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Photolytic Rearrangement of 2-Isobutyl-1,2-oxazaspiro[2.5]octane. Sensitized Photoisomerization of Oxaziridines

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The use of oxaziridines in organic synthesis is well documented.[1] A particularly interesting application is the photoisomerization of spiro oxaziridines into the corresponding ring-expanded lactams using UV light.[1,2] This reaction has been shown to proceed in yields of ca. 80% in a stereoselective and regioselective manner in which the migrating carbon is located anti to the lone pair on the nitrogen (Scheme 1).[2b,3] The mechanism for oxaziridines containing an *N*-alkyl group has been proposed to involve an initial homolytic fragmentation of the N–O bond on the singlet excited state surface ($n \rightarrow \sigma^*_{NO}$), internal conversion to the ground-state surface, and migration of a ring carbon atom.[3b,c]

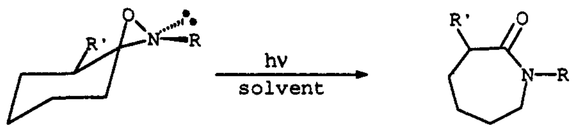
This mechanism presupposes that the excited state is localized on the oxaziridine, which is typically not the case when R contains an aromatic group. Absorption in the UV of most substituted aromatics is generally at a longer wavelength than that of *N*-alkyl-substituted oxaziridines ($\lambda_{max} < 210$ nm).[2a] More specifically, the wavelength generally used in the photolysis of oxaziridines is 254 nm, a wavelength at which absorption by an aryl substituent (ϵ_{254} 200–10^4 M^{-1} cm^{-1}) far exceeds that of the oxaziridine chromophore (ϵ_{254} ca. 50 M^{-1} cm^{-1}). One may therefore assume that excitation is initially localized on the aromatic ring. In fact, there is anecdotal evidence that the presence of an aromatic ring, either within the substrate or as the solvent, facilitates the photoinduced rearrangement. Despite this, it is generally held that triplet photosensitization of oxaziridines is ineffective in eliciting lactam formation.[2] We therefore set out to study the photosensitization of 2-isobutyl-1,2-oxazaspiro[2.5]octane (**1**) with a number of benzene derivatives. Compound **1** was prepared by treatment of the corresponding *N*-isobutyl imine with MCPBA in CH_2Cl_2 at 0 °C.[3b] For sensitization studies, solutions were prepared such that the concentration of the aromatic was ca. 0.5 M and that of **1** varied from 0.04 to 0.1 M, with a total of four different concentrations being used.[4] Direct photolyses were run in hexane and acetonitrile for purposes of comparison and gave quantum efficiencies for the disappearance of starting material (ϕ_{dis}) and the formation of lactam (ϕ_{app}) of $\phi_{dis} = \phi_{app} = 0.29 \pm 0.05$.[5]

All four aromatics were indeed found to be efficient sensitizers. Assuming singlet sensitization (see below), a Stern–Volmer kinetic analysis gives eq 1, and all four sensitizers did indeed give good linear double-reciprocal plots.[6] Using singlet lifetimes (τ_{sens}) measured for each sensitizer in the absence of **1**, the k_{sens} values derived from the slopes and the ϕ_{max} values

$$\frac{1}{\phi_{app}} = \frac{1}{\phi_{max}} + \frac{1}{k_{sens}\tau_{sens}\phi_{max}[1]} \qquad (1)$$

derived from the intercepts are presented in Table 1.[7]

Scheme 1



1: R = isobutyl
R'= H

2: R = isobutyl
R'= H

Table 1. Sensitizer Singlet Lifetimes, Sensitization Rate Constants, and Maximum ϕ_{app}

solvent	sensitizer	τ_{sens}/ns	$k_{sens}/10^9$ M^{-1} s^{-1}	ϕ_{max}
CH_3CN	*N*,*N*-dimethylaniline	0.8	9.6	0,49
	anisole	9	1.3	0.59
	toluene	20	1.5	0.61
	benzonitrile	8	0.96	0.44
hexane	*N*,*N*-dimethylaniline	0.7	20	0.77
	toluene	30	1.6	0.73
	benzonitrile	12	1.6	0.63

The following observations are made regarding the mechanism for aryl photosensitization: (a) Triplet energy transfer: Triplet sensitization studies indicate that the lactam is not a photoproduct under such conditions.[2] Our own studies with benzophenone in hexane, using a medium-pressure Hg lamp with a uranium yellow filter ($\lambda > 330$ nm), confirm these reports. This experiment gave *N*-isobutylcaproamide as the primary photoproduct with no evidence for lactam. The fact that ϕ_{max} for toluene in hexane is greater than the quantum efficiency for intersystem crossing for this sensitizer ($\phi_{isc} = 0.52$)[8] also eliminates this option.

(b) Singlet energy transfer: Fluorescence quenching studies of toluene by **1** indicate that the photosensitization must be singlet derived, as seen by a shortening of the toluene singlet excited state lifetime in hexane. The rate constant for quenching (3.4×10^9 M^{-1} s^{-1}) is comparable to that measured by sensitization (Table 1).[9] However, singlet/singlet energy transfer would be highly endothermic. Furthermore, the ϕ_{dis} for **1** of 0.29 in acetonitrile and hexane under direct photolysis conditions is significantly below the ϕ_{max} values for sensitization (Table 1). Alternative singlet mechanisms are required.

