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Direct UV Observation and Kinetic Studies of a α-Alkoxy Benzyloxy Radical

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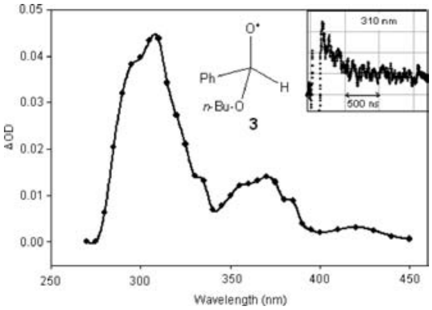
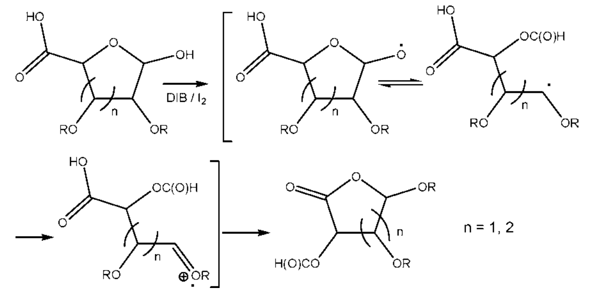
ABSTRACT



A α-alkoxy benzyloxy radical 3 was generated by laser flash photolysis of peroxyacetal 2, and its UV spectrum, decomposition pattern, reactivity with PPh_3, O_2, and *i*-PrOH, and quantum yield were explored. It was found that the radical 3 is very unstable and highly reactive and performs *β*-C-H scission much faster than *β*-C-O scission and H-abstraction.

The α-alkoxy alkoxy radicals (ROCH(O$^•$)R, **1**) can be intermediates of various reactions; the following are three examples. First, oxidation of ethers in air generates various peroxyacetals. These peroxyacetals may be decomposed into the α-alkoxy alkoxy radicals **1**.[1a] Some theoretical and kinetic studies on *β*-scission and oxidation of **1** have been done, but direct observation of the radical **1** is still absent.[1b−d] Second, since the early 1960s, photodynamic therapy has been developed for treatment of tumor cells, bacteria, and viruses by means of photosensitizer, oxygen, and light.[2a] The photosensitization reaction generates highly reactive singlet oxygen, which not only reacts with tumor cells, bacteria, or viruses but also attacks biological molecules such as α-tocopherol, forming the corresponding peroxyacetal, which decomposes into the α-alkoxy alkoxy radical.[2b] To determine out how these biological molecules are damaged, understanding properties of the α-alkoxy alkoxy radicals is necessary. Third, as shown in Scheme 1, oxidation of carbohydrates and their analogues by oxidants such as

Scheme 1. Oxidation of Carbohydrates and Their Analogues, Forming α-Alkoxy Alkoxy Radicals as Intermediates



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(1) (a) Carey, F. A. *Organic Chemistry*, 7th ed.; McGraw Hill: New York, 2008; pp 671−672. (b) Henon, E.; Bohr, F.; Sokolowski-Gomez, N.; Caralp, F. *Phys. Chem. Chem. Phys.* **2003**, *5*, 5431. (c) Orlando, J. J. *Phys. Chem. Chem. Phys.* **2007**, *9*, 4189. (d) Aschmann, S. M.; Atkinson, R. *Int. J. Chem. Kinet.* **1999**, *31*, 501.

(2) (a) Juzeniene, A.; Peng, Q.; Moan, J. *Photochem. Photobiol. Sci.* **2007**, *6*, 1234. (b) Halliwell, B.; Gutteridge, J. M. C. *Free Radicals in Biology and Medicine*, 4th ed.; Oxford University Press: New York, 2007; pp 69−78.

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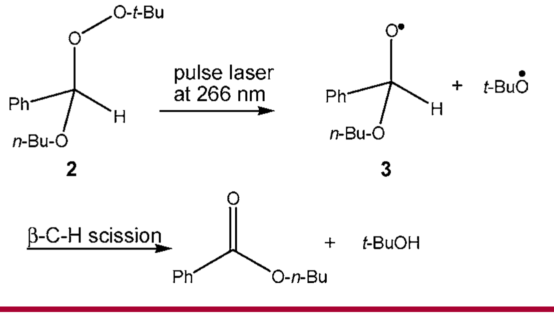
(diacetoxyiodo) benzene and iodine usually generates the corresponding α-alkoxy alkoxy radicals, followed by fragmentation into several types of useful chemicals.[3] However, the α-alkoxy alkoxy radicals that were claimed as intermediates in the oxidation of carbohydrates have not yet been identified.

