

Oxidative Cleavage of Epoxides with Ammonium Molybdate–H₂O₂ System: An Efficient Route to α -Hydroxy Ketones

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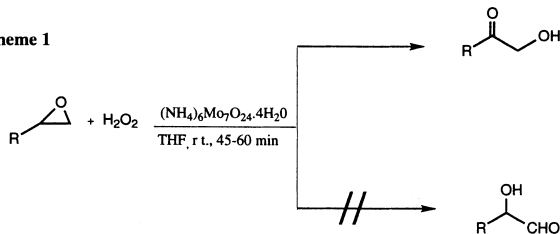
Epoxides are efficiently converted into α -hydroxy ketones by employing ammonium molybdate–H₂O₂ system. The α -hydroxy ketones are prepared without the formation of α -hydroxy aldehydes, via 1,2-diols as intermediates. The products are formed with excellent yields under very mild conditions.

Epoxides are valuable intermediates for asymmetric synthesis of complex organic compounds.¹ These are used in the synthesis of enantiomerically enriched compounds either by kinetic resolution of racemates² or asymmetric ring opening of meso epoxides.^{3,4}

α -Hydroxy ketones (α -ketols) are present in many of the biologically active compounds such as antitumour agents and drugs.^{5,6} Available methods for their preparation include the oxidation of ketones via enol ethers,⁷ or enolate anions,^{8,9} oxidation of diols,¹⁰ the acyloin¹¹ and benzoin¹² condensation, partial reduction of 1,2-diketones,¹³ oxidation of epoxides¹⁴ and alkenes,¹⁵ reaction of various acyl anion equivalents¹⁶ and acyl lithiums with ketones and aldehydes¹⁷ and reductive coupling reactions of acid halides with ketones and aldehydes.¹⁸ Among them, the oxidation of 1,2-diols and epoxides occupy a prominent position. To the best of our knowledge, there are only a few reports available in the literature for the oxidation of epoxides to α -hydroxy ketones.¹⁴ Hence it has been considered to be of great interest to develop mild and efficient methods for the oxidation of epoxides to the corresponding α -hydroxy ketones. Here we report a mild and efficient method for the oxidative ring opening of epoxides with ammonium molybdate–H₂O₂ system to corresponding α -hydroxy ketones (Scheme 1).

In the recent past molybdenum based reagents have emerged as efficient oxidants in organic synthesis.¹⁹ Ammonium molybdate catalyzes various oxidation reactions such as oxidation of alcohols,²⁰ olefin epoxidation²¹ and regioselective bromination.²²

Scheme 1



Oxidation of epoxides in presence of ammonium molybdate proceeds rapidly affording high yields of the corresponding α -hydroxy ketones. When the reaction is carried out in the absence of ammonium molybdate, the reaction did not proceed even on prolong time. Thus it is assumed that ammonium molybdate is essential for the oxidation of epoxides. Progress of the reaction

is monitored not only by a visible change in the color of the reaction mixture (from white to yellow) but also from tlc during the course of the reaction. After completion of the reaction as indicated by tlc the reaction mixture is filtered off, washed with water and extracted with chloroform to give the α -hydroxy ketones. The results are summarized in Table 1. The reaction proceeds very fast in the case of *N*-substituted epoxides (entries 1h–1j) when compared to *O*-substituted epoxides (entries 1a–1g). However, the reaction does not have any limitations with respect to the substitution which has been later confirmed by carrying out same reaction with styrene epoxide (entry 1k) to obtain 2-hydroxyacetophenone (entry 2k).

To explain the exact path of the reaction it is believed that reaction proceeds by epoxide ring opening to corresponding 1,2-diols which subsequently undergo oxidation selectively to give α -hydroxy ketones. Differentiation of secondary alcohol from primary is a key step in this. However, this has been confirmed independently by subjecting intermediary phenyl 1,2-ethanediol to the similar conditions which has generated the desired 2-hydroxyacetophenone [UV 245 nm; IR 3371 cm⁻¹ (OH), 1797 cm⁻¹ (C=O)]. In the earlier reports the above system was used for the selective oxidation of secondary alcohols in the presence of primary alcohols.²³ Therefore it is predicted that reaction proceeds via the formation of 1,2-diols which further undergo selective oxidation to give corresponding α -hydroxy ketones. The mechanism is similar to those reported in the literature.^{7b,10,14b,14h}

Table 1. Oxidative ring opening of epoxides with ammonium molybdate–H₂O₂ system

Entry	R	Reaction Time/ min	Product	Yield/ %
1a	C ₆ H ₅ OCH ₂	60	2a	96
1b	2-CH ₃ -C ₆ H ₄ OCH ₂	60	2b	94
1c	3-CH ₃ O-C ₆ H ₄ OCH ₂	60	2c	95
1d	4-CH ₃ O-C ₆ H ₄ OCH ₂	60	2d	94
1e	4-CH ₃ CONH-C ₆ H ₄ OCH ₂	60	2e	92
1f		60	2f	94
1g		60	2g	92
1h		45	2h	96
1i		45	2i	94
1j		45	2j	96
1k	C ₆ H ₅	45	2k	94

There have been some reports where the primary hydroxyl group of 1,2-diols is oxidized in presence of secondary alcohols.²⁴ The oxidation of 1,2-diols appears to be a straightforward route to prepare α -hydroxy aldehydes. However the present method provides α -hydroxy ketones without formation of α -hydroxy aldehydes.

