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Photochemical Generation and Absolute Reactivity of an Allene Oxide in Solution

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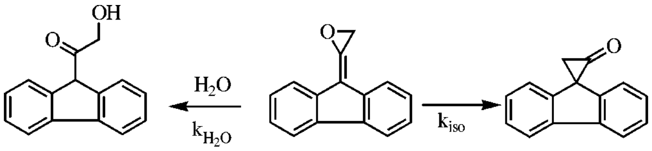
ABSTRACT



A method for the rapid photochemical generation of allene oxides is described that allows absolute rate constants for the reactions of these interesting reactive intermediates to be measured. The fluorenylideneallene oxide generated using this method was found to rearrange to the corresponding cyclopropanone with a rate constant of 0.0012 s^{-1} in TFE. The lifetime of the allene oxide was significantly reduced in the presence of nucleophiles such as halides, methanol, and water.

Allene oxides which contain a distinctive structural feature consisting of an epoxide with an exocyclic methylene group have been of interest to chemists for over 3 decades. Much of this interest has been directed toward understanding the mechanisms of the reactions of allene oxides, especially with regard to the isomerization to cyclopropanones and the addition of nucleophiles.[1−8] In recent years, allene oxides have emerged as useful reagents for organic synthesis, such as stereospecific [4 + 3] cycloaddition reactions[9] and the generation of chiral α-hydroxyketones.[10] In addition, allene oxides have also been postulated as reactive intermediates generated in the biosynthesis of prostaglandins and related cyclopentanoids in both plants and marine organisms.[11−16]

Most experimental studies of allene oxides have focused on examining the products from transient allene oxides generated thermally in situ from appropriate precursors. Results from these studies have firmly established the fundamental reactions of allene oxides to be addition of nucleophiles to give α-substituted ketones and isomerization to cyclopropanones, with the pathway followed being dependent on the nature and the position of the substituents.[6]

To fully understand the chemistry of these interesting intermediates, it would be useful to have methods with which to examine directly their dynamic behavior. This would provide information about the absolute rate constants[17] for isomerization to cyclopropanones and for bimolecular reactions such as the addition of nucleophiles which can be used to determine the mechanisms of the reactions. Our research

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(17) The lifetime of the allene oxide generated enzymatically from 8*R*-8-hydroperoxyeicosatetraenoic acid has been measured to be ca. 25 s in aqueous solution at 0 °C (ref 14).

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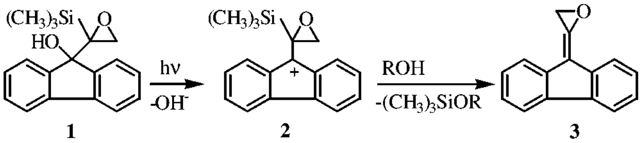
in this area involves developing methods for the rapid photochemical formation of allene oxides so that their reactivity can be directly examined using flash photolysis techniques. In this paper, we report our results concerning the photochemical generation of the fluorenylideneallene oxide and absolute rate constants for its rearrangement to the corresponding cyclopropanone and its reaction with nucleophiles.

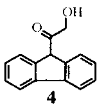
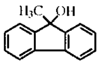
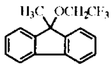
9-Hydroxy-9-(1-(trimethylsilyl)-1,2-epoxyethyl)fluorene (**1**) was prepared as the photochemical precursor to the desired fluorenylideneallene oxide **3**. This precursor was expected to give the allene oxide by initial photodehydroxylation to the substituted β-silyl-9-fluorenyl cation **2** followed by rapid solvent-assisted elimination of the silyl group, Scheme 1.

Scheme 1



Results from product studies provide convincing evidence that the allene oxide is indeed generated upon irradiation of **1**. Thus, GC analysis after steady-state irradiation[18] of **1**[19] in 50% CH_3CN/50% water (vol %) (10−60% conversion) indicated the presence of a single photoproduct. The product was isolated by column chromatography and identified by GC−MS and NMR as 9-(2-hydroxyacetyl)fluorene **4** (Table 1, entry 1).

