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Ultrasonic Assisted Dimeric Cinchona based Chiral Phase Transfer Catalysts for Highly Enanatioselective Synthesis of Epoxidation of α, β–Unsaturated Ketones

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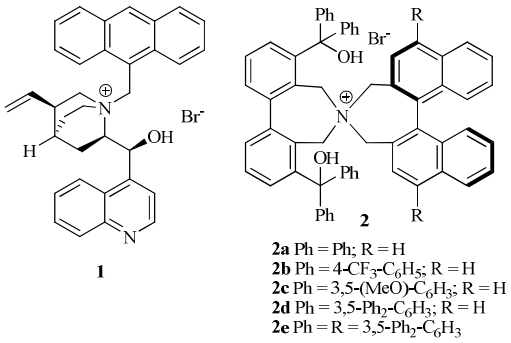
New types of bis-quaternary ammonium bromide as chiral multisite phase transfer catalysts derived from cinchona alkaloids have been developed and evaluated for the enantioselective epoxidation of chalcones in the presence of lower concentration of various oxidants, bases and ultrasonic irradiation condition. Under optimized conditions, excellent chemical yields of up to 98% along with the highest enantioselectivities of about 98% were obtained by using the reported catalysts.

1. Introduction

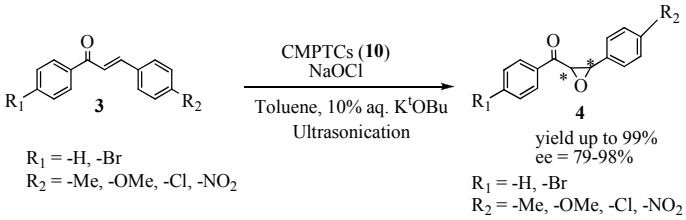
Enantioselective asymmetric epoxidation of electron deficient olefins, particularly α, β-unsaturated ketones such as chalcones, have been investigated and reported under bi functional chiral phase transfer catalysts.[1] The chiral phase transfer catalyst mediated reactions have unique features due to their simplicity and many advantages including non-metal containing compounds as well as environmental friendliness.[2] Recently Lygo et al.,[3] and Corey et al.,[4] have reported the 9-anthracenylmethyl group containing cinchona based chiral catalyst **1** with the commercially available 65% of sodium hypochlorite solution as an oxidant at -40°C for the effective epoxidation of chalcones with moderate yields and ee's. Further, Keiji Maruoka et al.,[5] reported the enantioselective epoxidation of chalcones with good yields and ee's in the presence of binapthyl based chiral catalysts **2** with 13% NaOCl at 0°C, but the reaction was carried out longer, i.e. 24-187 h. Even though there are numerous reports[6, 7] available for the enantioselective epoxidation of chalcones, their full potential is yet to be reached or explained in terms of both enantioselectivity and general applicability. Previously reported enantioselective epoxidation reactions were carried out at low temperature (-40°C – 0°C). Hence, we focused on the enantioselectivity and the chemical yield of epoxidation reactions (Scheme 1) using new types of bis-quaternary ammonium bromides as chiral multi-site phase transfer catalysts (CMPTCs **10**, Scheme 2) and ultrasonic irradiation effectively removing the need for temperature under mild reaction conditions. The chemicals such as catalysts, oxidants and bases are reduced with the substrate for simplifying the process in keeping with the basic principles of green chemistry.



1

2a Ph = Ph; R = H
2b Ph = 4-CF_3-C_6H_5; R = H
2c Ph = 3,5-(MeO)-C_6H_3; R = H
2d Ph = 3,5-Ph_2-C_6H_3; R = H
2e Ph = R = 3,5-Ph_2-C_6H_3

Fig. 1 Previously reported CPTCs.



Scheme 1 Enantioselective synthesis of chiral epoxidation of chalcones under CMPTC conditions.

