Structure−Kinetics Correlations in Isostructural Crystals of α-(ortho-Tolyl)-acetophenones: Pinning Down Electronic Effects Using Laser-Flash Photolysis in the Solid State

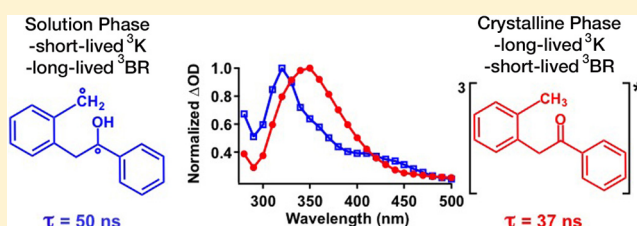Anoklase J.-L. Ayitou,[†] Kristen Flynn,[†] Steffen Jockusch,[‡] Saeed I. Khan,[†] and Miguel A. Garcia-Garibay*,[†]

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Ⓢ *Supporting Information*

ABSTRACT: Aqueous suspensions of nanocrystals in the 200−500 nm size range of isostructural α-(*ortho*-tolyl)-acetophenone (**1a**) and α-(*ortho*-tolyl)-*para*-methylacetophenone (**1b**) displayed good absorption characteristics for flash photolysis experiments in a flow system, with transient spectra and decay kinetics with a quality that is similar to that recorded in solution. In contrast to solution measurements, reactions in the solid state were characterized by a rate limiting hydrogen transfer reaction from the triplet excited state and a very short-lived biradical intermediate, which does not accumulate. Notably, the rate for δ-hydrogen atom transfer of **1a** (2.7×10^7 s^{-1}) in the crystalline phase is 18-fold larger than that of **1b** (1.5×10^6 s^{-1}). With nearly identical molecular and crystal structures, this decrease in the rate of δ-hydrogen abstraction can be assigned unambiguously to an electronic effect by the *para*-methyl group in **1b**, which increases the contribution of the $^3\pi,\pi^*$ configuration relative to the reactive ^{3}n,π^* configuration in the lowest triplet excited state. These results highlight the potential of relating single crystal X-ray structural data with absolute kinetics from laser flash photolysis.

Solution Phase
-short-lived ^{3}K
-long-lived ^{3}BR

Crystalline Phase
-long-lived ^{3}K
-short-lived ^{3}BR

τ = 50 ns

τ = 37 ns

INTRODUCTION

One of the long-standing and most promising objectives of solid state photochemistry is to correlate kinetic parameters with structural information from single crystal X-ray diffraction.[1,2] However, due to challenges in the determination of absolute kinetics in the solid state, this aim has remained elusive. In fact, optical analysis of species generated by pulsed-laser excitation in large single crystals and bulk powders are complicated by problems associated with their high optical densities, intense light scattering, multiphotonic events (such T−T annihilation), and interference by accumulated photo-products.[3] Knowing that crystals smaller than the wavelength of light can be suspended in water and behave as large supramolecular assemblies while retaining the structure of macroscopic crystals,[4] we showed that a promising approach to meet these challenges is based on the use of crystals in the 100−300 nm size range.[5] With a strongly diminished scattering and single excitations under low laser power, the resulting nanocrystalline suspensions may be used in a flow cell so that a fresh sample is exposed to every shot in a laser flash photolysis experiment.[6]

Hoping to document the effects of substituents on a solid state photoreaction, we explored the nanosecond spectroscopy and kinetics of crystalline α-(*ortho*-tolyl)-acetophenones **1a** and **1b** (Scheme 1).[7] These compounds are known to undergo an intramolecular hydrogen transfer reaction from their triplet excited states (^{3}K*) to form 1,5-biradicals (^{3}**1,5-BR**), which

