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The Juliá–Colonna Asymmetric Epoxidation Reaction of Chalcone Catalyzed by Length Defined Oligo- L-leucine: Importance of the *N*-Terminal Functional Group and Helical Structure of the Catalyst in the Asymmetric Induction

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Catalysts, oligo-L-leucine, for the Juliá–Colonna asymmetric epoxidation of chalcone with defined degrees of polymerization were prepared by a stepwise elongation method. The yield and enantioselectivity in the epoxidation increased with the degree of polymerization of the catalyst. The presence of an unprotected amine moiety at the *N*-terminus proved to be essential for high asymmetric induction. The IR characteristic absorption bands (the amide I region) of the catalysts suggested that helical structure in the catalyst is related to asymmetric induction.

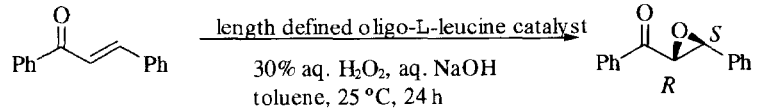
The epoxide group is an extremely versatile functionality in organic synthesis.[1] Thus, the field of asymmetric epoxidation has experienced extensive activity.[2–6] Among the developed methods, the Juliá–Colonna method, which utilizes poly amino acids as catalysts, has emerged as the first reliable method for the asymmetric epoxidation of electron-deficient olefins, with exceptionally high induction for chalcone.[7,8] Stemming from our interest in the chemistry of small-ring compounds, we have recently developed a highly diastereoselective method of glycidic ester, 2,3-epoxypropanoate, synthesis utilizing the Darzens protocol.[9] In conjunction with this work, we became attracted to the closely related Juliá–Colonna reaction, of which mechanistically little is known. As an initial study towards elucidation of the process, we have prepared oligo-L-leucine catalysts of defined length (degree varying from 5 to 20, as opposed to the catalytic mixture of oligo-L-leucines of varying chain lengths used in usual reactions) by stepwise syntheses (Scheme 2). Herein, we report on the correlation between the enantioselectivity, degree of polymerization of the catalyst, and the chain terminal functionality. Also presented are IR measurements suggestive of the role of α-helical structure of the catalysts on asymmetric induction. While this project was well underway, 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.[8e]

Results and Discussion

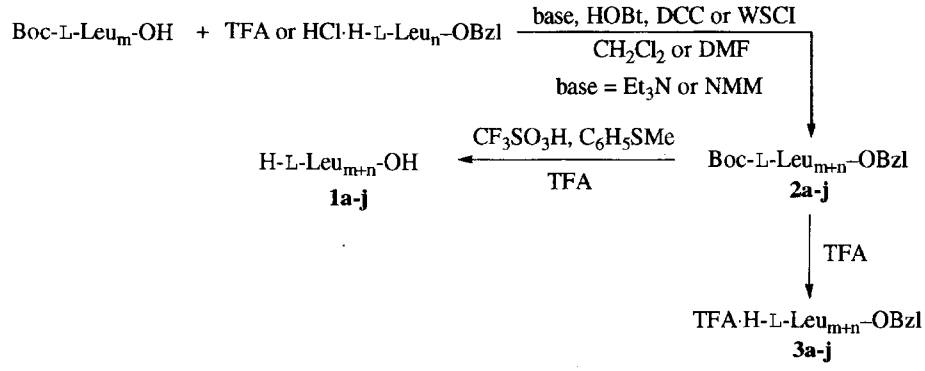
The *N*- and *O*-protected oligo-L-leucines, Boc–L-Leu$_{m+n}$–OBzl (**2a**—**j**), were prepared by the stepwise coupling of Boc–L-Leu$_m$–OH and H–L-Leu$_n$–OBzl.[10] The coupling reactions were mediated by dicyclohexylcarbodiimide (DCC) ($m+n$ = 2—5) or 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (WSCI) ($m+n > 5$) in the presence of 1-hydroxybenzotriazole (HOBt), as shown in Scheme 2. Deprotection of the *N*-terminus of Boc–L-Leu$_{m+n}$–OBzl (**2a**-**j**) was carried out by treatment with trifluoroacetic acid (TFA) to give TFA·H–L-Leu$_{m+n}$–OBzl (**3a**—**j**). The one-step deprotection of both *N*- and *C*-termini of Boc–L-Leu$_{m+n}$–OBzl (**2a**—**j**) was carried out by treatment with trifluoromethanesulfonic acid and methyl phenyl sulfide in TFA to give H–L-Leu$_{m+n}$–OH (**1a**—**j**). All of the synthetic leucine catalysts were fully characterized by ^{1}H NMR, and gave satisfactory combustion analyses and exact mass (FAB-MS or MALDI-MS).

Epoxidation reactions of chalcone in the presence of solid oligo-L-leucines (**1a**—**j**—**3a**—**j**) of various lengths were investigated at room temperature under triphasic conditions. In order to make comparisons, all reactions were terminated after 24 h.[11]

Table 1 and Fig. 1 show the chemical yield and enan-



Scheme 1. Juliá–Colonna asymmetric epoxidation using length defined oligo-L-leucine catslyst.



	m+n										
	5	7	8	9	10	11	12	13	14	15	20
H-L-Leu$_{m+n}$-OH	**1a**		**1b**	**1c**	**1d**	**1e**	**1f**	**1g**	**1h**	**1i**	**1j**
Boc-L-Leu$_{m+n}$-OBzl		**2a**	**2b**	**2c**	**2d**	**2e**	**2f**	**2g**	**2h**	**2i**	**2j**
TFA·H-L-Leu$_{m+n}$-OBzl		**3a**	**3b**	**3c**	**3d**	**3e**	**3f**	**3g**	**3h**	**3i**	**3j**

Scheme 2. Preparation of length defined oligo-L-leucines.

