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Organocatalytic Enantioselective aza-Michael Additions of N-Heterocycles to α,β-Unsaturated Enones

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A procedure for enantioselective organocatalytic conjugate additions of a variety of N-heterocycles to α,β-unsaturated enone systems is presented. The reactions are efficiently catalyzed by salts of 9-amino-9-deoxy-epiquinine (**3d**). Cyclic, acyclic, and aromatic enones can be used in reactions with 1*H*-benzotriazole (**1a**) or 5-phenyltetrazole derivatives **12**, providing the Michael addition products in high yields and with good to excellent enantioselectivities.

Introduction

Nitrogen-containing heterocycles and their derivatives have broad application in synthetic, materials, and biological chemistry, and as a result their synthesis and reactivity are subjects of considerable interest.[1] Conjugate addition reactions of nitrogen-centered heterocyclic nucleophiles to electron-deficient olefins serve as a powerful preparative method in the area of heterocyclic chemistry. An asymmetric version of this Michael addition process would furnish enantiomerically enriched adducts, but to date reports of this reaction are sparse. Jacobsen and Gandelman,[2] for example, accomplished additions of a range of different aromatic N-heterocyclic compounds to unsaturated ketones and imides with high enantioselectivities with the aid of a chiral Al-salen catalyst, and Miller and co-workers[3] have described the use of peptides as catalysts for asymmetric conjugations of azide to unsaturated imides with moderate to good enantioselectivity. In another report, Wang and co-workers[4] used 6′-hydroxyquinine as a catalyst for asymmetric additions of 1*H*-benzotriazole to nitroolefins and quinine-derived thiourea[5] for addition to aromatic enones with moderate enantioselectivities. MacMillan and co-worker[6] demonstrated the enantioselective formation of β-amino aldehydes through additions of *O*-(*tert*-butyldimethylsilyl)-protected carbamates to α,β-unsaturated aldehydes, Jørgensen and co-workers[7] succeeded in additions of 1,2,4-triazoles to α,β-unsaturated aldehydes with high enantioselectivities with the aid of a chiral 2-[bis(3,5-bis-trifluoromethylphenyl)(trimethylsilanyloxy)-methyl]pyrrolidine catalyst, and Vicario and co-workers[8] used a chiral imidazolidinone as catalyst for asymmetric additions of 5-phenyltetrazole to α,β-unsaturated aldehydes with high enantioselectivity. Zhong and co-workers[9] have developed a novel, practical, and highly enantio- and diastereoselective domino reaction based on the use of L-proline for the synthesis of functionalized tetrahydro-1,2-oxazines (THOs).

Chiral primary amines are also effective catalysts for enantioselective β-additions to α,β-unsaturated carbonyl compounds.[10] In the case of these α,β-unsaturated systems, the catalyst activates the substrate through the iminium ion mechanism, thereby facilitating the addition of the nucleophile to the β-carbon atom. This reaction protocol has been developed in its organocatalytic version for a number of different reactions such as Michael additions,[11] Diels–Alder reactions,[12] cyclopropanation reactions,[13] epoxidation reactions,[14] and aziridination reactions.[15]

Here we wish to describe a more general and efficient enantioselective process for organocatalytic conjugate additions of a broad spectrum of nucleophilic heterocycle species to enones, catalyzed by a primary amine organocatalyst derived from a cinchona alkaloid.[16] The reactions afford good yields and enantioselectivities with 1*H*-benzotriazole and tetrazole as nucleophiles and a diverse array of cyclic, acyclic, or aromatic enones as electrophiles.

Results and Discussion

In an exploratory study, a series of chiral amines were screened as bifunctional organocatalysts for their ability to promote the Michael addition reaction between 1*H*-benzotriazole (**1a**) and cyclohex-2-en-1-one (**2a**) in $PhCH_3$ at room temperature (Table 1). The results of this investigation revealed that the aminocatalysts **3a**–**f** differed significantly with regard to catalytic activity and stereo- and regiocontrol of the process. Interestingly, secondary amines such as **3a** (Table 1, Entry 1) afforded poor results. Because the rela-

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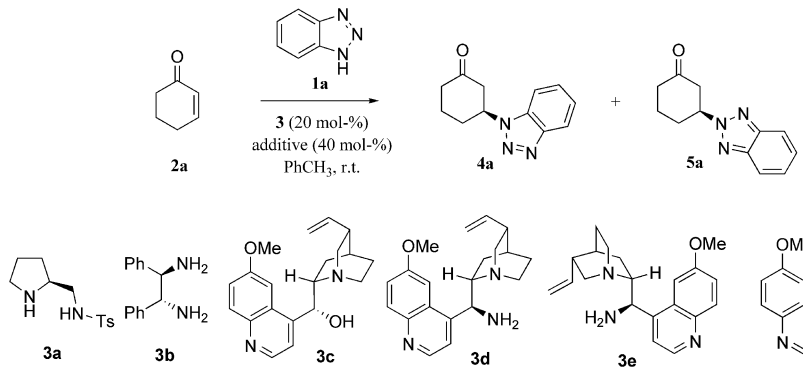
Table 1. Catalytic asymmetric Michael addition reaction between 1*H*-benzotriazole (**1a**) and cyclohex-2-en-1-one (**2a**).[a]



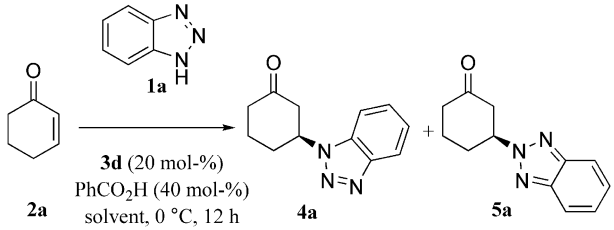
Entry	Cat.	Additive	Time [h]	Yield [%][b]		*ee* [%][c]	
				4a	**5a**	**4a**	**5a**
1	**3a**	$PhCO_2H$	24	30	10	0	0
2	**3b**	$PhCO_2H$	24	30	20	–74	–61
3	**3c**	–	24	50	25	0	0
4	**3d**	–	4	60	30	38	40
5[d]	**3d**	$PhCO_2H$	4	67	33	73	72
6	**3d**	$PhCO_2H$	3	72	28	86	83
7[e]	**3d**	$PhCO_2H$	12	72	24	90	90
8[f]	**3d**	$PhCO_2H$	24	42	15	75	80
9	**3d**	TFA[g]	4	66	33	55	65
10	**3d**	TMA[g]	4	60	40	45	81
11	**3e**	$PhCO_2H$	4	70	30	–80	–78
12	**3f**	$PhCO_2H$	4	75	25	55	58

[a] Reaction conditions: **1a** (0.125 mmol), **2a** (0.60 mmol), **3** (20 mol-%), and additive (40 mol-%) in $PhCH_3$ (1.25 mL) were stirred at room temperature. [b] Isolated yield. [c] Determined by HPLC analysis. [d] PhCOOH: 20 mol-%. [e] Reaction temperature: 0 °C. [f] Reaction temperature: –20 °C. [g] TFA = trifluoroacetic acid; TMA = *p*-methylmandelic acid.

tive bulkiness of secondary amines might be unfavorable for the formation of iminium ions with α,β-unsaturated ketones, we wondered whether primary amines might be more suitable for enone activation as a result of their reduced steric requirements.

Preliminary studies confirmed that the primary amine **3b** was able to promote the reaction with moderate catalytic efficiency, enantioselectivity, and regioselectivity (Table 1, Entry 2). Subsequently we found that 9-amino-9-deoxy-epiquinine (**3d**) provided the products in high yields (reaction time only 4 h; 90% total yield of **4a** and **5a**) but with poor enantioselectivities (38% *ee*, Entry 4). Of the systems tested, a combination of PhCOOH (40 mol-%) and **3d** (20 mol-%), which was very recently described as an effective catalyst for enone activation, has the most favorable characteristics in terms of reaction time (4 h) and enantioselectivity with respect both to **4a** and to **5a** (86% and 83%, respectively) at room temperature (Table 1, Entry 6). We also found that lowering the temperature to 0 °C resulted in an improved enantioselectivity without any significant lowering of yield, although with an increase in reaction time (Table 1, Entry 7). A much longer reaction time (24 h) was required when the reaction temperature was –20 °C (Table 1, Entry 8) and enantioselectivity was reduced. Solvent effects were also examined and it was found that $PhCH_3$ was ideal for this process (Table 2).

Table 2. Effect of solvent on the catalytic asymmetric Michael addition reaction between 1*H*-benzotriazole (**1a**) and cyclohex-2-en-1-one (**2a**).[a]



Entry	Solvent	Yield [%][b]		*ee* [%][c]	
		4a	**5a**	**4a**	**5a**
1	$PhCH_3$	72	24	90	90
2	CH_2Cl_2	70	30	56	64
3	$CHCl_3$	75	25	63	70
4	THF	69	31	83	72
5	CH_3OH	30	30	0	21
6	H_2O	20	60	0	–10

[a] Reaction conditions: **1a** (0.125 mmol), **2a** (0.60 mmol), **3d** (20 mol-%), and PhCOOH (40 mol-%) in solvent (1.25 mL) were stirred at 0 °C. [b] Isolated yield. [c] Determined by HPLC analysis.

Parts a and b of Figure 1 show the effects of the concentration of the reaction mixture and the mol ratio of cyclohexenone **2a** to 1*H*-benzotriazole (**1a**), respectively, on the

enantioselectivity for the Michael addition between 1*H*-benzotriazole and cyclohexenone. As can be seen from Figure 1 (a), an increase in the enantioselectivity (from 67 to 90% *ee* for **4a** and from 65 to 90% *ee* for **5a**) was observed with decreasing concentration of the reaction mixture (Figure 1, a), whereas at higher concentrations the enantioselectivity decreased. In addition, it was found that the enantioselectivity could be increased to 90% *ee* if the **2a**/**1a** mol ratio were increased to 4.8. In this regard, optimum conditions were found to depend significantly on the amount of **2a** and the concentration of **1a**.

