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An efficient organic solvent-free methyltrioxorhenium-catalyzed epoxidation of alkenes with hydrogen peroxide

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ABSTRACT

Methyltrioxorhenium/3-methylpyrazole has proved to be an efficient catalytic system for epoxidation of alkenes with aqueous 35% H_2O_2 in excellent yields under organic solvent-free conditions. The yields of epoxides by the organic solvent-free epoxidation are comparable to those using CH_2Cl_2 as the organic solvent. The epoxidations of simple alkenes under organic solvent-free conditions are slower than those in CH_2Cl_2, while the epoxidations of alkenols such as citronellol are faster than those in CH_2Cl_2.

1. Introduction

Epoxides are important compounds for both laboratory and industry as the intermediates and the final products for a wide range of chemicals.[1,2] Although a major method for producing epoxides in industry is dehydrochlorination of chlorohydrins,[2] direct epoxidation of alkenes is more favorable than the two-step procedure,[3] and extensive studies of direct epoxidation methods have been continued.[4] Various oxidants have been used for both laboratory and industrial epoxidations. Most of the oxidants are often hazardous and expensive, and in addition, form equimolar amounts of the deoxygenated compounds as waste, which are troublesome to remove from the epoxide products. The ideal alkene epoxidation procedure must be high yield and selectivity without any by-products through a simple and safe operation using a clean and cheap oxidant. In this context, H_2O_2 is one of the ideal oxidants, because of its high atom efficiency (47%) as oxidant and sole theoretical side product water.[5,6]

Currently, methyltrioxorhenium (CH_3ReO_3, MTO) is one of the most effective catalysts for epoxidation using aqueous H_2O_2.[7] In 1991, Herrmann and co-workers reported on the H_2O_2 epoxidation of various alkenes using MTO as a catalyst and *t*-BuOH as the solvent under homogeneous reaction medium conditions.[8] Although catalytic activity of MTO has proven to be very high, the disadvantage of the method is acid (MTO) catalyzed hydrolysis of epoxides produced during the reaction. Herrmann's group managed modest increases in selectivity by addition of tertiary nitrogen bases.[8,9] Since then, intense efforts have been made to improve the performance of this significant epoxidation.[10–17] Subsequently, Sharpless and co-workers found that the addition of 12 mol % pyridine (or substituted pyridines) under organic-aqueous biphasic conditions using CH_2Cl_2 as the organic solvent both suppressed epoxide ring-opening reaction and enhanced catalytic activity.[10] Shortly afterward Herrmann reported pyrazole as a superior additive to pyridine because pyrazole is not affected under the reaction conditions while pyridine is oxidized to pyridine *N*-oxide during epoxidation.[18] Recently, we reported 3-methylpyrazole as a superior additive to pyrazole because MTO/3-methylpyrazole system has higher catalytic activity and longer catalyst lifetime than MTO/pyrazole system.[19]

Generally, CH_2Cl_2 has been chosen as the solvent for MTO-catalyzed epoxidation, because fast rate, high yield, and high selectivity are obtained by using CH_2Cl_2.[10–19] From environmental and toxic points of view, this is certainly not the most appropriate solvent. The negative influences of CH_2Cl_2 on health and the environment[20] cancel out the advantages of aqueous H_2O_2. The use of environmentally friendly and lower toxic solvent instead of CH_2Cl_2 or organic solvent-free reaction is desirable. Although various alternative solvents have been investigated to lower the negative impact of CH_2Cl_2, only a limited success has been obtained. The change of the solvent from CH_2Cl_2 to fluorinated alcohols such as trifluoroethanol[21] and hexafluoro-2-propanol[22] allowed reduction of MTO loading. However, acid-sensitive epoxides undergo ring-opening leading to a mixture of compounds in these fluorinated

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alcohols.[21,22] Room temperature ionic liquids were also examined for MTO-catalyzed epoxidation. A higher MTO loading and use of UHP (urea hydrogen peroxide adduct) were required to obtain comparable results in ionic liquids to those in CH_2Cl_2.[23] Very recently dimethylcarbonate has been reported as the good solvent for MTO-catalyzed oxidations.[24] However, the paper reported only one example of alkene epoxidation (styrene) using UHP as the oxidant.

Herein, we wish to report an effective organic solvent-free epoxidation of alkenes with aqueous 35% H_2O_2 catalyzed by MTO using 3-methylpyrazole as an additive when alkenes are liquid. This reaction will be performed under entirely organic solvent-free and halide-free conditions, and avoids the solvent problem.

