

Manganese(III) Acetate Dihydrate Catalyzed Aerobic Epoxidation Of Unfunctionalized Olefins In Fluorous Solvents.

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Abstract: Manganese(III) acetate dihydrate is used as a catalyst for the epoxidation of various olefins with molecular oxygen/pivalaldehyde as an oxidant in perfluoro-2-butyltetrahydrofuran. Various types of olefins, including substituted styrenes, stilbenes and cyclic and acyclic alkenes were epoxidized in excellent yields at 25°C. The reaction is stereodependent. Regioselectivity is observed on epoxidation of limonene. Mono- and disubstituted olefins show interesting dichotomy in their reactivity in fluorous solvents such as perfluoro-2-butyltetrahydrofuran and 1,1,1,3,3,3-hexafluoro-2-propanol. © 1998 Elsevier Science Ltd. All rights reserved.

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INTRODUCTION

Epoxides are amongst the most synthetic intermediates for the preparation of natural products or epoxy resins. The inherent polarity and strain of their three membered ring makes them susceptible to reaction with a large number of reagents.¹ These epoxides are easily prepared from a variety of starting materials.² Peracids are frequently used for the conversion of olefins to epoxides. Another very interesting method is the oxidation by molecular oxygen with the advantage of a fairly safe, clean and abundant oxidant.^{3,4} The combination of three components - a transition metal, organic ligands and a reductant - creates an effective oxygenation system in aerobic reaction. The high solubility of molecular oxygen in perfluoro carbons^{5,6} together with the inertness of these solvents, suggested us to choose a "fluorous phase"^{7,8} in the aerobic epoxidation reaction.^{9,10} Transition metal catalyzed aerobic epoxidation of olefins have been reviewed.^{11,12} Mukaiyama et al¹³ showed that in the presence of metal catalyst [Ni(dmp)₂, Fe(acac)₃, Pd(acac)₂, Ru(acac)₃, Co(acac)₃, Mn(acac)₃, Mn(dpm)₂], olefins are monooxygenated into epoxides with molecular oxygen in the coexistence of aldehyde. Groves¹⁴ and Chandrasekaran¹⁵ reported a successful aerobic epoxidation of olefins with Ruthenium catalysts. Recently, Knochel et al⁹ used Ru(III) and Ni(II) complexes of perfluorinated 1,3-diketone for the aerobic epoxidation of olefins in fluorous medium. Pozzi and coworkers¹⁰ prepared perfluorocarbon soluble cobalt(II) complexes of tetraarylporphyrin for the epoxidation of unfunctionalized olefins.

Manganese(III) acetate dihydrate **1** was extensively used for the radical addition of acetic acid to olefins leading to lactones¹⁶ and for oxidative free-radical cyclisation reactions.^{17,18} The aim of the present work is to use this commercially available, inexpensive Mn(OAc)₃·2H₂O **1** as catalyst in the aerobic oxidation reaction of olefins in fluorous solvents.

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RESULTS AND DISCUSSION

The efficacy of catalyst **1** was investigated in various solvent systems. Results are listed in table 1. At first, we examined the oxidation of 1,2-dihydronaphthalene **2** with catalyst **1** (4 mol%), molecular oxygen as oxidant, and pivalaldehyde as the co-reductant in CH_2Cl_2 (5 mL, 25°C), and found that in these heterogeneous conditions the corresponding 1,2-epoxytetrahydronaphthalene **3** was obtained in 3 h in quantitative yield. There was no change in reaction time when the oxidation of olefin **2** was carried out in α,α,α -trifluorotoluene.

Table 1. $\text{Mn}(\text{OAc})_3 \cdot \text{H}_2\text{O}$ 1 Catalyzed Epoxidation of 1,2-Dihydronaphthalene **2** with O_2 /Pivalaldehyde^a

Entry	Solvent	Time (h)	Conversion ^b (%)	Epoxide ^b (%)
1.	CH_2Cl_2	3	100	quantitative
2.	PhCF_3	3	100	quantitative
3.	Perfluoro-2-butyltetrahydrofuran (FC-75)	1	100	quantitative
4.	$(\text{CH}_3)_2\text{CHOH}$	24	0	-
5.	$\text{CF}_3\text{CH}_2\text{OH}$	24	0	-
6.	$(\text{CF}_3)_2\text{CHOH}$ (HFIP)	24	0	-

a. 1,2-Dihydronaphthalene (2 mmol), catalyst **1** (4 mol%), pivalaldehyde (6 mmol), solvent (5 mL), O_2 bubbling, 25°C

b. Determined by GC analysis.


