A Simple Iron Catalyst for Terminal Alkene Epoxidation

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Experimental

All olefins were purchased from Aldrich and distilled prior to use. $\text{Fe}^{\text{III}}(\text{ClO}_4)_3$ hydrate, 1,10-phenanthroline, 32% peracetic acid, hydrogen peroxide 50% and acetonitrile were purchased from Aldrich and used directly. Gas chromatographic (GC) yields were determined using either a DB-5 capillary column [30m x 0.53 mm x 5 μm , He 15 psi] or DB-1 capillary column [15m x 0.25 mm x 0.1 μm , He 10 psi] on a HP 5890 GC. GC conditions for each substrate are listed below. Large-scale reactions were performed in high surface to volume flasks (e.g. Erlenmeyer flasks) with external cooling to assure appropriate heat dissipation. Isolated products were > 98% pure by GC.

Synthesis of $[(\text{phen})_2(\text{H}_2\text{O})\text{Fe}^{\text{III}}](\mu\text{-O})(\text{ClO}_4)_4$ stock solutions

In a 20 ml flask, $\text{Fe}^{\text{III}}(\text{ClO}_4)_3$ hydrate (0.197 g, 0.56 mmol) was dissolved in 0.5 ml water, then a 4.5 ml acetonitrile solution of phenanthroline (0.2 g, 1.1 mmol) was added. The green-brown solution is stirred for 5 min at RT. The stock solution (0.055 M) was stored at -20°C to ensure that no decomposition of the complex occurs. Excellent catalysis reproducibility was obtained over one month.

Preparation and titration of a 24% peracetic acid solution

In a 250 ml erlenmeyer flask equipped with a magnetic stir-bar, hydrogen peroxide 50% (28.3 g, 0.42 mol) was added to a glacial acetic acid (50 g, 0.83 mol), sulfuric acid (1 g, 0.01 mol) solution. The solution is stirred overnight at RT and then kept in the freezer in a plastic bottle. The peracetic acid weight % was determined by integrating the ^{13}C NMR shifts of acetic and peracetic acid in D_2O .

Epoxidation of Alkenes with **1** on GC Scale

An MeCN (0.2 mL) solution of alkene (0.33 mmole), **1** (8.25×10^{-7} moles, 7.5 μL of 0.055 M solution), and decane (internal standard, 8 mol%, 0.0026 mmole, 5 μL) was prepared in a 5 mL vial at 0°C with a stir-bar. 1.5 equivalents of 32% peracetic acid (0.49 mmole, 100 μL) dissolved in 0.1 ml MeCN was added dropwise over 30 seconds. The reaction was stirred for 5 min, diluted with Et_2O , and filtered through a basic alumina plug. The GC analysis of the solution provides the substrate conversion and product yield relative to the internal standard integration. The epoxide product was identified by a comparison of the GC retention time of an authentic sample and the reaction sample. In cases in which authentic samples were not readily available, the structures were assigned through a combination of GC/MS and ^1H NMR of an isolated sample.

GC Conditions:

Cyclooctene: 150°C isothermal for 10 min on DB-5 column. Cyclooctene $R_t = 1.84$ min, cyclooctene oxide $R_t = 3.24$ min. Product identity was confirmed with comparison to an authentic samples (Aldrich, 99% cyclooctene $R_t = 3.24$ min) and GC/MS ($[M^+] = 126$)

Cyclohexene: 120°C isothermal for 10 min on DB-5 column. Cyclohexene $R_t = 1.23$ min, cyclohexene oxide $R_t = 2.25$ min. Product identity was confirmed with comparison to an authentic samples (Aldrich, 98% cyclohexene oxide, $R_t = 2.25$ min) and GC/MS ($[M^+] = 98$).

