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Highly enantioselective transfer hydrogenation catalyzed by diasteromeric mixtures of axially chiral (a*R*,*S*)- and (a*S*,*S*)-Biscarbolines

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ABSTRACT

The mixtures of axially chiral (a*R*,*S*)- and (a*S*,*S*)-biscarboline alcohols were firstly used as catalysts in enantioselective 1,2- and 1,4-transfer hydrogenations of ketimines and β-enamino esters, respectively. This mixed axially chiral catalysts exhibited excellent enantioselectivity (up to 98%ee) in the transfer hydrogenations under mild reaction conditions.

1. Introduction

Hundreds of chiral catalysts have been developed [1–4], for example, axial acids (**1**) [5], phosphoric acids derivatives of BINOL and BINAP (**2**—**3**) [6], spiral ligands (**4**) [7], including P-containing piperazine (**5**) [8], Fe-, Ru-, and other ion-containing ligands (**6**—**7**), and have been widely applied for various asymmetric reactions [9]. The combined axial structures and active *N*—O functionality (**8**-**10**) have attracted many researchers' attentions (Fig. 1) [10]. Until now, all of the chiral catalysts reported and used in various asymmetric reactions are optically pure [11], such as the catalysts used in enantioselective transfer hydrogenations of ketimines with $HSiCl_3$ to produce chiral amines [12]. Among different reactions catalyzed by various chiral catalysts, an important asymmetric reduction led to the synthesis of chiral calcimimetic NPS R-568, an effective drug against hyperparathyroidism [13a,b]. Indeed, bioactive natural products with different absolute configurations may be synthetic targets [13c]. Some transfer hydrogenations of β-enamino esters with $HSiCl_3$ or ammonia borane reported recently [14a] exhibited very good enantioselectivities catalyzed by chiral optically pure ligands [14]. No doubt, to use optically pure chiral catalysts is based on a common sense that different stereogenic catalysts can control different transition state (TS) structure formations. These TS structures may have different TS barriers and form products with various absolute configurations. Few reports have shown that mixtures of axially chiral compounds can promote asymmetric reactions with high enantioselectivities until now.

Theoretically, if (1) two axially diastereomeric catalysts have high enough transition state (TS) barriers, which may guarantee the reaction to have high enantioselectivity, in catalytic procedures, and (2) both diastereomeric ligands promote the reactions to afford the same absolute configuration products. In this case, the mixtures of both diastereomeric catalysts may catalyze the asymmetric reactions in good enantioselectivities. Indeed, it is not very easy to obtain the optical pure chiral catalysts when chiral ligands have close polarities. Thus, to use mixtures of the diastereogenic catalysts is easy and economical in asymmetric reactions under this situation. It brings the convenience for some researchers to use mixtures of the diastereogenic catalysts. However, this is a challenge to find such mixtures of the diastereogenic catalysts in experiments.

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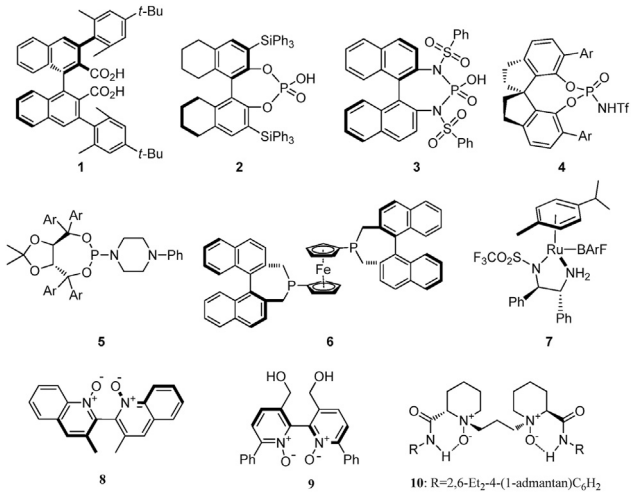


Fig. 1. Some typical previous effective catalysts.

2. Results and discussion

The asymmetric transfer hydrogenations have successfully attracted many researchers' attentions [15], including their uses in drug syntheses [13]. In our series of study of biscarboline ligands derived from L-tryptophane, we synthesized some derivatives and successfully achieved high enantioselectivities in reactions using these derivatives as chiral catalysts [16]. In our recent report, optically pure chiral catalyst (a*R*,*S*)-**11** exhibited excellent enantioselectivity in the 1,2- and 1,4-transfer hydrogenations of ketimines and β-enamino esters, respectively [17]. In the study, the predicted TS barriers showed that both catalysts, (a*R*,*S*)-**11** and (a*S*,*S*)-**11**, had relatively high barriers: 1.211 and 1.112 kcal/mol, at the B3LYP/6−311++G(2d,p) level (Fig. 2B and C). Importantly, it is predicted that both (a*R*,*S*)-**11** and (a*S*,*S*)-**11** may catalyze the reactions to afford (*S*)-product with 87.7%ee and 88.5%ee, theoretically. Thus, this matches the two key conditions to use mixtures as chiral catalysts to afford high %ee values mentioned above.

In our initial tests, high up to 95% enantioselectivity was recorded in the 1,2-transfer hydrogenations of *N*-(1-phenylethylidene)aniline using (a*S*,*S*)-**11**. This 95%ee is very close to 93%ee catalyzed by (a*R*,*S*)-**11**. Therefore, the questions emerged: did the high enantioselectivity achieved just happened occasionally using this specific substrate? Could it be widely applied for other substrates? It may be a good chance to study the diastereomeric mixtures of both (a*R*,*S*)-**11** and (a*S*,*S*)-**11** as catalysts in the transfer hydrogenations. In view of this point, we performed the transfer hydrogenations using the mixtures of axially chiral (a*R*,*S*)-**11** and (a*S*,*S*)-**11**, also the optically pure (a*R*,*S*)-**11** as chiral catalysts, respectively. The same ketimines and β-enamino esters were used in the hydrogenations using both mixtures and optically pure (a*R*,*S*)-**11**. Here we report the hydrogenations using mixtures of

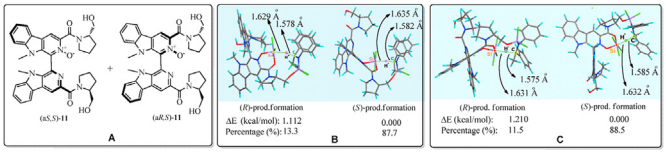
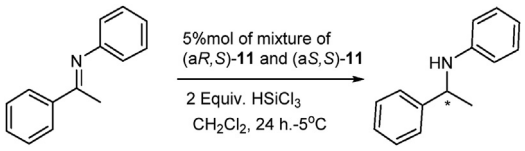


Fig. 2. (A) Axially chiral biscarboline alcohols (a*R*,*S*)-**11** and (a*S*,*S*)-**11**. (B) and (C) Two TS structures and their catalytic activation energy in 1,2-transfer hydrogenations of *N*-(1-phenylethylidene)aniline and the predicted %ee values. Plots B and C are copied from Ref.17 and modified here.

