

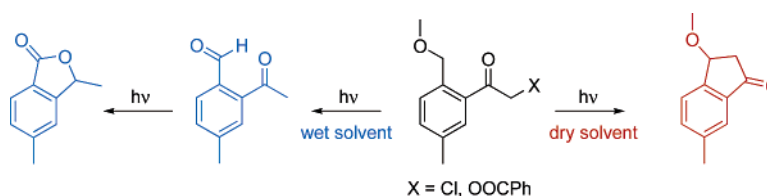
Photochemistry of 2-Alkoxyethyl-5-methylphenacyl Chloride and Benzoate

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Irradiation of 2-(alkoxymethyl)-5-methyl- α -chloroacetophenones (**1a–c**) and 2-(methoxymethyl)-5-methylphenacyl benzoate (**1d**) in dry, nonnucleophilic solvents afforded 3-alkoxy-6-methylindan-1-ones (**3a–c**) in very high chemical yields. 3-Methylisobenzofuran-1(3*H*)-one (**2**) was, however, isolated as a major photoproduct in the presence of trace amounts of water. Quenching experiments and laser flash spectroscopy revealed that the indanone derivatives **3** are formed by 1,5-hydrogen migration from the lowest triplet excited state of the acetophenones **1** and cyclization of the resulting photoenols. In contrast, production of the lactone **2** in wet solvents was found to result from two consecutive photochemical transformations. The photoenols produced by photolysis of **1a–c** add water as a nucleophile to form 2-acetyl-4-methylbenzaldehyde (**4**), which is further converted to **2** via a second, singlet state photoenolization process. Exhaustive photolysis of **1a** in methanol produced the acetal 2-(dimethoxymethyl)-5-methylacetophenone (**7a**) as the exclusive product. The remarkable selectivity of these photoreactions may well be useful in synthetic organic chemistry.

Introduction

The photochemistry of 2-alkylphenyl ketones has been the subject of numerous studies and the reaction mechanism is now well-established.^{1–13} For example, 2-methylacetophenone un-

dergoes intramolecular hydrogen abstraction via the triplet state to form a short-lived triplet enol ³E, yielding two isomeric photoenols, *E* and *Z*, while direct enolization from the lowest excited singlet state produces the *Z*-isomer only^{2,14–18} (Scheme 1). The *Z* isomer, having a lifetime similar to that of the triplet enol, is converted efficiently back to the starting molecule, but the *E* isomer may, in the absence of trapping agents such as

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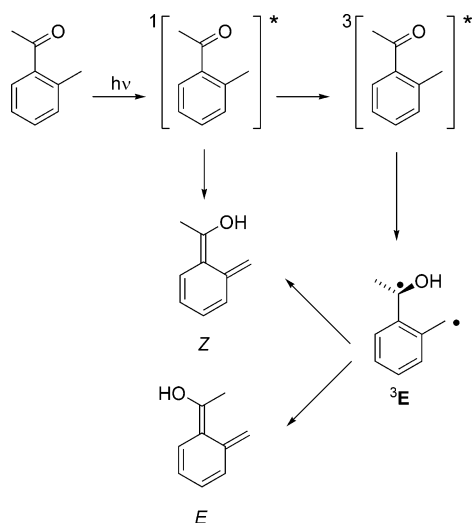
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SCHEME 1

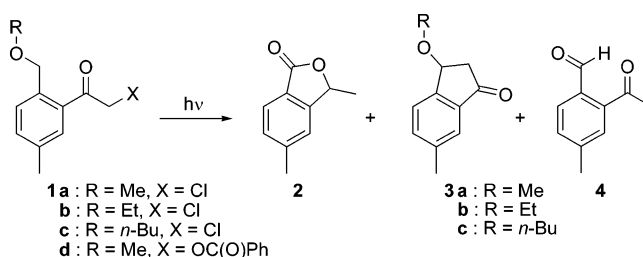


dienophiles, persist up to seconds because its reketonization requires proton transfer through the solvent. Photoenols may also cyclize to the corresponding cyclobutenols.¹⁹

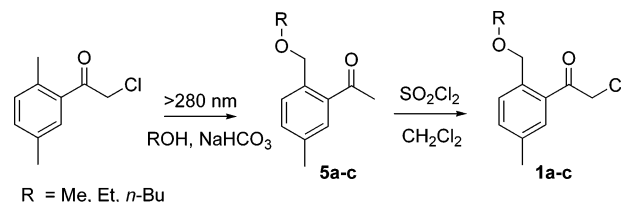
When leaving groups are present in an appropriate position, the primary photoenols can undergo elimination reactions. Thus, 2-substituted 2-ethylbenzophenones²⁰ or 2-ethylacetophenones^{21,22} release the substituent efficiently upon irradiation. Similarly, leaving groups on the α -carbon of 2-methylphenacyl compounds are efficiently released.^{23–25} Such chromophores were proposed as photoremovable protecting groups for various applications in organic synthesis or biochemistry.^{7,26,27}

There are other examples in which photoenolization is utilized in organic synthesis. A short-lived *E* photoenol can be, for example, trapped in a Diels–Alder fashion by electron-deficient dienophiles.^{28–31} The total syntheses of the antitumor agent hybocarpone or cytotoxic hamigerans were recently reported by Nicolaou and co-workers.^{32–34} Photoenols generated by photolysis of 2-tolualdehydes in the solid state react with the precursor aldehydes in hetero-Diels–Alder cycloaddition reac-

SCHEME 2



SCHEME 3. Synthesis of 1a–c Using a Photochemical Step



tions to afford *trans*-3-arylisochromanols.³⁵ A photoenolization–electrocyclization sequence was applied in the total synthesis of quinoidic natural product G-2N, a powerful antiretroviral agent.³⁶ Various functionalized 1-indanones were synthesized using photoenolization reactions by Wessig and co-workers.³⁷ The 1-indanone skeleton can also be prepared by conventional procedures, which are based on the pentanone ring closure and they incorporate intramolecular S_N reactions.^{38–44}

This paper reports our mechanistic study of unexpected phototransformations of 2-alkoxymethyl-5-methylphenacyl chloride or benzoate.

Results and Discussion

Products. Irradiation of 2-(methoxymethyl)-5-methyl- α -chloroacetophenone (**1a**) at $\lambda > 280$ nm was originally carried out to synthesize the corresponding indanone derivative 3-methoxy-6-methylindan-1-one (**3a**) via a photoenolization step and the following ring closure reaction, analogous to the reaction observed with similar systems.^{7,25,37,45} To our surprise, the lactone 3-methylisobenzofuran-1(3H)-one (**2**) was formed in high yield in addition to **3a** (Scheme 2). Methanol, methyl chloride, and a small amount of 2-acetyl-4-methylbenzaldehyde (**4**) were produced as side products. The product distribution was found to depend strongly on the solvent type (hexane, benzene, acetonitrile, or methanol) and to be extremely sensitive to moisture. To elucidate the mechanism of this photochemically initiated transformation, four acetophenone derivatives (**1a–d**) were synthesized and their reactions examined by common photochemical tools, laser flash photolysis (LFP), and quantum chemical calculations.

2-(Alkoxyethyl)-5-methyl- α -chloroacetophenones (**1a–c**) were prepared by photolysis of 2,5-dimethylphenacyl chloride²⁵ in alcohols, yielding the corresponding 2-(alkoxymethyl)-5-methylacetophenones (**5a–c**) (~50%), which were chlorinated using SO_2Cl_2 in the subsequent step (Scheme 3).

