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The Regio- and Stereo- Selective Epoxidation of Alkenes with Methyl Trioxorhenium and Urea-Hydrogen Peroxide Adduct.

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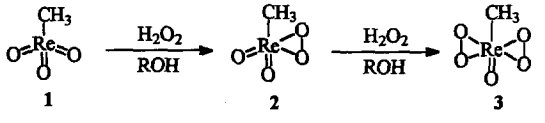
Abstract: Alkenes are expoxidized with methyltrioxorhenium and urea-hydrogen peroxide adduct in CH_2Cl_2 solution. Copyright © 1996 Elsevier Science Ltd

Methyl trioxorhenium (MTO) **1** is rapidly emerging as a versatile reagent,[1,2] and in combination with aqueous hydrogen peroxide forms peroxy adducts **2** and **3** which are capable of the epoxidation of alkenes,[3] the oxidation of amines,[4] sulphides,[5] phosphines,[6] alkynes[7], phenols,[8] and arenes,[9] and oxygen insertion into C-H bonds.[10] However, one of the potential shortcomings of this reagent combination, particularly for epoxidation, is the need for protic solvent (water, alcohol). Protic solvents may lead to the destruction of sensitive products[3] or a reduction in the stereoselectivity due to competitive hydrogen bonding by the solvent.[11] Urea hydrogen peroxide adduct (UHP) has been used successfully in combination with acid anhydrides[12] and several metal complexes[13] to perform oxidations, and it offers a solid, anhydrous source of hydrogen peroxide.[12a,14] An ongoing project in marine natural product synthesis led us to examine MTO/aq. hydrogen peroxide for both alkene and amine oxidations. Realizing the potential need for a non-protic variant of this reagent system, we initiated a study to examine UHP as a reoxidant of MTO in non-protic solvents for the catalytic epoxidation of alkenes.

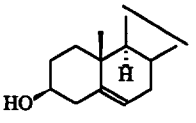
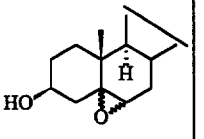
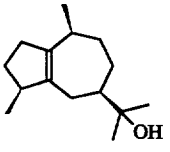
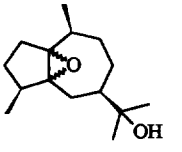
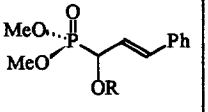
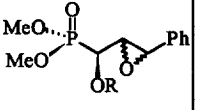
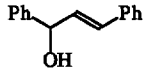
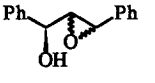
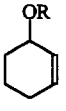
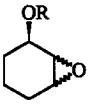
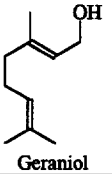
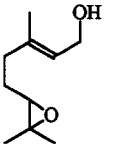
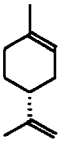
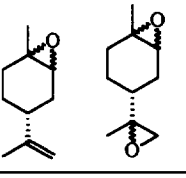
Scheme 1



1 **2** **3**

Urea hydrogen peroxide adduct is insoluble in non-polar organic solvents, however, addition of UHP (2 equiv.) to a methylene chloride solution of MTO (5 mol%) results in the rapid development of the yellow color characteristic of the peroxyrhenium intermediate **3**. Addition of cholesterol to the solution at room temperature

Table 1. The Epoxidation of Alkenes with Methyl Trioxorhenium and Urea-hydrogen Peroxide Adduct

Alkene Substrate	Entry	Conditions, Time	Results ratio, conversion	Product(s)	RCO_3H/DMD Comparison (ref)
 Cholesterol	i ii iii iv	CH_2Cl_2, 1.5 hr. + Na_2SO_4, 6 hr. PhMe, 3.5 hr. THF, 1 hr.	α/β, 4:1, 100 % α/β, 5:1, 100 % α/β, 4:1, 86 % α/β, 8:1, 50 % + decomp. products		MMPP, (ref 12a) α/β, 4:1, 88% DMD (ref 15) α/β, 1:1, 90%
 Guaiol	v vi	A, 1.5 hr. C, 1.5 hr.	α/β, 9:1, 96 % α/β, 9:1, 95 %		m-CPBA (ref 16) α/β, 6:4, high yield MPP, (ref 17) α/β, 69:31, 22%
	vii viii ix	A, 1.5 hr. C, 12 hr. (also *t*-BuOH) A, 4 hr.	For R = OH syn/anti, 3.5:1, 88 % -- no reaction-- for R = OCONHPh syn/anti, 1:3.8, 93 %		For R = OH m-CPBA (ref 18) 1:1, 100% yield DMD (ref 18) 1:1, 100% yield
	x	A, 2 hr.	syn/anti, 2:1, 97 %		NMR data (ref 19)
	xi xii xiii	A, 1 hr. C, 2-12 hr. (also *t*-BuOH) A, 24 hr.	For R = OH cis/trans, 6:1, 41 % decomp. products for R = OAc cis/trans, 1:2, 54 %		For R = OH, (ref 11) DMD in 97% CH_2Cl_2 cis/trans, 82:18, 77% for R=OAc, (ref 11) DMD in 50% CH_2Cl_2 cis/trans, 36:64, 84%
 Geraniol	xiv xv	A, 15 min. C, 30 min.	6,7-epoxide, 73% + 10% geraniol decomp. products and diepoxide		DMD (ref 20) 2,3 : 6,7 : diepoxide 10:69:21 at 40% con. 2:30:68 at 93%
 (R) (+) limonene	xvi xvii	A, 15 min. B, 30 min.	mixture of mono and di, approx 1:2, 52% mono only, 99%		(ref 21) mCPBA, 95:3 1,2 / 8,9 epoxides peroxyimidic, 62:36 1,2 / 8,9 epoxides and diepoxide 2%