Vinyl Cyclohexane: 150°C isothermal for 10 min on DB-5 column. Vinyl cyclohexane $R_t = 1.46$ min, 1,2 epoxyethylcyclohexane $R_t = 2.79$ min. Product identity confirmed by GC/MS ($[M^+] = 126$) and by ^1H NMR.

cis-2-heptene: 120°C isothermal for 10 min on DB-5 column. *Cis*-2-heptene $R_t = 1.3$ min, *cis*-2,3-epoxy heptane $R_t = 2.33$. Product identity confirmed by GC/MS ($[M^+] = 114$) and by ^1H NMR.

trans-2-heptene: 120° C isothermal for 10 min on DB-5 column. *Trans*-2-heptene R_t = 1.27 min, *trans*-2,3-epoxyheptane R_t = 2.08 min. Product identity confirmed GC/MS ($[M^+] = 114$) and by 1H NMR.

1-Heptene: 120° C isothermal for 10 min on DB-5 column. 1-heptene R_t = 1.22 min, 1,2-epoxyheptane R_t = 2.68 min. Product identity confirmed GC/MS ($[M^+] = 114$) and by 1H NMR.

Styrene: 70° C isothermal for 10 min on DB-1 column. styrene R_t = 0.84 min, styrene oxide R_t = 2.24 min, phenylacetaldehyde R_t = 1.97 min. Product confirmed by GC/MS ($[M^+] = 120$) and by 1H NMR.

Trans-β-methylstyrene: 70° C isothermal for 10 min on DB-1 column. *Trans*-β-methylstyrene R_t = 1.74 min, *trans*-β-methylstyrene oxide R_t = 3.13 min. Product confirmed by GC/MS ($[M^+] = 134$) and by 1H NMR.

Cis-β-methylstyrene: 70° C isothermal for 10 min on DB-1 column. *Cis*-β-methylstyrene R_t = 1.39 min, *cis*-β-methylstyrene R_t = 2.82 min, propiophenone R_t = 3.45 min. Product confirmed by GC/MS ($[M^+] = 134$) and by 1H NMR.

Trans-methylcinnamate: 120° C isothermal for 10 min on DB-1 column. *Trans*-methylcinnamate R_t = 2.17 min, *Trans*-methylcinnamate oxide R_t = 2.85 min. Product confirmed by GC/MS ($[M^+] = 178$) and by 1H NMR.

Ethyl Sorbate: 80° C isothermal for 10 min on DB-1 column. Ethyl sorbate R_t = 1.89 min, 4,5-epoxy-ethyl sorbate R_t = 3.27 min, 2,3-epoxy-ethyl sorbate R_t = 3.37 min. Product confirmed by GC/MS ($[M^+] = 156$) and by 1H NMR.

Ethyl Crotonate: 120° C isothermal for 10 min on DB-5 column. Ethyl crotonate R_t = 1.81 (*cis*), 1.89 (*trans*) min, ethyl crotonate oxide R_t = 3.09 min. Product confirmed by GC/MS ($[M^+] = 130$) and by 1H NMR.

Butadiene: 90° C isothermal for 10 min on DB-5 column. Butadiene could not be detected, butadiene monoepoxide R_t = 1.12 min. Product identity confirmed by GC/MS ($[M^+] = 86$) and by 1H NMR.

Butadiene monoepoxide: 90° C isothermal for 10 min on DB-5 column. Butadiene mono-epoxide R_t = 1.12 min, butadiene diepoxide R_t = 2.55, 2.71 min. Product identity confirmed GC/MS ($[M^+] = 102$) and by 1H NMR.

2-Cyclohexen-1-ol: 120° C isothermal for 10 min on DB-5 column. 2-cyclohexen-1-ol R_t = 2.37 min, 2-cyclohexene oxide-1-ol (*cis*) R_t = 4.43 min, 2-cyclohexene oxide-1-ol (*trans*) R_t = 5.22 min, 2-cyclohexen-1-one R_t = 2.82 min, 2-cyclohexene oxide-1-one R_t = 4.1 min. Product identity confirmed GC/MS ($[M^+] = 114$) and by 1H NMR.

