

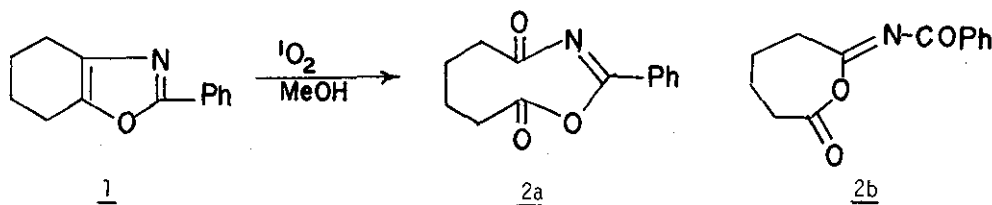
THE REACTION OF OXAZOLES WITH SINGLET OXYGEN. IV. IMINO ANHYDRIDE INTERMEDIATES

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Reaction of 2-aryl-4,5-polymethylene oxazoles with singlet oxygen yields N-aryl imino anhydrides. If the polymethylene bridge is large enough a further rearrangement to triamides may take place.

Previous reports on the reactions of singlet oxygen with oxazoles have shown that oxygen uptake leads to triamides, most probably, through intermediate imino anhydrides.^{1,2,3} While these imino anhydrides are too reactive to be isolated in the oxygenations of monocyclic oxazoles, they may be isolated in the case of fused-ring systems. Thus, the singlet oxygen oxidation of 2-phenylcyclohexeno-4,5-oxazole (1) in methanol leads to an imino anhydride postulated² to be either 2a or 2b. In this communication we describe oxygen-18 tracer studies supporting structure 2b, and report further examples showing the generality of the reaction.



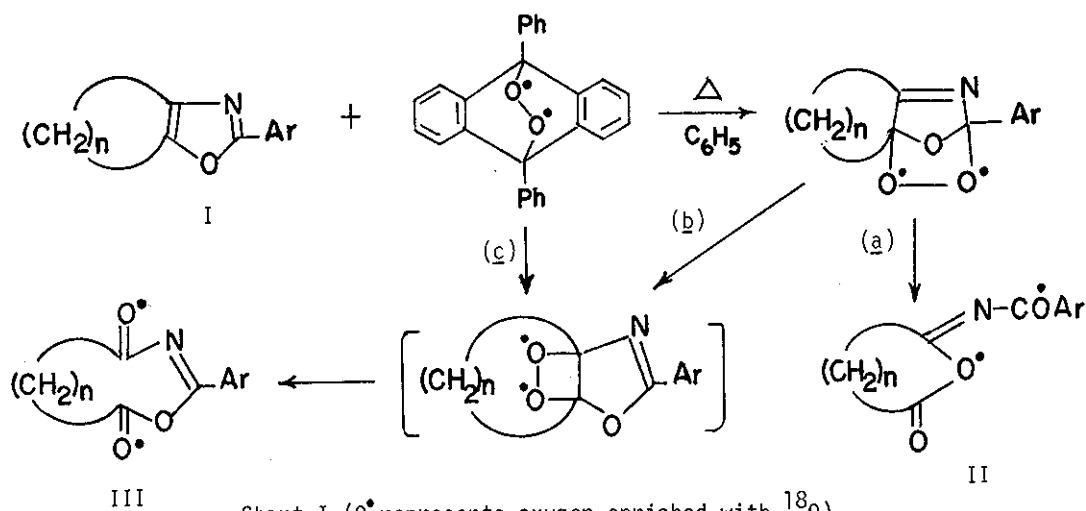
The reaction of a number of 2-aryl-4,5-polymethylene oxazoles (I) with singlet oxygen in methylene chloride yielded products corresponding to II (Table 1).^{4,5} A typical procedure is illustrated by the conversion of Ib to IIB: A solution of 2.88g of Ib in 2ℓ of freshly distilled methylene chloride was irradiated with

a 275 watt sun lamp in the presence of methylene blue for 6 hr while dry air was bubbled through the solution. Removal of solvent *in vacuo* and chromatography on silica gel (ether) yielded I Ib (87%), mp 94-95.5°. The product (I Ib) shows no NH band in the I.R., and has carbonyl peaks at 1745, 1680 and 1660 cm^{-1} . The NMR spectrum shows absorption at τ 2.0-2.5 (m, 5H), 6.8-7.2(m, 4H) and 7.9-8.3 (m, 6H). Refluxing I Ib overnight in water gave a virtually quantitative yield of benzamide and pimelic acid.