Some α-alkoxy alkoxy radicals have been claimed or assumed to be intermediates, which were formed in situ, in the following reactions, but they were not directly observed. Poranski, Jr. et al. used carbon-13 CIDNP to observe conventional photolysis of *tert*-butyl hydroperoxide (TBHP) in alcohols with the beam from a CW Hg/Xe arc source.[4] In this photolysis, peroxyhemiacetals were generated in situ, followed by decomposition into carbonyl compounds possibly through α-hydroxy alkoxy radical. Wallington et al. used modulated photolysis of $Cl_2/CH_3OCH_3/O_2/N_2$ mixtures or pulse radiolysis of $SF_6/CH_3OCH_3/O_2$ mixtures to generate $CH_3OCH_2O_2^{\bullet}$, whose self-reaction produced $CH_3OCH_2O^{\bullet}$, followed by β-C-H scission or reacting with molecular oxygen to form CH_3OCHO.[5] Using high-level *ab initio* calculations (CCSD(T)//MP2), Henon, et al. found that the activation energy of β-C-H scission is around 10 kcal/mol less than that of β-C-O scission for the decomposition of $ROCH_2O^{\bullet}$.[1b]

In this paper, we used peroxyacetal **2**[6] as a source of α-alkoxy benzyloxy radical **3** and explored this radical's UV spectrum, decomposition pattern, reactivity with PPh_3, oxygen, and isopropyl alcohol, and quantum yield. Laser flash photolysis of **2** in deoxygenated aqueous acetonitrile with a 266-nm pulse from a nanosecond Nd:YAG laser generated the radical **3**, which decomposed into *n*-butyl benzoate through β-C-H scission (Scheme 2). Product analysis by HPLC for the laser flash photolysis of **2** in aqueous acetonitrile showed that *n*-butyl benzoate was the product, but benzaldehyde was not found. Since only a small amount of **2** was consumed in a single shot of laser flash photolysis, **2** in deoxygenated 2:1 CD_3CN/D_2O was treated with many shots of pulse laser at 266 nm and monitored by ^1H NMR spectrometer. As shown in Figure 1, a series of the ^1H NMR spectra show that [**2**] kept decreasing and [*n*-butyl benzoate] kept increasing as the number of shots of pulse laser increased, but benzaldehyde from β-C-O scission was not observed. If the radical **3** undergoes H-abstraction, the unstable hemiacetal product would follow β-elimination to form benzaldehyde and *n*-butanol. However, benzaldehyde is not the reaction product, so it indicates that the β-C-H scission rate of **3** is much faster than its H-abstraction. On the other hand, when laser flash photolysis of **2** was carried out in deoxygenated CD_3CN without water, not only *n*-butyl benzoate from β-C-H scission but also benzaldehyde from β-C-O scission were observed in a ratio of 3:1. Because laser flash photolysis of **2** in aqueous acetonitrile produced a simple decomposition pattern, we did the rest of experiment in this solvent system. Laser flash photolysis of **2** in deoxygenated aqueous acetonitrile with many shots of the pulse laser was also monitored by conventional UV spectrophotometer. As shown in Figure 2, absorption at 230 nm (**2**: 2.3 × 10^{-4} M, $\varepsilon = 2392$ cm^{-1} M^{-1} at 230 nm) kept growing as the number of shots of pulse laser increased, generating the product of *n*-butyl benzoate ($\varepsilon = 10{,}000$ cm^{-1} M^{-1} at 230 nm). According to the above results, the radical **3**, generated by laser flash

Scheme 2. Generation of α-Alkoxy Benzyloxy Radical **3** from Laser Flash Photolysis of **2** in Deoxygenated Aqueous Acetonitrile, Followed by β-C-H Scission



