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INFLUENCE OF POLYMERIZATION DEGREE OF POLY-L-LEUCINE CATALYST AND SUBSTITUENT EFFECT ON THE JULIÁ-COLONNA ASYMMETRIC EPOXIDATION OF BENZALACETOPHENONES

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Abstract – The Juliá-Colonna asymmetric epoxidation reaction of substituted benzalacetophenone afforded the corresponding epoxide with high yield and high enantioselectivity, catalyzed by the specified length of poly-L-leucine (chain length n > 15). Poly-L-leucine catalysts have been prepared by the polymerization reaction of L-leucine-NCA with initiators (BnONa, *n*-$BuNH_2$, H_2O) and characterized by the MALDI-TOF Mass and IR analysis.

INTRODUCTION

The epoxide functionality has frequently been demonstrated to be a versatile and useful moiety for organic synthesis.[1] For this reason the synthesis of chiral oxirans is still a challenging target in the area of asymmetric induction. Recently, we have investigated the asymmetric induction in epoxidations and cyclopropanations by means of the (-)-8-phenylmenthyl moiety as a chiral auxiliary.[2] In the Juliá-Colonna asymmetric epoxidation reaction of benzalacetophenone, catalyzed by the length-defined poly-L-leucine (n > 15), the enantioselectivity is very attractive and high. This asymmetric epoxidation is interesting owing to its enzymatic behavior with respect to the substrate specificity. The Juliá-Colonna asymmetric epoxidation methodology[3] has been improved with the following viewpoint in organic synthesis: (1) *Two-phase* oxidation system (urea-hydrogen peroxide complex, DBU, poly-L-leucine, THF) required shorter reaction time than the original *three-phase* oxidation system (30% H_2O_2, aq. NaOH, poly-L-leucine, toluene).[4] (2) The Juliá-Colonna epoxidation of various type of enones which are different from benzalacetophenone have been developed.[5] (3) The quality of the poly-leucine catalysts was

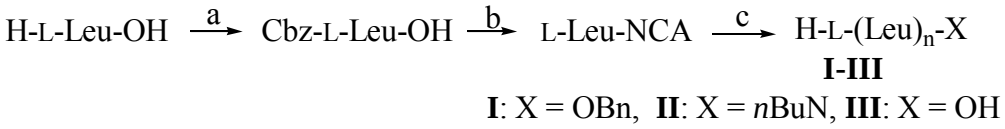
This paper is dedicated to Dr. Pierre Potier on the occasion of his 70th birthday.

improved by the immobilization of polyleucine on CLAMPS (cross-linked aminomethylpolystyrene).[6] (4) Recently, soluble poly-peptides have been tested for activity in Juliá-Colonna epoxidation.[7]

On the other hand, the mechanistic features of the Juliá-Colonna asymmetric epoxidation is not well known. In the Juliá-Colonna asymmetric epoxidation by means of oligo-L-leucine catalysts of defined length (degree varying from 5 to 20), the higher degree of polymerization of catalyst made the yields and selectivities higher.[8] Optimal conditions require leaving the *N*-terminus unprotected and having the number of leucine units at least *ca*. 15. A related and intriguing study on *polymer supported* oligo-L-leucine catalysts of specified length (degrees of 10 and 20 of varying enantiomer composition) was disclosed by Roberts and his co-workers.[9] The same tendency was found in the asymmetric epoxidation using polymer supported oligo-L-leucine catalysts. Our IR spectral measurements of the length defined oligo-L-leucines suggested that α-helical structure of the catalysts played an important role on the asymmetric induction. Here, we report the structural features of the poly-L-leucine catalysts and substituent effect on the asymmetric epoxidation of benzalacetophenones.

RESULTS AND DISCUSSION

The poly-L-leucines were prepared by polymerization of L-leucine *N*-carboxyanhydride (L-Leu-NCA) (Scheme 1).[10] Reaction of benzyloxycarbonyl-L-leucine (Cbz-L-Leu) with oxalyl chloride afforded L-Leu-NCA. The subsequent polymerization of L-Leu-NCA with initiators (BnONa, *n*-$BuNH_2$, H_2O) afforded poly-L-leucine catalysts (**I**-**III**) (Table 1). The amide I region in the IR spectra of poly-L-leucine (**I**-**II**) in the solid state was shown in Figure. 1. The IR spectra of poly-L-leucine (**IIa**, **IIb**, **IIc**, and **IId**) showed bands at 1630 cm^{-1} assigned to *β*-sheet structure and 1655 cm^{-1} assigned to helical structure.[11] The IR spectra of the amide I region of poly-L-leucine (**I** and **IIe**) showed strong absorption bands at 1655 cm^{-1} assigned to the helical structure and the shoulder bands at 1630 cm^{-1} assigned to *β*-sheet structure.



Scheme 1. *Reagents and conditions*: (a) CbzCl, 2N NaOH; (b) $(COCl)_2$, benzene; (c) initiator (BnONa For **I**, *n*-$BuNH_2$ for **II**, H_2O for **III**, MeCN).

