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Acid-Catalyzed Hydration of Di-*tert*-butylketene

Sir:

We report new evidence relevant to the mechanism of ketene hydration. Specifically di-*tert*-butylketene (**1**) undergoes hydration to the acid **2** in 50% water–acetonitrile with general acid catalysis and a solvent isotope effect k_{H^+}/k_{D^+} of 2.8. These facts indicate that the reaction occurs by rate-limiting proton transfer.

$$\underset{\mathbf{1}}{t\text{-Bu}_2\text{C=C=O}} + \text{H}_2\text{O} \xrightarrow{\text{H}^+} \underset{\mathbf{2}}{t\text{-Bu}_2\text{CHCO}_2\text{H}}$$

The reaction mechanisms of ketenes[1] are of interest because of their widespread use in acylations,[1] cycloadditions,[2] and other synthetic procedures.[3] Ketenes are also implicated as intermediates in reactions of various acyl derivatives with nucleophiles,[4] including reactions of biologically important molecules.[4c]

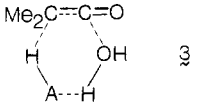
There has been intense recent interest in the protonation and hydration of ketenes. Studies on ketene itself include four independent measurements of the gas-phase proton affinity,[5] determination of gas-phase hydration kinetics,[6a] and a molecular orbital study of the site of protonation.[6b] The kinetics of hydration of dimethylketene in solution have been examined,[7] and the hydration of arylketenes in water have been studied.[8]

There was agreement on a value of the proton affinity of ketene of 194 ± 1 kcal/mol,[5] almost identical with that of isobutene (193.5 kcal/mol).[5b] There was some difference of opinion as to the site of protonation (eq 1): two groups favored

$$\text{CH}_2\text{=C=O} \xrightleftharpoons{\text{H}^+} \text{CH}_3\overset{+}{\text{C}}\text{=O} \quad \text{or} \quad \text{CH}_2\text{=}\overset{+}{\text{C}}\text{OH} \qquad (1)$$

C protonation,[5a,b] another reported that the position of protonation depended on the acidity of the proton donor,[5c] and one group favored O protonation.[5d]

In the studies of dimethylketene hydration in organic media, acid catalysis was observed[7] and a concerted addition of water involving the cyclic transition state **3** was proposed, where H–A represents the catalyzing acid. In the investigation of aryl-



3

ketenes the substrates were generated in situ by photochemical Wolff rearrangement and the rates of hydration were followed by the change in conductivity of the photolyzed solution (eq 2).[8]

$$\text{ArC(=O)CHN}_2 \xrightarrow{h\nu} \text{ArCH=C=O} \xrightarrow{\text{H}_2\text{O}} \text{ArCH}_2\text{CO}_2\text{H} \qquad (2)$$

In the latter study high rates of reaction were reported (first-order rate constants of 4×10^3 and 5×10^4 s^{-1} for *p*-tolyl- and *p*-nitrophenylketenes, respectively).[8] The reactions were reported to be independent of pH in the range 4–10.8, with solvent isotope effects k_{H_2O}/k_{D_2O} = 1.8–2.0, and the rates were correlated with σ_p^n constants with ρ = 1.19.

We have been able to correlate rates of alkene hydrations with considerable success.[9] In view of the interest in ketene hydration, and the indecisive nature of the previous studies of this reaction, further study appeared desirable.

Di-*tert*-butylketene (**1**)[10] offers great advantages for the study of mechanism of ketene hydration, in that it is stable to dimerization and to reaction with air and has both ultraviolet and visible chromophores which permit reliable spectral measurement of its rate of hydration. Rates of hydration of **1** were conveniently observed by monitoring the disappearance of its UV absorption maximum at 227 nm. In solutions of 50% aqueous acetonitrile at 25 °C in HCO_2H–HCO_2Na buffers at ionic strength 0.05 (NaCl) and a pH of 4.09, the rate law $k_{obsd} = k_{H^+}[H^+] + k_{HA}[HCO_2H]$ was closely followed, with k_{H^+} = 4.43 M^{-1} s^{-1} and $k_{HA} = 2.38 \times 10^{-2}$ M^{-1} s^{-1}. These rate constants gave a good fit to other rate data obtained for the pH range 3.67–4.50. At the pH value of 7.7 no reaction was discernible; so k_{H_2O} must be $<10^{-6}$ M^{-1} s^{-1}.

General acid catalysis was also observed at pH 3.30 using a HCl–KH_2PO_4 buffer in the same medium. The fit of the data was not so precise as in formic acid but gave values of k_{H^+} = 3.6 M^{-1} s^{-1} and $k_{HA'}$ = 0.90 M^{-1} s^{-1}.

Acid catalyzed hydration was also observed for H_2SO_4 in the range of 1.7×10^{-3} to 2.9×10^{-4} M H_2SO_4 in 50% water–acetonitrile. The acidity function of this medium has not been determined but k_{H^+} = 3.2 M^{-1} s^{-1} could be estimated,[10] and a solvent isotope effect of k_{H^+}/k_{D^+} = 2.8 at 9.00 $\times 10^{-4}$ M sulfuric acid was found. The observed values of k_{H^+} in the three acid systems are thus in reasonable agreement, with that in the formate buffers being the most reliable.

