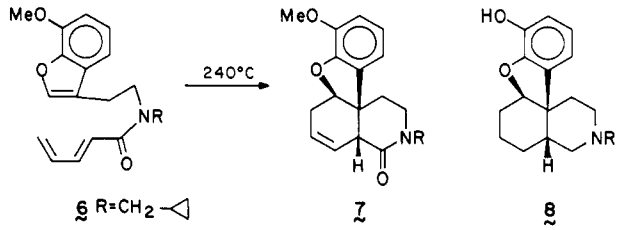
yield. Catalytic hydrogenation of **7** followed by borane reduction and demethylation furnished **8**,[6,16] the cis isomer of **2b**, mp 174-175 °C.



Intramolecular Diels-Alder reactions have also been carried out with substrates **3** where the benzofuran oxyen was replaced by sulfur and nitrogen and by one[17] or two methylenes. Details will be reported in future publications.

Supplementary Material Available: X-ray structure determination of 3-(cyclopropylmethyl)-2,3,4,4a,5,6,7,7a-octahydro-1*H*-benzofuro[3,2-*e*]isoquinolin-9-ol (14 pages). Ordering information is given on any current masthead page.

(16) NMR (220 MHz in $CDCl_3$): τ 3.2 (m, 1 H), 3.3 (m, 2 H), 5.7 (br s, width at half-height ca. 9 Hz, 1 H), 7.1-7.6 (br m, 4 H), 7.7 (d, J = 6 Hz, 2 H), 7.9-8.6 (br m, 9 H), 9.1 (m, 1 H); 9.5 (m, 2 H), and 9.9 (m, 2 H). The phenolic OH occurred as a very broad signal in the aromatic region.

(17) For an unsuccessful attempt to prepare decahydroindeno[1,2-*f*]isoquinolines, see: Smith, J. R. L.; Norman, R. O. C.; Rose, M. E.; Curran, A. C. W. *J. Chem. Soc., Perkin Trans. 1* **1979**, 2863.

Experimental Measurement of the Electron Affinity of the Hydroperoxy Radical

Veronica M. Bierbaum,* Robert J. Schmitt,† and Charles H. DePuy

Department of Chemistry, University of Colorado Boulder, Colorado 80309

Roy D. Mead, P. A. Schulz, and W. C. Lineberger*

Department of Chemistry, University of Colorado and Joint Institute for Laboratory Astrophysics University of Colorado and National Bureau of Standards Boulder, Colorado 80309

Received August 21, 1981

The hydroperoxy radical, HO_2, plays an important role in the chemistry of the atmosphere, in combustion processes, and in a variety of biological and chemical oxidative systems. However, the electron affinity of this species has never been measured directly. An estimate by Weiss[1] placed this quantity at 4.6 eV. Recently, Benson and Nangia[2] have obtained 1.85 ± 0.12 eV on the basis of a thermochemical cycle employing solution data. Using the flowing afterglow technique we have experimentally bracketed the gas-phase acidity of hydrogen peroxide

$$H_2O_2 \rightarrow H^+ + HO_2^- \qquad \Delta H = \Delta H°_{acid}(H_2O_2) \qquad (1)$$

to be 375.5 ± 3.3 kcal mol^{-1} and the electron affinity of the hydroperoxy radical

$$HO_2^- \rightarrow HO_2 + e^- \qquad \Delta H = EA(HO_2) \qquad (2)$$

to be 1.16 ± 0.15 eV. Using these results, we have performed threshold photodetachment of HO_2^- to obtain a more precise value, $EA(HO_2)$ = 1.19 ± 0.01 eV (27.4 ± 0.2 kcal mol^{-1}). Employing this value and well-established heats of formation of HO_2, H_2O_2, and H^+, we find $\Delta H_f°(HO_2^-)$ = -24.9 ± 0.7 kcal mol^{-1} and $\Delta H°_{acid}(H_2O_2)$ = 374.8 ± 0.7 kcal mol^{-1}.

In the flowing afterglow which has been described in detail previously,[3,4] ion-molecule reactions are carried out in helium buffer gas under thermal energy conditions. In order to determine the acidity of H_2O_2, the bracketing acids must have well-known acidities which are similar to that of H_2O_2. Moreover, they must react with HO_2^- exclusively by a simple proton-transfer process. This is a stringent requirement since HO_2^- has been found to be a potent gas-phase oxidant.[5] Fluoroform and hydrofluoric acid fulfill these requirements:

