ORGANIC LETTERS

2005
Vol. 7, No. 12
2485−2487

Photochemistry of 2-Nitrobenzyl Enol Ethers: Oxidative C═C Bond Scission

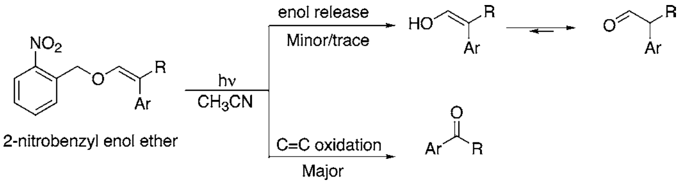
Promise K. Yong and Anamitro Banerjee*

Department of Chemistry, University of North Dakota,
Grand Forks, North Dakota 58202-9024

abanerjee@chem.und.edu

Received April 13, 2005

ABSTRACT



2-Nitrobenzyl enol ethers, when photolyzed in the presence of air, result in an oxidative C═C bond scission, forming a ketone as the major product (>60% yield). Enol release leads to the aldehyde as the minor product.

The photochemistry of 2-nitrobenzyl groups has been extensively studied in the past due to their utility as photoremovable protecting groups.[1] The 2-nitrobenzyl group has been used to photochemically release acids, alcohols, amines, phosphates, and ketones.[2] While the photochemistry of 2-nitrobenzyl esters has been studied, their enol ethers have never been investigated. We expected that photolysis of the 2-nitrobenzyl enol ethers could lead to (1) the release of the enol, which will then tautomerize to the keto form in the absence of an electrophile, and/or (2) a photoinduced intramolecular electron transfer leading to the oxidation of the enolic double bond. The photochemistry of benzyl enol ethers[3] and silyl enol ethers[4] has been studied in the past, but enol generation or oxidative cleavage has not been reported in these cases.[5] Enols have been generated photochemically in the past by H atom transfer (Norrish type II reaction),[6] OH insertion of a carbene,[7] and addition of water to ketenes.[8] These methods require specific solvents (water) or could generate specific kinds of enols. Enol release from a photoremovable group, in our opinion, would be a more convenient method to access the enols. On the other hand, oxidation of the enolic double bond could lead to the "release" of a ketone.

Our study of the photochemistry of 2-nitrobenzyl enol ethers indicates that the oxidative cleavage of the double bond is a major pathway in the presence of oxygen when 350 nm light is used.

The synthesis of the 2-nitrobenzyl enol ethers is described in Scheme 1. The commercially available 2-nitrobenzyl alcohol was converted to 1-methylsulfanylmethoxymethyl-2-nitrobenzene **2** in nearly 50% yield. Compound **2** was then

---

[1] (a) Yip, R. W.; Sharma, D. K.; Giasson, R.; Gravel, D. *J. Phys. Chem.* **1985**, *89*, 5328−5330. (b) Schupp, H.; Wong, W. K.; Schnabel, W. *J. Photochem.* **1987**, *36*, 85−97. (c) Blanc, A.; Bochet, C. G. *J. Am. Chem. Soc.* **2004**, *126*, 7174−7175. (d) Il'ichev, Y. V.; Schwörer, M. A.; Wirz, J. *J. Am. Chem. Soc.* **2004**, *126*, 4581−4595.

[2] (a) Pillai, V. N. R. *Organic Photochemistry*; Marcel Dekker: New York, 1987; Vol. 9. (b) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*; Wiley: New York, 1991. (c) Blanc, A.; Bochet, C. G. *J. Org. Chem.* **2003**, *68*, 1138−1141.

[3] Pinhey, J. T.; Schaffner, K. *Aust. J. Chem.* **1968**, *21*, 2265−2276.

[4] Bockman, T. M.; Shukla, D.; Kochi, J. K. *J. Chem. Soc., Perkin Trans. 2* **1996**, 1623−1632. (b) Bockman, T. M.; Kochi, J. K. *J. Chem. Soc., Perkin Trans. 2* **1996**, 1633−1643.

