ORGANIC LETTERS

2004
Vol. 6, No. 11
1797−1799

Photochemical Deuterium Exchange of the *m*-Methyl Group of 3-Methylbenzophenone and 3-Methylacetophenone in Acidic D_2O

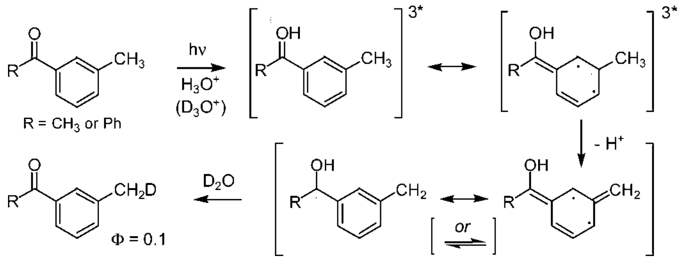
Lawrence A. Huck and Peter Wan*

Department of Chemistry, University of Victoria, P.O. Box 3065,
Victoria, British Columbia V8W 3V6, Canada

pwan@uvic.ca

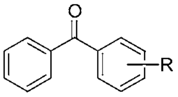
Received March 22, 2004

ABSTRACT

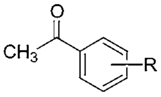


Photolysis of the title compounds in acidic aqueous solution results in “activation” of the distal *m*-methyl group, resulting in deuterium exchange ($\Phi \approx 0.1$) when D_2O is used. The reaction is not observed in neutral aqueous solution or in deuterated organic solvents such as CD_3CN. The reaction is best rationalized by a mechanism involving initial protonation at the carbonyl oxygen of the triplet excited state.

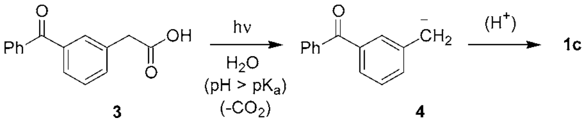
The photochemistry and photophysics of benzophenone (**1a**), acetophenone (**2a**), and related compounds are well-documented.[1a−e] Upon excitation there is rapid intersystem crossing to triplet state ($\Phi_{ST} \approx 1$) and the diradical-like character of the carbonyl moiety (in the n,π* configuration) makes possible reactions such as the Norrish Type I and II processes and hydrogen abstraction.[1e] The diradical-like character of the excited triplet state is useful for explaining much of the observed photochemistry of these compounds. In our continuing studies[2] of the photodecarboxylation of phenylacetic acids ($ArCH_2CO_2H$), we discovered that a variety of benzoyl and acetyl-substituted phenylacetic acids undergo efficient (Φ up to 0.7) photodecarboxylation (via the carboxylate form in aqueous solution), to give the corresponding methyl-substituted aromatic ketone products (e.g., eq 1 for 3-benzoylphenylacetic acid (**3**)). These photodecarboxylations most likely give rise to benzyl carbanion intermediates[3] (e.g. **4**) in the primary photochemical step. During the course of our investigations of these photo-



1a R = H
b R = *o*-CH_3
c R = *m*-CH_3
d R = *p*-CH_3



2a R = H
b R = *o*-CH_3
c R = *m*-CH_3
d R = *p*-CH_3



(1)

---

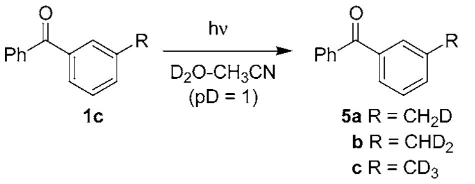
(1) See for example: (a) Turro, N. J. *Modern Molecular Photochemistry*; University Science Books: Mill Valley, CA, 1991. (b) Scaiano, J. C. *J. Photochem.* **1973/74**, *2*, 81. (c) Garcia-Garibay, M. A.; Campos, L. M. In *CRC Handbook of Organic Photochemistry and Photobiology*, 2nd ed.; Horspool, 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 52. (e) Zimmerman, H. E.; Schuster, D. I. *J. Am. Chem. Soc.* **1962**, *84*, 4527.

