Enantioselective and α-Regioselective Allylic Amination of Morita-Baylis-Hillman Acetates with Simple Aromatic Amines Catalyzed by Planarly Chiral Ligand/Palladium Catalyst

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An asymmetric allylic amination of Morita-Baylis-Hillman acetates with simple aromatic amines catalyzed by planarly chiral ligand/palladium-catalyst was developed in good yield with excellent α -regioselectivity (α/γ up to 30 : 1) and moderate enantioselectivity (up to 70% *ee*).

Keywords asymmetric allylic amination, Morita-Baylis-Hillman adducts, aromatic amines, palladium catalysis, diphosphine ligands

Introduction

The Morita-Baylis-Hillman (MBH) reactions have been proved to be one of the most successful methods for C-C bond forming reaction.^[1] Since three functionalized groups, the hydroxyl group, the double bond, and the carbonyl (cyano) group, lie closely in one molecule, the MBH adducts provide an opportunity for developing methodology in organic synthesis by ma-nipulating the functional groups.^[1b] Among the trans-formations of the MBH adduct,^[2] the palladium-catalyzed allylic substitution reaction has attracted considerable attentions.^[3] This type of reaction could proceed in two regioselective ways to give α - and γ -products because of the unsymmetrical allylic unit in the MBH adduct molecule (Scheme 1). Regioselective introduction of nucleophile to either the α - or γ -position of the allylic moiety seems to be an urgent requirement and is becoming a power tool in synthetic organic chemistry. For the α -product, the enantioselective control is another challenge problem. Accordingly, simultaneously regioselective and enantioselective allylic substitution reaction of MBH adduct has been becoming an attractive and challenge subject to the chemist in organic synthesis. Although asymmetric allylic amination of MBH adducts with nitrogen nucleophiles such as cyclic imides or aliphatic amines catalyzed by organocatalysts has been reported,^[4] the enantioselective amination using less active simple aromatic amines was still unde-veloped. Trost and coworkers^[5] reported palladium

catalyzed α -regioselective and enantioselective allylic substitution with *O*-nucleophile such as phenols and alcohols. However, there were only two examples of MBH adducts in Pd-catalyzed allylic amination.^[6] In 2002, Iqbal and co-workers^[7] firstly reported the palladium-catalyzed allylic amination of MBH acetates, but with the moderate regioselectivity ($\alpha/\gamma=3$: 1 to 6 : 1) and no enantioselectivity. Hamada and coworkers^[8] realized the asymmetric allylic amination reactions of MBH adducts, but evaded a problem of the regioselectivity due to the symmetry of the substrates used. Herein, we reported α -regioselective and enantioselective allylic amination of MBH acetates with the simple aromatic amines catalyzed by planarly chiral ligand/palladium catalysts.

Scheme 1 Allylic substitution of Morita-Baylis-Hillman adduct



Results and Discussion

Initially, we selected the allylic amination of MBH acetate 1a with aniline 2a as the model reaction. Using Pd₂(dba)₃ as a catalyst, various diphosphine ligands were tested. As shown in Table 1, ligands L1—L4 were

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mmol), K₂CO₃ (0.3 mmol), in DCM (2 mL) at 25 °C in nitrogen atmosphere. Pd₂(dba)₃ (5 mol%) and ligand (12.5 mol%) were used. ^b Determined by ¹H NMR of the mixture of crude products. ^c Determined by chiral HPLC.

not quite effective for this reaction and afforded the poor conversion (Table 1, Entries 1-4) probably because of the short distance between the two phosphine units in the ligands. Switching to L5-L7, which have longer distance between the two phosphine units, full

conversion was offered with poor α -regioselectivity (Entries 5-7). The ligand L8 with planar chirality showed the best α -regioselectivity ($\alpha : \gamma = 20 : 1$) and enantioselectivity (63% ee) (Entry 8). Ligand L9 having more steric hindrance was then used to increase the enantioselectivity (Entry 9). However, the γ -product 4a was obtained as the major product in 26% conversion, and for α -product **3a** only with 36% *ee*.

Subsequently, several metallic catalysts, bases and solvents were examined (Table 2). In contrast with other Pd-catalysts, $Pd_2(dba)_3$ could give the better α -regioselectivity and enantioselectivity (Entries 4 vs. 1-3). KOH was better than K_2CO_3 with excellent α -regioselectivity (α : γ = 30 : 1) and better enantioselectivity (66% ee) (Entry 8). Taking account of both regioselectivity and enantioselectivity, DCM was the best choice.