Table 1. Asymmetric Epoxidation of Chalcone Catalyzed by H–L-Leu$_{m+n}$–OH Catalysts

Entry	Catalyst	$m+n$	Yield/%	% ee[a]
1	**1a**	5	22	7
2	**1b**	8	20	10
3	**1c**	9	22	7
4	**1d**	10	46	13
5	**1e**	11	33	54
6	**1f**	12	24	25
7	**1g**	13	36	54
8	**1h**	14	52	41
9	**1i**	15	31	57
10	**1j**	20	37	56
11	None[b]	—	0	—
12	None[c]	—	0	—

a) Estimated by HPLC using a chiralcel OD column. b) This reaction was run in the absence of catalyst. c) The filtrate (the soluble portion) of the catalyst prepared by the conventional *N*-carboxyanhydride (2-oxazolin-5-one) polymerization method was used.

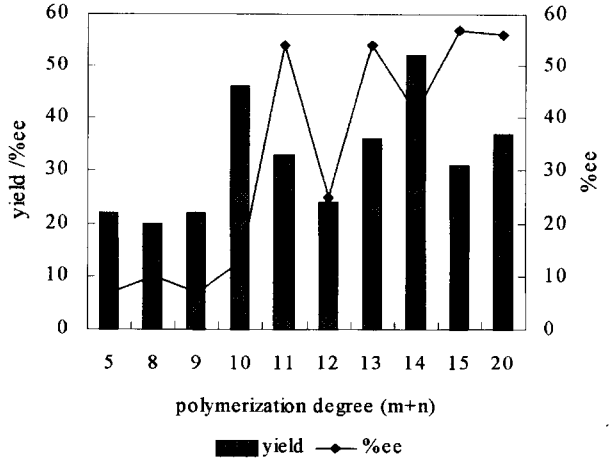


Fig. 1. Asymmetric epoxidation catalyzed by H–L-Leu$_{m+n}$–OH catalyst.

Table 2. Asymmetric Epoxidation of Chalcone Catalyzed by Boc–L-Leu$_{m+n}$–OBzl Catalysts

Entry	Catalyst	$m+n$	Yield/%	% ee[a]
1	**2a**	7	1	2
2	**2b**	8	6	4
3	**2c**	9	6	4
4	**2d**	10	4	15
5	**2e**	11	11	18
6	**2f**	12	6	22
7	**2g**	13	7	16
8	**2h**	14	12	20
9	**2i**	15	10	18
10	**2j**	20	11	41

a) Estimated by HPLC using a chiralcel OD column.

tioselectivity of the epoxidation of chalcone in the presence of H–L-Leu$_{m+n}$–OH (**1a**—**j**) catalysts. As the degree of polymerization of the catalyst increased, both the chemical yield and enantioselectivity sligthly increased (Entries 1—8). Only a minimal improvement was observed upon using higher polymer catalysts (Entries 9 and 10). It was confirmed that epoxidation does not occur in the absence of catalyst, thus dismissing the possibility of background reactions (Entries 11 and 12).

To elucidate the effect of *N*- and *C*-terminal groups of the catalysts, the epoxidation of chalcone was tested in the presence of Boc–L-Leu$_{m+n}$–OBzl (**2a**—**j**) in which both ends are protected, and TFA·H–L-Leu$_{m+n}$–OBzl (**3a**—**j**) in which only the *C*-terminus is protected. Table 2 and Fig. 2 show the yield and enantioselectivity of epoxidation in the presence of the former group of catalysts (**2a**—**j**). Both the chemical yield and enantioselectivity of the product were inferior compared with the corresponding unprotected H–L-Leu$_{m+n}$–OH

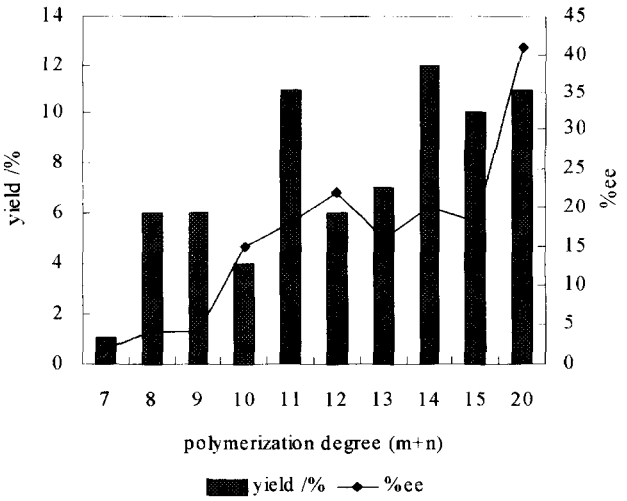


Fig. 2. Asymmetric epoxidation catalyzed by Boc–L-Leu$_{m+n}$–OBzl catalyst.

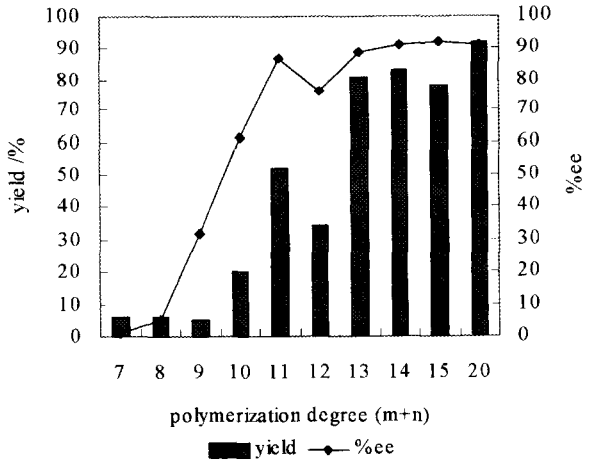


Fig. 3. Asymmetric epoxidation catalyzed by TFA·H–L-Leu$_{m+n}$–OBzl catalyst.

catalysts. The higher polymerized catalysts showed slightly better enantioselectivity (degree of polymerization > 10, entries 5—10).

