

within the experimental error except for 1,3-cyclohexadiene. The lifetimes reported for the acyclic examples are thus lifetimes for the triplet in the absence of dimerization. For 1,3-cyclohexadiene, a trivariate fit to eq 6 afforded $k_B \approx 2 \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$ and the parameters in the table ($R^2 = 0.99$). The lifetime for 1,3-cyclohexadiene triplet may be a minimum estimate in view of the complexities encountered with the paraquat technique on the microsecond time scale.^{10,11}

The lifetimes and k_{PQ} values show the trends expected from our previous study of styrene triplets.^{10,11} The most highly substituted acyclic triplet has the longest lifetime. The very long lifetime for the 1,3-cyclohexadiene triplet is consistent with its constraint to near planarity. Most interestingly, the lifetimes for the acyclics are strikingly similar to those for comparably substituted styrenes when comparison is made with regard to the more substituted (i.e., most readily twisted) double bond in the triplet; compare *p*-methoxy- β,β -dimethylstyrene triplet (48 ns¹⁰) to 2,5-dimethyl-2,4-hexadiene and anethole triplet (30 ns¹⁰) to the other two acyclic dienes. Vinylalkenes appear to have almost exactly the same lifetimes as identically substituted anisylalkenes. The absolute similarity reinforces our previous¹¹ argument that the degree of substitution at the twisted bond matters more than one might expect, and the nature of the substituents matters less.

We have attempted to determine the lifetime of the 2,3,4,5-tetramethyl-2,4-hexadiene triplet but have so far not been successful. Substantial yields of Ph₂COH apparently result from the quenching of ³Ph₂CO by this diene, as evidenced by the isolation of benzopinacol in >60% yield from the photoreaction and by the observation of a long-lived transient product in the decay of the ³Ph₂CO signal at 525 nm. This behavior is not surprising in view of the hindrance to planarity of the diene and the consequent expected increase in triplet energy. The ³Ph₂CO quenching rate is $4.7 \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, which is more nearly in the range of ³Ph₂CO quenching by simple olefins via exciplex formation¹²⁻¹⁴ than in the range of the ca. $5 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ typical for energy transfer to less hindered dienes.

Our lifetimes and known^{1,5} k_{BT} values for the acyclic diene triplets permit determination of k_B in some cases, by assuming negligible dependence of lifetime on the changes in solvent.¹⁵ For isoprene, we expect a triplet lifetime similar to *p*-methoxy- α -methylstyrene (31 ns¹⁰) by the analogy above and observe a transient with 27-ns lifetime (see table and caveats). The known¹ k_{BT} value affords $k_B \sim 2 \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$ at room temperature. Were this a simple radicallike addition of the "methylene" of the alkylmethylene triplet to ground-state isoprene, its rate should have been comparable to, or even slower than, the known¹⁶ addition of methyl radical to butadiene, $k = 2.7 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$ at 65 °C. Considering that a primary alkyl radical (a fair model for the methylene terminus) will be less reactive than the methyl radical and that the radical addition will be at least modestly activated,¹⁶ we suggest that the k_B for isoprene is at least 1 or 2 orders of magnitude too high for simple radicallike addition. Results of Saltiel⁵ for 2,4-hexadiene isomerization afforded k_{BT} of 0.0026 for *trans,trans* and 0.0064 for *cis,cis*; our 2,4-hexadiene triplet lifetime affords $k_B = 8 \times 10^4$ and $2 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$, respectively, also very high values considering the hindrance at the termini.¹⁷ Rate enhancements of this sort have previously been among the early hints of triplet exciplex involvement in other photoreactions.^{12,13,18} Our result now suggests that such is also likely in diene dimerization.

Acknowledgment. We thank the National Science Foundation (Grant CHE 7915228) and the Robert A. Welch Foundation (Grant AT-532) for financial support. Flash kinetic work was performed at the Center for Fast Kinetics Research at The University of Texas at Austin, supported by NIH Grant RR-0086 from the Biotechnology Branch of the Division of Research Resources and The University of Texas.

Registry No. Ph₂CO, 119-61-9; 2,5-dimethyl-2,4-hexadiene, 764-13-6; *trans,trans*-2,4-hexadiene, 5194-51-4; *trans*-2-methyl-1,3-pentadiene, 926-54-5; 1,3-cyclohexadiene, 592-57-4; 2,3,4,5-tetramethyl-2,4-hexadiene, 1114-06-3; PQ²⁺, 4685-14-7.

