water concentration is the increase in the solvent polarity.

In summary, complete pH–rate profiles for the ketenes **1**–**3** have been measured, and these substrates are interpreted to react in acid by rate-limiting protonation on carbon (C_γ in the case of **1**) and in the neutral and hydroxide reactions to proceed with rate-limiting nucleophilic attack in the ketene plane. For the first time, k_{H^+} values for arylketenes have been measured, and major electronic and steric effects of the substituents in **1**–**3** have been identified. An evaluation of the reliability of extrapolations of rate data in mixed solvents to pure water suggests this procedure can give useful estimates of rate constants.

Experimental Section

Ketene **1**[5,9] was prepared as reported,[9] except that sodium chlorite/hydrogen peroxide[12] was used to oxidize α-citral to acid **4**. Ketene **2**[10a] was obtained from the acid chloride as reported,[10a] from acid **8**.[10b] The acid t-BuCHPhCO_2H[10b] was obtained from t-BuCOPh by a general Wittig reaction, hydration, and oxidation

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[18] (a) Neuvonen, H. *J. Chem. Soc., Perkin Trans. 2* **1986**, 1141–1145. (b) Allen, J. M.; Venkatasubban, K. S. *J. Org. Chem.* **1985**, *50*, 5108–5110. (c) Gandour, R. D.; Coyne, M.; Stella, V. J.; Showen, R. L. *Ibid.* **1980**, *45*, 1733–1737.

[19] (a) Duhaime, R. M.; Weedon, A. C. *J. Am. Chem. Soc.* **1987**, *109*, 2479–2483. (b) Pollack, R. M.; Mack, J. P. G.; Eldin, S. *Ibid.* **1987**, *109*, 5048–5050.

[20] (a) Grunwald, E.; Winstein, S. *J. Am. Chem. Soc.* **1948**, *70*, 846–854. (b) Bentley, T. W.; Bowen, C. T.; Morten, D. H.; Schleyer, P. v. R. *Ibid.* **1981**, *103*, 5466–5475.

[21] The numerical data for the variation in rate of Ph_2C=C=O in aqueous dioxane as a function of water concentration was kindly provided to us by Professor D. P. N. Satchell.

sequence[10b] and was converted to 3 by zinc debromination[2a,b] of t-BuC(Br)PhCOCl.

For the product studies on 1, three 25-mL solutions of water/acetonitrile (20%/80%) were prepared: acid (2×10^{-2} M HCl), base (1×10^{-3} N NaOH), and neutral (buffered at pH 7.00 with sodium hydroxide/potassium monobasic phosphate). To each solution was added approximately 75 mg of ketene 1 directly from the VPC (OV-17 column at 120 °C and helium flow of 85 mL/min) without collection of the ketene. The solutions were allowed to react for 88 h at room temperature in acid and 39 h at 65 °C for the basic and buffered solutions. Ether (20 mL) was added to each solution, and the solutions were extracted against dilute acid and then saturated sodium chloride. The solutions were treated with diazomethane, extracted again with saturated sodium chloride, and dried over calcium sulfate. Excess ether was removed under reduced pressure. Relative quantities of the esters 9 and 10 were measured by VPC using the OV-17 column at 120 °C and a helium flow of 85 mL/min.

Kinetic measurements were carried out as reported previously[1a] by observing the decrease in the UV absorbance at 232 nm for 1 and 254 nm for 2 and 3.

Kinetic studies of 1 in NaOH solution below 0.1 M NaOH were carried out in solutions maintained at ionic strength $\mu = 0.1$ by the addition of NaCl, but above 0.1 M NaOH no NaCl was added and the ionic strengths were greater and increased with [NaOH]. The reactions maintained at $\mu = 0.1$ gave $k_{OH} = 0.122$ M^{-1} s^{-1}, whereas if all the reactions are considered together, $k_{OH} = 0.104$ M^{-1} s^{-1} is calculated.

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Registry No. 1, 61899-98-7; 2, 38082-08-5; 3, 57768-77-1; 9, 28043-10-9; 10, 49815-58-9; O_2, 7782-39-0.