Next, *C*-terminus-protected catalysts, TFA·H–L-Leu$_{m+n}$–OBzl (**3a—j**), were examined.[11] As shown in Table 3 and Fig. 3, compounds of degrees of polymerization of 9 and under were ineffective as catalysts (Entries 1—3). However, as in the case of catalysts **1a—j**, as the number of leucine units increased, both the yield and enantioselectivity improved, with optimum results with catalysts of and over 13 unit length.

A comparison of the results in Tables 1 and 3 with those in Table 2 indicates that a free terminal amine is preferable over a protected one for better results, whereas the functionality of the *C*-terminus (Tables 1 and 3) seems to be insignificant. Also, it was found that the longer the polymer is, the better the yield and enantioselectivity are for all three groups of catalysts. The required minimum degree of polymerization for optimum results seems to lie around 15 for the catalysts of both groups of unprotected amines.

The fact that the catalysts are practically insoluble under the reaction conditions implies the presence of strong intermolecular interaction between the catalyst chains. Thus, a plausible explanation for our experimental results is that as the lengths of the catalysts increase, the proportion of the moiety of the catalyst with the conformation required for asymmetric induction increases due to increasing entropy-favorable intra-chain hydrogen bonding interactions relative to inter-chain interactions which could lead to conformational randomization. The degree of polymerization of about 15 could be the point at which regulation of the required conformation initiates. Local regular conformations possible for such results would be either α-helical or β-sheet structure. The entropy considerations presented above suggest the former. Such structure has also been proposed (not on concrete evidence) in the original reports by Juliá and Colonna.[12]

Table 3. Asymmetric Epoxidation of Chalcone Catalyzed by TFA·H–L-Leu$_{m+n}$–OBzl Catalysts

Entry	Catalyst	$m+n$	Yield/%	% ee[a)]
1	**3a**	7	6	1
2	**3b**	8	6	5
3	**3c**	9	5	32
4	**3d**	10	20	61
5	**3e**	11	52	87
6	**3f**	12	34	76
7	**3g**	13	81	89
8	**3h**	14	83	91
9	**3i**	15	78	92
10	**3j**	20	92	91

a) Estimated by HPLC using a chiralcel OD column.

Reports on IR measurements of peptides have indicated the relationship between secondary amide structure, α-helical and β-sheet, and amide region I absorption frequencies, 1660 and 1630 cm^{-1}, respectively.[13] Thus, in order to obtain structural insight of the catalysts, IR measurements on solid samples were carried out. Since the epoxidation reactions were run in solution, the state of the catalyst may not be completely the same as in the solid state. However, since the catalysts remained undissolved in solution (with no apparent change), and the soluble portion of the catalyst prepared by the conventional leucine-*N*-carboxyanhydride (4-isobutyl-2-oxazolin-5-one) method showed no catalytic activity (Table 1, Entry 11), the solid state IR should reflect the state of the solution catalyst to a high degree.

The amide I region in the IR spectra of H–L-Leu$_{m+n}$–OH (**1**), Boc–L-Leu$_{m+n}$–OBzl (**2**), and TFA·H–L-Leu$_{m+n}$–OBzl (**3**) in the solid state are shown in Fig. 4. The IR spectra of H–L-Leu$_{m+n}$–OH (**1d**, **1i**, **1j**), in Fig. 4a, show strong bands at 1630 cm^{-1} indicating the presence of large portions of β-sheet structure. Also observable are shoulder bands at 1655 cm^{-1} assigned to the helical structure, of which the relative intensity appears to increase with the degree of polymerization. Figure 4b shows the amide I region of Boc–L-Leu$_{m+n}$–OBzl (**2d**, **2i**, **2j**), which proved to be least effective as catalysts among the three groups. Here, strong absorption bands at 1630 cm^{-1} assigned to the β-sheet structure are