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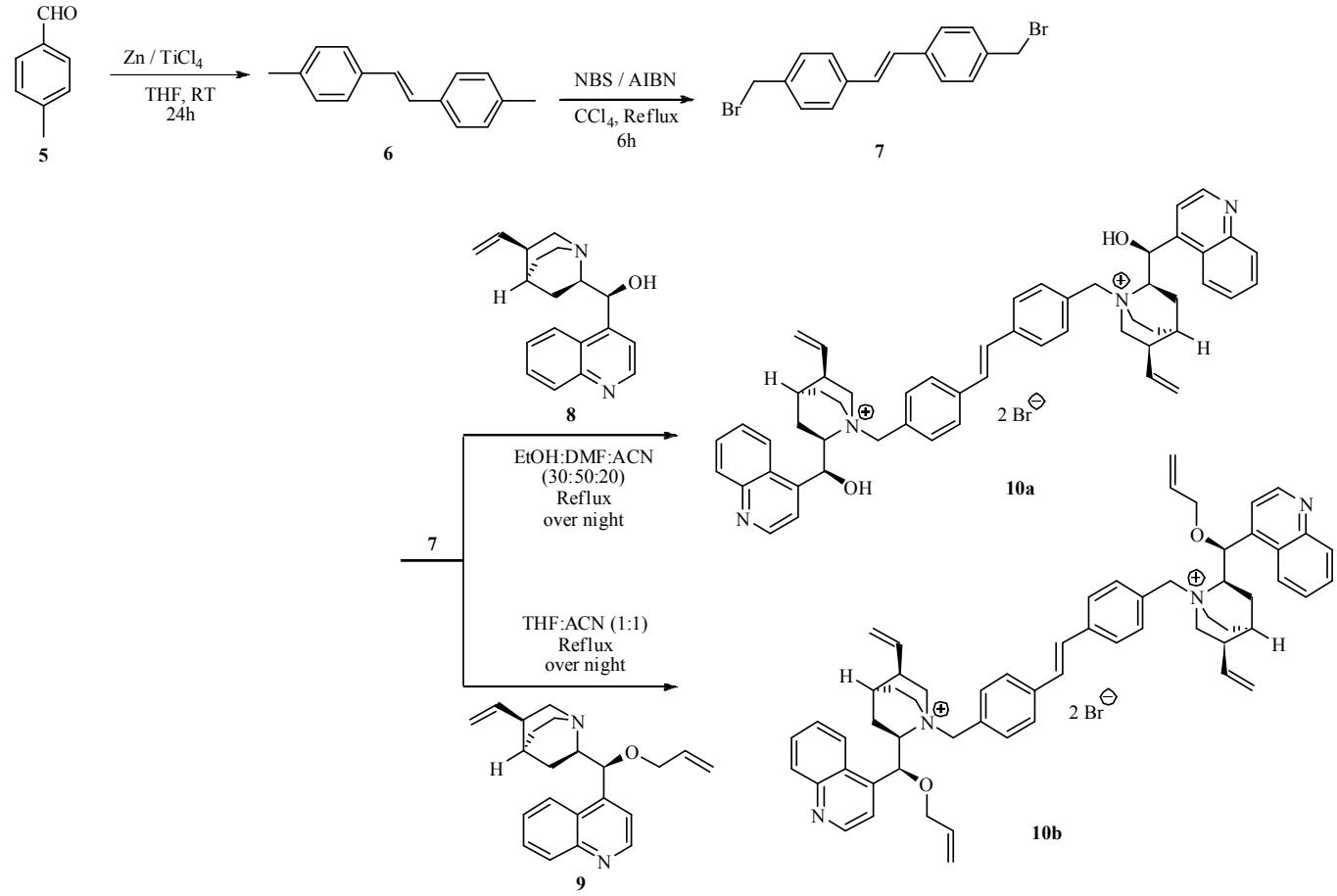
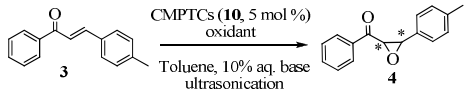


Scheme 2 Synthesis of bis quaternary ammonium ion as CMPTC for asymmetric epoxidation reaction.

2. Results and discussion

Asymmetric epoxidation serves as a versatile building block for the synthesis of metal free organic frameworks. The three-membered ring system containing epoxide is high ring strain intermediate, which is more useful for a variety of nucleophilic ring-opening reactions. Hence, we focused to optimize the reaction conditions. First, we focused our attention on finding optimal basic and oxidant conditions for the enantioselective epoxidation of chalcone in the presence of different bases under ultrasonic irradiation. It was found that (entries 1-24, Table 1), the maximum yields and ee's were obtained when K^tOBu was used as a base for the epoxidation reaction (entries 3 and 4, Table 1) rather than the other bases such as NaOH, KOH, K_2CO_3 and Cs_2CO_3. Further, we observed higher chemical yields (99%), and ee's (81%) for the epoxidation of chalcones in the presence of NaOCl as a oxidant with lesser time; i.e. less than 1 h and other oxidants such as H_2O_2, PMS, and APS used for this reaction gave good yields and moderate ee's. Stereoselectivity was not improved on changing the oxidants (entries 5-24, Table 1) nor by changing the base concentrations (entries 5-24, Table 1) for this reaction. Furthermore, we found from Table 1, that the dimeric catalyst **10a** showed a moderate yield (up to 98%) and enantiomeric excess (77-80%) in the presence of PMS, APS and H_2O_2 as oxidants (entries 5-8, Table 1), but the reaction times were somewhat higher (3-7 h). This may be due to the fact that longer reaction times would affect the epoxidation reaction rate which can reduce the yield and enantiomeric excess (entries 9-24, Table 1). The formation of higher chemical yields and ee's may be due to the interaction of oxidants (NaOCl) with the β carbon atom of chalcone from the upside direction in the 1, 4-addition to afford the configuration of *αS* and *βR* isomer **4**. The chalcone is located between the two cinchona units, either in **10a** or **10b** and the *β*-phenyl group of chalcone has a π-π stacking interaction with one of the quinoline moieties of the cinchona alkaloid and also the spacer chain of the stilbene aromatic group has π–π stacking interaction with the chalcone aromatic group (Figure 2). Similarly, the enolate anion of the carbonyl oxygen atom is placed as close to the R_4N^+ of the catalyst as possible due to van der Waals interactions (Figure 3). The formation of lower yields and ee's, when **10a** was used as a CMPTC, R_4N^+ of the catalyst is ion paired with the oxidant ion and also hydrogen bonded with the C_9 free –OH containing ammonium salt (**10a**).

Table 1 Effect of various bases, oxidants and CMPTCs (**10**) for enantioselective epoxidation reaction.

