Highly Enantioselective Epoxidation of α, β-Unsaturated Ketones Catalyzed by Chiral Multi-site Phase-Transfer Catalysts

Dr. P. Kottala Vijaya
Assistant Professor
PG & Research Department of Chemistry
Pope's College (Autonomous), Sawyerpuram - 628 152, India.

Abstract : The asymmetric epoxidation reaction of α, β-unsaturated ketones catalyzed by mesitylene based tris-quaternary ammonium bromide as chiral multi-site phase transfer catalysts derived from cinchona alkaloids. The CMPTCs was found to be a highly enantioselective PTC for epoxidation reaction at room temperature. Under optimized reaction conditions, excellent chemical yields upto 98% along with the highest enantioselectivity upto 99% were obtained by using the CMPTCs.

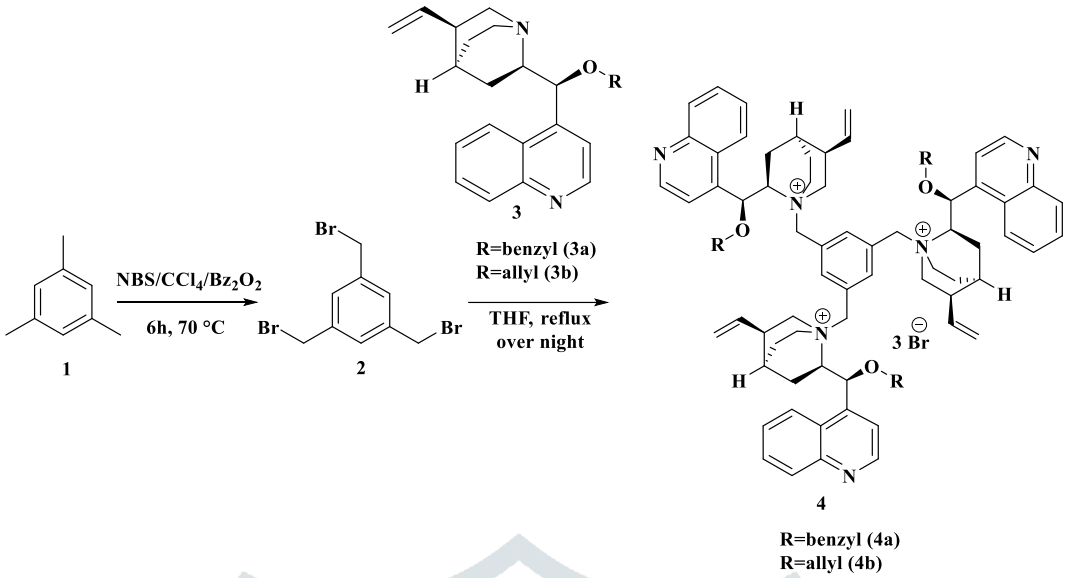
Epoxidation, cinchona alkaloids, enantioselective, phase transfer catalysts, asymmetric

I. INTRODUCTION

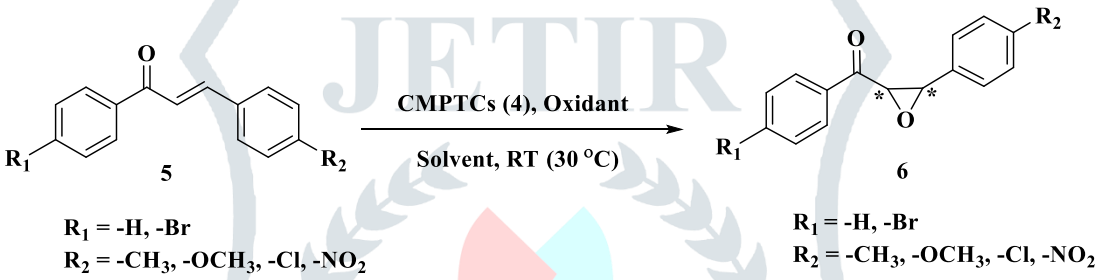
Asymmetric epoxidation is one of the most important transformations in organic synthesis, since it provides a straight forward access to various optically active epoxides, which are highly useful chiral building blocks for the synthesis of natural products and synthetic analogues with biological activities.[1] Much progress has been achieved in this field, since Sharpless *et al*. reported the discovery of titanium-catalyzed asymmetric epoxidation of allylic alcohols in the early 1980s.[2] The catalytic asymmetric epoxidation of electron-deficient olefins, particularly α,β-unsaturated ketones, has recently been the subject of numerous investigations reported and a number of useful methodologies involving different types of catalyst-reagent combinations have been elaborated.[3] Among these, the method utilizing chiral phase-transfer catalysis occupies a unique place, featuring many advantages including operational simplicity, non-metal containing catalyst, and environmental consciousness.[4] However, successful examples have been very limited since the pioneering work of Wynberg using alkylated cinchona alkaloids.[5]

