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Enantioselective Conjugate Addition of Both Aromatic Ketones and Acetone to Nitroolefins Catalyzed by Chiral Primary Amines Bearing Multiple Hydrogen-Bonding Donors

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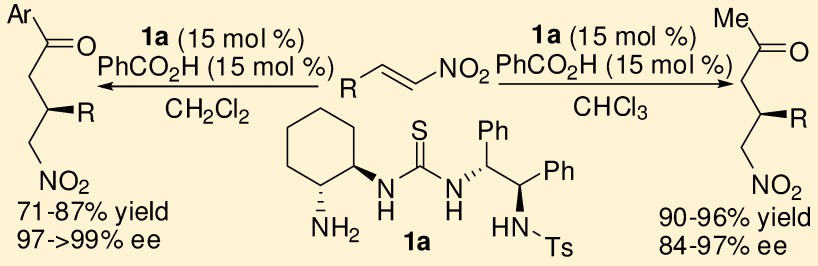
Supporting Information



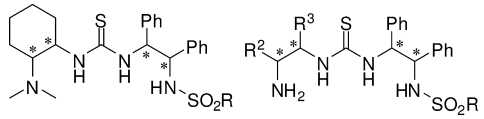
ABSTRACT: A new class of chiral primary amine catalysts bearing multiple hydrogen-bonding donors have been designed and synthesized. The newly developed bifunctional organocatalysts efficiently catalyzed not only enantioselective conjugate addition of aromatic ketones to nitroolefins in good yields (up to 87%) with excellent enantioselectivities (97→99% ee) but also enantioselective conjugate addition of acetone to nitroolefins in excellent yields (90−96%) with high enantioselectivities (up to 97% ee).

Design of new chiral organocatalysts to meet the needs of challenging asymmetric transformations is one of the most important undertakings in current asymmetric organocatalysis.[1] Direct conjugate addition of carbonyl compounds to nitroolefins represents a convenient access to bifunctional chiral nitroalkanes, which are valuable building blocks in organic synthesis and medicinal chemistry, and development of the chiral catalysts for such processes has received much attention.[2] Over the past years, impressive progress has been made in the development of metal-free organic catalysts for the enantioselective addition of 1,3-dicarbonyl compounds,[3] aldehydes,[4] and cyclic ketones[5] to nitroolefins. Nonetheless, the direct catalytic asymmetric conjugate addition of aromatic ketones to nitroolefins and the catalytic asymmetric conjugate reaction between acetone and nitroolefins remain the two most important challenges in this field.

Since the pioneering and independent work by Tsogoeva,[6] Jacobsen,[7] and Ma,[8] a few bifunctional chiral primary amines have been developed as effective organocatalysts for the asymmetric conjugate addition of acetone to nitroolefins[9] and the asymmetric conjugate reaction between aromatic ketones and nitroolefins,[10] respectively. However, despite these limited cases, few general catalyst systems with broad substrate scope have been reported for the asymmetric conjugate addition of both aromatic aromatic ketones and acetone to nitroolefins with enantiomeric excesses of over 90%.[11] Thus, we became interested in the development of a new class of *general* chiral organic catalysts to realize these two most challenging reactions in this field.

Recently, chiral multifunctional organocatalysts bearing multiple hydrogen-bonding donors have emerged as promising catalysts for asymmetric transformations.[12] Notably, Wang's group has recently developed a new class of bifunctional tertiary amine−thioureas bearing multiple hydrogen bonding donors for several catalytic asymmetric reactions via noncovalent catalysis (Scheme 1).[13] Inspired by this seminal work, and

Scheme 1. Two Types of Catalytic Modes in Organocatalysis



considering the importance and challenge of the direct catalytic asymmetric conjugate addition of both aromatic ketones and acetone to nitroolefins, together with our interest in chiral primary amine catalysis,[14] we envisioned that chiral primary amines bearing multiple hydrogen-bonding donors might serve

