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One-pot synthesis of α,β-epoxy ketones through domino reaction between alkenes and aldehydes catalyzed by proline based chiral organocatalysts

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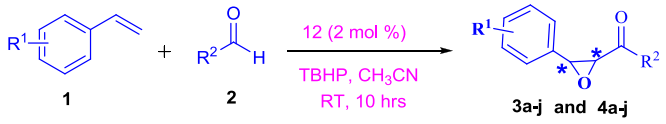
Abstract: A proline based metal free organocatalysts developed by new approach for the synthesis of epoxide derivatives through domino reaction. This domino reaction (oxidative coupling) allows the direct access to epoxides from various alkene and aldehyde through C–H functionalization and C–C/C–O bond formation. The catalytic efficiencies of the newly synthesized organocatalysts were also determined by domino reaction in presence of various functional groups containing aldehyde and alkene derivatives with very good yield (up to 95 %) and ee's (up to 99 %).

1. Introduction

α, *β*-Epoxy ketones are important intermediates and precursors in modern synthetic organic chemistry.[1] Further, they can be reliably functionalized to provide numerous products (e.g. pharmaceuticals, natural products, agricultural chemicals, fragrances, and inhibitors of cytosolic epoxide hydrolases) including *α*- and *β*-carbonyls, *α*, *β*-epoxy alcohols, 1,3-diols, etc.[2] In general, *α*, *β*-epoxy ketones can be prepared either by the Darzens reaction of *α*-halocarbonyl compounds with aldehydes under strong basic conditions[3] or epoxidation of *α*, *β*-unsaturated ketones, with various oxidants, catalyzed by different catalytic systems such as Lewis acids or phase-transfer catalysts.[4-10] An alternative method of oxidative coupling of aldehydes with styrenes catalyzed by base, with TBHP as an oxidant, has also been reported for its synthesis.[11] However, these methods were required either prefunctionalized starting materials, expensive metal catalysts, or often employ a large excess of aldehydes and oxidants (TBHP, H_2O_2) at high temperatures, thus resulting in low chemical yield and low atom economy of the process.[12]

Organocatalyzed reactions represented an attractive alternative method to metal-catalyzed processes, because of their low cost and benign environmental impact in comparison to organometallic catalysis. As organocatalysts, proline catalyst has a wide range of C–C, C–O, and C–N bond-forming reactions.[13] In addition, proline is an abundant chiral molecule that is inexpensive and bifunctional compound, such as carboxylic acid and amine portion. These two functional groups can act as an acid or base and can also facilitate the chemical transformations easily.[14] However, bifunctionalization of alkenes to different functional group such as aldehyde, alcohol, amine and peroxide is still a distinct challenge.[15,16] The catalyst design is important for enhancing enantiomeric excess, a C_3-symmetric proline catalyst has been found to be an excellent catalyst for domino reaction with higher reactivity and better asymmetric induction than the C_1-and C_2-symmetric catalyst. Herein, we wish to disclose a novel proline based organocatalyzed, metal-free and base free domino reaction (oxidative coupling) in presence of alkenes, aldehydes, and hydroperoxide to afford *α*, *β*-epoxy ketones with higher yield and excellent ee's under mild reaction conditions (Scheme 1). Our chiral organocatalysts itself act as a base as well as catalyst.

2. Results and discussion



R^1 = -H, 4-F, 4-Cl, 2-Cl, 4-Br, 3-Br, 2-Br, 4-NO_2, 4-OMe, 4-CH_3

R^2 = C_6H_5, 4-Cl-C_6H_4, 4-Br-C_6H_4, 4-OMe-C_6H_4, 3-OMe-C_6H_4, 2-OMe-C_6H_4, 4-CH_3-C_6H_4, 4-CF_3-C_6H_4, 4-C_2H_5-C_6H_4, C_5H_{11}

Scheme 1 Proline based organocatalytic domino reaction (oxidative coupling) of alkenes with aldehydes.

The scaffold 7 and 10, obtained from the modified procedure (Scheme 2).[17] Further, the proline based chiral C_3-symmetric organocatalysts (12a and 12b) synthesized by using compound 7 and 10 with chiral precursor proline, as depicted in (Scheme 2). The initial attempt an optimization of domino reaction, we carried out this reaction in different solvent condition, the product yields and ee's decreases gradually from polar to non-polar solvents (Table 1, entries 1-14).

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† Footnotes relating to the title and/or authors should appear here.
Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

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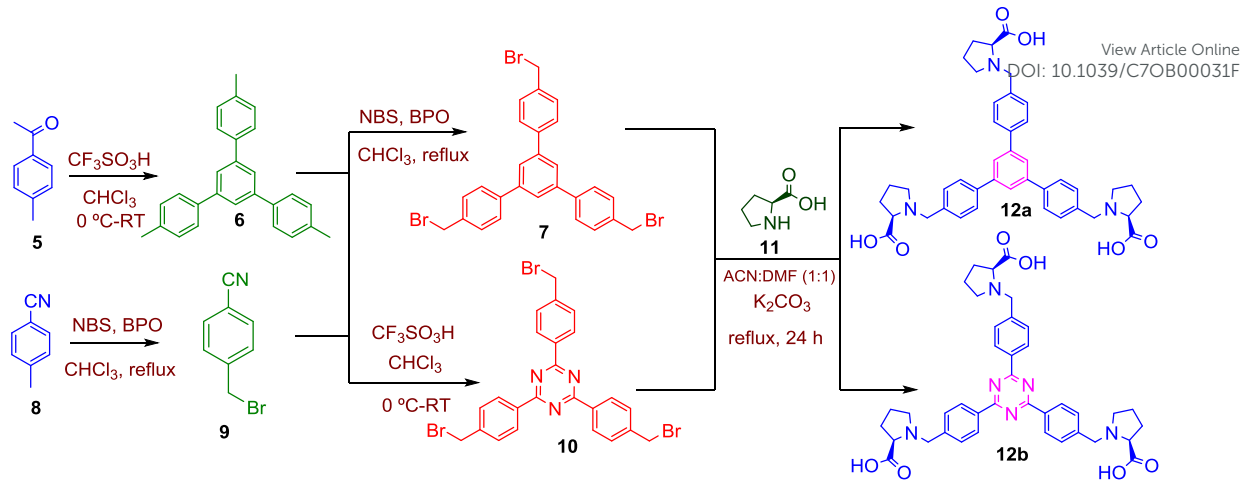
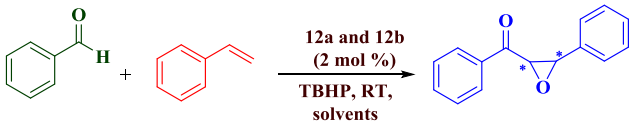


Scheme 2 Synthesis of proline based organocatalysts **12a** and **12b**.

Table 1 Effect of various solvents on domino reaction (oxidative coupling) between benzaldehyde and styrene.