Table 1
Effect of the different ratio of (a*R*,*S*)-**11** to (a*S*,*S*)-**11** on the enantioselectivity in 1,2-transfer hydrogenations of *N*-(1-phenylethylidene)aniline (**12**).



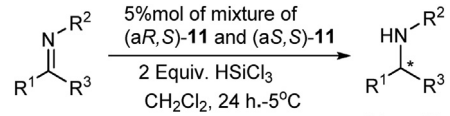
Entry	(a*R*,*S*)-11: (a*S*,*S*)-11	Yield (%)	Ee(%)	Config.
1	1:5	91	94	*S*
2	2:5	89	93.5	*S*
3	3:5	92	95	*S*
4	4:5	91	96	*S*
5	5:5	93	94	*S*
6	5:4	90	95	*S*
7	5:3	92	94.5	*S*
8	5:2	92	92	*S*
9	5:1	93	94.5	*S*
10	Optically pure (a*S*,*S*)-**11**	90	95	*S* [ref.17]

axially chiral (a*R*,*S*)-**11** and (a*S*,*S*)-**11** after the hydrogenations using optically pure (a*R*,*S*)-**11** as chiral catalyst was reported [17].

The mixtures of (a*R*,*S*)-**11** and (a*S*,*S*)-**11** were obtained with a ratio of 4:3 after the corresponding biscarboline alcohols reacted with *m*-CPBA (see SM for details) [16e]. Both could be separated by column chromatography from each other. Thus, the effect of different ratio of (a*R*,*S*)-**11** to (a*S*,*S*)-**11** on the enantioselective transfer hydrogenations was investigated first (Table 1). Interestingly, no matter what the ratio was used in experiments, the enantioselectivities were almost in the range of 92%–96%ee (Table 1, entries 1 to 9).

These good results encouraged us to investigate the enantioselectivities of 1,2-transfer hydrogenations using other ketimines catalyzed by the mixtures of (a*R*,*S*)-**11** and (a*S*,*S*)-**11**. Other thirteen ketimines were synthesized and used in the 1,2-transfer hydrogenations. As the expected, the enantioselectivities reached high up to 98%ee when substrates **19** and **20** were used (Table 2, entries 8 and 9). The lowest enantioselectivity was 91%ee (Table 2, entries 13

Table 2
Enantioselectivity in 1,2-transfer hydrogenations of ketimines using the mixtures of (a*R*,*S*)-**11** and (a*S*,*S*)-**11** (nearly 4:3).



12 to **25** **26** to **39**

Entry	Comp.	R [1], R^2, R^3	Prod.	Yield (%)	Ee (%)	Config
1	**12**	Ph, Ph, Me	**26**	90	95	*S*
2	**13**	4-F-Ph,Ph, Me	**27**	91	93	*S*
3	**14**	4-Cl-Ph,Ph, Me	**28**	90	95	*S*
4	**15**	4-Br-Ph, Ph, Me	**29**	91	94	*S*
5	**16**	4-NO_2-Ph,Ph,Me	**30**	90	93	*R*
6	**17**	4-Me-Ph, Ph, Me	**31**	90	92	*R*
7	**18**	4-MeO-Ph,Ph,Me	**32**	92	93	*S*
8	**19**	Ph, 4-MeO-Ph, Me	**33**	93	98	*S*
9	**20**	Ph, 4-EtO-Ph, Me	**34**	94	98	*S*
10	**21**	Ph, 4-Me-Ph, Me	**35**	90	92	*R*
11	**22**	Ph, 4- Et-Ph, Me	**36**	91	94	*S*
12	**23**	Ph, 4-Br-Ph, Me	**37**	92	95	*R*
13	**24**	Ph, Ph, Et	**38**	89	91	*S*
14	**25**	4-MeO-Ph,4-MeO-Ph,Me	**39**	90	91	*S*

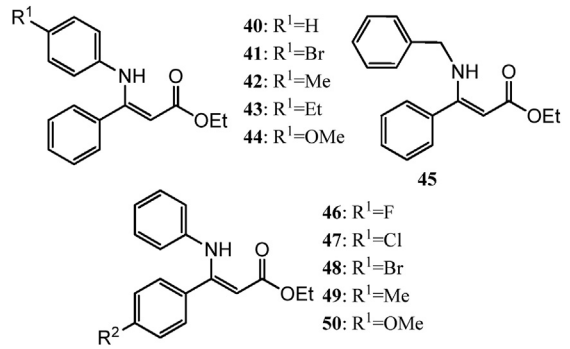
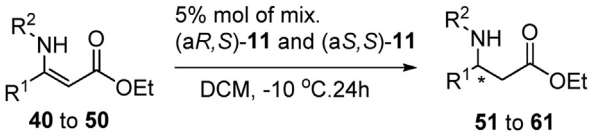


Fig. 3. The structures of 16 β-enamino esters (**40** to **50**).

Table 3
Enantioselectivities of sixteen β-enamino esters in 1,4-transfer hydrogenations using the mixtures of (a*R*,*S*)-**11** and (a*S*,*S*)-**11** with a ratio of 4:3.



Entry	Comp.	R [1], R^2	Prod.	Yield (%)	*Ee* (%)	Config.
1	**40**	Ph, Ph	**51**	90	96	*S*
2	**41**	Ph, 4-Br-Ph	**52**	91	95	*S*
3	**42**	Ph, 4-Me-Ph	**53**	89	92	*S*
4	**43**	Ph, 4-Et-Ph	**54**	91	95	*S*
5	**44**	Ph, 4-MeO-Ph	**55**	91	96	*S*
6	**45**	Ph, -Bn, Ph	**56**	90	92	*S*
7	**46**	4-F-Ph, Ph,	**57**	95	92	*S*
8	**47**	4-Cl-Ph, Ph	**58**	95	92	*S*
9	**48**	4-Br-Ph, Ph	**59**	89	91	*S*
10	**49**	4-Me-Ph, Ph	**60**	92	97	*S*
11	**50**	4-MeO-Ph, Ph	**61**	92	96	*S*

and 14). Most of the %ee values recorded in the 1,2-transfer hydrogenations are slightly smaller than those catalyzed by the single optically pure (a*R*,*S*)-**11** under similar reaction conditions [17].