In 1998, Lygo showed the effectiveness of a catalyst incorporating a 9-anthracenylmethyl group in the epoxidation of substituted chalcones with commercially available sodium hypochlorite,[6] and consecutively Corey reported that use of the same catalyst with freshly prepared 65% potassium hypochlorite at lower temperature (-40 °C) led to improve enantioselectivities.[7] Our group also reported the highly enanatioselective synthesis of epoxidation of α,β-unsaturated ketones under ultrasonic irradiation conditions with very good yield and ee's[8]. In 2014, Qinqin Qian *et al* reported the asymmetric epoxidation of unsaturated ketones catalyzed by heterobimetallic rare earth−lithium complexes bearing phenoxy-functionalized chiral diphenylprolinolate ligand (yield 60-79% and ee's 80-99%).[9] Similarly, Chao Zeng and co-workers reported highly enantioselective epoxidation of α,β-unsaturated ketones catalyzed by rare-earth amides $[(Me_3Si)_2N]_3RE(\mu\text{-}Cl)Li(THF)_3$ with phenoxy-functionalized chiral prolinols (yield 86-99% and ee's 87-99%).[10] Recently, Yu-Chang Liu et al., reported the enzymatic cascade for the asymmetric epoxidation of α,β-unsaturated ketones (yield 59-95% and ee's 85-99%).[11]

Despite such numerous impressive progresses,[12-30] the full potential of this reaction is yet to be realized in terms of both stereoselectivity and general applicability. This situation is largely due to the lack of well-designed, finely tuneable chiral catalysts. Herein, we wish to disclose our own solution to this difficulty by introducing a chiral multi-site phase transfer catalyst (CMPTCs). The synthesized new CMPTC **4** (Scheme 1) were showed their excellent catalytic reactivity in the asymmetric Michael addition of chalcones with diethylmalonate under mild reaction conditions with very good chemical yields (upto 98%) and ee's (upto 99%).[31] These previous successes led us to envision that CMPTCs **4** was might be highly enantioselective catalysts for the asymmetric epoxidation of α,β-unsaturated ketones with high chemical yield up to 98% and excellent enantiomeric excess up to 99% under mild reaction conditions (Scheme 2).



Scheme 1: Synthesis of chiral multi-site phase transfer catalysts **4 (4a/4b).**



Scheme 2: Enantioselective epoxidation of chalcones using CMPTCs **4 (4a/4b)** in aqueous/organic solvent media.

