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

\[
\begin{align*}
\text{MeO} & \quad \text{MeO} \\
\text{R} & \quad \text{R} \\
\text{C} & \quad \text{C} \\
\text{CH}_2 & \quad \text{CH}_2
\end{align*}
\]

240°C

Intramolecular Diels–Alder reactions have also been carried out with substrates 3 where the benzozenoxygen was replaced by sulfur and nitrogen and by one or two methylene groups. Details will be reported in future publications.

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

(16) NMR (220 MHz in CDCl₃): δ 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.


Experimental Measurement of the Electron Affinity of the Hydroperoxy Radical

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The hydroperoxy radical, HO₂, 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 Weiss1 placed this quantity at 18 kcal mol⁻¹. Recently, Benson and Nangia2 have obtained threshold photodetachment of HO₂⁻ to obtain a more precise value, \( \Delta H_{\text{EA}}(\text{HO}_2) = 37.55 \pm 3.3 \text{ kcal mol}^{-1} \), and the electron affinity of the hydroperoxy radical \( \text{HO}_2^{-} \rightarrow \text{HO}_2 + e^{-} \)

\[ \Delta H = \Delta H_{\text{EA}}(\text{HO}_2) \]

is given on any current masthead page.

\[ \Delta H = \Delta H_{\text{EA}}(\text{HO}_2) \]

(2)

to be 1.16 ± 0.15 eV. Using these results, we have performed threshold photodetachment of HO₂⁻ to obtain a more precise value, \( \text{EA} (\text{HO}_2) = 1.19 ± 0.01 \text{ eV} \) (27.4 ± 0.2 kcal mol⁻¹). Employing this value and well-established heats of formation of \( \text{H}_2\text{O}_2 \), \( \text{HO}_2 \), and \( \text{H}^+ \), we find \( \Delta H_{\text{EA}}(\text{HO}_2) = -24.9 ± 0.7 \text{ kcal mol}^{-1} \) and \( \Delta H_{\text{EA}}(\text{HO}_2) = 374.8 ± 0.7 \text{ kcal mol}^{-1} \).

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 \( \text{H}_2\text{O}_2 \) (97.5%) and \( \text{CF}_3 \) were determined by monitoring the pressure increase in a calibrated volume, while HF flow was determined using a calibrated mass flowmeter. A limit of the extent of possible decomposition of \( \text{H}_2\text{O}_2 \) was evaluated and included in the error limits.

The experimental results for reaction 3 are \( k_1 = 2.2 \times 10^{10} \text{ cm}^3 \text{ molecule}^{-1} \text{ s}^{-1} \) and \( k_2 = 2.8 \times 10^{10} \text{ cm}^3 \text{ molecule}^{-1} \text{ s}^{-1} \), yielding \( \Delta H = -1.3 \text{ kcal mol}^{-1} \). Using \( \Delta H_{\text{EA}}(\text{CF}_3) = 376.6 \text{ kcal mol}^{-1} \) yields \( \Delta H_{\text{EA}}(\text{H}_2\text{O}_2) = 375.3 \text{ kcal mol}^{-1} \) for reaction 4. \( k_1 = 1.7 \times 10^{12} \text{ cm}^3 \text{ molecule}^{-1} \text{ s}^{-1} \) and \( k_2 = 2.8 \times 10^{10} \text{ cm}^3 \text{ molecule}^{-1} \text{ s}^{-1} \), yielding \( \Delta H = +4.4 \text{ kcal mol}^{-1} \). Using \( \Delta H_{\text{EA}}(\text{HF}) = 371.3 \text{ kcal mol}^{-1} \) yields \( \Delta H_{\text{EA}}(\text{H}_2\text{O}_2) = 375.7 \text{ kcal mol}^{-1} \).

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We have found that proton-transfer equilibria involving \( \text{HO}_2^+ \) and \( \text{H}_2\text{O}_2 \) cannot be experimentally established because a rapid competing process occurs.

\[ \text{HO}_2^- + \text{H}_2\text{O}_2 \rightarrow \text{OH}^- + \text{H}_2\text{O} + \text{O}_2 \]
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 $^{12}$C$^{+}$ 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 $^{2}$A$^{+}$ 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$^{15,16}$ 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$_2$($^{2}$A$(^0$,(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 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 ± 0.01 eV.

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Selective hydroxylation of aromatic compounds is a difficult task in preparative organic chemistry. 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 or by circumventing the direct hydroxylation as exemplified by the catalytic asymmetric production of l-3,4-dihydroxyphenylalanine (l-DOPA). 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$^{17}$ 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, 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: t-DOPA$^{1}$ from L-tyrosine (I), d(-)-3,4-dihydroxyphenylglycine$^{2}$ from d(-)-p-

Preparative Hydroxylation of Aromatic Compounds Catalyzed by Peroxidase

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Catalyzed by Peroxidase

(5) (I) and (2) Due to the direct hydroxylation of L-tyrosine to form l-DOPA (Sih, C. J.; Foss, P. J.; Rosazza, J.; Lemberger, M. J. Am. Chem. Soc. 1969, 91, 6204. Florent, J.; Renaut, J. German Patent 1,279,730, 1970). This elegant process involves the condensation of 3,4-dihydroxybenzaldehyde with N-acetylglutamate, followed by asymmetric hydrogenation catalyzed by rhodium complexes and subsequent hydrolysis of the resultant N-acetyl-l-DOPA (Kowala, W. S.; Sabacky, M. J.; Vineyard, B. D. U.S. Patent 4,003,127, 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 way.
(8) 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.