That the high enantioselectivities obtained in the 1,2-transfer hydrogenations of ketimines may not hint the mixtures can be successfully used in 1,4-transfer hydrogenations with high %ee values since the β-enamino esters have larger steric hinderance than the ketimines. The steric hinderance of substrates may lead to higher TS barriers when using the diastereomeric mixtures. Thus, they might not promote the enantioselective reactions with high enantioselectivities. Thus, further total 16 β-enamino esters (**40** to **50**) were used in the 1,4-transfer hydrogenations and the %ee values were examined. The enantioselectivities reached high up to 97% in the 1,4-transfer hydrogenations. The specific substrate structures are illustrated below (Fig. 3).

The catalyst mixtures exhibited very high enantioselectivities from 90%ee to 97%ee in the 1,4-transfer hydrogenations using eleven substrates **40**–**50** (Table 3).

3. Summary

This is the first trial to use the diastereomeric mixtures of axially chiral biscarbolines as catalysts. The experimental results exhibited that the mixtures of (a*R*,*S*)-**11** and (a*S*,*S*)-**11** can catalyze 1,2-transfer hydrogenations of ketimines and 1,4-transfer hydrogenations of β-enamino esters with high enantioselectivities. Total 25 substrates were tested. Excellent enantioselectivities up to 98%ee were achieved. This result gives us a clue that some diastereogenic mixtures may be directly used in asymmetric reactions without further isolations economically.

4. Experimental

All reactions were carried out in oven-dried glassware and were allowed to proceed under a dried argon atmosphere with magnetic stirring. All solvents for the reactions were of reagent grade and were dried and distilled before use (dichloromethane from calcium hydride, DMF were stored with 4 Å MS). Thin layer chromatography was performed on TLC plates (GF254). Flash column chromatography was performed with silica gel (300–400 mesh). Enantiomeric excess was determined using chiral HPLC. Concentration unit for $[\alpha]_D$ is g/100 mL.

4.1. Synthesis of chiral catalyst 11

3-Chloroperoxybenzoic acid (4–8 equiv.) was added slowly to the anhydrous dichloromethane (60 mL) of intermediate 9,9′-dimethyl-9H, 9′H-[1,1′-bipyrido[3,4-b]indole]-3,3′-dicarboxylic acid (300 mg) in dichloromethane at room temperature. The solution was stirred for 10–32 h. The aqueous saturated solution of $NaHCO_3$ was added to quench the reaction at 0 °C after the reaction finished by TLC analysis. The organic phase was separated from water and the aqueous phase was then extracted three times with dichloromethane. The combined organic layers were washed with brine (15 × 3 mL) and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure. Yellow products (a*R*,*S*)-**11** and (a*S*,*S*)-**11** were obtained by column chromatography or plate chromatgraphy first. The isolated ratio was 4:3. Both were used to prepare mixture of (a*R*,*S*)-**11** and (a*S*,*S*)-**11** with different ratio (1:5 to 5:1) for catalystic reactions. Fianlly, the mixture of (a*R*,*S*)-**11** and (a*S*,*S*)-**11** were obtained by column chromatography and directly used in hydrogenations.

(a*S*,*S*)-3,3′-bis((*S*)-2-(hydroxymethyl)pyrrolidine-1-carbonyl)-9,9′-dimethyl-9H,9′H-[1,1′-bipyrido[3,4-b]indole] 2-oxide ((a*S*,*S*)-11): yield of 31%, $[\alpha]_D = -52.2$ (c 0.36, CH_2Cl_2), HR-MS-ESI *m/z* calcd for $C_{38}H_{40}N_6O_5$, $[M+Na]^+$ 655.2639, found: 655.2618. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.27 (s, 1 H, ArCH), 8.12 (m, 1H, ArCH), 8.07 (m, 2 H, ArCH), 7.61–7.58 (m, 2 H, ArCH), 7.37 (dd, J = 7.2, 4.0 Hz, 4 H, ArCH), 3.96 (dd, J = 20.6, 12.6 Hz, 2 H, CH), 3.83 (dd, J = 12.4, 7.6 Hz, 4 H, CH_2), 3.73–3.55 (m, 4 H, CH_2), 3.54 (s, 6 H, CH_3), 2.18–2.02 (m, 4 H, CH_2), 2.01–1.89 (m, 4 H, CH_2). ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.52 (CO), 166.55 (CO), 158.89 (ArC), 155.99 (ArC), 143.79 (ArC), 143.75 (2 × ArCH), 143.00 (ArC), 140.13 (ArC), 129.84 (ArC), 129.14 (2 × ArCH), 126.37 (ArCH), 121.79 (2 × ArCH), 120.96 (2 × ArCH), 120.00 (2 × ArCH), 114.14 (ArCH), 109.68 (2 × ArCH), 106.93 (2 × ArCH), 68.02 (CH), 63.71 (CH_2), 53.43 (CH_2), 32.00 (CH_3), 27.70 (CH_2), 21.69 (CH_2).

(a*R*,*S*)-3,3′-bis((*S*)-2-(hydroxymethyl)pyrrolidine-1-carbonyl)-9,9′-dimethyl-9H,9′H-[1,1′-bipyrido[3,4-b]indole] 2-oxide ((a*R*,*S*)-11), yield of 23%, $[\alpha]_D = +30.2$ (c 0.35, CH_2Cl_2), HR-MS-ESI *m/z* calcd for $C_{38}H_{40}N_6O_5$, $[M+Na]^+$ 655.2639, found: 655.2621. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.10 (s, 1 H, ArCH), 8.36 (s, 1H, ArCH), 8.17 (d, J = 7.6 Hz, 2 H, ArCH), 7.60 (m, 2 H, ArCH), 7.36 (m, 4 H), 3.95 (dd, J = 9.2, 5.5 Hz, 4 H, CH_2), 3.69 (m, 2 H, CH), 3.66–3.58 (m, 4 H, CH_2), 3.26 (s, 6 H, CH_3), 1.75 (dd, J = 11.6, 7.9 Hz, 4 H, CH_2), 1.56–1.50 (m, 4 H, CH_2). ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.75 (CO), 166.26 (CO), 157.16 (ArC), 154.50 (ArC), 145.85 (ArC), 143.05 (2 × ArCH), 140.28 (ArC), 138.29 (ArC), 129.09 (ArC), 128.52 (2 × ArCH), 127.00 (ArCH), 121.67 (2 × ArCH), 120.94 (2 × ArCH), 119.79 (2 × ArCH), 113.99 (ArCH), 109.66 (2 × ArCH), 107.66 (2 × ArCH), 68.02 (CH), 63.28 (CH_2), 55.73 (CH_2), 38.16 (CH_3), 32.03

(CH_2), 26.19 (CH_2).

