JOC The Journal of Organic Chemistry

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Enantioselective Friedel–Crafts Alkylation Reactions of 3-Substituted Indoles with Electron-Deficient Alkenes

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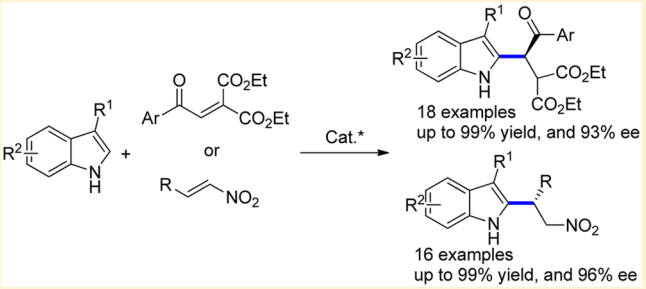
Supporting Information

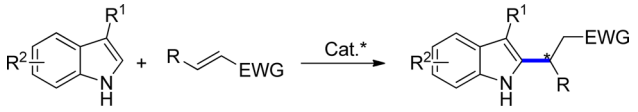
ABSTRACT: Highly enantioselective Friedel–Crafts C2-alkylation reactions of 3-substituted indoles with α,β-unsaturated esters and nitroalkenes were developed using chiral Lewis acids as catalysts, which afforded chiral indole derivatives bearing C2-benzylic stereogenic centers in good to excellent yields (up to 99%) and enantioselectivities (up to 96% ee).



Enantioselective Friedel–Crafts alkylation reaction represents one of the most significant approaches to the synthesis of chiral aromatic compounds bearing benzylic stereogenic centers.[1] In this research field, indoles have attracted considerable attention as popular aromatic substrates, and many efficient reactions have been developed to synthesize chiral indole derivatives.[2] However, most of the these transformations have predominantly focused on the C3-functionalization of indoles due to the higher nucleophilicity of the C3 position.[3] In contrast, the asymmetric Friedel–Crafts alkylation reactions occurring at the less reactive C2 position to deliver chiral indoles bearing C2-benzylic stereocenters have remained rarely exploited but are important structural motifs that frequently appear in numerous biologically active molecules and natural products.[4] Therefore, it is highly desirable to develop efficient an asymmetric Friedel–Crafts C2-alkylation reaction of indoles. For this purpose, the asymmetric Pictet–Spengler reaction of indoles has been well-established, while it was intrinsically limited to the intramolecular versions.[5] An indirect strategy has also been developed by incorporating asymmetric Friedel–Crafts alkylation of 4,7-dihydroindoles and a subsequent oxidation.[6] In comparison, the direct enantioselective C2-alkylation of 3-substituted indoles provides a promising access to C2-functionalized chiral indoles, while it still remains a challenge. To date, only β,γ-unsaturated α-ketoesters[7a−c] and β,γ-unsaturated α-ketimino esters[7d] were applied as alkylating agents for the C2-alkylation of 3-substituted indoles. Herein, we report the Friedel–Crafts C2-alkylation reactions of 3-substituted indoles with α,β-unsaturated esters and nitroalkenes as alkylating agents, which obtained C2-alkylated indoles in excellent enantioselectivities using chiral Lewis acid catalysts (Scheme 1).

Initially, we chose diethyl 2-benzylidenemalonate **2** as an alkylating agent to react with 3-methylindole **1a**. No reaction took place, and compound **2** remained inactive in the presence of a range of Lewis acid catalysts. Therefore, more active diethyl 2-(2-oxo-2-phenylethylidene)malonate **3a** was synthesized by introducing an additional carbonyl group and tested in the reaction with **1a** (Table 1). To our delight, the reaction between 3-methylindole **1a** and compound **3a** occurred smoothly in CH_2Cl_2 to afford the desired C2-alkylated product **4aa** in good yield by using $Cu(OTf)_2$ as a catalyst (entry 1). Moderate ee value and good yield were obtained when a chiral bisoxazoline ligand **L1** was introduced (entry 2). The reaction in THF led to excellent yield, while the enantioselectivity decreased to 21% (entry 3). Both yield and ee were decreased for the reaction in toluene (entry 4). Subsequent examination of chiral ligand revealed that (*S*)-^{i}Pr-bisoxazoline **L2** was the best choice, and product **4aa** was isolated in 99% yield and 93% ee (entry 5). Comparable results were obtained for ligand **L4** (entry 7), while moderate yield and ee value were afforded for ligand **L3** bearing a ^{t}Bu substituent (entry 6). Examination of other Lewis acids in the presence of ligand **L2** disclosed that moderate enantioselectivities were obtained for $Ni(OTf)_2$ and $Zn(OTf)_2$ in spite of the observed excellent yields (entries 8 and 9). $Mg(OTf)_2$ was also a suitable catalyst, but the yield and enantioselectivity were both lower (entry 10). Gratifyingly, both the yield and ee remained excellent when the reaction was performed at a lower catalyst loading (entry 11).

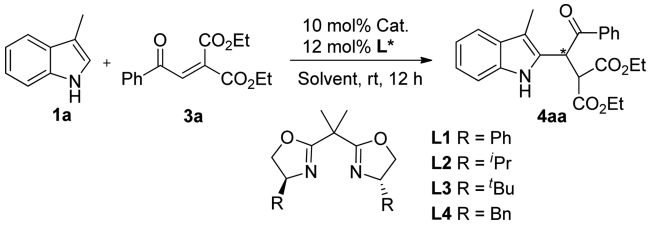
Scheme 1. Enantioselective Friedel–Crafts C2-Alkylation of 3-Substituted Indoles



Received: January 19, 2016
Published: March 9, 2016

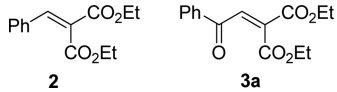
DOI: 10.1021/acs.joc.6b00123
J. Org. Chem. 2016, 81, 3023−3030

Table 1. Condition Optimization for the Reaction between 1a and 3a[a]



entry	cat.	L*	solvent	yield (%)[b]	ee (%)[c]
1[d]	$Cu(OTf)_2$		CH_2Cl_2	87	
2	$Cu(OTf)_2$	L1	CH_2Cl_2	86	48
3	$Cu(OTf)_2$	L1	THF	99	21
4	$Cu(OTf)_2$	L1	toluene	80	25
5	$Cu(OTf)_2$	L2	CH_2Cl_2	99	93
6	$Cu(OTf)_2$	L3	CH_2Cl_2	80	76
7	$Cu(OTf)_2$	L4	CH_2Cl_2	90	89
8	$Ni(OTf)_2$	L2	CH_2Cl_2	96	51
9	$Zn(OTf)_2$	L2	CH_2Cl_2	95	50
10	$Mg(OTf)_2$	L2	CH_2Cl_2	81	70
11[e]	$Cu(OTf)_2$	L2	CH_2Cl_2	96	93

[a]Conditions: **1a** (0.3 mmol), **3a** (0.2 mmol), 10 mol % of catalyst, and 12 mol % of **L*** in the solvent indicated (2.0 mL) at room temperature for 12 h. [b]Isolated yield. [c]Determined by chiral HPLC. [d]No ligand. [e]$Cu(OTf)_2$ (1 mol %) and **L2** (1.2 mol %).



With the optimal reaction conditions in hand, we investigated the scope of this reaction. A range of α,β-unsaturated esters (**3a**–**3k**) bearing different aryl substituents were tested. As shown in Table 2, all of the reactions of α,β-unsaturated esters (**3a**–**3h**) bearing either electron-donating or electron-withdrawing substituents on the phenyl ring occurred smoothly to afford the desired products in excellent yields. Enantioselectivities were generally excellent, while the halo-substituents (F, Cl, and Br) resulted in relatively lower ee values (entries 2–4). In addition, 2-naphthyl and heteroaryl substrates (**3i**–**3k**) were also successfully reacted with 3-methylindole **1a** to furnish the corresponding products **4ai**–**4ak** in excellent yields and good to excellent enantioselectivities (entries 9–11). The substituent effect of 3-substituted indole was then examined. Excellent yields and good enantioselectivities were achieved for 3-ethyl-, 3-isopropyl-, 3-benzyl-, and 3-phenyl-substituted indoles (**1b**–**1e**); however, the reactivity of **1c**, **1d**, and **1e** was relatively lower, and a higher catalyst loading was required to ensure excellent yields (entries 12–15). Moreover, good results were obtained for 3-methylindoles (**1f**–**1h**) bearing either electron-donating or electron-withdrawing substituents on the phenyl ring (entries 16–18).

The absolute configuration of bromo-product **4ab** was determined to be *S* based on its single-crystal X-ray structure. As shown in Scheme 2, a proposed model for asymmetric

Scheme 2. Proposed Asymmetric Induction Model and the Absolute Configuration of 4ab

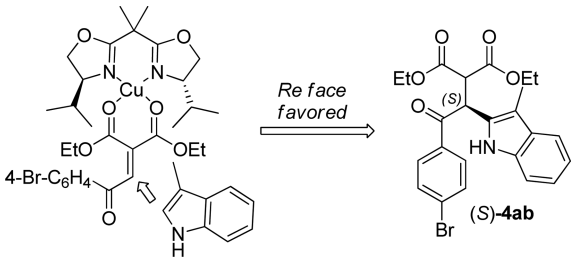
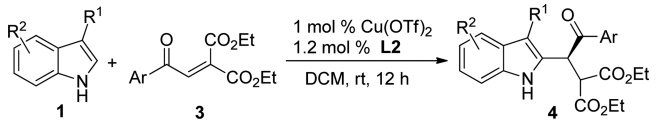