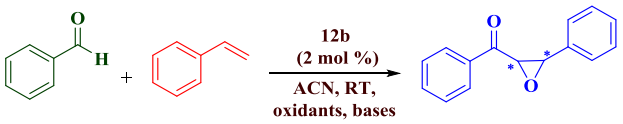


Ent.	Solvents	Cat.	Time (h)[a]	Yield (%)[b]	ee (%)[c]
1	Ethanol	**12a**	15	60	47
2	Ethanol	**12b**	15	65	59
3	1-butanol	**12a**	15	43	31
4	1-butanol	**12b**	15	51	41
5	Acetonitrile	**12a**	10	90	95
6	Acetonitrile	**12b**	10	95	99
7	DMSO	**12a**	10	85	89
8	DMSO	**12b**	10	90	92
9	THF	**12a**	10	78	79
10	THF	**12b**	10	85	86
11	Toluene	**12a**	24	Trace	-
12	Toluene	**12b**	24	Trace	-
13	Xylene	**12a**	24	n.r[e]	-
14	Xylene	**12b**	24	n.r[e]	-

[a] The domino reaction was carried out between the benzaldehyde (1 mmol), styrene (1 mmol), TBHP (2 equiv.) and solvents (2 mL) at room temperature with different time. [b] Isolated yield of purified material. [c] Enantiopurity was determined by HPLC analysis of epoxide product using a chiral column (Chiralcel OD-H) with hexane: IPA as an eluent. [d] Absolute configuration (2*R*,3*S*) was determined by comparison of the HPLC retention time using known literature data.[4-10] TBHP= *tert*-butyl hydrogen peroxide (70 % in water), [e] no reaction

The protic polar solvents such as ethanol and 1-butanol gave lower yields and ee's, due to hydrogen bonding solvents tending to decrease the reactivity of nucleophile (Table 1, entries 1-4). On the other hand, the aprotic polar solvents gave higher yields and ee's with lower reaction time (Table 1, entries 5-10). This may be due to the lack of hydrogen bonding in the solvent and the nucleophile is relatively "free" in solution, making them more reactive.

Table 2 Optimization of oxidants and bases for domino reaction (oxidative coupling) between benzaldehyde and styrene.



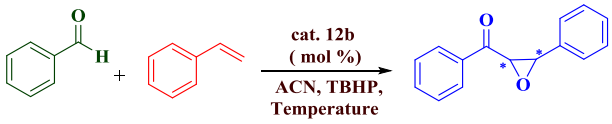
Ent.	Oxidant	Base	Time (h)[a]	Yield (%)[b]	ee (%)[c]
1	H_2O_2	K^{t}OBu	17	-	-
2	H_2O_2	TEA	17	20	31
3	H_2O_2	-	17	31	47
4	BQ	TEA	24	n.r[e]	-
5	BQ	-	24	Trace	-
6	APS	TEA	36	n.r[e]	-
7	APS	-	36	Trace	-
8	PMS	TEA	48	n.r[e]	-
9	PMS	-	48	Trace	-
10	TBHP	NaOH	10	-	-
11	TBHP	K^{t}OBu	10	-	-
12	TBHP	TEA	10	76	62
13	TBHP	Pyridine	10	57	41
14	TBHP	-	10	95	99

[a] The domino reaction was carried out between the benzaldehyde (1 mmol), styrene (1 mmol), oxidants (2 equiv.) and acetonitrile (2 mL) at room temperature with different time. [b] Isolated yield of purified material. [c] Enantiopurity was determined by HPLC analysis of epoxide product using a chiral column (Chiralcel OD-H) with hexane: IPA as an eluent. [d] Absolute configuration (2*R*,3*S*) was determined by comparison of the HPLC retention time using known literature data.[4-10] [e] no reaction. BQ = 1,4-benzoquinone, APS = ammonium peroxysulphate, PMS = potassium peroxy monosulphate.

Furthermore, these solvents do not participate in the reaction; they serve only as the reaction medium. Finally, in the presence of the non-polar solvents does not give any considerable effect in the reaction, even increased the reaction time to 24 hrs

(Table 1, entries 11-14), this may be due to the non-polar solvents have low dielectric constants (< 5) and hence reduce the binding ability of the organocatalysts. But, the enantiomeric excess as well as an excellent chemical yield was observed when the reaction was performed in acetonitrile as a solvent (Table 1, entry 5 and 6). Henceforth, we have chosen an acetonitrile as a suitable solvent for further investigations.

Table 3 Effect of temperature and concentration of catalyst on domino reaction (oxidative coupling) between benzaldehyde and styrene.



Ent.	Tempe-rature	mol % of cat.	Time (h)[a]	Yield (%)[b]	ee (%)[c]
1	65 °C	2	10	90	92
2	65 °C	5	10	86	89
3	65 °C	15	10	40	67
4	30 °C	2	10	95	99
5	30 °C	5	10	90	95
6	30 °C	15	10	48	80
7	0 °C	2	20	17	47
8	0 °C	5	20	15	31
9	0 °C	15	20	Trace	-
10	−10 °C	2	24	Trace	-
11	−10 °C	5	24	Trace	-
12	−10 °C	15	24	Trace	-

[a] The domino reaction was carried out between the benzaldehyde (1 mmol), styrene (1 mmol), TBHP (2 equiv.) and acetonitrile (2 mL) at various temperature with different time. [b] Isolated yield of purified material. [c] Enantiopurity was determined by HPLC analysis of epoxide product using a chiral column (Chiralcel OD-H) with hexane: IPA as an eluent. [d] Absolute configuration $(2R,3S)$ was determined by comparison of the HPLC retention time using known literature data.[4-10]

Further, we carried out the optimization of oxidants for the oxidative coupling of benzaldehyde and styrene by using 2 mol % of the organocatalyst 12a or 12b along with different oxidants in acetonitrile at room temperature. The reaction was carried out in the presence of H_2O_2 as an oxidant, we got our expected product with very low yield and ee's, obtained from more than 10 hrs (Table 2, entries 1-3). When using 1,4- benzoquinone, APS and PMS as oxidants in combination with the organocatalysts 12b in acetonitrile produced only a trace amount of desired product (Table 2, entries 4-9). In the presence of TBHP, the oxidative coupling reaction occured to give the corresponding product phenyl(3-phenyloxiran-2-yl)methanone with very good yields and ee's without adding any base (Table 2, entry 14). In addition to that, we investigated various inorganic and organic bases in the oxidative coupling reaction between the styrene and benzaldehyde. The α, β-epoxy ketones are not formed in the presence of strong bases like NaOH and K^{t}OBu (Table 2, entries1-14). This may be due to the formation of secondary product (i.e. cleavage of epoxide to diol formation) to the oxidative coupling reaction. Further, we selected TBHP as an oxidant and triethylamine as a base, we got better yield and poor enantioselectivity (Table 2, entry 12). Remarkably, without adding any base, we got a very good yield and ee's. This may be due to the presence of amine portion in the proline moiety of our organocatalysts which may act as a base to abstract the active hydrogen from the intermediate 19 (Scheme 3) to afford desired product. Hence, we conclude that, our organocatalyst itself acting as a base as well as catalyst.