Ketonization of Enols. Enol Content and Acid Dissociation Constants of Simple Carbonyl Compounds

Y. Chiang, A. J. Kresge,* and P. A. Walsh

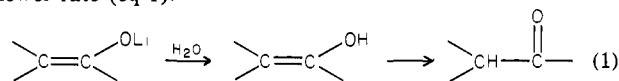
Department of Chemistry, University of Toronto
Scarborough College, West Hill
Ontario, Canada M1C 1A4

Received August 3, 1982

Enols and enolate ions are essential intermediates in a number of important reactions, and the accurate determination of enol contents of carbonyl compounds has therefore been the object of active investigation by chemists for many decades. Although reliable methods exist for determining keto-enol equilibrium constants of polyfunctional compounds such as β -diketones whose enol contents are high, these methods fail when enol contents become low, as is generally the case with simple monofunctional aldehydes and ketones; little accurate information on simple carbonyl compounds is consequently available. We report that we have now devised a new method of determining enol contents that is both accurate and sensitive, and we have used it to determine the keto-enol equilibrium and acid dissociation constants of the simple carbonyl compound isobutyraldehyde.

Our method is based upon the fact that a keto-enol equilibrium constant is equal to the ratio of enolization to ketonization rate constants, $K_E = k_E/k_K$; measurement of k_E and k_K will therefore lead directly to the desired equilibrium constant. Rates of enolization of simple aldehydes and ketones can be determined by a variety of methods, and an extensive literature exists on this subject. Determination of rates of ketonization of simple enols, however, presents a much more difficult problem; these quantities have seldom been measured directly, probably because of the widespread belief that the required enol substrates are very unstable substances. This is not quite true, however,¹ and in fact a recent report has shown that the enol of acetaldehyde has a half-life of 10 min in an aqueous acetonitrile solvent at 20 °C.² We have found comparable reactivities for several other simple enols in an essentially wholly aqueous medium at 25 °C.

We generate enols in aqueous solution by adding a small quantity of lithium enolate dissolved in an aprotic solvent, e.g., tetrahydrofuran, prepared by standard methods,³ to a large excess of water. Rapid proton transfer to oxygen then produces the enol, which subsequently isomerizes to the carbonyl compound at a slower rate (eq 1).



These solutions, when first prepared, have strong UV absorption maxima near 200 nm, similar to the spectra of corresponding

(12) (a) Caldwell, R. A.; James, S. P. *J. Am. Chem. Soc.* **1969**, *91*, 5184.

(b) Caldwell, R. A. *J. Am. Chem. Soc.* **1970**, *92*, 1439.

(13) Kochevar, I.; Wagner, P. J. *J. Am. Chem. Soc.* **1972**, *94*, 3859.

(14) Caldwell, R. A.; Sovocool, G. W.; Gajewski, R. P. *J. Am. Chem. Soc.* **1973**, *95*, 2549.

(15) Görner, H.; Schulte-Frohlinde, D. *J. Phys. Chem.* **1981**, *85*, 1835. This reference shows that the decay rate of perpendicular stilbene triplet is insensitive to a substantial change in solvent polarity.

(16) Ingold, K. U. In "Free Radicals"; Kochi, J. K., Ed.; Wiley: New York, 1973; Vol. I, pp 37-112; see especially pp 91-93.

(17) Saltiel⁵ has noted the effect of hindrance on relative dimerization rates.

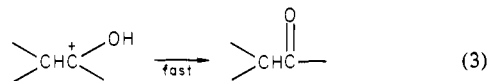
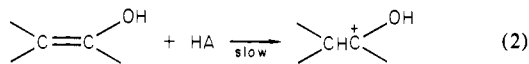
(18) Caldwell, R. A. *J. Am. Chem. Soc.* **1973**, *95*, 1690.

(1) Hart, H. *Chem. Rev.* **1979**, *79*, 515-528.

(2) Capon, B.; Rycroft, D. S.; Watson, T. C.; Zucco, C. *J. Am. Chem. Soc.* **1981**, *103*, 1761-1765. Capon, B.; Rycroft, D. S.; Watson, T. C. *J. Chem. Soc., Chem. Commun.* **1979**, 724-725.