Scheme 1
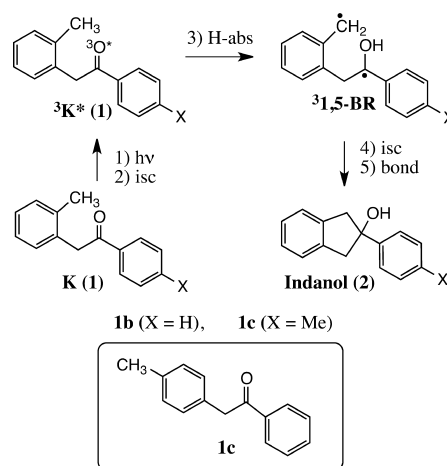
transform into the corresponding 2-hydroxy-indanols **2a** and **2b** in excellent chemical yields (Scheme 1). A notable feature of these ketones is that they have nearly identical conformations (Figure 1) and differ only by a *para*-methyl group (X = Me) in **1b**. We recognized that their isomorphism would provide us with an opportunity to quantify the electronic effect of the
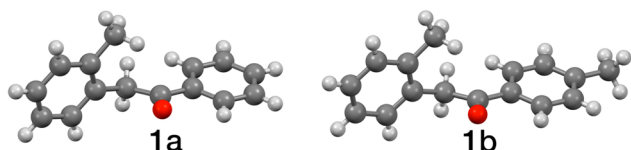
Figure 1. Molecular structures of ketones **1a** and **1b** illustrating their high similarity, which includes a suitable disposition for a δ-hydrogen transfer from the *ortho*-tolylmethyl group to the carbonyl oxygen.

para-methyl group,[8] which would be an excellent way to validate the broad potential of structure−kinetics correlation based on single crystal diffraction and kinetic studies based on suspended nanocrystals.

■ RESULTS AND DISCUSSION

In order to document the spectral characteristics of the triplet states, we also analyzed the aqueous crystalline suspension of α-(*para*-tolyl)-acetophenone (**1c**), which is unable to undergo the Norrish type II reaction. Ketones **1a**−**1c** were synthesized by $AlCl_3$-catalyzed Friedel−Crafts acylations using commercially available arylacetyl chlorides and benzene (**1a** and **1c**) or toluene (**1b**).[9] All three samples were purified by flash chromatography on silica gel and recrystallized from methylene chloride/pentane (1/10, v/v). X-ray diffraction data obtained from single crystals of **1a** and **1b** were solved in the space group $P2_1/c$ with remarkably similar molecular (Figure 1) and packing structures (Table 1).

**Table 1. Key Structural Parameters from Crystals of Ketones 1a and 1b**[a]

	1a	1b
mp [°C]	67−69	85−88
Space group (Z^b)	$P2_1/c$ (4)	$P2_1/c$ (4)
a [Å]	12.1826(10)	12.8879(11)
b [Å]	9.1323(7)	8.7706(7)
c [Å]	11.2711(11)	11.5969(10)
α, β, γ [deg]	90, 114.959(5), 90	90, 109.124(6), 90
η, θ, Δ [deg] (90, 180, 0)^c	78.3, 124.5, 69.3	76.9, 123.6, 72.8
d [Å] (2.5)^c	2.78	2.80

[a]Diffraction data acquired at 100 K. [b]Number of molecules per unit cell. [c]Please refer to Scheme 2 for the definition of these parameters. The values indicated in parentheses represent the "ideal" values according to Scheffer and Scott.[10]

Knowing that intramolecular hydrogen atom transfer in triplet ketones occurs from n,π^* excited states, and based on orbital and state correlation diagrams, Scheffer and Scott suggested that the rate of reaction should depend on the overlap between the transferring hydrogen atom and the n-orbital.[10] They suggested that an ideal ground state conformation would have angular ($\eta = 90°$, $\theta = 180°$, $\Delta = 0°$), and distance ($d = 2.5$ Å) parameters related to the best C−H···O=C orbital overlap, as indicated in Scheme 2.

A comparison of the geometric parameters reveals that the relation between the carbonyl oxygen and the closest transferrable δ-hydrogen in the case of **1a** and **1b** (Table 1) shows that they are very similar, with angles η, θ, and Δ that vary by less than 3.5° and C−H···O distances, d, that vary by 0.2 Å. Considering that these small differences fall within the range of molecular vibrational amplitudes captured by thermal ellipsoids at ambient temperatures,[11] one could expect that

Scheme 2

η, θ, Δ [°] Ideal: 90, 180, 0
d [Å] Ideal: 2.5 (Ref. 10)
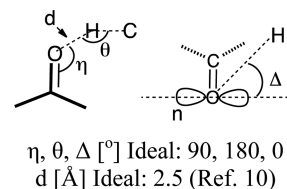
differences in reactivity between **1a** and **1b** could be related to the electronic influence of the *para*-methyl group (X = Me) in **1b** as compared to the aromatic hydrogen (X = H) in **1a**.