2. Results and discussion

We first examined organic solvent-free MTO-catalyzed epoxidation of cyclohexene using pyridine,[10] pyrazole,[18] and 3-methylpyrazole[19] as the additives (Table 1). These three additives have been reported to be effective for MTO-catalyzed cyclohexene epoxidation under CH_2Cl_2-aqueous biphasic conditions. Pyridine and 3-methylpyrazole are liquid at room temperature and soluble in cyclohexene. On the other hand, pyrazole is solid at room temperature and insoluble in cyclohexene.

The reaction without additive or organic solvent resulted in hydrolysis of the epoxide produced, and only a trace amount of the epoxide was detected (entry 1).

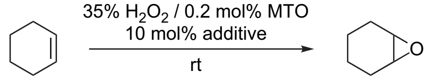
The epoxidation of cyclohexene with 0.2 mol % MTO in the presence of 10 mol % pyridine, pyrazole, or 3-methylpyrazole in CH_2Cl_2 gave quantitative conversion to cyclohexene oxide (entries 2, 4, and 6).[19]

When the epoxidation of cyclohexene was carried out without organic solvent in the presence of pyridine, the reaction stopped within 30 min with large amount of unreacted cyclohexene remained (entry 3). The yellow color of the reaction mixture, which indicates the presence of catalytically active peroxo rhenium species,[8] changed to colorless within 30 min. This indicated that the decomposition of MTO is rapid in the presence of pyridine under organic solvent-free conditions.[13c,25–27]

Although pyrazole is not dissolved in common alkenes, aqueous H_2O_2 dissolves pyrazole. When the epoxidations of cyclohexene were carried out without organic solvent in the presence of pyrazole (dissolved in aqueous H_2O_2 before mixing with cyclohexene and MTO), the reaction stopped within 1 h with low conversion of the alkene and low yield of epoxide (entry 5). It is reported that in CH_2Cl_2-aqueous H_2O_2 biphasic system the additive (pyridine) play an important role as phase-transfer catalyst,[10d] transporting the peroxo complexes of MTO from the aqueous layer into CH_2Cl_2. Because of the poor solubility of pyrazole in cyclohexene, pyrazole does not work as good phase-transfer catalyst in the cyclohexene-aqueous H_2O_2 biphasic system. This must be the reason of the unsatisfactory result using pyrazole.

Table 1

MTO-catalyzed epoxidation of cyclohexene with 35% H_2O_2[a]



Entry	Additive	Solvent[b]	Time (h)	Conversion[c] (%)	Epoxide[c,d] (%)
1	—[e]	—[f]	5	89	<1
2	Pyridine	CH_2Cl_2	5	99	>99
3	Pyridine	—[f]	0.5	14	14
4	Pyrazole	CH_2Cl_2	3	>99	>99
5	Pyrazole	—[f]	1	25	14
6	3-Methylpyrazole	CH_2Cl_2	1	>99	>99
7	3-Methylpyrazole	—[f]	3	>99	97

[a] Cyclohexene (20 mmol), 35% H_2O_2 (40 mmol), additive (2 mmol), MTO (0.04 mmol) at room temperature in CH_2Cl_2 (10 mL) or without organic solvent.

[b] The results of epoxidation in CH_2Cl_2 are from Ref. 19.

[c] Determined by GC analysis.

[d] Yield of cyclohexene oxide based on cyclohexene used.

[e] Reaction without additive.

[f] Reaction without organic solvent.

When the organic solvent-free epoxidations of cyclohexene were carried out with 3-methylpyrazole, compared with unsatisfactory results using pyridine and pyrazole, a good result was obtained. The reaction completed within 3 h to give 97% yield of cyclohexene oxide (entry 7). Because of the good solubility in cyclohexene, 3-methylpyrazole works as good phase-transfer catalyst in the cyclohexene-aqueous H_2O_2 biphasic system. And furthermore, the lower basicity of 3-methylpyrazole (p*K*a=3.3) than pyridine (p*K*a=5.2) must prevent the decomposition of MTO.[10d] These must be the reasons of the excellent result of 3-methylpyrazole as the additive.

The results in Table 1 clearly indicated that 3-methylpyrazole is an effective additive for organic solvent-free epoxidation of alkenes catalyzed by MTO with aqueous H_2O_2 as the terminal oxidant, and that pyridine and pyrazole are ineffective for this purpose.