10.1021/ol0494616 CCC: $27.50

decarboxylations in acidic solution (with the intent of uncovering possible acid catalysis), we discovered to our surprise that the methyl-substituted photoproducts from the meta series (**1c** and **2c**) were themselves quite photoreactive. This led to the present study wherein we report a new type of photochemical reaction of aromatic ketones that results in activation of a "distal" *m*-methyl group by the ketone that requires acid, and which results in exchange of the methyl group protons (in D_2O).

The *o*-methyl-substituted ketones **1b** and **2b** did not exhibit any unexpected photochemistry: photolysis in D_2O (CH_3CN cosolvent; $\approx 10^{-3}$ M, Rayonet RPR-100 photochemical reactor; 254 or 300 nm lamps; deaerated by argon purge; 5−10 min) resulted in efficient deuterium exchange at the *o*-methyl. This is not surprising because of the proximity of the methyl group to the carbonyl. In these ortho-substituted compounds, photolysis results in the well-known[4] intramolecular hydrogen atom abstraction process, giving rise to a photoenol. Deuterium incorporation at the methyl group is then achieved via the ketonization of the photoenol in D_2O. As expected, this reaction dominates the photochemistry of these ortho-substituted compounds, and in aqueous solution, the efficiency of this process was found to be pH independent (pH 1−7). The para analogues **1d** and **2d** would not be expected to react via this pathway. Indeed, photolysis of these isomers under the same conditions gave no reaction; no deuterium exchange was observed in aqueous D_2O solution in the pH(D) 1−7 range studied.

The meta derivatives **1c** and **2c** gave unexpected photochemistry. Whereas photolysis of dilute ($\approx 10^{-3}$ M) solutions in organic solvents such as CH_3CN or in neutral D_2O solution gave essentially no photochemistry under the conditions employed above, photolysis in acidic D_2O (CH_3CN cosolvent) (pD < 3) gave efficient exchange at the *m*-methyl group; no deuterium incorporation was observed at the methyl of the acetyl group for **2c** (eq 2). No reaction was observed when the solutions were left in the dark. The introduction of deuterium to the *m*-methyl group was readily observable in the ^1H (500 MHz) NMR spectrum (Figure 1). In this particular high conversion run ($\approx$70%, based on loss of substrate) for **1c**, the extent of deuterium incorporation was calculated to consist of 39% monodeuterated, 30% dideuterated, and 10% trideuterated product (**5a**, **5b**, and **5c**, respectively).[5] These results were confirmed by mass spectrometry. A quantum yield of 0.1 was estimated (based on low conversion experiments) for monodeuterium incorporation for both **1c** and **2c**, using the known photochemical deuterium incorporation into the benzylic methylene position of dibenzosuberene ($\Phi = 0.02$)[6] in 1:1 D_2O-CH_3CN.



(2)

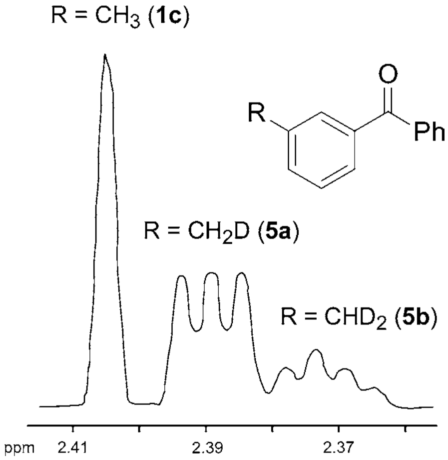


Figure 1. ^1H NMR (500 MHz, in $CDCl_3$) spectrum of the aromatic *m*-methyl region of recovered starting material **1c** on photolysis in 1:1 D_2O-CH_3CN (pD 1, 30 min). The NMR is consistent with a mixture of **1c**, **5a**, **5b** and **5c**, the amount of the trideuterio **5c** calculated by using the signals in the aromatic region (and subsequently confirmed by MS).