Nanocrystalline suspensions for the laser flash photolysis studies were prepared via the reprecipitation method[12] as described previously.[13] Dynamic light scattering (DLS) analyses showed mean particle sizes for **1a** and **1b** to be in 200−500 nm size range. While particles of **1c** were consistently larger, we were able to obtain reasonable transmission spectra. As illustrated for **1b** in Figure 2, a comparison of the powder X-
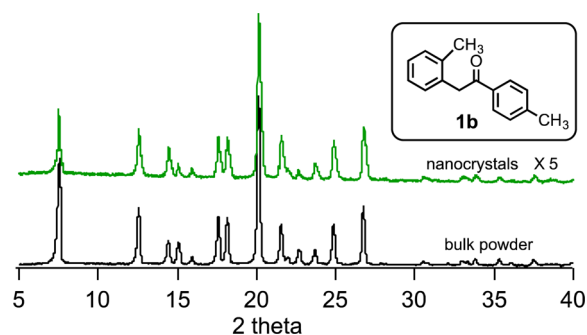

Figure 2. X-ray powder diffraction patterns of ketone **1b** obtained from bulk powder (bottom) and from nanocrystals collected by centrifugation of an aqueous suspension (top).

ray diffraction patterns (PXRD) of nanocrystalline samples collected by centrifugation and those obtained from powered single crystals confirmed that they both belong to the same polymorph (Figure 2). Similar results were obtained for **1a** and **1c**.

Nanocrystalline suspension prepared with a loading of 1.5 mg of ketone per 20 mL of water in the presence of submicellar (0.4×10^{-3} M) cetyltrimethylammonium bromide (CTAB) to passivate the crystal surfaces resulted in clear suspensions suitable for transmission UV−vis spectroscopic measurements. As shown in Figure 3 (and Figure S1), the spectrum obtained
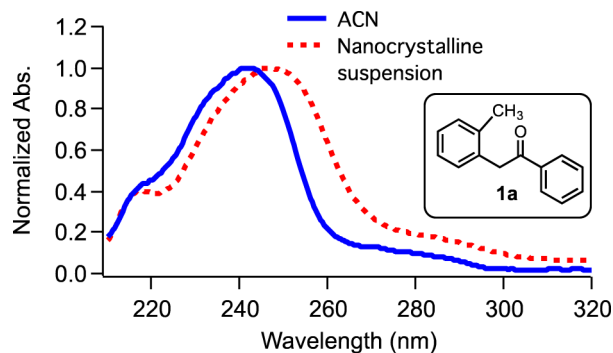

Figure 3. Transmission UV−vis spectra of **1a** in ACN and in an aqueous nanocrystalline suspension.

with nanocrystalline samples of **1a–c** are very similar to those obtained in acetonitrile (ACN), with the former being red-shifted by ca. 10 nm. Prior to laser flash photolysis measurements, and using a combination of ^{1}H NMR and GC analysis, we confirmed that the solid state photochemistry of **1a** and **1b** with nanocrystals matches the results with bulk solids previously reported by Wagner et al., with the formation of indanols **2a** and **2b** as the major photoproducts (ca. 90%) along with some unidentified minor components. Ready to explore the detection of the excited triplet states and biradical intermediates, we carried out transient absorption measurements with samples having an optical density of 0.3 at 266 nm. The fourth harmonic of a Nd:YAG laser was used as an excitation source. In order to avoid problems associated with the accumulation of photoproducts, all measurements were carried out in a flow system with the nanocrystalline suspension and solution samples pumped at a rate of 2–3 mL/min. Ketone **1c**, with no intramolecular H-abstraction pathway available in its structure was used as a test sample to determine the spectrum and kinetic characteristics of the acetophenone triplet in the solid state. The end-of-pulse spectrum obtained in acetonitrile (Figure 4A) is consistent with the one reported in
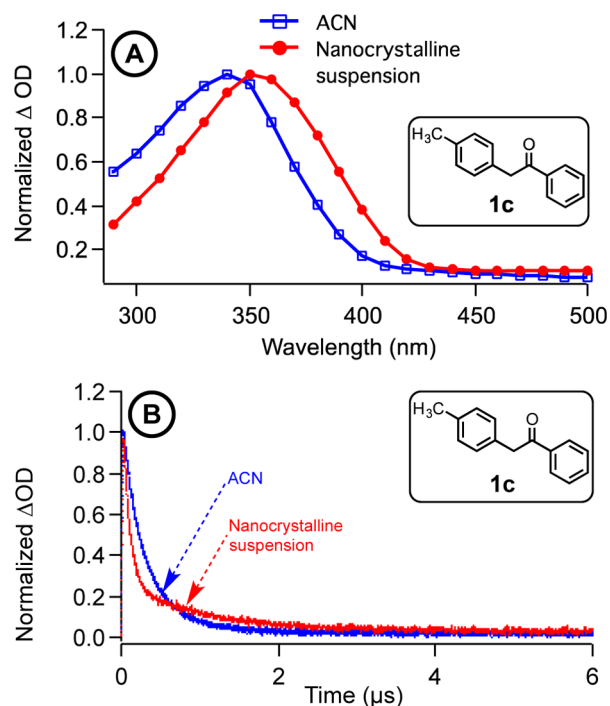
Shown in Figure 4B, the triplet decay of **1c** recorded in acetonitrile at 340 nm could be fit to a single exponential function with a lifetime of 308 ns, as expected for a triplet state that undergoes an α-cleavage reaction in a relatively low quantum yield.[16,17] By contrast, the triplet decay in the nanocrystalline suspension displayed significant heterogeneity, as is commonly observed for kinetic measurements in solids.[18] The data was fit to a double exponential function with a short-lived component of 88 ns and a long-lived component or 1.03 μs (Table 2).