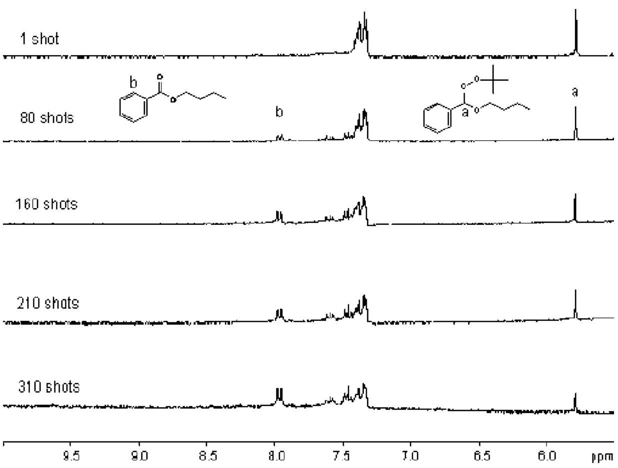


Figure 1. ^1H NMR spectra for laser flash photolysis of **2** in deoxygenated 2:1 CD_3CN/D_2O with many shots of pulse laser at 266 nm.

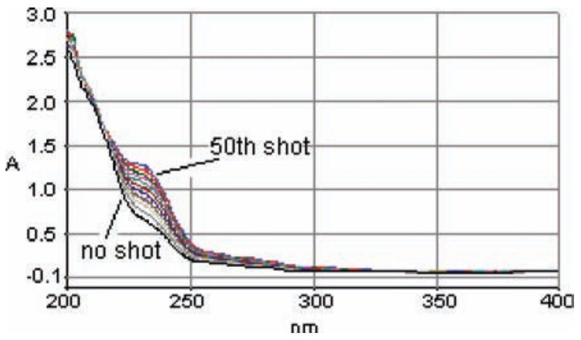


Figure 2. UV spectra for laser flash photolysis of **2** in deoxygenated 2:1 CH_3CN/H_2O with many shots of pulse laser at 266 nm.

photolysis of **2** in deoxygenated aqueous acetonitrile, follows β-C-H scission much faster than β-C-O scission and H-abstraction. The results confirm Henon's theoretical findings[1b] that β-C-H scission is much faster than β-C-O scission for the decomposition of $\mathrm{ROCH_2O^{\bullet}}$. In addition, photodecomposition of **2** produces the in-cage radical pair, **3** and *tert*-butoxy radical. *tert*-Butoxy radical is known to do H-abstraction from various H-atom donors, such as toluene, $\mathrm{Ph_2CHOH}$, and *i*-PrOH.[7] It is likely that *tert*-butoxy radical performs H-abstraction from the in-cage radical **3**, enhancing β-C-H scission rate of **3**. Recently, Orlando did atmospheric oxidation of diethyl ether and found that β-C-C(alkyl carbon) scission of $\mathrm{CH_3CH_2O\text{-}CH(O^{\bullet})CH_3}$ is much faster than β-C-H and β-C-O scissions because ethyl formate is the major product.[1c] Combining the result with our findings, one can draw the β-scission rate sequence of α-alkoxy alkoxy radicals: β-C-C(alkyl carbon) scission > β-C-H scission > β-C-O scission. This β-scission rate sequence is consistent with the results for oxidation of carbohydrates[3] shown in Scheme 1.

As shown in Figure 3, laser flash photolysis of **2** in deoxygenated 66.7% acetonitrile aqueous solution produces the transient absorption spectrum with a strong absorption maximum at around 310 nm and two weak absorption maxima at 370 and 420 nm. The transient decay at these maxima gives a reasonable fit to first-order kinetics with a lifetime of 158 ns and a rate constant of 4.4×10^6 s^{-1}. This is consistent with the known results that the electronic transition of alkoxyl radicals between the ground state and the first excited state lies around 300 nm.[8] In deoxygenated aqueous acetonitrile, photodecomposition of **2** generates two radicals: *tert*-butoxy radical and the radical **3**. Scaiano et al. reported that *tert*-butoxy radical has a very weak absorption maximum at 320 nm, but it is too weak to observe for kinetic study.[9] The other radical **3**, however, has a phenyl chromophore, which makes its molar absorptivity higher. In addition, benzyloxy and cumyloxy radicals were found to have weak visible light absorptions due to the $\pi \rightarrow \pi^*$ transition of intramolecular charge transfer from benzene ring to oxygen radical.[10] The weak visible light absorption at 420 nm for the radical **3** is likely to be attributed to the charge-transfer band. Hence, the transient we observed in Figure 3 is supposed to be the α-alkoxy benzyloxy radical **3**.

