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This article is dedicated to Professor Satoshi Ōmura in celebration of his 2015 Nobel Prize.

Regular Article

Chiral Integrated Catalysts Composed of Bifunctional Thiourea and Arylboronic Acid: Asymmetric Aza-Michael Addition of α,β-Unsaturated Carboxylic Acids

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The first intermolecular asymmetric Michael addition of nitrogen-nucleophiles to α,β-unsaturated carboxylic acids was achieved through a new type of arylboronic acid equipped with chiral aminothiourea. The use of $BnONH_2$ as a nucleophile gives a range of enantioenriched β-(benzyloxy)amino acid derivatives in good yields and with high enantioselectivity (up to 90% yield, 97% enantiomeric excess (ee)). The obtained products are efficiently converted to optically active β-amino acid and 1,2-diamine derivatives.

Key words aza-Michael addition; α,β-unsaturated carboxylic acid; integrated catalyst; thiourea; arylboronic acid; *O*-benzylhydroxylamine

Stereoselective functionalization of electron-deficient alkenes continues to play a fundamental role in modern organic synthesis. The catalytic asymmetric aza-Michael addition of α,β-unsaturated carboxylic acid derivatives has been extensively investigated as a powerful protocol for the synthesis of optically active β-amino acids,[1–4] which are frequently encountered as important structural components in biologically active natural products and pharmaceuticals.[5] However, simple α,β-unsaturated esters and amides have only been used in a limited number of successful studies because of their inherent low reactivity as Michael acceptors.[6,7] Instead, a variety of activated ester/amide surrogates possessing greater reactivity and rigidity, which enables them to interact with appropriate catalysts, have been developed for the Michael addition.[8] Recently, a range of activated carboxylates—specifically, α,β-unsaturated imides,[9,10] acyl pyrroles,[11] and acyl pyrazoles[12]—have been successfully applied in asymmetric metal- and organocatalyzed Michael additions to furnish the desired products with excellent enantioselectivity (Chart 1). However, this masked ester/amide strategy requires a stoichiometric amount of an activating auxiliary and additional protection and deprotection steps. From the perspective of atom and step economy, achieving a direct Michael reaction of α,β-unsaturated carboxylic acids without the use of any activating templates is highly desirable. Despite strong synthetic utility, the direct Michael addition of α,β-unsaturated carboxylic acids has never been reported, except for an enzyme-catalyzed aza-Michael addition[13,14]; very few strategies have been exploited to catalytically activate the hydroxy group of carboxylic acids *via* transient covalent bond formation.

By contrast, since the discovery by Yamamoto and Ishihara that electron-deficient arylboronic acids are efficient activators of carboxylic acids in direct amidation reactions,[15–18] a series of arylboronic acids have been developed for the activation of various functional groups, including α,β-unsaturated carboxylic acids,[19–21] alcohols,[22] carbonyl compounds,[23] and others.[24,25] Hall reported that different types of arylboronic acids could be used for the cycloaddition of α,β-unsaturated carboxylic acids to dienes and 1,3-dipoles.[20,21] Recently, we also revealed that aminoarylboronic acid was the best catalyst for the intramolecular hetero-Michael addition of α,β-unsaturated carboxylic acids bearing sulfonamides or phenols.[26] In addition, the asymmetric oxa-Michael addition could be achieved *via* a dual catalysis system consisting of bifunctional thiourea[27] and 3,5-bis-(trifluoromethyl)phenylboronic acid. On the basis of these results, we explored two activation strategies for the intermolecular asymmetric aza-Michael addition of α,β-unsaturated carboxylic acids (Chart 2): (i) synergistic activation of a nucleophile and an electrophile using a bimolecular dual catalyst system, and (ii) dual activation of a carboxylic acid moiety using structurally integrated catalysts composed of arylboronic acid and bifunctional *N*-arylthiourea moieties.[28,29] To perform the target reaction, both regioselectivity and enantioselectivity must be controlled by these catalytic systems. Herein, we report that a novel chiral hybrid catalyst remarkably promoted the intermolecular aza-Michael addition of *O*-benzylhydroxylamine to a wide range of α,β-unsaturated carboxylic acids, providing the Michael adducts with complete regioselectivity and high enantioselectivity.

Results and Discussion

We initially examined the aza-Michael addition of (*E*)-5-phenylpent-2-enoic acid **1a** with $BnONH_2$ under dual catalytic conditions [strategy (i)] using achiral arylboronic acids **4a**–**c** and aminothiourea **5** (Table 1). The reaction was performed in CCl_4 at room temperature with 10 mol% of each catalyst and 4 Å molecular sieves. Although the electron-deficient arylboronic acid **4a** gave no desired product **2a**, affording

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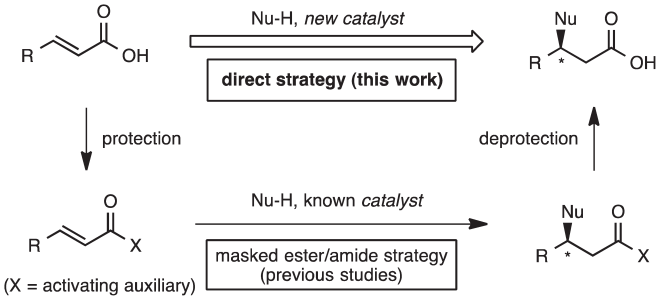


Chart 1. Direct Michael Addition to α,β-Unsaturated Carboxylic Acids

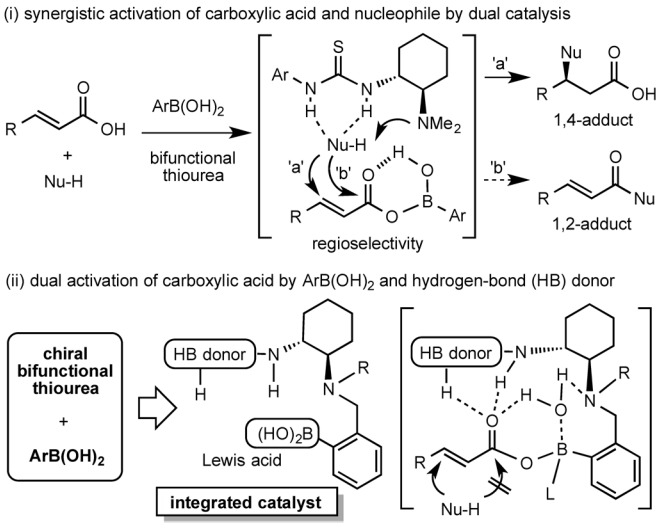
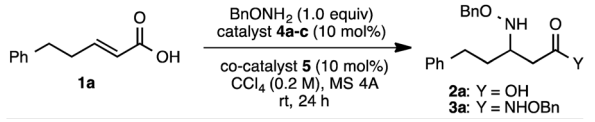
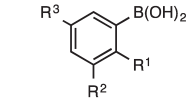


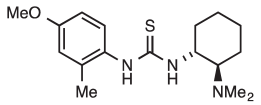
Chart 2. Asymmetric Michael Addition *via* (i) Dual Catalysis and (ii) Integrated Catalysis

Table 1. Intermolecular Aza-Michael Addition Catalyzed by **4a**–**c** and Co-catalyst **5**



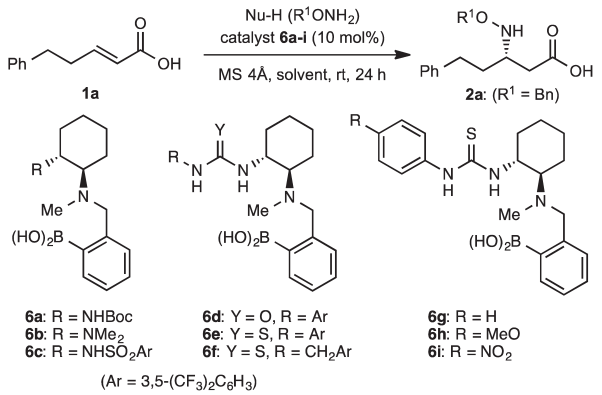
Catalyst	**2a**	**3a**
(a) **4a** and **5**:	0%	41%
(b) **4b** and **5**:	15% (0% ee)	6%
(c) **4c** and **5**:	29% (0% ee)	22%





only double-addition adduct **3a** in moderate yield, mixtures of **2a** and **3a** were obtained with other catalyst combinations **4b**/**5** and **c**/**5**, giving only racemic **2a** in low yields. To identify the catalytic effect of co-catalyst **5**, we then attempted the same reaction of **1a** in the absence of **5**, which clarified that merely using catalysts **4a**–**c** gave almost the same results as the dual catalytic systems. These results indicate that, in contrast to the intramolecular Michael addition of phenols and sulfonamides,[26] arylboronic acids **4** singularly promote the

Table 2. Optimization of the Aza-Michael Addition of R^1ONH_2 to **1a**[a]



Entry	Cat.	Nu-H	Solvent	Yield (%)[b]	Ee (%)[c]
1	**6a**	$BnONH_2$	CCl_4	40	58
2	**6b**	$BnONH_2$	CCl_4	24	9
3	**6c**	$BnONH_2$	CCl_4	0	—
4	**6d**	$BnONH_2$	CCl_4	52	33
5	**6e**	$BnONH_2$	CCl_4	81	80
6	**6f**	$BnONH_2$	CCl_4	79	77
7	**6g**	$BnONH_2$	CCl_4	73	87
8	**6h**	$BnONH_2$	CCl_4	65	78
9	**6i**	$BnONH_2$	CCl_4	83	90
10	**6i**	n-$C_7H_{15}ONH_2$	CCl_4	66	90
11	**6i**	Ph_2CHONH_2	CCl_4	77	76
12	**6i**	$BnONH_2$	MeO^tBu	11	24
13	**6i**	$BnONH_2$	$Cl_2C{=}CCl_2$	24	28
14	**6i**	$BnONH_2$	4-$CF_3C_6H_4Cl$	62	70
15[d]	**6i**	$BnONH_2$	CCl_4	0	—

a) Unless otherwise noted, the reaction was carried out with **1a** (1.0 mmol), nucleophile (1.0 equiv), and catalyst **6a**–**i** (0.1 equiv) at room temperature for 24 h. *b*) Isolated yield after treatment with $TMSCHN_2$. *c*) Estimated by chiral HPLC after treatment with $TMSCHN_2$. *d*) Without 4 Å molecular sieves.

Michael addition of $BnONH_2$ and that chiral thiourea **5** does not appear to participate in the activation of substrates in this catalytic cycle.

Because the dual catalysis system composed of arylboronic acid **4** and bifunctional thiourea **5** proved to be ineffective for the intermolecular Michael addition, we next designed a new type of catalyst **6** in which arylboronic acid **4b** and aminothiourea **5** were merged. We envisioned that the integrated catalyst would efficiently activate carboxylate anions *via* both Lewis acid-Lewis base and hydrogen-bonding interactions and that 1,2-addition of the nucleophile might be inhibited because of the crowded environment around the carboxylate complex (see strategy (ii) in Chart 2). To evaluate the functionality of the proposed catalysts, a series of integrated arylboronic acids **6a**–**i** bearing different hydrogen-bond-donating moieties were prepared and subsequently screened under various reaction conditions; the results are summarized in Table 2. As expected, all integrated catalysts, except sulfonamide **6c**, afforded the desired β-benzyloxyamino acid **2a** as a single product; in addition, the nature of the hydrogen-bond-donor moiety was observed to substantially affect the yield. Among catalysts **6a**–**e**, thiourea **6e** bearing a 3,5-bis(trifluoromethyl)phenyl group gave the best results in terms of yield and enantioselectivity (entries 1–5). Regarding the achiral *N*-substituent of the thiourea moiety, catalysts **6g** and **i** bearing phenyl and 4-nitrophenyl groups, respectively, exhibited higher enanti-

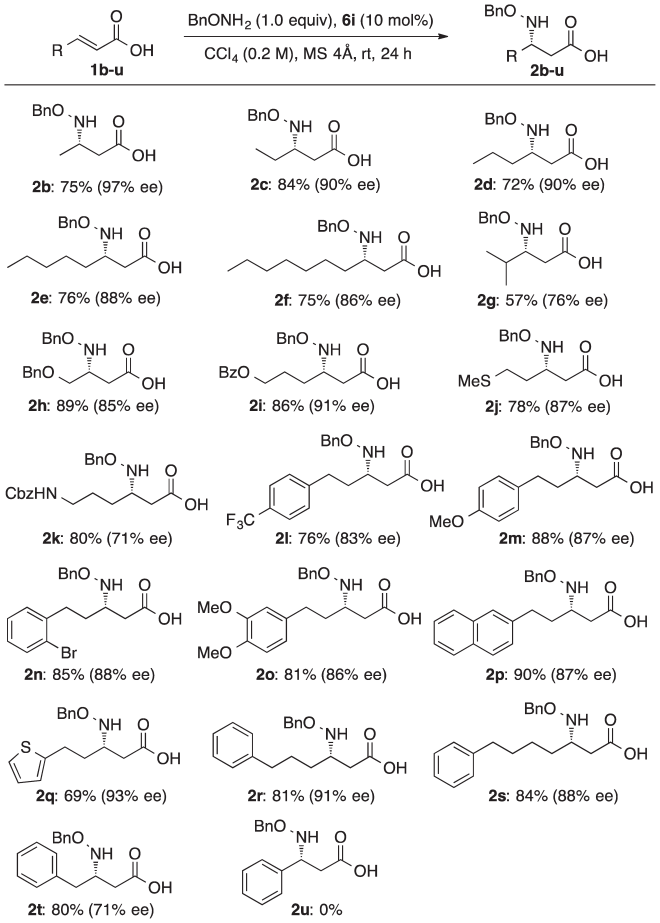


Chart 3. Scope of the Substrates **1** under the Optimized Conditions

oselectivities than electron-rich derivatives **6f** and **h** (entries 6–9). Further investigation of R^1ONH_2 and solvent revealed that the highest ee was obtained when the reaction was performed with **6i** in CCl_4 at room temperature in the presence of 4 Å molecular sieves, furnishing **2a** in 83% yield with 90% enatiomeric excess (ee) (entries 9–14).[30] Notably, the reaction gave no desired product in the absence of 4 Å molecular sieves in any solvent (entry 15).