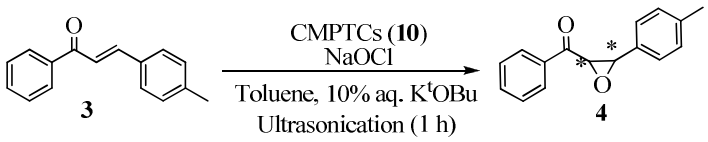


Entry	Base	Oxidant	Catalyst	Time (h)	Yield (%)[a]	% of ee[b] (Abs.Conf.)[c]
1	K^{t}OBu	H_2O_2	10a	3.0	95	73 (2*S*,3*R*)
2	K^{t}OBu	H_2O_2	10b	3.0	97	64 (2*S*,3*R*)
3	K^{t}OBu	NaOCl	10a	1.0	99	81 (2*S*,3*R*)
4	K^{t}OBu	NaOCl	10b	1.0	96	79 (2*S*,3*R*)
5	K^{t}OBu	PMS[d]	10a	3.5	98	78 (2*S*,3*R*)
6	K^{t}OBu	PMS[d]	10b	3.5	92	77 (2*S*,3*R*)
7	K^{t}OBu	APS[d]	10a	3.3	91	80 (2*S*,3*R*)
8	K^{t}OBu	APS[d]	10b	3.3	93	77 (2*S*,3*R*)
9	NaOH	H_2O_2	10a	3.5	94	73 (2*S*,3*R*)
10	NaOH	H_2O_2	10b	3.5	95	65 (2*S*,3*R*)
11	NaOH	NaOCl	10a	3.5	98	73 (2*S*,3*R*)
12	NaOH	NaOCl	10b	3.5	95	74 (2S,3R)
13	KOH	H_2O_2	10a	5.0	96	77 (2*S*,3*R*)
14	KOH	H_2O_2	10b	5.0	98	66 (2*S*,3*R*)
15	KOH	NaOCl	10a	5.0	95	72 (2*S*,3*R*)
16	KOH	NaOCl	10b	5.0	97	76 (2*S*,3*R*)
17	Cs_2CO_3	H_2O_2	10a	7.0	88	69 (2*S*,3*R*)
18	Cs_2CO_3	H_2O_2	10b	7.0	89	59 (2*S*,3*R*)
19	Cs_2CO_3	NaOCl	10a	7.0	91	67 (2*S*,3*R*)
20	Cs_2CO_3	NaOCl	10b	7.0	90	74 (2*S*,3*R*)
21	K_2CO_3	H_2O_2	10a	6.5	90	67 (2*S*,3*R*)
22	K_2CO_3	H_2O_2	10b	6.5	93	59 (2*S*,3*R*)
23	K_2CO_3	NaOCl	10a	6.5	98	78 (2*S*,3*R*)
24	K_2CO_3	NaOCl	10b	6.5	95	80 (2*S*,3*R*)

[a] Isolated yield of purified materials.
[b] Enantiomeric excess of **4** was determined by HPLC analysis using a chiral column (Phenomenex Chiralpack) with hexane-IPA as a solvent.
[c] The absolute configuration of **4** was determined to be (2*S*,3*R*) by comparison with the HPLC retention time using known standard.[8]
[d] PMS-Pottassium peroxy monosulphate, APS- Ammonium peroxysulphate.

With these optimized conditions, we then tested the epoxide reaction in the presence of different concentrations of catalysts **10** (Table 2). In general, all homogeneous catalysis reaction rates are directly proportional to the catalyst concentration. Based on the observed results, the catalyst amount was increased from 1 mol % to 15 mol % for the epoxidation reaction and the ee's reduced from 81% to 78% for **10a** and 84% to 79% for **10b** as catalysts respectively. This may be due to the catalyst poison taking place in this reaction irrespective of the catalysts **10a** and **10b** (entries 1-10, Table 2). Furthermore, the free C_9 –OH containing catalyst **10a** is more efficient than the allyl protected catalyst **10b** (entries 1-10, Table 2), because the free –OH containing the catalyst has more binding with the chalcone and oxidants. Similar reports were reported by Jew et. al., for the enantioselective epoxidation of chalcone in the presence of various cinchona based alkaloids as PTCs.[9]Generally, the enantioselective epoxidation reactions were not carried out with both the nucleophile and electrophile in the same phase. But, in our case, the epoxidation reaction is carried out in the presence of both the nucleophile and electrophile in the organic phase under phase-transfer reaction conditions, and also the reaction times were considerably less than the previously reported reaction.[7] Such fast enantioselective phase-transfer reactions may influence the chemical yields and the enantioselectivities.

Table 2 The asymmetric epoxidation of chalcone **3** under various concentration of CMPTCs **10** (**10a/ 10b**)



Entry	Catalyst	mol % of Catalyst	Time (min)	Yield (%)[a]	% of ee[b] (Abs.Conf.)[c]
1	10a	1.0	90	93	81 (2*S*,3*R*)
2	10a	3.0	75	95	81 (2*S*,3*R*)
3	10a	5.0	60	99	81 (2*S*,3*R*)
4	10a	10.0	45	96	79 (2*S*,3*R*)
5	10a	15.0	25	98	78 (2*S*,3*R*)
6	10b	1.0	90	95	84 (2*S*,3*R*)
7	10b	3.0	75	96	83 (2*S*,3*R*)
8	10b	5.0	60	96	79 (2*S*,3*R*)
9	10b	10.0	45	97	80 (2*S*,3*R*)
10	10b	15.0	25	98	79 (2*S*,3*R*)

[a] Isolated yield of purified materials.
[b] Enantiomeric excess of **4** was determined by HPLC analysis using a chiral column (Phenomenex Chiralpack) with hexane-IPA as a solvent.
[c] The absolute configuration of **4** was determined to be (2*S*,3*R*) by comparison of the HPLC retention time with known data. [8]