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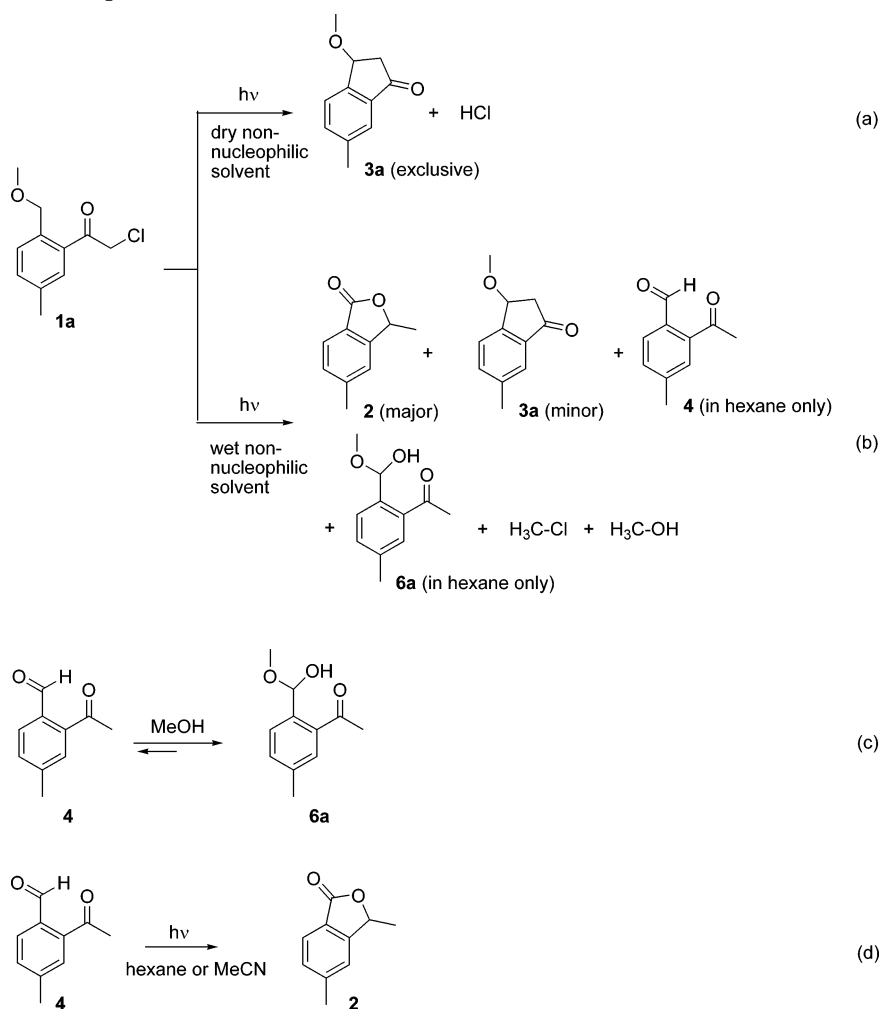
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SCHEME 4. Photolysis in Nonpolar Solvents



The chemical yields of lactone **2** and indanone **3a** in the photolysis of **1a** ($c = 5 \times 10^{-3}$ M) at >280 nm (polychromatic light was used in the preparative experiments) or 313 nm (quantum yield measurements) were found to be highly sensitive to the water content in all the solvents used. In dry solvents **3a** was formed exclusively, irrespective of the extent of conversion (Scheme 4a). Exhaustive irradiation provided **3a** in almost quantitative yields and the best results were obtained when HCl, produced as a side product, was trapped by NaHCO_3 to avoid possible chemical interferences. When benzene was used without drying (water content $\sim 0.05\%$), **2** was identified as the major product, while **3a** was formed in very low yield. The side products, methyl chloride and methanol, were detected by NMR as well as by a headspace analysis. Photolysis of **1a** in moist hexane afforded two minor products in addition to **2**, namely, 2-acetyl-4-methylbenzaldehyde (**4**), which was isolated in $\sim 15\%$ yield, and 2-hydroxy-2-(methoxymethyl)-5-methylacetophenone (**6a**) in trace amounts (Scheme 4b). The lactone **2** was eventually

isolated as the sole product formed after exhaustive irradiation. For analytical comparison, **6a** was alternatively prepared in high yield by methanolysis of **4** at 20°C (Scheme 4c). Exhaustive irradiation of **1a** in wet acetonitrile (polar, aprotic, and non-nucleophilic) led to the formation of a nearly equimolar mixture of the products **2** and **3a**. When pure 2-acetyl-4-methylbenzaldehyde (**4**), which had been isolated from the photolysis of **1a**, was irradiated in either hexane or acetonitrile solution, 3-methylisobenzofuran-1(3*H*)-one (**2**) was isolated in near quantitative yield (Scheme 4d).

Irradiation of **1a** in wet or dry CD_3OD to low conversions led to isotopic exchange at the 2-methylene position (*d*-**1a**), while exhaustive photolysis produced an acetal, 2-(dimethoxymethyl)-5-methylacetophenone (*d*-**7a**), as the exclusive product (Scheme 5). Compound **7a** was also photochemically synthesized from **1a**, to hydrolyze it to **4**, which was needed in our mechanistic studies and for analytical purposes. These results clearly indicated that the starting material undergoes a photo-

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SCHEME 5

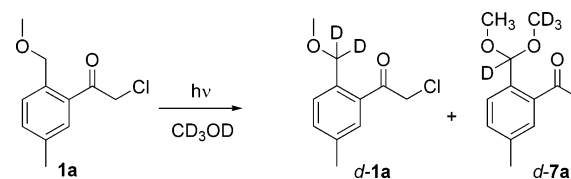


TABLE 1. Photochemistry of 2-Alkoxy-5-methylphenacyl Derivatives 1a–d^a

starting material	solvent	water content ^b	% yield (2) ^c	$\Phi_{1\rightarrow 2}$ ^d	% yield (3) ^c	$\Phi_{1\rightarrow 3}$ ^e
1a	hexane	dry	0	n.d.	98	0.022 ± 0.001
	hexane	wet	95	0.23 ± 0.01 ^f	3	0.007 ± 0.001
	benzene	dry	0	n.d.	95 ^g	0.08 ± 0.01
	benzene	wet	88	0.16 ± 0.01	10	0.022 ± 0.001
	acetonitrile	dry	0	n.d.	98	0.26 ± 0.01 ^g
	acetonitrile	wet	36	0.09 ± 0.01	62	0.16 ± 0.04 ^g
1b	acetonitrile	dry	0	n.d.	98	0.28 ± 0.01
	acetonitrile	wet	21	0.06 ± 0.01	76	0.22 ± 0.02
1c	acetonitrile	dry	0	n.d.	98	0.29 ± 0.02
	acetonitrile	wet	18	0.014 ± 0.008	80	0.26 ± 0.02
1d	hexane	dry	0	n.d.	98	0.050 ± 0.002 ^g
	hexane	wet	60	0.050 ± 0.002	35	0.031 ± 0.001 ^g
	acetonitrile	dry	0	n.d.	98	0.071 ± 0.006 ^g
	acetonitrile	wet	29	0.008 ± 0.002	69	0.056 ± 0.009 ^g

^a The starting material concentration was $3\text{--}5 \times 10^{-3}$ M; the samples degassed by purging with Ar; n.d. = not detected. ^b The water concentration in wet solvents was $5\text{--}50 \times 10^{-3}$ M. ^c Exhaustive Pyrex-filtered irradiation (>280 nm) in the presence of NaHCO_3 (GC). ^d The quantum yield of **2** formation at 313 nm (the conversions were kept below 10%). ^e The quantum yield of **3** formation at 313 nm (the conversions were kept below 10%). ^f The combined quantum yield for formation of **4** (almost the exclusive product at low conversions) and **2**; **6a** was formed in trace amounts. ^g **5a** was formed in trace amounts.