Under the optimized conditions, we next examined the substrate scope of the aza-Michael addition catalyzed by **6i** (Chart 3). Aliphatic substrates possessing different alkyl chains **1b**–**f** were initially screened as *β*-alkyl amino acids, which have proven to be more challenging synthetic targets. Irrespective of alkyl chain length, the reaction of the linear alkyl substrates **1b**–**f** proceeded smoothly to give the corresponding products in good yields and with high ee's (**2b**–**f**: 86-97% ee's). In contrast, a lower ee was observed with the branched aliphatic substrate **1g** (**2g**: 76% ee). Other aliphatic substrates bearing ether, ester and sulfide moieties **1h**–**j** were well-tolerated (**2h**–**j**: 85-91% ee's); however, the Cbz-carbamate **1k** gave only a moderate ee. A variety of (*E*)-5-arylpent-2-enoic acids **1l**–**q** bearing electron-deficient and electron-rich aryl and heteroaryl groups were used as Michael acceptors to afford the corresponding *β*-amino acid derivatives in good yields and with high enantioselectivities (**2l**–**q**: 83–93% ee's). We also evaluated a series of other aryl-substituted 2-alkenoic acids; substrates **1r** and **s**, with a phenyl group at their 6- and 7-positions, respectively, both underwent the Michael addition to deliver products with no loss of yield or enantioselectivity (**2r**, **s**: 88–91% ee's); however, introduction of a phenyl group at the 4-position resulted in a substantial decrease in enantioselectivity (**2t**: 71% ee) with no influence on the chemical yield. To our surprise, the same reaction with cinnamic acid (**1u**: R=Ph) did not proceed, resulting only in recovered starting material. The absolute configuration of products **2b**–**t** are presumed to have the *S* configuration.[30]

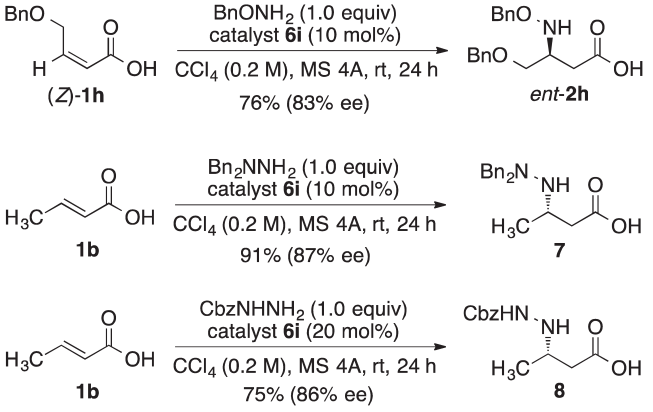


Chart 4. Scope of the Nucleophiles with (*Z*)- and (*E*)-Substrates

To gain insight into the reaction mechanism, the Michael addition with (*Z*)-4-benzyloxybut-2-enoic acid (*Z*)-**1h** was performed under the optimized conditions, providing the opposite enantiomer, *ent*-**2h**, in 76% yield and with a slightly lower enantioselectivity (83% ee) (Chart 4). We next explored the use of other nitrogen nucleophiles to extend the synthetic utility of the reaction and observed that Bn_2NNH_2 and $CbzNHNH_2$ underwent the Michael addition under the same conditions, giving the corresponding adducts **7** and **8** with enantioselectivities similar to those of (benzyloxy)amine derivatives **2a**–**s**. However, 20 mol% of **6i** was used for the reaction of **1b** with $CbzNHNH_2$, since a lower yield of **8** was observed (48%). Because the resulting hydrazine **8** possesses the same absolute configuration as **2b**,[30] the aza-Michael addition is considered to occur *via* a similar catalytic process, independent of the nucleophiles employed.

In the integrated catalysts, a Brønsted basic site together with Lewis acidic and hydrogen-bonding sites (*i.e.*, a tricoordinate boron atom and two thiourea–NH protons) are available to activate both acidic and basic substrates, such as a carboxylic acid. On the basis of the working hypothesis, together with the aforementioned experimental results, we propose the following plausible reaction mechanism[31] (Fig. 1): Deprotonation of carboxylic acid **1** by catalyst **6** results in the formation of binary complex **A** or **B** *via* coordination of the resulting carboxylate anion to a boron atom; multiple hydrogen-bonding interactions between the carbonyl moiety and both the N–H protons of thiourea and the hydroxy group of the borate anion would also be present. Participation of the borate hydroxy group facilitates preferential attack of the nucleophile on the *s-trans* form of the carboxylate anion (binary complex **B**), which, after protonation of the enolate intermediate C, provides (*S*)-adduct **2** in a highly enantioselective manner. The proposed mechanism rationalizes the need for the electron-deficient thiourea as a hydrogen-bond donor as well as the favored (*S*)-configuration of the products.

Finally, as a synthetic application of the aza-Michael addi-

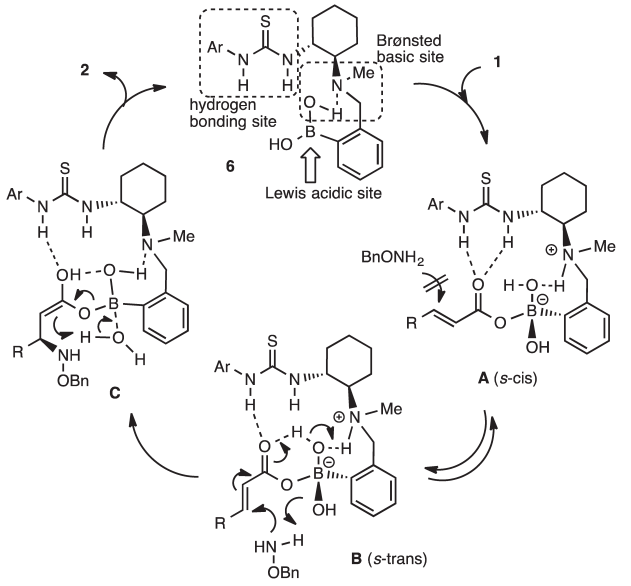


Fig. 1. Plausible Mechanism of Asymmetric Aza-Michael Addition

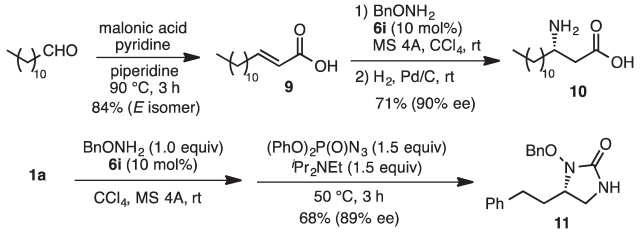


Chart 5. Synthetic Applications of the Asymmetric Aza-Michael Addition

tion, the asymmetric synthesis of (*R*)-3-aminododecanoic acid **10**,[30] which is a structural motif of the cyclic peptide epichlicin, was performed starting from undecanal and malonic acid in a three-step sequence *via* tridec-2-enoic acid **9** (60, 90% ee) (Chart 5). Further synthetic utility was demonstrated by the one-pot transformation of *α*,*β*-unsaturated carboxylic acid **1a** into enantio-enriched 1,2-diamine derivative **11** (68% yield, 89% ee) without isolation of the Michael adduct **2a**.

Summary

We have developed an intermolecular asymmetric aza-Michael addition of *α*,*β*-unsaturated carboxylic acids using new chiral integrated catalysts composed of arylboronic acid and bifunctional thiourea moieties. A wide range of *β*-amino acid derivatives could be rapidly and concisely synthesized with good to high enantioselectivity (up to 97% ee). The utility of these products was illustrated by the conversion into both an important *β*-amino acid fragment of biologically active peptides and a *vic*-diamine derivative. We believe that our concept will stimulate further development of innovative asymmetric reaction protocols through catalytic activation of hydroxy groups of various functional groups. Efforts to discover additional synthetic applications of our chiral integrated catalysts and to clarify the detailed reaction mechanism are currently underway in our laboratory.

Experimental

General Experimental Details All non-aqueous reactions were carried out under a positive atmosphere of argon in dried glassware unless otherwise noted. Solvents and materials were obtained from commercial suppliers and used without further purification. Column chromatography was performed on Cica silica gel 60 (230–400 mesh) or Fuji Silysia silica gel (NH, 100–200 mesh). Reactions and chromatography fractions were analyzed employing pre-coated silica gel plate (Merck Silica Gel 60 F254). All melting points were measured on BÜCHI M-565 melting point apparatus and are uncorrected. IR spectra were measured on JASCO FT/IR-4100. Unless otherwise noted, NMR spectra were obtained in $CDCl_3$. ^{1}H-NMR (400 MHz) spectra were recorded with JEOL ECP-400 spectrometers. Chemical shifts are reported relative to Me_4Si (δ 0.0) in $CDCl_3$, and residual solvents of CD_3CN (δ 1.94), acetone-d_6 (δ 2.05) and CD_3OD (δ 3.31). ^{13}C-NMR (100 MHz) spectra were also recorded using JEOL ECP-400 spectrometers. Chemical shifts are reported relative to $CDCl_3$ (δ 77.0), CD_3CN (δ 1.32, 118.3), acetone-d_6 (δ 29.8, 206.3) and CD_3OD (δ 49.0). ^{1}H-NMR multiplicities are reported as follows: br=broad; m=multiplet; s=singlet; d=doublet; t=triplet; q=quartet. High-resolution (HR)-MS were obtained on a Shimadzu LCMS-IT-TOF fitted with an electrospray ionization (ESI). Optical rotations were recorded on a JASCO P-2200 polarimater with a path length of 1 cm; concentrations are quoted in grams per 100 mL. $[\alpha]_D$ values are measured in 10^{-1} deg cm^2 g^{-1}. Enantiomeric excess was determined by HPLC analyses. Unless otherwise noted, all materials and solvent were purchased from Tokyo Kasei Co., Aldrich Inc., and other commercial suppliers and were used without purification. All non-commercially available substrates were prepared according to the literature procedure as indicated below.

Preparation of *α*,*β*-Unsaturated Carboxylic Acids

α,*β*-Unsaturated carboxylic acids **1b**–**f**, and **1u** were commercially available. **1k** was prepared according to the literature procedure.[26] Other *α*,*β*-unsaturated carboxylic acids **1a, g**, and **l**–**q** were prepared by following the general procedure as indicated below.

General Procedure for the Preparation of *α*,*β*-Unsaturated Carboxylic Acids (Procedure A)

3-Phenylpropionaldehyde (2.68 g, 20 mmol) and malonic acid (2.08 g, 20 mmol) were suspended in pyridine (1.6 mL) at room temperature, and the mixture was heated at 100°C for 3 h. After being cooled to 0°C, the reaction mixture was neutralized with 2 N aqueous HCl solution. The precipitate was then collected by filtration, and washed with cold water and *n*-hexane, which was further purified by recrystallization from ethyl acetate and *n*-hexane to give **1a** (1.96 g, 50%) as a white solid.

(*E*)-5-Phenylpent-2-enoic Acid (**1a**)

mp 101.9–102.2°C (ethyl acetate–*n*-hexane); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 10.55 (br s, 1H), 7.33–7.28 (m, 3H), 7.24–7.16 (m, 2H), 7.11 (dt, J_1=15.7 Hz, J_2=6.8 Hz, 1H), 5.85 (dt, J_1=15.7 Hz, J_2=1.6 Hz, 1H), 2.79 (t, J=7.8 Hz, 2H), 2.60–2.52 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 171.9, 151.0, 140.5, 128.5 (2C), 128.3 (2C), 126.2, 121.2, 34.1, 34.0; IR attenuated total reflection (ATR): 2938, 1685, 985 cm^{-1}; HR-MS (ESI): Calcd for $C_{11}H_{11}O_2$ $[M-H]^-$ 175.0765. Found 175.0772.

(*E*)-4-Methylpent-2-enoic Acid (**1g**)

1g was purified by distillation (1 Torr, 160°C), and obtained as a colorless oil (631 mg, 58%); ^{1}H-NMR (400 MHz, $CDCl_3$)

δ: 11.86 (brs, 1H), 7.07 (dd, J_1=15.7 Hz, J_2=6.7 Hz, 1H), 5.78 (dd, J_1=15.7 Hz, J_2=1.4 Hz, 1H), 2.56–2.43 (m, 1H), 1.08 (d, J=7.0 Hz, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 172.7, 158.3, 118.0, 31.1, 21.1 (2C); IR (ATR): 2968, 1699 cm^{-1}; HR-MS (ESI): Calcd for $C_6H_9O_2$ $[M-H]^-$ 113.0608. Found 113.0609.

(*E*)-5-(4-(Trifluoromethyl)phenyl)pent-2-enoic Acid (**1l**)

1l was prepared from 3-(4-(trifluoromethyl)phenyl)propanal (303 mg, 1.5 mmol), and purified by recrystallization from ethyl acetate and *n*-hexane. White solid (180 mg, 49%); mp 146.4–147.5°C (ethyl acetate–*n*-hexane); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 11.67 (brs, 1H), 7.55 (d, J=7.8 Hz, 2H), 7.29 (d, J=7.8 Hz, 2H), 7.09 (dt, J_1=15.7 Hz, J_2=6.9 Hz, 1H), 5.85 (d, J=15.7 Hz, 1H), 2.85 (t, J=7.7 Hz, 2H), 2.62–2.53 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 171.8, 150.2, 144.5, 128.7 (J=32.1 Hz), 128.6 (2C), 125.5 (J=3.8 Hz, 2C), 124.2 (J=271.7 Hz), 121.6, 33.9, 33.5; IR (ATR): 2916, 1694, 1650, 1321 cm^{-1}; HR-MS (ESI): Calcd for $C_{12}H_{10}F_3O_2$ $[M-H]^-$ 243.0638. Found 243.0636.

(*E*)-5-(4-Methoxyphenyl)pent-2-enoic Acid (**1m**)

1m was prepared from 3-(4-methoxyphenyl)propanal (300 mg, 1.8 mmol), and purified by recrystallization from ethyl acetate and *n*-hexane. Off-white solid (242 mg, 64%); mp 131.0–133.4°C (ethyl acetate–*n*-hexane); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 9.88 (brs, 1H), 7.15–7.05 (m, 3H), 6.84 (d, J=8.4 Hz, 2H), 5.84 (d, J=15.7 Hz, 1H), 3.79 (s, 3H), 2.73 (t, J=7.7 Hz, 2H), 2.56–2.48 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 171.6, 158.0, 151.2, 132.6, 129.2 (2C), 121.1, 113.9 (2C), 55.2, 34.3, 33.3; IR (ATR): 2931, 1682, 1640, 1242, 968 cm^{-1}; HR-MS (ESI): Calcd for $C_{12}H_{13}O_3$ $[M-H]^-$ 205.0870. Found 205.0870.

(*E*)-5-(2-Bromophenyl)pent-2-enoic Acid (**1n**)

1n was prepared from 3-(2-bromophenyl)propanal (300 mg, 1.4 mmol), and purified by recrystallization from ethyl acetate and *n*-hexane. Off-white solid (157 mg, 44%); mp 91.5–93.0°C (ethyl acetate–*n*-hexane); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 9.14 (brs, 1H), 7.54 (d, J=8.1 Hz, 1H), 7.28–7.05 (m, 4H), 5.87 (d, J=15.7 Hz, 1H), 2.91 (t, J=7.5 Hz, 2H), 2.61–2.53 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 171.7, 150.6, 139.8, 132.9, 130.3, 128.1, 127.6, 124.3, 121.3, 34.5, 32.3; IR (ATR): 2906, 1691 cm^{-1}; HR-MS (ESI): Calcd for $C_{11}H_{10}O_2Br$ $[M-H]^-$ 252.9870. Found 252.9866.

(*E*)-5-(3,4-Dimethoxyphenyl)pent-2-enoic Acid (**1o**)

1o was prepared from 3-(3,4-dimethoxyphenyl)propanal (291 mg, 1.5 mmol), and purified by recrystallization from ethyl acetate and *n*-hexane. Off-white solid (212 mg, 60%); mp 118.5–119.0°C (ethyl acetate–*n*-hexane); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 9.98 (brs, 1H), 7.11 (dd, J_1=15.7 Hz, J_2=6.7 Hz, 1H), 6.80 (d, J=8.1 Hz, 1H), 6.75–6.68 (m, 2H), 5.85 (d, J=15.7 Hz, 1H), 3.88 (s 3H), 3.86 (s 3H), 2.74 (t, J=7.5 Hz, 2H), 2.68–2.59 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 171.7, 151.1, 148.8, 147.4, 133.1, 121.1, 120.1, 111.6, 111.2, 55.9, 55.8, 34.2, 33.8; IR (ATR): 2836, 1677, 1642, 1237 cm^{-1}; HR-MS (ESI): Calcd for $C_{13}H_{15}O_4$ $[M-H]^-$ 235.0976. Found 235.0977.

