Generation of 6-methylene-2,4-cyclohexadienylideneketene by flash photolysis of benzocyclobutenone in aqueous solution and study of the reactions of this ketene in that medium

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Abstract: Flash photolysis of benzocyclobutenone in aqueous solution produced a transient species with a microsecond lifetime whose rates of decay were measured in perchloric acid, sodium hydroxide, and buffer solutions over the acidity range $[H^+] 1 \times 10^{-13} - 10^0$ M. This produced a rate profile, isotope effects, and buffer behaviour typical of ketene reactions, and that, together with product identification, served to identify this transient as 6-methylene-2,4-cyclohexadienylideneketene, formed by electrocyclic opening of the four-membered ring of benzocyclobutenone. Comparison of rates of reaction of this ketene with those of its saturated analog, pentamethyleneketene, produced some expected as well as some unexpected results.

Key words: cyclobutenone chemistry, electrocyclic ring opening, ketene hydration, rate profile, solvent isotope effects.

Résumé : La photolyse éclair de la benzocyclobuténone en solution aqueuse produit une entité transitoire de temps de vie de la microseconde dont on a mesuré les vitesses de décroissance dans l'acide perchlorique, l'hydroxyde de sodium et des solutions tampons dont l'acidité $[H^+]$ s'étale de 1×10^{-13} à 10^0 . Sur la base de ces données, on a établi que le profil de vitesse de réaction, les effets isotopiques et le comportement vis-à-vis des tampons sont typiques des réactions des cétènes et, en les combinant à l'identification du produit, on a pu établir que cette entité transitoire est le 6-méthy-lènecyclohexa-2,4-diénylidènecétène qui se forme par une ouverture électrocyclique du cycle à quatre chaînons de la benzocyclobuténone. Une comparaison des vitesses de réaction de ce cétène avec celles de son analogue saturé, pentaméthylènecétène, a conduit à des résultats dont quelques-uns étaient attendus alors que d'autres étaient inattendus.

Mots clés : chimie de la cyclobuténone, ouverture électrocyclique de cycle, hydratation d'un cétène, profil de vitesse de réaction, effets isotopiques de solvant.

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Introduction

Three decades ago, Don Arnold, studying the photochemistry of benzocyclobutenone (1) (1) corroborated an earlier observation (2) that irradiation of this ketone in methanol solution produced methyl 2-methylbenzoate (3). He then postulated that this reaction occured through electrocyclic opening of the four-membered ring to give 6methylene-2,4-cyclohexadienylideneketene (2) followed by the well-known addition of alcohols to ketenes to form the ester product (eq. [1]).



Support for this hypothesis was provided by subsequent observations (3) that irradiation of benzocyclobutenone in low-temperature hydrocarbon matrices converts it into an unstable but observable substance with UV and IR spectral properties expected of 6-methylene-2,4-cyclohexadienylideneketene. Additional evidence for this structural assignment came from a room-temperature flash photolytic study of benzocyclobutenone in ether solution that showed generation and decay of a transient species whose pattern of reactivity with added reagents agreed with expectation for this ketene (4).

We now add to these previous investigations a flash photolytic study of benzocyclobutenone in aqueous solution. This has allowed comparison of rates of hydration of 6methylene-2,4-cyclohexadienylideneketene with those of other ketenes, and that has revealed some interesting features concerning the reactivity of this substance.

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This paper is dedicated to Professor Don Arnold in appreciation for his many contributions to organic photochemistry.

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Experimental section

Materials

Benzocyclobutenone, a gift from Dr. P. Schiess, was made by flash vacuum pyrolysis of 2-methylbenzoyl chloride (5). 2-Methylbenzamide was prepared by treating 2-methylbenzoyl chloride (6) with concentrated aqueous ammonia (7). All other materials were the best available commercial grades.

Kinetics

Rate measurements were made using a nanosecond, eximer laser flash photolysis system operating at λ_{exc} = 248 nm that has already been described (8), and reactions were followed by monitoring absorbance decay at λ = 400 nm. Initial substrate (benzocyclobutenone) concentrations were ca. 1×10^{-5} M, and the temperature of all reacting solutions was controlled at 25.0 ± 0.05°C. The rate data so obtained conformed to the first-order rate law well, and observed first-order rate constants were obtained by leastsquares fitting of a single exponential function.