 Table 2
 Optimization of other reaction conditions^a



Entry	Pd	Base	Sol.	t/h C	onv. ^b /%	3a : 4 a ^b	<i>ee^c/%</i>
1	Pd ₂ (dba) ₃ CHCl ₃	K ₂ CO ₃	DCM	20	100	9.3:1	60
2	Pd(acac) ₂	K_2CO_3	DCM	20	100	5:1	55
3	$[Pd(C_3H_5)Cl]_2$	K ₂ CO ₃	DCM	16	100	2.7:1	39
4	Pd ₂ (dba) ₃	K ₂ CO ₃	DCM	24	100	20:1	63
5	Pd ₂ (dba) ₃	KOtBu	DCM	24	100	13.8:1	62
6	Pd ₂ (dba) ₃	KOAc	DCM	24	100	1:2.8	3.3
7	Pd ₂ (dba) ₃	KHCO ₃	DCM	24	97	24.3:1	65
8	Pd ₂ (dba) ₃	КОН	DCM	24	100	30:1	66
9	Pd ₂ (dba) ₃	DABCO	DCM	24	97	1.5:1	4
10	Pd ₂ (dba) ₃	NEt ₃	DCM	24	100	10:1	60
11	Pd ₂ (dba) ₃	КОН	THF	24	100	32.6:1	62
12	Pd ₂ (dba) ₃	КОН	toluene	24	97	11.4:1	49
13	Pd ₂ (dba) ₃	КОН	MeOH	24	low	_	_
14	Pd ₂ (dba) ₃	КОН	acetone	24	100	_	_
15	$Pd_2(dba)_3$	КОН	EA	24	100	13.8:1	49

^a All reactions were performed with **1a** (0.1 mmol), **2a** (0.3 mmol), base (0.3 mmol), in solvents (2 mL) at 25 °C in nitrogen atmosphere. Pd catalyst (10 mol%) and ligand (12.5 mol%) were used. ^b Determined by ¹H NMR of the mixture of crude products. ^c Determined by chiral HPLC.

With the optimized catalyst and reaction conditions in hand, we then investigated the substrate scope of allylic amination. Various MBH acetates were employed in the reaction (Table 3). When R^2 was ethyl, the best **Table 3** Substrate scope of the allylic amination^a

	OAc O R ¹	`OR ² + R ³ −NH ₂ 2	Pd ₂ (dba) ₃ 5 mol% L8 12.5 mol% KOH, DCM, r.t.	$R^{3}-\underline{N}H O$ R^{1} OR^{2} +	R^{1} O OR^{2} $N-R^{3}$ H	
Entry	1 , R ¹	R^2	2 , R ³	$3:4^{b}$	3 , Yield ^{<i>c</i>} /%	<i>ee^d/%</i>
1	1a, phenyl	Me	2a, phenyl	30:1	3a , 88	66
2	1b, phenyl	Et	2a, phenyl	25:1	3b , 90	70
3	1c, 3-Br-phenyl	Et	2a, phenyl	1:1	3c , 48	60
4	1d, 4-Br-phenyl	Et	2a, phenyl	13:1	3d , 88	64
5	1e, 4-Me-phenyl	Et	2a, phenyl	6:1	3e , 75	37
6	1f, 4-Cl-phenyl	Et	2a, phenyl	27:1	3f , 91	60
7	1g , naphthyl	Et	2a, phenyl	20:1	3g , 89	61
8	1b, phenyl	Et	2b, 3-Cl-phenyl	15:1	3h , 88	66
9	1b, phenyl	Et	2c , 3,5-Cl ₂ -phenyl	20:1	3i , 85	63
10	1b, phenyl	Et	2d, 4-Cl-phenyl	26:1	3j , 86	54
11	1b, phenyl	Et	2e , 3- CF ₃ -phenyl	21:1	3k , 89	57
12	1b, phenyl	Et	2f, 2-Me-phenyl	20:1	31 , 87	62
13	1b, phenyl	Et	2g , naphthyl	24:1	3m , 90	41