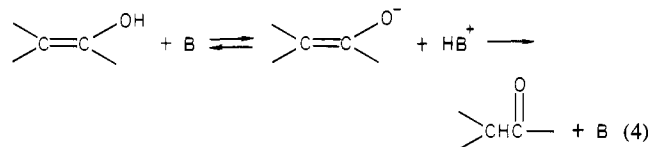
(3) House, H. O.; Gzuba, L. J.; Gall, M.; Olmstead, H. D. *J. Org. Chem.* **1969**, *34*, 2324-2336. House, H. O.; Gall, M.; Olmstead, H. D. *Ibid.* **1971**, *36*, 2361-2371.

methyl vinyl ethers. As ketonization proceeds, these maxima give way to weaker bands at longer wavelengths, which are characteristic of the carbonyl group, and this change can be used to measure the rates of these reactions. The process follows first-order kinetics with good precision, and observed first-order rate constants measured in dilute mineral acid solution are accurately proportional to hydronium ion concentration. The reaction shows general acid catalysis and gives substantial hydronium ion isotope effects; e.g., $k_{H^+}/k_{D^+} = 2.83 \pm 0.08$ for the enol of isobutyraldehyde. This mechanistic evidence is similar to that obtained for the hydrolysis of simple vinyl ethers,⁴ and it suggests that the rate-determining step in the present reaction is the same as that established for vinyl ether hydrolysis, namely rate-determining proton transfer from catalyst to substrate (eq 2); this is then



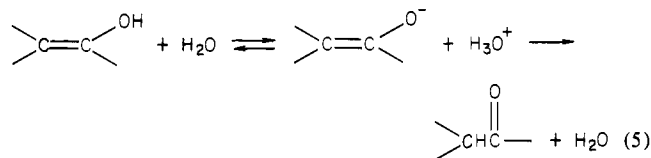
followed by proton loss from oxygen to give aldehyde or ketone product (eq 3). Such a two-step reaction scheme is consistent with current opinion on the mechanism of acid-catalyzed enolization of carbonyl compounds,⁵ which, by the principle of microscopic reversibility, must occur by the route of the present reaction taken in reverse.

In addition to acid catalysis, the present ketonization reactions show strong catalysis by bases, and the form of this base catalysis indicates a reaction path that involves rate-determining carbon protonation of the enolate anion (eq 4). This scheme is again



consistent with the accepted mechanism for base-catalyzed enolization of carbonyl compounds. At high pH, this base catalysis becomes saturated, and rate measurements made in the region of saturation can be used to give an estimate of the equilibrium constant for the first step of this base-catalyzed route (eq 4). Measurements made on the enol of isobutyraldehyde lead to the enol acidity constant $K_a = 2.4 \times 10^{-4}$ M, $pK_a = 11.63 \pm 0.03$, which is in good agreement with an approximate estimate, $pK_a = 11.7 \pm 1.0$, derived from free-energy relationships.⁶

The pH-rate profile of these ketonization reactions also shows an uncatalyzed region in which the process occurring may be identified as the reaction of eq 4 with $\text{B} = \text{H}_2\text{O}$ (eq 5). Observed

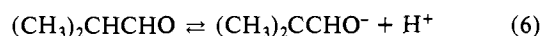


rate constants here are therefore products of the acid dissociation constants of the enols and rate constants for carbon protonation

of the enolate ions, $k_{\text{obsd}} = K_a k'_{H^+}$. Measurements on isobutyraldehyde enol give $k_{\text{obsd}} = 4.2 \times 10^{-4} \text{ s}^{-1}$, from which, since K_a has been evaluated, $k'_{H^+} = 1.8 \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$ may be obtained. This result is 8 orders of magnitude greater than the rate constant for carbon protonation of the un-ionized enol of isobutyraldehyde, $k_{H^+} = 0.59 \text{ M}^{-1} \text{ s}^{-1}$, which illustrates the very powerful activating influence of a negatively charged oxygen substituent on electrophilic addition to a carbon-carbon double bond.

We have also measured the rate of enolization of isobutyraldehyde, by iodine scavenging, and have found $k_{H^+} = 4.7 \times 10^{-5} \text{ M}^{-1} \text{ s}^{-1}$, in good agreement with an earlier determination.⁷ When this value is corrected for aldehyde hydrate formation⁸ and is combined with k_{H^+} for ketonization, the keto-enol equilibrium constant $K_E = 1.28 \times 10^{-4}$ and $pK_E = 3.90 \pm 0.01$ is obtained. This result is again consistent with an approximate recent estimate, $pK_E = 2.8 \pm 1.1$.^{6,9}

An acidity constant for the ionization of isobutyraldehyde as a carbon acid (eq 6) may be derived by combining the presently



determined values of pK_E and $pK_a(\text{enol})$: $pK_a(\text{carbon}) = pK_E + pK_a(\text{enol})$. The result, $pK_a(\text{carbon}) = 15.53 \pm 0.03$, is to our knowledge the first accurately determined empirically founded acidity constant of a simple carbonyl compound in aqueous solution.

This new method of investigating enol chemistry promises to be of general applicability, and we are in fact currently engaged in applying it to a variety of simple carbonyl compounds.

Acknowledgment. We are grateful to the Natural Sciences and Engineering Research Council of Canada and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for their financial support of this research.