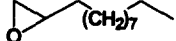
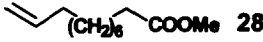
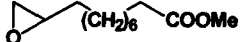
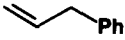
The catalytic epoxidation of olefin **2** was then examined in perfluoro-2-butyltetrahydrofuran (FC-75). In this non coordinating fluoruous solvent, the catalyst **1** is not soluble. Addition of pivalaldehyde (6 mmol) and dihydronaphthalene **2** (2 mmol) under an atmosphere of oxygen gave an heterogeneous two phase mixture which readily reacted over a period of only 1 h to yield 98% of epoxide **3**. At the end of the reaction, 5% aqueous K_2CO_3 (5 mL) was added. The three phases were easily separated. The fluoruous solvent was separated as the bottom phase and reused as such for a second run and the product epoxide was recovered from the hydrocarbon phase. It is worth noting that the starting olefin was recovered unchanged when the reaction was carried out in alcoholic solvents (Table 1) such as isopropyl alcohol (entry 4), trifluoroethanol (entry 5) and hexafluoropropanol (entry 6). Despite of the fast reaction in the heterogeneous biphasic system in FC-75, we carried out all further epoxidation studies in this solvent but with an addition of toluene (2 mL) in order to solve the problem of solubility and to facilitate further separations. Results are summarized in table 2.

Styrene **4** and α -methylstyrene **6** afforded rapidly the styrene oxide **5** and the 1,2-epoxy-2-phenylpropane **7** respectively in high yields. *Trans*-stilbene **8** afforded *trans*-stilbene oxide **9** as the only product in excellent yield. By contrast, the conversion of *cis*-stilbene **10** was only 30% even after a total reaction time of 18h, and the product epoxide is a mixture of *cis* and *trans* isomer (3:97). This indicates that the catalyst **1** is greatly stereodependent¹⁹ and the reaction is not stereospecific.

Cyclic olefins such as cyclohexene **12** and cyclooctene **14** afforded under the same reaction conditions 1,2-epoxycyclohexane **13** and 1,2-epoxycyclooctane **15** respectively in very good yields. 1-Phenyl-1,2-epoxy cyclohexane **17** which is highly unstable under the conditions of peracid epoxidation is quite stable in the present reaction conditions and was obtained in a quantitative yield.

Table 2. Epoxidation of olefins with catalyst $\text{Mn}(\text{OAc})_3 \cdot 2\text{H}_2\text{O}$ 1 and O_2 /pivalaldehyde in FC-75.^a

Entry	Substrate	Time (h)	Product	Yield (%) ^b
1.		1		85
2.		1		97
3.		2		100
4.		18	+ 11 3:97 9	24 ^c
5.		1		82
6.		0.75		92
7.		0.5		97
8.		2.5	+ 19a 82:18 19b	100 ^c
9.		4	+ 21a 81:19 21b	97 ^c
10.		4	+ 23a 74:26 23b	75 ^c
11.		1		96

12.		26	6		27	6
13.		28	6		29	11
14.		30	6	No reaction		-

(a) Olefin (2 mmol), catalyst 1 (0.08 mmol, 4 mol%), pivalaldehyde (6 mmol), FC-75 (5 mL), toluene (2 mL), O₂ bubbling, 25 °C.

(b) Isolated yields.

(c) Ratio determined from ¹H NMR.

It is worth to note that (Table 3), under the reaction conditions in the absence of catalyst, the starting olefins 1,2-dihydronaphthalene and styrene were recovered unchanged.^{20,21} Cyclooctene, (entry 4, table 3) underwent very slow oxidation without catalyst 1. GC analysis showed the presence of starting olefin and epoxide in the ratio of 27:73 even after 5 h (25°C).

Epoxidation of steroids was also undertaken by using catalyst 1. Under the present reaction conditions cholesteryl benzoate **18** yielded a mixture of epoxides **19a** and **19b** in which the hindered 5β,6β-epoxide **19a** is the major isomer (82:18) (entry 8, table 2). This ratio is comparable to those reported for Mn(dpm)₂ - 82:18; Mn(acac)₂ - 80:20; Ni(dmp)₂ - 69:31; Fe(acac)₃ - 67:33; Ru(acac)₃ - 76:24 in the aerobic epoxidation reaction. 3β,17β-Diacetoxyandrost-5-en **20** was converted smoothly into the 5β,6β-epoxide **21a** in high yield. Cholesterol **22** without any protection on hydroxyl group at the 3-position, was converted into the β-epoxide **23a** in good yield.