^{*a*} All reactions were performed with **1** (0.1 mmol), **2** (0.3 mmol), KOH (0.3 mmol), in DCM (2 mL) at 25 $^{\circ}$ C in nitrogen atmosphere. Pd₂(dba)₃ catalyst (5 mol%) and ligand **L8** (12.5 mol%) were used. ^{*b*} Determined by ¹H NMR of the mixture of crude products. ^{*c*} isolated yield. ^{*d*} Determined by chiral HPLC.

enantioselectivity was observed (Entry 2). The regioselectivity disappeared completely using the MBH acetate **1c** derived from 3-Br-benzaldehyde (Entry 3). For the MBH acetate **1e**, the enantioselectivity decreased to 37% (Entry 5). Various aniline derivatives tolerated this reaction and afforded the excellent α -regioselectivities and moderate enantioselectivities. When R³ was naphthyl, the enantioselectivity dropped slightly to 41% (Entry 13).

Compared with the known compound,^[9] the configuration of a newly created chiral center of **3b** was deduced as *S*. The transition state of the allylic amination reaction was proposed in Figure 1. After removing OAc, the MBH acetate **3** forms π -allylpalladium complex with Pd catalyst and the ligand. The palladium could also coordinate with the ethyl ester of MBH adduct to preferentially adopt the anti- π -allyl geometry and the bulky phanephos ligand approached to the less steric hindrance γ -position easily. Thus, the steric hindrance in α -position appeared to be less, aniline attacks



Figure 1 Proposed transition state.

the allylic intermediate from α -position and *Si*-face leading to the *S* enantiomer of the product.

Conclusions

In conclusion, the Morita-Baylis-Hillman acetates have been successfully employed in a planarly chiral ligand (L8)/palladium-catalyzed asymmetric allylic amination reaction with a variety of simple amines, aniline derivatives, in good yields with excellent α -regioselectivity and moderate enantioselectivity. This reaction provides an efficient method access to optically β -arylamino acid esters^[1a,1d,2b,10] that could be readily transformed into corresponding β -lactam derivatives.

Experimental

General methods

The ¹H NMR and ¹³C NMR spectra were recorded on Bruker-AV 300 spectrometer and chemical shift reported in CDCl₃ with tetramethylsilane as an internal standard. IR spectra were recorded on a Bruker tensor 27 infrared spectrometer. HRMS spectra were recorded on GCT-Mass Micromass spectrometer. All reactions were carried out in oven dried flasks. Common reagents were purchased from commercial sources and were used without further purification. The Morita-Baylis-Hillman acetates were prepared according to literature methods.^[11] All reactions were performed under nitrogen atmosphere.

Typical experimental procedures for allylic amination reaction

A solution of 5 mol% Pd₂(dba)₃ catalyst and 12.5 mol% ligand **L8** in 1 mL DCM was stirred at 25 °C for 0.5 h. Followed by a solution of MBH acetates **1a** (0.1 mmol) and aniline **2a** (0.3 mmol) in 1 mL DCM, 0.3 mmol KOH (1 mol/L) were added. The reaction mixture was stirred at 25 °C and monitored by TLC until the starting material disappeared. Then the reaction mixture was extracted by ethyl acetate. The organic phase was dried by Na₂SO₄, filtered and evaporated to afford a mixture of the crude products. The ratio of α - to γ -isomer was determined by ¹H NMR of the mixture at δ 5.41 and δ 7.91. The crude product was purified by flash column chromatography over silica gel (eluent: PE : EA=30 : 1) to give **3a** as a yellow oil (24 mg, 88%).

(S)-Methyl 2-[(phenylamino)(phenyl)methyl]acrylate (3a)^[12] Compound 3a was isolated as a yellow oil, $[\alpha]_{25}^{D}$ +71.3 (c 0.48, CH₂Cl₂), 66% ee; ¹H NMR (CDCl₃, 300 MHz) δ : 3.69 (s, 3H), 4.15 (s, 1H), 5.41 (s, 1H), 5.96 (s, 1H), 6.38 (s, 1H), 6.55—6.58 (m, 2H), 6.69—6.74 (m, 1H), 7.13—7.18 (m, 1H), 7.27—7.38 (m, 5H); ¹³C NMR (CDCl₃, 75MHz) δ : 52.0, 59.0, 113.5, 117.9, 126.2, 127.6, 127.9, 128.8, 129.2, 140.0, 140.6, 146.7, 166.7. The enantiomeric ratio was determined by HPLC on Chiralpak AS column (10/90, 2-propanol/hexane, 0.3 mL/min), t_{major} =9.7 min, t_{minor} =11.4 min.

