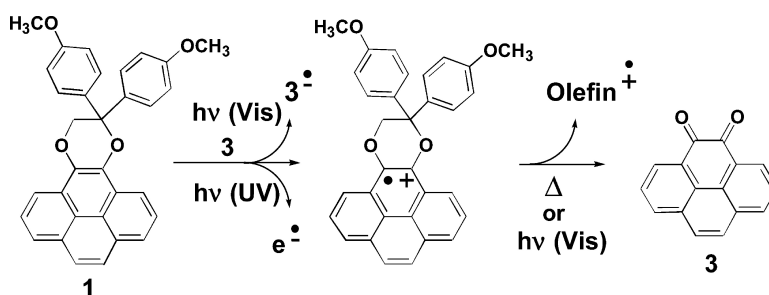Communication

Thermal and Photochemistry of a Pyrene Dihydrodioxin (PDHD) and Its Radical Cation: A Photoactivated Masking Group for *ortho*-Quinones

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Thermal and Photochemistry of a Pyrene Dihydrodioxin (PDHD) and Its Radical Cation: A Photoactivated Masking Group for *ortho*-Quinones

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In their classic work, Schönberg and Mustafa found that irradiation of *ortho*-quinones in the presence of olefins with visible light leads to the formation of dihydrodioxins (DHDs) (Scheme 1).[1] It was later observed that this reaction is reversed with UV light (364 nm),[2] and thus, this photochemistry might constitute a useful tool for masking highly reactive *ortho*-quinones. Using this masking strategy, dihydrodioxins have been shown to be effective DNA photocleaving agents.[3] In an effort to elucidate the mechanism of this quinone photorelease, we have studied the photochemistry of PDHDs **1** and **2** (Scheme 2), which are known to be among the more effective DHD-based DNA photocleaving agents. During the course of these studies, it has become clear that the photochemistry of PDHDs constitutes a unique example of an autosensitized PET system that proceeds through an unusually stable radical cation.

The relative quantum yields for pyrene-4,5-dione (**3**) release from PDHD **1** with UV light[4] have been found to be highly solvent dependent. The initial quantum yield in CCl$_4$ (Figure 1) is 0.078 ± 0.003, 23 times more efficient than that in benzene, and the isolated/purified yield of **3** is 78%. Since CCl$_4$ is known to function as an electron acceptor in photochemical reactions,[5] the effect of other, more conventional, electron acceptors on quinone release was investigated. Indeed, the addition of phenanthrenequinone or quinone **3** greatly accelerated the release of quinone **3** and makes it possible to trigger quinone release with visible light at wavelengths that are not absorbed by **1**.[6] In unsensitized reactions, UV light is only necessary for the initial release of a small amount of quinone **3**, which thereafter serves as a photosensitizer for further quinone release with visible light in the autosensitized mode. The release of **3** from the water-soluble PDHD **2** was also examined and found to be dramatically enhanced by the addition of methyl viologen[7] and FAD.[8] Finally, while the release of **3** does occur under anaerobic conditions, its rate is significantly increased in the presence of oxygen.

In general, DHDs are most interesting molecules in that they form relatively stable radical cations in solution.[9] PDHD **1** is no exception. Thus, treatment of **1** with tris(2,4-dibromophenyl)-aminium hexachloroantimonate (DBAHA) leads to the immediate formation of a red-orange solution of the radical cation **4** (Figure 2).[10] Radical cation **4** is stable for minutes to hours, depending upon the conditions of its generation, and ultimately decays with near-quantitative release of **3**. As shown in the inset in Figure 2, irradiation of the 453 nm band of **4** with visible light greatly accelerates its decomposition. These experiments provide direct evidence that **4** is not only thermally labile but also photochemically labile, and that both pathways lead to the extrusion of **3**.

In fact, the direct excitation of **1** with UV light also leads to the formation of radical cation **4** by photochemical electron ejection. This process can be observed by transient spectroscopy (Figure 3). Transient spectra of other DHD radical cations have been observed previously,[11] and these spectra exhibit behavior consistent with spectra generated by the aforementioned DBAHA process. In the