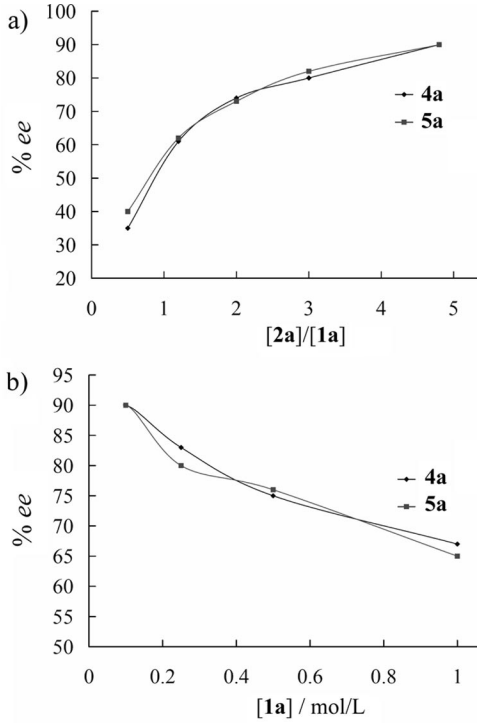
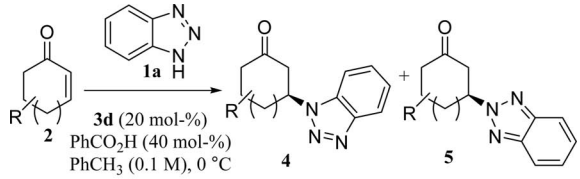


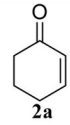
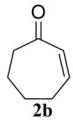
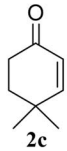
Figure 1. a) Enantioselectivity with respect to **4a** and **5a** against the concentration of **1a** in the Michael addition between 1*H*-benzotriazole (**1a**, 1 equiv.) and cyclohexenone **2a** (4.8 equiv.). b) Enantioselectivity with respect to **4a** and **5a** against the mol ratio of cyclohexenone **2a** to 1*H*-benzotriazole (**1a**); the concentration of **1a** is 0.1 mol L^{-1}.

Enantioselective organocatalytic Michael additions were first investigated with cyclic enones (Table 3). It was pleasing to find that as well as the known compounds **4a** and **5a**, the seven-membered congeners (Table 3, Entry 2) were also formed with similarly high yields (60% for **4b** and 30% for **5b**) and enantioselectivities (95% *ee* for **4b** and 97% *ee* for **5b**). Moreover, 4,4-dimethylcyclohex-2-en-1-one (**2c**) also served as an effective Michael acceptor with 1*H*-benzotriazole (**1a**), giving the major product **4c** in 83% yield and with 90% *ee* and excellent regioselectivity (Entry 3). In fact, only the five-membered cyclopent-2-en-1-one (Entry 4) gave only moderate enantioselectivity (63% *ee* for **4d** and 35% *ee* for **5d**), but retained the high yields (75% for **4d** and 15% for **5**d).

1*H*-Benzotriazole (**1a**) was next applied in additions with linear *E*-enones (Table 4). Again, it was most encouraging to see that they did indeed react with high yields and

Table 3. 1,4-Additions between 1*H*-benzotriazole (**1a**) and cyclic α,β-unsaturated enones **2**.[a]



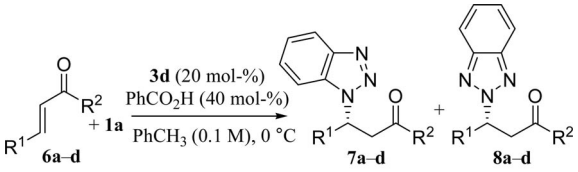
Entry	Enone	Time [h]	Yield [%][b]		*ee* [%][c]	
			4	**5**	**4**	**5**
1	 **2a**	12	72	24	90	90
2	 **2b**	12	60	30	95	97
3	 **2c**	15	83	<5	89	–
4	 **2d**	10	81	10	35	60

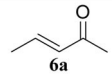
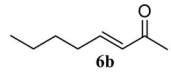
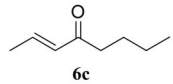
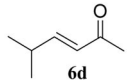
[a] Reaction conditions: **1a** (0.125 mmol), **2** (0.60 mmol), **3d** (20 mol-%), and $PhCO_2H$ (40 mol-%) were stirred at 0 °C in $PhCH_3$ (1.25 mL). [b] Isolated yield. [c] Determined by HPLC analysis.

enantioselectivities generally comparable with those obtained with the cyclohex-2-en-1-one systems **2**. Oct-3-en-2-one (**6b**, Entry 2) and oct-2-en-3-one (**6c**, Entry 3) worked just as well as the truncated linear enone pent-3-en-2-one (**6a**, Entry 1), all with very good yields and enantioselectivities. Furthermore, the branched example **6d** (Entry 4) also worked well and was obtained in good yields (75% for **7d** and 25% for **8d**), with retention of the high enantioselectivities (94% *ee* for **7d** and 97% *ee* for **8d**).

To explore the scope of the reactions further, a series of aromatic *E*-α,β-unsaturated enones (Table 5) were used as substrates in 1,4-additions with 1*H*-benzotriazole (**1a**). As a result of the poor solubilities of **9d** and **9f**, $PhCH_3/CHCl_3$ (7:3) was used instead. Because H_2O would be generated during the formation of an active iminium intermediate, the expected hydrogen-bonding interaction might be affected. Consequently, molecular sieves (4 Å) were added to remove the trace amounts of water. In this way, the *ee* value for the major product **10a** was raised from 86% to 90%, although the reaction time had to be extended, probably because the hydrolysis of the iminium salt to release the catalyst would be retarded after the completion of Michael addition (Entry 2). It was pleasing to find that these reactions also

Table 4. 1,4-Additions between 1*H*-benzotriazole (**1a**) and the linear α,β-unsaturated enones **6**.[a]



Entry	Enone	Time [h]	Yield [%][b]		*ee* [%][c]	
			7	**8**	**7**	**8**
1	 **6a**	5	75	18	90	93
2	 **6b**	6	70	20	94	97
3	 **6c**	6	66	33	95	99
4	 **6d**	7	75	20	96	97

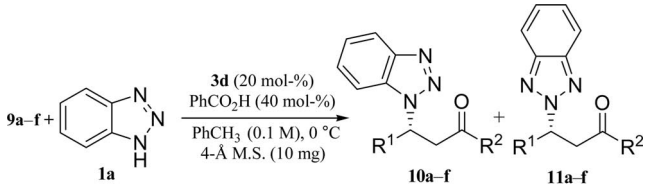
[a] Reaction conditions: **1a** (0.125 mmol), **6** (0.60 mmol), **3d** (20 mol-%), and $PhCO_2H$ (40 mol-%) were stirred at 0 °C in $PhCH_3$ (1.25 mL). [b] Isolated yield. [c] Determined by HPLC analysis.

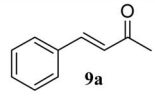
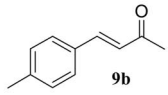
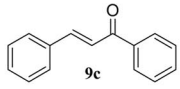
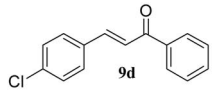
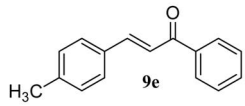
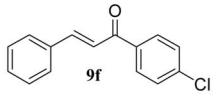
worked very well and that the Michael adducts were all formed in moderate yields and with generally excellent enantioselectivities. Both electron-withdrawing (Cl, Entries 5 and 7) and electron-donating (Me, Entries 4 and 6) substituents can be introduced on the aromatic ring without deterioration in yield or enantioselectivity.

Determination of the absolute configurations of the newly generated stereogenic centers was performed by chemical correlation as follows: the aza-Michael reaction between **9d** and 1*H*-benzotriazole, under the conditions very recently reported by Wang,[5] furnished levorotatory (*R*)-3-(1*H*-benzotriazol-1-yl)-3-(4-chlorophenyl)-1-phenylpropan-1-one {**10d**, $[a]_D^{25} = +9.7$ ($c = 0.6$, $CHCl_3$)}, whereas adduct **10d** as obtained by us in the presence of catalyst **3d** was in the form of the levorotatory isomer {$[a]_D^{25} = +26.8$ ($c = 0.6$, $CHCl_3$)}. For the reaction between **9** and **1a** we thus propose a plausible, albeit very naive, catalytic mode based on the absolute and relative configurations of the N-heterocycle derivative **10d** (Scheme 1). The ketiminium cation formed between **3d** and enone **9d** might adopt a *trans* conformation, and a hydrogen bond could be formed from the bridgehead nitrogen of **3d** and the NH group of 1*H*-benzotriazole (**1a**) to produce concerted communication. As a result of the steric hindrance and bifunctional effect, *re*-face selectivity would be enforced to give the desired Michael addition products **10d** and **11d**.

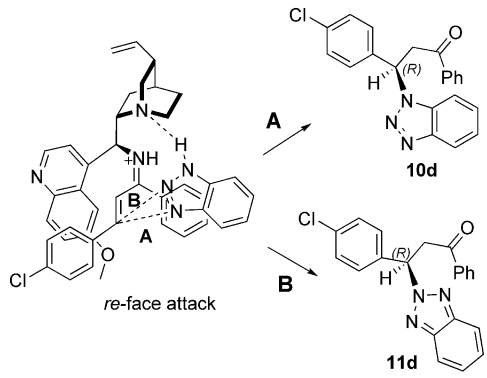
In further investigations, we examined the reactivities of other nitrogen heterocycles in these aza-Michael additions. The 5-phenyl-1*H*-tetrazole derivatives **12** served as effective Michael donors in reactions with α,β-unsaturated (*E*)-enones at lower temperatures (from 0 °C to –20 °C, Table 6),

Table 5. 1,4-Additions between 1*H*-benzotriazole (**1a**) and the aromatic α,β-unsaturated enones **9**.[a]



Entry	Enone	Time [h]	Yield [%][b]		*ee* [%][c]	
			10	**11**	**10**	**11**
1[d]	 **9a**	4	78	19	86	95
2		6	70	25	90	96
3	 **9b**	6	80	16	89	97
4	 **9c**	48	65	10	94	97
5[e]	 **9d**	72	70	15	93	96
6	 **9e**	48	52	12	95	95
7[e]	 **9f**	72	43	8	93	97

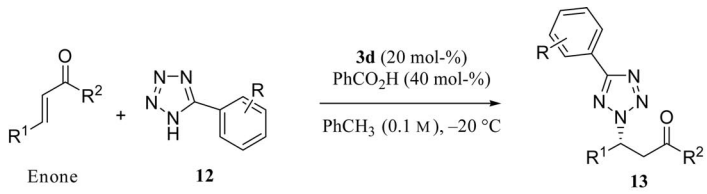
[a] Reaction conditions: **1a** (0.125 mmol), **9** (0.60 mmol), **3d** (20 mol-%), $PhCO_2H$ (40 mol-%), and mol. sieves (4 Å, 10 mg) were stirred at 0 °C in $PhCH_3$ (1.25 mL). [b] Isolated yield. [c] Determined by HPLC analysis. [d] Without mol. sieves. [e] $PhCH_3$/$CHCl_3$ (7:3) as solvent.



