

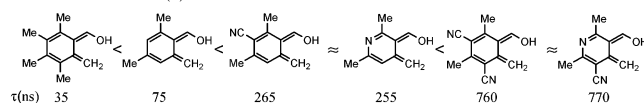
## Substituent Electronic Effects on the Persistence and Absorption Spectra of (*Z*)-*o*-Xylylenols. A Nanosecond Laser Flash Photolysis Study

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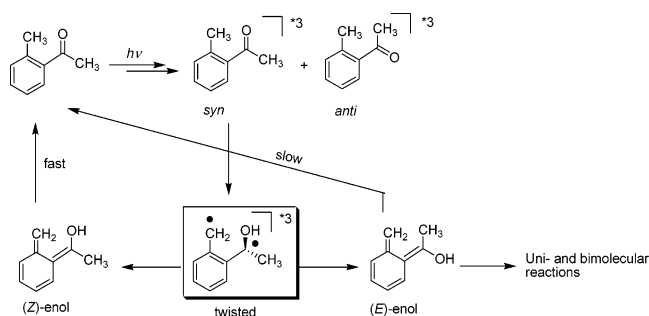
Order of the lifetimes of (*Z*)-enols:



A systematic investigation on a broad set of aldehydes reveals that the lifetimes of (*Z*)-photoenols can be modulated by variation of the substituents. We have found that the lifetimes of (*Z*)-enols (in benzene) can be varied by more than 1 order of magnitude with a judicious choice of the substituents that exert mesomeric and inductive effects as, for example, in the case of pentamethylbenzaldehyde ( $\tau = 35$  ns) and dicyanomethylaldehyde ( $\tau = 760$  ns). This study thus points to the fact that the electronic factors in conjunction with hydrogen bonding stabilization can considerably broaden the uni- as well as bimolecular chemistry based on photoenolization. Further, we have shown that the photoenols exhibit dramatic shifts in their absorption properties with variation of the substituents; although the photoenols have long been considered to be colored, their absorption properties have not been heretofore comprehensively examined.

After the finding by Yang and Rivas<sup>1</sup> that benzophenones containing an alkyl group at the *o*-position undergo intramolecular hydrogen transfer under the influence of light to yield dienols, the mechanism of photoenolization has been extensively investigated.<sup>2</sup> The presently accepted mechanism with regard to *o*-methylacetophenone, a representative *o*-alkylphenyl ketone, constitutes the following (Scheme 1):<sup>3–6</sup> intersystem crossing from the singlet-excited state leads to two conformationally isomeric *syn* and *anti* triplets. Whereas the *syn* triplet undergoes  $\gamma$ -hydrogen abstraction from the *o*-methyl group with a rate constant of  $>10^9$  s<sup>-1</sup>, the *anti* triplet has time to undergo competitive reactions before it can

SCHEME 1



get into the *syn* geometry from where it can undergo enolization; the bond rotation is solvent-dependent and thus determines the lifetime of the *anti* rotamer and its rate of enolization. Hydrogen abstraction by the *syn* triplet results in the formation of a 1,4-biradical, which is considered to be equivalent to a triplet-excited enol. Both Wirz<sup>3b</sup> and Scaiano<sup>6</sup> have identified the triplet-excited enol via direct detection of its absorption and based on the growth of the transient due to paraquat cation radical resulting from electron transfer, respectively. The triplet enol has been found to have a lifetime of ca. 530 ns in wet acetonitrile and resembles unconjugated type II biradicals in both its lifetime and reactivity. Spin inversion leads to two ground-state enols, i.e., *Z* and *E*. While the (*Z*)-enol is shorter-lived (ca. 1  $\mu$ s in nonpolar solvents), the (*E*)-enol is sufficiently long-lived (millisecond range) to lend itself to uni- and bimolecular reactions.<sup>2,7</sup> The shorter lifetime in the former case has been rationalized in terms of an extremely rapid [1,5]-sigmatropic hydrogen shift, which leads to regeneration of the precursor ketone.

