

Formal Intramolecular Photoredox Chemistry of Meta-Substituted Benzophenones

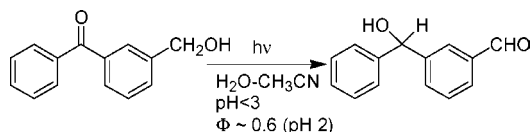
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ABSTRACT

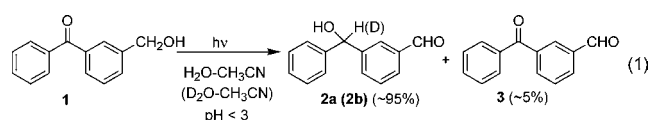


Photolysis of 3-(hydroxymethyl)benzophenone (**1**) in aqueous solution ($\text{pH} < 3$) results in clean formation of 3-formylbenzhydrol (**2**) at dilute ($<10^{-4}$ M) conditions. Evidence suggests that the highly efficient ($\Phi \sim 0.6$) reaction involves a unimolecular mechanism and an overall formal intramolecular photoredox process, which requires electronic communication between the 1,3-positions of the benzene ring, an unprecedented example of the photochemical meta effect. The photoredox reaction was not observed in organic solvents, where only photoreduction of the benzophenone moiety was observed.

Benzophenones have been well-studied photochemically and photophysically.¹ Typical photochemical reactions include Norrish Type I and II processes and intermolecular hydrogen abstraction. Much of the observed photochemistry may be rationalized as being due to the diradical character of the excited triplet state. For example, photolysis of a typical benzophenone in an organic solvent such as 2-propanol would result in hydrogen abstraction from the solvent by the ketone to generate a ketyl radical. This may result in subsequent formation of pinacol-type products or simple reduction of the ketone.¹ Benzophenones have also been observed to undergo photoinduced electron-transfer processes.² We report a new type of photochemistry of ap-

propriately meta-substituted benzophenones that is observed only in aqueous solution. These meta-substituted benzophenones undergo a clean (formal) intramolecular redox process (that does not formally involve an initial one electron transfer) in which the benzophenone ketone moiety is reduced to the alcohol and a meta-substituted alcohol group is oxidized to the aldehyde (or ketone). This mode of reactivity requires enhanced electronic communication between the 1,3-positions of the benzene ring, previously described as the photochemical meta effect.³

As the central example of these studies, 3-(hydroxymethyl)benzophenone (**1**) undergoes a highly efficient ($\Phi \sim 0.6$)⁴ intramolecular redox reaction in acidic ($\text{pH} < 3$) aqueous solution, to form 3-formylbenzhydrol (**2b**) (95%) with trace amounts of the fully oxidized 3-formylbenzophenone (**3**) (5%) (eq 1).⁵ This finding mirrors the highly



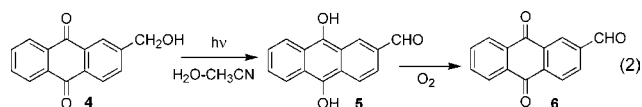
efficient ($\Phi \sim 0.8$) intramolecular photoredox reaction of 2-(hydroxymethyl)anthraquinone (**4**) (eq 2) to give 2-formyl-

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(1) (a) Turro, N. J. *Modern Molecular Photochemistry*; University Science Books: Mill Valley, CA, 1991. (b) Scaiano, J. C. *J. Photochem. 1973/74*, 2, 81. (c) Garcia-Garibay, M. A.; Campos, L. M. In *CRC Handbook of Organic Photochemistry and Photobiology*, 2nd ed.; Horspool, W. M., Lenci, F., Eds.; CRC Press: Boca Raton, FL, 2004; Chapter 48. (d) Wagner, P. J.; Klán, P. In *CRC Handbook of Organic Photochemistry and Photobiology*, 2nd ed.; Horspool, W. M., Lenci, F., Eds.; CRC Press: Boca Raton, FL, 2004; Chapter 48. (e) Zimmerman, H. E.; Schuster, D. I. *J. Am. Chem. Soc.* **1962**, 84, 4527.