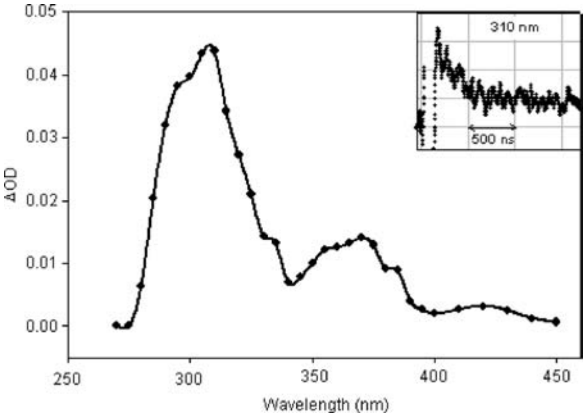


Figure 3. Transient absorption spectrum recorded 160 ns after 266-nm laser excitation of **2** in deoxygenated 66.7% acetonitrile aqueous solution.

Scaiano et al. reported that alkoxy radicals such as the *tert*-butoxy radical, generated by laser flash photolysis in 1:2 benzene/*t*-BuOO-*t*-Bu, can be quenched by $\mathrm{PPh_3}$ with a rate constant of 1.9×10^9 M^{-1} s^{-1}, producing a *tert*-butoxy-triphenylphosphoranyl radical with a lifetime of 900 μs and a maximum of the transient absorption spectrum at 430 nm.[11] Because $\mathrm{PPh_3}$ reacts very fast with alkoxy radicals at a diffusion rate, we tried to use it to quench the labile radical **3**. The transient generated by laser flash photolysis of **2** in deoxygenated 66.7% acetonitrile aqueous solution can also be quenched by $\mathrm{PPh_3}$ with a rate constant of 4.0×10^9 M^{-1} s^{-1}, producing another transient with a maximum absorption at around 400 nm (Figure 4). The decay rate constants of the transient absorption at 310 nm were found to be proportional to [$\mathrm{PPh_3}$], and the correlation curve fits the equation of $k_{\mathrm{obs}} = k_0 + k_{\mathrm{PPh_3}}[\mathrm{PPh_3}]$, where $k_0 = 4.0 \times 10^6$ s^{-1} and $k_{\mathrm{PPh_3}} = 4.0 \times 10^9$ M^{-1} s^{-1}. The k_0 is close to the

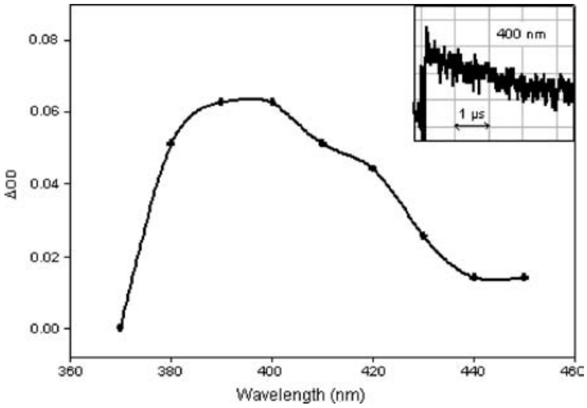


Figure 4. Transient absorption spectrum recorded 170 ns after 266-nm laser excitation of **2** in the presence of $\mathrm{PPh_3}$ in deoxygenated 66.7% acetonitrile aqueous solution.

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(3) (a) Francisco, C. G.; Martin, C. G.; Suarez, E. *J. Org. Chem.* **1998**, *63*, 2099. (b) Hernandez, R.; Leon, E. I.; Moreno, P.; Suarez, E. *J. Org. Chem.* **1997**, *62*, 8974. (c) de Armas, P.; Francisco, C. G.; Suarez, E. *J. Am. Chem. Soc.* **1993**, *115*, 8865. (d) Francisco, C. G.; Freire, R.; Gonzalez, C. C.; Suarez, E. *Tetrahedron: Asymmetry* **1997**, *8*, 1971.

(4) Moniz, W. B.; Sojka, S. A.; Poranski, C. F., Jr.; Birkle, D. L. *J. Am. Chem. Soc.* **1978**, *100*, 7940.