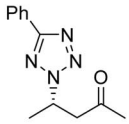
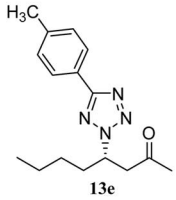
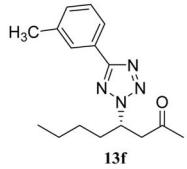
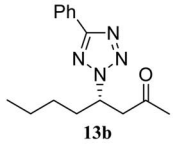
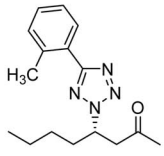
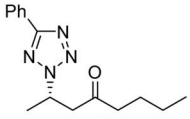
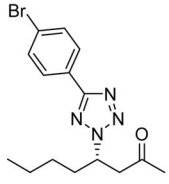
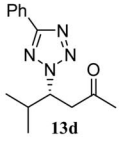
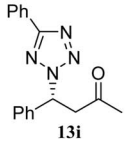
Scheme 1. Proposed mode of Michael addition between **1a** and **9d** with catalysis by the multifunctional salt of **3d**.

giving products **13** in 85–95% yields and with 90–98% *ee* values and excellent regioselectivities. Both electron-withdrawing (Cl, Entry 8) and electron-donating (Me, Entries 5–7) substituents can be introduced on the aromatic ring of 5-phenyl-1*H*-tetrazole without deterioration in yield or enantioselectivity. Moreover, the position of the substituent

Table 6. 1,4-Additions of 5-phenyltetrazole derivatives to α,β-unsaturated enones.[a]



Enone 12 13

Entry	Enone	Time [h]	Yield [%][b]	*ee* [%][c]	Entry	Enone	Time [h]	Yield [%][b]	*ee* [%][c]
1	 13a	5	88	90	6	 13e	3	87	96
2		3	93	96	7	 13f	3	91	97
3[d]	 13b	2	95	92	8	 13g	4	85	93
4	 13c	3	95	92	9	 13h	3	89	95
5	 13d	4	90	98	10[e]	 13i	4	95	91

[a] Reaction conditions: **12** (0.125 mmol), enone (0.60 mmol), **3d** (20 mol-%), and $PhCO_2H$ (40 mol-%) were stirred at –20 °C in $PhCH_3$ (1.25 mL). [b] Isolated yield. [c] Determined by HPLC analysis. [d] Reaction temperature 0 °C. [e] $PhCH_3/CHCl_3$ (7:3) as the solvent and mol. sieves (4 Å, 10 mg) as additives.

(a methyl group, for example) on the aromatic ring seems to have no influence except when in the *ortho*-position (Entry 7). Furthermore, we found that the use of mol. sieves (4 Å) as additives and $PhCH_3/CHCl_3$ (7:3) as the solvent were crucial in order to obtain high enantioselectivities in the Michael addition between 5-phenyl-1*H*-tetrazole (**12a**) and (*E*)-4-phenylbut-3-en-2-one (**9a**).

Conclusions

In summary, a procedure for enantioselective organocatalytic conjugate additions between a variety of N-heterocyclic compounds and α,β-unsaturated enone systems has been developed. The reactions are efficiently catalyzed by salts of 9-amino-9-deoxy-epiquinine (**3d**). Cyclic, acyclic, and aromatic enones can be used and the reactions with 1*H*-benzotriazole (**1a**) provide the Michael addition products in high yields and with good to excellent enantioselectivities. We found strong effects of the concentration of the reaction mixture and the ratio of cyclohexenone **2a** to 1*H*-benzotriazole (**1a**) on the enantioselectivity for the Michael addition between 1*H*-benzotriazole and cyclohexenone **2a**. Moreover, the 5-phenyl-1*H*-tetrazole derivatives **12** also served as effective Michael donors in reactions with α,β-unsaturated (*E*)-enones, giving products **13** in 85–95% yields and with 90–98% *ee* values and excellent regioselectivities.

Experimental Section

General: Commercial reagents were used as received, unless otherwise stated. Catalysts **3c**, **3d**, and **3f** were synthesized by literature procedures.[17] ^{1}H and ^{13}C NMR spectra were recorded with Bruker DPX 300 or 400 spectrometers. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard. Accurate mass data were obtained with an Agilent Technologies 6520 Accurate-Mass Q-TOF LC/MS instrument by electrospray ionization (ESI). Optical rotations were measured with a Perkin–Elmer 341 polarimeter at 20 °C. HPLC analysis was performed with a Shimadzu CTO-10AS instrument and a Chiralpak AD-H column purchased from Daicel Chemical Industries, LTD.

Typical Procedure for Additions of 1*H*-Benzotriazole to Cyclic α,β-Unsaturated Enones: PhCOOH (40 mol-%) was added to a stirred solution of catalyst **3d** (20 mol-%) in $PhCH_3$ (1.25 mL), and the solution was stirred for 5 minutes at room temperature. After addition of enone **2** (0.60 mmol), the mixture was stirred for 10 minutes. The benzotriazole **1a** (0.125 mmol) was added at 0 °C, and stirring was continued for the indicated time, resulting in a mixture of regioisomers. The crude reaction mixture was then loaded onto a silica gel column for purification (EtOAc/hexane, 1:5), to afford the Michael adduct.

(*S*)-3-(1*H*-Benzotriazol-1-yl)cyclohexanone (4a): The title compound was obtained by the General Procedure described above, from **1a** and **2a**. Yield 72% (19.4 mg). $[a]_D^{20}$ = + 21 (*c* = 0.5 in CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.10 [d, ^3J(H,H) = 8.3 Hz, 1 H, Ar-H], 7.54–7.52 (m, 2 H, Ar-H), 7.44–7.38 (m, 1 H, Ar-H), 5.10–5.00 (m, 1 H, N–CH), 3.32 [dd, ^3J(H,H) = 10.9, 14.4 Hz, 1 H, CH_2], 2.97 [dd, ^3J(H,H) = 4.5, 14.4 Hz, 1 H, CH_2], 2.59-2.39 (m, 4 H, CH_2), 2.27–2.16 (m, 1 H, CH_2), 1.93–1.77 (m, 1 H, CH_2) ppm. ^{13}C NMR (75 MHz, $CDCl_3$ 25 °C, TMS): δ = 206.7, 146.0, 132.1, 127.5, 124.3, 120.3, 109.0, 56.9, 47.1, 40.6, 31.0, 22.0 ppm. HRMS (ESI): calcd. for $C_{12}H_{14}N_3O$: 216.1131 [M + H]$^+$; found 216.1129; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 85:15, 1.0 mL min^{-1}): t_R (**4a** minor) = 13.6, t_R (**4a** major) = 17.4 min (90% *ee*).

(*S*)-3-(2*H*-Benzotriazol-2-yl)cyclohexanone (5a): The title compound was obtained by the General Procedure described above, from **1a** and **2a**. Yield 24% (6.4 mg). $[a]_D^{20}$ = +28.1 (*c* = 0.5 in CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.78 [dd, ^3J(H,H) = 2.7, 6.4 Hz, 2 H Ar-H], 7.31 [dd, ^3J(H,H) = 2.7, 6.4 Hz, 2 H, Ar-H], 5.23–5.10 (m, 1 H, N–CH), 3.18 [dd, ^3J(H,H) = 9.6, 14.6 Hz, 1 H, CH_2], 2.92 [dd, ^3J(H,H) = 4.5, 14.6 Hz, 1 H, CH_2], 2.46–2.36 (m, 4 H, CH_2), 2.03–1.96 (m, 1 H, CH_2), 1.83–1.71 (m, 1 H, CH_2) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 206.7, 144.1, 126.5, 118.1, 64.1, 46.7, 40.5, 31.5, 21.4 ppm. HRMS (ESI): calcd. for $C_{12}H_{13}N_3ONa$: 238.0951; found 238.0947 [M + Na]$^+$; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 95:5, 1.0 mL min^{-1}): t_R (**5a** major) = 15.8, t_R (**5a** minor) = 18.0 min (90% *ee*).

(*S*)-3-(1*H*-Benzotriazol-1-yl)cycloheptanone (4b): The title compound was obtained by the General Procedure described above, from **1a** and **2b**. Yield 60% (17.2 mg). $[a]_D^{20}$ = –20.2 (*c* = 0.5, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.08 [d, ^3J(H,H) = 8.3 Hz, 1 H, Ar-H], 7.57–7.48 (m, 2 H, Ar-H), 7.42–7.37 (m, 1 H, Ar-H), 5.05–4.96 (m, 1 H, N–CH), 3.64 [dd, ^3J(H,H) = 11.4, 14.1 Hz, 1 H, CH_2], 2.97 [ddd, ^3J(H,H) = 2.1, 3.9, 13.8 Hz, 1 H, CH_2], 2.83–2.33 (m, 4 H, CH_2), 2.16–2.05 (m, 2 H, CH_2), 1.97–1.84 (m, 1 H, CH_2), 1.70–1.59 (m, 1 H, CH_2) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 209.7, 146.1, 131.8, 127.4, 124.1, 120.3, 109.3, 56.4, 49.3, 44.0, 37.0, 26.5, 23.6 ppm. HRMS (ESI): calcd. for $C_{13}H_{16}N_3O$: 230.1288 [M + H]$^+$; found 230.1286; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 85:15, 1.0 mL min^{-1}): t_R (**4b** minor) = 14.5, t_R (**4b** major) = 16.6 min (95% *ee*).

(*S*)-3-(2*H*-Benzotriazol-2-yl)cycloheptanone (5b): The title compound was obtained by the General Procedure described above, from **1a** and **2b**. Yield 30% (8.6 mg). $[a]_D^{20}$ = +4.0 (*c* = 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.86 [dd, ^3J(H,H) = 3.1, 6.6 Hz, 2 H, Ar-H], 7.40 [dd, ^3J(H,H) = 3.1, 6.6 Hz, 2 H, Ar-H], 5.23–5.16 (m, 1 H, N–CH), 3.56 [dd, ^3J(H,H) = 10.8, 15.1 Hz, 1 H, CH_2], 3.08 [dd, ^3J(H,H) = 2.5, 15.1 Hz, 1 H, CH_2], 2.75–2.57 (m, 2 H, CH_2), 2.47–2.42 (m, 2 H, CH_2), 2.08–1.96 (m, 2 H, CH_2), 1.90–1.79 (m, 1 H, CH_2), 1.76–1.66 (m, 1 H, CH_2) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 209.4, 144.0, 126.4, 118.1, 63.3, 49.3, 44.2, 37.5, 26.6, 23.7 ppm. HRMS (ESI): calcd. for $C_{13}H_{15}N_3ONa$: 252.1107; found 252.1109 [M + Na]$^+$; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 95:5, 1.0 mL min^{-1}): t_R (**5b** minor) = 16.6, t_R (**5b** major) = 17.0 min (97% *ee*).

