Diazoacetaldehyde: completion of the rate profile for hydration of its photo-Wolff rearrangement product, ketene, in aqueous solution and kinetics and mechanism of acid-catalyzed hydrolysis of the diazoaldehyde †

Y. Chiang, A. J. Kresge * and V. V. Popik

Department of Chemistry, University of Toronto, Toronto, Ontario, M5S 3H6, Canada

Received (in Gainesville, FL) 12th February 1999, Accepted 9th April 1999

Ketene was generated flash photolytically by the photo-Wolff reaction of diazoacetaldehyde and rates of its hydration to acetic acid were measured in dilute aqueous sodium hydroxide solution. The results give the isotope effect, $k_{HO}/k_{DO} = 0.87$, on the hydroxide-ion catalytic coefficient for this reaction, and, together with literature information, they provide a complete rate law for the hydration of ketene in aqueous solution promoted by solvent related species: $k_{obs}/s^{-1} = 1.01 \times 10^4[H^+] + 3.65 \times 10^1 + 5.26 \times 10^4[HO^-]$. Rates of hydrolysis of diazoacetaldehyde in dilute perchloric acid solution were also measured and an inverse hydronium ion isotope effect was found: $k_{H^+}/k_{D^+} = 0.55$. That, plus the fact that hydrogen exchange of the diazo hydrogen atom of diazoacetaldehyde takes place more rapidly than its hydrolysis, shows that hydrolysis occurs through a mechanism involving pre-equilibrium protonation of diazo carbon followed by rate-determining loss of nitrogen.

The hydration of ketenes, **1**, to produce carboxylic acids, **2**, eqn. (1), is a much-studied reaction that has been examined

$$\underset{\mathbf{1}}{RR'C{=}C{=}O} + H_2O \longrightarrow \underset{\mathbf{2}}{RR'CHCO_2H} \qquad (1)$$

both empirically and theoretically.[1] In aqueous solution it occurs by acid- and base-catalyzed pathways as well as by an often prominent uncatalyzed route. For the prototypical substrate, ketene itself (**1**, R = R′ = H), values of the hydronium-ion catalytic coefficient and the uncatalyzed rate constant have been available,[2] but the same has not been true of the hydroxide-ion catalytic coefficient. We have now remedied that deficiency by measuring the rate of hydration of ketene in aqueous sodium hydroxide solutions.

The hydration of ketene in aqueous solution is a moderately rapid process that requires fast reaction techniques for measurement of its reaction rates. In the present study, we used flash photolytic methods, with diazoacetaldehyde, **3**, as the substrate; photolysis of this substance is known to produce ketene,[3] and ketene-derived products,[4] by a photo-Wolff reaction, as shown in eqn. (2).

$$\underset{\mathbf{3}}{N_2CHCHO} \xrightarrow{h\nu} CH_2{=}C{=}O + N_2 \qquad (2)$$

Diazo compounds such as diazoacetaldehyde also undergo acid-catalyzed hydrolysis, as illustrated in eqn. (3). This reaction has been studied extensively for a variety of diazo compounds, and several different mechanisms have been identified.[5] Little information, however, is available for hydrolysis of the simplest α-carbonyldiazo compound, diazoacetaldehyde: the only mention in the open literature[6] states the mechanism of the reaction and gives a reference to a generally unavailable thesis,[7] but provides no details. We have therefore examined this reaction of diazoacetaldehyde as well.

$$N_2CRCR'O + H_2O \xrightarrow{HA} HOCHRCR'O \qquad (3)$$

Experimental

Materials

Diazoacetaldehyde was prepared by formylation of diazomethane using formic acetic anhydride as the formylating agent.[8] The crude material was purified by the extraction procedure described in reference 9 followed by distillation at 2–3 Torr while keeping the heating bath temperature at 40–45 °C.[8] The IR spectrum of the material so obtained was consistent with that reported in the literature.[8] Its proton NMR spectra: δ_H (200 MHz; $CDCl_3$; Me_4Si) 9.61 (0.30 H, d, $J = 6.8$ Hz), 9.19 (0.67 H, s), 5.33 (0.74 H, s), 5.14 (0.29 H, d, $J = 7.0$ Hz); δ_H (200 MHz; D_2O) 9.36 (0.38 H, d, $J = 8.0$ Hz), 8.94 (0.61 H, s), 5.78 (0.63 H, s), 5.47 (0.38 H, d, $J = 8.1$ Hz), indicated restricted rotation about the C–C bond, giving rise to s-*cis* and s-*trans* isomers, present in the ratio 70 : 30 in $CDCl_3$ solution and 62 : 38 in D_2O solution. This phenomenon has been observed before,[10] and the ratio found here for $CDCl_3$ solution agrees well with the 69 : 31 ratio reported for that solvent.[10] The carbon-13 NMR spectra of the present preparation also indicated s-*cis*/s-*trans* isomerism: δ_C (50 MHz; $CDCl_3$; Me_4Si) 183.56, 183.15, 59.50, 56.39; δ_C (50 MHz; D_2O) 190.99, 190.29, 65.93, 62.29.

