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A simple and versatile method for alkene epoxidation using aqueous hydrogen peroxide and manganese salophen catalysts

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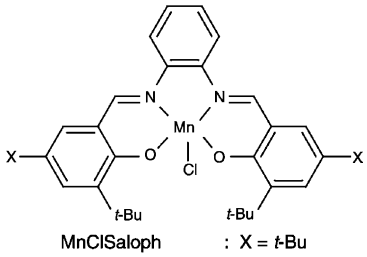
Abstract—We describe a simple and versatile method for the catalytic epoxidation of a broad range of olefins (e.g., ketones, esters, and alkyl halides) with aqueous H_2O_2 using manganese salophen catalysts. Low catalyst loading, short reaction times, and a simple reaction setup (e.g., no pH buffer is required) are salient features of the system, which unites the benefits of H_2O_2 as an oxidant with the versatility and modularity of salen-based catalysts.

The discovery of manganese salen complexes as epoxidation catalysts by Kochi[1] and their subsequent development in asymmetric catalysis, most notably by Jacobsen[2] and Katsuki,[3] represent landmark achievements in catalytic oxidation chemistry. High chemo-, stereo-, and regio-selectivities have been achieved when these salen catalyst platforms are used in concert with iodosylbenzene, sodium hypochlorite, and *m*-chloroperbenzoic acid as the primary oxidants. Recently, there has been a burgeoning interest in the development of catalytic epoxidation systems that employ 'green' oxidants such as H_2O_2.[4–20] The successful implementation of such systems becomes a worthwhile objective when issues of environmental compatibility,[21] high atom economy,[22,23] availability, and expense[24,25] are considered. Surprisingly, manganese salen complexes have only rarely been employed as epoxidation catalysts in conjunction with H_2O_2 as the primary oxidant.[26–32] In the few examples, turnover numbers (TON) are low (typically ~20), and the substrate scope is limited. We envisioned that more efficient oxidations may be realized when H_2O_2 is activated with catalysts that precisely position (or hang) an acid–base functionality over the face of a redox-active macrocycle.[33,34] Proton delivery from an acid–base functional group to a hydroperoxide bound to the metal unmasks the high-valent metal-oxo, that is, the active species in many oxidation cycles. We have shown this to be the case for 'Hangman' porphyrin complexes, which function as mono-oxygenase mimics,[35–37] and 'Hangman' salophen complexes,[38] which function as catalase mimics. During the course of these studies, we discovered that simple manganese salophen complexes, such as MnClSaloph and MnClSaloph-Br in Chart 1, could also promote, under certain conditions, the epoxidation of olefins using H_2O_2. In this letter, we show that olefin epoxidations can be efficiently performed with 30% H_2O_2 solutions and manganese salophen as the catalyst. Using our catalytic system, a broad range of olefins (e.g., ketones, esters, and alkyl halides are well tolerated) can be epoxidized at high turnover and in good yield. The results described herein add to the emerging literature of using H_2O_2 as a primary oxidant and unite the benefits of employing an environmentally benign oxidant with the versatility and modularity of salen-based catalysts.



MnClSaloph : X = *t*-Bu
MnClSaloph-OMe : X = OMe
MnClSaloph-Br : X = Br

Chart 1.

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For initial optimization studies, we chose to investigate the olefin epoxidation of the common benchmark, styrene. Table 1 illustrates the solvent effect on the efficacy of the epoxidation reaction in the presence of 1,5-dicyclohexylimidazole (DCI) as an additive. Of all the solvents used (Table 1, entries 1–9), DMF seems to be the only one that can promote efficient epoxidation (entry 7). In order to prevent potential solubility problems that can arise from using hydrophobic hydrocarbon substrates in a hydrophilic solvent such as DMF, CH_2Cl_2/DMF solvent mixtures were used. Indeed, the use of a CH_2Cl_2/DMF mixture in a ratio of 1 to 3 significantly improves conversion yields (entry 10). Interestingly, a higher CH_2Cl_2 concentration results in complete loss of epoxidation reactivity (entry 11).

