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5 Epoxidation of Allylic Alcohols

CONTENTS

In 1980, Katsuki and Sharpless[1] reported that, with the combination of a titanium(IV) alkoxide, an enantiomerically pure tartrate ester [for example (+)-diethyl tartrate ((+)-DET) or (+) di-iso-propyltartrate ((+)-DIPT)] and *tert*-butyl hydroperoxide, they were able to carry out the epoxidation of a variety of allylic alcohols in good yield and with a good enantiomeric excess (Figure 5.1).

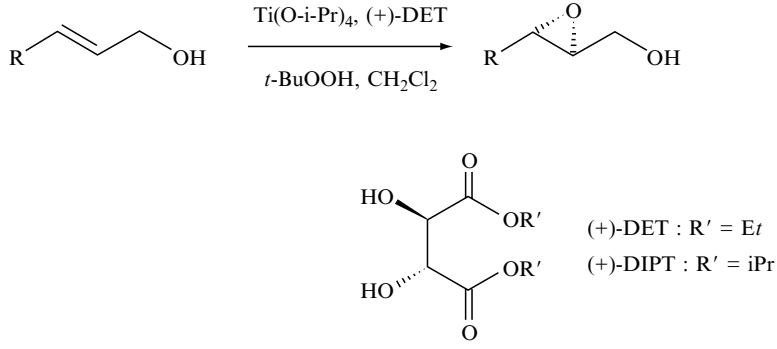


Figure 5.1 Allylic alcohol epoxidation using a chiral titanium(IV) complex.

Of fundamental importance to an understanding of the reaction and its mechanism is the fact that in solution there is rapid exchange of titanium ligands (Figure 5.2). After formation of the [titanium$(OR)_2$(tartrate)] complex, the two remaining alkoxide ligands are replaced in reversible exchange reactions by the *tert*-butyl hydroperoxide (TBHP) and the allylic alcohol to give the [titanium(tartrate)(allylic alcohol)(TBHP)] complex. The oxygen is then transferred from the coordinated hydroperoxide to the allylic alcohol[2].

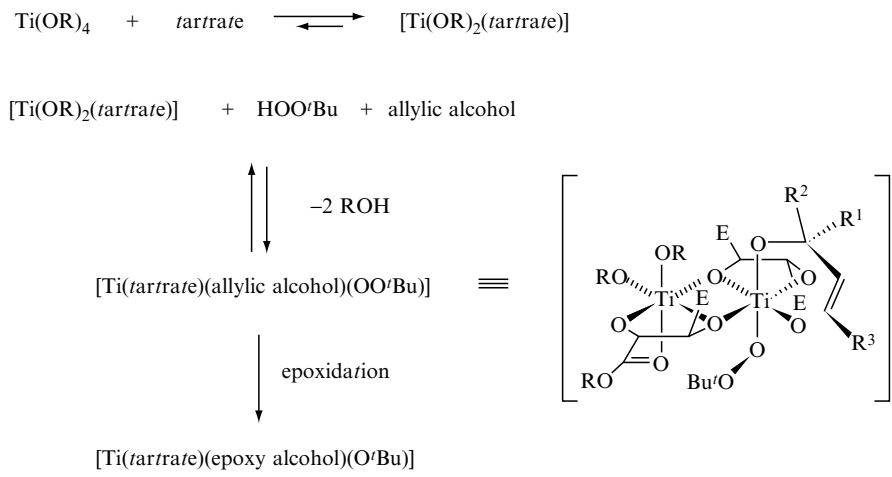
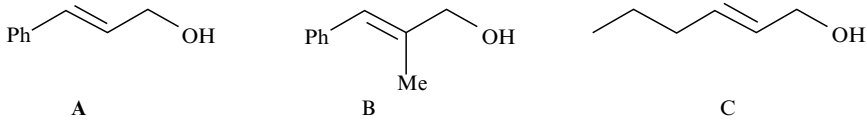
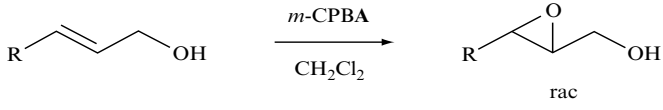


Figure 5.2 Mechanism of epoxidation using titanium(IV) chiral complex.

We will describe representative procedures for the epoxidation of a disubstituted aromatic allylic alcohol (A), a trisubstituted aromatic allylic alcohol (B) and a disubstituted aliphatic allylic alcohol (C).