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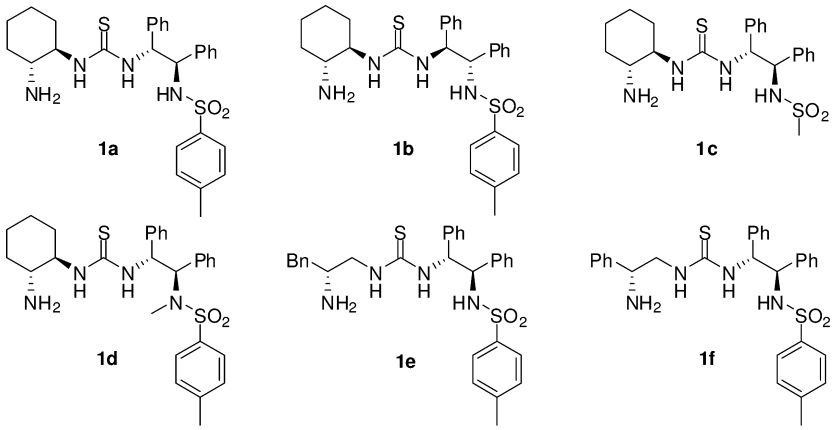
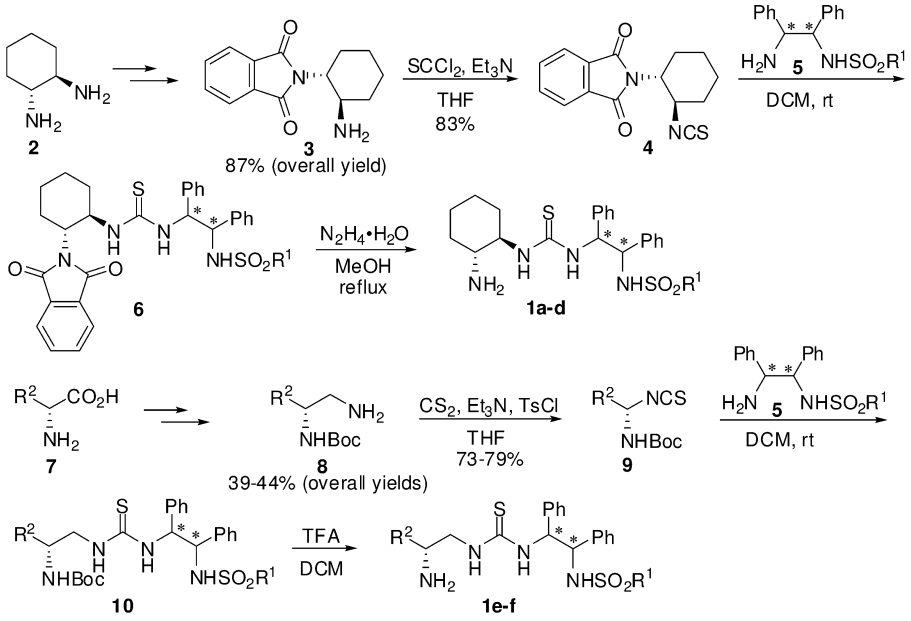


Figure 1. New class of chiral primary amine catalysts.

Scheme 2. Synthesis of Chiral Primary Amine Catalysts Bearing Multiple Hydrogen-Bonding Donors



as a new class of easily tunable bifunctional organic catalysts for the enantioselective conjugate addition of *both* aromatic ketones *and* acetone to nitroolefins.

As part of our interest in asymmetric organocatalysis,[14,15] herein we report a new class of *general* chiral primary amine catalysts bearing multiple hydrogen bonding donors which efficiently catalyzed enantioselective conjugate addition of aromatic ketones to nitroolefins and enantioselective conjugate reaction of acetone to nitroolefins which are two of the most challenging reactions in this field in good yields (up to 96%) with high to excellent enantioselectivities (up to >99% ee).

Designed chiral primary amine catalysts bearing multiple hydrogen-bonding donors (Figure 1) were readily synthesized by the following procedures described in Scheme 2. The organocatalysts **1a−d** were prepared from monoprotected chiral diamine **3**[16] in three steps. The preparation of chiral primary amine catalysts **1e,f** started with α-amino acids **7**. The treatment of Boc-protected chiral diamine **8**[17] with $CS_2/Et_3N/TsCl$ provided the corresponding isothiocyanates **9**.[18] Then the condensation of isothiocyanates **3** with the amine **5** in DCM gave the corresponding thioureas **10**. Removing the Boc protecting group from nitrogen with trifluoroacetic acid afforded the target catalysts **1e,f**.

With these catalysts in hand, we initially investigated the more challenging asymmetric conjugate addition of aromatic ketones to nitroolefins. Acetophenone **11a** and β-nitrostyrene **12a** were selected as the model substrates for initial optimization studies. To our delight, the newly designed catalysts **1a** prompted the desired reaction, providing the desired product **13a** in 72% yield and >99% ee (Table 1, entry 1). Interestingly, its diastereoisomer **1b** afforded the same level of asymmetric induction but moderate yield (entry 2). This seems to indicate that the (*R*,*R*)-1,2-diphenylethenediamine moiety matched the (*R*,*R*)-cyclohexanediamine moiety, and the configuration of the product was determined mainly by the latter, but the catalytic activity could be greatly enhanced by the former. Replacing the Ts group of **1a** with a less bulky group (Ms) decreased the catalytic activity significantly (26% yield) (entry 3). In order to investigate the effects of the chiral diamine scaffolds on the catalytic activities, the α-amino acid derived chiral primary amine catalysts bearing multiple hydrogen-bonding donors **1e,f** were evaluated. These catalysts promoted the desired reaction in moderate selectivity (entries 5

