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A novel method for the synthesis of chiral epoxides from styrene derivatives using chiral acids in presence of *Pseudomonas* lipase G6 [PSL G6] and hydrogen peroxide

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Abstract—Chiral epoxidation of styrene and its derivatives was carried out using series of chiral acids and urea hydrogen peroxide (UHP) or aqueous hydrogen peroxide (50%) in two phases under the catalytic influence of immobilized *Pseudomonas* lipase G6 [PSL G6] at 25–55 °C. A moderate to good yield and enantioselectivities of chiral epoxides were obtained.

1. Introduction

Chiral epoxides, more particularly substituted styrene oxides, are extremely important building blocks for the synthesis of enantiomerically pure biologically active molecules as well as other molecules.[1,2] Catalytic asymmetric epoxidation of olefinic compounds for direct preparation of epoxides is a useful technique for the synthesis of chiral compounds. The ability to produce the desired organic compounds in enantiomerically pure form from simple and readily available precursors in presence of a catalytic amount of chiral compound with substrate/catalyst molar ratio of 1–10 or more has tremendous practical implications.[3] Ever since the development by Sharpless and others,[4–8] the reports of acid catalyzed epoxidation of olefinic compounds are scarce compared to base[9] and transition metal complex[3,10] catalyzed epoxidations. This may be due to the possible acid catalyzed ring opening of the product epoxide during the reaction course. However, in the current context of environment friendliness of a chemical process, use of reusable small organic molecule as catalyst is desirable to avoid the step of metal and other waste treatments[11] that may be necessary due to trace metal turning up in the production of commercially important molecules. Further, the problem of acid catalyzed epoxide ring opening associated with the reaction can be avoided by strategic manipulations of the reaction conditions. After the studies of epoxidation of olefins using vanadium complex with L-proline hydroxamic acid by Sharpless and Verhoeven[12] and Malkov and Bourhani,[13] not much attention was paid to this molecule for its catalytic activity in any of its simple forms. The success of L-proline[14,15] as catalyst in oxygen transfer reaction to organic compounds gave us an impetus to explore its new possible activity in chiral epoxidation reactions of olefins. It is reported[16] that certain lipases catalyze the reaction of acid and hydrogen peroxide in the formation of peroxy acid. In our earlier studies[17,18] on isolation of novel lipases from hydrocarbon bearing soils and their characteristic features, we observed certain properties of the *Pseudomonas* lipase G6 in the enhancement of enantioselectivity in the products formed from transesterification reaction. Having observed such properties in PSL G6, we wanted to study the role of this enzyme in chiral epoxidation of certain substituted styrenes in presence of a mild chiral acid and hydrogen peroxide.

With this aim, we carried out the study of chiral epoxidation of a few substituted styrenes with urea hydrogen peroxides (UHP) or 50% hydrogen peroxide in presence of a protected L-proline and few other chiral acids at an ambient temperature.

2. Results and discussions

2.1. Epoxidation studies

Four acids and one ester viz. *N*-2,4-dinitrophenyl-L-proline (**a**), *N*-benzyl-L-proline methyl ester (**b**), L-(+)-tartaric acid (**c**), (*S*)-(−)-2-chloropropionic acid (**d**) and (*S*)-(+)-2-methylbutyric acid (**e**) were taken to study as a carrier of oxygen in the epoxidation reaction. At this stage, we studied the reaction with only substituted styrene derivatives to observe the selectivity (Scheme 1). The reaction was first carried out by stirring one of the acids either with UHP or 50% hydrogen peroxide in presence of *Pseudomonas* lipase G6 in catalytic

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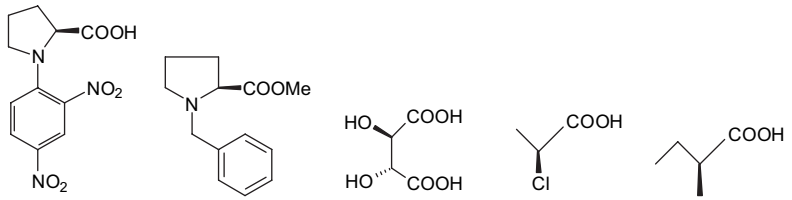
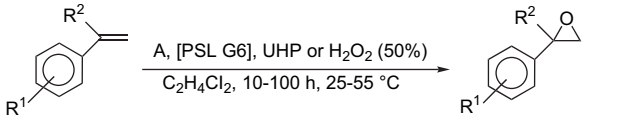


a **b** **c** **d** **e**

amount for about 2–3 h. Then the substrate styrene was added as a solution in dichloroethane and then stirred vigorously for several hours. Lipase catalyzes the formation of peroxy acid from the acid and hydrogen peroxide, which in turn transforms the styrene derivatives into the corresponding epoxide leaving behind the acid. The acid thus generated is again transformed into the corresponding peroxy acid by UHP or hydrogen peroxide in presence of lipase for further use in a catalytic cycle. The lipase and the chiral acid can be recycled in the subsequent reactions without any significant loss of catalytic activity. Among all these chiral acids and ester derivatives, *N*-2,4-dinitrophenyl-L-proline (**a**) shows the best results in affording good yields as well as enantioselectivity in the epoxidation of almost all the substrates (Table 1). The efficiency of the five chiral acids or esters showing good performance with respect to yield decreases in the order **a**>**c**>**d**>**b**>**e** and with respect to the enantioselectivity decreases in the order **a**>**b**>**c**>**d**>**e** excluding the substrate **3** and **10** in which the ee values decrease in the order **a**>**c**>**b**>**d**>**e**. We took the chiral acid (*S*)-(−)-2-chloropropionic acid (**d**) expecting that the electron withdrawing Cl group might help in the rapid formation of the respective peracid inside the reaction system and seemed to be the case as it is better than (*S*)-(+)-2-methylbutyric acid (**e**). Moreover, among all the substituted styrenes, α-methylstyrene and 4-methylstyrene (entries **11** and **12**, Table 1) did not produce any epoxide when the reaction was carried out in presence of (*S*)-(+)-2-methylbutyric acid (**e**) even after 100 h. Out of all the substrates, 3-nitrostyrene (entry **3**, Table 1) has been found to produce the highest yield (85%) and 2-nitrostyrene oxide (entry **2**, Table 1) has showed the highest enantiomeric excess (81%).