TABLE 2. Photochemistry of 4^a

solvent	water content ^b	$\Phi_{4\rightarrow 2}$
hexane	dry	0.032 ± 0.006
hexane	wet	0.030 ± 0.002
acetonitrile	dry	0.068 ± 0.003
acetonitrile	wet	0.061 ± 0.002

^a The starting material concentration was 3×10^{-3} M. The samples were degassed by purging with Ar and irradiated at 313 nm. ^b The water concentration in wet solvents was $5\text{--}50 \times 10^{-3}$ M.

enolization process^{2,46} and that the presence of nucleophilic methanol prevents the reactions observed in non-nucleophilic solvents.

Chemical and Quantum Yields. Table 1 documents the exceptional reaction selectivity of the photoinduced transformations of α -chloroacetophenones **1a–c** and of α -benzoyloxyacetophenone **1d**, which are observed in dry and wet non-nucleophilic solvents. Although indanone **3a** was the sole product formed by irradiation of **1a** in dry nonpolar solvents, the quantum yields $\Phi_{1a\rightarrow 3a}$ were relatively low. Addition of water suppressed these values further, while formation of lactone **2** ($\Phi_{1a\rightarrow 2}$) represented the main photodegradation pathway. In contrast, $\Phi_{1a\rightarrow 3a}$ was found to be high in dry acetonitrile and comparable to $\Phi_{1a\rightarrow 2}$ in wet acetonitrile. The ratio of the product concentrations, $[2]:[3]$, was found to be practically independent of the water concentration when more than equimolar water amounts were used. The replacement of a good leaving group (chloride in **1a**) by a poorer one (benzoate in **1d**) caused a considerable quantum efficiency decrease of indanone cyclization in acetonitrile and of lactone formation in both hexane and acetonitrile; nevertheless, exhaustive irradiation provided high chemical yields of both major products in wet solvents. The larger ethoxy and *n*-butoxy groups in **1b** and **1c**, respectively, somewhat affected both $\Phi_{1\rightarrow 2}$ and $\Phi_{1\rightarrow 3}$; lactone formation was slightly reduced with increasing size of the alkoxy substituent.

Table 2 lists the quantum yields of the production of lactone **2** by irradiation of 2-acetyl-4-methylbenzaldehyde **4**, the intermediate trapped during the photolysis of **1a** (Schemes 4b

and 4d). The quantum yields were low in both solvents and hardly affected by water addition. The quantum yield $\Phi_{4\rightarrow 2}$ is comparable to $\Phi_{1a\rightarrow 2}$ in wet acetonitrile, but it is almost an order of magnitude lower than $\Phi_{1a\rightarrow 2}$ in wet hexane. This will be discussed below; we emphasize here that $\Phi_{1\rightarrow 2}$ (Table 1) obtained in this solvent is the combined quantum yield for the formation of **2** and **4**. The latter was completely consumed upon exhaustive irradiation, which led to a 98% chemical yield of **2**.

An indanone moiety is known to be produced by photoenolization of similar substituted phenyl ketones containing good (halide, sulfate)^{24,25,45,47} or even poorer (carboxylate, carbonate)^{7,26,27} leaving groups in the α -position. Wessig and co-workers have utilized this reaction for the synthesis of 2,3-disubstituted indanones from the corresponding substituted 2-methyl and α -methylacetophenones.³⁷ We were initially interested in the synthesis of 3-alkoxyindanones, but the electron-donating substituent on the ortho methyl group of the phenacyl chloride **1a** significantly altered the anticipated behavior. Our first findings indicated that at least two different photochemical processes occurred when **1a** was photolyzed. While indanone **3a** was apparently formed directly from **1a**, the lactone **2** was unquestionably produced by photochemical transformation of **4**, a primary product isolated from photolysis of **1a**. Production of methyl chloride (Scheme 4b), in addition to methanol, was suggested to be a secondary substitution process, which is enabled by HCl release in the first photochemical step, especially at higher reaction conversions. This assumption was easily verified by equilibrating the solution of methanol and HCl under identical reaction conditions.

The excited state responsible for the reaction of **1a** was identified by facile quenching of product formation with a typical triplet quencher (piperylene). The formation of **3a** from **1a** in dry hexane or acetonitrile was prevented by addition of 3 M piperylene, while the production of **2** was quenched only in wet acetonitrile but not in wet hexane. Besides, piperylene addition had no effect on the formation of **2** from **4** in any of the solvents used. This indicates that the formation of indanone **3a** and of acetylbenzaldehyde **4** in acetonitrile is initiated from

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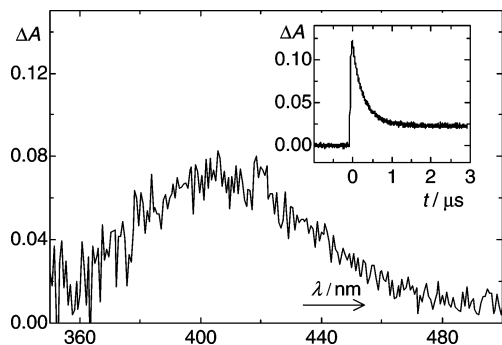


FIGURE 1. Transient absorption spectrum of **1a** in degassed acetonitrile at a delay of 20 ns after the flash. The inset shows a kinetic trace recorded at 390 nm. The long-lived end absorption decays to baseline on the ms time scale.

TABLE 3. Lifetimes τ of Transient Intermediates Formed by LFP (248 or 308 nm) of **1a**^a

solvent	$\tau(\text{Z-8a})/\mu\text{s}$, $\lambda_{\text{obs}} = 400 \text{ nm}$	$\tau(\text{E-8a})/\text{ms}$, $\lambda_{\text{obs}} = 400 \text{ nm}$
hexane ^b	ca. 20 ^c	very weak
acetonitrile dry (<0.05% of water)	0.29 ± 0.03	0.35 ± 0.05
acetonitrile wet (2.5% of water)	0.16 ± 0.04	0.15 ± 0.01
benzene dry (molecular sieve)	ca. 7 ^d	ca. 300 ^e
benzene (water-saturated)	0.9 ± 0.1	80 ± 10

^a Air-saturated solutions. The yields and lifetimes of the enol transients were not significantly affected by degassing. ^b Water saturation had no substantial effect. ^c Not accurately first-order; fitting of a biexponential rate law gave lifetimes of ca. 10 and 50 μs . ^d Not accurately first-order; fitting of a biexponential rate law gave lifetimes of ca. 5 and 10 μs . ^e Not accurately first-order; a minor component decayed with a lifetime of about 50 ms.

the triplet state, whereas **4**, and consequently **2**, are produced via a singlet pathway in hexane.

2-Alkylphenyl ketones are known to have π, π^* lowest triplet states.⁴⁸ Nevertheless, photoenolization from the triplet state is an efficient process,²⁵ presumably because the π, π^* and n, π^* triplet states are nearly degenerate.⁴⁹ Formation of the intermediates **6a** and **4**, which were isolated at lower conversions, an isotopic exchange signifying the photoenolization step, and observation of the phototransformation **4** \rightarrow **2** were the most important initial pieces of evidence required to interpret the following time-resolved study.

