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THE REACTION OF SINGLET OXYGEN WITH 4,5,6,7-TETRAHYDRO-2-METHYLBENZOTHIAZOLE

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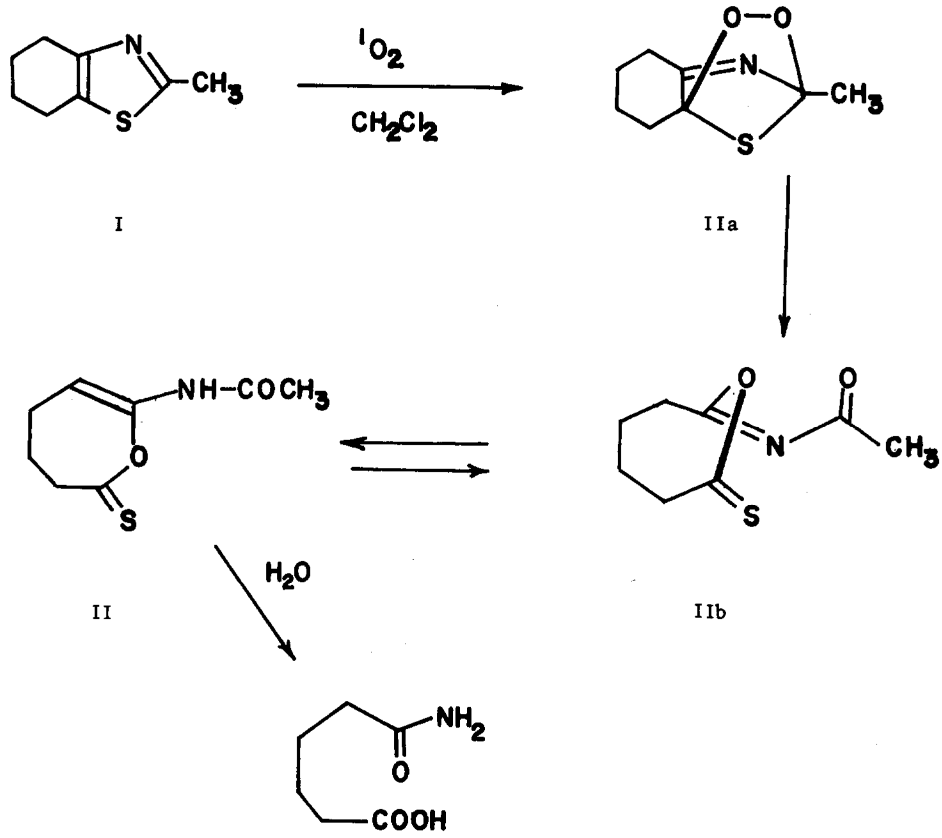
Previous studies on the oxidation of oxazoles with singlet oxygen [2,3] have shown that the observed products (triamides) are formed by a stepwise sequence involving first, endoperoxide formation, then, Baeyer-Villiger-like rearrangement to an imino anhydride, and finally, O-acyl to N-acyl transfer . Neither the endoperoxides nor the imino anhydrides could be isolated in any of the previous oxazole oxidations.

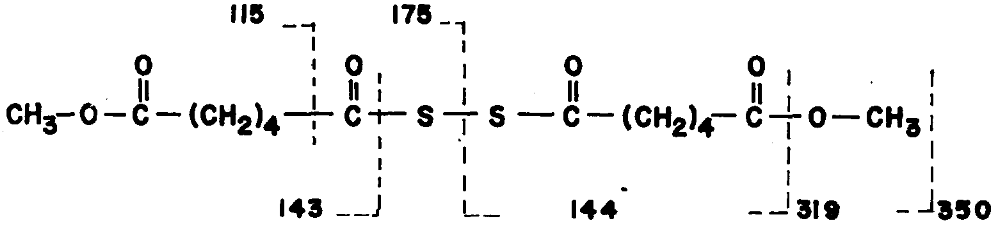
We now report the reaction of an alkyl thiazole with singlet oxygen in which an imino anhydride can be isolated as a stable product. As is discussed below, the formation of this intermediate appears to be a consequence of the special geometry of the fused ring system under study.

