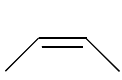
Catalysts for Fine Chemical Synthesis: Hydrolysis, Oxidation and Reduction. Volume 1
Edited by Stan M Roberts and Geraldine Poignant

ISBN: 0-471-98123-0

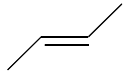
6 Epoxidation of Unfunctionalized Alkenes and α, β-Unsaturated Esters

CONTENTS

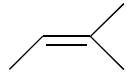
The methods developed by E. Jacobsen[1], using the salen – manganese complexes, and Y. Shi[2], using chiral ketones, permit the epoxidation of a large range of disubstituted *Z*- or *E*-alkenes and trisubstituted alkenes. The methodology of Zhang, using porphyrins, is complementary.



Disubstituted *Z*-alkene



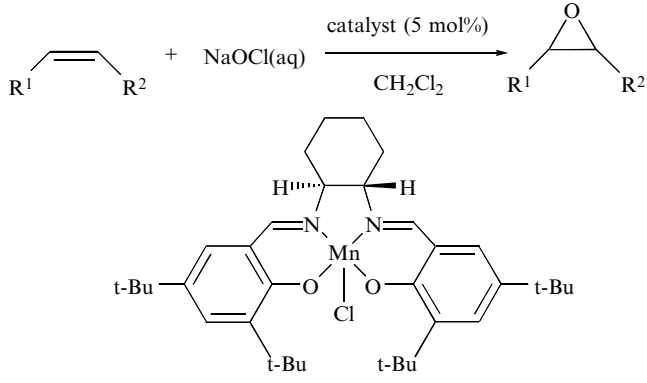
Disubstituted *E*-alkene



Trisubstituted alkene

6.1 ASYMMETRIC EPOXIDATION OF DISUBSTITUTED *Z*-ALKENES USING A CHIRAL SALEN–MANGANESE COMPLEX[1]

Epoxidation of a variety of alkenes may be effected in a biphasic reaction system consisting of aqueous sodium perchlorate at pH $\geq$ 9.5 and an organic phase containing catalytic levels of a soluble manganese(III) complex (Figure 6.1). The ideal pH range appears to be 10.5–11.5 for most applications, with non-water-miscible solvents such as dichloromethane, *tert*-butyl methyl ether or ethyl acetate as the organic solvent. At pH $\leq$ 11.5 no phase transfer catalysts are necessary for epoxidation to occur, due to the presence of a significant equilibrium concentration of HOCl. At low pH, equilibrium levels of Cl_2 can produce chlorinated by-product. Reactions with alkenes are carried out in an air atmosphere, without the need to exclude moisture or trace impurities.



catalyst: (*S*,*S*)-(–)-N,N′-Bis(3,5-di-tert-butylsalicylidene) -1,2-cyclohexanediaminomanganese(III) chloride

Figure 6.1 Epoxidation of *Z*-alkenes using a manganese(III) complex.

Mechanistically, the epoxidation appears to proceed via oxygen-atom transfer from the high-valent oxometallo intermediate (**A**) to organic substrates.

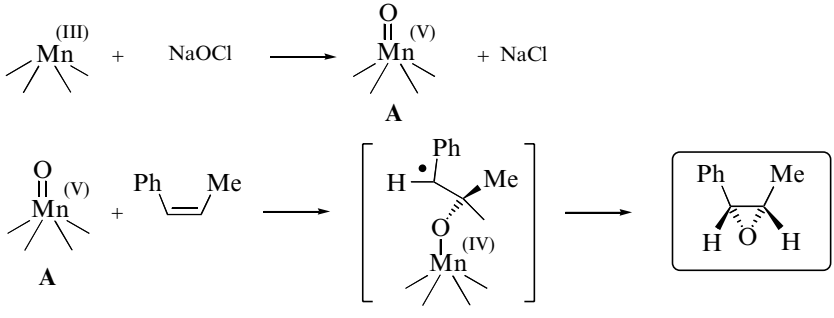
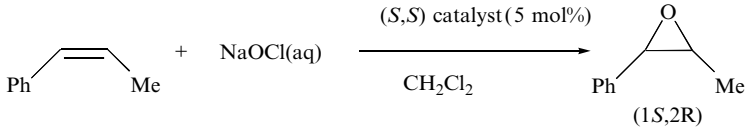


Figure 6.2 Mechanism of epoxidation using a manganese(III) complex.

There seems to be a direct attack of alkene at the oxometal, with C–O bond formation (Figure 6.2).