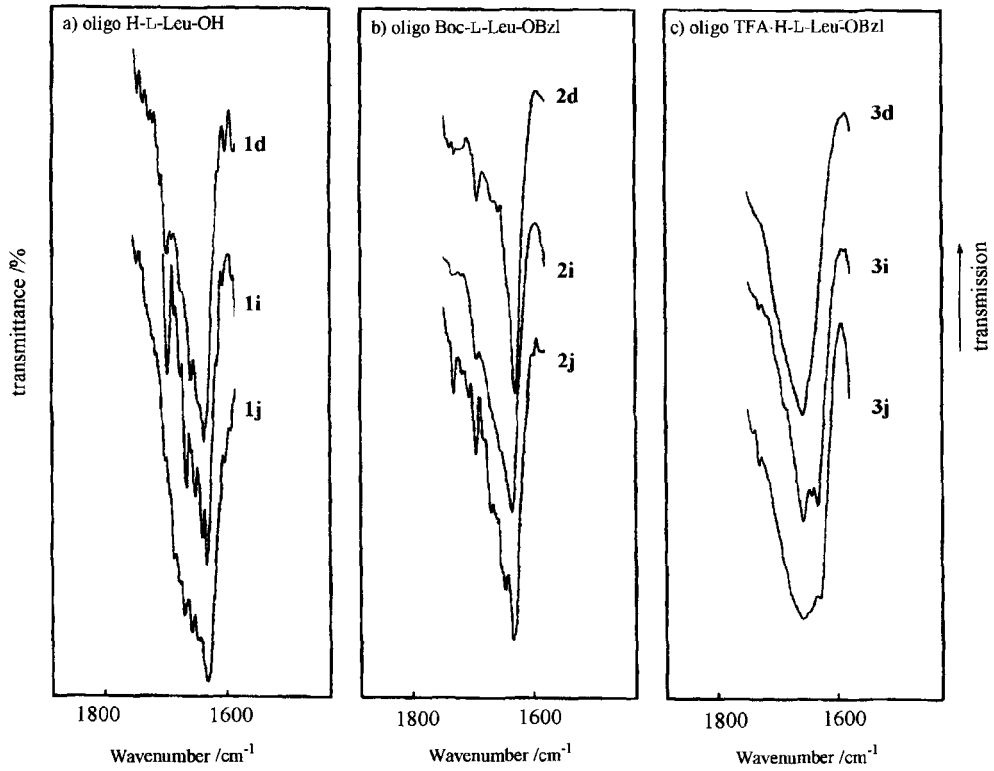


Fig. 4. IR spectra of oligo-L-leucine catslyst (**1d,i,j**, **2d,i,j**, **3d,i,j**).

seen, and the shoulder bands at 1655 cm^{-1} are relatively much weaker than those for the corresponding catalyst **1**. The IR spectra of the amide I region of TFA·H–L-Leu_{m+n}–OBzl are shown in Fig. 4c. In this case, a reversal of intensity was observed. All TFA·H–L-Leu_{m+n}–OBzl (**3d**, **3i**, **3j**) showed strong absorption bands at 1660 cm^{-1} assigned to helical structure with weaker bands at 1635 cm^{-1} assigned to the β-sheet structure.

A comprehensive qualitative analysis of the IR spectra clearly shows a relationship between the intensity of the band at 1655 cm^{-1} and enantioselectivity of the reactions; the stronger the absorption, higher the selectivity. These results support the assumption that the helical structure of the oligo-leucine catalysts plays an important role in the asymmetric induction process. Upon these grounds, the negative effect of terminal amine protection could be attributed to the incapability of the oligomeric compounds to assume the required helical structure.

Conclusion

In summary, our results show that in Juliá–Colonna asymmetric epoxidation, the higher the degree of polymerization of the catalyst is, the higher the yield and selectivity are. Optimal conditions require leaving the *N*-terminus unprotected and having the number of leucine units at least ca. 15. IR measurements suggest that the proportion of helical structure of the catalyst is related to the size of the catalyst and nature of the *N*-terminus, and thus controls the enantioselectivity. Since the levels of asymmetric induction observed here for long length catalysts are comparable with those of original Juliá–Colonna catalysts, our results support the original speculations made by Juliá and Colonna that α-helical structure of the catalysts is important for high asymmetric induction.

Experimental

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 spectrometer. High-resolution mass spectra (HRMS) were recorded on a JEOL SX-102A mass spectrometer under fast-atom bombardment (FAB) conditions. MALDI-TOF Mass spectra were recorded on a Bruker REFLEX.

General Procedure for the Stepwise Elongation Reaction. Boc–L-Leu_m–OH, TFA·H–L-Leu_n–OBzl or HCl·H–L-Leu_n–OBzl (1.12 mmol) and 1-hydroxybenzotriazole (HOBt) (1.89 mmol) were dissolved in DMF (45 ml). *N*-Methylmorpholine (NMM) (0.15 ml, 1.4 mmol) was added to the solution. The resulting mixture was cooled to −20 °C and stirred. After 1 h, a solution of 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (WSCI) (231 mg, 1.21 mmol) in CH_2Cl_2 (4 ml) was added to the reaction mixture. The mixture was stirred overnight at −20 to 25 °C. After the evaporation of CH_2Cl_2, the mixture was poured into ice-water. Continued stirring resulted in the precipitation of a white solid, which was filtered and washed with CH_2Cl_2. The white solid was used for subsequent reactions without further purification.

General Procedure for the Deprotection of Both *N*- and *C*-Termini of Boc–L-Leu_{m+n}–OBzl. A 1.0 M solution (3.2 ml) of CF_3SO_3H and C_6H_5SMe in TFA (1 M = 1 mol dm^{-3}) was added to Boc–L-Leu_{m+n}–OBzl (0.12 mmol), and the resulting mixture was stirred at 25 °C. After 3.5 h, DMF (50 ml) was added to the reaction mixture. The white solid which formed was filtered and washed with DMF and H_2O, and was used for subsequent reactions without further purification.

General Procedure for the Deprotection of *C*-Termini of

Boc–L-Leu$_{m+n}$–OBzl. A solution of Boc–L-Leu$_{m+n}$–OBzl (0.41 mmol) and 5% Pd/C (30.5 mg) in MeOH (5 ml) was stirred at 25 °C under a hydrogen atmosphere overnight. The reaction mixture was filtered and concentrated. The crude product was used for subsequent reactions without further purification.

H–L-Leu$_5$–OH (1a): 90%; ^{1}H NMR (500 MHz, TFA in $CDCl_3$) δ = 0.86—0.95 (30H, m), 1.54—1.75 (15H, m), 4.21 (1H, bs), 4.51—4.63 (4H, m), 7.32 (1H, bs), 7.56 (3H, bs), 7.77 (1H, bs), 7.87 (1H, bs), 8.05 (1H, bs); IR (KBr) 3264, 2961, 1632, 1550 cm^{-1}; FAB-HRMS *m/z* 584.4442, $[M+H]^+$. Calcd for $C_{30}H_{57}N_5O_6$: M, 584.4387.

H–L-Leu$_8$–OH (1b): 98%; ^{1}H NMR (500 MHz, TFA in $CDCl_3$) δ = 0.85—0.95 (48H, m), 1.45—1.75 (24H, m), 4.20—4.60 (8H, m), 7.40—8.00 (8H, m), the two protons (the amide and the carboxylic acid) were not observed due to the broadening of the signal; IR (KBr) 3264, 2961, 1632, 1550 cm^{-1}; MALDI-TOF MS 945.80 ($[M+Na]^+$). Anal. Calcd for $C_{48}H_{90}N_8O_9$: C, 62.44; H, 9.83; N, 12.14%. Found: C, 62.47; H, 10.00; N, 12.15%.

