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# ON THE MECHANISM OF PHOTOLYSIS OF 4-PHENYL-1,3,2-OXATHIAZOLYLIO-5-OXIDE IN ETHANOL

## EVIDENCE FOR KETENE INTERMEDIATES

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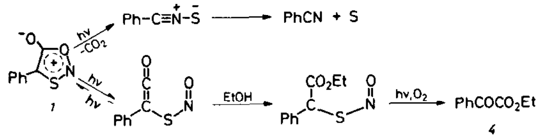
**Abstract**—Photolysis of 4-phenyl-1,3,2-oxathiazolylio-5-oxide (**1**) in ethanol in the presence of oxygen leads to benzonitrile (21%) and ethyl phenylglyoxylate (65%). Photolysis under an atmosphere of $^{15}$NO results in isotope exchange which is considered strong evidence for phenyl(nitrosothio)ketene (**2**) being in photolytic equilibrium with the starting material. In ethanolic solution saturated with nitric oxide the photolytic equilibrium is shifted towards the starting material resulting in formation of benzonitrile in 100% yield. Benzonitrile is formed by a competitive reaction route via benzonitrile sulfide.[1] Compound **2** does not undergo ethanolysis to ethyl(nitrosothio)phenylacetate (**3**). Ethyl phenylglyoxylate is probably formed via thiyl radical **6** resulting from homolytic scission of the S–NO bond in ketene **2**. Singlet molecular oxygen is present during photolysis of **1** but seems to be unimportant to the course of reaction.

Two reaction routes, one involving a fragmentation and the other a ring-opening, may account for the major part of the products formed in the photolysis of mesoionic 4-phenyl-1,3,2-oxathiazolylio-5-oxide (**1**).[1] The relative dominance of the two processes is biased at least by the nature of the solvent. In diethylether/methylene chloride, benzonitrile is the dominant product (77%) together with carbon dioxide and elemental sulfur.[2] Strong evidence has been presented that benzonitrile sulfide is a precursor to benzonitrile.[1-3] Photolysis of **1** in the protic solvent ethanol saturated with oxygen (1 atm) leads to benzonitrile (21%), ethyl benzoate (3%) and ethyl phenylglyoxylate (**4**) (65%). We have tentatively suggested the formation of the latter to involve ring-opening and ethanolysis as shown in Scheme 1.[1]



Scheme 1.

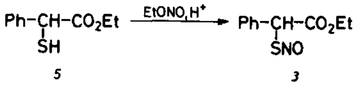
It has been shown in the meantime that the suggested ring-opening (**2**) can be observed spectroscopically in a $N_2$-matrix at 10 K.[4] In the present paper evidence will be given for the ring-opening in ethanolic solution at room temperature.

The question of whether phenyl (nitrosothio)ketene (**2**) undergoes ethanolysis with formation of **4** via **3** or undergoes alternative reactions leading to **4** is another problem investigated. In general the reaction between ketenes and alcohols is slow from a preparative point of view.[5] A few kinetic investigations have been undertaken but the rate expressions are complicated due to hydrogen bonding between alcohol molecules.[6] Furthermore, the rate of solvolysis has been found to vary strongly with the substituents.[7] Thus aldoketenes react far more reluctantly than ketoketenes.[8] It is not possible on this basis to predict an approximate lifetime of **2** with respect to solvolysis in ethanol but the reaction times reported in the literature cited do not exclude that **2** might be able to undergo alternative reactions.

As a first problem, the photolytic properties of authentic **3** will be treated. Secondly a direct oxidation of **1** will be considered and finally its photolysis under a nitric oxide and $^{15}$N-nitric oxide atmosphere will be described.