6.1.1 EPOXIDATION OF (*Z*)-METHYL STYRENE[3]



Materials and equipment

- Jacobsen's catalyst ((*S,S*)-(−)-*N*, *N*′-bis (3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediaminomanganese(III) chloride, 98%), 26 mg, 0.04 mmol, 0.04 eq
- (*Z*)-Methyl styrene, 1 mmol

  (*Z*)-Methyl styrene was easily obtained by hydrogenation of l-phenyl-l-propyne using Lindlar's catalyst (5% palladium on calcium carbonate, poisoned with lead) in *n*-hexane under an atmospheric pressure of hydrogen. The mixture, containing 90% of (*Z*)-methyl styrene and 10% of the over-reduced alkane, was used without further purification.
- Sodium hydrogenphosphate aqueous solution, 0.05 *M*, 5 mL
- Bleach (sodium hypochlorite, available chlorine 14%), 2.5 mL
- Sodium hydroxide solution, 1 *M*
- Hydrogen chloride solution, 1 *M*
- Dichloromethane, *n*-hexane, petroleum ether, diethyl ether, ethyl acetate, triethylamine
- Brine
- Sodium sulfate
- Silica gel 60 (0.063–0.04 mm)
- *p*-Anisaldehyde

- 100 mL Round-bottomed flask with a magnetic stirrer bar
- Magnetic stirrer
- Beaker, 100 mL
- Separating funnel, 100 mL
- Rotary evaporator
- pH-meter

Procedure

1. A solution was prepared by mixing an aqueous solution of sodium hydrogenphosphate (0.05 *M*, 5 mL) and a solution prepared with concentrated

bleach (sodium hypochlorite, 2.5 mL) in water (10 mL). The pH of the resulting solution was adjusted to pH 11.3 by addition of few drops of hydrogen chloride 1 *M* or sodium hydroxide 1 *M*. This solution was cooled using an ice-bath.

2. A 100 mL flask was filled with Jacobsen's catalyst (26 mg), (*Z*)-methyl styrene (1 mmol) and dichloromethane (1 mL). The solution was cooled with an ice-bath. To this solution was added the cold solution of bleach previously prepared (3.5 mL).
3. After 5 minutes the cooling bath was removed and the two-phase reaction mixture was stirred at room temperature. The reaction was monitored by TLC (eluent: petroleum ether–diethyl ether, 8:2). (*Z*)-Methyl styrene was UV active, R_f 0.85. The epoxide visualized with *p*-anisaldehyde dip stained yellow, R_f 0.63.
4. After 2 hours the reaction was quenched. The reaction mixture was transferred into a 100 mL beaker, *n*-hexane (10 mL) was added and stirred for 10 minutes.
5. The mixture was transferred into a separating funnel. The lower aqueous phase was separated and extracted with *n*-hexane (4 × 20 mL). The brown combined organic layers were washed with water (3 × 30 mL) and twice with brine (2 × 30 mL), dried over sodium sulfate, filtered and concentrated under reduced pressure, giving a brown oil (180 mg).

   In case of formation of an emulsion, this solution was mixed with the aqueous layer and extracted with *n*-hexane as explained in the earlier procedure.
6. The crude material was purified by flash chromatography on silica gel (20 g) buffered with 1 % triethylamine, using petroleum ether–ethyl acetate (9:1) as eluent to give the epoxide as a grey oil (104 mg, 0.78 mmol, 78 % yield).

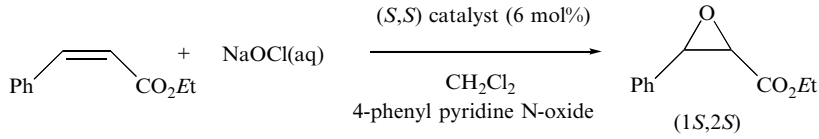
   The ee (90.5 %) was determined by GC analysis (Lipodex® E 25 m, 0.25 mm ID, temperatures: column 110 °C isotherm, injector 250 °C, detector 250 °C, mobile phase helium); (1*S*,2*R*)-enantiomer: R_t 7.8 min, (1*R*, 2*S*)-enantiomer: R_t 9.0 min.

   ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.35–7.31 (m, 5H, Ph); 4.07 (d, *J* 4.4 Hz, 1H, CH); 3.35 (qd, *J* 5.5 Hz, *J* 4.4 Hz, 1H, C*H*–CH_3); 1.09 (d, *J* 5.5 Hz, 3H, CH_3).

   IR ($CHCl_3$, cm^{-1}): 3091, 3069 (C–H epoxide), 3008 (C–H aromatic), 2972, 2934, 2877 (C–H aliphatic), 1730, 1604, 1495, 1451 (C=C), 1416, 1375, 1359, 1248 (C–OH, C–O–C), 1028, 1009, 955, 915, 851.

   Mass: calculated for $C_9H_{14}NO$: *m/z* 152.10754; found $[M + NH_4]^+$ 152.10743.