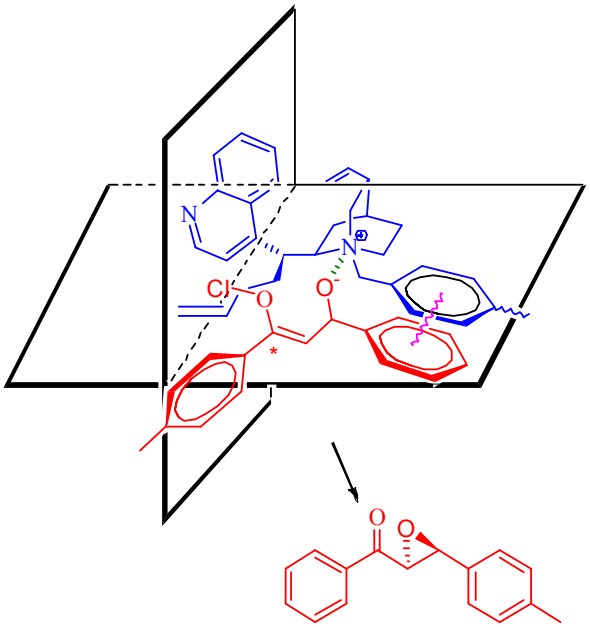


Fig. 2 Formation of π-π interaction between the spacer chain (aromatic) of all the CMPTCs with aromatic ring of the chalcones.

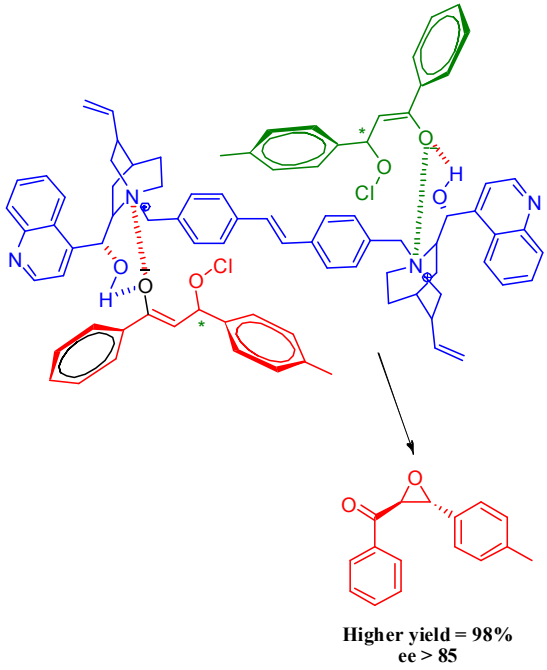
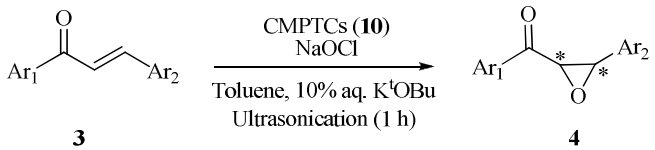


Fig. 3 C_2- symmetric *trans*-cinchona bis catalysts strong binding with the enolate anion of the chalcone and peroxides due to electrostatic attraction.

Table 3 Catalytic asymmetric epoxidation of chalcone derivatives **3** under CMPTCs conditions.



3 **4**

Entry	Enone (**3**)	Ar^1	Ar^2	Catalyst	Product[a]	Yield (%)[b]	% of ee[c]	Abs.conf.[d]
1	3a	Ph	4-Me-C_6H_4	10a	4a	99	81	(2*S*,3*R*)
2	3a	Ph	4-Me-C_6H_4	10b	4a	96	79	(2*S*,3*R*)
3	3b	Ph	4-OMe-C_6H_4	10a	4b	94	78	(2*S*,3*R*)
4	3b	Ph	4-OMe-C_6H_4	10b	4b	94	80	(2*S*,3*R*)
5	3c	Ph	4-Cl-C_6H_4	10a	4c	95	83	(2*S*,3*R*)
6	3c	Ph	4-Cl-C_6H_4	10b	4c	96	82	(2*S*,3*R*)
7	3d	Ph	4-NO_2-C_6H_4	10a	4d	97	93	(2*S*,3*R*)
8	3d	Ph	4-NO_2-C_6H_4	10b	4d	97	92	(2*S*,3*R*)
9	3e	4-Br- C_6H_4	4-Me-C_6H_4	10a	4e	95	78	(2*S*,3*R*)
10	3e	4-Br- C_6H_4	4-Me-C_6H_4	10b	4e	97	86	(2*S*,3*R*)
11	3f	4-Br- C_6H_4	4-OMe-C_6H_4	10a	4f	95	82	(2*S*,3*R*)
12	3f	4-Br- C_6H_4	4-OMe-C_6H_4	10b	4f	95	86	(2*S*,3*R*)
13	3g	4-Br- C_6H_4	4-Cl-C_6H_4	10a	4g	96	86	(2*S*,3*R*)
14	3g	4-Br- C_6H_4	4-Cl-C_6H_4	10b	4g	96	89	(2*S*,3*R*)
15	3h	4-Br- C_6H_4	4-NO_2-C_6H_4	10a	4h	98	98	(2*S*,3*R*)
16	3h	4-Br- C_6H_4	4-NO_2-C_6H_4	10b	4h	98	94	(2*S*,3*R*)

[a] The asymmetric epoxidation of chalcones **3** (0.1 mmol), NaOCl (1 mmol), CMPTCs **10** (**10a/10b**, 5 mol %), with 1 mL toluene and 0.5 mL of 10% K^{t}OBu in ultrasonic conditions.
[b] Isolated yield of purified materials.
[c] Enantiopurity of **4** was determined by HPLC analysis using a chiral column (Phenomenex Chiralpack) with hexane-IPA as a solvent.
[d] The absolute configuration of **4** was determined to be (2*S*,3*R*) by comparison of the HPLC retention time with known data.[8]

3. Conclusions

In summary, we have successfully synthesized bis-quaternary ammonium bromides as chiral phase transfer catalysts **10** for highly enantioselective epoxidation of various α, β-unsaturated ketones **3** under mild phase-transfer catalysis and ultrasonic irradiation conditions. In our system, the catalyst provides a ready to access wide range of useful synthetic transformations having higher chemical yields and enantiomeric purity. We believe that the new concept of the present synthetic design would be valid for the development of other enantioselective asymmetric phase-transfer reactions using the nucleophiles being supplied to an aqueous inorganic salt to prochiral electrophiles.