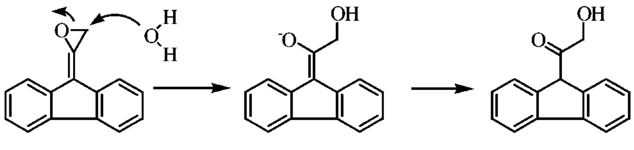
Table 1. Percent Yield of Products Generated upon Steady-State Irradiation of **1** (60% Conversion) in Various Solvents

Solution	% Yield of products		
	 **4**	 **5**	 **6**
50% CH_3CN:50% H_2O	100	0	0
50% TFE:50% H_2O	100	0	0
90% TFE:10% H_2O[a]	79	8	13
95% TFE:5% H_2O[a]	44	18	37
100% TFE:0% H_2O[a]	0	0	100

[a] A trace amount (<2%) of methylene fluorene was also detected as a product at lower conversions.

As demonstrated from previous studies,[6] nucleophilic addition to allene oxides generally occurs at the saturated carbon of the epoxide to give, in this case, a fluorenyl-substituted enol that rapidly tautomerizes to the observed product, Scheme 2. Isolation of 9-(2-hydroxyacetyl)fluorene therefore provides excellent evidence that the fluorenylideneallene oxide is indeed produced photochemically from **1**.

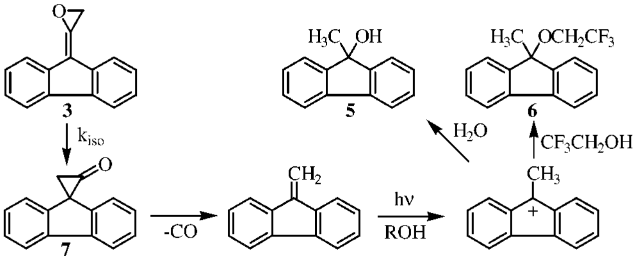
Scheme 2



In 50% 2,2,2-trifluoroethanol (TFE)/50% water, **4** was again the only product formed upon steady-state irradiation of **1** (Table 1, entry 2). However, as the water content decreased to 10% (Table 1, entry 3), GC analysis showed the appearance of two new products along with 9-(2-hydroxyacetyl)fluorene. These products were identified by GC and GC−MS as 9-methyl-9-fluorenol **5** and 9-methyl-9-(2,2,2-trifluoroethoxy)fluorene **6**. At even lower water content, the sum of the yields of **5** and **6** increased at the expense of 9-(2-hydroxyacetyl)fluorene **3**, and in neat TFE, **4** was no longer formed at all (Table 1, entry 5).

Products **5** and **6** are clearly not derived from direct addition of the solvent to the allene oxide. However, these products are still consistent with photochemical formation of the allene oxide that, as a result of the low nucleophilicity of TFE, isomerizes to fluorenylidenecyclopropanone **7** instead of undergoing nucleophilic attack, Scheme 3. Fluorenylidenecyclopropanone then rapidly decarbonylates to give methylenefluorene, which undergoes subsequent photoaddition of solvent to give the observed products.[20] Support for this mechanism comes from the detection by GC of trace amounts of methylenefluorene after short irradiation times. Furthermore, as shown in Table 1, the ratio of **5**:**6** decreased with decreasing water content, and in neat TFE, only the

Scheme 3



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[18] Hanovia 450-W medium-pressure Hg lamp.

[19] GC and UV analysis showed no evidence for thermal decomposition of **1** when dissolved for time periods up to 5 h in solvents such as TFE, HFIP, TFE/water mixtures, and CH_3CN/water mixtures.

[20] (a) Isolation of 9-methyl-9-(2,2,2-trifluoroethoxy)fluorene upon irradiation of precursors that photochemically generate methylenefluorene has been previously demonstrated. (b) Lew, C. S. Q.; McClelland, R. A.; Johnston, L. J.; Schepp, N. P. *J. Chem. Soc., Perkin Trans. 2* **1994**, 395−397.

TFE adduct **6** was formed. This is consistent with product formation via the 9-methyl-9-fluorenyl cation, with the amount of water adduct **5** decreasing as the water content in the mixture is reduced.

In neat 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP), a solvent that is even less nucleophilic than TFE, the sole product upon photolysis of **1** is 9-(1,1,1,3,3,3-hexafluoro-2-propoxy)-9-methylfluorene. This material is analogous to the trifluoroethoxy ether **6** isolated in neat TFE, indicating that the allene oxide **3** is still formed in HFIP, and its main reaction is again isomerization to the cyclopropanone **7**.