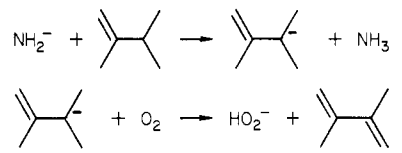
$$CF_3^- + H_2O_2 \rightleftarrows HO_2^- + HCF_3 \qquad (3)$$

$$F^- + H_2O_2 \rightleftarrows HO_2^- + HF \qquad (4)$$

We have found that proton-transfer equilibria involving HO_2^- and H_2O_2 cannot be experimentally established because a rapid competing process occurs.

$$HO_2^- + H_2O_2 \rightarrow OH^- + H_2O + O_2 \qquad (5)$$

Therefore equilibrium constants for reactions 3 and 4 were determined from measurements of forward and reverse rate constants, and a source of each ion which did not involve its conjugate acid was employed so that back reactions were minimized. CF_3^- was generated by electron impact on CF_4, F^- was produced by electron impact on NF_3, and HO_2^- was formed by chemical reaction.



Neutral reactants were added through a movable inlet, and rate constants were measured by monitoring the reactant ion density as a function of reaction distance. The flow rates of H_2O_2 (97.5%) and HCF_3 were determined by monitoring the pressure increase in a calibrated volume, while HF flow was determined by using a calibrated mass flowmeter. A limit of the extent of possible decomposition of H_2O_2 was evaluated and included in the error limits.

The experimental results for reaction 3 are $k_f = 2.2 \times 10^{-10}$ cm^3 molecule^{-1} s^{-1} and $k_r = 6.4 \times 10^{-11}$ cm^3 molecule^{-1} s^{-1}, yielding ΔH = -1.3 kcal mol^{-1}.[6] Using $\Delta H°_{acid}(HCF_3)$ = 376.6 kcal mol^{-1}[7] yields $\Delta H°_{acid}(H_2O_2)$ = 375.3 kcal mol^{-1}.

For reaction 4 $k_f = 2.0 \times 10^{-12}$ cm^3 molecule^{-1} s^{-1} and $k_r = 2.8 \times 10^{-10}$ cm^3 molecule^{-1} s^{-1}, yielding ΔH = +4.4 kcal mol^{-1}.[6] Using $\Delta H°_{acid}(HF)$ = 371.3 kcal mol^{-1}[7] yields $\Delta H°_{acid}(H_2O_2)$ = 375.7 kcal mol^{-1}.

Employing the average value $\Delta H°_{acid}(H_2O_2)$ = 375.5 kcal mol,$^{-1}$ reaction 1, $\Delta H_f°(H^+)$ = 367.2 kcal mol^{-1},[8] and $\Delta H_f°(H_2O_2)$ = -32.5 kcal mol^{-1}[8,9] yields $\Delta H_f°(HO_2^-)$ = -24.2 kcal mol^{-1}. Finally, using this latter value, reaction 2, and a recently determined value,[10] $\Delta H_f°(HO_2)$ = 2.5 kcal mol^{-1}, yields $EA(HO_2)$ = 1.16 ± 0.15 eV (26.7 ± 3.4 kcal mol^{-1}).

Once the results of the flowing afterglow experiments were available, a more precise determination of the EA using threshold

† Physical Organic Chemistry Department, SRI International, Menlo Park, CA 94025.

(1) Weiss, J. *Trans. Faraday Soc.* **1935**, *31*, 966.

(2) Benson, S. W.; Nangia, P. S. *J. Am. Chem. Soc.* **1980**, *102*, 2843.

(3) Ferguson, E. E.; Fehsenfeld, F. C.; Schmeltekopf, A. L. *Adv. At. Mol. Phys.* **1969**, *5*, 1.

(4) DePuy, C. H.; Bierbaum, V. M. *Acc. Chem. Res.* **1981**, *14*, 146.

(5) DePuy, C. H.; Bierbaum, V. M.; Schmitt, R. J.; Shapiro, R. H. *J. Am. Chem. Soc.* **1978**, *100*, 2920.

(6) Standard entropies for H_2O_2, HCF_3, HF, and F^- were obtained from ref 8 and 9. Entropies for CF_3^- and HO_2^- were estimated from those of isoelectronic neutrals.

(7) Bartmess, J. E.; McIver, R. T., Jr., In "Gas Phase Ion Chemistry"; Bowers, M. T., Ed.; Academic Press: New York, 1979.

(8) Stull, D. R.; Prophet, H. *Natl. Stand. Ref. Data Ser.* (*U.S. Natl. Bur. Stand.*) **1971**, *NSRDS-NBS 37*.

(9) Stull, D. R.; Westrum, E. F., Jr.; Sinke, G. C. "The Chemical Thermodynamics of Organic Compounds"; Wiley: New York, 1969.

(10) Howard, C. J. *J. Am. Chem. Soc.* **1980**, *102*, 6937.