Reductions of ketimines The ketimine (50 mg) and catalyst (6 mg) mixture of (a*S*,*S*)-**11** and (a*R*,*S*)-**11** were dissolved in anhydrous dichloromethane (20 mL) under nitrogen atmosphere and cooled to −10 °C. Trichlorosilane (2 equiv.) was added to the solution and stirred at −10 °C. After 24 h later, aqueous saturated solution of $NaHCO_3$ was added to quench the reaction after the reaction finished that was checked by TLC. The organic layer was separated from water and the aqueous phase was extracted with dichloromethane (15 × 3 mL). The combined organic layers were washed with brine (15 × 3 mL), and dried over anhydrous Na_2SO_4. The solvent was evaporated under vacuum. The product was obtained by column chromatography. These reactions were performed using both of the mixtures of (a*R*,*S*)-**11** and (a*S*,*S*)-**11** and optically pure (a*R*,*S*)-**11**, respectively, in a same low temperature equipment [17]. By checking with the TLC, the R_f values of the reaction products catalyzed by the either mixture of (a*R*,*S*)-**11** and (a*S*,*S*)-**11** or the optically pure **11** were the same. Chiral HPLC analysis for racemic products and the products indicated that the retention times are almost the same. The optical rotation (OR) values are almost the same with the reports and the OR signs for all products are the same with the reports too [17]. All results confirmed that the products catalyzed by either mixture of (a*R*,*S*)-**11** and (a*S*,*S*)-**11** or the optically pure (a*R*,*S*)-**11** are the same.

(*S*)−*N*-(1-phenylethyl)aniline (26): Light yellow viscous, yield of 90%, 95%ee, $[\alpha]_D$ = −13.1 (*c* 0.45, EtOH). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.29 (d, *J* = 5.5 Hz, 3 H, ArCH), 7.24 (t, *J* = 7.6 Hz, 2 H, ArCH), 7.05−7.01 (m, 2 H, ArCH), 6.56 (t, *J* = 7.3 Hz, 1 H, ArCH), 6.44 (d, *J* = 8.1 Hz, 2 H, ArCH), 4.41 (q, *J* = 6.7 Hz, 1 H, CH), 1.44 (d, *J* = 6.7 Hz, 3 H, CH_3). ^{13}C NMR (151 MHz, $CDCl_3$) δ 147.31 (ArC), 145.24 (ArC) 129.08 (2 × ArCH), 128.79 (2 × ArCH), 128.61 (2 × ArCH), 125.90 (ArCH), 122.22 (ArCH), 113.32 (2 × ArCH), 65.54 (CH), 19.18 (CH_3).

(*S*)−*N*-(1-(4-fluorophenyl)ethyl)aniline (27): Light yellow viscous, yield of 91%, 93%ee, $[\alpha]_D$ = −18.2 (c 0.055, EtOH). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.24 (dd, *J* = 8.2, 5.6 Hz, 2 H, ArCH), 7.01 (t, *J* = 7.8 Hz, 2 H, ArCH), 6.91 (t, *J* = 8.6 Hz, 2 H, ArCH), 6.57 (t, *J* = 7.3 Hz, 1 H, ArCH), 6.40 (d, *J* = 8.0 Hz, 2 H, ArCH), 4.38 (q, *J* = 6.7 Hz, 1 H, CH), 3.90 (s, 1 H, NH), 1.40 (d, *J* = 6.7 Hz, 3 H, CH_3). ^{13}C NMR (151 MHz, $CDCl_3$) δ 160.99 (ArC), 147.14 (ArC), 140.92 (ArC), 129.15 (2 × ArCH), 127.37 (2 × ArCH), 117.48 (ArC), 115.37 (2 × ArCH), 113.38 (2 × ArCH), 52.93 (CH), 25.13 (CH_3).

(*S*)−*N*-(1-(4-chlorophenyl)ethyl)aniline (28): Yellow viscous, yield of 90%, 95% ee, $[\alpha]_D$ = −13.0 (c 0.05, EtOH). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.20−7.15 (t, *J* = 7.6 Hz, 4 H, ArCH), 6.99 (m, 2H, ArCH), 6.58−6.53 (m, 1 H, ArCH), 6.39−6.35 (d, *J* = 8.3 Hz, 2H, ArCH), 4.35−4.31 (q, *J* = 6.7 Hz, 1 H, CH), 1.36 (d, *J* = 6.7 Hz, 3H, CH_3). ^{13}C NMR (151 MHz, $CDCl_3$) δ 147.08 (ArC), 143.93 (ArC), 132.47 (ArC), 129.23 (2 × ArCH), 128.87 (2 × ArCH), 127.34 (2 × ArCH), 117.60 (ArCH), 113.42 (2 × ArCH), 53.04 (CH), 25.12 (CH_3).

(*S*)−*N*-(1-(4-bromophenyl)ethyl)aniline (29): Light yellow oil, yield of 91%, 94% ee, $[\alpha]_D$ = −18.0 (*c* 0.046, EtOH). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.4 Hz, 2 H, ArCH), 7.24 (d, *J* = 8.6 Hz, 2 H, ArCH), 7.09 (dd, *J* = 8.4, 7.5 Hz, 2 H, ArCH), 6.65 (t, *J* = 7.3 Hz, 1 H, ArCH), 6.47 (d, *J* = 7.7 Hz, 2 H, ArCH), 4.43 (q, *J* = 6.7 Hz, 1 H, CH_2), 1.48 (d, *J* = 6.7 Hz, 3 H, CH_3). ^{13}C NMR (151 MHz, $CDCl_3$) δ 146.96 (ArC), 144.38 (ArC), 131.75 (2 × ArCH), 129.15 (2 × ArCH), 127.64 (2 × ArCH), 120.49 (ArC), 117.55 (ArCH), 113.32 (2 × ArCH), 53.06 (CH), 25.05 (CH_3).

(*R*)-*N*-(1-(4-nitrophenyl)ethyl)aniline (30): Light yellow oil, yield of 90%, 93%ee, $[\alpha]_D$ = +18.3 (*c* 0.039, EtOH). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.22 (dd, *J* = 9.0, 5.2 Hz, 4 H, ArCH), 7.13 (dt, *J* = 5.8, 2.5 Hz, 1 H, ArCH), 7.05 (d, *J* = 8.8 Hz, 2 H, ArCH), 6.27 (d, *J* = 8.8 Hz, 2 H, ArCH), 4.33 (q, *J* = 6.7 Hz, 1 H, CH), 3.94 (s, 1 H, NH), 1.40 (d, *J* = 6.7 Hz, 3 H, CH_3). ^{13}C NMR (151 MHz, $CDCl_3$) δ 145.19 (ArC), 143.60 (ArC), 130.75 (ArC), 127.69 (2 × ArCH), 126.01 (2 × ArCH), 124.73 (2 × ArCH), 113.90 (ArCH), 107.86 (2 × ArCH), 52.48 (CH), 23.85 (CH_3).