The observed general acid catalysis and the large solvent isotope effect unequivocally establish that **1** undergoes hydration by rate-limiting protonation. Carbon protonation to give the acylium ion is one likely path (eq 3), but protonation on oxygen (eq 4) is also possible.

$$t\text{-Bu}_2\text{C=C=O} \xrightarrow{\text{H}^+} t\text{-Bu}_2\text{CH}\overset{+}{\text{C}}\text{=O} \qquad (3)$$

$$t\text{-Bu}_2\text{C=C=O} \xrightarrow{\text{H}^+} t\text{-Bu}_2\text{C=}\overset{+}{\text{C}}\text{OH} \qquad (4)$$

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The low reactivity of **1** relative to the arylketenes is an item of some interest. The change in medium accounts for only a small portion of the difference,[12a] and geminal di-*tert*-butyl groups do not cause a steric barrier to protonation.[12b] Generation of the arylketenes in an excited state by eq 2 could lead to enhanced reaction rates in these cases.[12c] In any event these ketenes are all quite reactive in solution relative to alkenes such as isobutene ($k_{H^+} = 3.71 \times 10^{-4}$ s^{-1} at 25 °C),[13] even though the proton affinities of ketene and isobutene are the same in the gas phase.

The relative stability of **1** to neutral and basic hydrolysis may reflect a steric barrier to nucleophilic attack. Quantitative reactivity comparisons of **1** and less hindered ketenes will be illuminating in this regard.

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Supplementary Material Available: Tables of original rate constants (4 pages). Ordering information is given on any current masthead page.

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Book Reviews

Fortschritte der Chemie organischer Naturstoffe (Progress in the Chemistry of Organic Natural Products). Edited by W. HERZ, H. GRISEBACH, and G. W. KIRBY. Springer-Verlag, Vienna–New York. 1977. x + 620 pp. $118.70.

For the past 40 years "Zechmeister" has provided invaluable accounts of the many facets of natural product chemistry. As usual, the articles in the present volume reflect the broad canvas of the field ranging from the isoprenoids and alkaloids of tobacco to the hypothalamus regulating hormone. Intervening chapters survey the chemistry of the eremophilane and related sesquiterpenoids, phytoalexins, carbazole alkaloids, uropygial gland lipids, and the use of plant tissue culture in the study of secondary metabolism. Particular articles will be a standard source of reference for the specialist, but there is much to interest his noncommitted colleague, who may find it a source of new synthetic challenges, or bizarre transformations to test his arrow-pushing skills. The high standards of authorship and presentation associated with this series have been fully maintained in the present volume. It is particularly commendable that the "old-fashioned" though very helpful practice of including the titles of papers in the reference quotation is still retained. Despite the bilingual title of the series, five of the eight articles are in English.

Regrettably, only the exceedingly affluent, or the fortunate reviewer, can aspire to having a copy on his own bookshelf.

C. W. Bird, *Queen Elizabeth College*

Horizons in Biochemistry and Biophysics. Volume I. Edited by E. QUIGLIARIELLO (University of Bari), F. PALMIERI (University of Bari), and THOMAS P. SINGER (University of California, School of Medicine). Addison-Wesley, Reading, Mass. 1974. xiii + 344 pp. $6.75 paper; $13.50 cloth.

This book is the first in a series which is designed to keep people in various scientific areas abreast with "major conceptual and methodological advances and important discoveries in biochemistry and biophysics".

Volume I contains nine chapters. The articles are vastly different in their content and emphasis; they vary from a chapter on photosynthesis to one on clinical aspects of genetic disease. Obviously no attempt was made by the editors to localize emphasis in each volume. Perhaps this is good; there are chapters to interest people in vastly different areas. This book tends to remind one of *Chemical Reviews*. This varied emphasis along with the modest price of the paperback version may interest many in entering subscriptions.

The articles themselves are generally well written and well referenced. They are largely free of typographical errors, and most are of high quality both in scientific content and literary style. Most are excellent reviews of present knowledge and contain indications of areas where research is still needed.

On picking up the book the first thing that strikes one's eye is the fact that it is reproduced from a typewritten manuscript rather than from set type. The resulting uneven right margins make one feel like one is reading a preliminary draft rather than a book, which detracts from the quality of the volume.

All things considered, this volume is a good addition to most scientific bookshelves.

Robert R. Pavlis, *College of the Virgin Islands*

The Synthesis of Prostaglandins. By ABHIJIT MITRA (Columbia University). John Wiley & Sons, Inc., New York. 1977. xiii + 444 pp. $22.50.

This text is a comprehensive review of the reactions and mechanisms pertaining to prostaglandin synthesis. It is a well-documented book with many references to the 1977 literature.

The book begins with a brief introductory chapter reviewing the original isolation of the prostaglandins. A short discussion of their