Table 1. Synthesis of poly-L-leucine catalysts (**I-III**)

entry	initiator	X	product	distribution of polymerization	polymerization degree most frequent	polymerization degree second frequent
1	BnOH/NaH	BnO	**I**	7-12	8	12
2	*n*-$BuNH_2$	*n*-BuNH	**IIa**	4-12	7	
3	*n*-$BuNH_2$	*n*-BuNH	**IIb**	2-23	6	17
4	*n*-$BuNH_2$	*n*-BuNH	**IIc**	3-23	7	16
5	*n*-$BuNH_2$	*n*-BuNH	**IId**	3-22	7	15
6	*n*-$BuNH_2$	*n*-BuNH	**IIe**	5-20	9	16
7	H_2O	OH	**III**	---	8[a)]	

[a] average degree of polymerization estimated by ^{1}H NMR

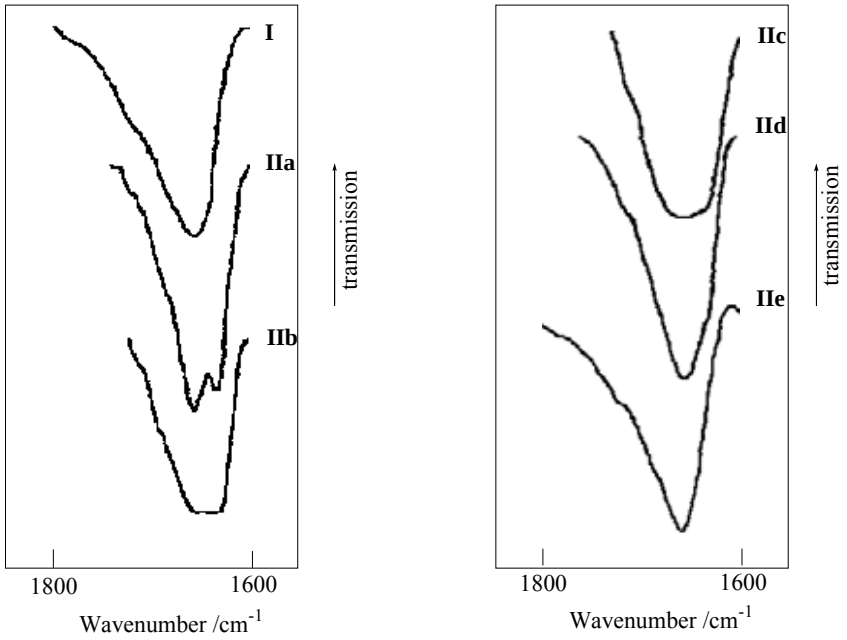


Figure 1. IR spectra of poly-L-leucine catalysts (**I** and **IIa-e**).

The poly-L-leucine catalysts (**I-III**) were characterized by MS spectra using MALDI-TOF technique (Table 1 and Figure 2). The mass weight (*m*/*z*) of the poly-L-leucine catalyst (**I**) distributed from 945 (n = 7) to 1504 (n = 12). The most frequent polymerization degrees was 1035 (n = 8) and the second frequent polymerization degree was 1488 (n = 12) (Table 1, entry 1). The distribution of polymerizaton of the poly-L-leuine catalyst (**IIa**) was narrow (n = 4 to 12) compared with that of **IIb-e** and the most frequent polymerization degree was n = 7 (Table 1, entry 2). The distribution of polymerization of the poly-L-leucine catalysts (**IIb-e**) was relatively wide and more highly polymerized poly-L-leucine (n > 15) was contained in the catalysts (Table 1, entries 3-6). The average degree of polymerization in

poly-L-leucine (**III**) was n = 8, which was estimated by integral values of ^{1}H NMR spectrum (Table 1, entry 7).