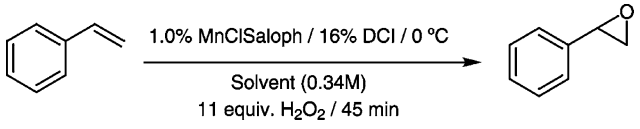
With an optimal solvent system established, we turned our attention to address additive effects. In the presence of 0.5% catalyst, different ligands with pK_a values ranging from 0.8 to 11 were surveyed. As can be seen from Table 2, the nucleophilicity/basicity of the added ligands is a critical factor for the efficacy of epoxidation. Although many reactions employ 4-phenylpyridine *N*-oxide (PPO) as an additive,[39–41] a negligible amount of product is obtained when PPO or other coordinating ligands with p$K_a < 7$ (entries 1 and 2) are employed. Enhanced activity is observed, however, when the epoxidation reaction is carried out using bases with p$K_a > 7$ (entries 3–5). No product was observed when the reaction is carried out in the absence of an additive (entry 6).

One of the more attractive features of using salen-based catalysts is the ability to tune reactivity by altering the X-substituent on the macrocyclic ring.[1,42–44] We sought to probe the electronic effects on catalyst performance for various X substituents appended to the salen at the 5 and 5′ positions of the macrocycle. Table 3 illustrates that epoxidation reactivity is reduced significantly for a catalyst bearing an electron-rich salophen ligand (i.e., X = OMe). On the other hand, good reactivity can be achieved with catalysts containing less electron donating groups (i.e., X = *t*-Bu or Br).

Control experiments were performed with unligated manganese since it is known that simple manganese salts can catalyze olefin epoxidations. For instance, Burgess et al. described olefin epoxidations in the presence of Mn^{2+} salts in a hydrogen carbonate buffer,[45,46] and moreover, olefin epoxidations have been reported in the absence of transition metal catalysts.[47] Notwithstanding, our experiments indicate that Mn^{2+} and Mn^{3+} salts are ineffective catalysts under our experimental conditions (Table 4). In addition, no product was observed in the absence of any transition metals. The results in Table 3, as well as in Table 4, stress the importance of the metal-supporting salophen scaffold. Presumably, a high valent salophen Mn^{V} oxo species[48–51] is involved in the catalytic epoxidation reaction.

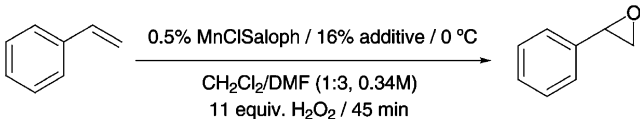
The epoxidation method can be applied to a wide range of olefins. As can be seen from Table 5, unfunctionalized

Table 1. Manganese salophen catalyzed epoxidation of styrene: solvent screen



Entry	Solvent	GC yield (%)
1	Toluene	<5
2	CH_2Cl_2	<5
3	THF	<5
4	CH_3CN	<5
5	CH_3NO_2	<5
6	MeOH	7
7	DMF	85
8	DMA	5
9	NMP	6
10	CH_2Cl_2/DMF (1:3)	99
11	CH_2Cl_2/DMF (1:1)	6

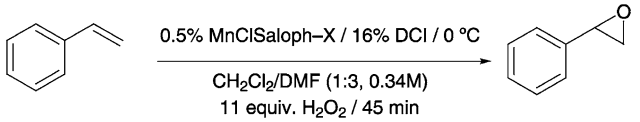
Table 2. Additive effect in manganese salophen catalyzed epoxidation of styrene



Entry	Additive	pK_a	GC yield (%)
1	4-PPO	0.8	<5
2	Pyridine	5.2	5
3	DCI[a]	7.0	97
4	DMAP	9.2	88
5	Quinuclidine	11.0	73
6	—	—	<5

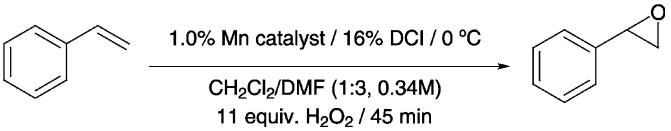
[a] pK_a reported for imidazole.