Product analyses

Product compositions were determined by HPLC using a Varian Vista 5500 instrument with a NovoPak C_{18} reversephase column and methanol–water (50:50, v/v) as the eluent. Reaction solutions containing substrate at similar concentrations as used for the kinetic measurements (ca. 1×10^{-5} M) were subjected to a single pulse from a microsecond flash photolysis system (9), and products were identified by comparing retention times and UV spectra with those of authentic samples.

Results and discussion

Reaction identification

Flash photolysis of benzocyclobutenone in aqueous solution produced a transient species with strong absorbance at $\lambda = 400$ nm. This is the wavelength at which 6-methylene-2,4-cyclohexadienylideneketene showed a strong absorption band when generated in low-temperature matrices (3) or in ether solution at room temperature (4), which indicates that this ketene is generated by irradiation of this precursor in an aqueous solvent just as in these other media. Additional support for this conclusion comes from the fact that 2-methylbenzoic acid (4) was found to be the only product formed by flash photolysis of benzocyclobutenone in unbuffered water and in 0.001 M aqueous perchloric acid solution (eq. [2]) consistent with the known proclivity of ketenes to react with water giving carboxylic acid products (10*a*).





In aqueous ammonium ion – ammonia buffers, 2-methylbenzamide (5) was formed as well (eq. [3]) which again is consistent with the known reaction of ketenes with ammonia and amines to give amide products (10b, 11).

Rate profile

Rates of decay of 6-methylene-2,4-cyclohexadienylideneketene were measured in aqueous perchloric acid and sodium hydroxide solutions and in acetic acid, biphosphate ion, tris-(hydroxymethyl)methylammonium ion, and ammonium ion buffers. The ionic strength of these solutions was maintained at 0.10 M through the addition of sodium perchlorate as required, except in the case of perchloric acid solutions at concentrations greater than 0.1 M, where the ionic strength was equal to the acid concentration. These data are summarized in Tables S1-S3.²

The measurements in buffers were made using series of solutions of varying buffer concentration but constant buffer ratio and therefore, because the ionic strength was constant, constant hydronium ion concentration. In each solution series, observed first-order rate constants proved to be linear functions of buffer concentration, and the data were therefore analyzed by least-squares fitting of the buffer dilution expression shown as eq. [4]. The zero-buffer-

$$[4] k_{obs} = k_{intcpt} + k_{buff}[buffer]$$

concentration intercepts obtained in this way (k_{intept}), together with the rate constants obtained in perchloric acid and sodium hydroxide solutions, are displayed as the rate profile shown in Fig. 1. Hydronium ion concentrations of the buffer solutions needed for this purpose were obtained by calculation using acidity constants of the buffer acids from the literature and activity coefficients recommended by Bates (12).

This rate profile shows a long uncatalyzed portion extending from $[H^+] = 1 \times 10^{-1}$ to $[H^+] = 1 \times 10^{-11}$, with weak hydroxide ion catalysis and even weaker hydronium ion catalysis. Such behavior is typical of ketene hydrations, where the hydroxide ion reaction is only moderately faster than uncatalyzed hydration and acid catalysis is often not observed.³ This profile therefore provides further evidence that the transient species observed is a ketene.

As is often the case for acid-catalyzed reactions in concentrated acid solutions, rates of hydration of 6-methylene-2,4-cyclohexadienylideneketene in perchloric acid solutions more concentrated than 0.1 M increased more steeply than in direct linear proportion to acid concentration. The data were therefore treated by the Cox–Yates method using the X_0 excess acidity function (14). The analysis was done by least-squares fitting of eq. [5], where H⁺

[5]
$$k_{obs} = k_{uc} + k_{H^+} [H^+] 10^{mX_o}$$

² Tables of rate data (Tables S1–S4) have been deposited and may be purchased from the Depository of Unpublished Data, Document Delivery, CISTI, National Research Council Canada, Ottawa ON, K1A OS2, Canada (http://www.nrc.ca/cisti/irm/unpub_e.shtml for information on ordering electronically).