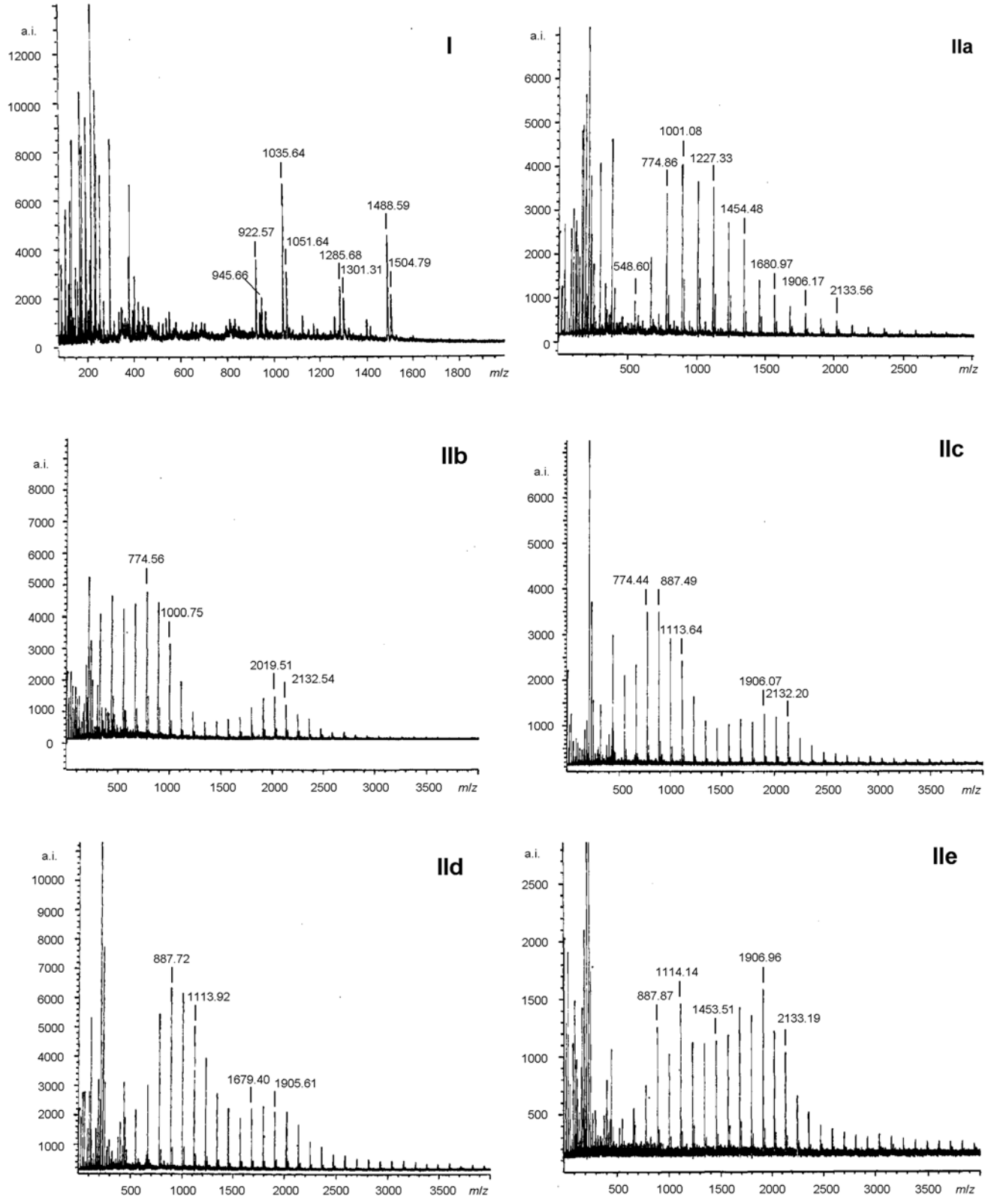
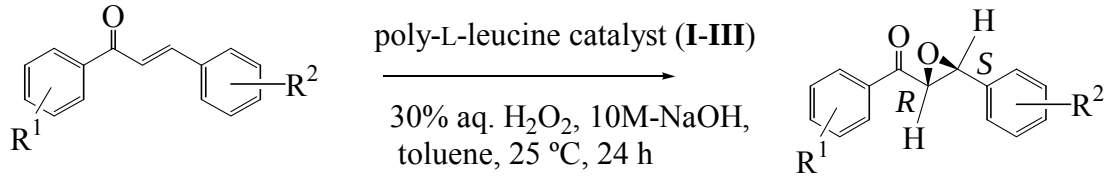


Figure 2. MS spectra of poly-L-leucine catalysts (**I** and **IIa-e**).



1 :	R^1 = H, R^2 = H	**2** :	R^1 = H, R^2 = H
3a :	R^1 = *o*-MeO, R^2 = H	**4a** :	R^1 = *o*-MeO, R^2 = H
3b :	R^1 = *m*-MeO, R^2 = H	**4b** :	R^1 = *m*-MeO, R^2 = H
3c :	R^1 = *p*-MeO, R^2 = H	**4c** :	R^1 = *p*-MeO, R^2 = H
5a :	R^1 = *o*-Me, R^2 = H	**6a** :	R^1 = *o*-Me, R^2 = H
5b :	R^1 = *m*-Me, R^2 = H	**6b** :	R^1 = *m*-Me, R^2 = H
5c :	R^1 = *p*-Me, R^2 = H	**6c** :	R^1 = *p*-Me, R^2 = H
7a :	R^1 = *o*-Cl, R^2 = H	**8a** :	R^1 = *o*-Cl, R^2 = H
7b :	R^1 = *m*-Cl, R^2 = H	**8b** :	R^1 = *m*-Cl, R^2 = H
7c :	R^1 = *p*-Cl, R^2 = H	**8c** :	R^1 = *p*-Cl, R^2 = H
9a :	R^1 = H, R^2 = *o*-MeO	**10a** :	R^1 = H, R^2 = *o*-MeO
9b :	R^1 = H, R^2 = *m*-MeO	**10b** :	R^1 = H, R^2 = *m*-MeO
9c :	R^1 = H, R^2 = *p*-MeO	**10c** :	R^1 = H, R^2 = *p*-MeO
11a :	R^1 = H, R^2 = *o*-Me	**12a** :	R^1 = H, R^2 = *o*-Me
11b :	R^1 = H, R^2 = *m*-Me	**12b** :	R^1 = H, R^2 = *m*-Me
11c :	R^1 = H, R^2 = *p*-Me	**12c** :	R^1 = H, R^2 = *p*-Me
13a :	R^1 = H, R^2 = *o*-Cl	**14a** :	R^1 = H, R^2 = *o*-Cl
13b :	R^1 = H, R^2 = *m*-Cl	**14b** :	R^1 = H, R^2 = *m*-Cl
13c :	R^1 = H, R^2 = *p*-Cl	**14c** :	R^1 = H, R^2 = *p*-Cl

Scheme 2. Juliá-Colonna asymmetric epoxidation of benzalacetophenones catalyzed by poly-L-leucine.

