Enantioselective Conjugate Addition of N-Heterocycles to α,β-Unsaturated Ketones Catalyzed by Chiral Primary Amines

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Received 29 January 2009

Abstract: A new organocatalytic enantioselective conjugate addition reaction of nitrogen-centered heterocycles with α,β-unsaturated ketones has been developed. Promoted by a chiral cinchona alkaloid derived primary amine, the reaction affords the adducts in moderate to high enantioselectivities.

Key words: primary amines, N-heterocycles, enones, conjugate addition, catalysis

Recently, much attention has been focused on the development of new protocols for the asymmetric synthesis of nitrogen-containing heterocycles because of their broad utility in organic synthesis and medicinal chemistry.[1,2] The conjugate addition of appropriate nitrogen-centered heterocycles to electron-poor alkenes (e.g., aza-Michael) represents one of the most efficient approaches to their synthesis.[3,4] Surprisingly, only a handful of catalytic asymmetric versions of the processes can be identified in the literature. Jacobsen and co-workers disclosed an elegant chiral salen–aluminum-catalyzed conjugate addition of a range of aromatic N-heterocyclic compounds to α,β-unsaturated ketones and imides with high enantioselectivities.[5] Sibi and co-workers also reported chiral-organometallic-mediated highly enantioselective conjugate addition of nitrogen species to α,β-unsaturated systems.[6] Jørgensen and co-workers described an organocatalytic conjugate addition of aromatic N-heterocycles to α,β-unsaturated aldehydes using a chiral secondary amine.[7] Recently we and other groups have successfully developed the hydrogen-bond-mediated asymmetric catalytic conjugation of N-heterocycles to nitroolefins and enones with moderate to good enantioselectivities.[8–10] Nevertheless, the utilization of chiral amine covalently catalyzed conjugate addition of N-heterocycles to enones has not been reported. Herein we wish to disclose an unprecedented promotion of such a process by a chiral primary amine, resulting in good regioselectivities and moderate to high enantioselectivities.

In the exploratory studies, aimed at seeking optimal reaction conditions, eight aminocatalysts **1a–h** (Figure 1) were screened for a model aza-Michael addition reaction of 1*H*-benzotriazole (**2**) with (*E*)-4-phenylbut-3-en-2-one (**3a**) (Table 1). The reaction was initially carried out in the presence of 20 mol% catalyst at room temperature in chloroform. The results of this investigation revealed that aminocatalysts **1a–h** differed significantly with regard to catalytic activity and stereo- and regiocontrol of the process. 1,1,1-Trifluoro-*N*-[(*S*)-pyrrolidin-2-ylmethyl]methanesulfonamide (**1a**) and cinchona alkaloid derived thiourea **1f** were good promoters for the process, providing the products in high yields but with poor enantioselectivities and moderate regioselectivities (Table 1, entries 1 and 6). The use of chiral cyclohexane-1,2-diamine-based thioureas **1b**, **1c**, and **1e** resulted in sluggish reactions (entries 2, 3, and 5), whereas catalyst **1d** gave good yields (**4a**, 13%; **5a**, 60%) and moderate ee values (**4a**, 49% ee; **5a**, 54% ee) (entry 4). Among the catalysts probed, the cinchona alkaloid derived primary amines **1g** and **1h** showed superior activities (reaction time only 3 h; >98% total yield of **4a** and **5a**; entries 7 and 8),[11] but with **1g** giving a much higher enantioselectivity.

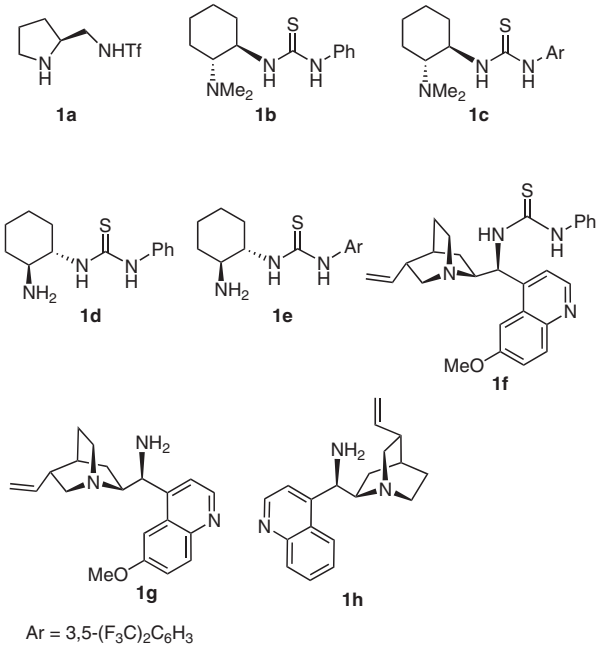
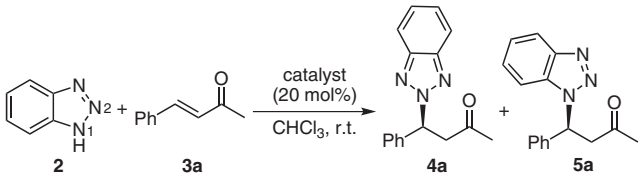


Figure 1 Structures of screened organocatalysts

SYNTHESIS 2009, No. 9, pp 1564–1572
Advanced online publication: 14.04.2009
DOI: 10.1055/s-0029-1216636; Art ID: C00409SS

Table 1 Results of Exploratory Studies of Catalytic Asymmetric Conjugate Addition Reactions of 1*H*-Benzotriazole (**2**) with (*E*)-4-Phenylbut-3-en-2-one (**3a**)[a]

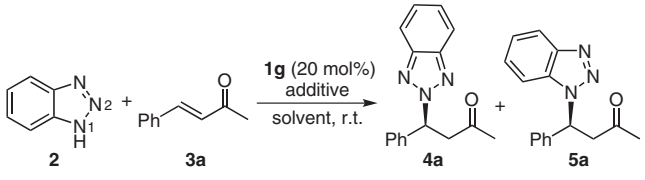


Entry	Catalyst	Time (h)	Yield[b] (%)		ee[c,d,e] (%)	
			4a	**5a**	**4a**	**5a**
1	**1a**	72	30	70	–3.5	12
2	**1b**	168	trace	21	n.d.	–32
3	**1c**	168	trace	trace	n.d.	n.d.
4	**1d**	72	13	60	49	54
5	**1e**	168	trace	57	n.d.	28
6	**1f**	96	27	63	12.5	0
7	**1g**	3	31	69	86	53
8	**1h**	3	40	58	–70	–17

[a] Reaction conditions: **2** (1 equiv), **3a** (2 equiv), cat. (20 mol%), $CHCl_3$, r.t.
[b] Isolated yield.
[c] The ee values were determined by chiral HPLC analysis (Chiralpak AS-H).
[d] n.d. = not determined.
[e] Negative ee values indicate that the opposite enantiomer of **4a** was formed in excess.

