# Efficient Epoxidation of Alkenes with Aqueous Hydrogen Peroxide Catalyzed by Methyltrioxorhenium and 3-Cyanopyridine

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The epoxidation of alkenes with 30% aqueous hydrogen peroxide is catalyzed efficiently by methyltrioxorhenium (MTO) in the presence of pyridine additives. The addition of 1−10 mol % of 3-cyanopyridine increases the system's efficiency for terminal and trans-disubstituted alkenes resulting in high isolated yields of the corresponding epoxides. The system allows for epoxidation of alkenes with various functional groups. Alkenes leading to acid-sensitive products are efficiently epoxidized using a mixture of pyridine and 3-cyanopyridine as additives. This method is operationally very simple and uses an environmentally benign oxidant. The effects of different pyridine additives on the alkene conversion and the catalyst lifetime are discussed.

## Introduction

Three-membered ring systems containing one heteroatom, e.g., epoxides and aziridines, serve as important building blocks for a wide variety of chemical compounds. The search for and development of efficient and selective methods for the preparation of epoxides is therefore of high importance. Although base-promoted dehydrochlorination of chlorohydrins is one of the most employed methods, the direct oxidation of alkenes represents the most cost-effective and elegant method for the production of epoxides. The major advantage of direct epoxidation using various environmentally benign oxygen sources such as hydrogen peroxide, alkyl hydroperoxides, or most desireful, molecular oxygen, is the limited amount of byproducts formed from the oxidant. Whereas dehydrochlorinations always produce equimolar amounts of hydrogen chloride, the only byproduct formed in hydrogen peroxide mediated epoxidations is water. Various peracids commonly used to transform alkenes to epoxides also suffer from the same disadvantage of producing equimolar amounts of byproducts, namely the parent acids, and thus need to be buffered to prevent epoxide ring opening via acidic activation.

Despite numerous procedures described in the literature there is still a lack of a highly efficient, general, and, most important, neutral method for epoxidation of alkenes.[1] The problem with most of the current methods is the inherent acidity (Brönsted or Lewis), which may lead to ring cleavage of the formed epoxides. Although some alkenes react directly with a variety of oxidants, the use of transition-metal catalysts often increases the

efficiency of the process. This field has been extensively studied, but there are only a few systems that show good applicability and reliability.[2] Currently, one of the more successful transition metal catalyzed epoxidations uses aqueous hydrogen peroxide as oxidant in the presence of sodium tungstate as the catalyst. This system was originally found by Payne and Williams in 1959.[3] Venturello et al. improved the system by addition of phosphoric acid and quaternary ammonium salts,[4] and more recently, Noyori et al. found that changing the additives to (aminomethyl)phosphonic acid and methyltrioctylammonium hydrogensulfate further enhanced the sodium tungstate catalyzed epoxidation of alkenes.[5] With this method it is possible to epoxidize a wide variety of alkenes; however, sensitive epoxides undergo ring-opening reactions due to the inherent Lewis acidity of the system. The industrially used process based on a heterogeneous titanium substituted silicate (TS-1) catalyst introduced by *Enichem* represents another efficient catalytic epoxidation system using hydrogen peroxide as oxidant.[6] This system shows high preference for epoxidation of small unbranched terminal alkenes, but recent developments in this area, by taking into account the size of the zeolite pores, have increased the range of substrates working in this system.[7]

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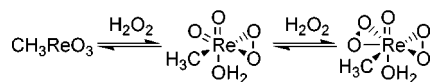
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(2) For a recent review on transition metal catalyzed epoxidation reactions, see: Sheldon, R. A. *In Applied Homogeneous Catalysis with Organometallic compounds*; Cornils, B., Herrmann, W. A., Eds.; VCH: Weinheim, 1996.

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(7) Murugavel, R.; Roesky, H. W. *Angew. Chem., Int. Ed. Engl.* **1997,** *36,* 477 and references therein.

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<div align="center">

**Scheme 1**

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$$CH_3ReO_3 \; \rightleftharpoons \; \underset{H_3C}{\overset{O}{\underset{OH_2}{\overset{O}{\text{Re}}}}} \overset{O}{\underset{O}{}} \; \overset{H_2O_2}{\rightleftharpoons} \; \underset{H_3C}{\overset{O}{\underset{OH_2}{\overset{O}{\text{Re}}}}} \overset{O}{\underset{O}{}}$$

We have previously reported on the effects of various heterocyclic additives, i.e., pyridine and pyridine derivatives, in the methyltrioxorhenium (MTO)-catalyzed epoxidation of alkenes with aqueous hydrogen peroxide.[8] MTO was originally introduced as a catalyst for alkene epoxidation by Herrmann et al. in 1991.[9,10]

Despite the fact that this organometallic compound on first glance may seem to be unstable under oxidation reaction conditions, it has proven to be an excellent catalyst for a variety of oxidative processes.[11] In the original MTO process for epoxidation of alkenes, the use of aqueous-free hydrogen peroxide in *tert*-butyl alcohol was essential for a successful outcome of the reaction. However, the Lewis acidity of the catalyst restricted the system to alkenes leading to less acid-sensitive epoxides.[12] The use of the hydrogen peroxide−urea complex as the terminal oxidant somewhat improved the substrate scope of the system, though at the cost of lower reactivity.[13]

There are two peroxo complexes formed in the reaction between MTO and hydrogen peroxide, the monoperoxo and the bisperoxo complexes as shown in Scheme 1. Espenson and co-workers have shown that with excess of hydrogen peroxide the bisperoxo-complex is the most abundant; however, both peroxo intermediates can take part in the oxygen-transfer step.[14]

Our continuing search for ligand-accelerated catalytic

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(10) For the original preparation of MTO, see; Beattie, I. R.; Jones, P. J. *Inorg. Chem.* **1979**, *18*, 2318.