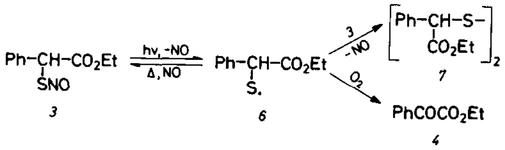
### RESULTS AND DISCUSSION

*Photolysis of ethyl (nitrosothio)phenylacetate* (**3**). Compound **3** was prepared by the acid catalyzed action of ethyl nitrite on ethyl mercaptophenylacetate [eqn (1)].



$$\underset{\substack{\text{SH}\\ 5}}{\text{Ph–CH–CO}_2\text{Et}} \xrightarrow{\text{EtONO,H}^+} \underset{\substack{\text{SNO}\\ 3}}{\text{Ph–CH–CO}_2\text{Et}} \qquad (1)$$

Photolysis ($\lambda > 390$ nm) of an ethanolic solution of **3** under an oxygen atmosphere led to ethyl phenylglyoxylate (**3**) in 2% yield. Along with this, only dithiodi(2-(ethyl phenylacetate)) (**7**) was formed (Scheme 2).



Scheme 2.

Scheme 2 shows the assumed reaction pathway for the photolysis of **3**. The initial step is cleavage of the S–NO bond with formation of a thiyl radical **6**. This has three potential partners for further reactions. First, the starting material itself may serve as scavenger forming the observed disulfide **7**. This rationalisation is in agreement with Barret *et al.*,[9] who reported upon the spectra and photochemistry of alkyl and benzyl *S*-nitrosothiols. They found the corresponding disulfides to be the only products, but gave no information about the influence of oxygen. In the case of **3** oxygen may be the second possible reaction partner and responsible for the formation of small amounts of ethyl phenylglyoxylate (**4**). Third, nitric oxide is known to be a thiyl scavenger.[10] Thus the photolytic step is *a priori* thermally reversible.

Two simple types of experiments support this model. Fig. 1 shows the rate of conversion in two evenly irradiated samples of **3** in ethanol under argon and oxygen, respectively. The identical shapes of these curves illustrate that scavenging of thiyl radicals is fairly insensitive to the presence of oxygen. The deviation of the curves from a zero-order reaction (constant light input and total absorption) agrees well with the assumed reversibility of the primary photochemical step. With decreasing concentration of **3** the rate of disulfide formation is reduced and nitric oxide competes more efficiently for **6** resulting in a slower rate of conversion.

In the other type of experiment it was found that the relative yields of **4** and **7** show dependence upon the concentration of **3** which is to be expected if the formulations in Scheme 2 are correct. In order to reproduce the concentration which **3** could be expected to achieve if formed photolytically from **1** at constant rate, **3** was "bled" slowly through a capillary into irradiated ethanol. This approach led to an enhanced yield of ethyl phenylglyoxylate at the expense of disulfide but the yield never exceeded 7% in a number of experiments.

Authentic **3** was also photolyzed together with equimolar amounts of **1** in the presence of oxygen. The yield of ethyl phenylglyoxylate (**4**) (57% based on **1**) was less than when **1** was photolyzed alone (65%). However, the yield of benzonitrile rose to 39%. This increase is most probably due to the nitric oxide formed photolytically from **3** (see below). When **3** was "bled" slowly through a capillary into the reaction chamber during photolysis of **1** the yields of benzonitrile (21%) and ethyl phenylglyoxylate (65%) were unchanged compared to the photolysis of **1** without additives. Apparently, the steady-state concentration achieved by nitric oxide during the latter reactions is too small to interfere.

Photolysis of **3** with or without oxygen thus always leads to disulfide as the main product. By contrast disulfide formation has not been observed in the photochemical reactions of **1** in a number of experiments under varying conditions. These results clearly rule out **3** as an intermediate in the photochemical conversion of **1** into **4**.

*Experiments with singlet molecular oxygen* ($O_2(^1\Delta_g)$). Photolysis ($\lambda > 390$ nm)† of **1** under an argon atmosphere produces benzonitrile (49%) together with *ca.* 20 unidentified compounds. Formation of ethyl phenylglyoxylate (**4**) and ethyl benzoate is dependent on the presence of oxygen. A direct oxidation of the mesoion with $O_2(^1\Delta_g)$ is possible. **1** was photolyzed ($\lambda > 390$ nm) together with 2,3-dimethyl-2-butene (30% v/v in ethanol) and the photolysis products examined (GLC) according to the procedure of Foote.[11] 2,3-Dimethyl-3-butene-2-ol which was formed in *ca* 40% yield (based on **1**) is commonly believed to indicate the presence of $O_2(^1\Delta_g)$.[11,12]‡ This result required a separate investigation of the reaction between $O_2(^1\Delta_g)$ and **1**. Thus **1** was photolyzed ($\lambda > 560$ nm) together with methylene blue and oxygen under conditions where only methylene blue receives light.§ GLC analysis revealed 8% ethyl phenylglyoxylate together with several unidentified products but no benzonitrile. The absence of the latter implies that **1** had been properly screened by the filter, but the low yield of **4** excludes direct reaction between **1** and $O_2(^1\Delta_g)$ as a major pathway in the photolytic conversion of **1** to **4**. Compound **3** was reacted with $O_2(^1\Delta_g)$ in the same manner. GLC analysis revealed from 0 to 1% ethyl phenylglyoxylate.