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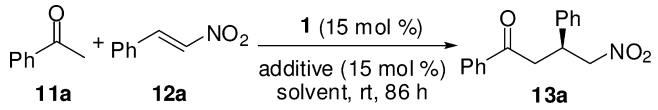
Table 1. Conjugate Addition of Acetophenone to β-Nitrostyrene[a]

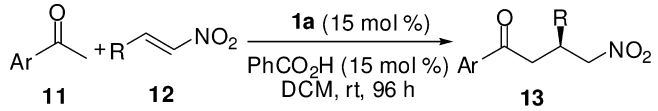


11a 12a 13a

entry	catalyst	solvent	additive	yield[b] (%)	ee[c] (%)
1	**1a**	DCM	$PhCO_2H$	**72**	**>99**
2	**1b**	DCM	$PhCO_2H$	50	>99
3	**1c**	DCM	$PhCO_2H$	26	>99
4	**1d**	DCM	$PhCO_2H$	27	>99
5	**1e**	DCM	$PhCO_2H$	30	76
6	**1f**	DCM	$PhCO_2H$	22	72
7	**1a**	$CHCl_3$	$PhCO_2H$	60	>99
8	**1a**	DCE	$PhCO_2H$	14	95
9	**1a**	THF	$PhCO_2H$	14	97
10	**1a**	toluene	$PhCO_2H$	45	97
11	**1a**	DCM	4-$NO_2C_6H_4CO_2H$	32	>99
12	**1a**	DCM	4-$MeOC_6H_4CO_2H$	58	>99
13	**1a**	DCM	$PhCO_2H$	61	>99[d]
14	**1a**	DCM	none	trace	N.D.

[a]Reactions carried out on a 0.2 mmol scale. General conditions: β-nitrostyrene (0.2 mmol), acetophenone (0.6 mmol), $PhCO_2H$ (0.03 mmol), and catalyst (15 mol %) were stirred in 0.2 mL of solvent at rt for 96 h. [b]Isolated yield. [c]Enantiomeric excess (ee) was determined by HPLC analysis using a chiral stationary phase. [d]5 mol % of $PhCO_2H$ was used.

Table 2. Conjugate Addition of Aromatic Ketones to Nitroolefins[a]



11 12 13

entry	Ar	R	13	yield[b] (%)	ee[c] (%)
1	Ph	Ph	**13a**	72	>99
2	4-Me-C_6H_4	Ph	**13b**	75	98
3	4-MeO-C_6H_4	Ph	**13c**	73	98
4	4-NO_2-C_6H_4	Ph	**13d**	81	>99
5	4-CF_3-C_6H_4	Ph	**13e**	87	98
6	4-Br-C_6H_4	Ph	**13f**	80	98
7	Ph	4-Me-C_6H_4	**13g**	75	>99
8	Ph	4-MeO-C_6H_4	**13h**	72	>99
9	Ph	4-Cl-C_6H_4	**13i**	71	>99
10	Ph	4-Br-C_6H_4	**13j**	77	>99
11	Ph	2-Br-C_6H_4	**13k**	71	99
12	Ph	4-CF_3-C_6H_4	**13l**	80	97
13	Ph	3-CF_3-C_6H_4	**13m**	79	98
14	Ph	2-CF_3-C_6H_4	**13n**	83	>99
15	Ph	2-furyl	**13o**	71	98

[a]Reactions carried out on a 0.2 mmol scale. General conditions: nitroolefin (0.2 mmol), aromatic ketone (0.6 mmol), $PhCO_2H$ (0.03 mmol), and catalyst (15 mol %) were stirred in 0.2 mL of CH_2Cl_2 at rt for 96 h. [b]Isolated yield. [c]Enantiomeric excess (ee) was determined by HPLC analysis using a chiral stationary phase.

and 6); however, this represents the first example of chiral primary amine−thiourea-type catalysts derived from acyclic α-amino acids. In order to evaluate the role the multiple hydrogen-bonding donors played in this system, a control experiment was performed with the catalyst **1d** in which the sulfonamide $NMeSO_2Ts$ was methylated. The use of the catalyst **1d** led to poor catalytic activity (27% yield after 96 h) (entry 4). This indicates that the third NH of sulfonamide on the 1,2-diphenylethenediamine moiety played a significant role in this conjugate addition reaction.