5.1 NON-ASYMMETRIC EPOXIDATION



Materials and equipment

- Allylic alcohol, 1 mmol
- Anhydrous dichloromethane, 10 mL
- *m*-Chloroperbenzoic acid (MCPBA, *m*-CPBA), 1 mmol
- Saturated aqueous solution of sodium hydrogencarbonate, 40 mL
- Dichloromethane
- Magnesium sulfate
- Silica gel 60 (0.063–0.04 mm)

- 50 mL Round-bottomed flask with a magnetic stirrer bar
- Magnetic stirrer
- Ice-bath
- Separating funnel, 250 mL
- Rotary evaporator

Procedure

1. In a 50 mL round-bottomed flask was dissolved the allylic alcohol (1 mmol) in dry dichloromethane (10 mL). The mixture was cooled with an ice-bath, stirred, and *m*-chloroperbenzoic acid (1 mmol) was added.
2. The ice-bath was removed, the reaction mixture was stirred at room temperature and monitored by TLC. After completion of the reaction dichloromethane (10 mL) was added.
3. The reaction mixture was transferred into a separating funnel. The aqueous layer was extracted with dichloromethane (10 mL). The combined organic layers were washed with a aqueous solution of sodium hydrogencarbonate (2×20 mL), then with water (30 mL), dried over magnesium sulfate, filtered and the solvent removed under reduced pressure.
4. The residue was purified by flash chromatography over silica gel.
   See below for the method of purification for each product.

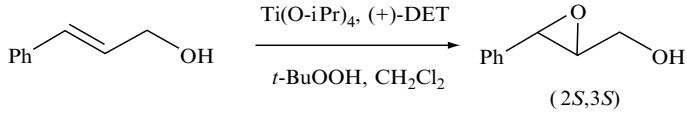
5.2 ASYMMETRIC EPOXIDATION USING A CHIRAL TITANIUM COMPLEX

The following three procedures need to be carried out under strictly anhydrous conditions.

- Before each reaction, the molecular sieves (4 Å in powder form or 3 Å as pellets) were activated by heating for 2 hours at 400 °C, then cooled under vacuum in a desiccator.
- Dry dichloromethane was stored on preactivated molecular sieves 3 Å in pellets (4 Å sieves should not to be used).
- The tartrate esters can be used as obtained from Aldrich Chemical Co. or Fluka Chemical Corp. If the yield and/or the enantiomeric excess is/are

lower than expected, the reaction should be repeated with tartrate distilled under high vacuum and stored under vacuum or in an inert atmosphere.
- An anhydrous solution of 5.5 M of *tert*-butyl hydroperoxide in *iso*octane stored over molecular sieves is available from Fluka.
- Liquid allylic alcohols ((E)-2-methyl-3-phenyl-2-propenol and (E)-2-hexen-1-ol) were stored over preactivated 3 Å molecular sieves.
- Titanium *iso*propoxide needs to be manipulated carefully with gloves and eye protection. If the yield and/or the enantiomeric excess is/are lower than expected, the catalyst should be distilled under vacuum (b.p 78–79.5 °C, 1.1 mmHg).

5.2.1 EPOXIDATION OF CINNAMYL ALCOHOL[3,4]



Materials and equipment

- L-(+)-Di*iso*propyl tartrate ((+)-DIPT), 400 mg, 2 mmol, 0.1 eq
- Dichloromethane stored over preactivated 3 Å molecular sieves, 43 mL
- Activated powdered 4 Å molecular sieves, 500 mg
- Titanium isopropoxide, 297 μL, 1 mmol, 0.05 eq
- Anhydrous solution of 5.5 *M* of *tert*-butyl hydroperoxide in isooctane stored over molecular sieves, 5.5 mL, 30 mmol, 1.5 eq
- Cinnamyl alcohol, 2.68 g, 20 mmol
- Aqueous solution of sodium hydroxide 30 % saturated with sodium chloride, 6 mL
- Celite®
- Brine
- Magnesium sulfate
- Silica gel 60 (0.063–0.04 mm)
- (*R*)-(+)-α-Methoxy-α-(trifluoromethyl)phenylacetyl chloride (MTPA chloride) or the (*S*)-enantiomer, 5 mg, 0.02 mmol
- 4-Dimethylaminopyridine (DMAP), 5 mg, 0.04 mmol
- Dichloromethane, diethyl ether, petroleum ether, ethyl acetate, *n*-hexane
- *p*-Anisaldehyde

- 50 mL Two-necked flask with a magnetic stirrer bar
- Magnetic stirrer
- Cooling bath (acetone/Dri-ice) equipped with contact thermometer, −5 °C
- Büchner funnel with glass frite (30 mL, porosity n°3)

