213. Self-Sensitized Photo-Oxygenation of 1-Benzyl-3,4-dihydroisoquinolines

Preliminary Communication

by **Ned H. Martin**[1]) and **Charles W. Jefford**

Department of Organic Chemistry, University of Geneva, CH-1211 Geneva 4

(10.VI.81)

Summary

The air oxidation of 1-benzyl-3,4-dihydroisoquinolines is shown to be a self-sensitized photo-oxidation proceeding *via* singlet oxygen.

Introduction. - The autoxidation of alkoxy-substituted 1-benzyl-3,4-dihydroisoquinolines (**2**) to give the corresponding 1-benzoyl derivatives (**3**) has been known for many years [1]. Adventitious oxidations of **2** have been observed on work-up after *Bischer-Napieralski* cyclization of the starting amide **1** [2] [3]. Similar unexpected conversion of **2** to **3** was also reported to occur during chromatography over alumina [4]. In other cases, where the benzoyl derivative was required synthetically, reaction times of some two weeks were required to complete the oxidation [5]. In a preliminary study we have demonstrated that this oxidation can be accomplished more efficiently by dye-sensitized photo-oxygenation [6]. We have further investigated this potentially useful, mild, selective oxidation and now report that the rate of reaction varies markedly with light intensity.

In the dark, oxidation of the parent compound 1-benzyl-3,4-dihydroisoquinoline (**4**) by triplet oxygen proceeds very slowly. Less than 2% is oxidized in 12 days when a solution of **4** (20 mM) in chloroform is maintained under an oxygen atmosphere at 10°. In a room illuminated with fluorescent light[2]), the half oxidation time of **4** is 6 days. Exposure of the same solution to irradiation by two 500 W tungsten filament lamps[3]) under an oxygen atmosphere effects 50% reaction in 17 h. When methylene blue (0.25 mM) is used as sensitizer, the reaction half-life is shortened to 9 h under ordinary room light and to 2.5 min when two 500 W projector lamps are employed *(Table)*. 3,4-Dihydropapaverine (**5**) is oxidized more

---

[1]) Author to whom correspondence should be addressed; on leave from the University of North Carolina at Wilmington, P.O. Box 3725, Wilmington, North Carolina 28406, USA.

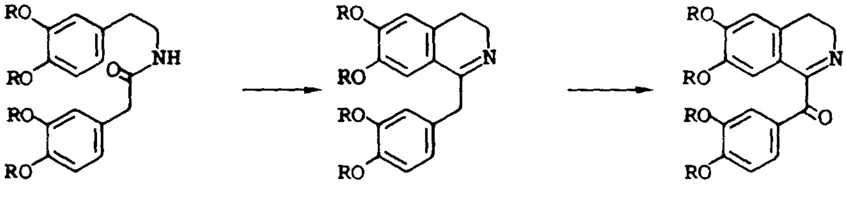
[2]) The radiant flux density in a typical laboratory is 10^{-5} to 10^{-4} watts/cm^2, and is sufficient for the photo-oxidation.

[3]) Light from *Sylvania* FFX projector bulbs was passed through a *Jena* KV filter to block radiation below 400 nm.

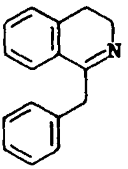
0018-019X/81/7/2189-04$01.00/0

Table. *Half-lives of reactants* **4** *and* **5** *on oxygenation*

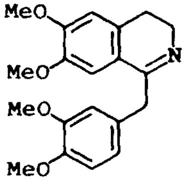
	Self-sensitized		Methylene blue-sensitized	
Reactant	**4**	**5**	**4**	**5**
Dark	10 d	⩾ 12 d	-	-
Room light	112 h	148 h	38 h	9 h
2 × 500 W	2.8 h	17 h	4.4 min	2.5 min



1 **2** **3**



4



5

rapidly than **4** in the absence of methylene blue, requiring 112 h in room light and just 2.8 h when two 500 W lamps are used to achieve in both cases 50% oxidation. The methylene blue photo-sensitized oxidation of **5** proceeds with half-lives of 38 h and 4.4 min respectively for the two light sources *(Table)*. It is significant that the dye-sensitized photo-oxygenation of the tetramethoxy compound is slower than that of the unsubstituted compound, however the rate order is reversed when methylene blue is omitted as sensitizer.

An explanation of this rate difference may lie in the different long wavelength absorption characteristics. The tetramethoxy compound **5** absorbs at 360 nm ($\log\varepsilon = 2.66$), whereas the unsubstituted 1-benzyl-3,4-dihydroisoquinoline (**4**) absorbs less intensely and at shorter wavelength ($\lambda_{max} = 345$, $\log\varepsilon = 2.33$). Consequently, the faster photo-oxygenation of **5** over **4** may be ascribed to the greater self-sensitization of the former as its absorption spectrum is closer to the irradiation wavelength used3)4).

Both the self-sensitized and dye-sensitized reactions are mediated by singlet oxygen and verification of its intermediacy was obtained from the following evidence: 1) The rate of oxidation in the light is unaffected by the radical inhibitor 2,6-di-*t*-butyl-*p*-cresol (1 mM), but is retarded considerably by addition of DABCO

---

4) A complete re-examination of the substituent effects on the rates of photo-oxygenation is in progress.