The effect of an acid additive, reaction medium, catalyst loading, and reaction temperature on the catalytic efficiency of **1g** was evaluated next. As indicated in Table 2, the various different acid additives gave very diverse results (entries 1–6). Stronger Brønsted acids such as trifluoroacetic acid, *p*-toluenesulfonic acid, and hydrochloric acid (entries 2–5) resulted in excellent regioselectivities, to give the Michael N1-adduct **5a** exclusively, but the enantioselectivities were disappointing (8–17%). When acetic acid was used as additive, the ee of the major product **5a** was slightly lower (44%, Table 2, entry 1) than without the use of additive (53%, Table 1, entry 7). The use of phosphoric acid as additive and a lower temperature of 0 °C resulted in significantly higher enantioselectivities of both **4a** and **5a** (95% and 75% respectively) (entry 7). Probing solvent effects showed that increasing the polarity of the reaction medium resulted in decreased ee values, yields, and reaction activities, for example with propan-2-ol (entry 8), *N*,*N*-dimethylformamide (entry 9), brine (entry 11), tetrahydrofuran (entry 12), and ethyl acetate (entry 13). A further lowering of the reaction temperature to –14 °C and –30 °C resulted in prolonged reaction times without an improvement in enantioselectivity and yield (entries 14 and 15). Lowering the catalyst loading to ten mol% **1g** resulted in an enhanced enantioselectivity of **5a** (79% ee, entry 16 vs 10) without the enantioselectivity of **4a** being sacrificed. Asymmetric counterion-directed catalysis (ACDC)[12] has recently been recognized as an attractive strategy for improving enantioselective transformations. We therefore probed the effect of (*S*)-binol and L-*N*-Boc-phenylglycine on the enantioselectivity of the reaction, and found that the enantioselectivity was improved, although the yield was poor with L-

Table 2 Optimization of Reaction Conditions for Catalytic Asymmetric Conjugate Addition Reactions of 1*H*-Benzotriazole (**2**) with (*E*)-4-Phenylbut-3-en-2-one (**3a**)[a]



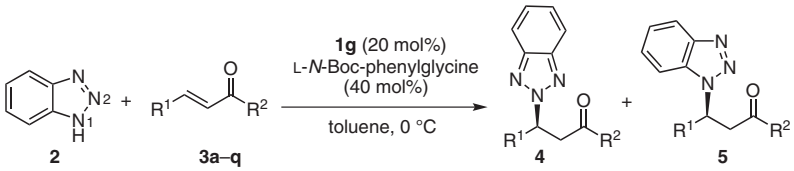
Entry	Solvent	Additive	Time (h)	Yield[b] (%)		ee[c,d] (%)	
				4a	**5a**	**4a**	**5a**
1	$CHCl_3$	AcOH	3	33	66	88	44
2	$CHCl_3$	TFA	3	<5	88	n.d.	15
3	$CHCl_3$	PTSA	3	<5	88	n.d.	17
4	$CHCl_3$	d-CSA	3	<5	84	n.d.	8
5	$CHCl_3$	HCl (2 N)	3	<5	99	n.d.	21
6	$CHCl_3$	H_3PO_4	3	43	56	90	62
7[e]	$CHCl_3$	H_3PO_4	17	30	57	95	75
8[e]	*i*-PrOH	H_3PO_4	36	23	45	85	19
9[e]	DMF	H_3PO_4	36	<5	30	n.d.	0
10[e]	toluene	H_3PO_4	36	26	68	95	76
11[e]	brine	H_3PO_4	36	23	64	75	9
12[e]	THF	H_3PO_4	36	<5	19	n.d.	64
13[e]	EtOAc	H_3PO_4	36	<5	38	n.d.	52
14[f]	$CHCl_3$	H_3PO_4	48	42	42	97	76
15[g]	$CHCl_3$	H_3PO_4	68	<5	23	n.d.	76
16[e,h]	toluene	H_3PO_4	17	38	60	95	79
17[e,i]	toluene	(*S*)-binol	17	36	62	95	84
18[e]	toluene	L-*N*-Boc-phenylglycine	34	<5	39	n.d.	82

[a] Reaction conditions: **2** (1 equiv), **3a** (2 equiv), **1g** (20 mol%), solvent, r.t.
[b] Isolated yield.
[c] The ee values were determined by chiral HPLC analysis (Chiralpak AS-H).
[d] n.d. = not determined.
[e] The reaction was performed at 0 °C.
[f] The reaction was performed at –14 °C.
[g] The reaction was performed at –30 °C.
[h] Catalyst **1g** (10 mol%) and H_3PO_4 (20 mol%) were used.
[i] Catalyst **1g** (20 mol%) and (*S*)-binol (20 mol%) were used.

N-Boc-phenylglycine (entries 17 and 18). The absolute configuration of **4a** and **5a** was determined to be *S*.[13]

Having established the optimized reaction conditions, we then probed the scope and limitations of **1g**-promoted enantioselective conjugate addition of 1*H*-benzotriazole (**2**) to a range of α,β-unsaturated ketones **3** in the presence of L-*N*-Boc-phenylglycine as additive in toluene. The results are summarized in Table 3. Under the reaction conditions, the processes proceeded smoothly to give adduct **5** as the major product, with **4** as a minor one, in moderate to high enantioselectivities for both regioisomers. The conjugate processes are tolerant of significant structural variations of R^1 and R^2 in enones **3**. The electronic effects of the aromatic system R^1 in enones **3** have limited influence on the reaction outcome. Generally, good to high ee values of products **5** were observed with enones **3** bearing electron-neutral (entry 1), electron-withdrawing (entries 2–6), as well as electron-donating (entries 7–10) substituents. A low yield was obtained with unsaturated ketone **3i**, even after a long reaction time (110 h), because of its poor solubility in toluene at 0 °C (entry 9). However, when chloroform was used as the solvent, a significantly higher total yield of up to 99% resulted, with a slight decrease in the ee value for **5i** (74%), but high ee for **4i** (94%) (entry 10). It seems that steric effects influence the regioselectivity of the conjugate addition. The more hindered 2-substituted substrates gave dominant N1-addition products (entries 4–6 and 8). The **1g**-catalyzed enantioselective conjugate addition processes were also applicable to heterocyclic (entries 11 and 12) and aliphatic (entries 13 and

Table 3 Scope of Catalytic Asymmetric Conjugate Addition Reactions of 1*H*-Benzotriazole (**2**) with Enones **3**[a]