The photoenols, referred to also as *o*-xylylenols when derived specifically from *o*-alkylphenyl carbonyl compounds,<sup>8</sup> may in principle undergo thermal conrotatory cyclization to synthetically useful benzocyclobutenols<sup>9</sup> or react with dienophiles in a Diels–Alder cycloaddition fashion.<sup>2,7</sup> The vast thermal cyclization as well as bimolecular cycloaddition chemistry known to date is tenable with the configuration of the photoenol being “*E*”. The (*Z*)-enols have long remained elusive. Wirz and Wagner demonstrated in their seminal laser flash photolysis study that the lifetimes of (*Z*)-enols can be significantly increased via *hydrogen-bonding* to polar protic/aprotic

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(1) Yang, N. C.; Rivas, C. *J. Am. Chem. Soc.* **1961**, 83, 2213.

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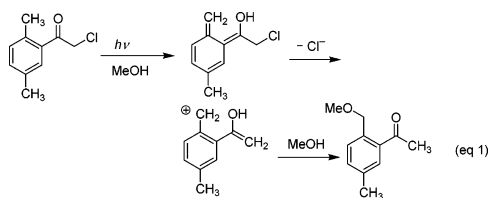
(b) Hagg, R.; Wirz, J.; Wagner, P. *J. Helv. Chim. Acta* **1977**, 60, 2595.

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(5) (a) Das, P. K.; Scaiano, J. C. *J. Photochem.* **1980**, 12, 85. (b) Small, R. D., Jr.; Scaiano, J. C. *J. Am. Chem. Soc.* **1977**, 99, 7713.

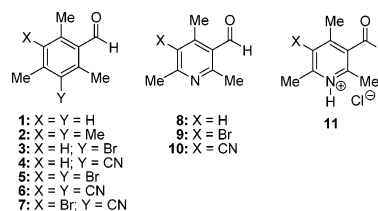
(6) Das, P. K.; Encinas, M. V.; Small, R. D., Jr.; Scaiano, J. C. *J. Am. Chem. Soc.* **1979**, 101, 6965.

solvents, yet the synthetic utility of (*Z*)-enols was considered remote.<sup>3b</sup> In a most recent work that focuses on exploitation of photoenolization toward the development of photoremovable protecting groups, Pelliccioli et al.<sup>10</sup> have shown for the first time that predominant reactivity in the case of *o*-methylphenacyl halides (eq 1) emanates from (*Z*)-enols when generated in polar protic solvents under aerobic conditions due to longer lifetimes.<sup>11</sup>



The lifetimes of (*E*)-enols have also been shown to be crucial for efficient photodeprotection of alcohols from benzophenone esters.<sup>12,13</sup> In fact, the success of bimolecular trapping reactions also appears to be determined by the lifetimes of the photoenols, which are influenced by the substituents.<sup>14</sup> This dependence of the reactivity on the lifetimes and our own recent work on the solid-state photochemistry of *o*-methylaromatic aldehydes,<sup>15</sup> which has led us to uncover remarkable effects of electronic and hydrogen-bonding factors on the solid-state lifetimes of (*E*)-enols,<sup>16</sup> spurred us to undertake the present investigation. Accordingly, we defined the following two objectives. First, to examine the extent to which *electronic factors* alone modulate the lifetimes of photoenols; while considerable enhancement via *hydrogen-bonding* to the polar protic/aprotic solvents has been demonstrated, the influence of *electronic factors* remains singularly unexplored. Second, to explore the manifestation of variations in the electronic factors on the absorption properties of photoenols, which are, in general, considered to be colored intermediates, but have surprisingly not been examined for their absorption properties in a comprehensive manner thus far. Herein, we report our results of a laser flash photolysis study of (*Z*)-enols derived from a broad set of sterically hindered mesitaldehydes **1–7** and their het-

## CHART 1



eroaromatic analogues **8–11** (Chart 1). Our preference for mesitaldehydes was dictated by their convenient synthetic access<sup>15</sup> as well as the lifetimes of the derived (*Z*)-enols, which are in the nanosecond–microsecond range and are therefore (i) accessible by nanosecond laser flash photolysis and (ii) readily discriminated from the longer-lived (*E*)-enols.