The typical procedure involves stirring a mixture of the ammonium molybdate (1 mmol) and epoxide (1 mmol) in THF. Hydrogen peroxide (2 mL of 30% aqueous solution) was added and the reaction proceeded at room temperature. After completion of reaction as indicated by tlc, the reaction mixture was filtered off and washed with water, extracted with chloroform. The organic layer was separated and dried over Na_2SO_4 . The residue was purified by silica gel using hexane : ethyl acetate (7 : 3) as eluent to get pure product in good yield. All the products have been characterized by ^1H NMR, IR, mass spectroscopy.

In conclusion, a synthetically useful and practical approach for the preparation of α -hydroxy ketones in one-pot by the opening of epoxides with ammonium molybdate- H_2O_2 system has been developed. This method has a potential for the preparation of α -hydroxy ketones of biological interest.

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References and Notes

- 1 a) A. Johnson and K. B. Sharpless, in I. Ojima, ed., "Catalytic Asymmetric Synthesis," VCH, New York (1993), Chapter 4.1.
- 2 a) K. Maruoka, S. Nagahara, T. Ooi, and H. Yamamoto, *Tetrahedron Lett.*, **30**, 5607 (1989). b) S. Pedragosa-Moreau, A. Archelas, and R. Furstoss, *J. Org. Chem.*, **58**, 5533 (1993). c) P. L. Barli, G. Berti, and E. Mastrorilli, *Tetrahedron*, **49**, 6263 (1993).
- 3 a) H. Yamashita and T. Mukaiyama, *Chem Lett.*, **1985**, 1643. b) S. G. Davies and P. Warner, *Tetrahedron Lett.*, **26**, 4815 (1985). c) M. Emziane, K. I. Sutowardeyo, and D. Sinou, *J. Organomet. Chem.*, **346**, C-7 (1988). d) H. Su, L. Walder, Z. D. Zhang, and R. Scheffold, *Helv. Chim. Acta*, **71**, 1073 (1988). e) H. Yamashita, *Bull. Chem. Soc. Jpn.*, **61**, 1213 (1988). f) M. Hayashi, K. Kohmura and N. Oguni, *Synlett*, **1991**, 774. g) W. A. Nugent, *J. Am. Chem. Soc.*, **114**, 2768 (1992). h) M. Mischitz and K. Faber, *Tetrahedron Lett.*, **35**, 81 (1994).
- 4 a) M. Hayashi, K. Ono, H. Hoshimi, and N. Ogini, *J. Chem. Soc., Chem. Commun.*, **1994**, 2699. b) Z. Zhang and R. Scheffold, *Helv. Chim. Acta*, **76**, 2602 (1993).
- 5 Y. Tamura, T. Yakura, J.-I. Haruta, and Y. Kita, *Tetrahedron Lett.*, **26**, 3837 (1985).
- 6 a) Y. Tamura, H. Annoura, H. Yamamoto, H. Kondo, Y. Kita, and H. Fujioka, *Tetrahedron Lett.*, **28**, 5709 (1987). b) S.-I. Murahashi, T. Naota, and H. Hanaoka, *Chem Lett.*, **1993**, 1767 and references cited therein.
- 7 a) G. M. Rubottom, M. A. Vezquez, and D. R. Pelegrina, *Tetrahedron Lett.*, **15**, 4319 (1974). b) H. Yamamoto, M. Tsuda, S. Sakaguchi, and Y. Ishi, *J. Org. Chem.*, **62**, 7174 (1997) and references cited therein.
- 8 R. M. Moriarty, H. Hu, and S. C. Gupta, *Tetrahedron Lett.*, **22**, 1283 (1981).
- 9 C. Betancor, C. G. Francisco, R. Freire, and E. Suarez, *J. Chem. Soc., Chem. Commun.*, **1988**, 947.
