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Cu(OTf)$_2$-Catalyzed Asymmetric Friedel–Crafts Alkylation Reaction of Indoles with Arylidene Malonates Using Bis(sulfonamide)-Diamine Ligands

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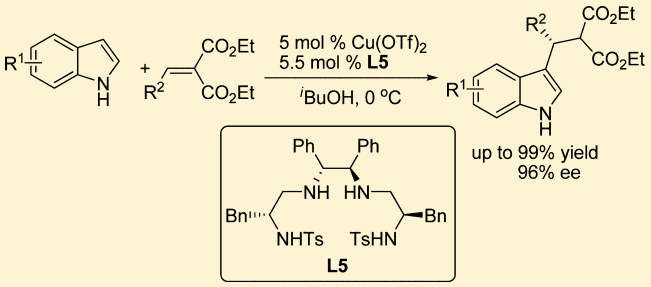
Supporting Information

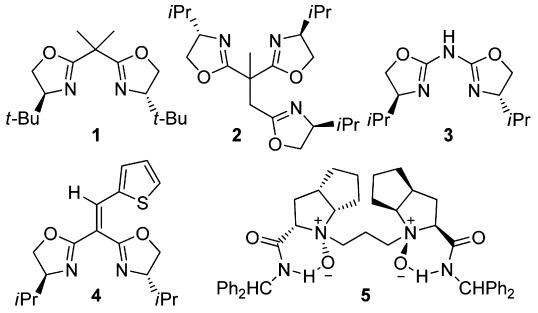
ABSTRACT: A highly efficient Cu-catalyzed asymmetric Friedel–Crafts alkylation reaction of indoles with arylidene malonates using simple, stable, and easily prepared bis-sulfonamide diamine ligands was developed. The desired products were obtained in up to 99% yield with 96% ee.



INTRODUCTION

Chiral indole architectures have been identified as privileged compounds due to their common occurrence in a wide variety of medicinal chemistry lead compounds as well as bioactive nature products.[1] During the past decades, the asymmetric Friedel–Crafts alkylation reaction of indoles has proved to be one of the most powerful methodologies in providing optical active indole derivatives.[2] Meanwhile, the enantioselective Friedel–Crafts alkylation of indoles with alkylidene malonates is intriguing. In 2001, a C_2-symmetric chiral bis(oxazoline) **1**-Cu(II) catalyst was used in the pioneering work of Jørgensen and co-workers[3] providing good yields and moderate enantioselectivities (Scheme 1). Subsequently, impressive improvement was achieved by Tang's group[4] using pseudo-C_3-symmetric tris(oxazoline) ligand **2** in which an additional oxazoline moiety coordinated with the copper center in an apical position affording high enantioselectivities (up to 93% ee). Furthermore, Reiser et al.[5] disclosed that meticulously tuning the ratio of azabis(oxazoline) ligand **3**/Cu(II) played a vital role in obtaining excellent enantioselectivity in this reaction. Heteroarylidenemalonate-derived bis(oxazoline) **4**-Cu(II) developed by Fu et al.[6] could also serve as an efficient catalyst for this transformation. Recently, Feng et al.[7] found that *N*,*N*′-dioxide scandium(III) complexes could effectively promote the asymmetric Friedel–Crafts alkylation of indoles with arylidene malonates. Although tremendous efforts have been devoted and considerable progress have been made, the catalysts involved therein were limited to bis- or trisoxazoline[8]–Cu(II) complexes and *N*,*N*′-dioxide[9] **5**–scandium(III) complexes. Given the great utility of this reaction, exploration of efficient alternative catalysts especially for developing simple, stable, readily available chiral ligands is still highly desirable.

Scheme 1. Ligands Reported in the Asymmetric Friedel–Crafts Alkylation of Indoles with Alkylidene Malonates



Our recently developed chiral bis-sulfonamide diamine ligands, designed to be simple, cheap, easily prepared, and stable, with their metal complexes were described to be effective catalysts for the enantio- and diastereoselective Henry reaction[10] as well as the asymmetic Friedel–Crafts addition of indole to nitroalkenes.[11] As a part of our continuing interest and ongoing research in making bis-sulfonamide diamine ligands as structurally versatile and widely applicable ligands, we demostrated herein the highly effective Cu-catalyzed asymmetric Friedel–Crafts alkylation reaction of indoles with arylidene malonates using bis-sulfonamide diamine ligands affording the products in up to 99% yield with 96% ee.

RESULTS AND DISCUSSION

In order to determine the optimal reaction condition, initial studies were conducted between model substrates of indole **6a** and benzylidene malonate **7a**. Some representative results were summarized in Table 1. Treatment of this reaction with

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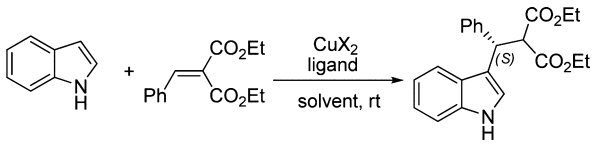
Table 1. Optimization of Reaction Conditions[a]



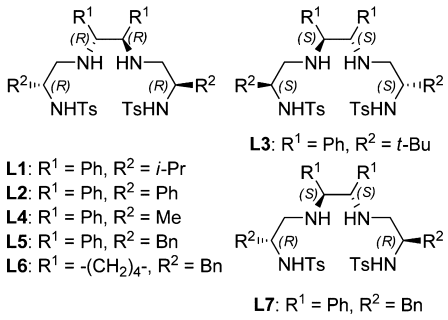
6a 7a 8a

entry	ligand	X in CuX_2	solvent	yield (%)	ee (%)[b]
1	**L1**	OTf	EtOH	90	60
2	**L1**	ClO_4	EtOH	96	38
3	**L2**	OTf	EtOH	73	0
4	**L3**	OTf	EtOH	97	13 (−)
5	**L4**	OTf	EtOH	98	69
6	**L5**	OTf	EtOH	95	82
7	**L6**	OTf	EtOH	89	0
8	**L7**	OTf	EtOH	99	30
9	**L5**	OTf	MeOH	86	59
10	**L5**	OTf	^{i}PrOH	99	77
11	**L5**	OTf	^{n}PrOH	99	86
12	**L5**	OTf	^{n}BuOH	99	83
13	**L5**	OTf	^{i}BuOH	98	89
14	**L5**	OTf	^{t}BuOH	97	78
15[c]	**L5**	OTf	^{i}BuOH	99	92
16[c,d]	**L5**	OTf	^{i}BuOH	98	95

[a]Unless otherwise noted, all reactions were performed with indole **6a** (0.25 mmol) and benzylidene malonate **7a** (0.3 mmol) with 5 mol % catalyst {CuX_2 (5 mol %), ligand (5 mol %)} in 1 mL of solvent for 6−12 h. [b]Determined by chiral HPLC analysis. [c]The reaction was performed at 0 °C. [d]The reaction was performed when the ligand/metal ratio was 1.1/1.0.