Laser Flash Photolysis. LFP of **1a** in hexane and acetonitrile at 248 nm, or in benzene at 308 nm, gave broad transient absorptions, $\lambda_{\text{max}} \approx 400 \text{ nm}$ (Figure 1), which are assigned to the photoenol intermediates **8a**. The decay of the photoenols usually obeyed biexponential kinetics (Table 3, Figure 1). The amplitudes and the decays of these transients were not significantly affected by the presence of oxygen, but depended strongly on the solvent and on the presence of water. By analogy to the results obtained with parent 2-methylphenacyl chloride and with use of the arguments given there,²⁵ we assign the major components of the decay traces to the photoenols with Z-configuration of the enol function ((1Z)-2-chloro-1-(6-(methoxymethylene)-3-methylcyclohexa-2,4-dienylidene)ethanol; **Z-8a**; Scheme 6). The minor components are attributed to the E-photoenol ((1E)-2-chloro-1-(6-(methoxymethylene)-3-meth-

ylcyclohexa-2,4-dienylidene)ethanol; **E-8a**; Scheme 6). The latter is formed only by the triplet pathway, i.e., via the triplet state of the ketone and of the enol, ³E; it is suppressed in the presence of 2 M piperylene. The yield of **Z-8a** was generally much higher than that of **E-8a**. Z-Photoenols undergo fast reketonization and their lifetimes are usually on the order of hundreds of nanoseconds in nonpolar solvents.^{2,7,14,25} The observed microsecond lifetimes (Table 3) indicate that **Z-8a** is stabilized by an intramolecular hydrogen bond, particularly in nonpolar solvents, and/or by resonance stabilization from an adjacent methoxy group.

LFP of **1a** in acetonitrile also caused the rapid formation of a short-lived transient with $\lambda_{\text{max}} = 340 \text{ nm}$. The lifetime of this transient, $\tau \approx 2.2 \mu\text{s}$, was reduced to about 250 ns in aerated solution and it was assigned to the triplet enol, ³E (Scheme 6), in accord with the literature.^{7,25} The lifetime of ³E is somewhat longer than usual, which may be attributed to biradical stabilization by the electron-donating methoxy group.

Assignment of the major components to the Z- and E-enols of **8a** does not identify the configuration of the double bond bearing the methoxy group ((6Z) or (6E); Figure 2). Presumably, both isomers are formed in comparable yields and they have slightly different lifetimes: In several cases, the enol decay traces recorded at 400 nm did not fit a first-order rate law accurately (footnotes of Table 3). Ab initio DFT calculations employing B3LYP/6-31+G** were carried out to determine the relative energies of the photoenol isomers and to evaluate the stabilization of **Z-8a** by hydrogen bonding (Figure 2). The $\text{—O—H}\cdots\text{O}(\text{CH}_3)$ distance was found to be 1.651 Å in the (6Z)-isomer of **Z-8a**. The angle between those two substituents was calculated to be 159.3°, which is close to a linear geometry typical for strong hydrogen bonds. No such intramolecular arrangement is achievable in the (6E)-**Z-8a** (**1**). The hydrogen atom in this isomer is not coplanar with the double bond system. The calculations validated attribution of the observed longer lifetimes of **Z-8a** (Table 3) to hydrogen bonding. The calculations also showed that the energy of the (6E)-isomer of **E-8a** is higher than that of the (6Z)-isomer by 4.1 kcal mol⁻¹ (not shown), which may be explained by a steric hindrance of the methylene group hydrogens and the hydrogen atom of the double bond.

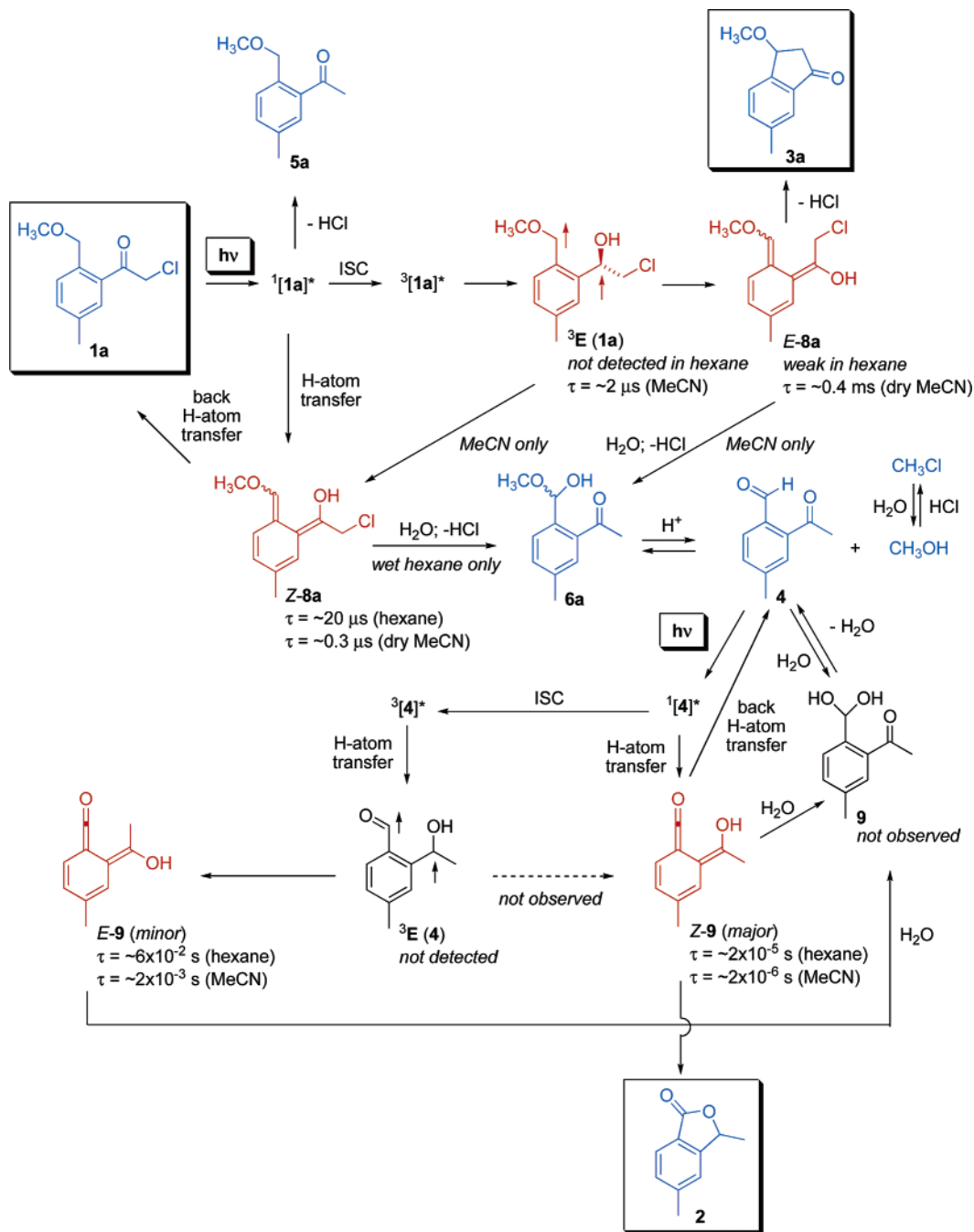
Formation of **6a**, which could be isolated in trace amounts from a hexane solution, is a logical intermediate to obtain **4**. Moreover, the observed increase in the quantum yield $\Phi_{1\rightarrow3}$ that occurs at the expense of $\Phi_{1\rightarrow2}$ when the alkoxy group in **1a–c** becomes larger suggests an increasing steric influence on the nucleophilic attack of water to the double bond of the photoenol.