(*E*)-5-(Naphthalen-2-yl)pent-2-enoic Acid (**1p**)

1p was prepared from 3-(naphthalen-2-yl)propanal (500 mg, 2.7 mmol), and purified by recrystallization from ethyl acetate and *n*-hexane. Off-white solid (313 mg, 51%); mp 108.5–110.0°C (ethyl acetate–*n*-hexane); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 11.36 (brs, 1H), 7.85–7.74 (m, 3H), 7.62 (s, 1H), 7.49–7.39 (m, 2H), 7.31 (d, J=8.1 Hz, 1H), 7.15 (dd, J_1=15.7 Hz, J_2=6.7 Hz, 1H), 5.87 (d, J=15.7 Hz, 1H), 2.95 (t, J=7.5 Hz, 2H), 2.70–2.58 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 171.9, 151.0, 138.0, 133.5, 132.1, 128.1, 127.6, 127.5, 126.9, 126.5, 126.0, 125.4, 121.3, 34.3, 33.9; IR (ATR): 2829, 1682, 1639, 1129 cm^{-1}; HR-MS (ESI): Calcd for $C_{15}H_{13}O_2$ $[M-H]^-$ 225.0921. Found 225.0923.

(*E*)-5-(Thiophen-2-yl)pent-2-enoic Acid (**1q**)

1q was prepared from 3-(thiophen-2-yl)propanal (280 mg, 2 mmol), and purified by recrystallization from ethyl acetate and *n*-hexane. Off-white solid (247 mg, 68%); mp 93.2–95.9°C (ethyl acetate–*n*-hexane); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 11.36 (brs, 1H), 7.16–7.05 (m, 2H), 6.95–6.89 (m, 1H), 6.81 (d, J=3.5 Hz, 1H), 5.87 (d, J=15.7 Hz, 1H), 3.02 (t, J=7.5 Hz, 2H), 2.67–2.58 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 171.7, 150.2, 143.1, 126.8, 124.6, 123.5, 121.6, 34.1, 28.3; IR (ATR): 2938, 1677, 974, 920, 851 cm^{-1}; HR-MS (ESI): Calcd for $C_9H_9O_2S$ $[M-H]^-$ 181.0329. Found 181.0336.

α,β-Unsaturated carboxylic acids **1h**, **j**, and **1r-t** were generally prepared by following the general procedure as indicated below.

General Procedure for the Preparation of α,β-Unsaturated Carboxylic Acids (Procedure B1)

To a stirred solution of benzyloxyacetaldehyde (3.0 mmol) in toluene (15 mL) was added *tert*-butyl 2-(triphenylphosphoranylidene)acetate (1.7 g, 4.5 mmol). After being stirred at room temperature for 6 h, the reaction mixture was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (*n*-hexane–ethyl acetate=100 : 1 to 20 : 1) to afford ***E*-1h-[O*t*Bu]** (530 mg, 81%) as a colorless oil, along with ***Z*-1h-[O*t*Bu]** (44 mg, 7%).

tert-Butyl (*E*)-4-(Benzyloxy)but-2-enoate (***E*-1h-[O*t*Bu]**)

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.39–7.27 (m, 5H), 6.88 (dt, J_1=15.7 Hz, J_2=4.5 Hz, 1H), 6.04 (dt, J_1=15.7 Hz, J_2=2.0 Hz, 1H), 4.56 (s, 2H), 4.16 (dd, J_1=4.5 Hz, J_2=2.0 Hz, 2H), 1.48 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 165.6, 142.9, 137.7, 128.4 (2C), 127.8, 127.6 (2C), 123.3, 80.4, 72.7, 68.7, 28.1 (3C); IR (ATR): 1713, 1154 cm^{-1}; HR-MS (ESI): Calcd for $C_{15}H_{20}O_3Na$ $[M+Na]^+$ 271.1305. Found 271.1306.

tert-Butyl (*Z*)-4-(Benzyloxy)but-2-enoate (***Z*-1h-[O*t*Bu]**)

Colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.40–7.22 (m, 5H), 6.33 (dt, J_1=11.9 Hz, J_2=4.6 Hz, 1H), 5.73 (d, J=11.9 Hz, 1H), 4.62 (dd, J_1=4.6 Hz, J_2=2.6 Hz, 2H), 4.54 (s, 2H), 1.45 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 165.4, 146.8, 137.9, 128.3 (2C), 127.7 (2C), 127.6, 121.3, 80.5, 72.7, 68.4, 28.1 (3C); IR (ATR): 1710, 1154 cm^{-1}; HR-MS (ESI): Calcd for $C_{15}H_{20}O_3Na$ $[M+Na]^+$ 271.1305. Found 271.1305.

General Procedure for the Preparation of α,β-Unsaturated Carboxylic Acids (Procedure B2)

To a stirred solution of **(*E*)-1h-[O*t*Bu]** (232 mg, 0.93 mmol) in dichloromethane (DCM) (2.0 mL) was added trifluoroacetic acid (TFA) (2.0 mL) dropwise at 0°C. After being stirred for 3 h, the reaction mixture was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (*n*-hexane–ethyl acetate=10 : 1 to 2 : 1) to afford the corresponding α,β-unsaturated acid **(*E*)-1h** as an off-white solid (156 mg, 87%).

(*E*)-4-(Benzyloxy)but-2-enoic Acid (**(*E*)-1h**)

mp 48.1–48.9°C (ethyl acetate–*n*-hexane); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 10.47 (brs, 1H), 7.40–7.27 (m, 5H), 7.10 (dt, J_1=15.7 Hz, J_2=4.0 Hz, 1H), 6.16 (d, J=15.7 Hz, 1H), 4.58 (s, 2H), 4.23–4.19 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 171.6, 147.1, 137.5, 128.5 (2C), 127.9, 127.6 (2C), 120.4, 72.8, 68.4; IR (ATR): 2839, 1699, 1657, 1136 cm^{-1}; HR-MS (ESI):

Calcd for $C_{11}H_{11}O_3$ $[M-H]^-$ 191.0714. Found 191.0716.

(*Z*)-4-(benzyloxy)but-2-enoic Acid (**(*Z*)-1h**)

Colorless oil (90.4 mg, 94%); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 10.61 (br s, 1H), 7.41–7.28 (m, 5H), 6.58 (dt, J_1=11.9 Hz, J_2=4.8 Hz, 1H), 5.86 (d, J=11.9 Hz, 1H), 4.64 (dd, J_1=4.8 Hz, J_2=2.5 Hz, 2H), 4.56 (s, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 171.1, 151.1, 137.7, 128.5 (2C), 127.83, 127.78 (2C), 118.9, 72.9, 68.5; IR (ATR): 3032, 1698, 1646, 1100 cm^{-1}; HR-MS (ESI): Calcd for $C_{11}H_{11}O_3$ $[M-H]^-$ 191.0714. Found 191.0713.

(*E*)-5-(Methylthio)pent-2-enoic Acid (**1j**)

Colorless oil (70.4 mg, 82%, in 2 steps); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 11.35 (br s, 1H), 7.09 (dt, J_1=15.7 Hz, J_2=6.8 Hz, 1H), 5.90 (d, J=15.7 Hz, 1H), 2.64 (t, J=6.8 Hz, 2H), 2.58–2.51 (m, 2H), 2.13 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 171.9, 149.6, 121.8, 32.2, 31.8, 15.5; IR (ATR): 3026, 1698 cm^{-1}; HR-MS (ESI): Calcd for $C_6H_9O_2S$ $[M-H]^-$ 145.0329. Found 145.0331.

(*E*)-6-Phenylhex-2-enoic Acid (**1r**)

Colorless oil (180 mg, 78%, in 2 steps); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 9.36 (br s, 1H), 7.32–7.24 (m, 2H), 7.22–7.14 (m, 3H), 7.10 (dd, J_1=15.7 Hz, J_2=6.9 Hz, 1H), 5.84 (d, J=15.7 Hz, 1H), 2.65 (t, J=7.7 Hz, 2H), 2.31–2.20 (m, 2H), 1.87–1.76 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 172.0, 151.9, 141.5, 128.40 (2C), 128.39 (2C), 126.0, 121.0, 35.2, 31.7, 29.4; IR (ATR): 3026, 1694 cm^{-1}; HR-MS (ESI): Calcd for $C_{12}H_{13}O_2$ $[M-H]^-$ 189.0921. Found 189.0922.

(*E*)-7-Phenylhept-2-enoic Acid (**1s**)

By following the general procedure B, **1s** was prepared from 5-phenylpentanal, and obtained as a colorless oil (96.8 mg, 68%, in 2 steps); ^{1}H-NMR (400 MHz, $CDCl_3$) δ, 7.32–7.25 (m, 2H), 7.22–7.14 (m, 3H), 7.07 (dd, J_1=15.7 Hz, J_2=6.9 Hz, 1H), 5.82 (d, J=15.7 Hz, 1H), 2.62 (t, J=7.7 Hz, 2H), 2.30–2.22 (m, 2H), 1.71–1.62 (m, 2H), 1.57–1.47 (m, 2H), one O–H proton was not observed; ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 171.8, 152.1, 142.1, 128.4 (2C), 128.3 (2C), 125.8, 120.7, 35.6, 32.2, 30.9, 27.4; IR (ATR): 3026, 1693 cm^{-1}; HR-MS (ESI): Calcd for $C_{13}H_{15}O_2$ $[M-H]^-$ 203.1078. Found 203.1076.

(*E*)-4-Phenylbut-2-enoic Acid (**1t**)

White solid (205 mg, 37%, in 2 steps, recrystallized from ethyl acetate and *n*-hexane); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 10.66 (br s, 1H), 7.36–7.29 (m, 2H), 7.28–7.16 (m, 4H), 5.82 (d, J=15.7 Hz, 1H), 3.56 (d, J=7.0 Hz, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 171.8, 152.1, 137.2, 128.8 (2C), 128.7 (2C), 126.8, 121.6, 38.5; IR (ATR): 2918, 1668 cm^{-1}; HR-MS (ESI): Calcd for $C_{10}H_9O_2$ $[M-H]^-$ 161.0608. Found 161.0611.

Procedure for the Preparation of **1i**

To a stirred solution of *tert*-butyl (*E*)-6-hydroxyhex-2-enoate (186 mg, 1.0 mmol) in DCM (2.0 mL) were added benzoyl chloride (180 μL, 1.5 mmol) and pyridine (120 μL, 1.5 mmol) at 0°C. After being stirred at room temperature for 3 h, the reaction mixture was quenched with 1 N aqueous HCl solution, and extracted with ethyl acetate three times. The combined organic layer was washed with saturated aqueous $NaHCO_3$ solution, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (*n*-hexane–ethyl acetate=20 : 1 to 10 : 1) to afford the **(*E*)-1i-[O*t*Bu]** as a colorless oil (300 mg). Deprotection of *tert*-butyl ester was performed by following the general procedure B2 to give **1i** (82.6 mg, 71%, in 2 steps) as a colorless oil.

(*E*)-6-(Benzoyloxy)hex-2-enoic Acid (**1i**)

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.10–8.01 (m, 2H), 7.62–7.53 (m, 1H), 7.49–7.42 (m, 2H), 7.14 (dt, J_1=15.7 Hz, J_2=6.9 Hz, 1H), 5.90 (d, J=15.7 Hz, 1H), 4.37 (t, J=6.4 Hz, 2H), 2.43 (dt, J_1=J_2=6.9 Hz, 2H), 2.04–1.93 (m, 2H), one O–H proton was not observed; ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 171.6, 166.5, 150.6, 133.0, 130.0, 129.5 (2C), 128.4 (2C), 121.4, 64.0, 29.0, 27.1; IR (ATR): 3065, 1717, 1695, 1275 cm^{-1}; HR-MS (ESI): Calcd for $C_{13}H_{13}O_4$ $[M-H]^-$ 233.0819. Found 233.0816.

Preparation of Hydroxylamine Derivatives

O-Benzylhydroxylamine, *O*-(*tert*-butyldimethylsilyl)hydroxylamine, 1,1-diphenylhydrazine, and benzyl carbamate were commercially available. Other nucleophiles were prepared as indicated below.

Procedure for the Preparation of *O*-Benzhydrylhydroxylamine (**S-2**)

To a stirred solution of diphenylmethanol (921 mg, 5.0 mmol), 2-hydroxyisoindoline-1,3-dione (978 mg, 6.0 mmol), and triphenylphosphine (1.57 g, 6.0 mmol) in tetrahydrofuran (THF) (20 mL) was added diisopropyl azodicarboxylate (DIAD) (1.2 mL, 1.5 mmol) at 0°C. After being stirred at room temperature for 1 h, the reaction mixture was concentrated *in vacuo*. The produced precipitate was collected by filtration and successively washed with *n*-hexane to afford the product **S-1** (850 mg) as white solid, which was used for the next step without further purification. To a stirred solution of **S-1** (658 mg, *ca.* 2.0 mmol) in EtOH (10 mL) was added hydrazine monohydrate (200 μL, 4.0 mmol) at room temperature. After being stirred at the same temperature for 1 h, the reaction mixture was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (*n*-hexane–ethyl acetate=20 : 1 to 10 : 1) to afford **S-2** as a colorless oil (390 mg, 50%, in 2 steps). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.38–7.23 (m, 10H), 5.64 (br s, 1H), 5.43 (br s, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 140.9 (2C), 128.5 (4C), 127.7 (2C), 127.1 (4C), 88.6; IR (ATR): 2926 cm^{-1}; HR-MS (ESI): Calcd for $C_{13}H_{14}NO$ $[M+H]^+$ 200.1070. Found 200.1067.

Procedure for the Preparation of *O*-Heptylhydroxylamine (**S-4**)

To a stirred solution of heptan-1-ol (580 mg, 5.0 mmol), 2-hydroxyisoindoline-1,3-dione (984 mg, 6.0 mmol), and triphenylphosphine (1.57 g, 6.0 mmol) in THF (20 mL) was added DIAD (1.2 mL, 1.5 mmol) at 0°C. After being stirred at room temperature for 1 h, the reaction mixture was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (*n*-hexane–ethyl acetate=10 : 1) to afford the product **S-3** as a yellow oil (1.39 g). To a stirred solution of **S-3** (523 mg, *ca.* 2.0 mmol) in DCM (10 mL) was added hydrazine monohydrate (500 μL, 10 mmol) at room temperature. After being stirred at the same temperature for 2 h, the reaction mixture was washed with H_2O, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (*n*-hexane–ethyl acetate=4 : 1 to 2 : 1) to afford **S-4** as a colorless oil (171 mg, 65%, in 2 steps). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 5.34 (br s, 2H), 3.66 (t, J=6.7 Hz, 2H), 1.62–1.53 (m, 2H), 1.37–1.23 (m, 8H), 0.88 (t, J=7.0 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 7.62, 31.8, 29.2, 28.4, 25.9, 22.6, 14.1; IR (ATR): 2930 cm^{-1}; HR-MS (ESI): Calcd for $C_7H_{18}NO$ $[M+H]^+$ 132.1383. Found 132.1385.

Preparation of Boronic Acid Catalysts

Catalysts (**6a**–**i**) were generally prepared as indicated below.

General Procedure for the Preparation of **6** (Procedure C)

To a stirred solution of *tert*-butyl ((1*R*,2*R*)-2-aminocyclo-

hexyl)carbamate (107 mg, 0.5 mmol) in DCM (5.0 mL) were added Na_2SO_4 (500 mg, 3.5 mmol) and 2-formylphenylboronic acid (113 mg, 0.75 mmol) at room temperature under argon atmosphere. The reaction mixture was stirred at room temperature for 3 h, before the addition of $NaBH(OAc)_3$ (318 mg, 1.5 mmol) at the same temperature. After being stirred for 3 h, the reaction mixture was quenched with 1 N aqueous HCl solution, and extracted with $CHCl_3$ twice. The combined organic layer extracts were washed with saturated aqueous $NaHCO_3$ solution and brine, dried over $MgSO_4$, and concentrated *in vacuo*. The crude **S-5** (159 mg) was used for the next step without further purification. To a solution of **S-5** (159 mg, 0.5 mmol) in DCM (5.0 mL) was added 37% aqueous formaldehyde solution (200 μL, 2.5 mmol) followed by $NaBH(OAc)_3$ (212 mg, 1.0 mmol) at room temperature under argon atmosphere. After being stirred at the same temperature for 3 h, the reaction mixture was quenched with 1 N aqueous HCl solution (pH=*ca.* 1), and extracted with $CHCl_3$ twice. The combined organic layer extracts were washed with saturated aqueous $NaHCO_3$ solution (pH=*ca.* 6) and brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (NH; *n*-hexane–ethyl acetate=4 : 1 to ethyl acetate only) to afford **6a** as a white amorphous (84.6 mg, 47%, in 2 steps).