(*R*)-*N*-(1-(p-tolyl)ethyl)aniline (31): Light yellow oil, yield of 90%, 92% ee, $[\alpha]_D$ = +13.3 (c 0.055, EtOH). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.15 (d, *J* = 7.2 Hz, 2 H, ArCH), 7.03 (t, *J* = 7.4 Hz, 2 H, ArCH), 7.00 (m, 2 H, ArCH), 6.57−6.54 (m, 1 H, ArCH), 6.44−6.42 (m, 2 H, ArCH), 4.37 (q, *J* = 6.7 Hz, 1 H, CH), 3.87 (s, 1 H, NH), 2.22 (s, 3 H, CH_3), 1.40 (d, *J* = 6.7 Hz, 3 H, CH_3). ^{13}C NMR (151 MHz, $CDCl_3$) δ 147.45 (ArC), 142.31 (ArC), 136.45 (ArC), 129.39 (2 × ArCH), 129.16 (2 × ArCH), 125.84 (2 × ArCH), 117.24 (ArCH), 113.37 (2 × ArCH), 53.21 (CH), 25.07 (CH_3), 21.13 (CH_3).

(*S*)−*N*-(1-(4-methoxyphenyl)ethyl)aniline (32): Light yellow oil, yield of 92%, 92%ee, $[\alpha]_D$ = −14.9 (c 0.039, EtOH). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.21−7.18 (m, 2 H, ArCH), 7.01 (t, *J* = 7.0 Hz, 2H, ArCH), 6.78 (d, *J* = 8.0 Hz, 2 H, ArCH), 6.57 (d, *J* = 6.8 Hz, 1 H, ArCH), 6.44 (d, *J* = 7.6 Hz, 2 H, ArCH), 4.37 (d, *J* = 6.2 Hz, 1 H, CH), 4.19 (s, 1 H, NH), 3.71 (s, 3 H, CH_3), 1.42 (d, *J* = 6.2 Hz, 3 H, CH_3). ^{13}C NMR (151 MHz, $CDCl_3$) δ 157.54 (ArC), 146.39 (ArC), 136.30 (ArC), 128.07 (2 × ArCH), 125.90 (2 × ArCH), 116.21 (ArCH), 113.04 (2 × ArCH), 112.37 (2 × ArCH), 54.25 (CH), 51.86 (CH_3), 23.91 (CH_3).

(*S*)-4-methoxy-*N*-(1-phenylethyl)aniline (33): Light yellow oil, yield of 93%, 98% ee, $[\alpha]_D$ = −7.5 (c 0.05, EtOH). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.28 (d, *J* = 7.6 Hz, 2 H, ArCH), 7.23 (t, *J* = 7.5 Hz, 2 H, ArCH), 7.14 (t, *J* = 7.2 Hz, 1 H, ArCH), 6.61 (d, *J* = 8.8 Hz, 2 H, ArCH), 6.39 (d, *J* = 8.8 Hz, 2 H, ArCH), 4.33 (q, *J* = 6.7 Hz, 1 H, CH), 3.61 (s, 3 H, CH_3), 1.42 (d, *J* = 6.7 Hz, 3 H, CH_3). ^{13}C NMR (151 MHz, $CDCl_3$) δ 151.01 (ArC), 144.44 (ArC), 140.52 (ArC), 127.58 (2 × ArCH), 125.81 (2 × ArCH), 124.90 (ArCH), 113.80 (2 × ArCH), 113.65 (2 × ArCH), 54.74 (CH), 53.33 (CH_3), 24.01 (CH_3).

(*S*)-4-ethoxy-*N*-(1-phenylethyl)aniline(34): Light yellow oil, yield of 94%, 98%ee, $[\alpha]_D$ = −18.3 (c 0.035, EtOH). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.29 (d, *J* = 7.6 Hz, 2 H, ArCH), 7.23 (t, *J* = 7.6 Hz, 2 H, ArCH), 7.14 (t, *J* = 7.3 Hz, 1 H, ArCH), 6.61 (d, *J* = 8.9 Hz, 2 H, ArCH), 6.45 (d, *J* = 8.5 Hz, 2 H, ArCH), 4.34 (q, *J* = 6.7 Hz, 1 H, CH), 3.83 (q, *J* = 7.0 Hz, 2 H, CH_2), 1.46 (d, *J* = 6.7 Hz, 3 H, CH_3), 1.26 (t, *J* = 7.0 Hz, 3 H, CH_3). ^{13}C NMR (151 MHz, $CDCl_3$) δ 151.78 (ArC), 144.80 (ArC), 140.85 (ArC), 128.58 (2 × ArCH), 126.95 (2 × ArCH), 126.12 (2 × ArCH), 115.62 (ArCH), 114.38 (2 × ArCH), 64.04 (CH), 55.03 (CH_3), 14.96 (CH_2), 8.61 (CH_3).

(*R*)-4-methyl-*N*-(1-phenylethyl)aniline (35): Light yellow oil, yield of 90%, 92%ee, $[\alpha]_D$ = +10.2 (c 0.035, EtOH). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.28 (d, *J* = 7.4 Hz, 2 H, ArCH), 7.23 (t, *J* = 7.6 Hz, 2 H, ArCH), 7.14 (dd, *J* = 12.5, 5.2 Hz, 1 H, ArCH), 6.82 (d, *J* = 8.1 Hz, 2 H, ArCH), 6.35 (d, *J* = 8.3 Hz, 2 H, ArCH), 4.37 (q, *J* = 6.7 Hz, 1 H, CH), 2.10 (s, 3 H, CH_3), 1.42 (d, *J* = 6.7 Hz, 3 H, CH_3). ^{13}C NMR (151 MHz, $CDCl_3$) δ 144.40 (ArC), 144.00 (ArC), 128.56 (2 × ArCH), 127.57 (ArC), 125.76 (2 × ArCH), 125.36 (2 × ArCH), 124.84 (ArCH), 112.43 (2 × ArCH), 52.67 (CH), 23.98 (CH_3), 19.30 (CH_3).

(*S*)-4-ethyl-*N*-(1-phenylethyl)aniline (36): Light yellow oil, yield of 91%, 94%ee, $[\alpha]_D$ = −8.0 (c 0.042, EtOH). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.26 (d, *J* = 7.6 Hz, 2 H, ArCH), 7.20 (t, *J* = 7.5 Hz, 2 H, ArCH), 7.11 (t, *J* = 7.2 Hz, 1 H, ArCH), 6.83 (d, *J* = 8.2 Hz, 2 H, ArCH), 6.36 (d, *J* = 8.3 Hz, 2 H, ArCH), 4.35 (q, *J* = 6.7 Hz, 1 H, CH), 3.77 (s, 1 H, NH), 2.39 (q, *J* = 7.6 Hz, 2 H, CH_2), 1.39 (d, *J* = 6.7 Hz, 3 H, CH_3), 1.05 (t, *J* = 7.6 Hz, 3 H, CH_3). ^{13}C NMR (151 MHz, $CDCl_3$) δ 144.48 (ArC), 144.27 (ArC), 131.98 (ArC), 127.56 (2 × ArCH), 127.37 (2 × ArCH), 125.76 (2 × ArCH), 124.85 (ArCH), 112.40 (2 × ArCH), 52.70 (CH), 26.84 (CH_2), 23.96 (CH_3), 14.79 (CH_3).