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9,10-dihydroxyanthracene (**5**).⁶ The final product was 2-formyl-



anthraquinone (**6**), which arose via (thermal) air oxidation of the initially formed **5**. At that time, we also studied the corresponding (hydroxymethyl)benzophenone derivatives **1** and **7** (in neutral aqueous solution) and found they reacted only via hydrogen abstraction from the CH₃CN cosolvent, yielding pinacol-type photoreduction products.⁷ In contrast, photolysis of **1** in aqueous solution (1:1 H₂O–CH₃CN, water at pH < 3) resulted in UV–vis spectral changes with an isosbestic point (Figure 1)⁸ consistent with an entirely

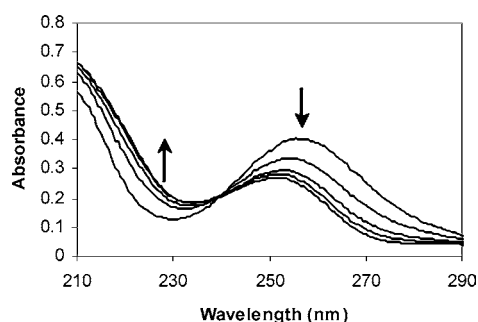


Figure 1. UV–vis traces for **1** with increasing photolysis time. Samples ($\sim 10^{-5}$ M, 1:1 H₂O–CH₃CN; pH 2, Ar purged) were drawn from a semipreparative photolysis and diluted before recording spectra traces. Each trace is 60 s apart. The resulting spectrum is essentially identical to that of authentic 3-formylbenzhydrol (**2**).

different reaction than observed at pH 7,⁹ viz. eq 1. Aside from simple photoreduction, the para isomer **7** did not undergo photoredox chemistry and was not studied further. The above are consistent with a meta effect that has been observed by Wirz and co-workers for the photochemical hydration of benzophenone.¹⁰

(3) (a) Zimmerman, H. E. *J. Am. Chem. Soc.* **1995**, *117*, 8988. (b) Zimmerman, H. E. *J. Phys. Chem. A* **1998**, *102*, 5616.

(4) Quantum yield of reaction was estimated by comparison with the photoredox chemistry of 2-hydroxymethylanthraquinone ($\Phi \sim 0.8$).⁶

(5) Rayonet RPR 100 photochemical reactor, 300 nm lamps, argon purged continuously.

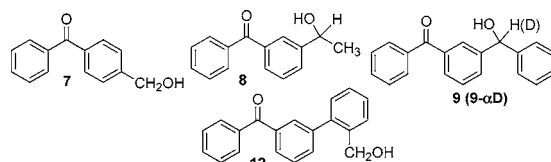
(6) Lukeman, M.; Xu, M.; Wan, P. *J. Chem. Soc., Chem. Commun.* **2002**, 136.

(7) The photoreaction in these solvents was characterized by gradual loss of the main UV–vis absorption band (255 nm) and with the formation of new NMR signals, consistent with pinacol-type products.

(8) To maintain consistency with regards to concentration dependence of the photolysis, the UV–vis traces followed a semipreparative photolysis by halting the photolysis, removing aliquots, diluting them precisely, and taking UV–vis spectra. The photolysis was then continued and the cycle repeated.

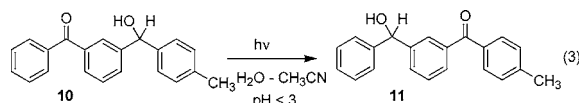
(9) At concentrations below 10^{-4} M, a residual photoredox pathway is observable at pH 7 but was much less efficient compared to pH's < 3. Photolysis in pure CH₃CN at these lower concentrations still yielded only photoreduction products.

(10) Ramseier, M.; Senn, P.; Wirz, J. *J. Phys. Chem. A* **2003**, *107*, 3305.



The photoredox reaction is apparently unaffected by dilution and was observed down to the lowest substrate concentration in which we were able to follow the reaction ($\sim 10^{-6}$ M). However, the amount of side product increases rapidly above $\sim 10^{-3}$ M.¹¹ These observations suggest that the photoredox reaction is unimolecular with respect to the starting material but that the photoreduction side reaction is a bimolecular process. Photolysis under oxygen gave exclusively **3**, suggesting that its trace yield observed under argon arises via residual oxygenation (of either **2** or a reactive intermediate leading to **2**). Decreasing the pH to 1 or 0 gave even higher yields of **2** consistent with acid catalysis of the photoreaction. Photolysis of **1** in 1:1 pD 2 D₂SO₄–CH₃CN resulted in the formation of **2-αD** (**2b**), indicating that the methine proton arises from water, not from acetonitrile. This is consistent with a water-mediated intramolecular photoredox reaction.¹²

The observed photochemical behavior is unaffected by relatively minor structural changes as evidenced by 3-(1'-hydroxyethyl)benzophenone (**8**) and 3-benzoylbenzhydrol (**9**), both of which show the same photoredox behavior. As **9** would only interchange the ketone and alcohol moieties, resulting in the same structure upon intramolecular photoredox reaction, **9-αD** was used instead and was shown to exchange the deuterium for a proton at the methine position on photolysis in acidic H₂O, consistent with the water-mediated intramolecular redox process. While similar to **9**, the photoreaction of **10** can be monitored by NMR. When photolyzed in acidic (pH < 2) aqueous solution, **10** undergoes the equivalent photoredox reaction (eq 3) but unlike **1** or **8**, whose product are benzhydrols and less photoreactive than the starting benzophenone, the photoproduct of **11** also contains a benzophenone, leading to a photostationary state after about 30% conversion. Intramolecular photoredox chemistry was also observed in the biphenyl example **12**, strengthening the evidence that electronic transmission is possible through a biphenyl ring.¹³ Secondary photochemistry was however, evident above approximately 10% conversion, complicating this initial study.



