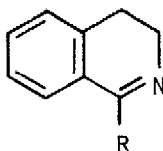




aromatization of the dihydroisoquinoline ring, and that the rate of reaction is approximately four times the rate of oxidation by ground state molecular oxygen.

In order to examine the scope and mechanism of this new synthetic application of singlet oxygen, a series of 1-alkyl-3,4-dihydroisoquinolines (Table 2) was prepared by Bischler-Napieralski cyclization of the corresponding 2-phenylethylamides, and the reaction time for 99% conversion to the ketone was determined. The photooxidations were performed on 0.01 M solutions

Table 2



<u>Compound</u>	<u>R</u>	<u>Reaction Time</u> <sup>a</sup>
<u>4a</u>	- CH <sub>3</sub>	N.R.
<u>4b</u>	- CH <sub>2</sub> CH <sub>3</sub>	48 hr.
<u>4c</u>	- CH(CH <sub>3</sub> ) <sub>2</sub>	N.R.
<u>4d</u>	- CH(CH <sub>3</sub> )C <sub>6</sub> H <sub>5</sub>	60 hr. <sup>b</sup>
<u>4e</u>	- CH <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	12 hr.
<u>4f</u>	- CD <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	12 hr.
<u>4g</u>	- CH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> (p-OCH <sub>3</sub> )	6 hr.
<u>4h</u>	- CH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> (p-Cl)	24 hr.
<u>4i</u>	- CH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> (p-NO <sub>2</sub> )	50 hr.

<sup>a</sup> 99% oxidation by GLC

<sup>b</sup> only fragmentation products observed (vide infra)

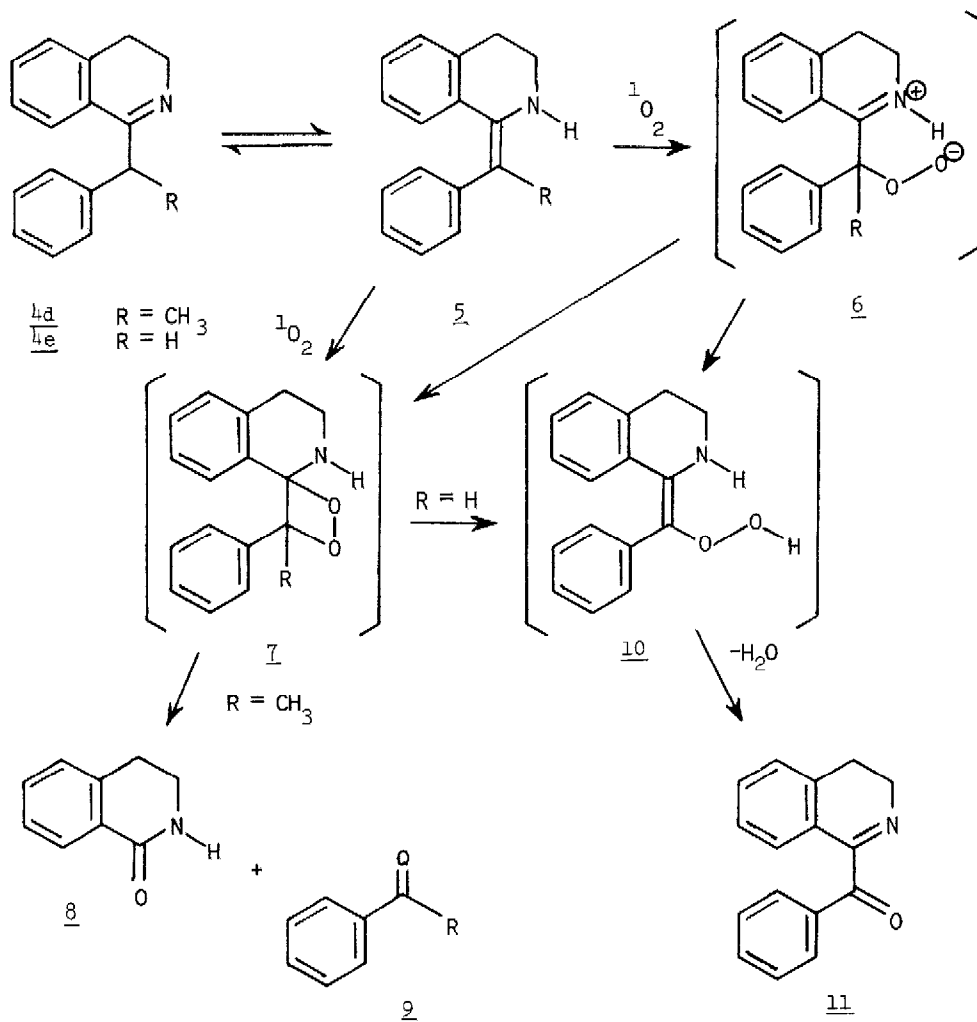
of the 3,4-dihydroisoquinolines in chloroform containing Methylene Blue (ca. 10<sup>-4</sup> M) as sensitizer at ambient temperature under an oxygen atmosphere. A 40 watt tungsten filament lamp provided irradiation. The usual tests<sup>4</sup> were performed to ensure that singlet rather than triplet oxygen was the reacting species. The structures of the oxidation products from 4b and 4d-i were unambiguously determined using ir, pmr, and ms.