(*R*)-4-bromo-*N*-(1-phenylethyl)aniline(37): Light yellow oil, yield of 92%, 95% ee, $[\alpha]_D$ = +31.3 (c 0.026, EtOH). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.25−7.21 (m, 4 H, ArCH), 7.14 (dt, *J* = 8.5, 2.9 Hz, 1 H, ArCH), 7.06 (d, *J* = 8.8 Hz, 2 H, ArCH), 6.28 (d, *J* = 8.8 Hz, 2 H, ArCH), 4.33 (q, *J* = 6.7 Hz, 1 H, CH_2), 3.95 (s, 1 H, NH), 1.41 (d, *J* = 6.7 Hz, 3 H, CH_3). ^{13}C NMR (151 MHz, $CDCl_3$) δ 145.15 (ArC), 143.57 (ArC), 130.73 (2 × ArCH), 127.68 (2 × ArCH), 126.00

(2 × ArCH), 124.71 (ArCH), 113.87 (ArC), 107.76 (2 × ArCH), 52.45 (CH), 23.88 (CH_3).

(*S*)−*N*-(1-phenylpropyl)aniline(38): Light yellow oil, yield of 89%, 91% ee, $[\alpha]_D = -47.2$ (c 0.01, EtOH). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.25 (dt, J = 15.0, 7.5 Hz, 4 H, ArCH), 7.15 (t, J = 6.9 Hz, 1 H, ArCH), 7.00 (t, J = 7.9 Hz, 2 H, ArCH), 6.55 (t, J = 7.3 Hz, 1 H, ArCH), 6.44 (d, J = 7.8 Hz, 2 H, ArCH), 4.15 (t, J = 6.7 Hz, 1 H, CH), 3.67 (s, 1 H, NH), 1.75 (m, 2 H, CH_2), 0.88 (t, J = 7.4 Hz, 3 H, CH_3). ^{13}C NMR (151 MHz, $CDCl_3$) δ 146.51 (ArC), 142.91 (ArC), 128.05 (2 × ArCH), 127.47 (2 × ArCH), 125.85 (2 × ArCH), 125.46 (ArCH), 116.10 (ArCH), 112.22 (2 × ArCH), 58.71 (CH), 30.64 (CH_2), 9.79 (CH_3).

(*S*)-4-methoxy-*N*-(1-(4-methoxyphenyl)ethyl)aniline(39): Light yellow oil, yield of 90%, 91% ee, $[\alpha]_D = +18.3$ (c 0.016, EtOH). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.11 (dd, J = 13.9, 7.7 Hz, 3 H, ArCH), 7.04 (t, J = 7.6 Hz, 2 H, ArCH), 6.86−6.83 (m, 1 H, ArCH), 6.81 (d, J = 7.2 Hz, 2 H, ArCH), 4.12 (q, J = 6.7 Hz, 1 H, CH), 2.09 (s, 6H, CH_3), 1.24 (t, J = 6.7 Hz, 3 H, CH_3). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.51 (ArC), 154.84 (ArC), 144.11 (ArC), 138.72 (ArC), 129.57 (2 × ArCH), 119.85 (2 × ArCH), 113.26 (2 × ArCH), 112.70 (2 × ArCH), 62.20 (CH), 54.45 (CH_3), 50.42 (CH_3), 25.27 (CH_3).

4.2. Reduction of β-enamino esters

β-Keto ester (50 mg), catalyst mixture **11** (6 mg) were dissolved in anhydrous dichloromethane (30 mL). The mixture was stirred until it completely dissolved at room temperature. The solution was then cooled to −10 °C. Trichlorosilane (2 equiv.) was added into the solution and it was stirred at −10 °C for 24 h. The reaction was quenched with saturated solution of $NaHCO_3$ after reaction finished checked by TLC. The organic layer was separated from the aqueous phase and the aqueous layer was extracted by dichloromethane (15 × 3 mL). The combined organic layers were washed with brine (15 × 3 mL) and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure. White material was obtained by column chromatography.

(*S*)-Ethyl 3-phenyl-3-(phenylamino)propanoate(51) : Light yellow solid, yield of 90%, 96% ee, $[\alpha]_D = -1.8$ (c 0.55, CH_2Cl_2), HR-MS-ESI *m/z* calcd for $C_{17}H_{19}NO_2$, $[M+Na]^+$ 292.1308, found: 292.1298. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30 (d, J = 7.4 Hz, 2 H, ArCH), 7.24 (t, J = 7.6 Hz, 2 H, ArCH), 7.17−7.14 (m, 1 H, ArCH), 7.02 (dd, J = 8.4, 7.5 Hz, 2 H, ArCH), 6.62−6.57 (m, 1 H, ArCH), 6.48 (d, J = 7.8 Hz, 2 H, ArCH), 4.77−4.74 (t, J = 6.1, 1 H, CH), 4.02 (pd, J = 7.7, 3.7 Hz, 2 H, CH_2), 2.75−2.69 (m, 2 H, CH_2), 1.10 (t, J = 7.1 Hz, 3 H, CH_3). ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.13 (CO), 145.80 (ArC), 141.18 (ArC), 128.11 (2 × ArCH), 127.72 (2 × ArCH), 126.40 (2 × ArCH), 125.23 (ArCH), 116.74 (ArCH), 112.65 (2 × ArCH), 59.77 (CH_2), 53.99 (CH), 41.90 (CH_2), 13.10 (CH_3).

(*S*)-Ethyl 3-((4-bromophenyl)amino)-3-phenylpropanoate(52): Light yellow solid, yield of 91%, 95%ee, $[\alpha]_D = +15.0$ (c 0.58, CH_2Cl_2), HR-MS-ESI *m/z* calcd for $C_{17}H_{18}BrNO_2$, $[M+Na]^+$ 370.0413, found: 370.0399. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.28−7.23 (m, 2 H, ArCH), 7.01 (t, J = 7.8 Hz, 2 H, ArCH), 6.91 (t, J = 8.5 Hz, 2 H, ArCH), 6.59 (t, J = 7.3 Hz, 1 H, ArCH), 6.45 (d, J = 7.8 Hz, 2 H, ArCH), 4.72 (t, J = 6.5 Hz, 1 H, CH), 4.04−3.98 (m, 2 H, CH_2), 4.48 (s, 1 H, NH), 2.68 (m, 2 H, CH_2), 1.09 (t, J = 7.1 Hz, 3 H, CH_3). ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.94 (CO), 146.68 (ArC), 137.96 (ArC), 129.19 (2 × ArCH), 127.88 (2 × ArCH), 118.00 (ArCH), 115.67 (2 × ArCH), 115.53 (ArC), 113.75 (2 × ArCH), 60.83 (CH_2), 54.43 (CH), 42.90 (CH_2), 14.13 (CH_3).