Table 2. Laser Flash Photolysis-Derived Triplet and Biradical Lifetimes of α-(ortho-Aryl)-acetophenones

| | $\tau_{\text{triplet-state}}$ (ns) | | $\tau_{1,5\text{-biradical}}$ (ns) | |
ketone	ACN[a]	NC[b]	ACN[a]	NC[b]
1a	6[c]	37	50 and 650[e]	f
1b	ca. 70[d] (50 and 309)[e]	660	f	f
1c	ca. 308[d] (210 and 548)[e]	(88 and 1030)[e]	g	g

[a]Acetonitrile. [b]Nanocrystalline suspension. [c]Reference 18. [d]Single exponential fit. [e]Double exponential fit. [f]The triplet biradical was not observable. [g]Not applicable.

Knowing that the triplet excited state of ketone **1a** undergoes a hydrogen transfer reaction with a time constant of ca. 6 ns in solution,[19] which is shorter than the time resolution of our experimental setup, we assigned the end-of-pulse spectrum (blue open squares) in Figure 5A to the corresponding triplet 1,5-biradical (^{3}**1,5-BR**). As expected for a chromophore that has benzyl and benzylketyl radicals, the spectrum has a λ_{max} at 320 nm and decays with some heterogeneity with lifetimes of

Figure 4. (A) Triplet spectra of α-(para-tolyl)-acetophenone (**1c**) in ACN and as a nanocrystalline suspension. (B) Triplet decay kinetics detected at λ = 340 nm with residual corresponding to double exponential functions. (A_1 = 0.69 and τ_1 = 210 ns and A_2 = 0.31 and τ_2 = 548 ns for acetonitrile and A_1 = 0.79 and τ_1 = 88 ns and A_2 = 0.22 and τ_2 = 1030 ns for nanocrystals).

the literature with a λ_{max} at 340 nm and a spectral width covering from ca. 290 to 400 nm.[14] The spectrum obtained in the nanocrystalline suspension is an excellent match, but shows a red shift of ca. 10 nm. Furthermore, while the spectrum in solution is effectively quenched by molecular oxygen, the one obtained in the nanocrystalline suspension is not affected, as previously reported for nanocrystals of triplet benzophenones.[6b,15]
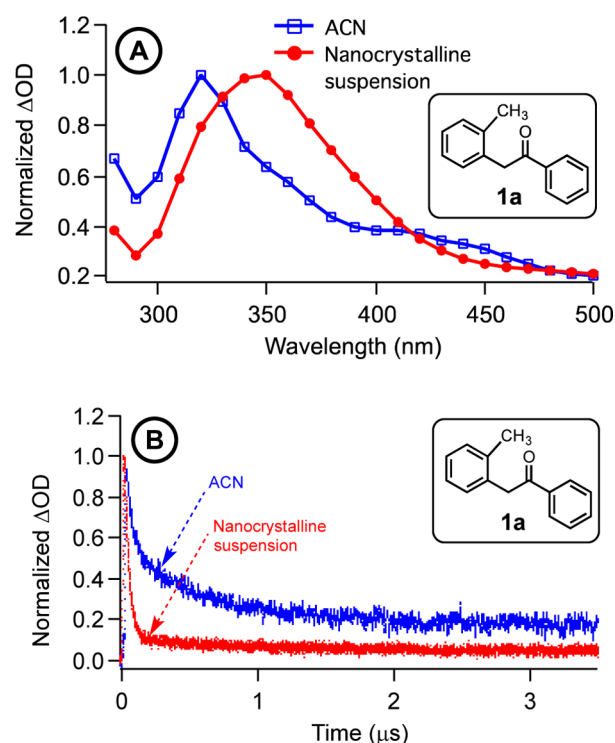