II. EXPERIMENTAL SECTION

2.1 Materials and methods

All the chemicals and reagents used in this work were of analytical grade. Mesitylene, allylbromide, (+)-cinchonine were obtained from Alfa Aesar. N-Bromosuccinimide, *p*-tolualdehyde, 4-chlorobenzaldehyde, 4-methoxybenzaldehyde, 4-nitrobenzaldehyde, acetophenone and 4-bromoacetophenone were obtained from Sigma Aldrich. Benzyl chloride, sodium hydroxide and potassium hydroxide were obtained from Merck and all the solvents obtained were of laboratory grade. The melting points were measured in open capillary tubes and are uncorrected. The ^{1}H and ^{13}C NMR spectra were recorded on Bruker (Avance) 300 and 400 MHz NMR instruments using TMS as an internal standard, $CDCl_3$ and DMSO-d^6 as solvents. Standard Bruker software was used throughout. Chemical shifts are given in parts per million (δ-scale) and the coupling constants are given in Hertz. Silica gel-G plates (Merck) were used for TLC analysis with a mixture of n-hexane and ethyl acetate as an eluent. Column chromatography was carried out in silica gel (60–120 mesh) using n-hexane, DCM, methanol and ethyl acetate as an eluents. Electro spray Ionization Mass Spectrometry (ESI-MS) analyses were recorded on a LCQ Fleet, Thermo Fisher Instruments Limited, US. ESI-MS was performed in the positive ion mode. The collision voltage and ionization voltage were -70 V and -4.5 kV, respectively, using nitrogen as an atomization and desolvation gas. The desolvation temperature was set at 300ºC. The relative amount of each component was determined from the LC-MS chromatogram, using the area normalization method. HPLC was recorded on a SHIMADZU LC-6AD using a chiral column (Chiralcel OD-H), and HPLC grade n-hexane and isopropanol as solvents.

2.2 Preparation of 1,3,5-tribromomesitylene (2)[32]

Mesitylene **1** (10 ml, 72.0 mmol), NBS (44.8 g, 252 mmol), a catalytic amount of benzoyl peroxide and CCl_4 (100 ml) were taken in a 150 ml RB flask. The reaction mixture was refluxed for about 6 hrs at 70ºC. After the completion of reaction time, the formed solid was removed by filtration at room temperature and the required filtrate was washed with water and extracted with DCM; the combined organic layer was washed with brine, dried over sodium sulphate and concentrated. The crude product was purified using column chromatography using 5% ethyl acetate and n-hexane as an eluent. Pale yellow solid, yield is 96%, m.p. 86–87ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.35 (s, 3H), 4.45 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 139.00, 129.55, 32.19.

2.3 Synthesis of mesitylene based CMPTCs (4)

A mixture of 1,3,5-tribromomesitylene **2** (0.1 g, 10 mmol), and cinchona derivatives **3** (0.30 g, 30 mmol) was dissolved in 5 ml of THF and heated to reflux overnight; the white solid was filtered, washed with diethylether and dried to get pure tri-site chiral PTC (86% yield of **4a** and 88% yield of **4b**).

2.3.1 Mesitylene based benzylcinchonine (4a)

^{1}H NMR (400 MHz, DMSO) δ_H 9.04 (d, *J* = 4.4 Hz, 3H), 8.45 (d, *J* = 8.5 Hz, 3H), 8.20 (d, *J* = 8.4 Hz, 3H), 8.01 (d, *J* = 8.8 Hz, 3H), 7.92 (t, *J* = 7.6 Hz, 3H), 7.87–7.78 (m, 6H), 7.62 (d, *J* = 7.5 Hz, 6H), 7.51 (t, *J* = 7.5 Hz, 6H), 7.41 (d, *J* = 7.4 Hz, 3H), 6.61 (s, 3H), 5.96 (ddd, *J* = 17.3 Hz, 10.3 Hz, 6.9 Hz, 6H), 5.20 (d, *J* = 12.8 Hz, 3H), 5.09 (d, *J* = 10.6 Hz, 3H), 4.94 (t, *J* = 14.4 Hz, 6H), 4.79 (d, *J* = 12.5 Hz, 3H), 4.65 (d, *J* = 11.8 Hz, 3H), 4.02 (s, 6H), 3.91 (d, *J* = 9.0 Hz, 3H), 3.81 (s, 3H), 3.69 (s, 3H), 3.10 (d, *J* = 7.7 Hz, 3H), 1.97 (s, 3H), 1.74 (dd, *J* = 20.6 Hz, 9.1 Hz, 6H), 1.35 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ_C 150.31, 148.04, 147.99, 142.08, 141.42, 138.51, 137.30, 136.96, 129.87, 129.72, 128.62, 128.49, 128.44, 128.37, 128.24, 128.10, 127.86, 127.69, 127.31, 125.15, 116.39, 70.27, 58.97, 48.37, 47.46, 36.55, 30.67, 26.50, 25.76. ESI-MS $(M)^{3+}$; 1510.67.