Warning: health and explosion hazard. Diazoacetaldehyde, like most volatile diazo compounds, is a possible carcinogen that attacks the liver and pancreas; it also explodes with unusual violence when overheated, and bath temperatures required for its distillation should not be raised above 50 °C.[9]

All other materials were the best available commercial grades.

Kinetics

Rates of hydration of ketene were measured using a conventional flash photolysis system that has already been

---

† Tables S1 and S2 are available as supplementary data. For direct electronic access see http://www.rsc.org/suppdata/p2/1999/1107, otherwise available from BLDSC (SUPPL. NO. 57537, pp. 4) or the RSC Library. See Instructions for Authors available *via* the RSC web page (http:www.rsc.org/authors).

described,[11] whose cell compartment was thermostatted at 25.0 ± 0.05 °C. The reaction was monitored by following the decrease in ketene absorbance at $\lambda = 215$ or 222 nm. The data obtained at $\lambda = 215$ nm conformed to the first-order rate law well, and observed first-order rate constants were evaluated by least-squares fitting of an exponential function. At $\lambda = 222$ nm, however, the first-order drop in absorbance was followed by a further downward drift; the data were therefore analyzed by least-squares fitting of an exponential plus linear function. Observed first-order rate constants determined in this way agreed well with analogous results obtained by $\lambda = 215$ nm where no downward drift occurred.

Rates of hydrolysis of diazoacetaldehyde were measured by monitoring the decrease in substrate absorbance at $\lambda = 275$ nm, using a Cary 2200 spectrometer whose cell compartment was thermostatted at 25.0 ± 0.05 °C. The data so obtained fit the first-order rate law well, and observed first-order rate constants were determined by least-squares fitting of an exponential function.

Product studies

The products of ketene hydration and diazoacetaldehyde hydrolysis were determined by carrying out the reactions in D_2O solution and then examining the NMR spectra of the solutions so obtained, using spectra of authentic samples to confirm identification. Ketene was generated in these experiments by irradiation of diazoacetaldehyde with a Sylvania Model H44GS-100 high pressure mercury lamp.

Results

Ketene hydration

The principal product formed upon irradiation of 0.4 M diazoacetaldehyde in dilute aqueous sodium hydroxide solution was found to be acetic acid, as expected. A minor amount, *ca.* 10%, of glycolaldehyde, existing largely as the hydrate, was found as well. This substance is the product expected from insertion of formylcarbene, formed by photolysis of diazoacetaldehyde,[4,9] into an O–H bond of solvent water. Such insertions are characteristic reactions of carbenes,[12] which, in the case of α-carbonylcarbenes, have recently been shown to occur *via* enol intermediates, according to eqn. (4).[13]

$$N_2CHCHO \xrightarrow[-N_2]{h\nu} \ddot{C}HCHO \xrightarrow{H_2O} CHOH{=}CHOH \longrightarrow CH_2OHCHO \quad (4)$$

Rates of hydration of ketene, produced by flash photolysis of *ca.* 5×10^{-5} M solutions of diazoacetaldehyde, were measured in dilute sodium hydroxide solutions in H_2O at 7 different concentrations over the range [NaOH] = 0.0004–0.0025 M and in D_2O at 4 different concentrations over the range [NaOD] = 0.0006–0.002 M. Replicate determinations (2–6) were made at most concentrations. The data so obtained are summarized in Table S1.†

Observed first-order rate constants obtained in this way proved to be directly proportional to sodium hydroxide concentration; linear least squares analysis produced the following relationships: H_2O: $k_{obs}/s^{-1} = (3.70 \pm 0.22) \times 10^1 + (5.26 \pm 0.21) \times 10^4[NaOH]$; D_2O: $k_{obs}/s^{-1} = (2.11 \pm 0.36) \times 10^1 + (6.06 \pm 0.31) \times 10^4[NaOD]$.