The following study was done to determine whether **2** is produced exclusively by secondary photolysis of 2-acetyl-4-methylbenzaldehyde (**4**), an isolated intermediate obtained from **1a**. For the kinetic studies discussed above, solutions were exposed only to a single laser flash. New transients appeared upon re-excitation of the solutions with a second laser pulse, and these new contributions were the same as those obtained by LFP of **4**. Two transients, with $\lambda_{\text{max}} \sim 400$ and 370 nm, were detected (Table 4). While the lifetimes and amplitudes of the former (major) species were independent of the presence of oxygen in both hexane and acetonitrile, both were diminished significantly in the latter (minor) contribution. The photochemistry of *o*-dicarbonyl compounds has been investigated previously.^{3,50,51} For example, that of 2-phthalaldehyde was reported

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SCHEME 6. Photochemistry of 1a in Wet Hexane or Acetonitrile (Blue: Isolated Compounds; Red: Transients Detected; Black: Anticipated Species)



to yield phthalide as a major product.^{52,53} For 2-benzoylbenzaldehyde in benzene or acetonitrile intramolecular hydrogen transfer leads to the formation of two ketene-enols: *E* ($\tau = 1$ ms), showing absorption at 340 and 400 nm, and *Z* ($\tau = 1.5$ μ s) with $\lambda_{\text{max}} \sim 360$ and 430 nm.⁵⁰ By analogy, we assign the transient with $\lambda_{\text{max}} = 400$ nm to *Z*-**9** and that with $\lambda_{\text{max}} = 370$ nm to *E*-**9** (Table 4; Scheme 6). The lifetime of *E*-**9** is reduced in aerated solutions, which may indicate oxidation by O₂, as

observed in the study on 2-phthalaldehyde.³ This intermediate probably regenerates the starting material **4** by nucleophilic addition of water. On the other hand, **Z-9** must be the precursor of **2** because the lactone is formed by a singlet pathway, which gives the *Z*-enol exclusively. The efficiency of this reaction was, of course, lowered by a back hydrogen transfer to regenerate the starting material (**4**). As shown above (Tables 1 and 2), the quantum yield $\Phi_{1a \rightarrow 2}$ is comparable to $\Phi_{4 \rightarrow 2}$ in wet acetonitrile, but is an order of magnitude higher in wet hexane. The quantum inefficiency in hexane could be explained by a fast reketonization and/or by a formation of nonproductive *E-9*, which decays via nucleophilic addition of water (Scheme 6). The rate constant for quenching of the *E*-ketene-enol (from 2-benzoyl-

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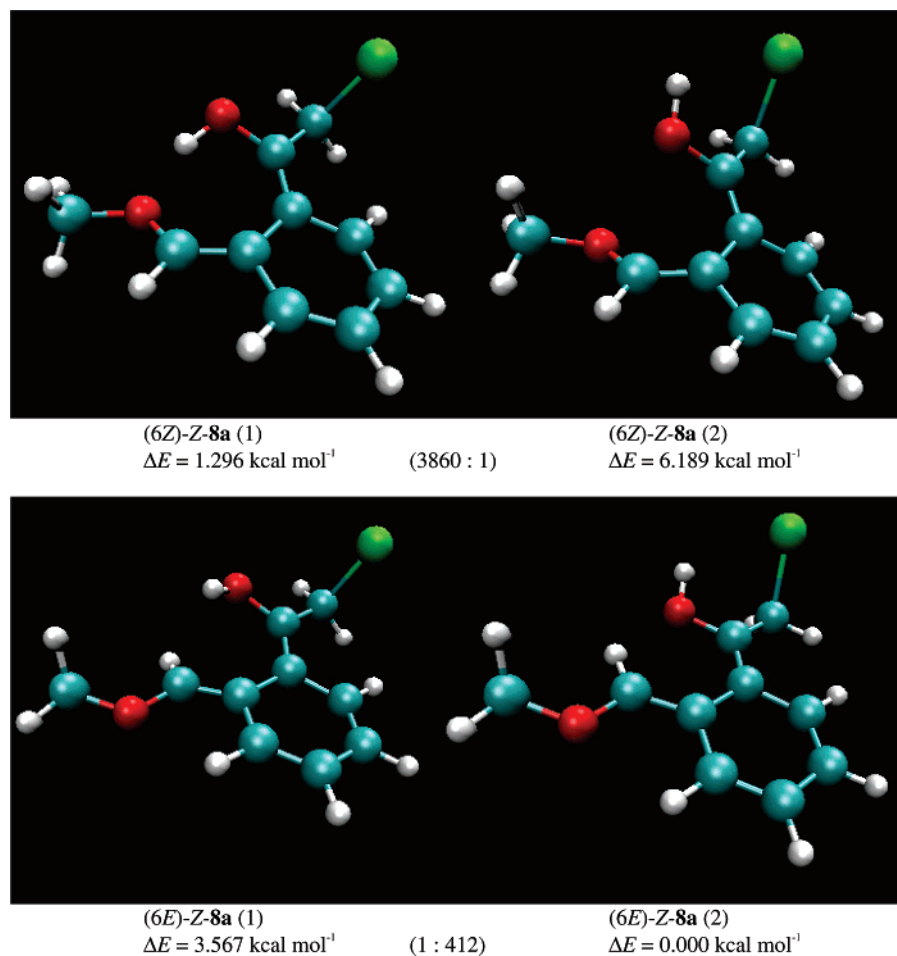


FIGURE 2. 3D representation and relative standard Gibbs free energies at 298.15 K of the fully optimized B3LYP/6-31+G** local minima of the ground-state enol Z-8a (without the 5-methyl group). The numbers (1) and (2) designate opposite conformations of the OH group. The relative population of the conformers in each pair is given in parentheses.

TABLE 4. Lifetimes τ /s of the Transients from 4^a

conditions	Z-9 ($\lambda_{\text{max}} = 400 \text{ nm}$) ^b	E-9 ($\lambda_{\text{max}} = 370 \text{ nm}$) ^c
degassed hexane	$(2.1 \pm 0.1) \times 10^{-5}$	$(5.8 \pm 0.1) \times 10^{-2}$
aerated hexane	$(2.0 \pm 0.1) \times 10^{-5}$	$(5.7 \pm 0.1) \times 10^{-4}$
degassed acetonitrile	$(2.0 \pm 0.2) \times 10^{-6}$	$(1.7 \pm 0.3) \times 10^{-3}$
aerated acetonitrile	$(1.96 \pm 0.05) \times 10^{-6}$	$(7.3 \pm 0.3) \times 10^{-4}$

^a Lifetimes measured by LFP (248 nm pulse; 280 nm filter). ^b Major transient; the yields were not affected by oxygen. ^c The transient yields diminished in the presence of O₂ by ~35% in MeCN and 25% in hexane.

benzaldehyde) by water has been found by Netto-Ferreira and Scaiano to be $1.1 \times 10^3 \text{ M}^{-1} \text{ s}^{-1}$ in acetonitrile.⁵⁰

In conclusion, Scheme 6 shows a complete mechanistic proposal of the photochemical transformation of **1a** into the major products **3a** and **2**. It includes short-lived transients detected by LFP, productive or nonproductive isolated as well as hypothetical intermediates, and byproducts, such as methanol, methyl chloride, or the acetophenone derivative **5a** that is produced in traces, apparently by homolytic C–Cl bond cleavage. The production of the major products was found to be very sensitive to the water content and the polarity of the solvents. By analogy to previous work,^{23–25,37} we expected cyclization to indanone to take place from the triplet excited ketone. The surprising lactone formation was found to be a consequence of two consecutive photochemical transformations that occur in the presence of nucleophilic water. The high

reaction selectivity, controlled by traces of water in the reaction system, is unquestionably a very intriguing result, which could be utilized in organic synthesis.