The commercially available (Fluka) mesitaldehyde **1** was distilled prior to its use, and the crystalline pentamethylbenzaldehyde **2** was used as received. All other aldehydes were available from our recent work.<sup>15</sup> The nanosecond time-resolved laser flash photolysis (308-nm excitation) of all of the aldehydes **1–11** was carried out in benzene as an inert nonpolar solvent. Although the lifetimes of (*Z*)-*o*-xylylenols in benzene ( $<1 \mu\text{s}$ ) are shorter than that in polar and protic solvents,<sup>3b</sup> the substituent electronic effects could be more reliably determined, since bimolecular reactions, including acid–base-catalyzed reactions,<sup>17</sup> are less likely to compete on this time scale in a nonpolar solvent. As an exception, acetonitrile was employed to probe the absorption characteristics in the case of the salt **11** due to insufficient solubility in benzene.

The solutions of aldehydes **1–10** in benzene (ca. 0.2–0.4 mM) were saturated with oxygen by purging for ca. 10 min prior to flash photolysis. In oxygenated solutions, the triplet species (i.e., triplet ketone and the triplet biradical)<sup>3b</sup> are efficiently quenched, such that the corresponding absorptions disappear from the transient spectra, leaving only the characteristic absorptions responsible for *o*-xylylenols to allow a straightforward data analysis. This approach to extract enol lifetimes and spectra has been previously successfully applied to *o*-methylacetophenone.<sup>3b</sup> Figure 1 shows typical transient absorption observed for a solution (ca. 0.2 mM) of mesitaldehyde **1** in benzene under nitrogen- and oxygen-saturated conditions. As can be seen, the absorptions assigned to triplet aldehyde and the triplet biradical at ca. 330 and 350 nm, respectively, in the absence of oxygen disappear when the spectra are recorded in O<sub>2</sub>-saturated solutions. A similar spectral simplification was uniformly observed for all aldehydes.

To further reduce the residual influence of the triplet aldehyde and the triplet biradical absorptions, the transient decays were monitored at wavelengths 20–30 nm longer than the maximum. The decays were found to be biexponential for all of the aldehydes. Whereas one of the components decayed in the time scale of nanoseconds, the second component was found to be very long-lived (several microseconds).<sup>18</sup> These fast- and slow-decaying components in all of the cases were assigned to (*Z*)- and

(10) Pelliccioli, A. P.; Klán, P.; Zabadal, M.; Wirz, J. *J. Am. Chem. Soc.* **2001**, *123*, 7931.

(11) This is particularly important if the photodeprotection must be carried out under aerobic conditions; in the presence of oxygen, predominant reactivity from the singlet-excited state leads specifically to the formation of (*Z*)-enols, while the triplet-excited state and the triplet biradicals responsible for photoenols are quenched by molecular oxygen.

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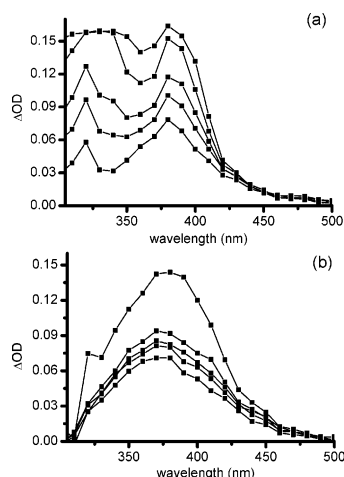
(13) For photodeprotections based on photoenolization, see: (a) Pika, J.; Konosonoks, A.; Robinson, R. M.; Singh, P. N. D.; Gudmundsdóttir, A. D. *J. Org. Chem.* **2003**, *68*, 1964. (b) Klán, P.; Pelliccioli, A. P.; Pospisil, T.; Wirz, J. *Photochem. Photobiol. Sci.* **2002**, *1*, 920–923. (c) Litérák, J.; Wirz, J.; Klán, P. *Photochem. Photobiol. Sci.* **2005**, *4*, 43. (d) Atemnkeng, W. N.; Louisiana, L. D., II; Yong, P. K.; Vettero, B.; Banerjee, A. *Org. Lett.* **2003**, *5*, 4469.

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(16) In the solid state, the molecular stacking and crystal lattice forces mask the true effects of hydrogen bonding and electronic factors and thus preclude assessment of lifetimes as well as the absorption properties in a rational manner.