Epoxidation reactions of benzalacetophenone (**1**) with 30% aqueous H_2O_2/10M-NaOH in the presence of poly-L-leucine catalysts were carried out (Scheme 2). Table 2 shows the stereoselectivity in the epoxidation of **1** catalyzed by poly-L-leucine (**I-III**). In the presence of poly-L-leucine catalysts (**I** and **IIa**), chemical yields were very low (Table 2, entries 1, 2). The catalytic low activity may be attributed to the low degree of polymerization. Moreover, the enantioselectivity of the reaction using the poly-L-leucine catalyst (**IIa**) was considerably lower than that of the other catalysts (Table 2, entry 2). Both the chemical yield and enantioselectivity of the product in the reaction using poly-L-leucine (**IIb-e**

Table 2. Asymmetric epoxidation of benzalacetophenone catalyzed by various poly-L-leucine

entry	poly-L-leucine	%ee	yield %
1	**I**	90	39
2	**IIa**	70	18
3	**IIb**	92	75
4	**IIc**	91	83
5	**IId**	93	87
6	**IIe**	90	85
7	**III**	93	73

and **III**) were significantly higher relative to those of original Juliá-Colonna catalysts (Table 2, entries 3-7). The functional groups (*n*-BuN and OH) at *C*-terminus are more favorable than the BnO group for the asymmetric induction and the preparation of the catalyst.

Judging from the asymmetric induction of the epoxidation along with the IR spectral features, the longer the chain length of the poly-L-leucine is, the higher the distribution of α-helix structures.[12] The α-helical structure of the catalysts played an important role on the asymmetric induction.

The asymmetric epoxidation of a series of substituted benzalacetophenones by the poly-L-leucine catalyst (**III**) was examined (Tables 3 and 4). Both the chemical yield and enantioselectivity in the reaction of *p*-substituted benzalacetophenones by the poly-L-leucine catalyst (**III**) were comparable to those of the unsubstituent substrate (**1**) (Table 3, entries 4, 7, 10; Table 4, entries 4, 7, 10). In the asymmetric epoxidation reaction of *m*-substituted benzalacetophenones by the poly-L-leucine catalyst (**III**), the enantioselectivity was also high (Table 3, entries 3, 6, 9; Table 4, entries 3, 6, 9), while the reaction yields

Table 3. Epoxidation of substituted benzalacetophenones catalyzed by poly-L-leucines catalyst (**III**)

entry	substrate	R_1	R_2	product	yield (%)[a]	%ee[b]
1	**1**	H	H	**2**	73	93
2	**3a**	*o*-MeO	H	**4a**	27 (64)	81
3	**3b**	*m*-MeO	H	**4b**	58 (82)	92
4	**3c**	*p*-MeO	H	**4c**	72 (97)	97
5	**5a**	*o*-Me	H	**6a**	27 (49)	81
6	**5b**	*m*-Me	H	**6b**	47 (53)	94
7	**5c**	*p*-Me	H	**6c**	84 (84)	97
8	**7a**	*o*-Cl	H	**8a**	48 (76)	76
9	**7b**	*m*-Cl	H	**8b**	74 (95)	92
10	**7c**	*p*-Cl	H	**8c**	77 (93)	94

a) Reaction yield in parenthesis.
b) The ratios were determined by HPLC analysis using a chiralcel-OD.

Table 4. Epoxidation of substituted benzalacetophenones catalyzed by poly-L-leucines catalyst (**III**)

entry	substrate	R_1	R_2	product	yield (%)[a]	%ee[b]
1	**1**	H	H	**2**	73	93
2	**9a**	H	*o*-MeO	**10a**	39 (43)	67
3	**9b**	H	*m*-MeO	**10b**	45 (54)	90
4	**9c**	H	*p*-MeO	**10c**	66 (69)	85
5	**11a**	H	*o*-Me	**12a**	46 (57)	87
6	**11b**	H	*m*-Me	**12b**	65 (81)	98
7	**11c**	H	*p*-Me	**12c**	66 (76)	93
8	**13a**	H	*o*-Cl	**14a**	92 (97)	54
9	**13b**	H	*m*-Cl	**14b**	83 (92)	95
10	**13c**	H	*p*-Cl	**14c**	87 (91)	94

a) Reaction yield in parenthesis.
b) The ratios were determined by HPLC analysis using a chiralcel-OD.

were comparable to or lower than that of the unsubstituted substrate (**1**). The *o*-substituent remarkably affected to both the yield and the enantioselectivity (Table 3, entries 2, 5, 8; Table 4, entries 2, 5, 8). The reaction was deaccelerated by the *o*-substituent and the favorable attack of the nucleophile may be disturbed to lower the enantioselectivity.