Experimental Section

Materials and Methods. NMR spectra were recorded on a 300 MHz spectrometer; ¹H and ¹³C NMR data were measured in CDCl₃ with tetramethylsilane as an internal standard. Gas chromatography was performed on a gas chromatograph equipped with a 15-m column (5% diphenyldimethylsiloxane). Mass spectra were recorded on a spectrometer in positive mode with EI. UV spectra were obtained with matched 1.0-cm quartz cells. All solvents were purified by distillation before use. Hexane and benzene were dried over sodium wire; acetonitrile was dried over CaCl₂. 2,5-Dimethylphenacyl chloride was prepared as described.⁴⁵

Quantum Yield Measurements. The quantum yield measurements were accomplished on an optical bench consisting of a high-pressure 350 W Hg lamp, a 1/8 m monochromator with grating 200–1600 nm set to 313 nm, and a 1 cm quartz cell containing the sample solution (degassed by purging with argon). The light intensity was monitored by a Si photodiode detector (UV enhanced) with a multifunction optical power meter. The concentration of all solutions was adjusted to approximately $\sim 5 \times 10^{-3} \text{ M}$, if not stated otherwise. A solution of valerophenone in hexane was used as an actinometer ($\Phi = 0.30$ for acetophenone formation).⁵⁴ The irradiated samples were analyzed using gas chromatography and hexadecane was used as an internal standard. The reaction conversions

were kept below 10% in order to prevent interference from the photoproducts. Each sample was measured at least five times and the relative standard deviation is shown in the tables.

Steady-State Quenching Studies. The steady-state quenching studies were performed on a merry-go-round apparatus that assured identical irradiation conditions. Samples in Pyrex tubes (13 × 120 mm) were purged with argon for 15 min before irradiation. Three argon-purged tubes of each sample were irradiated simultaneously with a medium-pressure 125 W Tesla mercury lamp.

Laser Flash Photolysis Measurements (LFP). The sample solutions were excited at 248 nm using a KrF excimer laser (pulse energy ~ 150 mJ, pulse duration ~ 25 ns) or at 308 nm (XeCl, 150 mJ, 25 ns). A pulsed Xenon arc provided the monitoring beam (cell path length 4.5 cm, orthogonal to the excitation pulse). The monitoring light beam leaving the sample cell could be directed either to a polychromator that was equipped with a gated image intensifier and a diode array to measure absorbance difference spectra at selected delay times after excitation, or to a monochromator-photomultiplier unit to monitor the time dependence of the transient absorption at given wavelengths. The photomultiplier output was fed to 50 Ω on a digital oscilloscope. The data from both an OMA and oscilloscope were analyzed by computer. Solutions were degassed by three freeze–pump–thaw cycles and sealed under vacuum before the measurements to avoid quenching of the transients by oxygen. The samples were freshly prepared from cyclohexane or methanol (not dried) stock solutions and discarded after each laser shot.

Photochemical Synthesis of 2-Alkoxyethyl-5-methyl-acetophenones (5a–c). 2,5-Dimethylphenacyl chloride (8.5 g; 46.5 mmol) was dissolved in an aliphatic alcohol (MeOH, EtOH, or *n*-BuOH) (1.2 L), NaHCO₃ (2 g) was added, and the solution was purged with argon for 15 min. This stirred mixture was irradiated with a 400 W mercury UV lamp through a Pyrex filter (>280 nm) for 20 h at room temperature until the conversion was complete (GC). The excess solvent was removed under reduced pressure and the residue was extracted with methylene chloride (100 mL) and washed two times with water (50 mL) and brine (50 mL). The organic layer was then dried over MgSO₄ and CH₂Cl₂ was removed in vacuo. The corresponding product, 2-(alkoxyethyl)-5-methylacetophenone, was separated by flash column chromatography (silica gel; hexane/diethyl ether, 4:1). 6-Methyl-indan-1-one was isolated as a byproduct.²⁵

2-(Methoxymethyl)-5-methylacetophenone (5a). 5a was synthesized from MeOH. Yield, 4.64 g (56%). The analytical data were published in our preceding article.⁷

2-(Ethoxymethyl)-5-methylacetophenone (5b). 5b was synthesized from EtOH. Yield, 2.2 g (25%); colorless oil. ¹H NMR (300 MHz, CDCl₃) (ppm): δ 1.25 (t, *J* = 7.1 Hz, 3H), 2.39 (s, 3H), 2.57 (s, 3H), 3.57 (q, *J* = 7.1 Hz, 2H), 4.74 (s, 2H), 7.29 (d, *J* = 7.6 Hz, 1H), 7.49 (s, 1H), 7.53 (d, *J* = 7.6 Hz, 1H). ¹³C NMR (75.5 MHz) (ppm): δ 15.4, 21.2, 29.4, 66.4, 70.7, 128.2, 129.8, 132.5, 136.7, 137.0, 137.1, 202.0. MS (EI, 70 eV): *m/z* = 192 (M⁺), 177, 163, 147, 117, 91.

2-(*n*-Butoxymethyl)-5-methylacetophenone (5c). 5c was synthesized from *n*-BuOH. Yield, 1.9 g (19%); colorless oil. ¹H NMR (300 MHz, CDCl₃) (ppm): δ 0.93 (t, *J* = 7.6 Hz, 3H), 1.35–1.45 (m, 2H), 1.55–1.65 (m, 2H), 2.39 (s, 3H), 2.57 (s, 3H), 3.51 (t, *J* = 7.0 Hz, 2H), 4.74 (s, 2H), 7.28 (d, *J* = 7.6 Hz, 1H), 7.50 (s, 1H), 7.53 (d, *J* = 7.6 Hz, 1H). ¹³C NMR (75.5 MHz) (ppm): δ 14.1 (broad), 19.6, 21.1, 29.3, 32.0, 70.9, 128.1, 129.9, 132.5, 136.6, 136.8, 136.9, 201.9. MS (EI, 70 eV): *m/z* = 220 (M⁺), 205, 191, 177, 163, 147, 117, 91.

Synthesis of 2-Alkoxyethyl-5-methyl- α -chloroacetophenones (1a–c). Freshly distilled SO₂Cl₂ (0.45 mL; 5.6 mmol) was added dropwise to a stirred solution of 2-(alkoxyethyl)-5-methylacetophenone (5a–c) (5.6 mmol) in dry methylene chloride (50 mL)

under an argon atmosphere and the mixture was stirred for 30 min at 20 °C. The reaction was then quenched with aqueous NaHCO₃ (20 mL). The layers were separated and the aquatic layer was extracted with methylene chloride (2 × 20 mL). Combined organic layers were washed with brine (20 mL) and dried over MgSO₄, and the solvent was removed under reduced pressure. The corresponding product was separated by flash column chromatography (silica gel; hexane/methylene chloride/ethyl acetate, 33:66:1).