From the obtained results (Table 3, entries 1-12), which shows that the concentration of the catalyst and temperature was affected the chemical yields and ee's of the desired product, it can be noted from the Table 3, the 2 mol % of the catalyst gave a higher chemical yields and excellent ee's when compared to others. This may be due to the catalyst poison may take place in this reaction irrespective of the organocatalyst 12b. Furthermore, the temperature of the reaction medium strongly affected the product yields and ee's. From the observed results, higher chemical yields and ee's were obtained at room temperature, when compared to other temperature conditions, i.e. 65 °C, 0 °C and -10 °C (Table 3, entries 1–12). In summary, from these investigations, the optimized reaction conditions are: concentration of organocatalysts (2 mol %), acetonitrile as a solvent, TBHP (2 equiv.) as an oxidant and room temperature. Furthermore, we carried out the oxidative coupling reaction between benzaldehyde and styrene by using C_1-, C_2-and C_3-symmetric proline based organocatalysts. From the observed results, we found that C_3-symmetric proline catalysts (12a and 12b) is more efficient catalyst than the C_1- and C_2-symmetric catalysts (Table S1, entries 1-4, See ESI). This may be due to the presence of multiactive sites in C_3-symmetric proline catalysts compared to others.

The scope of both alkenes and aldehydes was investigated at above mentioned optimized reaction conditions in the presence of organocatalysts 12a and 12b (Table 4 and Table 5). The results in Table 4 show that the oxidative coupling reaction of 4-methylbenzaldehyde successfully proceeded with either electron-withdrawing or electron-donating substituents on the styrene ring. The addition of an electron-withdrawing group at any position on the styrene ring allows the coupling reaction with 4-methylbenzaldehyde to form the desired product in high yields and ee's (Table 4, entries 1–7). The above results also show that the appropriate product is obtained with higher yield when styrene was used as a reactant (Table 4, entry 8). It is interesting to note that the use of a substrate having an electron-donating group such as methyl and methoxy group on the styrene ring resulted in a moderate yields and good ee's (Table 4, entries 9 and 10).

From the observed results of Table 5, it is evident that benzaldehyde with various substituents (such as -Cl, -Br, -CH_3, -OCH_3, -CH_2CH_3 and -CF_3) at the para position can react with styrene to form the desired products in high yields and ee's (Table 5, entries 1–4 and 7-9). Using 2- or 3-methoxyl benzaldehyde as reactants, the product yields obtained 43 % and 64 % respectively, and moderate ee's (Table 5, entries 5 and 6).

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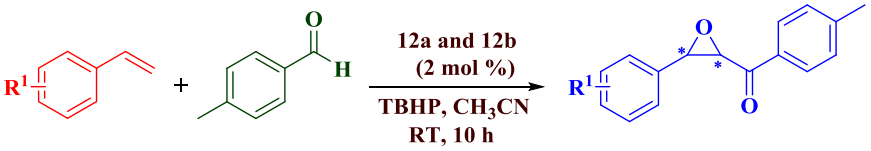
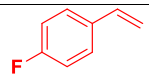
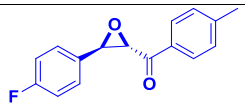
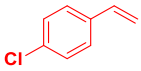
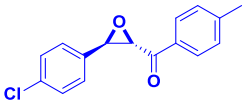
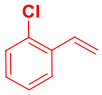
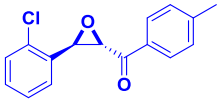
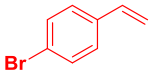
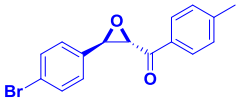
Table 4 Scope of styrene compounds.



Entry	Substrate[a]	Substrate code	Product	Product code	Catalyst	Yield (%)[b]	ee (%)[c]
1		**1a**		**3a**	**12a**	85	88
					12b	90	94
2		**1b**		**3b**	**12a**	83	87
					12b	92	95
3		**1c**		**3c**	**12a**	80	80
					12b	86	90
4		**1d**		**3d**	**12a**	90	91
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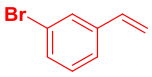
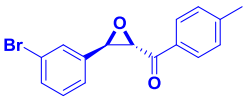
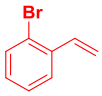
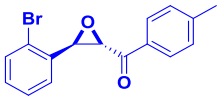
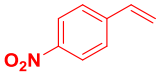
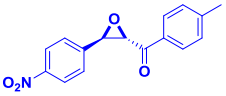
5		**1e**		**3e**	**12a**	80	83
					12b	87	93
6		**1f**		**3f**	**12a**	81	85
					12b	89	92
7		**1g**		**3g**	**12a**	84	90
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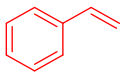
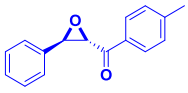
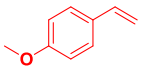
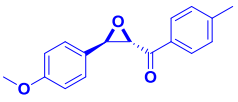
8		**1h**		**3h**	**12b**	90	87
					12a	95	95
9		**1i**		**3i**	**12b**	62	84
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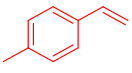
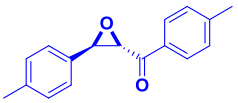
10		**1j**		**3j**	**12b**	60	86
					12a	72	91

[a] The domino reaction was carried out between the 4-methylbenzaldehyde (1 mmol), various styrene (1 mmol), TBHP (2 equiv.) and acetonitrile (2 mL) at room temperature. [b] Isolated yield of purified material. [c] Enantiopurity was determined by HPLC analysis of epoxide product using a chiral column (Chiralcel OD-H) with hexane: IPA as an eluent. [d] Absolute configuration ($2R,3S$) was determined by comparison of the HPLC retention time using known literature data.[4-10]

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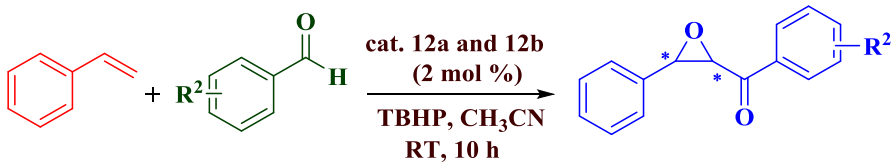
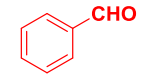
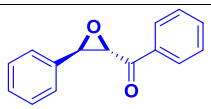
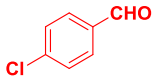
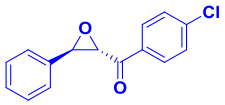
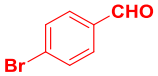
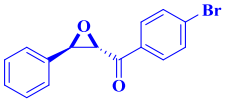
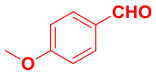
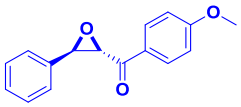
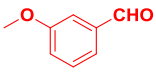
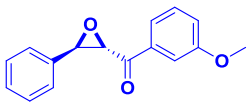
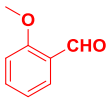
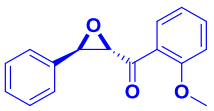
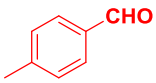
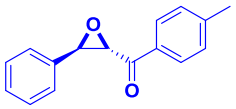
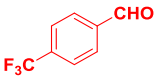
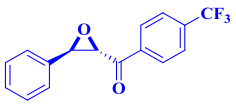
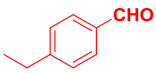
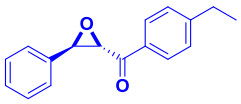
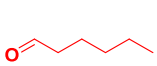
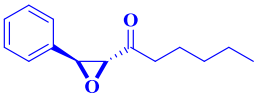
Table 5 Scope of aldehyde compounds.