A. alkene (100 mg), UHP (3 equiv.), MTO (0.05 equiv.), CH_2Cl_2 (2 mL) at 20 °C; **B.** alkene (100 mg), UHP (2 equiv.), MTO (0.05 equiv.), CH_2Cl_2 (2 mL) at 20 °C; **C.** alkene (100 mg), 30% aq. H_2O_2 (2 equiv.), MTO (0.05 equiv.), EtOH (2 mL) at 20 °C

immediately discharged the yellow color. After stirring at room temperature for two hours the yellow color returned at which point an aqueous workup gave the α and β epoxides in a 4:1 ratio (Table 1, entry I). The epoxidation of cholesterol proceeded equally well in toluene, but a reaction in THF resulted in the formation of

additional products. In an attempt in insure completely anhydrous reaction conditions, 3Å and 4Å molecular sieves were added to the reaction mixture. In both experiments the rate of epoxidation was significantly retarded, perhaps due to the competitive absorption of H_2O_2 by the sieves. The effect of adding anhydrous Na_2SO_4 was similar, however the reduction in reaction rate was smaller. The oxidation of cholesterol required six hours to go to completion giving the epoxides in a 5:1 ratio (α/β).

A range of alkenes were selected to examine the regio- and stereoselectivity of epoxidation using the MTO/UHP system in CH_2Cl_2. In a typical procedure, MTO (0.05 equiv.) is added to a suspension of UHP (3.0 equiv.) in CH_2Cl_2 (2 mL) at room temperature. The mixture is stirred for 10 mins where upon the solution becomes yellow. The alkene (100 mg) is added to the mixture and stirring is continued until the reaction is complete (t.l.c. or g.c. analysis). The reaction mixture is diluted with CH_2Cl_2 and washed with H_2O, aq. $Na_2S_2O_3$, dried over Na_2SO_4, filtered and evaporated *in vacuo* to give the crude epoxide.

MTO/UHP in CH_2Cl_2 showed a similar selectivity to the common peracids in the oxidation of cholesterol. However, with guaiol, a much better selectivity was seen. The selectivity in the epoxidation of guaiol is probably sterically controlled and was independent of solvent with ethanol and CH_2Cl_2 giving similar results. Allylic alcohols showed good selectivity for the syn epoxide (vii, x, and xi), suggesting a hydrogen bonded transition state. In comparison, the oxidation of acetoxy cyclohexene (xiii) gave a modest excess of the trans epoxide. When the epoxidation of cyclohexenol is run in ethanol or *t*-butanol, only products from epoxide ring opening are observed. More surprisingly, the allylic hydroxyphosphonate failed to give any expoxide in ethanol or *t*-butanol solution.[22] Interestingly, the allylic hydroxyphosphonate and the carbamate (ix) derivative showed a preference for opposite diastereoisomers. The diastereoisomers were correlated by converting the epoxy alcohol (syn) into the epoxy carbamate with phenyl isocyanate. The stereochemistry was determined by X-ray crystallography on the major epoxide isomer (anti) from oxidation of the carbamate.[23] The regioselectivity, demonstrated in the oxidation of geraniol and limonene, is consistent with the results of other electrophilic epoxidizing agents, with the more substituted alkene reacting faster.