(*R*)-3-(1*H*-Benzotriazol-1-yl)-4,4-dimethylcyclohexanone (4c): The title compound was obtained by the General Procedure described above, from **1a** and **2c**. Yield 83% (25.2 mg). $[a]_D^{20}$ = +6.1 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.08 [d, ^3J(H,H) = 8.4 Hz, 1 H, Ar-H], 7.50 [d, ^3J(H,H) = 3.6 Hz, 2 H, Ar-H], 7.40–7.36 (m, 1 H, Ar-H), 4.78 [dd, ^3J(H,H) = 5.1, 10.0 Hz, 1 H, N–CH], 3.46 [ddd, ^3J(H,H) = 1.0, 10.0, 15.6 Hz, 1 H, CH_2], 2.84 [ddd, ^3J(H,H) = 1.6, 5.1, 15.7 Hz, 1 H, CH_2], 2.75–2.67 (m, 1 H, CH_2), 2.57–2.49 (m, 1 H, CH_2), 2.10–2.03 (m, 1 H, CH_2), 1.83–1.75 (m, 1 H, CH_2), 1.34 (s, 3 H, CH_3), 1.10 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 207.1, 145.2, 133.8, 127.5, 124.0, 120.1, 109.5, 64.1, 43.6, 37.5, 36.2, 36.0, 28.0, 21.9 ppm. HRMS (ESI): calcd. for $C_{14}H_{18}N_3O$: 244.1444 [M + H]$^+$; found 244.1447; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 85:15, 1.0 mL min^{-1}): t_R (**4c** minor) = 12.0, t_R (**4c** major) = 14.1 min (89% *ee*).

(*S*)-3-(1*H*-Benzotriazol-1-yl)cyclopentanone (4d): The title compound was obtained by the General Procedure described above, from **1a** and **2d**. Yield 81% (20.3 mg). $[a]_D^{20}$ = +5.0 (*c* = 0.2, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.10 [d, ^3J(H,H) = 8.4 Hz, 1 H, Ar-H], 7.58–7.52 (m, 2 H, Ar-H), 7.44–7.40 (m, 1 H, Ar-H), 5.50-5.44 (m, 1 H, N–CH), 3.12 [dd, ^3J(H,H) = 18.5, 5.9 Hz, 1 H, CH_2], 2.94 [dd, ^3J(H,H) = 7.7, 18.6 Hz, 1 H, CH_2], 2.51-2.44 (m, 1 H, CH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$ 25 °C, TMS): δ = 214.0, 146.2, 132.5, 127.7, 124.4, 120.3, 109.1, 55.9, 44.1, 36.7, 29.7 ppm. HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 85:15, 1.0 mL min^{-1}): t_R (**4d** minor) = 13.9, t_R (**4d** major) = 17.0 min (34% *ee*).

(*S*)-3-(2*H*-Benzotriazol-2-yl)cyclopentanone (5d): The title compound was obtained by the General Procedure described above, from **1a** and **2d**. Yield 10% (2.5 mg). $[a]_D^{20}$ = +15.0 (*c* = 0.2, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.86 [dd, ^3J(H,H) = 3.1, 6.6 Hz, 2 H, Ar-H], 7.86 [dd, ^3J(H,H) = 3.1, 6.6 Hz, 2 H, Ar-H], 5.69–5.63 (m, 1 H, N–CH), 3.01 [ddd, ^3J(H,H) = 6.19, 18.65, 26.28 Hz, 2 H, CH_2], 2.72–2.66 (m, 3 H, CH_2), 2.42–2.35 (m, 1 H, CH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$ 25 °C, TMS): δ = 214.5, 144.3, 126.6, 118.1, 63.3, 44.7, 36.2, 30.3 ppm. HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 95:5, 1.0 mL min^{-1}): t_R (**5a** major) = 12.3, t_R (**5a** minor) = 13.9 min (60% *ee*).

Typical Procedure for Additions of 1*H*-Benzotriazole to Linear α,β-Unsaturated Enones: PhCOOH (40 mol-%) was added to a stirred solution of catalyst **3d** (20 mol-%) in $PhCH_3$ (1.25 mL) and the solution was stirred for 5 minutes at room temperature. After addition of the enone **6** (0.60 mmol), the mixture was stirred for 10

minutes. The benzotriazole **1a** (0.125 mmol) was added at 0 °C, and stirring was continued for the indicated time, resulting in a mixture of regioisomers. The crude reaction mixture was then loaded onto a silica gel column for purification (EtOAc/hexane, 1:5), to afford the Michael adduct.

(*S*)-4-(1*H*-Benzotriazol-1-yl)pentan-2-one (7a): The title compound was obtained by the General Procedure described above, from **1a** and **6a**. Yield 75% (19.0 mg). $[a]_D^{20}$ = +15.4 (c = 0.5, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.04 [d, ^3J(H,H) = 8.4 Hz, 1 H, Ar-H], 7.64 [d, ^3J(H,H) = 8.4 Hz, 1 H, Ar-H], 7.50 [t, ^3J(H,H) = 7.6 Hz, 1 H, Ar-H], 7.36 [t, ^3J(H,H) = 7.6 Hz, 1 H, Ar-H], 5.45–5.33 (m, 1 H, N–CH), 3.60 [dd, ^3J(H,H) = 7.7, 18.0 Hz, 1 H, CH_2], 3.15 [dd, ^3J(H,H) = 5.7, 18.0 Hz, 1 H, CH_2], 2.15 (s, 3 H, $COCH_3$), 1.68 [d, ^3J(H,H) = 6.8 Hz, 3 H, CH_3] ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 205.2, 145.8, 132.6, 127.2, 124.0, 119.8, 109.7, 50.2, 49.1, 30.4, 21.2 ppm. HRMS (ESI): calcd. for $C_{11}H_{14}N_3O$: 204.1131 [M + H]$^+$; found 204.1133; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 90:10, 1.0 mL min^{-1}): t_R (**7a** minor) = 11.1, t_R (**7a** major) = 11.8 min (90% *ee*).

(*S*)-4-(2*H*-Benzotriazol-2-yl)pentan-2-one (8a): The title compound was obtained by the General Procedure described above, from **1a** and **6a**. Yield 18% (4.5 mg). $[a]_D^{20}$ = +16.1 (c = 0.5, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.77 [dd, ^3J(H,H) = 3.1, 6.6 Hz, 2 H, Ar-H], 7.29 [dd, ^3J(H,H) = 3.1, 6.6 Hz, 2 H, Ar-H], 5.50–5.38 (m, 1 H, N–CH), 3.46 [dd, ^3J(H,H) = 7.2, 17.7 Hz, 1 H, $COCH_2$], 2.99 [dd, ^3J(H,H) = 6.4, 17.7 Hz, 1 H, $COCH_2$], 2.11 (s, 3 H, $COCH_3$), 1.63 [d, ^3J(H,H) = 6.8 Hz, 3 H, CH_3] ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 204.7, 144.0, 126.2, 118.0, 58.4, 49.2, 30.4, 21.4 ppm. HRMS (ESI): calcd. for $C_{11}H_{13}N_3ONa$: 226.0951 [M + Na]$^+$; found 226.0947; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 90:10, 1.0 mL min^{-1}): t_R (**8a** minor) = 6.5, t_R (**8a** major) = 6.9 min (93% *ee*).

(*S*)-4-(1*H*-Benzotriazol-1-yl)octan-2-one (7b): The title compound was obtained by the General Procedure described above, from **1a** and **6b**. Yield 70% (21.4 mg). $[a]_D^{20}$ = +9.3 (c = 0.6, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.03 [d, ^3J(H,H) = 8.4 Hz, 1 H, Ar-H], 7.65 [d, ^3J(H,H) = 8.4 Hz, 1 H, Ar-H], 7.49 [t, ^3J(H,H) = 7.6 Hz, 1 H, Ar-H], 7.36 [t, ^3J(H,H) = 7.6 Hz, 1 H, Ar-H], 5.29–5.20 (m, 1 H, N–CH), 3.57 [dd, ^3J(H,H) = 8.4, 18.0 Hz, 1 H, OCH_2], 3.13 [dd, ^3J(H,H) = 5.0, 18.0 Hz, 1 H, OCH_2], 2.24–2.13 (m, 1 H, CH_2), 2.01 (s, 3 H, $COCH_3$), 2.01–1.89 (m, 1 H, CH_2), 1.31–1.13 (m, 3 H, CH_2CH_2), 1.01–0.91 (m, 1 H, CH_2), 0.79 (t, J = 7.2 Hz, 3 H, CH_2CH_2) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 205.3, 145.6, 133.5, 127.2, 123.9, 119.8, 109.8, 54.5, 48.2, 45.1, 30.4, 28.0, 22.1, 13.8 ppm. HRMS (ESI): calcd. for $C_{14}H_{20}N_3O$: 246.1601 [M + H]$^+$; found 246.1600; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 95:5, 1.0 mL min^{-1}): t_R (**7b** minor) = 15.8, t_R (**7b** major) = 16.9 min (94% *ee*).

(*S*)-4-(3*H*-Benzotriazol-2-yl)octan-2-one (8b): The title compound was obtained by the General Procedure described above, from **1a** and **6b**. Yield 20% (6.1 mg). $[a]_D^{20}$ = +17.4 (c = 0.6, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.86 [dd, ^3J(H,H) = 3.1, 6.5 Hz, 2 H, Ar-H], 7.37 [dd, ^3J(H,H) = 3.1, 6.5 Hz, 2 H, Ar-H], 5.42–5.30 (m, 1 H, N–CH), 3.49 [dd, ^3J(H,H) = 7.8, 17.6 Hz, 1 H, $COCH_2$], 3.08 [dd, ^3J(H,H) = 5.8, 17.6 Hz, 1 H, $COCH_2$], 2.14 (s, 3 H, $COCH_3$), 2.11–1.91 (m, 1 H, CH_2), 1.31–0.97 (m, 4 H, CH_2CH_2), 0.82 [t, ^3J(H,H) = 7.0 Hz, 3 H, CH_3] ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 204.8, 143.9, 126.2, 118.1, 62.8, 48.1, 35.4, 30.3, 27.8, 22.1, 13.8 ppm. HRMS (ESI): calcd. for $C_{14}H_{19}N_3ONa$: 268.1420 [M + Na]$^+$; found 268.1416; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 95:5, 1.0 mL min^{-1}): t_R (**8b** minor) = 5.8, t_R (**8b** major) = 6.4 min (97% *ee*).