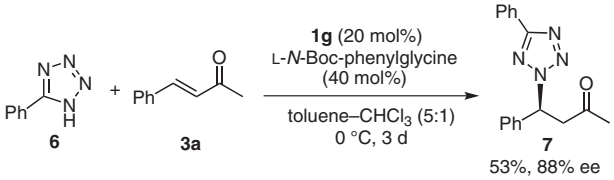


Entry	3	R^1	R^2	Time (h)	Yield[b] (%)		ee[c,d] (%)	
					4	5	4	5
1[e]	**3a**	Ph	Me	17	36	62	95	84
2	**3b**	4-BrC_6H_4	Me	63	16	83	95	81
3	**3c**	4-FC_6H_4	Me	63	18	81	92	69
4	**3d**	2-BrC_6H_4	Me	63	<5	92	n.d.	78
5	**3e**	2-IC_6H_4	Me	63	<5	98	n.d.	86
6	**3f**	2-$O_2NC_6H_4$	Me	63	<5	60	n.d.	77
7	**3g**	4-$MeOC_6H_4$	Me	63	10	87	95	81
8	**3h**	2-$MeOC_6H_4$	Me	63	7	90	92	78
9	**3i**	1,3-benzodioxol-5-yl	Me	110	<5	14	n.d.	88
10[f]	**3i**	1,3-benzodioxol-5-yl	Me	34	12	87	94	74
11	**3j**	2-furyl	Me	110	13	86	71	38
12	**3k**	2-thienyl	Me	64	21	60	88	67
13	**3l**	Bn	Me	64	16	60	91	79
14	**3m**	styryl	Me	64	11	69	83	75
15	**3n**	*n*-C_5H_{11}	Me	64	<5	62	n.d.	63
16	**3o**	Ph	Et	64	20	79	97	78
17[f]	**3p**	4-$MeOC_6H_4$	Ph	72	<5	21	n.d.	75
18[f]	**3q**	Ph	Ph	72	<5	29	n.d.	83

[a] Reaction conditions: **2** (1 equiv), **3** (2 equiv), **1g** (20 mol%), L-*N*-Boc-phenylglycine (40 mol%), toluene, 0 °C.
[b] Isolated yield.
[c] The ee values were determined by chiral HPLC analysis (see experimental section).
[d] n.d. = not determined.
[e] (*S*)-binol (20 mol%) was used as additive instead of L-*N*-Boc-phenylglycine.
[f] $CHCl_3$ was used as solvent.

15) enones. Variation of the R^2 moieties gave mixed results. Aliphatic R^2 substituents behaved similarly to the methyl group (entry 16). However, low yields were obtained for both products (entries 17 and 18), with moderate to good enantioselectivities for the major products, when the R^2 groups are aromatic. Again, as a result of the poor solubilities of **3p** and **3q** in toluene, chloroform was used instead.

In further investigations, we examined the reactivity of other nitrogen heterocycles in this aza-Michael addition (Scheme 1). 5-Phenyl-1*H*-tetrazole (**6**) served as an effective Michael donor in reaction with (*E*)-4-phenylbut-3-en-2-one (**3a**), giving product **7** in 53% yield, 88% ee, and excellent regioselectivity. Unfortunately, however, the process for 1*H*-[1,2,4]triazole was sluggish (<5% yield even after 5 d).



Scheme 1 Conjugate addition of heterocycle **6** to (*E*)-4-phenylbut-3-en-2-one (**3a**) promoted by catalyst **1g**

In summary, motivated by the broad synthetic utility of nitrogen-containing heterocycles and the lack of efficient asymmetric methods for their preparation, we have developed a new catalytic conjugate addition reaction of N-heterocycles with α,β-unsaturated ketones. The process, efficiently catalyzed by cinchona alkaloid derived primary amine **1g**, provides the corresponding adducts in good to high enantiomeric excesses. A range of unsaturated ketones and N-heterocycles can be applied in the reaction. Further investigations aimed at expanding the scope of the conjugate addition process and its applications in biological studies are underway in our laboratory.

Commercially obtained reagents were used as received, unless specified otherwise. ^{1}H and ^{13}C NMR spectra were recorded on Bruker Avance-400 spectrometers. Chemical shifts are reported relative to TMS or the solvent resonances as internal standard. Optical rotations were measured on a Rudolph Research Analytical Autopol III automatic polarimeter. MS was performed on a Micromass GCT CA055 spectrometer. Mass spectra (ESI) were obtained from the University of New Mexico mass spectral facility. TLC was performed on glass plates precoated with silica gel GF254, and spots were visualized with UV light. Flash column chromatography was performed on silica gel. HPLC was carried out on an Agilent 1100 HPLC system with Daicel columns.

Conjugate Addition of *N*-Heterocycle 2 to Enone 3b (Table 3, entry 2); Typical Procedure

1*H*-Benzotriazole (**2**; 36 mg, 0.3 mmol, 1 equiv) was added to a soln of **3b** (135 mg, 0.6 mmol, 2 equiv), 9-epi-9-aminoquinine (**1g**; 19 mg, 0.06 mmol, 20 mol%), and L-*N*-Boc-phenylglycine (30 mg, 0.12 mmol, 40 mol%) in toluene (1 mL), and the resulting mixture was stirred for 63 h at 0 °C. The reaction mixture was directly purified by column chromatography (silica gel, EtOAc–hexane, 1:10 to 1:5) to afford adducts **4b** [yield: 17 mg (16%)] and **5b** [yield: 86 mg (83%)].

(*S*)-4-(2*H*-Benzotriazol-2-yl)-4-phenylbutan-2-one (4a)[5e] (Table 3, entry 1)

Compound **4a** was prepared according to the typical procedure described above for **4b** and **5b**.

Yield: 36%; $[\alpha]_D^{28}$ –29 (*c* 0.9, $CHCl_3$).

HPLC (Chiralpak AS-H, hexane–*i*-PrOH, 60:40, flow rate 0.5 mL/min, λ = 254 nm): t_R (minor) = 16.39 min, t_R (major) = 11.65 min, 97% ee.

(*S*)-4-(1*H*-Benzotriazol-1-yl)-4-phenylbutan-2-one (5a)[5e,9b] (Table 3, entry 1)

Compound **5a** was prepared according to the typical procedure described above for **4b** and **5b**.

Yield: 62%; $[\alpha]_D^{27}$ –20 (*c* 1.0, $CHCl_3$).

HPLC (Chiralpak AS-H, hexane–*i*-PrOH, 60:40, flow rate 1 mL/min, λ = 254 nm); t_R (major) = 5.79 min (major), t_R (minor) = 6.48 min, 84% ee.

(*S*)-4-(2*H*-Benzotriazol-2-yl)-4-(4-bromophenyl)butan-2-one (4b)[5e] (Table 3, entry 2)

Compound **4b** was prepared according to the typical procedure described above for **4b** and **5b**.

Yield: 16%; $[\alpha]_D^{30}$ +72 (*c* 0.95, $CHCl_3$).

HPLC (Chiralpak AD-H, hexane–*i*-PrOH, 70:30, flow rate 1 mL/min, λ = 254 nm): t_R (minor) = 6.85 min, t_R (major) = 8.74 min, 95% ee.

(*S*)-4-(1*H*-Benzotriazol-1-yl)-4-(4-bromophenyl)butan-2-one (5b)[5e] (Table 3, entry 2)

Compound **5b** was prepared according to the typical procedure described above for **4b** and **5b**.