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(12) MTO has, due to its high Lewis acidity, successfully been employed as the catalyst for Diels Alder reactions; see: Zhu, Z.; Espenson, J. H. *J. Am. Chem. Soc.* **1997**, *119*, 3507.

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oxidation systems[15] led to the discovery that pyridine had a beneficial influence on the rate of the MTO-catalyzed epoxidation of cyclooctene.[8a] This discovery also allowed the introduction of the relatively safe and environmentally friendly 30% aqueous hydrogen peroxide as oxidant. With the addition of pyridine, epoxidations could be performed in a biphasic water−organic solvent system, selectively giving epoxides in high yields with a low catalyst loading. The addition of pyridine promotes an increase in the rate of the reaction and protects the formed epoxide from possible ring-opening reactions, catalyzed by the Lewis acidic metal center. This system turned out to be most effective for more electron-rich systems such as tetra-, tri-, and cis-disubstituted alkenes. Trans-disubstituted and terminal alkenes react slower with electrophilic oxygen-transfer reagents and thus required prolonged reaction times to reach acceptable conversion. The addition of 3-cyanopyridine instead of pyridine to the epoxidation system resulted in high conversion of terminal alkenes to their corresponding epoxides.[8b] Herrmann et al. introduced pyrazole as an additive promoting efficient epoxidation of alkenes.[16] This system has properties similar to the pyridine systems and a comparison of which amine additive to choose depending on the nature of the substrate was recently published.[8c] Herein we report a comprehensive study of the MTO-catalyzed epoxidation of alkenes with aqueous hydrogen peroxide in the presence of pyridine additives.

## Results and Discussion

**Epoxidation Conditions.** The inability of the simple pyridine system to fully convert terminal alkenes into their corresponding epoxides led us to search for other additives that could enhance the catalytic process. Styrene, representing a terminal alkene and a progenitor for a very acid-sensitive epoxide, was chosen as the model substrate for this investigation. Screening the reaction with different functionalized pyridines showed that heterocycles containing electron-releasing substituents, thus having a higher basicity, such as 4-*tert*-butyl- and 4-methoxypyridine did protect the formed epoxide from ring cleavage but had a negative effect on the catalyst lifetime, leading to lower conversion. On the other hand, pyridine derivatives with electron-withdrawing substituents (less basic) and particularly the meta-substituted ones, 3-cyanopyridine, 3-fluoropyridine, methyl nicotinate and nicotinic acid, allowed the reaction to reach high conversion. The disadvantage, though, was the inability of these additives to protect the epoxide from the occurrence of various side reactions, resulting in product mixtures of benzaldehyde, benzoic acid, phenyl-1,2-ethylene glycol, and only trace amounts of the epoxide (Table 1).

Table 1 also shows the influence of the pyridines on the $^1$H NMR chemical shift of the methyl group in MTO. The change in chemical shift serves as a guide to how strongly the additives coordinate to the rhenium center and reflects the Lewis base strength of the pyridines. The addition of more basic pyridines substantially decrease the chemical shift of MTO, which would indicate a strong

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**Table 1. Influence of Pyridine Additives on the Epoxidation of Styrene with Aqueous Hydrogen Peroxide Catalyzed by MTO**

| additive | $pK_a$ | chemical shift[a] $\delta$ $(-\Delta\delta))$ | conversion[b] (%) | yield of epoxide (%) |
|---|---|---|---|---|
| no additive | | 2.62 | 100 | 5 |
| 2-cyanopyridine | −0.26 | 2.62 (0) | 99 | 3 |
| 3-cyanopyridine | 1.45 | 2.40 (0.22) | 100 | 1 |
| 4-cyanopyridine | 1.9 | 2.42 (0.2) | 100 | 7 |
| 3-chloropyridine | 2.81 | 2.22 (0.4) | 95 | 87 |
| 3-fluoropyridine | 2.97 | 2.22 (0.4) | 98 | 97 |
| methyl picolinate | 2.65 | 2.62 (0) | 85 | 13 |
| methyl nicotinate | 3.25 | 2.13 (0.51) | 93 | 86 |
| methyl isonicotinate | 3.26 | 2.18 (0.44) | 94 | 90 |
| quinoline | 4.87 | 2.46 (0.16) | 62 | 62 |
| pyridine | 5.17 | 1.85 (0.77) | 70 | 70 |
| 2-picoline | 5.97 | 2.59 (0.03) | 14 | 14 |
| 3-picoline | 5.60 | 1.85 (0.77) | 58 | 58 |
| 4-picoline | 6.03 | 1.84 (0.78) | 63 | 63 |
| 4-*tert*-butylpyridine | 5.99 | 1.70 (0.92) | 69 | 69 |
| 4-methoxypyridine | 6.62 | 1.79 (0.83) | 63 | 63 |

[a] The $^1$H NMR chemical shift of the methyl group in MTO in the presence of 10 equiv of pyridine additives in $CD_2Cl_2$ at 25 °C. The numbers in parentheses are the differences between the chemical shift for MTO and the observed chemical shift upon addition of the pyridines. [b] Reactions were run using 30% aqueous $H_2O_2$, styrene, additive, and $MeReO_3$ in a 400:200:20:1 molar ratio at 24 °C for 17 h. Alkene concentration: 1.3 M in $CH_2Cl_2$. The conversion of styrene was determined by GC analysis with respect to internal standard.