(*S*)-2-(1*H*-Benzotriazol-2-yl)octan-4-one (7c): The title compound was obtained by the General Procedure described above, from **1a** and **6c**. Yield 66% (20.2 mg). $[a]_D^{20}$ = +7.9 (c = 0.7, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.02 [d, ^3J(H,H) = 8.4 Hz, 1 H, Ar-H], 7.62 [d, ^3J(H,H) = 8.4 Hz, 1 H, Ar-H], 7.48 [t, ^3J(H,H) = 7.3 Hz, 1 H, Ar-H], 7.34 [t, ^3J(H,H) = 7.6 Hz, 1 H, Ar-H], 5.44–5.36 (m, 1 H, N–CH), 3.55 [dd, ^3J(H,H) = 7.8, 17.7 Hz, 1 H, $COCH_2$], 3.09 [dd, ^3J(H,H) = 5.7, 17.7 Hz, 1 H, $COCH_2$], 2.45–2.30 (m, 2 H, CH_2), 1.66 [d, ^3J(H,H) = 6.8 Hz, 3 H, CH_3], 1.49–1.42 (m, 2 H, CH_2), 1.24–1.15 (m, 2 H, CH_2), 0.82 [t, ^3J(H,H) = 7.3 Hz, 3 H] ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 207.8, 145.8, 132.6, 127.2, 123.9, 119.8, 109.7, 50.2, 48.3, 43.1, 25.5, 22.1, 21.2, 13.7 ppm. HRMS (ESI): calcd. for $C_{14}H_{20}N_3O$: 246.1601 [M + H]$^+$; found 246.1603; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 95:5, 1.0 mL min^{-1}): t_R (**7c** minor) = 12.7, t_R (**7c** major) = 15.7 min (95% *ee*).

(*S*)-2-(2*H*-Benzotriazol-2-yl)octan-4-one (8c): The title compound was obtained by the General Procedure described above, from **1a** and **6c**. Yield 33% (10.1 mg). $[a]_D^{20}$ = –22.7 (c = 0.8, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.85 [dd, ^3J(H,H) = 3.1, 6.5 Hz, 2 H, Ar-H], 7.37 [dd, ^3J(H,H) = 3.1, 6.6 Hz, 2 H, Ar-H], 5.57–5.44 (m, 1 H, N–CH), 3.49 [dd, ^3J(H,H) = 7.1, 17.5 Hz, 1 H, $COCH_2$], 3.04 [dd, ^3J(H,H) = 6.6, 17.5 Hz, 1 H, $COCH_2$], 2.43 [t, ^3J(H,H) = 7.4 Hz, 2 H, CH_2], 1.70 [d, ^3J(H,H) = 6.7 Hz, 3 H, $COCH_3$], 1.53 [td, ^3J(H,H) = 7.4, 15.2 Hz, 2 H, CH_2], 1.32–1.20 (m, 2 H, CH_2), 0.86 [t, ^3J(H,H) = 7.3 Hz, 3 H, CH_3] ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 207.2, 144.0, 126.2, 118.2, 58.5, 48.3, 43.0, 25.6, 22.2, 21.4, 13.9 ppm. HRMS (ESI): calcd. for $C_{14}H_{19}N_3ONa$: 268.1420 [M + Na]$^+$; found 268.1418; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 95:5, 1.0 m min^{-1}): t_R (**8c** minor) = 7.6, t_R (**8c** major) = 9.0 min (99% *ee*).

(*R*)-4-(1*H*-Benzotriazol-1-yl)-5-methylhexan-2-one (7d): The title compound was obtained by the General Procedure described above, from **1a** and **6d**. Yield 75% (21.7 mg). $[a]_D^{20}$ = –25.0 (c = 0.6, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.02 [d, ^3J(H,H) = 8.3 Hz, 1 H, Ar-H], 7.64 [d, ^3J(H,H) = 8.4 Hz, 1 H, Ar-H], 7.49 [t, ^3J(H,H) = 7.5 Hz, 1 H, Ar-H], 7.35 [t, ^3J(H,H) = 8.1 Hz, 1 H, Ar-H], 5.06–5.00 (m, 1 H, N–CH), 3.75 [dd, ^3J(H,H) = 9.9, 17.8 Hz, 1 H, $COCH_2$], 3.10 [dd, ^3J(H,H) = 3.5, 17.8 Hz, 1 H, $COCH_2$], 2.44–2.32 (m, 1 H, CH), 2.09 (s, 3 H, $COCH_3$), 1.00 [d, ^3J(H,H) = 6.8 Hz, 3 H, CH_3], 0.79 [d, ^3J(H,H) = 6.7 Hz, 3 H, CH_3] ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 205.5, 145.4, 134.1, 127.2, 123.9, 119.8, 110.0, 59.9, 45.1, 33.3, 30.5, 19.6, 19.0 ppm. HRMS (ESI): calcd. for $C_{13}H_{18}N_3O$: 232.1444 [M + H]$^+$; found 232.1440; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 90:10, 1.0 mL min^{-1}): t_R (**7d** minor) = 8.8, t_R (**7d** major) = 9.2 min (96% *ee*).

(*R*)-4-(2*H*-Benzotriazol-2-yl)-5-methylhexan-2-one (8d): The title compound was obtained by the General Procedure described above, from **1a** and **6d**. Yield 20% (5.8 mg). $[a]_D^{20}$ = –5.6 (c = 0.6, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.84 [dd, ^3J(H,H) = 3.1, 6.6 Hz, 2 H, Ar-H], 7.34 [dd, ^3J(H,H) = 3.1, 6.6 Hz, 2 H, Ar-H], 5.44–5.35 (m, 1 H, N–CH), 3.49 [dd, ^3J(H,H) = 7.8, 17.6 Hz, 1 H, $COCH_2$], 3.08 [dd, ^3J(H,H) = 5.8, 17.6 Hz, 1 H, $COCH_2$], 2.14 (s, 3 H, $COCH_3$), 2.11–1.90 (m, 2 H, CH_2), 1.35–1.23 (m, 3 H, CH_3), 1.09–0.95 (m, 1 H, CH), 0.82 [t, ^3J(H,H) = 7.02, 7.0 Hz, 3 H, CH_3] ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 204.8, 143.9, 126.2, 118.1, 62.85, 48.1, 35.4, 30.3, 27.8, 22.1, 13.8 ppm. HRMS (ESI): calcd. for $C_{13}H_{17}N_3ONa$: 254.1264 [M + Na]$^+$; found 254.1261; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 95:5, 1 mL min^{-1}): t_R (**8d** minor) = 7.8, t_R (**8d** major) = 9.7 min (97% *ee*).

Typical Procedure for Additions of 1*H*-Benzotriazole to Aromatic α,β-Unsaturated Enones: PhCOOH (40 mol-%) and MS (4 Å, 10 mg) were added to a stirred solution of catalyst **3d** (20 mol-%) in $PhCH_3$ (1.25 mL) and the solution was stirred for 5 minutes at room temperature. After addition of an enone **9** (0.60 mmol), the mixture was stirred for 10 minutes. The benzotriazole **1a** (0.125 mmol) was added at 0 °C, and stirring was continued for the indicated time, resulting in a mixture of regioisomers. The crude reaction mixture was then loaded onto a silica gel column for purification (EtOAc/hexane, 1:5), to afford the Michael adduct.

(*R*)-4-(1*H*-Benzotriazol-1-yl)-4-phenylbutan-2-one (10a): The title compound was obtained by the General Procedure described above, from **1a** and **9a**. Yield 70% (23.2 mg). $[\alpha]_D^{20}$ = +24.1 (*c* = 0.6, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.02 [d, ^3J(H,H) = 8.1 Hz, 1 H, Ar-H], 7.41–7.29 (m, 8 H, Ar-H), 6.31 [dd, ^3J(H,H) = 4.6, 9.4 Hz, 1 H, N–CH], 4.27 [dd, ^3J(H,H) = 9.4, 17.7 Hz, 1 H, $COCH_2$], 3.31 [dd, ^3J(H,H) = 4.6, 17.7 Hz, 1 H, $COCH_2$], 2.24 (s, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 204.6, 146.3, 138.8, 133.0, 129.1, 128.5, 127.3, 126.6, 124.1, 119.8, 110.0, 58.3, 48.8, 30.4 ppm. HRMS (ESI): calcd. for $C_{16}H_{15}N_3ONa$: 288.1107 [M + Na]$^+$; found 288.1110; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 90:10, 1 m min^{-1}): t_R (**10a** minor) = 19.8, t_R (**10a** major) = 20.8 min (90% *ee*).

(*R*)-4-(2*H*-Benzotriazol-2-yl)-4-phenylbutan-2-one (11a): The title compound was obtained by the General Procedure described above, from **1a** and **9a**. Yield 25% (8.3 mg). $[\alpha]_D^{20}$ = +35 (*c* = 0.6, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.84 [dd, ^3J(H,H) = 3.1, 6.5 Hz, 2 H, Ar-H], 7.37–7.29 (m, 7 H, Ar-H), 6.53 [dd, ^3J(H,H) = 4.9, 9.5 Hz, 1 H, N–CH], 4.16 [dd, ^3J(H,H) = 9.6, 17.9 Hz, 1 H, $COCH_2$], 3.32 [dd, ^3J(H,H) = 4.9, 17.8 Hz, 1 H, $COCH_2$], 2.23 (s, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 204.2, 144.3, 138.6, 128.9, 128.6, 126.8, 126.3, 118.2, 65.6, 48.5, 30.3 ppm. HRMS (ESI): calcd. for $C_{16}H_{15}N_3ONa$: 288.1107 [M + Na]$^+$; found 288.1119; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 90:10, 1 mL min^{-1}): t_R (**11a** minor) = 13.6, t_R (**11a** major) = 18.2 min (96% *ee*).

(*R*)-4-(1*H*-Benzotriazol-1-yl)-4-(4-methylphenyl)butan-2-one (10b): The title compound was obtained by the General Procedure described above, from **1a** and **9b**. Yield 80% (27.9 mg). $[\alpha]_D^{20}$ = +11.7 (*c* = 0.65, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.01 [d, ^3J(H,H) = 8.3 Hz, 1 H, Ar-H], 7.40–7.28 (m, 3 H, Ar-H), 7.18 [d, ^3J(H,H) = 8.1 Hz, 2 H, Ar-H], 7.10 [d, ^3J(H,H) = 8.0 Hz, 2 H, Ar-H], 6.27 [dd, ^3J(H,H) = 4.8, 9.3 Hz, 1 H, N–CH], 4.25 [dd, ^3J(H,H) = 9.3, 17.7 Hz, 1 H, $COCH_2$], 3.30 [dd, ^3J(H,H) = 4.8, 17.7 Hz, 1 H, $COCH_2$], 2.28 (s, 3 H, CH_3), 2.24 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 204.7, 146.2, 138.4, 138.4, 135.8, 132.9, 129.7, 127.3, 126.5, 124.1, 119.8, 110.1, 58.2, 48.8, 30.5, 21.1 ppm. HRMS (ESI): calcd. for $C_{17}H_{17}N_3ONa$: 302.1264 [M + Na]$^+$; found 302.1266; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 90:10, 1.0 mL min^{-1}): t_R (**11b** minor) = 15.8, t_R (**11b** major) = 22.3 min (89% *ee*).