The results (Table 2) indicate that oxidation proceeds readily when R = benzyl or substituted benzyl, consistent with a reaction mechanism (Scheme 2) in which the rate-determining step involves attack by electrophilic singlet oxygen on an intermediate enamine (5)<sup>5</sup>. Substrates having substituents that lack an aromatic ring which can stabilize an intermediate enamine through conjugation either do not react (4a, 4c) or react sluggishly (4b). Albrecht et. al.<sup>8</sup> have shown that an equilibrium exists between enamines and imines of this general type, and furthermore that electron withdrawing substituents on the aromatic ring increase the equilibrium concentration of enamine. Interestingly, our results show that the rate of photooxidation is inversely related to the equilibrium concentration of enamine. A Hammett-type plot of the log of the reaction rate constant versus  $\sigma_p$  gives a  $\rho$  value of -0.8, indicative of a mechanism

which is relatively insensitive to substituent effects, and which has a rate that is retarded by electron withdrawing groups. These data are interpreted in terms of a mechanism involving an endothermic rate determining step in which electron withdrawing substituents (e.g.,  $p\text{-NO}_2$  and  $p\text{-Cl}$ ) stabilize the reactant relative to the transition state, and therefore raise the energy of activation and lower the reaction rate. Electron donating substituents ( $p\text{-OCH}_3$ ) have the opposite effect, destabilizing the reactant relative to the transition state and therefore enhancing the rate.

Additional evidence for the presence of enamine in equilibrium with the dihydroisoquinoline is found in the observation that dissolution of 4e in methanol- $d_1$  provides a facile means of exchange of the benzylic protons and conversion to the didetero compound 4f. A comparison of singlet oxygen oxidation rates between 4e and 4f shows no deuterium isotope effect.

Scheme 2



The reaction of singlet oxygen with compound 4d offers further insight into the reaction mechanism. The sole observed products (8 and 9) are the result of cleavage of an intermediate dioxetane (7), which may arise directly as a result of [2 + 2] addition or upon closure of an initially formed zwitterionic peroxide (6).<sup>10</sup>

Confirmation of a possible zwitterionic peroxide intermediate was sought by means of a solvent trapping experiment using methanol,<sup>11</sup> but no trapped product was observed. We conclude that either the dioxetane 7 is the initial product of photooxidation or the initially formed zwitterionic peroxide (6) is too short lived to be trapped. Either intermediate can give rise to the enaminohydroperoxide 10 which spontaneously dehydrates, probably via a six-membered ring transition state. Further work is underway to distinguish between these mechanistic possibilities.

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#### References and Notes

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11. See C. W. Jefford and C. G. Rimbault, J. Am. Chem. Soc. 100, 6437 (1978).

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