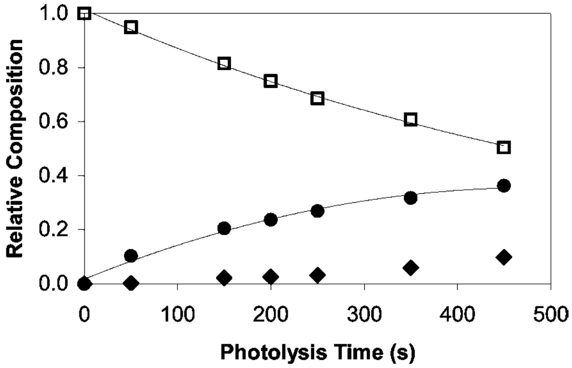


Figure 2. Plot of the yield of deuterium exchange of the *m*-methyl protons of **1c** on photolysis (300 nm) of a 10^{-3} M solution in 1:1 D_2O-CD_3CN (D_2O at pD 1): □, **1c** (CH_3); ●, **5a** (CH_2D); ◆, **5b** (CHD_2). At these conversions, the yield of **5c** (CD_3) was negligible.

In lower conversion experiments, the change in isotopic composition of the aromatic *m*-methyl group of **1c** was monitored vs photolysis time by NMR (Figure 2). As expected, there is a decrease in the amount of the starting ketone (**1c**), with a concomitant increase in the monodeuterated product (**5a**). Slower growth of the dideuterio (**5b**)

---

(2) Xu, M.; Wan, P. *J. Chem. Soc., Chem. Commun.* **2000**, 2147.

(3) (a) Laferrière, M.; Sanramé, C. N.; Scaiano, J. C. *Org. Lett.* **2004**, *6*, 873. (b) Cosa, G.; Llauger, L.; Scaiano, J. C.; Miranda, M. A. *Org. Lett.* **2002**, *4*, 3083. (c) Martinez, L. J.; Scaiano, J. C. *J. Am. Chem. Soc.* **1997**, *119*, 11066.

(4) Sammes, P. G. *Tetrahedron* **1976**, *32*, 405.

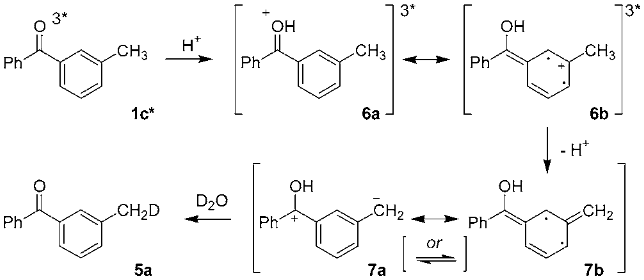
(5) In these high-conversion runs, other products were observed in the product mixture that include a "dimer", $[m\text{-PhCOPhCH}_2]_2$, which is formally derived via coupling of two $m\text{-PhCOPhCH}_2^{\bullet}$ radicals.

(6) Budac, D.; Wan, P. *J. Org. Chem.* **1992**, *57*, 887.

is observed, since its formation, of course, requires the presence of **5a**. Because this was a low conversion run, the amount of trideuterio **5c** was negligible.

As with the para isomer, a classical photoenol (via intramolecular hydrogen abstraction) cannot form with the meta compounds. Clearly there is another mechanism responsible for the observed exchange that requires acid, and that cannot operate for the para isomers. In proposing a mechanism, there are some additional noteworthy points to consider: (i) The enhanced photoreactivity displayed by the meta derivatives appears to be another example of meta activation, first delineated by Zimmerman,[7] for substituted benzenes with electron-withdrawing or -donating substituents. (ii) Experiments with a variety of solvent combinations indicate that the source of deuterium is D_2O (in aqueous solution) and not deuterated aprotic organic solvents. (iii) Experiments at a variety of different substrate concentrations revealed that the photoexchange took place without decrease in efficiency even at the lowest concentrations used in semipreparative experiments ($\approx 10^{-5}$ M). Photolysis at high concentrations gave increasing yields of side reactions presumably due to competing intermolecular hydrogen abstractions between substrate molecules. (iv) These ketones are insufficiently basic to be protonated in the ground state in the pH values used in our experiments (pH >0). It is generally believed, however, that an electronic redistribution in the excited state (toward the carbonyl) makes aromatic ketones much stronger bases.[8] Our preliminary laser flash photolysis experiments[9] of **1c** in pH 7 and 1 are in agreement with this expectation; that is, there is acid quenching of the well-known benzophenone triplet transient at 525 nm.[10] Indeed, Wirz and co-workers[11] have also recently shown that the acid quenching of triplet excited benzophenone itself is due to protonation of the carbonyl oxygen. In addition, a meta hydrate is formed predominantly, via nucleophilic attack of the corresponding carbocation by water.[11]