Entry	Substrate[a]	Substrate code	Product	Product code	Catalyst	Yield (%)[b]	ee (%)[c]
1		**2a**		**4a**	**12a**	90	95
					12b	95	99
2		**2b**		**4b**	**12a**	89	92
					12b	94	98
3		**2c**		**4c**	**12a**	87	92
					12b	93	97
4		**2d**		**4d**	**12a**	85	86
					12b	90	92
5		**2e**		**4e**	**12a**	43	67
					12b	53	75
6		**2f**		**4f**	**14a**	52	60
					12b	64	73
7		**2g**		**4g**	**12a**	60	87
					12b	72	95
8		**2h**		**4h**	**12a**	87	82
					12b	91	93
9		**2i**		**4i**	**12a**	85	88
					12b	90	97
10		**2j**		**4j**	**12a**	37	65
					14b	44	71

[a] The domino reaction was carried out between various aldehydes (1 mmol), styrene (1 mmol), TBHP (2 equiv.) and Acetonitrile (2 mL) at room temperature.[b] Isolated yield of purified material. [c] Enantiopurity was determined by HPLC analysis of epoxide product using a chiral column (Chiralcel OD-H) with hexane: IPA as an eluent. [d] Absolute configuration was (2*R*,3*S*) determined by comparison of the HPLC retention time using known literature data.[4-10]

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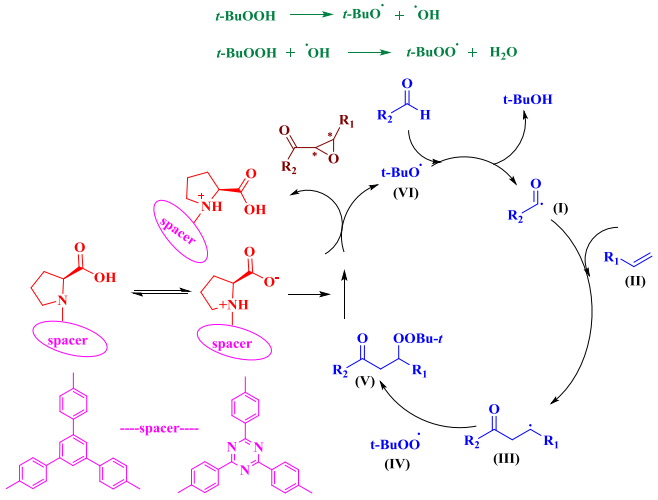
Compared to various aldehyde, the alkyl aldehyde (caproaldehyde) is less reactive, than the aryl aldehyde, due to generate a poor acyl radical which can reduce the product yields and ee's (Table 5, entry 10). Further, the results demonstrate that changing the para position of the aryl substituents of the aldehyde has an obvious influence on this oxidative coupling reaction. Among the newly synthesized organocatalysts 12b gave better yields and ee's than 12a. This may be due to the electron rich nitrogen present in the central core moiety of the chiral organocatalyst 12b. This is in very good agreement with the observed results. Therefore, this metal-free organocatalytic synthetic procedure can be successfully extended to a variety of styrene- and aldehyde-based substrates. The plausible mechanism of domino reaction followed by a radical mechanism (Scheme 3).[11] The butoxide radical (**VI**) abstract the proton from the aldehyde to form the acyl radical (**I**), then it is coupled with alkene (**II**) to form the intermediate (**III**) and (**V**) respectively. In this stage our chiral organocatalyst play a crucial role (acting as a base as well as catalyst), that is amine part of the proline moiety abstract the proton from the intermediate (**V**) to form the desired α, β-epoxy ketone and eliminate the butoxide radical (**VI**) which is used for another cycle.



Scheme 3 Probable catalytic cycle for domino reaction (oxidative coupling) of aldehydes with alkenes (styrenes)

3. Conclusions

In conclusion, first time we designed and synthesized a novel proline based organocatalysts, the catalytic efficiencies were successfully applied to one-pot synthetic procedure for the domino reaction (oxidative coupling) of alkenes with aldehydes, thus leading to a synthesis of the α, β-epoxy ketones in moderate to good yields with excellent ee's. The salient features of the methodology are: 1) metal and base-free synthesis, 2) milder reaction conditions, and 3) functional-group tolerance and excellent enantioselectivity. This work demonstrates a facile method for the synthesis of α, β-epoxy ketones and further investigation of this reaction is underway in our laboratory.

4. Experimental section

Materials and methods

All the chemicals and reagents used in this work were of analytical grade. 4-Methylacetophenone, 4-Methylbenzonitrile, trifluoroacetic acid, n-Bromosuccinamide, benzoyl peroxide, 1,4-Benzoquinone, Ammonium peroxysulphate, Potassium peroxy monosulphate were purchased from Alfe Aesar. L-Proline, *tert*-butyl hydroperoxide, 4-Fluorostyrene, 4-Chlorostyrene, 4-Bromostyrene, 3-Bromostyrene, 2-Bromostyrene, 4-Nitrostyrene, 4-Methylstyrene, Benzaldehyde, 4-Chlorobenzaldehyde, 4-bromobenzaldehyde, 2-Chlorobenzaldehyde, 4-Methoxybenzaldehyde, Styrene, 3-Methoxybenzaldehyde, 2-Methoxybenzaldehyde, 4-Methylbenzaldehyde, 4-Ethylbenzaldehyde, 4-(trifluoromethyl)benzaldehyde and Caproaldehyde were purchased from Sigma Aldrich. Potassium carbonate was purchased from Merck and all the solvents were obtained from laboratory grade. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker (Avance) 300 MHz and 400 MHz NMR instrument using TMS as an internal standard and $CDCl_3$ as a solvent. Standard Bruker software was used throughout. Chemical shifts were 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 and ethyl acetate as an eluent. The HPLC was recorded in SHIMADZU LC-6AD with Chiral column (Chiralcell OD-H), using HPLC grade *n*-hexane and isopropanol as mobile phase solvents. High Resolutin mass spectroscopic (HRMS) data were obtained using Bruker Apex IV RTMS. Optical rotations were measured on Rudolph Research Analytical AUTOPOL-II (readability ± 0.01°) and AUTOPOL-IV (readability ± 0.001°) automatic polarimeters.

Preparation of 1,3,5-tris(methylphenyl)benzene (6).

4-methylacetophenone **5** (2 g, 14.90 mmol) was added to trifluoromethane sulfonic acid (6 mL) in small portions at 0 °C. After the addition, the mixture was warmed to room temperature and stirred for about 24 h. After completion of reaction, the reaction mixture was quenched with a saturated NH_4OH aqueous solution, extracted with EtOAc, and dried with anhydrous Na_2SO_4. The crude product was purified by silica gel column chromatography (hexane/EtOAc) to get pure orange colour solid product **6** (4.25 g,

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yield 83 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 (s, 3H), 7.61 (d, *J* = 7.9 Hz, 6H), 7.30 (d, *J* = 8.0 Hz, 6H), 2.43 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 142.10, 138.34, 137.19, 129.48, 127.13, 124.51, 21.09.

Preparation of 1,3,5-tris(*p*-bromomethylphenyl)benzene (7).

A mixture of 1,3,5-tris(methylphenyl)benzene **6** (3 g, 8.60 mmol), NBS (4.6 g, 25.84 mmol) and benzoyl peroxide (50 mg) was refluxed in chloroform (70 mL) for about 24 h. After completion of the reaction, the solvent was evaporated under reduced pressure and then ethyl acetate and H_2O was added. The organic layer was extracted and washed with brine solution (3 x 75 mL), dried over sodium sulphate, and concentrated in vacuum, compound **7** was obtained as a yellow solid (4.10 g, yield 81 %).^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.70 (s, 3H), 7.55 (d, *J* = 7.9 Hz, 6H), 7.25 (d, *J* = 8.0 Hz, 6H), 4.56 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 142.29, 138.52, 137.38, 129.67, 127.31, 124.69, 33.37.