4. Experimental section

4.1. Materials and Methods

All the chemicals and reagents used in this work were of analytical grade. Allylbromide, (+)-Cinchonine were obtained from Alfa Aesar, 4-methylbezaldehyde, N-bromosuccinimide, Potassium *tert*-butoxide, Cesium carbonate and Potassium carbonate were obtained from Sigma Aldrich, Sodium hyroxide, Pottassium hydroxide, were obtained from Merck and all the Solvents were obtained from 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 a Bruker (Avance) 300 and 400 MHz NMR instrument using TMS as internal standard and $CDCl_3$ as a solvent. 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. Coloumn chromatography was carried out in silica gel (60-120 mesh) using n-hexane and ethyl acetate as an eluent. Electrospray Ionization Mass Spectrometry (ESI-MS) analyses were recorded in LCQ Fleet, Thermo Fisher Instruments Limited, US. ESI-MS was performed in positive ion mode. The collision voltage and ionization voltage were −70 V and −4.5 kV, respectively, using nitrogen as atomization and desolvation gas. The desolvation temperature was set at 300 ˚C. The relative amount of each component was determined from the LC-MS chromatogram, using the area normalization method. The HPLC were recorded in SHIMADZU LC-6AD with Chiral Column (Phenomenex Chiralpack), using HPLC grade n-hexane and isopropanol solvents.

4.2. Preparation of (*E*)-4, 4'-Dimethylstilbene (6)[10]

4-methylbenzaldehyde **5** (1 mmol), Zn (5 mmol) was dissolved in THF and the reaction mass was cooled to 0°C. Further, $TiCl_4$ (5 mmol) was added slowly into the reaction mass under Nitrogen atmosphere. Finally the reaction mixture was stirred at room temperature for about 24h, after completion of the starting material; the reaction mixture was poured into the saturated NH_4Cl solution and filtered through celite pad, extracted with ethyl acetate and washed with brine solution and concentrated it. The crude material was purified by column chromatography (n-hexane as an eluent). Yield is 96%.^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.41 (d, J = 8.1 Hz, 2H), 7.17 (d, J = 8.2 Hz, 2H), 7.05 (s, 1H), 2.36 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 137.18, 134.79, 129.30, 127.68, 126.28, 21.12.

4.3. Preparation of (*E*)-4, 4'-bis(bromomethyl)stilbene (7)[11]

The (*E*)-4, 4'-Dimethylstilbene **6** was brominated by NBS and CCl_4 in the presence of AIBN. After refluxing 6hrs, completion of starting material, the reaction mixture was quenched with water and extracted with ethyl acetate, washed with brine and dried over sodium sulphate. Concentrated it and purified by column chromatography (Pet. ether as eluent). Yield is 60%, m.p. 176–178°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.49 (d, J = 7.8 Hz, 2H), 7.43 (d, J = 8.1 Hz, 2H), 7.29 (s, 1H), 4.54 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 139.11, 138.44, 129.44, 128.33, 127.73, 32.72.

4.4. Preparation of *O*- Allylcinchonine (9)[12]

To the solution of (+)-Cinchonine **8** (3 g, 0.01mmol) in dried DMF was added NaH (0.61 g, 60% suspension in mineral oil, 0.025 mmol). The resulting mixture was stirred at room temperature for 2h. Then allylbromide (1.35 g, 0.01mmol) was added drop wisely in 5 minutes. The resulting mixture was stirred overnight. When the reaction was completed, brine (35 ml) was added carefully and the resulting mixture was extracted with ethyl acetate (3×20 ml), the organic phase was washed with brine (3×50 ml), dried over sodium sulphate, and concentrated in vacuo. The residue was purified by chromatography ($MeOH/CH_2Cl_2$: 1/10) to give a yellow oil (3.205 g, 87%yield).^{1}H NMR (300 MHz, $CDCl_3$) δ_H 8.88 (d, J = 4.4 Hz, 1H), 8.16 – 8.08 (m, 2H), 7.71 (dd, J = 8.2, 7.1 Hz, 1H), 7.59 – 7.53 (m, 1H), 7.48 (d,J = 4.3 Hz, 1H), 5.98 – 5.86 (m, 1H), 5.70 (dd, J = 12.0,

5.1 Hz, 1H), 5.22 (dd, *J* = 12.0, 5.1Hz, 3H), 4.96 (d, *J* = 10.0 Hz, 1H), 4.87 (d, *J* = 10.4 Hz, 1H), 3.97 – 3.91 (m, 1H), 3.87 – 3.80 (m, 1H), 3.40 (s, 1H), 3.07 (dd, *J* = 13.0, 10.3 Hz, 2H), 2.62 (d, *J* = 4.3 Hz, 1H), 2.24 (s, 1H), 1.78 (s, 1H), 1.51 (d, *J* = 10.0 Hz, 3H), 1.24 (s, 1H), 0.87 – 0.76 (m, 1H).^{13}C NMR (75 MHz, $CDCl_3$) δ_C 150.05, 148.40, 146.52, 141.80, 134.31, 130.35, 129.09, 126.72, 126.41, 123.10, 118.39, 116.89, 114.23, 70.08, 60.53, 57.01, 43.17, 39.93, 27.79, 22.03.