2.3.2 Mesitylene based allylcinchonine (4b)

^{1}H NMR (400 MHz, DMSO) δ_H 9.05 (d, *J* = 4.2 Hz, 3H), 8.49 (d, *J* = 8.5 Hz, 3H), 8.17 (d, *J* = 7.9 Hz, 3H), 7.94–7.89 (m, 3H), 7.86 (d, *J* = 7.9 Hz, 3H), 7.73 (d, *J* = 4.3 Hz, 3H), 6.53 (s, 3H), 6.35–6.26 (m, 3H), 6.02–5.95 (m, 3H), 5.55–5.45 (m, 6H), 5.34 (d, *J* = 9.8 Hz, 6H), 5.16 (d, *J* = 10.6 Hz, 6H), 4.86 (d, *J* = 12.2 Hz, 3H), 4.43 (dd, *J* = 12.8 Hz, 5.3 Hz, 3H), 4.02 (s, 12H), 3.76 (s, 3H), 3.21 (s, 3H), 1.96 (s, 3H), 1.76 (s, 12H), 1.24 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ_C 150.41, 150.16, 148.00, 140.70, 137.02, 134.25, 129.81, 129.67, 129.18, 127.69, 125.16, 124.08, 119.67, 118.15, 116.56, 72.90, 69.35, 67.48, 62.25, 55.79, 53.77, 36.10, 26.18, 22.30, 21.12. ESI-MS (M^{3+}); 1359.75.

2.4 General method for synthesis of chalcones (5a–h)[33]

Acetophenone or 4-bromoacetophenone (5 mmol) and aromatic aldehydes (5 mmol) were dissolved in 2 mL of ethanol and 10% sodium hydroxide was added, the mixture was stirred for 5 min. After completion of the reaction, the mixture was poured into ice; the precipitate was filtered and recrystallized with ethanol, to get pure chalcone.

2.5 General procedure for catalytic epoxidation of enones under CMPTCs conditions (6a-h)

To a mixture of enone **5** (10 mg 0.1 mmol), NaOCl (1 mmol) and CMPTCs **4** (**4a/4b,** 1 mol%) was dissolved in 1 ml solvents (like Toluene, DCM, $CHCl_3$, CCl_4, cyclohexane, xylene, benzene, THF) and added 0.5 ml of 5% aqueous bases (like NaOH, KOH, K_2CO_3, Na_2CO_3, Cs_2CO_3, Na^{t}BuO, K^{t}BuO) Then the reaction mixture was stirred for 2 hrs at room temperature (30ºC), after that the reaction mixture was extracted with ethyl acetate, washed with water (3 × 2 ml), then washed with brine solution (5 ml), dried over sodium sulphate and concentrated it. The crude product was purified by column chromatography on silica gel (ethyl acetate and petether [1:9] as an eluent), to afford the corresponding product **6**. The enantiomeric excess of epoxide **6** was determined by chiral stationary-phase HPLC analysis.

2.6 Characterization of epoxidation compounds (6a-h)

2.6.1 *trans*-(2*S*, 3*R*)-epoxy-3-(4-methylphenyl)-1-phenylproan-1-one (6a)

White solid; (98% yield). m.p. 69–71ºC; 99% ee's, determined by HPLC [Chiralcel OD-H, *n*-hexane /*i*-propanol = 85/15, 1mL/min, λ = 254 nm, t (major) = 2.921 min, t (minor) = 4.163 min]. ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.82 (d, *J* = 7.5 Hz, 2H), 7.44 (t, *J* = 7.3 Hz, 1H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.06 (d, *J* = 7.9 Hz, 2H), 6.96 (d, *J*= 7.9 Hz, 2H), 4.42 (d, *J* = 6 Hz, 1H), 4.33 (d, *J* = 6 Hz, 1H), 2.18 (s, 3H).^{13}C NMR (75 MHz, $CDCl_3$) δ_C 197.69, 137.37, 136.85, 136.63, 133.00, 129.09, 128.13, 128.06, 65.14, 58.22, 21.03.