*Photolysis under an atmosphere of nitric oxide.* As a consequence of the experiments described so far, we investigated alternative reaction modes of **2**. Excitation

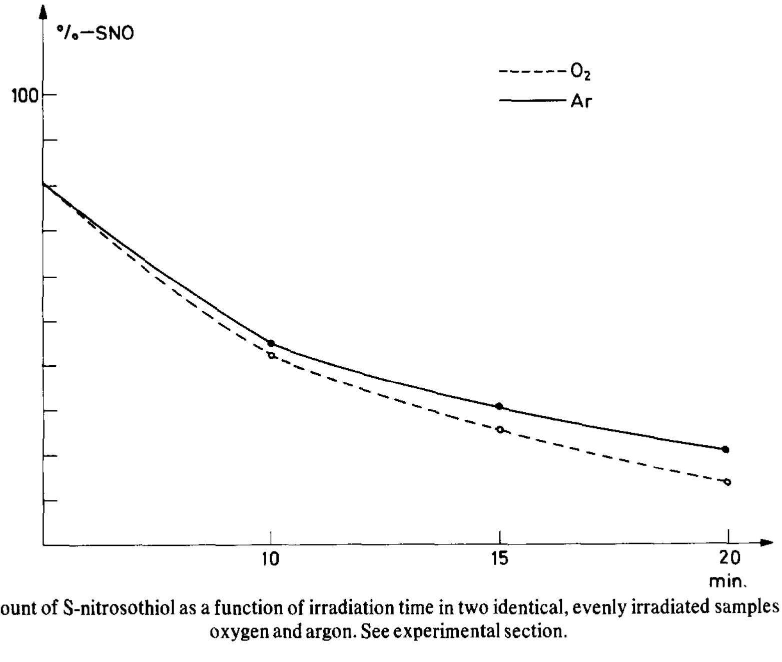


Fig. 1. Amount of S-nitrosothiol as a function of irradiation time in two identical, evenly irradiated samples of **3** under oxygen and argon. See experimental section.

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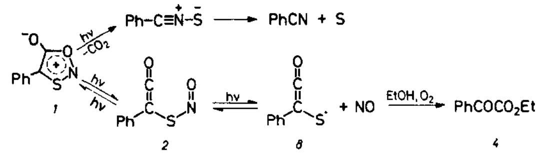
†See Ref. 2 for the electronic spectrum of 1.

‡It must be pointed out, however, that the same product may be formed when 2,3-dimethyl-2-butene is exposed to oxygen together with a radical capable of abstracting a hydrogen atom from the alkene.[13]

§Independent experiments with methylene blue, oxygen and 2,3-dimethyl-2-butene showed that easily detectable amounts of $O_2(^1\Delta_g)$ was produced under the experimental conditions.

(directly or by energy transfer) is expected to cause scission of the sulfur nitrogen bond[9] of **2** leading to the resonance stabilized thiyl radical **8** (Scheme 3).



Scheme 3.

This homolytic reaction is strongly supported by photolysis experiments in ethanolic solutions saturated with nitric oxide ($10^{-2}$ M[14]). A 6–7 times slower rate of conversion relative to an analogous photolysis under argon was observed. Furthermore GLC analysis showed 100% conversion of the starting material to benzonitrile which is to be compared with 49% under argon. Apparently the high concentration of nitric oxide efficiently reverses the second photolytic step (from **8** to **2**); the only drain being the irreversible formation of benzonitrile.