Conclusion

Our results supported the original speculations made by Juliá and Colonna that α-helical structure of the catalysts was important for the high asymmetric induction. The *o*-hetero substituent on phenyl group attached at vinyl position of benzalacetophenone influences both the reactivity and the enantioselectivity.

EXPERIMENRAL

General Methods

NMR spectra were recorded on a JEOL GSX-270 or a JMN-LA500 instrument and calibrated using TMS as an internal reference (δ=0.0). IR spectra were recorded on a JASCO-FT/IR7300 spectrophotometer. High-resolution mass spectra (HRMS) were recorded on a JEOL SX-102A mass spectrometer under fast-atom bombardment (FAB) conditions. MALDI-TOF MS spectra were recorded on a BRUKER REFLEX.

General Procedure for the Preparation of L-Leucine-NCA[13]

Benzyloxyacarbonyl-L-leucine (Cbz-L-Leu) (4.61 g, 17.4 mmol) was dissolved in benzene (20 mL). $(COCl)_2$ (2 mL) was slowly added to the solution and the reaction mixture was warmed at 60 to 70 ºC for 15 min. After the reaction mixture was cooled to 25 ºC, hexane-ether (1 : 1) was added to the mixture. The white solid which formed was filtered and recrystallized from CH_2Cl_2/hexane (2.85 g): mp 72-73 ºC: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.99 (3 H, d, *J* = 6.4 Hz), 1.01 (3 H, d, *J* = 6.4 Hz), 1.69 (1 H, m), 1.83 (2 H, m), 4.34 (1 H, dd, *J* = 4.4, 8.8 Hz), 6.19 (1 H, m).

General Procedure for the Polymerization of L-Leucine-NCA

Appropriate amount of initiator in CH_3CN was added to a solution of L-leucine-NCA in CH_3CN. The reaction mixture was stirred at 25 ºC for 5 days. The solvent was evaporated under reduced pressure. Dry Et_2O was added to the residue to form a white solid, which was formed and filtered. The white soiled was washed with ether and CH_2Cl_2 and used for subsequent reactions without further purification.

General Procedure for the Asymmetric Epoxidation Using Oligo-L-Leucine as Catalyst

An aliquot (1.7 mL) of a solution of NaOH (0.8 g, 20 mmol) in 30% aqueous H_2O_2 (10 mL, 88.2 mmol) was added to a mixture of oligo-L-leucine catalyst (100 mg) and benzalacetophenones (**1**) (100 mg, 0.48 mmol) in toluene (1.7 mL) at 0 °C. The mixture was allowed to warm to rt and was vigorously stirred for 24 h. The insoluble catalyst was filtered off and the filtrate was washed with water and brine, dried over Na_2SO_4, and evaporated. The crude product was purified by preparative TLC [silica gel, petroleum ether/ether = 10 : 1 (v/v)] to give pure sample (**2**). The enantiomeric excess of the product (**2**) was determined by HPLC analysis [hexane/2-propanol = 9 : 1 (v/v), 254 nm] using chiralcel OD (Daicel Chemical Industries, Ltd.).

***trans*-(2*R*,3*S*)-2,3-Epoxy-1,3-diphenylpropan-1-one (2)**[14]

$[\alpha]^{25}_D$ = -300° (*c* 0.06, MeOH); CD (*i*PrOH) $\Delta\varepsilon_{318}$ = -5.0; $\Delta\varepsilon_{257}$ = -6.6; $\Delta\varepsilon_{247}$ = 0; $\Delta\varepsilon_{231}$ = 7.6 (C = 0.043 mg/ml); ^{1}H NMR (270 MHz, $CDCl_3$) δ 4.08 (1 H, d, *J* = 2.0 Hz), 4.29 (1 H, d, *J* = 2.0 Hz), 7.43-8.06 (10 H, m); ^{13}C NMR (68 MHz, $CDCl_3$) δ 58.4, 60.7, 124.0 (x2), 125.6, 128.3, 128.7, 128.8, 129.1, 130.0, 134.0, 134.8, 135.3, 137.6, 192.5; HRMS (EI) Calcd for $C_{15}H_{12}O_2$ [M^+] 224.0837. Found 224.0843.

***trans*-(2*R*,3*S*)-2,3-Epoxy-1-(2'-methoxyphenyl)-3-phenylpropan-1-one (4a)**[15]

$[\alpha]^{25}_D$ = -13.0° (*c* 0.23, hexane); ^{1}H NMR (270 MHz, $CDCl_3$) δ 3.59 (3 H, s, OMe), 4.01 (1 H, d, *J* = 2.0 Hz), 4.31 (1 H, d, *J* = 2.0 Hz), 7.08-7.84 (9 H, m); ^{13}C NMR (68 MHz, $CDCl_3$) δ 55.6, 59.8, 64.5, 111.6, 121.1, 125.8, 126.0, 127.3, 128.4, 128.6, 128.7, 130.7, 134.9, 136.5, 159.6, 194.9; HRMS (EI) Calcd for $C_{16}H_{14}O_3$ [M^+] 254.0943. Found 254.0955.