Figure 5. (A) Triplet absorption spectra (end-of-pulse) of α-(ortho-tolyl)-acetophenone (**1a**) in ACN (λ_{max} = 320 nm) and in nanocrystalline suspension (λ_{max} = 340 nm). (B) Triplet decay kinetics detected at the respective λ_{max}.

ca. 50 and 650 ns (Figure 5B, ACN; Table 2). The 50 ns component is associated with the time needed for the triplet biradical to intersystem cross to the singlet state, which is expected to form the expected photoproduct, rapidly. The observation of a long-lived component with τ = 650 ns is in good agreement with reports by Scaiano and Wagner and their co-workers of a transient species formed by secondary excitation of the triplet 1,5-biradical.[20,21]

Notably, the spectrum obtained in nanocrystals of **1a** (filled red circles in Figure 5A) has the distinctive characteristics of the triplet ketone excited state with λ_{max} at 350 nm. The transient decays with a time constant of 37 ns (Figure 5B, nanocrystals), consistent with a lifetime limited by the hydrogen transfer reaction and a 1,5-biradical that rapidly converts to product, without being able to accumulate. These observations indicate that the time constant for hydrogen transfer in crystals of **1a** is increased by a factor of ca. 6 (37 ns) compared with the time constant in solution (6 ns). These results are consistent with a favorable solid state hydrogen abstraction geometry (Figure 1) and would imply an accelerated rate of intersystem crossing for the 1,5-biradical in the solid state, which is in agreement with suggestions that biradicals with orthogonal p-orbitals facilitate intersystem crossing by a spin−orbit coupling mechanism.[22]

The similar solid state structural parameters for the *ortho*-tolyl ketones **1a** and **1b** suggest that they should have analogous chemical behavior. However, flash photolysis of *para*-methyl-substituted ketone **1b** carried out in ACN solution resulted in detection of a transient with a spectrum that corresponds to the triplet excited state (Figure S3), which has a lifetime of ca. 70 ns. This is consistent with a relatively strong electronic perturbation by the electron donating *para*-methyl group, which is known to render triplet arylketones less reactive as a result of an increased contribution of the $^3\pi,\pi^*$ state mixed with the reactive $^3n,\pi^*$ state configuration.

Measurements carried out in nanocrystalline samples also revealed a transient consistent with the triplet excited state ketone (Figure S3), which has a much longer hydrogen transfer time constant of ca. 0.66 μs (Figure 6). Taking these results
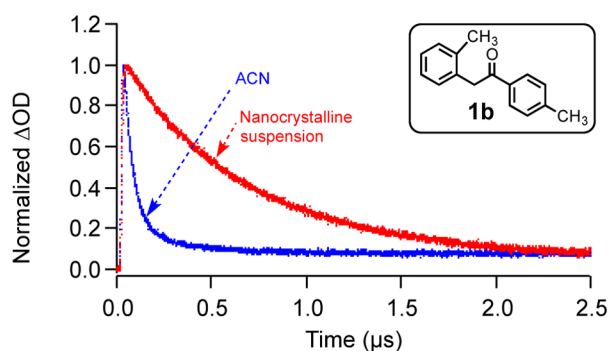

Figure 6. Triplet decay kinetics detected at the respective λ_{max} of α-(*ortho*-tolyl)-*para*-methylacetophenone (**1b**) in ACN (λ_{max} = 340 nm) and in nanocrystalline suspension (λ_{max} = 360 nm).

together, one can deduce that hydrogen transfer is the rate-limiting step for triplet decay in both solids and that the ^{3}**1,5-BR** must be able to intersystem cross and form the product with rates that are significantly greater than those observed in solution. Based on the structural similarity between **1a** and **1b**, one can assign the ca. 18-fold difference in H-transfer rates in the solid state to the effect of the *para*-methyl group on the electronic configuration of the triplet state. It is interesting to

point out that the rate of γ-hydrogen abstraction for the corresponding valerophenones in nonpolar benzene is reported to be 12.5×10^7 s^{-1} for the unsubstituted compound and 1.8×10^{-7} s^{-1} for the structure with the *para*-methyl group.[8] These correspond to a 6.9-fold difference, suggesting an electronic effect on the rate of reaction that is about half as large in solution compared with the one in the solid state.