2-[(1*R*,2*R*)-2-(*tert*-Butoxycarbonylamino)cyclohexan-1-yl]-*N*-methyl-(2-aminomethyl)]phenylboronic Acid (**6a**)

^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 8.35 (brs, 1H), 8.00–7.86 (m, 1H), 7.42–7.28 (m, 2H), 7.22–7.10 (m, 1H), 4.65 (brs, 1H), 3.82–3.70 (m, 2H), 3.70–3.55 (m, 1H), 2.43–2.33 (m, 1H), 2.28 (s, 3H), 2.08–1.94 (m, 2H), 1.83–1.74 (m, 1H), 1.70–1.59 (m, 1H), 1.45 (s, 9H), 1.34–1.20 (m, 2H), 1.15–0.97 (m, 2H), one O–H or N–H proton was not observed; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ: 155.4, 141.3, 136.4, 130.5, 130.1, 127.5, 79.2, 77.3, 62.5, 60.5, 58.2, 34.5, 34.1, 28.4 (3C), 25.0, 24.8. One carbon peak could not be observed; IR (ATR): 3343, 2932, 1704, 1446, 1366, 1173 cm^{-1}; HR-MS (ESI): Calcd for $C_{19}H_{32}BN_2O_4$ $[M+H]^+$ 363.2453. Found 363.2454; $[\alpha]_D^{25}$+35.4 (*c* 0.99, $CHCl_3$).

2-[*N*-[(1*R*,2*R*)-2-(*N*,*N*-Dimethylamino)cyclohaxan-1-yl]-*N*-methyl-(2-aminomethyl)]phenylboronic Acid (**6b**)

By following the general procedure C, **6b** was prepared from (1*R*,2*R*)-N^1,N^1-dimethylcyclohexane-1,2-diamine (427 mg, 3.0 mmol), and purified by column chromatography on silica gel (NH; *n*-hexane–ethyl acetate=4 : 1 to ethyl acetate–methanol 8 : 2). Colorless oil (302 mg, 35%, in 2 steps); ^{1}H-NMR (CD_3CN, 400 MHz) δ: 9.15 (brs, 1H), 7.70 (d, J=7.0 Hz, 1H), 7.28–7.12 (m, 3H), 3.74 (d, J=12.5 Hz, 1H), 3.65 (d, J=12.5 Hz, 1H), 2.36 (ddd, J_1=J_2=11.1 Hz, J_3=3.2 Hz, 1H), 2.23 (ddd, J_1=J_2=11.0 Hz, J_3=3.0 Hz, 1H), 2.14 (s, 3H), 1.94 (s, 6H), 1.96–1.88 (m, 1H), 1.73–1.65 (m, 1H), 1.65–1.52 (m, 2H), 1.24–0.77 (m, 4H), one O–H proton was not observed; ^{13}C-NMR (CD_3CN, 100 MHz) δ: 143.5, 136.4, 131.2, 130.4, 127.7, 64.4, 60.4, 58.8, 40.4 (2C), 35.1, 26.1, 26.0, 24.5, 22.5. One carbon peak could not be observed; IR (ATR): 2932, 1445, 1382, 1280, 1178, 1135 cm^{-1}; HR-MS (ESI): Calcd for $C_{16}H_{28}BN_2O_2$ $[M+H]^+$ 291.2241. Found 291.2246; $[\alpha]_D^{22}$−51.7 (*c* 0.99, $CHCl_3$).

2-[[(1*R*,2*R*)-2-(3,5-Bis(trifluoromethyl)phenylsulfonamido)-cyclohexan-1-yl]-*N*-methyl-(2-aminomethyl)]phenylboronic Acid (**6c**)

By following the general procedure C, **6c** was prepared from *N*-((1*R*,2*R*)-2-aminocyclohexyl)-3,5-bis(trifluoromethyl)-benzenesulfonamide (200 mg, 0.51 mmol), and purified by column chromatography on silica gel (NH; *n*-hexane–ethyl acetate=2 : 1 to ethyl acetate–methanol=8 : 2). White amorphous (54.9 mg, 20%, in 2 steps); ^{1}H-NMR (CD_3CN, 400 MHz) δ: 7.97 (s, 1H), 7.93 (s, 2H), 7.55 (d, J=6.7 Hz, 1H), 7.21–7.13 (m, 2H), 6.93 (d, J=6.9 Hz, 1H), 3.96 (d, J=15.1 Hz, 1H), 3.43 (d, J=15.3 Hz, 1H), 3.05–2.90 (m, 2H), 2.74 (ddd, J_1=J_2=11.1 Hz, J_3=3.0 Hz, 1H), 2.40–2.17 (m, 4H), 2.06–1.99 (m, 1H), 1.78–1.69 (m, 1H), 1.64–1.55 (m, 1H), 1.34–1.15 (m, 2H), 1.14–0.95 (m, 2H), two O–H or N–H protons were not observed; ^{13}C-NMR (CD_3CN, 100 MHz) δ: 146.7, 141.1, 133.4, 132.3 (J=33.9 Hz, 2C), 128.8, 128.1 (J=3.8 Hz, 2C), 127.6, 125.8 (J=3.7 Hz), 123.8 (J=271 Hz, 2C), 123.5, 69.7, 60.2, 56.9, 41.8, 32.7, 25.0, 24.6, 24.5. One carbon peak could not be observed; IR (ATR): 2944, 1358, 1135, cm^{-1}; HR-MS (ESI): Calcd for $C_{22}H_{26}BF_6N_2O_4S$ $[M+H]^+$ 539.1609. Found 539.1615; $[\alpha]_D^{26}$+12.8 (*c* 1.00, $CHCl_3$).

2-[[(1*R*,2*R*)-2-(3-(3,5-Bis(trifluoromethyl)phenyl)ureido)-cyclohexan-1-yl]-*N*-methyl-(2-aminomethyl)]phenylboronic Acid (**6d**)

By following the general procedure C, **6d** was prepared from 1-((1*R*,2*R*)-2-aminocyclohexyl)-3-(3,5-bis(trifluoromethyl)-phenyl)urea (185 mg, 0.5 mmol) (MeOH was used as solvent instead of DCM due to insolubility), and purified by column chromatography on silica gel (NH; *n*-hexane–ethyl acetate=2 : 1 to ethyl acetate–methanol 7 : 3). White amorphous (131 mg, 51%, in 2 steps); ^{1}H-NMR (CD_3CN, 400 MHz) δ: 9.61 (brs, 1H), 8.44 (brs, 1H), 7.80 (s, 2H), 7.62–7.56 (m, 1H), 7.42–7.34 (m, 2H), 7.30–7.24 (m, 1H), 7.23 (s, 1H), 6.42 (brs, 1H), 3.89–3.80 (m, 2H), 3.64 (d, J=12.8 Hz, 1H), 2.35 (s, 3H), 2.25 (ddd, J_1=J_2=11.3 Hz, J_3=2.9 Hz, 1H), 2.02–1.95 (m, 1H), 1.76–1.65 (m, 2H), 1.58–1.50 (m, 1H), 1.35–0.82 (m, 4H), one O–H or N–H proton was not observed; ^{13}C-NMR (CD_3CN, 100 MHz) δ: 155.2, 143.4, 142.5, 137.2, 131.5 (J=33.1 Hz, 2C), 131.3 (2C), 127.8, 124.4 (J=272 Hz, 2C), 117.7 (J=2.9 Hz, 2C), 114.5 (J=3.6 Hz), 61.1, 60.3, 50.4, 35.3, 34.5, 26.0, 25.3, 22.3. One carbon peak could not be observed; IR (ATR): 3312, 2934, 1566, 1385, 1277, 1175, 1129 cm^{-1}; HR-MS (ESI) : Calcd for $C_{23}H_{27}BF_6N_3O_3$ $[M+H]^+$ 518.2048. Found 518.2048; $[\alpha]_D^{24}$+43.7 (*c* 0.99, $CHCl_3$).

2-[[(1*R*,2*R*)-2-(3-(3,5-Bis(trifluoromethyl)phenyl)thioureido)-cyclohexan-1-yl]-*N*-methyl-(2-aminomethyl)]phenylboronic Acid (**6e**)

By following the general procedure C, **6e** was prepared from 1-((1*R*,2*R*)-2-aminocyclohexyl)-3-(3,5-bis(trifluoromethyl)-phenyl)thiourea (771 mg, 2.0 mmol), and purified by column chromatography on silica gel (NH; *n*-hexane–ethyl acetate=4 : 1 to ethyl acetate–methanol 8 : 2). White amorphous (520 mg, 49%, in 2 steps); ^{1}H-NMR (CD_3CN, 400 MHz) δ: 8.93 (brs, 2H), 8.03 (s, 2H), 7.67 (d, J=6.4 Hz, 1H), 7.59 (s, 1H), 7.35–7.26 (m, 2H), 7.20 (d, J=6 Hz, 1H), 7.17–7.08 (m, 1H), 4.51–4.38 (m, 1H), 3.77 (d, J=12.6 Hz, 1H), 3.65 (d, J=12.6 Hz, 1H), 2.47 (ddd, J_1=J_2=11.3 Hz, J_3=3.0 Hz 1H), 2.19 (s, 3H), 2.04–1.93 (m, 2H), 1.76–1.67 (m, 1H), 1.63–1.54 (m, 1H), 1.37–0.90 (m, 4H), one O–H or N–H proton was not observed; ^{13}C-NMR (CD_3CN, 100 MHz) δ: 181.6, 142.7, 142.5, 136.8, 131.6 (J=33.1 Hz, 2C), 131.1, 131.0, 127.9, 124.4 (J=271.7 Hz, 2C), 124.2, 117.9 (J=3.4 Hz, 2C), 62.1, 60.3, 55.5, 35.3, 33.1, 25.6, 25.4, 22.5. One carbon peak could not be observed; IR (ATR): 3277, 2933, 1541, 1469, 1382, 1277, 1176,

1133 cm^{-1}; HR-MS (ESI): Calcd for $C_{23}H_{27}BF_6N_3O_2S$ $[M+H]^+$ 534.1820. Found 534.1823; $[\alpha]_D^{24}$+44.7 (*c* 1.06, $CHCl_3$).

2-[[(1*R*,2*R*)-2-(3-(3,5-Bis(trifluoromethyl)benzyl)thioureido)-cyclohexan-1-yl]-*N*-methyl-(2-aminomethyl)]phenylboronic Acid (**6f**)

By following the general procedure C, **6f** was prepared from 1-((1*R*,2*R*)-2-aminocyclohexyl)-3-(3,5-bis(trifluoromethyl)-benzyl)thiourea (200 mg, 0.5 mmol), and purified by column chromatography on silica gel (NH; *n*-hexane–ethyl acetate=4 : 1 to ethyl acetate–methanol=7 : 3). White amorphous (159 mg, 58%, in 2 steps); ^{1}H-NMR (CD_3CN, 400 MHz) δ: 9.02 (brs, 1H), 7.91 (s, 2H), 7.84 (s, 1H), 7.76 (d, *J*=6.7 Hz, 1H), 7.28–7.19 (m, 2H), 7.23 (d, *J*=6.7 Hz, 1H), 7.10 (brs, 1H), 6.45 (brs, 1H), 4.99–4.80 (m, 2H), 4.51–4.32 (m, 1H), 3.73 (dd, *J*=12.7 Hz, 2H), 2.47 (ddd, J_1=J_2=11.4 Hz, J_3=3.2 Hz, 1H), 2.18 (s, 3H), 2.06–1.94 (m, 2H), 1.80–1.72 (m, 1H), 1.66–1.56 (m, 1H), 1.40–1.16 (m, 2H), 1.13–0.95 (m, 2H), one O–H or N–H proton was not observed; ^{13}C-NMR (CD_3CN, 100 MHz) δ: 183.4, 144.3, 142.5, 136.8, 131.6 (*J*=33.1 Hz, 2C), 131.2, 130.8, 128.4 (*J*=3.3 Hz, 2C), 127.9, 124.5 (*J*=271.7 Hz, 2C), 121.4 (*J*=3.8 Hz), 62.6, 60.5, 55.7, 46.9, 34.7, 33.7, 25.6, 25.4, 22.7. One carbon peak could not be observed; IR (ATR): 3285, 2940, 1548, 1446, 1375, 1278, 1170, 1132 cm^{-1}; HR-MS (ESI): Calcd for $C_{24}H_{29}BF_6N_3O_2S$ $[M+H]^+$ 548.1977. Found 548.1987; $[\alpha]_D^{23}$+38.1 (*c* 0.99, $CHCl_3$).

2-[[*N*-Methyl-(1*R*,2*R*)-2-(3-phenylthioureido)cyclohexan-1-yl]-(2-aminomethyl)]phenylboronic Acid (**6g**)

By following the general procedure C, **6g** was preparerd from 1-((1*R*,2*R*)-2-aminocyclohexyl)-3-(3,5-bis(trifluoromethyl)-benzyl)thiourea (249 mg, 1.0 mmol), and purified by column chromatography on silica gel (NH; *n*-hexane–ethyl acetate=4 : 1 to ethyl acetate–methanol=8 : 2). White amorphous (256 mg, 65%, in 2 steps), recrystallization from acetone afforded colorless prisms suitable for X-ray diffraction analysis (see below); ^{1}H-NMR (CD_3CN, 400 MHz) δ: 8.57 (brs, 1H), 7.73 (d, *J*=6.7 Hz, 1H), 7.43–7.37 (m, 2H), 7.36–7.25 (m, 4H), 7.21 (d, *J*=6.4 Hz, 1H), 7.16–7.10 (m, 1H), 7.10 (brs, 1H), 6.62 (brs, 1H), 4.64–4.52 (m, 1H), 3.77 (d, *J*=12.5 Hz, 1H), 3.65 (d, *J*=12.5 Hz, 1H), 2.43 (ddd, J_1=J_2=11.4 Hz, J_3=3.4 Hz, 1H), 2.27 (s, 3H), 2.07–1.97 (m, 2H), 1.80–1.71 (m, 1H), 1.66–1.58 (m, 1H), 1.40–1.16 (m, 2H), 1.11–0.93 (m, 2H), one O–H or N–H proton was not observed; ^{13}C-NMR (CD_3CN, 100 MHz) δ: 181.4, 142.5, 139.7, 136.7, 131.2, 130.8, 129.6 (2C), 127.9, 125.8, 125.6 (2C), 61.5, 60.3, 55.5, 35.6, 33.5, 25.6, 25.4, 22.6. One carbon peak could not be observed; IR (ATR): 3276, 2933, 1535, 1448 cm^{-1}; HR-MS (ESI): Calcd for $C_{21}H_{29}BN_3O_2S$ $[M+H]^+$ 398.2072. Found 398.2071; $[\alpha]_D^{25}$+46.2 (*c* 1.00, $CHCl_3$).