Table 1. Epoxidation catalyzed by **1** and **2** using Peracetic Acid^a

	Alkenes	Catalysts	Conversion ^b %	GC Yield %
			± 2	± 2
1	Vinyl cyclohexane	1	95	93
		2	99	96
2	Styrene	1 ^c	100	63
		2	100	60
3	<i>Cis</i> -β-methyl styrene	1	100	74
		2	100	76
4	<i>Trans</i> -methyl cinnamate	1	87	87
		2	89	89

^a Reaction conditions: olefin (1.1 M in CH₃CN), **catalyst** (0.25 mole %), 32% CH₃CO₃H (2 equiv) in acetic acid/water added rapidly at 0°C, 5 min. ^b Yields determined by GC using nitrobenzene as an internal standard, average over at least two runs. ^c 0.375 mole %.

1: [((phen)₂(H₂O)Fe^{III})₂(μ-O)](ClO₄)₄

2: [((phen)₂(H₂O)Fe^{III})₂(μ-O)](NO₃)₄

Figure 1. Dependence of vinyl-cyclohexane oxide formation at 1 min vs. the pH of reaction solution using 24% sulfuric acid free peracetic acid. Reaction pH was adjusted by addition of HClO_4 prior to the start of the reaction. Reactions were quenched after 1 min by the addition of Et_3N , and epoxide formation was determined by GC.

Isolated Epoxidations:

Vinyl Cyclohexane

Caution this reaction is very exothermic

A solution containing vinyl cyclohexane (1 g, 0.0093 mole) and 24% peracetic acid (5.7g, 18 mmole) in 18 mL of MeCN in a 125 mL Erlenmeyer flask was cooled in an ice bath. To this solution, a 0.05 M solution of **1** (0.454 mL) was added via a syringe over the course of 2 min with stirring. After an additional 3 min, the reaction flask was removed from the ice bath, and 2 g of K₂CO₃ in 100 mL H₂O were added. The solution was extracted with pentane (3 x 40 mL). The combined organic volume was washed with saturated NaHCO₃ (2 x 50 mL), dried over K₂CO₃, and filtered through a glass frit. Removal of the solvent under vacuum gave 1.05 g of 1,2 epoxy ethylcyclohexane (90%, 1.14 g theoretical). [M⁺] = 126. ¹H NMR (CD₃Cl) δ = 2.71 (2H, m), 2.52 (1H, t), 1.88 (1H, dd), 1.75-1.65 (4H, m), 1.28-1.1 (6H, m), 0.9 (1H, t). ¹³C NMR CD₃Cl δ = 56.7, 46.0, 40.4, 29.7, 28.9, 26.3, 25.7, 25.5.

Trans- β -methylstyrene

Caution this reaction is very exothermic

A solution containing *trans*- β -methylstyrene (0.25 g, 0.0021 mole) and 24% peracetic acid (0.501 g, 4.2 mmole) in 4 mL of MeCN in a 100 mL Erlenmeyer flask was cooled in an ice bath. To this solution, a 0.05 M solution of **1** (0.105 mL) was added via a syringe over the course of 2 min with stirring. After an additional 3 min, the reaction flask was removed from the ice bath, and 2 g of K₂CO₃ in 50 mL H₂O were added. The solution was extracted with ether (3 x 20 mL). The combined organic volume was washed with saturated NaHCO₃ (2 x 25 mL), dried over MgSO₄, and filtered through a glass frit. Solvent removal under vacuum gave 0.265 g of *trans*- β -methylstyrene oxide (96%, 0.275 g theoretical). [M⁺] = 134.2. ¹H NMR (CD₃Cl) δ = 7.3 (5H, m), 3.59 (1H, s), 3.06 (1H, q), 1.47 (3H, d). ¹³C NMR (CD₃Cl) δ = 137.72, 128.37, 125.5, 59.51, 58.99, 17.89.

Trans-methyl cinnamate

Caution this reaction is very exothermic

A solution containing *trans*-methyl cinnamate (0.5 g, 0.0031 mole) and 32% peracetic acid (1.46 g, 6.0 mmole) in 6 mL of MeCN in a 100 mL Erlenmeyer flask was cooled in an ice bath. To this solution, a 0.055 M solution of **1** (0.308 mL) was added via a syringe over the course of 2 min with stirring. After an additional 3 min, the reaction flask was removed from the ice bath, and 3 g of K₂CO₃ in 50 mL H₂O were added. The solution was extracted with ether (3 x 20 mL). The combined organic volume was washed with saturated NaHCO₃ (2 x 25 mL), dried over MgSO₄, and filtered through a glass frit. Solvent removal under vacuum gave 0.48 g of 3-phenyl-oxirane-2-carboxylic acid methyl ester (86%, 0.55 g theoretical). [M⁺] = 178. ¹H NMR (CD₃Cl) δ = 7.37-7.2 (5H, m), 4.09 (1H, s), 3.82 (1H, s), 3.52 (1H, s). ¹³C NMR (CD₃Cl) δ = 168.56, 134.78, 128.7, 125.68, 57.84, 56.56, 52.47.