(*R*)-4-(2*H*-Benzotriazol-2-yl)-4-(4-methylphenyl)butan-2-one (11b): The title compound was obtained by the General Procedure described above, from **1a** and **9b**. Yield 16% (5.6 mg). $[\alpha]_D^{20}$ = +8.2 (*c* = 0.65, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.83 [dd, ^3J(H,H) = 3.1, 6.6 Hz, 2 H, Ar-H], 7.35–7.11 (m, 6 H, Ar-H), 6.49 [dd, ^3J(H,H) = 5.1, 9.4 Hz, 1 H, N–CH], 4.13 [dd, ^3J(H,H) = 9.4, 17.7 Hz, 1 H, $COCH_2$], 3.31 [dd, ^3J(H,H) = 5.1, 17.7 Hz, 1 H, $COCH_2$], 2.29 (s, 3 H, CH_3), 2.22 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 204.3, 114.2, 138.5, 135.7, 129.6, 126.7, 126.3, 118.2, 65.4, 48.4, 30.4, 21.1 ppm. HRMS (ESI): calcd. for $C_{17}H_{17}N_3ONa$: 302.1264 [M + Na]$^+$; found 302.1267; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 90:10, 1.0 mL min^{-1}): t_R (**11b** minor) = 10.5, t_R (**11b** major) = 12.0 min (97% *ee*).

(*R*)-3-(1*H*-Benzotriazol-1-yl)-1,3-diphenylpropan-1-one (10c): The title compound was obtained by the General Procedure described above, from **1a** and **9c**. Yield 65% (21.2 mg). $[\alpha]_D^{20}$ = +23.1 (*c* = 0.6, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.03 [d, ^3J(H,H) = 7.9 Hz, 2 H, Ar-H], 7.88–7.32 (m, 12 H, Ar-H), 6.83 (m, 1 H, N–CH), 4.76 [dd, ^3J(H,H) = 9.0, 18.0 Hz, 1 H], 3.91 [dd, ^3J(H,H) = 5.0, 18.0 Hz, 1 H] ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 195.9, 146.2, 139.1, 136.3, 133.6, 133.0, 129.1, 128.7, 128.5, 128.3, 127.4, 126.8, 124.1, 119.9, 110.0, 58.4, 44.3 ppm. HRMS (ESI): calcd. for $C_{21}H_{17}N_3ONa$: 350.1624; found 350.1627 [M + Na]$^+$; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 70:30, 1.0 mL min^{-1}): t_R (**10c** minor) = 16.0, t_R (**10c** major) = 19.1 min (94% *ee*).

(*R*)-3-(2*H*-Benzotriazol-2-yl)-1,3-diphenylpropan-1-one (11c): The title compound was obtained by the General Procedure described above, from **1a** and **9c**. Yield 10% (4.1 mg). $[\alpha]_D^{20}$ = +137.5 (*c* = 0.4, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.02–7.30 (m, 14 H, Ar-H), 6.78 [dd, ^3J(H,H) = 5.0, 9.0 Hz, 1 H, Ar-H], 4.73 [dd, ^3J(H,H) = 9.0, 18.0 Hz, 1 H, $COCH_2$], 3.89 [dd, ^3J(H,H) = 5.0, 18.0 Hz, 1 H, $COCH_2$] ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 195.5, 144.1, 138.8, 136.2, 133.5, 130.9, 128.9, 128.7, 128.2, 126.8, 126.2, 118.2, 65.7, 44.1 ppm. HRMS (ESI): calcd. for $C_{21}H_{17}N_3ONa$: 350.1624; found 350.1626 [M + Na]$^+$; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 95:5, 1.0 m min^{-1}): t_R (**11c** minor) = 36.8, t_R (**11c** major) = 45.2 min (97% *ee*).

(*R*)-3-(1*H*-Benzotriazol-1-yl)-3-(4-chlorophenyl)-1-phenylpropan-1-one (10d): The title compound was obtained by the General Procedure described above, from **1a** and **9d**. Yield 70% (31.6 mg). $[\alpha]_D^{20}$ = +26.8 (*c* = 0.85, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.03 [d, ^3J(H,H) = 8.3 Hz, 1 H, Ar-H], 7.94 [d, ^3J(H,H) = 8.4 Hz, 2 H, Ar-H], 7.51–7.29 (m, 10 H, Ar-H), 6.54 [dd, ^3J(H,H) = 4.8, 8.9 Hz, 1 H, N–CH], 4.85 [dd, ^3J(H,H) = 9.0, 17.8 Hz, 1 H, $COCH_2$], 3.81 [dd, ^3J(H,H) = 4.8, 17.8 Hz, 1 H, $COCH_2$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 195.7, 146.5, 140.5, 137.6, 136.1, 134.5, 133.8, 133.0, 129.3, 128.8, 128.3, 17.6, 124.2, 120.0, 109.7, 57.7, 44.4 ppm. HRMS (ESI): calcd. for $C_{21}H_{17}ClN_3O$: 362.1055 [M + H]$^+$; found 362.1058; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 70:30, 1.0 mL min^{-1}): t_R (**10d** minor) = 18.7, t_R (**10d** major) = 31.3 min (93% *ee*).

(*R*)-3-(2*H*-Benzotriazol-2-yl)-3-(4-chlorophenyl)-1-phenylpropan-1-one (11d): The title compound was obtained by the General Procedure described above, from **1a** and **9d**. Yield 15% (6.8 mg). $[\alpha]_D^{20}$ = +89.7 (*c* = 0.9, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.00 [d, ^3J(H,H) = 7.8 Hz, 2 H, Ar-H], 7.83 [d, ^3J(H,H) = 7.4 Hz, 2 H, Ar-H], 7.6 [t, ^3J(H,H) = 7.3 Hz, 1 H, Ar-H], 7.59 [t, ^3J(H,H) = 7.5 Hz, 1 H, Ar-H], 7.42 [d, ^3J(H,H) = 7.5 Hz, 2 H, Ar-H], 7.35 [d, ^3J(H,H) = 7.2 Hz, 2 H, Ar-H], 7.30 [d, ^3J(H,H) = 7.6 Hz, 2 H, Ar-H], 6.75 [t, ^3J(H,H) = 6.8 Hz, 1 H, N–CH], 4.65 [dd, ^3J(H,H) = 8.3, 18.0 Hz, 1 H, $COCH_2$], 3.92 [dd, ^3J(H,H) = 5.4, 18.0 Hz, 1 H, $COCH_2$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 195.3, 144.2, 137.3, 136.2, 134.5, 133.7, 129.1, 128.7, 128.4, 128.2, 126.5, 118.2, 65.1, 44.0 ppm. HRMS (ESI): calcd. for $C_{21}H_{16}N_3ONa$: 384.0874 [M + Na]$^+$; found 384.070; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 70:30, 1.0 mL min^{-1}): t_R (**11d** minor) = 11.7, t_R (**11d** major) = 14.7 min (96% *ee*).

(*R*)-3-(1*H*-Benzotriazol-1-yl)-3-(4-methylphenyl)-1-phenylpropan-1-one (10e): The title compound was obtained by the General Procedure described above, from **1a** and **9e**. Yield 52% (22.2 mg).

$[\alpha]_D^{20}$ = +76.4 (*c* = 0.95, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.00 [t, ^3J(H,H) = 8.8 Hz, 3 H, Ar-H], 7.59–7.28 (m, 8 H, Ar-H), 7.12 [d, ^3J(H,H) = 7.9 Hz, 2 H, Ar-H], 6.54 [dd, ^3J(H,H) = 5.0, 8.6 Hz, 1 H, N–CH], 4.83 [dd, ^3J(H,H) = 8.7, 17.8 Hz, 1 H, $COCH_2$], 3.88 [dd, ^3J(H,H) = 5.0, 17.9 Hz, 1 H, $COCH_3$], 2.29 (s, 3 H, $ArCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 196.0, 146.2, 138.4, 136.3, 136.1, 133.6, 133.1, 129.7, 128.7, 128.3, 127.3, 126.7, 124.0, 119.9, 110.0, 58.2, 44.5, 21.1 ppm. HRMS (ESI): calcd. for $C_{22}H_{20}N_3O$: 342.1601 $[M + H]^+$; found 342.1604; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 65:35, 1.0 mL min^{-1}): t_R (**10e** minor) = 15.8, t_R (**10e** major) = 23.2 min (95% *ee*).

(*R*)-3-(2*H*-Benzotriazol-2-yl)-3-(4-methylphenyl)-1-phenylpropan-1-one (11e): The title compound was obtained by the General Procedure described above, from **1a** and **9e**. Yield 12% (5.1 mg). $[\alpha]_D^{20}$ = +99.5 (*c* = 0.4, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.00 [d, ^3J(H,H) = 7.7 Hz, 2 H, Ar-H], 7.82 [d, ^3J(H,H) = 8.6 Hz, 2 H, Ar-H], 7.57 [t, ^3J(H,H) = 7.3 Hz, 1 H, Ar-H], 7.46 [t, ^3J(H,H) = 7.5 Hz, 2 H, Ar-H], 7.37–7.32 (m, 4 H, Ar-H), 7.14 [d, ^3J(H,H) = 7.7 Hz, 2 H, Ar-H], 6.74 [dd, ^3J(H,H) = 5.4, 8.5 Hz, 1 H, N–CH], 4.70 [dd, ^3J(H,H) = 8.8, 17.9 Hz, 1 H, $COCH_2$], 3.89 [dd, ^3J(H,H) = 5.1, 17.9 Hz, 1 H, $COCH_2$], 2.30 (s, 3 H, Ar-CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 195.6, 144.2, 138.5, 136.4, 135.9, 133.5, 129.6, 128.7, 128.2, 126.9, 126.2, 118.3, 65.6, 44.1, 21.1 ppm. HRMS (ESI): calcd. for $C_{22}H_{19}N_3ONa$: 364.1420 $[M + Na]^+$; found 364.1418; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 65:35, 1.0 mL min^{-1}): t_R (**11e** minor) = 10.1, t_R (**11e** major) = 10.8 min (95% *ee*).