(S)-Ethyl 2-(phenyl(phenylamino)methyl)acrylate (3b)^[12] Compound 3b was isolated as a yellow oil, $[\alpha]_{25}^{D}$ +81.8 (*c* 0.50, CH₂Cl₂), 70% *ee*; ¹H NMR (CDCl₃, 300 MHz) δ : 1.20 (t, J = 7.2 Hz, 3H), 4.08—4.19 (m, 3H), 5.41 (s, 1H), 5.93 (s, 1H), 6.38 (s, 1H), 6.57 (d, J=7.8 Hz, 2H), 6.71 (t, J=7.2 Hz, 1H), 7.15 (t, J=7.8 Hz, 2H), 7.27—7.33 (m, 5H); ¹³C NMR (CDCl₃, 75MHz) δ : 14.1, 59.0, 60.8, 113.5, 117.9, 126.0, 127.6, 127.8, 128.8, 129.2, 140.3, 140.8, 146.8, 166.2. The enantiomeric ratio was determined by HPLC on Chiralpak AS column (10/90, 2-propanol/hexane, 0.3 mL/min), $t_{major}=9.4$ min, $t_{minor}=11.6$ min.

(S)-Ethyl 2-((3-bromophenyl)(phenylamino)methyl)acrylate (3c) Compound 3c was isolated as a yellow oil, $[\alpha]_{25}^{D}$ +47.1 (c 0.24, CH₂Cl₂), 60% ee; ¹H NMR (CDCl₃, 300 MHz) δ : 1.23 (t, J=7.2 Hz, 3H), 4.14–4.19 (m, 3H), 5.37 (d, J=5.4 Hz, 1H), 5.92 (s, 1H), 6.41 (s, 1H), 6.57 (d, J=7.8 Hz, 2H), 6.73 (t, J=7.5 Hz, 1H), 7.13–7.17 (m, 3H), 7.19 (d, J=3.3 Hz, 1H), 7.23 (d, J=5.4 Hz, 1H), 7.30 (s, 1H); ¹³C NMR (CDCl₃, 75MHz) δ: 14.1, 58.6, 61.0, 113.5, 118.2, 122.8, 126.2, 126.7, 129.3, 130.3, 130.5, 130.9, 139.9, 143.1, 146.5, 165.9; IR (KBr) v_{max}: 3475, 2981, 1699, 1509 cm⁻¹; ESI-HRMS *m/z* calcd for C₁₈H₁₉BrNO₂ 360.0594 (M^+) , found 360.0588. The enantiometric ratio was determined by HPLC on Chiralpak AS column (5/95, 2-propanol/hexane, 0.6 mL/min), t_{major}=10.5 min, $t_{\rm minor} = 12.4$ min.

(S)-Ethyl 2-((4-bromophenyl)(phenylamino)methyl)acrylate (3d) Compound 3d was isolated as a yellow oil, $[\alpha]_{25}^{D}$ +57.6 (*c* 0.50, CH₂Cl₂), 64% *ee*; ¹H NMR (CDCl₃, 300 MHz) δ : 1.22 (t, *J*=7.2 Hz, 3H), 4.11—4.19 (m, 3H), 5.36 (d, *J*=5.4 Hz, 1H), 5.91 (s, 1H), 6.39 (s, 1H), 6.56 (d, *J*=8.1 Hz, 2H), 6.73 (t, *J*= 7.2 Hz, 1H), 7.16 (t, *J*=7.8 Hz, 2H), 7.25 (d, *J*=7.2 Hz, 2H), 7.46 (d, *J*=8.4 Hz, 2H); ¹³C NMR (CDCl₃, 75 MHz) δ : 14.1, 58.6, 61.0, 113.6, 118.2, 121.7, 126.5, 129.3, 131.9, 139.9, 140.0, 146.5, 166.0; IR (KBr) ν_{max} : 3391, 2981, 1711, 1502 cm⁻¹; ESI-HRMS *m/z* calcd for C₁₈H₁₉BrNO₂ 360.0594 (M⁺), found 360.0588. The enantiomeric ratio was determined by HPLC on Chiralpak AS column (5/95, 2-propanol/hexane, 0.6 mL/min), *t*_{major}=11.2 min, *t*_{minor}=12.8 min.