- Syringes
- Separating funnel, 250 mL
- Rotary evaporator

Procedure

1. A 50 mL two-necked flask equipped with a stirrer bar was placed in an oven at 120 °C overnight, cooled under vacuum and flushed with nitrogen.
2. The flask was filled with activated powdered 4 Å molecular sieves (500 mg), dry dichloromethane (40 mL) and L-(+)-diisopropyl tartrate (400 mg).
3. The mixture was cooled to −5 °C with the cooling bath, stirred and titanium isopropoxide (297 μL) was added. After cooling the bath to −20 °C, a solution of *tert*-butyl hydroperoxide (5.5 *M* in *iso*octane, 5.5 mL) was added and the mixture was stirred at −20 °C for 1 hour.
4. The solution of cinnamyl alcohol (2.68 g in 3 mL of dry dichloromethane) was added dropwise over 1 hour via a syringe.
5. The reaction was monitored by TLC (eluent: petroleum ether–diethyl ether, 1:1). The visualization of the cinnamyl alcohol (UV active) with *p*-anisaldehyde dip gave a blue stain, R_f 0.35, and a brown stain for the epoxycinnamyl alcohol, R_f 0.25.
6. After being stirred for 2 hours at −15 °C, the reaction was quenched with water (6 mL) and the mixture was stirred for 30 minutes at this temperature. The solution was warmed to room temperature. Hydrolysis of the tartrate was then effected by adding an aqueous solution of sodium hydroxide (30 %) saturated with sodium chloride (6 mL) and stirring vigorously for 1 hour.
7. A Büchner funnel with glass frite was packed with 2 cm Celite®. The two-phase mixture was filtered over the pad of Celite®, transferred into a separating funnel and the organic layer was separated.
8. The aqueous phase was washed with dichloromethane (3 × 10 mL) and the combined organic phases were dried (magnesium sulfate) and evaporated under reduced pressure to afford crude product.
9. The crude material was purified by flash chromatography over silica gel (150 g) using ethyl acetate-*n*-hexane (1:9) as eluent to give (*2S,3S*)-2,3-epoxy-3-phenyl-1-propanol as a white solid (2.08 g, 70 %).

   The ee (92 %) was determined by HPLC analysis (Chiralpak® OD column, flow 1 mL/min, isopropanol–*n*-hexane; 1:9); (2*R*,3*R*)-enantiomer: R_t 12.3 min, (2*S*,3*S*)-enantiomer: R_t 13.4 min or by analysis of the corresponding Mosher esters.

Derivatization with MTPA chloride

Esterification of chiral alcohols with (R)-(+)-α-methoxy-α-(trifluoromethyl)-phenylacetyl chloride (MTPA chloride) or its (S)-enantiomer as homochiral auxiliaries affords the corresponding diastereoisomeric (R)- or (S)-Mosher esters, respectively.

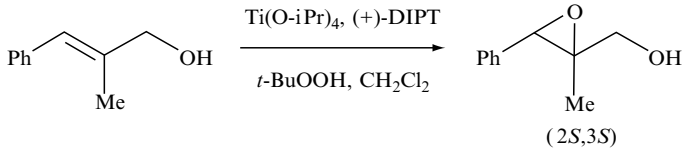
In a NMR tube, to a solution of the epoxy alcohol (2.5 mg) in $CDCl_3$ (0.5 mL) was added 4-dimethylaminopyridine (5 mg) and (R)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride (5 mg). The mixture was allowed to stand overnight at room temperature. The reaction was monitored by TLC to ensure complete consumption of the starting material. ^1H and ^{19}F NMR spectra were carried out on the crude reaction mixture. In the ^{19}F NMR spectrum, each enantiomer gave a signal; an additional signal at −71.8 ppm was ascribed to residual MTPA. (^{19}F NMR (250 MHz, $CDCl_3$): δ − 70.7 (s, (2*R*,3*R*)-enantiomer); −72.0 (s, (2*S*,3*S*)-enantiomer)).

^1H NMR (200 MHz, $CDCl_3$): δ 7.37–7.27 (m, 5H, Ph); 4.06 (ddd, *J* 10.5 Hz, *J* 4.9 Hz, *J* 3.0 Hz, C*H*–CH_2); 3.94 (d, *J* 3 Hz, 1H, C*H*–Ph); 3.81 (dd, *J* 12.5 Hz, *J* 4.9 Hz, 1H, C*Ha*Hb); 3.24 (m, 1H, CHa*Hb*), 2.05 (br, 1H, OH).

IR ($CHCl_3$, cm^{-1}): 3603, 3450 (O–H), 3060 (C–H epoxide), 3010 (C–H aromatic), 2927, 2875 (C–H aliphatic), 1606, 1461 (C=C), 1390, 1308, 1289, 1203 (C–OH, C–O–C), 1103, 1079, 1023, 882, 861, 838.

Mass: calculated for $C_9H_{10}O_2$: *m/z* 150.06808; found $[M]^{+\circ}$ 150.06781.

