Pergamon

Tetrahedron Letters, Vol. 35, No. 25, pp. 4303-4306, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)00816-7

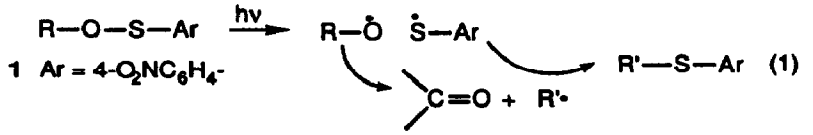
Demonstration of the Synthetic Utility of the Generation of Alkoxy Radicals by the Photo-Induced, Homolytic Dissociation of Alkyl 4-Nitrobenzenesulfenates.

Daniel J. Pasto* and François Cottard

Department of Chemistry and Biochemistry, University of Notre Dame
Notre Dame, IN USA 46556

Abstract: The synthetic utility of the generation and study of the reactions of alkoxy radicals generated by the photo-induced, homolytic dissociation of alkyl 4-nitrobenzenesulfenates is demonstrated. The efficient formation of remotely substituted alcohol derivatives, and the addition of the alkoxy radical to a remotely situated C=C is illustrated.

Recent studies in the author's laboratories have focused on the photo-induced, homolytic dissociation of *t*-alkyl and *t*-homoallyl 4-nitrobenzenesulfenates (1) with the primary emphasis focusing on the reactions of the alkyl and substituted allyl radicals, formed by the β-scission of the initially formed alkoxy radicals, with the 4-nitrophenylthiyl radical [eq (1)].[1] The initially studied systems were chosen such as to favor the β-scission of the alkoxy radical[2] and to preclude intramolecular hydrogen-atom abstraction and the addition of the alkoxy radical center to a remote site of unsaturation. In the present communication we wish to present the results of a preliminary study on the use of the photo-induced, homolytic dissociation of alkyl 4-nitrobenzenesulfenates to generate and study the reactions of alkoxy radicals.



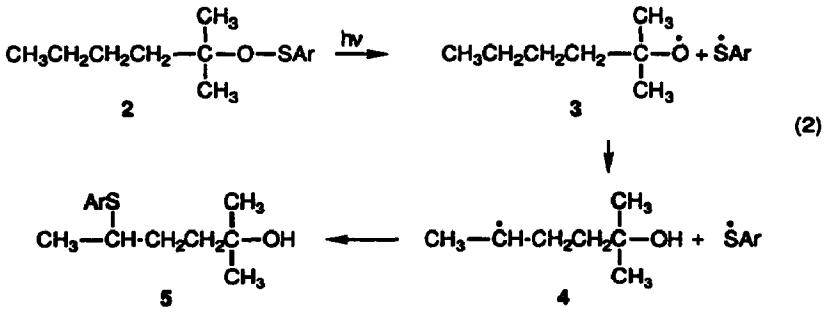
Prior methods employed to generate alkoxy radicals include the photo- and thermally-induced homolytic dissociation of dialkyl peroxides, alkyl hypochlorites,[3,4] the photo-induced decomposition of nitrite esters,[5] the AIBN-initiated reactions of tributylstannane with N-alkoxypyridine-2-thiones,[6] and by the ring opening of β,γ-epoxyalkyl radicals.[7] The above mentioned procedures proved not to be applicable for the generation of the substituted allyl radicals (by the β-scission of substituted *t*-homoallyloxy radicals) required for the study of the regioselectivity of the reactions of substituted allyl radicals. Attempts to prepare the hypochlorites of the substituted *t*-homoallyl alcohols resulted in electrophilic attack on the C=C.[1a] The highly electrophilic conditions required for the preparation of the nitrite esters also precluded the use of that method. The use of the N-alkoxypyridine-2-thione protocol did not appear to be universally feasible, while the ring opening of β,γ-epoxyalkyl radicals was not applicable. These complications are not encountered in the preparation of alkyl 4-nitrobenzenesulfenates containing remote unsaturation in the alkyl group.[1b] Furthermore, *pri-*, *sec-*

and *t*-alkyl 4-nitrobenzenesulfenates are easily prepared from the corresponding alcohol and 4-nitrobenzenesulfenyl chloride, and can be readily purified by chromatography on silica gel.[1]