Another salient feature of the present epoxidation is the high regioselectivity. Thus, in the oxidation of limonene **24**, the monoepoxide **25** (entry 11, table 2) was the only product isolated in very good yield. As this result strongly suggests a low reactivity of non activated terminal olefins with our reagent system, we checked the reaction with 1-dodecene **26**, 10-methylundecenoate **28** and allylbenzene **30**. Effectively the reaction provided corresponding epoxides in very poor yield.

Table 3 : Reaction of Olefins with O₂/Pivalaldehyde without Catalyst 1^a

Entry	Substrate	Solvent	Time (h)	Yield (%) ^b (Olefin:epoxide)
1.	1,2-Dihydronaphthalene	FC-75	16	no reaction
2.	"	PhCF ₃	16	no reaction
3.	Styrene	FC-75	5 ^c	96:4
4.	Cyclooctene	FC-75	5 ^c	27:73

a. Olefin (2 mmol), pivalaldehyde (6 mmol), solvent (5 mL), O₂ bubbling, 25°C.

b. Determined by GC analysis and it is relative yield

c. With reaction time of 16 h the conversion was identical.

Surprisingly when the reaction was performed in hexafluoropropanol (HFIP) as solvent, the low reactive monosubstituted olefins **26** and **28** yielded the corresponding epoxides **27** (91%) and **29** (89%) in 3 to 5 h (Table 4). Allylbenzene **30** also yielded the epoxide **31** in excellent yield. The influence of this fluoruous medium is particularly essential in the epoxidation of low reactive olefins since in non fluoruous solvents, reactions completely failed (in ^tPrOH) or occurred in very poor yield (about 10% in CH₂Cl₂). In contrast, when the reactions were performed in HFIP with di- and trisubstituted olefins, limonene **24** and 1,2-dihydronaphthalene **2**, the starting olefins were recovered (entries 4 and 5, table 4). For comparison we checked the reaction of **26** with Mn(OAc)₂·4H₂O instead of Mn(OAc)₃·2H₂O as catalyst. Under the similar reaction conditions, the olefin **26** did not give epoxide even after 24h.

Table 4: Epoxidation of Olefin with O₂/Pivalaldehyde in (CF₃)₂CHOH^a

Entry	Substrate	Time (h)	Product	Yield(%) ^b
1.	1-Dodecene 26	3	1,2-epoxydodecane 27	91
2.	10-methylundecenoate 28	4.5	10,11-epoxymethylundecanoate 29	89
3.	Allylbenzene 30	5	(2,3-epoxypropyl)benzene 31	90
4.	Limonene 24	24	no reaction	--
5.	1,2-Dihydronaphthalene 2	24	no reaction	--

a. Olefin (2 mmol), catalyst **1** (4 mol%), pivalaldehyde (6 mmol), hexafluoropropanol (5 mL), O₂ bubbling, 25°C.

b. Isolated Yield.

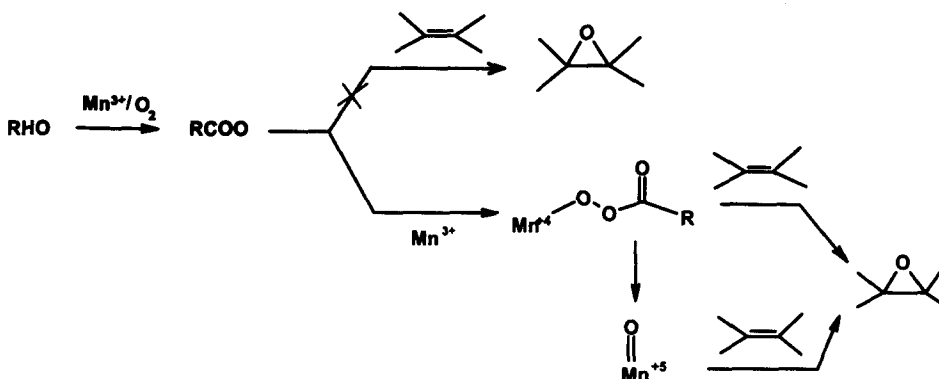
The reactivity of olefins presents an interesting dichotomy in the present epoxidation study. The less reactive monosubstituted olefins underwent epoxidation in a perfluorous alcoholic solvent (HFIP) in which di- and trisubstituted olefins were unreactive. Conversely, more reactive di- and trisubstituted olefins easily reacted in FC-75 in which monosubstituted olefins were unreactive.