(*S*)-Ethyl 3-phenyl-3-(p-tolylamino)propanoate(53): Light yellow solid, yield of 89%, 92%ee, $[\alpha]_D = -9.1$ (c 0.55, CH_2Cl_2), HR-MS-ESI *m/z* calcd for $C_{18}H_{21}NO_2$, $[M+Na]^+$ 306.1465, found: 306.1454. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.29 (d, J = 7.6 Hz, 2 H, ArCH), 7.23 (t, J = 7.6 Hz, 2 H, ArCH), 7.15 (dd, J = 11.6, 4.0 Hz, 1 H, ArCH), 6.83 (d, J = 8.2 Hz, 2 H, ArCH), 6.40 (d, J = 8.3 Hz, 2 H, ArCH), 4.72 (t, J = 6.7 Hz, 1 H, CH), 4.02 (qd, J = 7.1, 4.7 Hz, 2 H, CH_2), 2.73−2.68 (m, 2 H, CH_2), 2.10 (s, 3 H, CH_3), 1.10 (t, J = 7.1 Hz, 3 H, CH_3). ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.21 (CO), 144.56 (ArC), 142.38 (ArC), 129.65 (2 × ArCH), 128.73 (ArC), 127.38 (2 × ArCH), 126.97 (2 × ArCH), 126.30 (ArC), 113.87 (2 × ArCH), 60.76 (CH_2), 55.31 (CH), 42.96 (CH_2), 20.31 (CH_3), 14.15 (CH_3).

(*S*)-Ethyl 3-((4-ethylphenyl)amino)-3-phenylpropanoate(54): Light yellow solid, yield of 91%, 95%ee, $[\alpha]_D = -10.4$ (c 0.45, CH_2Cl_2), HR-MS-ESI *m/z* calcd for $C_{19}H_{23}NO_2$, $[M+Na]^+$ 320.1621, found: 320.1611. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.29 (d, J = 7.4 Hz, 2 H, ArCH), 7.22 (t, J = 7.6 Hz, 2 H, ArCH), 7.14 (t, J = 7.3 Hz, 1 H, ArCH), 6.85 (d, J = 8.3 Hz, 2 H, ArCH), 6.42 (d, J = 8.4 Hz, 2 H, ArCH), 4.71 (t, J = 6.7 Hz, 1 H, CH), 4.03−3.97 (m, 2 H, CH_2), 2.69 (dd, J = 7.9, 6.4 Hz, 2 H, CH_2), 2.40 (q, J = 7.6 Hz, 2 H, CH_2), 1.09 (t, J = 7.1 Hz, 3 H, CH_3), 1.06 (t, J = 7.6 Hz, 3 H, CH_3). ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.22 (CO), 144.81 (ArC), 142.51 (ArC), 133.58 (2 × ArCH), 128.75 (ArC), 128.48 (2 × ArCH), 127.40 (2 × ArCH), 126.33 (ArC), 113.84 (2 × ArCH), 60.77 (CH_2), 55.35 (CH), 43.01 (CH_2), 27.91 (CH_2), 15.86 (CH_3), 14.17 (CH_3).

(*S*)-Ethyl 3-(benzylamino)-3-phenylpropanoate(56): Light yellow solid, yield of 90%, 92%ee, $[\alpha]_D = +27.3$ (c 0.47, CH_2Cl_2), HR-MS-ESI *m/z* calcd for $C_{18}H_{21}NO_2$, $[M+Na]^+$ 306.1465, found: 306.1456. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30−7.16 (m, 10 H), 4.60 (t, J = 6.4 Hz, 1 H, CH), 4.19 (d, J = 6.4 Hz, 2 H, CH_2), 4.10−4.06 (m, 2 H, CH_2), 1.20 (t, J = 7.1 Hz, 3 H, CH_3). ^{13}C NMR (151 MHz, $CDCl_3$) δ 169.36 (CO), 138.26 (ArC), 135.00 (ArC), 128.23 (2 × ArCH), 127.59 (2 × ArCH), 127.36 (2 × ArCH), 126.89 (2 × ArCH), 125.87 (2 × ArCH), 60.45 (CH2), 57.76 (CH), 52.38 (CH_2), 47.36 (CH_2), 13.57 (CH_3).

(*S*)-ethyl 3-((4-methoxyphenyl)amino)-3-phenylpropanoate(55): Light yellow solid, yield of 91%, 96%ee, $[\alpha]_D = -14.2$ (c 0.58, CH_2Cl_2). HR-MS-ESI *m/z* calcd for $C_{18}H_{21}NO_3$, $[M+Na]^+$ 322.1414, found: 322.1401. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36 (d, J = 7.4 Hz, 2 H, ArCH), 7.31 (t, J = 7.6 Hz, 2 H, ArCH), 7.23 (t, J = 7.3 Hz, 1 H, ArCH), 6.73−6.65 (m, 2 H, ArCH), 6.52 (d, J = 8.9 Hz, 2 H, ArCH), 4.74 (t, J = 6.7 Hz, 1 H, CH), 4.10 (m, 2 H, CH_2), 3.69 (s, 3 H, CH_3), 2.78 (d, J = 6.7 Hz, 2 H, CH_2), 1.19 (t, J = 7.1 Hz, 3 H, CH_3). ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.23 (CO), 151.38 (ArC), 141.37 (ArC), 139.90 (ArC), 127.70 (2 × ArCH), 126.38 (2 × ArCH), 125.32 (ArCH), 114.23 (2 × ArCH), 113.75 (2 × ArCH), 59.72 (CH_2), 55.04 (CH), 54.69 (CH_3), 41.89 (CH_2), 13.12 (CH_3).