5.2.2 EPOXIDATION OF (*E*)-2-METHYL-3-PHENYL-2-PROPENOL[4]



Materials and equipment

- L-(+)-Diisopropyl tartrate ((+)-DIPT), 350 mg, 1.5 mmol, 0.075 eq
- Dichloromethane stored over preactivated 3 Å molecular sieves, 50 mL
- Activated powdered 4 Å molecular sieves, 1.2 g
- Titanium *iso*propoxide, 297 μL, 1 mmol, 0.05 eq
- Anhydrous solution of 5.5 *M* of *tert*-butyl hydroperoxide in isooctane stored over molecular sieves, 7.2 mL, 40 mmol, 2 eq
- (*E*)-2-Methyl-3-phenyl-2-propenol, 3 g, 2.9 mL, 20 mmol
- Aqueous solution of sodium hydroxide (30 %) saturated with sodium chloride, 6 mL
- Celite®
- Brine
- Sodium sulfate
- Silica gel 60 (0.063–0.04 mm)
- Dichloromethane, diethyl ether, petroleum ether, methanol
- *p*-Anisaldehyde

- 50 mL Two-necked flask with a magnetic stirrer bar
- Magnetic stirrer
- Acetone/Dry ice cooling bath equipped with contact thermometer, −35 °C
- Syringes
- Büchner funnel with glass frite, 30 mL
- Glass wool
- Separating funnel, 250 mL
- Rotary evaporator

Procedure

1. A 50 mL two-necked flask equipped with a stirrer bar was placed in an oven at 120 °C overnight, cooled under vacuum and flushed with nitrogen.
2. The flask was filled with dry dichloromethane (50 mL) and L-(+)-diisopropyl tartrate (350 mg). The mixture was cooled to −35 °C using the cooling bath, then activated powdered 4 Å molecular sieves (1.2 g), titanium *iso*propoxide (297 μL) and a solution of *tert*-butyl hydroperoxide (5.5 *M* in *iso*octane, 7.2 mL) were added sequentially. The mixture was stirred at −35 °C for 1 hour.
3. The (*E*)-2-methyl-3-phenyl-2-propenol (2.9 mL) was added dropwise via a syringe over 30 minutes.
4. The reaction was monitored by TLC (eluent: petroleum ether–diethyl ether, 6:4). 2-Methyl-3-phenyl-2-propenol (UV active) visualized with a *p*-anisaldehyde dip stained blue, R_f 0.50 and the epoxide stained brown, R_f 0.33.
5. The mixture was stirred for 2.5 hours at −35 °C, then the bath was warmed to 0 °C and the reaction quenched by the addition of water (6 mL). The resulting mixture was stirred for 30 minutes.
6. The solution was warmed to room temperature. Hydrolysis of the tartrate was then effected by adding an aqueous solution of sodium hydroxide (30 %) saturated with sodium chloride (6 mL) and stirring vigorously for 1 hour.
7. The mixture was transferred into a separating funnel. The aqueous phase was extracted with dichloromethane (2 × 30 mL). Then the combined organic layer phase were dried over sodium sulfate, filtered and concentrated under reduced pressure to give a yellow oil.

   If the phase separation does not occur, the reaction mixture is transferred into a separating funnel. A small amount of methanol is added to the mixture (5 mL) followed by a very brief shaking. Immediate phase separation often occurs, allowing for the simple removal of the lower organic phase. If the emulsion is still a problem, then the mixture is filtered once or twice through a small plug of glass wool washed with dichloromethane.
8. The crude material was purified by flash chromatography over silica gel (100 g) using petroleum ether–diethyl ether (8:2) as eluent to give (2*S*,3*S*)-2-methyl-3-phenyloxiranemethanol as a white solid (3 g, 18.6 mmol, 93 %).

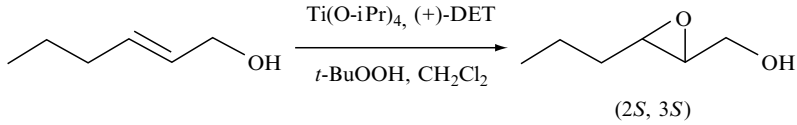
   The ee (94.5 %) was determined by HPLC (Chiralpak® OD column, flow 1 mL/min, ethanol–*n*-hexane; 1:99); (2*S*,3*S*)-enantiomer: R_t 16.0 min,

(2*R*,3*R*)-enantiomer: R_t 13.5 min. The analysis of the ester derived from (+)-MTPA chloride did not give any resolution by ^{19}F NMR.

^1H NMR (200 MHz, $CDCl_3$): δ 7.23–7.34 (m, 5H, Ph); 4.19 (s, 1H, C*H*); 3.68–3.88 (m, 2H, CH_2); 1.84–1.77 (m, 1H, O*H*); 1.06 (s, 3H, CH_3).

