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Received March 20, 1980

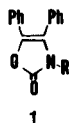
Dedicated to Professor John C. Sheehan on the occasion of his sixty-fifth birthday.

The photochemical cleavage of 4,5-diaryl-4-oxazolin-2-one protecting groups is discussed as an alternative to reduction or chemical oxidation of the heterocyclic system. Ultraviolet irradiation in air of oxazolinone (**1**) in methanol leads to photooxygenation of the protecting group, affording the corresponding benzamide and benzoate ester. Reduction of the intermediate photoproduct leads to complete removal of the protecting group. A mechanism for this photolysis is proposed and evidence in support of this mechanism is reported.

J. Heterocyclic Chem., **17**, 1807 (1980).

Sir:

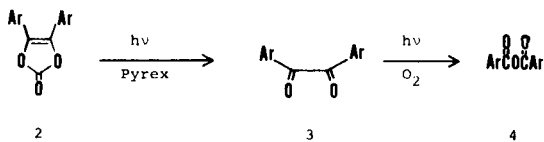
The 4,5-diphenyl-4-oxazolin-2-one (Ox) amine protecting group (1,2) **1** has properties which should make it extremely attractive in the synthesis of natural products. The Ox group replaces both hydrogens of a primary amine, preventing side reactions which may occur at the acidic hydrogens of amide or urethane protecting groups. The group is very stable toward solvolysis in both acid and alkali, conditions which severely limit the use of Schiff



base- or phthaloyl-derived protecting groups in similar applications (3). In addition, Ox derivatives tend to be highly crystalline, highly fluorescent solids, yet are easily soluble in organic solvents.

One significant difficulty associated with the Ox group involves removal of the protecting group. While hydrogenolysis, dissolving metal reduction, or peracid cleavage all are satisfactory in simple applications, in complex syntheses, a number of functional groups may interfere with these methods of removal. We wish to report photochemical transformations of the Ox group which may greatly increase its usefulness in complex syntheses.

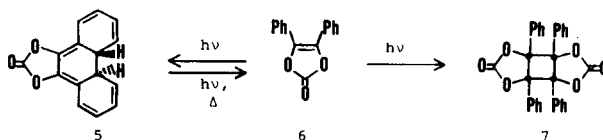
The *cis*-stilbene moiety present in the diaryloxazolinone ring system is known to impart a rich photochemistry to other heterocyclic systems. Irradiations of cyclic carbonates **2a** and **2b** are reported to lead to photodecarbonylation affording the corresponding diketones **3a** and **3b**. In oxygen **3a** and **3b** are further photooxidized to the anhydrides **4a** and **4b** (4). In contrast to this



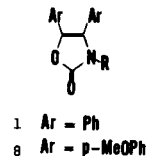
a. Ar = *p*-MePh

b. Ar = *p*-MeOPh

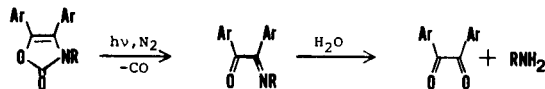
behavior, upon irradiation the parent cyclic carbonate **6** behaves like a stilbene derivative and reversibly cyclizes to **5** or dimerizes to **7** depending on concentration. It is believed that all of these cyclic carbonate transformations occur *via* excited singlet states (4).



These observations led us to investigate the photochemistry of the Ox group **1** and its dimethoxy-derivative



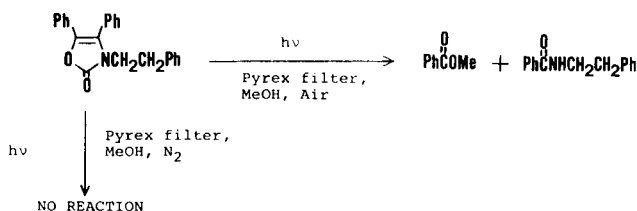
8. If one or both of these derivatives would behave upon irradiation as the cyclic carbonates **2**, photodecarbonylation could lead to a mild method of deprotection.