Cyclohexene

Caution this reaction is very exothermic

A solution containing cyclohexene (1.0 g, 0.0121 mole) and 24% peracetic acid (7.68 g, 24 mmole) in 24 mL of MeCN in a 125 mL Erlenmeyer flask was cooled in an ice bath. To this solution, a 0.11 M solution of **1** (0.121 mL) was added via a syringe over the course of 2 min with stirring. After an additional 3 min, the reaction flask was removed from the ice bath, and 2 g of K₂CO₃ in 100 mL H₂O were added. The solution was extracted with pentane (3 x 60 mL). The combined organic volume was washed with saturated NaHCO₃ (2 x 50 mL), dried over K₂CO₃, and filtered through a glass frit. Removal of the solvent under vacuum gave 0.99 g of cyclohexene oxide (85%, 1.16 g theoretical). [M⁺] = 98. ¹H NMR (CD₃Cl) δ = 3.1 (2H, s), 1.58-1.45 (4H, m), 1.05-0.89 (4H, m). ¹³C NMR (CD₃Cl) δ = 52.09, 24.35, 19.35.

Cyclooctene

Caution this reaction is very exothermic

A solution containing cyclooctene (1 g, 0.0093 mole) and 24% peracetic acid (5.77g, 18 mmole) in 18 mL of MeCN in a 125 mL Erlenmeyer flask was cooled in an ice bath. To this solution, a 0.055 M solution of **1** (0.090 mL) was added via a syringe over the course of 2 min with stirring. After an additional 3 min, the reaction flask was removed from the ice bath, and 2 g of K₂CO₃ in 100 mL H₂O were added. The solution was extracted with pentane (3 x 60 mL). The combined organic volume was washed with saturated NaHCO₃ (2 x 50 mL), dried over K₂CO₃, and filtered through a glass frit. Solvent removal under vacuum gave 1.03 g of cyclooctene oxide (90%, 1.14 g theoretical). [M⁺] = 126. ¹H NMR (CD₃Cl) δ = 2.89 (2H, m), 2.16 (2H, m), 1.2-1.7 (10H, m). ¹³C NMR (CD₃Cl) δ = 55.64, 26.52, 26.26, 25.57.

Ethyl Sorbate

Caution this reaction is very exothermic

A solution containing ethyl sorbate (0.5 g, 0.0036 mole) and 24% peracetic acid (1.69 g, 5.3 mmole) in 4 mL of MeCN in a 125 mL Erlenmeyer flask was cooled in an ice bath. To this solution, a 0.055 M solution of **1** (0.08 mL) was added via a syringe over the course of 2 min with stirring. After an additional 3 min, the reaction flask was removed from the ice bath, and 1 g of K₂CO₃ in 50 mL H₂O were added. The solution was then extracted with ether (3 x 20 mL). The combined organic volume was washed with saturated NaHCO₃ (2 x 25 mL), dried over MgSO₄, and filtered through a glass frit. Solvent removal under vacuum gave 0.5 g of 4,5-epoxy-ethyl sorbate (89%, 0.56 g theoretical). [M⁺] = 156. ¹H NMR (CD₃Cl) δ = 1.29 (3H, t), 1.39 (3H, d), 2.98 (1H, qd), 3.18 (1H, dd), 4.20 (2H, q), 6.13 (1H, d), 6.67 (1H, d). ¹³C NMR (CD₃Cl) δ = 14.05, 17.36, 57.10, 57.28, 60.47, 123.53, 144.56, 165.61.