different copper salts revealed that only $Cu(OTf)_2$ and $Cu(ClO_4)_2·6H_2O$ promoted the reaction with promising results in the presence of bis-sulfonamide diamine ligand **L1** (Scheme 2) derived from (1*R*,2*R*)-1,2-diphenylethylenediamine. Cu-

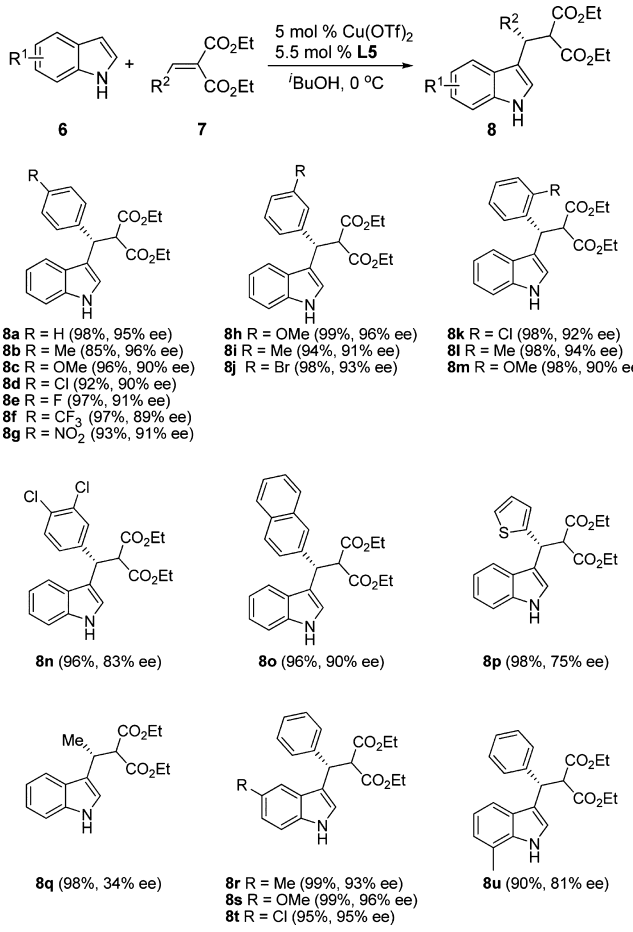
Scheme 2. Bis(sulfonamide)-diamine Ligands



$(OTf)_2$ displayed greater competence in comparison to $Cu(ClO_4)_2·6H_2O$ providing the desired product in 90% yield with 60% ee (Table 1, entries 1 and 2). Further optimization of the reaction condition by focusing on screening the structure of bis-sulfonamide diamine ligands indicated that different substituents R^1 and R^2 of the bis-sulfonamide diamine ligand had a dramatic effect on both the reactivity and enantioselectivity of this transformation (Table 1, entries 3−6). To our disappointment, when ligand **L2** with R^2 as a phenyl group was used which showed the best performance in previous work with the asymmetic Friedel−Crafts addition of indole to nitroalkenes, only a racemic product was obtained in 73% yield (Table 1, entry 3). Better results were observed when substituent R^2 was an alkyl group (Table 1, entries 1, 4, 5, 6). Fortuitously, significant enhancement of the enantioselectivity was obtained when substituent R^2 as a benzyl group was employed, providing the desired product in 95% yield with 82% ee (Table 1, entry 6). Sequential investigation on modifying the substituent R^1 group indicated that the ligand containing (1*R*,2*R*)-cyclohexane-1,2-diamine moiety or (1*S*,2*S*)-1,2-diphenylethylenediamine moiety showed poor induction on the level of enantioselectivity (Table 1, entries 7 and 8). An evaluation of solvent effects showed that alcohol was a more appropriate solvent, with isobutyl alcohol as the best choice (Table 1, entry 13). Subsequently, decreasing the temperature to 0 °C slightly improved the enantioselectivity (Table 1, entry 15). Further improvement of the enantioselectivity was observed when the ligand/metal ratio was meticulously tuned to 1.1/1.0 (Table 1, entry 16).

With the optimized reaction conditions established, we next sought to explore the generality of this transformation. Various structurally different arylidene malonates and indoles were evaluated (Table 2). Both the electronic property and steric hindrance on arylidene malonate were tolerated (Table 2,

Table 2. Cu-Catalyzed Asymmetric Friedel−Crafts Alkylation of Indoles 6 with Various Arylidiene Malonates 7[a−c]



[a]Unless otherwise noted, all reactions were performed with indole **6** (0.25 mmol) and aryldiene malonate **7** (0.3 mmol) with 5 mol % $Cu(OTf)_2$, and 5.5 mol % **L5** in 1 mL of solvent at 0 °C. [b]Determined by chiral HPLC analysis. [c]Determined to be S by comparison of optical rotation with that in ref 5a.

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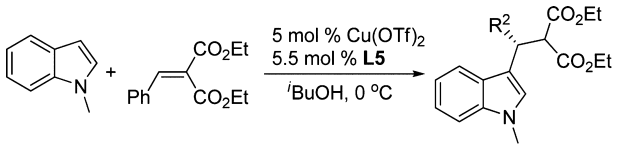
entries **8a**–**8m**). The reaction proceeded smoothly and afforded the corresponding products in excellent yields and enantioselectivities, regardless of the presence of electron-withdrawing or -donating groups on the *para*- (Table 2, **8b**–**8g**), *meta*- (Table 2, **8h**–**8j**), or *ortho*-position (Table 2, **8k**–**8m**) of the phenyl ring in arylidene malonate. In addition, disubstituted, condensed-ring, and heterocyclic arylidene malonates also served as competent substrates for this transformation albeit with slightly lower enantioselectivities (Table 2, **8n**–**8p**). Unfortunately, when ethylidene malonate was employed, the reaction proceeded in 98% yield with only 34% ee (Table 2, **8q**). Meanwhile, the substituents on the indolyl scaffold were investigated. High yields and enantioselectivities were achieved in the case of indoles containing electron-withdrawing or -donating groups at the 5, 6, or 7 position (Table 2, **8r**–**8u**).