IR ($CHCl_3$, cm^{-1}): 3589, 3450, (O–H), 3060 (C–H epoxide), 3010 (C–H aromatic), 2938, 2878 (C–H aliphatic), 1713, 1603, 1493, 1452 (C=C), 1385, 1204 (C–OH, C–O–C), 1095, 1058, 1029, 980, 924, 898, 850.

5.2.3 EPOXIDATION OF (*E*)-2-HEXEN-1-OL[4]



(2*S*, 3*S*)

Materials and equipment

- L-(+)-Diethyl tartrate ((+)-DET), 250 mg, 1.2 mmol, 0.06 eq
- Dichloromethane stored over preactivated 3 Å molecular sieves, 40 mL
- Activated powdered 4 Å molecular sieves, 600 mg
- Titanium isopropoxide, 297 μL, 1 mmol, 0.05 eq
- Anhydrous solution of 5.5 *M* of *tert*-butyl hydroperoxide in *iso*octane stored over molecular sieves, 7.2 mL, 40 mmol, 2 eq
- (*E*)-2-Hexen-1-ol, 2 g, 20 mmol
- Solution of ferrous sulfate heptahydrate, 6.6 g, 24 mmol, and tartaric acid, 2 g, 12 mmol, in deionized water, 20 mL
- Sodium hydroxide solution in saturated brine, 30 %, 50 mL
- Sodium sulfate
- Silica gel 60 (0.063–0.04 mm)
- (*R*)-(+)-α-Methoxy-α-(trifluoromethyl)phenylacetyl chloride (MTPA chloride) or the (*S*)-enantiomer, 5 mg, 0.02 mmol
- 4-Dimethylaminopyridine (DMAP), 5 mg, 0.04 mmol
- *n*-Hexane, ethyl acetate, diethyl ether, triethylamine
- *p*-Anisaldehyde

- 50 mL Two-necked flask with a magnetic stirrer bar
- Magnetic stirrer
- Acetone/Dri-ice cooling bath equipped with contact thermometer, −20 °C
- Syringes
- Beaker, 100 mL
- Separating funnel, 250 mL
- Rotary evaporator

Procedure

1. A 50 mL two-necked flask equipped with a stirrer bar was placed in an oven at 120 °C overnight, cooled under vacuum and flushed with nitrogen.
2. To the flask was added dry dichloromethane (30 mL), activated powdered 4 Å molecular sieves (600 mg) and L-(+)-diethyl tartrate (250 mg).
3. After the mixture was cooled to −20 °C, titanium isopropoxide (297 μL) was added. The reaction mixture was stirred at −20 °C as a solution of *tert*-butyl hydroperoxide (5.5 *M* in *iso*octane, 7.2 mL) was added via a syringe at a moderate rate (over 5 minutes). The mixture was stirred at −20 °C for 30 minutes.
4. The solution of (*E*)-2-hexen-1-ol (2 g) in dry dichloromethane (10 mL) was added dropwise via a syringe over a period of 20 minutes, while the temperature was maintained between −20 °C and −15 °C.
5. The reaction mixture was stirred for an additional 2.5 hours at −20 °C. The reaction was monitored by TLC (eluent: *n*-hexane–ethyl acetate, 7:3). The products were visualized with a *p*-anisaldehyde dip; 2-hexenol stained purple, R_f 0.49 and the epoxide stained dark blue, R_f 0.22.
6. After completion of the reaction a 100 mL beaker containing the solution of ferrous sulfate–tartaric acid (20 mL) was pre-cooled at 0 °C by means of an ice-water bath. The epoxidation reaction mixture was allowed to warm to 0 °C and then was poured slowly onto the pre-cooled, stirring ferrous sulfate solution. The two-phase mixture was stirred for 5–10 minutes; the aqueous layer became brown.
7. The mixture was transferred into a separating funnel. The phases were separated and then the aqueous phase was extracted with diethyl ether (2 × 30 mL). The combined organic layers were treated with the pre-cooled solution of 30 % sodium hydroxide in saturated brine (50 mL).
8. The two-phase mixture was stirred vigorously for 1 hour at 0 °C and then diluted with 50 mL of water. The mixture was transferred into a separating funnel and the phases were separated. The aqueous layer was extracted with diethyl ether (2 × 50 mL) and the combined organic layers dried over sodium sulfate, filtered and concentrated under reduced pressure yielding a colourless oil.