(*R*)-3-(1*H*-Benzotriazol-1-yl)-1-(4-chlorophenyl)-3-phenylpropan-1-one (10f): The title compound was obtained by the General Procedure described above, from **1a** and **9f**. Yield 43% (19.4 mg). $[\alpha]_D^{20}$ = +21.2 (*c* = 0.85, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.03 [t, ^3J(H,H) = 8.3 Hz, 1 H, Ar-H], 7.94 [d, ^3J(H,H) = 8.4 Hz, 2 H, Ar-H], 7.51–7.29 (m, 10 H, Ar-H), 6.54 [dd, ^3J(H,H) = 4.8, 8.9 Hz, 1 H, N–CH], 4.85 [dd, ^3J(H,H) = 9.0, 17.8 Hz, 1 H, $COCH_2$], 3.81 [dd, ^3J(H,H) = 4.8, 17.8 Hz, 1 H, $COCH_2$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 194.8, 146.2, 140.2, 138.9, 134.6, 129.7, 129.2, 129.1, 128.6, 127.5, 126.7, 124.2, 119.9, 114.1, 109.9, 58.4, 44.4 ppm. HRMS (ESI): calcd. for $C_{21}H_{17}ClN_3O$: 362.1055 $[M + H]^+$; found 362.1058; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 70:30, 1.0 mL min^{-1}): t_R (**10f** minor) = 20.6, t_R (**10f** major) = 23.7 min (93% *ee*).

(*R*)-3-(2*H*-Benzotriazol-2-yl)-1-(4-chlorophenyl)-3-phenylpropan-1-one (11f): The title compound was obtained by the General Procedure described above, from **1a** and **9f**. Yield 8% (3.61 mg). $[\alpha]_D^{20}$ = +117.5 (*c* = 0.6, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.03 [t, ^3J(H,H) = 8.3 Hz, 1 H, Ar-H], 7.94 [d, ^3J(H,H) = 8.4 Hz, 2 H, Ar-H], 7.51–7.29 (m, 10 H, Ar-H), 6.54 [dd, ^3J(H,H) = 4.8, 8.9 Hz, 1 H, N–CH], 4.85 [dd, ^3J(H,H) = 9.0, 17.8 Hz, 1 H, $COCH_2$], 3.81 [dd, ^3J(H,H) = 4.8, 17.8 Hz, 1 H, $COCH_2$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 194.5, 144.2, 140.1, 138.7, 134.6, 129.7, 129.1, 129.0, 128.7, 126.8, 126.3, 118.3, 65.7, 44.1 ppm. HRMS (ESI): calcd. for $C_{21}H_{16}N_3ONa$: 384.0874 $[M + Na]^+$; found 384.077; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 70:30, 1.0 mL min^{-1}): t_R (**10f** minor) = 11.5, t_R (**10f** major) = 14.6 min (97% *ee*).

Typical Procedure for Additions of 5-Phenyltetrazole Derivatives to α,β-Unsaturated Enones: PhCOOH (40 mol-%) was added to a stirred solution of catalyst **3d** (20 mol-%) in $PhCH_3$ (1.25 mL) and the solution was stirred for 5 minutes at room temperature. After addition of an enone **2** (0.60 mmol), the mixture was stirred for 10 minutes. The 5-phenyltetrazole derivative **12** (0.125 mmol) was added at –20 °C, and stirring was continued for the indicated time, resulting in a single of regioisomers. The crude reaction mixture was then loaded onto a silica gel column for purification (EtOAc/hexane, 1:5), to afford the Michael adduct.

(*S*)-4-(5-Phenyl-2*H*-tetrazol-2-yl)pentan-2-one (13a): The title compound was obtained by the General Procedure described above, from **12a** and **6a**. Yield 88% (20.2 mg). $[\alpha]_D^{20}$ = –15 (*c* = 1.5, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$ 25 °C, TMS): δ = 8.07–8.04 (m, 2 H, Ar-H), 7.42–7.39 (m, 3 H, Ar-H), 5.45–5.33 (m, 1 H, N–CH), 3.39 [dd, ^3J(H,H) = 7.0, 17.9 Hz, 1 H, $COCH_2$], 2.97 [dd, ^3J(H,H) = 6.6, 17.8 Hz, 1 H, $COCH_2$], 2.14 (s, 3 H, $COCH_3$), 1.61 [d, ^3J(H,H) = 6.8 Hz, 3 H, CH_3] ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 204.1, 164.9, 130.2, 128.8, 127.5, 126.8, 55.9, 48.4, 30.3, 20.9 ppm. HRMS (ESI): calcd. for $C_{12}H_{15}N_4O$: 231.1240 $[M + H]^+$; found 231.1244; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 95:5, 1.0 mL min^{-1}): t_R (**13a** minor) = 13.7, t_R (**13a** major) = 14.3 min (90% *ee*).

(*S*)-4-(5-Phenyl-2*H*-tetrazol-2-yl)octan-2-one (13b): The title compound was obtained by the General Procedure described above, from **12a** and **6b**. Yield 93% (43.5 mg). $[\alpha]_D^{20}$ = +1.4 (*c* = 1.1, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.09–8.06 (m, 2 H, Ar-H), 7.41–7.40 (m, 3 H, Ar-H), 5.36–5.27 (m, 1 H, N–CH), 3.34 [dd, ^3J(H,H) = 7.7, 17.9 Hz, 1 H, $COCH_2$], 3.00 [dd, ^3J(H,H) = 5.84, 17.9 Hz, 1 H, $COCH_2$], 2.12 (s, 3 H, $COCH_3$), 1.99-1.81 (m, 2 H, CH_2), 1.26–1.14 (m, 2 H, CH_2), 0.78 [t, ^3J(H,H) = 6.9 Hz, 3 H, CH_3] ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 204.2, 164.8, 130.3, 128.8, 127.5, 126.8, 60.1, 47.2, 34.7, 30.3, 27.6, 22.09, 13.8 ppm. HRMS (ESI): calcd. for $C_{15}H_{21}N_4O$: 273.1710 $[M + H]^+$; found 273.1707; HPLC analysis (Chiralpak AD-H, hexanes/propan-2-ol, 95:5, 1.0 mL min^{-1}): t_R (**13b** minor) = 11.2, t_R (**13b** major) = 12.3 min (96% *ee*).

(*S*)-2-(5-Phenyl-2*H*-tetrazol-2-yl)octan-4-one (13c): The title compound was obtained by the General Procedure described above, from **12a** and **6c**. Yield 95% (32.3 mg). $[\alpha]_D^{20}$ = –20.4 (*c* = 1.3, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.15–8.12 (m, 2 H, Ar-H), 7.49–7.46 (m, 3 H, Ar-H), 5.54-5.45 (m, 1 H, N–CH), 3.43 [dd, ^3J(H,H) = 7.1, 17.7 Hz, 1 H, $COCH_2$], 3.02 [dd, ^3J(H,H) = 6.6, 17.7 Hz, 1 H, $COCH_2$], 2.47 [t, ^3J(H,H) = 7.4 Hz, 2 H, $COCH_2$], 1.68 [d, ^3J(H,H) = 6.7 Hz, 3 H, CH_3], 1.59–0.87 (m, 7 H, $CH_2CH_2CH_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 206.6, 164.8, 130.2, 128.8, 127.5, 126.8, 56.0, 47.6, 43.0, 25.6, 22.2, 20.9, 13.8 ppm. HRMS (ESI): calcd. for $C_{15}H_{21}N_4O$: 273.1710 $[M + H]^+$; found 273.1709; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 90:10, 1.0 mL min^{-1}): t_R (**13c** minor) = 8.1, t_R (**13c** major) = 8.8 min (92% *ee*).

(*S*)-4-(5-Phenyl-2*H*-tetrazol-2-yl)-5-methylhexan-2-one (13d): The title compound was obtained by the General Procedure described above, from **12a** and **6d**. Yield 90% (29.0 mg). $[\alpha]_D^{20}$ = –5.8 (*c* = 1.3, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.16–8.14 (m, 2 H, Ar-H), 7.49–7.46 (m, 3 H, Ar-H), 5.28–5.23 (m, 1 H, N–CH), 3.59 [dd, ^3J(H,H) = 9.8, 17.9 Hz, 1 H, $COCH_2$], 3.00 [dd, ^3J(H,H) = 3.9, 17.9 Hz, 1 H, $COCH_2$], 2.38–2.40 (m, 1 H, CH), 2.21 (s, 3 H, $COCH_3$), 0.97 [d, ^3J(H,H) = 6.8 Hz, 3 H, CH_3], 0.90 [d, ^3J(H,H) = 6.8 Hz, 3 H, CH_3] ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 204.4, 164.5, 130.2, 128.8, 127.5, 126.8, 65.0, 43.4, 32.9, 30.4, 18.6, 18.4 ppm. HRMS (ESI): calcd. for $C_{14}H_{19}N_4O$: 259.1553 $[M + H]^+$; found 259.1557; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 95:5, 1.0 mL min^{-1}): t_R (**13d** minor) = 9.8, t_R (**13d** major) = 10.3 min (98% *ee*).

(*S*)-4-(5-*p*-Tolyl-2*H*-tetrazol-2-yl)octan-2-one (13e): The title compound was obtained by the General Procedure described above,

from **12b** and **6b**. Yield 87% (25.0 mg). $[a]_D^{20}$ = –5.2 (*c* = 0.65, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.03 [d, ^3J(H,H) = 7.92 Hz, 2 H Ar-H], 7.29 [d, ^3J(H,H) = 7.92 Hz, 2 H, Ar-H], 5.40–5.34 (m, 1 H, N–CH), 3.40 [dd, ^3J(H,H) = 7.6, 17.8 Hz, 1 H, $COCH_2$], 3.06 [dd, ^3J(H,H) = 6.0, 17.9 Hz, 1 H, $COCH_2$], 2.41 (s, 3 H, Ar-CH_3), 2.19 (s, 3 H, $COCH_3$), 2.08–1.88 (m, 2 H, CH_2), 1.38–1.06 (m, 4 H, CH_2CH_2), 0.85 [t, ^3J(H,H) = 7.03, 3 H, CH_3] ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 204.2, 164.9, 140.4, 129.5, 126.8, 124.8, 60.0, 47.2, 34.7, 30.4, 27.6, 22.1, 21.5, 13.8 ppm. HRMS (ESI): calcd. for $C_{16}H_{23}N_4O$: 287.1866 $[M + H]^+$; found 287.1869; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 95:5, 1.0 mL min^{-1}): t_R (**13e** minor) = 13.2, t_R (**13e** major) = 16.0 min (96% *ee*).