Table 2. Substrate Scope for the Reaction of α,β-Unsaturated Esters 3[a]



entry	1	Ar	4	yield (%)[b]	ee (%)[c]
1	**1a** (R^1 = Me, R^2 = H)	Ph (**3a**)	**4aa**	99	93
2	**1a** (R^1 = Me, R^2 = H)	4–Br-C_6H_4 (**3b**)	**4ab**	92	81(*S*)
3	**1a** (R^1 = Me, R^2 = H)	4–F-C_6H_4 (**3c**)	**4ac**	95	88
4	**1a** (R^1 = Me, R^2 = H)	2–Cl-C_6H_4 (**3d**)	**4ad**	98	55
5	**1a** (R^1 = Me, R^2 = H)	4-MeO-C_6H_4 (**3e**)	**4ae**	98	93
6	**1a** (R^1 = Me, R^2 = H)	4-Me-C_6H_4 (**3f**)	**4af**	96	92
7	**1a** (R^1 = Me, R^2 = H)	2-Me-C_6H_4 (**3g**)	**4ag**	96	92
8	**1a** (R^1 = Me, R^2 = H)	3,4-$(MeO)_2$-C_6H_3 (**3h**)	**4ah**	97	90
9	**1a** (R^1 = Me, R^2 = H)	2-naphthyl (**3i**)	**4ai**	98	90
10	**1a** (R^1 = Me, R^2 = H)	2-thienyl (**3j**)	**4aj**	98	91
11	**1a** (R^1 = Me, R^2 = H)	2-furyl (**3k**)	**4ak**	97	86
12	**1b** (R^1 = Et, R^2 = H)	Ph (**3a**)	**4ba**	93	91
13[d]	**1c** (R^1 = iPr, R^2 = H)	Ph (**3a**)	**4ca**	99	85
14[d]	**1d** (R^1 = Bn, R^2 = H)	Ph (**3a**)	**4da**	95	79
15[d]	**1e** (R^1 = Ph, R^2 = H)	Ph (**3a**)	**4ea**	99	88
16	**1f** (R^1 = Me, R^2 = 5-MeO)	Ph (**3a**)	**4fa**	99	84
17	**1g** (R^1 = Me, R^2 = 6-Cl)	Ph (**3a**)	**4ga**	98	82
18	**1h** (R^1 = Me, R^2 = 7-Me)	Ph (**3a**)	**4ha**	99	86

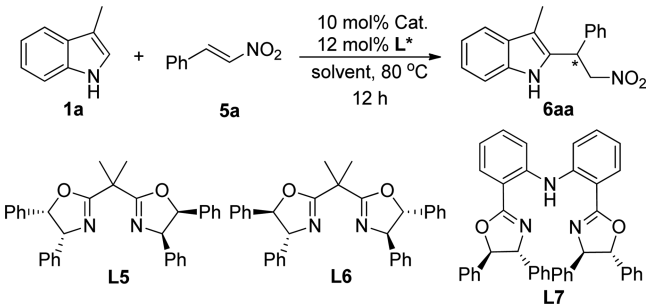
[a]Reactions conditions: **1** (0.3 mmol), **3** (0.2 mmol), $Cu(OTf)_2$ (1 mol %), and **L2** (1.2 mol %) in CH_2Cl_2 (2.0 mL) at room temperature for 12 h. [b]Isolated yield. [c]Determined by chiral HPLC. [d]$Cu(OTf)_2$ (5 mol %) and **L2** (6 mol %).

DOI: 10.1021/acs.joc.6b00123
J. Org. Chem. 2016, 81, 3023–3030

induction is depicted. Substrate **3b** is activated by the chiral catalyst through 1,5-coordination of two carbonyl oxygen atoms of ester to Cu(II), and the *Re* face approach of 3-methylindole is favorable to result in the *S* configuration of product **4ab**.

Due to the above success, nitroalkene, a popular alkylating agent for the asymmetric C3-alkylation of indoles,[8] was also investigated in the reaction with 3-substituted indole. Therefore, 3-methylindole **1a** and *β*-nitrostyrene **5a** were chosen as model substrates for condition optimization. The reaction was smoothly promoted by the complex of $Cu(OTf)_2$ and chiral bisoxazoline ligand **L5**, leading to the desired product **6aa** in 73% yield and 50% ee in toluene at 80 °C for 12 h (Table 3, entry 1). $Zn(OTf)_2$ showed a higher activity, resulting in excellent product yield and the same ee value (entry 4). $Ni(OTf)_2$, $Ni(ClO_4)_2·6H_2O$, and $Zn(ClO_4)_2·6H_2O$ led to inferior results (entries 2, 3, and 5), although nickel salts have been found to be efficient catalysts for the asymmetric Friedel–Crafts reaction of indole with *β,β*-disubstituted nitroalkenes.[8a,d] When Du's bisoxazoline **L7**[9] was used as a ligand, the enantioselectivity was remarkably improved to 92% (entry 11); however, poor enantioselectivities were obtained for other ligands (**L1**–**L4** and **L6** in entries 6–10). Subsequent solvent screening showed that no reaction occurred in THF, and inferior results were obtained in 1,2-dichloroethane (entries 12 and 13). The catalyst loading could be decreased to 5 and 1 mol %, although yield and enantioselectivity were both slightly decreased for the latter (entries 14 and 15).

Table 3. Optimization of the Reaction between 1a and 5a[a]



entry	cat.	L*	solvent	yield (%)[b]	ee (%)[c]
1	$Cu(OTf)_2$	**L5**	toluene	73	50
2	$Ni(OTf)_2$	**L5**	toluene	65	31
3	$Ni(ClO_4)_2·6H_2O$	**L5**	toluene	92	5
4	$Zn(OTf)_2$	**L5**	toluene	97	50
5	$Zn(ClO_4)_2·6H_2O$	**L5**	toluene	88	29
6	$Zn(OTf)_2$	**L1**	toluene	91	11
7	$Zn(OTf)_2$	**L2**	toluene	85	9
8	$Zn(OTf)_2$	**L3**	toluene	81	5
9	$Zn(OTf)_2$	**L4**	toluene	93	11
10	$Zn(OTf)_2$	**L6**	toluene	98	28
11	$Zn(OTf)_2$	**L7**	toluene	98	92
12	$Zn(OTf)_2$	**L7**	CH_2ClCH_2Cl	43	58
13	$Zn(OTf)_2$	**L7**	THF	nr[d]	
14[e]	$Zn(OTf)_2$	**L7**	toluene	97	92
15[f]	$Zn(OTf)_2$	**L7**	toluene	91	90

[a]Reactions conditions: **1a** (0.6 mmol), **5a** (0.4 mmol), 10 mol % of catalyst, and 12 mol % of **L*** in the indicated solvent (4.0 mL) at 80 °C for 12 h. [b]Isolated yield. [c]Determined by chiral HPLC. [d]No reaction. [e]$Zn(OTf)_2$ (5 mol %) and **L7** (6 mol %). [f]$Zn(OTf)_2$ (1 mol %) and **L7** (1.2 mol %).

We then investigated the scope of 3-substituted indole and nitroalkene. A range of nitrostyrenes bearing different substituents on the phenyl ring were reacted with 3-methylindole **1a** under the optimal conditions. Yields and enantioselectivities were both excellent for all of the reactions (Table 4, entries 2–8). The same good results were also obtained for 1-naphthyl and 2-thienyl nitroalkenes (entries 9 and 10). Note that the reaction of a cinnamaldehyde-derived nitroalkene substrate **5k** took place smoothly to afford the product **6ak** in 72% yield and 90% ee (entry 11). The substituent effect of 3-substituted indole was then examined. Good results were observed for the reactions of 3-ethyl and 3-phenyl indoles (**1b** and **1e**) with nitrostyrene **5a**, although the yield for product **6ea** was slightly lower (entries 12 and 13). Other indoles (**1f**, **1h**, **1i**) bearing additional substituents at the C5–C7 position were also tested, and the reactions with **5a** produced the corresponding adducts (**6fa**, **6ha**, and **6ia**) in excellent yields and enantioselectivities (entries 14–16). The absolute configuration of product **6ae** was determined to be *R* on the basis of the X-ray diffraction of its single-crystal structure. According to the asymmetric induction model proposed by Du and co-workers,[9b] the nucleophilic attack of 3-methylindole **1a** to nitroalkene **5e** was favored in the *Re* face and thus resulted in the *R* configuration of the product.

In conclusion, we have developed highly enantioselective Friedel–Crafts C2-alkylation reactions of 3-substituted indoles with *α,β*-unsaturated esters and nitroalkenes as alkylating agents by using Cu- or Zn-based chiral Lewis acids as catalysts. The reaction provides a straightforward access to the synthesis of chiral inoles bearing C2-benzylic stereogenic centers.

EXPERIMENTAL SECTION

General Information. Column chromatography was carried out on silica gel (200–300 mesh). ^1H NMR spectra were recorded at 500 MHz in $CDCl_3$, and ^{13}C NMR spectra were recorded at 125 MHz in $CDCl_3$. Melting points were determined on a microscopic apparatus and were uncorrected. All new products were further characterized by HRMS obtained on a TOF LC/MS mass spectrometer equipped with an ESI source; copies of their ^1H NMR and ^{13}C NMR spectra are provided. Enantiomeric excesses (ee) were determined by chiral high-performance liquid chromatography (chiral HPLC). Optical rotation values were measured with instruments operating at λ = 589 nm, corresponding to the sodium D line at the temperatures indicated. *α,β*-Unsaturated ester **3** was also prepared according to the known methods.[10,11]

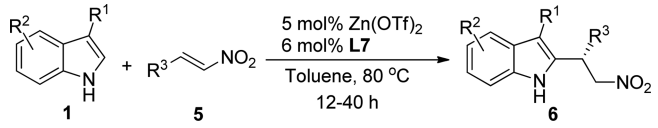
*Diethyl 2-(2-(4-Bromophenyl)-2-oxoethylidene)malonate (**3b**):* Yellow solid; yield 29% (1.2 g); mp = 50–52 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.86–7.83 (m, 2H), 7.79 (s, 1H), 7.68–7.66 (m, 2H), 4.36 (q, J = 7.0 Hz, 2H), 4.31 (q, J = 7.0 Hz, 2H), 1.37 (t, J = 7.0 Hz, 3H), 1.28 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.2, 164.2, 162.7, 136.8, 134.9, 132.3, 130.2, 129.6, 62.5, 62.0, 14.0, 13.7; HRMS m/z (ESI+) calcd for $C_{15}H_{16}BrO_5$ ($[M + H]^+$) 355.0176, found 355.0174.