Additional support for formation of fluorenylideneallene oxide upon irradiation of **1** is provided by the spectroscopic properties and the kinetic behavior of intermediate species observed in time-resolved experiments. Laser[21] irradiation of **1** in neat TFE generated an absorption spectrum characterized by maxima at 300 and 315 nm, Figure 1a. This spectrum contains features expected for a compound like the fluorenylideneallene oxide with a methylenefluorene chromophore.[22] The absorption at 305 and 315 nm does not decay over a time period of 10 ms, which is the longest time-scale available on our laser system. In fact, the same absorption band can still be observed when a solution of **1** is irradiated with a laser pulse and then quickly placed into a conventional UV−vis spectrometer, Figure 1a. At the longer times now available, the absorption bands can be observed to decay, Figure 1b. The decay fits nicely to a first-order expression giving a rate constant of 1.2×10^{-3} s^{-1}.

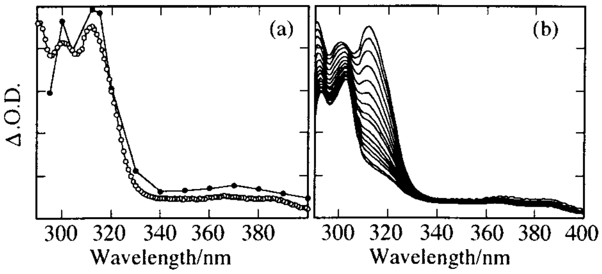


Figure 1. (a) Absorption spectra obtained 100 ns (●) and 5 s (○) after a single 308 nm laser pulse of a solution of **1** in neat TFE. (b) Absorption spectra taken at 120 s time intervals after a single 308 nm laser pulse of a solution of **1** in neat TFE at 24 °C.

The β-silyl-9-fluorenyl cation **2** (Scheme 1), which leads to the fluorenylideneallene oxide, was not detected in TFE. However, in the less nucleophilic HFIP, a transient with a maximum at 480 nm, a shoulder at 420 nm, and another band below 350 nm is observed immediately after laser irradiation of **1**, Figure 2a. All of these bands decay rapidly with the same rate constant of 1×10^7 s^{-1}, which is insensitive to the presence or absence of oxygen but increases as the nucleophilicity of the solvent is increased by addition of TFE or water. These observations are all consistent with identification of the transient as the substituted 9-fluorenyl cation generated by photodehydroxylation of **1**.[20,23,24]

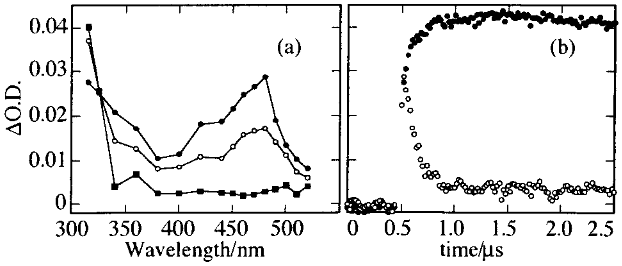
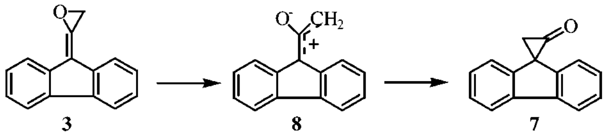


Figure 2. (a) Transient absorption spectra taken 20 (●), 100 (○), and 700 ns (■) after 266 nm laser irradiation of **1** in HFIP. (b) Time-resolved absorption changes at 315 (●) and 480 nm (○) generated upon 266 nm laser irradiation of **1** in HFIP.

Importantly, as shown in Figure 2b, the decay of the carbocation is accompanied by an increase in absorption at 315 nm. This is consistent with the identification of the transient at 315 nm as the allene oxide **3** which grows in upon solvent-assisted loss of the trimethylsilyl group from the initially formed carbocation, Scheme 1. Once formed, the fluorenylideneallene oxide is long-lived in HFIP and decays with a first-order rate constant of 0.0054 s^{-1}.