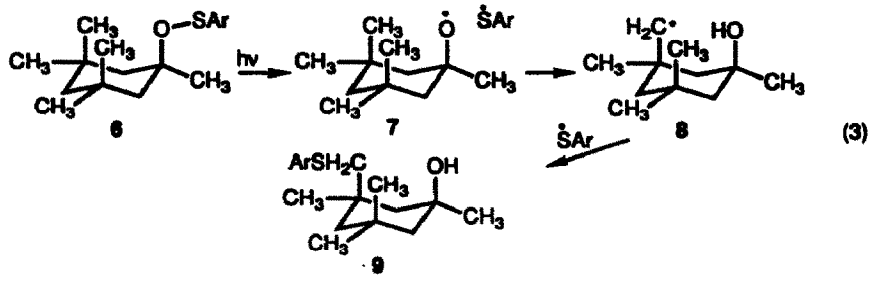
The reactions of the alkoxy radicals of interest are the intramolecular hydrogen-atom transfer leading to remote functionalization, and addition to a remote π system. Intramolecular H-atom transfer reactions in alkoxy radicals have been observed to occur only *via* six-centered transition structures.[4,7c,8] The preference for δ-H-atom abstraction has been attributed to a more favorable entropy of activation, while ε-H-atom abstraction is enthalpically favored.[9] In the addition to a δ,ε-C=C, formation of a five-membered ring, tetrahydrofuran derivative is favored over six-membered ring, tetrahydropyran formation.[5,10] In contrast, addition to an ε,ζ-C≡C produces both six- and seven-membered ring products.[11]

The reactions reported herein have been carried out in benzene-d_6 solution (~10^{-3} M) and were monitored by ^{1}H NMR spectroscopy, or in regular benzene for larger-scale reactions.[12] The solution of the alkyl 4-nitrobenzenesulfenates were irradiated with 350 nm wavelength light using a Rayonet Photochemical Chamber reactor, model PRP-100, at ~35 °C. The ^{1}H NMR spectra of the product solutions indicated the clean formation of only the products shown in the following reaction equations. The products were readily isolated using chromatographic techniques in 60-75% yield.

The photo-induced, homolytic dissociation of *t*-heptyl 4-nitrobenzenesulfenate (**2**)[13] results in the formation of **5** as the only detectable product; its formation being illustrated in eq (2). The structure of the product is indicated by the presence of a high-field methyl doublet indicating that H-atom abstraction has occurred as shown.[13] Of interest here is to note that the rate of intramolecular H-atom abstraction to form the carbon-centered radical **4** is faster than that of β-scission of **3**. In the case of **2** the alkoxy carbon atom is *tertiary* which favors β-scission, but the alkyl radical that would be formed on β-scission is a *primary* alkyl radical which disfavors β-scission.[3]

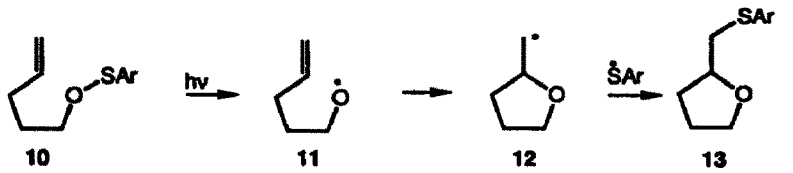


The photo-induced decomposition of the sulfenate **6**[14] cleanly produces the remotely substituted product **9** in 62% isolated yield [eq (3)]. The ^{1}H NMR spectrum of the product shows four high-field methyl singlets, and three high-field sets and one low-field set of AB doublets representing the four sets of diastereotopic methylene protons which is consistent only with a product having the structure shown as **9**.[14,15] There is no indication for the formation of any product being derived from β-scission of the alkoxy radical **7**. Again, although the alkoxy radical is *tertiary*, the radical formed on β-scission would be a *primary* alkyl radical which disfavors β-scission.[3]



(3)

The photo-induced, homolytic dissociation of 4-pent-1-enyl 4-nitrobenzenesulfenate (**10**)[16] results in the formation of only **13** (by ^{1}H NMR) which was isolated in 75% yield after chromatography on silica gel [eq (4)]. The structure of the product is definitively indicated by the ^{1}H NMR spectrum of the product which shows the presence of an A-XY spin system for the CH-CH_2-SAr portion of the molecule.[16]



(4)

The preliminary results outlined in this communication indicate that the photo-induced, homolytic dissociation of alkyl 4-nitrobenzenesulfenates is a very efficient and selective method for the generation of alkoxy radicals, and for the study of their chemistry. Further studies are under way to extend these investigations to other systems having remotely situated C=C, C≡C, and C=C=C functions.