2.6.2 *trans*-(2*S*, 3*R*)-epoxy-3-(4-methoxylphenyl)-1-phenylproan-1-one (6b)

Pale yellow solid; (98% yield). m.p. 81–82ºC; 99% ee's, determined by HPLC [Chiralcel OD-H, *n*-hexane /*i*-propanol = 85/15, 1mL/min, λ = 254 nm, t (major) = 2.785 min, t (minor) = 6.502 min]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.11 (d, *J* = 7.0 Hz, 2H), 7.75 – 7.66 (m, 3H), 7.61 (d, *J* = 7.5 Hz, 2H), 7.04 (d, *J* = 8.7 Hz, 2H), 4.42 (d, *J* = 6 Hz, 1H), 4.33 (d, *J* = 6 Hz, 1H), 2.39 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 197.69, 161.52, 144.51, 132.38, 130.06, 128.39, 128.24, 119.59, 114.26, 65.14, 58.22, 55.22.

2.6.3 *trans*-(2*S*, 3*R*)-epoxy-3-(4-chlorophenyl)-1-phenylproan-1-one (6c)

Yellow solid; (95% yield). m.p. 68–71ºC; 99% ee's, determined by HPLC [Chiralcel OD-H, *n*-hexane /*i*-propanol = 85/15, 1mL/min, λ = 254 nm, t (major) = 2.794 min, t (minor) = 8.829 min]. ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 8.03 (d, *J* = 7.0 Hz, 2H), 7.62 – 7.56 (m, 3H), 7.55 – 7.51 (m, 2H), 7.40 (d, *J* = 8.5 Hz, 2H), 4.42 (d, *J* = 6 Hz, 1H), 4.33 (d, *J* = 6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 197.69, 137.93, 133.30, 132.85, 129.51, 129.15, 128.59, 128.42, 65.14, 58.22.

2.6.4 *trans*-(2*S*, 3*R*)-epoxy-3-(4-nitrophenyl)-1-phenylproan-1-one (6d)

Yellow solid; (98% yield). m.p. 140–142ºC; 99% ee, determined by HPLC [Chiralcel OD-H, *n*-hexane /*i*-propanol = 85/15, 1mL/min, λ = 254 nm, t (major) = 3.316 min, t (minor) = 9.412 min]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.31 (d, *J* = 8.8 Hz, 2H), 7.82 (dd, *J* = 17.9, 11.1 Hz, 3H), 7.66 (dd, *J* = 11.4, 7.6 Hz, 2H), 7.60 – 7.51 (m, 2H), 4.42 (d, *J* = 6 Hz, 1H), 4.33 (d, *J* = 6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 197.69, 148.56, 141.05, 137.53, 133.38, 128.94, 128.83, 128.60, 124.22, 65.14, 58.22.

2.6.5 *trans*-(2*S*, 3*R*)-epoxy-1-(4-bromophenyl)-3-(4-methylphenyl)proan-1-one (6e)

White solid; (97% yield). m.p. 100–101ºC; 98% ee, determined by HPLC [Chiralcel OD-H, *n*-hexane /*i*-propanol = 85/15, 1mL/min, λ = 254 nm, t (major) = 2.865 min, t (minor) = 8.647 min]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.2 Hz, 2H), 7.67 – 7.57 (m, 4H), 6.94 (d, *J* = 8.6 Hz, 2H), 4.42 (d, *J* = 6 Hz, 1H), 4.33 (d, *J* = 6 Hz, 1H), 2.18 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 197.69, 161.87, 137.23, 131.85, 130.36, 129.96, 127.42, 118.98, 114.38, 65.14, 58.22, 21.03.