coordination to rhenium.[17] This effectively blocks the Lewis acidic metal center from epoxide coordination which in term is leading to better epoxide protection. The less basic pyridines have no or little influence on the chemical shift and can therefore be assumed to have a much weaker coordination to the metal, a situation leading to a decreased yield of epoxide. In summary, these results showed that highly basic additives protect the epoxide but are detrimental to the catalyst lifetime, decomposing MTO into a perrhenic acid pyridine adduct and methanol (eq 1). Less basic additives, however, allowed higher conversion at the cost of lower selectivity.

$$CH_3ReO_3 \xrightarrow[\text{pyridine}]{H_2O_2} HOReO_3 \cdot 2py + CH_3OH \quad (1)$$

Employing these observations in the epoxidation of 1-decene, a substrate giving an epoxide less sensitive for nucleophilic ring cleavage than styrene oxide, resulted in a system where the addition of 10 mol % 3-cyanopyridine effectively gave full conversion of the alkene in only 17 h. Figure 1 shows that 3-cyanopyridine turned out to be, as in the previous study of styrene epoxidation, the additive of choice and that the reaction with no additive surprisingly led to higher conversion of the alkene than in the case where pyridine was added.

It is worth noting that the epoxidation of 1-decene containing 3-cyanopyridine was very fast up to about 85−90% conversion, when the rate suddenly substantially decreased. In the following workup of the reaction a white precipitate was isolated and characterized as 3-cyanopyridine N-oxide. In fact, MTO has previously been used as a catalyst for the oxidation of amines to nitrones and in one example pyridine to its N-oxide.[11c] However, the oxidation of this additive did compete with the epoxida-
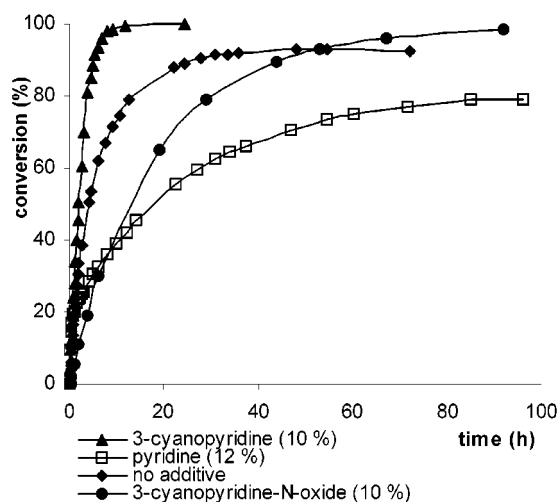


**Figure 1.** Influence of different additives on the epoxidation of 1-decene with 30% aqueous hydrogen peroxide (2 equiv) catalyzed by MTO (0.5 mol %) in dichloromethane at 24 °C.

tion only late in the process at high alkene conversion. Employing 3-cyanopyridine N-oxide as an additive resulted in overall much lower reaction rate, which can explain the decrease in reaction rate observed at high alkene conversion when 3-cyanopyridine is used as additive.[18] We have recently investigated the scope of this system, and a number of pyridines were successfully transformed in high yields to their corresponding N-oxides.[19]
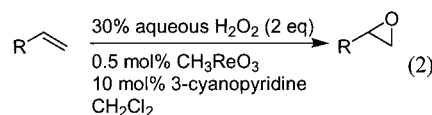


In conclusion, terminal alkenes can efficiently be epoxidized in high yields as a result of changing the additive to 3-cyanopyridine. The conditions are summarized in eq 2. For alkenes leading to more sensitive epoxides, a mixture of pyridine and 3-cyanopyridine (10 mol %, respectively) as additives was successfully employed to give epoxides in high yield.[20]

The enhanced yields obtained employing 3-cyanopyridine as an additive led us to further investigate the use of this additive for the epoxidation of higher substituted alkenes. First we examined trans-disubstituted alkenes, which typically required longer reaction times using the parent pyridine as an additive. Performing the MTO-catalyzed epoxidation of *trans*-3-decene in the presence of pyridine (12 mol %) and 3-cyanopyridine (10 mol %), respectively, showed that using the functionalized pyridine resulted in full conversion of the olefin after 7 h whereas the reaction containing pyridine required >20 h. The substantially shorter reaction time observed with 3-cyanopyridine as the additive led us to further investigate how various factors as amount of catalyst, amount of additive and the alkene concentration influence the
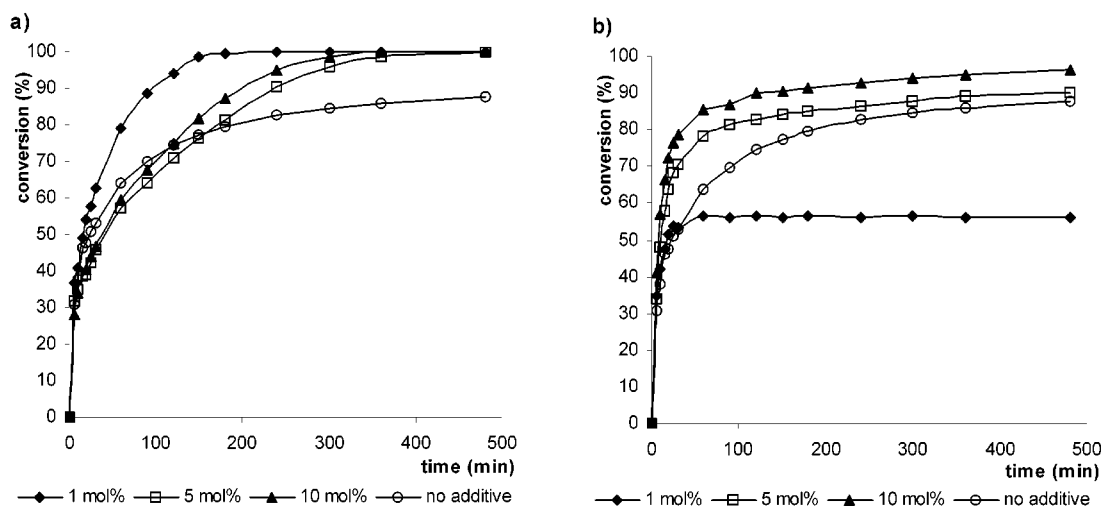
(17) Complexation constants have been determined for the reaction between a number of pyridines and MTO; see: Wang, W.-D.; Espenson, J. H. *J. Am. Chem. Soc.* **1998**, *120*, 11335.