References:

1. a) Pasto, D. J.; L'Hermine, G. *J. Org. Chem.* **1990**, *55*, 5815. b) Pasto, D. J.; L'Hermine, G. *Tetrahedron*, **1993**, *49*, 3259.
2. The β-scission of alkoxy radicals is favored by increased substitution at the carbinol carbon atom, and by increasing stability of the radical formed.
3. Walling, C.; Clark, R. T. *J. Am. Chem. Soc.* **1974**, *96*, 4530.
4. Walling, C.; Padwa, A. *J. Am. Chem. Soc.* **1963**, *85*, 1593.
5. For reviews see: Barton, D. H. R. *Pure Appl. Chem.* **1968**, *16*, 1. Hesse, R. H. *Adv. Free-Radical Chem.* **1969**, *3*, 83.
6. Beckwith, A. L. J.; Hay, B. P. *J. Am. Chem. Soc.* **1988**, *110*, 415.
7. a) Krosley, K. W.; Gleicher, G. J.; Clapp, G. E. *J. Org. Chem.* **1992**, *57*, 840. b) Russell, G. A.; Shi, B. Z., Talk #98, Division of Organic Chemistry, National ACS Meeting, Denver, CO, April, 1993. c) Rawal, V. H.; Newton, R. C.; Krishnamurthy, V. *J. Org. Chem.* **1990**, *55*, 5181. d) Murphy, F. A.; Patterson, C. W.; Wooster, N. F. *J. Chem. Soc., Chem. Commun.* **1988**, 294. e) Johns, A.; Murphy, J. A. *Tetrahedron Lett.* **1988**, *29*, 837. f) Barton, D. H. R.; Motherwell, R. S.; Motherwell, W. B. *J. Chem.*

Soc., Perkin Trans. I, **1981**, 2363. g) Carlson, R. G.; Huber, J. H.-A.; Henton, D. E. *J. Chem. Soc., Chem. Commun.* **1973**, 233.