(S)-Ethyl 2-((phenylamino)(*p*-tolyl)methyl)acrylate (3e) Compound 3e was isolated as a yellow oil, $[\alpha]_{25}^{D}$ +76.8 (*c* 0.42, CH₂Cl₂), 37% *ee*; ¹H NMR (CDCl₃, 300 MHz) δ : 1.13 (t, *J*=7.2 Hz, 3H), 2.25 (s, 3H), 4.00–4.11 (m, 3H), 5.29 (s, 1H), 5.85 (s, 1H), 6.28 (s, 1H), 6.48 (d, *J*=8.1 Hz, 2H), 6.62 (t, *J*=7.5 Hz, 1H), 7.04–7.09 (m, 4H), 7.18 (d, *J*=8.1 Hz, 2H); ¹³C NMR (CDCl₃, 75 MHz) δ : 14.1, 21.2, 58.7, 60.8, 113.4, 117.8, 125.7, 127.5, 129.2, 129.4, 137.5, 137.8, 140.4, 146.8, 166.3; IR (KBr) ν_{max} : 3437, 2982, 1713, 1504 cm⁻¹; ESI-HRMS *m/z* calcd for C₁₉H₂₂NO₂ 296.1645 (M⁺), found 296.1642. The enantiomeric ratio was determined by HPLC on Chiralpak AS column (5/95, 2-propanol/hexane, 0.6 mL/min), t_{major} =8.8 min, t_{minor} =9.9 min.

(S)-Ethyl 2-((4-chlorophenyl)(phenylamino)methyl)acrylate (3f) Compound 3f was isolated as a yellow oil, $[\alpha]_{25}^{D}$ +71.6 (*c* 0.50, CH₂Cl₂), 54% *ee*; ¹H NMR (CDCl₃, 300 MHz) δ : 1.22 (t, *J*=7.2 Hz, 3H), 4.11—4.19 (m, 3H), 5.38 (s, 1H), 5.92 (s, 1H), 6.39 (s, 1H), 6.57 (d, *J*=7.8 Hz, 2H), 6.73 (t, *J*=7.2 Hz, 1H), 7.16 (t, *J*=7.5 Hz, 2H), 7.31 (s, 4H); ¹³C NMR (CDCl₃, 75 MHz) δ : 14.1, 58.5, 61.0, 113.5, 118.1, 126.4, 128.9, 129.2, 133.5, 139.3, 140.1, 146.5, 166.0; IR (KBr) ν_{max} : 3402, 2961, 1711, 1501 cm⁻¹; ESI-HRMS *m/z* calcd for C₁₈H₁₉CINO₂ 316.1098 (M⁺), found 316.1094. The enantiomeric ratio was determined by HPLC on Chiralpak AS column (5/95, 2-propanol/hexane, 0.6 mL/min), t_{major} =11.0 min, t_{minor} =12.5 min.

(S)-Ethyl 2-[(naphthalen-2-yl)(phenylamino)methyl]acrylate (3g) Compound 3g was isolated as a yellow oil, $[\alpha]_{25}^{D}$ +128.8 (c 0.52, CH₂Cl₂), 61% ee; ¹H NMR (CDCl₃, 300 MHz) δ : 1.19 (t, J=7.2 Hz, 3H), 4.09—4.17 (m, 2H), 4.24 (br, 1H), 5.58 (s, 1H), 5.99 (s, 1H), 6.44 (s, 1H), 6.62 (d, J=7.8 Hz, 2H), 6.73 (t, J= 7.5 Hz, 1H), 7.14—7.19 (m, 2H), 7.46—7.48 (m, 3H), 7.79—7.84 (m, 4H); ¹³C NMR (CDCl₃, 75 MHz) δ : 14.1, 59.1, 60.9, 113.5, 118.0, 125.8, 126.1, 126.2, 127.7, 128.1, 128.6, 129.2, 133.0, 133.4, 138.1, 140.4, 146.8, 166.3; IR (KBr) v_{max} : 3407, 2980, 1711, 1502 cm⁻¹; ESI-HRMS *m*/*z* calcd for C₂₂H₂₂NO₂ 332.1645 (M⁺), found 332.1641. The enantiomeric ratio was determined by HPLC on Chiralpak AS column (5/95, 2-propanol/hexane, 0.6 mL/min), $t_{\text{major}} = 12.0$ min, $t_{\text{minor}} = 14.4$ min.