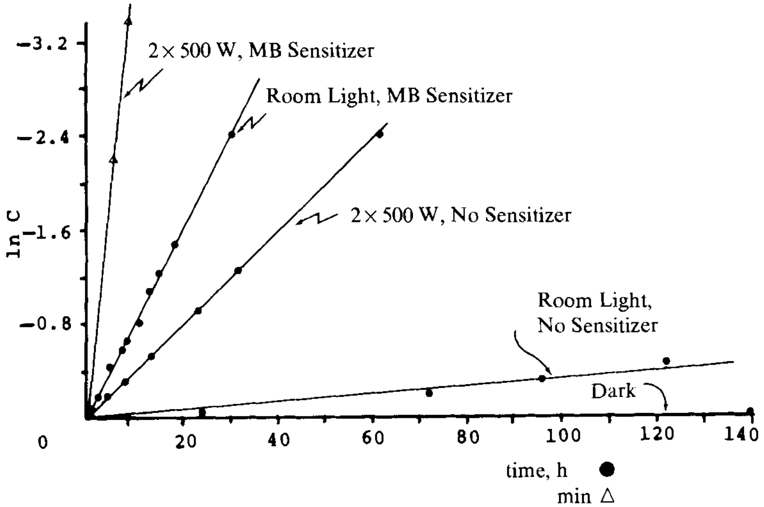


Fig. 1. *Natural logarithm of the concentration* (c) *of 1-benzyl-3,4-dihydroisoquinoline* (**4**) *during oxygenation* vs. *time*

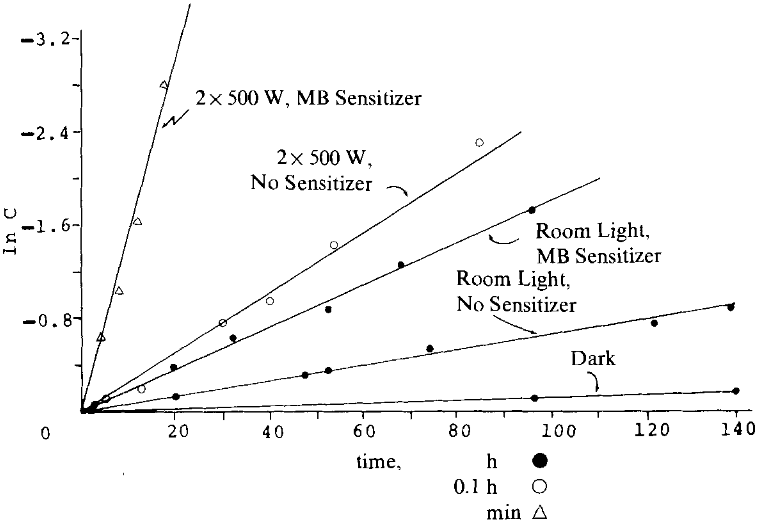


Fig. 2. *Natural logarithm of the concentration* (c) *of 3,4-dihydropapaverine* (**5**) *during oxygenation* vs. *time*

(1-10 mM), a known quencher of singlet oxygen [7]; 2) Oxidation ceases immediately when irradiation is stopped; 3) When the natural logarithm of the concentration of substrate under various oxygenation conditions is plotted against time, straight lines are obtained indicating that the reaction is of *pseudo* first-order[5]. Similar plots are obtained for both the dye-sensitized and self-sensitized photo-

---

[5] Analyses were performed by gas-liquid chromatography using dibutylphthalate as internal standard.

oxygenations (*Fig. 1* and *2*); 4) The same oxidation products are obtained when 1,4-dimethylnaphthalene endoperoxide [8] is used to generate singlet oxygen in the dark; 5) The same product is obtained regardless of the sensitizer/solvent combination used, *viz.* methylene blue/chloroform, *meso*-tetraphenylporphine/carbon tetrachloride, rose bengal/methanol and methylene blue/acetonitrile.

These results are at variance with those originally reported [6]. It is now seen that those experiments where a low intensity light source was used involve radicals and not singlet oxygen. Further details of this investigation will be reported later.

We are indebted to the *Swiss National Science Foundation* for support of this work. We thank Dr. *Charles Stalder* for measurements of the light intensity.

REFERENCES

[1] *J.S. Buck, R.D. Haworth & W.H. Perkin*, jr., J. Chem. Soc. *125*, 2176 (1924).

[2] *R.S. Livshits, G.I. Baslevskaya, M.S. Bainova, O.E. Dobrovinskaya & N.A. Preobrazhenskii*, J. Gen. Chem. (U.S.S.R.) *17*, 1671 (1947); Chem. Abstr. *42*, 2606 (1948).

[3] *A. Lindenmann*, Helv. Chim. Acta *32*, 69 (1949).

[4] *T. Kametani & K. Fukumoto*, J. Pharm. Soc. Jpn *83*, 1031 (1963).

[5] *T. Kametani, H. Matsumoto, Y. Satoh, H. Nemoto & K. Fukumoto*, J. Chem. Soc. Perkin I, *1977*, 376.

[6] *N.H. Martin, P.B. Belt & S.L. Champion*, Tetrahedron Lett. *21*, 2613 (1980).

[7] *C. Ouannès & T. Wilson*, J. Am. Chem. Soc. *90*, 6527 (1968); *R.S. Davidson & K.R. Trethewey, ibid.* *98*, 4008 (1976).

[8] *H.H. Wasserman & D.L. Larsen*, J. Chem. Soc. Chem. Commun. *1972*, 253.