H–L-Leu$_9$–OH (1c): 92%; ^{1}H NMR (500 MHz, TFA in $CDCl_3$) δ = 0.79—0.94 (54H, m), 1.45—1.76 (27H, m), 4.22 (1H, m), 4.42—4.60 (8H, m), 7.17 (1H, m), 7.28 (3H, m), 7.47 (1H, d, J = 6.6 Hz), 7.53 (1H, d, J = 7.8 Hz), 7.65 (2H, d, J = 7.3 Hz), 7.77 (1H, d, J = 7.6 Hz), 7.90 (1H, d, J = 7.8 Hz), 7.95 (1H, d, J = 7.3 Hz); IR (KBr) 3264, 2958, 1631, 1549 cm^{-1}; MALDI-TOF MS 1058.88 ($[M+Na]^+$). Anal. Calcd for $C_{54}H_{101}N_9O_{10}$: C, 62.58; H, 9.82; N, 12.16%. Found: C, 62.58; H, 9.97; N, 11.92%.

H–L-Leu$_{10}$–OH (1d): 59%; mp 260 °C (decomp); ^{1}H NMR (500 MHz, TFA in $CDCl_3$) δ = 0.75—1.03 (60H, m), 1.48—1.87 (30H, m), 4.15—4.55 (10H, m), 7.15—8.37 (10H, m), two protons (of an amide and a carboxylic acid) were not observed due to broadening of the signals; IR (KBr) 3263, 2959, 2870, 1655, 1635, 1542 cm^{-1}; MALDI-TOF MS 1171.70 ($[M+Na]^+$). Anal. Calcd for $C_{60}H_{112}N_{10}O_{11}$: C, 62.69; H, 9.82; N, 12.18%. Found: C, 62.74; H, 9.57; N, 12.17%.

H–L-Leu$_{11}$–OH (1e): 59%; ^{1}H NMR (500 MHz, TFA in $CDCl_3$) δ = 0.83—1.04 (66H, m), 1.52—1.84 (33H, m), 4.21—4.47 (11H, m), 7.26—8.22 (13H, m); IR (KBr) 3288, 3084, 2965, 1629, 1542 cm^{-1}; MALDI-TOF MS 1398.15 ($[M+Na]^+$). Anal. Calcd for $C_{66}H_{123}N_{11}O_{12}$: C, 62.78; H, 9.82; N, 12.20%. Found: C, 62.80; H, 10.03; N, 12.17%.

H–L-Leu$_{12}$–OH (1f): 55%; ^{1}H NMR (500 MHz, TFA in $CDCl_3$) δ = 0.76—1.06 (72H, m), 1.46—1.90 (36H, m), 4.08—4.62 (12H, m), 7.19—8.32 (14H, m); IR (KBr) 3269, 2958, 1626, 1555 cm^{-1}; MALDI-TOF MS 1397.68 ($[M+Na]^+$). Anal. Calcd for $C_{72}H_{134}N_{12}O_{13}$: C, 62.84; H, 9.82; N, 12.22%. Found: C, 62.62; H, 9.99; N, 12.45%.

H–L-Leu$_{13}$–OH (1g): 68%; ^{1}H NMR (500 MHz, TFA in $CDCl_3$) δ = 0.79—1.05 (78H, m), 1.49—1.93 (39H, m), 4.04—4.51 (13H, m), 7.14—8.25 (15H, m); IR (KBr) 3266, 2959, 1633, 1554 cm^{-1}; MALDI-TOF MS 1512.15 ($[M+Na]^+$). Anal. Calcd for $C_{78}H_{145}N_{13}O_{14}$: C, 62.92; H, 9.81; N, 12.23%. Found: C, 62.83; H, 9.80; N, 12.23%.

H–L-Leu$_{14}$–OH (1h): 43%; ^{1}H NMR (500 MHz, TFA in $CDCl_3$) δ = 0.81—1.03 (84H, m), 1.50—1.89 (42H, m), 4.08—4.99 (14H, m), 7.23—8.96 (16H, m); IR (KBr) 3279, 2957, 2873, 1694, 1631, 1543 cm^{-1}; MALDI-TOF MS 1624.91 ($[M+Na]^+$). Anal. Calcd for $C_{84}H_{156}N_{14}O_{15}$: C, 62.97; H, 9.81; N, 12.24%. Found: C, 62.98; H, 9.86; N, 12.47%.

H–L-Leu$_{15}$–OH (1i): 81%; ^{1}H NMR (500 MHz, TFA in $CDCl_3$) δ = 0.71—1.02 (90H, m), 1.42—1.90 (45H, m), 4.03—4.62 (15H, m), 7.35—8.30 (15H, m), the protons (of an amide and a carboxylic acid) were not observed due to broadening of the signals; IR (KBr) 3275, 2930, 1631, 1548 cm^{-1}; MALDI-TOF MS 1738.43 ($[M+Na]^+$). Anal. Calcd for $C_{90}H_{167}N_{15}O_{16}$: C, 63.02; H, 9.81; N, 12.25%. Found: C, 62.95; H, 9.90; N, 12.29%.

H–L-Leu$_{20}$–OH (1j): 34%; ^{1}H NMR (500 MHz, TFA in $CDCl_3$) δ = 0.75—1.03 (120H, m), 1.50—1.91 (60H, m), 3.85—4.57 (20H, m), 7.05—8.44 (20H, m), two protons (of an amide and a carboxylic acid) were not observed due to broadening of the signal; IR (KBr) 3262, 2959, 1657, 1630 cm^{-1}; MALDI-TOF MS 2302.90 ($[M+Na]^+$).