(18) The epoxidation of 1-decene with 30% aqueous hydrogen peroxide catalyzed by MTO containing 3-cyanopyridine N-oxide (10 mol %) as additive shows a first-order kinetics for the alkene.

(19) Copéret, C.; Adolfsson, H.; Khuong, T.-A. V.; Yudin, A. K.; Sharpless, K. B. *J. Org. Chem.* **1998**, *63*, 1742.
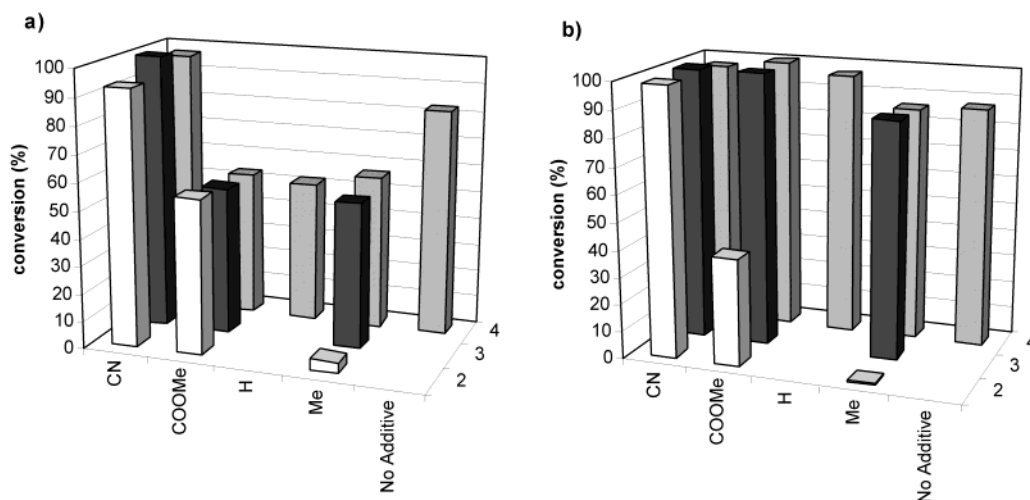
(20) For the scope of the MTO-catalyzed epoxidation of terminal alkenes in the presence of 3-cyanopyridine, see ref 8b.

**Figure 2.** Reaction profiles for the epoxidation of *trans*-3-decene with 30% aqueous hydrogen peroxide catalyzed by MTO (0.3 mol %) in the presence of various amounts of (a) 3-cyanopyridine and (b) pyridine, respectively.



**Figure 3.** Plots showing the influence of varying the amount additive in the epoxidation of *trans*-3-decene with 30% aqueous hydrogen peroxide (2 equiv) catalyzed by MTO (0.3 mol %) at ambient temperature: (a) 1 mol % additive, reaction time 4 h; (b) 10 mol % additive, 8 h.

MTO-catalyzed epoxidation of trans-substituted alkenes with aqueous hydrogen peroxide.

We initially focused on the amount of catalyst required for achieving full conversion. When the reaction conditions from the above epoxidation of terminal alkenes were used, i.e., 10 mol % of 3-cyanopyridine, 2 equiv of 30% aqueous hydrogen peroxide at an alkene concentration of 2 M in dichloromethane, varying the amount of MTO showed that the minimum catalyst loading necessary for full conversion of *trans*-3-decene to *trans*-3,4-epoxydecane was 0.3 mol % compared to 0.5 mol % required in the pyridine system.

We then focused our attention upon the additive and more so upon the importance of electronic and steric effects from various pyridine additives on the epoxidation of *trans*-3-decene. Figure 2 shows the reaction profiles for the epoxidation of *trans*-3-decene with aqueous hydrogen peroxide catalyzed with 0.3 mol % MTO in the presence of various amounts of 3-cyanopyridine and pyridine, respectively. Interestingly, the lower amount of 3-cyanopyridine resulted in higher conversion in shorter time while the opposite is true for pyridine where the catalytic activity completely is lost after 1 h using

the lower amount of the additive. Thus, full conversion of *trans*-3-decene was obtained after only 4 h using 1 mol % of 3-cyanopyridine (Figure 2a).

To further investigate the importance of the additives, we extended the study using the following substituted pyridines: 2-, 3-, and 4-cyanopyridine, the methyl esters of picolinic, nicotinic, and isonicotinic acid, the parent pyridine, and 2-, 3-, and 4-picoline. The reaction without any additive was also included for comparison. Thus, screening the epoxidation reaction using exactly the same conditions in each case, i.e., 0.3 mol % MTO, 2 equiv of 30% aqueous hydrogen peroxide at an alkene concentration of 2 M in dichloromethane, and varying only the amount and substituent of the pyridine additive gave the following results: Using 1 mol % of additive showed that the cyanopyridines, independently on the position of substitution, gave high conversion of the alkene within only a short time (Figure 3a), whereas all the other additives in the study typically showed low conversion. It is worth pointing out that 3-cyanopyridine still was the best of the additives.