Diazoacetaldehyde hydrolysis

Glycolaldehyde, again existing largely as the hydrate, was found to be the only product formed upon hydrolysis of 0.5 M diazoacetaldehyde in 0.1 M DCl in D_2O solution, as expected on the basis of eqn. (3). Proton NMR spectra taken at various time intervals during the course of this reaction also showed that signals of the diazo proton disappeared more rapidly than hydrolysis took place, the latter as judged by the disappearance of signals from the diazoacetaldehyde aldehyde proton.

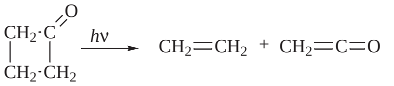
Rates of hydrolysis of diazoacetaldehyde were measured in dilute perchloric acid solutions in H_2O and in D_2O at 5 different concentrations over the range 0.02–0.1 M for each solvent. Three replicate determinations were made at each concentration. Substrate concentrations were *ca.* 5×10^{-5} M. The data so obtained are summarized in Table S2.†

Observed first-order rate constants obtained in this way were directly proportional to perchloric acid concentration, and linear least squares analysis produced the hydronium-ion catalytic coefficients $k_{H^+} = (2.23 \pm 0.01) \times 10^{-2}\ M^{-1}\ s^{-1}$ and $k_{D^+} = (4.08 \pm 0.05) \times 10^{-2}\ M^{-1}\ s^{-1}$. These results agree well with catalytic coefficients that can be calculated from the data of reference 7, kindly provided to us by Professor H. Dahn: $k_{H^+} = 2.18 \times 10^{-2}\ M^{-1}\ s^{-1}$ and $k_{D^+} = 4.07 \times 10^{-2}\ M^{-1}\ s^{-1}$.

Discussion

Ketene hydration

The rate constant for the uncatalyzed hydration of ketene determined here as the intercept of the k_{obs} *vs.* [NaOH] relationship, $k_o = 37.0 \pm 2.2\ s^{-1}$, agrees very well with the value of this constant measured directly in neutral aqueous solution, $k_o = 36.5 \pm 0.4\ s^{-1}$.[2a] The isotope effect on this rate constant determined here as the ratio of H_2O and D_2O intercepts, $k_o^H/k_o^D = 1.75 \pm 0.32$, also agrees well with the directly measured value, $k_o^H/k_o^D = 1.59 \pm 0.02$.[2a] These previously measured values were determined using ketene generated by a reaction, photolytic cycloreversion of cyclobutanone, eqn. (5), different from the one used here. The good agreement of results obtained with ketene from two different sources reinforces the conclusion that both reactions were in fact producing the same substance, ketene, and that the transient changes observed in both flash photolytic studies were ketene hydration reactions.



(5)

The isotope effect provided by the ratio of hydroxide ion catalytic coefficient determined here in H_2O and D_2O, $k_{HO}/k_{DO} = 0.87 \pm 0.06$, is characteristic of hydroxide-ion-catalyzed ketene hydrations: for five other ketenes this isotope effect was found to lie in the range $k_{HO}/k_{DO} = 0.76$–0.97.[14] The weakly inverse values of these isotope effects are consistent with the nature of this reaction, which involves nucleophilic attack of hydroxide ion on the carbonyl carbon atom of the ketene[1] in a process that consumes hydroxide ion but includes no breaking or making of bonds to isotopically substituted hydrogen.

The present determination of the hydroxide-ion catalytic coefficient for the hydration of ketene completes the rate law for this reaction in aqueous solution promoted by solvent related species, eqn. (6).

$$k_{obs}/s^{-1} = (1.01 \times 10^4)\,[H^+] + (3.65 \times 10^1) + (5.26 \times 10^4)\,[HO^-] \quad (6)$$

Diazoacetaldehyde hydrolysis

The hydronium-ion catalytic coefficients for the hydrolysis of diazoacetaldehyde determined here provide the isotope effect $k_{H^+}/k_{D^+} = 0.55 \pm 0.01$ on this reaction. The inverse ($k_H/k_D < 1$) nature of this isotope effect implies that this is a pre-equilibrium hydron transfer process, *i.e.* that hydron transfer occurs in a rapidly established equilibrium step preceeding the rate-determining stage; if the hydron transfer step itself were rate-determining, the isotope effect would have been in the normal ($k_H/k_D > 1$) direction.[15]