2.6.6 *trans*-(2*S*, 3*R*)-epoxy-1-(4-bromophenyl)-3-(4-methoxylphenyl)proan-1-one (6f)

Pale yellow solid; (96% yield). m.p. 81–82ºC; 98% ee, determined by HPLC [Chiralcel OD-H, *n*-hexane /*i*-propanol = 85/15, 1mL/min, λ = 254 nm, t (major) = 3.327 min, t (minor) = 8.631 min]. ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.88 (d, *J* = 8.5 Hz, 2H), 7.64 (d, *J* = 8.5 Hz, 2H), 7.54 (d, *J* = 8.1 Hz, 2H), 7.23 (d, *J* = 7.9 Hz, 2H), 4.42 (d, *J* = 6 Hz, 1H), 4.33 (d, *J* = 6 Hz, 1H), 2.39 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C =197.69, 145.41, 137.06, 131.84, 129.97, 129.72, 128.51, 127.66, 65.14, 58.22, 21.24.

2.6.7 *trans*-(2*S*, 3*R*)-epoxy-1-(4-bromophenyl)-3-(4-chlorophenyl)proan-1-one (6g)

White solid; (94% yield). m.p. 65–66ºC; 96% ee, determined by HPLC [Chiralcel OD-H, *n*-hexane /*i*-propanol = 85/15, 1mL/min, λ = 254 nm, t (major) = 3.215 min, t (minor) = 10.888 min]. ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.88 (d, *J* = 8.3 Hz, 2H), 7.64 (d, *J* = 6.9 Hz, 2H), 7.57 (d, *J* = 6.9 Hz, 2H), 7.40 (d, *J* = 8.7 Hz, 2H), 4.42 (d, *J* = 6 Hz, 1H), 4.33 (d, *J* = 6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C =197.69, 168.44, 167.81, 136.57, 133.07, 131.89, 129.92, 129.58, 129.20, 128.00, 65.14, 58.22.

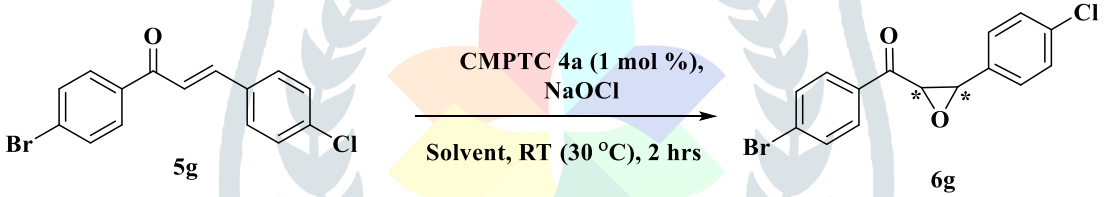
2.6.8 *trans*-(2*S*, 3*R*)-epoxy-1-(4-bromophenyl)-3-(4-nitrophenyl)proan-1-one (6h)

White solid; (97% yield). m.p. 130–132ºC; 99% ee, determined by HPLC [Chiralcel OD-H, *n*-hexane /*i*-propanol = 85/15, 1mL/min, λ = 254 nm, t (major) = 6.113 min, t (minor) = 17.080 min]. ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 8.30 (d, *J* = 8.7 Hz, 2H), 7.80 (d, *J* = 8.5 Hz, 2H), 7.69 (d, *J* = 8.5 Hz, 2H), 7.60 (d, *J* = 8.7 Hz, 2H), 4.42 (d, *J* = 6 Hz, 1H), 4.33 (d, *J* = 6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 197.69, 148.56, 141.05, 137.53, 133.38, 128.94, 128.83, 128.60, 124.22, 65.14, 58.22.

III. RESULTS AND DISCUSSION

First we focused our attention on finding an optimal reaction condition for the enantioselective epoxidation of chalcone **5g** in the presence of different solvents, bases and oxidant under room temperature.