*Diethyl 2-(2-(4-Fluorophenyl)-2-oxoethylidene)malonate (**3c**):* Yellow solid; yield 34% (0.8 g); mp = 51–53 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.05–7.99 (m, 2H), 7.81 (s, 1H), 7.23–7.16 (m, 2H), 4.36 (q, J = 7.0 Hz, 2H), 4.31 (q, J = 7.0 Hz, 2H), 1.37 (t, J = 7.0 Hz, 3H), 1.28 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 187.6, 166.3 (d, J = 257.2 Hz), 164.1, 162.7, 136.5, 135.1, 132.5 (d, J = 2.4 Hz), 131.5 (d, J = 10.2 Hz), 116.1 (d, J = 21.3 Hz), 62.3, 61.8, 13.9, 13.6; HRMS m/z (ESI+) calcd for $C_{15}H_{16}FO_5$ ($[M + H]^+$) 295.0976, found 295.0977.

*Diethyl 2-(2-(2-Chlorophenyl)-2-oxoethylidene)malonate (**3d**):* Yellow sticky oil; yield 60% (1.1 g); ^1H NMR (500 MHz, $CDCl_3$) δ 7.67 (s, 1H), 7.65 (d, J = 8.5 Hz, 1H), 7.48 (dd, J = 9.0, 1.5 Hz, 2H), 7.40–7.36 (m, 1H), 4.36–4.27 (m, 4H), 1.36–1.28 (m, 6H); ^{13}C

DOI: 10.1021/acs.joc.6b00123
J. Org. Chem. 2016, 81, 3023–3030

Table 4. Substrate Scope for the Reaction of Nitroalkenes[a]



entry	1	R^3	6	yield (%)[b]	ee (%)[c]
1	**1a** (R^1 = Me, R^2 = H)	Ph (**5a**)	**6aa**	97	92
2	**1a** (R^1 = Me, R^2 = H)	4-Me-C_6H_4 (**5b**)	**6ab**	97	93
3	**1a** (R^1 = Me, R^2 = H)	4-MeO-C_6H_4 (**5c**)	**6ac**	99	90
4	**1a** (R^1 = Me, R^2 = H)	4−Cl-C_6H_4 (**5d**)	**6ad**	95	93
5	**1a** (R^1 = Me, R^2 = H)	4−Br-C_6H_4 (**5e**)	**6ae**	99	91(*R*)
6	**1a** (R^1 = Me, R^2 = H)	3-MeO-C_6H_4 (**5f**)	**6af**	97	93
7	**1a** (R^1 = Me, R^2 = H)	2-MeO-C_6H_4 (**5g**)	**6ag**	99	91
8	**1a** (R^1 = Me, R^2 = H)	3,4-$(MeO)_2$-C_6H_3 (**5h**)	**6ah**	99	92
9	**1a** (R^1 = Me, R^2 = H)	1-naphthyl (**5i**)	**6ai**	98	91
10	**1a** (R^1 = Me, R^2 = H)	2-thienyl (**5j**)	**6aj**	95	92
11	**1a** (R^1 = Me, R^2 = H)	PhCh=CH (**5k**)	**6ak**	72	90
12	**1b** (R^1 = Et, R^2 = H)	Ph (**5a**)	**6ba**	96	94
13	**1e** (R^1 = Ph, R^2 = H)	Ph (**5a**)	**6ea**	86	96
14	**1f** (R^1 = Me, R^2 = 5-MeO)	Ph (**5a**)	**6fa**	92	91
15	**1h** (R^1 = Me, R^2 = 7-Me)	Ph (**5a**)	**6ha**	99	95
16	**1i** (R^1 = Me, R^2 = 6-F)	Ph (**5a**)	**6ia**	97	92

[a]Reactions conditions: **1** (0.6 mmol), **5** (0.4 mmol), $Zn(OTf)_2$ (5 mol %), and **L7** (6 mol %) in toluene (4.0 mL) at 80 °C for 12 h. [b]Isolated yield. [c]Determined by chiral HPLC.

NMR (125 MHz, $CDCl_3$) δ 189.2, 163.3, 161.8, 135.8, 135.6, 134.5, 132.3, 131.6, 129.8, 129.7, 126.1, 61.4, 61.0, 13.0, 12.8; HRMS *m*/*z* (ESI+) calcd for $C_{15}H_{16}ClO_5$ ($[M + H]^+$) 311.0681, found 311.0684.

*Diethyl 2-(2-Oxo-2-(o-tolyl)ethylidene)malonate (**3g**):* Yellow sticky oil; yield 38% (1.2 g); ^1H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 6.0 Hz, 2H), 7.35−7.30 (m, 1H), 7.19 (dd, *J* = 12.5, 7.5 Hz, 2H), 4.23 (q, *J* = 7.0 Hz, 2H), 4.13 (q, *J* = 7.0 Hz, 2H), 2.45 (s, 3H), 1.24 (t, *J* = 7.0 Hz, 3H), 1.14 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 191.8, 163.9, 162.6, 139.1, 138.0, 135.5, 135.1, 132.3, 131.7, 129.8, 125.5, 61.9, 61.4, 20.7, 13.6, 13.3; HRMS *m*/*z* (ESI+) calcd for $C_{16}H_{19}O_5$ ($[M + H]^+$) 291.1227, found 291.1225.

*Diethyl 2-(2-(Naphthalen-2-yl)-2-oxoethylidene)malonate (**3i**):* Yellow solid; yield 50% (0.6 g); mp = 51−52 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.50 (s, 1H), 8.05 (dd, *J* = 9.0, 2.0 Hz, 1H), 8.02 (s, 1H), 8.00 (s, 1H), 7.93 (dd, *J* = 19.5, 8.5 Hz, 2H), 7.66−7.64 (m, 1H), 7.62−7.58 (m, 1H), 4.40 (q, *J* = 7.0 Hz, 2H), 4.31 (q, *J* = 7.0 Hz, 2H), 1.40 (t, *J* = 7.0 Hz, 3H), 1.27 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.9, 164.4, 162.9, 136.4, 136.0, 135.5, 133.5, 132.4, 131.2, 129.7, 129.1, 128.9, 127.8, 127.1, 123.6, 62.4, 61.9, 14.0, 13.7; HRMS *m*/*z* (ESI+) calcd for $C_{19}H_{19}O_5$ ($[M + H]^+$) 327.1227, found 327.1226.

*Diethyl 2-(2-(Furan-2-yl)-2-oxoethylidene)malonate (**3k**):* Yellow solid; yield 34% (1.7 g); mp = 52−53 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.70 (d, *J* = 1.0 Hz, 1H), 7.39 (d, *J* = 4.0 Hz, 1H), 6.64 (dd, *J* = 3.5, 1.5 Hz, 1H), 4.40 (q, *J* = 7.0 Hz, 2H), 4.35 (q, *J* = 7.0 Hz, 2H), 1.36 (t, *J* = 7.0 Hz, 3H), 1.36 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.4, 164.6, 162.6, 152.5, 147.9, 137.5, 131.8, 119.6, 113.0, 62.3, 61.8, 13.8, 13.7; HRMS *m*/*z* (ESI+) calcd for $C_{13}H_{15}O_6$ ($[M + H]^+$) 267.0863, found 267.0861.

General Procedure for the Friedel−Crafts Reaction. To a dried Schlenk tube were added $M(OTf)_2$ (1 or 5 mol %) and chiral ligand (1.2 or 6 mol %) under N_2, and the solvent (2.0 or 4.0 mL) was then introduced via syringe. The resulting mixture was stirred at room temperature for 1 h, after which 3-substituted indole (0.3 or 0.6 mmol) and α,β-unsaturated ester (0.2 mmol) or nitroalkene (0.4 mmol) were added. The resulting mixture was stirred at the indicated temperature until the reaction was completed (monitored by TLC). The solvent was then removed under vacuum, and the residue was purified by chromatography on silica gel, eluting with ethyl acetate/petroleum ether 1:10 (v/v) to afford the products.

*(S)-Diethyl 2-(1-(3-Methyl-1H-indol-2-yl)-2-oxo-2-phenylethyl)-malonate (**4aa**):* Yellow solid; yield 99% (80.7 mg); mp = 121−122 °C; $[\alpha]_D^{25}$ = −189.4 (*c* 1.0, CH_2Cl_2); 93% ee [Daicel Chiralcel AD-H column (25 cm × 0.46 cm i.d.), *n*-hexane/*i*-PrOH = 80/20, 1.0 mL/min, 254 nm; t_{major} = 27.1 min, t_{minor} = 34.3 min]; ^1H NMR (500 MHz, $CDCl_3$) δ 8.07 (s, 1H), 8.05−8.02 (m, 2H), 7.55−7.52 (m, 1H), 7.49−7.40 (m, 3H), 7.26 (d, *J* = 8.0 Hz, 1H), 7.16−7.12 (m, 1H), 7.07−7.04 (m, 1H), 5.69 (d, *J* = 11.5 Hz, 1H), 4.56 (d, *J* = 11.5 Hz, 1H), 4.26−4.12 (m, 2H), 4.01−3.91 (m, 2H), 2.38 (s, 3H), 1.21 (t, *J* = 7.0 Hz, 3H), 0.92 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.5, 167.9, 167.8, 136.4, 135.9, 133.5, 128.9, 128.7, 126.1, 122.4, 119.2, 118.7, 110.8, 110.7, 62.0, 61.6, 54.7, 44.4, 13.8, 13.5, 8.6; HRMS *m*/*z* (ESI+) calcd for $C_{24}H_{26}NO_5$ ($[M + H]^+$) 408.1805, found 408.1813.

*(S)-Diethyl 2-(2-(4-Bromophenyl)-1-(3-methyl-1H-indol-2-yl)-2-oxoethyl)malonate (**4ab**):* Yellow solid; yield 92% (89.5 mg); mp = 116−117 °C; $[\alpha]_D^{25}$ = −94.2 (*c* 1.0, CH_2Cl_2); 81% ee [Daicel Chiralcel AD-H column (25 cm × 0.46 cm i.d.), *n*-hexane/*i*-PrOH = 80/20, 1.0 mL/min, 254 nm; t_{major} = 19.5 min, t_{minor} = 49.6 min]; ^1H NMR (500 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.88 (d, *J* = 8.5 Hz, 2H), 7.58 (d, *J* = 8.5 Hz, 2H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.26 (d, *J* = 8.0 Hz, 1H), 7.15 (t, *J* = 7.5 Hz, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 5.61 (d, *J* = 11.0 Hz, 1H), 4.53 (d, *J* = 11.0 Hz, 1H), 4.25−4.13 (m, 2H), 4.01−3.93 (m, 2H), 2.36 (s, 3H), 1.23 (t, *J* = 7.0 Hz, 3H), 0.92 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.6, 167.9, 167.6, 136.4, 134.7, 132.0, 130.1, 128.9, 128.9, 125.7, 122.6, 119.4, 118.8, 111.0, 110.8, 62.1, 61.7, 54.6, 44.4, 13.9, 13.6, 8.6; HRMS *m*/*z* (ESI+) calcd for $C_{24}H_{25}BrNO_5$ ($[M + H]^+$) 486.0911, found 486.0911.

