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Ene-like Addition of an Oxoammonium Cation to Alkenes: Highly Selective Route to Allylic Alkoxyamines

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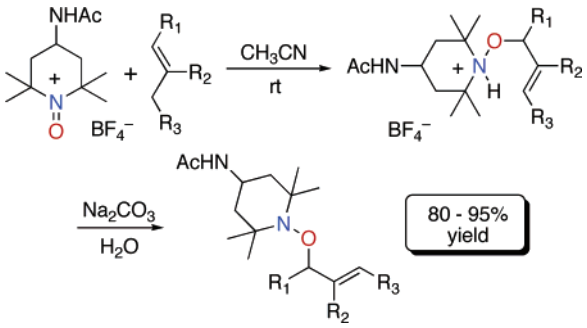
ABSTRACT



The oxoammonium cation of 4-acetamido-2,2,6,6-tetramethylpiperidine-1-oxoammonium tetrafluoroborate (1) adds rapidly at room temperature in an ene-like fashion to trisubstituted alkenes to afford allylic alkoxyamines in high yield.

Oxoammonium salts are widely used, either catalytically or stoichiometrically, for the oxidation of alcohols,[1] but little is known concerning their potential reactions with alkenes. The reactions of oxoammonium salts with the enol form of ketones and 1,3-diones to give 1,2-diketones and 1,2,3-triketones, respectively, have been known for some time.[2] Oxoammonium halides are known to add to electron-rich alkenes, such as enol ethers and styrenes, to give 1,2-addition products;[3] stabilized enolates have been trapped by oxoammonium salts to afford alkoxyamines;[4] and conjugated alkenes are reported to undergo allylic oxidation when treated with electrochemically generated oxoammonium cations.[5] Herein we report that 4-acetamido-2,2,6,6-tetramethylpiperidine-1-oxoammonium tetrafluoroborate[6] (**1**) adds rapidly, cleanly, and selectively in an ene-like fashion to trisubstituted alkenes in acetonitrile at room temperature to afford a novel route to allylic alkoxyamines.[7] Such alkoxyamines are widely used as initiators of "living" free-radical polymerizations.[8]

(1) For reviews, see: (a) Bobbitt, J. M.; Flores, C. L. *Heterocycles* **1988**, *27*, 509. (b) de Nooy, A. E. J.; Besemer, A. C.; van Bekkum, H. *Synthesis* **1996**, 1153. (c) Merbouh, N.; Bobbitt, J. M.; Brückner, C. *Org. Prep. Proced. Int.* **2004**, *36*, 1.

(2) (a) Golubev, V. A.: Miklyush, R. V. *J. Org. Chem. U.S.S.R.* **1972**, *8*, 1376. (b) Hunter, D. H.; Barton, D. H. R.; Motherwell, W. J. *Tetrahedron Lett.* **1984**, *25*, 603. (c) Liu, Y.-C.; Ren, T.; Guo, Q.-X. *Chin. J. Chem.* **1996**, *14*, 252.

(3) (a) Takata, T.; Tsujino, Y.; Nakanishi, S.; Nakamura, K.; Yoshida, E.; Endo, T. *Chem. Lett.* **1999**, 937. (b) Church, K. M.; Holloway, L. M.; Matley, R. C.; Brower, R. J. *Nucleosides Nucleotides* **2004**, *23*, 1723.

(4) Schämann, M.; Schäfer, H, J. *Synlett* **2004**, 1601.

(5) Breton, T.; Liagre, D.; Belgsir, E. M. *Tetrahedron Lett.* **2005**, *46*, 2487.

(6) Bobbitt, J. M.; Merbouh, N. *Organic Syntheses*; Wiley: New York, 2005; Vol. 82, p 80. The 4-acetamido group on **1** raises the melting point of the salt and results in a much increased stability relative to salts derived from TEMPO.