(5) (a) Jenkin, M. E.; Hayman, G. D.; Wallington, T. J.; Hurley, M. D.; Ball, J. C.; Nielsen, O. J.; Ellermann, T. *J. Phys. Chem.* **1993**, *97*, 11712. (b) Wallington, T. J.; Hurley, M. D.; Ball, J. C.; Straccia, A. M.; Platz, J.; Christensen, L. K.; Sehested, J.; Nielsen, O. J. *J. Phys. Chem. A* **1997**, *101*, 5302.

(6) (a) **Synthetic procedure.** To benzaldehyde (2 mmol) and 4 Å molecular seives (0.5 g) in $\mathrm{CHCl_3}$ (2 mL) at rt was added $\mathrm{TiCl_4}$ (0.1 mmol, 10% in $\mathrm{CHCl_3}$). The mixture was stirred at rt for 1 h. Toluene solution of TBHP (1.7 mmol) and *n*-butanol (1 mmol) were added into the mixture, followed by stirring at rt condition for 2 d. The product **3** was purified by column chromatography with silica gel as stationary phase and hexane/EtOAc as mobile phase. (b) Ochiai, M.; Ito, T.; Takahashi, H.; Nakanishi, A.; Toyonari, M.; Sueda, T.; Goto, S.; Shiro, M. *J. Am. Chem. Soc.* **1996**, *118*, 7716.

rate constant (4.4×10^6 s^{-1}) that is associated with the transient decay at 310 nm in the absence of PPh_3. The decay of the transient absorption at 400 nm, generated by quenching of **3** with PPh_3, is slower than its growth and follows first-order kinetics with a lifetime of 1.7 μs. Hence, the quenching experimental result is consistent with the assignment of the radical **3**.

The transient absorption at 310 nm can also be quenched by O_2 efficiently, forming *n*-butyl benzoate through β-C-H scission, which is consistent with O_2 quenching of other alkoxy radicals.[12] The O_2 solubility in acetonitrile and water at 1 atm O_2 and 298 K is reported to be 9.1 and 1.39×10^{-3} M.[13a] The equilibrium between oxygen dissolved in a solvent ($[O_2]_s$) and molecular oxygen in the gas phase ($[O_2]_g$) is temperature-dependent.[13b] Hence, the equilibrium constant of $([O_2]_s)/([O_2]_g)$ in 66.7% acetonitrile aqueous solution at 298 K is assumed to be 1.63×10^{-3} M atm^{-1}. The transient **3** generated by laser flash photolysis of **2** in 66.7% acetonitrile aqueous solution was quenched by various $[O_2]_s$, which was controlled by $[O_2]_g$. The quenching rate constant (k_{O_2}) for the transient absorption at 310 nm was calculated to be 6.6×10^8 M^{-1} s^{-1}. It is consistent with O_2 quenching for $ClCH_2O^{\bullet}$ ($k_{O_2} = 1.9 \times 10^8$ $M^{-1}s^{-1}$).[14] Similarly, reactions of other α-alkoxy alkoxy radicals with molecular oxygen also produced esters through β-C-H scission.[1c,5] Usually, intensities and decay rates of oxygen-center tertiary alkoxy radicals, such as cumyloxy radicals, *tert*-butoxy radical, and aroyloxy radicals, are unaffected by molecular oxygen.[10,15] Hence, the transient, which absorbs at 310 nm and is affected by molecular oxygen, is not *tert*-butoxy radical but the radical **3**.

Because *i*-PrOH is a good H-atom donor, we used it as a quencher for the radical **3** to perform H-abstraction, producing butoxy(phenyl)methanol, followed by β-elimination to form benzaldehyde, which was confirmed by HPLC with an authentic sample. The transient **3** generated by laser flash photolysis of **2** in deoxygenated 66.7% acetonitrile aqueous solution was quenched by various [*i*-PrOH]. The correlation between the decay rate constants of the transient absorption at 310 nm and [*i*-PrOH] gave the quenching rate constant ($k_{i\text{-PrOH}}$) of 1.3×10^6 M^{-1} s^{-1}, which is consistent with the *i*-PrOH quenching rate constant ($k_{i\text{-PrOH}} = 1.8 \times 10^6$ M^{-1} s^{-1})[7] for $(CH_3)_3CO^{\bullet}$. The H-abstraction of α-alkoxy alkoxy radicals might also be found in conventional photolysis of TBHP in alcohols, in which peroxyhemiacetals were generated in situ.[4] Decomposition of the peroxyhemiacetals into carbonyl compounds is assumed to go through α-hydroxy alkoxy radicals, followed by (1) H-abstraction from alcohols and (2) β-elimination.