***trans*-(2*R*,3*S*)-2,3-Epoxy-1-(3'-methoxyphenyl)-3-phenylpropan-1-one (4b)**

$[\alpha]^{25}_D$ = -199.3° (*c* 0.30, hexane); ^{1}H NMR (270 MHz, $CDCl_3$) δ 3.84 (3 H, s, OMe), 4.07 (1 H, d, *J* = 1.5 Hz), 4.28 (1 H, d, *J* = 1.5 Hz), 7.14-7.59 (9 H, m); ^{13}C NMR (68 MHz, $CDCl_3$) δ 55.4, 59.4, 61.0, 112.2, 112.4, 120.5, 120.9, 125.7, 128.7, 129.0, 129.5, 129.8, 135.4, 136.7, 159.9, 190.8; HRMS (EI) Calcd for $C_{16}H_{14}O_3$ [M^+] 254.0943. Found 254.0953.

***trans*-(2*R*,3*S*)-2,3-Epoxy-1-(4'-methoxyphenyl)-3-phenylpropan-1-one (4c)**[16]

$[\alpha]^{25}_D$ = -231.2° (*c* 0.23, hexane); ^{1}H NMR (270 MHz, $CDCl_3$) δ 3.87 (3 H, s, OMe), 4.06 (1 H, d, *J* = 2.0 Hz), 4.25 (1 H, d, *J* = 2.0 Hz), 6.59 (2 H, d, *J* = 8.8 Hz), 7.36-7.40 (5 H, m), 8.01 (2 H, d, *J* = 8.8 Hz); ^{13}C NMR (68 MHz, $CDCl_3$) δ 55.6, 59.2, 60.9, 113.8 (x2), 114.1, 125.8, 128.2, 128.6, 129.0, 130.8 (x2), 131.4, 135.8, 164.3, 191.4; HRMS (EI) Calcd for $C_{16}H_{14}O_3$ [M^+] 254.0943. Found 254.0952.

***trans*-(2*R*,3*S*)-2,3-Epoxy-1-(2'-methylphenyl)-3-phenylpropan-1-one (6a)**[4d]

$[\alpha]^{25}_{D}$ = -125.6° (*c* 0.20, hexane); ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.54 (3 H, s, CH_3), 4.04 (1 H, d, *J* = 2.0 Hz), 4.11 (1 H, d, *J* = 2.0 Hz), 7.23-7.69 (9 H, m); ^{13}C NMR (68 MHz, $CDCl_3$) δ 21.0, 59.5, 62.4, 125.5, 125.8, 127.1, 128.5, 128.6, 128.8, 128.9, 129.0, 132.1, 132.3, 135.5, 138.9, 196.6; HRMS (EI) Calcd for $C_{16}H_{14}O_2$ [M^+] 238.0994. Found 238.0999.

trans-(2*R*,3*S*)-2,3-Epoxy-1-(3'-methylphenyl)-3-phenylpropan-1-one (6b)[17]

$[\alpha]^{25}_{D}$ = -169.2° (*c* 0.15, hexane); ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.38 (3 H, s, CH_3), 4.04 (1 H, d, *J* = 2.0 Hz), 4.26 (1 H, d, *J* = 2.0 Hz), 7.31-7.78 (9 H, m); ^{13}C NMR (68 MHz, $CDCl_3$) δ 21.3, 59.4, 60.9, 125.6 (x2), 125.8 (x2), 128.8 (x2), 129.0 (x2), 134.8 (x2), 135.6, 138.8, 193.2; HRMS (EI) Calcd for $C_{16}H_{14}O_2$ [M^+] 238.0994. Found 238.0988.

trans-(2*R*,3*S*)-2,3-Epoxy-1-(4'-methylphenyl)-3-phenylpropan-1-one (6c)[16]

$[\alpha]^{25}_{D}$ = -165.8° (*c* 0.24, hexane); ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.39 (3 H, s, CH_3), 4.06 (1 H, d, *J* = 2.0 Hz), 4.25 (1 H, d, *J* = 2.0 Hz), 7.25 (2 H, d, *J* = 8.5 Hz), 7.31-7.37 (5 H, m), 7.88 (2 H, d, *J* = 8.5 Hz); ^{13}C NMR (68 MHz, $CDCl_3$) δ 21.8, 59.3, 60.9, 125.8 (x2), 126.6, 128.4, 128.5, 128.7, 129.0, 129.2, 129.6, 133.1, 135.6, 145.1, 192.6; HRMS (EI) Calcd for $C_{16}H_{14}O_2$ [M^+] 238.0994. Found 238.0998.

trans-(2*R*,3*S*)-2,3-Epoxy-1-(2'-chlorophenyl)-3-phenylpropan-1-one (8a)[4d]