CONCLUSION

We have confirmed that ketone crystals in the 200−500 nm size range form a stable, free-flowing aqueous suspension, which make it possible to do transmission spectroscopy in the UV−visible range. Taking advantage of laser flash photolysis with nanocrystalline isostructural samples of two α-(*ortho*-tolyl)acetophe-nones, we were able to determine the rates of hydrogen atom transfer, which vary from 2.7×10^7 s^{-1} for the parent acetophenone chromophore to 1.5×10^6 s^{-1} for the acetophenone with a *para*-methyl group. An 18-fold rate difference between the two compounds can be associated with the electronic effect of the methyl group, which alters the configuration of the triplet excite state. These results bode well for structure−kinetic correlations based on single crystal X-ray diffraction and laser flash photolysis data.

ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b11657.

Synthesis and characterization of ketones **1a**−**1c**, dynamic light scattering (DLS) data, UV−Vis absorption and laser flash photolysis absorption, and kinetics measurements (PDF)
Crystallographic structure of **1a** (CIF)
Crystallographic structure of **1b** (CIF)

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Notes
The authors declare no competing financial interest.

ACKNOWLEDGMENTS

REFERENCES

(1) (a) Schmidt, G. M. *Solid State Photochemistry*; Verlag Chemie: New York, 1976. (b) Hollingsworth, M. D.; McBride, J. M. *Adv. Photochem.* **1990**, *15*, 279. (c) Scheffer, J. R.; Garcia-Garibay, M.; Nalamasu, O. *Org. Photochem.* **1987**, *8*, 249. (d) Ramamurthy, V.; Venkatesan, K. *Chem. Rev.* **1987**, *87*, 433.

(2) An approach based on laser excitation of single crystal and X-ray diffraction detection to follow changes in real time also gaining momentum: (a) Techert, S. *Crystallogr. Rev.* **2006**, *12*, 25. (b) Makal, A.; Benedict, J. B.; Trzop, E.; Sokolow, J.; Fournier, B.; Chen, Y.; Kalinowski, J. A.; Graber, T.; Henning, R.; Coppens, P. *J. Phys. Chem. A* **2012**, *116*, 3359. (c) Coppens, P.; Zheng, S.-L. *Supramolecular Photochemistry: Controlling Photochemical Processes*; Ramamurthy, V., Inoue, Y., Eds.; John Wiley & Sons: Hoboken, NJ, 2011.

(3) (a) Wilkinson, F.; Willsher, C. J. *Appl. Spectrosc.* **1984**, *38*, 897. (b) Wilkinson, F. *J. Chem. Soc., Faraday Trans. 2* **1986**, *82*, 2073.

(4) (a) Kasai, H.; Nalwa, H. S.; Oikawa, H.; Okada, S.; Matsuda, H.; Minami, N.; Kakuta, A.; Ono, K.; Mukoh, A.; Nakanishi, H. *Jpn. J. Appl. Phys.* **1992**, *31*, L1132. (b) Baba, K.; Kasai, H.; Okada, S.; Oikawa, H.; Nakanishi, H. *Opt. Mater.* **2003**, *21*, 591−594.

(5) Chin, K. K.; Natarajan, A.; Campos, L. M.; Johansson, E.; Shepherd, H.; Garcia-Garibay, M. A.; Gard, M. N. *Chem. Commun.* **2007**, *41*, 4266.

(6) (a) Lebedeva, N. V.; Tarasov, V. F.; Resendiz, M. J. E.; Garcia-Garibay, M. A.; White, R. C.; Forbes, M. D. E. *J. Am. Chem. Soc.* **2010**, *132*, 82. (b) Simoncelli, S.; Kuzmanich, G.; Gard, M. N.; Garcia-Garibay, M. A. *J. Phys. Org. Chem.* **2010**, *23*, 376.