R^1 = H, 4-Cl, 3-Cl, 2-Cl, 4-Br, 3-Br, 2-Br, 4-NO_2, 3-NO_2, 2-NO_2, 4-Me

R^2 = H, CH_3 A= Chiral acids/ ester **a, b, c, d** and **e**

Scheme 1.

Styrene was readily transformed into (*S*)-styrene oxide (entry **1**, Table 1, 73% yield) accompanied by a small amount of benzaldehyde (2%) and phenylacetaldehyde (~0.8%) with '**a**'. It is to be noted that addition of extra amount of oxidant did not enhance the yield or produce new products.

2.2. Mechanistic studies

The mechanism for olefin epoxidation by peroxyacids was initially proposed by Bartlett.[19] Later, more evidence for this mechanism has been provided by a number of research groups[20] (Scheme 2). The mechanism demands the orientation of the peroxy acid in 'C' or 'U' shape with preferred *S*-cis conformation in the peroxy acid functionality to achieve chirality in the epoxide formed from the olefin.[8] Keeping this in mind, a systematic study of the formation of enantiomerically pure chiral epoxides from styrene derivatives was carried out in presence of 'C' or 'U' shaped *N*-2,4-dinitrophenyl-L-proline (**a**), *N*-benzyl-L-proline methyl ester (**b**), L-(+)-tartaric acid (**c**) and simple chiral acids (*S*)-(−)-2-chloropropionic acid (**d**) and (*S*)-(+)-2-methylbutyric acid (**e**).

Since the enantioselectivity of all the product epoxides in the case of the *N*-2,4-dinitrophenyl-L-proline (**a**) catalyzed reaction has been shown to be better (70–81%), the bulky *N*-2,4-dinitrophenyl group in the peroxy acid formed during the reaction course probably orient in such a way that oxygen transfer to the olefinic bond of styrene from the peroxy group is hindered in one side resulting in preferential insertion from the opposite side compared to the other acids.

2.3. Solvent effect

The catalytic epoxidation of styrene derivatives was studied in various solvents for better yield and selectivity (Table 2). Among all the solvents used, dry dichloroethane was observed to give the best results for the epoxidation of styrene derivatives. Slight improvement in conversion (60%) of 3-nitrostyrene to 3-nitrostyrene oxide was observed on changing the solvent system to hexane/water/sodium bicarbonate solution (entry **7**) at pH 9–10.

3. Conclusion

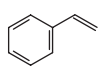
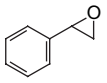
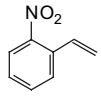
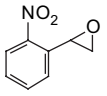
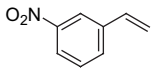
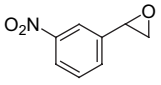
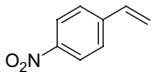
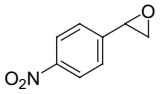
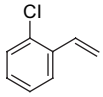
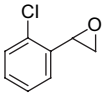
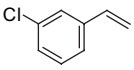
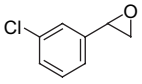
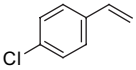
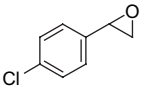
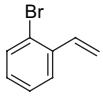
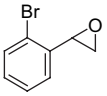
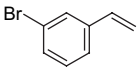
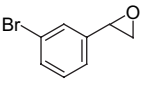
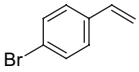
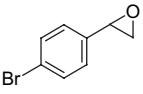
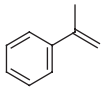
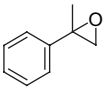
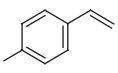
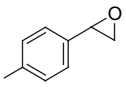
In conclusion, we have developed a convenient, cheap, recyclable and catalytic method for enantioselective epoxidation of substituted styrene using chiral acids or esters and UHP or H_2O_2 (50%) in presence of *Pseudomonas* lipase G6 under mild condition for the synthesis of chiral building block, which is used for the synthesis of biologically active compounds.

4. Experimental

4.1. General methods

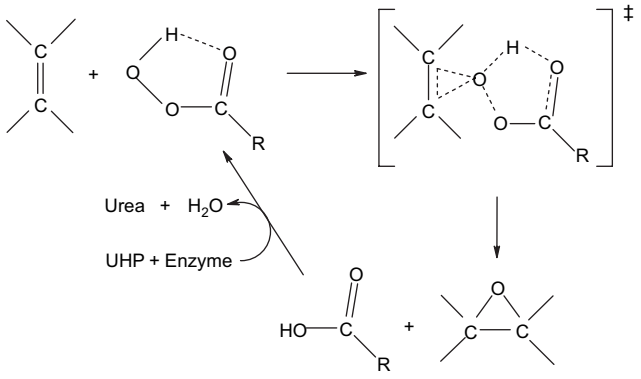
All the IR, ^1H and ^{13}C NMR and mass spectra were recorded on FTIR System-2000 PERKIN–ELMER, AVANCE-DPX-300 MHz FTNMR BRUKER standard and WATERS Micro-mass ZQ 4000 (ESI Probe) spectrometers, respectively. The chemical shifts are reported in parts per million relative

Table 1. Epoxidation of the styrene derivatives using UHP in presence of chiral acid and *Pseudomonas* lipase G6 in dry dichloroethane solvent

