Rhenium-Catalyzed Epoxide Deoxygenation: Scope and Limitations

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Abstract: Transfer of oxygen atoms from epoxides to triphenylphosphine is efficiently catalyzed by Tp′ReO$_3$ [Tp′ = hydrido-*tris*-(3,5-dimethylpyrazolyl)borate] in benzene at 75–105 ºC. The reaction tolerates a wide variety of functional groups including ketones (conjugated or non-conjugated to the new double bond), esters, nitriles, ethers, silyl ethers and phthalimides. Relative rates vary with substitution pattern and electronics; in general, monosubstituted and 2,2-disubstituted epoxides react fastest, and *cis*-2,3-disubstituted systems react faster than *trans*. Electron-withdrawing substituents promote the reaction.

Key words: epoxide deoxygenation, rhenium catalysis, O-atom transfer

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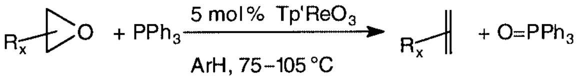
Recent work in our laboratories led to the discovery of an efficient, rhenium-catalyzed deoxygenation of epoxides (Equation 1).[1] This reaction is of interest for several reasons. Our primary focus has been on mechanism in as much as removal of oxygen from an epoxide is the microscopic reverse of alkene epoxidation. Other applications include completing a protection/deprotection cycle for alkenes[2] and conversion of biomass-derived substrates to useful organic compounds.[3] Relatively few general methods exist for removing oxygen atoms from epoxides; the best tend to use stoichiometric reagents and harsh reaction conditions that do not tolerate wide substrate functionalization.[4–7] The rhenium-catalyzed reaction is singular in that it preserves the stereochemistry about the incipient C=C bond; Vedejs' method[4b] employing LiPPh$_2$ as an example leads to inversion of stereochemistry at one center, i.e., a *trans*-epoxide generates a *cis*-alkene.



Equation 1

While transition metal reagents are known[7] that preserve stereochemistry, none save a recent report[8] are catalytic in the metal. We report here the scope and limitations of the rhenium-catalyzed reactions with regard to epoxide substitution pattern and other functional groups in the molecule.

The examined substrates and the results of catalytic deoxygenation are shown in Table 1. The general conditions for this screening were to use 0.2 M epoxide in benzene and drying over CaH$_2$. Because reactions were followed by NMR spectroscopy, 1,4-di-*tert*-butylbenzene was added as an integration standard. PPh$_3$ (1.5 equiv) was added as the stoichiometric reductant, and the solution was added to 0.05 equivalent solid Tp′ReO$_3$. The mixture was sealed under vacuum. The sample was immersed in a thermostated bath initially at 75 °C and over the course of the initial 100 hours the sample was periodically removed for spectroscopic measurement of conversion. The first column of Table 1 shows the production of alkene at that time. After 100 hours, all samples that had not undergone complete conversion were subjected to an additional period at 105 °C; the second column in Table 1 shows the length of that time, and the third column shows the conversion to alkene (usually complete) at the end of that time.

Several observations must be noted. The material balance for all substrates (the sum of alkene plus epoxide divided by initial epoxide concentrations) was within experimental uncertainty of 100% for all systems. With the exception of the extremely slow *trans*-2-butene oxide, those substrates with stereochemistry (entries 1, 11, 14) show complete stereospecificity; *trans*-2-butene oxide (entry 16) does show small amounts of *cis*-2-butene forming after an extremely long time. All substrates save *trans*-2-butene oxide could be pushed to completion, given sufficient time and temperature.

Some general trends are apparent from the data. First, *trans*-disubstitution slows the reaction considerably. Based on earlier mechanistic studies implicating a rhenium-epoxide complex as a reactive intermediate, such a geometry likely creates a steric clash with the Tp′ ligand that interferes with epoxide binding. Notably, the tetrasubstituted epoxide tetramethylethylene oxide does not undergo reaction to any observable extent. Somewhat surprisingly, the trisubstituted epoxide (entry 13) proceeds faster than *trans*-2-butene oxide, indicating that steric factors alone do not completely account for reactivity trends.

Mechanistic investigation of this system[9] has revealed that the catalytic cycle is composed of two competing manifolds, but that both are consistent with initial coordination of epoxide to Re(V). In one, direct fragmentation leads to alkene. For styrene and *cis*-stilbene, this was shown to be the dominant path. The second manifold led to formation of a rhenium diolate via ring expansion (yet with retention of configuration); these diolates are known

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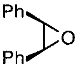
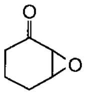
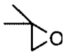
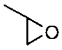
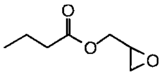
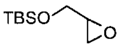
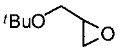
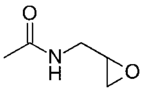
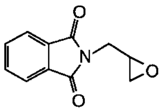
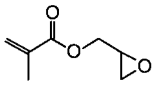
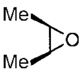
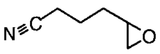
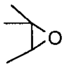
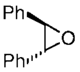
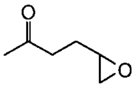
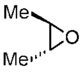
Table 1 The Examined Substrates and Results of Catalytic Deoxygenation

Substrate	Conversion, 100 h/75 °C	2nd Time, h/ 105 °C	Total Conv., %
	>95		
	>95 (25 h)		
	82	48	>95
	55	48	>95
	39	288	87
	39	144	>95
	38	144	>95
	Trace[12]	–	–
	28	294	85
	30	288	83
	26	288	>95
	18	1317	>95
	16	1104	>95
	14	48	>95
	6	1317	>95
	Trace	1317	39
	–	1317	–

to thermally fragment to alkene also. The consequence of this mechanism for interpreting the reactivity patterns is that steric factors certainly play a role in coordination of the epoxide and perhaps in defining the barrier to fragmentation, but that electronic factors will probably dominate in determining how fast 'direct' fragmentation is compared with ring expansion/fragmentation.