Since the above data are in accord with either structure I Ib or IIIb, we employed oxygen-18 labeling techniques to distinguish between the two possibilities.

Table I

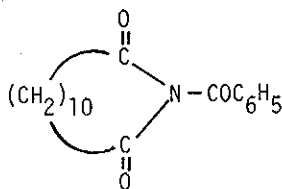
Oxazole (I)	Imino Anhydride (II)
Ia, Ar=C ₆ H ₅ ; n=4	I Ia, m.p. 125-6° (65%)
Ib, Ar=C ₆ H ₅ ; n=5	I Ib, m.p. 94-95.5° (87%)
Ic, Ar=C ₆ H ₅ ; n=6	I Ic, m.p. 100-1° (80%)
Id, Ar=p-CH ₃ C ₆ H ₄ ; n=4	I Id, m.p. 171-2° (60%)
Ie, Ar=p-CH ₃ OC ₆ H ₄ ; n=4	I Ie, m.p. 151-2° (55%)



As pictured in Chart I, incorporation of singlet oxygen into the product could take place by paths a, b or c. Using a singlet oxygen source enriched with oxygen-18, path a would lead to IIb having the labeling pattern shown, while paths b or c would lead to IIIb in which both carbonyl oxygens contain the extra oxygen-18.⁶

Reaction of Ib with the known singlet oxygen donor, diphenylanthracene peroxide, containing 4% $^{18}\text{O}_2$, for 48 hr in refluxing benzene gave the di-oxygen-18 labelled intermediate IIb, upon preparative tlc.⁷ The mass spectrum of unlabelled IIb shows a weak parent peak at 245 amu as well as significant peaks at 105 amu ($\text{C}_6\text{H}_5\text{CO}$, 100%); 140 amu ($\text{C}_7\text{H}_{10}\text{NO}_2$, 8%); and 217 amu ($\text{C}_{13}\text{H}_{15}\text{NO}_2$, 5%). The mass spectrum of labelled IIb indicated that $4.2 \pm 0.3\%$ of molecular oxygen-18 had been incorporated in the parent peak at 245 amu with no detectable mono-oxygen-18 incorporation. In addition, the benzoyl peak at 105 amu showed a p+2 oxygen-18 enrichment of $4.4 \pm 0.2\%$, and the remaining atom of oxygen-18 ($3.8 \pm 0.2\%$) was found in the other portion of the molecule at 140 amu. These results firmly established the structure of IIb and related products (Table I) as N-aryloisoimides.

The isolation of N-aryloisoimides (II) is of special interest in view of the ready rearrangement to triamides observed earlier.¹ It appears that the geometric restrictions imposed on the system by the polymethylene bridge prevents the isoimide from attaining the correct molecular alignment for rearrangement. In accord with this view, it was considered likely that if the 4,5-polymethylene bridge on the oxazole was large enough, the chemical behavior would approach that of the monocyclic 2-aryl-4,5-dialkyloxazoles. Accordingly, the oxazole (I, $n=10$; $\text{Ar}=\text{C}_6\text{H}_5$) was prepared and photooxidized under the usual conditions (vide supra). After chromatography of the product on silica gel, the triamide (IV) was obtained as a viscous oil (70%). The NMR spectrum of IV shows τ 2.0-2.6 (m, 5H), 7.25-7.5 (m, 4H) and 8.0-8.8 (m, 16H). The I.R. spectrum of the triamide is distinctive, showing no -NH absorption, a very broad carbonyl band at 1715 cm^{-1} , and additional amide bands at 1250 and 1200 cm^{-1} .



IV

References

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3. H.H. Wasserman, F.J. Vinick and Y.C. Chang, J. Amer. Chem. Soc., 1972, 94, 7180.
4. Earlier studies have shown that 4,5-condensed oxazoles unsubstituted in the 2-position yield ω-cyano acids as the main products in methylene chloride.
5. Satisfactory elemental analyses were obtained for all new compounds.
6. Dioxetanes have been shown to be intermediates in the reactions of enamines and related systems with singlet oxygen. (a) C.S. Foote, A.A. Dzakpasu and J.W.-P Liu, Tetrahedron Lett., 1975, 1247; (b) H.H. Wasserman and S. Terao, ibid., 1975, 1735.
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