

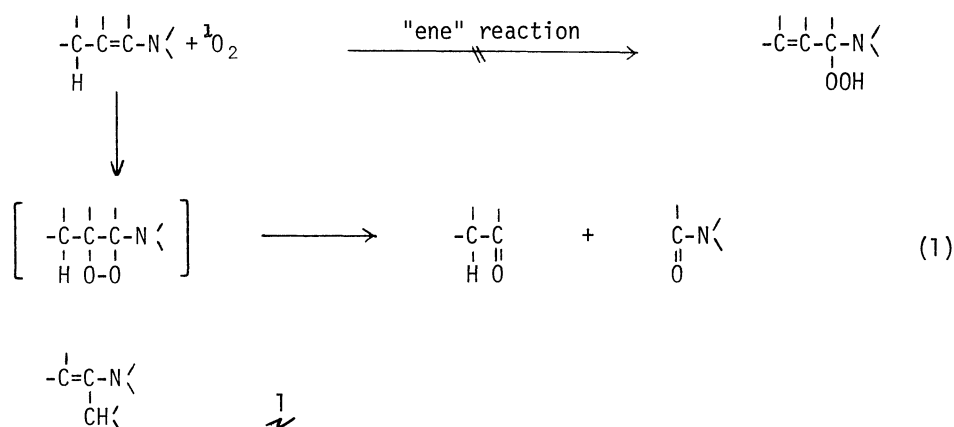
PHOTOINDUCED REACTIONS. LXV.  
PHOTOSENSITIZED OXYGENATION OF 2-METHYLINDOLES <sup>1)</sup>

Isao SAITO, Mitsuru IMUTA, and Teruo MATSUURA

Department of Synthetic Chemistry, Faculty of Engineering, Kyoto University  
Sakyo-ku, Kyoto 606

Photosensitized oxygenation of 2-methylindole and 1,2-dimethylindole gave 2-methyl-2-[3-(2-methylindolyl)]indoxyl and its N,N'-dimethyl derivative, respectively, which were possibly formed through a hydroperoxide intermediate, whereas 1,2,3-trimethylindole underwent oxidative 2,3-cleavage to give o-(N-acetyl-N-methyl)aminoacetophenone.

It is known that enamines react with singlet oxygen, produced usually in the dye-sensitized photo-oxygenation system, to undergo  $\alpha,\beta$ -cleavage through a 1,2-dioxetane intermediate (eq. 1),<sup>2,3)</sup> although its formation has not been experimentally confirmed. Among them, tertiary enamines having allylic hydrogen at  $\gamma$ -carbon undergo  $\alpha,\beta$ -cleavage but not "ene" reaction<sup>4)</sup> to form an allylic hydroperoxide as shown in eq. 1.<sup>2a, 2b, 8)</sup> Moreover, there have been a few examples of the reaction of singlet

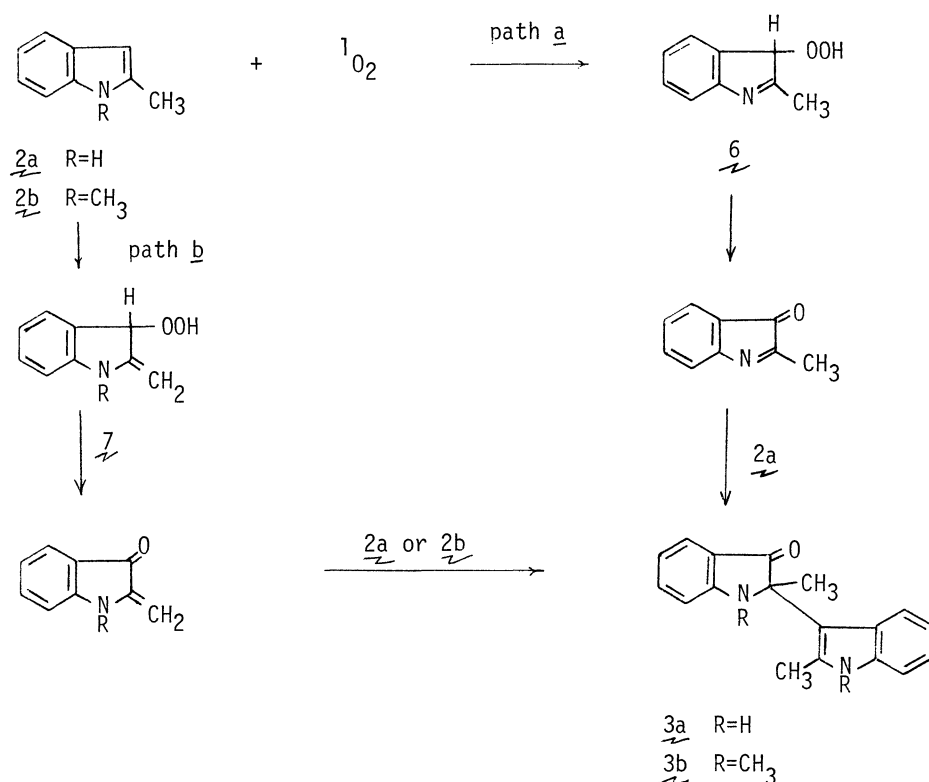


oxygen with enamines of type 1 having allylic hydrogen on a carbon atom substituted at the  $\alpha$ -position.<sup>6)</sup> However, in such cases no "ene" reaction was observed. In this respect, we examined reaction of singlet oxygen with 2-methylindoles, which have the partial structure 1, in order to know whether or not 1,2-cleavage is predominant over "ene" reaction in such a case.