To elucidate the mechanism and clarify the observed sense of asymmetric induction, we attempted to cultivate the single crystal of the bis-sulfonamide diamine ligand **L5**/Cu(II) complex in various solvents but failed. Fortunately, we examined the composition of the catalyst by ESI-MS and found that the MS peak at 998.2078 could be assigned as [**L5**-Cu(OTf)]$^+$ (m/z calculated for $[C_{47}H_{50}N_4O_7S_3CuF_3]^+$: 998.2084 (see Supporting Information). Subsequently, a control experiment with *N*-methyl indole and benzylidene malonate **7a** was conducted under the optimal reaction conditions to produce the corresponding product **8v** in 95% yield with only 64% ee (Scheme 3), which indicated that the

Scheme 3. Control Experiment of *N*-Methyl Indole with Benzylidene Malonate



8v 95% yield, 64% ee

indolic proton plays a vital role in the enantioselectivity. In addition, screening of the ligands showed that the (1*R*,2*R*)-1,2-diphenylethylenediamine moiety is indispensible in achieving an excellent yield and enantioselectivity, while a ligand containing the (1*R*,2*R*)-cyclohexane-1,2-diamine moiety only provided a racemic product (Table 1, entry 7). Notably, the phenyl group as substituent R^2 also gave a racemic product (Table 1, entry 3). In contrast, the *i*-Pr (**L1**, 60% ee), Me (**L4**, 69% ee), Bn (**L5**, 82% ee), or even *t*-Bu (**L3**, 13% ee) group as substituent R^2 all showed the ability to induce enantioselectivity (Table 1, entries 1, 4, 5, and 6). These results revealed that the additional sp^3 carbon in the R^2 group directly connected to the backbone of the ligand greatly impacted the enantioselectivity. Meanwhile, the benzyl group was the optimal R^2 substituent and arylidene malonates were more suitable substrates, which might suggest that a π–π stacking existed between the aryl group of arylidene malonate and the benzyl group R^2 of **L5**. Furthermore, it is noteworthy that the optimal solvent, isobutyl alcohol, not only accelerated the reaction but also increased the enatioselectivities.[12] Tang's group[4c] proved that alcohol was involved in the H-transfer step of the catalytic circle to acceletate the reaction and coordinated to the copper center in the active transition state. We presume that alcohol plays the same role in this transformation.

Based on the above results and analysis, a plausible working model was proposed, as shown in Figure 1. We envision that

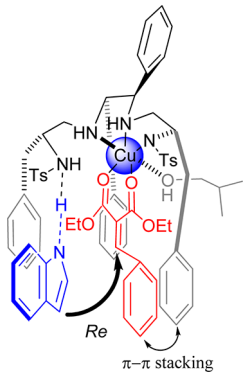
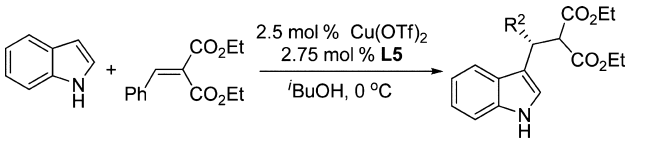


Figure 1. Proposed transition state model of catalyst **L5**-Cu(OTf)$_2$.

catalyst **L5**-Cu(OTf)$_2$ acts in a bifunctional manner. A weak hydrogen bond is formed between the indolic proton and the nitrogen atom which is linked with the tosyl substituent. As a result, the ability of this nitrogen atom to coordinate with the Cu(II) center diminishes. A distorted octahedral geometry at the copper center[4c] is taken into consideration in which the remaining three nitrogen atoms of ligand **L5** take three coordinate positions, where one nitrogen atom is in an apical space and both carboxyl moieties of arylidene malonate occupy two equatorial positions with isobutyl alcohol coordinated in the another apical position. Arylidene malonate is activated by chelating to the Cu(II) center. In addition, the π–π stacking between the aryl group of arylidene malonate and the benzyl group R^2 of **L5** turned the arylidene malonate in a fixed position. One phenyl group of (1*R*,2*R*)-1,2-diphenylethylenediamine moiety shields the back portion of arylidene malonate, thus directing the indole to attack the *Re* face and provide the product with the configuration of *S*.

To further demonstrate the synthetic potential of this strategy, benzylidene malonate (5 mmol, 1.24g) underwent reaction under the optimal conditions with a lower catalyst loading (2.5 mol %). It is noteworthy that the product was obtained by simple filtration as a white solid in 90% yield with 98% ee (Scheme 4).

Scheme 4. Reaction Carried out on a Large Scale



5 mmol

1.64g, 90% yield, 98% ee

CONCLUSIONS

In summary, we have developed a highly efficient Cu-catalyzed asymmetric Friedel–Crafts alkylation reaction of indoles with arylidene malonates using simple, stable, and easily prepared bis-sulfonamide diamine ligands. Several substrates of arylidene malonates and indoles with various substituents were investigated, and the corresponding products were obtained in excellent yields and with high ee. Moreover, a gram scale experiment was performed. The excellent yield and ee from the simple process illustrated its practicality.

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EXPERIMENTAL SECTION

General Considerations. All reactions were carried out under an atmosphere of argon using standard Schlenk techniques, unless otherwise noted. ^{1}H and ^{13}C NMR spectra were recorded at 400 and 100 MHz respectively using $CDCl_3$ as the solvent. Tetramethylsilane (δ = 0) or $CDCl_3$ (δ = 7.27) serves as the internal standard for ^{1}H NMR, and $CDCl_3$ (77.16 ppm), for ^{13}C NMR. Coupling constants (J) are reported in Hz and refer to apparent peak multiplications. The abbreviations *s*, *d*, *t*, *q*, and *m* stand for singlet, doublet, triplet, quartet, and multiplet in that order. Optical rotations were measured with MCP 200. HRMS data were obtained with an HPLC-Q-TOF mass spectrometer. Flash column chromatography was performed on silica gel (300−400 mesh). TLC analysis was performed using silica gel GF254 and visualized by fluorescence quenching under UV light. The enantiomeric excesses were determined by HPLC analysis with chiral HPLC columns (Chiralcel AD-H, OJ-H, OD-H, and AS-H).

Commercially available reagents were used throughout without further purification. All solvents were purified according to the standard procedures.

General Procedure for the Asymmetric Friedel−Crafts Alkylation Reaction. Under an argon atmosphere, the bis-(sulfonamide)-diamine ligand (10.8 mg, 0.0138 mmol, 5.5 mol %) and $Cu(OTf)_2$ (4.5 mg, 0.0125 mmol, 5 mol %) were dissolved in *i*-BuOH (1 mL), and the mixture was stirred at room temperature in a 25 mL Schlenk tube for 2 h to give the catalyst. After being placed in a freezer at a temperature of 0 °C, this mixture was added to aryldiene malonate (0.3 mmol, 1.2 equiv). After the mixture was stirred for 15 min, indole was added (0.25 mmol, 1.0 equiv). The reaction was stirred at 0 °C and monitored by TLC. When the reaction was finished (∼2−12 h), the solvent was evaporated under reduced pressure. The crude residue was purified by column chromatography (CH_2Cl_2/petroleum ether = 1:1) to afford the desired product.