(7) Alkoxyamines are typically prepared either by trapping a carbon-centered radical with a nitroxide or via a Meisenheimer rearrangement. For leading references, see: (a) Braslau, R.; Burrill, L. C., Sianno, M.; Naik, N.; Howden, R. K.; Mahal, L. K. *Macromolecules* **1997**, *30*, 6445. (b) Barclay, G. G.; Hawker, C. J.; Ito, H.; Ornellana, A.; Malenfant, P. R. L.; Sinta, R. F. *Macromolecules* **1998**, *31*, 1024. (c) Cadot, C.; Dalko, P. I.; Cossy, J. *J. Org. Chem.* **2002**, *67*, 7193. (d) Braslau, R.; Tsimelzon, A.; Gewandter, *J. Org. Lett.* **2004**, *6*, 2233. (e) Wetter, C.; Jantos, K.; Woithe, K.; Studer, A. *Org. Lett.* **2003**, *5*, 2899. (f) Albini, A. *Synthesis* **1993**, 263. (g) Anderson, C. D.; Shea, K. J.; Rychnovsky, S. D. *Org. Lett.* **2005**, *7*, 4879.

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We were prompted to explore the reactions of **1** with alkenes following an observation made some time ago in the course of a study of the oxidation of various alcohols with stoichiometric quantities of oxoammonium salt: the oxidation of citronellol was accompanied by reaction at the carbon−carbon double bond to give products that were not identified at the time.[9]

The reactions of a variety of representative alkenes with **1** were surveyed by analysis of aliquots taken from a series of reactions in which approximately 0.2 M solutions of alkene and a hydrocarbon standard (heptane or octane) in acetonitrile containing an equimolar quantity of **1** were allowed to stand at room temperature. The disappearance of alkene was monitored by capillary GC as a function of time. The results of these experiments, illustrated graphically in Figure 1, indicate that, of the alkenes surveyed, only those having a trisubstituted double bond (i.e., 1-methylcyclohexene and 2-methyl-2-pentene) react rapidly with **1** at room temperature.[10] Terminal alkenes (i.e., 1-octene), *gem*-disubstituted alkenes (i.e., 2-methyl-1-pentene), and 1,2-disubstituted alkenes (i.e., cyclohexene) fail to react under these conditions, and tetrasubstituted alkenes (i.e., 2,3-dimethyl-2-butene) react very slowly. In short, the reaction of **1** with alkenes at room temperature appears to be highly selective for trisubstituted substrates. The product of the reaction of **1** with a trisubstituted alkene is an allylic alkoxyamine salt that is readily converted to the free base upon treatment with aqueous Na_2CO_3 (Table 1).

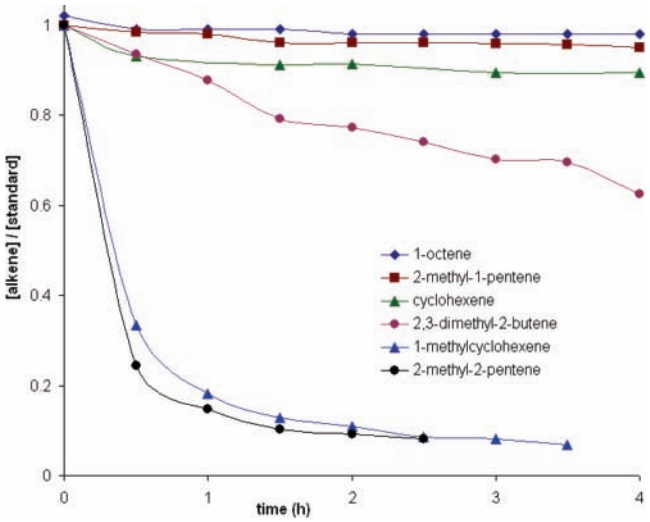
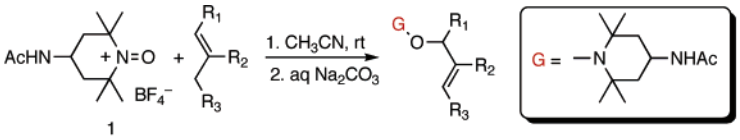
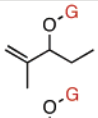
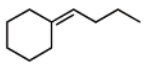
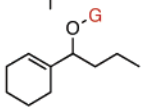
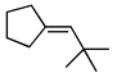
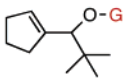
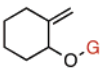
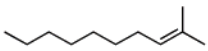
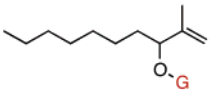
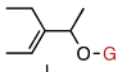
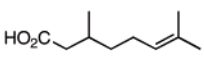
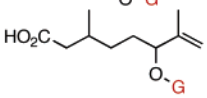
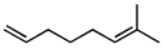
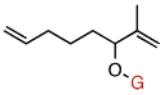