Preparation of *p*-cyanobenzylbromide (9).

A mixture of *p*-toluonitrile **8** (5 g, 42.68 mmol), NBS (7.6 g, 42.70 mmol) and benzoyl peroxide (50 mg) was refluxed in chloroform (100 mL) for about 24 h. After completion of the reaction, the solvent was evaporated under reduced pressure and then ethyl acetate and H_2O was added. The organic layer was extracted and washed with brine solution (3 x 75 ml), dried over sodium sulphate, and concentrated in vacuum, compound **9** was obtained as a white solid (7.7 g, yield 92 %). This product was used for the next step without any further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.64 (d, *J* = 8.2 Hz, 2H), 7.50 (d, *J* = 8.2 Hz, 2H), 4.47 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 142.86, 132.61, 129.74, 118.38, 112.21, 31.49.

Preparation of 2, 4, 6-Tris-(4-bromomethyl-phenyl)-[1, 3, 5]triazine (10).

p-Cyanobenzylbromide **9** (2.50 g, 12.8 mmol) was added to trifluoromethane sulfonic acid (3 mL) in small portions at 0 °C. After the addition, the mixture was warmed to room temperature and stirred for about 24 h, and then the reaction mixture was poured into ice, neutralized by ammonium hydroxide. The solid phase was collected by filtration. The white powder product was used for the next step without any further purification. (1.80 g, yield 72 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 8.72 (d, *J* = 8.3 Hz, 6H), 7.60 (d, *J* = 8.2 Hz, 6H), 4.59 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 142.86, 132.61, 129.74, 118.38, 112.21, 31.49.

Synthesis of proline based C_3-symmetric organocatalysts (12a).

A mixture of 1,3,5-tris(*p*-bromomethylphenyl)benzene **7** (0.5 g, 10 mmol), L-proline **11** (0.29 g, 30 mmol) was dissolved in 1: 1 ratio of DMF: ACN solvent mixture and heated to reflux for overnight. The reaction mass was poured into cold water the white solid was filtered, washed with diethylether and dried it, to get pure chiral multifunctional organocatalyst **12a** (1.0 g, yield 85 %). IR (KBr) cm^{-1}: 3415, 3340, 3020, 2604, 1705, 1585, 1356, 1210, 1162; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 12.36 (br, 3H), 8.05 (s, 3H), 7.46 (d, *J* = 8.1 Hz, 6H), 7.41 (d, *J* = 7.5 Hz, 6H), 3.69 (s, 6H), 3.21 (t, *J* = 6.9 Hz, 3H), 2.40-2.30 (m, 6H), 1.91-1.77 (m, 6H), 1.64-1.54 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 174.60, 139.50, 137.48, 129.50, 127.22, 126.11, 73.29, 62.18, 57.61, 29.11, 21.99; HRMS calculated for $C_{42}H_{45}N_3O_6$: 687.3308, found: 687.3309.

Synthesis of proline based triazine containing C_3-symmetric organocatalysts (12b).

A mixture of 2,4,6-tris-(4-bromomethyl-phenyl)-[1,3,5]triazine **10** (0.5 g, 10 mmol), L-proline **11** (0.29 g, 30 mmol) was dissolved in 1: 1 ratio of DMF: ACN solvent mixture and heated to reflux for overnight. The reaction mass was poured into cold water the white solid was filtered, washed with diethylether and dried it, to get pure chiral C_3-symmetric organocatalyst **12b** (1.02 g, yield 87 %). IR (KBr) cm^{-1}: 3396, 3320, 3012, 2140, 1725, 1695, 1585, 1340, 1150; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H12.38 (br, 3H), 8.06 (d, *J* = 11.3 Hz, 6H), 7.46 (d, *J* = 9.4 Hz, 6H), 3.57 (s, 6H), 3.21 (t, *J* = 8.0 Hz, 3H), 2.41-2.30 (m, 6H), 1.96-1.71 (m, 6H), 1.64-1.54 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 174.61, 171.58, 138.65, 133.43, 129.34, 125.51, 73.64, 62.08, 57.68, 29.70, 22.03; HRMS calculated for $C_{39}H_{42}N_6O_6$: 690.3166, found: 687.3167.

Synthesis of proline based triazine containing C_2-symmetric organocatalysts (12c).

A mixture of 2,4,6-tris-(4-bromomethyl-phenyl)-[1,3,5]triazine **10** (0.5 g, 10 mmol), L-proline **11** (0.19 g, 20 mmol) was dissolved in 1: 1 ratio of DMF: ACN solvent mixture and heated to reflux for overnight. The reaction mass was poured into cold water the white solid was filtered, washed with diethylether and dried it, to get pure chiral C_2-symmetric organocatalyst **12c** with 84 %. Yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ_H12.32 (br, 2H), 8.58 (d, *J* = 7.8 Hz, 6H), 7.43 (d, *J* = 8.01 Hz, 6H), 4.56 (s, 2H), 3.62 (s, 4H), 3.21 (t, *J* = 6.3 Hz, 2H), 2.40-2.30 (m, 4H), 1.95-1.70 (m, 4H), 1.64-1.56 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 174.22, 172.16, 171.04, 138.66, 138.11, 134.01, 132.13, 129.54, 129.33, 126.14, 125.44, 73.74, 62.17, 57.27, 33.32, 29.22, 22.01.

Synthesis of proline based triazine containing C_1-symmetric organocatalysts (12d).

A mixture of 2,4,6-tris-(4-bromomethyl-phenyl)-[1,3,5]triazine **10** (0.5 g, 10 mmol), L-proline **11** (0.09 g, 10 mmol) was dissolved in 1: 1 ratio of DMF: ACN solvent mixture and heated to reflux for overnight. The reaction mass was poured into cold water the white solid was filtered, washed with diethylether and dried it, to get pure chiral C_1-symmetric organocatalyst **12d** with 85 %. Yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ_H12.30 (br, 1H), 8.59 (d, *J* = 7.4 Hz, 6H), 7.46 (d, *J* = 6.4 Hz, 6H), 4.56 (s, 4H), 3.61 (s, 2H), 3.21 (t, *J* = 4.4 Hz, 1H), 2.40-2.31 (m, 2H), 1.96-1.71 (m, 2H), 1.64-1.57 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 173.24, 172.19, 171.06, 138.71, 138.20, 134.18, 132.13, 129.54, 129.38, 126.16, 125.53, 74.64, 62.40, 57.34, 33.48, 29.45, 22.14.

General procedure for domino reaction (oxidative coupling reaction).

The proline based organocatalyst 12a or 12b (0.1 mmol), acetonitrile (2 mL), TBHP (70 % in water, 2 equiv.), benzaldehyde (1 mmol) were taken into the round bottom flask. Further, a slow addition of styrene (1 mmol) is added to the reaction mixture. The mixture was stirred at room temperature for about 10 h. After that H_2O (5 mL) and CH_2Cl_2 (5 mL) were added, the phases were separated and the organic layer was washed with water (2 x 5 mL). The organic phase was subsequently evaporated under reduced pressure to give the crude product. The product was purified by

column chromatography on silica gel using petroleum ether/ethyl acetate as an eluent.