   This procedure works well for most hydrophobic epoxy alcohols. The key advantage is that it is possible to remove tartrate, titanium isopropoxide and *tert*-butyl hydroperoxide, as those different compounds are not easily separated through distillation or recrystallization.
9. The crude material was purified by flash chromatography over silica gel (100 g), buffered with 1 % triethylamine, using *n*-hexane–diethyl ether (3:1) as eluent to give (2*S*,3*S*)-3-propyloxiranemethanol as a colourless oil (2 g, 15.3 mmol, 80 %).

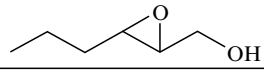
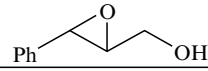
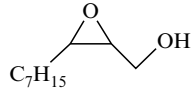
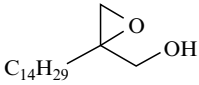
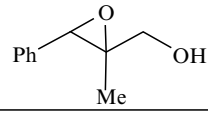
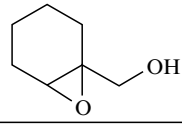
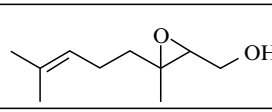
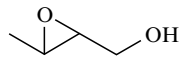
   The ee (93 %) was determined by GC analysis (Lipodex® E, 25 m, 0.25 mm ID, temperatures: column 70 °C isotherm, injector 250 °C, detector 250 °C, mobile phase helium); (2*S*,3*S*)-enantiomer: R_t 53.6 min,

(2*R*, 3*R*)-enantiomer: R_t 52.6 min. The ee can be determined by analysis of the ester derived from (+)-MTPA chloride (^{19}F NMR (250 MHz, $CDCl_3$): δ − 70.8 (s, (2*R*,3*R*)-enantiomer); −72.0 (s, (2*S*,3*S*)-enantiomer)).

^{1}H NMR (200 MHz, $CDCl_3$): δ 3.91 (d, *J* 13.5 Hz, 1H); 3.60 (dd, *J* 13.4 Hz, *J* 4.1 Hz, 1H); 2.94 (m, 2H); 2.53 (m, 1H); 1.53 (m, 4H); 0.96 (t, *J* 7.1 Hz, 3H, CH_3).

IR ($CHCl_3$, cm^{-1}: 3589 (C–O), 3009, 2965, 2937, 2877 (C–H), 1458 (C–H, CH_3), 1382, 1203 (C–OH, C–O–C), 1095, 1030, 970, 924, 897, 848.

Table 5.1 Catalytic asymmetric epoxidation of allylic alcohols using a combination of titanium *iso*propoxide. enantiomerically pure tartrate ester ((+)-DET or (+)-DIPT) and *tert*-butyl hydroperoxide (yield and enantiomeric excess, according to the relevant publication)[4].

	Yield %	ee % (configuration)
	85*	94 (2*S*,3*S*)*
	89*	>98 (2*S*,3*S*)*
	74	86 (2*S*,3R)
	91	96 (*S*)
	79*	>98 (2*S*,3*S*)*
	77	93
	95	91 (2*S*,3R)
	70	91 (2*S*,3*S*)

* Reaction described above

5.2.4 CONCLUSION

This method, specific for the epoxidation of allylic alcohols, gives good results if the reaction is carried out under strictly anhydrous conditions, otherwise the yield or the enantiomeric excess can decrease, sometimes dramatically.This can explain the small differences between the results obtained during the validation experiments and the published results. All the different reagents are commercially available; they can be used as received but in case of low yield and/or enantiomeric excess they should be distilled and dried under an inert atmosphere. Table 5.1 gives some other examples of substrates which can be epoxidized using the procedure described above.

5.3 ASYMMETRIC EPOXIDATION OF (*E*)-UNDEC-2-EN-1-OL USING POLY(OCTAMETHYLENE TARTRATE)

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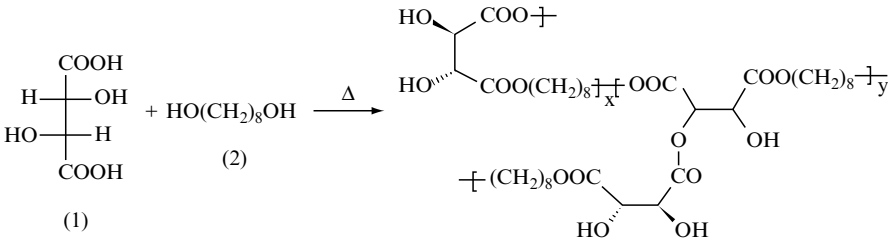
5.3.1 SYNTHESIS OF BRANCHED POLY(OCTAMETHYLENE-L-(+)-TARTRATE)[5]



Materials and equipment

- L-(+)-Tartaric acid, 10.0 g, 0.067 mol
- 1,8-Octanediol, 11.7 g, 0.080 mol
- *p*-Toluene sulfonic acid, 0.6 g
- Ethyl acetate
- *n*-Hexane