Boc–L-Leu$_7$–OBzl (2a): 81%; mp 273 °C (decomp); ^{1}H NMR (500 MHz, TFA in $CDCl_3$) δ = 0.82—0.94 (42H, m), 1.41—1.69 (21H, m), 1.46 (9H, s), 4.11—4.65 (7H, m), 5.20 (1H, d, J = 12.2 Hz), 5.21 (1H, d, J = 12.2 Hz), 7.15—7.97 (12H, m); IR (KBr) 3268, 3085, 2958, 1630, 1548 cm^{-1}; MALDI-TOF MS 1035.56 ($[M+Na]^+$), 922.48 ($[M-Boc+Na]^+$). Anal. Calcd for $C_{54}H_{93}N_7O_{10}$: C, 64.84; H, 9.37; N, 9.80%. Found: C, 64.86; H, 9.32; N, 9.94%.

Boc–L-Leu$_8$–OBzl (2b): 79%; ^{1}H NMR (500 MHz, TFA in $CDCl_3$) δ = 0.83—0.94 (48H, m), 1.40—1.72 (24H, m), 1.44 (9H, s), 4.10—4.66 (8H, m), 5.20 (1H, d, J = 12.2 Hz), 5.22 (1H, d, J = 12.2 Hz), 6.54—7.86 (13H, m); MALDI-TOF MS 1035.74 ($[M-Boc+Na]^+$); IR (KBr) 3273, 2958, 1630, 1542, 1167 cm^{-1}. Anal. Calcd for $C_{60}H_{104}N_8O_{11}$: C, 64.72; H, 9.41; N, 10.06%. Found: C, 64.52; H, 9.49; N, 10.32%.

Boc–L-Leu$_9$–OBzl (2c): 94%; ^{1}H NMR (500 MHz, TFA in $CDCl_3$) δ = 0.82—0.90 (54H, m), 1.44 (9H, s), 1.48—1.60 (27H, m), 4.11—4.60 (9H, m), 5.19 (1H, d, J = 11.9 Hz), 5.24 (1H, d, J = 11.9 Hz), 7.22 (1H, m), 7.32—7.30 (5H, m), 7.52—7.80 (8H, m); IR (KBr) 3262, 2964, 1629, 1541 cm^{-1}; MALDI-TOF MS 1148.72 ($[M-Boc+Na]^+$). Anal. Calcd for $C_{66}H_{115}N_9O_{12}$: C, 64.62; H, 9.45; N, 10.28%. Found: C, 64.53; H, 9.49; N, 10.32%.

Boc-L-Leu$_{10}$-OBzl (2d): 90%; ^{1}H NMR (500 MHz, TFA in $CDCl_3$) δ = 0.83—0.93 (60H, m), 1.44—1.72 (30H, m), 1.44 (9H, s), 4.12—4.67 (10H, m), 5.20 (2H, m), 7.20—7.97 (15H, m); IR (KBr) 3268, 2956, 2870, 1630, 1545 cm^{-1}; MALDI-TOF MS 1262.49 ($[M-Boc+Na]^+$). Anal. Calcd for $C_{72}H_{126}N_{10}O_{13}$: C, 64.54; H, 9.48; N, 10.45%. Found: C, 64.40; H, 9.48; N, 10.63%.

Boc–L-Leu$_{11}$–OBzl (2e): 91%; ^{1}H NMR (500 MHz, TFA in $CDCl_3$) δ = 0.85—0.95 (66H, m), 1.44 (9H, s), 1.43—1.69 (33H, m), 4.09—4.67 (11H, m), 5.20 (2H, m), 7.16—7.97 (16H, m); IR (KBr): 3266, 2958, 1630, 1542, 1386, 1368, 1279, 1159 cm^{-1}. Anal. Calcd for $C_{78}H_{137}N_{11}O_{14}$: C, 64.48; H, 9.50; N, 10.60%. Found: C, 64.44; H, 9.50; N, 10.60%.

Boc–L-Leu$_{12}$–OBzl (2f): 93%; ^{1}H NMR (500MHz, TFA in $CDCl_3$) δ = 0.84—0.94 (72H, m), 1.44—1.79 (36H, m), 1.46 (9H, s), 4.01—4.67 (12H, m), 5.13 (2H, m), 7.13—8.12 (17H, m); MALDI-TOF MS 1488.64 ($[M-Boc+Na]^+$); IR (KBr) 3266, 2957, 1694, 1630, 1549, 1164, 718 cm^{-1}. Anal. Calcd for $C_{84}H_{148}N_{12}O_{15}$: C, 64.42; H, 9.52; N, 10.73%. Found: C, 64.50; H, 9.28; N, 10.83%.

Boc-L-Leu$_{13}$-OBzl (2g): 83%; ^{1}H NMR (500 MHz, TFA in $CDCl_3$) δ = 0.77—0.91 (78H, m), 1.46 (9H, s), 1.44—1.86 (39H, m), 4.13—4.63 (13H, m), 5.15 (2H, m), 7.16—8.22 (18H, m); IR (KBr) 3264, 2960, 1632, 1542 cm^{-1}; MALDI-TOF MS 1601.84 ($[M-Boc+Na]^+$). Anal. Calcd for $C_{90}H_{159}N_{13}O_{16}$: C, 64.37; H, 9.54; N, 10.84%. Found: C, 64.29; H, 9.79; N, 10.92%.