We then investigated the influence of the amount of 3-methylpyrazole added on the cyclohexene epoxidation under organic solvent-free conditions. As can be seen from Figure 1, the efficient epoxidation required 10 mol % or higher amount of 3-methylpyrazole.[28] For comparison and general applicability, the amount of 3-methylpyrazole (10 mol %) was maintained for all experiments.

MTO-catalyzed epoxidations of a variety of alkenes using 3-methylpyrazole as an additive under organic solvent-free conditions were examined. The results are summarized in Table 2.

Cyclic alkenes, 1-methylcyclohexene, 1-phenylcyclohexene, cyclopentene, cycloheptene, and cyclooctene, required longer reaction time compared to the reaction in CH_2Cl_2 with comparable conversions and yields of epoxides (entries 1–10).

MTO-catalyzed epoxidation of 1-octene, aliphatic terminal alkene, was slower under organic solvent-free conditions than that

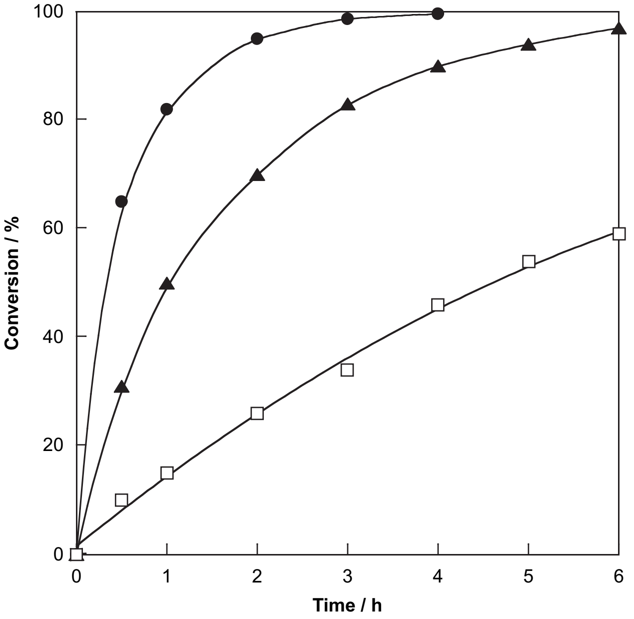
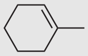
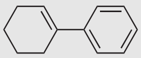
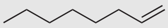
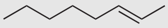
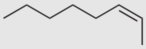
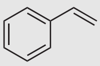
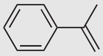
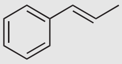
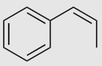
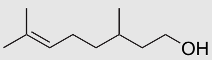
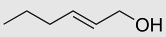
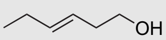


Figure 1. Time course of MTO-catalyzed epoxidation of cyclohexene with different amounts of 3-methylpyrazole under organic solvent-free conditions. Conditions: cyclohexene (10 mmol), 35% H_2O_2 (20 mmol), MTO (0.02 mmol), and 3-methylpyrazole at 20 °C. Analysis by GC: (●) Curve A: 1.5 mmol (15 mol %) 3-methylpyrazole. (▲) Curve B: 1.0 mmol (10 mol %) 3-methylpyrazole. (□) Curve C: 0.5 mmol (5 mol %) 3-methylpyrazole. The curve of 20 mol % 3-methylpyrazole lapped over that of 15 mol %.

Table 2
MTO-catalyzed epoxidation of various alkenes with 35% H_2O_2 in the presence of 3-methylpyrazole[a,b]