6.1.2 EPOXIDATION OF (*Z*)-ETHYL CINNAMATE[4]



Materials and equipment

- Jacobsen's catalyst (*S*,*S*)-(−)-*N*,*N*′-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexane diaminomanganese(III) chloride, 98 %), 108 mg, 0.166 mmol, 6.5 mol%
- (*Z*)-Ethyl cinnamate, 500 mg, 2.55 mmol

  The (*Z*)-ethyl cinnamate was obtained by hydrogenation of ethyl phenyl propiolate using Lindlar's catalyst (5 % palladium on calcium carbonate, poisoned with lead) in *n*-hexane under an atmospheric pressure of hydrogen. The mixture, containing 75 % of the (*Z*)-ethyl cinnamate, 22 % of the over-reduced alkane and 3 % of the (*E*)-ethyl cinnamate, was used without further purification. 666 mg of this mixture contains 500 mg of (*Z*)-ethyl cinnamate (2.55 mmol).
- 4-Phenylpyridine *N*-oxide, 116 mg, 0.680 mmol, 0.25 eq
- Sodium hydrogenphosphate aqueous solution 0.05 *M*, 10 mL
- Bleach (sodium hypochlorite, available chlorine 14 %), 5 mL
- Sodium hydroxide solution, 1 *M*
- Hydrogen chloride solution, 1 *M*
- Dichloromethane, petroleum ether, diethyl ether, *tert*-butyl methyl ether, ethyl acetate
- Celite®
- Brine
- Sodium sulfate
- Silica gel 60 (0.063–0.04 mm)
- *p*-Anisaldehyde

- 100 mL Flask with a magnetic stirrer bar
- Magnetic stirrer
- Beaker, 100 mL
- Separating funnel, 250 mL
- Rotary evaporator
- pH-meter

Procedure

1. A solution was prepared by mixing an aqueous solution of sodium hydrogenphosphate (0.05 *M*, 10 mL) and a solution prepared with concentrated bleach (sodium hypochlorite, 5 mL) in water (20 mL). The pH of the resulting solution was adjusted to 11.25 by addition of few drops of hydrogen chloride 1 *M* or sodium hydroxide 1 *M*.
2. A 100 mL flask, was filled with (*Z*)-ethyl cinnamate, (666 mg of the mixture containing 75 % of (*Z*)-ethyl cinnamate), 4-phenylpyridine *N*-oxide (116 mg) and dichloromethane (6 mL). Jacobsen's catalyst (108 mg) was then added.
3. The resulting organic solution and the buffered bleach (16 mL) were cooled separately using an ice-bath and then combined at 4 °C in the flask.
4. After 5 minutes the cooling bath was removed and the two-phase reaction mixture was stirred at room temperature. The reaction was monitored by TLC (eluent: petroleum ether–diethyl ether, 9:1). (*Z*)-Ethyl cinnamate was UV active, R_f 0.42. The epoxide visualized with *p*-anisaldehyde dip stained yellow, R_f 0.28.
5. After 12 hours of stirring the two-phase mixture at room temperature, the reaction was quenched. The reaction mixture was transferred into a 100 mL beaker, *tert*-butyl methyl ether (50 mL) was added and the solution was stirred for 10 minutes.
6. The mixture was transferred into a separating funnel. The aqueous phase was separated and extracted with *tert*-butyl methyl ether (2 × 20 mL). The brown combined organic layers were filtered through a pad of Celite®, and then washed with water (2 × 40 mL) and with brine (2 × 40 mL), dried over sodium sulfate, filtered and concentrated under reduced pressure, giving a brown oil (700 mg).
7. The crude material was purified by flash chromatography on silica gel (20 g) using petroleum ether–ethyl acetate (95:5) as eluent to give a yellow oil (286 mg) which was a mixture of 77 % (*Z*)-ethyl 3-phenylglycidate (1.14 mmol, 45 % yield) and 23 % of (*E*)-ethyl 3-phenylglycidate (0.34 mmol).

   The ee (91.5 %) was determined by GC analysis (Lipodex® C 25 m, 0.25 mm ID, temperatures: column 110 °C isotherm, injector 250 °C, detector 250 °C, mobile phase helium). (1*R*, 2*R*)-(*Z*)-enantiomer: R_t 41.4 min, (1*S*,2*S*)-(*Z*)-enantiomer: R_t 42.6 min.

   (*Z*)-Ethyl 3-phenylglycidate ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.42–7.30 (m, 5H, Ph); 4.27 (d, *J* 4.4 Hz, 1H, CH); 4.01 (q, *J* 7.15 Hz, 2H, CH_2); 3.83 (d, *J* 4.4 Hz, 1H, CH); 1.02 (t, *J* 7.15 Hz, 3H, CH_3).

   (*E*)-Ethyl 3-phenylglycidate ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.42–7.30 (m, 5H, Ph); 4.291 (q, *J* 7.15 Hz, 2H, CH_2); 4.09 (d, *J* 1.65 Hz, 1H, CH); 3.51 (d, *J* 1.65 Hz, 1H, CH); 1.33 (t, *J* 7.15 Hz, 3H, CH_3).

