HETEROCYCLES, Vol.12, No.1, 1979

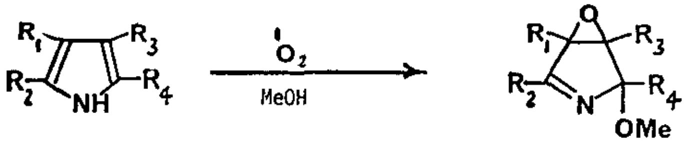
REACTIONS OF SINGLET OXYGEN WITH HETEROCYCLIC SYSTEMS

Harry H. Wasserman
Department of Chemistry, Yale University, New Haven, Connecticut 06520

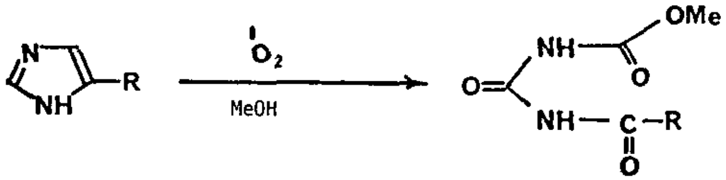
In recent years it has become evident that singlet oxygen plays an important role in many processes affecting living systems. In large part, the participation of this excited species in such biochemical processes occurs through oxidation of various heterocyclic compounds. Our studies have attempted to elucidate the oxidation pathways and clarify the mechanisms of such reactions.

The heterocyclic systems investigated have included pyrroles, imidazoles, oxazoles, thiazoles, thiophenes, benzofurans and various heterocyclophanes. The results have shown that singlet oxygen may bring about complex changes which are not caused by other reagents. These changes result not so much from unusual modes of initial attack by singlet oxygen upon the heterocyclic molecule but rather from the decomposition of the intermediate endoperoxide, dioxetane or other peroxidic species. These second-stage reactions often involve intramolecular interactions leading to novel products.

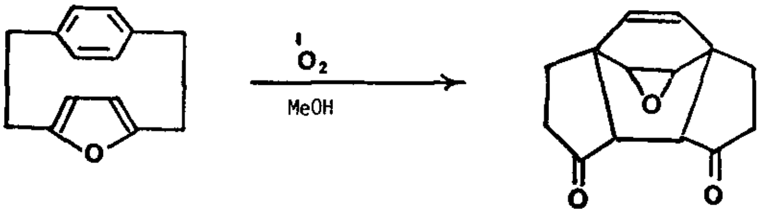
Among the reactions of special interest are the formation of 3,4-epoxides in pyrrole oxidation (equation 1); the oxidative destruction of imidazoles related to the photodynamic effect (equation 2); the intramolecular oxygen transfer observed in furanophane oxidation (equation 3); and the conversion of oxazoles to triamides (equation 4). The unusual oxidation of oxazoles in polar media has been studied in detail and shown to involve an intermediate imino anhydride. In nonpolar solvents other reactions become predominant (equation 5).



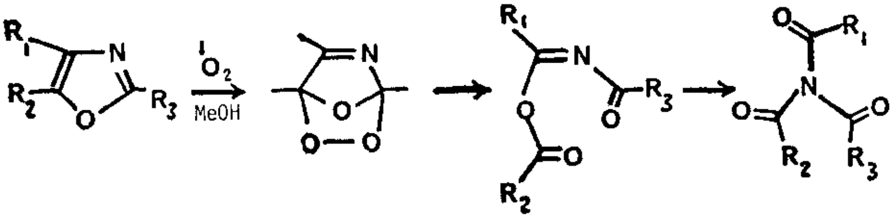
(1)



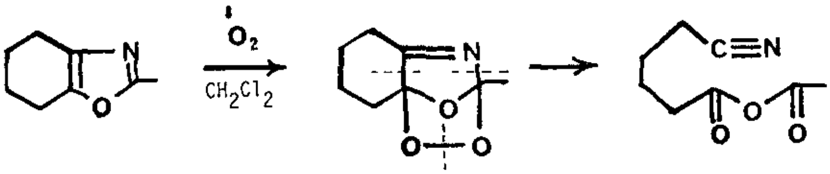
(2)



(3)



(4)



(5)

The reactions of singlet oxygen with enamines are related to the pathways by which a number of heterocyclic systems including indoles, imidazoles and purines undergo photooxidation. Our studies on the reactions of simpler acyclic and cyclic enamines have shown that the oxidation may result in carbon-carbon double bond cleavage or α-oxidation depending on the geometry of the system. Singlet oxygen oxidation of enamines has been developed into a useful *synthetic method for the formation* of α-keto lactones and α-keto lactams, as well as α-diketones.