Increasing the amount of additives successively from 1 mol % to 10 mol % resulted in longer reaction times

(5−8 h) to reach full conversion (3-cyanopyridine). The reaction mixtures containing 10 mol % of additives showed very small differences and went almost to completion within 8 h, the exceptions being the 2-substituted pyridines, methyl picolinate, and 2-picoline, where the former effectively slows down the reaction and the latter completely inhibits the epoxidation of the alkene. In conclusion, the additive of choice for trans-disubstituted alkenes turned out to be, as in the case of epoxidation of terminal alkenes, 3-cyanopyridine, with the big difference that only 1 mol % additive was required for full conversion in a short time.

The alkene concentration was also demonstrated to be of importance, and an increase of the concentration of *trans*-3-decene from 2 to 3 M with respect to the organic solvent, using 0.3 mol % MTO, 10 mol % 3-cyanopyridine, and 2 equiv of 30% aqueous hydrogen peroxide, dramatically shortened the reaction time to only 3 h. For best results in general, however, alkene concentrations of 2 M is recommended, due to the potential change of reaction medium (low polarity) obtained when higher concentrations are used. It is worth pointing out that transition metal catalyzed oxygen transfer reaction typically works better when the amount hydrocarbon solvents is kept at a low level, due to decreased solvation of the active catalysts.[21] The optimized conditions for epoxidation of trans-disubstituted alkenes are summarized in eq 3.

$$R\diagdown\diagup R' \xrightarrow[\substack{0.3\ mol\%\ CH_3ReO_3 \\ 1\text{-}2\ mol\%\ 3\text{-cyanopyridine} \\ CH_2Cl_2}]{30\%\ aqueous\ H_2O_2\ (2\ eq)} R\diagdown\overset{O}{\triangle}\diagup R' \quad (3)$$
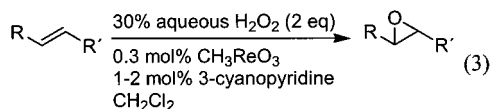
Employing 3-cyanopyridine as the additive for the epoxidation of cis-disubstituted or other more electron-rich alkenes (tri- or tetrasubstituted alkenes) did not result in any improvements compared to when the parent pyridine was added. In fact, lower reaction rates and less product protection was typically observed; thus, for faster reacting alkenes (more electron-rich substrates) the system containing 12 mol % pyridine gives the best results in terms of conversion and selectivity.

**The Role of the Additive.** Addition of pyridine or pyridine derivatives to the MTO-catalyzed epoxidation of alkenes clearly have an improving effect, both in increasing the rate of the reaction and protecting the formed epoxide from Lewis acid mediated nucleophilic ring-opening reactions. The origin of the rate-improving effect is still not fully understood, but several observations of the reaction indicates that the pyridine or pyridine derivatives play an important role as phase-transfer catalysts, transporting the peroxo complexes of MTO from the aqueous layer into the organic phase. This can easily be observed from the bright yellow color of the peroxo complexes of MTO,[17] that in the absence of any additive is only observed in the aqueous layer, whereas upon addition of pyridine or a pyridine derivative, the yellow peroxo complexes are transported into the organic phase. Further evidence indicating that the pyridine additives act as phase-transfer agents comes from ob-
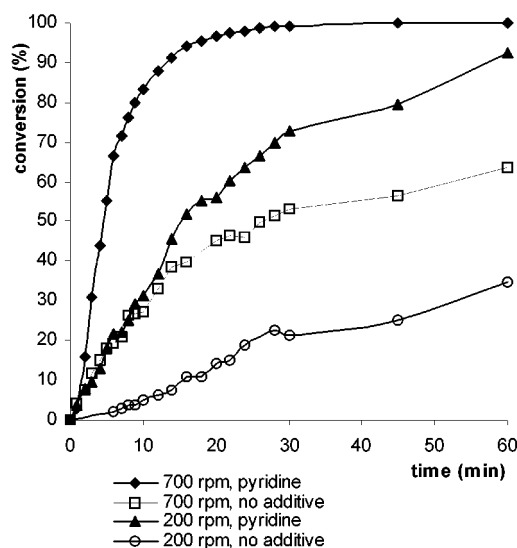


**Figure 4.** Effect of different stirring rates in the biphasic epoxidation of cyclooctene with aqueous hydrogen peroxide catalyzed by MTO with or without pyridine additive.

**Scheme 2**
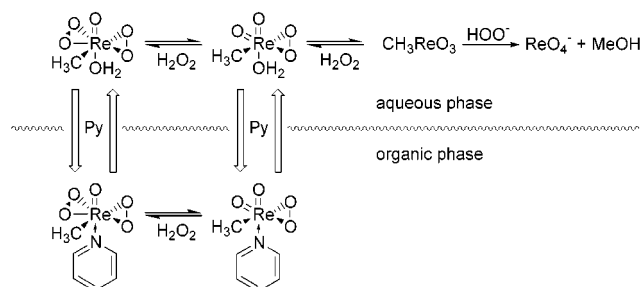


serving the reaction profile obtained when the epoxidation reaction is performed with different stirring rates (Figure 4).