2-(Methoxymethyl)-5-methyl- α -chloroacetophenone (1a). Yield, 0.5 g (42%); colorless crystals; mp 41–43 °C (hexane). IR (KBr): 2925, 2821, 1691, 1261, 1106 cm^{−1}. ¹H NMR (300 MHz, CDCl₃) (ppm): δ 2.40 (s, 3H), 3.41 (s, 3H), 4.61 (s, 4H), 7.32 (d, *J* = 7.6 Hz, 1H), 7.35 (s, 1H), 7.42 (d, *J* = 7.6 Hz, 1H). ¹³C NMR (75.5 MHz) (ppm): δ 21.2, 48.1, 58.8, 72.6, 128.7, 129.0, 133.1, 134.6, 136.6, 137.4, 195.1. MS (EI, 30 eV): *m/z* = 212 (M⁺), 176, 163, 145, 133, 117, 105, 91, 79, 65. Anal. Calcd for C₁₁H₁₃ClO₂: C, 62.12; H, 6.16. Found: C, 62.06; H, 6.12.

2-(Ethoxymethyl)-5-methyl- α -chloroacetophenone (1b). Yield, 0.51 g (40%); colorless crystals. ¹H NMR (300 MHz, CDCl₃) (ppm): δ 1.24 (t, *J* = 7.1 Hz, 3H), 2.39 (s, 3H), 3.55 (q, *J* = 7.1 Hz, 2H), 4.64 (s, 2H), 4.68 (s, 2H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.35 (s, 1H), 7.46 (d, *J* = 8.0 Hz, 1H). ¹³C NMR (75.5 MHz) (ppm): δ 15.3, 21.2, 48.4, 66.6, 70.6, 128.7, 128.8, 132.8, 135.0, 136.6, 137.3, 195.4. MS (EI, 30 eV): *m/z* = 227 (M⁺), 191, 176, 163, 145, 133, 117, 105, 91, 79, 65.

2-(*n*-Butoxymethyl)-5-methyl- α -chloroacetophenone (1c). Yield, 0.57 g (40%); colorless crystals. ¹H NMR (300 MHz, CDCl₃) (ppm): δ 0.93 (t, *J* = 7.6 Hz), 1.24–1.34 (m, 2H), 1.55–1.65 (m, 2H), 2.39 (s, 3H), 3.49 (t, *J* = 6.6 Hz, 2H), 4.64 (s, 2H), 4.67 (s, 2H), 7.32 (d, *J* = 8.1 Hz, 1H), 7.36 (s, 1H), 7.47 (d, *J* = 8.1 Hz, 1H). ¹³C NMR (75.5 MHz) (ppm): δ 14.1, 19.6, 21.2, 31.9, 48.3, 70.8, 71.2, 128.8, 132.9, 134.9, 136.9, 137.3, 195.3. MS (EI, 30 eV): *m/z* = 255 (M⁺), 219, 204, 190, 176, 163, 145, 133, 117, 105, 91, 79, 65.

Preparative Irradiation of 2-(Alkoxyethyl)-5-methyl- α -chloroacetophenones. The stirred solution of 2-(alkoxyethyl)-5-methyl- α -chloroacetophenone (1a–c) (2.4 mmol) in acetonitrile (200 mL) was purged with argon for 15 min and irradiated with a 400 W mercury UV lamp through a Pyrex filter (>280 nm) for 12 h until the conversion was complete (GC). NaHCO₃ (1 g) was then added and the solvent removed under reduced pressure. The residue was extracted with methylene chloride (50 mL) and washed twice with water (50 mL) and once with brine (50 mL). The organic layer was dried over MgSO₄ and CH₂Cl₂ was removed in vacuo. The products (3-methylisobenzofuran-1(3*H*)-one (2) and 3-alkoxy-6-methylindan-1-ones (3a–c)) were separated by flash column chromatography (silica gel; hexane/methylene chloride/ethyl acetate, 33:66:1). A trace amount of 2-hydroxy-2-(methoxymethyl)-5-methylacetophenone (6a) was identified by GC-MS ((EI, 30 eV): *m/z* = 193 (M⁺), 177, 161, 145, 133, 115, 105, 91, 77, 65).

3-Methylisobenzofuran-1(3*H*)-one (2). Yield, 45%; colorless crystals; mp 104–105.5 °C (hexane). IR (KBr): 2987, 2929, 1745, 1614, 1043 cm^{−1}. ¹H NMR (300 MHz, CDCl₃) (ppm): δ 1.53 (d, *J* = 6.6 Hz, 3H), 2.41 (s, 3H), 5.43 (q, *J* = 6.6 Hz, 1H), 7.19 (s, 1H), 7.24 (d, *J* = 7.6 Hz, 1H), 7.65 (d, *J* = 7.6 Hz, 1H). ¹³C NMR (75.5 MHz) (ppm): δ 20.3, 22.0, 77.4, 121.9, 123.1, 125.2, 130.1, 145.3, 151.8, 170.4. MS (EI, 70 eV): *m/z* = 162 (M⁺), 147, 119, 91, 77, 65, 51. Anal. Calcd for C₁₀H₁₀O₂: C, 74.06; H, 6.21. Found: C, 73.92; H, 6.22.

3-Methoxy-6-methylindan-1-one (3a). 3a was synthesized from 1a. Yield, 43%; yellow crystals. IR (KBr): 2929, 1718, 1284, 1091 cm^{−1}. ¹H NMR (300 MHz, CDCl₃) (ppm): δ 2.37 (s, 3H), 2.61 (dd, *J*₁ = 18 Hz, *J*₂ = 2.3 Hz, 1H), 2.94 (dd, *J*₁ = 18 Hz, *J*₂ = 6.3 Hz, 1H), 3.43 (s, 3H), 4.94 (dd, *J*₁ = 6.3 Hz, *J*₂ = 2.3 Hz, 1H), 7.42 (d, *J* = 7.9 Hz, 1H), 7.49 (s, 1H), 7.53 (d, *J* = 7.9 Hz, 1H). ¹³C NMR (75.5 MHz) (ppm): δ 21.2, 43.8, 56.9, 76.6, 123.2, 126.2, 136.1, 137.0, 139.7, 150.7, 203.0. MS (EI, 70 eV): *m/z* = 176 (M⁺), 161, 145, 133, 115, 105, 91, 77, 65, 51. Anal. Calcd for C₁₁H₁₂O₂: C, 74.98; H, 6.86. Found: C, 75.08; H, 6.91.

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3-Ethoxy-6-methylindan-1-one (3b). **3b** was synthesized from **1b**. Yield, 43%; yellow crystals. ^1H NMR (300 MHz, CDCl_3) (ppm): δ 1.28 (t, $J = 7.1$ Hz, 3H), 2.42 (s, 3H), 2.68 (dd, $J_1 = 18.5$ Hz, $J_2 = 2.6$ Hz, 1H), 2.95 (dd, $J_1 = 18.5$ Hz, $J_2 = 6.3$ Hz, 1H), 3.66 (q, $J = 7.1$ Hz, 2H), 5.06 (dd, $J_1 = 6.3$ Hz, $J_2 = 2.6$ Hz, 1H), 7.49 (d, $J = 7.9$ Hz, 1H), 7.57 (s, 1H), 7.60 (d, $J = 7.9$ Hz, 1H). ^{13}C NMR (75.5 MHz) (ppm): δ 15.6, 21.4, 44.7, 65.3, 75.2, 123.3, 126.4, 136.3, 137.2, 139.8, 151.3, 203.5. MS (EI, 70 eV): $m/z = 190$ (M^+), 175, 161, 145, 133, 115, 105, 91, 77, 65, 51.

