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DIRECTED OXIDATIVE CYCLIZATION OF 5-HYDROXYALKENES WITH RHENIUM OXIDE.

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Abstract: 5-Hydroxyalkenes react with rhenium(VII) oxide (Re_2O_7) to provide 2-hydroxymethyltetrahydrofurans. Oxidative cyclization occurs with overall *syn* addition to the alkenes in moderate yields with little tendency toward oxidation of alcohols to carbonyl compounds.

Despite the fact that rhenium(VII) oxide is isoelectronic with osmium tetroxide, few parallels in reactivity have been observed.[1] *Herein, we report the first observation of oxidation of unactivated alkenes with rhenium oxide under mild conditions*. The key to increased reactivity of rhenium is presumed to be a combination of both effective molarity and electronegativity of the ligating substituent.[2]

The oxidation of alkenes by d^0 transition metals has generated much excitement in recent years due to progress in stereochemical control[3] and catalytic applications.[4] These advances have occurred despite a lack of clear understanding of the mechanism involved in these oxidations. In 1977, Sharpless proposed that oxametallocyclobutanes were intermediates in the oxidation of alkenes by d^0 transition metals.[3e,5] In 1980, Goddard and Rappe[6] showed that oxametallocyclobutane intermediates were consistent with *ab initio* calculations on the reaction of CrO_2Cl_2 with ethlyene. Other work on the oxidation of alkenes by osmium tetroxide has supported a [3+2] cycloaddition mechanism.[3f,7]

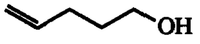
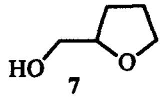
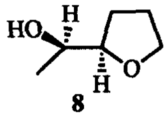
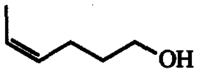
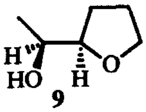
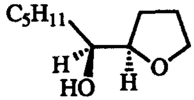
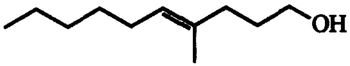
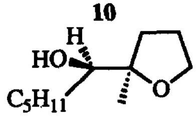
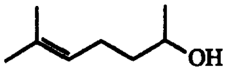
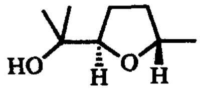
It is of interest whether oxidative cyclizations of 1,5-dienes by permanganate[8] and 5,6-dihydroxyalkenes by Cr(VI) oxo species[9] are mechanistically related to dihydroxylation of alkenes by osmium tetroxide. For this reason, we have embarked upon a study of the oxidation of alkenes by rhenium(VII) oxo compounds, in the hope that covalent linkage of an alkene to the oxo species would provide information about the transition state of these reactions.

The general procedure is as follows: To a solution of 1 mmol of 5-hydroxyalkenes and 1.1 mmol of 2,6-lutidine in 5 ml of methylene chloride at room temperature was added 1.1 mmol of Re_2O_7.[10] The rhenium(VII) oxide dissolved rapidly providing a red solution that gradually yielded a black precipitate as the reaction proceeded. After 1 hr, 1.1 mmol of 2,6-lutidine followed by 1.1 mmol of rhenium(VII) oxide were added. This sequence was repeated again after another hour. After 8 hrs, 10 mmol of sodium hydroperoxide was added as a 1M aqueous solution. The resulting colorless mixture was stirred for 30 minutes, then diluted with 10 ml of methylene chloride. The organic layer was washed with 10 ml of 1N HCl to remove 2,6-lutidine followed by 10 ml of saturated NaCl solution The products were then purified by flash chromatography on silica gel.

The first step in this reaction is presumed to be formation of a perrhenate ester,[11] and perrhenic acid which dissolved upon the addition of one equivalent of alcohol, resulting in red solution. In the absence of added base, non-oxidative acid catalyzed cyclization of substrates with trisubstituted double bonds was observed. A number of solvents and bases were employed. However, the combination of methylene chloride and 2,6-lutidine provided the highest yields. For example, when pyridine or other less hindered bases are employed, the order of addition of rhenium and base must be reversed and the red solution rapidly precipitates a fine black powder upon addition of pyridine. That the putative perrhenate esters undergo rapid, if incomplete, reaction upon addition of ligands such as pyridine is suggestive of formation oxametallocyclobutanes which then reductively eliminate. Unless the perrhenate ester is preformed, nucleophilic bases and solvents compete effectively with the alkene for the metal coordination site and no oxidation is observed.

Table 1 outlines oxidation of several representative 5-hydroxyalkenes.[12] Substrates **2** and **3** confirm overall *syn* addition to the alkene. The product of rhenium oxidation of **2** was identical to that obtained by epoxidation of **3** and acid catalyzed cyclization. The complementary experiment involving the formation of tetrahydrofuran **9** was also performed. Oxidation of alkenes **4** and **5** provide products which are less volatile leading to an improvement in isolated yields. Substrates **5** and **6** also demonstrate the cyclization of more hindered alkenes.

Table 1. Oxidation of 5-Hydroxyalkenes by Re_2O_7.

Entry	Substrate	Product[a]	Yield(%)[b]
1	 **1**	 **7**	59
2	 **2**	 **8**	47
3	 **3**	 **9**	59
4	 **4**	 **10**	88
5	 **5**	 **11**	86
6	 **6**	 **12**	62

a. Products 7-9 were isolated as the acetate. All products showed proper IR, ^{1}H NMR, ^{13}C NMR, and HRMS. *b*. Isolated yields.