(*S*)-Ethyl 3-(4-fluorophenyl)-3-(phenylamino)propanoate(57): Light yellow solid, yield of 95%, 92%ee, $[\alpha]_D = +5.0$ (c 0.57, CH_2Cl_2), HR-MS-ESI *m/z* calcd for $C_{17}H_{18}FNO_2$, $[M+Na]^+$ 310.1214, found: 310.1206. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.25 (m, 2 H, ArCH), 7.01 (t, J = 7.8 Hz, 2 H, ArCH), 6.90 (t, J = 8.6 Hz, 2 H, ArCH), 6.59 (t, J = 7.3 Hz, 1 H, ArCH), 6.45 (d, J = 8.2 Hz, 2 H, ArCH), 4.72 (t, J = 6.6 Hz, 1 H, CH), 4.48 (t, J = 6.6 Hz, 1 H, CH), 4.04−3.98 (m, 2 H, CH_2), 2.68 (d, J = 6.6 Hz, 2 H, CH_2), 1.09 (t, J = 7.1 Hz, 3 H, CH_3). ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.93 (CO), 162.91 (ArC), 146.69 (ArC), 137.95 (ArC), 129.19 (2 × ArCH), 127.94 (2 × ArCH), 118.00 (ArCH), 115.67 (2 × ArCH), 113.76 (2 × ArCH), 60.82 (CH_3), 54.44 (CH), 42.90 (CH_2), 14.13 (CH_3).

(*S*)-Ethyl 3-(4-chlorophenyl)-3-(phenylamino)propanoate(58): Light yellow solid, yield of 95%, 92%ee, $[\alpha]_D = -13.2$ (c 0.5, CH_2Cl_2), HR-MS-ESI *m/z* calcd for $C_{17}H_{18}ClNO_2$, $[M+Na]^+$ 326.0918, found: 326.0911. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.22 (dd, J = 20.1, 8.5 Hz, 4 H, ArCH), 7.02 (t, J = 7.9 Hz, 2 H, ArCH), 6.60 (t, J = 7.3 Hz, 1 H, ArCH), 6.44 (d, J = 7.9 Hz, 2 H, ArCH), 4.71 (t, J = 6.6 Hz, 1 H, CH), 4.50 (s, 1 H, NH) 4.05−3.99 (m, 2 H, CH_2), 2.72−2.66 (m, 2 H, CH_2), 1.11 (t, J = 7.1 Hz, 3 H, CH_3). ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.84 (CO), 146.57 (ArC), 140.82 (ArC), 133.13 (ArC), 129.20 (2 × ArCH), 128.93 (2 × ArCH), 127.73 (2 × ArCH), 118.07 (ArCH), 113.73 (2 × ArCH), 60.89 (CH_2), 54.48 (CH), 42.74 (CH_2), 14.13 (CH_3).

(*S*)-Ethyl 3-(4-bromophenyl)-3-(phenylamino)propanoate(59): Light yellow solid, yield of 89%, 91%ee, $[\alpha]_D = -14.0$ (c 0.65, CH_2Cl_2), HR-MS-ESI *m/z* calcd for $C_{17}H_{18}BrNO_2$, $[M+Na]^+$ 370.0413, found: 370.0406. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35 (d, $J = 8.3$ Hz, 2 H, ArCH), 7.19–7.16 (m, 2 H, ArCH), 7.02 (t, $J = 7.8$ Hz, 2 H, ArCH), 6.60 (t, $J = 7.3$ Hz, 1 H, ArCH), 6.44 (d, $J = 8.1$ Hz, 2 H, ArCH), 4.69 (t, $J = 6.6$ Hz, 1 H, CH), 4.50 (s, 1 H, NH), 4.02 (qd, $J = 7.1$, 3.1 Hz, 2 H, CH_2), 2.71–2.65 (m, 2 H, CH_2), 1.11 (t, $J = 7.1$ Hz, 3 H, CH_3). ^{13}C NMR (151 MHz, $CDCl_3$) δ 169.78 (CO), 145.51 (ArC), 140.34 (ArC), 130.84 (2 × ArCH), 128.17 (2 × ArCH), 127.07 (2 × ArCH), 120.18 (ArC), 117.05 (ArCH), 112.70 (2 × ArCH), 59.87 (CH_2), 53.50 (CH), 41.65 (CH_2), 13.11 (CH_3).

(*S*)-Ethyl 3-(phenylamino)-3-(p-tolyl)propanoate(60): Light yellow solid, yield of 92%, 97%ee, $[\alpha]_D = -15.2$ (c 0.65, CH_2Cl_2), HR-MS-ESI *m/z* calcd for $C_{18}H_{21}NO_2$, $[M+Na]^+$ 306.1465, found: 306.1456. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.17 (m, 2 H, ArCH), 7.05–6.99 (m, 4 H, ArCH), 6.57 (t, $J = 7.3$ Hz, 1 H, ArCH), 6.47 (d, $J = 7.9$ Hz, 2 H, ArCH), 4.72 (t, $J = 6.7$ Hz, 1 H, CH), 4.43 (s, 1 H, NH), 4.04–3.98 (m, 2 H, CH_2), 2.71–2.68 (m, 2 H, CH_2), 2.22 (s, 3 H, CH_3), 1.10 (t, $J = 7.1$ Hz, 3 H, CH_3). ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.13 (CO), 145.94 (ArC), 138.23 (ArC), 135.97 (ArC), 128.40 (2 × ArCH), 128.10 (2 × ArCH), 125.15 (2 × ArCH), 116.70 (ArCH), 112.69 (2 × ArCH), 59.68 (CH_2), 53.77 (CH), 41.91 (CH_2), 20.01 (CH_3), 13.11 (CH_3).

(*S*)-Ethyl 3-(4-methoxyphenyl)-3-(phenylamino)propanoate(61): Light yellow oil, yield of 92%, 96%ee, $[\alpha]_D = -22.3$ (c 0.55, CH_2Cl_2), HR-MS-ESI *m/z* calcd for $C_{18}H_{21}NO_3$, $[M+Na]^+$ 322.1414, found: 322.1407. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.21 (t, $J = 6.8$ Hz, 2 H, ArCH), 7.02 (t, $J = 6.2$ Hz, 2 H, ArCH), 6.77 (d, $J = 6.9$ Hz, 2 H, ArCH), 6.58 (t, $J = 6.2$ Hz, 1 H, ArCH), 6.48 (d, $J = 7.2$ Hz, 2 H, ArCH), 4.71 (s, 1 H, CH), 4.43 (s, 1 H, NH), 4.02 (m, 2 H, CH_2), 3.69 (s, 3 H, CH_3), 2.70 (d, $J = 3.9$ Hz, 2 H, CH_2), 1.11 (t, $J = 7.2$ Hz, 3 H, CH_3). ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.16 (CO), 158.91 (ArC), 146.92 (ArC), 134.25 (ArC), 129.12 (2 × ArCH), 127.41 (2 × ArCH), 117.73 (ArCH), 114.15 (2 × ArCH), 113.73 (2 × ArCH), 60.69 (CH_2), 55.23 (CH), 54.49 (CH_3), 42.93 (CH_2), 14.08 (CH_3).

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tet.2021.131924.

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