Yield: 83%; $[\alpha]_D^{30}$ +9.5 (*c* 1.0, $CHCl_3$).

HPLC (Chiralpak AS-H, hexane–*i*-PrOH, 70:30, flow rate 1 mL/min, λ = 254): t_R (minor) = 7.50 min, t_R (major) = 10.07 min, 81% ee.

(*S*)-4-(2*H*-Benzotriazol-2-yl)-4-(4-fluorophenyl)butan-2-one (4c) (Table 3, entry 3)

Compound **4c** was prepared according to the typical procedure described above for **4b** and **5b**.

Yield: 18%; $[\alpha]_D^{31}$ +97 (*c* 0.75, $CHCl_3$).

HPLC (Chiralpak AD-H, hexane–*i*-PrOH, 70:30, flow rate 1 mL/min, λ = 254 nm): t_R (minor) = 6.23 min, t_R (major) = 7.88 min, 92% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85–7.87 (dd, *J* = 3.1, 6.6 Hz, 2 H), 7.36–7.41 (m, 4 H), 7.00–7.04 (t, *J* = 8.7 Hz, 2 H), 6.51–6.55 (dd, *J* = 5.3, 9.1 Hz, 1 H), 4.10–4.16 (dd, *J* = 9.1, 17.8 Hz, 1 H), 3.32–3.38 (dd, *J* = 5.3, 17.8 Hz, 1 H), 2.25 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 203.9, 163.9, 161.5, 144.2, 134.5, 134.4, 128.8, 128.7, 126.5, 118.2, 116.0, 115.8, 64.9, 48.5, 30.3.

ESI-HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_{16}H_{14}FN_3NaO$: 306.1019; found: 306.1021.

(*S*)-4-(1*H*-Benzotriazol-1-yl)-4-(4-fluorophenyl)butan-2-one (5c) (Table 3, entry 3)

Compound **5c** was prepared according to the typical procedure described above for **4b** and **5b**.

Yield: 81%; $[\alpha]_D^{31}$ +49 (*c* 3.95, $CHCl_3$).

HPLC (Chiralpak AD-H, hexane–*i*-PrOH, 70:30, flow rate 1 mL/min, λ = 254 nm): t_R (minor) = 7.00 min, t_R (major) = 8.36 min, 69% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.05–8.07 (d, *J* = 8.3 Hz, 1 H), 7.43 (s, 2 H), 7.36–7.39 (m, 1 H), 7.30–7.33 (dd, *J* = 5.2, 8.6 Hz, 2 H), 7.00–7.04 (t, *J* = 8.5 Hz, 2 H), 6.31–6.35 (dd, *J* = 4.9, 8.9 Hz, 1 H), 4.22–4.29 (dd, *J* = 9.0, 17.8 Hz, 1 H), 3.32–3.38 (dd, *J* = 4.9, 17.8 Hz, 1 H), 2.27 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 204.4, 163.8, 161.3, 146.0, 134.6, 134.6, 132.8, 128.5, 128.4, 127.5, 127.2, 124.3, 119.8, 116.1, 115.9, 109.9, 57.6, 48.7, 30.3.

ESI-HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{14}FN_3NaO$: 306.1019; found: 306.1025.

(*S*)-4-(1*H*-Benzotriazol-1-yl)-4-(2-bromophenyl)butan-2-one (5d) (Table 3, entry 4)

Compound **5d** was prepared according to the typical procedure described above for **4b** and **5b**.

Yield: 92%; $[\alpha]_D^{31}$ +166 (*c* 4.5, $CHCl_3$).

HPLC (Chiralcel OD-H, hexane–*i*-PrOH, 70:30, flow rate 1 mL/min, λ = 254 nm): t_R (minor) = 7.66 min, t_R (major) = 6.82 min, 78% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.04–8.06 (d, *J* = 8.3 Hz, 1 H), 7.61–7.64 (dd, *J* = 1.7, 7.6 Hz, 1 H), 7.49–7.51 (d, *J* = 8.3 Hz, 1 H), 7.42–7.45 (m, 1 H), 7.34–7.38 (dt, *J* = 1.0, 7.0 Hz, 1 H), 7.14–7.22 (m, 2 H), 7.02–7.04 (dd, *J* = 2.1, 7.4 Hz, 1 H), 6.81–6.85 (dd, *J* = 3.2, 10.7 Hz, 1 H), 4.24–4.31 (dd, *J* = 10.7, 17.8 Hz, 1 H), 3.20–3.26 (dd, *J* = 3.2, 17.8 Hz, 1 H), 2.28 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 203.8, 145.9, 137.9, 133.2, 133.1, 130.0, 128.4, 128.1, 127.7, 124.4, 122.0, 119.7, 110.1, 57.3, 47.3, 30.1.

ESI-HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{14}BrN_3NaO$: 368.0218; found: 368.0211.

(*S*)-4-(1*H*-Benzotriazol-1-yl)-4-(2-iodophenyl)butan-2-one (5e) (Table 3, entry 5)

Compound **5e** was prepared according to the typical procedure described above for **4b** and **5b**.

Yield: 98%; $[\alpha]_D^{31}$ +226.5 (*c* 5.9, $CHCl_3$).

HPLC (Chiralpak AD-H, hexane–*i*-PrOH, 60:40, flow rate 1 mL/min, λ = 254 nm): t_R (minor) = 7.92 min, t_R (major) = 6.49 min, 86% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.04–8.06 (d, *J* = 8.3 Hz, 1 H), 7.89–7.91 (m, 1 H), 7.43 (s, 2 H), 7.36–7.39 (m, 1 H), 7.30–7.33 (dd, *J* = 5.2, 8.6 Hz, 2 H), 7.00–7.04 (t, *J* = 8.5 Hz, 2 H), 6.31–6.35 (dd, *J* = 4.9, 8.9 Hz, 1 H), 4.22–4.29 (dd, *J* = 9.0, 17.8 Hz, 1 H), 3.32–3.38 (dd, *J* = 4.9, 17.8 Hz, 1 H), 2.27 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 203.7, 146.0, 140.9, 139.9, 133.1, 130.2, 129.3, 127.6, 124.4, 119.7, 110.3, 97.3, 62.4, 47.5, 30.1.

ESI-HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{14}IN_3NaO$: 414.0079; found: 414.0071.

(*S*)-4-(1*H*-Benzotriazol-1-yl)-4-(2-nitrophenyl)butan-2-one (5f) (Table 3, entry 6)

Compound **5f** was prepared according to the typical procedure described above for **4b** and **5b**.

Yield: 60%; $[\alpha]_D^{30}$ +361 (*c* 2.15, $CHCl_3$).