³See, for example, ref. (13).

Fig. 1. Rate profile for the hydration of 6-methylene-2,4cyclohexadienylideneketene in aqueous solution at 25°C.



represents the hydronium ion, with [H⁺] and X_o as independent variables, and $k_{\rm uc}$, $k_{\rm H^+}$, and *m* as parameters to be determined by the fit. This gave $k_{\rm uc} = (1.35 \pm 0.01) \times 10^5 \, {\rm s}^{-1}$, $k_{\rm H^+} = (1.45 \pm 0.03) \times 10^5 \, {\rm M}^{-1} \, {\rm s}^{-1}$, and $m = 1.20 \pm 0.03$. This value of *m* was then used to calculate the quantity [H⁺]10^{*m*X_o}, which was used as the abscissa for the rate profile of Fig. 1. Because X_o becomes equal to zero at hydronium ion concentrations less than 0.1 M, and $10^{$ *m* X_o} consequently becomes equal to unity, [H⁺]10^{*m*X_o} differs from [H⁺] only at [H⁺] > 0.1.

With this definition of the abscissa, the rate law that applies to the rate profile of Fig. 1 is the expression shown in eq. [6]. Least-squares fitting of this expression gave $k_{\rm H^+} = (1.44 \pm 0.01) \times 10^5 \, {\rm M^{-1}} \, {\rm s^{-1}}$, $k_{\rm uc} = (1.35 \pm 0.01) \times 10^5 \, {\rm s^{-1}}$, and $k_{\rm HO^-} = (9.26 \pm 0.06) \times 10^6 \, {\rm M^{-1}} \, {\rm s^{-1}}$. It is

[6]
$$k_{\text{obs}} = k_{\text{H}^+}[\text{H}^+]10^{mX_{\text{o}}} + k_{\text{uc}} + k_{\text{HO}^-}[\text{HO}^-]$$

gratifying that the values of $k_{\rm H^+}$ and $k_{\rm uc}$ obtained in this way are in excellent agreement with those produced by the Cox–Yates analysis of the perchloric acid data.

It has been observed that substituent effects on the rates of uncatalyzed ketene hydration (k_{uc}) are remarkably similar to those on the rates of hydroxide-ion catalyzed hydration (k_{HO^-}) and this similarlity has been used to support a common nucleophilic reaction mechanism for both processes (10*a*). It has also led to the good correlaton of rate constants for these two reactions illustrated in Fig. 2 (15). This figure also shows that the presently determined data fit this correlation well, thus substantiating identification of the presently observed transient species as 6-methylene-2,4-cyclohexadienylideneketene.

Isotope effects

Rates of hydration of 6-methylene-2,4-cyclohexadienylideneketene were also measured in moderately concentrated solutions of HCl in H₂O and DCl in D₂O. These data are summarized in Table S4² and are displayed in Fig. 3.

Once again, observed rate constants increased more steeply than in direct proportion to acid concentration, and the Cox–Yates method (14) using the X_0 scale for HCl (16) was used to analyze the data. The X_0 scale has not been determined for DCl in D₂O solution, but other acidity func-

Fig. 2. Correlation of rates of uncatalyzed (k_{uc}) and hydroxideion-catalyzed (k_{HO^-}) ketene hydration; 6-methylene-2,4-cyclohexadienylideneketene (\bullet), other ketenes (O).

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Fig. 3. Reaction of 6-methylene-2,4-cyclohexadienylideneketene in aq HCl-H₂O (O) and DCl-D₂O (Δ) solutions at 25°C.



tions are known to be the same for D_2O as for H_2O solutions of hydrochloric (17) and perchloric (18) acids when the comparison is made at the same molar acid concentration. It seems reasonable to assume that the same would be true for the X_0 scale, and values of X_0 for HCl in H_2O were therefore used for the D_2O solutions.