*(S)-Ethyl 2-Ethoxycarbonyl-3-(3-indolyl)-3-phenyl Propanoate (**8a**).*[5a] By following the general procedure, the compound was obtained as a white solid: 90 mg, 98% yield, and 95% ee; $[\alpha]^{20}_D$ = +63.4 (*c* 1.0, CH_2Cl_2); [lit.:[5a] $[\alpha]^{25}_D$ = +65.4 (*c* 1.0, CH_2Cl_2) for 99% ee]; R_f = 0.3 (petroleum ether/EtOAc = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.55 (d, *J* = 7.9 Hz, 1H), 7.37 (d, *J* = 7.5 Hz, 2H), 7.29 (d, *J* = 8.1 Hz, 1H), 7.23 (t, *J* = 7.6 Hz, 2H), 7.19−7.09 (m, 3H), 7.03 (t, *J* = 7.5 Hz, 1H), 5.08 (d, *J* = 11.8 Hz, 1H), 4.29 (d, *J* = 11.8 Hz, 1H), 4.05−3.93 (m, 4H), 1.00 (q, *J* = 7.3 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.2, 168.0, 141.5, 136.3, 128.5, 128.3, 126.9, 122.4, 121.0, 119.7, 119.6, 117.2, 111.1, 61.6, 61.5, 58.5, 43.0, 13.91, 13.88. HPLC: Chiralcel OD-H column, hexanes/*i*-PrOH = 88/12, UV = 254 nm, flow rate = 1.0 mL/min, t_1 = 12.5 min (maj.), t_2 = 14.9 min.

*(S)-Ethyl 2-Ethoxycarbonyl-3-(3-indolyl)-3-(p-methylphenyl) Propanoate (**8b**).*[5a] By following the general procedure, the compound was obtained as a white solid: 95 mg, white solid in 85% yield and 96% ee; $[\alpha]^{20}_D$ = +52.5 (*c* 0.8, CH_2Cl_2); [lit.:[5a] $[\alpha]^{25}_D$ = +26.7 (c 0.5, CH_2Cl_2) for 94% ee]; R_f = 0.35 (petroleum ether/EtOAc = 8/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.55 (d, *J* = 7.9 Hz, 1H), 7.24 (d, *J* = 7.9 Hz, 3H), 7.12−7.08 (m, 2H), 7.03−7.00 (m, 3H), 5.04 (d, *J* = 11.8 Hz, 1H), 4.28 (d, *J* = 11.8 Hz, 1H), 4.02−3.95 (m, 4H), 2.23 (s, 3H), 1.03 (t, *J* = 7.1 Hz, 3H), 0.96 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.3, 168.1, 138.5, 136.3, 136.3, 129.1, 128.1, 126.88, 122.2, 121.0, 119.5, 119.5, 117.1, 111.1, 61.54, 61.51, 58.5, 42.6, 21.1, 13.9, 13.8. HPLC: Chiralcel OD-H column, hexanes/*i*-PrOH = 90/10, UV = 254 nm, flow rate = 0.5 mL/min, t_1 = 33.9 min, t_2 = 36.4 min (maj.).

*(S)-Ethyl 2-Ethoxycarbonyl-3-(3-indolyl)-3-(p-methoxylphenyl) Propanoate (**8c**).*[5b] By following the general procedure, the compound was obtained as a white solid: 95 mg, 96% yield, and 90% ee; $[\alpha]^{20}_D$ = +67.0 (*c* 1.0, CH_2Cl_2); [lit.:[5b] $[\alpha]^{25}_D$ = +53.3 (*c* 1.0, CH_2Cl_2) for 84% ee]; R_f = 0.22 (petroleum ether/EtOAc = 8/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.52 (d, *J* = 7.9 Hz, 1H), 7.27 (d, *J* = 7.7 Hz, 3H), 7.17−7.07 (m, 2H), 7.02 (t, *J* = 7.4 Hz, 1H), 6.76 (d, *J* = 7.3 Hz, 2H), 5.03 (d, *J* = 11.7 Hz, 1H), 4.24 (d, *J* = 11.7 Hz, 1H), 4.00 (q, *J* = 7.0 Hz, 4H), 3.72 (s, 3H), 1.04 (t, *J* = 7.1 Hz, 3H), 0.98 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.2, 168.0, 158.4, 136.4, 133.7, 129.3, 126.8, 122.3, 120.8, 119.59, 119.57, 117.4, 113.8, 111.1, 110.1, 61.6, 61.5, 58.7, 55.3, 42.2, 14.0, 13.9. HPLC: Chiralcel OD-H column, hexanes/*i*-PrOH = 88/12, UV = 254 nm, flow rate = 0.9 mL/min, t_1 = 17.7 min, t_2 = 21.0 min (maj.).

*(S)-Ethyl 2-Ethoxycarbonyl-3-(3-indolyl)-3-(p-chlorophenyl) Propanoate (**8d**).*[5a] By following the general procedure, the compound was obtained as a white solid: 93 mg, 92% yield, and 90% ee; $[\alpha]^{20}_D$ = +44.7 (*c* 1.0, CH_2Cl_2); [lit.:[5a] $[\alpha]^{25}_D$ = +48.2 (*c* 1.0, CH_2Cl_2) for 98% ee]; R_f = 0.31 (petroleum ether/EtOAc = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.48 (d, *J* = 7.8 Hz, 1H), 7.30−7.27 (m, 3H), 7.20−7.18 (m, 2H), 7.13−7.11 (m, 2H), 7.03 (t, *J* = 7.4 Hz, 1H), 5.06 (d, *J* = 11.7 Hz, 1H), 4.25 (d, *J* = 11.7 Hz, 1H), 4.08−3.93 (m, 4H), 1.05 (t, *J* = 7.0 Hz, 3H), 0.98 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.0, 167.8, 140.1, 136.4, 132.6, 129.7, 128.6, 126.6, 122.5, 121.0, 119.8, 119.3, 116.6, 111.2, 61.7, 58.3, 42.3, 14.0, 13.9. HPLC: Chiralcel OD-H column, hexanes/*i*-PrOH = 88/12, UV = 254 nm, flow rate = 0.5 mL/min, t_1 = 20.1 min, t_2 = 21.9 min (maj.).

*(S)-Ethyl 2-ethoxycarbonyl-3-(3-indolyl)-3-(p-fluorophenyl) Propanoate (**8e**).*[6c] By following the general procedure, the compound was obtained as a white solid: 93 mg, 97% yield, and 91% ee; $[\alpha]^{20}_D$ = +79.9 (*c* 1.0, CH_2Cl_2); [lit.:[6c] $[\alpha]^{25}_D$ = −77.3 (*c* 0.2, CH_2Cl_2) for 83% ee]; R_f = 0.29 (petroleum ether/EtOAc = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.49 (d, *J* = 7.8 Hz, 1H), 7.37−7.27 (m, 3H), 7.21−7.09 (m, 2H), 7.03 (t, *J* = 7.0 Hz, 1H), 6.92 (t, *J* = 7.9 Hz, 2H), 5.07 (d, *J* = 11.6 Hz, 1H), 4.23 (d, *J* = 11.6 Hz, 1H), 4.04−3.97 (m, 4H), 1.09−0.96 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.0, 167.9, 161.8 (d, J_{C-F} = 245.4 Hz), 137.3 (d, J_{C-F} = 3.3 Hz), 136.4, 129.9 (d, J_{C-F} = 8.0 Hz), 126.7, 122.5, 120.9, 119.7, 119.4, 117.0, 115.3 (d, J_{C-F} = 21.3 Hz), 111.2, 61.7, 61.6, 58.6, 42.3, 14.0, 13.9. HPLC: Chiralcel AS-H column, hexanes/*i*-PrOH = 90/10, UV = 254 nm, flow rate = 1.0 mL/min, t_1 = 19.1 min (maj.), t_2 = 27.8 min.