Registry No. D₂, 7782-39-0; isobutyraldehyde, 78-84-2; isobutyraldehyde enol, 56640-70-1.

(7) Talvik, A. J.; Hidmaa, S. O. *Org. React. (NY, Engl. Transl.)* **1968**, *5*, 121-126.

(8) Green, L. R.; Hine, J. J. *Org. Chem.* **1973**, *38*, 2801-2806.

(9) Guthrie, J. P. *Can. J. Chem.* **1979**, *57*, 797-802.

Use of the *N*-Oxide of *p*-Cyano-*N,N*-dimethylaniline as an "Oxygen" Donor in a Cytochrome P-450 Model System

Michael W. Nee and Thomas C. Bruice*

Department of Chemistry
University of California at Santa Barbara
Santa Barbara, California 93106

Received July 16, 1982

Iodosobenzene, organic peracids, and hydroperoxides have been employed with *meso*-(tetraphenylporphinato)iron(III) chloride [TPPFe^{III}Cl] to model the oxidation reactions of cytochrome P-450.¹ The products formed when peracids or hydroperoxides are employed with either TPPFe^{III}Cl or cytochrome P-450 are similar to those obtained in Fenton-type reactions,²⁻⁴ whereas

(1) (a) Groves, J. T.; Nemo, T. E.; Myers, R. S. *J. Am. Chem. Soc.* **1979**, *101*, 1032-1033. (b) Chang, C. K.; Kuo, M.-S. *Ibid.* **1979**, *101*, 3413-3415. (c) Mansuy, D.; Bartoli, J.-F.; Chottard, J.-C.; Lange, M. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 909-910. (d) Mansuy, D.; Dansette, P. M.; Pecquet, F.; Chottard, J.-C. *Biochem. Biophys. Res. Commun.* **1980**, *96*, 433-439. (e) Gold, A.; Ivey, W.; Brown, M. *J. Chem. Soc., Chem. Commun.* **1981**, 293-295. (f) Chang, C. K.; Ebina, F. *Ibid.* **1981**, 778-779. (g) Groves, J. T.; Haushalter, R. C.; Nakamura, M.; Nemo, T. E.; Evans, B. J. *J. Am. Chem. Soc.* **1981**, *103*, 2884-2886. (h) Lindsay Smith, J. R.; Sleath, P. R. *J. Chem. Soc., Perkin Trans. 2*, **1982**, 1009-1015.

(2) Blake, R. C., II; Coon, M. J. *J. Biol. Chem.* **1981**, *256*, 12127-12133.

(3) (a) Groves, J. T.; McClusky, G. A. *J. Am. Chem. Soc.* **1976**, *98*, 859-861. (b) Groves, J. T.; Van Der Puy, M. *Ibid.* **1976**, *98*, 5280-5297.

(4) But see ref 1g.

(4) Salomaa, P.; Kankaanpera, A.; Lajunen, M. *Acta Chem. Scand.* **1966**, *20*, 1790-1801. Kresge, A. J.; Chiang, Y. *J. Chem. Soc. B* **1967**, 53-57; 58-61. Kresge, A. J.; Chen, H. L.; Chiang, Y.; Murrill, E.; Payne, M. A.; Sagatys, D. S. *J. Am. Chem. Soc.* **1971**, *93*, 413-423. Kresge, A. J.; Sagatys, D. S.; Chen, H. L. *Ibid.* **1977**, *99*, 7228-7233. Okuyama, T.; Fueno, T.; Nakatsuji, H.; Fujimoto, J. *Ibid.* **1967**, *89*, 5826-5831. Kreevoy, M. M.; Eliason, R. E. *J. Phys. Chem.* **1968**, *72*, 1313-1316.

(5) Bell, R. P.; Jones, P. J. *J. Chem. Soc.* **1953**, 88-92. Lienhard, G. E.; Wang, T.-C. *J. Am. Chem. Soc.* **1969**, *91*, 1146-1153. Toulllec, J.; Dubois, J. E. *J. Am. Chem. Soc.* **1974**, *96*, 3524-3532. Hegarty, A. F.; Jencks, W. P. *J. Am. Chem. Soc.* **1975**, *97*, 7188-7189. Albery, W. J.; Gelles, J. S. *J. Chem. Soc., Faraday Trans. 1* **1982**, *78*, 1569-1578. Albery, W. J. *Ibid.* **1982**, *78*, 1579-1590.

(6) Guthrie, J. P.; Cullimore, P. A. *Can. J. Chem.* **1979**, *57*, 240-248. Guthrie, J. P. *Ibid.* **1979**, *57*, 1177-1185.