Characterization of α,β-epoxy ketones.

(3-(4-Fluorophenyl)oxiran-2-yl)(*p*-tolyl)methanone (3a). Yield 90 % ; ee 94 % ; $[\alpha]^{25}_{D}$ = +17.4 (c= 0.19, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.91 (d, *J* = 5.0 Hz, 2H), 7.38 – 7.32 (m, 2H), 7.29 (d, *J* = 5.0 Hz, 2H), 7.10 (t, *J* = 8.1 Hz, 2H), 4.24 (d, *J* = 1.1 Hz, 1H), 4.06 (d, *J* = 1.2 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 192.58, 164.26, 145.23, 133.84, 131.23, 129.42, 128.55, 127.41, 115.70, 115.42, 60.77, 58.69, 21.58. The enantiomeric excess was determined by HPLC, Chiralcel (OD-H), 254 nm, hexane: IPA 95: 5, flow rate: 1 mL min^{-1}, retention time: 20.16 min (major) and 46.15 min (minor). The absolute stereochemistry of the α,β-epoxy ketone was assigned as (2*R,* 3*S*) by comparison of the optical data with a known literatures reported value.[4-10]

(3-(4-Chlorophenyl)oxiran-2-yl)(*p*-tolyl)methanone (3b). Yield 92 % ; ee 95 % ; $[\alpha]^{25}_{D}$ = +19.2 (c= 0.21, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.82 (d, *J* = 6.8 Hz, 2H), 7.30 (d, *J* = 6.5 Hz, 2H), 7.23 (dd, *J* = 7.0, 3.1 Hz, 4H), 4.16 (d, *J* = 1.3 Hz, 1H), 3.98 (d, *J* = 1.2 Hz, 1H), 2.37 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 192.13, 145.32, 134.92, 134.34, 132.92, 129.57, 129.25, 128.73, 127.14, 60.80, 58.54, 21.84. The enantiomeric excess was determined by HPLC, Chiralcel (OD-H), 254 nm, hexane: IPA 95: 5, flow rate: 1 mL min^{-1}, retention time: 16.89 min (major) and 44.97 min (minor). The absolute stereochemistry of the α,β-epoxy ketone was assigned as (2*R,* 3*S*) by comparison of the optical data with a known literature reported value. [4-10]

(3-(2-Chlorophenyl)oxiran-2-yl)(*p*-tolyl)methanone (3c). Yield 86 % ; ee 90 % ; $[\alpha]^{25}_{D}$ = +24.1 (c= 0.12, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.96 (d, *J* = 6.2 Hz, 2H), 7.41 – 7.37 (m, 2H), 7.35 – 7.27 (m, 4H), 4.40 (d, *J* = 1.2 Hz, 1H), 4.15 (d, *J* = 1.3 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 192.27, 145.34, 133.96, 133.39, 132.97, 129.61, 129.37, 128.51, 127.28, 126.19, 60.01, 57.05, 21.78. The enantiomeric excess was determined by HPLC, Chiralcel (OD-H), 254 nm, hexane: IPA 95: 5, flow rate: 1 mL min^{-1}, retention time: 15.98 min (major) and 34.27 min (minor). The absolute stereochemistry of the α,β-epoxy ketone was assigned as (2*R,* 3*S*) by comparison of the optical data with a known literature reported value. [4-10]

(3-(4-Bromophenyl)oxiran-2-yl)(*p*-tolyl)methanone (3d). Yield 94 % ; ee 97 % ; $[\alpha]^{25}_{D}$ = +19.4 (c= 0.17, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.91 (d, *J* = 6.9 Hz, 2H), 7.54 (d, *J* = 6.0 Hz, 2H), 7.30 (d, *J* = 5.4 Hz, 2H), 7.23 (d, *J* = 5.4 Hz, 2H), 4.22 (d, *J* = 1.3 Hz, 1H), 4.04 (d, *J* = 1.2 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 192.34, 145.35, 134.53, 133.03, 131.96, 129.63, 128.49, 127.42, 123.10, 60.84, 58.66, 21.76. The enantiomeric excess was determined by HPLC, Chiralcel (OD-H), 254 nm, hexane: IPA 95: 5, flow rate: 1 mL min^{-1}, retention time: 11.98 min (major) and 20.20 min (minor). The absolute stereochemistry of the α,β-epoxy ketone was assigned as (2*R,* 3*S*) by comparison of the optical data with a known literature reported value. [4-10]

(3-(3-Bromophenyl)oxiran-2-yl)(*p*-tolyl)methanone (3e). Yield 84 % ; ee 93 % ; $[\alpha]^{25}_{D}$ = +27.1 (c= 0.24, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.91 (d, *J* = 5.0 Hz, 2H), 7.49 (dd, *J* = 6.9, 2.6 Hz, 2H), 7.34 – 7.27 (m, 4H), 4.24 (d, *J* = 1.6 Hz, 1H), 4.04 (d, *J* = 1.4 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 192.12, 145.40, 138.09, 132.96, 132.07, 130.32, 129.61, 128.57, 124.57,123.03, 60.77, 58.32, 21.79. The enantiomeric excess was determined by HPLC, Chiralcel (OD-H), 254 nm, hexane: IPA 95: 5, flow rate: 1 mL min^{-1}, retention time: 17.90 min (major) and 40.93 min (minor). The absolute stereochemistry of the α,β-epoxy ketone was assigned as (2*R,* 3*S*) by comparison of the optical data with a known literature reported value. [4-10]

(3-(2-Bromophenyl)oxiran-2-yl)(*p*-tolyl)methanone (3f). Yield 89 % ; ee 92 % ; $[\alpha]^{25}_{D}$ = +29.4 (c= 0.20, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.97 (d, *J* = 7.0 Hz, 2H), 7.56 (dd, *J* = 9.3, 1.0 Hz, 1H), 7.36 (dd, *J* = 9.4, 2.0 Hz, 2H), 7.28 (d, *J* = 8.7 Hz, 2H), 7.26 (s, 1H), 4.34 (d, *J* = 1.4 Hz, 1H), 4.15 (d, *J* = 1.4 Hz, 1H), 2.45 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 192.15, 145.17, 135.57, 132.71, 130.00, 129.57, 128.58, 128.03, 127.84, 126.52, 122.54, 60.05, 59.35, 21.85. The enantiomeric excess was determined by HPLC, Chiralcel (OD-H), 254 nm, hexane: IPA 95: 5, flow rate: 1 mL min^{-1}, retention time: 14.97 min (major) and 37.86 min (minor). The absolute stereochemistry of the α,β-epoxy ketone was assigned as (2*R,* 3*S*) by comparison of the optical data with a known literature reported value. [4-10]