Entry	Alkene	Epoxide	Chiral acid used	Temperature (°C)	Time (h)	Yield[a] (%)	ee[b] (%)
1			**a**	25	15	73	75
			b	30	30	68	74
			c	25	17	71	73
			d	25	20	70	68
			e	50	50	20	—
2			**a**	25	14	80	81
			b	50	30	73	78
			c	40	15	78	75
			d	40	18	76	70
			e	55	90	28	—
3			**a**	25	10	85	76
			b	30	30	78	70
			c	25	15	82	75
			d	25	15	80	70
			e	50	90	30	—
4			**a**	25	12	77	80
			b	45	30	69	77
			c	30	15	75	76
			d	30	17	74	71
			e	50	90	25	—
5			**a**	25	15	79	77
			b	45	35	73	74
			c	40	20	76	72
			d	40	20	75	67
			e	55	90	26	—
6			**a**	25	17	65	75
			b	45	35	61	73
			c	40	20	63	71
			d	40	22	63	60
			e	55	90	12	—
7			**a**	25	15	76	80
			b	45	35	70	78
			c	40	18	75	75
			d	40	20	74	73
			e	55	90	15	—
8			**a**	30	15	69	75
			b	45	45	60	73
			c	40	18	67	70
			d	40	20	65	63
			e	55	100	10	—
9			**a**	30	18	63	73
			b	45	50	60	70
			c	40	20	62	70
			d	40	25	61	67
			e	55	100	5	—
10			**a**	30	15	71	78
			b	45	35	65	76
			c	40	20	70	77
			d	40	20	69	70
			e	55	90	13	—
11			**a**	40	40	55	78
			b	50	60	47	77
			c	40	45	51	71
			d	40	45	50	70
			e	55	100	—	—
12			**a**	40	20	60	70
			b	50	50	52	67
			c	45	25	55	63
			d	45	25	53	60
			e	55	100	—	—

[a] Crude yield determined by ^{1}H NMR (300 MHz).
[b] Determined from optical rotation data, HPLC and GC analyses.

to $CHCl_3$ (δ=7.26), CH_3COCH_3 (δ=2.17) for ^{1}H and relative to the central $CDCl_3$ resonance (δ=77.0), CD_3COCD_3 resonance (δ=30, 205) for ^{13}C NMR. Flash chromatography (FC) was carried out using Merck silica gel 60 (230–400 mesh). Optical rotation was measured on a Jasco Digital P-1020 polarimeter. The enantiomeric excess (ee) of the



Scheme 2.

Table 2. Effect of solvents on the epoxidation of 3-nitrostyrene using UHP or H_2O_2 (50%) in presence of *N*-2,4-dinirophenyl-L-proline and *Pseudomonas* lipase G6

Entry	Oxidant	Solvent	Conversion (%)
1	UHP	Dry dichloroethane	83
2	UHP	Dry dimethoxymethane	75
3	UHP	Dry tetrahydrofuran	60
4	UHP	Dry dimethylformamide	50
5	H_2O_2 (50%)	Hexane	50
6	H_2O_2 (50%)	Hexane/water (4:1)	40
7	H_2O_2 (50%)	Hexane/$NaHCO_3$/water	60
8	H_2O_2 (50%)	Ethanol	45
9	H_2O_2 (50%)	Ethanol/water (9:1)	55

products was determined by chiral HPLC using Chiralcel OD, Chiralcel OJ, Chiralpak AD, Chiralpak AS and Chiralpak OT columns with hexane/2-propanol as eluent and GC analysis using Chiraldex. G-PN column (Astec.), Chiraldex. G-TA column and CP-cyclodextrin-b-2,3,6-M-19 capillary column.

4.2. Materials

All the chemicals and dry solvents were purchased from Aldrich Chemicals and Acros Organics. The enzyme *Pseudomonas* lipase G6 [PSL G6] belongs to the Biotechnology Division of this laboratory. It was isolated from the soil sample[17] of petroleum hydrocarbon contaminated area of Borhola oil field, Assam, India and was immobilized in Sol–Gel-Ak following standard method.

4.3. General procedures for the preparation of chiral acid and ester

4.3.1. *N*-2,4-Dinitrophenyl-L-proline (a).[21] To a solution or suspension of L-proline (0.5 g, 4.35 mmol) in 10 mL of water and sodium hydrogen carbonate (1.0 g, 11.90 mmol), a solution of 1-fluoro-2,4-dinitrobenzene (0.8 g, 4.30 mmol) in 5 mL of ethanol was added. The reaction mixture was shaken vigorously and allowed to stand for 1 h with intermittent vigorous shaking. A 5 mL saturated solution of sodium chloride was added to it and extracted with ether (3×5 mL) to remove the unchanged reagent. The aqueous layer was then poured into 20 mL of cold 5% hydrochloric acid with vigorous agitation to make it acidic to congo red. The product precipitated was then collected by suction filtration and recrystallized from ethyl acetate to get 95% yield (1.15 g, yellow solid). Found: C, 46.8; H, 3.9; N, 14.6%. $C_{11}H_{11}O_6N_3$ requires: C, 47.0; H, 3.9; N, 14.9%. R_f (40% CH_2Cl_2/hexane) 0.25; $[\alpha]_D^{24}$ −103.52 (*c* 2.10, $CHCl_3$) {lit.[22] reported as molar rotation, $[M]_D^{24}$ −1978 (*c* 0.2, glacial CH_3COOH)}; δ_H (300 MHz, $CDCl_3$) 1.95 (2H, m, $CH_2CH_2CH_2$), 2.08 (2H, m, CH_2CH_2CHN), 3.54 (2H, t, *J* 2.1, CH_2CH_2N), 3.95 (1H, t, *J* 4.1, $CH_2CHCOOH$), 7.04 (1H, d, *J* 2.0, NCCHCH arom.), 8.12 (1H, d, *J* 2.0, $CHCHCNO_2$ arom.), 8.96 (1H, s, $O_2NCCHCNO_2$ arom.), 11.45 (1H, s, NCHCOOH); δ_C (300 MHz, $CDCl_3$) 27.4 (CH_2), 33.6 (CH_2), 54.8 (CH_2), 65.4 (NCH), 119.4 (CH arom.), 126.2 (CH arom.), 130.1 (CH arom.), 138.7 (CH arom.), 139.0 (CNO_2 arom.), 148.2 (CNO_2 arom.), 176.4 (COOH); IR (KBr) 1715, 1604, 1582, 1524, 1500, 1337 cm^{-1}.