- 100 mL Three-necked round-bottomed flask with a magnetic stirrer bar; N_2 cylinder and bubbler; oil bath; hot-plate stirrer; vacuum distillation equipment

Procedure

1. The tartaric acid, 1,8-octanediol and *p*-toluene sulfonic acid were placed in the flask and the latter flushed with N_2. A positive pressure of N_2 was then maintained throughout. The mixture was stirred as the temperature was raised to 140 °C to achieve a homogeneous solution; the temperature was then allowed to fall to 125 °C and the reaction left to proceed for 3 days.
2. Water and excess diol were removed by distillation under high vacuum to yield a solid mass. The latter was swollen in refluxing ethyl acetate (sufficient to make the mass mobile) and the resulting mixture poured into *n*-hexane (~3 fold volume excess).
3. The solid was recovered by decanting off the solvents and the polymer dried under vacuum at 40 °C for 6 hours and at room temperature for 2 days to yield 16.6 g (95%) of poly(octamethylene tartrate) (**3**).

   $[\alpha]_D^{25} = +9$ (c 1.6, THF).

   ^{1}H NMR (400 MHz, DMSO-d_6, 70 °C): δ 5.75 (br s), 5.41 (d, *J* 3.2 Hz), 4.62 (d, *J* 2.9 Hz), 4.37 (s, 2H), 4.09 (t, *J* 6.5 Hz, 4H), 1.58 (m, 4H), 1.30 (m, 9H).

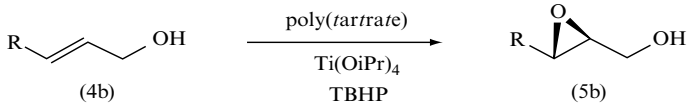
   Note 1 – small signals δ = 5.41 and 4.62 correspond to methine H atoms on tartrate branch points; the ratio of these intensities to the total intensity of all tartrate methine resonances allows estimation of the percentage branching.

   Note 2 – the percentage branching can vary with precise reaction conditions, up to ~ 10% gives optimal results; products insoluble in DMSO are crosslinked and should be discarded.

   FTIR (KBr, cm^{-1}) 3450 (OH), 2932, 2857 (C–H aliphatic), 1743 (C=O ester).

   Poly(octamethylene tartrate) can be used directly in place of dialkyl tartrates in the Sharpless epoxidation of allylic alcohols.

5.3.2 ASYMMETRIC EPOXIDATION OF (*E*)-UNDEC-2-EN-1-OL



(4b) (5b)

R = C_3H_7, (4a,5a); C_8H_{17}, (4b,5b); Ph (4c,5c) (see Table 5.2)

Materials and equipment

- Dry CH_2Cl_2 (over $CaCl_2$)
- Powdered activated 4 Å molecular sieves

- Poly(octamethylene-L(+)-tartrate)
- $Ti(OiPr)_4$
- Anhydrous *tert*-butylhydroperoxide (TBHP) (in *iso*-octane). See refs 5.6 for preparation and standardization
- (*E*)-Undec-2-en-1-ol (**4**, $R = C_8H_{17}$)
- Diethyl ether, toluene, petroleum ether
- NaOH, NaCl, $MgSO_4$, Celite

- Three-necked round-bottomed flask
- Magnetic stirrer
- N_2 supply
- Gas bubbler
- Syringe
- Bücher funnel, flask
- Filter paper
- −20 °C Cold bath
- Rotary evaporator