(3-(4-Nitrophenyl)oxiran-2-yl)(*p*-tolyl)methanone (3g). Yield 93 % ; ee 98 % ; $[\alpha]^{25}_{D}$ = +34.1 (c= 0.15, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 8.17 (d, *J* = 5.4 Hz, 2H), 7.59-7.45 (m, 4H), 6.75 (d, *J* = 6.6 Hz, 2H), 4.42 (d, *J* = 1.2 Hz, 1H), 4.35 (d, *J* = 1.3 Hz, 1H), 2.39 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 192.59, 147.43, 142.66, 137.61, 129.30, 128.95, 128.73, 126.13, 123.83, 60.96, 59.42, 21.32. The enantiomeric excess was determined by HPLC, Chiralcel (OD-H), 254 nm, hexane: IPA 95: 5, flow rate: 1 mL min^{-1}, retention time: 26.71 min (major) and 34.93 min (minor). The absolute stereochemistry of the α,β-epoxy ketone was assigned as (2*R,* 3*S*) by comparison of the optical data with a known literature reported value. [4-10]

(3-Phenyloxiran-2-yl)(*p*-tolyl)methanone (3h). Yield 95 % ; ee 95 % ; $[\alpha]^{25}_{D}$ = +23.2 (c= 0.17, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.84 (d, *J* = 6.4 Hz, 2H), 7.36 – 7.27 (m, 5H), 7.20 (d, *J* = 6.2 Hz, 2H), 4.21 (d, *J* = 1.7 Hz, 1H), 3.99 (d, *J* = 1.9 Hz, 1H), 2.34 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 192.59, 147.43, 142.66, 137.61, 129.29, 128.95, 128.73, 126.13, 123.83, 60.96, 59.42, 21.32. The enantiomeric excess was determined by HPLC, Chiralcel (OD-H), 254 nm, hexane: IPA 95: 5, flow rate: 1 mL min^{-1}, retention time: 10.69 min (major) and 31.72 min (minor). The stereochemistry of the α,β-epoxy ketone was assigned as (2*R,* 3*S*) by comparison of the optical data with a known literature reported value. [4-10]

(3-(4-Methoxyphenyl)oxiran-2-yl)(*p*-tolyl)methanone (3i). Yield 73 % ; ee 91 % ; $[\alpha]^{25}_{D}$ = +21.4 (c= 0.12, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.41 (d, *J* = 6.0 Hz, 2H), 7.28 (d, *J* = 6.7 Hz, 2H), 6.89 (d, *J* = 6.9 Hz, 2H), 6.75 (d, *J* = 6.6 Hz, 2H), 4.42 (d, *J* = 1.8 Hz, 1H), 4.35 (d, *J* = 1.6 Hz, 1H), 3.82 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 192.19, 160.14, 142.84, 129.23, 128.91, 128.73, 127.85, 125.15, 114.18, 61.71, 59.43, 55.81, 21.30. The enantiomeric excess was determined by HPLC, Chiralcel (OD-H), 254 nm, hexane: IPA 95: 5, flow rate: 1 mL min^{-1}, retention time: 15.13 min (major) and 48.04 min (minor). The absolute stereochemistry of the α,β-epoxy ketone was assigned as (2*R,* 3*S*) by comparison of the optical data with a known literature reported value. [4-10]

***p*-Tolyl(3-*p*-tolyloxiran-2-yl)methanone (3j).** Yield 72 % ; ee 91 % ; $[\alpha]^{25}_{D}$ = +20.3 (c= 0.16, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.91 (d,

J = 7.8 Hz, 2H), 7.30 – 7.27 (m, 4H), 7.22 (d, *J* = 7.0 Hz, 2H), 4.28 (d, *J* = 1.4 Hz, 1H), 4.04 (d, *J* = 1.3 Hz, 1H), 2.42 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 192.65, 151.13, 135.67, 133.28, 128.92, 128.75, 128.63, 128.40, 125.80, 61.05, 59.27, 21.78, 21.27. The enantiomeric excess was determined by HPLC, Chiralcel (OD-H), 254 nm, hexane: IPA 95: 5, flow rate: 1 mL min^{-1}, retention time: 25.21 min (major) and 42.85 min (minor). The stereochemistry of the α,β-epoxy ketone was assigned as (2*R,* 3*S*) by comparison of the optical data with a known literature reported value. [4-10]

Phenyl(3-phenyloxiran-2-yl)methanone (4a). Yield 95 % ; ee 99 % ; [α] $^{25}_D$ = +31.4 (c= 0.17, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 8.01 (d, *J* = 4.0 Hz, 2H), 7.62 (t, *J* = 6.5 Hz, 1H), 7.49 (t, *J* = 8.5 Hz, 2H), 7.42 – 7.36 (m, 5H), 4.30 (d, *J* = 1.8 Hz, 1H), 4.08 (d, *J* = 1.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 193.11, 135.56, 133.96, 129.05, 128.89, 128.78, 128.39, 125.81, 61.01, 59.36. The enantiomeric excess was determined by HPLC, Chiralcel (OD-H), 254 nm, hexane: IPA 95: 5, flow rate: 1 mL min^{-1}, retention time: 20.45 min (major) and 40.33 min (minor). The stereochemistry of the α,β-epoxy ketone was assigned as (2*R,* 3*S*) by comparison of the optical data with a known literature reported value. [4-10]

(4-Chlorophenyl)(3-phenyloxiran-2-yl)methanone (4b). Yield 94 % ; ee 98 % ; [α] $^{25}_D$ = +34.2 (c= 0.19, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.97 (d, *J* = 7.0 Hz, 2H), 7.47 (d, *J* = 7.5 Hz, 2H), 7.40 – 7.33 (m, 5H), 4.23 (d, *J* = 1.1 Hz, 1H), 4.08 (d, *J* = 1.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 192.06, 104.65, 135.26, 133.70, 129.83, 129.27, 129.16, 128.80, 125.74, 61.06, 59.39. The enantiomeric excess was determined by HPLC, Chiralcel (OD-H), 254 nm, hexane: IPA 95: 5, flow rate: 1 mL min^{-1}, retention time: 12.10 min (major) and 32.64 min (minor). The absolute stereochemistry of the α,β-epoxy ketone was assigned as (2*R,* 3*S*) by comparison of the optical data with a known literature reported value. [4-10]

(4-Bromophenyl)(3-phenyloxiran-2-yl)methanone (4c). Yield 93 % ; ee 97 % ; [α] $^{25}_D$ = +39.1 (c= 0.21, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.90 (d, *J* = 6.7 Hz, 2H), 7.65 (d, *J* = 6.4 Hz, 2H), 7.44 – 7.38 (m, 3H), 7.34 (dt, *J* = 4.6, 2.1 Hz, 2H), 4.23 (d, *J* = 1.4 Hz, 1H), 4.07 (d, *J* = 1.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 192.42, 135.23, 134.13, 132.28, 129.86, 129.46, 129.21, 128.86, 125.79, 61.07, 59.42. The enantiomeric excess was determined by HPLC, Chiralcel (OD-H), 254 nm, hexane: IPA 95: 5, flow rate: 1 mL min^{-1}, retention time: 25.13 min (major) and 49.28 min (minor). The absolute stereochemistry of the α,β-epoxy ketone was assigned as (2*R,* 3*S*) by comparison of the optical data with a known literature reported value. [4-10]