Scheme 1
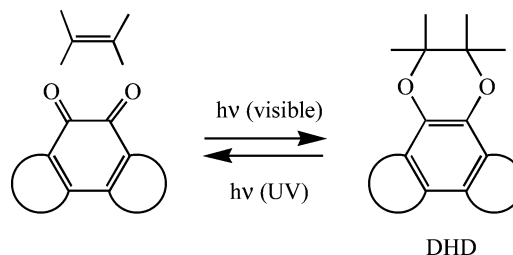
Scheme 2
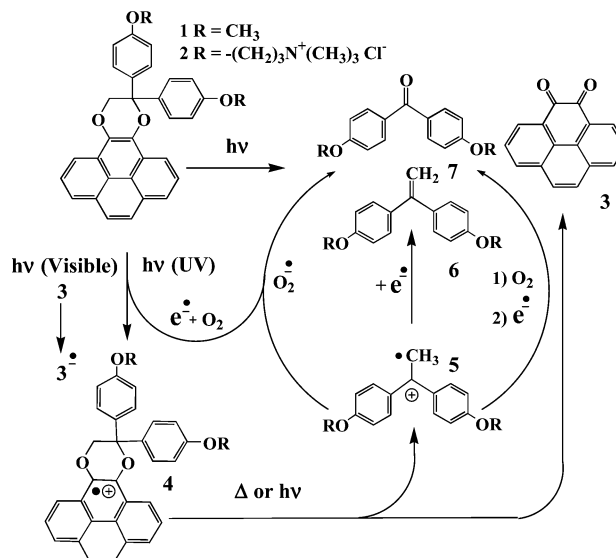
case of **4**, the very conspicuous band at $\lambda_{max} = 453$ nm can be observed by transient spectroscopy in a number of solvents. Many of these solvents, such as CCl$_4$, produce unidentified transients that tend to obscure the spectrum of **4**. However, in acetonitrile, a pristine spectrum of **4** is obtained, as shown in Figure 3. Under these conditions, the lifetime of **4** ($\tau = 6.3 \pm 0.1$ μs) tends to be much shorter than when it is generated using the DBAHA method. This is certainly due to the occurrence of reverse electron-transfer processes in the photosystem that are not active under the DBAHA conditions.

These observations are summarized in Scheme 2, where some possible pathways for the fragmentation of **4** are outlined. Thus, **4** probably extrudes **3** and the olefin-derived radical cation **5**, which might either acquire an electron by reverse electron transfer to form **6** or participate in a radical chain mechanism to generate another molecule of **4** by any of several possible routes.[12] Alternatively, **5** might react with molecular oxygen to form benzophenone **7**.[13] Some variation on these pathways is supported by the observation that olefin **6** and corresponding benzophenone **7** are formed as major products in these reactions.
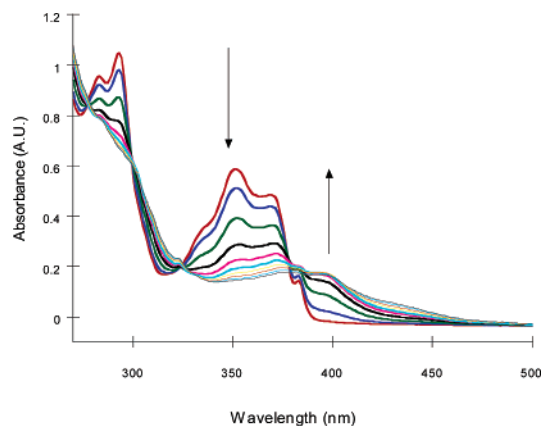
Figure 1. Absorption spectra of **1** upon UV irradiation (364 nm for 120 s) in CCl$_4$.
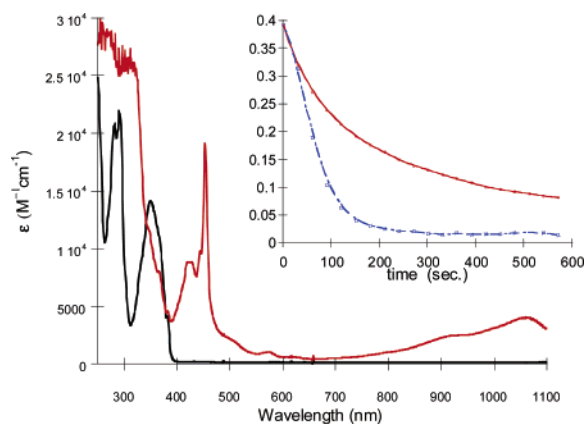

Figure 2. Absorption spectra of **1** (black) and its radical cation **4** (red) in hexanes/CH$_2$Cl$_2$ (98:2). Inset: normalized absorption (450 nm) of **4** as a function of time; thermal decay (red) and irradiation at 457−514 nm (blue).
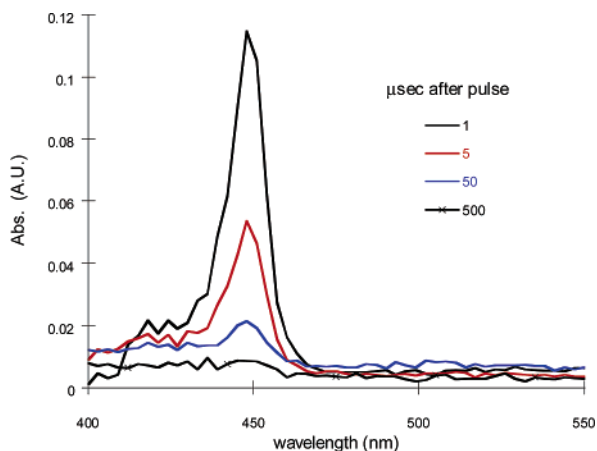

Figure 3. Transient absorption spectrum of radical cation **4** in ACN, generated with 350 nm irradiation.