Depending upon the reagent and the reaction conditions, oxidation of olefins into epoxide can follow different pathways. Recently, Nam and Valentine reported²² that the possible active species present in the aerobic epoxidation using O₂/aldehyde in the presence of metal catalyst could be a peroxyacid, an acylperoxy radical, a metal-peroxy complex or a metal-oxo species.

When cyclopentanone and cyclohexanone were treated with the catalyst **1** in the presence of O₂/pivalaldehyde in FC-75, no lactones were isolated, starting ketones being recovered. These results combined with non-stereospecific reaction of *cis*-stilbene oxidation suggests that the active oxidant in the present epoxidation is not a simple carboxylic peracid directly generated from aldehyde in autooxidation manner. According to Nam and Valentine, acylperoxy radical generated from O₂/aldehyde can react with olefins either directly or with metal to form metal-peroxy complexes. This metal-peroxy species can directly transfer an oxygen atom to olefins or form metal-oxo species which can in turn promote the oxidation. In our case also, the epoxidation of olefin can occur in FC-75 either by the direct reaction of metal-peroxy species with olefins or through metal oxo species (Scheme 1).

The difference in reactivity of olefin in FC-75 and hexafluoropropanol is particularly striking. The high selectivity for the epoxidation of low reactive monosubstituted olefins in hexafluoropropanol is not yet clear. Further study of this line is under progress.

Scheme 1



CONCLUSION

The present results show that i) the commercially available and inexpensive Mn(OAc)₃·2H₂O is a good epoxidation reagent: high yields, regioselectivity and stereodependence. ii) results are comparable to those reported for other transition metals complexed with expensive ligands. iii) fluoruous solvents are particularly efficient for this reaction: they reduce reaction time and facilitate separating phases. iv) furthermore, HFIP has been proved to highly improve epoxidation reaction of non reactive terminal olefins.

EXPERIMENTAL SECTION

Manganese(III) acetate dihydrate, 1,1,1,3,3,3-hexafluoro-2-propanol were obtained from Aldrich. Perfluoro-2-butyrtetrahydrofuran (FC-75), was purchased from Interchim. α,α,α -Trifluorotoluene was purchased from ACROS. ¹H NMR spectra were recorded at 200 MHz in CDCl₃. TLC were performed on 0.25 mm Merck precoated silica plates (60F-254). All olefins were commercially available and freshly distilled or recrystallized before use.

Typical Procedure for Epoxidation of Olefin in FC-75. To a stirred solution of 1,2-dihydronaphthalene, 2 (0.26 g, 2 mmol) in FC-75 (5 mL) and toluene (2 mL) at 25°C was added Mn(OAc)₃·2H₂O (21.4 mg, 4 mol%). To this heterogeneous biphasic solution pivalaldehyde (0.51 g, 6 mmol) was added under an atmosphere of oxygen (bubbling throughout the experiment). The reaction was followed by tlc and glc. After complete disappearance of olefin 2, a solution of 5% aqueous K₂CO₃ was added and the three phase system was stirred for an additional 15 min (25°C). The fluoruous phase was removed by phase separation. The reaction mixture was extracted with ether (3 x 20 mL) and it was washed with brine and dried (MgSO₄). Removal of solvent followed by silica gel column chromatographic purification afforded 1,2-epoxytetrahydronaphthalene 3²⁴ as a yellow viscous oil (0.285g, 97%). ¹H NMR (CDCl₃) δ 1.75 (m, 1H), 2.40 (m, 1H), 2.55 (m, 1H), 2.75 (m, 1H), 3.70 (m, 1H), 3.85 (d, 1H, J = 4.2 Hz), 7.00 - 7.40 (m, 4H).

Styrene oxide 5.²³ Yield 0.21 g, (85%); ¹H NMR δ 2.6 (dd, J = 2.6, 5.4 Hz, 1H), 3.0 (dd, J = 4, 5.4 Hz, 1H), 3.7 (dd, J = 2.6, 4Hz, 1H), 7.17 (m, 5H).