2-[[(1*R*,2*R*)-2-(3-(4-Methoxyphenyl)thioureido)cyclohexan-1-yl]-*N*-methyl-(2-aminomethyl)]phenylboronic Acid (**6h**)

By following the general procedure C, **6h** was prepared from 1-((1*R*,2*R*)-2-aminocyclohexyl)-3-(4-methoxyphenyl)-thiourea (300 mg, 1.07 mmol), and purified by column chromatography on silica gel (NH; *n*-hexane–ethyl acetate=4 : 1 to ethyl acetate–methanol=8 : 2). White amorphous (191 mg, 42%, in 2 steps); ^{1}H-NMR (CD_3CN, 400 MHz) δ: 8.57 (brs, 1H), 8.00 (brs, 1H), 7.71 (d, *J*=6.7 Hz, 1H), 7.34–7.24 (m, 2H), 7.22 (d, *J*=8.7 Hz, 2H), 7.16 (d, *J*=6.7 Hz, 1H), 6.88 (d, *J*=8.7 Hz, 2H), 6.04 (brs, 1H), 4.60–4.44 (m, 1H), 3.78 (s, 3H), 3.74 (d, *J*=12.8 Hz, 1H), 3.65 (d, *J*=12.8 Hz, 1H), 2.43–2.33 (m, 1H), 2.29 (s, 3H), 2.05–1.95 (m, 2H), 1.78–1.70 (m, 1H), 1.64–1.55 (m, 1H), 1.38–1.16 (m, 2H), 1.06–0.92 (m, 2H), one O–H or N–H proton was not observed; ^{13}C-NMR (CD_3CN, 100 MHz) δ: 181.8, 158.7, 142.6, 136.6, 131.2, 130.7, 128.4 (2C), 127.8, 115.0 (2C), 114.3, 61.6, 60.3, 56.0, 55.7, 35.7, 33.6, 25.6, 25.4, 22.9. One carbon peak could not be observed; IR (ATR): 2933, 1511, 1448 cm^{-1}; HR-MS (ESI): Calcd for $C_{22}H_{31}BN_3O_3S$ $[M+H]^+$ 428.2178. Found 428.2179; $[\alpha]_D^{23}$+23.2 (*c* 0.99, $CHCl_3$).

2-[[*N*-Methyl-(1*R*,2*R*)-2-(3-(4-nitrophenyl)thioureido)-cyclohexan-1-yl]-(2-aminomethyl)]phenylboronic Acid (**6i**)

By following the general procedure C, **6i** was prepared from 1-((1*R*,2*R*)-2-aminocyclohexyl)-3-(4-nitrophenyl)thiourea (886 mg, 3.0 mmol) (MeOH was used as solvent instead of DCM due to insolubility), and purified by column chromatography on silica gel (NH; *n*-hexane–ethyl acetate=4 : 1 to ethyl acetate–methanol=7 : 3). Yellow amorphous (531 mg, 56%, in 2 steps); ^{1}H-NMR (acetone-d_6, 400 MHz) δ: 9.47 (brs, 2H), 7.99 (d, *J*=9.3 Hz, 2H), 7.85–7.75 (m, 3H), 7.65 (d, *J*=6.7 Hz, 1H), 7.30–7.17 (m, 3H), 4.57–4.43 (m, 1H), 3.71 (dd, *J*=12.8 Hz, 2H), 2.56 (ddd, J_1=J_2=11.3 Hz, J_3=3.2 Hz, 1H), 2.20 (s, 3H), 2.11–1.97 (m, 2H), 1.75–1.65 (m, 1H), 1.60–1.50 (m, 1H), 1.38–0.90 (m, 4H), one O–H or N–H proton was not observed; ^{13}C-NMR (acetone-d_6, 100 MHz) δ: 180.7, 147.5, 143.3, 142.5, 136.5, 130.9, 130.7, 127.7, 124.8 (2C), 121.9 (2C), 62.5, 60.5, 55.2, 35.3, 33.2, 25.6, 25.5, 22.5 One carbon peak could not be observed; IR (ATR): 3267, 2936, 1596, 1329, 1261 cm^{-1}; HR-MS (ESI): Calcd for $C_{21}H_{28}BN_4O_4S$ $[M+H]^+$ 443.1923. Found 443.1920; $[\alpha]_D^{22}$+22.3 (*c* 1.01, $CHCl_3$).

General Procedure for Asymmetric Aza-Michael Addition of *α,β*-Unsaturated Carboxylic Acids and Their Derivatization to Determine the Enantiomeric Excess

General Procedure (D)

To a stirred suspension of *α,β*-unsaturated carboxylic acid **1** (0.1 mmol), boronic acid catalyst (0.01 mmol), and activated MS 4 Å (50 mg) in CCl_4 (0.25 mL), was added hydroxylamine derivatives (0.1 mmol) in CCl_4 (0.25 mL) at room temperature. The reaction mixture was stirred at the room temperature for 24 h. The reaction mixture was directly purified by flash chromatography on silica gel (*n*-hexane–ethyl acetate=4 : 1 to ethyl acetate–methanol=7 : 3) to afford crude **2** as a colorless oil. To a crude solution of **2** in toluene/methanol (0.75 mL/0.25 mL) at 0°C, was added trimethylsilyldiazomethane ($TMSCHN_2$) in Et_2O (0.25 mL, 2.0 M, 0.5 mmol, 5.0 equiv). The reaction mixture was stirred at 0°C for 30 min, before being quenched with AcOH until yellow solution changed to be colorless. The reaction mixture was purified by flash chromatography on silica gel to afford methyl esters **2-[OMe]**. When it was difficult to separate the enantiomers of methyl ester **2-[OMe]** by chiral HPLC, **2-[OMe]** was further modified by *N*-benzoylation as shown below.

General Procedure (E)

To a stirred solution of **2-[OMe]** (0.05 mmol) in THF (1.0 mL) were added benzoyl chloride (23 μL, 0.20 mmol) and pyridine (12 μL, 0.15 mmol) at 0°C. After being stirred at room temperature for 3 h, the reaction mixture was quenched with 1 N aqueous HCl solution (pH=*ca.* 1), and extracted with ethyl acetate. The combined organic layer was washed with saturated aqueous $NaHCO_3$ solution (pH=9) and brine,, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel to afford *N*-benzoyl compound **(2-[*N*Bz, OMe])**.

Methyl (*S*)-3-((Benzyloxy)amino)-5-phenylpentanoate (**2a-[OMe]**)

Colorless oil (25.9 mg, 83, 90% ee with cat. **6i**); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.36–7.23 (m, 7H), 7.21–7.14 (m, 3H), 5.86 (brs, 1H), 4.69 (s, 2H), 3.64 (s, 3H), 3.36–3.28 (m, 1H), 2.78–2.58 (m, 3H), 2.47 (dd, J_1=15.8 Hz, J_2=4.8 Hz, 1H), 1.94–1.82 (m, 1H), 1.76–1.65 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 172.7, 141.7, 137.8, 128.37 (2C), 128.34 (2C), 128.32 (2C), 128.30 (2C), 127.7, 125.9, 76.5, 57.0, 51.5, 36.8, 33.5, 32.4; IR (ATR): 1735 cm^{-1}; HR-MS (ESI): Calcd for $C_{19}H_{24}NO_3$ $[M+H]^+$ 314.1751. Found 314.1754; HPLC [Chiralcel IC, *n*-hexane–2-propanol=99 : 1, 1.0 mL/min, λ=254 nm, retention times: (major) 20.9 min (minor) 17.4 min]; $[\alpha]_D^{21}$−4.5 (*c* 0.99, $CHCl_3$) for 90% ee. **2a-[OMe]** was converted to the corresponding known compound **S-6** and its absolute configuration was determined to be *S* (Chart S1 in the Supplementary Materials).

(*S*)-*N*-(Benzyloxy)-3-((benzyloxy)amino)-5-phenylpentanamide (**3a**)

Colorless oil (16.6 mg, 41% with cat. **4a** + **5**); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 9.06 (brs, 1H), 7.40–7.10 (m, 15H), 4.87 (s, 2H), 4.71 (brs, 1H), 4.50 (s, 2H), 3.18–3.08 (m, 1H), 2.68–2.59 (m, 2H), 2.40–2.31 (m, 2H), 1.88–1.77 (m, 1H), 1.71–1.59 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 169.3, 141.2, 137.2, 135.6, 129.0 (2C), 128.64, 128.58 (2C), 128.44 (4C), 128.37 (2C), 128.30 (2C), 128.1, 126.0, 77.9, 76.3, 56.7, 36.0, 33.1, 32.2; IR (ATR): 3198, 1657, 1496, 1456 cm^{-1}; HR-MS (ESI): Calcd for $C_{25}H_{29}N_2O_3$ $[M+H]^+$ 405.2173. Found 405.2174.

Methyl (*S*)-3-((Benzhydryloxy)amino)-5-phenylpentanoate (**2aA-[OMe]**)

Colorless oil (30.1 mg, 77, 76% ee with cat. **6i**); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.36–7.22 (m, 12H), 7.20–7.11 (m, 3H), 5.82 (brs, 1H), 5.69 (s, 1H), 3.59 (s, 3H), 3.39–3.31 (m, 1H), 2.75–2.57 (m, 3H), 2.50 (dd, J_1=15.7 Hz, J_2=4.9 Hz, 1H), 1.96–1.84 (m, 1H), 1.77–1.65 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 172.7, 141.7, 141.6, 141.5, 128.4 (2C), 128.33 (4C) 128.30 (2C), 127.49, 127.46, 127.2 (2C), 127.1 (2C), 125.9, 86.8, 57.1, 51.5, 37.0, 33.6, 32.4; IR (ATR): 1731 cm^{-1}; HR-MS (ESI): Calcd for $C_{25}H_{28}NO_3$ $[M+H]^+$ 390.2064. Found 390.2062; HPLC [Chiralcel IB, *n*-hexane–2-propanol=99 : 1, 1.0 mL/min, λ=254 nm, retention times: (major) 10.1 min (minor) 12.9 min]; $[\alpha]_D^{21}$−2.0 (*c* 0.98, $CHCl_3$) for 76% ee.

Methyl (*S*)-3-((Heptyloxy)amino)-5-phenylpentanoate (**2aB-[OMe]**)

Colorless oil (21.1 mg, 66, 90% ee with cat. **6i**); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.33–7.12 (m, 5H), 5.73 (brs, 1H), 3.70–3.62 (m, 5H), 3.35–3.24 (m, 1H), 2.81–2.56 (m, 3H), 2.51–2.43 (m, 1H), 1.94–1.80 (m, 1H), 1.77–1.63 (m, 1H), 1.57–1.48 (m, 2H), 1.34–1.20 (m, 8H), 0.93–0.84 (m, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 172.8, 141.8, 128.4 (2C), 128.3 (2C), 125.9, 74.5, 56.9, 51.5, 36.7, 33.6, 32.4, 31.8, 29.2, 28.7, 26.1, 22.6, 14.1; IR (ATR): 1734 cm^{-1}; HR-MS (ESI): Calcd for $C_{19}H_{32}NO_3$ $[M+H]^+$ 322.2377. Found 322.2377; $[\alpha]_D^{24}$−8.2 (*c* 1.00, $CHCl_3$) for 90% ee.

Methyl (*S*)-3-(*N*-(Heptyloxy)benzamido)-5-phenylpentanoate (**2aB-[*N*Bz, OMe]**)

Colorless oil (19.4 mg, 91, 90% ee with cat. **6i**); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.65–7.60 (m, 2H), 7.47–7.35 (m, 3H), 7.30–7.24 (m, 2H), 7.22–7.14 (m, 3H), 4.92–4.50 (m, 1H), 3.90–3.68 (m, 1H), 3.69 (s, 3H), 2.89 (dd, J_1=15.7 Hz, J_2=8.4 Hz, 1H), 2.83–2.73 (m, 1H), 2.73–2.57 (m, 2H), 2.24–2.11 (m, 1H), 1.96–1.85 (m, 1H), 1.77–1.63 (m, 1H), 1.50–1.45 (m, 2H), 1.41–1.10 (m, 8H), 0.87 (t, J=7.0 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 171.4, 171.2, 141.1, 134.8, 130.4, 128.4 (2C), 128.3 (2C), 128.0 (4C) 126.0, 77.2, 56.5, 51.8, 37.5, 34.6, 32.7, 31.6, 28.9, 28.0, 25.7, 22.5, 14.0; IR (ATR): 1740, 1652 cm^{-1}; HR-MS (ESI): Calcd for $C_{26}H_{36}NO_4$ $[M+H]^+$ 426.2639. Found 426.2638; HPLC [Chiralcel IC, *n*-hexane–2-propanol=80 : 20, 1.0 mL/min, λ=254 nm, retention times: (major) 14.4 min (minor) 11.0 min]; $[\alpha]_D^{21}$+8.6 (*c* 1.03, $CHCl_3$) for 90% ee.

Methyl (*S*)-3-((Benzyloxy)amino)butanoate (**2b-[OMe]**)

Colorless oil (16.7 mg, 75, 97% ee with cat. **6i**); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.38–7.26 (m, 5H), 5.73 (brs, 1H), 4.69 (s, 2H), 3.65 (s, 3H), 3.54–3.44 (m, 1H), 2.60 (dd, J_1=15.7 Hz, J_2=7.0 Hz, 1H), 2.37 (dd, J_1=15.7 Hz, J_2=5.8 Hz, 1H), 1.13 (d, J=6.7 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 172.6, 137.7, 128.3 (4C), 127.8, 76.6, 53.0, 51.5, 38.6, 17.9; IR (ATR): 1739, 1218 cm^{-1}; HR-MS (ESI): Calcd for $C_{12}H_{18}NO_3$ $[M+H]^+$ 224.1281. Found 224.1280; HPLC [Chiralcel IC, *n*-hexane–2-propanol=99 : 1, 1.0 mL/min, λ=254 nm, retention times: (major) 15.6 min (minor) 13.5 min]; $[\alpha]_D^{28}$+10.1 (*c* 1.02, $CHCl_3$) for 97% ee (Lit[10]: $[\alpha]_D^{25}$−4.66 (*c* 0.75, $CHCl_3$) for 40% ee, (*R*) enantiomer).

Methyl (*S*)-3-((Benzyloxy)amino)pentanoate (**2c-[OMe]**)

Colorless oil (20.0 mg, 84, 90% ee with cat. **6i**); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.38–7.26 (m, 5H), 5.71 (brs, 1H), 4.68 (s, 2H), 3.65 (s, 3H), 3.28–3.19 (m, 1H), 2.56 (dd, J_1=15.7 Hz, J_2=7.7 Hz, 1H), 2.45 (dd, J_1=15.7 Hz, J_2=4.9 Hz, 1H), 1.63–1.52 (m, 1H), 1.49–1.38 (m, 1H), 0.93 (t, J=7.4 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 173.0, 137.8, 128.36 (2C), 128.31 (2C), 127.7, 76.5, 59.0, 51.5, 36.6, 24.7, 10.4; IR (ATR): 1737, 1200 cm^{-1}; HR-MS (ESI): Calcd for $C_{13}H_{20}NO_3$ $[M+H]^+$ 238.1438. Found 238.1432; $[\alpha]_D^{26}$+10.3 (*c* 0.99, $CHCl_3$) for 90% ee.