*(S)-Ethyl 2-Ethoxycarbonyl-3-(3-indolyl)-3-(p-trifluoromethyl-phenyl) Propanoate (**8f**).*[5b] By following the general procedure, the compound was obtained as a white solid: 105 mg, 97% yield, and 89% ee; $[\alpha]^{20}_D$ = +45.1 (*c* 1.0, CH_2Cl_2); [lit.:[5b] $[\alpha]^{25}_D$ = +15.2 (*c* 0.5, CH_2Cl_2) for 90% ee]; R_f = 0.37 (petroleum ether/EtOAc = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (s, 1H), 7.49−7.45 (m, 5H), 7.31−7.29 (m, 1H), 7.19−7.13 (m, 2H), 7.05−7.03 (m, 1H), 5.15 (d, *J* = 11.5 Hz, 1H), 4.30 (d, *J* = 11.6 Hz, 1H), 4.00−3.99 (m, 4H), 1.01−0.99 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.8, 167.7, 145.8, 136.4, 129.0, 128.7, 126.5, 125.5 (q, J_{C-F} = 4.0 Hz), 122.7, 121.2, 112.0, 119.2, 116.2, 111.3, 61.80, 61.77, 58.05, 42.70, 13.86. HPLC: Chiralcel OJ-H column, Hexanes/*i*-PrOH = 90/10, UV = 254 nm, flow rate = 1.0 mL/min, t_1 = 21.3 min, t_2 = 27.1 min (maj.).

*(S)-Ethyl 2-Ethoxycarbonyl-3-(3-indolyl)-3-(p-nitrophenyl) Propanoate (**8g**).*[5b] By following the general procedure, the compound was obtained as a yellow solid: 95 mg, 93% yield, and 91% ee; $[\alpha]^{20}_D$ = +9.3 (*c* 1.0, CH_2Cl_2); [lit.:[5b] $[\alpha]^{25}_D$ = +6.9 (*c* 1.0, CH_2Cl_2) for 80% ee]; R_f = 0.26 (petroleum ether/EtOAc = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (s, 1H), 8.10 (d, *J* = 8.7 Hz, 2H), 7.55 (d, *J* = 8.7 Hz, 2H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.32 (d, *J* = 8.2 Hz, 1H), 7.22 (d, *J* = 2.3 Hz, 1H), 7.16 (t, *J* = 7.3 Hz, 1H), 7.05 (t, *J* = 7.3 Hz, 1H), 5.20 (d, *J* = 11.6 Hz, 1H), 4.32 (d, *J* = 11.6 Hz, 1H), 4.07−3.99 (m, 4H), 1.07 (t, *J* = 7.1 Hz, 3H), 1.01 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.6, 167.5, 149.4, 146.8, 136.3, 129.3, 126.4, 123.8, 122.8, 121.3, 120.1, 119.0, 115.5, 111.4, 61.9, 57.8, 42.6, 14.0, 13.9. HPLC: Chiralcel AS-H column, hexanes/*i*-PrOH = 90/10, UV = 254 nm, flow rate = 1.0 mL/min, t_1 = 33.4 min (maj.), t_2 = 49.3 min.

*(S)-Ethyl 2-Ethoxycarbonyl-3-(3-indolyl)-3-(m-methoxylphenyl) Propanoate (**8h**).*[7a] By following the general procedure, the compound was obtained as a white solid: 98 mg, 99% yield, and 96% ee; $[\alpha]^{20}_D$ = +52.5 (*c* 0.8, CH_2Cl_2); [lit.:[7a] $[\alpha]^{27}_D$ = −49.6 (*c* 0.222, CH_2Cl_2) for 92% ee]; R_f = 0.26 (petroleum ether/EtOAc = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.57 (d, *J* = 7.9 Hz, 1H), 7.25 (d, *J* = 8.3 Hz, 1H), 7.17−7.06 (m, 3H), 7.02 (t, *J* = 7.4 Hz, 1H), 6.96 (d, *J* = 7.7 Hz, 1H), 6.91 (s, 1H), 6.67 (dd, *J* = 8.1, 2.1 Hz, 1H), 5.05 (d, *J* = 11.9 Hz, 1H), 4.29 (d, *J* = 11.9 Hz, 1H), 4.03−3.94 (m, 4H), 3.71 (s, 3H), 1.03 (t, *J* = 7.1 Hz, 3H), 0.95 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.3, 168.1, 159.7, 143.3, 136.4, 129.5, 126.9, 122.4, 121.2, 120.8, 119.7, 119.5, 116.9, 114.4,

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112.1, 111.3, 61.68, 61.65, 58.5, 55.3, 43.0, 14.0, 13.9. HPLC: Chiralcel OD-H column, Hexanes/*i*-PrOH = 90/10, UV = 254 nm, flow rate = 1.0 mL/min, t_1 = 21.6 min, t_2 = 28.1 min (maj.).

*(S)-Ethyl 2-Ethoxycarbonyl-3-(3-indolyl)-3-(m-methylphenyl) Propanoate (**8i**).*[7a] By following the general procedure, the compound was obtained as a white solid: 89 mg, 94% yield, and 91% ee; $[\alpha]^{20}_D$ = +53.1 (*c* 0.8, CH_2Cl_2); [lit.:[7a] $[\alpha]^{26}_D$ = −60.5 (*c* 0.2, CH_2Cl_2) for 90% ee]; R_f = 0.29 (petroleum ether/EtOAc = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.57 (d, *J* = 7.9 Hz, 1H), 7.26 (d, *J* = 8.1 Hz, 1H), 7.20−7.07 (m, 5H), 7.03 (t, *J* = 7.5 Hz, 1H), 6.94 (d, *J* = 7.3 Hz, 1H), 5.04 (d, *J* = 11.9 Hz, 1H), 4.29 (d, *J* = 11.9 Hz, 1H), 4.03−3.93 (m, 4H), 2.25 (s, 3H), 1.01 (t, *J* = 7.1 Hz, 3H), 0.96 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.0, 167.8, 141.2, 137.6, 136.0, 128.8, 128.0, 127.3, 126.6, 124.9, 122.0, 120.8, 119.3, 119.2, 116.8, 110.8, 61.3, 61.2, 58.3, 42.6, 21.3, 13.6, 13.6. HPLC: Chiralcel AS-H column, Hexanes/*i*-PrOH = 90/10, UV = 254 nm, flow rate = 1.0 mL/min, t_1 = 17.8 min (maj.), t_2 = 19.9 min.