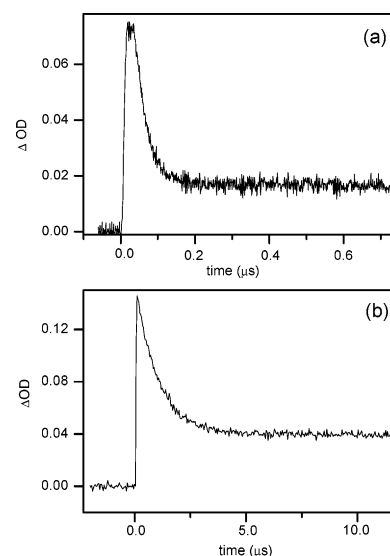
(17) Scaiano, J. C.; Wintgens, V.; Netto-Ferreira, J. C. *Tetrahedron Lett.* **1992**, *33*, 5905.



**FIGURE 1.** Transient absorption spectra obtained by 308-nm laser flash photolysis of mesitaldehyde **1** in  $N_2$ -purged (a) and  $O_2$ -saturated (b) benzene; the spectra were recorded after delay intervals of 0.1, 0.3, 0.7, 1.1, and 2.5  $\mu s$ . Notice the simplification of the transient absorption spectra upon purging with  $O_2$ .

(*E*)-enols, respectively. The typical decay profiles recorded for two of the aldehydes (i.e., **2** and **6**) are shown in Figure 2. The lifetimes of the (*Z*)-enols determined under both  $N_2$ - and  $O_2$ -purged conditions were found to be comparable (as well as the related absorbances), attesting to the fact that molecular oxygen does not affect the lifetimes as has been shown previously.<sup>3b</sup> Consolidated in Table 1 are the lifetimes assigned to (*Z*)-photoenols. Also recorded in Table 1 are their absorption maxima. It should be noted that, during the spectral acquisition as well as transient decay measurements, the solutions, after a few laser shots, were periodically replaced with fresh ones to exclude spectral and temporal variations related to secondary photolysis of photoproducts; however, except for variations in the signal intensity, no significant changes were observed.

A perusal of the results in Table 1 shows that the increasing methyl substitution leads to a substantial reduction in the lifetimes of (*Z*)-enols; whereas the photoenol derived from mesitaldehyde lives for 75 ns, the lifetime in the case of pentamethylbenzaldehyde **2** decreases to 35 ns. Remarkable is the influence of cyano substitution. Relative to mesitaldehyde **1**, monosubstitution as in **4** leads to an increase by ca. 200 ns, while disubstitution as in **6** raises the lifetime further to 760 ns. In a noteworthy contrast, bromo-substitution appears



**FIGURE 2.** Typical biexponential decays observed for the transients attributed to (*Z*)- and (*E*)-photoenols derived from (a) pentamethylbenzaldehyde **2** and (b) dicyanomethylaldehyde **6** upon 308-nm laser flash photolysis in  $O_2$ -saturated benzene.

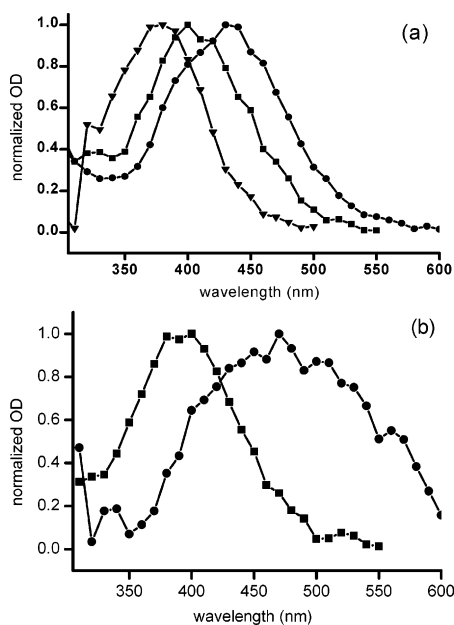
**TABLE 1. Lifetimes and Absorption Maxima Assigned to (*Z*)-Enols Obtained by Laser Flash Photolysis of Aromatic Aldehydes 1–11**

