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# Photoinduced Reactions. XXXIV. Photosensitized Oxygenation of 2,4,5-Triphenylthiazole[1]

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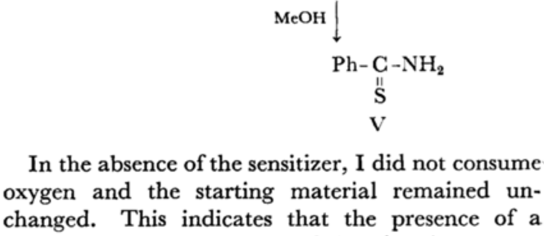
In connection with the photodynamic action of the biological systems, photosensitized oxygenation of a thiazole was investigated. Photooxidation of 2,4,5-triphenylthiazole in methanol in the presence of rose bengal resulted in the formation of benzil and benzamide. On the other hand, photooxidation of 2,4,5-triphenylthiazole in chloroform containing methylene blue as a sensitizer gave *N,N*-dibenzoylthiobenzamide in good yield. Possible mechanisms for these reactions, involving an *endo*-peroxide or a zwitterionic peroxide, are discussed.

Recently much attention has been drawn to the photosensitized oxygenation of five-membered heterocyclic bases in relation to the photodynamic action of the biological systems.[2] Although the photosensitized oxygenation of imidazoles,[3] pyrroles,[4] oxazoles,[5] indoles[6] and purines[7] has been studied extensively, the photooxidation of thiazole, which is an important part of thiamine, has never been investigated. In this paper, the photosensitized oxygenation of 2,4,5-triphenylthiazole is described. The results provide further information regarding the structure of the peroxide intermediate and the manner of its decomposition in the photosensitized oxygenation of five-membered heterocyclic compounds.

When a methanol solution of 2,4,5-triphenylthiazole (I) was subjected to photosensitized oxygenation in the presence of rose bengal, 0.45 mol equivalent of oxygen was consumed and benzil (II) and benzamide (III) were obtained in 11 and 18% yield, respectively.

On the other hand, when photosensitized oxygenation was carried out in chloroform using methylene blue as sensitizer, I afforded a different product. Thus, I gave, after consumption of 0.9 mol equivalent of oxygen, a red-colored compound $C_{21}H_{15}NO_2S$, an oxygen adduct of I, in 30% yield. The IR spectrum showed a broad carbonyl absorption band at 1700 cm$^{-1}$. In its UV spectrum a weak absorption maximum was observed at 500 m$\mu$. Treatment of the adduct with boiling methanol gave thiobenzamide (V) in 50% yield. The adduct gave tribenzamide (VI) in aqueous silver nitrate solution in 10% yield. These reactions and spectral data are known to be generally found in the case of *N*-acylthiobenzamides.[8] The above results led us to assign structure IV to the adduct.



In the absence of the sensitizer, I did not consume oxygen and the starting material remained unchanged. This indicates that the presence of a sensitizer is a necessary condition for the present photooxygenation.

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[1] Part XXXIII. T. Matsuura and K. Ogura, This Bulletin, **42**, 2971 (1969).

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[3] H. H. Wasserman, K. Stiller and M. B. Floyd, *Tetrahedron Letters*, **1968**, 3277; M. Tomita, M. Irie and T. Ukita, *ibid.*, **1968**, 4933; T. Matsuura and M. Ikari, *Kogyo Kagaku Zassi* (*J. Chem. Soc. Japan, Ind. Chem. Sect.*), **72**, 179 (1969) and references cited therein.

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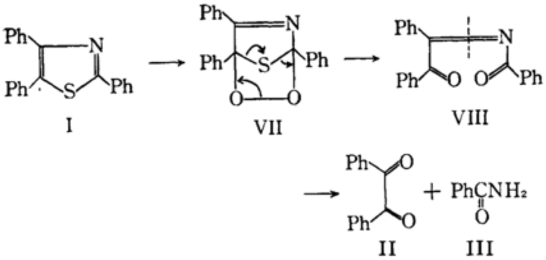
[5] H. H. Wasserman and M. B. Floyd, *Tetrahedron*, Suppl. No. 7, 441 (1966).

[6] Z. Yoshida and M. Kato, *J. Am. Chem. Soc.*, **76**, 311 (1954); *Nippon Kagaku Zassi* (*J. Chem. Soc. Japan, Pure Chem. Sect.*), **75**, 112 (1954).

[7] T. Matsuura and I. Saito, *Tetrahedron Letters*, **1968**, 3273; *Tetrahedron*, **24**, 6609 (1968); **25**, 541, 549, 557 (1969) and references cited therein.