$[\alpha]^{25}_{D}$ = -157.3° (*c* 0.25, hexane); ^{1}H NMR (270 MHz, $CDCl_3$) δ 4.10 (1 H, d, *J* = 1.7 Hz), 4.16 (1 H, d, *J* = 1.7 Hz), 7.30-7.64 (9 H, m); ^{13}C NMR (68 MHz, $CDCl_3$) δ 60.4, 62.8, 125.8, 127.1, 128.4, 128.5, 128.6, 128.8, 129.0, 130.4, 130.6, 132.1, 135.2, 136.5, 196.3, HRMS (EI) Calcd for $C_{15}H_{11}O_2{}^{35}Cl$ [M^+] 258.0448. Found 258.0444.

trans-(2*R*,3*S*)-2,3-Epoxy-1-(3'-chlorophenyl)-3-phenylpropan-1-one (8b)

$[\alpha]^{25}_{D}$ = -175.0° (*c* 0.19, hexane); ^{1}H NMR (270 MHz, $CDCl_3$) δ 4.08 (1 H, d, *J* = 1.7 Hz), 4.24 (1 H, d, *J* = 1.7 Hz), 7.43-8.00 (9 H, m); ^{13}C NMR (68 MHz, $CDCl_3$) δ 59.5, 61.0, 125.8, 126.5, 128.4 (x2), 128.9, 129.0, 129.2, 130.2, 133.9, 135.1, 135.3, 136.8, 192.0; HRMS (EI) Calcd for $C_{15}H_{11}O_2{}^{35}Cl$ [M^+] 258.0448. Found 258.0473.

trans-(2*R*,3*S*)-2,3-Epoxy-1-(4'-chlorophenyl)-3-phenylpropan-1-one (8c)[16]

$[\alpha]^{25}_{D}$ = -208.4° (*c* 0.41, hexane); ^{1}H NMR (270 MHz, $CDCl_3$) δ 3.79 (1 H, d, *J* = 1.7 Hz), 4.24 (1 H, d, *J* = 1.7 Hz), 7.43-7.99 (9 H, m); ^{13}C NMR (68 MHz, $CDCl_3$) δ 59.3, 61.0, 125.7 (x2), 128.7 (x2), 128.8, 128.9, 129.2 (x2), 129.7, 133.6, 135.2, 140.4, 192.0; HRMS (EI) Calcd for $C_{15}H_{11}O_2{}^{35}Cl$ [M^+] 258.0448. Found 258.0447.

***trans*-(2*R*,3*S*)-2,3-Epoxy-3-(2'-methoxyphenyl)-1-phenyl-3-propan-1-one (10a)**[18]

^{1}H NMR (270 MHz, $CDCl_3$) δ 3.85 (3 H, s, OMe), 4.20 (1 H, d, *J* = 2.0 Hz), 4.40 (1 H, d, *J* = 2.0 Hz), 6.89-8.04 (9 H, m); ^{13}C NMR (68 MHz, $CDCl_3$) δ 55.4, 55.7, 60.4, 110.3, 120.7, 124.2, 125.5, 128.4 (x2), 128.7 (x2), 129.6, 133.8, 135.6, 158.2, 193.7; HRMS (EI) *m*/*z* Calcd for $C_{16}H_{14}O_3$ [M^+] 254.0943. Found 254.0942.

***trans*-(2*R*,3*S*)-2,3-Epoxy-3-(3'-methoxyphenyl)-1-phenyl-3-propan-1-one (10b)**

^{1}H NMR (270 MHz, $CDCl_3$) δ 3.82 (3 H, s, OMe), 4.05 (1 H, d, *J* = 1.7 Hz), 4.28 (1 H, d, *J* = 1.7 Hz), 6.90-8.02 (9 H, m); ^{13}C NMR (68 MHz, $CDCl_3$) δ 55.3, 59.3, 60.9, 110.8, 114.7, 118.2, 128.3, 128.5, 128.1, 129.7, 129.8, 133.7, 135.4, 137.1, 160.1, 193.0; HRMS (EI) Calcd for $C_{16}H_{14}O_3$ [M^+] 254.0943. Found 254.0943.

***trans*-(2*R*,3*S*)-2,3-Epoxy-1-(4'-methoxyphenyl)-3-phenyl-3-propan-1-one (10c)**[19]

$[\alpha]^{25}_D$ = -78.9° (*c* 0.19, hexane); ^{1}H NMR (270 MHz, $CDCl_3$) δ 3.83 (3 H, s, OMe), 4.02 (1 H, d, *J* = 1.7 Hz), 4.29 (1 H, d, *J* = 1.7 Hz), 6.91-8.02 (9 H, m); ^{13}C NMR (68 MHz, $CDCl_3$) δ 55.2, 55.4, 75.2, 113.6, 113.9, 114.3, 128.4, 128.5, 129.0, 129.2, 129.7, 130.2, 132.0, 133.2, 134.0, 190.8; HRMS (EI) Calcd for $C_{16}H_{14}O_3$ [M^+] 254.0943. Found 254.0949.