8. For a review see: Brun, P.; Waegell, B. *Reactive Intermediates*, Vol. 3, Abramovich, R. A., ed., Plenum Press, New York, 1983, p 367.
9. Dorigo, A. E.; Houk, K. N. *J. Am. Chem. Soc.* **1987**, *109*, 2195.
10. Kraus, G. A.; Thurston, J. *Tetrahedron Lett.* **1987**, *28*, 4011, and references cited therein.
11. See fn 5c.
12. It was necessary to use benzene as the solvent for the reactions described herein in order to avoid intermolecular hydrogen atom abstraction by the alkoxy radicals (see ref 1).
13. ^{1}H NMR of **2**: δ ($CDCl_3$) 0.95 (t, J = 7.20 Hz, 3 H), 1.28 (s, 6 H), 1.35 (m, 4 H), 1.60 (m, 2 H), 7.30 (d, J = 9.08 Hz, 2 H), 8.20 (d, J = 9.08 Hz). ^{13}C NMR of **2**: δ ($CDCl_3$) 22.9, 25.0, 26.4, 40.7, 86.6, 119.9, 123.7, 144.5, 154.2. HR-FAB-MS; calcd for ($C_{13}H_{19}NO_3S$ + H^+) 270.116, found 270.115. ^{1}H NMR of **5**: δ ($CDCl_3$) 1.23 (s, 6 H), 1.40 (d, J = 6.60 Hz, 3 H), 1.60 (m, 4 H), 7.35 (d, J = 9.02 Hz, 2 H), 8.15 (d, J = 9.02 Hz, 2 H). ^{13}C NMR of **5**: ($CDCl_3$) δ 20.9, 29.3, 29.4, 30.9, 40.6, 42.0, 70.6, 124.0, 127.6, 145.0, 147.1. HR-EIMS: calcd for $C_{13}H_{19}NO_3S$ 269.109, found 269.109.
14. ^{1}H NMR of **8**: δ ($CDCl_3$) 0.89 (s, 6 H), 1.05 (d, J = 13.80 Hz, 1 H), 1.17 (d, J = 15.90 Hz, 2 H), 1.20 (s, 9 H), 1.35 (dt, J = 13.80, 1.80 Hz, 1 H), 1.50 (dt, J = 15.90, 1.80 Hz, 2 H), 7.30 (d, J = 9.08 Hz, 2 H), 8.20 (d, J = 8.09 Hz, 1 H). ^{13}C NMR of **8**: δ ($CDCl_3$) 28.5, 31.4, 34.3, 36.1, 50.6, 51.7, 72.3, 119.9, 123.7, 144.5, 154.2. HR-EIMS; no parent ion, fragment ion calcd for $C_{10}H_{19}O^+$ 155.144, found 155.143. ^{1}H NMR of **9**: δ ($CDCl_3$) 0.93 (s, 3 H), 1.05 (s, 3 H), 1.12 (d, J = 14.10 Hz, 1 H), 1.20 (d, J cannot be determined due to overlap with one of the methyl singlets, 1 H), 1.22 (s, 3 H), 1.24 (s, 3 H), 1.25 (d, J cannot be determined due to overlap with one of the methyl singlets, 1 H), 1.55 (dt, J = 14.40, 2.1 Hz, 1 H), 1.75 (dt, J = 14.10, 2.1 Hz, 1 H), 1.90 (dt, J = 14.40, 2.1 Hz, 1 H), 3.50 (d, J = 11.40 Hz, 1 H), 3.60 (d, J = 11.40 Hz, 1 H), 7.30 (d, J = 9.30 Hz, 2 H), 8.10 (d, J = 9.30 Hz, 2 H). ^{13}C NMR of **9**: δ ($CDCl_3$) 28.2, 31.2, 32.2, 34.1, 35.4,36.2, 42.6, 47.8, 50.4, 72.2, 123.8, 126.2, 144.6, 149.3. HR-FAB-MS: calcd for ($C_{17}H_{25}NO_3S$ + H^+) 324.163, found 324.163.
15. The conformation illustrated for **9** is not intended to imply that it is the only, or the major, conformation of **9** existing in solution, but is employed for ease in following the course of the reaction.
16. ^{1}H NMR of **10**: δ ($CDCl_3$) 1.80 (m, 2 H), 2.20 (m, 2 H), 3.90 (t, J = 6.50 Hz, 2 H), 5.00 (m, 2 H), 5.80 (ddt, J = 16.31, 10.20, 1.00 Hz, 1 H), 7.20 (d, J = 9.03 Hz, 2 H), 8.20 (d, J = 9.03 Hz, 2 H). ^{13}C NMR of **10**: δ ($CDCl_3$) 29.3, 29.5, 78.6, 78.6, 115.4, 119.7, 124.0, 137.1, 144.9, 151.5. HR-FAB-MS: calcd for ($C_{11}H_{13}NO_3S$ + H^+) 240.069, found 240.069. ^{1}H NMR of **13**: δ ($CDCl_3$) 1.70 (m, 1 H), 1.95 (m, 2 H), 2.10 (m, 1 H), 3.19 (dd, J = 13.10, 5.86 Hz, 1 H), 3.23 (dd, J = 13.10, 6.03 Hz, 1 H), 3.78 (m, 1 H), 3.92, (m 1 H), 7.40 (d, J = 8.96 Hz, 2 H), 8.15 (d, J = 8.96 Hz, 2 H). ^{13}C NMR of **13**: δ 25.8, 31.2, 37.2, 65.5, 77.0, 123.9, 126.3, 145.0, 147.4. HR-FAB-MS: calcd for ($C_{11}H_{13}NO_3S$ + H^+) 240.069, found 240.069.

(*Received in USA* 27 *January* 1994; *revised* 29 *March* 1994; *accepted* 21 *April* 1994)