Synthesis and Reactions of α-Carbomethoxy-*N*-phenylmaleimide and Related Electrophilic Ethylenes

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Received November 1, 1988

The synthesis of α-carbomethoxy-*N*-phenylmaleimide (CNPM) was accomplished by way of a Diels–Alder precursor from α-carbomethoxymaleic anhydride and cyclopentadiene, conversion of the anhydride functionality to *N*-phenylmaleimide, and finally thermolysis. Reactions of this highly electrophilic new olefin with donor olefins were studied. The Diels–Alder product with cyclopentadiene and unstable [2 + 2] cycloadducts with *N*-vinylcarbazole were obtained. With styrene and *p*-methoxystyrene, double Diels–Alder adducts were formed. Anionic oligomerization of CNPM occurred with triethylamine. Various trialkyl ethylenetricarboxylates have been synthesized in a one-step reaction using poly(methyl glyoxylate) and dialkyl malonates. The synthesis of α-carbomethoxymaleic anhydride has been optimized. Attempts to synthesize new carboalkoxymaleic anhydrides (and in turn other carboalkoxy-*N*-phenylmaleimides) from their corresponding trialkyl ethylenetricarboxylates have failed.

Introduction

We have been interested in spontaneous cycloaddition and polymerization reactions of tri-substituted electrophilic olefins with electron-donor olefins.[1-6]

Of the electrophilic olefins studied, α-carbomethoxymaleic anhydride, CMA, is much more reactive than other trisubstituted olefins in cycloaddition reactions with electron-rich olefins and dienes.[6] Confining two substituents in the maleic anhydride ring minimizes steric hindrance and hence increases reactivity. CMA is even more reactive than tetracyanoethylene in [4 + 2] cycloadditions.

CMA had been synthesized by reaction of trimethyl ethylenetricarboxylate with phosphorus pentoxide at 150–160 °C.[5] We have improved the synthesis of CMA. It was used as the starting material for the synthesis of a novel cyclic trisubstituted electrophilic olefin, α-carbomethoxy-*N*-phenylmaleimide, CNPM. Its reactivity with various electron-rich olefins and its polymerization tendencies will be examined.

Attempts to synthesize other α-carboalkoxymaleic anhydrides will also be described.

Results

Synthesis of Trialkyl Ethylenetricarboxylates. Trimethyl ethylenetricarboxylate was previously synthesized by a multistep procedure starting from dimethyl malonate and methyl chloroacetate.[2] We now introduce a one-step synthesis, which consists of a Knoevenagel reaction of methyl glyoxylate 1 with dimethyl malonate in acetic anhydride. Three possible products are formed in this reaction: trimethyl ethylenetricarboxylate **3a**, its acetate adduct **4**, and the acylal of methyl glyoxylate **5**. The yield of each compound depends on the reaction time and temperature.

Many different experimental conditions were attempted to maximize the yield of trimethyl ethylenetricarboxylate **3a** from monomeric methyl glyoxylate. When the reaction

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[1] Hall, H. K., Jr. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 440.

[2] Hall, H. K., Jr.; Daly, R. C. *Macromolecules* **1975**, *8*, 22.

[3] Hall, H. K., Jr.; Abdelkader, M. *J. Org. Chem.* **1981**, *46*, 2948.

[4] Hall, H. K., Jr.; Padias, A. B.; Pandya, A.; Tanaka, H. *Macromolecules* **1987**, *20*, 247.

[5] Hall, H. K., Jr.; Rhoades, J. W.; Nogues, P.; Wai, G. *Polym. Bull.* **1981**, *4*, 629.

[6] Hall, H. K., Jr.; Nogues, P.; Rhoades, J. W.; Sentman, R. C.; Detar, M. *J. Org. Chem.* **1982**, *47*, 1451.

[7] Abdelkader, M.; Padias, A. B.; Hall, H. K., Jr. *Macromolecules* **1987**, *20*, 949.

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