4,5,6,7-Tetrahydro-2-methylbenzothiazole[4] (I) (3.66g) was irradiated with a 275 watt sunlamp in 1500 ml of methylene chloride in the presence of methylene blue while pure oxygen was bubbled through the solution. After 20 hr, the solvent was removed in vacuo and the residue purified by chromatography on silica gel (10% ethyl acetate in methylene chloride) to yield II (67%) mp 105°. The nmr spectrum of this product shows: a NH proton at 1.82τ (exchangeable with D_2O); a one-proton broad triplet ($J \approx 7.5$) in the olefinic region at 3.42τ; a two-proton broad triplet ($J \approx 7$) at 7.18τ; a four-proton multiplet at 7.30-8.10τ; and a sharp singlet at 7.90τ corresponding to methyl protons in a N-acetyl group. The ir spectrum has NH absorption at 3200 cm^{-1} and amide and thio ester groups at 1665, 1525, 1260 and 1080 cm^{-1}.[5] Compound II could be hydrolyzed to adipamic acid, indicating that the double bond is part of an enamide system. The above data are clearly in accord with the N-acetylthio isoimide structure, II.[6]

When the photooxygenation of the thiazole (I) was run in methanol, a different product (IV) was isolated. Work-up of the reaction mixture as described above gave a white crystalline



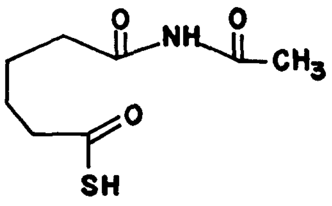
compound, mp 31-2° (55%). The elemental analysis of (IV) corresponds to a disulfide, $C_7H_{11}O_3S_2$, suggesting that an oxidative coupling had taken place. The ir spectrum shows the presence of an ester carbonyl at 1735 cm^{-1}, while the nmr spectrum has a methoxyl singlet at 6.34τ, two 2-proton multiplets at 7.23 and 7.72τ, and a multiplet at 8.0-8.5τ corresponding to four aliphatic protons. On warming this product in water, monomethyl adipate was obtained. The only structure in accord with these data is the disulfide (IV) formed, most probably from oxidation of the methyl ester of monothioadipic acid. The mass spectrum of IV confirms the assigned structure, showing a parent peak at m/e 350 and peaks at 175 and 115 resulting from cleavage of the disulfide bridge and loss of COS. Other major peaks at m/e 319 144 and 143 are explained by the following fragmentation pattern.



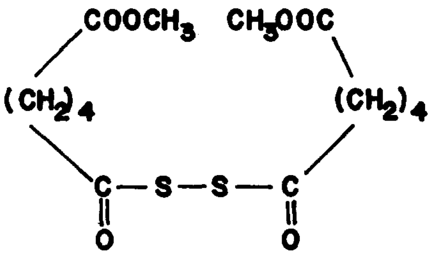
$$CH_3-O-\overset{O}{\overset{\|}{C}}-(CH_2)_4-\overset{O}{\overset{\|}{C}}-S-S-\overset{O}{\overset{\|}{C}}-(CH_2)_4-\overset{O}{\overset{\|}{C}}-O-CH_3$$

The formation of II may be explained by the same mechanism as that shown to operate in related oxazole oxidations.[3] Uptake of singlet oxygen leads to the transannular peroxide IIa which undergoes a Baeyer-Villiger type of rearrangement to the N-acylthioimino anhydride IIb. Proton shift then leads to the enamine tautomer, II. In the photooxygenations of 2,4,5-triphenylthiazole[7] and various monocyclic oxazoles[2,3] previously studied, intermediates corresponding to II have not been isolated. Instead, these labile imino anhydrides undergo rapid rearrangement to triamides. In the case reported here, the geometry of II does not appear to favor intramolecular thioacyl transfer from oxygen to nitrogen.[8]

The production of IV in the polar solvent may result from the same reaction course observed in the methylene chloride oxidation. It is reasonable to assume that in methanol, the initially formed thio isoimide, IIb, or its tautomer II, undergoes hydrolysis by water in the methanol to form III, followed by methanolysis and oxidation to the diacyl disulfide (IV).[9]



III



IV

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4. F. Asinger, M. Thiel and H.G. Hauthal, Ann., 634, 131 (1959).
5. L.J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, New York, 294 (1954).
6. All new compounds possess the correct elemental analyses and spectral properties in agreement with the postulated structures.
7. In the first reported study on thiazole photooxidation, T. Matsuura and I. Saito, Bull. Soc. Chem., Japan, 42, 2973 (1969) obtained benzil and benzamide from 2,4,5-triphenylthiazole in methanol. In chloroform, they isolated N,N-dibenzoylthiobenzamide.
8. Recent studies have shown that certain 4,5-polymethylene-2-phenyloxazoles also yield N-aroyl isoimides on reaction with singlet oxygen (H.H. Wasserman and G.R. Lenz, manuscript in preparation.)
9. That hydrolysis of II is much faster than alcoholysis was demonstrated by the quantitative recovery of II after refluxing overnight in absolute alcohol. On the other hand, refluxing of II in water gave virtually a quantitative yield of adipamic acid.

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