Table 3.1 Effect of solvent on asymmetric epoxidation reaction



Entry	Solvent	Yield (%)[a]	% of ee[b]	Abs.Conf[c]
1	Benzene	57	66	2*S*, 3*R*
2	CCl_4	60	59	2*S*, 3*R*
3	$CHCl_3$	83	93	2*S*, 3*R*
4	Cyclohexane	55	63	2*S*, 3*R*
5	DCM	94	96	2*S*, 3*R*
6	THF	91	93	2*S*, 3*R*
7	Toluene	80	79	2*S*, 3*R*
8	Xylene	58	66	2*S*, 3*R*

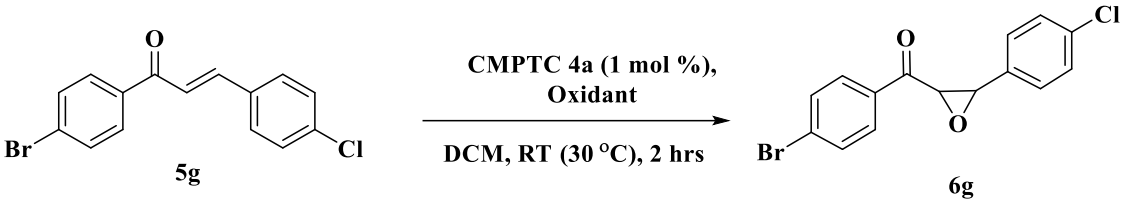
[a] Isolated yield.

[b] Enantiomeric excess of **6** was determined by HPLC analysis using a chiral column [Chiralcel OD-H] with hexane-IPA as an eluent.

[c] The absolute configuration of **6** was determined by comparison of the HPLC retention time with known data.[8]

The asymmetric epoxidation reaction was carried out in different solvents using CMPTC **4a** under room temperature. The obtained results (Table 3.1) show that, the change of solvent is found to be an important decisive factor in the epoxidation reaction due to their polarity, degree of solvation and dielectric constant of the solvents. The product yield and ee's have been found to decrease gradually, using polar to non polar solvents (enties 1–8, Table 3.1). In the case of toluene, cyclohexane and benzene they are nonpolar solvents, the degree of solvation of CMPTC is considerably less. Hence, the degree of decay due to solvation of CMPTC's of the catalyst is almost minimized. So, the interaction between $R_4N^+$of the catalyst and oxidant is more in polar solvents.[34] This is in turn improves the potential of the catalyst as well as effective attraction of the substrate and catalyst and hence the reaction yield and ee's are found to be higher in presence of DCM (entry 5, Table 3.1).

Table 3.2 Effect of oxidant on asymmetric epoxidation reaction

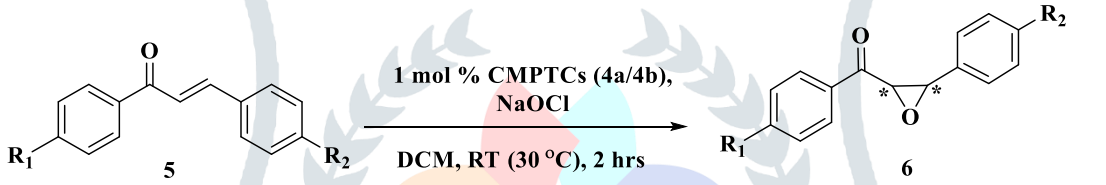


Entry	Oxidant	Yield (%)[a]	% of ee[b]	Abs.Conf[c]
1	APS[d]	55	38	2*S*, 3*R*
2	H_2O_2	79	63	2*S*, 3*R*
3	NaOCl	94	96	2*S*, 3*R*
4	Air	70	63	2*S*, 3*R*
5	PMS[e]	23	11	2*S*, 3*R*

[a] Isolated yield.
[b] Enantiomeric excess of **6** was determined by HPLC analysis using a chiral column [Chiralcel OD-H] with hexane-IPA as an eluent.
[c] The absolute configuration of **6** was determined by comparison of the HPLC retention time with known data.[8]
[d]APS – ammonium peroxysulphate, [e] PMS – potassium peroxy monosulphate

Furthermore, we carried out the optimization of oxidant for the enantioselective epoxidation of chalcone **5g** by using 1 mol% of the CMPTC **4a** along with different oxidant in DCM at room temperature. Further, we observed NaOCl gave higher chemical yield and ee's when compared the other oxidants such as H_2O_2, PMS, air and APS (entries 1-5, Table 3.2).

Table 3.3 Asymmetric epoxidation reaction of chalcone derivatives **5** under the optimized conditions.