- 10 a) S. K. Kang, K. Y. Jung, C. H. Park, E. Y. Namkoong, and T. H. Kim, *Tetrahedron Lett.*, **36**, 6287 (1995). b) T. Morimoto, M. Hirano, K. Iwasaki, and T. Ishikawa, *Chem. Lett.*, **1994**, 53. c) R. Curci, D. Luccia, A. Annadinioi, C. Fusco, and A. Rosa, *Tetrahedron Lett.*, **37**, 115 (1994). d) P. Bovicelli, P. Lupatelli, and A. Sanetti, *Tetrahedron Lett.*, **35**, 8477 (1994). e) F. Macrouhi, J. L. Namy, and H. B. Kagan, *Tetrahedron Lett.*, **38**, 7183 (1997).
- 11 J. J. Bloomfield, D. C. Owsley, C. Ainsworth, and R. E. Robertson, *J. Org. Chem.*, **40**, 393 (1975).
- 12 J. P. Kuebrich, R. L. Schowen, M. S. Wang, and M. E. Lupton, *J. Am. Chem. Soc.*, **93**, 1214 (1971).
- 13 T. L. Ho and G. A. Olah, *Synthesis*, **1976**, 815.
- 14 a) T. M. Santosuso and D. Swern, *J. Org. Chem.*, **40**, 2764 (1975). b) E. Hasegawa, K. Ishiyama, H. Kashiwazaki, T. Horaguchi, and T. Shimizu, *Tetrahedron Lett.*, **31**, 4045 (1990). c) Y. Zhu, Y. Tu, H. Yu, and Y. Shi, *Tetrahedron Lett.*, **39**, 7819 (1998). d) D. Villemin and M. Hammadi, *Synth. Commun.*, **25**, 3141 (1995). e) T. Cohen and T. Tsuji, *J. Org. Chem.*, **26**, 1681 (1961). f) T. Tsuji, *Bull. Chem. Soc. Jpn.*, **62**, 645 (1971). g) E. Ruiz-Hitzky and B. Casal, *J. Catal.*, **92**, 291 (1985). h) A. R. Katritzky, A. K. Heck, J. Li, A. Wells, and C. Gart, *Synth. Commun.*, **26**, 2657 (1996). i) T. Tsuji, *Tetrahedron Lett.*, **1966**, 2416. j) B. M. Trost and M. J. Fray, *Tetrahedron Lett.*, **29**, 2163 (1988) and references cited therein.
- 15 N. S. Srinivas and D. G. Lee, *Synthesis*, **1979**, 520.
- 16 A. R. Katritzky, Z. Yang, and J. N. Lam, *J. Org. Chem.*, **56**, 6917 (1991).
- 17 T. Hiiro, Y. Morita, T. Inoue, N. Kambe, A. Ogawa, I. Ryu, and N. J. Sonoda, *J. Am. Chem. Soc.*, **112**, 455 (1990).
- 18 S. M. Ruder, *Tetrahedron Lett.*, **33**, 2621 (1992).
- 19 a) B. M. Trost and M. Lautens, *J. Am. Chem. Soc.*, **104**, 5543 (1982). b) B. M. Trost and M. Lautens, *J. Am. Chem. Soc.*, **105**, 3343 (1983). c) B. M. Trost, B. Peterson, and M. Lautens, *Tetrahedron Lett.*, **24**, 4525 (1983). d) B. M. Trost, J.-I. Yoshida, and M. Lautens, *J. Am. Chem. Soc.*, **105**, 4494 (1983).
- 20 a) S. E. Jacobson, D. A. Miccigrosso, and F. Mares, *J. Org. Chem.*, **44**, 921 (1979). b) H. Tomioka, K. Takai, K. Oshima, H. Nozaki, and K. Toriumi, *Tetrahedron Lett.*, **21**, 4843 (1980).
- 21 a) H. Mimoun, in "The Chemistry of Functional Group Peroxides", ed. by S. Patai, Wiley, New York (1982). p. 463. b) H. Minoun, *Pure Appl. Chem.*, **53**, 2389 (1981). c) R. A. Sheldon, J. K. Kochi, in "Metal Catalyzed Oxidation of Organic Compounds," Academic Press, New York (1981) p. 48.
- 22 B. M. Choudary, Y. Sudha, and P. N. Reddy, *Synlett*, **1994**, 450.
- 23 B. M. Trost and Y. Mosuyama, *Tetrahedron Lett.*, **25**, 173 (1984).
- 24 a) H. Tomioka, K. Takai, K. Oshima, and H. Nozaki, *Tetrahedron Lett.*, **22**, 1605 (1981). b) S. Kanemoto, K. Oshima, S. Matsubara, K. Takai, and H. Nozaki, *Tetrahedron Lett.*, **24**, 2185 (1983). c) T. Inokuchi, S. Matsumoto, T. Nishiyama, and S. Torii, *J. Org. Chem.*, **55**, 462 (1990). d) J. Einhorn, C. Einhorn, F. Ratajczak, and J. L. Pierre, *J. Org. Chem.*, **61**, 7452 (1996).