Rose bengal-sensitized photooxygenation of 2-methylindoles was carried out in methanol at room temperature under irradiating with a tungsten-bromine lamp. 2-Methylindole (2a) gave a dimeric product 3a<sup>11)</sup> in almost quantitative yield. 1,2-Dimethylindole (2b) gave 3b<sup>12)</sup> in 80% yield, whose spectral properties are quite similar to those of 3a. In both cases, a half mole equivalent of oxygen was absorbed. In contrast, 1,2,3-trimethylindole (4)<sup>13)</sup> absorbed one mole equivalent of oxygen under the conditions to give o-(N-acetyl-N-methyl)aminoacetophenone (5)<sup>14,15)</sup> in 92% yield, showing that oxidative 2,3-cleavage occurred. All the starting materials did not absorb oxygen at appreciable rate in the dark.

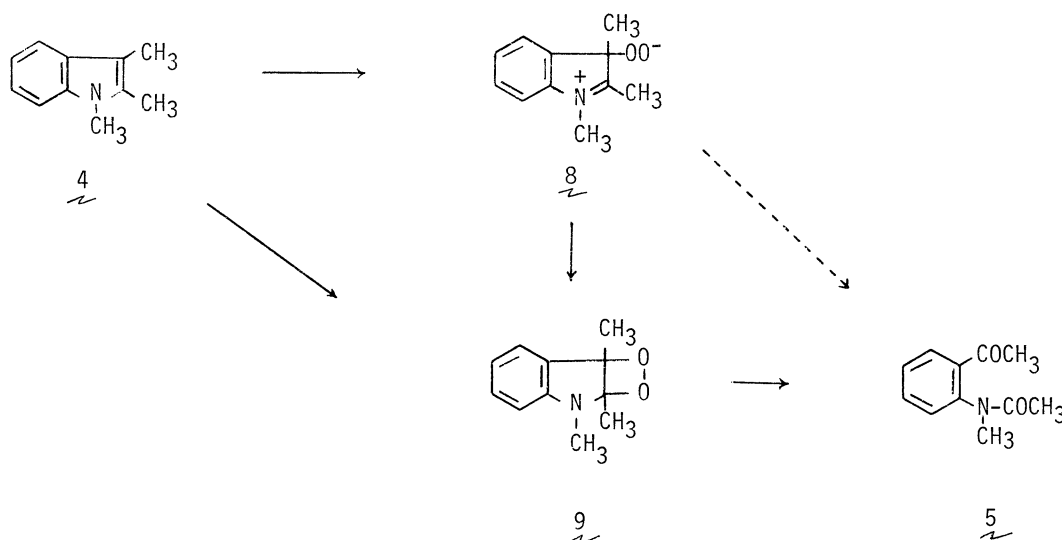
The formation of the dimeric products, 3a and 3b, may be rationalized as shown in Scheme 1, involving a hydroperoxide intermediate, 6 (path a) or 7 (path b). The same mechanism involving 6 (R=H) has been proposed for the formation of 3a in the autoxidation of 2a.<sup>16)</sup> Considering the fact that singlet oxygen adds to the enamine system  $\text{-}\overset{|}{\text{C}}=\overset{|}{\text{C}}\text{-}\overset{|}{\text{N}}\text{H}$  to give the product  $\text{-}\overset{|}{\text{C}}(\text{OOH})\text{-}\overset{|}{\text{C}}=\text{N-}$ ,<sup>3)</sup> it is more likely that 3a is formed via path a but not via path b. However, 3b must be formed through the "ene" reaction product 7 (R=CH<sub>3</sub>) because of the lack of NH hydrogen in 2b.

Scheme 1.



Scheme 2 illustrates two possible pathways for the formation of 5 from 4, involving a zwitterionic peroxide 8<sup>2c,17)</sup> and/or a dioxetane intermediate 9, although available experimental data cannot distinguish between two modes of addition of singlet oxygen; i.e. stepwise and concerted.<sup>19)</sup>

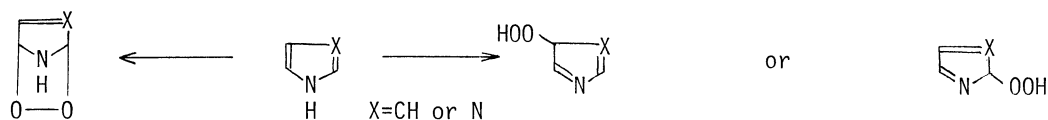
Scheme 2.



