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PHOTOOXYGENATION OF ENAMINES - A
PARTIAL SYNTHESIS OF PROGESTERONE

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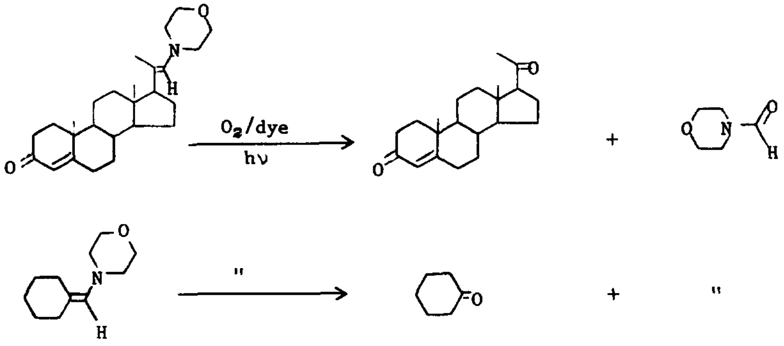
The growing interest in singlet oxygen has resulted in a number of examples demonstrating the usefulness of this reagent as a synthetic tool (1). We wish now to report a further example of this utility. We have found that certain enamines which were stable to ground state oxygen were cleanly cleaved by photooxygenation to form two carbonyl fragments.

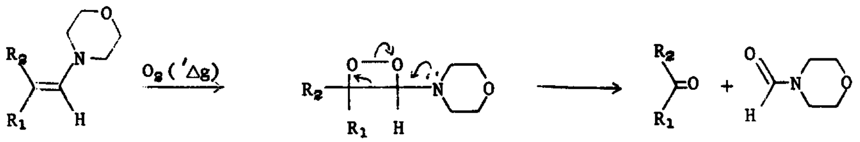
3-Ketobisnor-4-cholen-22-al was selectively converted to the 22-morpholine enamine by a standard procedure (2). Photooxygenation (3) of a slurry of 5.0 g. of the pure enamine in 25 ml. of DMF at 15° using rose bengal as the sensitizer afforded, after 17.5 hrs., a quantitative yield of progesterone, m.p. 126-128°, $[\alpha]_D$ +176° (dioxane). This product was identified by comparison of its n.m.r. spectrum and mobility in both t.l.c. and g.l.c. with that of an authentic sample. The other fragment from this cleavage was shown by direct g.l.c. analysis of the



reaction mixture to be 4-morpholinecarboxaldehyde. Similarly, the morpholine enamine of cyclohexanecarboxaldehyde (b.p. 100-106°/8 mm., n_D^{25} 1.5020) upon photooxygenation (methanol solution, rose bengal dye) produced cyclohexanone and 4-morpholinecarboxaldehyde as the only products as determined by direct g.l.c. analysis. The cyclohexanone in the mixture was isolated as the 2,4-dinitrophenylhydrazone, m.p. 159-160°. In both of these examples, no experimental evidence (t.l.c. or g.l.c.) for any intermediates could be found.

This cleavage of the carbon-carbon double bond is envisioned simply as the 1,2-cycloaddition of the singlet ($'\Delta$ g) oxygen molecule to the enamine and subsequent decomposition of this postulated intermediate to the two carbonyl fragments.

Proposed Mechanism:



REFERENCES

1. See for example: T. J. Katz, V. Balogh and J. Schulman, J. Am. Chem. Soc., 90, 734 (1968) and J. A. Marshall and A. R. Hochstetler, J. Org. Chem., 31, 1020 (1966).
2. M. E. Herr and F. W. Heyl, J. Am. Chem. Soc., 74, 3627 (1952).
3. The photo-reactor used in these examples was similar to that described by Nickon and Bagli [J. Am. Chem. Soc., 83, 1498 (1961)] except that it was fitted with a cold finger. This was illuminated with four 15-watt fluorescent tubes. No reaction would take place in these examples if either the light or dye was omitted.