*(S)-Diethyl 2-(2-(4-Fluorophenyl)-1-(3-methyl-1H-indol-2-yl)-2-oxoethyl)malonate (**4ac**):* Yellow solid; yield 95% (80.8 mg); mp = 102−103 °C; $[\alpha]_D^{25}$ = −142.5 (*c* 1.0, CH_2Cl_2); 88% ee [Daicel Chiralcel AD-H column (25 cm × 0.46 cm i.d.), *n*-hexane/*i*-PrOH = 80/20, 1.0 mL/min, 254 nm; t_{major} = 18.0 min, t_{minor} = 40.9 min]; ^1H NMR (500 MHz, $CDCl_3$) δ 8.10−8.03 (m, 3H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.26 (d, *J* = 8.0 Hz, 1H), 7.17−7.05 (m, 4H), 5.63 (d, *J* = 11.5 Hz, 1H), 4.54 (d, *J* = 11.5 Hz, 1H), 4.25−4.14 (m, 2H), 4.01−3.92 (m, 2H), 2.37 (s, 3H), 1.22 (t, *J* = 7.0 Hz, 3H), 0.92 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.0, 167.9, 167.7, 166.0 (d, *J* = 256.1 Hz), 136.4, 132.3 (d, *J* = 2.7 Hz), 131.4 (d, *J* = 9.4 Hz), 128.8, 125.9, 122.5, 119.3, 118.7, 115.9 (d, *J* = 22.0 Hz), 110.8, 110.8, 62.1,

DOI: 10.1021/acs.joc.6b00123
J. Org. Chem. 2016, 81, 3023−3030

61.7, 54.6, 44.3, 13.9, 13.6, 8.6; HRMS *m*/*z* (ESI+) calcd for $C_{24}H_{25}FNO_5$ ([M + H]$^+$) 426.1711, found 426.1716.

*(S)-Diethyl 2-(2-(2-chlorophenyl)-1-(3-methyl-1H-indol-2-yl)-2-oxoethyl)malonate (**4ad**):* Yellow solid; yield 98% (86.6 mg); mp = 123−124 °C; $[\alpha]_D^{25}$ = −55.3 (*c* 1.0, CH_2Cl_2); 55% ee [Lux 5u Cellulose-2 column (25 cm × 0.46 cm i.d.), *n*-hexane/*i*-PrOH = 80/20, 1.0 mL/min, 254 nm; t_{minor} = 5.4 min, t_{major} = 8.7 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (s, 1H), 7.73−7.70 (m, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.34−7.31 (m, 2H), 7.28−7.25 (m, 2H), 7.17−7.14 (m, 1H), 7.08−7.04 (m, 1H), 5.50 (d, *J* = 10.5 Hz, 1H), 4.51 (d, *J* = 10.5 Hz, 1H), 4.25−4.20 (m, 2H), 4.03−3.97 (m, 2H), 2.19 (s, 3H), 1.25 (t, *J* = 7.0 Hz, 3H), 0.95 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.1, 167.9, 167.8, 137.3, 136.4, 132.0, 131.9, 130.8, 129.2, 128.8, 126.6, 125.0, 122.4, 119.2, 118.7, 111.8, 110.9, 62.1, 61.7, 53.8, 48.4, 13.9, 13.6, 8.4; HRMS *m*/*z* (ESI+) calcd for $C_{24}H_{25}ClNO_5$ ([M + H]$^+$) 442.1416, found 442.1422.

*(S)-Diethyl 2-(2-(4-Methoxyphenyl)-1-(3-methyl-1H-indol-2-yl)-2-oxoethyl)malonate (**4ae**):* Yellow solid; yield 98% (85.8 mg); mp = 128−129 °C; $[\alpha]_D^{25}$ = −97.3 (*c* 1.0, CH_2Cl_2); 93% ee [Daicel Chiralcel AD-H column (25 cm × 0.46 cm i.d.), *n*-hexane/*i*-PrOH = 80/20, 1.0 mL/min, 254 nm; t_{major} = 26.3 min, t_{minor} = 64.5 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (s, 1H), 8.05−8.00 (m, 2H), 7.47 (d, *J* = 7.5 Hz, 1H), 7.25 (d, *J* = 8.0 Hz, 1H), 7.15−7.11 (m, 1H), 7.08−7.03 (m, 1H), 6.93−6.88 (m, 2H), 5.65 (d, *J* = 11.0 Hz, 1H), 4.54 (d, *J* = 11.0 Hz, 1H), 4.23−4.12 (m, 2H), 4.00−3.91 (m, 2H), 3.84 (s, 3H), 2.38 (s, 3H), 1.21 (t, *J* = 7.0 Hz, 3H), 0.91 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.9, 167.9, 167.9, 164.0, 136.2, 131.1, 128.9, 128.7, 126.7, 122.3, 119.2, 118.6, 113.9, 110.8, 110.3, 61.9, 61.6, 55.5, 54.7, 43.9, 13.9, 13.6, 8.6; HRMS *m*/*z* (ESI+) calcd for $C_{25}H_{28}NO_6$ ([M + H]$^+$) 438.1911, found 438.1912.

*(S)-Diethyl 2-(1-(3-Methyl-1H-indol-2-yl)-2-oxo-2-(p-tolyl)ethyl)-malonate (**4af**):* Yellow solid; yield 96% (80.9 mg); mp = 126−127 °C; $[\alpha]_D^{25}$ = −103.1 (*c* 1.0, CH_2Cl_2); 92% ee [Daicel Chiralcel AD-H column (25 cm × 0.46 cm i.d.), *n*-hexane/*i*-PrOH = 80/20, 1.0 mL/min, 254 nm; t_{major} = 23.2 min, t_{minor} = 47.9 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.94 (d, *J* = 8.5 Hz, 2H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.24 (t, *J* = 10.5 Hz, 3H), 7.15−7.11 (m, 1H), 7.05 (t, *J* = 8.0 Hz, 1H), 5.67 (d, *J* = 11.0 Hz, 1H), 4.55 (d, *J* = 11.0 Hz, 1H), 4.23−4.13 (m, 2H), 3.99−3.93 (m, 2H), 2.38 (s, 3H), 2.37 (s, 3H), 1.21 (t, *J* = 7.0 Hz, 3H), 0.91 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.1, 167.9, 167.8, 144.6, 136.3, 133.3, 129.4, 128.9, 128.8, 126.4, 122.3, 119.2, 118.7, 110.8, 110.6, 62.0, 61.6, 54.6, 44.1, 21.6, 13.9, 13.6, 8.6; HRMS *m*/*z* (ESI+) calcd for $C_{25}H_{28}NO_5$ ([M + H]$^+$) 422.1962, found 422.1966.

*(S)-Diethyl 2-(1-(3-Methyl-1H-indol-2-yl)-2-oxo-2-(o-tolyl)ethyl)-malonate (**4ag**):* Yellow solid; yield 96% (80.9 mg); mp = 139−140 °C; $[\alpha]_D^{25}$ = −204.1 (*c* 1.0, CH_2Cl_2); 92% ee [Daicel Chiralcel AD-H column (25 cm × 0.46 cm i.d.), *n*-hexane/*i*-PrOH = 80/20, 1.0 mL/min, 254 nm; t_{major} = 25.3 min, t_{minor} = 60.0 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.88 (d, *J* = 7.5 Hz, 1H), 7.46 (d, *J* = 7.5 Hz, 1H), 7.33 (td, *J* = 7.5, 1.0 Hz, 1H), 7.27 (s, 1H), 7.23 (t, *J* = 7.5 Hz, 1H), 7.15 (td, *J* = 8.5, 1.5 Hz, 2H), 7.08−7.05 (m, 1H), 5.51 (d, *J* = 11.0 Hz, 1H), 4.54 (d, *J* = 11.0 Hz, 1H), 4.26−4.19 (m, 2H), 4.00−3.92 (m, 2H), 2.34 (s, 3H), 2.25 (s, 3H), 1.25 (t, *J* = 7.0 Hz, 3H), 0.92 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.6, 168.1, 167.7, 138.9, 137.1, 136.3, 131.7, 131.6, 128.9, 128.5, 126.0, 125.6, 122.4, 119.2, 118.7, 111.0, 110.8, 62.1, 61.6, 54.5, 47.3, 20.7, 14.0, 13.6, 8.4; HRMS *m*/*z* (ESI+) calcd for $C_{25}H_{28}NO_5$ ([M + H]$^+$) 422.1962, found 422.1967.

*(S)-Diethyl 2-(2-(3,4-Dimethoxyphenyl)-1-(3-methyl-1H-indol-2-yl)-2-oxoethyl)malonate (**4ah**):* Yellow solid; yield 97% (90.7 mg); mp = 169−170 °C; $[\alpha]_D^{25}$ = −100.3 (*c* 1.0, CH_2Cl_2); 90% ee [Lux 5u Cellulose-2 column (25 cm × 0.46 cm i.d.), *n*-hexane/*i*-PrOH = 80/20, 1.0 mL/min, 254 nm; t_{minor} = 10.0 min, t_{major} = 18.8 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.75 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.54 (d, *J* = 2.0 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.25 (d, *J* = 8.0 Hz, 1H), 7.15−7.12 (m, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.87 (d, *J* = 8.5 Hz, 1H), 5.66 (d, *J* = 11.5 Hz, 1H), 4.55 (d, *J* = 11.5 Hz, 1H), 4.23−4.15 (m, 2H), 4.00−3.92 (m, 2H), 3.92 (s, 3H), 3.89 (s, 3H), 2.40 (s, 3H), 1.22 (t, *J* = 7.0 Hz, 3H), 0.91 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.8, 167.9, 167.9, 153.8, 149.0, 136.3, 128.8, 128.7, 126.8, 123.5, 122.3, 119.1, 118.6, 110.9, 110.8, 110.2, 110.1, 61.9, 61.5, 56.0, 55.7, 54.6, 43.9, 13.8, 13.5, 8.6; HRMS *m*/*z* (ESI+) calcd for $C_{26}H_{30}NO_7$ ([M + H]$^+$) 468.2017, found 468.2027.