(4-Methoxyphenyl)(3-phenyloxiran-2-yl)methanone (4d). Yield 90 % ; ee 92 % ; [α] $^{25}_D$ = +33.2 (c= 0.15, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 8.02 (d, *J* = 4.3 Hz, 2H), 7.44 – 7.33 (m, 5H), 6.95 (d, *J* = 6.3 Hz, 2H), 4.25 (d, *J* = 1.8 Hz, 1H), 4.07 (d, *J* = 1.9 Hz, 1H), 3.88 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 191.36, 164.34, 135.79, 130.76, 128.93, 128.73, 128.65, 125.80, 114.24, 60.88, 59.11, 55.54. The enantiomeric excess was determined by HPLC, Chiralcel (OD-H), 254 nm, hexane: IPA 95: 5, flow rate: 1 mL min^{-1}, retention time: 15.11 min (major) and 36.83 min (minor). The absolute stereochemistry of the α,β-epoxy ketone was assigned as (2*R,* 3*S*) by comparison of the optical data with a known literature reported value. [4-10]

(3-Methoxyphenyl)(3-phenyloxiran-2-yl)methanone (4e). Yield 64 % ; ee 75 % ; [α] $^{25}_D$ = +41.4 (c= 0.20, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.58 (d, *J* = 6.1 Hz, 1H), 7.53 (t, *J* = 4.8 Hz, 1H), 7.43 – 7.35 (m, 6H), 7.15 (dd, *J* = 5.4, 2.4 Hz, 1H), 4.28 (d, *J* = 1.4 Hz, 1H), 4.07 (d, *J* = 1.1 Hz, 1H), 3.84 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 192.93, 160.04, 136.83, 135.55, 129.85, 129.03, 128.76, 125.81, 121.00, 120.57, 61.05, 59.42, 55.46. The enantiomeric excess was determined by HPLC, Chiralcel (OD-H), 254 nm, hexane: IPA 95: 5, flow rate: 1 mL min^{-1}, retention time: 16.06 min (major) and 34.89 min (minor). The absolute stereochemistry of the α,β-epoxy ketone was assigned as (2*R,* 3*S*) by comparison of the optical data with a known literature reported value. [4-10]

(2-Methoxyphenyl)(3-phenyloxiran-2-yl)methanone (4f). Yield 52 % ; ee 73 % ; [α] $^{25}_D$ = +47.2 (c= 0.23, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.85 (dd, *J* = 5.4, 1.4 Hz, 1H), 7.57 – 7.49 (m, 1H), 7.44 – 7.33 (m, 5H), 7.05 (t, *J* = 4.0 Hz, 1H), 6.93 (d, *J* = 6.1 Hz, 1H), 4.31 (d, *J* = 1.0 Hz, 1H), 4.00 (d, *J* = 1.0 Hz, 1H), 3.57 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 194.88, 159.54, 136.55, 134.86, 130.76, 128.61, 128.52, 126.08, 125.83, 121.08, 111.56, 64.46, 59.76, 55.59. The enantiomeric excess was determined by HPLC, Chiralcel (OD-H), 254 nm, hexane: IPA 95: 5, flow rate: 1 mL min^{-1}, retention time: 22.86 min (major) and 42.40 min (minor). The absolute stereochemistry of the α,β-epoxy ketone was assigned as (2*R,* 3*S*) by comparison of the optical data with a known literature reported value. [4-10]

(3-Phenyloxiran-2-yl)(*p*-tolyl)methanone (4g). Yield 95 % ; ee 95 % ; [α] $^{25}_D$ = +23.2 (c= 0.17, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.84 (d, *J* = 6.4 Hz, 2H), 7.36 – 7.27 (m, 5H), 7.20 (d, *J* = 6.2 Hz, 2H), 4.21 (d, *J* = 1.7 Hz, 1H), 3.99 (d, *J* = 1.9 Hz, 1H), 2.34 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 192.59, 147.43, 142.66, 137.61, 129.29, 128.95, 128.73, 126.13, 123.83, 60.96, 59.42, 21.32. The enantiomeric excess was determined by HPLC, Chiralcel (OD-H), 254 nm, hexane: IPA 95: 5, flow rate: 1 mL min^{-1}, retention time: 10.69 min (major) and 31.72 min (minor). The stereochemistry of the α,β-epoxy ketone was assigned as (2*R,* 3*S*) by comparison of the optical data with a known literature reported value. [4-10]

(3-Phenyloxiran-2-yl)(4-(trifluoromethyl)phenyl)methanone (4h). Yield 91 % ; ee 93 % ; [α] $^{25}_D$ = +47.2 (c= 0.19, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 8.12 (d, *J* = 7.2 Hz, 2H), 7.76 (d, *J* = 7.2 Hz, 2H), 7.41 (d, *J* = 6.9 Hz, 3H), 7.39 – 7.34 (m, 2H), 4.26 (d, *J* = 1.3 Hz, 1H), 4.09 (d, *J* = 1.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 192.59, 137.93, 135.07, 129.32, 129.26, 128.91, 128.83, 125.80, 61.46, 59.65. The enantiomeric excess was determined by HPLC, Chiralcel (OD-H), 254 nm, hexane: IPA 95: 5, flow rate: 1 mL min^{-1}, retention time: 13.93 min (major) and 44.10 min (minor). The absolute stereochemistry of the α,β-epoxy ketone was assigned as (2*R,* 3*S*) by comparison of the optical data with a known literature reported value. [4-10]

(4-Ethylphenyl)(3-phenyloxiran-2-yl)methanone (4i). Yield 90 % ; ee 97 % ; [α] $^{25}_D$ = +44.3 (c= 0.21, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.94 (d, *J* = 6.0 Hz, 2H), 7.45 – 7.34 (m, 5H), 7.31 (d, *J* = 6.1 Hz, 2H), 4.28 (d, *J* = 1.4 Hz, 1H), 4.07 (d, *J* = 1.2 Hz, 1H), 2.72 (q, *J* = 8.6 Hz, 2H), 1.26 (t, *J* = 8.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 192.55, 151.42, 135.65, 133.26, 128.99, 128.72, 128.61, 128.41, 125.84, 61.05, 59.24, 29.07, 15.06. The enantiomeric excess was determined by HPLC, Chiralcel (OD-H), 254 nm, hexane: IPA 95: 5,

flow rate: 1 mL min^{-1}, retention time: 21.98 min (major) and 33.29 min (minor). The absolute stereochemistry of the α,β-epoxy ketone was assigned as (2*R,* 3*S*) by comparison of the optical data with a known literature reported value. [4-10]

1-(3-Phenyloxiran-2-yl)hexan-1-one (4j). Yield 44 % ; ee 71 % ; $[\alpha]_D^{25}$ = +61.4 (c= 0.24, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ_H 7.36 (s, 3H), 7.28 (d, *J* = 7.0 Hz, 2H), 3.97 (d, *J* = 1.0 Hz, 1H), 3.51 (d, *J* = 1.0 Hz, 1H), 2.61 – 2.39 (m, 2H), 1.69 – 1.60 (m, 2H), 1.31 (d, *J* = 2.7 Hz, 4H), 0.91 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 206.15, 136.26, 128.88, 128.68, 128.62, 125.75, 63.14, 58.07, 37.79, 31.33, 22.84, 22.45, 13.95. The enantiomeric excess was determined by HPLC, Chiralcel (OD-H), 254 nm, hexane: IPA 95: 5, flow rate: 1 mL min^{-1}, retention time: 20.63 min (major) and 40.76 min (minor). The absolute stereochemistry of the α,β-epoxy ketone was assigned as (2*R,* 3*S*) by comparison of the optical data with a known literature reported value. [4-10]

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