1-Heptene

Caution this reaction is very exothermic

A solution containing 1-heptene (1 g, 10.2 mmole) and 32% peracetic acid (4.8g, 20.4 mmole) in 20 mL of MeCN in a 125 mL Erlenmeyer flask was cooled in an ice bath. To this solution, a 0.050 M solution of **1** (0.5 mL, 0.025 mmole) was added via a syringe over the course of 2 min with stirring. After an additional 3 min, the reaction flask was removed from the ice bath, and 2 g of K₂CO₃ in 100 mL H₂O were added. The solution was extracted with pentane (3 x 40 mL). The combined organic volume was washed with saturated NaHCO₃ (2 x 50 mL), dried over K₂CO₃, and filtered through a glass frit. Removal of the solvent under vacuum gave 1.01 g of 1,2-epoxyheptane (88%, 1.16 g theoretical). [M⁺] = 114. ¹H NMR (CD₃Cl) δ = 2.91 (1H, m), 2.73 (1H, t), 2.45 (1H, q), 1.6-0.9 (11H, m). ¹³C NMR (CD₃Cl) δ = 52.36, 47.08, 32.41, 31.57, 25.6, 22.53, 13.93.

1-Octene, 1 gram scale

Caution this reaction is very exothermic

A solution containing 1-octene (1.0 g, 8.9 mmole) and 24% peracetic acid (5.6 g, 18 mmole) in 18 mL of MeCN in a 125 mL Erlenmeyer flask was cooled in an ice bath. To this solution, a 0.05 M solution of **1** in MeCN (0.404 mL, 0.022 mmole) was added dropwise over the course of 2 min with stirring. After an additional 3 min 100 mL of water was added, followed by the careful addition of 2 g K_2CO_3 . The solution was then extracted with pentane (3 x 40 mL). The combined organic volume was washed with saturated NaHCO_3 (2 x 30 mL), dried over K_2CO_3 , and filtered through a glass frit. Removal of the solvent under vacuum gave 1.05 g of 1,2-epoxyoctane (92%, 1.14 g theoretical). $[\text{M}^+] = 128$. ^1H NMR (CD_3Cl) $\delta = 2.84$ (1H, m), 2.69 (1H, m), 2.41 (1H, m), 1.51-1.20 (10H, m), 0.81 (3H, t). ^{13}C NMR CD_3Cl $\delta = 52.05, 46.94, 32.38, 31.65, 29.0, 25.82, 22.44, 14.0$.

1-Octene, 0.1 mole scale

Caution this reaction is very exothermic

A solution containing 1-octene (11.2 g, 0.10 mole) and 24% peracetic acid (63.3 g, 0.2 mole) in 200 mL of MeCN in a 1 L Erlenmeyer flask was cooled to -30°C in an acetone bath that was maintained between -35°C and -40°C by addition of dry ice. To this solution, a stock solution of **2** [$\text{Fe}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ (0.202 g, 0.5 mmole) and phenanthroline (0.180 g, 1.0 mmole) in 12 mL of 8/2 MeCN/ H_2O] was added dropwise over the course of 5 min while maintaining the reaction temperature below -25°C . The reaction was maintained at -30°C for 5 min, and then slowly warmed over 30 min to -5°C . If the reaction temperature rose more than $5^\circ/\text{min}$ than the temperature of the acetone bath was lowered by addition of dry ice. The reaction was removed from the acetone bath and 20 g K_2CO_3 in 600 mL of water was slowly added to the reaction. The solution was extracted with pentane (3 x 400 mL). The combined organic volume was washed with saturated NaHCO_3 (2 x 300 mL), dried over K_2CO_3 , and filtered. Removal of the solvent under vacuum gave 11.0 g of 1,2-epoxyoctane (86%, 12.6 g theoretical). $[\text{M}^+] = 128$. ^1H NMR (CD_3Cl) $\delta = 2.84$ (1H, m), 2.69 (1H, m), 2.41 (1H, m), 1.51-1.20 (10H, m), 0.81 (3H, t). ^{13}C NMR CD_3Cl $\delta = 52.05, 46.94, 32.38, 31.65, 29.0, 25.82, 22.44, 14.0$.