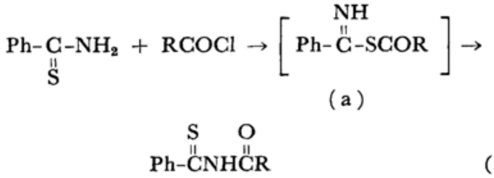
[8] J. Goerdeler and H. Horstmann, *Chem. Ber.*, **93**, 663 (1960).

The formation of benzil (II) and benzamide (III) in the photosensitized oxygenation of I in methanol is well rationalized by a pathway involving a cyclic peroxide VII (Scheme 1). Such a cyclic peroxide is commonly recognized as an intermediate in the photosensitized oxygenation of five-membered heterocycles, *i. e.*, imidazoles,³⁾ pyrroles,⁴⁾ oxazoles,⁵⁾ isoindoles⁹⁾ and isobenzothiophenes.¹⁰⁾ The initially formed peroxide VII could undergo rearrangement to form a Schiff base VIII, which is hydrolysed to give II and III. The loss of a sulfur atom from VII has analogy in the photosensitized oxygenation of 1,3-diphenylisobenzothiophene leading to the *o*-dibenzoylbenzene.¹⁰⁾



Scheme 1

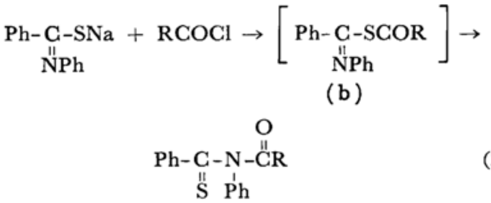
In inert solvents such as chloroform, the photosensitized oxygenation of I takes a different course. Such a solvent effect on photooxidation has also been observed in the cases of purines⁷⁾ and oxazoles.¹¹⁾ Two mechanisms seem to account for the formation of IV from I. In this case a zwitterionic peroxide IXa or IXb³,⁷,¹²⁾ is proposed for the first step intermediate. As shown in Scheme 2, IX could be rearranged to a four-membered cyclic peroxide X (path a), which undergoes ring cleavage to give *N*-benzoyl-*S*-benzoylisothiobenzamide (XI). Such a photooxidative cleavage of C=C double bond is analogous to the photooxidation of 1,2,3,4-tetraphenylpyrrole leading to α-*N*-benzoylamino-α′-benzoylstilbene.¹³⁾ The isothiobenzamide (XI) would then undergo further intramolecular rearrangement to give IV. Such a type of rearrangement has been proposed in the reaction of acyl chloride with thiobenzamide (Eq. (1))⁸⁾ and *N*-phenylthiobenzamide (Eq. (2)).¹⁴⁾ *S*-Benzoylisothiobenzamide (a) in the former and *N*-phenyl-*S*-benzoylisothiobenzamide (b) in the latter case are considered to be an intermediate.



$$\text{Ph-}\underset{\underset{S}{\|}}{C}\text{-NH}_2 + \text{RCOCl} \rightarrow \left[\ \text{Ph-}\overset{\overset{NH}{\|}}{C}\text{-SCOR}\ \right] \rightarrow$$

(a)

$$\text{Ph-}\overset{\overset{S}{\|}}{C}\text{NH}\overset{\overset{O}{\|}}{C}\text{R} \qquad (1)$$



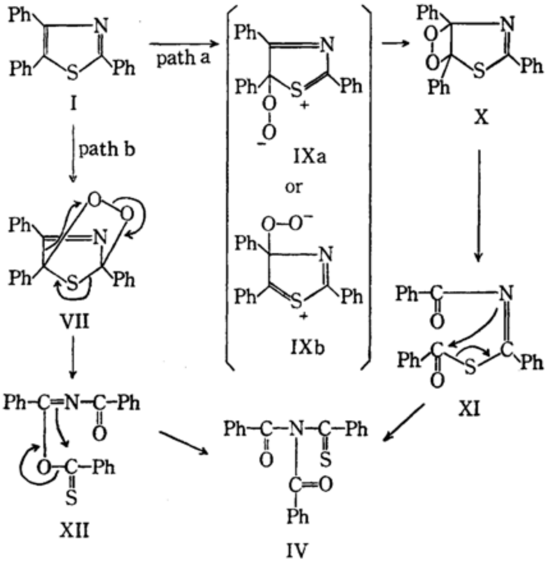
$$\text{Ph-}\underset{\underset{NPh}{\|}}{C}\text{-SNa} + \text{RCOCl} \rightarrow \left[\ \text{Ph-}\underset{\underset{NPh}{\|}}{C}\text{-SCOR}\ \right] \rightarrow$$