4.3.2. *N*-Benzyl-L-proline methyl ester (b).[23] Benzyl chloride (6.25 mL, 55 mmol) was added to a stirred solution of L-proline (5 g, 43 mmol), 35 mL of water, 22 mL of 2 M NaOH, KI (110 mg, 0.65 mmol) and 1 M tetrabutylammonium hydroxide (0.45 mL, 0.4 mmol) under N_2, and the mixture was heated to 65 °C for 2 h. Excess of 2 M NaOH (6 mL) and benzyl chloride (2.2 mL, 19 mmol) were added, and after further reaction for 1 h the mixture was neutralized with ~6 mL of 1 M HCl to pH 7. Partial concentration in vacuo and addition of ethanol (50 mL) produced a solid, which was washed with 50 mL of ethanol; the washings were concentrated to afford 12.5 g of crude *N*-benzyl-L-proline (containing salts) as previously described, but without chromatography. Acetyl chloride (7.5 g, 95 mmol) was added dropwise to 25 mL of anhydrous methanol under N_2 at −10 °C followed by crude *N*-benzyl-L-proline (12.5 g) in 20 mL of anhydrous methanol, and the solution was heated at 50 °C for 18 h. After cooling to −10 °C, additional acetyl chloride (2.0 g, 25 mmol) was added dropwise, and the mixture was heated at 50 °C for 3 h. Partial concentration in vacuo, dilution with 100 mL of Et_2O at 0 °C, washing with 35 mL of 2 M NaOH (with further addition of 2 M NaOH until pH 12) and brine, drying ($MgSO_4$) and concentration yielded 7.15 g of *N*-benzyl-L-proline methyl ester as a yellow oil (65 mmol, 75% from (*R*)-(+)-proline). Found: C, 71.28; H, 7.79; N, 6.42%. $C_{13}H_{17}O_2N$ requires: C, 71.23; H, 7.76; N, 6.39%. R_f (40% CH_2Cl_2/hexane) 0.21; $[\alpha]_D^{24}$ +73.3 (*c* 2.15, $CHCl_3$) {lit.[23] $[\alpha]_D^{24}$ +73.8 (*c* 2.15, $CHCl_3$)}; δ_H (300 MHz, $CDCl_3$) 1.70–2.25 (4H, m, CH_2CH_2), 2.39 (1H, dd, *J* 16.5 and 8.3, $NCHCH_2$), 3.06 (1H, m, $NCHHCH_2$), 3.24 (1H, dd, *J* 8.6 and 6.3 , $NCHHCH_2$), 3.57 (1H, d, *J* 12.6, PhCHHN), 3.64 (3H, s, OCH_3), 3.88 (1H, d, *J* 12.6, PhCHHN), 7.35–7.25 (5H, m, 5×CH, arom.); IR (neat) 1748, 1733 cm^{-1}.

4.4. General procedure for epoxidation reaction

The standard epoxidation reaction was performed at room temperature by adding 0.5 g (3.35 mmol) of 3-nitrostyrene to a stirred mixture of catalytic amount of immobilized *Pseudomonas* lipase G6[17] (50 mg), 100 mg (0.36 mmol) of *N*-2,4-dinitrophenyl-L-proline (**a**) and 3 g (32 mmol) of UHP in 15 mL dry dichloroethane. The reaction was monitored by TLC and GC at regular intervals. It was observed that the reaction was complete in 10 h giving the maximum yield 85%. The reaction mixture was then filtered and

washed with water (3×20 mL) to remove urea. The enzyme lipase was washed further with a solvent mixture of acetonitrile/water (8:2) to recycle it at least for the next 3–4 reactions. The filtrate was extracted with ethyl acetate (3×20 mL) and neutralized with $NaHCO_3$ solution. Finally, the organic layer was concentrated in rotavapor and the crude product was purified by silica gel chromatography and identified using ^1H NMR, ^{13}C NMR, IR and mass spectral analysis and subjected to optical rotation and HPLC to measure the value of enantiomeric excess.

Similarly other chiral acids and esters were employed in the chiral epoxidation of styrene and its derivatives such as *N*-benzyl-L-proline methyl ester (**b**), L-(+)-tartaric acid (**c**), (*S*)-(−)-2-chloropropionic acid (**d**) and (*S*)-(+)-2-methylbutyric acid (**e**).

4.4.1. (*R*)-(+)-Phenyloxirane (1).[24] Yield 73%, oil. (Found: C, 79.91; H, 6.65. C_8H_8O requires: C, 79.97; H, 6.71%.) R_f (40% CH_2Cl_2/hexane) 0.55; $[\alpha]_D^{22}$ +33.67 (*c* 1.01, PhH) {lit.[24] $[\alpha]_D^{22}$ +44.8 (*c* 1.00, PhH), *R*}. The enantiomeric excess was determined by HPLC analysis using a Chiralcel OD column and showed it to be 75% ee [^{i}PrOH/hexane 0.2:99.8; flow rate 0.2 $cm^3\,min^{-1}$; t_R (*S*) 56.79 min and t_R (*R*) 60.99 min]; ν_{max} (neat/cm^{-1}) 1496, 1476, 1452, 1390; δ_H (300 MHz, $CDCl_3$) 2.81 (1H, dd, *J* 2.6 and 5.5, HCOC*H*H), 3.15 (1H, dd, *J* 4.1 and 5.5, HCOCH*H*), 3.87 (1H, dd, *J* 2.6 and 4.0, PhC*H*OCH_2), 7.26–7.36 (5H, m, 5×C*H*, arom.); δ_C (300 MHz, $CDCl_3$) 51.2 (CH_2), 52.4 (CH), 125.5, 128.2, 128.4 and 137.6 (6×C–Ph). MS *m*/*z* (rel intensity %): 122 (M+2, 15), 121 (M+1, 43), 120 (M^+, 20), 105 (100), 91 (68), 77 (88).