(*S*)-Ethyl 2-[((3-chlorophenyl)amino)(phenyl)methyl]acrylate (3h) Compound 3h was isolated as a yellow oil, $[\alpha]_{25}^{D}$ +86.4 (*c* 0.50, CH₂Cl₂), 66% *ee*; ¹H NMR (CDCl₃, 300 MHz) δ : 1.21 (t, *J*=7.2 Hz, 3H), 4.10—4.27 (m, 3H), 5.37 (d, *J*=5.4 Hz, 1H), 5.89 (s, 1H), 6.40 (s, 1H), 6.42—6.46 (m, 1H), 6.54—6.56 (m, 1H), 6.66—6.69 (m, 1H), 7.05 (t, *J*=8.1 Hz, 1H), 7.29—7.30 (m, 5H); ¹³C NMR (CDCl₃, 75 MHz) δ : 14.4, 59.3, 61.2, 112.0, 113.5, 118.1, 126.4, 127.8, 128.3, 129.2, 130.5, 135.3, 140.3, 140.5, 148.2, 166.4; IR (KBr) v_{max} : 3415, 2990, 1703, 1595 cm⁻¹; ESI-HRMS *m*/*z* calcd for C₁₈H₁₉CINO₂ 316.1099 (M⁺), found 316.1093. The enantiomeric ratio was determined by HPLC on Chiralpak AS column (5/95, 2-propanol/ hexane, 0.6 mL/min), t_{major} =10.6 min, t_{minor} =12.2 min.

(S)-Ethyl 2-[((3,5-dichlorophenyl)amino)(phenyl)methyl]acrylate (3i) Compound 3i was isolated as a yellow oil, $[\alpha]_{25}^{D}$ +76.8 (c 0.60, CH₂Cl₂), 63% ee; ¹H NMR (CDCl₃, 300 MHz) δ : 1.21 (t, J=7.2 Hz, 3H), 4.10—4.21 (m, 2H), 4.37 (d, J=6.0 Hz, 1H), 5.35 (d, J=6.0 Hz, 1H), 5.86 (s, 1H), 6.41 (s, 1H), 6.43 (s, 2H), 6.69 (s, 1H), 7.32—7.36 (m, 5H); ¹³C NMR (CDCl₃, 75 MHz) δ : 14.0, 58.9, 61.0, 111.6, 117.7, 126.3, 127.3, 128.1, 128.9, 135.4, 139.6, 139.7, 148.3, 165.9; IR (KBr) v_{max} : 3414, 2981, 1710, 1591 cm⁻¹; ESI-HRMS *m/z* calcd for C₁₈H₁₈Cl₂NO₂ 350.0709 (M⁺), found 350.0705. The enantiomeric ratio was determined by HPLC on Chiralpak AS column (5/95, 2-propanol/ hexane, 0.6 mL/min), t_{major} =10.1 min, t_{minor} =11.4 min.

(S)-Ethyl 2-[((4-chlorophenyl)amino)(phenyl)methyl]acrylate (3j) Compound 3j was isolated as a yellow oil, $[\alpha]_{25}^{D}$ +80.2 (c 0.46, CH₂Cl₂), 54% ee; ¹H NMR (CDCl₃, 300 MHz) δ : 1.21 (t, J=7.2 Hz, 3H), 4.10—4.20 (m, 3H), 5.34 (s, 1H), 5.88 (s, 1H), 6.38 (s, 1H), 6.49 (d, J=8.7 Hz, 2H), 7.091 (d, J=9.0 Hz, 2H), 7.28—7.34 (m, 5H); ¹³C NMR (CDCl₃, 75 MHz) δ : 14.1, 59.1, 60.9, 114.6, 122.5, 126.0, 127.5, 127.9, 128.5, 128.8, 129.0, 140.1, 140.3, 145.3, 166.1; IR (KBr) v_{max} : 3413, 2982, 1712, 1497 cm⁻¹; ESI-HRMS *m/z* calcd for C₁₈H₁₉ClNO₂ 316.1099 (M⁺), found 316.1093. The enantiomeric ratio was determined by HPLC on Chiralpak AS column (5/95, 2-propanol/hexane, 0.6 mL/min), t_{major} =11.0 min, t_{minor} =12.5 min.