Table 3. Electronic effects on the epoxidation of styrene



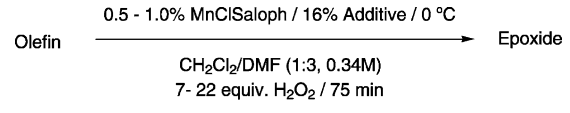
X	GC yield (%)
t-Bu	97
OMe	6
Br	94

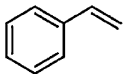
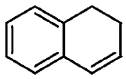
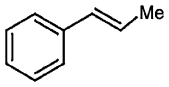
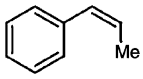
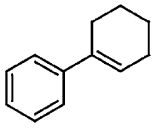
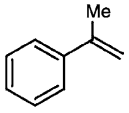
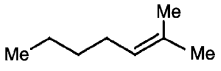
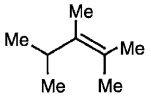
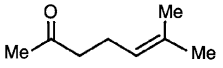
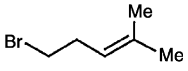
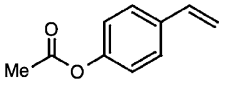
Table 4. Control experiments using simple manganese salts as epoxidation catalysts



Catalyst	GC yield (%)
$Mn(OAc)_2{\cdot}4H_2O$	0
$MnCl_2$	0
$Mn(OAc)_3{\cdot}2H_2O$	0
—	0

Table 5. Manganese salophen catalyzed epoxidation of olefins

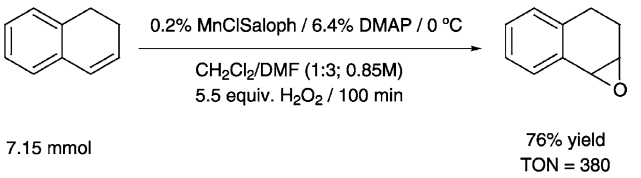


Entry	Olefin	Additive	Yield (%)[a]	TON
1		DCI	90	180
2		DMAP	77	154
3		DMAP	70	140
4		DMAP	59[b]	118
5		DCI	51	102
6		DCI	60[c]	120
7		DCI	78	78
8		DCI	69	69
9		DCI	39	78
10		DCI	62	62
11		DCI	61	61
12		DCI	68	136

[a] Isolated yields.
[b] 1.1:1 cis:trans ratio of products obtained (see SI).
[c] 79% oxidized product obtained, 19% of which was 2-phenyl-propionaldehyde (see SI).

aromatic (entries 1–6) as well as aliphatic (entries 7–9) olefins are suitable substrates. Furthermore, our conditions tolerate functional groups such as ketones (entry 10), alkyl bromides (entry 11), and esters (entry 12). The low catalyst loading, the short reaction time, simplicity of reaction setup (e.g., no pH buffer is required), and the broad substrate scope are salient features of our catalytic system. The TONs that have been achieved with our method are among the highest reported for manganese-salen-catalyzed epoxidation using H_2O_2.

We have scaled up the catalytic epoxidation of 1,2-dihydronaphthalene (Eq. 1). Using just 0.2% catalyst, the reaction goes to completion within 100 min, and the desired product can be obtained in 76% isolated yield, corresponding to a TON of 380.



(1)

In conclusion, we have developed a simple and versatile method for alkene epoxidation employing manganese salophen catalysts and aqueous H_2O_2 as the primary oxidant. Implementing the experimental conditions described here, a wide range of unfunctionalized and functionalized olefins can be epoxidized with high TON. The method is distinguished from sodium hypochlorite oxidations inasmuch as it is not necessary to precisely control the pH.[52] Additionally, the oxidation features a high atom economy and the reaction does not suffer from the undesirable organic by-products of iodosylbenzene and organic peracid oxidations. Our results establish that hydrogen peroxide may be used effectively as an oxidant for salophen-mediated oxidation catalysis.

Acknowledgements

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Supplementary data

Synthesis and characterization of salophen complexes and procedures for epoxidation reactions. This material is available free of charge via the Internet at http://pubs.acs.org. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.01.074.

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