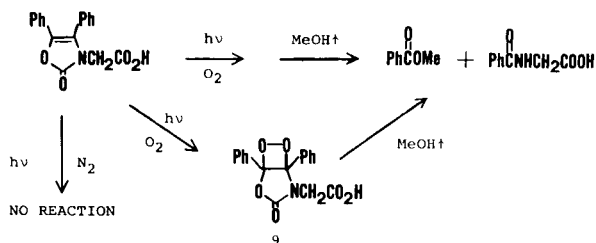
We quickly observed that lengthy ultraviolet irradiation of oxazolinone derivatives of amino acids on silica thin layer chromatography plates led to formation of ninhydrin active materials corresponding to the parent amino acids.

When the Ox derivative of 2-phenylethylamine was irradiated at room temperature in methanol (Pyrex filter) without protection from atmospheric oxygen, methyl benzoate and *N*-benzoyl-2-phenylethylamine could be isolated in 80% and 94% yield. While such a result would be consistent with the occurrence of the desired photoreaction, it was surprising then that no photoreaction occurred when the photolysis was attempted under a nitrogen atmosphere. No photoproducts could be detected even upon

lengthy irradiations. Such an observation would not be consistent with an initial photodecarbonylation initiating the cleavage.

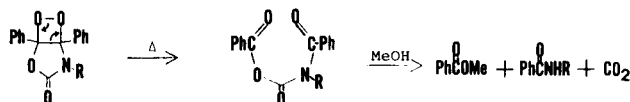


Interestingly, a similar irradiation of the oxazolinone derivative of glycine without protection from oxygen afforded an intermediate photoproduct, stable at room temperature, which fragmented in refluxing methanol affording methyl benzoate and hippuric acid (60% yield, not optimized). Again, no reaction was observed when the irradiation was done under a nitrogen atmosphere.

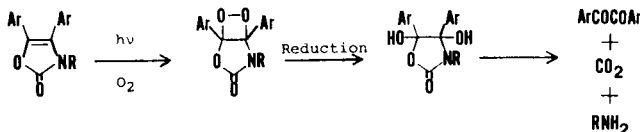


These observations are consistent with an initial photooxygenation of the oxazolinone, ultimately leading to cleavage of the ring system. Two possible mechanisms for this photooxygenation are apparent: free radical oxygenation or singlet oxygen addition. Irradiation in the presence of a free radical scavenger (0.1M 2,6-di-*t*-butylphenol) showed no significant decrease in the rate of cleavage of the oxazolinone, strongly suggesting that a free radical mechanism is not operative (5).

While singlet oxygen oxygenations of electron rich double bonds are well documented (6), the rapid photooxygenation of the heterocyclic system without a suitable sensitizer is without precedent. Treatment of the oxazolinone at 10° in methanol with hydrogen peroxide-sodium hypochlorite, a source of chemically generated singlet oxygen (7), rapidly and quantitatively cleaved the heterocycle, affording essentially the same products as the photoreaction. This strongly implicates singlet oxygen in the photoreaction, and requires that the highly fluorescent diaryloxazolinone itself acts as a photosensitizer for generation of singlet oxygen. The observed photooxygenation intermediate would be a 1,2-dioxetane **9**. It is well known that 1,2-dioxetanes thermally fragment to carbonyl compounds (6). In the case of the oxazolinone, such a fragmentation would lead, upon solvolysis of the unstable intermediate dibenzoylcarbamate, to the observed products.



Although the described photooxygenation does convert the oxazolinone protecting group into the corresponding benzamide, a useful transformation in its own right, it would be advantageous to completely remove the oxazolinone group under photolytic conditions. The possibility for such a conversion was suggested by the isolation of the intermediate 1,2-dioxetane in the Ox-glycine irradiation. Reduction of the dioxetane would lead, upon solvolysis, to diketone, carbon dioxide, and the corresponding amine. Irradiation of Ox-alanine at -30° in air, followed by zinc-acetic acid reduction afforded the zinc salt of the amino acid in nearly quantitative yield.



Preliminary photolyses of the corresponding dianisyl-oxazolinones **8** indicate that these compounds undergo similar photoreactions, although at faster rates than the diphenyl derivatives. A detailed investigation into the scope and limitations of these methods of photochemical deprotection in peptide and natural product synthesis is currently underway.

Acknowledgement

The authors gratefully acknowledge financial support from a Schering-Plough Foundation, Inc. Grant of Research Corporation. We also wish to thank Mr. David Palmer for assistance in the initial stages of this project.

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