R_1 = -H, -Br
R_2 = -CH_3, -OCH_3, -Cl, -NO_2

R_1 = -H, -Br
R_2 = -CH_3, -OCH_3, -Cl, -NO_2

Entry	Chalcone	R_1	R_2	Catalyst	Product	Yield (%)[a]	% of ee[b]	Abs.Conf[c]
1	5a	H	CH_3	4a	6a	98	98	2*S*, 3*R*
2	5a	H	CH_3	4b	6a	98	99	2*S*, 3*R*
3	5b	H	OCH_3	4a	6b	98	98	2*S*, 3*R*
4	5b	H	OCH_3	4b	6b	98	99	2*S*, 3*R*
5	5c	H	Cl	4a	6c	95	98	2*S*, 3*R*
6	5c	H	Cl	4b	6c	95	99	2*S*, 3*R*
7	5d	H	NO_2	4a	6d	98	99	2*S*, 3*R*
8	5d	H	NO_2	4b	6d	98	99	2*S*, 3*R*
9	5e	Br	CH_3	4a	6e	97	98	2*S*, 3*R*
10	5e	Br	CH_3	4b	6e	97	98	2*S*, 3*R*
11	5f	Br	OCH_3	4a	6f	96	98	2*S*, 3*R*
12	5f	Br	OCH_3	4b	6f	96	98	2*S*, 3*R*
13	5g	Br	Cl	4a	6g	94	96	2*S*, 3*R*
14	5g	Br	Cl	4b	6g	94	96	2*S*, 3*R*
15	5h	Br	NO_2	4a	6h	97	99	2*S*, 3*R*
16	5h	Br	NO_2	4b	6h	97	98	2*S*, 3*R*

[a] Isolated yield.
[b] Enantiomeric excess of **6** was determined by HPLC analysis using a chiral column [Chiralcel OD-H] with hexane-IPA as an eluent.
[c] The absolute configuration of **6** was determined by comparison of the HPLC retention time with known data.[8]

Further, the catalytic efficiency was studied via the epoxidation reaction of chalcones **5** under the optimized reaction conditions described above (1 mol% of the catalyst **4a** and **4b**, DCM, room temperature), are listed in Table 7.1.3. The observed results suggested that independent of the substitution on the aryl group of the chalcones, both the electron withdrawing and electron donating groups were present on the aryl groups which could not affect the product yields and ee's. We found an excellent product yield and higher enantiomeric excess (entries 1–16, Table 3.3). This may be due to the π–π stacking interaction between the benzyl

group of the tris-ammonium catalysts with the aryl group of the chalcone which further influenced the interaction between the enolated ions of the chalcone and the electron deficient sites of the R_4N^+ of the catalysts **(Figure 3.1)**.

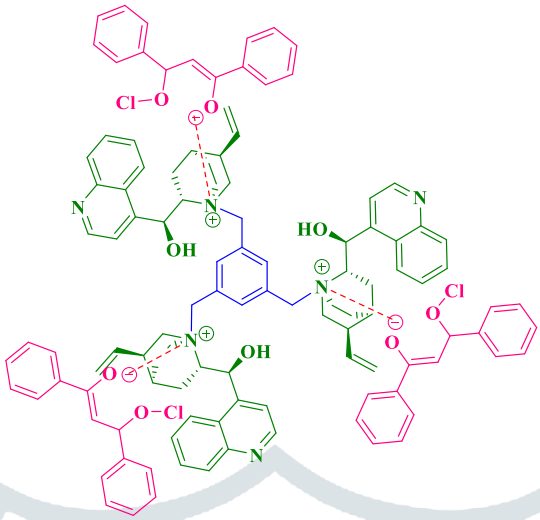


Figure 3.1. Possible formation of ion pair interaction between the enolated ions of the chalcone and R_4N^+ of catalyst.

IV. CONCLUSIONS

We have successfully synthesized and studied the catalytic efficiencies of mesitylene based tris-quaternary ammonium bromides via the epoxidation reaction of chalcones with very good chemical yields (upto 98%) and enantiomeric excess (upto 99%) at lower concentrations of base and catalysts under room temperature conditions.

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