HPLC (Chiralcel OD-H, hexane–*i*-PrOH, 60:40, flow rate 1 mL/min, λ = 254 nm): t_R (minor) = 10.52 min, t_R (major) = 7.67 min, 77% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.04–8.06 (d, *J* = 8.3 Hz, 1 H), 8.01–8.03 (d, *J* = 7.9 Hz, 1 H), 7.43–7.54 (m, 4 H), 7.31–7.39 (m, 2 H), 7.09–7.12 (dd, *J* = 4.2, 9.3 Hz, 1 H), 4.24–4.30 (dd, *J* = 9.3, 18.0 Hz, 1 H), 3.47–3.53 (dd, *J* = 4.2, 18.0 Hz, 1 H), 2.28 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 203.2, 147.9, 145.9, 134.0, 133.9, 133.1, 129.4, 128.9, 128.0, 124.9, 124.6, 119.8, 109.9, 52.9, 48.4, 29.9.

ESI-HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{14}N_4NaO_3$: 333.0964; found: 333.0970.

(*S*)-4-(2*H*-Benzotriazol-2-yl)-4-(4-methoxyphenyl)butan-2-one (4g) (Table 3, entry 7)

Compound **4g** was prepared according to the typical procedure described above for **4b** and **5b**.

Yield: 10%; $[\alpha]_D^{29}$ +30 (*c* 1.1, $CHCl_3$).

HPLC (Chiralpak AD-H, hexane–*i*-PrOH, 70:30, flow rate 1 mL/min, λ = 254 nm): t_R (minor) = 8.14 min, t_R (major) = 10.28 min, 95% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84–7.87 (dd, *J* = 3.1, 6.6 Hz, 2 H), 7.34–7.37 (m, 4 H), 6.84–6.87 (dd, *J* = 2.0, 6.7 Hz, 2 H), 6.48–6.52 (dd, *J* = 5.2, 9.2 Hz, 1 H), 4.09–4.16 (dd, *J* = 9.2, 17.7 Hz, 1 H), 3.76 (s, 3 H), 3.32–3.38 (dd, *J* = 5.2, 7.7 Hz, 1 H), 2.23 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 204.3, 159.7, 144.1, 130.7, 128.2, 126.3, 118.2, 114.3, 65.1, 55.3, 48.5, 30.3.

ESI-HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{17}N_3NaO_2$: 318.1218; found: 318.1227.

(*S*)-4-(1*H*-Benzotriazol-1-yl)-4-(4-methoxyphenyl)butan-2-one (5g) (Table 3, entry 7)

Compound **5g** was prepared according to the typical procedure described above for **4b** and **5b**.

Yield: 87%; $[\alpha]_D^{29}$ +42 (*c* 0.35, $CHCl_3$).

HPLC (Chiralpak AD-H, hexane–*i*-PrOH, 70:30, flow rate 1 mL/min, λ = 254 nm): t_R (minor) = 8.62 min, t_R (major) = 10.11 min, 81% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00–8.02 (d, *J* = 8.2 Hz, 1 H), 7.23–7.42 (m, 5 H), 6.81–6.83 (d, *J* = 8.5 Hz, 2 H), 6.26–6.29 (dd, *J* = 4.8, 9.0 Hz, 1 H), 4.19–4.26 (dd, *J* = 9.1, 17.6 Hz, 1 H), 3.74 (s, 3 H), 3.29–3.35 (dd, *J* = 4.8, 17.6 Hz, 1 H), 2.23 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 204.7, 159.6, 146.1, 132.9, 130.8, 127.9, 127,3, 124.1, 119.7, 114.4, 110.1, 57.9, 55.3, 48.8, 30.4.

ESI-HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{17}N_3NaO_2$: 318.1218; found: 318.1228.

(*S*)-4-(2*H*-Benzotriazol-2-yl)-4-(2-methoxyphenyl)butan-2-one (4h) (Table 3, entry 8)

Compound **4h** was prepared according to the typical procedure described above for **4b** and **5b**.

Yield: 7%; $[\alpha]_D^{29}$ +159 (*c* 0.3, $CHCl_3$).

HPLC (Daicel Chiralpak AD-H, hexane–*i*-PrOH, 70:30, flow rate 1 mL/min, λ = 254 nm): t_R (minor) = 6.14 min, t_R (major) = 9.41 min, 92% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87–7.89 (dd, *J* = 3.1, 6.6 Hz, 2 H), 7.36–7.39 (dd, *J* = 3.1, 6.6 Hz, 2 H), 7.24–7.28 (m, 1 H), 7.01–7.05 (dd, *J* = 3.7, 10.6 Hz, 1 H), 6.92–6.94 (d, *J* = 8.2 Hz, 1 H), 6.81–6.85 (t, *J* = 7.7 Hz, 1 H), 6.77–6.79 (dd, *J* = 1.7, 7.7 Hz, 1 H), 4.05–4.12 (dd, *J* = 10.6, 17.7 Hz, 1 H), 3.91 (s, 3 H), 3.20–3.26 (dd, *J* = 3.7, 7.7 Hz, 1 H), 2.25 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 204.7, 155.6, 144.1, 129.4, 127.6, 126.7, 126.2, 120.9, 118.3, 110.8, 60.0, 55.7, 47.5, 30.1.

ESI-HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{17}N_3NaO_2$: 318.1218; found: 318.1223.

(*S*)-4-(1*H*-Benzotriazol-1-yl)-4-(2-methoxyphenyl)butan-2-one (5h) (Table 3, entry 8)

Compound **5h** was prepared according to the typical procedure described above for **4b** and **5b**.

Yield: 90%; $[\alpha]_D^{30}$ +110 (*c* 1.0, $CHCl_3$).

HPLC (Chiralpak AD-H, hexane–*i*-PrOH, 70:30, flow rate 1 mL/min, λ = 254 nm); t_R (minor) = 6.65 min, t_R (major) = 7.22 min, 78% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99–8.01 (d, *J* = 8.2 Hz, 1 H), 7.48–7.50 (d, *J* = 8.3 Hz, 1 H), 7.36–7.40 (m, 1 H), 7.30–7.33 (m, 1 H), 7.22–7.27 (m, 1 H), 6.96–6.98 (d, *J* = 7.6 Hz, 1 H), 6.89–6.91 (d, *J* = 8.3 Hz, 1 H), 6.80–6.83 (m, 1 H), 4.21–4.28 (ddd, *J* = 1.9, 10.5, 17.7 Hz, 1 H), 3.90 (s, 3 H), 3.22–3.28 (dd, *J* = 3.5, 7.7 Hz, 1 H), 2.22 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 204.8, 155.8, 145.9, 133.2, 129.5, 127.2, 127.1, 126.9, 124.0, 121.1, 119.5, 110.7, 110.3, 55.6, 51.8, 47.1, 30.3.

ESI-HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{17}N_3NaO_2$: 318.1218; found: 318.1230.

(*S*)-4-(1,3-Benzodioxol-5-yl)-4-(1*H*-benzotriazol-1-yl)butan-2-one (5i) (Table 3, entry 9)

Compound **5i** was prepared according to the typical procedure described above for **4b** and **5b**.

