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A Mild, Convenient, Non-Acidic Conversion of Enol Ethers into Alcohols Using $Hg(OAc)_2$ - $NaBH_4$

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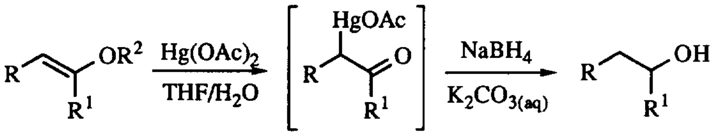
Abstract: Alkyl enol ethers can be converted into the corresponding alcohols in good to excellent yields by treatment with aqueous $Hg(OAc)_2$ - $NaBH_4$ in one reaction flask. This method is sufficiently mild to allow the survival of acid-sensitive groups such as silyl ethers, THP-protected alcohols and *N*-Boc-protected amines. © 1997, Elsevier Science Ltd. All rights reserved.

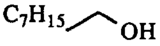
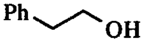
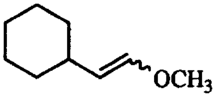
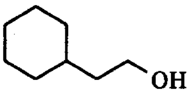
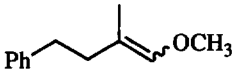
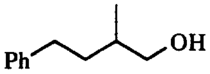
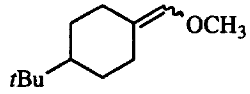
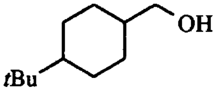
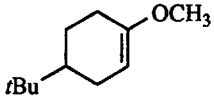
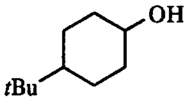
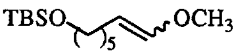
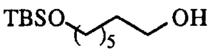
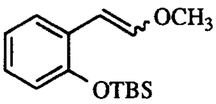
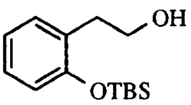
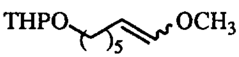
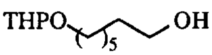
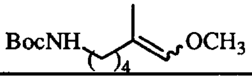
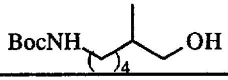
Alkyl enol ethers can be hydrolyzed under acid catalysis to the corresponding aldehyde or ketone.[1,2] Typically, acids such as aqueous HCl,[3,4] H_2SO_4,[5] H_3PO_4,[6] and $HClO_4$[4,7] as well as *p*-toluenesulfonic,[8] formic,[9] acetic,[10] oxalic[11] and trichloroacetic acids[12] have been used as catalysts. Unfortunately, many complex organic molecules decompose under strongly acidic conditions. Additionally, many widely used protecting groups are acid sensitive.[13] Although Bu_4NF-Lewis acid mixtures[14] and benzyltriethylammonium borohydride-TMSCl[15] have been reported to hydrolyze alkyl enol ethers, no evidence of compatibility with common acid-sensitive protecting groups was described.

Recently, as part of the synthesis of a vitamin D analog, Posner and Dai needed to convert an enol ether into an alcohol in a substrate which proved to be especially acid sensitive.[16] This conversion was finally effected by sequential treatment with aqueous $Hg(OAc)_2$ and $NaBH_4$,[17,18] allowing for hydrolysis and subsequent reduction in one reaction vessel and without substrate decomposition.[16] Solvomercuration-demercuration[17] has been used to convert glycals to glycosides[19] and as a means of accessing mixed acetals.[20] However, to the best of our knowledge, oxymercuration-demercuration has not been systematically studied in the conversion of alkyl enol ethers into alcohols. Herein we wish to report our finding that oxymercuration-demercuration is a general, mild and non-acidic method for converting alkyl enol ethers into alcohols.



A typical procedure is as follows: the alkyl enol ether was dissolved in THF (~ 3 mL/mmol of enol ether), cooled to 0°C and 1.2 equivalents of $Hg(OAc)_2$ in H_2O (~ 3 mL/mmol of $Hg(OAc)_2$) was added. After TLC indicated disappearance of the enol ether substrate (typically 15 - 30 minutes), 4 equivalents of $NaBH_4$ dissolved

Table: Results of Oxymercuration-Demercuration of Alkyl Enol Ethers

entry	alkyl enol ether	product	isolated yield
1			81%
2			71%
3			78%
4			83%
5			87% cis:trans = 2.5:1[a]
6			76% cis:trans = 7:93[b]
7			87%
8			83%
9			72%
10			87%[c]

[a] Cis:trans ratio determined by nmr.

[b] Cis:trans ratio determined by gas chromatography.

[c] Product gave satisfactory ^1H and ^{13}C nmr and IR spectra. All other products were spectrally consistent with authentic compounds or data reported in the literature

in saturated aqueous K_2CO_3 (~ 0.75 mL/mmol of $NaBH_4$) were added and the reaction mixture was warmed to room temperature. After 15 - 30 minutes, ethyl acetate and H_2O were added and the reaction mixture was subjected to extractive work up followed by column chromatography to give the alcohol product.

The generality of this method is demonstrated by the variety of enol ethers that can be converted into alcohols. 1,2-Disubstituted alkyl enol ethers were cleanly converted into primary alcohols (entries 1 - 3). 1,2,2-Trisubstituted alkyl enol ethers also yielded primary alcohols (entries 4, 5) while 1,1,2-trisubstituted alkyl enol ethers produced secondary alcohols (entry 6).