Figure 1. Reaction of various alkenes with oxoammonium salt **1**.

Table 1. Ene-like Addition of **1** to Alkenes[a]

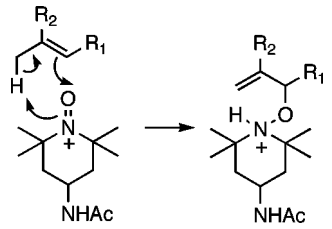


entry	alkene	product	time (h)	% yield[b]
1			4	93
2			3	60
3			3	80
4			1.5	95[c]
5			3	86
6			4	75
7			4	94
8			2	80

[a] Reactions were conducted by stirring approximately 0.2 M solutions of the alkene and one molar equivalent of **1** at room temperature. [b] Isolated yield of chromatographically pure, crystalline product. [c] Two molar equivalents of **1** were used.

The addition of **1** to a trisubstiuted alkene is formally equivalent to an ene-like addition of the oxoammonium cation to the carbon−carbon π-bond of the alkene with concomitant, if not simultaneous, removal of an allylic proton as depicted in Scheme 1. Thus, unlike oxoammonium halides,

Scheme 1



which add in a 1,2-fashion to electron-rich alkenes,[3] addition of the non-nucleophilic tetrafluorborate salt results in trans-position of the π-bond.

As demonstrated by the results summarized in Table 1, the addition of **1** to a trisubstituted alkene occurs rapidly and cleanly under very mild conditions. Within a few hours at room temperature, a solution of the alkene and an equimolar quantity of **1** in acetonitrile is converted to the addition product from which the allylic alkoxyamine may be isolated in good to excellent yield. Not surprisingly, the addition reaction is even more rapid when an excess of **1** is used (Table 1, entry 4); the excess oxoammonium salt may be removed by adding methanol prior to workup.

As might be anticipated, the addition appears to be highly regioselective: in every instance, the less highy substituted carbon of the π-bond is attacked by the oxoammonium cation to give a secondary allylic alkoxyamine. Moreover, the substantial preference for addition of **1** to trisubstituted carbon−carbon π-bonds may be exploited for chemoselective addition to dienes containing a terminal and a trisubstituted π-bond (Table 1, entry 8).

The pronounced selectivity for trisubstituted double bonds in the addition of **1** to alkenes is likely related to the need for a relatively electron-rich π-system. Such a rationale is consistent with prior work demonstrating that the 1,2-addition of oxoammonium halides to alkenes is restricted to electron-rich substrates.[3] The rather slow reaction of **1** with a tetrasubstituted alkene (Figure 1) may be a reflection of the crowded steric environment in the transition state for the process.

In summary, the facile and selective ene-like addition of oxoammonium tetrafluoroborate salts such as **1** to trisubstituted alkenes provides a novel route to secondary allylic alkoxyamines.

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Supporting Information Available: Detailed experimental procedures and NMR spectra of products. This material is available free of charge via the Internet at http://pubs.acs.org.

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(8) (a) Benoit, D.; Chaplinski, V.; Braslau, R.; Hawker, C. J. *J. Am. Chem. Soc.* **1999**, *121*, 3904. (b) Hawker, C. J.; Bosman, A. W.; Harth, E. *Chem. Rev.* **2001**, *101*, 3661.

(9) Bobbitt, J. M. *J. Org. Chem.* **1998**, *63*, 9367.

(10) It should be noted that solutions of **1** in acetonitrile are not stable at elevated temperatures, and for this reason, no attempt was made to conduct reactions at temperatures above ambient.