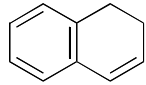
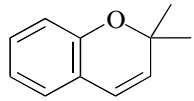
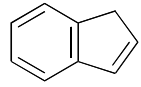
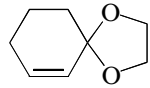
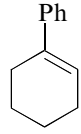
   IR ($CHCl_3$, cm^{-1}): 3070 (C–H epoxide), 3012 (C–H aromatic), 2988, 2943, 2911, 2876 (C–H aliphatic), 1748 (C=O), 1455 (C=C), 1416, 1375 (CH_2, CH_3), 1394, 1301 (C–O), 1190 (C–O–C)), 1108, 1052, 1027, 917.

   Mass: calculated for $C_{11}H_{12}O_3$: *m/z* 192.07864; found $[M]^{+\bullet}$ 192.07855.

6.1.3 CONCLUSION

Epoxidation using manganese – salen complexes is very easy to carry out; it occurs under aqueous conditions and commercial house bleach can be used as the oxidant. The results are similar to those reported in the literature; Table 6.1 gives other examples of alkenes which can be epoxidized using the same procedure. This method gives good results, especially for disubstituted *Z*-alkenes but trisubstituted alkenes can be epoxidized as well.

Table 6.1 Epoxidation of disubstituted *Z*-alkenes by (*S,S*)-salen–manganese complex (results according to the literature[1,5]).

	3. *Y*ield%	ee %
Ph, Me	84*	91*
	67	92
	87	98
	80	88
Me_3Si, C_6H_{11}	65	98
	63	94
Ph, CO_2Et	67*	97*
Trisubstituted alkene: 	75	92

* Reaction described above

6.2 ASYMMETRIC EPOXIDATION OF DISUBSTITUTED *E*-ALKENES USING A D-FRUCTOSE BASED CATALYST[2]

Among many other methods for epoxidation of disubstituted *E*-alkenes, chiral dioxiranes generated *in situ* from potassium peroxomonosulfate and chiral ketones have appeared to be one of the most efficient. Recently, Wang *et al.*[2] reported a highly enantioselective epoxidation for disubstituted *E*-alkenes and trisubstituted alkenes using a D- or L-fructose derived ketone as catalyst and oxone as oxidant (Figure 6.3).

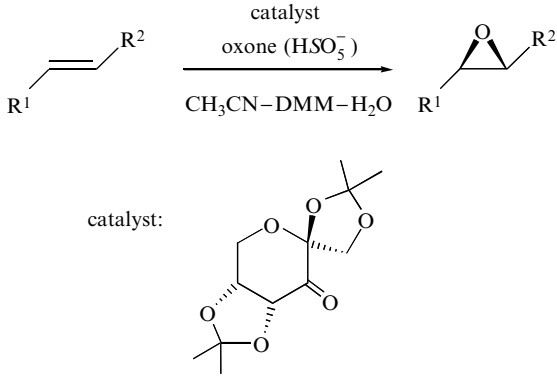


Figure 6.3 Epoxidation of *E*-alkenes by a ketone derived from D-fructose.

The ketone catalyst is readily prepared from D-fructose by ketalization and oxidation. The other enantiomer of this ketone, prepared from L-sorbose,

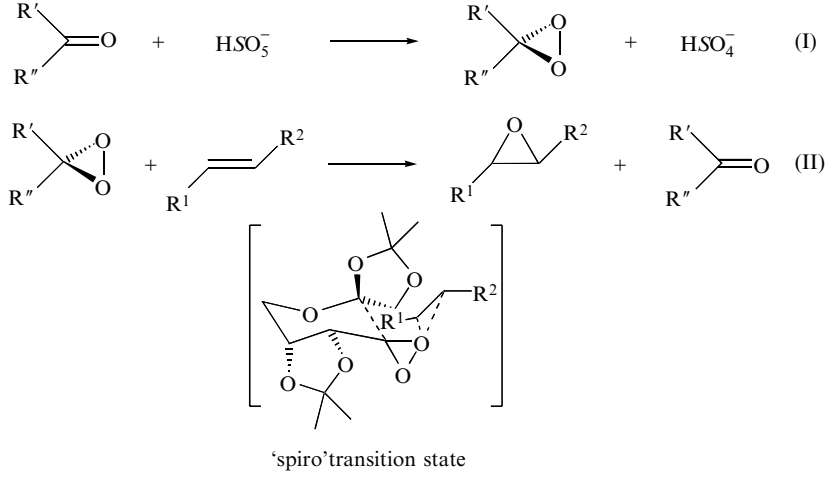


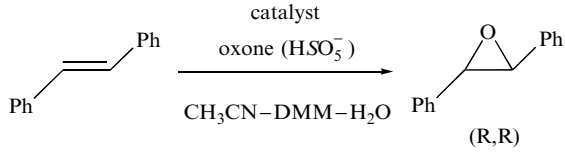
Figure 6.4 Mechanism of epoxidation by a chiral ketone catalyst.

shows the same enantioselectivity for the epoxidation[6]. The dioxirane is generated *in situ* from potassium monoperoxosulfate and the ketone catalyst (I, Figure 6.4). During the oxygen-atom transfer reaction from the dioxirane to the *E*-alkene (II, Figure 6.4), a 'spiro' transition state was proposed to give the (*E*)-epoxide.

