A Synthetically Useful, Self-Assembling MMO Mimic System for Catalytic Alkene Epoxidation with Aqueous H$_2$O$_2$

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Received March 26, 2001

Revised Manuscript Received May 31, 2001

The discovery of efficient and practical epoxidation methods that utilize aqueous H$_2$O$_2$ as terminal oxidant stands as an important objective in synthetic chemistry. While significant advances have been made in identifying catalysts for peroxide-based epoxidations, important challenges remain; these include the development of highly reactive systems that effect rapid substrate conversion with high selectivity, and the use of inexpensive, environmentally friendly metals in coordination environments that can be adapted to sterically and electronically tunable biomimetic triad ligands. Nature has evolved a variety of remarkable oxidative enzymes that may point to a solution. For example, in addition to its well-known biological role in the selective hydroxylation of small hydrocarbons, methane monoxygenase (MMO) is an efficient and selective catalyst for epoxidation of small terminal olefins (i.e. ethylene, propylene, 1-butene). Moreover, oxidized MMO (diiron(III)) displays this oxidative activity with H$_2$O$_2$. In this paper we describe a new protocol that employs low loadings of an inexpensive, easily prepared iron-tetrantadent ligand complex and 50% aqueous H$_2$O$_2$ to effect epoxidation of a wide variety of aliphatic olefins—including terminal olefins—within 5 min in 60–90% isolated yields (e.g. Scheme 1). On the basis of spectroscopic and crystallographic data, it is shown that this catalyst system self-assembles under the reaction conditions to form a μ-oxo, carboxylate-bridged diiron(III) complex reminiscent of the μ-hydroxy, carboxylate-bridged diiron(III) core found in the hydroxylase active site of oxidized methane monoxygenase.

A variety of interesting synthetic non-heme iron complexes have been identified as functional mimics of MMO. For example, both mononuclear and pre-assembled binuclear iron perchlorate complexes of the mep ligand (mep = N,N′-dimethyl-N,N′-bis(2-pyridylmethyl)-ethane, 1,2-diamine) effect hydroxylation of cyclohexane in the presence of aqueous H$_2$O$_2$ with modest catalytic activity (2–5 turnovers). Thus far, however, the application of functional MMO model systems to preparative oxidation chemistry has been prevented by low catalyst turnover numbers, poor selectivity for product formation (often attributed to generation of free hydroxy radicals), and the requirement for large excesses of substrate relative to oxidant. Nonetheless, the (mep)iron system appeared to hold special promise for epoxidation catalysis because it was demonstrated to effect oxidation without the participation of free hydroxy radicals. This feature, combined with the synthetically accessible and tunable nature of the mep ligand, prompted us to investigate its potential utility in epoxidation catalysis.

We evaluated mononuclear [Fe(II)(mep)(CH$_3$CN)$_2$](ClO$_4$)$_2$ complex (5 mol %) for epoxidation of 1-decene in the presence of varying amounts of H$_2$O$_2$. With 4 equiv of oxidant, complete conversion of alkene was achieved; however, epoxide was produced in only 40% yield and a variety of over-oxidized byproducts were detected. Use of the corresponding SbF$_6$ complex led to a substantially more efficient reaction, with only 1.5 equiv of H$_2$O$_2$ required to effect complete conversion of alkene, and with selectivity for formation of 1,2-epoxydeca-1,6-diene improved to 71%. A screen of additives and solvents revealed that improvement to 82% selectivity for epoxide formation was possible with the addition of as little as 1 equiv of acetic acid with respect to catalyst. Moreover, the acetic acid-containing system was very well-behaved, with reductions in catalyst loading (S/C up to 100) and increases in H$_2$O$_2$ addition rates (from dropwise to rapid addition) resulting in no change in selectivity for epoxide formation. In contrast, the system lacking acetic acid as additive displayed significant decreases in epoxide yield both at lower catalyst loadings and with increased addition rates of H$_2$O$_2$.


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of MMO, it is likely that a “carboxylate shift” is responsible for generating the coordination site required for catalysis.\textsuperscript{13}

Further optimization of reaction conditions and a preliminary investigation of substrate scope led to the results shown in Table 1.\textsuperscript{14} A wide range of aliphatically substituted alkenes proved to be excellent substrates for epoxidation with catalyst 2.\textsuperscript{15} Terminal olefins (entries 1–5), which are normally least reactive to electrophilic oxidants and typically require long reaction times with any of the known epoxidation methods (e.g. 12 h to several days with peracid reagents), were found to undergo epoxidation within 5 min and in 60–90% isolated yields. The reaction is operationally simple in that it is insensitive to air and moisture and product isolation is effected simply by distillation or filtration through a short plug of silica. To our knowledge, this is the first example of an MMO model system that is useful for preparative oxidation chemistry. The mep ligand framework is modular in nature and promises to be a very useful template for chiral ligand design. Experiments aimed toward developing enantioselective variants of this epoxidation catalyst are underway.

Acknowledgment. This work was supported by the NIH (GM-43214) and a postdoctoral fellowship to M.C.W. from the NIH (1 F32 GM20077-01). The crystal structure analysis was performed by Dr. Richard Staples (Harvard University).

Supporting Information Available: Complete experimental details of catalyst synthesis, epoxidation reactions, crystallization, UV–Vis studies (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

JA015884G


(14) General procedure: A CH\textsubscript{3}CN solution of olefin (0.24 mmol, 0.16 M), 1 (0.007 mmol, 3 mol %, S/C = 33), and CH\textsubscript{3}CO\textsubscript{2}H (30 mol %) was cooled to 4 °C with rapid stirring in a screw cap glass vial. Nitrobenzene (40 mol %, 0.097 mmol) was added as internal standard. A CH\textsubscript{3}CN solution of 50 wt % H\textsubscript{2}O\textsubscript{2} (1.5 equiv, 0.36 mmol, 0.36–5.0 M depending on scale) was precooled to 4 °C and added dropwise over 2 min. Reaction progress was monitored by GC, and in all cases complete conversion of olefin was observed within 5 min with epoxide as the only detectable product. However, small amounts of polar, carboxylic acid-containing byproducts were detected by NMR and IR analysis. Epoxide was isolated by extraction of the crude reaction mixture into pentane and purification through a short plug of silica.

(15) In contrast, substrates bearing aromatic substituents underwent decomposition to unidentified products.