*(S)-Diethyl 2-(1-(3-Methyl-1H-indol-2-yl)-2-(naphthalen-2-yl)-2-oxoethyl)malonate (**4ai**):* Yellow solid; yield 98% (89.7 mg); mp = 140−141 °C; $[\alpha]_D^{25}$ = +13.2 (*c* 1.0, CH_2Cl_2); 90% ee [Lux 5u Cellulose-2 column (25 cm × 0.46 cm i.d.), *n*-hexane/*i*-PrOH = 80/20, 1.0 mL/min, 254 nm; t_{minor} = 6.2 min, t_{major} = 10.6 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.16 (s, 1H), 8.05 (dd, *J* = 9.0, 1.5 Hz, 1H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.85 (dd, *J* = 13.5, 9.0 Hz, 2H), 7.59 (t, *J* = 7.0 Hz, 1H), 7.54 (t, *J* = 7.0 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.25 (d, *J* = 8.0 Hz, 1H), 7.13 (t, *J* = 7.5 Hz, 1H), 7.04 (t, *J* = 7.5 Hz, 1H), 5.86 (d, *J* = 11.0 Hz, 1H), 4.62 (d, *J* = 11.0 Hz, 1H), 4.24−4.13 (m, 2H), 4.05−3.92 (m, 2H), 2.46 (s, 3H), 1.21 (t, *J* = 7.0 Hz, 3H), 0.94 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.5, 167.9, 167.9, 136.3, 135.8, 133.0, 132.4, 130.7, 129.7, 128.9, 128.8, 128.6, 127.7, 126.8, 126.3, 124.1, 122.4, 119.3, 118.7, 110.8, 110.7, 62.1, 61.7, 54.7, 44.4, 13.9, 13.6, 8.7; HRMS *m*/*z* (ESI+) calcd for $C_{28}H_{28}NO_5$ ([M + H]$^+$) 458.1962, found 458.1969.

*(S)-Diethyl 2-(1-(3-Methyl-1H-indol-2-yl)-2-oxo-2-(thiophen-2-yl)ethyl)malonate (**4aj**):* Yellow solid; yield 98% (81.0 mg); mp = 107−108 °C; $[\alpha]_D^{25}$ = −196.3 (*c* 1.0, CH_2Cl_2); 91% ee [Lux 5u Cellulose-2 column (25 cm × 0.46 cm i.d.), *n*-hexane/*i*-PrOH = 80/20, 1.0 mL/min, 254 nm; t_{minor} = 5.9 min, t_{major} = 7.5 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (s, 1H), 7.86 (dd, *J* = 4.0, 1.0 Hz, 1H), 7.64 (dd, *J* = 5.0, 1.0 Hz, 1H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.26 (s, 1H), 7.17−7.14 (m, 1H), 7.11−7.05 (m, 2H), 5.48 (d, *J* = 11.5 Hz, 1H), 4.52 (d, *J* = 11.5 Hz, 1H), 4.24−4.15 (m, 2H), 4.00−3.93 (m, 2H), 2.39 (s, 3H), 1.21 (t, *J* = 7.0 Hz, 3H), 0.92 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.8, 167.7, 167.6, 142.3, 136.3, 134.8, 133.2, 128.8, 128.4, 126.4, 122.5, 119.3, 118.8, 110.9, 110.9, 62.1, 61.7, 54.3, 45.6, 13.9, 13.6, 8.7; HRMS *m*/*z* (ESI+) calcd for $C_{22}H_{24}NO_5S$ ([M + H]$^+$) 414.1370, found 414.1363.

*(S)-Diethyl 2-(2-(Furan-2-yl)-1-(3-methyl-1H-indol-2-yl)-2-oxoethyl)malonate (**4ak**):* Yellow solid; yield 97% (77.1 mg); mp = 119−120 °C; $[\alpha]_D^{25}$ = −121.5 (*c* 1.0, CH_2Cl_2); 86% ee [Lux 5u Cellulose-2 column (25 cm × 0.46 cm i.d.), *n*-hexane/*i*-PrOH = 80/20, 1.0 mL/min, 254 nm; t_{minor} = 6.6 min, t_{major} = 10.1 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (s, 1H), 7.60 (d, *J* = 1.0 Hz, 1H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.29 (d, *J* = 3.5 Hz, 1H), 7.26 (s, 1H), 7.17−7.13 (m, 1H), 7.10−7.04 (m, 1H), 6.52 (dd, *J* = 4.0, 2.0 Hz, 1H), 5.51 (d, *J* = 11.5 Hz, 1H), 4.52 (d, *J* = 11.5 Hz, 1H), 4.25−4.13 (m, 2H), 4.01−3.93 (m, 2H), 2.38 (s, 3H), 1.22 (t, *J* = 7.0 Hz, 3H), 0.93 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 185.4, 167.8, 167.5, 151.5, 147.2, 136.3, 128.7, 125.9, 122.4, 119.2, 118.9, 118.7, 112.7, 111.3, 110.9, 62.1, 61.6, 53.8, 44.3, 13.8, 13.6, 8.5; HRMS *m*/*z* (ESI+) calcd for $C_{22}H_{24}NO_6$ ([M + H]$^+$) 398.1598, found 398.1602.

*(S)-Diethyl 2-(1-(3-Ethyl-1H-indol-2-yl)-2-oxo-2-phenylethyl)-malonate (**4ba**):* Yellow solid; yield 93% (78.4 mg); mp = 121−122 °C; $[\alpha]_D^{25}$ = −172.6 (*c* 1.0, CH_2Cl_2); 91% ee [Lux 5u Cellulose-2 column (25 cm × 0.46 cm i.d.), *n*-hexane/*i*-PrOH = 80/20, 1.0 mL/min, 254 nm; t_{minor} = 5.3 min, t_{major} = 7.1 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (s, 1H), 8.07−8.03 (m, 2H), 7.56−7.50 (m, 2H), 7.44 (t, *J* = 8.0 Hz, 2H), 7.27 (s, 1H), 7.17−7.11 (m, 1H), 7.07−7.02 (m, 1H), 5.71 (d, *J* = 11.5 Hz, 1H), 4.58 (d, *J* = 11.5 Hz, 1H), 4.27−4.12 (m, 2H), 4.01−3.90 (m, 2H), 2.92−2.79 (m, 2H), 1.26−1.19 (m, 6H), 0.91 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.9, 167.9, 167.8, 136.6, 136.0, 133.6, 128.8, 128.6, 128.0, 125.2, 122.4, 119.2, 119.2, 117.6, 110.9, 62.1, 61.6, 55.0, 44.1, 17.6, 14.9, 13.9, 13.6; HRMS *m*/*z* (ESI+) calcd for $C_{25}H_{28}NO_5$ ([M + H]$^+$) 422.1962, found 422.1964.

*(S)-Diethyl 2-(1-(3-Isopropyl-1H-indol-2-yl)-2-oxo-2-phenylethyl)-malonate (**4ca**):* Yellow solid; yield 99% (86.2 mg); mp = 175−176 °C; $[\alpha]_D^{25}$ = −106.7 (*c* 1.0, CH_2Cl_2); 85% ee [Lux 5u Cellulose-2 column (25 cm × 0.46 cm i.d.), *n*-hexane/*i*-PrOH = 80/20, 1.0 mL/min, 254 nm; t_{minor} = 4.7 min, t_{major} = 6.4 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, *J* = 7.0 Hz, 3H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 2H), 7.26 (s, 1H), 7.15−7.09 (m, 1H), 7.01 (t, *J* = 7.5 Hz, 1H), 5.75 (d, *J* = 11.5 Hz, 1H), 4.58 (d, *J* =

DOI: 10.1021/acs.joc.6b00123
J. Org. Chem. 2016, 81, 3023−3030

11.5 Hz, 1H), 4.25−4.13 (m, 2H), 4.00−3.96 (m, 2H), 3.40 (dt, J = 14.0, 7.0 Hz, 1H), 1.44 (d, J = 7.0 Hz, 3H), 1.37 (d, J = 7.0 Hz, 3H), 1.22 (t, J = 7.0 Hz, 3H), 0.94 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.8, 167.9, 167.8, 137.0, 135.8, 133.6, 128.8, 128.6, 126.4, 124.3, 122.0, 121.5, 120.7, 118.8, 111.1, 62.0, 61.6, 54.9, 44.2, 26.3, 22.8, 22.5, 13.9, 13.6; HRMS m/z (ESI+) calcd for $C_{26}H_{30}NO_5$ ($[M + H]^+$) 436.2118, found 436.2119.

*(S)-Diethyl 2-(1-(3-Benzyl-1H-indol-2-yl)-2-oxo-2-phenylethyl)-malonate (**4da**):* Yellow solid; yield 95% (91.9 mg); mp = 153−154 °C; $[\alpha]_D^{25}$ = −92.2 (c 1.0, CH_2Cl_2); 79% ee [Daicel Chiralcel AD-H column (25 cm × 0.46 cm i.d.), n-hexane/i-PrOH = 80/20, 1.0 mL/min, 254 nm; t_{major} = 17.5 min, t_{minor} = 19.6 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.63 (s, 1H), 7.85 (dd, J = 7.0, 4.0 Hz, 2H), 7.46 (t, J = 7.5 Hz, 1H), 7.37 (d, J = 8.0 Hz, 1H), 7.32 (d, J = 8.0 Hz, 1H), 7.25−7.15 (m, 8H), 7.03 (t, J = 7.5 Hz, 1H), 5.81 (d, J = 11.0 Hz, 1H), 4.70 (dd, J = 11.0, 4.0 Hz, 1H), 4.38−4.27 (m, 2H), 4.27−4.14 (m, 2H), 4.07−3.93 (m, 2H), 1.22 (t, J = 7.0 Hz, 3H), 0.96 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.9, 167.9, 167.8, 140.3, 136.4, 135.5, 133.4, 128.8, 128.7, 128.5, 128.3, 127.1, 125.9, 122.4, 119.5, 119.4, 113.5, 110.9, 62.0, 61.7, 55.1, 44.1, 29.7, 13.8, 13.6; HRMS m/z (ESI+) calcd for $C_{30}H_{30}NO_5$ ($[M + H]^+$) 484.2118, found 484.2124.