A remarkable difference between reaction modes of 2b and 4 should be attributed to the methyl substituent at position 3. Although the role of the methyl group remains to be elucidated, one of the possible roles may be its electron-donating ability which causes the indole nucleus to be more electron-rich so that the oxidative 2,3-cleavage occurs predominantly over the "ene" reaction. A similar example has been reported in the preceding communication.<sup>1)</sup>

## REFERENCES AND NOTES

- 1) Part LXIV: I. Saito and T. Matsuura, Chemistry Lett., preceding communication.
- 2) For examples see, (a) C. S. Foote and J. W.-P. Lin, Tetrahedron Lett., 3267 (1968); (b) J. F. Huber, ibid., 3271 (1968); (c) T. Matsuura and I. Saito, ibid., 3273 (1968); Tetrahedron, 24, 6609 (1969); 25, 541, 549 (1969); (d) H. H. Wasserman, K. Stiller, and M. B. Floyd, Tetrahedron Lett., 3277 (1968); (e) G. Rhodes and P. D. Gardner, Ann. N.Y. Acad. Sci., 171, 151 (1970); (f) H. H. Wasserman and A. Liberles, J. Amer. Chem. Soc., 82, 2086 (1960); (g) D. A. Lightner and G. B. Quistad, Angew. Chem., 84, 216 (1972); (h) D. A. Lightner and L. K. Low, Chem. Commun., 625 (1972).
- 3) It has been reported that singlet oxygen adds to enamines having an NH hydrogen such as purines,<sup>2c)</sup> pyrroles<sup>2g,2h,5,6)</sup> and imidazoles<sup>2c,7)</sup> to give an endo-peroxide (1,4-addition) or a hydroperoxide as the initial product.



- 4) C. S. Foote, *Accounts Chem. Res.*, 1, 104 (1968).
- 5) (a) H. H. Wasserman and A. Liberles, *J. Amer. Chem. Soc.*, 82, 2086 (1960); (b) G. Rio, A. Ranjon and O. Pouchot, *Compt. Rend.*, 263, 634 (1966).
- 6) (a) G. B. Quistad and D. A. Lightner, *Tetrahedron Lett.*, 4417 (1971); *Chem. Commun.*, 1099 (1971); (b) L. K. Low and D. A. Lightner, *ibid.*, 116 (1972).
- 7) E. H. White and M. J. C. Harding, *Photochem. Photobiol.*, 4, 1124 (1965).
- 8) 3-Methylindole<sup>9)</sup> and tryptophan<sup>9,10)</sup> having a  $-\overset{|}{\text{CH}}-\overset{|}{\text{C}}=\overset{|}{\text{C}}-\text{NH}-$  moiety are known, on photosensitized oxygenation, to undergo 2,3-cleavage. In these cases, a 3-hydroperoxyindolenine intermediate was proposed as the precursor of the dioxetane which undergoes 2,3-cleavage.
- 9) G. Rhodes and P. D. Gardner (Reported by J. D. Spikes and M. L. MacKnight), *Ann. N. Y. Acad. Sci.*, 171, 151 (1970).
- 10) Z. Yoshida and M. Kato, *Nippon Kagaku Zasshi*, 75, 112 (1954).
- 11) B. Witkop and J. B. Patrick, *J. Amer. Chem. Soc.*, 73, 713 (1951).
- 12) This product exhibits following spectral properties which are consistent with structure 3b: IR (Nujol) 1695  $\text{cm}^{-1}$ ; UV (EtOH) 228 ( $\epsilon$  88400), 265 (10800), 286 (7670), and 425 nm (3320); NMR ( $d_6$ -acetone)  $\tau$  2.26-3.36m (8H), 6.30s (3H), 7.10s (3H), 7.63s (3H), and 8.13s (3H). Satisfactory microanalyses were obtained for all new compounds.
- 13) E. F. J. Janetzky and P. E. Verkade, *Rec. Trav. Chim. Pays-Bas*, 65, 691 (1946).
- 14) This product exhibits following spectral properties which are consistent with structure 5: IR (Neat) 1695 and 1660  $\text{cm}^{-1}$ ; UV (EtOH) 227 ( $\epsilon$  8280) and 285 nm (110); NMR ( $\text{CDCl}_3$ )  $\tau$  2.13-2.81m (4H), 6.80s (3H), 7.47s (3H), and 8.23s (3H); MS  $m/e$  191.
- 15) In different solvents, 5 was obtained in virtually the same yield: 90% in acetone at room temperature; 95% in methanol-pyridine (50:1) at 0°C.
- 16) R. J. Sundberg, "The Chemistry of Indoles", Academic Press, New York-London (1970), p.289.
- 17) A peroxirane intermediate<sup>18)</sup> may be regarded as one of the possible forms of such a zwitterionic peroxide. Evidence for the formation of such a zwitterionic peroxide has been reported.<sup>2c)</sup>
- 18) D. R. Kearns, *Chem. Rev.*, 71, 395 (1971) and references cited therein.
- 19) Direct cleavage of 8 to 5 may not be ruled out as one of possible pathways.

( Received September 14, 1972 )