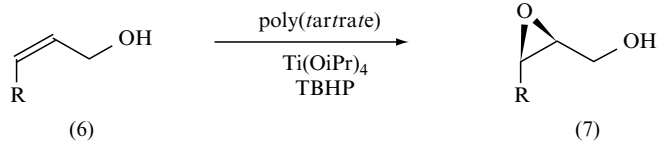
Procedure

1. An oven-dried three-necked round-bottomed flask (100 mL) equipped with a magnetic stir bar, nitrogen inlet, septum and bubbler was charged with CH_2Cl_2 (35 mL dried over $CaCl_2$), powdered activated 4 Å molecular sieves (0.3 g) and poly(octamethylene-L-(+)-tartrate) (1.56 g, 0.0059 mol tartrate, 6% branching). The flask was cooled to −20°C and $Ti(OiPr)_4$ (0.85 g, 0.0030 mol) added via a syringe.
2. The mixture was stirred for 1 hour at −20 °C and then anhydrous TBHP (7.5 mL, 3.2 M in *iso*-octane) also added slowly via a syringe. The mixture was again stirred at −20 °C for 1 hour. (*E*)-Undec-2-en-1-ol (1 g, 0.0059 mol) in CH_2Cl_2 (5 mL) was added dropwise by syringe such that the temperature was maintained between −15 and −20 °C. The reaction mixture was stirred at −20 °C for 6 hours and then placed in a freezer overnight.
3. The polymer–ligand–Ti complex was filtered off and washed thoroughly with CH_2Cl_2. The recovered solution was then quenched with aqueous NaOH (30%, 10 mL, saturated with NaCl) and diethyl ether added (50 mL) after which the cold bath was removed and the stirred mixture allowed to warm up to 10 °C. Stirring was continued for 10 minutes at 10 °C whereupon sufficient magnesium sulfate and Celite were added to absorb all the aqueous phase. After a final 15 minutes stirring the mixture was allowed to settle and the solution filtered through a pad of Celite and washed with diethyl ether. The solvents were removed under vacuum and the excess TBHP removed by azeotropic distillation with a little added toluene. The crude product was purified by recrystallization from petroleum ether to yield a white solid (0.55 g, 50%).

- ee = 88 % determined by ^{1}H NMR analysis of the Mosher ester; $[\alpha]_D^{25} = -22$(c 1.33, $CHCl_3$).
- ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.88 (dd, *J*2, 13 Hz, 1H), 3.59 (ddd, *J*5, 7, 10 Hz, 1H), 2.87–2.96 (m, 2H), 2.68 (br s), 1.24–1.55 (m, 14H), 0.85 (t, *J* 7 Hz, 3H).
- FTIR ($CHCl_3$ cm^{-1}): 1237 (in phase epoxy); 933–817 (out of phase epoxy).

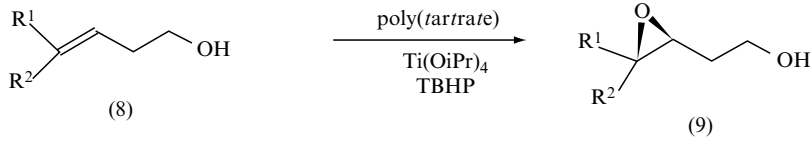
Utility and Scope

Use of poly(octamethylene tartrate) in place of dialkyl tartrates offers practical utility since the branched polymers yield *hetereogeneous* Ti complex catalysts which can be removed by filtration. Overall the work-up procedure is considerably simplified relative to the conventional Sharpless system. In addition, significant induction is shown in the epoxidation of (*Z*)-allylic alcohols[7] and even with homoallylic[8] species where the dialkyltartrates give very poor results Figure 5.3. Table 5.2 is illustrative of the scope using the polymer ligand.



(6) (7)

R=C_2H_5,(6a,7a); C_3H_7,(6b,7b); $PhCH_2OCH_2$ (6c,7c)



(8) (9)

R^1= C_2H_5	R^2= H	(8a,9a)
R^1= H	R^2= C_2H_5	(8b,9b)
R^1= CH_3	R^2= CH_3	(8c,9c)
R^1= H	R^2= H	(8d,9d)

Figure 5.3 Oxidation of some (*Z*)-allylic alcohols and some homoallylic alcohols using poly(tartrate).

Table 5.2 Asymmetric epoxidation of *cis*- and *trans*-allylic and homoallylic alcohols using poly(octamethylene tartrate)/Ti(O*i*Pr)$_4$/TBHP.

Alkene	Epoxide	Poly(tartrate) % branching	Molar ratio alkene:Ti:tartrate	Temperature (°C)	Time	Isolated[a] Yield (%)	Ee(%)
4a	5a[b]	3	10:25:5	−20	6h	53	87[h]
4b	5b[b]	6	10:2:6	−15	12h	40	98[h]
4c	5cc	10	10:10:20	−20	7d	51	86[i]
6b	7b[c]	10	10:10:40	−20	6d	48	80[i]
6c	7c[c]	10	10:20:40	−20	6d	18	68[i]
8a	9a[d]	8	10:20:40	−20	5d	45	54[j]
8b	9b[e]	10	10:20:40	−20	21d	20	51[j]
8c	9c[f]	3	10:10:20	−20	1d	31	36[j]
8d	9d[g]	10	10:20:40	−20	14d	20	80[j]

a) GC yield typically much higher; scope for improvement in isolation
b) (2*S*-*trans*)isomer using L-(+)-polytartrate
c) (2*S*-*cis*)isomer using L-(+)-polytartrate
d) (3*R*, 4*R*)isomer using L-(+)-polytartrate
e) (3*R*, 4*S*)isomer using L-(+)-polytartrate
f) (3*R*)isomer using L-(+)-polytartrate
g) (3*R*)isomer using L-(+)-polytartrate
h) marginally lower than with dialkyltartrate
i) marginally better than with dialkyltartrate
j) substantially better than with dialkyltartrate

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