The quantum yield for the formation of **3** in laser flash photolysis of **2** in deoxygenated 66.7% acetonitrile aqueous solution was evaluated to be 0.027 according to the equation $[A_{450}(SO_4^{-\bullet})/A_{310}(\mathbf{3})] = [\varepsilon_{450}(SO_4^{-\bullet}) \times \Phi(SO_4^{-\bullet})]/[\varepsilon_{310}(\mathbf{3}) \times \Phi(\mathbf{3})]$,[16] which can be reformulated into $[A_{450}(SO_4^{-\bullet})/[\mathbf{3}]] = [\varepsilon_{450}(SO_4^{-\bullet}) \times \Phi(SO_4^{-\bullet})]/[\Phi(\mathbf{3})]$. Potassium peroxodisulfate ($K_2S_2O_8$) was used as the chemical actinometer, and we used the solution of **2** with the same optical densities at 266 nm as that of $K_2S_2O_8$. The formation of a sulfate radical ($SO_4^{-\bullet}$), which was generated by laser flash photolysis of $K_2S_2O_8$, was monitored at 450 nm ($\varepsilon_{450}(SO_4^{-\bullet}) = 1400$ M^{-1} cm^{-1}, $\Phi(SO_4^{-\bullet}) = 1.4$),[16] and $A_{450}(SO_4^{-\bullet})$ was measured. The concentration of the transient **3** in a single shot of laser flash photolysis of **2** was calculated on the basis of generated [*n*-butyl benzoate] in 80 shots of laser at 266 nm, which was calculated from their ^{1}H NMR spectra (Figure 1).

In conclusion, the α-alkoxy benzyloxy radical **3** is very unstable and highly reactive and performs β-C-H scission much faster than β-C-O scission and H-abstraction.

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Supporting Information Available: Experimental procedures and ^{1}H and ^{13}C NMR spectra and characterization of **2** and *n*-butyl benzoate. This material is available free of charge via the Internet at http://pubs.acs.org.

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(7) Lusztyk, J.; Kanabus-Kaminska, J. M. In *CRC Handbook of Organic Photochemistry*; Scaiano, J. C., Ed.; CRC Press: Boca Raton, FL, 1989; Vol. II, p 184.

(8) Chatgilialoglu, C. In *CRC Handbook of Organic Photochemistry*; Scaiano, J. C., Ed.; CRC Press: Boca Raton, FL, 1989; Vol. II, pp 3–11.

(9) Chatgilialoglu, C.; Ingold, K. U.; Scaiano, J. C.; Woynar, H. *J. Am. Chem. Soc.* **1981**, *103*, 3231.

(10) (a) Avila, D. V.; Lusztyk, J.; Ingold, K. U. *J. Am. Chem. Soc.* **1992**, *114*, 6576. (b) Avila, D. V.; Ingold, K. U.; Di Nardo, A. A.; Zerbetto, F.; Zgierski, M. Z.; Lusztyk, J. *J. Am. Chem. Soc.* **1995**, *117*, 2711. (c) Baciocchi, E.; Bietti, M.; Salamone, M.; Steenken, S. *J. Org. Chem.* **2002**, *67*, 2266.

(11) Griller, D.; Ingold, K. U.; Patterson, L. K.; Scaiano, J. C.; Small, R. D., Jr. *J. Am. Chem. Soc.* **1979**, *101*, 3780.

(12) Devolder, P. *J. Photochem. Photobiol. A: Chem.* **2003**, *157*, 137.

(13) (a) Murov, S. L.; Carmichael, I.; Hug, G. L. *Handbook of Photochemistry*; Marcel Dekker: New York, 1993. (b) Tromans, D. *Hydrometallurgy* **1998**, *48*, 327.

(14) Wu, F.; Carr, R. W. *Chem. Phys. Lett.* **1999**, *305*, 44.

(15) (a) Chateauneuf, J.; Lusztyk, J.; Ingold, K. U. *J. Am. Chem. Soc.* **1988**, *110*, 2877. (b) Chateauneuf, J.; Lusztyk, J.; Ingold, K. U. *J. Am. Chem. Soc.* **1988**, *110*, 2886.

(16) Othmen, K.; Boule, P.; Richard, C. *New J. Chem.* **1999**, *23*, 857.