4.4.2. (*R*)-(−)-(2-Nitrophenyl)-oxirane (2).[25] Yield 80%, light yellow solid, mp 51–52 °C. (Found: C, 58.20; H, 4.28; N, 8.51. $C_8H_7NO_3$ requires: C, 58.18; H, 4.27; N, 8.48%.) R_f (25% EtOAc/hexane) 0.52; $[\alpha]_D^{19.5}$ −85.6 (*c* 1.50, $CHCl_3$) {lit.[25] $[\alpha]_D^{19.5}$ −107.2 (*c* 1.65, $CHCl_3$), *R*}. The enantiomeric excess was determined by HPLC analysis using Chiralcel OD column and showed it to be 81% ee (eluent at *V*=0.8 $mLmin^{-1}$, hexane/2-propanol 9:1); ν_{max} (neat/cm^{-1}) 3150, 2997, 1532, 1353, 1254, 899, 859, 809, 737, 684; δ_H (300 MHz, $CDCl_3$) 2.67 (1H, dd, *J* 2.5 and 5.4, HCOC*H*H), 3.30 (1H, dd, *J* 4.2 and 5.4, HCOCH*H*), 4.48 (1H, dd, *J* 2.5 and 4.2, PhC*H*OCH_2), 7.41–7.56 (1H, m, 1×C*H*, arom.), 7.57–7.77 (2H, m, 2×C*H*, arom.) and 8.14 (1H, dd, *J* 1.21 and 8.13, 1×C*H*, arom.); δ_C (300 MHz, $CDCl_3$) 50.5 (CH_2), 51.6 (CH), 124.6, 128.5, 128.8, 131.7, 133.5, 149.1 (6×C–Ph); MS *m*/*z* (rel intensity %): 165 (M^+, 0.3), 149 (2), 135 (21), 105 (10), 104 (10), 91 (79), 89 (21), 79 (71), 77 (100).

4.4.3. (*R*)-(−)-(3-Nitrophenyl)-oxirane (3).[25] Yield 85%, yellow oil. (Found: C, 58.22; H, 4.28; N, 8.50. $C_8H_7NO_3$ requires: C, 58.18; H, 4.27; N 8.48%.) R_f (25% EtOAc/hexane) 0.50; $[\alpha]_D^{20}$ −1.91(*c* 2.5, $CHCl_3$) {lit.[25] $[\alpha]_D^{18}$ +2.5 (*c* 2.8, $CHCl_3$), *S*}. The enantiomeric excess was determined by HPLC analysis using a Chiralpak AD column and showed it to be 76% ee [hexane/2-propanol 9:1; flow rate 0.8 $cm^3\,min^{-1}$]; ν_{max} (neat/cm^{-1}) 3113, 2995, 1517, 1343, 1301, 1042, 983, 888, 788, 740; δ_H (300 MHz, $CDCl_3$) 2.80 (1H, dd, *J* 2.5 and 4.8, HCOC*H*H), 3.21 (1H, dd, *J* 3.9 and 4.8, HCOCH*H*), 3.97 (1H, dd, *J* 2.5 and 3.9, PhC*H*OCH_2), 7.40–7.75 (2H, m, 2×C*H*, arom.) and 8.01–8.24 (2H, m, 2×C*H*, arom.); δ_C (300 MHz, $CDCl_3$) 51.7 (CH_2), 51.9 (CH), 126.0, 126.4, 145.4 and 148.6 (6×C–Ph); MS *m*/*z* (rel intensity %): 165 (M^+, 18), 150 (32), 136 (68), 120 (25), 105 (17), 90 (100), 77 (22), 74 (12), 65 (52), 63 (59).

4.4.4. (*R*)-(−)-(4-Nitrophenyl)-oxirane (4).[26] Yield 77%, solid, mp 84–85 °C (lit.[26] mp 84 °C). (Found: C, 58.21; H, 4.28; N, 8.51. $C_8H_7NO_3$ requires: C, 58.18; H, 4.27; N, 8.48%.) R_f (25% EtOAc/hexane) 0.48; $[\alpha]_D^{22}$ −30.31 (*c* 1.40, $CHCl_3$) {lit.[29] $[\alpha]_D^{22}$ −36.0 (*c* 1.25, $CHCl_3$), 95% ee, *R*}. The enantiomeric excess was determined by HPLC analysis using a Chiralpak OT column and showed it to be 80% ee [^{i}PrOH/hexane 1:40; flow rate 0.2 $cm^3\,min^{-1}$; t_R (*S*) 52.40 min and t_R (*R*) 56.47 min]; ν_{max} (KBr/cm^{-1}) 1606, 1522, 1345; δ_H (300 MHz, $CDCl_3$) 2.79 (1H, dd, *J* 2.6 and 5.5, HCOC*H*H), 3.24 (1H, dd, *J* 4.0 and 5.5, HCOCH*H*), 3.97 (1H, dd, *J* 2.6 and 4.0, PhC*H*OCH_2), 7.45–7.47 (2H, m, 2×C*H*, arom.) and 8.21–8.24 (2H, m, 2×C*H*, arom.); δ_C (300 MHz, $CDCl_3$) 51.7 (CH_2), 51.9 (CH), 126.0, 126.4, 145.4 and 148.6 (6×C–Ph).

4.4.5. (*R*)-(−)-(2-Chlorophenyl)-oxirane (5).[27] Yield 79%, oil. (Found: C, 62.08; H, 4.53. C_8H_7OCl requires: C, 62.09; H, 4.53%.) R_f (40% EtOAc/hexane) 0.58; $[\alpha]_D^{22}$ −24.8 (*c* 1.32, $CHCl_3$) {lit.[27] $[\alpha]_D^{25}$ +32.2 (*c* 1.19, $CHCl_3$), 99% ee, *S*}. The enantiomeric excess was determined by HPLC analysis using a Chiralpak OT column and showed it to be 77% ee [^{i}PrOH/hexane 1:40; flow rate 0.2 $cm^3\,min^{-1}$; t_R (*S*) 52.40 min and t_R (*R*) 56.47 min]; ν_{max} (neat/cm^{-1}) 3061, 2993, 1699, 1593, 1482, 1442, 1383, 1249, 1121, 1053, 1035, 880, 755; δ_H (300 MHz, $CDCl_3$) 2.60 (1H, dd, *J* 2.6 and 5.6, HCOC*H*H), 3.12 (1H, dd, *J* 4.1 and 5.6, HCOCH*H*), 4.14 (1H, dd, *J* 2.6 and 4.1, PhC*H*OCH_2), 7.15–7.30 (4H, m, 4×C*H*, arom.); δ_C (300 MHz, $CDCl_3$) 51.2 (CH_2), 51.8 (CH), 126.7, 126.6, 133.9 and 136.1 (6×C–Ph). MS *m*/*z* (rel intensity %): 156, 154 (M^+, 4, 16), 155, 153 (M^+−1, 10, 23), 134 (9), 124 (28), 119 (75), 91 (33), 89 (100), 63 (17).