4.5. Synthesis of CMPTCs (10) from (*E*)-4, 4-bis(bromomethyl)stilbene (7)

4.5.1. Synthesis of Cinchonine (contains free C_9-OH) based CMPTC (10a)

A mixture of (*E*)-4, 4-bis(bromomethyl)stilbene **7** (0.1g, 10 mmol), *O*- Allylcinchonine **9** (30 mmol) was dissolved in 5 ml of THF:ACN (1:1 ratio) and was refluxed for overnight, the white solid was filtered off, washed with diethylether and dried it, to get pure di-site chiral PTC (**10a**). (95% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 8.90 (d, *J* = 4.2 Hz, 2H), 8.07 (d, *J* = 8.3 Hz, 2H), 7.97 (d, *J* = 4.7 Hz, 4H), 7.92 (s, 2H), 7.85 (d, *J* = 4.4 Hz, 2H), 7.80 (d, *J* = 7.9 Hz, 2H), 7.66 (dd, *J* = 19.1, 5.9 Hz, 4H), 7.61 (d, *J* = 8.4 Hz, 2H), 7.36 (s, 2H), 6.05 (s, 2H), 5.84 (dd, *J* = 17.5, 7.5 Hz, 2H), 5.58 (d, *J* = 11.9 Hz, 2H), 5.32 – 5.19 (m, 2H), 5.14 (s, 4H), 4.20 (s, 2H), 3.67 – 3.58 (m, 2H), 3.29 – 3.13 (m, 4H), 3.13 – 2.96 (m, 4H), 2.91 (d, *J* = 12.2 Hz, 2H), 1.83 (d, *J* = 18.1 Hz, 4H), 1.73 – 1.65 (m, 4H), 1.61 – 1.56 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 150.10, 149.41, 148.11, 147.81, 139.12, 134.67, 130.21, 129.83, 129.76, 129.00, 126.75, 125.30, 122.90, 119.58, 118.38, 115.65, 69.97, 59.99, 49.94, 49.10, 39.29, 27.83, 25.32, 21.78, 20.12. ESI-MS (M^{3+}); 954.74.

4.5.2. Synthesis of Allylated cinchonine based CMPTC (10b)

A mixture of (*E*)-4, 4'-bis(bromomethyl)stilbene **7** (0.1g, 10 mmol), *O*- Allylcinchonine **9** (30 mmol) was dissolved in 5 ml of EtOH:DMF:ACN (30:50:20 v/v) and heated to reflux for about overnight, the off white solid was filtered, washed with diethylether and dried it, to get pure di-site chiral PTC (**10b**). (96% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 8.92 (d, *J* = 3.4 Hz, 2H), 8.23 – 8.02 (m, 6H), 8.03 – 7.95 (m, 2H), 7.82 (d, *J* = 7.7 Hz, 4H), 7.73 (d, *J* = 6.3 Hz, 4H), 7.57 (d, *J* = 7.7 Hz, 2H), 7.49 (s, 2H), 6.27 – 5.99 (m, 4H), 5.96 – 5.82 (m, 2H), 5.39 (d, *J* = 17.8 Hz, 4H), 5.30 – 5.14 (m, 6H), 4.58 – 4.41 (m, 2H), 4.21 (s, 4H), 4.03 – 3.94 (m, 2H), 3.53 – 3.33 (m, 4H), 2.83 (d, *J* = 9.9 Hz, 2H), 2.42 (d, *J* = 10.9 Hz, 2H), 2.09 (s, 4H), 1.92 – 1.68 (m, 8H). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 149.77, 148.43, 142.43, 135.89, 134.97, 133.26, 132.49, 132.40, 130.33, 130.11, 129.91, 128.17, 125.39, 123.49, 119.93, 118.20, 117.87, 70.59, 70.45, 60.11, 49.33, 48.32, 37.01, 27.52, 22.98, 22.16, 18.47. ESI-MS (M^{3+}); 1034.93.

4.6. General method A for synthesis of chalcones (3a-h)[12, 13]

Acetophenone (5 mmol) and aromatic aldehyde (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.

4.6.1. Preparation of (*E*)–1–phenyl-3-*p*-tolylprop-2-en-1-one (3a).

Synthesized according to General method A using *p*-tolualdehyde (1.09 g, 5 mmol) and acetophenone (1 g, 5 mmol); white solid; (98% yield).m.p. 96-97 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 8.05 – 8.00 (d, *J* = 8.0 Hz, 2H), 7.80 (d, *J* = 15.7 Hz, 1H), 7.59 – 7.48 (m, 6H), 7.24 (d, *J* = 8.0 Hz, 2H), 2.40 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 190.32, 144.82, 141.05, 138.37, 132.71, 132.18, 129.75, 128.62, 128.52, 121.09, 121.0, 21.53.