Methyl (*S*)-3-(*N*-(Benzyloxy)benzamido)pentanoate (**2c-[*N*Bz, OMe]**)

Colorless oil (13.9 mg, 81, 90% ee with cat. **6i**); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.65 (d, J=7.0 Hz, 2H), 7.51–7.37 (m, 3H), 7.34–7.28 (m, 3H), 7.26–7.07 (m, 2H), 4.91–4.48 (m, 3H), 3.68 (s, 3H), 2.85 (dd, J_1=15.4 Hz, J_2=8.4 Hz, 1H), 2.58 (dd, J_1=15.4 Hz, J_2=5.2 Hz, 1H), 1.95–1.81 (m, 1H), 1.72–1.57 (m, 1H), 0.98 (t, J=7.0 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 171.7, 171.6, 135.0, 134.6, 130.5, 129.4 (2C), 128.7, 128.4 (2C), 128.13 (2C), 128.11 (2C), 78.1, 58.9, 51.8, 37.2, 25.9, 11.0; IR (ATR): 1740, 1655 cm^{-1}; HR-MS (ESI): Calcd for $C_{20}H_{24}NO_4$ $[M+H]^+$ 342.1700. Found 342.1699; HPLC [Chiralcel IC, *n*-hexane–2-propanol=80 : 20, 1.0 mL/min, λ=254 nm, retention times: (major) 19.1 min (minor) 12.8 min]; $[\alpha]_D^{26}$+20.9 (*c* 1.00, $CHCl_3$) for 90% ee.

Methyl (*S*)-3-((Benzyloxy)amino)hexanoate (**2d-[OMe]**)

Colorless oil (18.0 mg, 72, 90% ee with cat. **6i**); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.38–7.27 (m, 5H), 5.79 (brs, 1H), 4.68 (s, 2H), 3.65 (s, 3H), 3.36–3.27 (m, 1H), 2.57 (dd, J_1=15.7 Hz, J_2=7.5 Hz, 1H), 2.44 (dd, J_1=15.7 Hz, J_2=5.2 Hz, 1H), 1.59–1.45 (m, 1H), 1.44–1.30 (m, 3H), 0.90 (t, J=7.0 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 172.9, 137.8, 128.36 (2C), 128.29 (2C), 127.7, 76.5, 57.3, 51.5, 37.0, 34.1, 19.2, 14.1; IR (ATR): 1737, 1195 cm^{-1}; HR-MS (ESI): Calcd for $C_{14}H_{22}NO_3$ $[M+H]^+$ 252.1594. Found 252.1596; $[\alpha]_D^{21}$+9.8 (*c* 1.03, $CHCl_3$) for 90% ee.

Methyl (*S*)-3-(*N*-(Benzyloxy)benzamido)hexanoate (**2d-[*N*Bz, OMe]**)

Colorless oil (10.8 mg, 61, 90% ee with cat. **6i**); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.65 (d, J=7.0 Hz, 2H), 7.51–7.37 (m, 3H), 7.35–7.27 (m, 3H), 7.27–7.00 (m, 2H), 5.04–4.40 (m, 3H), 3.68 (s, 3H), 2.85 (dd, J_1=15.4 Hz, J_2=8.4 Hz, 1H), 2.56 (dd, J_1=15.4 Hz, J_2=4.3 Hz, 1H), 1.94–1.77 (m, 1H), 1.76–1.20 (m, 3H), 0.88 (t, J=6.4 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 171.6, 171.5, 135.0, 134.5, 130.5, 129.4 (2C), 128.7, 128.4 (2C), 128.1 (4C), 78.1, 57.1, 51.8, 37.4, 34.9, 19.5, 13.8; IR (ATR): 1739, 1655 cm^{-1}; HR-MS (ESI): Calcd for $C_{21}H_{26}NO_4$ $[M+H]^+$ 356.1856. Found 356.1850; HPLC [Chiralcel IC, *n*-hexane–2-propanol=80 : 20, 1.0 mL/min, λ=254 nm, retention times: (major) 17.4 min (minor) 12.2 min]; $[\alpha]_D^{23}$+17.4 (*c* 1.00, $CHCl_3$) for 90% ee.

Methyl (*S*)-3-((Benzyloxy)amino)octanoate (**2e-[OMe]**)

Colorless oil (21.3 mg, 76, 88% ee with cat. **6i**); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.38–7.26 (m, 5H), 5.79 (br s, 1H), 4.67 (s, 2H), 3.64 (s, 3H), 3.35–3.25 (m, 1H), 2.57 (dd, J_1=15.7 Hz, J_2=7.5 Hz, 1H), 2.44 (dd, J_1=15.7 Hz, J_2=4.9 Hz, 1H), 1.57–1.47 (m, 1H), 1.42–1.19 (m, 7H), 0.88 (t, J=6.8 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 173.0, 137.8, 128.37 (2C), 128.30 (2C), 127.7, 76.5, 57.6, 51.5, 37.0, 31.8, 31.8, 25.7, 22.5, 14.0; IR (ATR): 1735, 1204 cm^{-1}; HR-MS (ESI): Calcd for $C_{16}H_{26}NO_3$ $[M+H]^+$ 280.1907. Found 280.1909; $[\alpha]_D^{31}$+2.2 (*c* 1.00, $CHCl_3$) for 88% ee.

Methyl (*S*)-3-(*N*-(Benzyloxy)-4-methylbenzamido)octanoate (**2e-[*N*-4-toluoyl, OMe]**)

Colorless oil (15.1 mg, 76, 88% ee with cat. **6i**); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.56 (d, J=8.1 Hz, 2H), 7.38–7.15 (m, 7H), 4.98–4.46 (m, 3H), 3.67 (s, 3H), 2.82 (dd, J_1=15.7 Hz, J_2=8.4 Hz, 1H), 2.54 (dd, J_1=15.7 Hz, J_2=5.7 Hz, 1H), 2.40 (s, 3H), 1.90–1.85 (m, 1H), 1.73–1.15 (m, 7H), 0.85 (t, J=7.1 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 171.6, 171.4, 140.9, 134.8, 132.0, 129.4 (2C), 128.8 (2C), 128.6, 128.4 (2C), 128.2 (2C), 77.8, 57.7, 51.8, 37.4, 32.7, 31.4, 26.0, 22.4, 21.5, 13.9; IR (ATR): 1740, 1652 cm^{-1}; HR-MS (ESI): Calcd for $C_{24}H_{32}NO_4$ $[M+H]^+$ 398.2326. Found 398.2326; HPLC [Chiralcel IC, *n*-hexane–2-propanol=80 : 20, 1.0 mL/min, λ=254 nm, retention times: (major) 19.2 min (minor) 12.2 min]; $[\alpha]_D^{22}$+11.0 (*c* 1.00, $CHCl_3$) for 88% ee.

Methyl (*S*)-3-((Benzyloxy)amino)decanoate (**2f-[OMe]**)

Colorless oil (23.1 mg, 75, 86% ee with cat. **6i**); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.37–7.26 (m, 5H), 5.79 (br s, 1H), 4.67 (s, 2H), 3.64 (s, 3H), 3.34–3.25 (m, 1H), 2.57 (dd, J_1=15.5 Hz, J_2=7.7 Hz, 1H), 2.44 (dd, J_1=15.5 Hz, J_2=4.9 Hz, 1H), 1.57–1.47 (m, 1H), 1.42–1.19 (m, 11H), 0.88 (t, J=6.8 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 172.9, 137.8, 128.36 (2C), 128.28 (2C), 127.7, 76.5, 57.6, 51.5, 37.0, 31.9, 31.8, 29.5, 29.1, 26.0, 22.6, 14.1; IR (ATR): 1737, 1199 cm^{-1}; HR-MS (ESI): Calcd for $C_{18}H_{30}NO_3$ $[M+H]^+$ 308.2220. Found 308.2222; $[\alpha]_D^{24}$+2.6 (*c* 0.96, $CHCl_3$) for 86% ee.

Methyl (*S*)-3-(*N*-(Benzyloxy)benzamido)decanoate (**2f-[*N*Bz, OMe]**)

Colorless oil (17.5 mg, 85, 86% ee, with cat. **6i**); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.65 (d, J=7.0 Hz, 2H), 7.51–7.38 (m, 3H), 7.35–7.27 (m, 3H), 7.26–7.03 (m, 2H), 5.00–4.35 (m, 3H), 3.68 (s, 3H), 2.84 (dd, J_1=15.4 Hz, J_2=8.4 Hz, 1H), 2.58 (dd, J_1=15.4 Hz, J_2=4.3 Hz, 1H), 1.91–1.77 (m, 1H), 1.70–1.15 (m, 11H), 0.86 (t, J=6.8 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 171.6, 171.5, 135.0, 134.7, 130.5, 129.4 (2C), 128.7, 128.4 (2C), 128.1 (4C), 77.2, 57.1, 51.8, 37.4, 32.7, 31.7, 29.3, 29.1, 26.3, 22.6, 14.1; IR (ATR): 1740, 1657 cm^{-1}; HR-MS (ESI): Calcd for $C_{25}H_{34}NO_4$ $[M+H]^+$ 412.2482. Found 412.2483; HPLC [Chiralcel IC, *n*-hexane–2-propanol=90 : 10, 1.0 mL/min, λ=254 nm, retention times: (major) 23.3 min (minor) 16.3 min]; $[\alpha]_D^{25}$+1.3 (*c* 1.00, $CHCl_3$) for 86% ee.

Methyl (*R*)-3-((Benzyloxy)amino)-4-methylpentanoate (**2g-[OMe]**)

Colorless oil (14.3 mg, 57, 76% ee, with cat. **6i**); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.39–7.27 (m, 5H), 5.81 (br s, 1H), 4.67 (s, 2H), 3.64 (s, 3H), 3.16 (ddd, J_1=9.7 Hz, J_2=J_3=3.9 Hz, 1H), 2.47 (dd, J_1=15.7 Hz, J_2=4.6 Hz, 1H), 2.42 (dd, J_1=15.7 Hz, J_2=7.8 Hz, 1H), 1.97–1.84 (m, 1H), 0.94 (t, J=7.0 Hz, 3H), 0.90 (t, J=7.0 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 173.4, 137.8, 128.4 (2C), 128.3 (2C), 127.7, 76.2, 62.7, 51.6, 33.9, 29.0, 19.2, 18.2; IR (ATR): 1737, 1202 cm^{-1}; HR-MS (ESI): Calcd for $C_{14}H_{22}NO_3$ $[M+H]^+$ 252.1594. Found 252.1594; $[\alpha]_D^{23}$+8.6 (*c* 1.02, $CHCl_3$) for 76% ee.

Methyl (*R*)-3-(*N*-(Benzyloxy)benzamido)-4-methylpentanoate (**2g-[*N*Bz, OMe]**)

Colorless oil (16.0 mg, 90, 76% ee with cat. **6i**); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.66 (d, J=7.0 Hz, 2H), 7.50–7.37 (m, 3H), 7.36–6.94 (m, 5H), 5.00–4.20 (m, 3H), 3.70 (s, 3H), 2.89 (dd, J_1=15.4 Hz, J_2=9.9 Hz, 1H), 2.76–2.67 (m, 1H), 2.20–2.08 (m, 1H), 1.12–0.93 (m, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 172.1, 171.4, 135.1, 134.5, 130.4, 129.2 (2C), 128.6, 128.3 (2C), 128.1 (4C), 77.8, 63.1, 51.8, 35.4, 31.4, 20.2, 19.8; IR (ATR): 1738, 1650 cm^{-1}; HR-MS (ESI): Calcd for $C_{21}H_{26}NO_4$ $[M+H]^+$ 356.1856. Found 356.1854; HPLC [Chiralcel IC, *n*-hexane–2-propanol=90 : 10, 1.0 mL/min, λ=254 nm, retention times: (major) 28.3 min (minor) 18.9 min]; $[\alpha]_D^{22}$+24.6 (*c* 1.01, $CHCl_3$) for 76% ee.

Methyl (*R*)-4-(Benzyloxy)-3-((benzyloxy)amino)butanoate (**2h-[OMe]**)

Colorless oil (58.9 mg, 89, 85% ee with cat. **6i**); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.37–7.26 (m, 10H), 6.08 (br s, 1H), 4.67 (s, 2H), 4.52 (d, J=12.2 Hz, 1H), 4.48(d, J=12.2 Hz, 1H), 3.64 (s, 3H), 3.62–3.52 (m, 3H), 2.61 (dd, J_1=15.9 Hz, J_2=7.0 Hz, 1H), 2.48 (dd, J_1=15.9 Hz, J_2=5.5 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 172.4, 138.0, 137.6, 128.36 (2C), 128.35 (2C), 128.29 (2C), 127.8, 127.65, 127.61 (2C), 76.4, 73.2, 69.3, 57.2, 51.6, 34.2; IR (ATR): 1734, 1099 cm^{-1}; HR-MS (ESI): Calcd for $C_{19}H_{24}NO_4$ $[M+H]^+$ 330.1700. Found 330.1703; HPLC [Chiralcel IC, *n*-hexane–2-propanol=98 : 2, 1.0 mL/min, λ=254 nm, retention times: (major) 20.1 min (minor) 17.9 min]; $[\alpha]_D^{26}$+3.2 (*c* 1.02, $CHCl_3$) for 85% ee.

Methyl (*S*)-4-(Benzyloxy)-3-((benzyloxy)amino)butanoate (***ent*-2h-[OMe]**)

Colorless oil (24.9 mg, 76, 83% ee with cat. **6i**); HPLC [Chiralcel IC, *n*-hexane–2-propanol=98 : 2, 1.0 mL/min, λ=254 nm, retention times: (major) 17.9 min (minor) 20.1 min]; $[\alpha]_D^{25}$−3.0 (*c* 1.03, $CHCl_3$) for 83% ee.

(*S*)-4-((Benzyloxy)amino)-6-methoxy-6-oxohexyl Benzoate (**2i-[OMe]**)

Colorless oil (31.9 mg, 86, 91% ee with cat. **6i**); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.10–8.01 (m, 2H), 7.62–7.53 (m, 1H), 7.49–7.42 (m, 2H), 7.37–7.27 (m, 5H), 5.87 (br s, 1H), 4.68 (s, 2H), 4.30 (t, J=6.5 Hz, 2H), 3.65 (s, 3H), 3.39–3.30 (m, 1H), 2.63 (dd, J_1=15.9 Hz, J_2=7.8 Hz, 1H), 2.46 (dd, J_1=15.9 Hz, J_2=4.9 Hz, 1H) 1.95–1.49 (m, 4H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 172.7, 166.6, 137.7, 132.9, 130.2, 129.5 (2C), 128.39

(2C), 128.32 (2C), 128.30 (2C), 127.8, 76.5, 64.7, 57.1, 51.6, 36.7, 28.4, 25.4; IR (ATR): 1732, 1278 cm^{-1}; HR-MS (ESI): Calcd for $C_{21}H_{26}NO_5$ $[M+H]^+$ 372.1805. Found 372.1806; HPLC [Chiralcel IC, *n*-hexane–2-propanol=95 : 5, 1.0 mL/min, λ=254 nm, retention times: (major) 22.2 min (minor) 18.9 min]; $[\alpha]_D^{26}$+1.5 (*c* 0.96, $CHCl_3$) for 91% ee.

Methyl (*R*)-3-((Benzyloxy)amino)-5-(methylthio)pentanoate (**2j-[OMe]**)

Colorless oil (22.2 mg, 78, 91% ee with cat. **6i**); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.39–7.27 (m, 5H), 5.93 (brs, 1H), 4.67 (s, 2H), 3.66 (s, 3H), 3.46 −3.36 (m, 1H), 2.64 (dd, J_1=15.9 Hz, J_2=7.5 Hz, 1H), 2.60 −2.51 (m, 2H), 2.46 (dd, J_1=15.9 Hz, J_2=5.1 Hz, 1H), 2.09 (s, 3H), 1.92–1.78 (m, 1H), 1.74–1.61 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 172.6, 137.7, 128.4 (2C), 128.3 (2C), 127.8, 76.5, 56.5, 51.6, 36.6, 31.1, 30.8, 15.4; IR (ATR): 2918, 1734, 1437, 1207 cm^{-1}; HR-MS (ESI): Calcd for $C_{14}H_{22}NO_3S$ $[M+H]^+$ 284.1315. Found 284.1318; $[\alpha]_D^{23}$−7.0 (*c* 1.02, $CHCl_3$) for 87% ee.