Boc–L-Leu$_{14}$–OBzl (2h): 92%; ^{1}H NMR (500 MHz, TFA in $CDCl_3$) δ = 0.81—1.07 (84H, m), 1.46 (9H, s), 1.43—1.96 (42H, m), 4.08—4.64 (14H, m), 5.20 (2H, m), 7.28—8.26 (19H, m); IR (KBr) 3274, 2956, 1630, 1549 cm^{-1}; MALDI-TOF MS 1715.23 ($[M-Boc+Na]^+$). Anal. Calcd for $C_{96}H_{170}N_{14}O_{17}$: C, 64.33; H, 9.56; N, 10.94%. Found: C, 66.43; H, 9.53; N, 11.00%.

Boc-L-Leu$_{15}$-OBzl (2i): 67%; mp 260 °C (decomp); ^{1}H NMR (500 MHz, TFA in $CDCl_3$) δ = 0.77—1.06 (90H, m), 1.35—2.07 (54H, m), 3.71—4.71 (15H, m), 5.14 (1H, d, J = 12.5 Hz), 5.18 (1H, d, J = 12.5 Hz), 7.32—7.45 (5H, m), 7.58—8.71 (15H, m); MALDI-TOF MS 1828.50 ([M − Boc + Na + H]$^+$); IR (KBr) 3270, 2872, 1631, 1540 cm^{-1}. Anal. Calcd for $C_{102}H_{181}N_{15}O_{18}$: C, 64.29; H, 9.57; N, 11.03%. Found: C, 64.17; H, 9.75; N, 11.09%.

Boc-L-Leu$_{20}$-OBzl (2j): 71%; mp 265 °C (decomp); ^{1}H NMR (500 MHz, TFA in $CDCl_3$) δ = 0.72—1.08 (120H, m), 1.38—2.05 (69H, m), 3.83—4.68 (20H, m), 5.12—5.22 (2H, m), 7.29—7.45 (5H, m), 7.50—8.52 (20H, m); MALDI-TOF MS 2394.36 ([M − Boc + Na + H]$^+$); IR (KBr) 3314, 2926, 1631, 1544 cm^{-1}. Anal. Calcd for $C_{132}H_{236}N_{20}O_{23}$: C, 64.15; H, 9.62; N, 11.33%. Found: C, 64.07; H, 9.66; N; 11.33%.

General Procedure for the Deprotection of *N*-Termini of Boc-L-Leu$_{m+n}$-OBzl. TFA (2.0 ml, 26 mmol) was added to Boc-L-Leu$_{m+n}$-OBzl (0.13 mmol) at −16 °C. After 2 h, the reaction mixture was warmed to 25 °C and stirred for 7 h. Excess TFA was removed to dryness by successive azeotropic evaporation with CH_2Cl_2 (10 ml) under reduced pressure. Dry Et_2O (100 ml) was added to the residue to form a white solid, which was formed and filtered. The white solid was used for subsequent reactions without further purification.

TFA·H-L-Leu$_7$-OBzl (3a): 95%; ^{1}H NMR (500 MHz, TFA in $CDCl_3$) δ = 0.82—0.94 (42H, m), 1.47—1.71 (21H, m), 4.16 (1H, m), 4.45—4.61 (6H, m), 5.17 (1H, d, J = 12.2 Hz), 5.18 (1H, d, J = 12.2 Hz), 7.31—7.47 (5H, m), 7.62—8.05 (9H, m); MALDI-TOF MS 922.46 ([M − TFA + Na]$^+$); IR (KBr) 3264, 2960, 1695, 1635, 1557, 1204, 1139, 721, 697 cm^{-1}. Anal. Calcd for $C_{51}H_{86}F_3N_7O_{10}$: C, 60.39; H, 8.55; N, 9.67%. Found: C, 60.25; H, 8.65; N, 9.65%.

TFA·H-L-Leu$_8$-OBzl (3b): 95%; ^{1}H NMR (500 MHz, TFA in $CDCl_3$) δ = 0.82—0.98 (48H, m), 1.46—1.74 (24H, m), 4.23—4.62 (8H, m), 5.19 (1H, d, J = 11.9 Hz), 5.20 (1H, d, J = 11.9 Hz), 7.24—7.47 (5H, m), 7.50—7.99 (10H, m); IR (KBr) 3266, 2959, 1734, 1636, 1541, 1203, 1140, 722, 697 cm^{-1}; MALDI-TOF MS 1036.2959 ([M − TFA + Na]$^+$.) Anal. Calcd for $C_{57}H_{97}F_3N_8O_{11}$: C, 60.72; H, 8.67; N, 9.94%. Found: C, 60.64; H, 8.86; N, 10.02%.

TFA·H-L-Leu$_9$-OBzl (3c): 93%; ^{1}H NMR (500 MHz, TFA in $CDCl_3$) δ = 0.80—1.00 (54H, m), 1.46—1.76 (27H, m), 4.41—4.64 (9H, m), 5.19 (1H, d, J = 12.2 Hz), 5.20 (1H, d, J = 12.2 Hz), 7.32—8.09 (16H, m); IR (KBr) 3261, 2962, 1669, 1633, 1542 cm^{-1}; MALDI-TOF MS 1148.72 ([M − TFA + Na]$^+$). Anal. Calcd for $C_{63}H_{108}F_3N_9O_{12}$: C, 60.99; H, 8.77; N, 10.16%. Found: C, 61.17; H, 8.51; N, 10.35%.

TFA·H-L-Leu$_{10}$-OBzl (3d): 90%; ^{1}H NMR (500 MHz, TFA in $CDCl_3$) δ = 0.82—0.99 (60H, m), 1.46—1.78 (30H, m), 4.24—4.65 (10H, m), 5.27 (2H, m), 7.31—8.13 (17H, m); IR (KBr) 3313, 2960, 2873, 1660, 1543 cm^{-1}; MALDI-TOF MS 1262.10 ([M − TFA + Na]$^+$). Anal. Calcd for $C_{69}H_{119}F_3N_{10}O_{13}$: C, 61.22; H, 8.86; N, 10.35%. Found: C, 61.20; H, 8.71; N, 10.43%.