4.4.6. (*R*)-(−)-(3-Chlorophenyl)-oxirane (6).[28] Yield 65%, light oil. (Found: C, 62.10; H, 4.52. C_8H_7OCl requires: C, 62.09; H, 4.53%.) R_f (40% EtOAc/hexane) 0.55; $[\alpha]_D^{22}$ −8.41 (*c* 1.56, $CHCl_3$) {lit.[28] $[\alpha]_D^{20}$ +11.1 (*c* 1.23, $CHCl_3$), 99% ee, *S*}. The enantiomeric excess was measured by capillary GC analysis using Chiraldex. G-PN column (Astec) and showed it to be 75% ee. ν_{max} (neat/cm^{-1}) 3059, 2993, 1602, 1575, 1481, 1435, 1386, 1079, 999, 880, 823, 692; δ_H (300 MHz, $CDCl_3$) 2.68 (1H, dd, *J* 2.6 and 5.4, HCOC*H*H), 3.07 (1H, dd, *J* 4.0 and 5.4, HCOCH*H*), 3.76 (1H, dd, *J* 2.6 and 4.0, PhC*H*OCH_2), 7.09–7.20 (4H, m, 4×C*H*, arom.); δ_C (300 MHz, $CDCl_3$) 51.2 (CH_2), 51.8 (CH), 126.7, 126.6, 133.9 and 136.1 (6×C–Ph). MS *m*/*z* (rel intensity %): 157, 155 (M+1, 0.8, 1.4), 156, 154 (M^+, 10, 24), 141 (15), 139 (14), 125 (50), 111 (11), 91 (56), 89 (100).

4.4.7. (*R*)-(−)-(4-Chlorophenyl)-oxirane (7).[29] Yield 76%, oil. (Found: C, 62.11; H, 4.51. C_8H_7OCl requires: C, 62.09; H, 4.53%.) R_f (40% EtOAc/hexane) 0.51; $[\alpha]_D^{22}$ −19.79 (*c* 1.00, $CHCl_3$) {lit.[29] $[\alpha]_D^{20}$ −24.0 (*c* 1.08, $CHCl_3$), 97% ee, *R*}. The enantiomeric excess was determined by HPLC analysis using a Chiralcel OJ column and

showed it to be 80% ee [hexane/2-propanol 9:1; flow rate 0.8 $cm^3\ min^{-1}$]; ν_{max} (neat/cm^{-1}) 3054, 2992, 2920, 1602, 1496, 1478, 1417, 1381, 1199, 1090, 1015, 987, 879, 831, 769; δ_H (300 MHz, $CDCl_3$) 2.68–2.69 (1H, dd, *J* 2.6 and 5.4, HCOC*H*H), 3.08 (1H, dd, *J* 4.0 and 5.4, HCOCH*H*), 3.77 (1H, dd, *J* 2.6 and 4.0, PhC*H*OCH_2), 7.13–7.26 (4H, m, 4×C*H*, arom.); δ_C (300 MHz, $CDCl_3$) 51.2 (CH_2), 51.8 (CH), 126.7, 126.6, 133.9 and 136.1 (6×C–Ph). MS *m*/*z* (rel intensity %): 156, 154 (M+1, 2, 8), 155, 153 (M^+, 3, 7), 138 (3), 125 (40), 119 (39), 91 (29), 89 (100), 63 (34), 50 (17).

4.4.8. (*R*)-(+)-(2-Bromophenyl)-oxirane (8).[25] Yield 69%, oil. (Found: C, 54.05; H, 3.16. C_8H_7OBr requires: C, 54.05; H, 3.15%.) R_f (30% EtOAc/hexane) 0.54; $[\alpha]_D^{18}$ +51.52 (*c* 1.10, $CHCl_3$), 75% ee {lit.[25] $[\alpha]_D^{18}$ +68.7 (*c* 1.12, $CHCl_3$), *R*}. The enantiomeric excess was measured by capillary GC analysis using Chiraldex. G-PN column (Astec); ν_{max} (neat/cm^{-1}) 3055, 2991, 2916, 1569, 1472, 1440, 1381, 1248, 1045, 1026, 879, 753; δ_H (300 MHz, CD_3COCD_3) 2.65 (1H, dd, *J* 2.6 and 5.9, HCOC*H*H), 3.17 (1H, dd, *J* 4.1 and 5.9, HCOCH*H*), 4.13 (1H, dd, *J* 2.6 and 4.1, PhC*H*OCH_2), 7.08–7.38 (3H, m, 3×C*H*, arom.), 7.54 (1H, dd, *J* 1.1 and 8.0, 1×C*H*, arom.); δ_C (300 MHz, $CDCl_3$) 50.5 (CH_2), 51.7 (CH), 123.5, 127.6, 128.6, 129.4, 132.8, 136.8 (6×C–Ph); MS *m*/*z* (rel intensity %): 200, 198 (M^+, 17, 18), 199, 197 (M^+-1, 16, 15), 185 (1), 171 (9), 169 (10), 141 (1), 120 (7), 119 (84), 91 (63), 90 (41), 89 (100).