0002-7863/81/1503-6262$01.25/0

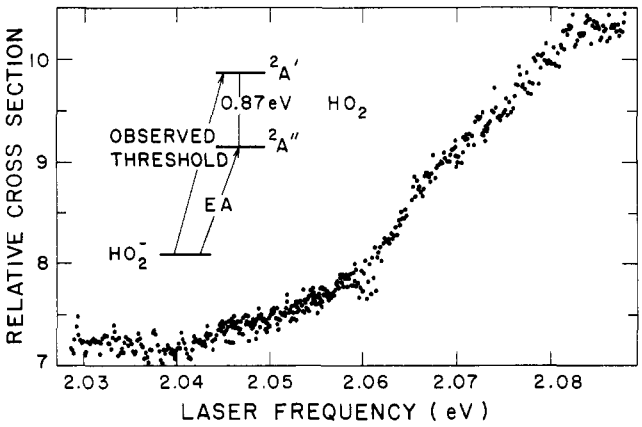


Figure 1. Relative photodetachment cross section for HO_2^- and energy level diagram showing ion and neutral states. The observed threshold of the $^2A'$ state of HO_2 is at 2.06 eV. Consequently the electron affinity (EA) of HO_2 is 1.19 eV.

photodetachment spectroscopy was possible. This technique, which has produced electron affinities for many atomic and molecular species, is described in detail elsewhere.[11] A mass analyzed beam of HO_2^- was crossed with a tunable dye laser beam. The ions were made by an electric discharge in O_2 and 2,3-dimethyl-1-butene under conditions which typically produce ions characterized[12,13] by a temperature of 1500 K. Electrons and neutrals generated by photodetachment were collected and counted to produce a plot of photodetachment cross section vs. photon energy. In order to observe a photodetachment threshold using convenient dye laser technology, a search was made for the onset of photodetachment to the $^2A'$ excited state of the neutral, which lies[14] 0.872 eV above the ground state.

The data, shown in Figure 1, display a strong onset near 2.06 eV for detachment to the excited state. Modeling[13,15] of the cross section in this region places the electron affinity of the excited state slightly above the onset, but the exact position is relatively insensitive (±0.003 eV) to the details of the model. The photodetachment cross section was featureless near 1000 and 1300 cm^{-1} both above and below this feature where other thresholds involving the lower frequency vibrations of the neutral or ion might appear. Involvement of the highest frequency vibration would be inconsistent with the flowing afterglow measurement, so the absence of other thresholds indicates that the threshold observed corresponds to the $HO_2^-(0,0,0) \rightarrow HO_2\ ^2A'(0,0,0)$ threshold. Photodetachment spectra down to photon energies of 1.75 eV showed little decrease in cross section. This observation alone indicates the EA to be substantially smaller than 1.75 eV, inconsistent with the current literature value[2] of 1.85 eV but supporting this determination of 1.19 eV.

Two different methods have been used to determine the EA of HO_2. By measuring forward and reverse rate constants with a flowing afterglow apparatus, the EA is found to be 1.16 ± 0.15 eV. Threshold photodetachment provides both a consistency check on this value and improves the precision of the determination, giving $EA(HO_2) = 1.19 \pm 0.01$ eV.

Acknowledgment. The flowing afterglow research was supported by the U.S. Army Research Office (DAAG29-79-G-0012) and the National Science Foundation (CHE79-09750). The laser photodetachment work was supported by National Science Foundation Grants PHY79-04928 and CHE78-18424.

(11) Slater, J.; Read, F. H.; Novick, S. E.; Lineberger, W. C. *Phys. Rev. A* **1978**, *17*, 201.
(12) Novick, S. E.; Engelking, P. C.; Jones, P. L.; Futrell, J. H.; Lineberger, W. C. *J. Chem. Phys.* **1979**, *70*, 2652.
(13) Engelking, P. C.; Corderman, R. R.; Wendoloski, J. J.; Ellison, G. B.; ONeil, S. V.; Lineberger, W. C. *J. Chem. Phys.* **1981**, *74*, 5460.
(14) Tuckett, R. P.; Freedman, P. A.; Jones, W. J. *Mol. Phys.* **1979**, *37*, 379; **1979**, *37*, 403.
(15) Hotop, H.; Patterson, T. A.; Lineberger, W. C. *J. Chem. Phys.* **1974**, *60*, 1806.