(*S*)-4-(5-*m*-Tolyl-2*H*-tetrazol-2-yl)octan-2-one (13f): The title compound was obtained by the General Procedure described above, from **12c** and **6b**. Yield 91% (32.5 mg). $[a]_D^{20}$ = –2.4 (*c* = 0.85, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.97 (s, 1 H, Ar-H), 7.94 [d, ^3J(H,H) = 7.7 Hz, 1 H, Ar-H], 7.37 [t, ^3J(H,H) = 7.6 Hz, 1 H, Ar-H], 7.27 [d, ^3J(H,H) = 8.3 Hz, 1 H, Ar-H], 5.40–5.34 (m, 1 H, N–CH), 3.40 [dd, ^3J(H,H) = 7.6, 17.8 Hz, 1 H, $COCH_2$], 3.06 [dd, ^3J(H,H) = 6.0, 17.9 Hz, 1 H, $COCH_2$], 2.41 (s, 3 H, Ar-CH_3), 2.19 (s, 3 H, $COCH_3$), 2.08-1.88 (m, 2 H, CH_2), 1.38–1.06 (m, 4 H, CH_2CH_2), 0.85 [t, ^3J(H,H) = 7.03 Hz, 3 H, CH_3] ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 204.2, 165.0, 138.6, 131.0, 128.8, 127.4, 127.3, 124.0, 60.1, 47.2, 34.7, 30.4, 27.6, 22.1, 21.4, 13.8 ppm. HRMS (ESI): calcd. for $C_{16}H_{23}N_4O$: 287.1866 $[M + H]^+$; found 287.1869; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 95:5, 1.0 mL min^{-1}): t_R (**13f** minor) = 9.9, t_R (**13f** major) = 10.8 min (97% *ee*).

(*S*)-4-(5-*o*-Tolyl-2*H*-tetrazol-2-yl)octan-2-one (13g): The title compound was obtained by the General Procedure described above, from **12d** and **6b**. Yield 85% (30.4 mg). $[a]_D^{20}$ = –4.2 (*c* = 0.85, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.01 [d, ^3J(H,H) = 7.2 Hz, 1 H, Ar-H], 7.38–7.29 (m, 3 H, Ar-H), 5.44–5.34 (m, 1 H, N–CH), 3.43 [dd, ^3J(H,H) = 7.7, 17.8 Hz, 1 H, $COCH_2$], 3.07 [dd, ^3J(H,H) = 5.9, 17.8 Hz, 1 H, $COCH_2$], 2.62 (s, 3 H, Ar-CH_3), 2.20 (s, 3 H, $COCH_3$), 2.09–1.91 (m, 2 H, CH_2), 1.43–1.11 (m, 4 H, CH_2CH_2), 0.86 [t, ^3J(H,H) = 7.1 Hz, 3 H, CH_3] ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 204.2, 165.2, 137.4, 131.3, 129.8, 129.4, 126.6, 126.0, 59.9, 47.2, 34.7, 30.4, 27.6, 22.1, 21.7, 13.8 ppm. HRMS (ESI): calcd. for $C_{16}H_{23}N_4O$: 287.1866 $[M + H]^+$; found 287.1868; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 95:5, 1.0 mL min^{-1}): t_R (**13g** minor) = 9.5, t_R (**13g** major) = 10.6 min (93% *ee*).

(*S*)-4-[5-(*p*-Bromophenyl)-2*H*-tetrazol-2-yl]octan-2-one (13h): The title compound was obtained by the General Procedure described above, from **12e** and **6b**. Yield 89% (34.2 mg). $[a]_D^{20}$ = –1.2 (*c* = 0.85, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.08 [d, ^3J(H,H) = 8.4 Hz, 2 H, Ar-H], 7.46 [d, ^3J(H,H) = 8.4 Hz, 2 H, Ar-H], 5.41–5.35 (m, 1 H, N–CH), 3.41 [dd, ^3J(H,H) = 7.8, 17.9 Hz, 1 H, $COCH_2$], 3.07 [dd, ^3J(H,H) = 5.8, 17.9 Hz, 1 H, $COCH_2$], 2.19 (s, 3 H, CH_3), 2.07–1.86 (m, 2 H, CH_2), 1.38–1.21 (m, 4 H, CH_2CH_2), 0.86 [t, ^3J(H,H) = 7.1 Hz, 3 H, CH_3] ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 204.2, 164.0, 136.2, 129.1, 128.1, 126.1, 60.2, 47.1, 34.7, 30.3, 27.6, 22.0, 13.8 ppm. HRMS (ESI): calcd. for $C_{15}H_{20}ClN_4O$: 307.1320 $[M + H]^+$; found 307.1320; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 95:5, 1.0 mL min^{-1}): t_R (**13h** minor) = 12.5, t_R (**13h** major) = 14.1 min (95% *ee*).

(*R*)-4-Phenyl-4-(5-phenyl-2*H*-tetrazol-2-yl)butan-2-one (13i): PhCOOH (40 mol-%) and mol. sieves (4 Å, 10 mg) were added to a stirred solution of catalyst **3d** (20 mol-%) in $PhCH_3/CHCl_3$ (7:3, 1.25 mL) and the solution was stirred for 5 minutes at room temperature. After addition of enone **9a** (0.60 mmol), the mixture was stirred for 10 minutes. 5-Phenyltetrazole (**12a**, 0.125 mmol) was added at –20 °C, and stirring was continued for the indicated time, resulting in a single regioisomer. The crude reaction mixture was then loaded onto a silica gel column for purification (EtOAc/hexane, 1:5), to afford the Michael adduct. Yield 95% (43.9 mg). $[a]_D^{20}$ = +58.2 (*c* = 1.3, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.14–8.11 (m, 2 H, Ar-H), 7.46–7.45 (m, 3 H, Ar-H), 7.41–7.32 (m, 5 H, Ar-H), 6.47 [dd, ^3J(H,H) = 5.0, 9.4 Hz, 1 H, N–CH], 4.04 [dd, ^3J(H,H) = 9.4, 18.0 Hz, 1 H, $COCH_2$], 3.33 [dd, ^3J(H,H) = 5.0, 18.0 Hz, 1 H, $COCH_2$], 2.38 (s, 3 H, $COCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 203.6, 165.0, 137.4, 130.3, 129.1, 129.0, 128.8, 126.9, 126.8, 63.1, 48.1, 30.3 ppm. HRMS (ESI): calcd. for $C_{17}H_{17}lN_4O$: 293.1397 $[M + H]^+$; found 293.1400; HPLC (Chiralpak AD-H, hexanes/propan-2-ol, 90:10, 1.0 mL min^{-1}): t_R (**13i** major) = 17.2, t_R (**13i** minor) = 18.0 min (91% *ee*).

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[1] A. R. Katritzky, A. F. Pozharskii, *Handbook of Heterocyclic Chemistry*, 2nd ed., Pergamon, Oxford, **2002**.
[2] M. Gandelman, E. N. Jacobsen, *Angew. Chem. Int. Ed.* **2005**, *44*, 2393–2397.
[3] a) S. J. Miller, *Acc. Chem. Res.* **2004**, *37*, 601–610; b) D. J. Guerin, S. J. Miller, *J. Am. Chem. Soc.* **2002**, *124*, 2134–2136; c) T. E. Hortsmann, D. J. Guerin, S. J. Miller, *Angew. Chem. Int. Ed.* **2000**, *39*, 3635–3638; d) D. J. Guerin, T. E. Horstmann, S. J. Miller, *Org. Lett.* **1999**, *1*, 1107–1109.
[4] J. Wang, H. Li, L. Zu, W. Wang, *Org. Lett.* **2006**, *8*, 1391–1394.
[5] J. Wang, L. Zu, H. Li, H. Xie, W. Wang, *Synthesis* **2007**, 2576–2580.
[6] Y. K. Chen, M. Yoshida, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2006**, *128*, 9328–9329.
[7] P. Dinér, M. Nielsen, M. Marigo, K. A. Jørgensen, *Angew. Chem. Int. Ed.* **2007**, *46*, 1983–1987.
[8] U. Uria, J. L. Vicario, D. Badía, L. Carrillo, *Chem. Commun.* **2007**, *27*, 2509–2511.
[9] M. Lu, D. Zhu, Y. Lu, Y. Hou, B. Tan, G. Zhong, *Angew. Chem. Int. Ed.* **2008**, *47*, 10187–10191.
[10] a) H. Kim, C. Yen, P. Preston, J. Chin, *Org. Lett.* **2006**, *8*, 5239–5242; b) J.-W. Xie, L. Yue, W. Chen, W. Du, J. Zhu, J.-G. Deng, Y.-C. Chen, *Org. Lett.* **2007**, *9*, 413–415; c) S. B. Tsogoeva, S. B. Jagtap, *Synlett* **2004**, 2624–2626; d) N. J. A. Martin, B. List, *J. Am. Chem. Soc.* **2006**, *128*, 13368–13369.
[11] a) J.-W. Xie, W. Chen, R. Li, M. Zeng, W. Du, L. Yue, Y.-C. Chen, Y. Wu, J. Zhu, J.-G. Deng, *Angew. Chem. Int. Ed.* **2007**, *46*, 389–392; b) G. Bartoli, M. Bosco, A. Carlone, F. Pesciaioli, L. Sambri, P. Melchiorre, *Org. Lett.* **2007**, *9*, 1403–1405; c) S. H. McCooey, S. J. Connon, *Org. Lett.* **2007**, *9*, 599–602; d) Y.-Q. Yang, G. Zhao, *Chem. Eur. J.* **2008**, *14*, 10888–10891; e) X. Lu, L. Deng, *Angew. Chem. Int. Ed.* **2008**, *47*, 7710–7710; f) B. Tan, P. J. Chuan, X. Zeng, M. Lu, G. Zhong, *Org. Lett.* **2008**, *10*, 3489–3492.
[12] P. R. Singh, K. Bartelso, Y. Wang, H. Su, X. Lu, L. Deng, *J. Am. Chem. Soc.* **2008**, *130*, 2422–2423.
[13] J. Lv, J. Zhang, Zh. Lin, Y. Wang, *Chem. Eur. J.* **2009**, *15*, 972–979.

[14] a) X. Wang, C. M. Reisinger, B. List, *J. Am. Chem. Soc.* **2008**, *130*, 6070–6071; b) X. Lu, Y. Liu, B. Sun, B. Cindric, L. Deng, *J. Am. Chem. Soc.* **2008**, *130*, 8134–8135.
[15] F. Pesciaioli, F. D. Vincentiis, P. Galzerano, G. Bencivenni, G. Bartoli, A. Mazzanti, P. Melchiorre, *Angew. Chem. Int. Ed.* **2008**, *47*, 8703–8706.
[16] After our original submission, enantioselective conjugate additions of *N*-heterocycles to α,β-unsaturated ketones in the presence of the L-*N*-Boc-phenylglycine salt of a primary amine derived from a chiral cinchona alkaloid (20 mol-%), affording moderate to good levels of enantioselectivity (*ee* values ranging from 38–88% for Michael N1 adducts), were reported; see: G. Luo, S. Zhang, W. Duan, W. Wang, *Synthesis* **2009**, 1564–1572.
[17] B. Vakulya, S. Varga, A. Csámpai, T. Soós, *Org. Lett.* **2005**, *7*, 1967–1969.

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