4.4.9. (*R*)-(+)-(3-Bromophenyl)-oxirane (9).[25] Yield 63%, oil. (Found: C, 54.04; H, 3.13. C_8H_7OBr requires: C, 54.05; H, 3.15%.) R_f (30% EtOAc/hexane) 0.51; $[\alpha]_D^{27}$ +8.45 (*c* 1.10, $CHCl_3$), 73% ee {lit.[25] $[\alpha]_D^{27}$ +4.0 (*c* 1.12, $CHCl_3$), 35% ee, *R*}. The enantiomeric excess was determined by HPLC analysis using a Chiralpak AS column (eluent at V=0.8 mL min^{-1}; hexane/2-propanol 9:1). ν_{max} (neat/cm^{-1}) 3057, 2992, 1600, 1571, 1478, 1431, 1385, 1369, 1201, 1070, 997, 877, 786, 691; δ_H (300 MHz, $CDCl_3$) 2.77 (1H, dd, *J* 2.5 and 5.4, HCOC*H*H), 3.15 (1H, dd, *J* 4.1 and 5.4, HCOCH*H*), 3.81 (1H, dd, *J* 2.5 and 4.1, PhC*H*OCH_2), 7.10–7.50 (4H, m, 4×C*H*, arom.); δ_C (300 MHz, $CDCl_3$) 51.0 (CH_2), 52.2 (CH), 122.5, 127.6, 130.0, 131.0, 131.7, 136.7 (6×C–Ph); MS *m*/*z* (rel intensity %): 200, 198 (M^+, 23, 23), 199, 197 (M^+-1, 32, 32), 69 (27), 141 (16), 119 (67), 91 (60), 89 (100).

4.4.10. (*R*)-(−)-(4-Bromophenyl)-oxirane (10).[30] Yield 71%, oil. (Found: C, 54.05; H, 3.14. C_8H_7OBr requires: C, 54.05; H, 3.15%.) R_f (30% EtOAc/hexane) 0.49; $[\alpha]_D^{23}$ −10.9 (*c* 1.2, $CHCl_3$) {lit.[30] $[\alpha]_D^{20}$ +13.6 (*c* 1.46, $CHCl_3$), 98% ee, *S*}. The enantiomeric excess was determined by HPLC analysis using a Chiralcel OJ column and showed it to be 78% ee (eluent at V=0.8 mLmin^{-1}; hexane/2-propanol 100:1); ν_{max} (neat/cm^{-1}) 3051, 2991, 2919, 1595, 1490, 1415, 1378, 1101, 1073, 1011, 987, 878, 828; δ_H (300 MHz, $CDCl_3$) 2.73 (1H, dd, *J* 2.7 and 5.4, HCOC*H*H), 3.13 (1H, dd, *J* 3.6 and 5.4, HCOCH*H*), 3.81 (1H, dd, *J* 2.7 and 3.6, PhC*H*OCH_2), 7.05–7.18 (2H, m, 2×C*H*, arom.), 7.40–7.48 (2H, m, 2×C*H*, arom.); δ_C (300 MHz, $CDCl_3$) 50.6 (CH_2), 52.0 (CH), 121.1, 128.6, 131.6, 135.8 (6×C–Ph); MS: *m*/*z* (rel intensity %): 200, 198 (M^+, 4), 199, 197 (M−1, 3), 169 (14), 119 (41), 89 (100), 63 (36).

4.4.11. (*R*)-(+)-α-Methylstyrene oxide (11).[27,31] Yield 55%, oil. (Found: C, 80.59; H, 7.45. $C_9H_{10}O$ requires: C, 80.60; H, 7.46%.) R_f (40% CH_2Cl_2/hexane) 0.51; $[\alpha]_D^{25}$ +6.1 (*c* 2.85, $CHCl_3$) {lit.[27] $[\alpha]_D^{25}$ −7.8 (*c* 3.84, $CHCl_3$), 99% ee, *S*}. The enantiomeric excess was determined by a Hewlett–Packard 5890 gas chromatograph equipped with an FID detector, using a Chiraldex G-TA capillary column and showed it to be 78% ee; ν_{max} (neat/cm^{-1}) 1496, 1476, 1452, 1390; δ_H (300 MHz, $CDCl_3$) 1.62 (3H, s, CH_3), 2.65 (1H, d, *J* 5.5, OC*H*H), 2.84 (1H, d, *J* 5.5, OCH*H*), 7.21–7.40 (5H, m, 5×C*H*, arom.); δ_C (300 MHz, $CDCl_3$) 21.5 (CH_3), 56.6 (CH_2), 56.8 (PhCO), 125.2, 127.4, 128.2 and 141.1 (6×C–Ph).

4.4.12. (*R*)-(−)-4-Methylstyrene oxide (12).[27,30] Yield 60%, oil. (Found: C, 80.59; H, 7.45. $C_9H_{10}O$ requires: C, 80.60; H, 7.46%.) R_f (40% CH_2Cl_2/hexane) 0.45; $[\alpha]_D^{25}$ −13.63 (*c* 1.77, $CHCl_3$) {lit.[27] $[\alpha]_D^{25}$ +19.5 (*c* 1.97, $CHCl_3$), 99% ee, *S*}. The enantiomeric excess was determined with a Hewlett–Packard 5890 gas chromatograph equipped with an FID detector, using a CP-cyclodextrin-*b*-2,3,6-M-19 capillary column and showed it to be 70% ee; ν_{max} (neat/cm^{-1}) 1495, 1475, 1450, 1395; δ_H (300 MHz, $CDCl_3$) 2.45 (3H, s), 2.91 (1H, dd, *J* 2.4 and 5.5, HCOC*H*H), 3.24 (1H, dd, *J* 4.2 and 5.5, HCOCH*H*), 3.84 (1H, dd, *J* 2.4 and 4.2, PhC*H*OCH_2), 7.31–7.40 (4H, m, 4×C*H*, arom.); δ_C (300 MHz, $CDCl_3$) 20.7 (CH_3), 50.9 (CH_2), 52.2 (CH), 125.4, 128.9, 134.4 and 137.8 (6×C–Ph).