TFA·H-L-Leu$_{11}$-OBzl (3e): 95%; ^{1}H NMR (500 MHz, TFA in $CDCl_3$) δ = 0.82—0.96 (66H, m), 1.42—1.70 (33H, m), 4.10—4.68 (11H, m), 5.16—5.26 (2H, m), 7.20—7.88 (16H, m), two protons (of an amide and TFA) were not observed due to broadening of the signals; IR (KBr) 3280, 2958, 1667, 1632, 1549 cm^{-1}; MALDI-TOF MS 1489.19 ([M + Na]$^+$). Anal. Calcd for $C_{75}H_{130}F_3N_{11}O_{14}$: C, 61.41; H, 8.93; N, 10.50%. Found: C, 61.52; H, 8.97; N, 10.31%.

TFA·H-L-Leu$_{12}$-OBzl (3f): 90%; ^{1}H NMR (500 MHz, TFA in $CDCl_3$) δ = 0.84—0.96 (72H, m), 1.49—1.82 (36H, m), 4.10—4.65 (12H, m), 5.13 (2H, m), 7.13—8.14 (17H, m); MALDI-TOF MS 1487.43 ([M − TFA + Na]$^+$); IR (KBr) 3298, 3265, 2959, 1635, 1540, 1471, 1204, 721 cm^{-1}. Anal. Calcd for $C_{81}H_{141}F_3N_{12}O_{15}$: C, 61.57; H, 8.99; N, 10.64%. Found: C, 61.51; H, 9.00; N, 10.65%.

TFA·H-L-Leu$_{13}$-OBzl (3g): 80%; ^{1}H NMR (500 MHz, TFA in $CDCl_3$) δ = 0.77—1.04 (78H, m), 1.46—1.94 (39H, m), 4.04—4.92 (13H, m), 5.06—5.19 (2H, m), 7.17—8.46 (18H, m), two protons (the amide) were not observed due to broadening of the signals; IR (KBr) 3286, 2962, 1655, 1633, 1542 cm^{-1}; MALDI-TOF MS 1602.14 ([M − TFA + Na]$^+$). Anal. Calcd for $C_{87}H_{152}F_3N_{13}O_{16}$: C, 64.65; H, 9.64; N, 11.53%. Found: C, 64.75; H, 9.65; N, 11.27%.

TFA·H-L-Leu$_{14}$-OBzl (3h): 64%; ^{1}H NMR (500 MHz, TFA in $CDCl_3$) δ = 0.62—0.97 (84H, m), 1.38—1.93 (42H, m), 3.99—4.61 (14H, m), 5.04—5.17 (2H, m), 7.18—8.49 (19H, m), two protons (of an amide and TFA) were not observed due to broadening of the signals; IR (KBr) 3281, 2959, 1660, 1636, 1544 cm^{-1}; MALDI-TOF MS 1714.33 ([M − TFA + Na]$^+$). Anal. Calcd for $C_{93}H_{163}F_3N_{14}O_{17}$: C, 61.84; H, 9.10; N, 10.86%. Found: C, 61.98; H, 8.98; N, 10.94%.

TFA·H-L-Leu$_{15}$-OBzl (3i): 85%; mp 245 °C (decomp); ^{1}H NMR (500 MHz, TFA in $CDCl_3$) δ = 0.52—1.17 (90H, m), 1.35—2.19 (45H, m), 3.87—4.79 (15H, m), 5.09 (1H, d, J = 12.2 Hz), 5.14 (1H, d, J = 12.2 Hz), 7.34—8.23 (20H, m), two protons (of an amide and TFA) were not observed due to broadening of the signals; IR (KBr) 3308, 2959, 1660, 1635, 1543 cm^{-1}; MALDI-TOF MS 1262.09 ([M − TFA + Na]$^+$). Anal. Calcd for $C_{99}H_{174}F_3N_{15}O_{18}$: C, 62.65; H, 8.97; N, 10.74%. Found: C, 62.59; H, 9.17; N, 10.95%.

TFA·H-L-Leu$_{20}$-OBzl (3j): 70%; mp 250 °C (decomp); ^{1}H NMR (500 MHz, TFA in $CDCl_3$) δ = 0.67—1.05 (120H, m), 1.40—2.05 (60H, m), 3.90—4.78 (20H, m), 5.05—5.22 (2H, m), 7.29—8.57 (25H, m), two protons (of an amide and TFA) were not observed due to broadening of the signals; IR (KBr) 3296, 2960, 1663, 1632, 1543 cm^{-1}; MALDI-TOF MS 2392.98 ([M − TFA + Na]$^+$). Anal. Calcd for $C_{129}H_{229}F_3N_{20}O_{23}$: C, 62.34; H, 9.29; N, 11.27%. Found: C, 62.18; H, 9.42; N, 11.27%.

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) in 30% aqueous H_2O_2 (10 ml) was added to a mixture of oligo-L-leucine catalyst (100 mg) and chalcone (100 mg) in toluene (1.7 ml) at 0 °C. The mixture was allowed to warm to room temperature and was vigorously stirred for 24 h. The insoluble catalyst was filtered off and the filtrate was washed with water and brine, dried with Na_2SO_4, and evaporated. The crude product was purified by preparative TLC [silica gel, petroleum ether –diethyl ether = 10 : 1 (v/v)]. The enantiomeric excess of the product was estimated 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-diphenylpropane-1-one:**[14] ^{1}H NMR (270 MHz, $CDCl_3$) δ = 4.08 (1H, d, J = 2.0 Hz), 4.29 (1H, d, J = 2.0 Hz), 7.43—8.06 (10H, m); EI-HRMS m/z 224.0843 M$^+$. Calcd for $C_{15}H_{12}O_2$: M$^+$, 224.0837; 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).

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