(S)-Ethyl 2-((phenylamino)(3-(trifluoromethyl)phenyl)methyl)acrylate (3k) Compound 3k was isolated as a yellow oil, $[\alpha]_{25}^{D}$ +60.4 (*c* 0.54, CH₂Cl₂), 57% *ee*; ¹H NMR (CDCl₃, 300 MHz) δ : 1.21 (t, *J*=7.2 Hz, 3H), 4.11—4.21 (m, 2H), 4.40 (s, 1H), 5.43 (s, 1H), 5.89 (s, 1H), 6.40 (s, 1H), 6.76 (d, *J*=8.1 Hz, 1H), 6.79 (s, 1H), 6.95 (d, *J*=7.8 Hz, 1H), 7.21—7.36 (m, 6H); ¹³C NMR (CDCl₃, 75MHz) δ : 14.0, 58.9, 61.0, 109.9 (d, *J*=3.9 Hz), 114.3 (d, *J*=3.9 Hz), 116.1, 122.4, 126.1, 127.4, 128.0, 128.8, 129.6, 131.3, 131.7, 140.0 (d, *J*= 10.4 Hz), 146.9, 166.0; IR (KBr) ν_{max} : 3382, 2986, 1704, 1493 cm⁻¹; ESI-HRMS *m/z* calcd for C₁₉H₁₈F₃NO₂ 349.3508 (M⁺), found 349.3507. The enantiomeric ratio was determined by HPLC on Chiralpak AS column (5/95, 2-propanol/hexane, 0.6 mL/min), t_{major} =8.4 min, t_{minor} =9.3 min.

(S)-Ethyl 2-((o-tolylamino)(phenyl)methyl)acrylate (3l) Compound 3l was isolated as a yellow oil, $[\alpha]_{25}^{D}$ +62.0 (c 0.46, CH₂Cl₂), 62% ee; ¹H NMR (CDCl₃, 300 MHz) δ : 1.24 (t, J=7.2 Hz, 3H), 2.18 (s, 3H), 4.08 (br, 1H), 4.11—4.24 (m, 2H), 5.50 (s, 1H), 5.93 (s, 1H), 6.41 (s, 1H), 6.54 (d, J=7.8 Hz, 1H), 6.70 (d, J=7.2 Hz, 1H), 7.08—7.13 (m, 2H), 7.28—7.33 (m, 4H); ¹³C NMR (CDCl₃, 75 MHz) δ : 14.4, 17.9, 59.2, 61.1, 111.3, 117.8, 122.5, 126.2, 127.3, 127.8, 129.1, 130.4, 140.7, 141.2, 145.0, 166.6; IR (KBr) ν_{max} : 3412, 2981, 1712, 1510; ESI-HRMS *m/z* calcd for C₁₉H₂₂NO₂ 296.1645 (M⁺), found 296.1641. The enantiomeric ratio was determined by HPLC on Chiralpak AS column (5/95, 2-propanol/hexane, 0.6 mL/min), t_{major} =7.5 min, t_{minor} =8.0 min.

(S)-Ethyl 2-[((naphthalen-1-yl)amino)(phenyl)methyl]acrylate (3m) Compound 3m was isolated as a yellow oil, $[\alpha]_{25}^{D}$ +26.3 (*c* 0.40, CH₂Cl₂), 41% *ee*; ¹H NMR (CDCl₃, 300 MHz) δ : 3.73 (s, 3H), 4.91—4.92 (d, *J*=3.9 Hz, 1H), 5.62 (d, *J*=4.2 Hz, 1H), 6.00 (s, 1H), 6.40 (s, 1H), 6.51 (d, *J*=7.2 Hz, 1H), 7.23—7.47 (m, 9H), 7.78—7.80 (m, 2H); ¹³C NMR (CDCl₃, 75 MHz) δ : 52.0, 59.1, 106.0, 118.0, 119.9, 123.4, 124.9, 125.8, 126.2, 126.5, 127.7, 128.0, 128.8, 128.9, 134.3, 139.6, 140.6, 141.6, 166.8; IR (KBr) v_{max} : 3419, 2980, 1711, 1580 cm⁻¹; ESI-HRMS *m/z* calcd for C₂₁H₂₀NO₂ 318.1408 (M⁺), found 318.1405. The enantiomeric ratio was determined by HPLC on Chiralpak AS column (5/95, 2-propanol/hexane, 0.6 mL/min), t_{major} =8.9 min, t_{minor} =10.3 min.

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