The solvents have a remarkable effect on the catalytic activity (entry 1 and entries 7−10). The chlorocarbon solvents seem to be promising (entries 1 and 7). Interestingly, however, the use of $ClCH_2CH_2Cl$ led to the conjugate adduct in only 14% yield (entry 8).

The presence of acid additives was also crucial for the reaction to occur. Without any additive, the reaction became sluggish (entry 14). Among the acids examined, benzoic acid was found to be the best additive.

Under the optimized reaction conditions, the substrate scope with respect to both aromatic ketones and nitroolefins was examined. As shown in Table 2, the reaction has a broad substrate scope with respect to both aromatic ketones and nitroolefins. A wide range of electron-rich and electron-deficient aromatic ketones underwent smoothly the conjugate addition reactions of β-nitrostyrene in good yield (73−87%)

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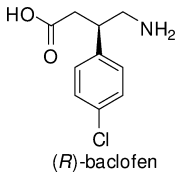
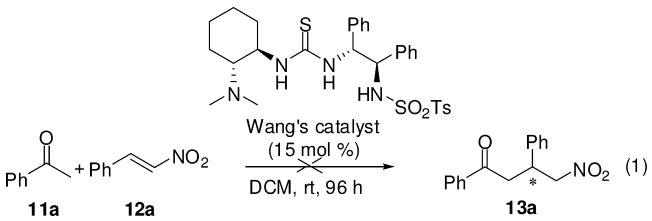
with excellent enantioselectivities (98→99% ee) (entries 2−6, Table 2). With regard to nitroolefins, it appears that the position and the electronic property of the substituents for aromatic rings of nitroalkenes are well tolerated by the conjugate addition reactions. Whether electron-withdrawing (entries 9−14, Table 2), -donating (entries 7−8, Table 2), or -neutral (entry 1, Table 2) groups on aromatic rings were used, the reactions proceeded smoothly to give the desired adducts in good yields (71−83%) with excellent enantioselectivities (97→99% ee). Moreover, a heteroaromatic nitroolefin was also a suitable substrate for this nitro-Michael addition (entry 15).[19]

Notably, the products of the Michael addition of aromatic ketones are useful intermediates for a variety of further elaborated structures such as chiral pyrrolidines,[10a] γ-lactams, and γ-amino acids.[20] For example, the product **13i** can be transformed into the therapeutically useful GABAB receptor agonist (*R*)-baclofen hydrochloride through a three-step route involving Baeyer−Villiger oxidation followed by reduction and subsequent hydrolysis.[20]



(*R*)-baclofen

To gain insight into the reaction mechanism, we performed the reaction between acetophenone **11a** and β-nitrostyrene **12a** with Wang's catalyst. The catalytic asymmetric Michael addition did not occur after 96 h (eq 1).



On the basis of the above results, a bifunctional mechanism involving hydrogen bonding and enamine formation has been proposed to account for the enantioselectivity observed (Figure 2). The primary amine activates the aromatic ketone through

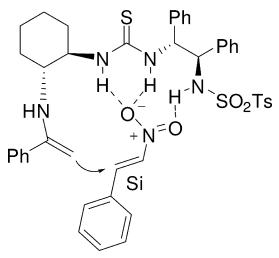


Figure 2. Proposed transition-state model for the Michael addition of aromatic ketones with β-nitrostyrene.

the formation of an enamine intermediate promoted by the acid additive, while the multiple hydrogen-bonding functionality interacts with the nitro group to enhance the electrophilicity of nitroolefin.

Having proven excellent stereocontrol performance of the chiral primary amine catalyst **1a**, we next turned our attention to investigate the direct conjugate addition of acetone to nitroolefins with the chiral catalyst **1a**. Acetone is still one of the most problematic substrates for the nitro-Michael addition. Acetone and β-nitrostyrene **12a** were selected as the model substrates in the preliminary screening. In the presence of 15 mol % of catalyst **1a** and DCM as solvent, the desired conjugate prodcut **14a** was obtained in 90% yield and 84% ee. Then we investigated the effects of the solvents on the conjugate reaction. As summarized in Table 3, the use of $CHCl_3$ led to the best results (92% yield, 96% ee, entry 2). The acid additives were also examined. Among the acid additives examined, $PhCO_2H$ was still the optimal additive.

With the optimized reaction conditions in hand, the scope of the reaction was investigated (Table 4). It appears that the position and the electronic property of the substituents for aromatic rings of nitroolefins have little effects on the conjugate addition. A wide range of nitroolefins underwent the conjugate addition reactions of acetone in high yields (90−96%) with good enantioselectivities (84−97% ee) (entries 1−8).