For this method, all glassware needs to be carefully washed to be free of any trace of metals which catalyse the decomposition of oxone.

6.2.1 EPOXIDATION OF (*E*)-STILBENE

This reaction can be carried out at different temperatures (room temperature, −10 °C or −20 °C) but the reaction at room temperature gave a good compromise between the yield and the enantiomeric excess.



Materials and equipment

- (*E*)-Stilbene, 181 mg, 1 mmol
- Distilled water
- Aqueous solution of ethylenediamine tetraacetic acid disodium salt (Na_2(EDTA)), 4×10^{-4} *M*, 20 mL
- Buffer: sodium tetraborate decahydrate 0.05 *M* ($Na_2B_4O_7.10H_2O$) in aqueous Na_2(EDTA)4×10^{-4} *M*, 10 mL
- Tetrabutylammonium hydrogensulfate, 15 mg, 0.04 mmol
- Ketone catalyst derived from fructose, 77.4 mg, 0.3 mmol, 0.3 eq*
- Solution of potassium peroxymonosulfate (oxone), 1 g, 1.6 mmol, 1.6 eq, in aqueous solution of 4×10^{-4} *M* Na_2(EDTA), 6.5 mL
- Solution of potassium carbonate, 930 mg, 6.74 mmol in water, 6.5 mL
- Acetonitrile (5 mL), dimethoxymethane (10 mL), pentane (5 mL), diethyl ether, *n*-hexane, triethylamine
- Brine
- Sodium sulfate
- Silica gel 60 (0.063–0.04 mm)
- *p*-Anisaldehyde

* *The ketone catalyst was kindly provided by Professor Y. Shi (Colorado State University, Fort Collins, Colorado)*

- 50 mL Three-necked flask with magnetic stirrer bar
- Magnetic stirrer
- Glass graduated cylinders
- Two addition funnels, 10 mL
- Separating funnel, 250 mL
- Rotary evaporator
- pH-meter

Procedure

1. In a 50 mL three-necked flask with a magnetic stirrer bar was dissolved (*E*)-stilbene (181 mg) in acetonitrile–dimethoxymethane (15 mL, 1/2, v/v). Buffer (10 mL), tetrabutylammonium hydrogensulfate (15 mg) and ketone catalyst (77.4 mg) were added with stirring.

   The mixture of organic solvent and borate buffer results in a solution of pH above 10, and with the addition of K_2CO_3 it rarely falls below that value.
2. The flask was equipped with two addition funnels; one of them was filled with the solution of oxone (1 g) in aqueous Na_2(EDTA) (4×10^{-4} *M*, 6.5 mL) and the other one with a solution of potassium carbonate (930 mg) in distilled water (6.5 mL). The two solutions were added dropwise as slowly as possible over a period of 1 hour.

   To maximize the conversion and enantioselectivity a steady and uniform addition rate of oxone and K_2CO_3 must be achieved. On a small scale (1 mmol substrate), this is easily done with a syringe pump.
3. The reaction was monitored by TLC (eluent: *n*-hexane–diethyl ether, 9:1). (*E*)-Stilbene was UV active, R_f 0.82. The epoxide (UV active) stained blue with *p*-anisaldehyde, R_f 0.70.
4. After completion of the addition, the reaction was stirred for 1 hour and immediately quenched by addition of water (10 mL) and pentane (5 mL).
5. The reaction mixture was transferred into a separating funnel and was extracted with *n*-hexane (4×40 mL). The combined organic layers were washed with brine, dried over sodium sulfate, filtered and concentrated under reduced pressure to give a colourless oil (200 mg).
6. The crude material was purified by flash chromatography on silica gel (60 g), buffered with 1 % of triethylamine, using *n*-hexane–diethyl ether (95:5) to afford (*R,R*)-(*E*)-stilbene oxide as a colourless oil (123 mg, 0.62 mmol, 62 %).

   The ee (96 %) was determined by HPLC (Chiralpak® AD column, flow 1 mL/min, ethanol–*n*-hexane; 1:9); (*R,R*)-enantiomer: R_t 5.6 min, (*S,S*)-enantiomer: R_t 10.1 min.

   ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.54–7.12 (m, 10H, Ph); 3.87 (s, 2H, CH).

   IR ($CHCl_3$, cm^{-1}): 3093, 3070 (C–H epoxide), 3012 (C–H aromatic), 2399, 1604, 1496, 1461, 1453 (C=C), 1230 (C–O–C), 1071, 1028, 925, 872, 838.