In summary, MTO/UHP in non-polar, non-protic solvents is a useful reagent for the stereoselective epoxidation of alkenes. The reactivity and selectivity are complementary to the peracids and DMD. The non-protic reaction conditions help to avoid unwanted epoxide ring opening reactions, insuring epoxide survival, and unlike hydrogen peroxide (of >35% aq. soln.), UHP can be shipped and is relatively safe.[12a]

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References and Notes

1. Herrmann, W. A.; Kuchler, J. G.; Weichselbaumer, G.; Herdtweck, E.; Kiprof, P. *J. Organomet. Chem.* **1989**, *272*, 351; Herrmann, W. A.; Kühn, F. E.; Fischer, R. W.; Thiel, W. R.; Romao, C. C. *Inorg Chem.* **1992**, *31*, 4431; Yamazaki, S. Epenson, J. H.; Huston, P. *Inorg. Chem.* **1993**, *32*, 4683.
2. Zhu, Z.; Espenson, J. H. *J. Org. Chem.* **1995**, *60*, 7090; Herrmann, W. A.; Wang, M. *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 1641; Herrmann, W. A.; Wagner, W.; Flessner, U. N.; Volkhardt, U.; Komber, H. *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 1636; Zhu, Z.; Espenson, J. H. *J. Org. Chem.* **1996**, *61*, 324.
3. Herrmann, W. A.; Fischer, R. W.; Marz, D. W. *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 1638; Herrmann, W. A.; Fischer, R. W.; Scherer, W.; Wauch, M. U. *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 1157; Herrmann, W. A.; Fischer, R. W.; Rauch, M. U.; Scherer, W. *J. Mol. Catal.* **1994**, *86*, 243; Al-Ajlouni, A. M.; Espenson, J. H. *J. Am. Chem. Soc.* **1995**, *117*, 9243.
4. Zhu, Z.; Espenson, J. H. *J. Org. Chem.* **1995**, *60*, 1326.
5. Adam, W.; Mitchell, C. M.; Saha-Moller, C. R.; *Tetrahderon* **1994**, *50*, 13121; Vasell, K. A.; Espenson, J. H. *Inorg. Chem.* **1994**, *33*, 5491.
6. Abu-Omar, M. M.; Espenson, J. H. *J. Am. Chem. Soc.* **1995**, *117*, 272.
7. Zhu, Z.; Espenson, J. H. *J. Org. Chem.* **1995**, *60*, 7728.
8. Adam, W.; Herrmann, W. A.; Lin, J.; Saha-Möller, C. R. *J. Org Chem.* **1994**, *59*, 8281.
9. Adam, W.; Herrmann, W. A.; Lin, J.; Saha- Möller, C. R.; Fischer, R. W.; Correia, J. D. G. *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 2475.
10. Murray, R. W.; Iyanar, K.; Chen, J.; Wearing, J. T. *Tetrahedron Lett.* **1995**, *36*, 6415.
11. Murray, R. W.; Singh, M.; Williams, B. L.; Moncrieff, H. M. *Tetrahedron Lett.* **1995**, *36*, 2437
12. a) Heaney, H. *Aldrichchimica Acta* **1993**, *26*, 35; b) Cooper, M. S.; Heaney, H.; Newbold, A. J.; Sanderson, W. R. *Syn. Lett.* **1990**, 533; c) Ballini, R.; Marcantoni, E.; Petrini, M. *Tetrahedron Lett.* **1992**, *33*, 4835.
13. Marcantoni, E.; Petrini, M.; Polimanti,O. *Tetrahedron Lett.* **1995**, *36*, 3561.
14. Lu, C. S.; Hughes, E. W.; Giguere, P.A. *J. Am. Chem. Soc.* **1941**, *63*, 1507
15. Marples, B. A.; Muxworthy, J. P.; Baggaley, K. H. *Tetrahedron Lett.* **1991**, *32*, 533.
16. Baker, J. A.; Lam, B.V. Schlueter, D. C.; Winter, R. E. K. W. Abstracts of Meetings, 28th Midwest Regional Meeting of the American Chemical Society, Columbia, MO, 1993, **Abs 199**.
17. Pesnelle, P. *Researches* **1966**, *15*, 33.
18. De la Cruz, A.; Spilling, C. D. unpublished results
19. Kawakami, T.; Shibata, I.; Baba, A.; Matsuda, H. *J. Org. Chem.* **1993**, *58*, 7608.
20. Cicala, G.; Curci, R.; Fiorentino, M.; Laricchiuta, O. *J. Org. Chem.* **1982**, *47*, 2670.
21. Carlson R. G.; Behn, N. S.; Cowles, C. *J. Org. Chem.* **1971**, *36*, 3832.
22. This reaction was run on 3 separate occasions, including a reaction run in parallel with guaiol. No epoxide was seen in the crude ^{1}H and ^{31}P NMR spectra and all the starting material was recovered.
23. Boehlow, T. R.; De la Cruz, A.; Rath, N. P.; Spilling, C. D. *Acta Cryst. Sec. C* in preparation.

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