In summary, we have developed a new class of easily tunable chiral primary amine catalysts bearing multiple hydrogen-bonding donors. These chiral primary amines as general catalysts efficiently catalyzed enantioselective conjugate addition of aromatic ketones to nitroolefins and conjugate reaction of acetone to nitroolefins, which are two of the most challenging reactions in this field in good to excellent yields and high to excellent enantioselectivities. The corresponding products are useful intermediates for a variety of further elaborated structures such as chiral pyrrolidines, γ-lactams, and γ-amino acids.

■ EXPERIMENTAL SECTION

^{1}H NMR and ^{13}C NMR spectra were recorded on a 300 MHz spectrophotometer. Chemical shifts (δ) are expressed in ppm, and *J* values are given in Hz. The enantiomeric excess was determined by HPLC using Chiralpak AD-H and Chiralpak AS-H columns with *n*-hexane and 2-propanol as eluents. High-resolution mass spectrometry (HRMS) was recorded on a spectrometer. Optical rotations were measured on a polarimeter. Flash column chromatography was performed on silica gel (230−400 mesh). All chemicals and solvents were used as received without further purification unless otherwise stated.

Preparation of Chiral Primary Amines 1a−d. The isothiocyanate **4**[16] (1.0 mmol) and the amine **5** (1.0 mmol) were placed in a 25 mL vial equipped with a Teflon-coated stir bar. Dry CH_2Cl_2 (10 mL) was added. The resulting solution was stirred at room temperature overnight until the reaction was complete (monitored by TLC). After removal of the solvent, the crude product was dissolved in MeOH (2 mL), and $N_2H_4{\cdot}H_2O$ (5 mmol) was added. The resulting mixture was stirred under reflux until the reaction was complete (monitored by TLC). After filtration, the filtrate was evaporated under vacuum and purified through column chromatography on silica gel (petroleum ether/ethyl acetate as the eluents) to afford the desired catalyst **1a−d** as a white solid.

Data for 1a. Amorphous solid, 408 mg, 78% yield. $[\alpha]^{20}_D$ = +114.7 (*c* 1.0 $CHCl_3$). ^{1}H NMR (300 MHz, CD_3OD): δ = 7.88 (s, 2H), 7.42−7.45 (d, *J* = 8.4 Hz, 2H), 7.11 (s, 3H), 7.04−7.07(d, *J* = 7.5 Hz, 4H), 6.94−7.01 (dd, *J* = 6.3, 5.7 Hz, 3H), 6.85−6.87 (d, *J* = 6.3 Hz, 2H), 5.79−5.82 (d, *J* = 9.9 Hz, 1H), 4.62−4.65 (d, *J* = 9.9 Hz, 1H), 4.06−4.13 (dd, *J* = 7.2, 7.2 Hz, 1H), 2.50 (s, 1H), 2.27 (s, 3H), 1.95−2.00 (m, 3H), 1.73 (s, 2H), 1,07−1.33 (m, 6H). ^{13}C NMR (75 MHz, CD_3OD): δ = 184.5, 144.2, 140.1, 139.9, 139.5, 130.3, 129.4, 129.1, 129.0, 128.9, 128.7, 128.5, 127.8, 65.0, 63.8, 61.1, 56.5, 34.6, 33.0, 26.1, 25.9, 21.4. HRMS: calcd for $C_{28}H_{35}N_4O_2S_2$ $[M]^+$ 523.2201, found 523.2217.

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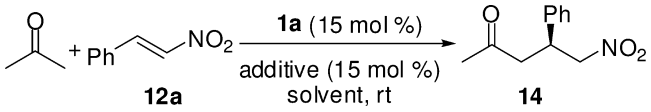
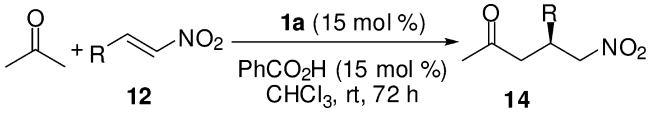
Table 3. Conjugate Addition of Acetone to Nitrostyrene[a]



entry	solvent	additive	yield[b] (%)	ee[c] (%)
1	DCM	$PhCO_2H$	90	84
2	$CHCl_3$	$PhCO_2H$	**92**	**96**
3	DCE	$PhCO_2H$	85	95
4	toluene	$PhCO_2H$	77	80
5	*m*-xylene	$PhCO_2H$	75	86
6	Et_2O	$PhCO_2H$	68	88
7	THF	$PhCO_2H$	80	75
8	$CHCl_3$	CH_3CO_2H	93	92
9	$CHCl_3$	CF_3CO_2H	trace	N.D.
10	$CHCl_3$	4-$NO_2C_6H_4CO_2H$	84	88
11	$CHCl_3$	4-$MeOC_6H_4CO_2H$	89	90
12	$CHCl_3$	PhOH	trace	N.D.