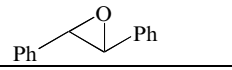
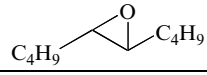
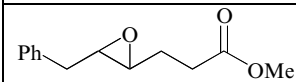
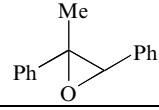
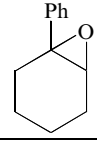
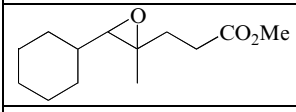
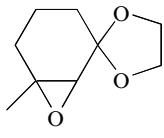
   Mass: calculated for $C_{14}H_{12}O$: *m/z* 196.08882; found $[M]^{+\bullet}$ 196.08861.

6.2.2 CONCLUSION

Epoxidation using a chiral fructose-derived ketone is easy to carry out, as it occurs in aqueous conditions. The reactions were performed without any modification of the published procedure. The glassware has to be free of trace metal, which can decompose the oxone; the use of a plastic spatula is recommended and the volumes must be measured using glass-graduated cylinders. Table 6.2 gives different examples of epoxides which can be obtained using the method prescribed.

Shi's method gives good results for disubstituted *E*-alkenes compared to the Jacobsen epoxidation previously described, which is more specific for disubstituted *Z*-alkenes. Concerning the epoxidation of trisubstituted alkenes, the epoxidation of 1-phenyl-1-cyclohexene could not be validated because of

Table 6.2 Epoxidation of disubstituted *E*-alkenes and trisubstituted alkenes by ketone derived from D-fructose[2].

	*Y*ield %	ee % (configuration)
	78*	>99 (R,R)*
	70	91 (R,R)
	68	92 (R,R)
	89	95.5 (R,R)
	94	98 (R,R)
	89	94 (R,R)
	41	97.2(R,R)

* Reaction described above

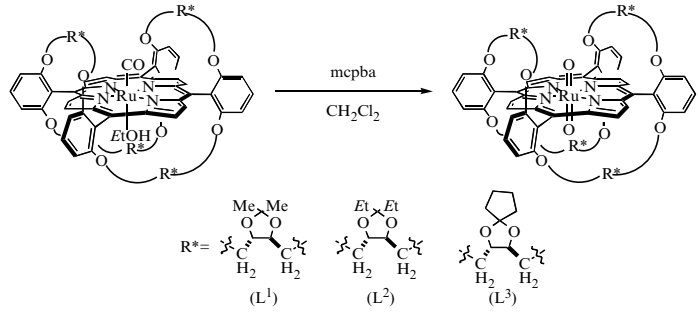
the difficulties in the determination of the enantiomeric excess; however, the yields were similar to the results given in the literature for both methods.

6.3 ENANTIOSELECTIVE EPOXIDATION OF (*E*)-β-METHYLSTYRENE BY D_2-SYMMETRIC CHIRAL *TRANS*-DIOXORUTHENIUM(VI) PORPHYRINS

RUI ZHANG, WING-YIU YU and CHI-MING CHE*

Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong

6.3.1 PREPARATION OF THE *TRANS*-DIOXORUTHENIUM(VI) COMPLEXES WITH D_2 SYMMETRIC PORPHYRINS (H_2L^{1-3})[7]



Materials and equipment

- Dichloromethane (freshly distilled over P_2O_5 under a nitrogen atmosphere), 5 mL
- *m*-Chloroperoxybenzoic acid (AR, Aldrich), 100 mg
- [$Ru^{II}(L^{1-3})$ (CO) (EtOH)], 0.07 mmol
- Acetone (AR)–CH_2Cl_2 (1:1), 20 mL
- Aluminum oxide (Brockman Grade II–III, basic), 20 g

- 10 mL Round-bottom flask with a magnetic stirrer bar
- Magnetic stirrer
- Vacuum pump

Procedure

1. A dichloromethane solution of [$Ru^{II}(L^{1-3})$ (CO) (EtOH)] (0.07 mmol) was added to a well-stirred dichloromethane solution of *m*-chloroperoxybenzoic acid (100 mg, 0.62 mmol) in a 10 mL round-bottomed flask. After 3 to 5 minutes stirring, the mixture was poured onto a short dry alumina column.

The completion of the oxidation can be checked by monitoring the disappearance and emergence of the Soret bands of the Ru(II) ($\lambda_{max} = 426$ nm) and the Ru(VI) ($\lambda_{max} =$ ca.440 nm) complexes using UV–vis spectroscopy. (Note: a prolonged reaction time (10 minutes) could result in lower product yields.)

2. The product complex was eluted by CH_2Cl_2/acetone (1:1 v/v). After solvent evaporation, a dark purple residue (~80 mg) was obtained. Yield: ~80 %.
3. The solid can be kept in a fridge (4 °C) for about one month without deterioration.