Entry	Alkene	Solvent	MTO (mol %)	Temperature (°C)	Time (h)	Conversion[c] (%)	Epoxide[c] (%)
1		CH_2Cl_2	0.1	10	5	>99	>99
2		—[d]	0.1	10	9	>99	>99
3		CH_2Cl_2	0.1	rt	3	>99	95
4		—[d]	0.1	10	9	>99	85
5		CH_2Cl_2	0.1	rt	2.5	>99	>99
6		—[d]	0.1	10	6	>99	>99
7		CH_2Cl_2	0.1	rt	3	>99	>99
8		—[d]	0.1	rt	7	>99	89
9		CH_2Cl_2	0.1	rt	2	>99	>99
10		—[d]	0.1	rt	3	>99	>99
11		CH_2Cl_2	0.5	rt	8	98	91
12		—[d]	0.5	rt	8	74	62
13		CH_2Cl_2	0.1	rt	5	>99	>99[e]
14		—[d]	0.1	rt	24	96	85[e]
15		CH_2Cl_2	0.1	rt	3	>99	>99[f]
16		—[d]	0.1	rt	8	>99	90[f]
17		CH_2Cl_2	0.5	rt	4	>99	97[g]
18		—[d]	0.5	rt	0.5	82	43[h]
19		—[d]	0.5	10	2.5	>99	98[i]
20		CH_2Cl_2	0.1	rt	3	>99	92
21		—[d]	0.1	10	5	>99	97
22		CH_2Cl_2	0.1	rt	5	>99	>99[e]
23		—[d]	0.1	10	5	>99	>99[e]
24		CH_2Cl_2	0.1	rt	5	>99	>99[f]
25		—[d]	0.1	10	7	>99	>99[f]
26		CH_2Cl_2	0.1	10	4	>99	97
27		—[d]	0.1	10	2	>99	>99
28		—[d]	0.04	10	4	>99	95
29		CH_2Cl_2	0.2	rt	8	>99	>99[e]
30		—[d]	0.2	10	8	>99	>99[e]
31		CH_2Cl_2	0.2	rt	6	>99	99[e]
32		—[d]	0.2	10	2	>99	95[e]

[a] Alkene (20 mmol), 35% H_2O_2 (40 mmol), 3-methylpyrazole (2 mmol), in CH_2Cl_2 (10 mL) or without organic solvent.
[b] The results of epoxidation in CH_2Cl_2 are from Ref. 19.
[c] Yields of epoxides based on alkenes used. Determined by GC analysis.
[d] Reaction without organic solvent.
[e] *trans*-Epoxide.
[f] *cis*-Epoxide.
[g] Styrene glycol (2%) and benzaldehyde (1%) were also produced.
[h] Styrene glycol (24%) and benzaldehyde (5%).
[i] Only trace amounts of styrene glycol and benzaldehyde were detected.

in CH_2Cl_2 (entries 11 and 12). The internal alkenes such as *trans*- and *cis*-2-octene were also converted to the corresponding epoxides under organic solvent-free conditions in somewhat lower yield of epoxides at longer reaction times compared to the epoxidation in CH_2Cl_2 (entries 13–16).

Styrene oxide is known to be very prone to ring-opening reaction. Although MTO-catalyzed epoxidation of styrene in CH_2Cl_2 afforded excellent yield of the epoxide (entry 17), the same epoxidation without organic solvent at room temperature resulted in the formation of large amount of styrene glycol (24%) and benzaldehyde (5%) with lower amount of epoxide (43%) in 82% conversion at 30 min (entry 18). The longer reaction time caused hydrolysis of the epoxide (after 2.5 h, conversion 95%, styrene oxide 5%, styrene glycol 50%, and benzaldehyde 9%). A marked improvement was observed when the reaction was performed at 10 °C. The reaction was faster than that in CH_2Cl_2 at room temperature, and complete conversion and excellent yield of the epoxide were obtained (entry 19).

Organic solvent-free MTO-catalyzed epoxidation of α-methylstyrene, *cis*- and *trans*-β-methylstyrene proceeded smoothly at 10 °C to give the corresponding epoxides in excellent yields within comparable reaction times to the reaction in CH_2Cl_2 at room temperature (entries 20–25).

Citronellol was converted to the corresponding epoxide in excellent yield with 0.1 mol % MTO within 2 h at 10 °C. The reaction is faster than that in CH_2Cl_2 (entries 26 and 27). A complete conversion of citronellol to the corresponding epoxide quantitatively was also observed with reduced amount of MTO (0.04 mol %) with prolonged reaction time (entry 28). A scale-up epoxidation of citronellol (20 g) was examined. The epoxidation and work-up were carried out under entirely CH_2Cl_2 and any chlorine containing compounds free conditions, and 16.7 g (76%) of corresponding epoxide was isolated (see detail Section 4).

Homoallylic alcohol, *trans*-3-hexen-1-ol, and allylic alcohol, *trans*-2-hexene-1-ol were also converted to the corresponding epoxides in excellent yields (entries 30 and 32). The rate of epoxidation of *trans*-3-hexen-1-ol under organic solvent-free condition at 10 °C is faster than that in CH_2Cl_2 at room temperature. The rate of epoxidation of *trans*-2-hexene-1-ol was slower than those of *trans*-3-hexen-1-ol and citronellol.