[a]Reactions carried out on a 0.2 mmol scale. General conditions: nitroolefin (0.2 mmol), acetone (2 mmol), $PhCO_2H$ (0.03 mmol), and catalyst (15 mol %) were stirred in 0.2 mL of solvent at rt for 72 h. [b]Isolated yield. [c]Enantiomeric excess (ee) was determined by HPLC analysis using a chiral stationary phase.

Table 4. Conjugate Addition of Acetone to Various Nitroolefins[a]



entry	R	14	yield[b] (%)	ee[c] (%)
1	Ph	**14a**	92	96
2	4-Me-C_6H_4	**14b**	90	97
3	4-MeO-C_6H_4	**14c**	91	93
4	4-Br-C_6H_4	**14d**	94	96
5	4-Cl-C_6H_4	**14e**	93	93
6	2-Br-C_6H_4	**14f**	92	90
7	3-CF_3-C_6H_4	**14g**	91	84
8	2-furyl	**14h**	96	94

[a]Reactions carried out on a 0.2 mmol scale. General conditions: nitroolefin (0.2 mmol), acetone (2 mmol), $PhCO_2H$ (0.03 mmol), and catalyst (15 mol %) were stirred in 0.2 mL of $CHCl_3$ at rt for 72 h. [b]Isolated yield. [c]Enantiomeric excess (ee) was determined by HPLC analysis using a chiral stationary phase.

Data for 1b. Amorphous solid, 397 mg, 76% yield. $[\alpha]^{20}_D$ = −153.3 (*c* 1.0 $CHCl_3$). ^{1}H NMR (300 MHz, CD_3OD): δ = 7.88 (s, 2H), 7.42−7.45 (d, *J* = 8.4 Hz, 2H), 7.11 (s, 3H), 7.04−7.07 (d, *J* = 7.5 Hz, 4H), 6.94−7.01 (dd, *J* = 6.3, 5.7 Hz, 3H), 6.85−6.87 (d, *J* = 6.3 Hz, 2H), 5.79−5.82 (d, *J* = 9.9 Hz, 1H), 4.62−4.65 (d, *J* = 9.9 Hz, 1H), 4.06−4.13 (dd, *J* = 7.2, 7.2 Hz, 1H), 2.50 (s, 1H), 2.27 (s, 3H), 1.95−2.00 (m, 3H), 1.73 (s, 2H), 1,07−1.33 (m, 6H). ^{13}C NMR (75 MHz, CD_3OD): δ = 184.5, 144.2, 140.1, 139.9, 139.5, 130.3, 129.4, 129.1, 129.0, 128.9, 128.7, 128.5, 127.8, 65.0, 63.8, 61.1, 56.5, 34.6, 33.0, 26.1, 25.9, 21.4. HRMS: calcd for $C_{28}H_{35}N_4O_2S_2$ $[M]^+$ 523.2201, found 523.2217.

Data for 1c. Amorphous solid, 317 mg, 71% yield. $[\alpha]^{20}_D$ = +81.2 (*c* 0.9 $CHCl_3$). ^{1}H NMR (300 MHz, CD_3OD): δ = 7.90 (s, 1H), 7.17−7.21 (d, *J* = 13.8 Hz, 10H), 5.85−5.87 (d, *J* = 8.7 Hz, 1H), 4.80−4.83 (d, *J* = 9.9 Hz, 2H), 4.10 (s, 1H), 2.71 (s, 3H), 2.56 (s, 1H), 1.98 (s, 2H), 1,74 (s, 2H), 1.12−1.30 (m, 5H). ^{13}C NMR (75 MHz, CD_3OD): δ = 184.4, 140.6, 140.1, 129.6, 129.4, 129.2, 129.1, 128.9, 128.7, 64.7, 63.8, 61.0, 56.1, 41.9, 34.6, 33.1, 26.0, 25.8. HRMS: calcd for $C_{22}H_{31}N_4O_2S_2$ $[M]^+$ 447.1888, found 447.1893.

Data for 1d. Amorphous solid, 403 mg, 75% yield. $[\alpha]^{20}_D$ = +51.4 (*c* 0.4 $CHCl_3$). ^{1}H NMR (300 MHz, CD_3OD): δ = 7.60−7.62 (d, *J* = 7.5 Hz, 2H), 7.33−7.35 (d, *J* = 7.8 Hz, 2H), 7.25−7.27 (d, *J* = 7.8 Hz, 2H), 7.08−7.18 (m, 8H), 6.44−6.48 (d, *J* = 11.4 Hz, 1H), 5.50−5.51 (d, *J* = 11.4 Hz, 1H), 4.25 (s, 1H), 2.85 (s, 3H), 2.72 (s, 1H), 2.37 (s, 3H), 2.02−2.03 (d, *J* = 4.5 Hz, 2H), 1.19 (s, 1H), 1.78 (s, 2H), 0.99−1.35 (m, 5H). ^{13}C NMR (75 MHz, CD_3OD): δ = 184.1, 144.9, 140.8, 138.4, 135.9, 130.7, 130.6, 129.5, 129.4, 129.2, 128.6, 128.4, 65.9, 59.7, 58.7, 56.2, 33.6, 33.1, 31.3, 25.9, 25.6, 21.5. HRMS: calcd for $C_{29}H_{37}N_4O_2S_2$ $[M]^+$ 537.2357, found 537.2347.