Preparative Hydroxylation of Aromatic Compounds Catalyzed by Peroxidase

Alexander M. Klibanov,* Zina Berman, and Barbara N. Alberti

Laboratory of Applied Biochemistry
Department of Nutrition and Food Science
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139

Received July 10, 1981

Selective hydroxylation of aromatic compounds is a difficult task in preparative organic chemistry.[1] The problem is particularly severe when the compounds to be hydroxylated (or their products) are optically active and/or unstable, since in these instances the reaction should be conducted rapidly and under mild conditions in order to prevent racemization and decomposition. Therefore, such hydroxylations are often carried out either by microbiological means[2] or by circumventing the direct hydroxylation as exemplified by the catalytic asymmetric production of L-3,4-dihydroxyphenylalanine (L-DOPA).[3] Both of these approaches have serious shortcomings: the former is laborious, time consuming, and usually provides relatively low yields; the latter has only a limited applicability and employs extremely O_2-unstable catalysts.

Mason and co-workers have discovered[4,5] that horse radish peroxidase, in addition to its usual peroxidatic and catalytic activities, can also catalyze the hydroxylation of some aromatic compounds by molecular oxygen in the presence of dihydroxyfumaric acid as a hydrogen donor. However, the yields obtained were very low and the process lacked specificity, apparently due to considerable nonenzymatic hydroxylation. Therefore, the preparative potential of this reaction has never been explored.

In this work we have found that under certain conditions the reaction in Scheme I, catalyzed by peroxidase,[6] can be used for fast, convenient, and selective hydroxylations which afford yields up to 70%. Three important drugs have been produced as examples using this enzymatic hydroxylation: L-DOPA[7] from L-tyrosine (I), D-(−)-3,4-dihydroxyphenylglycine[8] from D-(−)-*p*-

(1) Gunstone, F. D. *Adv. Org. Chem.* **1960**, *1*, 103. Norman, R. O. C.; Taylor, R. "Electrophilic Substitution in Benzenoid Compounds"; Elsevier: Amsterdam, 1965; Chapters 5 and 12. Stoddart, J. F. "Comprehensive Organic Chemistry"; Pergamon Press: Oxford, 1979; Vol. 1.
(2) For a review, see: Sih, C. J.; Rosazza, J. P. In "Applications of Biochemical Systems in Organic Chemistry"; Jones, J. B., Sih, C. J., Perlman, D., Eds.; Wiley: New York, 1976; Part I, pp 69–106. Sih, C. J.; Abushanab, E.; Jones, J. B. *Annu. Rep. Med. Chem.* **1977**, *12*, 298–308.
(3) Instead of direct hydroxylation of L-tyrosine to form L-DOPA (Sih, C. J.; Foss, P.; Rosazza, J.; Lemberger, M. *J. Am. Chem. Soc.* **1969**, *91*, 6204. Florent, J.; Renaut, J. German Patent 2 102 793, 1970), this elegant process involves the condensation of 3,4-dihydroxybenzaldehyde with *N*-acetylglycine, followed by asymmetric hydrogenation catalyzed by rhodium complexes and subsequent hydrolysis of the resultant *N*-acetyl-L-DOPA (Knowles, W. S.; Sabacky, M. J.; Vineyard, B. D. U.S. Patent 4 005 127, 1977. For a general review, see: Merrill, R. E. *CHEMTECH* **1981**, *11*, 118–127). Clearly, this approach, while excellent for L-DOPA, cannot be used for the production of a number of hydroxylated aromatic compounds, e.g., dihydroxyphenylglycine and adrenaline prepared in this work.
(4) Mason, H. S.; Onopryenko, I.; Buhler, D. *Biochim. Biophys. Acta* **1957**, *24*, 225–226. Mason, H. S. *Proc. Int. Symp. Enzyme Chem.* **1958**, 220.
(5) Buhler, D.; Mason, H. S. *Arch. Biochem. Biophys.* **1961**, *92*, 424–437.
(6) It is noteworthy that both peroxidases (EC 1.11.1.7) used in this study, horse radish peroxidase and lactoperoxidase from cow milk, are readily available from most commercial suppliers of biochemicals; they are relatively inexpensive and stable during storage and operation. The particular preparations of the horse radish peroxidase and lactoperoxidase used in this work were obtained from Sigma and had a specific activity of 175 and 80 purpurogallin units/mg, respectively.
(7) L-DOPA is widely used for the treatment of Parkinson's disease: Barbeau, A., Ed. "L-DOPA and Parkinsonism"; F. A. Davis: Philadelphia, 1970. Stern, D., Ed. "The Clinical Uses of L-DOPA"; Lankaster Medical and Technical Publishing: London, 1975. Recently, it has been found that L-DOPA and its derivatives also possess an antitumor activity: Wick, M. M.; Byers, L.; Frei, E.; *Science (Washington, DC)* **1977**, *197*, 468. Wick, M. M. *Nature (London)* **1977**, *269*, 512–513.
(8) Should this compound be readily available, it has the potential to become an important intermediate in the synthesis of semisynthetic antibiotics, including the cephalosporin-type antibiotics.

0002-7863/81/1503-6263$01.25/0