As shown above, the epoxidation of simple cyclic alkenes and aliphatic alkenes under organic solvent-free conditions is generally slower than that in CH_2Cl_2. This is because the solubility of the catalytically active peroxo rhenium complexes is lower in those alkenes compared to in CH_2Cl_2 solution. On the other hand, the results that the epoxidation of styrenes and alkenols is faster than in CH_2Cl_2 indicated that the peroxo complexes are dissolved in these alkenes at high concentrations. In every alkene, the yields of epoxides by MTO-catalyzed epoxidations using 3-methylpyrazole under organic solvent-free conditions are comparable with those obtained by epoxidation in CH_2Cl_2.

Although various catalytic epoxidations with aqueous H_2O_2 under organic solvent-free conditions have been reported, most of them are tungstate-based catalysts.[29] The method described in this paper is superior to previously reported methods in terms of low catalyst loading and high epoxide selectivity. The outstanding advantage is the excellent yields of acid-sensitive epoxides such as styrene oxide.[29b,c]

3. Conclusions

We have explored and succeeded for the first time in performing MTO-catalyzed epoxidation with aqueous 35% H_2O_2 under organic solvent-free conditions using 3-methylpyrazole as an additive. The use of 3-methylpyrazole is significant for achieving high epoxides' yields. Pyridine and pyrazole were inferior to 3-methylpyrazole as the additive for organic solvent-free epoxidation. This method will exclude CH_2Cl_2 and any chlorine containing compounds from the reaction system, and will avoid negative impact of CH_2Cl_2.

4. Experimental

All reagents obtained were from commercial sources unless otherwise noted and were used without further purification. Methyltrioxorhenium was prepared according to the reported procedure.[30] The concentration of hydrogen peroxide was determined by iodometric titration before use. The progress of the reaction was monitored by GC analysis. The conversion of alkenes and yield of epoxides were determined by GC internal standard method. GC analyses were performed on Shimadzu GC-2010 (FID detector) equipped with GL Sciences InertCap 1 column (30 m length×0.25 mm ID×0.25 μm film thickness).

4.1. Cyclohexene epoxidation (Table 1, entry 7)

A 50-mL flask equipped with a stirbar was charged with cyclohexene (2.03 mL, 20 mmol), 3-methylpyrazole (161 μL, 2.0 mmol, 10 mol %), and MTO (10 mg, 0.020 mmol, 0.1 mol %). H_2O_2 (35%, 3.36 mL, 40 mmol) was added all at once to the stirring solution. The resulted two-phase mixture was stirred vigorously (1000 rpm) at room temperature. The progress of the reaction was monitored at appropriate interval by GC analysis of small aliquots of the organic phase. The conversion of cyclohexene and yield of cyclohexene oxide were determined by GC internal standard method. The GC internal standard material (*n*-undecane) was added just before the first analysis.

4.2. Procedure for 20 g scale epoxidation of citronellol

A 200-mL flask equipped with a stirbar was charged with citronellol (20 g, 128 mmol), 3-methylpyrazole (1.03 mL, 12.8 mmol, 10 mol %), and MTO (31.9 mg, 0.128 mmol, 0.1 mol %). The flask was cooled to 10 °C by applying an external cooling bath. H_2O_2 (35%, 21.5 mL, 256 mmol) was added dropwise to the stirring solution from dropping funnel (ca. 50 min). During the H_2O_2 addition the temperature of the solution was kept below 22 °C. The resulted two-phase mixture was stirred vigorously (1000 rpm) at 10 °C. The reaction was completed after 2 h. AcOEt was added to the reaction mixture, and the mixture was washed successively with aqueous solution of Na_2SO_4 (two times) and with aqueous solution of $Na_2S_2O_3$. Then the organic layer was washed with aqueous solution of tartaric acid (5 g in 50 mL H_2O) to remove 3-methylpyrazole, followed with aqueous solution of $NaHCO_3$. The organic layer was dried over anhydrous Na_2SO_4, and AcOEt was distilled out by evaporator. The residual oil was dried under vacuum to give crude citronellol oxide (18.5 g). Vacuum distillation (1 Torr, 122–123 °C) afforded citronellol oxide as colorless oil (16.7 g, 76%, >96% purity by GC). The physical data agreed with that previously reported.[31]

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