More significantly, the non-acidic reaction conditions permit the survival of such acid-sensitive protecting groups[13] as silyl and THP ethers and *N*-Boc-protected amines (entries 7 - 10). It is noteworthy that, although aryl silyl ethers are typically more susceptible to hydrolysis than alkyl silyl ethers under basic conditions,[21] the TBS-protected phenol is stable under these reaction conditions (entry 8).

In summary, we have developed a general, one-flask procedure for the conversion of enol ethers into the corresponding alcohols under mild, non-acidic conditions. The method is particularly useful as it is compatible with acid-sensitive protecting groups. If the carbonyl compound is the desired product, this method coupled with a mild oxidation technique[22] represents an alternative to the harsh, acidic conditions typically used to hydrolyze alkyl enol ethers. We continue to investigate other aspects of this reaction and its mechanism.

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References

1. Larock, R. C. *Comprehensive Organic Transformations*; VCH: New York, 1989.
2. March, J. *Advanced Organic Chemistry*; 4 ed.; Wiley: New York, 1992.
3. a) Engel, C. R.; Just, G. *J. Am. Chem. Soc.* **1954**, *76*, 4909 - 4914.
   b) Nussbaum, A. L.; Yuan, E.; Dimer, D.; Oliveto, E. P. *J. Org. Chem.* **1961**, *26*, 3925 - 3928.
4. Kluge, A. F.; Cloudsdale, I. S. *J. Org. Chem.* **1979**, *44*, 4847 - 4852.
5. Earnshaw, C.; Wallis, C. J.; Warren, S. *J. Chem. Soc., Perkin Trans. 1* **1979**, 3099 - 3106.
6. Schulde, H. *Tetrahedron* **1975**, *31*, 89 - 92.
7. Levine, S. G. *J. Am. Chem. Soc.* **1958**, *80*, 6150 - 6151.
8. Novak, J.; Salemink, C. A. *Tetrahedron Lett.* **1981**, *22*, 1063 - 1064.
9. a) Magnus, P.; Roy, G. *J. Chem. Soc., Chem. Commun.* **1979**, 822 - 823.
   b) Jenneskens, L. W.; Krul, A. H. P.; Kraakman, P. A.; Moene, W.; de Wolf, W. H.; Bickelhaupt, F. *J. Org. Chem.* **1986**, *51*, 2162 - 2168.
10. Wollenberg, R. H.; Albizati, K. F.; Peries, R. *J. Am. Chem. Soc.* **1977**, *99*, 7365 - 7367.
11. Weinstein, B.; Fenselau, A. H. *J. Org. Chem.* **1965**, *30*, 3209 - 3211.
12. Corey, E. J.; Tius, M. A. *Tetrahedron Lett.* **1980**, *21*, 3535 - 3538.
13. Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*; Wiley: New York, 1991.

14. a) Gevorgyan, V.; Yamamoto, Y. *J. Chem. Soc., Chem. Commun.* **1994**, 59 - 60.
    b) Gevorgyan, V.; Yamamoto, Y. *Tetrahedron Lett.* **1995**, *36*, 7765 - 7766.
15. Baskaran, S.; Chidambaram, N.; Narasimhan, N.; Chandrasekaran, S. *Tetrahedron Lett.* **1992**, *33*, 6371 - 6374.
16. Posner, G. H.; Dai, H. *Bioorg. Med. Chem. Lett.* **1993**, *3*, 1829 - 1834.
17. Larock, R. C. *Solvomercuration/Demercuration Reactions in Organic Synthesis*; Springer-Verlag: New York, 1986.
18. a) Barton, D. H. R.; Gero, S. D.; Cleophax, J.; Machado, A. S.; Quiclet-Sire, B. *J. Chem. Soc., Chem. Commun.* **1988**, 1184 - 1186.
    b) Barton, D. H. R.; Augy-Dorey, S.; Camara, J.; Dalko, P.; Delaumeny, J. M.; Gero, S. D.; Quiclet-Sire, B.; Stutz, P. *Tetrahedron* **1990**, *46*, 215 - 230.
19. a) Inglis, G. R.; Schwarz, J. C. P.; McLaren, L. *J. Chem. Soc.* **1962**, 1014 - 1019.
    b) Honda, S.; Kakehi, K.; Takai, H.; Takiura, K. *Carbohydrate Res.* **1973**, *29*, 477 - 487.
    c) Mukhopadhyay, A. J.; Suryawanshi, S. N.; Bhakuni, D. S. *Ind. J. Chem.* **1988**, *27B*, 1009 - 1011.
    d) Lipshutz, B. H.; Pegram, J. J.; Morey, M. C. *Tetrahedron Lett.* **1981**, *22*, 4603 - 4606.
20. Boeckman, R. K., Jr.; Flann, C. J. *Tetrahedron Lett.* **1983**, *24*, 4923 - 4926.
21. Davies, J. S.; Higginbotham, C. L.; Tremeer, E. J.; Brown, C.; Treadgold, R. C. *J. Chem. Soc., Perkin Trans. 1* **1992**, 3043 - 3048.
22. for example, see: Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480 - 2482.

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