In the epoxidation of cyclooctene with 30% aqueous hydrogen peroxide catalyzed by MTO (0.3 mol %) with a stirring rate at 200 rpm we observed a dramatic increase in conversion of the alkene when pyridine was added compared to the reaction without any additive. This effect was even more pronounced when the rate of stirring was increased to 700 rpm. On the negative side, the more basic pyridines also display a clearly detrimental effect on the catalyst lifetime (Scheme 2).
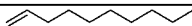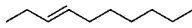
MTO is known to be stable under acidic conditions but when treated with base under oxidative aqueous conditions, the formation of perrhenic acid and methanol is an important side reaction.[22] Even a weak base like water can act destructively on the catalyst, forming a perrhenic acid−base adduct, which under these conditions is a completely inactive oxygen-transfer catalyst.[23] This explains why the system containing pyridine as the sole additive is only able to successfully epoxidize electron-rich and thereby faster reacting alkenes, since these

(21) The use of saturated hydrocarbon solvents in metal catalyzed oxidations reactions is known to dramatically change the catalyst composition and thereby decreasing the catalytic activity; see: Woddard, S. S.; Finn, M. G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1991**, *113*, 106.

(22) (a) Abu-Omar, M. M.; Hansen, P. J.; Espenson, J. H. *J. Am. Chem. Soc.* **1996**, *118*, 4966. (b) Yudin, A. K.; Sharpless, K. B. Unpublished results.

(23) Inorganic rhenium compounds are inactive as oxidation catalysts in the presence of aqueous hydrogen peroxide. This problem can, however, be overcome using bistrimethylsilyl peroxide (BTSP) as the terminal oxidant; see: (a) Yudin, A. K.; Sharpless K. B. *J. Am. Chem. Soc.* **1997**, *119*, 11536. (b) Coperét, C.; Adolfsson, H.; Chiang, J. P.; Yudin, A. K.; Sharpless, K. B. *Tetrahedron Lett.* **1998**, *39*, 761.

### Table 2.   Relative Initial Rates of Alkene Epoxidation[a]

| Alkene | No Additive | Pyridine (12 mol%) | 3-Cyanopyridine (10 mol%) | 3-Cyanopyridine (1 mol%) |
|---|---|---|---|---|
| (structure) | 1 | 2.2 (1) | 3.6 (1) | 2.3 (1) |
| (structure) | 11 | 17 (7.7) | 9 (2.5) | 15 (6.5) |
| (structure) | 11 | 33 (15) | 7 (2) | 12 (5) |
| (structure) | 13 | 25 (11) | 7.3 (2) | 17 (7.4) |
| (structure) | 43 | 62 (28) | 24 (6.7) | 42 (18) |
| (structure) | 56 | 56 (25) | 29 (8) | 60 (26) |

[a] Reactions were run using 30% aqueous $H_2O_2$, alkene, and $MeReO_3$ in a 2000:1000:3 molar ratio at 24 °C with stirring at 700 rpm. Amounts of additive as noted above. Alkene concentration: 2 M in $CH_2Cl_2$. The initial rates were determined by GC analysis of the conversion for each alkene, respectively, and the relative rates were calculated from the observed rate constants with the initial rate for 1-decene without additive normalized to 1. The numbers in parentheses are the relative initial rates for each additive, respectively.

reactions are fast enough to occur before a considerable amount of the catalyst is decomposed. 3-Cyanopyridine, however, being less basic than the parent pyridine, has a less detrimental effect on the catalyst lifetime and can therefore serve as an additive for slower reacting alkenes. In a recent study, Espenson and Wang investigated the effects of pyridine on the equilibrium and kinetics in the MTO/aqueous hydrogen peroxide system.[17] The observed results indicated that the accelerating effect obtained upon addition of pyridine is strongly connected to the Brönsted basicity of the heterocycle. Thus, the presence of pyridine increases the concentration of the mono-hydrogen peroxide anion ($HOO^-$), which results in a faster formation of the peroxo-complexes of MTO. The higher concentration of $HOO^-$ is also increasing the rate of MTO decomposition. The latter is in agreement with the fact that, in the presence of the less basic 3-cyanopyridine, the lifetime of the catalyst seems to be considerable longer. The isolation of 3-cyanopyridine *N*-oxide after the epoxidation reaction speaks clearly against the possibility that the additive is involved in a oxygen transfer process similar to the Payne epoxidation.[24] The latter reaction would lead to the formation 3-pyridinecarboxamide or its *N*-oxide. The Payne epoxidation also requires a stoichiometric amount of the nitrile.
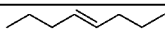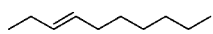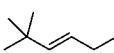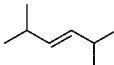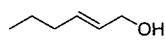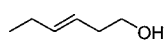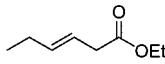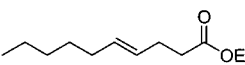
**Catalytic Performance.** High initial rates are of great significance in a system where catalyst decomposition is an important side reaction competing with the reaction path leading to product. Thus, lower conversion can be expected for slow reacting substrates since longer reaction times results in more catalyst deactivation. This is indeed true for the MTO catalyzed epoxidation of alkenes where the lifetime of the catalyst certainly is limited, especially under basic reaction conditions (vide supra). The differences between the two epoxidation systems discussed above (pyridine and 3-cyanopyridine as additives respectively) are clearly visualized when comparing the relative initial rates these systems show for alkenes with various substitution patterns. As shown in Table 2, the pyridine system shows a reactivity toward the alkenes following the expected order for electrophilic epoxidations, where a rate increase is expected when the electron density of the substrates increases.