Yield: 14%; $[\alpha]_D^{31}$ +56 (*c* 0.75, $CHCl_3$).

HPLC (Chiralpak AD-H, hexane–*i*-PrOH, 70:30, flow rate 1 mL/min, λ = 254 nm): t_R (minor) = 9.44 min, t_R (major) = 10.78 min, 88% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.05–8.07 (d, *J* = 8.1 Hz, 1 H), 7.36–7.49 (m, 3 H), 6.83–6.85 (dd, *J* = 1.6, 8.0 Hz, 1 H), 6.78 (d, *J* = 1.6 Hz, 1 H), 6.74–6.76 (d, *J* = 8.0 Hz, 1 H), 6.23–6.27 (dd, *J* = 4.7, 9.0 Hz, 1 H), 5.92–5.95 (d, *J* = 9.3 Hz, 2 H), 4.20–4.27 (dd, *J* = 9.2, 17.7 Hz, 1 H), 3.30–3.35 (dd, *J* = 4.8, 17.7 Hz, 1 H), 2.27 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 204.7, 148.3, 147.8, 146.0, 132.9, 132.5, 127.4, 127.2, 124.2, 120.3, 119.7, 110.1, 108.5, 107.0, 101.4, 58.2, 48.7, 30.4.

ESI-HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{15}N_3NaO_3$: 332.1011; found: 332.1007.

(*S*)-4-(2*H*-Benzotriazol-2-yl)-4-(2-furyl)butan-2-one (4j) (Table 3, entry 11)

Compound **4j** was prepared according to the typical procedure described above for **4b** and **5b**.

Yield: 13%; $[\alpha]_D^{31}$ –15 (*c* 0.5, $CHCl_3$).

HPLC (Chiralcel OD-H, hexane–*i*-PrOH, 60:40, flow rate 1 mL/min, λ = 254 nm): t_R (minor) = 6.36 min, t_R (major) = 5.59 min, 71% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85–7.88 (dd, *J* = 3.1, 6.6 Hz, 2 H), 7.36–7.39 (m, 3 H), 6.61–6.65 (dd, *J* = 5.6, 8.7 Hz, 1 H), 6.43–6.44 (d, *J* = 3.3 Hz, 1 H), 6.34–6.36 (dd, *J* = 1.9, 3.3 Hz, 1 H), 4.03–4.10 (dd, *J* = 8.7, 17.8 Hz, 1 H), 3.51–3.57 (dd, *J* = 5.6, 7.8 Hz, 1 H), 2.26 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 203.5, 150.3, 144.2, 143.1, 126.5, 118.3, 110.6, 108.7, 59.0, 45.6, 30.2.

ESI-HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{13}N_3NaO_2$: 278.0905; found: 278.0910.

(*S*)-4-(1*H*-Benzotriazol-1-yl)-4-(2-furyl)butan-2-one (5j) (Table 3, entry 11)

Compound **5j** was prepared according to the typical procedure described above for **4b** and **5b**.

Yield: 86%; $[\alpha]_D^{30}$ –23 (*c* 1.2, $CHCl_3$).

HPLC (Chiralcel OD-H, hexane–*i*-PrOH, 60:40, flow rate 0.5 mL/min, λ = 254 nm): t_R (minor) = 13.94 min, t_R (major) = 13.16 min, 38% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01–8.04 (d, *J* = 8.4 Hz, 1 H), 7.58–7.60 (d, *J* = 8.4 Hz, 1 H), 7.45–7.49 (m, 1 H), 7.33–7.37 (m, 2 H), 6.47–6.51 (dd, *J* = 5.3, 8.8 Hz, 1 H), 6.30 (s, 2 H), 4.04–4.11 (dd, *J* = 8.8, 17.8 Hz, 1 H), 3.52–3.58 (dd, *J* = 5.3, 17.8 Hz, 1 H), 2.22 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 203.8, 150.6, 145.9, 142.9, 132.9, 127.6, 124.2, 119.8, 110.7, 110.0, 108.2, 51.8, 45.6, 30.2.

ESI-HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{13}N_3NaO_2$: 278.0905; found: 278.0898.

(*S*)-4-(2*H*-Benzotriazol-2-yl)-4-(2-thienyl)butan-2-one (4k) (Table 3, entry 12)

Compound **4k** was prepared according to the typical procedure described above for **4b** and **5b**.

Yield: 21%; $[\alpha]_D^{31}$ +42 (*c* 0.85, $CHCl_3$).

HPLC (Chiralpak AD-H, hexane–*i*-PrOH, 70:30, flow rate 1 mL/min, λ = 254 nm): t_R (minor) = 7.49 min, t_R (major) = 8.92 min, 88% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85–7.88 (dd, *J* = 3.1, 6.6 Hz, 2 H), 7.36–7.39 (dd, *J* = 3.1, 6.6 Hz, 2 H), 7.25–7.27 (dd, *J* = 1.0, 5.1 Hz, 1 H), 7.16–7.17 (d, *J* = 3.4 Hz, 1 H), 6.94–6.96 (dd, *J* = 3.6, 5.1 Hz, 1 H), 6.80–6.84 (dd, *J* = 5.4, 9.0 Hz, 1 H), 4.12–4.19 (dd, *J* = 9.0, 17.7 Hz, 1 H), 3.48–3.54 (dd, *J* = 5.4, 7.8 Hz, 1 H), 2.24 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 203.5, 144.2, 140.8, 126.9, 126.5, 126.4, 126.1, 118.3, 61.0, 48.9, 30.3.

ESI-HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{13}N_3NaOS$: 294.0677; found: 294.0687.

(*S*)-4-(1*H*-Benzotriazol-1-yl)-4-(2-thienyl)butan-2-one (5k) (Table 3, entry 12)

Compound **5k** was prepared according to the typical procedure described above for **4b** and **5b**.

Yield: 60%; $[\alpha]_D^{31}$ –14.5 (*c* 2.3, $CHCl_3$).

HPLC (Chiralpak AD-H, hexane–*i*-PrOH, 70:30, flow rate 1 mL/min, λ = 254 nm): t_R (minor) = 8.48 min, t_R (major) = 7.67 min, 67% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.02–8.05 (d, *J* = 8.3 Hz, 1 H), 7.56–7.58 (d, *J* = 8.3 Hz, 1 H), 7.44–7.48 (m, 1 H), 7.33–7.37 (m, 1 H), 7.22–7.23 (d, *J* = 5.1 Hz, 1 H), 7.03–7.04 (d, *J* = 3.4 Hz, 1 H), 6.90–6.92 (m, 1 H), 6.60–6.62 (dd, *J* = 5.0, 8.9 Hz, 1 H), 4.21–4.27 (dd, *J* = 8.9, 17.8 Hz, 1 H), 3.48–3.54 (dd, *J* = 5.0, 17.8 Hz, 1 H), 2.23 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 204.0, 145.9, 141.3, 132.8, 127.6, 127.0, 126.0, 125.9, 124.3, 119.9, 109.9, 53.6, 49.2, 30.3.