This system exhibits significant tolerance of functionality. Our initial report noted several important exceptions to this tolerance: free alcohols impede catalysis (forming unreactive bis-alkoxyrhenium compounds). We presume that given the propensity for primary amines to condense with metal oxo ligands,[10] such functionality would also be precluded. However, common protection strategies (ethers or silyl ethers for alcohols; phthalimide for a primary amine) adequately circumvent some of these limitations. Use of a carboxamide led to a separate reaction (attack of the carbonyl oxygen on the epoxide), but use of a phthalimide avoided this and provided adequate protection of the amine.

All monosubstituted epoxides in this series react at comparable rates, showing that the specific functional group does not impose enough variation in inductive effect to perturb the fundamental reactivity. Halogen substituents were not part of this study but were previously shown to be compatible with the reaction. Nitro groups are better O-atom donors than are epoxides,[11] as are sulfoxides; these were not tested.

Several functional groups (ketone, ester, nitrile) are conceivable competitors for binding to the metal. Some rate retardation is observed (entries 12 and 15), but as with all other substrates these will proceed to completion. Notable also is that production of a conjugated α,β-unsaturated ketone is much faster than production of the non-conjugated product; this is likely a reflection of the previously-noted electronic effect favoring production of electron-deficient C=C bonds.

While most of this study was performed on the scale of NMR samples, preparative reactions confirmed the scalability of the reaction. A mixture of 1-dodecene oxide (0.62 mL, 2.82 mmol), PPh_3 (0.88 g, 3.36 mmol) and $Tp'ReO_3$ (0.080 g, 0.15 mmol) was heated to reflux in 30 mL benzene under Ar for 86 hours. [Care must be taken to exclude atmospheric O_2 to prevent aerobic oxidation of the catalytically active Re(V) intermediate.] Removal of solvent, followed by chromatography on silica (with hexane as eluent) gave 1-dodecene (447 mg, 2.66 mmol, 94% yield) after removal of the chromatographic solvent in vacuo. A similar reaction with *cis*-stilbene oxide, run for 24 hours, gave a 91.5% isolated yield after chromatography.

In summary, catalytic reduction of epoxides by triphenylphosphine using $Tp'ReO_3$ catalyst is an efficient, effective means for deoxygenation, providing high yields of alkene stereospecifically. The reaction is highly tolerant of other functionality in the substrate.

Deoxygenation of Alkenes; Small Scale

Epoxide (commercial, or generated from MCPBA oxidation of the corresponding alkene) (0.56 mmol), 1,4-di-*tert*-butylbenzene (1.6 mg, 0.0085 mmol) and PPh_3 (0.61 mmol) were weighed and dissolved in C_6D_6 (3 mL), then dried over solid CaH_2 for a minimum of 3 h and then filtered. An aliquot (0.5 mL) of this solution was added to solid $Tp'ReO_3$ (2.4 mg, 0.0045 mmol)[13] and sealed under vacuum in an NMR tube. The mixture was immersed in a water–glycol bath thermostated at 75.0 ± 0.2 °C for 100 h. The conversion was measured by ^{1}H NMR, via comparing integrals of alkene and epoxide proton signals with those of the 1,4-di-*tert*-butylbenzene standard and comparing the initial epoxide/di-*tert*-butylbenzene ratio. Those compounds, which had not been completely converted to alkene, were further heated to 105 ºC and periodically measured by NMR until the reaction was complete.

Deoxygenation of 1-Dodecene Oxide

A mixture of 1-dodecene oxide (0.62 mL, 2.82 mmol), PPh_3 (0.88 g, 3.36 mmol) and $Tp'ReO_3$ (0.080 g, 0.15 mmol) was heated to reflux in benzene (30 mL) under Ar for 86 h. [Care must be taken to exclude atmospheric O_2 to prevent aerobic oxidation of the catalytically active Re (V) intermediate.] Removal of solvent, followed by chromatography on silica (eluent: hexane) gave 1-dodecene (447 mg, 2.66 mmol, 94% yield) after removal of the chromatographic solvent in vacuo.

Deoxygenation of *cis*-Stilbene Oxide

A mixture of *cis*-stilbene oxide (1.50 g, 7.65 mmol) and PPh_3 (2.21 g, 8.42 mmol) was added to $Tp'ReO_3$ (0.20 g, 0.38 mmol) in benzene (10 mL) and heated to reflux for 24 h under Ar. Removal of solvent, followed by chromatography on silica (eluent: hexane) gave *cis*-stilbene (1.26 g, 7.00 mmol, 91.5%) after removal of solvent in vacuo.

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(12) After 4 h, a trace of alkene was observed. However, the major product was reaction of the carbonyl oxygen to form 2-methyl-5-hydroxymethyloxazoline.

(13) $Tp'ReO_3$ was prepared by the method of Mayer, et al.: (a) Matano, Y.; Northcutt, T. O.; Brugman, J.; Bennett, B. K.; Lovell, S.; Mayer, J. M. *Organometallics* **2000**, *19*, 2781. (b) In this method Re_2O_7 reacted with 2 equivalents trifluoroacetic anhydride in THF, followed by addition of KTp′. The solid trioxo complex precipitates and is collected by filtration and washed.