[5] Newcomb and co-workers have previously reported generation of enol ether radical cations by bond heterolysis of photochemically generated radicals. See: Horner, J. H.; Taxil, E.; Newcomb, M. *J. Am. Chem. Soc.* **2002**, *124*, 5402−5410 and references therein.

[6] (a) Chen, C.-P.; Wagner, P. J. *J. Am. Chem. Soc.* **1976**, *98*, 239−241. (b) Haag, R.; Wirz, J.; Wagner, P. J. *Helv. Chim. Acta* **1977**, *60*, 2595−2607. (c) Henin, F.; Muzart, J.; Pete, J.-P.; M'boungou-M'passi, A.; Rau, H. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 416−418. (d) Pelliccioli, A. P.; Klán, P.; Zabadal, M.; Wirz, J. *J. Am. Chem. Soc.* **2001**, *123*, 7931−7932. (e) Detalle, J.-F.; Riahi, A.; Steinmetz, V.; Henin, F.; Muzart, J. *J. Org. Chem.* **2004**, *69*, 6528−6532.

[7] Bakulev, V. A.; Chiang, Y.; Kresge, A. J.; Meng, Q.; Morzherin, Y. Y.; Popok, V. V. *J. Am. Chem. Soc.* **2001**, *123*, 2681−2682 and references therein.

[8] (a) Almstead, J.-I. K.; Urwyler, B.; Wirz, J. *J. Am. Chem. Soc.* **1994**, *116*, 954−960. (b) Wagner, B. D.; Arnold, B. R.; Brown, G. S.; Lusztyk, J. *J. Am. Chem. Soc.* **1998**, *120*, 1827−1834.

10.1021/ol0508072 CCC: $30.25

Scheme 1. Synthesis of 2-Nitrobenzyl Enol Ether

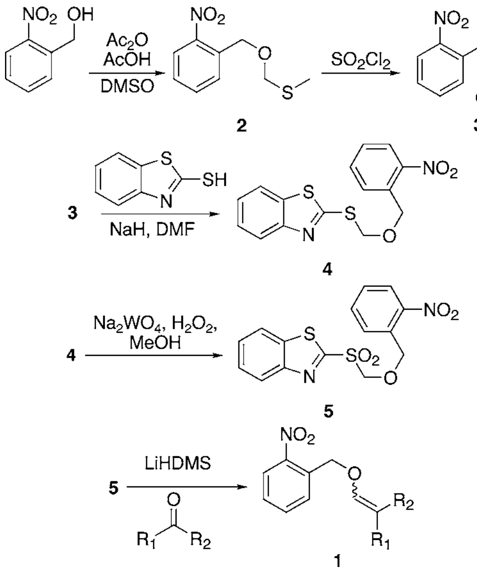
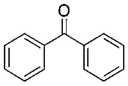
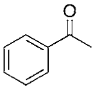
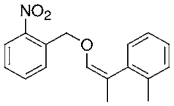
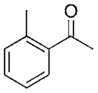
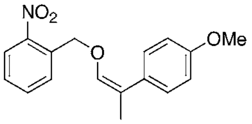
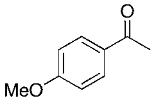
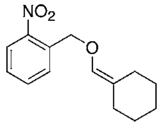
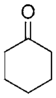
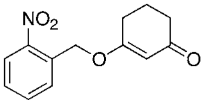
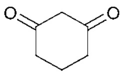


Table 1. Yields of C═C Cleavage Products from Photolysis of 2-Nitrobenzyl Enol Ethers

	compound	major product	yield
1a	$R_1 = R_2 = Ph$		63%[a]
1b	$R_1 = Me; R_2 = Ph$		62%
1c			48%
1d			63%
1e			22%
1f			~100[b]

[a] Nearly 23% 2,2-diphenylacetaldehyde was obtained as the minor product. The yield of the minor product did not change significantly when the reaction was carried out under O_2. [b] Nearly quantitative yields of 1,3-cyclohexanedione were obtained when the photolysis was carried out for 6 h (low conversions) or when $\lambda > 320$ nm was used.