Methyl (*R*)-3-(*N*-(Benzyloxy)benzamido)-5-(methylthio)-pentanoate (**2j-[*N*Bz, OMe]**)

Colorless oil (14.0 mg, 72, 87% ee with cat. **6i**); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.65 (d, *J*=7.0 Hz, 2H), 7.52–7.39 (m, 3H), 7.35–7.28 (m, 3H), 7.26–7.04 (m, 2H), 4.90–4.63 (m, 3H), 3.68 (s, 3H), 2.87 (dd, J_1=15.7 Hz, J_2=8.1 Hz, 1H), 2.68–2.45 (m, 3H), 2.24–2.10 (m, 1H), 2.06 (s, 3H), 1.93–1.80 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 171.7, 171.2, 134.6, 134.4, 130.7, 129.4 (2C), 128.8, 128.5 (2C), 128.2 (2C), 128.1 (2C), 78.1, 56.5, 51.9, 37.2, 32.0, 30.6, 15.4; IR (ATR): 2922, 1738, 1653 cm^{-1}; HR-MS (ESI): Calcd for $C_{21}H_{26}NO_4S$ $[M+H]^+$ 388.1577. Found 388.1577; HPLC [Chiralcel IC, *N*-hexane/2-propanol=80/20, 1.0 mL/min, λ=254 nm, retention times: (major) 22.8 min (minor) 16.3 min]; $[\alpha]_D^{23}$−2.0 (*c* 1.01, $CHCl_3$) for 87% ee.

Methyl (*S*)-3-((Benzyloxy)amino)-6-(((benzyloxy)carbonyl)-amino)hexanoate (**2k-[OMe]**)

Colorless oil (32.0 mg, 80, 71% ee with cat. **6i**); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.38–7.27 (m, 10H), 5.78 (brs, 1H), 5.09 (s, 2H), 4.86 (brs, 1H), 4.65 (s, 2H), 3.64 (s, 3H), 3.31–3.22 (m, 1H), 3.20–3.11 (m, 2H), 2.59 (dd, J_1=15.8 Hz, J_2=7.4 Hz, 1H), 2.42 (dd, J_1=15.8 Hz, J_2=4.9 Hz, 1H) 1.64–1.34 (m, 4H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 172.7, 156.3, 137.7, 136.6, 128.5 (2C), 128.4 (2C), 128.3 (2C) 128.11 (2C), 128.09, 127.8, 76.4, 66.6, 57.1, 51.6, 40.8, 36.8, 29.0, 26.5; IR (ATR): 2950, 1726, 1255 cm^{-1}; HR-MS (ESI): Calcd for $C_{22}H_{29}N_2O_5$ $[M+H]^+$ 401.2071. Found 401.2076; HPLC [Chiralcel IC, *N*-hexane/2-propanol=80/20, 1.0 mL/min, λ=254 nm, retention times: (major) 13.7 min (minor) 12.3 min]; $[\alpha]_D^{23}$+2.0 (*c* 1.00, $CHCl_3$) for 71% ee.

Methyl (*S*)-3-((Benzyloxy)amino)-5-(4-(trifluoromethyl)-phenyl)pentanoate (**2l-[OMe]**)

Colorless oil (29.0 mg, 76, 83% ee with cat. **6i**); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.52 (d, *J*=8.1 Hz, 2H), 7.38–7.24 (m, 7H), 5.88 (brs, 1H), 4.69 (s, 2H), 3.65 (s, 3H), 3.32–3.24 (m, 1H), 2.83–2.60 (m, 3H), 2.47 (dd, J_1=15.9 Hz, J_2=4.9 Hz, 1H), 1.94–1.82 (m, 1H), 1.77–1.65 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 172.6, 145.9, 137.8, 128.7 (2C), 128.38 (2C), 128.34 (2C), 128.2 (*J*=32.4 Hz), 127.8, 125.3 (*J*=3.8 Hz, 2C), 124.3 (*J*=271.7 Hz), 76.5, 56.8, 51.6, 36.6, 33.2, 32.2; IR (ATR): 1734, 1325 cm^{-1}; HR-MS (ESI): Calcd for $C_{20}H_{23}F_3NO_3$ $[M+H]^+$ 382.1625. Found 382.1624; HPLC [Chiralcel IB, *n*-hexane–2-propanol=98 : 2, 1.0 mL/min, λ=254 nm, retention times: (major) 9.9 min (minor) 8.7 min]; $[\alpha]_D^{22}$−5.2 (*c* 0.97, $CHCl_3$) for 80% ee.

Methyl (*S*)-3-((Benzyloxy)amino)-5-(4-methoxyphenyl)pentanoate (**2m-[OMe]**)

Colorless oil (30.2 mg, 88, 87% ee with cat. **6i**); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.39–7.26 (m, 5H), 7.08 (d, *J*=8.7 Hz, 2H), 6.82 (d, *J*=8.7 Hz, 2H), 5.88 (brs, 1H), 4.69 (s, 2H), 3.78 (s, 3H), 3.64 (s, 3H), 3.37–3.27 (m, 1H), 2.71–2.55 (m, 3H), 2.47 (dd, J_1=15.7 Hz, J_2=4.9 Hz, 1H), 1.91–1.78 (m, 1H), 1.73–1.60 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 172.8, 157.8, 137.8, 133.7, 129.2 (2C), 128.34 (2C), 128.31 (2C), 127.7, 113.8 (2C), 76.5, 57.0, 55.2, 51.5, 36.8, 33.8, 31.4; IR (ATR): 1736, 1513, 1248 cm^{-1}; HR-MS (ESI): Calcd for $C_{20}H_{26}NO_4$ $[M+H]^+$ 344.1856. Found 344.1856; HPLC [Chiralcel IB, *n*-hexane–2-propanol=95 : 5, 1.0 mL/min, λ=254 nm, retention times: (major) 8.7 min (minor) 7.4 min]; $[\alpha]_D^{25}$−3.3 (*c* 0.99, $CHCl_3$) for 87% ee.

Methyl (*S*)-3-((Benzyloxy)amino)-5-(2-bromophenyl)pentanoate (**2n-[OMe]**)

Colorless oil (33.0 mg, 84, 88% ee with cat. **6i**); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.51 (dd, J_1=7.8 Hz, J_2=0.9 Hz, 1H), 7.39–7.26 (m, 5H), 7.24–7.16 (m, 2H), 7.08–7.02 (m, 1H), 5.91 (brs, 1H), 4.71 (s, 2H), 3.65 (s, 3H), 3.39–3.31 (m, 1H), 2.90–2.72 (m, 2H), 2.66 (dd, J_1=15.9 Hz, J_2=7.8 Hz, 1H), 2.51 (dd, J_1=15.9 Hz, J_2=4.9 Hz, 1H), 1.91–1.80 (m, 1H), 1.77–1.66 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 172.7, 141.0, 137.8, 132.8, 130.3, 128.4 (2C), 128.3 (2C), 127.8, 127.7, 127.5, 124.3, 76.5, 57.1, 51,6, 36.7, 32.8, 32.0; IR (ATR): 1733 cm^{-1}; HR-MS (ESI): Calcd for $C_{19}H_{23}NO_3Br$ $[M+H]^+$ 392.0856. Found 392.0862; HPLC [Chiralcel IC, *n*-hexane–2-propanol=99 : 1, 1.0 mL/min, λ=254 nm, retention times: (major) 16.7 min (minor) 15.2 min]; $[\alpha]_D^{21}$−1.9 (*c* 0.98, $CHCl_3$) for 88% ee.

Methyl (*S*)-3-((Benzyloxy)amino)-5-(3,4-dimethoxyphenyl)-pentanoate (**2o-[OMe]**)

Colorless oil (30.3 mg, 81, 86% ee with cat. **6i**); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.38–7.27 (m, 5H), 6.78 (d, *J*=8.1 Hz, 1H), 6.73–6.68 (m, 2H), 5.86 (brs, 1H), 4.69 (s, 2H), 3.86 (s, 6H), 3.65 (s, 3H), 3.38–3.28 (m, 1H), 2.73–2.55 (m, 3H), 2.48 (dd, J_1=15.7 Hz, J_2=4.9 Hz, 1H), 1.93–1.80 (m, 1H), 1.77–1.55 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 172.8, 148.8, 147.2, 137.8, 134.3, 128.32 (2C), 128.31 (2C), 127.8, 120.1, 111.6, 111.1, 76.5, 57.0, 55.9, 55.8, 51.5, 36.8, 33.7, 32.0; IR (ATR): 1731, 1590, 1260, 1236 cm^{-1}; HR-MS (ESI): Calcd for $C_{21}H_{28}NO_5$ $[M+H]^+$ 374.1962. Found 374.1963; HPLC [Chiralcel IB, *n*-hexane–2-propanol=90 : 10, 1.0 mL/min, λ=254 nm, retention times: (major) 10.7 min (minor) 9.6 min]; $[\alpha]_D^{26}$−4.9 (*c* 0.97, $CHCl_3$) for 86% ee.

Methyl (*S*)-3-((Benzyloxy)amino)-5-(naphthale*n*-2-yl)pentanoate (**2p-[OMe]**)

Colorless oil (32.7 mg, 90, 87% ee with cat. **6i**); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.83–7.73 (m, 3H), 7.60 (s, 1H), 7.48–7.38 (m, 2H), 7.38–7.27 (m, 6H), 5.90 (brs, 1H), 4.71 (s, 2H), 3.64 (s, 3H), 3.40–3.30 (m, 1H), 2.94–2.77 (m, 2H), 2.66 (dd, J_1=15.7 Hz, J_2=7.5 Hz, 1H), 2.50 (dd, J_1=15.7 Hz, J_2=4.9 Hz, 1H), 2.03–1.92 (m, 1H), 1.86–1.74 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 172.8, 139.2, 137.8, 133.6, 132.0, 128.37 (2C), 128.33 (2C), 128.0, 127.8, 127.6, 127.4, 127.2, 126.3, 125.9, 125.2, 76.5, 57.0, 51.6, 36.8, 33.4, 32.5; IR (ATR): 1735 cm^{-1}; HR-MS (ESI): Calcd for $C_{23}H_{26}NO_3$ $[M+H]^+$ 364.1907. Found 364.1904; HPLC [Chiralcel IC, *n*-hexane–2-propanol=95 : 5, 1.0 mL/min, λ=254 nm, retention

times: (major) 9.2 min (minor) 8.4 min]; $[\alpha]_D^{23}$ −5.2 (*c* 1.04, $CHCl_3$) for 87% ee.

Methyl (*S*)-3-((Benzyloxy)amino)-5-(thiophen-2-yl)pentanoate (**2q-[OMe]**)

Colorless oil (22.1 mg, 69, 93% ee with cat. **6i**); ^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 7.38–7.27 (m, 5H), 7.11 (d, *J*=5.2 Hz, 1H), 6.91 (dd, J_1=5.2 Hz, J_2=3.5 Hz, 1H), 6.78 (d, *J*=3.5 Hz, 1H), 5.88 (brs, 1H), 4.69 (s, 2H), 3.65 (s, 3H), 3.38–3.28 (m, 1H), 3.00–2.84 (m, 2H), 2.64 (dd, J_1=15.9 Hz, J_2=7.8 Hz, 1H), 2.46 (dd, J_1=15.9 Hz, J_2=4.8 Hz, 1H), 1.99–1.87 (m, 1H), 1.83–1.70 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 172.7, 144.5, 137.8, 128.4 (2C), 128.3 (2C), 127.8, 126.8, 124.3, 123.1, 76.5, 56.7, 51.6, 36.6, 33.8, 26.5; IR (ATR): 1732 cm^{-1}; HR-MS (ESI): Calcd for $C_{17}H_{22}NO_3S$ $[M+H]^+$ 320.1315. Found 320.1314; HPLC [Chiralcel IC, *n*-hexane–2-propanol=98 : 2, 1.0 mL/min, *λ*=254 nm, retention times: (major) 11.3 min (minor) 10.2 min]; $[\alpha]_D^{29}$ −8.9 (*c* 1.03, $CHCl_3$) for 93% ee.

Methyl (*S*)-3-((Benzyloxy)amino)-6-phenylhexanoate (**2r-[OMe]**)

Colorless oil (26.6 mg, 81, 91% ee with cat. **6i**); ^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 7.37–7.24 (m, 7H), 7.21–7.14 (m, 3H), 5.78 (brs, 1H), 4.64 (s, 2H), 3.63 (s, 3H), 3.36–3.27 (m, 1H), 2.63–2.53 (m, 3H), 2.43 (dd, J_1=15.7 Hz, J_2=5.2 Hz, 1H), 1.78–1.51 (m, 3H), 1.48–1.36 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 172.9, 142.1, 137.8, 128.4 (4C), 128.3 (4C), 127.8, 125.8, 76.5, 57.4, 51.5, 36.9, 35.7, 31.4, 27.8; IR (ATR): 1736 cm^{-1}; HR-MS (ESI): Calcd for $C_{20}H_{26}NO_3$ $[M+H]^+$ 328.1907. Found 328.1906; HPLC [Chiralcel IB, *n*-hexane–2-propanol=99 : 1, 1.0 mL/min, *λ*=254 nm, retention times: (major) 14.2 min (minor) 12.3 min]; $[\alpha]_D^{27}$ −3.3 (*c* 1.00, $CHCl_3$) for 91% ee.

Methyl (*S*)-3-((Benzyloxy)amino)-7-phenylheptanoate (**2s-[OMe]**)

Colorless oil (28.7 mg, 84, 88% ee with cat. **6i**); ^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 7.37–7.24 (m, 7H), 7.20–7.14 (m, 3H), 5.76 (brs, 1H), 4.65 (s, 2H), 3.64 (s, 3H), 3.33–3.24 (m, 1H), 2.63–2.52 (m, 3H), 2.43 (dd, J_1=15.7 Hz, J_2=4.9 Hz, 1H), 1.66–1.51 (m, 3H), 1.45–1.32 (m, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 172.9, 142.2, 137.8, 128.38 (2C), 128.35 (2C), 128.29 (2C), 238.24 (2C), 127.7, 125.6, 76.4, 57.5, 51.5, 37.0, 35.7, 31.7, 31.4, 25.7; IR (ATR): 1734 cm^{-1}; HR-MS (ESI): Calcd for $C_{21}H_{28}NO_3$ $[M+H]^+$ 374.1962. Found 374.1963; HPLC [Chiralcel IB, *n*-hexane–2-propanol=98 : 2, 1.0 mL/min, *λ*=254 nm, retention times: (major) 15.7 min (minor) 11.7 min]; $[\alpha]_D^{27}$ +1.0 (*c* 1.03 $CHCl_3$) for 88% ee.

Methyl (*S*)-3-((Benzyloxy)amino)-4-phenylbutanoate (**2t-[OMe]**)

Colorless oil (23.9 mg, 80, 68% ee with cat. **6i**); ^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 7.39–7.27 (m, 10H), 5.80 (brs, 1H), 4.69 (s, 2H), 3.64 (s, 3H), 3.62–3.52 (m, 1H), 2.91 (dd, J_1=13.6 Hz, J_2=7.2 Hz, 1H), 2.73 (dd, J_1=13.6 Hz, J_2=6.7 Hz, 1H), 2.58 (dd, J_1=15.8 Hz, J_2=7.7 Hz, 1H), 2.44 (dd, J_1=15.8 Hz, J_2=5.4 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 172.6, 138.0, 137.6, 129.4 (2C), 128.5 (2C), 128.4 (2C), 128.3 (2C), 127.8, 126.5, 76.6, 58.9, 51.6, 38.0, 36.4; IR (ATR): 1734 cm^{-1}; HR-MS (ESI): Calcd for $C_{18}H_{22}NO_3$ $[M+H]^+$ 300.1594. Found 300.1596; $[\alpha]_D^{21}$ −18.3 (*c* 1.13, $CHCl_3$) for 71% ee.