The product studies described above show that the main reaction of the allene oxide in neat TFE and neat HFIP is isomerization to the cyclopropanone. Thus, it is reasonable to conclude that the rate constants of 0.0012 and 0.0054 s^{-1} for the decay of the allene oxide in TFE and HFIP, respectively, represent the rate constants, k_{iso}, for the isomerization reaction in those solvents. The observation that the allene oxide isomerizes over four times more rapidly in HFIP than in TFE provides some insight into questions concerning the presence or absence of a zwitterionic oxyallyl species **8** as an intermediate in the isomerization reaction. In particular, formation of the oxyallyl intermediate, Scheme 4, bears some similarity to the formation of ion pairs in traditional ionization reactions that typically proceed more rapidly in HFIP than in TFE. On the other hand, if isomerization is concerted, little charge separation will develop in the transition state, and the reaction is likely to be less sensitive to solvent ionizing ability. Thus, the observation that the rate constant for the conversion of the fluorenylideneallene oxide to the cyclopropanone in HFIP is greater than that in TFE is

Scheme 4



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[21] Lambda-physik excimer laser, XeCl (308 nm) gas mixture, ca. 100 mJ/pulse, 10 ns pulse width, or Spectra-Physics Nd:YAG laser, 4th harmonic (266 nm), ca. 30 mJ/pulse, 6 ns pulse width.

[22] Harcourt, M. P.; O'Ferrall, R. A. M. *J. Chem. Soc., Perkins Trans. 2* **1995**, 1414−1425.

more consistent with the formation of the zwitterionic oxyallyl intermediate.

Given that one of the main reactions of allene oxides is the addition of nucleophiles, the decay of the fluorenylideneallene oxide was measured as a function of the concentration of halides, methanol, and water. Observed rate constants, k_{obs}, for the decay of the allene oxide in TFE were found to increase in a linear manner as a function of increasing nucleophile concentration. Linear least-squares analysis of the relationships between k_{obs} and nucleophile concentration gave the second-order rate constants summarized in Table 2.

Table 2. Second-Order Rate Constants for the Reaction of the Fluorenylideneallene Oxide **3** with Various Nucleophiles in TFE (at 24 °C)

nucleophile	k_{Nu} (M^{-1} s^{-1})	nucleophile	k_{Nu} (M^{-1} s^{-1})
Cl^-	1.0 ± 0.1	H_2O	$(1.2 \pm 0.2) \times 10^{-3}$
Br^-	3.9 ± 0.2	CH_3OH	$(4.4 \pm 0.4) \times 10^{-3}$
I^-	23.1 ± 1.2		

The magnitude of the second-order rate constants clearly illustrates the relatively high electrophilicity of allene oxides. Furthermore, the observations that the decay of the fluorenylideneallene oxide depends on the concentration of nucleophiles and that the second-order rate constants for nucleophilic addition follow expected nucleophilicity trends indicate that the mechanism for addition involves rate-determining attack of the intact allene oxide rather than rate-determining formation and subsequent trapping of an oxyallyl intermediate.[7] A third mechanism whereby an oxyallyl intermediate is formed in a rapid preequilibrium and then trapped by the nucleophile is possible. While this mechanism cannot be ruled out, most evidence to date consistently indicates that oxyallyl intermediates collapse to the more thermodynamically stable cyclopropanones and not to the higher energy allene oxide.[2,25]

In summary, we have developed a technique for the rapid photochemical generation of reactive allene oxides that allows the dynamics of these species to be determined directly, both in the presence and absence of nucleophiles. Our results show that the fluorenylideneallene oxide generated using this method decays with rate constants of 0.0012 s^{-1} in TFE and 0.0054 s^{-1} in HFIP, which represent isomerization to the corresponding cyclopropanone. The allene oxide also reacts rapidly with nucleophiles with rate constants that reflect the relatively high electrophilicity of the allene oxide. Further studies into the effect of structure on the absolute rate constants for reactions of allene oxides and on the mechanisms for these reactions are currently in progress.

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Supporting Information Available: Synthetic procedures and spectral data for precursor and products and procedures for product studies and kinetics experiments. This material is available free of charge via the Internet at http://pubs.acs.org.

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