Least-squares analysis using eq. [5] gave $k_{uc} = (1.37 \pm 0.02) \times 10^5 \text{ s}^{-1}$, $k_{\text{H}^+} = (1.39 \pm 0.09) \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$, and $m = (1.64 \pm 0.17)$ for the H₂O solutions and $k_{uc} = (9.35 \pm 0.01) \times 10^4 \text{ s}^{-1}$, $k_{\text{D}^+} = (4.66 \pm 0.02) \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$, and $m = (1.40 \pm 0.10)$ for the D₂O solutions. These values of k_{uc} and k_{H^+} agree well with those determined for H₂O solutions of HClO₄ (vide supra). The difference between the HCl and HClO₄ values of *m*, on the other hand, is somewhat greater than their combined standard deviations, suggesting that medium effects are not quite the same in concd HCl as in concd HClO₄ solutions.

These data provide the isotope effects $k_{\rm H^+}/k_{\rm D^+} = 2.98 \pm 0.25$ and $(k_{\rm uc})_{\rm H_2O}/(k_{\rm uc})_{\rm D_2O} = 1.46 \pm 0.03$. Acid-catalyzed hydration of ketenes is known to occur by rate-determining protonation of the β -carbon atom of the ketene, followed by rapid reaction of the acylium ion thus formed with water

(10c, 19). In the present case, protonation is more likely to occur on the *exo*-carbon atom of the methylene group, because that will regenerate a benzene ring and benefit from a gain of benzene resonance energy (eq. [7]). In any event, there will be a hydron in flight in

the rate-determining step of this reaction and the isotope effect will consequently have a primary component. It will, however, have an inverse secondary component as well, produced by tightening of the hydrogen–oxygen bonds of the transition state moiety on its way to becoming a water molecule. The isotope effect observed $(k_{\rm H^+}/k_{\rm D^+} = 2.98)$ is in fact a typical value for such a process (20).

Uncatalyzed hydration of ketenes, on the other hand, occurs through nucleophilic attack of a water molecule on the carbon atom of the ketene carbonyl group, generating an enol intermediate, which then ketonizes in a fast subsequent step (10a, 15) (eq. [8]). Formation of the

enol could occur either through a zwitterion, or the zwitterion could be avoided by simultaneous proton shuffling. In either case, the solvent isotope effect would be small because there would be no primary component; in zwitterion formation because no hydron transfer takes place, and in simultaneous proton shuffling because the hydron transfer here is between oxygen atoms with the hydron lying in a stable potential well at the transition state and consequently not being in flight (21). The isotope effect observed ($k_{\rm H}/k_{\rm D} = 1.46$) is a typical value for such a process (15).

Reaction in buffers

The rate measurements in acetic acid and ammonium ion buffers were each made at four different buffer ratios, which allowed separation of the buffer-dependent rate constants of eq. [4] (k_{buff}) into their buffer base (k_B) and buffer acid (k_{HA}) components. This was done through the use of eq. [9], in which f_A is the fraction of buffer present in the acid form.

[9]
$$k_{\text{buff}} = k_{\text{B}} + (k_{\text{HA}} - k_{\text{B}})f_{\text{A}}$$

Least-squares fitting of this equation gave $k_{\rm B} = (1.23 \pm 0.07) \times 10^6 \,{\rm M}^{-1} \,{\rm s}^{-1}$ and $k_{\rm HA} = -(8.84 \pm 5.26) \times 10^4 \,{\rm M}^{-1} \,{\rm s}^{-1}$ for the acetic acid buffers, and $k_{\rm B} = (1.72 \pm 0.11) \times 10^6 \,{\rm M}^{-1} \,{\rm s}^{-1}$ and $k_{\rm HA} = (1.76 \pm 8.99) \times 10^4 \,{\rm M}^{-1} \,{\rm s}^{-1}$ for the ammonium ion buffers. In both cases, therefore, the buffer-dependent reaction was wholly of the basic type.