(b)

$$\text{Ph-}\underset{\underset{S}{\|}}{C}\text{-}\underset{\underset{Ph}{|}}{N}\text{-}\overset{\overset{O}{\|}}{C}\text{R} \qquad (2)$$

An alternative pathway (path b) involving a cyclic peroxide VII, which is analogous to the photosensitized oxygenation of oxazole,⁵⁾ may also account for the formation of IV. The peroxide VII could be rearranged to give XII, which undergoes an intramolecular rearrangement, analogous to *N*-benzoylisoimide, to give IV.⁵⁾ The formation of the *endo*-peroxide VII may occur either directly from I or stepwise *via* the zwitterionic peroxide IXa.

Although the above two modes of the formation of IV cannot be distinguished from the available results, path a seems to be more favorable considering the reaction of Eq. (2).



Scheme 2

## Experimental

**Photosensitized Oxygenation of 2,4,5-Triphenylthiazole (I). A. In Methanol.** A solution of 2,4,5-

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12) C. S. Foote and J. W. P. Lin, *Tetrahedron Letters*, **1968**, 3267.

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triphenylthiazole[15] (I) (2.8 g. 9 mmol) in methanol (300 m*l*) containing rose bengal (50 mg) was irradiated at room temperature by a 100 W high-pressure mercury lamp through a Pyrex cooling jacket. During irradiation oxygen was bubbled by means of a circulating pump through a sintered-glass joint which was attached to the bottom of the reaction vessel. Oxygen consumption was manometrically followed. Oxygen absorption ceased after oxygen (105 m*l*, 4.2 mmol) had been taken up for 24 hr. After removal of the solvent *in vacuo*, the residue was chromatographed on a neutral alumina column (50 g). Elution with chloroform (400 m*l*) gave unchanged starting material (I) (0.95 g, 34% recovery). Further elution with chloroform (*ca.* 600 m*l*) gave benzil (II) (135 mg, 11% based on the reacted starting material). Recrystallization from ethanol gave yellow prisms, mp 93—94°C, which were identical with an authentic sample by comparison of their IR spectra. Chloroform (1000 m*l*) eluted benzamide (III) (95 mg, 18% based on reacted I). Recrystallization from ethanol gave crystals, mp 128°C.

**B. In Chloroform.** A solution of 2,4,5-triphenylthiazole (I) (2.4 g, 7.7 mmol) in dry chloroform (200 m*l*) containing methylene blue (50 mg) was irradiated by a 100 W high-pressure mercury lamp for 10 hr as described above, until oxygen (170 m*l*, 6.8 mmol) was consumed. The solvent was removed *in vacuo*, and the residue was dissolved in ether (100 m*l*). The ethereal solution was treated with Norit. After removal of the solvent, the residue was crystallized from ether to give *N*,*N*-dibenzoylthiobenzamide (IV) (0.78 g, 30%). Recrystallization from ether (5 m*l*) gave red-colored crystals, mp 102—103°C. $\lambda_{max}^{cyclohexane}$ 224 m$\mu$ ($\varepsilon$ 29000), 233 (25000), and 500 (150); $\nu_{max}^{Nujol}$ 1700, 1600, and 1300—1200 cm$^{-1}$.

Found: C, 73.43; H, 4.47; N, 4.08; S, 9.24%. Calcd for $C_{21}H_{15}NO_2S$: C, 73.04; H, 4.63; N, 4.06; S, 9.28%.

**Reactions of *N*,*N*-Dibenzoylthiobenzamide (IV). A. With Methanol.** A solution of IV (100 mg) in methanol (40 m*l*) was boiled for 10 min. A thin layer chromatographic analysis (silica gel, chloroform-ethanol (20 : 1)) of the mixture showed that it consisted of at least five compounds among which thiobenzamide (V), (20 mg, 50%) was isolated by preparative thin layer chromatography.

**B. With Silver Nitrate.** To a suspension of IV (100 mg) in the mixture of methanol (10 m*l*) and water (10 m*l*) silver nitrate (400 mg) was added, according to the procedure of Goerdeler and Horstmen.[8] The solution was acidified, diluted with water (50 m*l*), and then extracted with ether (100 m*l*). After removal of ether, ethanol was added to the residue. The ethanol-insoluble solid was collected by filtration and was crystallized from boiling ethanol (*ca.* 80 m*l*) to give tribenzamide (VI) (10 mg, 10%), mp 198—200°C (lit,[16] mp 201—202°C), which was identical with the authentic sample prepared according to the method of Curtius[16] (by IR).

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