ESI-HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{13}N_3NaOS$: 294.0677; found: 294.0682.

(*R*)-4-(2*H*-Benzotriazol-2-yl)-5-phenylpentan-2-one (4l) (Table 3, entry 13)

Compound **4l** was prepared according to the typical procedure described above for **4b** and **5b**.

Yield: 16%; $[\alpha]_D^{31}$ +66.5 (*c* 0.65, $CHCl_3$).

HPLC (Chiralcel OD-H, hexane–*i*-PrOH, 80:20, flow rate 1 mL/min, λ = 254 nm): t_R (minor) = 6.68 min, t_R (major) = 6.16 min, 91% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84–7.86 (dd, *J* = 3.1, 6.5 Hz, 2 H), 7.37–7.39 (dd, *J* = 3.1, 6.5 Hz, 2 H), 7.21–7.24 (m, 3 H), 7.07–7.09 (m, 2 H), 5.64–5.71 (m, 1 H), 3.51–3.58 (dd, *J* = 8.4, 17.7 Hz, 1 H), 3.45–3.50 (dd, *J* = 7.0, 13.7 Hz, 1 H), 3.24–3.30 (dd, *J* = 7.4, 13.7 Hz, 1 H), 3.02–3.07 (dd, *J* = 5.3, 17.7 Hz, 1 H), 2.14 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 204.7, 144.0, 136.4, 129.1, 128.7, 127.1, 126.3, 118.1, 63.8, 46.6, 41.8, 30.3.

ESI-HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{17}N_3NaO$: 302.1269; found: 302.1270.

(*R*)-4-(1*H*-Benzotriazol-1-yl)-5-phenylpentan-2-one (5l) (Table 3, entry 13)

Compound **5l** was prepared according to the typical procedure described above for **4b** and **5b**.

Yield: 60%; $[\alpha]_D^{31}$ +57.5 (*c* 2.5, $CHCl_3$).

HPLC (Chiralcel OD-H, hexane–*i*-PrOH, 60:40, flow rate 1 mL/min, λ = 254 nm): t_R (minor) = 7.26, min, t_R (major) = 5.89 min, 79% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97–7.99 (m, 1 H), 7.29–7.34 (m, 2 H), 7.26–7.28 (dd, *J* = 1.9, 5.1 Hz, 1 H), 7.12–7.13 (m, 3 H), 7.43–7.54 (m, 4 H), 6.94–6.96 (m, 2 H), 5.40–5.43 (m, 1 H), 3.66–3.73 (dd, *J* = 8.3, 18.0 Hz, 1 H), 3.29–3.33 (m, 2 H), 3.20–3.26 (dd, *J* = 5.0, 18.0 Hz, 1 H), 2.13 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 205.1, 145.4, 136.6, 133.5, 128.9, 128.6, 127.1, 127.0, 123.8, 119.5, 109.6, 56.2, 47.3, 41.8, 30.4.

ESI-HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{17}N_3NaO$: 302.1269; found: 302.1268.

(*S*,*E*)-4-(2*H*-Benzotriazol-2-yl)-6-phenylhex-5-en-2-one (4m) (Table 3, entry 14)

Compound **4m** was prepared according to the typical procedure described above for **4b** and **5b**.

Yield: 11%; $[\alpha]_D^{31}$ +31.5 (*c* 0.5, $CHCl_3$).

HPLC (Chiralpak AD-H, hexane–*i*-PrOH, 70:30, flow rate 1 mL/min, λ = 254 nm): t_R (minor) = 7.51 min, t_R (major) = 9.23 min, 83% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87–7.90 (dd, *J* = 3.1, 6.6 Hz, 2 H), 7.40–7.41 (d, *J* = 2.8 Hz, 1 H), 7.35–7.40 (m, 3 H), 7.25–7.32 (m, 3 H), 6.66–6.70 (d, *J* = 5.8 Hz, 1 H), 6.45–6.51 (dd, *J* = 7.8, 15.8 Hz, 1 H), 6.12–6.18 (m, 1 H), 3.78–3.85 (dd, *J* = 8.2, 17.6 Hz, 1 H), 3.26–3.32 (dd, *J* = 5.8, 17.6 Hz, 1 H), 2.24 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 204.0, 144.2, 135.6, 133.9, 128.9, 128.6, 128.4, 127.3, 126.8, 126.4, 126.0, 118.2, 64.2, 47.6, 30.5.

ESI-HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{17}N_3NaO$: 314.1269; found: 314.1266.

(*S*,*E*)-4-(1*H*-Benzotriazol-1-yl)-6-phenylhex-5-en-2-one (5m) (Table 3, entry 14)

Compound **5m** was prepared according to the typical procedure described above for **4b** and **5b**.

Yield: 69%; $[\alpha]_D^{31}$ –62 (*c* 2.7, $CHCl_3$).

HPLC (Chiralpak AD-H, hexane–*i*-PrOH, 70:30, flow rate 1 mL/min, λ = 254 nm): t_R (minor) = 7.76 min, t_R (major) = 9.59 min, 75% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.06–8.09 (d, *J* = 8.4 Hz, 1 H), 7.65–7.67 (d, *J* = 8.4 Hz, 1 H), 7.47–7.51 (m, 1 H), 7.36–7.40 (m, 1 H), 7.25–7.34 (m, 5 H), 6.53–6.57 (d, *J* = 5.9 Hz, 1 H), 6.41–6.47 (dd, *J* = 7.2, 15.9 Hz, 1 H), 5.96–6.02 (m, 1 H), 3.91–3.97 (dd, *J* = 8.4, 17.8 Hz, 1 H), 3.30–3.36 (dd, *J* = 5.3, 17.7 Hz, 1 H), 2.24 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 204.5, 145.9, 135.4, 133.2, 133.0, 128.7, 128.4, 127.5, 126.7, 126.1, 124.3, 119.8, 110.1, 56.6, 47.4, 30.5.

ESI-HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{17}N_3NaO$: 314.1269; found: 314.1271.

(*R*)-4-(1*H*-Benzotriazol-1-yl)nonan-2-one (5n) (Table 3, entry 15)

Compound **5n** was prepared according to the typical procedure described above for **4b** and **5b**.

Yield: 62%; $[\alpha]_D^{31}$ +5 (*c* 2.4, $CHCl_3$).

HPLC (Daicel Chiralcel OD-H, hexane–*i*-PrOH, 60:40, flow rate 0.5 mL/min, λ = 254 nm): t_R (minor) = 9.61 min, t_R (major) = 9.03 min, 63% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.04–8.06 (d, *J* = 8.4 Hz, 1 H), 7.64–7.66 (d, *J* = 8.4 Hz, 1 H), 7.49–7.53 (m, 1 H), 7.35–7.39 (m, 1 H), 5.25–5.29 (m, 1 H), 3.54–3.61 (dd, *J* = 8.3, 17.9 Hz, 1 H), 3.10–3.16 (dd, *J* = 5.0, 17.9 Hz, 1 H), 2.15–2.12 (m, 1 H), 2.12 (s, 3 H), 1.91–2.00 (m, 1 H), 1.20–1.22 (m, 5 H), 1.00–1.03 (m, 1 H), 0.79–0.82 (t, *J* = 6.7 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 205.3, 145.6, 133.5, 127.2, 123.9, 119.8, 109.8, 54.5, 48.2, 35.3, 31.1, 30.4, 25.6, 22.3, 13.8.