*(S)-Ethyl 2-Ethoxycarbonyl-3-(3-indolyl)-3-(m-bromophenyl) Propanoate (**8j**).*[6a] By following the general procedure, the compound was obtained as a white solid: 109 mg, 98% yield, and 93% ee; $[\alpha]^{20}_D$ = +55.7 (*c* 1.0, CH_2Cl_2); [lit.:[7a] $[\alpha]^{25}_D$ = +24.0 (*c* 0.2, CH_2Cl_2) for 99% ee]; R_f = 0.37 (petroleum ether/EtOAc = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.56−7.44 (m, 2H), 7.35−7.21 (m, 3H), 7.18−7.00 (m, 4H), 5.04 (d, *J* = 11.7 Hz, 1H), 4.25 (d, *J* = 11.7 Hz, 1H), 4.09−3.91 (m, 4H), 1.07−0.96 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 167.8, 144.0, 136.3, 131.4, 130.0, 127.1, 126.6, 122.5, 122.5, 121.2, 119.8, 119.3, 116.3, 111.3, 61.7, 58.2, 42.6, 13.94, 13.85. HPLC: Chiralcel OD-H column, Hexanes/*i*-PrOH = 88/12, UV = 254 nm, flow rate = 0.9 mL/min, t_1 = 12.0 min, t_2 = 15.1 min (maj.).

*(S)-Ethyl 2-Ethoxycarbonyl-3-(3-indolyl)-3-(o-chlorophenyl) Propanoate (**8k**).*[7a] By following the general procedure, the compound was obtained as an oil: 99 mg, 99% yield, and 92% ee; $[\alpha]^{20}_D$ = +51.6 (*c* 0.8, CH_2Cl_2); [lit.:[7a] $[\alpha]^{25}_D$ = +22.6 (*c* 0.5, CH_2Cl_2) for 90% ee]; R_f = 0.26 (petroleum ether/EtOAc = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.68 (d, *J* = 7.9 Hz, 1H), 7.39 (d, *J* = 7.7 Hz, 1H), 7.31 (d, *J* = 7.9 Hz, 1H), 7.25 (d, *J* = 8.1 Hz, 1H), 7.18−6.99 (m, 5H), 5.66 (d, *J* = 11.7 Hz, 1H), 4.40 (d, *J* = 11.7 Hz, 1H), 4.07−3.88 (m, 4H), 1.02 (t, *J* = 7.1 Hz, 3H), 0.94 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.0, 167.7, 139.2, 136.1, 134.1, 130.0, 129.1, 127.9, 127.0, 126.8, 122.3, 122.1, 119.7, 119.6, 115.8, 111.2, 61.7, 61.6, 57.7, 38.7, 13.83, 13.79. HPLC: Chiralcel OD-H column, Hexanes/*i*-PrOH = 90/10, UV = 254 nm, flow rate = 1.0 mL/min, t_1 = 15.8 min, t_2 = 23.9 min (maj.).

*(S)-Ethyl 2-Ethoxycarbonyl-3-(3-indolyl)-3-(o-methylphenyl) Propanoate (**8l**).*[6b] By following the general procedure, the compound was obtained as a white solid: 95 mg, 98% yield, and 94% ee; $[\alpha]^{20}_D$ = −51.9 (*c* 0.8, CH_2Cl_2); [lit.:[6b] $[\alpha]^{25}_D$ = +11.2 (*c* 0.2, CH_2Cl_2) for 90% ee]; R_f = 0.43 (petroleum ether/EtOAc = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.61 (d, *J* = 7.9 Hz, 1H), 7.36 (d, *J* = 7.6 Hz, 1H), 7.26−7.21 (m, 1H), 7.17−7.01 (m, 5H), 6.95 (d, *J* = 2.4 Hz, 1H), 5.32 (d, *J* = 11.8 Hz, 1H), 4.34 (d, *J* = 11.8 Hz, 1H), 3.98 (q, *J* = 7.1 Hz, 2H), 3.88 (q, *J* = 7.1 Hz, 2H), 2.45 (s, 3H), 0.99 (t, *J* = 7.1 Hz, 3H), 0.89 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 168.0, 140.2, 136.4, 136.1, 130.8, 126.8, 126.6, 126.4, 126.1, 122.5, 122.1, 119.6, 119.4, 116.5, 111.1, 61.6, 61.5, 58.6, 38.1, 20.1, 13.8, 13.7. HPLC: Chiralcel OD-H column, hexanes/*i*-PrOH = 90/10, UV = 254 nm, flow rate = 0.8 mL/min, t_1 = 11.6 min, t_2 = 14.2 min (maj.).

*(S)-Ethyl 2-Ethoxycarbonyl-3-(3-indolyl)-3-(o-methoxylphenyl) Propanoate (**8m**).* Unknown compound; by following the general procedure, the compound was obtained as a white solid: 97 mg, 98% yield, and 90% ee; $[\alpha]^{20}_D$ = +22.9 (*c* 0.8, CH_2Cl_2); R_f = 0.29 (petroleum ether/EtOAc = 4/1); mp 94−96 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.68 (d, *J* = 7.8 Hz, 1H), 7.31 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.23 (d, *J* = 8.1 Hz, 1H), 7.16 (d, *J* = 2.3 Hz, 1H), 7.12−7.02 (m, 3H), 6.86−6.76 (m, 2H), 5.47 (d, *J* = 11.8 Hz, 1H), 4.55 (d, *J* = 11.8 Hz, 1H), 3.98−3.91 (m, 4H), 3.81 (s, 3H), 0.98 (t, *J* = 7.1 Hz, 3H), 0.92 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.6, 168.3, 157.2, 135.9, 129.9, 129.1, 127.9, 127.2, 121.9, 120.6, 119.5, 119.3, 116.5, 111.04, 110.98, 61.4, 61.3, 57.0, 55.5, 36.8, 13.9, 13.8. HPLC: Chiralcel OD-H column, hexanes/*i*-PrOH = 90/10, UV = 254 nm, flow rate = 0.8 mL/min, t_1 = 15.9 min, t_2 = 23.0 min (maj.); HRMS (ESI, *m*/*z*) Calculated for $[C_{23}H_{25}NO_5 + Na]^+$ 418.1630, found 418.1642.