aldehyde	lifetime (ns) <sup>a</sup>	$\lambda_{max}$ (nm) <sup>b</sup>
mesitaldehyde ( <b>1</b> )	75	375
pentamethylbenzaldehyde ( <b>2</b> )	35	380
3-bromomesitaldehyde ( <b>3</b> )	95	385
3-cyanomesitaldehyde ( <b>4</b> )	265	400
3,5-dibromomesitaldehyde ( <b>5</b> )	125	375
3,5-dicyanomethylaldehyde ( <b>6</b> )	760	430
3-cyano-5-bromomesitaldehyde ( <b>7</b> )	300	400
2,4,6-collidine-3-carboxaldehyde ( <b>8</b> )	255	385
	[5800] <sup>c</sup>	[395] <sup>c</sup>
5-bromo-2,4,6-collidine-3-carboxaldehyde ( <b>9</b> )	225	385
5-cyano-2,4,6-collidine-3-carboxaldehyde ( <b>10</b> )	770	420
3-formyl-2,4,6-trimethylpyridinium hydrochloride ( <b>11</b> )	[8300] <sup>c</sup>	[470] <sup>c</sup>

<sup>a</sup> The lifetimes in  $O_2$ -saturated  $C_6H_6$  solutions, error  $\pm 10$  ns, or 10%, whichever is larger. <sup>b</sup> Maximum of the absorption band assigned to (*Z*)-*o*-xylylenol, error  $\pm 10$  nm. <sup>c</sup> Data in square brackets refer to values in  $O_2$ -saturated  $CH_3CN$  solution.

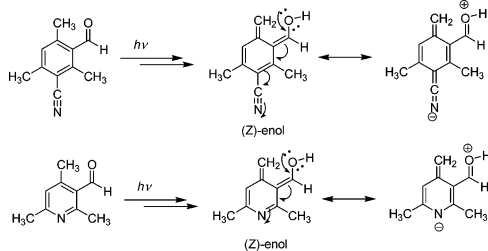
to exert only a marginal and less significant influence as reflected by the lifetimes of the (*Z*)-enols of 3-bromomesitaldehyde **3** and 3,5-dibromomesitaldehyde **5**. Strikingly, the lifetime of the enol obtained from 2,4,6-collidine-3-carboxaldehyde **8** is comparable to that of the enol obtained from cyanomesitaldehyde **4**. Evidently, the endocyclic nitrogen stabilizes the (*Z*)-enol to an equal extent as does the cyano-substituent in **4**. In line with this interpretation, the (*Z*)-enol of the cyano-substituted 2,4,6-collidine-3-carboxaldehyde **10** exhibits a lifetime, which is remarkably comparable to that derived from dicyanomethylaldehyde **5**. In accordance with these substituent electronic effects (cyano group versus endocyclic nitrogen), the absorption spectral features of "comparable" enols are also very similar. Note also the vastly red-shifted and broad absorption as well as the lengthened lifetime observed in the case of the salt of pyridine-3-carboxaldehyde **11** when compared to its precursor **8** (Figure 3). Due to solubility reasons, this comparison

(18) Exceptions were aldehydes **3** and **4**, in which an additional third exponent with a lifetime of ca. 3–5  $\mu s$  needed to be included; this was tentatively assigned to the formation of a regioisomeric enol, which is possible for these substrates as well as for aldehydes **7–11** due to their lower symmetry. It is likely that the lifetimes for the two regioisomeric (*Z*)-enols in the case of **7** are comparable such that no third component was observed. A similar absence of a third component in all of the pyridine derivatives **8–11** is presumably due to preferential formation of one regioisomeric (*Z*)-enol via H-abstraction from the methyl group at the fourth position. It is noteworthy that ab initio calculations (6-31G\*\*) for analogous 2,6-dichloro-4-methylpyridine-3-carboxaldehyde (cf. Sarkar, T. K.; Ghosh, S. K.; Moorthy, J. N.; Fang, J.-M.; Nandy, S. K.; Sathyamurthy, N.; Chakraborty, D. *Tetrahedron Lett.* **2000**, *41*, 6909) as well as X-ray crystallographic analysis<sup>15c</sup> of aldehyde **10** have indeed revealed a preference for the formyl oxygen to orient toward the methyl group at the fourth position such that only one regioisomeric enol may result.



**FIGURE 3.** Comparison of the normalized absorption spectra of (*Z*)-enols obtained by 308-nm laser flash photolysis of (a): mesitaldehyde **1** (▼), 3-cyanomesitaldehyde **4** (■), and 3,5-dicyanomesitaldehyde **6** (●), and (b): 2,4,6-collidine-3-carboxaldehyde **8** (■) and its HCl salt **11** (●). Notice the shifts in the absorption maxima.