By means of isotopically labelled nitric oxide it has been shown that the selective quenching effect of nitric oxide is at least not entirely physical.[15] Compound **1** was photolyzed in ethanol under an atmosphere of $^{15}NO$ (95% isotopically labelled). Starting material was recovered after 15% conversion and it was found from the mass spectrum (Fig. 2) that 17% incorporation of $^{15}N$ in **1** had taken place. In another run 24% incorporation was found after 17% conversion. No exchange was observed when **1** was stored under $^{15}NO$ in the dark.

These findings are considered strongly supportive for the existence of the two ketenes, **2** and **8**, and the ring-closure from **2** to **1** (Scheme 3) since direct exchange of NO with excited **1** seems highly improbable.

Clearly, the experiments with $^{15}NO$ does not prove that **8** is a precursor of ethyl phenylglyoxylate (**4**) but it seems likely that it may be trapped either by the solvent or oxygen and converted to ethyl phenylglyoxylate (**4**) as depicted in Scheme 3.

## EXPERIMENTAL

The photolytic reactions were carried out using light from a medium pressure Hg-lamp (Hanau Q-700). For $\lambda > 390$ nm a filter was used consisting of 1 cm solutions acetone saturated with anthracene. Samples were cooled by means of tap water during photolysis. GLC analysis were carried out on a Pye Unicam 104 chromatograph, dual FID, connected to a Varian aerograph 477 electronic integrator, on a 2 m, 1/4 in. column with 10% SE-30 or 10% polypropylenglycol on gaschrom Q 100/120 mesh (Applied Science Lab. Inc.) with nitrogen as carrier gas. Benzyl cyanide was used as internal standard for quantitative measurements. Analysis and calibration mixtures were run at the same column temperature in the range from 90° to 150°.

*Determination of* –SNO. The amount of S-nitrosothiol in the various samples was determined by the method of Saville.[16] This is based on the formation of an equivalent amount of nitrous acid on mercuric ion assisted hydrolysis. Nitrous acid reacts with sulfanilamide and N-1-naphthylethylenediamine to form an azo dye. The amount of azo dye formed is determined by absorption spectroscopy. Ammonium sulfamate can be added to the samples to remove excess nitrous acid without interference with the determination of S-nitrosothiol. The difference between determination with and without prior addition of ammonium sulfamate reflects the amount of nitrous gases present (by reaction of nitric oxide and nitrogen dioxide with oxygen and water to yield nitrous acid). Standard solutions of cysteine were run in parallel with every determination according to procedure.[16]

*Ethyl* (*nitrosothio*)*phenylacetate* (**3**). Ethyl mercaptophenylacetate (0.1–0.5 g) was dissolved in diethylether or dimethylether/methylene chloride 1:5 (5 ml) and the equivalent amount of ethylnitrite added to the cold solution (0°). On addition of a catalytic amount of sulfuric acid the soln attained a deep red color. After 10 min. it was washed with ice-water (2 × 2 ml) and dried over $MgSO_4$ at 0°. During all these operations the soln was