*(S)-Diethyl 2-(2-Oxo-2-phenyl-1-(3-phenyl-1H-indol-2-yl)ethyl)-malonate (**4ea**):* Yellow solid; yield 99% (93.0 mg); mp = 154−155 °C; $[\alpha]_D^{25}$ = −198.6 (c 1.0, CH_2Cl_2); 88% ee [Daicel Chiralcel AD-H column (25 cm × 0.46 cm i.d.), n-hexane/i-PrOH = 80/20, 1.0 mL/min, 254 nm; t_{major} = 22.2 min, t_{minor} = 24.4 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (s, 1H), 7.67 (dd, J = 8.0, 1.0 Hz, 2H), 7.57−7.52 (m, 3H), 7.51−7.48 (m, 2H), 7.47−7.43 (m, 2H), 7.35 (d, J = 8.0 Hz, 1H), 7.24−7.18 (m, 3H), 7.09−7.05 (m, 1H), 5.81 (d, J = 11.0 Hz, 1H), 4.74 (d, J = 11.0 Hz, 1H), 4.25−4.13 (m, 2H), 4.12−3.92 (m, 2H), 1.19 (t, J = 7.0 Hz, 3H), 0.93 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.2, 167.9, 167.9, 136.4, 135.2, 134.2, 133.5, 129.8, 128.9, 128.9, 128.4, 127.7, 126.9, 126.3, 122.9, 120.1, 119.6, 118.7, 111.0, 62.1, 61.8, 54.5, 43.7, 13.9, 13.6; HRMS m/z (ESI+) calcd for $C_{29}H_{28}NO_5$ ($[M + H]^+$) 470.1962, found 470.1964.

*(S)-Diethyl 2-(1-(5-Methoxy-3-methyl-1H-indol-2-yl)-2-oxo-2-phenylethyl)malonate (**4fa**):* Yellow solid; yield 99% (86.6 mg); mp = 127−128 °C; $[\alpha]_D^{25}$ = −174.4 (c 1.0, CH_2Cl_2); 84% ee [Lux 5u Cellulose-2 column (25 cm × 0.46 cm i.d.), n-hexane/i-PrOH = 80/20, 1.0 mL/min, 254 nm; t_{minor} = 6.9 min, t_{major} = 9.6 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04−8.01 (m, 2H), 7.97 (s, 1H), 7.53 (t, J = 7.5 Hz, 1H), 7.43 (t, J = 7.5 Hz, 2H), 7.14 (d, J = 8.5 Hz, 1H), 6.90 (d, J = 2.0 Hz, 1H), 6.80 (dd, J = 9.0, 2.5 Hz, 1H), 5.67 (d, J = 11.5 Hz, 1H), 4.54 (d, J = 11.5 Hz, 1H), 4.23−4.13 (m, 2H), 4.01−3.93 (m, 2H), 3.84 (s, 3H), 2.35 (s, 3H), 1.21 (t, J = 7.0 Hz, 3H), 0.93 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.4, 167.9, 167.8, 153.9, 135.8, 133.6, 131.5, 129.2, 128.7, 128.7, 126.8, 112.5, 111.6, 110.5, 100.8, 62.0, 61.6, 55.9, 54.7, 44.4, 13.9, 13.6, 8.7; HRMS m/z (ESI+) calcd for $C_{25}H_{28}NO_6$ ($[M + H]^+$) 438.1911, found 438.1914.

*(S)-Diethyl 2-(1-(6-Chloro-3-methyl-1H-indol-2-yl)-2-oxo-2-phenylethyl)malonate (**4ga**):* Yellow solid; yield 98% (86.6 mg); mp = 130−131 °C; $[\alpha]_D^{25}$ = −111.4 (c 1.0, CH_2Cl_2); 82% ee [Lux 5u Cellulose-2 column (25 cm × 0.46 cm i.d.), n-hexane/i-PrOH = 80/20, 1.0 mL/min, 254 nm; t_{minor} = 5.2 min, t_{major} = 7.3 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (s, 1H), 8.04−8.01 (m, 2H), 7.55 (t, J = 7.5 Hz, 1H), 7.45 (t, J = 8.0 Hz, 2H), 7.36 (d, J = 8.5 Hz, 1H), 7.24 (d, J = 1.5 Hz, 1H), 7.02 (dd, J = 8.5, 2.0 Hz, 1H), 5.66 (d, J = 11.5 Hz, 1H), 4.53 (d, J = 11.5 Hz, 1H), 4.22−4.13 (m, 2H), 4.03−3.91 (m, 2H), 2.35 (s, 3H), 1.21 (t, J = 7.0 Hz, 3H), 0.92 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.4, 167.8, 167.7, 135.6, 135.8, 133.7, 128.8, 128.7, 128.5, 127.5, 120.1, 119.6, 111.0, 110.8, 62.1, 61.7, 54.7, 44.2, 13.9, 13.7, 8.5; HRMS m/z (ESI+) calcd for $C_{24}H_{25}ClNO_5$ ($[M + H]^+$) 442.1416, found 442.1421.

*(S)-Diethyl 2-(1-(3,7-Dimethyl-1H-indol-2-yl)-2-oxo-2-phenylethyl)malonate (**4ha**):* Yellow solid; yield 99% (83.5 mg); mp = 140−141 °C; $[\alpha]_D^{25}$ = −158.2 (c 1.0, CH_2Cl_2); 86% ee [Lux 5u Cellulose-2 column (25 cm × 0.46 cm i.d.), n-hexane/i-PrOH = 80/20, 1.0 mL/min, 254 nm; t_{minor} = 4.5 min, t_{major} = 5.6 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05−8.02 (m, 2H), 7.93 (s, 1H), 7.55−7.52 (m, 1H), 7.45−7.41 (m, 2H), 7.32 (d, J = 8.0 Hz, 1H), 7.00−6.93 (m, 2H), 5.70 (d, J = 11.0 Hz, 1H), 4.58 (d, J = 11.0 Hz, 1H), 4.23−4.15 (m, 2H), 4.00−3.93 (m, 2H), 2.43 (s, 3H), 2.38 (s, 3H), 1.22 (t, J = 7.0 Hz, 3H), 0.94 (t, J = 7.0 Hz, 3H);^{13}C NMR (125 MHz, $CDCl_3$) δ 197.7, 167.9, 167.7, 135.9, 135.8, 133.6, 128.7, 128.5, 125.8, 123.1, 120.0, 119.5, 116.4, 111.4, 62.0, 61.7, 54.7, 44.3, 16.5, 13.9, 13.6, 8.8; HRMS m/z (ESI+) calcd for $C_{25}H_{28}NO_5$ ($[M + H]^+$) 422.1962, found 422.1962.

*(R)-3-Methyl-2-(2-nitro-1-phenylethyl)-1H-indole (**6aa**):* Yellow solid; yield 97% (108.8 mg); mp = 144−146 °C; $[\alpha]_D^{25}$ = −84.5 (c 1.0, CH_2Cl_2); 92% ee [Daicel Chiralcel AD-H column (25 cm × 0.46 cm i.d.), n-hexane/i-PrOH = 85/15, 1.0 mL/min, 254 nm; t_{minor} = 7.6 min, t_{major} = 9.3 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (s, 1H), 7.56 (d, J = 7.5 Hz, 1H), 7.41 (t, J = 7.0 Hz, 2H), 7.37−7.30 (m, 3H), 7.26 (d, J = 8.0 Hz, 1H), 7.19 (td, J = 1.0, 2.0 Hz, 1H), 7.14 (t, J = 7.0 Hz, 1H), 5.27 (t, J = 8.0 Hz, 1H), 5.09 (dd, J = 8.5, 13.0 Hz, 1H), 4.96 (dd, J = 8.0, 13.0 Hz, 1H), 2.37 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.0, 135.8, 130.6, 129.4, 129.1, 128.1, 127.3, 122.3, 119.7, 118.8, 110.8, 109.5, 77.6, 41.1, 8.6; HRMS m/z (ESI+) calcd for $C_{17}H_{17}N_2O_2$ ($[M + H]^+$) 281.1285, found 281.1290.

*(R)-3-Methyl-2-(2-nitro-1-(p-tolyl)ethyl)-1H-indole (**6ab**):* Yellow solid; yield 97% (114.2 mg); mp = 94−97 °C; $[\alpha]_D^{25}$ = −74.1 (c 1.0, CH_2Cl_2); 93% ee [Daicel Chiralcel AD-H column (25 cm × 0.46 cm i.d.), n-hexane/i-PrOH = 85/15, 1.0 mL/min, 254 nm; t_{minor} = 6.9 min, t_{major} = 7.8 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (s, 1H), 7.55 (d, J = 7.5 Hz, 1H), 7.25−7.19 (m, 5H), 7.17 (td, J = 1.0, 7.0 Hz, 1H), 7.12 (td, J = 1.0, 8.0 Hz, 1H), 5.23 (t, J = 8.0 Hz, 1H), 5.07 (dd, J = 8.0, 12.5 Hz, 1H), 4.95 (dd, J = 7.5, 13.0 Hz, 1H), 2.37 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.9, 135.7, 133.9, 130.8, 130.1, 129.2, 127.2, 122.3, 119.6, 118.7, 110.8, 109.3, 77.8, 40.8, 21.1, 8.6; HRMS m/z (ESI+) calcd for $C_{18}H_{19}N_2O_2$ ($[M + H]^+$) 295.1441, found 295.1446.