Preparation of Chiral Primary Amines 1e,f. The isothiocyanate **9**[18] (1.0 mmol) and the amine **5** (1.0 mmol) were placed in a 50 mL vial equipped with a Teflon-coated stir bar. Dry CH_2Cl_2 (10 mL) was added. The resulting solution was stirred at room temperature overnight until the reaction was complete (monitored by TLC). After removal of the solvent, the crude product was dissolved in CH_2Cl_2 (20 mL), and CF_3CO_2H (9 mL) was added dropwise at 0 °C. The resulting mixture was stirred under at room temperature until the reaction was complete (monitored by TLC). The reaction mixture was evaporated under vacuum. The resulting residue was extracted with CH_2Cl_2, and the separated organic phase was washed by saturated aqueous $NaHCO_3$. The combined organic phase was dried over anhydrous Na_2SO_4. After removal of solvent, the crude product was purified through column chromatography on silica gel (petroleum ether/ethyl acetate as the eluents) to afford the desired catalysts **1e,f.**

Data for 1e. Amorphous solid, 380 mg, 68% yield. $[\alpha]^{20}_D$ = +26.5 (*c* 1.0 $CHCl_3$). ^{1}H NMR (300 MHz, CD_3OD): δ = 7,49−7.51 (d, *J* = 7.5 Hz, 2H), 7.21−7.29 (m, 6H), 7.03−7.09 (m, 8H), 6.93−6.97 (m, 5H), 5.79−5.81 (d, *J* = 6.9 Hz, 1H), 4.69−4.72 (d, *J* = 9.3 Hz, 1H),

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3.67 (s, 1H), 3.37−3.41 (d, J = 12.6 Hz, 1H), 3.29−3.32 (d, J = 11.1 Hz, 1H), 2.76−2.79 (d, J = 8.1 Hz, 1H), 2.56−2.62 (d, J = 7.2 Hz, 1H), 2.24 (s, 3H). ^{13}C NMR (75 MHz, CD_3OD): δ = 184.9, 144.2, 139.9, 139.7, 139.6, 139.5, 130.5, 130.4, 129.8, 129.5, 129.1, 129.0, 128.8, 128.5, 128.0, 127.8, 65.1, 64.1, 53.7, 50.5, 41.7, 21.7. HRMS: calcd for $C_{31}H_{34}N_4O_2S_2$ $[M]^+$ 558.2123, found 558.2092.

Data for 1f. Amorphous solid, 343 mg, 63% yield. $[\alpha]^{20}_D$ = +27.0 (c 1.0 $CHCl_3$). ^{1}H NMR (300 MHz, CD_3OD): δ = 7.47−7.50 (d, J = 7.8 Hz, 2H), 7.18−7.41 (m, 6H), 6.79−7.10 (m, 13H), 5.745(s, 1H), 4.64−4.68 (d, J = 9.6 Hz, 1H), 4.20−4.24 (t, J = 6.3 Hz, 1H), 3.72−3.74 (d, J = 6.3 Hz, 2H), 2.28 (s, 3H). ^{13}C NMR (75 MHz, CD_3OD): δ = 184.8, 144.2, 143.8, 139.9, 139.6, 130.3, 129.8, 129.4, 129.1, 129.0, 128.7, 128.4, 127.9, 127.9, 127.2, 64.9, 64.0, 56.1, 52.8, 21.5. HRMS: calcd for $C_{30}H_{32}N_4O_2S_2$ $[M]^+$ 544.1967, found 544.1957.

General Procedure for 1a-Catalyzed Asymmetric Michael Addition of Aromatic Ketones to Nitroolefins. The nitroolefin (0.2 mmol), aromatic ketone (0.6 mmol), $PhCO_2H$ (0.03 mmol), and catalyst **1a** (0.03 mmol) were placed in a 1.5 mL vial equipped with a Teflon-coated stir bar. DCM (0.2 mL) was added under air. The vial was capped with a white polyethylene stopper, and the resulting mixture was stirred at room temperature until the reaction was complete (monitored by TLC). Then the mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate as the eluents) to afford the desired product. The enantiomeric excess of the pure product was determined by chiral HPLC analysis.