ESI-HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{21}N_3NaO$: 282.1582; found: 282.1595.

(*S*)-1-(2*H*-Benzotriazol-2-yl)-1-phenylpentan-3-one (4o) (Table 3, entry 16)

Compound **4o** was prepared according to the typical procedure described above for **4b** and **5b**.

Yield: 20%; $[\alpha]_D^{31}$ +90 (*c* 0.85, $CHCl_3$).

HPLC (Chiralpak AD-H, hexane–*i*-PrOH, 70:30, flow rate 1 mL/min, λ = 254 nm): t_R (minor) = 7.19 min, t_R (major) = 9.47 min, 97% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85–7.87 (dd, *J* = 3.1, 6.6 Hz, 2 H), 7.28–7.40 (m, 7 H), 6.57–6.61 (dd, *J* = 5.1, 9.4 Hz, 1 H), 4.10–4.17 (dd, *J* = 9.4, 17.5 Hz, 1 H), 3.30–3.36 (dd, *J* = 5.1, 17.5 Hz, 1 H), 2.45–2.62 (m, 2 H), 1.03–1.07 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 206.9, 144.2, 138.8, 128.9, 128.5, 126.8, 126.3, 118.2, 65.7, 47.4, 36.4, 7.53.

ESI-HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{17}N_3NaO$: 302.1269; found: 302.1278.

(*S*)-1-(1*H*-Benzotriazol-1-yl)-1-phenylpentan-3-one (5o) (Table 3, entry 16)

Compound **5o** was prepared according to the typical procedure described above for **4b** and **5b**.

Yield: 79%; $[\alpha]_D^{32}$ +43.5 (*c* 3.3, $CHCl_3$).

HPLC (Chiralpak AD-H, hexane–*i*-PrOH, 70:30, flow rate 1 mL/min, λ = 254 nm): t_R (minor) = 6.93 min, t_R (major) = 7.64 min, 78% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.02–8.04 (d, *J* = 8.3 Hz, 1 H), 7.39–7.43 (m, 2 H), 7.27–7.34 (m, 6 H), 6.34–6.38 (dd, *J* = 4.8, 9.4 Hz, 1 H), 4.21–4.28 (dd, *J* = 9.4, 17.5 Hz, 1 H), 3.28–3.34 (dd, *J* = 4.8, 17.5 Hz, 1 H), 2.32–2.65 (m, 2 H), 2.01–1.05 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 207.4, 146.0, 138.9, 133.0, 129.1, 128.6, 127.4, 126.6, 124.2, 119.8, 110.0, 58.5, 47.7, 36.5, 7.45.

ESI-HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{17}N_3NaO$: 302.1269; found: 302.1263.

(*S*)-3-(1*H*-Benzotriazol-1-yl)-3-(4-methoxyphenyl)-1-phenylpropan-1-one (5p)[9b] (Table 3, entry 17)

Compound **5p** was prepared according to the typical procedure described above for **4b** and **5b**.

Yield: 21%; $[\alpha]_D^{31}$ –12 (*c* 1.25, $CHCl_3$).

HPLC (Chiralpak AD-H, hexane–*i*-PrOH, 70:30, flow rate 1 mL/min, λ = 254 nm): t_R (minor) = 21.78 min, t_R (major) = 29.72 min, 74% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.03–8.05 (d, *J* = 8.3 Hz, 1 H), 7.99–8.01 (dd, *J* = 1.4, 8.5 Hz, 2 H), 7.54–7.60 (m, 2 H), 7.42–7.49 (m, 3 H), 7.34–7.38 (m, 3 H), 6.85–6.87 (d, *J* = 8.8 Hz, 2 H), 6.53–6.57 (dd, *J* = 5.2, 8.5 Hz, 1 H), 4.79–4.85 (dd, *J* = 8.5, 17.9 Hz, 1 H), 3.89–3.95 (dd, *J* = 5.2, 17.9 Hz, 1 H), 3.76 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.0, 196.1, 159.6, 158.1, 146.2, 136.3, 135.9, 133.6, 133.0, 132.9, 131.3, 131.1, 129.1, 128.7, 128.6, 128.2, 128.1, 128.0, 127.3, 124.0, 119.8, 114.4, 113.6, 110.0, 58.0, 55.3, 55.1, 44.5.

ESI-HRMS: *m/z* [M + Na]$^+$ calcd for $C_{22}H_{19}N_3NaO$: 380.1375; found: 380.1389.

(*S*)-3-(1*H*-Benzotriazol-1-yl)-1,3-diphenylpropan-1-one (5q)[9b] (Table 3, entry 18)

Compound **5q** was prepared according to the typical procedure described above for **4b** and **5b**.

Yield: 29%; $[\alpha]_D^{31}$ –19.5 (*c* 1.5, $CHCl_3$).

HPLC (Chiralcel OD-H, hexane–*i*-PrOH, 80:20, flow rate 1 mL/min, λ = 254 nm): t_R (minor) = 12.55 min, t_R (major) = 11.35 min, 83% ee.

(*S*)-4-Phenyl-4-(5-phenyl-2*H*-tetrazol-2-yl)butan-2-one (7)

Compound **7** was prepared according to the typical procedure described above for **4b** and **5b**.

Yield: 53%; $[\alpha]_D^{32}$ +51 (*c* 3.3, $CHCl_3$).

HPLC (Chiralcel OD-H, hexane–*i*-PrOH, 80:20, flow rate 1 mL/min, λ = 254 nm): t_R (minor) = 16.45 min, t_R (major) = 13.47 min, 88% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14–8.16 (m, 2 H), 7.46–7.50 (m, 3 H), 7.34–7.39 (m, 5 H), 6.48–6.51 (dd, *J* = 5.1, 9.3 Hz, 1 H), 4.02–4.09 (dd, *J* = 9.3, 17.9 Hz, 1 H), 3.32–3.38 (dd, *J* = 5.0, 17.9 Hz, 1 H), 2.26 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 203.5, 165.0, 137.4, 130.3, 129.1, 128.9, 128.8, 127.4, 126.9, 126.8, 63.1, 48.1, 30.3.

ESI-HRMS: *m/z* [M + Na]$^+$ calcd for $C_{17}H_{16}N_4NaO$: 315.1222; found: 315.1226.

Acknowledgment

We are grateful for financial support from the School of Pharmacy, East China University of Science & Technology and the National Science Foundation of China (0801031005), and the National Science Foundation (CHE-0704015).

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