3-(*n*-Butoxy)-6-methylindan-1-one (3c). **3c** was synthesized from **1c**. Yield, 52%; yellow crystals. ^1H NMR (300 MHz, CDCl_3) (ppm): δ 0.95 (t, $J = 7.3$ Hz, 3H), 1.40–1.45 (m, 2H), 1.59–1.64 (m, 2H), 2.42 (s, 3H), 2.67 (dd, $J_1 = 18.5$ Hz, $J_2 = 2.6$ Hz, 1H), 3.00 (dd, $J_1 = 18.5$ Hz, $J_2 = 6.3$ Hz, 1H), 3.62 (t, $J = 6.6$ Hz, 2H), 5.06 (dd, $J_1 = 6.3$ Hz, $J_2 = 2.6$ Hz, 1H), 7.49 (d, $J = 7.9$ Hz, 1H), 7.57 (s, 1H), 7.60 (d, $J = 7.9$ Hz, 1H). ^{13}C NMR (75.5 MHz) (ppm): δ 14.0 (broad), 19.5, 21.4, 32.2, 44.6, 69.7, 75.3, 123.3, 126.4, 136.3, 137.2, 139.7, 151.3, 203.4. MS (EI, 70 eV): $m/z = 218$ (M^+), 203, 189, 175, 161, 145, 133, 115, 105, 91, 77, 65, 51.

Preparative Irradiation of 2-(Methoxymethyl)-5-methyl- α -chloroacetophenone (1a) in Methanol. The stirred solution of 2-(methoxymethyl)-5-methyl- α -chloroacetophenone (**1a**) (0.5 g; 2.4 mmol) in methanol (200 mL) was purged with argon for 15 min and irradiated with a 400 W mercury UV lamp through a Pyrex filter (>280 nm) for 11 h until the conversion was complete (GC). NaHCO_3 (1 g) was then added and the solvent removed under reduced pressure. The residue was extracted with methylene chloride (50 mL) and washed two times with water (50 mL) and one time with brine (50 mL). The organic layer was dried over MgSO_4 and CH_2Cl_2 was removed in vacuo. The crude product (2-(dimethoxymethyl)-5-methylacetophenone (**7a**)) was not purified and served for identification purposes only.

2-(Dimethoxymethyl)-5-methylacetophenone (7a). Yield, 0.4 g (80%); colorless oil. ^1H NMR (300 MHz, CDCl_3) (ppm): δ 2.40 (s, 3H), 2.56 (s, 3H), 3.37 (s, 6H), 5.79 (s, 1H), 7.28 (d, $J = 7.6$ Hz, 1H), 7.29 (s, 1H), 7.56 (d, $J = 7.6$ Hz, 1H). ^{13}C NMR (75.5 MHz) (ppm): δ 21.1, 30.4, 54.1, 101.5, 127.3, 128.2, 131.3, 133.9, 138.4, 139.7, 203.9. MS (EI, 70 eV): $m/z = 207$ (M^+), 193, 177, 161, 145, 133, 115, 105, 91, 77.

Alternative Synthesis of 2-Acetyl-4-methylbenzaldehyde (4). The mixture of 2-(dimethoxymethyl)-5-methylacetophenone (**7a**) (250 mg, 1.2 mmol) in acetone (5 mL) was added to an aqueous HCl (5%; 20 mL). The mixture was stirred for 5 h until the conversion was complete (GC). The reaction mixture was then extracted with methylene chloride (3×10 mL). The combined organic layers were washed with brine (10 mL) and dried over MgSO_4 , and CH_2Cl_2 was removed in vacuo.

2-Acetyl-4-methylbenzaldehyde (4). Yield, 150 mg (80%); colorless solid. IR (KBr): 2921, 2873, 1687, 1602, 1359, 1268, 1186 cm^{-1} . ^1H NMR (300 MHz, CDCl_3) (ppm): δ 2.49 (s, 3H), 2.63 (s, 3H), 7.43 (d, $J = 7.6$ Hz, 1H), 7.46 (s, 1H), 7.79 (d, $J = 7.6$ Hz, 1H), 10.17 (s, 1H). ^{13}C NMR (75.5 MHz) (ppm): δ 21.9, 29.3, 129.1, 130.3, 132.3, 133.5, 141.4, 144.5, 191.9, 201.9. MS

(EI, 70 eV): $m/z = 162$ (M^+), 147, 134, 119, 105, 91, 77, 65. Anal. Calcd for $\text{C}_{10}\text{H}_{10}\text{O}_2$: C, 74.06; H, 6.21. Found: C, 73.90; H, 6.23.

Synthesis of 2-(Methoxymethyl)-5-methylphenacyl Benzoate (1d). 2-(Methoxymethyl)-5-methyl- α -chloroacetophenone (**1a**) (1.15 g, 5.4 mmol) in acetone (30 mL) was added to a stirred solution of benzoic acid (1 g, 8.1 mmol), triethylamine (0.9 mL, 6.5 mmol), and NaI (0.9 g, 6 mmol) in acetone (120 mL) and the reaction mixture was refluxed for 6.5 h. Acetone was then evaporated in vacuo and the residue was dissolved in benzene (50 mL) and washed twice with water (20 mL) and twice with saturated NaHCO_3 (20 mL). The combined aqueous layers were washed twice with benzene (20 mL) and dried over MgSO_4 and the solvent was removed under reduced pressure, yielding a crude product (brown solid), which was purified by recrystallization (hexane).

2-(Methoxymethyl)-5-methylphenacyl Benzoate (1d). Yield, 1.1 g (69%); colorless crystals; mp 47–49 °C (hexane). ^1H NMR (300 MHz, CDCl_3) (ppm): δ 2.42 (s, 3H), 3.44 (s, 3H), 4.70 (s, 2H), 5.44 (s, 2H), 7.35–8.15 (m, 8H). ^{13}C NMR (75.5 MHz) (ppm): δ 21.2, 58.8, 67.9, 72.5, 128.5, 128.7, 128.8, 129.6, 130.2, 133.2, 133.5, 133.8, 136.9, 137.2, 166.26, 196.2. MS (EI, 70 eV): $m/z = 299$ (M^+), 267, 193, 176, 163, 146, 133, 119, 105, 91, 77.

Photochemical Experiments in an NMR Tube. A solution of the starting material in dry benzene (dried over a 4 Å molecular sieve) in an NMR tube was purged with argon for 15 min and irradiated with a 125 W mercury UV lamp through a Pyrex filter (>280 nm) for 1 h. ^1H NMR spectra were measured in the corresponding time intervals.

Headspace Analyses. The samples were equilibrated in tightly sealed headspace vials for 24 h, and the head air concentrations of methyl chloride were measured using GC-MS.

Quantum Chemical Calculations. The quantum chemical calculations were performed using the Gaussian 03 software package using density functional theory employing the B3LYP functional with the 6-31+G** basis set. The wave functions were checked for internal stability. Ideal gas standard Gibbs free energies at 298.15 K were estimated using the calculated vibrational frequencies.

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Supporting Information Available: ^1H and ^{13}C NMR spectra for compounds **1b–d**, **3b–c**, **5b–c**, and **7a**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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