#### SCHEME 2



needs to be made in acetonitrile as the solvent (values in square brackets in Table 1).

What is the origin of stabilization of the photoenols? We have previously related the stabilization of photoenols to mesomeric effects as exhibited in Scheme 2 involving delocalization of the lone pairs of one of the regioisomeric enols;<sup>15c</sup> of course, a similar mesomeric effect applies for the other isomer as well. This stabilizing resonance effect, which manifests itself also in the absorption spectra (Figure 3), is clearly reflected in the lifetimes of the (*Z*)-enols derived from cyano-substituted and heteroatom-containing aldehydes, most pronounced for the strongly electron-withdrawing protonated nitrogen in the pyridinium ion **11**, cf. Scheme 2. The opposite (i.e., a destabilizing influence) emerges for groups with positive inductive effect; in these cases, like for the enol derived from **2**, the (*Z*)-enol lifetime is shortened, although the absorption maximum is not significantly shifted (Table 1). The influence of halogens at meta positions, for which both inductive and resonance effects operate and may balance each other, is only marginal on the enol lifetimes (75, 95, and 125 ns for **1**, **3**, and **5**, respectively) with no perceptible influence on their absorption spectra. In contrast, the absorption maximum shifts from 380 nm

for the (*Z*)-enol of pentamethylbenzaldehyde **2** to ca. 420–430 nm for that in the case of dicyanomesitaldehyde **4** and its heteroatom “analogue” **10**. Evidently, substitution modifies the electronic nature of the enols leading to shorter or longer lifetimes and hypsochromically or bathochromically shifted absorptions, respectively. Thus, the strategy involving stabilization of (*Z*)-enols via electronic factors in conjunction with the previously documented hydrogen bonding<sup>3b</sup> should be important in (i) realizing heretofore unprecedented bimolecular trapping reactions of (*Z*)-enols and (ii) increasing the potential of photodeprotection protocols,<sup>19</sup> under aerobic conditions, based on (*Z*)-photoenols,<sup>10,13</sup> which are putatively generated from the singlet-excited states. Further, as the absorption characteristics of (*E*)-enols are virtually indistinguishable from those of the (*Z*)-enols, the remarkable changes uncovered herein for the latter with variation of substituents should facilitate the design and development of photochromic materials<sup>20</sup> based on photoenolization.<sup>21</sup>

In conclusion, a systematic investigation on a broad set of aldehydes reveals that the lifetimes of (*Z*)-photoenols can be modulated by a variation of the substituents. We have found that the lifetimes of (*Z*)-enols can be varied by more than 1 order of magnitude with a judicious choice of the substituents that exert mesomeric and inductive effects as, for example, in the case of pentamethylbenzaldehyde ( $\tau = 35$  ns) and dicyanomesitaldehyde ( $\tau = 760$  ns). Thus, the electronic factors in conjunction with hydrogen bonding stabilization may increase the potential of uni- as well as bimolecular chemistry based on photoenolization. It is further shown that substituents exert a dramatic influence on the absorption properties of photoenols, which have long been considered to be colored.

#### Experimental Section

With the exception of the commercially available aldehydes **1** and **2**, all other aldehydes (**3–11**) were available from our recent work.<sup>15</sup>

The transient experiments were carried out with an LKS.60/S nanosecond laser flash photolysis spectrometer (Applied Photophysics) by using a GSI Lumonics Pulsemaster PM-846 excimer laser running on XeCl for excitation (308 nm, ca. 150 mJ pulse energy, 15-ns pulse width). The transient data were recorded with a 54830B 600 MHz Infiniium oscilloscope (Agilent Technologies) and processed with the instrument-own software. Transient spectra were recorded in a step-scan mode with 5-/10-nm intervals. Samples (ca. 3 mL) were prepared in fused long-neck quartz cuvettes to allow bubbling with oxygen gas for 10–15 min. The optical density of all samples was adjusted to  $0.4 \pm 0.1$  at 308 nm.

**Acknowledgment.** J.N.M. is thankful to AvH Foundation for supporting the collaborative effort at the International University Bremen, Germany, and to the Department of Science and Technology (DST), India, for generous financial support.

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