*(R)-2-(1-(4-Methoxyphenyl)-2-nitroethyl)-3-methyl-1H-indole (**6ac**):* Yellow solid; yield 99% (112.9 mg); mp = 70−72 °C; $[\alpha]_D^{25}$ = −64.5 (c 1.0, CH_2Cl_2); 90% ee [Daicel Chiralcel AD-H column (25 cm × 0.46 cm i.d.), n-hexane/i-PrOH = 85/15, 1.0 mL/min, 254 nm; t_{minor} = 10.1 min, t_{major} = 13.1 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (s, 1H), 7.61 (d, J = 7.5 Hz, 1H), 7.28−7.17 (m, 5H), 6.93 (dt, J = 3.5, 10.0 Hz, 2H), 5.22 (t, J = 8.0 Hz, 1H), 5.00 (dd, J = 8.0, 12.5 Hz, 1H), 4.90 (dd, J = 8.0, 13.0 Hz, 1H), 3.83 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.1, 135.7, 131.0, 129.1, 129.0, 128.4, 122.1, 119.5, 118.6, 114.6, 110.8, 109.0, 77.7, 55.2, 40.4, 8.5; HRMS m/z (ESI+) calcd for $C_{18}H_{19}N_2O_3$ ($[M + H]^+$) 311.1390, found 311.1395.

*(R)-2-(1-(4-Chlorophenyl)-2-nitroethyl)-3-methyl-1H-indole (**6ad**):* Yellow solid; yield 95% (119.6 mg); mp = 85−88 °C; $[\alpha]_D^{25}$ = −53.3 (c 1.0, CH_2Cl_2); 93% ee [Daicel Chiralcel AD-H column (25 cm × 0.46 cm i.d.), n-hexane/i-PrOH = 85/15, 1.0 mL/min, 254 nm; t_{minor} = 7.4 min, t_{major} = 8.8 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (s, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.37 (dt, J = 2.5, 9.0 Hz, 2H), 7.27−7.22 (m, 3H), 7.20 (td, J = 1.0, 7.0 Hz, 1H), 7.14 (td, J = 1.5, 8.0 Hz, 1H), 5.24 (t, J = 8.0 Hz, 1H), 5.06 (dd, J = 8.0, 13.0 Hz, 1H), 4.95 (dd, J = 7.0, 13.0 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.8, 135.6, 134.1, 130.0, 129.6, 129.1, 128.7, 122.6, 119.8, 118.8, 110.9, 109.8, 77.5, 40.6, 8.7; HRMS m/z (ESI+) calcd for $C_{17}H_{16}ClN_2O_2$ ($[M + H]^+$) 315.0895, found 315.0892.

*(R)-2-(1-(4-Bromophenyl)-2-nitroethyl)-3-methyl-1H-indole (**6ae**):* Yellow solid; yield 99% (142.2 mg); mp = 109−110 °C; $[\alpha]_D^{25}$ = −31.0 (c 1.0, CH_2Cl_2); 91% ee [Daicel Chiralcel AD-H column (25 cm × 0.46 cm i.d.), n-hexane/i-PrOH = 85/15, 1.0 mL/min, 254 nm; t_{minor} = 7.7 min, t_{major} = 9.4 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.55 (d, J = 7.5 Hz, 1H), 7.54−7.49 (m, 2H), 7.28−7.25 (m, 1H), 7.21−7.12 (m, 4H), 5.21 (t, J = 8.0 Hz, 1H), 5.05 (dd, J = 13.0, 8.0 Hz, 1H), 4.95 (dd, J = 13.0, 7.5 Hz, 1H), 2.34 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.2, 135.9, 132.5, 129.9, 129.1, 129.0, 122.6, 122.1, 119.8, 118.8, 110.8, 109.8, 77.4, 40.7, 8.6; HRMS m/z (ESI+) calcd for C17H16BrN2O2($[M + H]^+$) 359.0390, found 359.0379.

*(R)-2-(1-(3-Methoxyphenyl)-2-nitroethyl)-3-methyl-1H-indole (**6af**):* Yellow solid; yield 97% (120.4 mg); mp = 108−110 °C; $[\alpha]_D^{25}$ = −81.0 (c 1.0, CH_2Cl_2); 93% ee [Daicel Chiralcel AD-H column (25

DOI: 10.1021/acs.joc.6b00123
J. Org. Chem. 2016, 81, 3023−3030

cm × 0.46 cm i.d.), *n*-hexane/*i*-PrOH = 85/15, 1.0 mL/min, 254 nm; t_{minor} = 9.2 min, t_{major} = 10.5 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (s, 1H), 7.55 (d, J = 7.5 Hz, 1H), 7.33 (t, J = 8.0 Hz, 1H), 7.25 (d, J = 8.0 Hz, 1H), 7.18 (t, J = 7.0 Hz, 1H), 7.13 (t, J = 8.0 Hz, 1H), 6.91 (d, J = 8.0 Hz, 1H), 6.88 (dd, J = 2.5, 8.5 Hz, 1H), 6.85 (s, 1H), 5.24 (t, J = 8.0 Hz, 1H), 5.07 (dd, J = 8.5, 13.0 Hz, 1H), 4.93 (dd, J = 7.5, 13.0 Hz, 1H), 3.81 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.3, 138.6, 135.7, 130.5, 130.4, 129.1, 122.3, 119.6, 119.3, 18.8, 113.8, 113.0, 110.8, 109.4, 77.5, 55.3, 41.1, 8.6; HRMS m/z (ESI +) calcd for $C_{18}H_{19}N_2O_3$ ([M + H]$^+$) 311.1390, found 311.1394.

(R)-2-(1-(2-Methoxyphenyl)-2-nitroethyl)-3-methyl-1H-indole ***(6ag)****:* Yellow solid; yield 99% (122.9 mg); mp = 135−136 °C; $[\alpha]_D^{25}$ = −66.0 (c 1.0, CH_2Cl_2); 91% ee [Daicel Chiralcel AD-H column (25 cm × 0.46 cm i.d.), *n*-hexane/*i*-PrOH = 90/10, 1.0 mL/min, 254 nm; t_{minor} = 11.7 min, t_{major} = 12.6 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.41(s, 1H), 7.54(d, J = 7.5 Hz, 1H), 7.33−7.28 (m, 2H), 7.24 (dd, J = 2.0, 7.5 Hz, 1H), 7.17 (td, J = 1.5, 7.0 Hz, 1H), 7.11 (td, J = 1.0, 8.0 Hz, 1H), 6.99−6.95 (m, 2H), 5.36 (t, J = 7.5 Hz, 1H), 5.19 (dd, J = 7.5, 12.5 Hz, 1H), 5.05 (dd, J = 8.0, 13.0 Hz, 1H), 4.00 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.6, 135.4, 131.1, 129.6, 129.2, 108.7, 125.4, 121.9, 121.4, 119.2, 118.5, 111.6, 110.6, 108.9, 77.0, 55.7, 38.5, 8.4; HRMS m/z (ESI+) calcd for $C_{18}H_{19}N_2O_3$ ([M + H]$^+$) 311.1390, found 311.1398.

(R)-2-(1-(3,4-Dimethoxyphenyl)-2-nitroethyl)-3-methyl-1H-indole ***(6ah)****:* Yellow solid; yield 99% (134.8 mg); mp = 102−104 °C; $[\alpha]_D^{25}$ = −68.2 (c 1.0, CH_2Cl_2); 92% ee [Daicel Chiralcel AD-H column (25 cm × 0.46 cm i.d.), *n*-hexane/*i*-PrOH = 85/15, 1.0 mL/min, 254 nm; t_{minor} = 13.1 min, t_{major} = 15.4 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (s, 1H), 7.55 (d, J = 7.5 Hz, 1H), 7.25 (d, J = 8.0 Hz, 1H), 7.18 (td, J = 1.0, 7.0 Hz, 1H), 7.13 (td, J = 1.0, 7.5 Hz, 1H), 6.90 (t, J = 1.0 Hz, 2H), 6.78 (s, 1H), 5.22 (dd, J = 2.0, 8.5 Hz, 1H), 5.06 (dd, J = 9.0, 13.0 Hz, 1H), 4.93 (dd, J = 7.0, 13.0 Hz, 1H), 3.89 (s, 3H), 3.85 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.7, 148.9, 135.7, 130.8, 129.4, 129.2, 122.2, 119.6, 118.8, 118.7, 111.8, 111.4, 110.8, 109.0, 77.7, 56.0, 55.9, 40.9, 8.6; HRMS m/z (ESI+) calcd for $C_{19}H_{21}N_2O_4$ ([M + H]$^+$) 341.1496, found 341.1485.

(R)-3-Methyl-2-(1-(naphthalen-1-yl)-2-nitroethyl)-1H-indole ***(6ai)****:* Yellow solid; yield 98% (129.5 mg); mp = 56−59 °C; $[\alpha]_D^{25}$ = −45.2 (c 1.0, CH_2Cl_2); 91% ee [Daicel Chiralcel AD-H column (25 cm × 0.46 cm i.d.), *n*-hexane/*i*-PrOH = 85/15, 1.0 mL/min, 254 nm; t_{minor} = 8.5 min, t_{major} = 10.5 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03−8.01 (m, 1H), 7.91−7.89 (m, 2H), 7.58−7.49 (m, 5H), 7.45 (s, 1H), 7.16−7.09 (m, 3H), 6.05 (t, J = 8.0 Hz, 1H), 5.25 (dd, J = 8.5, 13.0 Hz, 1H), 5.05 (dd, J = 7.5, 13.0 Hz, 1H), 2.51 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.7, 134.3, 132.6, 131.3, 130.4, 129.2, 129.16, 129.08, 127.2, 126.4, 125.3, 122.9, 122.8, 122.3, 119.6, 118.8, 110.8, 109.1, 77.2, 37.3, 8.7; HRMS m/z (ESI+) calcd for $C_{21}H_{19}N_2O_2$ ([M + H]$^+$) 331.1441, found 331.1443.