$[Ru^{VI}(L^1)O_2]$ (**1a**): ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.65 (d, *J* 4.7 Hz, 4H), 8.55 (d, *J* 4.7 Hz, 4H), 7.77 (t, *J* 6.5 Hz, 4H), 7.22–7.38 (m, meta-H overlapped with a solvent peak, 8H), 4.91 (d, *J* 10.4 Hz, 4H), 4.62 (d, *J* 9.0 Hz, 4H), 4.43 (t, *J* 9.0 Hz, 4H), 4.22 (d, *J* 10.1 Hz, 4H), 3.76 (d, *J* 9.0 Hz, 4H), 2.60 (t, *J* 8.5 Hz, 4H), 0.77 (s, 12H), −0.78 (s, 12H).

IR (KBr): 818 ($\nu_{Ru=O}$), 1018 cm^{-1} (oxidation state marker band).

UV–vis (CH_2Cl_2) λ_{max}/nm (log ε/$dm^3mol^{-1}cm^{-1}$): 442 (5.12), 536 (4.07).

FAB–MS *m/z*: 1379 (M^+, 18 %), 1363 (M^+–O, 30 %), 1347 (M^+–2O, 100 %).

$[Ru^{VI}(L^2)O_2]$ (**1b**): ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.64 (d, *J* 4.7 Hz, 4H), 8.53 (d, *J* 4.7 Hz, 4H), 7.74 (m, 4H), 7.37–7.30 (m, meta-H overlapped with a solvent peak, 8H), 4.98 (d, *J* 10.4 Hz, 4H), 4.60 (d, *J* 8.8 Hz, 4H), 4.44 (t, *J* 8.9 Hz, 4H), 4.23 (d, *J* 10.4 Hz, 4H), 3.74 (d, *J* 8.8 Hz, 4H), 2.63 (t, *J* 8.7 Hz, 4H), 1.02 (m, 8H), 0.53 (t, *J* 7.2 Hz, 12H), −0.25 (m, 8H), −1.37 (t, *J* 7.3 Hz, 12H).

IR (KBr): 821 ($\nu_{Ru=O}$), 1019 cm^{-1} (oxidation state marker band).

UV–vis (CH_2Cl_2): λ_{max}/nm (log ε/$dm^3mol^{-1}cm^{-1}$) 443 (5.15), 534 (4.02).

FAB–MS: *m/z* 1491 (M^+, 9 %), 1475 (M^+–O, 20 %), 1459 (M^+–2O, 100 %).

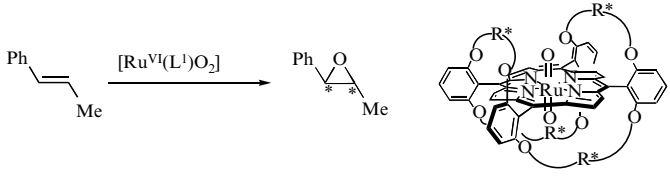
$[Ru^{VI}(L^3)O_2]$ (**1c**): ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.67 (d, *J* 4.6 Hz, 4H), 8.56 (d, *J* 4.6 Hz, 4H), 7.76 (m, 4H), 7.20–7.37 (m, meta-H overlapped with a solvent peak, 8H), 4.88 (d, *J* 9.3 Hz, 4H), 4.60 (d, *J* 9.4 Hz, 4H), 4.64 (t, *J* 9.0 Hz, 4H), 4.24 (d, *J* 10.1 Hz, 4H), 3.77 (d, *J* 8.6 Hz, 4H), 2.57 (t, *J* 8.6 Hz, 4H), 0.83 (m, 12H), 0.60 (m, 12H), −0.32 (m, 4H), −1.16 (m, 4H).

IR (KBr): 819 ($\nu_{Ru=O}$), 1019 cm^{-1} (oxidation state marker band).

UV–vis (CH_2Cl_2) λ_{max}/nm (log ε/$dm^3mol^{-1}cm^{-1}$): 441 (5.03), 535 (4.02).

FAB–MS *m/z*: 1483 (M^+, 8 %), 1467 (M^+–O, 22 %), 1451 (M^+–2O, 100 %).

6.3.2 ENANTIOSELECTIVE EPOXIDATION OF (*E*)-β-METHYLSTYRENE



Materials and equipment

- Benzene (freshly distilled over sodium/benzophenone under a nitrogen atmosphere), 5 mL
- (*E*)-β-Methylstyrene (purified by simple distillation), 118 mg, 1 mmol
- $[Ru^{VI}(L^1)O_2]$, 20–40 mg, 0.015–0.03 mmol
- Pyrazole (Hpz) (AR, Aldrich), 30 mg, 0.4 mmol
- Petroleum ether (AR) and CH_2Cl_2 (AR)
- Silica gel (70–230 mesh ASTM)

- 10 mL Round-bottomed flask with a magnetic stirrer bar
- Magnetic stirrer plate
- Glass column for chromatography
- Rotary evaporator
- HP-UV 8543 Ultraviolet–visible spectrophotometer
- HP5890 Series II Gas Chromatograph equipped with a chiraldex G-TA capillary column and a flame ionization detector

Procedure

1. In an ice-cooled (0 °C) 10 mL round-bottomed flask equipped with a magnetic stirrer bar were placed dry benzene (5 mL), (*E*)-β-methylstyrene (118 mg) and pyrazole (30 mg) under an argon atmosphere. $[Ru^{VI}(L^1)O_2]$ (20–40 mg) was added to the mixture with stirring. The resulting solution was stirred for overnight at 0 °C under an inert atmosphere.
2. The reaction was monitored by a UV–vis spectrophotometer, and the completion of the reaction was confirmed by the disappearance of the Soret band at 442 nm.
3. The mixture was passed through a silica gel column and eluted initially with petroleum ether to remove the unreacted alkene. The product epoxide was collected by using CH_2Cl_2 as the eluent.