***trans*-(2*R*,3*S*)-2,3-Epoxy-3-(2'-methylphenyl)-1-phenyl-3-propan-1-one (12a)**[20]

$[\alpha]^{25}_D$ = -39.2° (*c* 0.16, hexane); ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.73 (3 H, s, CH_3), 4.22 (2 H, d, *J* = 1.5 Hz), 7.20-8.07 (9 H, m); ^{13}C NMR (68 MHz, $CDCl_3$) δ 18.8, 57.7, 60.1, 124.2, 126.4, 128.3, 128.5, 128.6, 128.7, 128.9, 130.1, 133.9, 134.0, 135.5, 136.3, 193.4; HRMS (EI) Calcd for $C_{16}H_{14}O_2$ [M^+] 238.0994. Found 238.1001.

***trans*-(2*R*,3*S*)-2,3-Epoxy-3-(3'-methylphenyl)-1-phenyl-3-propan-1-one (12b)**[21]

$[\alpha]^{25}_D$ = -157.9° (*c* 0.17, hexane); ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.32 (3 H, s, CH_3), 3.98 (1 H, d, *J* = 1.7 Hz), 4.24 (1 H, d, *J* 1.7), 7.12-7.96 (9 H, m); ^{13}C NMR (68 MHz, $CDCl_3$) δ 21.3, 59.4, 60.9, 123.0, 126.2 (x2), 128.3 (x2), 128.6, 128.8 (x2), 132.4, 135.4, 135.5, 138.6, 193.1; HRMS (EI) Calcd for $C_{16}H_{14}O_2$ [M^+] 238.0994. Found 238.0982.

***trans*-(2*R*,3*S*)-2,3-Epoxy-3-(4'-methylphenyl)-1-phenyl-3-propan-1-one (12c)**[22]

$[\alpha]^{25}_D$ = -135.0° (*c* 0.11, hexane); ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.32 (3 H, s, CH_3), 3.98 (1 H, d, *J* = 2.0 Hz), 4.23 (1 H, d, *J* = 2.0 Hz), 7.13-7.64 (9 H, m); ^{13}C NMR (68 MHz, $CDCl_3$) δ 20.9, 59.1, 60.7, 125.4,

127.9, 128.5, 128.6, 129.0, 129.3, 129.8, 132.1, 133.6, 135.1, 138.7, 159.1, 192.9; HRMS (EI) Calcd for $C_{16}H_{14}O_2$ [M^+] 238.0994. Found 238.0986.

***trans*-(2*R*,3*S*)-2,3-Epoxy-3-(2'-chlorophenyl)-1-phenyl-3-propan-1-one (14a)**[23]

mp 48-49 °C; $[\alpha]^{25}_D$ = -12.1° (*c* 0.12, hexane); ^{1}H NMR (270 MHz, $CDCl_3$) δ 4.06 (1 H, d, *J* = 1.7 Hz), 4.26 (1 H, d, *J* = 1.7 Hz), 7.24-8.02 (9 H, m); ^{13}C NMR (68 MHz, $CDCl_3$) δ 58.4, 60.7, 124.0, 125.6, 128.3 (x2), 128.7, 128.8, 129.1, 130.0, 134.0, 134.8, 135.3, 137.6, 192.5; HRMS (EI) Calcd for $C_{15}H_{11}O_2{}^{35}Cl$ [M^+] 258.0448. Found 258.0440.

***trans*-(2*R*,3*S*)-2,3-Epoxy-3-(3'-chlorophenyl)-1-phenyl-3-propan-1-one (14b)**[17]

mp 74 °C; $[\alpha]^{25}_D$ = -137.5° (*c* 0.17, hexane); ^{1}H NMR (270 MHz, $CDCl_3$) δ 4.17 (1 H, d, *J* = 2.0 Hz), 4.41 (1 H, d, *J* = 2.0 Hz), 7.30-8.07 (9 H, m); ^{13}C NMR (68 MHz, $CDCl_3$) δ 57.0, 59.9, 126.0, 127.2, 128.3 (x2), 128.4 (x2), 128.8, 129.2, 129.7, 133.2, 133.9, 135.2, 192.6; MS (EI) *m*/*z* 258.0496 [M^+], 260.0404 [M^+].

***trans*-(2*R*,3*S*)-2,3-Epoxy-3-(4'-chlorophenyl)-1-phenyl-3-propan-1-one (14c)**[19]

mp 114 °C; $[\alpha]^{25}_D$ = -168.0° (*c* 0.45, hexane); ^{1}H NMR (270 MHz, $CDCl_3$) δ 4.06 (1 H, d, *J* = 2.0 Hz), 4.25 (1 H, d, *J* = 2.0 Hz), 7.29-8.01 (9 H, m); ^{13}C NMR (68 MHz, $CDCl_3$) δ 58.6, 60.8, 127.1 (x2), 128.2 (x2), 127.6 (x2), 128.0 (x2), 128.9, 134.0, 134.8, 135.3, 192.7; HRMS Calcd for $C_{15}H_{11}O_2{}^{35}Cl$ [M^+] 258.0448. Found 258.0445.

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