converted to the chloromethyl ether **3**.[9] The chloromethyl ether decomposes during purification by column chromatography or when stored. As a result, we followed its formation by TLC and converted the crude chloromethyl ether to 2-(2-nitrobenzyloxymethanesulfanyl)benzothiazole **4**, which was then oxidized to 2-{[(2-nitrobenzyloxy)methyl]-sulfonyl}benzothiazole **5**. The compound **5** was converted to the target 2-nitrobenzyl enol ether **1** by Julia olefination.[10] The different enol ethers synthesized are listed in Table 1. When symmetric ketones were not used ($R_1 \neq R_2$), a mixture of *E* and *Z* isomers was formed. So far, we have not been able to separate these two isomers. Since the release of the enol or the C═C oxidation will lead to the same set of aldehyde or ketone for both the isomers, we did not resolve the isomers. The enol ether **1f** was synthesized as per published procedures.[11]

The photolysis of the 2-nitrobenzyl enol ethers was carried out in a Rayonet photochemical reactor with 350 nm light. The reaction was followed with TLC, and the irradiation was stopped after 2 h 45 min. The product mixture was then analyzed by GC-MS, and the products were identified by their mass spectra as well as by their retention times. The yields of the major products (listed in Table 1) were calculated from the concentration curves obtained using authentic samples. It was found that for enol ethers **1a**−**d**, the photolysis led to an oxidative C═C cleavage to produce a ketone as the major product. The enol ether **1e** produced only 22% cyclohexanone, and a mixture of polymeric adducts and rearrangement products was detected by GC-MS as major decomposition products. Only trace amounts of the expected aldehydes were detected for all the enol ethers (except **1a**, in which case 2,2-diphenylacetaldehyde was obtained in 23% yield). 2-Nitrosobenzaldehyde (along with other unidentified decomposition byproducts) was detected as a byproduct (possibly the result of secondary photolysis of the formic acid ester). Control experiments ruled out the possibility of secondary photolysis of the released enols in their keto forms (we assume that the enols will undergo rapid tautomerism to the keto form prior to absorption of another photon) as a possible pathway for the oxidative cleavage products under these conditions.[12]

The enol ethers **1a** and **1b** were photolyzed under nitrogen and under oxygen. The photolysis in the absence of oxygen (under nitrogen) reduced the yield of benzophenone and acetophenone to 23 and 32%, respectively. Under oxygen, however, the yield of the enol release increased marginally for the enol ethers (69% for **1a** and 65% for **1b**) when compared to photolysis under air. The marginal improvements in oxidative cleavage yields in the presence of oxygen, as well as the decline in the yields when the photolysis was

---

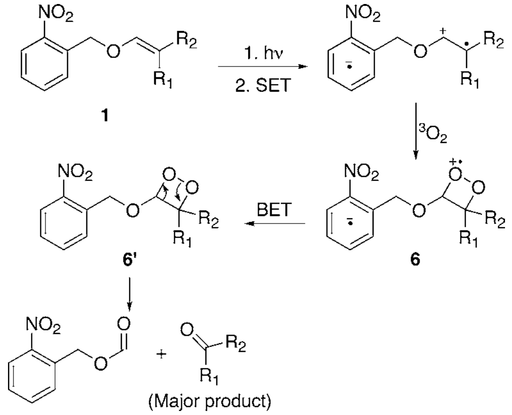
(9) (a) Benneche, T.; Strande, P.; Undheim, K. *Synthesis* **1983**, 762−763. (b) Schwartz, M. E.; Breaker, R. R.; Asteriadis, G. T.; deBear, J. S.; Gough, G. R. *Bioorg. Med. Chem. Lett.* **1992**, *2*, 1019−1024.

(10) Surprenant, S.; Chan, W. Y.; Berthelette, C. *Org. Lett.* **2003**, *5*, 4851−4854.

(11) Wu, C.-S.; Huang, J.-L.; Sun, Y.-S.; Yang, D.-Y. *J. Med. Chem.* **2002**, *45*, 2222−2228.

(12) Clennan, E. L.; Pan, G.-L. *Org. Lett.* **2003**, *5*, 4979−4982.