(R)-3-Methyl-2-(2-nitro-1-(thiophen-2-yl)ethyl)-1H-indole ***(6aj)****:* Yellow solid; yield 95% (108.8 mg); mp = 86−88 °C; $[\alpha]_D^{25}$ = −97.5 (c 1.0, CH_2Cl_2); 92% ee [Daicel Chiralcel AD-H column (25 cm × 0.46 cm i.d.), *n*-hexane/*i*-PrOH = 85/15, 1.0 mL/min, 254 nm; t_{minor} = 8.5 min, t_{major} = 11.2 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88(s, 1H), 7.62(d, J = 8.0 Hz, 1H), 7.31−7.29 (m, 2H), 7.25 (td, J = 1.5, 7.0 Hz, 1H), 7.20 (td, J = 1.5, 8.0 Hz, 1H), 7.03 (dd, J = 3.5, 5.0 Hz, 1H), 7.00 (dt, J = 1.0, 3.0 Hz, 1H), 5.50 (t, J = 7.5 Hz, 1H), 5.03 (dd, J = 8.0, 13.0 Hz, 1H), 4.90 (dd, J = 7.5, 13.0 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.1, 135.7, 129.9, 128.9, 127.2, 125.4, 125.0, 122.5, 119.6, 118.9, 110.9, 109.5, 78.2, 36.8, 8.5; HRMS m/z (ESI+) calcd for $C_{15}H_{15}N_2O_2S$ ([M + H]$^+$) 287.0849, found 287.0851.

(R)-3-Methyl-2-(1-nitro-4-phenylbut-3-en-2-yl)-1H-indole ***(6ak)****:* Yellow solid; yield 72% (88.2 mg); mp = 69−71 °C; $[\alpha]_D^{25}$ = −38.3 (c 1.0, CH_2Cl_2); 90% ee [Daicel Chiralcel AD-H column (25 cm × 0.46 cm i.d.), *n*-hexane/*i*-PrOH = 85/15, 1.0 mL/min, 254 nm; t_{minor} = 7.6 min, t_{major} = 10.4 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.58 (d, J = 7.0 Hz, 1H), 7.39−7.28 (m, 6H), 7.22 (td, J = 1.0, 7.0 Hz, 1H), 7.17 (td, J = 1.0, 7.5 Hz, 1H), 6.57 (dd, J = 0.5, 16 Hz, 1H), 6.38 (dd, J = 6.0, 16.5 Hz, 1H), 4.85 (dd, J = 10.5, 14.5 Hz, 1H), 4.78−4.73 (m, 2H), 2.37(s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.0, 135.8, 133.5, 129.7, 129.2, 128.7, 128.3, 126.5, 124.5, 122.4, 119.7, 118.7, 110.8, 109.6, 78.0, 38.9, 8.6; HRMS m/z (ESI+) calcd for $C_{19}H_{19}N_2O_2$ ([M + H]$^+$) 307.1441, found 307.1447.

(R)-3-Ethyl-2-(2-nitro-1-phenylethyl)-1H-indole ***(6ba)****:* Yellow solid; yield 96% (113.0 mg); mp = 113−115 °C; $[\alpha]_D^{25}$ = −122.3 (c 1.0, CH_2Cl_2); 94% ee [Daicel Chiralcel AD-H column (25 cm × 0.46 cm i.d.), *n*-hexane/*i*-PrOH = 85/15, 1.0 mL/min, 254 nm; t_{minor} = 6.7 min, t_{major} = 8.4 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (s, 1H), 7.61 (d, J = 7.5 Hz, 1H), 7.41 (t, J = 7.0 Hz, 2H), 7.36−7.26 (m, 4H), 7.19 (t, J = 2.0 Hz, 1H), 7.14 (t, J = 2.5 Hz, 1H), 5.28 (t, J = 8.0 Hz, 1H), 5.12 (dd, J = 8.5, 13.0 Hz, 1H), 4.95 (dd, J = 7.5, 12.5 Hz, 1H), 2.86 (q, J = 7.5 Hz, 2H), 1.30 (t, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.2, 136.1, 130.3, 129.4, 128.14, 128.06, 127.2, 122.3, 119.6, 119.1, 116.4, 110.9, 77.9, 40.9, 17.5, 15.6; HRMS m/z (ESI+) calcd for $C_{18}H_{19}N_2O_2$ ([M + H]$^+$) 295.1441, found 295.1448.

(R)-2-(2-Nitro-1-phenylethyl)-3-phenyl-1H-indole ***(6ea)****:* Yellow solid; yield 86% (117.8 mg); mp = 139−140 °C; $[\alpha]_D^{25}$ = −91.0 (c 1.0, CH_2Cl_2); 96% ee [Daicel Chiralcel AD-H column (25 cm × 0.46 cm i.d.), *n*-hexane/*i*-PrOH = 85/15, 1.0 mL/min, 254 nm; t_{minor} = 6.8 min, t_{major} = 9.5 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.59 (d, J = 8.0 Hz, 1H), 7.53−7.48 (m, 4H), 7.43−7.40 (m, 3H), 7.37−7.31 (m, 4H), 7.24 (t, J = 7.0 Hz, 1H), 7.15 (t, J = 8.0 Hz, 1H), 5.28 (t, J = 8.0 Hz, 1H), 5.01 (dd, J = 8.5, 13.5 Hz, 1H), 4.91 (dd, J = 7.0, 13.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.1, 135.6, 134.0, 130.9, 129.8, 129.4, 128.7, 128.2, 128.0, 127.4, 127.1, 122.8, 120.5, 119.6, 116.9, 111.0, 77.7, 41.2; HRMS m/z (ESI+) calcd for $C_{22}H_{19}N_2O_2$ ([M + H]$^+$) 343.1441, found 343.1443.

(R)-5-Methoxy-3-methyl-2-(2-nitro-1-phenylethyl)-1H-indole ***(6fa)****:* Yellow solid; yield 92% (114.2 mg); mp = 178−180 °C; $[\alpha]_D^{25}$ = −95.3 (c 1.0, CH_2Cl_2); 91% ee [Daicel Chiralcel AD-H column (25 cm × 0.46 cm i.d.), *n*-hexane/*i*-PrOH = 85/15, 1.0 mL/min, 254 nm; t_{minor} = 10.2 min, t_{major} = 11.8 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (s, 1H), 7.42−7.39 (m, 2H), 7.36−7.30 (m, 3H), 7.14 (d, J = 9.0 Hz, 1H), 6.98 (d, J = 2.5 Hz, 1H), 6.83 (dd, J = 2.5, 8.5 Hz, 1H), 5.24 (t, J = 8.0 Hz, 1H), 5.08 (dd, J = 8.0, 13.0 Hz, 1H), 4.96 (dd, J = 8.0, 13.0 Hz, 1H), 3.87 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.2, 137.0, 131.5, 130.9, 129.5, 129.4, 128.1, 127.3, 112.4, 111.6, 109.2, 100.7, 77.6, 56.0, 41.2, 8.7; HRMS m/z (ESI+) calcd for $C_{18}H_{19}N_2O_3$ ([M + H]$^+$) 311.1390, found 311.1394.

(R)-3,7-Dimethyl-2-(2-nitro-1-phenylethyl)-1H-indole ***(6ha)****:* Yellow solid; yield 99% (116.5 mg); mp = 108−110 °C; $[\alpha]_D^{25}$ = −49.8 (c 1.0, CH_2Cl_2); 95% ee [Daicel Chiralcel AS-H column (25 cm × 0.46 cm i.d.), *n*-hexane/*i*-PrOH = 85/15, 1.0 mL/min, 254 nm; t_{minor} = 12.3 min, t_{major} = 14.4 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (s, 1H), 7.43−7.39 (m, 3H), 7.36−7.31 (m, 3H), 7.07 (t, J = 7.5 Hz, 1H), 7.00 (d, J = 7.0 Hz, 1H), 5.28 (t, J = 8.0 Hz, 1H), 5.13 (dd, J = 8.0, 13.0 Hz, 1H), 5.01 (dd, J = 8.0, 13.0 Hz, 1H), 2.41 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.2, 135.4, 129.4, 139.4, 128.1, 127.3, 127.2, 123.0, 122.9, 120.0, 116.5, 110.2, 77.8, 41.2, 16.5, 8.8; HRMS m/z (ESI+) calcd for $C_{18}H_{19}N_2O_2$ ([M + H]$^+$) 295.1441, found 295.1445.

(R)-6-Fluoro-3-methyl-2-(2-nitro-1-phenylethyl)-1H-indole ***(6ia)****:* Yellow solid; yield 97% (115.7 mg); mp = 142−144 °C; $[\alpha]_D^{25}$ = −83.2 (c 1.0, CH_2Cl_2); 92% ee [Daicel Chiralcel AD-H column (25 cm × 0.46 cm i.d.), *n*-hexane/*i*-PrOH = 85/15, 1.0 mL/min, 254 nm; t_{minor} = 7.2 min, t_{major} = 8.4 min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (s, 1H), 7.45−7.40 (m, 3H), 7.35 (t, J = 7.0 Hz, 1H), 7.31 (d, J = 7.0 Hz, 2H), 6.92 (td, J = 2.5, 9.5 Hz, 1H), 6.91−6.86 (m, 1H), 5.23 (t, J = 8.0 Hz, 1H), 5.09 (dd, J = 8.0, 13.0 Hz, 1H), 4.97 (dd, J = 8.0, 12.5 Hz, 1H), 2.34 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.1(d, J = 237.5 Hz), 136.9, 135.7 (d, J = 12.5 Hz), 130.8 (d, J = 37.5 Hz), 129.5, 128.2, 127.2, 125.7, 119.5 (d, J = 10.0 Hz), 109.6, 108.3 (d, J = 25 Hz), 97.3 (d, J = 25 Hz), 77.6, 41.1, 8.6; HRMS m/z (ESI+) calcd for $C_{17}H_{16}FN_2O_2$ ([M + H]$^+$) 299.1190, found 299.1190.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00123.

DOI: 10.1021/acs.joc.6b00123
J. Org. Chem. 2016, 81, 3023−3030

X-ray data for **4ab** (CIF)
X-ray data for **6ae** (CIF)
Full experimental and characterization data, including ^{1}H and ^{13}C NMR for all new compounds, and chiral HPLC spectra for the products (PDF)

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

We are grateful for the generous financial support by the National Natural Science foundation of China (Nos. 21372202 and 21522207), the Program for New Century Excellent Talents in University (NCET-12-1086), and the Natural Science foundation of Zhejiang Province (LR14B020001).

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DOI: 10.1021/acs.joc.6b00123
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