A similar analysis could not be carried out for the biphosphate and tris-(hydroxymethyl)methylammonium ion buffers because measurements here were made at only one buffer ratio. It seems fair to assume, however, that the buffer-dependent reaction here was also wholly of the basic type, inasmuch as the acid and base strengths of the components of these buffers lie between those (acetic acid and ammonium ion) for which analysis using eq. [9] showed only a

Table 1. Buffer base rate constants $(k_{\rm B})$ for the reaction of 6methylene-2,4-cyclohexadienylideneketene in aqueous solution at 25°C.^{*a*}

Base	pK_a (BH)	$k_{\rm B}~(10^6~{\rm M}^{-1}~{\rm s}^{-1})$
CH ₃ CO ₂	4.76	1.23
HPO_4^{2-}	7.20	1.01
(CH ₂ OH) ₃ CNH ₂	8.07	0.283
NH ₃	9.25	1.72

^{*a*}Ionic strength = 0.10 M (NaClO₄).

Table 2. Comparison of rates of hydration of 6-methylene-2,4cyclohexadienylideneketene with those of an analogous ketene not having a cyclohexadienyl structure.^{*a*}

Substrate	$k_{\rm HO^-} ~({\rm M^{-1}~s^{-1}})$	$k_{\rm uc} ({\rm s}^{-1})$	$k_{\rm H^+} \ ({\rm M^{-1}} \ {\rm s^{-1}})$
~~~ ⁰	$9.26 \times 10^{6}$	$1.35 \times 10^{5}$	$1.44 \times 10^{5}$
	$6.24 \times 10^{3}$	$2.30 \times 10^{1}$	$2.78 \times 10^{3}$

^aAqueous solution, 25°C; data for pentamethyleneketene from ref. (15).

base reaction. Using this reasonable assumption, the bufferdependent rate constants for the biphosphate and tris-(hydroxymethyl)methylammonium buffers ( $k_{buff}$ ) were transformed into buffer base rate constants. The results, together with the buffer base rate constants obtained from acetic acid and ammonium ion buffers, are listed in Table 1.

Inspection of Table 1 shows that the reactivity of the buffer bases does not increase regularily with buffer base strength, as it would if the buffer bases were acting as proton transfer agents. Tris-(hydroxymethyl)methylamine, for example, is a stronger base than either acetate or hydrogen phosphate ions, and yet its rate of reaction is only a quarter of that of the ions. The reactivity order shown by Table 1, on the other hand, is what might be expected if the buffer bases were reacting as nucleophiles: tris-(hydroxymethly)methylamine, with its large bulk, should be a poorer nucleophile than the other smaller bases of this table. Bases, of course, react with ketenes as nucleophiles and not as proton transfer agents (11), and the data in Table 1, therefore, provide still more evidence that the substance produced by photolysis of benzocyclobutenone is 6-methylene-2,4-cyclohexadienylideneketene.

#### Reactivity

Rates of hydration of the presently studied ketene are considerably faster than those of other ketenes whose reactions do not convert a cyclohexadienyl structure into an aromatic benzene ring. The data assembled in Table 2 provide a comparison with pentamethyleneketene (15), a substrate also possessing a six-membered carbocyclic ring. It may be seen that the present ketene is the much more reactive substance, by a factor of 1500, corresponding to a free energy of activation difference of  $\delta G^{\neq} = 4.3$  kcal mol⁻¹, for the hydroxide-ion-catalyzed process and by a factor of 5900 or  $\delta \Delta G^{\neq} = 5.1$  kcal mol⁻¹ for the uncatalyzed reaction. The greater difference for the slower uncatalyzed hydration is of course

understandable as operation of the reactivity-selectivity principle.