Methyl (*S*)-3-((Benzyloxy)amino)-4-phenylbutanoate (**2t-[*N*Bz, OMe]**)

Colorless oil (18.5 mg, 92, 71% ee with cat. **6i**); ^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 7.45–7.03 (m, 15H), 5.18–4.43 (m, 3H), 3.67 (s, 3H), 3.20–3.07 (m, 1H), 2.90 (dd, J_1=15.7 Hz, J_2=8.7 Hz, 1H), 2.96–2.73 (m, 1H), 2.67–2.50 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 171.5, 171.4, 137.2, 134.8 (2C), 130.4, 129.6 (2C), 129.4 (2C), 128.7, 128.5 (2C), 128.4 (2C), 127.9 (2C), 127.7 (2C), 126.8, 77.6, 59.7, 51.8, 38.6, 36.6; IR (ATR): 3029, 1736, 1658 cm^{-1}; HR-MS (ESI): Calcd for $C_{25}H_{26}NO_4$ $[M+H]^+$ 404.1856. Found 404.1855; HPLC [Chiralcel IB, *n*-hexane–2-propanol=98 : 2, 1.0 mL/min, *λ*=254 nm, retention times: (major) 15.8 min (minor) 11.4 min]; $[\alpha]_D^{21}$ −25.0 (*c* 0.98, $CHCl_3$) for 71% ee.

Methyl (*S*)-3-(2,2-Dibenzylhydrazinyl)butanoate (**7-[OMe]**)

To a stirred suspension of *α*,*β*-unsaturated carboxylic acid **1b** (8.7 mg, 0.1 mmol), boronic acid catalyst **6i** (4.4 mg, 0.01 mmol), and activated MS 4 Å (50 mg) in CCl_4 (0.25 mL) was added 1,1-diphenylhydrazine (21.6 mg, 0.1 mmol) in CCl_4 (0.25 mL) at room temperature. The reaction mixture was stirred at the room temperature for 24 h. The reaction mixture was directly purified by flash chromatography on silica gel (*n*-hexane–ethyl acetate=4 : 1 to ethyl acetate–methanol=7 : 3) to afford crude as a colorless oil. To the solution of the crude in toluene/methanol (0.75 mL/0.25 mL) at 0°C, was added $TMSCHN_2$ in Et_2O (0.25 mL, 2.0 M, 0.5 mmol). The reaction mixture was stirred at 0°C for 30 min, before being quenched with AcOH until yellow solution changed to be colorless. The reaction mixture was purified by flash chromatography on silica gel (*n*-hexane–ethyl acetate=10 : 1 to 7 : 1) to afford a colorless oil (28.4 mg, 91, 87% ee with cat. **6i**); ^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 7.37–7.22 (m, 10H), 3.70 (d, *J*=13.0 Hz, 2H), 3.65 (d, *J*=13.0 Hz, 2H), 3.64 (s, 3H), 3.30–3.21 (m, 1H), 2.60 (brs, 1H), 2.51 (dd, J_1=15.4 Hz, J_2=6.1 Hz, 1H), 2.05 (dd, J_1=15.4 Hz, J_2=6.7 Hz, 1H), 0.95 (d, *J*=6.4 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 173.2, 137.8 (2C), 129.6 (4C), 128.1 (4C), 127.0 (2C), 60.3 (2C), 51.3, 49.3, 40.3, 19.2; IR (ATR): 2927, 1735 cm^{-1}; HR-MS (ESI): Calcd for $C_{19}H_{25}N_2O_2$ $[M+H]^+$ 313.1911. Found 313.1915; HPLC [Chiralcel OD-H, *n*-hexane–2-propanol=99 : 1, 1.0 mL/min, *λ*=254 nm, retention times: (major) 9.6 min (minor) 7.9 min]; $[\alpha]_D^{20}$ −4.9 (*c* 1.01 $CHCl_3$) for 87% ee.

Benzyl (*S*)-2-(4-Methoxy-4-oxobutan-2-yl)hydrazine-1-carboxylate (**8-[OMe]**)

To a stirred suspension of *α*,*β*-unsaturated carboxylic acid **1b** (86 mg, 1.0 mmol), boronic acid catalyst **6i** (89 mg, 0.2 mmol), and activated MS 4 Å (500 mg) in CCl_4 (2.5 mL) was added benzyl carbamate (167 mg, 0.1 mmol) in CCl_4 (2.5 mL) at room temperature. The reaction mixture was stirred at the room temperature for 24 h. The reaction mixture was purified by flash chromatography on silica gel (*n*-hexane–ethyl acetate=4 : 1 to ethyl acetate–methanol=7 : 3) to afford crude **2** as a colorless oil. To the solution of the crude **2** in toluene/methanol (7.5/2.5 mL) at 0°C, was added $TMSCHN_2$ in Et_2O (2.5 mL, 2.0 M, 5.0 mmol, 5.0 equiv.). The reaction mixture was stirred at 0°C for 30 min, before being quenched with AcOH until yellow solution changed to be colorless. The reaction mixture was purified by flash chromatography on silica gel (*n*-hexane–ethyl acetate=4 : 1 to 2 : 1) to afford a colorless oil (200 mg, 75, 86% ee with cat. **6i**); ^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 7.41–7.30 (m, 5H), 6.29 (brs, 1H), 5.14 (s, 2H), 4.30 (brs, 1H), 3.66 (s, 3H), 3.53–3.43 (m, 1H), 2.47 (dd, J_1=15.4 Hz, J_2=6.7 Hz, 1H), 2.34 (dd, J_1=15.4 Hz, J_2=6.1 Hz, 1H), 1.11 (d, *J*=6.4 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 172.4, 157.3, 135.9, 128.6 (2C), 128.3, 128.2 (2C),

67.2, 52.4, 51.6, 39.5, 18.5; IR (ATR): 3304, 1726, 1261 cm^{-1}; HR-MS (ESI): Calcd for $C_{13}H_{19}N_2O_4$ $[M+H]^+$ 267.1339. Found 267.1339; HPLC [Chiralcel IC, *n*-hexane–2-propanol=90 : 10, 1.0 mL/min, λ=254 nm, retention times: (major) 30.6 min (minor) 27.4 min]; $[\alpha]_D^{22}$−7.3 (*c* 0.99 $CHCl_3$) for 86% ee. **8-[OMe]** was converted to the corresponding known compound **S-8** and its absolute configuration was determined to be *S* (Chart S2 in the Supplementary Materials).

(*E*)-Tetradec-2-enoic Acid (**9**)

To a stirred suspension of the dodecanal (370 mg, 2.0 mmol) and malonic acid (210 mg, 2.0 mmol) in pyridine (0.5 mL), was added piperidine (20 μL) at room temperature. The mixture was heated at 90°C for 3 h. After being cooled to 0°C, the reaction mixture was neutralized with aqueous 2 N HCl solution (pH=*ca.* 1), and extracted with ethyl acetate. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (*n*-hexane–ethyl acetate=10 : 1 to 4 : 1) to afford **9** as a colorless solid (402 mg, 89, 95% α,β-isomer; >99% *E*-isomer), which was further purified by recrystallization from ethyl acetate/*n*-hexane at 0°C. mp 36.5–36.8°C (ethyl acetate–*n*-hexane); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.86 (br s, 1H), 7.09 (dd, J_1=15.7 Hz, J_2=7.0 Hz, 1H), 5.82 (dd, *J*=15.7 Hz, 1H), 2.23 (q, *J*=7.0 Hz, 2H), 1.51–1.42 (m, 2H), 1.36–1.22 (m, 16H), 0.88 (t, *J*=6.7 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 172.0, 152.6, 120.5, 32.3, 31.9, 29.61, 29.59, 29.50, 29.4, 29.3, 29.1, 27.8, 22.7, 14.1; IR (ATR): 2915, 1694 cm^{-1}; HR-MS (ESI): Calcd for $C_{14}H_{25}O_2$ $[M-H]^+$ 225.1860. Found 225.1859.

(*S*)-3-Aminotetradecanoic Acid (**10**)

To a stirred suspension of α,β-unsaturated carboxylic acid **9** (22.7 mg, 0.1 mmol), boronic acid catalyst **1i** (4.4 mg, 0.01 mmol), and activated MS 4 Å (50 mg) in CCl_4 (0.25 mL) was added *O*-benzylhydroxylamine (12.4 mg, 0.1 mmol) in CCl_4 (0.25 mL) at room temperature. The reaction mixture was stirred at the room temperature for 24 h. The reaction mixture was directly purified by flash chromatography on silica gel (*n*-hexane–ethyl acetate=4 : 1 to ethyl acetate–methanol=7 : 3) to afford crude adduct (37.9 mg) as a colorless oil. To this crude solution in methanol (5.0 mL) was added 10% Pd/C (30 mg), and then the mixture was subjected to an atmosphere of hydrogen gas (300 kPa) for 24 h. The catalyst was filtered off and the solvent was evaporated to give the crude aminoacid **10**, which was purified by column chromatography on silica gel (ethyl acetate only to $CHCl_3$–MeOH=6 : 4) and (NH; ethyl acetate only to $CHCl_3$–MeOH=8 : 2) to afford **10** (17.2 mg, 71%, in 2 steps) as a colorless solid; mp 188.0–189.6°C (methanol : H_2O); ^{1}H-NMR (400 MHz, CD_3OD) δ: 3.25–3.18 (m, 1H), 2.39 (dd, J_1=16.8 Hz, J_2=3.5 Hz, 1H), 2.18 (dd, J_1=16.8 Hz, J_2=9.3 Hz, 1H), 1.55–1.48 (m, 2H), 1.36–1.14 (m, 18H), 0.80 (t, *J*=6.7 Hz, 3H), one O–H and two N–H protons were not observed; ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 177.9, 50.9, 39.2, 34.1, 33.0, 30.70, 30.68, 30.59, 30.45, 30.43, 30.42, 26.4, 23.7, 14.4; IR (ATR): 2919, 2850, 1565, 1391 cm^{-1}; HR-MS (ESI): Calcd for $C_{14}H_{30}NO_2$ $[M+H]^+$ 244.2271. Found 244.2273; $[\alpha]_D^{28}$+12.5 (*c* 0.83 CH_3OH) for 90% ee (Lit[32]: $[\alpha]_D^{25}$+16.0 (*c* 0.90, H_2O) for (*S*) enantiomer).

Methyl (*S*)-3-Benzamidotetradecanoate (**10-[*N*Bz, OMe]**)

To a solution of **10** (12.1 mg, 0.05 mmol) in toluene/methanol (0.75 mL/0.25 mL) at 0°C, was added $TMSCHN_2$ in Et_2O (125 μL, 0.25 mmol). The reaction mixture was stirred at 0°C for 30 min, before being quenched with AcOH until yellow solution changed to be colorless. The reaction mixture was concentrated *in vacuo*. The crude ester (15 mg) was used for the next step without further purification. To a stirred solution of crude ester (15 mg) in THF (1.0 mL) were added benzoyl chloride (23 μL, 0.20 mmol) and pyridine (12 μL, 0.15 mmol) at 0°C. After being stirred at room temperature for 3 h, the reaction mixture was quenched with aqueous 1 N HCl solution (pH=*ca.* 1), and extracted with ethyl acetate. The organic layer was washed with saturated aqueous $NaHCO_3$ solution (pH=9), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (*n*-hexane–ethyl acetate=10 : 1 to 2 : 1) to afford a white solid (16.0 mg, 89%, in 2 steps); mp 95.3–95.5°C (ethyl acetate–*n*-hexane); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.79 (d, *J*=7.2 Hz, 2H), 7.50 (dd, J_1=J_2=7.2 Hz, 1H), 7.44 (dd, J_1=J_2=7.2 Hz, 2H), 6.90 (br d, *J*=9.3 Hz, 1H), 4.49–4.38 (m, 1H), 3.71 (s, 3H), 2.70 (dd, J_1=15.9 Hz, J_2=4.8 Hz, 1H), 2.63 (dd, J_1=15.9 Hz, J_2=4.6 Hz, 1H), 1.73–1.53 (m, 2H), 1.43–1.21 (m, 18H), 0.87 (t, *J*=6.7 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 172.7, 166.7, 134.6, 131.4, 128.5 (2C), 126.9 (2C), 51.7, 46.3, 38.0, 34.2, 31.9, 29.60, 29.59, 29.53, 29.47, 29.36, 29.31, 26.3, 22.7, 14.1; IR (ATR): 3298, 2921, 1736, 1639 cm^{-1}; HR-MS (ESI): Calcd for $C_{22}H_{36}NO_3$ $[M+H]^+$ 362.2690. Found 362.2690; HPLC [Chiralcel IA, *n*-hexane–2-propanol=95 : 5, 1.0 mL/min, λ=254 nm, retention times: (major) 10.3 min (minor) 12.3 min]; $[\alpha]_D^{20}$−31.5 (*c* 1.02 $CHCl_3$) for 90% ee.

(*S*)-1-(Benzyloxy)-5-phenethylimidazolidi*n*-2-one (**11**)

To a stirred suspension of α,β-unsaturated carboxylic acid **1a** (17.7 mg, 0.1 mmol), boronic acid catalyst **6i** (4.6 mg, 0.01 mmol), and activated MS 4 Å (50 mg) in CCl_4 (0.25 mL) was added a solution of *O*-benzylhydroxylamine (12.4 mg, 0.1 mmol) in CCl_4 (0.25 mL) at room temperature. The reaction mixture was stirred at the room temperature for 24 h, before the successive addition of *O*-diphenylphosphoryl azide (32 μL, 0.15 mmol) and *N*,*N*-diisopropylethylamine (25 μL, 0.15 mmol) at room temperature. The reaction mixture was heated at 50°C for 3 h. Then, the reaction mixture was directly purified by flash chromatography on silica gel (*n*-hexane–ethyl acetate=4 : 1 to ethyl acetate only) to afford the product **11** as a colorless oil (20.2 mg, 68, 89% ee). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.44 (dd, J_1=7.5 Hz, J_2=1.4 Hz, 2H), 7.37–7.24 (m, 5H), 7.23–7.17 (m, 1H), 7.11 (d, *J*=7.2 Hz, 2H), 5.60 (s, 1H), 5.10 (d, *J*=10.7 Hz, 1H), 4.92 (d, *J*=10.7 Hz, 1H), 3.61–3.50 (m, 1H), 3.32 (dd, J_1=J_2=8.1 Hz, 1H), 2.98 (dd, J_1=J_2=9.0 Hz, 1H), 2.58 (t, *J*=8.1 Hz, 2H), 2.10–1.99 (m, 1H), 1.77–1.64 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 164.4, 140.8, 136.0, 129.5 (2C), 128.5 (2C), 128.43, 128.35 (2C), 128.2 (2C), 126.1, 78.6, 60.5, 42.2, 32.9, 31.3; IR (ATR): 1735 cm^{-1}; HR-MS (ESI): Calcd for $C_{18}H_{21}N_2O_2$ $[M+H]^+$ 297.1598. Found 297.1596; HPLC [Chiralcel IB, *n*-hexane–2-propanol=90 : 10, 1.0 mL/min, λ=254 nm, retention times: (major) 13.9 min (minor) 16.3 min]; $[\alpha]_D^{25}$+69.4 (*c* 0.98, $CHCl_3$) for 89% ee.

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interest.

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