Scheme 1. Proposed Mechanism for the Acid-Catalyzed Deuterium Exchange of the *m*-Methyl Group for **1c**



Our proposed mechanism (Scheme 1) begins with protonation of the carbonyl oxygen of triplet excited **1c**, to give carbocation **6a/6b**, still assumed to be electronically excited.[11,12] On the basis of the above results of Zimmerman[7] and Wirz,[11] the resultant carbocation should have most of its positive charge localized at the meta position (i.e., represented by resonance structure **6b**). Neutralization of this positively charged species is achieved by the loss of a proton from the methyl group to give **7a**/**7b** (non-Kekulé meta enol). We have no information regarding the spin multiplicity of **7b** but evidence that zwitterionic **7a** may be the dominant resonance structure (with the aromatic ring restored; an equilibrium would be used if there is a change in spin from **7b** to **7a**) comes from the fact that reaction with D_2O gives the observed product. This process is remarkable because it formally allows the deprotonation of an aromatic methyl group ($pK_a \sim 25$) in an acid medium! In the case of acetophenone **2c**, deprotonation is selective for the *less* acidic methyl, as no deuterium incorporation was observed at the α-methyl ($pK_a \sim 20$).

In summary, our results show that proton quenching of aromatic ketone triplets can lead to activation of the *m*-methyl group, resulting in formation of a non-Kekulé-type meta enol, and subsequent deuterium incorporation at the aromatic methyl group. The observed chemistry may be interpreted as arising via the enhanced electron-withdrawing power[13] of the carbonyl group in the excited triplet state, which effectively activates a distal *m*-methyl group. These findings open up a new area of research in the mechanistic photochemistry of aromatic ketones, a topic of central importance in organic photochemistry.

Acknowledgment. This work was supported by the Natural Sciences and Engineering Research Council (NSERC) of Canada. We thank Matt Lukeman for some preliminary flash experiments.

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

OL0494616

---

[7] (a) Zimmerman, H. E.; Sandel, V. R. *J. Am. Chem. Soc.* **1963**, *85*, 915. (b) Zimmerman, H. E. *J. Am. Chem. Soc.* **1995**, *117*, 8988. (c) Zimmerman, H. E. *J. Phys. Chem. A* **1998**, *102*, 5616.

[8] Ireland, J. F.; Wyatt, P. A. H. *Adv. Phys. Org. Chem.* **1976**, *12*, 131.

[9] Laser flash photolysis data obtained with nitrogen-purged solutions of **1c** ($\sim 10^{-4}$ M, $OD_{266} = 0.4$.) in 1:1 H_2O-CH_3CN, aqueous pH adjusted with H_2SO_4/NaOH as required (266 nm excitation). The triplet transient of **1c** (525 nm)[10] decayed with first-order kinetics, having a lifetime (τ) of 9000 ns at pH 7, decreasing to $\tau = 200$ ns at pH 1.

[10] Buettner, A. V.; Dedinas, J. *J. Phys. Chem.* **1971**, *75*, 187.

[11] Ramseier, M.; Senn, P.; Wirz, J. *J. Phys. Chem. A* **2003**, *107*, 3305.

[12] One referee has argued that structure **6b** could be a ground-state species, that is, with a long σ bond joining the meta radicals, to give a non-Kekulé-type benzene structure. This would lead to a similar structure for **7b**, although the overall mechanism would not change.

[13] The apparent charge-transfer character of these aromatic ketone triplets (in aqueous solution) requires further study.