   The epoxide and aldehyde were identified and quantified by capillary GLC equipped with a Chiraldex G-TA column using 4-bromochlorobenzene as the internal standard (oven temp: 110 °C, carrier gas: He, flow rate: 60–65 mL min^{-1}, split ratio 100:1, detector: FID at 250 °C, (*1S*, *2S*)-(*E*)-β-methylstyrene oxide: $R_t = 6.98$ min; (*1R*, *2R*)-(*E*)-β-methylstyrene oxide: $R_t = 7.81$ min.) The enantiopurity of the *1R*,*2R*-epoxide = 70 % ee, Yield = 90 % (>99 % trans).

6.3.3 CONCLUSION

A D_2-symmetric chiral *trans*-dioxoruthenium(VI) porphyrin, $[Ru^{VI}(L^1)O_2]$, bifacially encumbered by four threitol units can effect enantioselective epoxidation of (*E*)-β-methylstyrene in up to 70 % ee. For the asymmetric styrene oxidation, a lower enantioselectivity of 40 % ee was obtained (c.f. 62 % ee, see Table 6.3) when

Table 6.3 Epoxidation of some aromatic alkenes by $[Ru^{VI}(L^1)O_2]$ (1a).

entry	alkenes	solvent	epoxide yield (%)	% ee (abs. config.)
1		C_6H_6	64[c]	62 (R)
		C_6H_6	62	40 (R)[d]
		CH_2Cl_2	39	41 (R)
		MeCN	13	33 (R)
2		C_6H_6	75	60 (R)
3		C_6H_6	90 (>99 % trans)	67 (1R,2R)
		C_6H_6(0°C)	90 (>99 % trans)	70 (1R,2R)
		CH_2Cl_2	58 (>99 % trans)	32 (1R,2R)
		*E*tOAc	82 (>99 % trans)	38 (1R,2R)
4		C_6H_6	70	76 (1R,2R)
5		C_6H_6	75 (> 99% cis)	40 (1R,2*S*)
		CH_2Cl_2	68 (95% cis, 5% trans)	18 (1R,2*S*)
6		C_6H_6	88	20 (1R,2*S*)

the reaction was carried out without pyrazole. It is believed that the pyrazole could prevent the Ru(IV) intermediate from undergoing further reduction to a Ru(II) porphyrin by forming the $[Ru^{IV}(L^1)(pz)_2]$ complex, where the Ru(II) species is known to racemize chiral epoxides[8]. The asymmetric (*E*)-β-methylstyrene epoxidation by $[Ru^{VI}(L^1)O_2]$ exhibits remarkable solvent dependence. Benzene is the solvent of choice, and the use of polar solvents such as dichloromethane or ethyl acetate would lead to lower enantioselectivities of 32 and 38% ee, respectively. Other dioxoruthenium derivatives bearing *gem*-diethyl, $[Ru^{VI}(L^2)O_2]$, and *gem*-cyclopentyl groups, $[Ru^{VI}(L^3)O_2]$, at the threitol units afforded a lower ee of 60% and 55% ee for the styrene oxidation.

Table 6.3 depicts the results of the asymmetric epoxidation of some aromatic alkenes.

REFERENCES

1. Jacobsen, E.N., Zhang, W., Muci, A.R., Ecker, J.R., Deng, L. *J. Am. Chem. Soc.,* 1991, **113**, 7063.
2. Wang, Z.-X., Tu, Y., Frohn, M., Zhang, J.-R., Shi, Y. *J. Am. Chem. Soc.,* 1997, **119**, 11224.
3. Zhang, W., Jacobsen, E.N. *J. Org. Chem.*, 1991, **56**, 2296.
4. Deng, L., Jacobsen, E.N. *J. Org. Chem.*, 1992, **57**, 4320.
5. Bennani, Y.L., Hanessian, S. *Chemical Reviews*, 1997, **1997**, 3161.

6. Mio, S., Kumagawa, Y., Sugai, S. *Tetrahedron*, 1991, **47**, 2133.
7. Zhang, R., Yu, W.-Y., Lai, T.-S., Che, C.-M. *Chem. Commun*., 1999, 409.
8. Groves, J.T., Ahn, K.T., Quinn, R. *J. Am. Chem. Soc*., 1988, **110**, 4217.