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References and notes

1. Smith, G. J. *Synthesis* **1984**, *8*, 629.
2. Besse, P.; Veschambre, H. *Tetrahedron* **1994**, *50*, 8885.
3. Xia, Q.-H.; Ge, H.-Q.; Ye, C.-P.; Liu, Z.-M.; Su, K.-X. *Chem. Rev.* **2005**, *105*, 1603.
4. Swern, D. *Organic Peroxides*; Swern, D., Ed.; Wiley Interscience: New York, NY, 1971; Vol. 2.
5. Fringuelli, G.; Pizzo, S. *Synth. Commun.* **1989**, *19*, 1939.
6. Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5976.
7. Freccero, M.; Gandolfi, R.; Sarzi-Amade, M.; Rastelli, A. *J. Org. Chem.* **2004**, *69*, 7479.
8. Rebek, J., Jr.; Marshall, L.; McManis, J.; Wolak, R. *J. Org. Chem.* **1986**, *51*, 1649.
9. (a) Adamo, M. F. A.; Agarwal, V. K.; Sage, M. A. *J. Am. Chem. Soc.* **2000**, *122*, 8317; (b) Ho, C.-Y.; Chen, Y.-C.; Wong, M.-K.; Yang, D. *J. Org. Chem.* **2005**, *70*, 898; (c) Vachon, J.; Lauper, C.; Ditrich, K.; Lacour, J. *Tetrahedron: Asymmetry* **2006**, *17*, 2334.
10. (a) Jacobsen, E. N. *Comprehensive Organometallic Chemistry*; 1995; Vol. 12, Chapter II, p 1; (b) Rossiter, B. E.; Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 464; (c) Jian, L. V.; Wang, X.; Liu, J.; Zhang, L.; Wang, Y. *Tetrahedron: Asymmetry* **2006**, *17*, 330; (d) Lane, B. S.; Vogt, M.; DeRose, V. J.; Burgess, K. *J. Am. Chem. Soc.* **2002**, *124*, 11948;

(e) Lane, B. S.; Burgess, K. *Chem. Rev.* **2003**, *103*, 2457; (f) McGarrigle, E. M.; Gilheany, D. G. *Chem. Rev.* **2005**, *105*, 1564; (g) Galia, M.; Fish, R. H.; Newmann, R. *Org. Lett.* **2003**, *5*, 3547; (h) Marchi-Deapierre, C.; Jorge-Robin, H.; Thibon, A.; Menage, S. *Chem. Commun.* **2007**, 1166.
11. (a) Houk, K. N.; List, B. *Acc. Chem. Res.* **2004**, *37*, 488; (b) Shi, Y. *Acc. Chem. Res.* **2004**, *37*, 487.
12. Sharpless, K. B.; Verhoeven, T. R. *Aldrichimica Acta* **1979**, *12*, 63.
13. Bourhani, Z.; Malkov, A. V. *Synlett* **2006**, 3525.
14. Cordova, A.; Sunden, H.; Engqvist, M.; Ibrahem, I.; Casas, J. *J. Am. Chem. Soc.* **2004**, *126*, 8914.
15. List, B. *Tetrahedron* **2002**, *58*, 5573.
16. Bjorkling, F.; Godtfredsen, S. E.; Kirk, O. *J. Chem. Soc., Chem. Commun.* **1990**, 1301.
17. Kanwar, L.; Hazarika, S.; Goswami, A.; Dutta, N. N.; Hazarika, A. K.; Goswami, P. *J. Chem. Technol. Biotechnol.* **2002**, *77*, 898.
18. Goswami, A.; Goswami, J. *Tetrahedron Lett.* **2006**, *47*, 6923.
19. (a) Bartlett, P. D. *Rec. Chem. Prog.* **1950**, *11*, 47 and **1957**, *18*, 111; (b) Back, R. D.; Glukhovtsev, M. N.; Gonzalez, C.; Marquez, M.; Estevez, C. M.; Baboul, A. G.; Schlegel, H. B. *J. Phys. Chem. A* **1997**, *101*, 6092.
20. (a) Lynch, B. M.; Pausacker, K. H. *J. Chem. Soc.* **1955**, 1525; (b) Schwartz, N. N.; Blumbergs, J. H. *J. Org. Chem.* **1964**, *29*, 1976; (c) Vilka, M. *Bull. Soc. Chim. Fr.* **1959**, 1401; (d) Renolen, P.; Ugelstad, J. *J. Chim. Phys.* **1960**, *57*, 634; (e) House, H. O.; Ro, R. S. *J. Am. Chem. Soc.* **1958**, *80*, 2428; (f) Ogata, Y.; Tabushi, I. *J. Am. Chem. Soc.* **1961**, *83*, 3440; (g) Curci, R.; DiPrete, R. A.; Edwards, J. O.; Modena, G. *J. Org. Chem.* **1970**, *35*, 740.
21. (a) Furniss, B. S.; Hannaford, A. J.; Smith, P. W. G.; Tatchell, A. R. *Vogel's Textbook of Practical Organic Chemistry*, 5th ed.; The Bath: London, 1991; p 1279; (b) *Dictionary of Organic Compounds*, 6th ed.; University Press: Cambridge, 1996; Vol. 6, p 5416.
22. Rao, K. R.; Sober, H. A. *J. Am. Chem. Soc.* **1954**, *76*, 1328.
23. Corey, E. J.; Link, J. O. *J. Org. Chem.* **1991**, *56*, 442.
24. Corey, E. J.; Shibata, S.; Bakshi, R. K. *J. Org. Chem.* **1988**, *53*, 2861.
25. Jin, H.; Li, Z.-Y.; Dong, X.-W. *Org. Biomol. Chem.* **2004**, *2*, 408.
26. Pedragosa-Moreau, S.; Morisseau, C.; Baratti, J.; Zylber, J.; Archelas, A.; Furstoss, R. *Tetrahedron* **1997**, *53*, 9707.
27. Spelberg, J. H. L.; Rink, R.; Kellogg, R. M.; Janssen, D. B. *Tetrahedron: Asymmetry* **1998**, *9*, 459.
28. Tanaka, K.; Yasuda, M. *Tetrahedron: Asymmetry* **1998**, *9*, 3275.
29. Moussou, P.; Archelas, A.; Baratti, J.; Furstoss, R. *J. Org. Chem.* **1998**, *63*, 3532 and references cited therein.
30. Pedragosa-Moreau, S.; Morisseau, C.; Baratti, J.; Zylber, J.; Archelas, A.; Furstoss, R. *J. Org. Chem.* **1996**, *61*, 7402.
31. Johnson, C. R.; Kirchhoff, R. A.; Reischer, R. J.; Katekar, G. F. *J. Am. Chem. Soc.* **1973**, *95*, 4287.