(7) (a) Zand, A.; Park, B.-S.; Wagner, P. J. *J. Org. Chem.* **1997**, *62*, 2326. (b) Wagner, P. J.; Zand, A.; Park, B.-S. *J. Am. Chem. Soc.* **1996**, *118*, 12856.

(8) (a) Wagner, P. J.; Kemppainen, A. E.; Schott, H. N. *J. Am. Chem. Soc.* **1973**, *95*, 5604. (b) Wagner, P. J.; Truman, R. J.; Scaiano, J. C. *J. Am. Chem. Soc.* **1985**, *107*, 7093.

(9) See Supporting Information, section S8.

(10) Scheffer, J. R.; Scott, C. In *CRC Handbook of Organic Photochemistry and Photobiology*; Hospool, W., Lenci, F., Eds.; CRC Press: Boca Raton, FL, 2004; p 54-1.

(11) Bürgi, H.-B.; Capelli, S. C. *Helv. Chim. Acta* **2003**, *86*, 1625.

(12) Kasai, H.; Nalwa, H. S.; Oikawa, H.; Okada, S.; Matsuda, H.; Minami, N.; Kakuta, A.; Ono, K.; Mukoh, A.; Nakanishi, H. *Jpn. J. Appl. Phys.* **1992**, *31*, L1132.

(13) Veerman, M.; Resendiz, M. J. E.; Garcia-Garibay, M. A. *Org. Lett.* **2006**, *8*, 2615.

(14) (a) Lutz, H.; Breheret, E.; Lindqvist, L. *J. Phys. Chem.* **1973**, *77*, 1758. (b) Samanta, S.; Mishra, B. K.; Pace, T. C. S.; Sathyamurthy, N.; Bohne, C.; Moorthy, J. N. *J. Org. Chem.* **2006**, *71*, 4453. (c) Wismontski-Knittel, T.; Kilp, T. *J. Phys. Chem.* **1984**, *88*, 110. (d) Netto-Ferreira, J. C.; Scaiano, J. C. *J. Photochem. Photobiol., A* **1988**, *45*, 109. (e) Wilkinson, F.; Willsher, C. J.; Casal, H. L.; Johnston, L. J.; Scaiano, J. C. *Can. J. Chem.* **1986**, *64*, 539.

(15) Kuzmanich, G.; Simoncelli, S.; Gard, M. N.; Spänig, F.; Henderson, B. L.; Guldi, D. M.; Garcia-Garibay, M. A. *J. Am. Chem. Soc.* **2011**, *133*, 17296.

(16) As reported in ref 17, the quantum yield of α-cleavage for **1c** in benzene is 0.1, and it is known to be smaller in polar solvents. We could not detect any product formation in acetonitrile.

(17) Lewis, F. D.; Hoyle, C. H.; Magyar, J. G.; et al. *J. Org. Chem.* **1975**, *40*, 488.

(18) Albery, W. J.; Bartlett, P. N.; Wilde, C. P.; Darwent, J. R. *J. Am. Chem. Soc.* **1985**, *107*, 1854.

(19) The rate of hydrogen abstraction of **1a** in benzene is 1.6×10^8 s^{-1}: Wagner, P. J.; Wang, L. *Org. Lett.* **2006**, *8*, 645.

(20) Wagner, P. J.; Hasegawa, T.; Zhou, B.; Ward, D. L. *J. Am. Chem. Soc.* **1991**, *113*, 9640.

(21) Scaiano, J. C.; Wagner, P. J. *J. Am. Chem. Soc.* **1984**, *106*, 4626.

(22) (a) Ounsworth, J.; Scheffer, J. R. *J. Chem. Soc., Chem. Commun.* **1986**, 232. (b) Scheffer, J. R.; Dzakpasu, A. A. *J. Am. Chem. Soc.* **1978**, *100*, 2163. (c) Ariel, S.; Evans, S. V.; Garcia-Garibay, M. A.; Harkness, B. R.; Omkaram, N.; Scheffer, J. R.; Trotter, J. *J. Am. Chem. Soc.* **1988**, *110*, 5591. (d) Turro, N. J.; Weiss, D. S. *J. Am. Chem. Soc.* **1968**, *90*, 2185. (e) Wagner, P. J. *Top. Curr. Chem.* **1976**, *66*, 1.