*(S)-Ethyl 2-Ethoxycarbonyl-3-(3-indolyl)-3-(3,4-dichlorophenyl) Propanoate (**8n**).*[7a] By following the general procedure, the compound was obtained as a white solid: 104 mg, 96% yield, and 83% ee; $[\alpha]^{20}_D$ = +40.0 (*c* 0.8, CH_2Cl_2); [lit.:[7a] $[\alpha]^{25}_D$ = −42.8 (*c* 0.208, CH_2Cl_2) for 83% ee]; R_f = 0.34 (petroleum ether/EtOAc = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.45 (d, *J* = 1.9 Hz, 1H), 7.31 (dd, *J* = 8.2, 2.9 Hz, 2H), 7.22 (dd, *J* = 8.3, 2.0 Hz, 1H), 7.19−7.13 (m, 2H), 7.06 (t, *J* = 7.4 Hz, 1H), 5.05 (d, *J* = 11.6 Hz, 1H), 4.24 (d, *J* = 11.6 Hz, 1H), 4.08−3.99 (m, 4H), 1.10 (t, *J* = 7.1 Hz, 3H), 1.00 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.7, 167.6, 142.0, 136.3, 132.4, 130.9, 130.4, 130.3, 127.9, 126.4, 122.7, 121.1, 120.0, 119.2, 115.9, 111.3, 110.1, 61.9, 61.8, 58.0, 42.0, 14.0, 13.9. HPLC: Chiralcel AS-H column, hexanes/*i*-PrOH = 95/5, UV = 254 nm, flow rate = 1.0 mL/min, t_1 = 33.5 min (maj.), t_2 = 39.0 min.

*(S)-Ethyl 2-Ethoxycarbonyl-3-(3-indolyl)-3-(2-naphthyl) Propanoate (**8o**).*[7a] By following the general procedure, the compound was obtained as a white solid: 100 mg, 96% yield, and 90% ee; $[\alpha]^{20}_D$ = +45.5 (*c* 0.8, CH_2Cl_2); [lit.:[7a] $[\alpha]^{25}_D$ = −38.4 (*c* 0.320, CH_2Cl_2) for 80% ee]; R_f = 0.14 (petroleum ether/EtOAc = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.86 (s, 1H), 7.81−7.67 (m, 3H), 7.58 (d, *J* = 7.9 Hz, 1H), 7.49−7.36 (m, 3H), 7.28 (d, *J* = 8.1 Hz, 1H), 7.23 (s, 1H), 7.12 (t, *J* = 7.5 Hz, 1H), 7.01 (t, *J* = 7.5 Hz, 1H), 5.27 (d, *J* = 11.8 Hz, 1H), 4.42 (d, *J* = 11.8 Hz, 1H), 4.02 (q, *J* = 7.1 Hz, 2H), 3.98−3.89 (m, 2H), 1.01 (t, *J* = 7.1 Hz, 3H), 0.92 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.2, 168.0, 139.0, 136.3, 133.5, 132.6, 128.2, 128.0, 127.7, 126.9, 126.69, 126.66, 126.1, 125.7, 122.4, 121.2, 119.7, 119.5, 117.0, 111.1, 61.7, 61.6, 58.4, 43.0, 13.90, 13.87. HPLC: Chiralcel AD-H column, hexanes/*i*-PrOH = 80/20, UV = 254 nm, flow rate = 1.0 mL/min, t_1 = 20.8 min (maj.), t_2 = 22.9 min.

*(S)-Ethyl 2-Ethoxycarbonyl-3-(3-indolyl)-3-(2-thienyl) Propanoate (**8p**).*[6a] By following the general procedure, the compound was obtained as a white solid: 91 mg, 98% yield, and 75% ee; $[\alpha]^{20}_D$ = +51.1 (*c* 1.0, CH_2Cl_2); [lit.:[6a] $[\alpha]^{25}_D$ = +62.0 (*c* 0.25, CH_2Cl_2) for 99% ee]; R_f = 0.34 (petroleum ether/EtOAc = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.63 (d, *J* = 7.9 Hz, 1H), 7.31 (d, *J* = 8.1 Hz, 1H), 7.19−7.12 (m, 2H), 7.12−7.04 (m, 2H), 6.99 (d, *J* = 3.2 Hz, 1H), 6.87−6.85 (m, 1H), 5.40 (d, *J* = 11.4 Hz, 1H), 4.32 (d, *J* = 11.4 Hz, 1H), 4.17−4.06 (m, 2H), 3.94 (q, *J* = 7.1 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 167.6, 145.9, 136.3, 126.5, 126.5, 125.2, 124.4, 122.4, 121.7, 119.8, 119.5, 116.6, 111.2, 61.8, 61.6, 59.5, 38.1, 14.0, 13.7. HPLC: Chiralcel OD-H column, hexanes/*i*-PrOH = 95/5, UV = 254 nm, flow rate = 1.0 mL/min, t_1 = 30.5 min, t_2 = 33.2 min (maj.).

*(S)-Ethyl 2-Ethoxycarbonyl-3-(3-indolyl)-3-methylpropanoate (**8q**).*[6a] By following the general procedure, the compound was obtained as a colorless oil: 74 mg, 98% yield, and 34% ee; $[\alpha]^{20}_D$ = −1.0 (*c* 1.1, CH_2Cl_2); [lit.:[6a] $[\alpha]^{25}_D$ = +1.5 (*c* 0.2, CH_2Cl_2) for 34% ee]; R_f = 0.34 (petroleum ether/EtOAc = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (s, 1H), 7.69 (d, *J* = 7.8 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.18 (t, *J* = 7.3 Hz, 1H), 7.12 (t, *J* = 7.4 Hz, 1H), 7.02 (d, *J* = 2.2 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.92 (q, *J* = 7.1 Hz, 3H), 3.83 (d, *J* = 9.9 Hz, 1H), 1.48 (d, *J* = 6.9 Hz, 3H), 1.28 (t, *J* = 7.1 Hz, 3H), 0.93 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.9, 168.7, 136.3, 126.4, 122.0, 121.6, 119.3, 119.3, 117.9, 111.3, 61.4, 61.2, 58.8, 31.8, 19.8, 14.2, 13.7. HPLC: Chiralcel OD-H column, Hexanes/*i*-PrOH = 90/10, UV = 254 nm, flow rate = 0.7 mL/min, t_1 = 14.3 min (maj.), t_2 = 16.4 min.