Epoxidation of cis- and trans-disubstituted alkenes is stereospecific and gives the corresponding epoxides with retention of configuration. The relative initial rate between *cis*- and *trans*-alkenes ($Z/E = 2:1$) are somewhat higher than the ratio observed when *m*-chloroperbenzoic acid is used as the oxidation reagent (3-octene, $Z/E = 1.2:1$).[5b] This is in sharp contrast to dimethyldioxirane (3-hexene, $Z/E = 8.3:1$)[25] and the sodium tungstate system developed by Noyori et al. (3-octene, $Z/E = 7.3:1$)[5b] which show a much higher reactivity toward *cis*-alkenes. The situation changes dramatically when using 10 mol % of 3-cyanopyridine as the additive. Relative initial rates for this system show a much smaller difference between terminal and disubstituted alkenes, which in terms explains the observed reactivity of this system where reactions performed on terminal alkenes with 3-cyanopyridine as the additive works better than when the unfunctionalized pyridine is added. There is practically no difference in initial rates between cis- and trans-disubstituted alkenes for the system containing 3-cyanopyridine ($Z/E = 1:1.2$), and in contrast to the pyridine system, the *trans*-alkenes react slightly faster. Interestingly, with the exception of terminal alkenes, the system containing 1 mol % of 3-cyanopyridine shows higher initial reactivity toward each class of alkenes compared to when 10 mol % of the additive is present. The similar relative initial rates observed for the systems containing pyridine and 1 mol % 3-cyanopyridine indicate that the latter could be the additive of choice also for more substituted alkenes. In our hands, however, the simple pyridine system performs with full satisfaction in epoxidations of alkenes other than terminal- and trans-disubstituted ones.

**Scope and Limitations.** With the optimized conditions in hand, we then investigated the catalytic activity of the above system containing 1 mol % of 3-cyanopyridine as additive on various trans-disubstituted alkenes. As listed in Table 3 this epoxidation method shows high applicability on a wide variety of substrates. Linear as well as the sterically more demanding branched alkenes are all epoxidized in good yields (entry 1−4) and in shorter reaction times compared to the previously reported pyridine containing system. Severe steric hindrance in positions next to the alkene did not dramati-
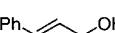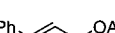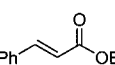
(24) Payne, G. B. *Tetrahedron* **1962**, *18*, 763.

(25) Baumstark, A. L.; Vasquez, P. C. *J. Org. Chem.* **1988**, *53*, 3437.

**Table 3. Epoxidation of *trans*-Alkenes with Hydrogen Peroxide, Catalyzed by Methyltrioxorhenium in the Presence of 3-cyanopyridine[a]**

| Entry | Alkene | mmol | MTO mmol | py-3-CN mmol | $CH_2Cl_2$ mL | Time | Yield |
|---|---|---|---|---|---|---|---|
| 1 | | 30 | 0.09 | 0.3 | 9 | 12 h | 97% |
| 2 | | 10 | 0.03 | 0.2 | 1.6 | 6 h | 98% |
| 3 | | 10 | 0.03 | 0.2 | 2 | 18 h | 85% |
| 4 | | 20 | 0.06 | 0.2 | 6 | 12 h | 89% |
| 5 | OH | 10 | 0.02 | 0.2 | 1.2 | 6 h | 80%[c] |
| 6 | OH | 10 | 0.02 | 0.2 | 1.2 | 6 h | 92%[c] |
| 7 | OEt | 20 | 0.06 | 0.2 | 6 | 19 h | 89% |
| 8 | OEt | 20 | 0.06 | 0.2 | 4.8 | 18 h | 89% |

[a] 30% aqueous $H_2O_2$ (2 equiv) used unless otherwise noted. [b] Isolated yield. [c] 50% aqueous $H_2O_2$ (2 equiv).

**Table 4. Epoxidation of Phenyl-Substituted *trans*-Alkenes with Hydrogen Peroxide, Catalyzed by Methyltrioxorhenium in the Presence of 3-Cyanopyridine and Pyridine[a]**

| Entry | Alkene | mmol | MTO mmol | py-3-CN mmol | py mmol | $CH_2Cl_2$ mL | Time | Yield[b] |
|---|---|---|---|---|---|---|---|---|
| 1 | Ph | 10 | 0.03 | 1 | 0.5 | 2.3 | 7 h | 90% |
| 2 | Ph—Ph | 300 | 1.5 | 30 | 30 | 50 | 17 h | 92% |
| 3 | Ph—OH | 10 | 0.03 | 1 | 0.5 | 2.3 | 7 h | 86% |
| 4 | Ph—OAc | 10 | 0.03 | 1 | 0.5 | 1.9 | 20 h | 96% |
| 5 | Ph—OEt | 20 | 0.1 | 2 | - | 12 | 6 h | 20%[c] |

[a] 30% aqueous $H_2O_2$ (2 equiv) used in all entries. [b] Isolated yield. [c] Conversion to epoxide, no diol was detected. No further conversion after 20 h.