1,2-Epoxy-2-phenylpropane 7.²⁴ Yield 0.26 g, (97%); ¹H NMR δ 1.7 (s, 3H), 2.8 (d, J = 5.41 Hz, 1H), 3.0 (d, J = 5.4 Hz, 1H), 7.2 - 7.4 (m, 5H).

trans-Stilbene oxide **9**.²⁵ Yield 0.39 g (100%); ¹H NMR δ 3.88 (s, 2H), 7.4 (s, 10 H).

Cis- and trans-Stilbene oxide **11**.²⁵ Yield 0.09 g (24%); ¹H NMR δ 3.88 (s, *trans*-isomer), 4.35 (s, *cis*-isomer).

1,2-Epoxy cyclohexane **13**.²³ Yield 0.16 g (82%); ¹H NMR δ 1.1 - 1.5 (m, 4H), 1.7 - 2.0 (m, 4H), 3.2 (m, 2H).

1,2-Epoxy cyclooctane **15**.²³ Yield 0.23 g (92%); ¹H NMR δ 1.1 - 1.7 (m, 10H), 2.0 - 2.2 (m, 2H), 2.8 - 2.9 (m, 2H).

1-Phenyl-1,2-epoxycyclohexane **17**.²⁶ Yield 0.34 g (97%); ¹H NMR δ 1.2 - 1.8 (m, 4H), 2.0 - 2.4 (m, 4H), 3.0 (t, J = 2 Hz, 1H), 7.2 - 7.4 (m, 5H).

5β, 6β-Epoxycholestanyl-3-benzoate **19**.¹³ Yield 1.01 g (100%); ¹H NMR δ 2.9 (d, J = 4.3 Hz, H_{6β}), 3.1 (d, J = 1.8 Hz, H_{6α}).

5β,6β-Epoxyandrostanyl-3β,17β-diacetate **21**.²⁷ Yield 0.76 g (97%); ¹H NMR δ 2.8 (d, J = 4.6 Hz, H_{6β}), 3.0 (d, J = 2.2 Hz, H_{6α}).

5β,6β-Epoxycholestan-3-ol **23**.¹³ Yield 0.6 g (75%); ¹H NMR δ 2.9 (d, J = 4.3 Hz, H_{6β}), 3.0 (d, J = 2.2 Hz, H_{6α}).

1,2-Epoxy-*p*-menth-8-ene **25**.²⁸ Yield 0.29 g (96%); ¹H NMR δ 1.3 (s, 3H), 1.4 - 2.1 (m, 10H), 3.0 (br t, J = 3 Hz, 1H), 4.6 (br s, 1H), 4.7 (m, 1H).

Typical Procedure for Epoxidation of Olefin in Hexafluoropropanol. To a stirred solution of 1,2-dodecene **26** (0.308 g, 2 mmol) in hexafluoropropanol (5 mL) at 25°C was added Mn(OAc)₃·2H₂O (21 mg, 4 mol%). To this solution pivalaldehyde (0.51 g, 6 mmol) was added under an atmosphere of oxygen (bubbling throughout the experiment). The reaction was followed by tlc and glc. After complete disappearance of olefin **26** (3 h), the crude product was poured into 5% aqueous K₂CO₃ solution and extracted with ether (3 x 30 mL) and it was washed with brine and dried (MgSO₄). Removal of solvent followed by silica gel column purification afforded 1,2-epoxydodecane **27**²³ as an oil (0.31g, 91%). ¹H NMR δ 0.9 (t, J = 6 Hz, 3H), 1.2 - 1.6 (m, 18H), 2.5 (dd, J = 5, 2.7 Hz, 1H), 2.8 (dd, J = 5.05, 4 Hz, 1H), 2.9 (br m, 1H).

10,11-Epoxyethylundecanoate **29**²³ Yield 0.38 g (89%); ¹H NMR δ 1.1 - 1.6 (m, 14H), 2.3 (t, J = 7.38 Hz, 2H), 2.5 (dd, J = 2.71, 4.92 Hz, 1H), 2.7 (dd, J = 4.92, 4.26 Hz, 1H), 2.9 (br m, 1H), 3.6 (s, 3H).

2,3-(Epoxypropyl)benzene **31**²⁹ Yield 0.24 g, (90%); ¹H NMR δ 2.4 - 3.3 (m, 5H), 7.2 - 7.5 (m, 5H).

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