On the basis of these observations, we are extending the study of this photochemistry into DNA cleaving agents that can undergo internally sensitized quinone release.[6c]

Supporting Information Available: Synthesis and characterization of **1** and **2**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(4) In this work, all irradiations were conducted with an argon ion laser: UV (364 nm) or all visible lines (457−514 nm).

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(7) (a) Yoon, K. B. *Chem. Rev.* **1993**, *93*, 321. (b) For a biological application, see: Dunn, D. A.; Lin, V. H.; Kochevar, I. E. *Biochemistry* **1992**, *31*, 11620−11625.

(8) Lu, C.-Y.; Yao, S.-D.; Lin, N.-Y. *Chem. Phys. Lett.* **2000**, *330*, 389−396.

(9) (a) Carle, A. B. A Mechanistic Investigation of the Photochemistry and Thermal Activation of 2,2- and 2,3-Diaryl, and 2,2,3-Triaryl-2,3-dihydrophenanthro[9,10-b]dioxins: A New Class of 1,4-Dioxene-based DNA Cleaving Agents. Ph.D. Thesis, University of Cincinnati, Cincinnati, OH, 2002. (b) Venkitachalam, S. Synthesis of Masked, Water-soluble Phenanthrenequinones as DNA Cleaving Agents and an Investigation of Possible Mechanisms for the Photochemical Release of Phenanthrenequinone. Ph.D. Thesis, University of Cincinnati, Cincinnati, OH, 1998.

(10) The radical cation of pyrene is well-known and characterized by a single intense, sharp band at ∼453 nm. For a transient spectrum of pyrene radical cation in solution (λ_{max} = 445 nm), see: (a) Schomburg, H.; Staerk, H.; Weller A. *Chemical Physics Lett.* **1973**, *22*, 1−4. For time-resolved diffuse reflectance specta in zeolites (λ_{max} = 450 nm), see: (b) Iu, K.-K.; Thomas, J. K. *J. Phys. Chem.* **1991**, *95*, 506−509. (c) Hashimoto, S. *Chem. Phys. Lett.* **1996**, *252*, 236−242. (d) Shida, T. *Electronic Absorption Spectra of Radical Ions*, Physical Science Data 34; Elsevier: Amsterdam, 1988. In contrast, absorption of protonated pyrene in a zeolite (H−Py$^+$) occurs at λ_{max} = 513 nm: (e) Liu, X.; Iu, K.-K.; Thomas, J. K.; He, H.; Klinowski, J. *J. Am. Chem. Soc.* **1994**, *116*, 11811−11818. Finally, **5**, which one might expect to observe under DBAHA conditions and has λ_{max} = 360 nm: (f) Al-Ekabi, H.; Kawata, H.; de Mayo, P. *J. Org. Chem.* **1988**, *53*, 1471−1474.

(11) The corresponding radical cation derived from the phenanthrenequinone DHD can be generated both thermally, with DBAHA, and photochemically but displays a broad relatively featureless absorption envelope extending from ∼450 to 750 nm. Transient studies were conducted by Monica Barra Guelph-Waterloo, Centre for Graduate Work in Chemistry and Biochemistry.

(12) Direct chain propagation is not very likely since **6** is more easily oxidized than **1** (E_{ox}(**6**) = +1.32 V, and E_{ox}(**1**) = +1.45 V, both vs an SCE): (a) Gollnick, K.; Schnatterer, A.; Utschick, G. *J. Org. Chem.* **1993**, *58*, 6049−6056. However, chains involving oxygen-containing intermediates (not shown in Scheme 2) are a distinct possibility: (b) Mattes, S. L.; Farid, S. In *Organic Photochemistry*; Padwa, A., Ed.; Marcel Dekker: New York, 1983; Vol. 6, pp 223−326.

(13) The yields of **6** and **7** are variable, depending upon reaction conditions, but are 14 and 10%, respectively, for a total of 24% at 4% conversion and 27% yield of **3** in acetonitrile. These pathways are particularly interesting since they may proceed through a dioxetane intermediate: Lakshminarasimhan, P.; Thomas, K. J.; Johnston, L. J.; Ramamurthy, V. *Langmuir* **2000**, *16*, 9360−9367. See also 12b, above. Dioxetane decomposition, in turn, will produce excited benzophenone, which could undergo hydrogen abstraction from the DNA causing strand cleavage. Thus, the quinone unmasking process might not only produce an embedded quinone that could cleave the DNA upon the further absorption of light but also produce an active DNA cleaving agent in the primary unmasking process, as well.

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