*(S)-Ethyl 2-Ethoxycarbonyl-3-[3-(5-methylindolyl)]-3-phenyl-propanoate (**8r**).*[6a] By following the general procedure, the compound was obtained as a white solid: 94 mg, 99% yield, and 93% ee; $[\alpha]^{20}_D$ = +36.0 (*c* 1.0, CH_2Cl_2); [lit.:[6a] $[\alpha]^{25}_D$ = +24.0 (*c* 0.5, CH_2Cl_2) for 97% ee]; R_f = 0.29 (petroleum ether/EtOAc = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (s, 1H), 7.34 (d, *J* = 7.7 Hz, 2H), 7.30 (s, 1H), 7.19 (t, *J* = 7.5 Hz, 2H), 7.16−7.07 (m, 3H), 6.91 (d, *J* = 8.3 Hz, 1H), 5.01 (d, *J* = 11.8 Hz, 1H), 4.24 (d, *J* = 11.8 Hz, 1H), 3.99−3.92 (m, 4H), 2.35 (s, 3H), 0.99−0.94 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.1, 168.0, 141.6, 134.6, 128.6, 128.4, 128.2, 127.0,

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126.7, 123.8, 121.1, 119.0, 116.4, 110.7, 61.5, 61.4, 58.6, 42.9, 21.6, 13.83, 13.80. HPLC: Chiralcel OD-H column, hexanes/*i*-PrOH = 85/15, UV = 254 nm, flow rate = 0.9 mL/min, t_1 = 10.9 min, t_2 = 13.1 min (maj.).

*(S)-Ethyl 2-Ethoxycarbonyl-3-[3-(5-methoxyindolyl)]-3-phenylpropanoate (**8s**).*[5a] By following the general procedure, the compound was obtained as a white solid: 98 mg, 99% yield, and 96% ee; $[\alpha]^{20}_D$ = +12.1 (*c* 1.0, CH_2Cl_2); [lit.:[5a] $[\alpha]^{25}_D$ = +11.3 (*c* 1.0, CH_2Cl_2) for 89% ee]; R_f = 0.29 (petroleum ether/EtOAc = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.36 (d, *J* = 7.4 Hz, 2H), 7.25−7.21 (m, 2H), 7.16−7.11 (m, 3H), 6.96 (d, *J* = 2.2 Hz, 1H), 6.78 (dd, *J* = 8.8, 2.3 Hz, 1H), 5.02 (d, *J* = 11.8 Hz, 1H), 4.26 (d, *J* = 11.8 Hz, 1H), 4.03−3.95 (m, 4H), 3.77 (s, 3H), 1.02−0.97 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.2, 168.0, 154.0, 141.5, 131.5, 128.5, 128.3, 127.2, 126.9, 121.7, 116.8, 112.6, 111.8, 101.3, 61.6, 61.5, 58.5, 55.9, 43.0, 13.9. HPLC: Chiralcel OD-H column, hexanes/*i*-PrOH = 85/15, UV = 254 nm, flow rate = 0.9 mL/min, t_1 = 14.9 min, t_2 = 18.2 min (maj.).

*(S)-Ethyl 2-Ethoxycarbonyl-3-[3-(7-chloroindolyl)]-3-phenylpropanoate (**8t**).*[6a] By following the general procedure, the compound was obtained as a white solid: 95 mg, 95% yield, and 95% ee; $[\alpha]^{20}_D$ = +47.8 (*c* 1.0, CH_2Cl_2); [lit.:[6a] $[\alpha]^{25}_D$ = +60.0 (*c* 0.25, CH_2Cl_2) for 98% ee]; R_f = 0.31 (petroleum ether/EtOAc = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.43 (d, *J* = 8.5 Hz, 1H), 7.33 (d, *J* = 7.5 Hz, 2H), 7.29−7.21 (m, 3H), 7.18−7.12 (m, 2H), 6.99 (dd, *J* = 8.5, 1.6 Hz, 1H), 5.03 (d, *J* = 11.8 Hz, 1H), 4.26 (d, *J* = 11.8 Hz, 1H), 4.04−3.95 (m, 4H), 1.00 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.1, 167.8, 141.2, 136.7, 128.5, 128.3, 128.2, 127.0, 125.4, 121.7, 120.4, 120.3, 117.3, 111.1, 61.7, 61.6, 58.4, 42.8, 13.9. HPLC: Chiralcel OD-H column, hexanes/*i*-PrOH = 88/12, UV = 254 nm, flow rate = 0.8 mL/min, t_1 = 11.2 min, t_2 = 13.1 min (maj.).

*(S)-Ethyl 2-Ethoxycarbonyl-3-[3-(7-methylindolyl)]-3-phenylpropanoate (**8u**).*[6b] By following the general procedure, the compound was obtained as a white solid: 92 mg, 97% yield, and 81% ee; $[\alpha]^{20}_D$ = +74.3 (*c* 0.8, CH_2Cl_2); [lit.:[6b] $[\alpha]^{25}_D$ = +23.5 (*c* 0.2, CH_2Cl_2) for 99% ee]; R_f = 0.57 (petroleum ether/EtOAc = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.40−7.35 (m, 3H), 7.27−7.06 (m, 4H), 7.00−6.87 (m, 2H), 5.07 (d, *J* = 11.9 Hz, 1H), 4.30 (d, *J* = 11.8 Hz, 1H), 4.04−3.94 (m, 4H), 2.40 (s, 3H), 1.00 (q, *J* = 7.2 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.2, 168.0, 141.6, 135.9, 128.4, 128.3, 126.8, 126.3, 122.9, 120.7, 120.2, 119.8, 117.6, 117.2, 61.6, 61.5, 58.5, 43.1, 16.6, 13.9. HPLC: Chiralcel OD-H column, hexanes/*i*-PrOH = 80/20, UV = 254 nm, flow rate = 0.6 mL/min, t_1 = 9.4 min, t_2 = 10.9 min (maj.).

*(S)-Ethyl 2-Ethoxycarbonyl-3-[3-(N-methylindolyl)]-3-phenylpropanoate (**8v**).*[7a] By following the general procedure, the compound was obtained as a white solid: 92 mg, 95% yield, and 64% ee; $[\alpha]^{20}_D$ = +47.0 (*c* 0.8, CH_2Cl_2); [lit.:[7a] $[\alpha]^{25}_D$ = +11.8 (*c* 0.25, CH_2Cl_2) for 45% ee]; R_f = 0.28 (petroleum ether/EtOAc = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.9 Hz, 1H), 7.36 (d, *J* = 7.4 Hz, 2H), 7.27−7.08 (m, 5H), 7.06−6.98 (m, 2H), 5.06 (d, *J* = 11.8 Hz, 1H), 4.27 (d, *J* = 11.8 Hz, 1H), 4.04−3.92 (m, 4H), 3.71 (s, 3H), 1.01−0.99 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.1, 168.0, 141.8, 137.1, 128.5, 128.3, 127.3, 126.8, 125.8, 121.9, 119.6, 119.1, 115.5, 109.2, 61.5, 61.5, 58.6, 43.0, 32.9, 13.90, 13.87. HPLC: Chiralcel OD-H column, hexanes/*i*-PrOH = 90/10, UV = 254 nm, flow rate = 1.0 mL/min, t_1 = 25.7 min (maj.), t_2 = 32.7 min.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H, ^{13}C spectra; HRMS spectra; copy of HPLC for racemic and chiral compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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