Scheme 2. Proposed Mechanism of C═C Oxidative Cleavage[a]



[a] SET: single-electron transfer. BET: back electron transfer.

carried out in the presence of nitrogen, lead us to believe that molecular oxygen was involved in the reaction. While singlet oxygen is known to form dioxetane rings with alkene via [2 + 2] cyclizations,[13] it is unlikely to occur in this case, as there is no known source of singlet oxygen. The triplet oxygen has been shown to form an adduct with alkene radical cations, which can then cyclize to form a dioxetane radical cation ring.[14] On the basis of these observations and literature reports, we propose the following mechanism for the oxidative cleavage of C═C for the enol ethers (Scheme 2). Photolysis of **1** leads to its excited singlet state with the 2-nitrobenzyl group acting as the chromophore. Schore and Turro have shown that excited singlet states of ketones can be quenched by enol ethers via an electron-transfer pathway to produce ion radical pairs.[15] We believe that in this case, the enol ether quenches the 2-nitrobenzyl chromophore by an intramolecular electron transfer to form the zwitterionic species. The aromatic rings on the double bond help stabilize the electron-deficient double bond, which is consistent with our observation that the yield of the oxidative cleavage drops when no aromatic rings are present (entry **1e**). 3-(2-Nitrobenzyloxy)cyclohex-2-enone, **1f**, when photolyzed for prolonged periods of time, produced only 1,3-cyclohexanedione (no C═C oxidative cleavage products were detected). The lack of reactivity of **1f** under these conditions is consistent with the proposed electron-transfer mechanism. The alkene cation radical then reacts with molecular oxygen to form a dioxetane radical cation **6**. On the basis of previous reports, it is likely that the dioxetane ring formation occurs via a peroxy radical intermediate.[16] The back electron transfer from the nitrobenzyl ring to the dioxetane ring occurs to form the compound **6′**. The dioxetane ring then decomposes to form the products.

The reduced yield of the oxidative cleavage products under nitrogen is not negligible and cannot be explained by traces of dissolved oxygen. This leads us to believe that an alternate pathway exists for this reaction under these conditions. It is possible that under nitrogen, traces of dissolved water could hydrate the radical cation leading to the ketone. Alternatively, the oxygen of the nitro goup could transfer to form the ketone. These possible pathways could at best be a minor pathway in the presence of air or oxygen since the ketone yields are substantially higher under these conditions even though the same solvent is used.

Due to the high yields of the products obtained, we believe that this reaction could be useful to synthetic chemists. In the future, we will investigate the substitution effects and the possibility of using an external excited-state electron acceptor to the alkyl enol ether in order to carry out these reactions. This will simplify the synthesis of the enol ethers, maximize the yields of the ketone, reduce the possibility of rearrangements, and offer flexibility with respect to the use of the electron acceptor. We also plan to study the possibility of using vinyl halides for these types of oxidative cleavage reactions.

Acknowledgment. The authors thank ND-EPSCoR, the ND-EPSCoR "Network in Catalysis" program (NSF-EPS-0132289), and the University of North Dakota for funding this research. The authors also thank Ms. Ann Cody, Ms. Judy Miska, and Ms. Yan Liang for their help in the synthesis of the enol ethers.

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

OL0508072

---

(13) Schank, K.; Weiter, M.; Keasalar, R. *Helv. Chim. Acta* **2002**, *85*, 2105−2124.

(14) (a) Nelsen, S. F.; Akaba, R. *J. Am. Chem. Soc.* **1981**, *103*, 2096−2097. (b) Clennan, E. L.; Simmons, W.; Almgren, C. W. *J. Am. Chem. Soc.* **1981**, *103*, 2098−2099.

(15) Schore, N. E.; Turro, N. J. *J. Am. Chem. Soc.* **1975**, *97*, 2482−2488.

(16) *Reactive Intermediate Chemistry*; Moss, R. A., Platz, M. S., Jones, M., Jr., Eds.; Wiley-Interscience: Hoboken, NJ, 2004.