cally affect either the yield or the reaction time. This is to be compared to the epoxidation of *trans*-2,5-dimethyl-3-hexene catalyzed by MTO (0.5 mol %) and pyridine (12 mol %) where only 68% was obtained after 17 h. Functional groups as alcohols or esters do not interfere with the epoxidation reaction and good yields were obtained with allylic and homoallylic 1-hexanols, in this case with a catalyst amount of only 0.2 mol % (entry 5 and 6). High yields were also obtained in the epoxidation of noncon-jugated unsaturated esters (entry 7 and 8). Alkenes yielding epoxides more sensitive to nucleophilic ring opening, e.g., phenyl-substituted alkenes, required a mixture of 3-cyanopyridine and pyridine (10 and 5−10 mol % respectively) for a successful outcome of the reaction. These results are presented in Table 4. The yield of *trans*-stilbene was significantly increased using the mixture of pyridines compared to the system containing only pyridine as the additive[8a] (entry 2). The epoxidation of cinnamyl acetate with 0.5 mol % MTO and 12 mol % pyridine resulted in 54% conversion, whereas using the *cocktail* (3-cyanopyridine and pyridine) and only 0.3 mol % catalyst gave a significantly higher yield (entry 4). The role of the two pyridines used in the

cocktail is not clear, but performing reactions on phenyl-substituted alkenes using only one of the additives results in lower yields of epoxides (cf. Table 1; epoxidation of styrene). For high selectivity in epoxidations of the alkenes in Table 4 the following requirements need to met: (1) the MTO catalyst must be stabilized against decomposition, and (2) the products need to be protected against ring opening. The *cocktail* provides a combination which satisfy these criterea. Electron-poor alkenes as ethyl cinnamate did not perform well under these epoxidation conditions (entry 5).

**Conclusions**

We have shown that changing the additive from pyridine to 3-cyanopyridine in the MTO-catalyzed epoxidation of alkenes with the environmental friendly oxidant aqueous hydrogen peroxide has several beneficial effects. Epoxidation of terminal alkenes can efficiently be accomplished in high yields using 10 mol % 3-cyanopyridine and 0.5 mol % catalyst. Trans-disubstituted alkenes were successfully epoxidized using only 0.3 mol % catalyst and 1−2 mol % 3-cyanopyridine. Alkenes leading to acid-

sensitive epoxides were oxidized in high yields using a cocktail consisting of pyridine and 3-cyanopyridine. Pyridine is, however, still the additive of choice for epoxidation of more electron-rich alkenes. The epoxidation system shows high tolerance toward functional groups in the substrates. The role of the additives in the system can to a great extent be explained by phase-transfer effects, where the pyridine additives take part in the transfer of the active peroxospecies of MTO into the organic solvent. Basic additives were shown to be very deleterious to the lifetime of the catalyst, presumable due to the formation of higher concentrations of HOO$^-$. The obtained enhancement of the system using 3-cyanopyridine as an additive can partly be explained by its lower p$K_a$, which in term is leading to a slower decomposition rate of the catalyst.

### Experimental Section

All reagents and solvents were purchased and used without further purification. All reactions were carried out at ambient temperature (24 °C, water bath) under air.

**Procedure for the Relative Initial Rate Determination.** In a 20 mL scintillation vial were added alkene (10 mmol), MTO (0.03 mmol), additive, cyclooctane or dodecane (100 $\mu$l) as internal standard, and CH$_2$Cl$_2$ to give a 2.0 M concentration of the alkene in the organic solvent. The stirring was set to 700 rpm, temperature regulated to 24 °C (water bath), and 2 mL of aqueous H$_2$O$_2$ (20 mmol) was added. The reaction was monitored by taking aliquots (40 $\mu$L) at different time intervals (initially every 30 s for the faster reacting alkenes). The samples were quenched by addition of the aliquots to MnO$_2$, diluted with ethyl acetate (2 mL), and dried with Na$_2$SO$_4$. The samples were analyzed by GC, and the initial rates were determined from the conversion of alkene versus time plots by comparing the slopes of the straight lines obtained.

**Standard Procedure for Epoxidation of Trans-Disubstituted Alkenes Exemplified for *trans*-3-Decene.** To a 20 mL scintillation vial were added *trans*-3-decene (1.40 g, 10 mmol), 3-cyanopyridine (0.2 mL 1 M in CH$_2$Cl$_2$, 0.2 mmol), MTO (0.3 mL 0.1 M in CH$_2$Cl$_2$, 0.03 mmol), and 1.6 mL of CH$_2$Cl$_2$. The flask was placed in a water bath (24 °C), and 30% aqueous hydrogen peroxide (2.26 mL, 20 mmol) was added.

The reaction mixture was stirred for 6 h when MnO$_2$ was added in portions. When no more oxygen gas evolution was observed, the phases were separated and the aqueous layer was washed with CH$_2$Cl$_2$ (2 × 20 mL). The combined organic phases were dried with Na$_2$SO$_4$ (s), and the solvent was removed under reduced pressure. The obtained crude was distilled under vacuum to yield 1.53 g (98%) of *trans*-3,4-epoxydecane.

**Standard Procedure for Epoxidation of Phenyl-Substituted Alkenes Exemplified for *trans*-Stilbene.** To a 250 mL Erlenmeyer flask were added *trans*-stilbene (54.07 g, 300 mmol), 3-cyanopyridine (3.12 g, 30 mmol), pyridine (2.37 g, 30 mmol), MTO (374 mg, 1.5 mmol), and 50 mL of CH$_2$Cl$_2$. The flask was placed in a water bath (24 °C), and 30% aqueous hydrogen peroxide (68 mL, 600 mmol) was added. The reaction mixture was stirred for 17 h when MnO$_2$ was added in portions. When no more oxygen gas evolution was observed, the phases were separated and the aqueous layer was washed with CH$_2$Cl$_2$ (2 × 200 mL). The combined organic phases were dried with Na$_2$SO$_4$ (s), and the solvent was removed under reduced pressure. The obtained crude was recrystallized from ethanol to yield 54.16 g (92%) of *trans*-stilbene oxide: mp 68–70 °C (65–67 °C).

**Supporting Information Available:** Spectroscopic characterization of the products and plots for relative initial rate determinations. This material is available free of charge via the Internet at http://pubs.acs.org.

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