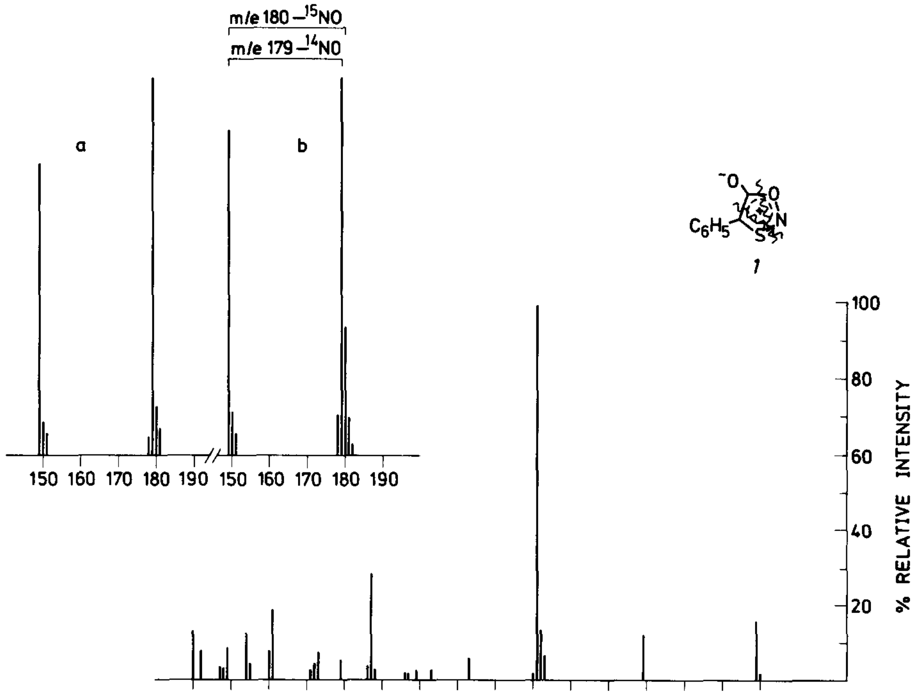


Fig. 2. Mass spectrum of 4-phenyl-1,3,2-oxathiazolylio-5-oxide (**1**), and enlarged (× 10) section of mass spectra before (a) and after photolysis (b) under $^{15}NO$.

protected against light. The purity of the S-nitrosothiol from this preparation was determined according to Saville (see above) to be 81%. The remaining 19% is believed to be unreacted thiol and disulfide **8** since these are the only products found after photolysis besides **4** (see below). For different purposes the soln was diluted with methylene chloride, diethyl ether or EtOH. When EtOH was used as the sole solvent washing with water was omitted. On evaporation of the solvent *in vacuo* **3** was obtained as a dark red oil. After a few min at room temp red fumes of nitrogen dioxide was formed. Due to this instability elemental analysis was not carried out. In dilute solns **3** appears to be considerably more stable. Thus a $2\times10^{-2}$ M soln of **3** in EtOH flushed with $O_2$ was not decolorized after 16 hr in the dark. However, on exposure to sunlight the same soln was decolorized in a few min.

*Photolysis of* **3**. (a) The concentration of **3** in EtOH (initially $2.28\times10^{-3}$ M) in two evenly irradiated ($\lambda > 390$ nm) samples under argon and oxygen, respectively, was monitored during photolysis according to the method of Saville (see above). The results are displayed in Fig. 1. (b) Compound **3** (prepared from 0.991 g ethyl mercaptophenylacetate) dissolved in a mixture of ether (40 ml) and ethanol (250 ml) was irradiated ($\lambda > 390$ nm) until the red color of the solution had disappeared (2.5 hr).

GLC analysis revealed **4** in 2% yield based on the amount ethyl (nitrosothio)phenylacetate determined according to Saville (see above). The remaining material was worked up by means of preparative TLC after removal of solvent *in vacuo* (silica gel, benzene/petroleumether 1:1). Compound **8** was identified by comparison with an authentic sample (IR) and isolated in 78% yield (based on ethyl (nitrosothio)phenylacetate). Unreacted ethyl mercaptophenylacetate (0.076 g) was isolated too. No other products was observed by GLC or TLC. (c) A soln of **3** (prepared from 21.15 mg ethyl mercaptophenylacetate) in ethanol (5 ml) was "bled" through a capillary during 5 hr into the photolysis chamber ($\lambda > 390$ nm) containing ethanol (100 ml) constantly flushed with oxygen. According to GLC analysis carried out on the solution after concentration *in vacuo* ethyl phenylglyoxylate was formed in 7% yield.

*Photolysis of* **1** *under argon and oxygen atmospheres*. Two identical solutions of **1** (13.96 mg) in EtOH (4 ml) (a) and (b) were placed in two ampoules flushed for 10 min with argon and oxygen, respectively. After sealing, the samples were irradiated ($\lambda >$ 390 nm). Solution (a) was colorless after 140 min and solution (b) after 100 min. According to the gas chromatograms benzonitrile (49%) had been formed in solution (a) while benzonitrile (21%), ethyl phenylglyoxylate (65%) and ethyl benzoate (3%) had been formed in solution (b).

*Photolysis of* **1** *under a nitric oxide atmosphere*. Argon was bubbled through a soln of **1** (20.26 mg) in EtOH (5 ml) contained in an ampoule (10 ml) for 15 min. Nitric oxide was then bubbled through the soln for 15 min and the sealed ampoule irradiated ($\lambda > 390$ nm) until the yellow color of **1** had disappeared (12 hr). GLC analysis showed that benzonitrile was formed in 100% yield.