Laser flash photolysis¹⁴ of **1** in 1:1 H₂O–CH₃CN led to a transient spectrum consisting of two peaks ($\lambda_{\text{max}} = 325$ nm,

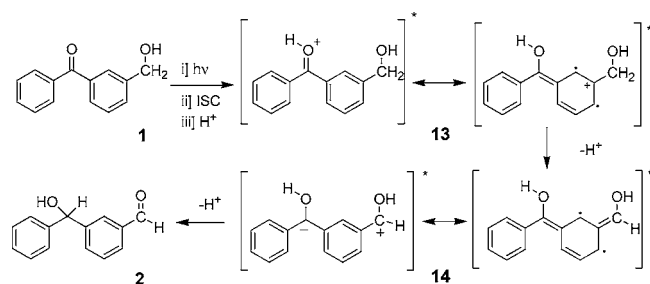
(11) Semipreparative photolysis⁵ at pH 2 ($\sim 10^{-3}$ M) gave a product mixture consisting of 65% (**2**), 30% simple photoreduction, and 5% **3**. When the photolysis was carried out at $\sim 10^{-4}$ M, **2** (95%) and **3** (5%) were the only products.

(12) Some deuteration of the aldehyde proton was observed on extended photolysis. This is due to deuterium photoexchange of the aldehyde proton in D₂O in a manner analogous to that observed by Görner and Kuhn (Görner, H.; Kuhn, H. *J. Phys. Chem.* **1986**, *90*, 5946–5955).

$\lambda_{\text{max}} = 525 \text{ nm}$) that may be assigned to the triplet excited state of the molecule as this is consistent with the well-known benzophenone triplet.¹⁰ Decreasing the pH of the solution led to significant quenching of that transient ($\tau_{\text{pH } 7} = 9.5 \mu\text{s}$, $\tau_{\text{pH } 2} = 60 \text{ ns}$) strongly suggesting that it is the protonated triplet state that leads to the observed products via a mechanism not unlike that which Wirz and co-workers have proposed for the photochemical hydration of benzophenone in acidic aqueous solvents.¹⁰

The proposed preliminary mechanism, shown in Scheme 1, is consistent with our findings. At the pH values used in

Scheme 1. Proposed Mechanism for the Intramolecular Photoredox Behavior Observed for 3-(Hydroxymethyl)benzophenone (**1**)



the experiments ($\text{pH} > 0$), protonation of the ketone in the ground state is negligible. However, excited-state ketones are much stronger bases ($\text{p}K_{\text{a}}(\text{S}_0) = -5.7$, $\text{p}K_{\text{a}}^*(\text{T}_1) = -0.4$).^{10,15} Protonation of the excited triplet state leads to an intermediate with a positive charge at the meta position (**13**), which has also been postulated as an intermediate for the

deuteration of 3-methylbenzophenone¹⁶ and analogous to the intermediate postulated for the acid-catalyzed photohydration of benzophenone.¹⁰ The observed isotopic effect of 1.55, observed from deuterium isotope effect exchange experiments involving the photolysis of α -monodeuterated **1**, is evidence that deprotonation of the benzylic proton of the biradical intermediate to form **14** is an integral part of the mechanism. The origin of **3** could be due to reaction of **14** with molecular oxygen. This is consistent with the observation that by purging with oxygen only **3** is produced. In contrast **2** may be formed by attack of water at the positive benzylic carbon and protonation at the negative benzhydryl carbon. This is consistent with the deuterium incorporation studies. The unimolecularity of the mechanism with respect to substrate is emphasized by photolyses at low concentration which minimize the formation of oligomeric reduction products while leaving the intramolecular redox reaction unaffected.

Although this mechanism requires additional verification, the observations are largely consistent with the proposed reaction mechanism. This general reaction involves a hitherto unknown pathway and is therefore an important mechanistic alternative to the conventionally held view of benzophenones being used as hydrogen abstractors or as triplet sensitizers.

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Supporting Information Available: Experimental procedures and spectral data of important compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(14) 266 nm Nd:YAG with a flow cell purged with N_2 , $\sim 10^{-5} \text{ M}$, $\text{OD}_{266} = 0.4$.

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