The hydronium-ion-catalyzed reaction of 6-methylene-2,4-cyclohexadienylideneketene is also faster than that of pentamethyleneketene, but now the difference, a factor of 52 or  $\delta \Delta G^{\neq} = 2.3$  kcal mol⁻¹, is much less than those for the hydroxide ion and uncatalyzed processes. This is surprising, because the hydronium ion catalysis of 6-methylene-2,3cyclohexadienylideneketene hydration presumably takes place by rate-determining proton transfer to the exo-carbon atom of the methylene group, as shown in eq. [7]. This immediately converts a cyclohexadienyl structure into an aromatic ring and profits from a gain in benzene resonance energy. The hydroxide-ion-catalyzed and uncatalyzed reactions, on the other hand, occur by nucleophilic attack on the ketene's carbonyl carbon atom (10a, 15), as illustrated for the uncatalyzed process in eq. [8]. Because this nucleophilic attack occurs in the ketene molecular plane (4), it puts negative charge into an orbital that is orthogonal to the cyclohexadienyl  $\pi$  system. Delocalization of this charge into the  $\pi$ system therefore does not occur, and this suggests that aromatization of the cyclohexadienyl ring in the reaction's rate-determining transition state does not take place; the reaction therefore does not benefit from a gain in benzene resonance energy.

These arguments lead to the expectation that hydroniumion-catalyzed hydration of 6-methylene-2,4-cyclohexadienylideneketene should be faster than that of pentamethyleneketene by an amount greater than those for the hydroxide-ion-catalyzed and uncatalyzed reactions, contrary to the data presented in Table 2. The reason for this unexpected difference is not clear.

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- D.R. Arnold, E. Hedeya, V.Y. Merritt, L.A. Karniscky, and M.E. Kent. Tetrahedron Lett. 3917 (1972).
- 2. M.P. Cava and R.J. Spangler. J. Am. Chem. Soc. 89, 4550 (1967).
- (a) A. Krantz. J. Am. Chem. Soc. 96, 4992 (1974); (b) N.P. Hacker and N.J. Turro. J. Photochem. 22, 131 (1983).
- 4. P. Schiess, M. Eberle, M. Huys-Francotte, and J. Wirz. Tetrahedron Lett. 25, 2201 (1984).
- P. Schiess and M. Heitzmann. Angew. Chem. Int. Ed. Engl. 16, 469 (1977).
- 6. H.G. Tanner and P.A. Lasselle. J. Am. Chem. Soc. 48, 2163 (1926).
- R.L. Shriner and R.C. Fuson. The systematic identification of organic compounds. Wiley, New York. 1948. pp. 157–158.
- J. Andraos, Y. Chiang, C.G. Huang, A.J. Kresge, and J.C. Scaiano. J. Am. Chem. Soc. 115, 10 605 (1993).
- Y. Chiang, M. Hojatti, J.R. Keeffe, A.J. Kresge, N. P. Schepp, and J. Wirz. J. Am. Chem. Soc. 109, 4000 (1987).
- (a) T.T. Tidwell. Ketenes. Wiley-Interscience, New York. 1995; pp. 571–587; (b) T.T. Tidwell. Ketenes. Wiley-Interscience, New York. 1995. pp. 589–590; (c) T.T. Tidwell. Ketenes. Wiley-Interscience, New York. 1995. 585–587.
- 11. J. Andraos and A.J. Kresge. J. Am. Chem. Soc. 114, 5643 (1992).
- 12. R.G. Bates. Determination of pH theory and practice. Wiley-Interscience, New York. 1973. p. 49.
- Y. Chiang, A.J. Kresge and V.V. Popik. J. Am. Chem. Soc. 117, 9165 (1995).
- 14. R.A. Cox. Adv. Phys. Org. Chem. 35, 1 (2000).
- 15. J. Andraos and A.J. Kresge. Can. J. Chem. 78, 508 (2000).
- 16. R.A. Cox and K. Yates. Can. J. Chem. 59, 2116 (1981).
- 17. E. Hogfeldt and J. Bigeleisen. J. Am. Chem. Soc. 82, 15 (1960).
- R.A. Cox, S.-O. Lam, R.A. McClelland, and T.T. Tidwell. J. Chem. Soc., Perkin Trans. 2, 272 (1979).
- (a) J. Andraos and A.J. Kresge. J. Photochem. Photobiol. A.
  57, 165 (1991); (b) J. Andraos, A. J. Kresge, and N. P. Schepp. Can. J. Chem. 73, 539 (1995).
- A.J. Kresge, D.S. Sagatys and H.L. Chen. J. Am. Chem. Soc. 99, 7228 (1977).
- C.G. Swain, D.A. Kuhn, and R.L. Schowen. J. Am. Chem. Soc. 87, 1553 (1965).