However, these two substrates were sensitive toward acid catalyzed cyclization. Intriguingly, oxidation of alkenol **6** provided a *trans* to *cis* ratio of 33:1.[13,14]

Rhenium(VII) oxide displays advantages over other similar oxidants since oxidation of the starting and product alcohols to aldehydes or ketones is minimal and yields are generally higher than those observed in permanganate and chromium oxidations. Rhenium(VII) oxide is less expensive per gram than osmium tetroxide.[10,15] However, a stoichiometric excess of rhenium(VII) was employed here in order to drive reactions to completion . One explanation for the requirement of more than one equivalent of rhenium(VII) oxide is that the product hydroxymethyltetrahydrofurans were observed to tightly bind rhenium (VII) according to ^{1}H NMR (400 MHz) spectroscopy. The stereospecificity of these oxidative cyclizations is the subject of further investigation.

Acknowledgment. We thank Mr. R. Boyce for kindly providing cleavage data on 5-methyl-2-(1-hydroxy-1-methylethyl)tetrahydrofuran **12**.

References and Notes

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2. (a) Perrhenyl chloride has been reported to react with alkenes to provide chlorohydrins: see Teranishi, A.Y.; Ph.D. thesis.Massachusetts Institute of Technology (1973). (b) Rhenium oxide has been reported to react with alkenes in refluxing acetic anhydride to provide 1,2-diacetoxy alkanes. see: *Chem. Abstr.* 69(13):51647y.
3. For examples of stoichiometric asymmetric osmylations involving external chiral amine ligands: (a) Yamada, T.; Narasaka, K. *Chem. Lett.* **1986**, 131. (b) Tokles, M.; Snyder, J. K. *Tetrahedron Lett.* **1986**, *27*, 3951. (c) Annunziata, R.; Cinquini, M.; Cozzi, F.; Raimondi, L.; Stefanelli, S. *Ibid.* **1987**, *28*, 3139. (d) Tomioka, K.; Nakajima, M.; Koga, K. *J. Am. Chem. Soc.* **1987**, *109*, 6213. (e) Hentges, S. G.; Sharpless, K. B. *Ibid.***1980**, *102*, 4263. (f) Corey, E. J.; Jardine, P. D.; Virgil, S.; Yuen, P.-W.; Connell, R. D. *Ibid.* **1989**, *111*, 9243. (g) Wai, J. S. M.; Marko, I.; Svendsen, J. S.; Finn, M. G.; Jacobsen, E. N.; Sharpless, K. B. *Ibid.* **1989**, *111*, 1123. (h) Svendsen, J. S.; Marko, I.; Jacobsen, E. N.; Pulla Rao, Ch.; Bott, S.; Sharpless, K. B. *J. Org. Chem.* **1989**, *54*, 2263. (i) Hirama, M.; Oishi, T.; Ito, S. *J. Chem. Soc. Chem. Commun.* **1989**, 665.
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7. (a) Jorgensen, K. A.; Hoffmann, R. *Ibid.* **1986**, *108*, 1867. (b) Christensen, D.; Jorgensen, K. A. *J. Org. Chem.* **1989**, *54*, 126. (c) Casey, C. P. *J. Chem. Soc. Chem. Commun* . **1983**, 126.

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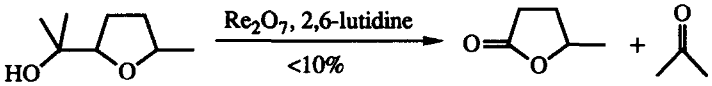
9. Walba, D.M.; Stoudt, G.S. *Tetrahedron Lett.* **1982**, *23*, 727.

10. Rhenium(VII) oxide (Re_2O_7) is readily available from Aldrich, ~16$/g.

11. Edwards, P.; Wilkinson, G. *J. Chem. Soc. Dalton Trans.* **1984**, 2695. However, use of perrhenyl chloride led to oxidation of the alcohol and less than 10% of tetrahydrofuran was observed under otherwise identical conditions.

12. 4-Hydroxyalkenes and 6-hydroxyalkenes provide no oxidative cyclization. Allylic hydroxyalkenes are oxidized rapidly to α,β-unsaturated aldehydes or ketones which will be reported later.

13. However, caution should be exercised before imputing energetic values to the ratio observed, since we have observed that cyclization product **12** is cleaved to lactone under reaction conditions at slow but unequal rates for *cis* and *trans* isomers. These results will be reported later in fuller detail than that possible here.



12

14. The preparation of **12** has previously been described: Mori, K.; Puapoomchareon, P. *Liebigs Ann. Chem.* **1987**, 271. The assignment of the *trans* stereochemistry of **12** is based on the C-13 NMR spectrum. see: (a) Michael, J.P.; Ting, P.C.; Bartlett, P.A. *J. Org. Chem.* **1985**, *50*, 2416. (b) Thomas, A. F.; Thommen, W.; Hagaman, E. W.; Wenkert, E. *Helv. Chim. Acta* . **1984**, *57*, 2055. (c) Eliel, E. L.; Rao, H. B.; Pietrusiewicz, K. M. *Org. Magn. Reson.* **1985**, *26*, 311.

15. Osmium tetroxide ~71$/g from Aldrich.

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