*Photolysis of* **1** *under a* $^{15}$*N-nitric oxide atmosphere*. **1** (18.2 mg), recrystallized from acetonitrile, was dissolved in abs EtOH (4 ml) and placed in an ampoule (10 ml). After removal of $O_2$ by repeated freeze-pump-thaw cycles (liq. nitrogen) $^{15}$NO was introduced (*ca* 30 mmol prepared[16] from $Na^{15}NO_2$ 95.0% isotopically labelled, Isomet Corporation). The ampoule was sealed and irradiated ($\lambda > 390$ nm) for 35 min. The ampoule was opened, the solvent removed *in vacuo* and the resulting material washed with small amounts of hexane to yield 15.4 mg of **1** corresponding to 85% recovery. Both this material and authentic **1** was submitted to mass spectroscopy on a AEI MS 902 instrument with an inlet temp. at 50°. The mass spectrum of authentic **1** is displayed in Fig. 2. The most characteristic fragmentation is loss of NO from the molecular ion. The spectrum of the sample achieved from photolysis under $^{15}$NO (Fig. 2(b)) showed that $^{15}$N had been incorporated to the extent of 17% calc. from the spectra in Fig. 2(a) and (b). In another experiment 83% of **1** was recovered and 24% $^{15}$N had been incorporated. The peak at *m/e* 180 in Fig. 2(b) was found by peak matching to be a doublet consisting of ions with mass weights 180.0074 and 180.0011. Calc. for $M^+$ (179) + 1, 180.0065 and for $C_8H_5{}^{15}NO_2S$, 180.0012. No $^{15}$N exchange had taken place when **1** was stored under $^{15}$NO in the dark for 18 hr.

*Photolysis of mixtures of* **1** *and* **3**. (a) A mixture of **3** (prepared from 20.08 mg ethyl mercaptophenylacetate) and **1** (20.32 mg) in absolute ethanol (5 ml) was irradiated ($\lambda > 390$ nm) until the color had disappeared (*ca* 4 hr). According to the gas chromatogram ethyl phenylglyoxylate (**4**) and benzonitrile had been formed in 57% and 39%, respectively, based on **1**. (b) A soln of **3** was "bled" slowly through a capillary into the photolysis chamber containing equimolar amounts of **1** in EtOH. The yields of benzonitrile and ethyl phenylglyoxylate (**4**) were 21% and 65%, respectively.

*Formation of* $O_2(^1\Delta_g)$ *during photolysis of* **1**. Heterocycle **1** (23.57 mg) dissolved in a mixture of abs EtOH (5 ml) and 2,3-dimethyl-2-butene (2 ml) was irradiated ($\lambda > 390$ nm) while $O_2$ was bubbled through the soln. The yellow color of the soln disappeared after 8.5 hr and trimethylphosphite (2.6 ml) was added. On comparison with an authentic sample, GLC revealed that approximately 40% 2,3-dimethyl-3-butene-2-ol (based on **1**) had been formed. This indicates the presence of $O_2(^1\Delta_g)$ during photolysis.[11]

*Reaction of* **1** *with* $O_2(^1\Delta_g)$. **1** (19.7 mg) and methylene blue (3.2 mg, sensitizer for photolytic formation of $O_2(^1\Delta_g)$[11]) in abs EtOH (10 ml) was photolysed for 20 hr through a filter transmitting $\lambda > 560$ nm (1 cm acetone saturated with eosin) while a slow stream of oxygen was bubbled through the soln. All starting material was converted according to TLC. GLC analysis showed that ethyl phenylglyoxylate (**4**) had been formed in 8% yield.

*Reaction of* **3** *with* $O_2(^1\Delta_g)$. A soln of **3** (from 18.28 mg ethyl mercaptophenylacetate) and methylene blue (50 mg) in EtOH (150 ml) was photolysed as above ($\lambda > 560$ nm). After 4 hr TLC showed that **3** had disappeared and that **7** was the main product. The yield of ethyl phenylglyoxylate never exceeded 1% in a series of experiments (GLC).

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