(c) Electron transfer: The possibility of photosensitization by reversible electron transfer has not been discussed in the literature, except in a footnote concerning the comment of a referee.[10] Our data do not support such an option. We observe neither the expected dependence of k_{sens} on sensitizer ionization potential nor any obvious effect of solvent dielectric constant (the latter has been noted in previous reports).[2b,11]

(d) "Nonvertical" singlet processes: The endothermicity of aryl/oxaziridine Franck–Condon singlet energy transfer requires

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(1) For a recent review, see: Davis, F. A.; Sheppard, A. C. *Tetrahedron* **1989**, *45*, 5703–5742.

(2) See, for example: (a) Kobayashi, Y. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 3467–3470. (b) Oliveros, E.; Riviere, M.; Lattes, A. *Nouv. J. Chim.* **1979**, *3*, 739–752.

(3) (a) Aube, J.; Wang, Y.; Hammond, M.; Tanol, M.; Takusagawa, F.; Vander Velde, D. *J. Am. Chem. Soc.* **1990**, *112*, 4879–4891. (b) Lattes, A.; Oliveros, E.; Riviere, M.; Belzecki, C.; Mostowicz, D.; Abramskj, W.; Piccinni-Leopardi, C.; Germain, G.; Van Meerssche, M. *J. Am. Chem. Soc.* **1982**, *104*, 3929–3934. (c) Oliveros, E.; Riviere, M.; Malrieu, J. P.; Teichteil, C. *J. Am. Chem. Soc.* **1979**, *101*, 318–322.

(4) All photolyses were carried out in a Rayonet Reactor (New England Ultraviolet Company), using four 254-nm lamps, after degassing with argon. Greater than 99% of the light was absorbed by the sensitizers.

(5) Quantum efficiencies were determined using GLC with an internal standard and 1-phenyl-2-butene actinometry; cf.: Morrison, H.; Pajak, J.; Peiffer, J. *J. Am. Chem. Soc.* **1971**, *93*, 3978–3985. Morrison, H.; Peiffer, R. *J. Am. Chem. Soc.* **1968**, *90*, 3428–3432.

(6) The correlation coefficient for toluene in hexane was 0.95; all others were greater than 0.99.

(7) k_{sens} is the rate constant for aryl sensitization, and ϕ_{max} is the maximum quantum efficiency for the appearance of **2**, in which all aryl excited states are intercepted by **1** (i.e., the limit as the concentration of **1** goes to infinity).

(8) Schloman, W. W., Jr.; Morrison, H. *J. Am. Chem. Soc.* **1977**, *99*, 3342–3345.

(9) It should be noted that the fluorescence study was done with a toluene concentration of 2.4 mM, whereas the photochemical experiments involve a concentration of 0.59 M.

(10) Boyd, D. R.; Campbell, R. M.; Coulter, P. B.; Grimshaw, J.; Neill, D. C.; Jennings, W. B. *J. Chem. Soc., Perkin Trans. 1* **1985**, 849–855.

(11) The possibility of intramolecular electron transfer in oxaziridines has not been ruled out nor yet actively explored. Interestingly, the photoisomerization of a dilute *N*-tryptophan-substituted oxaziridine is reported to proceed best in acetonitrile; cf.: Langlois, Y.; Pouilhes, A.; Genin, D.; Andriamialisoa, R. Z.; Langlois, N. *Tetrahedron* **1983**, *39*, 3755–3761. Studies of intramolecular systems are in progress.

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a significant nuclear distortion in the acceptor concomitant with sensitization, i.e., a "nonvertical" energy-transfer process.[12] Such "nonvertical" processes are poorly understood; there have been several mechanistic proposals,[13] including the formation of exciplex intermediates.[14,15]

The utility of this photoreaction in asymmetric synthesis necessitates a better understanding of the photosensitization mechanism. Further experiments designed to provide a more detailed analysis of the oxaziridine sensitization process (for example, dependence on sensitizer singlet energy), as well as the potential extension of these observations to other three-membered-ring heterocycles, are in progress.

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(12) Michl, J.; Bonačić-Koutecky, V. *Electronic Aspects of Organic Photochemistry*; John Wiley & Sons, Inc.: New York, 1990; p 83.

(13) See, for example: Saltiel, J.; Marchand, G. R.; Kirkor-Kaminska, E.; Smothers, W. K.; Mueller, W. B.; Charlton, J. L. *J. Am. Chem. Soc.* **1984**, *106*, 3144–3151. Balzani, V.; Bolletta, F.; Scandola, F. *J. Am. Chem. Soc.* **1980**, *102*, 2152–2163 and references therein.

(14) Turro, N. J.; Dalton, J. C.; Weiss, D. S. *Org. Photochem.* **1970**, *2*, 1. Turro, N. J. *Modern Molecular Photochemistry*; W. A. Benjamin: Menlo Park, CA, 1978; p 346.

(15) We note that, though the triplet energy of oxaziridines has not been determined, it seems likely that an endothermic process is involved in, e.g., benzophenone sensitization as well.