4.6.2. Preparation of (*E*)-3-(4-methoxyphenyl)-1-phenylprop-2-en-1-one (3b).

Synthesized according to General method A using 4-methoxybenzaldehyde (1.11 g, 5 mmol) and acetophenone (1 g, 5 mmol); pale yellow solid; (98% yield)).m.p. 80-82 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (d, *J* = 7.0 Hz, 2H), 7.81 (d, *J* = 15.6 Hz, 1H), 7.65 – 7.57 (m, 3H), 7.51 (d, *J* = 7.3 Hz, 2H), 7.43 (d, *J* = 15.6 Hz, 1H), 6.95 (d, *J* = 8.7 Hz, 2H), 3.87 (s, 3H).^{13}C NMR (75 MHz, $CDCl_3$) δ_C 190.17, 161.33, 144.32, 138.14, 132.19, 129.87, 128.20, 128.05, 127.24, 119.40, 114.07, 54.56.

4.6.3. Preparation of (*E*)–3–(4-chlorophenyl)-1-phenylprop-2-en-1-one (3c).

Synthesized according to General method A using 4-chlorobenzaldehyde (1.17 g, 5 mmol) and acetophenone (1 g, 5 mmol); pale yellow solid; (98% yield)).m.p. 113-114 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 8.03 (d, *J* = 7.0 Hz, 2H), 7.77 (d, *J* = 15.7 Hz, 1H), 7.64 – 7.55 (m, 3H), 7.55 – 7.51 (m, 2H), 7.49 (d, *J* = 15.7 Hz, 1H), 7.40 (d, *J* = 8.5 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 190.07, 143.18, 137.93, 133.30, 132.85, 129.51, 129.15, 128.59, 128.42, 122.37.

4.6.4. Preparation of (*E*)-3-(4-nitrophenyl)-1-phenylprop-2-en-1-one (3d).

Synthesized according to General method A using 4-nitrobenzaldehyde (1.23 g, 5 mmol) and acetophenone (1 g, 5 mmol); orange solid; (98% yield)).m.p. 138-140 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.31 (d, *J* = 8.8 Hz, 2H), 8.06 (d, *J* = 8.4 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). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 189.66, 148.56, 141.51, 141.05, 137.53, 133.38, 128.94, 128.83, 128.60, 125.72, 124.22.

4.6.5. Preparation of (*E*)–1–(4-bromophenyl)-3-*p*-tolylprop-2-en-1-one (3e).

Synthesized according to General method A using 4-methylbenzaldehyde (0.66 g, 5 mmol) and 4-bromoacetophenone (1 g, 5 mmol); white solid; (98% yield)).m.p. 145-147ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.2 Hz, 2H), 7.81 (d, *J* = 15.6 Hz, 1H), 7.69 – 7.58 (m, 4H), 7.37 (d, *J* = 15.6 Hz, 1H), 6.96 (d, *J* = 8.6 Hz, 2H), 3.88 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 189.32, 161.87, 145.26, 137.23, 131.85, 130.36, 129.96, 127.61, 127.42, 118.98, 114.38, 21.53.

4.6.6. Preparation of (*E*)–1–(4-bromophenyl)-3-(4-methoxyphenyl) prop-2-en-1-one (3f).

Synthesized according to General method A using 4-methoxybenzaldehyde (0.75 g, 5 mmol) and 4-bromoacetophenone (1 g, 5 mmol); white solid; (98% yield)).m.p. 165-167 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.88 (d, *J* = 8.5 Hz, 2H), 7.80 (d, *J* = 15.7 Hz, 1H), 7.64 (d, *J* = 8.5 Hz, 2H), 7.54 (d, *J* = 8.1 Hz, 2H), 7.43 (d, *J* = 15.7 Hz, 1H), 7.23 (d, *J* = 7.9 Hz, 2H), 2.39 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 189.34, 145.41, 141.26, 137.06, 131.84, 129.95, 129.72, 128.54, 127.66, 120.52, 120.43, 21.10.

4.6.7. Preparation of (*E*)–1–(4-bromophenyl)-3-(4-chlorophenyl)prop-2-en-1-one (3g).

Synthesized according to General method A using 4-chlorobenzaldehyde (0.76 g, 5 mmol) and 4-bromoacetophenone (1 g, 5 mmol); white solid; (98% yield)).m.p. 164-168 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.88 (d, *J* = 6.9 Hz, 2H), 7.76 (d, *J* = 15.7 Hz, 1H), 7.65 (d, *J* = 8.3 Hz, 2H), 7.57 (d, *J* = 6.9 Hz, 2H), 7.48 (d, *J* = 15.7 Hz, 1H), 7.40 (d, *J* = 8.7 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 188.89, 143.74, 136.61, 136.57, 133.07, 131.89, 129.92, 129.58, 129.20, 121.69.

4.6.8. Preparation of (*E*)–1–(4-bromophenyl)-3-(4-nitrophenyl) prop-2-en-1-one (3h).

Synthesized according to General method A using 4-nitrobenzaldehyde (0.76 g, 5 mmol) and 4-bromoacetophenone (1 g, 5 mmol); orange solid; (98% yield)).m.p. 164-168 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.30 (d, *J* = 8.7 Hz, 2H), 7.90 (t, *J* = 9.5 Hz, 2H), 7.80 (d, *J* = 8.5 Hz, 3H), 7.69 (d, *J* = 8.5 Hz, 2H), 7.60 (d, *J* = 15.7 Hz, 2H).^{13}C NMR (75 MHz, $CDCl_3$) δ_C 189.66, 148.56, 141.51, 141.05, 137.53, 133.38, 128.94, 128.83, 128.60, 125.72, 124.22.