There are two basic sites in diazoacetaldehyde: the carbonyl oxygen atom and the diazo carbon atom, and the isotope effect itself does not distinguish which of these sites is undergoing reversible pre-equilibrium hydronation. Hydronation on carbon, however, would lead to exchange of the diazo hydrogen, whereas hydronation on oxygen would not, and our observation that the NMR signal of the diazo proton disappears more rapidly than hydrolysis takes place, when the reaction is conducted in D_2O solution (*vide supra*), indicates that hydrogen exchange does take place. The acid-catalyzed hydrolysis of diazoacetaldehyde may therefore be assigned a mechanism consisting of rapid pre-equilibrium hydronation of diazo carbon followed by rate-determining displacement of nitrogen by a water molecule, as shown in eqn. (7).

$$N_2CHCHO + H^+ \rightleftharpoons {}^+N_2CH_2CHO \xrightarrow[-H^+]{H_2O} HOCH_2CHO + N_2 \quad (7)$$

This mechanistic assignment is the same as that mentioned in reference 6. It is supported further by a comparison of the rate of hydrolysis determined here with the rate of protonation of the diazo carbon atom of diazoacetaldehyde, determined earlier in a study of diazo hydrogen exchange made using all three isotopes of hydrogen.[6] The protonation rate constant obtained there, for the reaction in aqueous solution at 0 °C, is $k = 5.3 \times 10^{-2}\ M^{-1}\ s^{-1}$. This value is already greater than $k_{H^+} = 2.2 \times 10^{-2}\ M^{-1}\ s^{-1}$ obtained here for the hydrolysis reaction at 25 °C, and, for both reactions at 25 °C, the difference will be even greater. This, then, provides direct evidence that protonation of diazoacetaldehyde on its diazo carbon atom is faster than hydrolysis, and that the reaction mechanism is the pre-equilibrium scheme shown in eqn. (7).

Acknowledgements

We are grateful to Professor Hans Dahn for providing us with parts of reference 7 and to the Natural Sciences and Engineering Research Council of Canada for financial support of this work.

References

1 For a brief review, see T. T. Tidwell, *Ketenes*, Wiley, New York, 1995, pp. 11–12; 572–587. A recent theoretical study appears in J. P. Guthrie, *Can. J. Chem.*, 1999, **77**, in the press.
2 (*a*) J. Andraos and A. J. Kresge, *J. Photochem. Photobiol. A: Chem.*, 1991, **57**, 165; (*b*) E. Bothe, A. M. Dessouki and D. Schulte-Frohlinde, *J. Phys. Chem.*, 1987, **65**, 1719.
3 A. Kranz, *J. Chem. Soc., Chem. Commun.*, 1973, 670.
4 K.-P. Zeller, *Tetrahedron Lett.*, 1977, 707; *Chem. Ber.*, 1979, **112**, 678.
5 See, *e.g.* M. Regitz and G. Maas, *Diazo Compounds Properties and Synthesis*, Academic Press, New York, 1986, pp. 96–165.
6 H. Dahn, R. Malherbe and P. Beaud, *Helv. Chim. Acta*, 1971, **54**, 2202.
7 B. Favre, PhD Thesis, Univ. de Lausanne, 1971.
8 J. Hooz and G. F. Morrison, *Org. Prep. Proced. Int.*, 1971, **3**, 227.
9 J. Kuczera, Z. Janousek and Z. Arnold, *Collect. Czech. Chem. Commun.*, 1970, **35**, 3618.
10 F. Kaplan and G. K. Meloy, *J. Am. Chem. Soc.*, 1966, **88**, 950.
11 Y. Chiang, M. Hojatti, J. R. Keeffe, A. J. Kresge, N. P. Schepp and J. Wirz, *J. Am. Chem. Soc.*, 1987, **109**, 4000.
12 W. Kirmse, *Carbene Chemistry*, 2nd edn., Academic Press, New York, 1971, pp. 423–430.
13 Y. Chiang, A. J. Kresge, P. Pruszynski, N. P. Schepp and J. Wirz, *Angew. Chem., Int. Ed. Engl.*, 1991, **30**, 1366; Y. Chiang, E. A. Jefferson, A. J. Kresge, V. V. Popik and R.-Q. Xie, *J. Phys. Org. Chem.*, 1998, **11**, 610.
14 J. Andraos, Y. Chiang, S. J. Eustace, A. J. Kresge, S. W. Paine, V. V. Popik and K. Sung, *Can. J. Chem.*, 1999, **77**, 459.
15 J. R. Keeffe and A. J. Kresge, in *Techniques of Chemistry*, Volume VI, *Investigation of Rates and Mechanisms of Reactions*, ed. C. F. Bernasconi, Wiley-Interscience, New York, 1986, Part 1, pp. 763–764.

Paper 9/01238I