4.7. General procedure for catalytic epoxidation of enones under CMPTCs conditions (4a-h).

To a mixture of enone **4** (10 mg 0.1 mmol), NaOCl (1 mmol) and CMPTCs **10** (**10a/10b,** 5 mol%) was dissolved in 1 ml of toluene and added 0.5 ml of 10% aq. K^{t}OBu. Then the reaction mixture was ultra sonicated until chalcone disappeared (detected by TLC), after that the reaction mixture was extracted with ethyl acetate, washed with water (3× 2 ml). Further, the reaction mixture was washed with brine (5ml), dried over sodiumsulphate and concentrated it. The crude material was purified by column chromatography with petroleum ether and ethyl acetate as eluent gave the epoxidation

product. The enantiomeric excess was determined by chiral stationary-phase HPLC analysis.

4.7a. Characterization of Epoxidation Compounds (4a-h).

***trans*-(2*S*, 3*R*)-Epoxy-3-(4-methylphenyl)-1-phenylproan-1-one (4a)**. White solid, m.p. 69-71°C; ^{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. The enantiomeric excess was determined by HPLC, Phenomenex Chiralpack, 254 nm, hexane: IPA = 90:10, flow rate = 1 mL/min, retention time: 7.81 min (major), 19.29 min (minor).

***trans*-(2*S*, 3*R*)-Epoxy-3-(4-methoxylphenyl)-1-phenylproan-1-one (4b)**. Light yellow solid, m.p. = 81-82°C; ^{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. The enantiomeric excess was determined by HPLC, Phenomenex Chiralpack, 254 nm, hexane: IPA = 90:10, flow rate = 1 mL/min, retention time: 7.88 min (major), 37.12 min (minor).

***trans*-(2*S*, 3*R*)-Epoxy-3-(4-chlorophenyl)-1-phenylproan-1-one (4c)**. Yellow solid, m.p. = 68-71°C; ^{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. The enantiomeric excess was determined by HPLC, Phenomenex Chiralpack, 254 nm, hexane: IPA = 90:10, flow rate = 1 mL/min, retention time: 7.87 min (major), 20.11 min (minor).

***trans*-(2*S*, 3*R*)-Epoxy-3-(4-nitrophenyl)-1-phenylproan-1-one (4d).** Yellow solid m.p. = 140-142°C; ^{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. The enantiomeric excess was determined by HPLC, Phenomenex Chiralpack, 254 nm, hexane: IPA = 90:10, flow rate = 1 mL/min, retention time: 7.90 min (major), 61.97 min (minor).

***trans*-(2*S*, 3*R*)-Epoxy-1-(4-bromophenyl)-3-(4-methylphenyl)proan-1-one (4e).** White solid, m.p. 100-101°C; ^{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. The enantiomeric excess was determined by HPLC, Phenomenex Chiralpack, 254 nm, hexane: IPA = 90:10, flow rate = 1 mL/min, retention time: 7.89 min (major), 46.84 min (minor).

***trans*-(2*S*, 3*R*)-Epoxy-1-(4-bromophenyl)-3-(4-methoxylphenyl)proan-1-one (4f).** Light yellow solid, m.p. = 81-82°C; ^{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. The enantiomeric excess was determined by HPLC, Phenomenex Chiralpack, 254 nm, hexane: IPA = 90:10, flow rate = 1 mL/min, retention time: 7.88 min (major), 23.46 min (minor).

***trans*-(2*S*, 3*R*)-Epoxy-1-(4-bromophenyl)-3-(4-chlorophenyl)proan-1-one (4g).** White solid, m.p. 65-66°C; ^{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. The enantiomeric excess was determined by HPLC, Phenomenex Chiralpack, 254 nm, hexane: IPA = 90:10, flow rate = 1 mL/min, retention time: 7.91 min (major), 22.60 min (minor).

***trans*-(2*S*, 3*R*)-Epoxy-1-(4-bromophenyl)-3-(4-nitrophenyl)proan-1-one (4h).** White solid, m.p. 130-132°C; ^{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. The enantiomeric excess was determined by HPLC, Phenomenex Chiralpack, 254 nm, hexane: IPA = 90:10, flow rate = 1 mL/min, retention time: 7.91 min (major), 63.48 min (minor).

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Graphical Abstract

Ultrasonic Assisted Dimeric Cinchona based Chiral Phase Transfer Catalysts for Highly Enanatioselective Synthesis of Epoxidation of α, β-Unsaturated Ketones

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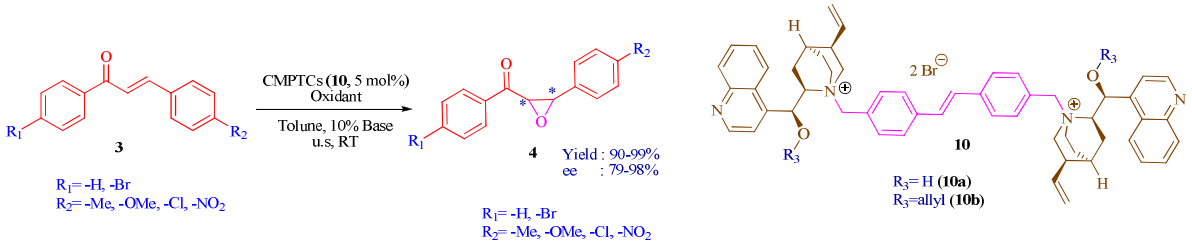

R_1= -H, -Br
R_2= -Me, -OMe, -Cl, $-NO_2$

R_1= -H, -Br
R_2= -Me, -OMe, -Cl, $-NO_2$

R_3= H **(10a)**
R_3=allyl **(10b)**