*(S)-4-Nitro-1,3-diphenylbutan-1-one (**13a**).*[8] 38.8 mg, 72% yield. $[\alpha]^{20}_D$ = −26.2 (c = 1.0 M, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.90−7.93 (d, J = 8.4 Hz, 2H), 7.55−7.59 (t, J = 7.2 Hz, 1H) 7.42−7.47 (t, J = 7.5 Hz, 2H), 7.29−7.35 (m, 5H), 4.80−4.86 (dd, J = 6.6, 6.6 Hz, 1H), 4.65−4.72 (dd, J = 8.1, 8.1 Hz, 1H), 4.18−4.27 (m, 1H), 3.37−3.53 (m, 2H). HPLC (Chiralpak AD-H, 2-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ = 254 nm): t_{major}= 15.9 min, t_{minor} (not found).

*(S)-4-Nitro-3-phenyl-1-p-tolylbutan-1-one (**13b**).*[8] 42.5 mg, 75% yield. $[\alpha]^{20}_D$ = −34.0 (c = 0.6 M, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.80−7.85 (d, J = 8.1 Hz, 2H), 6.99−7.59 (m, 7H), 4.80−4.86 (dd, J = 6.6, 6.6 Hz, 1H), 4.64−4.71 (dd, J = 8.1, 8.1 Hz, 1H), 4.17−4.26 (m, 1H), 3.31−3.49 (m, 2H), 2.19 (s, 3H). HPLC (Chiralpak AD-H, 2-propanol/hexane =10/90, flow rate 1.0 mL/min, λ = 254 nm): t_{major} = 18.6 min, t_{minor} = 30.2 min.

*(S)-1-(4-Methoxyphenyl)-4-nitro-3-phenylbutan-1-one (**13c**).*[8] 43.7 mg, 73% yield. $[\alpha]^{20}_D$ = −27.7 (c = 0.6 M, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.88−7.91 (d, J = 7.2 Hz, 2H), 7.23−7.35 (m, 5H), 6.90−6.92 (d, J = 6.9 Hz, 2H), 4.80−4.87 (dd, J = 6.6, 6.3 Hz, 1H), 4.64−4.71 (dd, J = 8.1, 8.1 Hz, 1H), 4.10−4.25 (m, 2H), 3.86 (s, 3H), 3.31−3.46 (m, 2H). HPLC (Chiralpak AD-H, 2-propanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 254 nm): t_{major} = 23.4 min, t_{minor} = 37.3 min.

*(S)-4-Nitro-1-(4-nitrophenyl)-3-phenylbutan-1-one (**13d**).* Amorphous solid, 51 mg, 81% yield. $[\alpha]^{20}_D$ = −27.3 (c = 1.0 M, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.26−8.29 (d, J = 8.7 Hz, 2H), 8.04−8.07 (d, J = 8.4 Hz, 2H), 7.27−7.36 (m, 5H), 4.78−4.85 (dd, J = 7.2, 6.9 Hz, 1H), 4.67−4.74 (dd, J = 7.2, 7.2 Hz, 1H), 4.18−4.27 (m, 1H), 3.51−5.53 (m, 2H). ^{13}C NMR (75 Hz, $CDCl_3$): δ = 195.5, 150.5, 140.7, 138.6, 129.2, 129.1, 128.1, 127.4, 124.0, 79.4, 42.1, 39.2. HPLC (Chiralpak AD-H, 2-propanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm): t_{major} = 43.1 min, t_{minor} (not found). HRMS: calcd for $C_{16}H_{14}N_2O_5$ $[M + Na]^+$ 337.0800, found 337.0798.

*(S)-4-Nitro-3-phenyl-1-(4-(trifluoromethyl)phenyl)butan-1-one (**13e**).* Amorphous solid, 58.7 mg, 87% yield. $[\alpha]^{20}_D$ = −24.8 (c = 1.0 M, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.99−8.02 (d, J = 8.1 Hz, 2H), 7.70−7.73 (d, J = 8.1 Hz, 2H), 7.26−7.43 (m, 5H), 4.78−4.85 (dd, J = 6.9, 7.2 Hz, 1H), 4.67−4.73 (dd, J = 7.5, 7.2 Hz, 1H), 4.18−4.27 (m, 1H), 3.43−3.56 (m, 2H). ^{13}C NMR (75 Hz, $CDCl_3$): δ = 196.0, 139.1, 138.8, 135.0, 134.6, 129.2, 128.4, 128.0, 127.4, 125.8, 79.4, 41.8, 39.2. HPLC (Chiralpak AD-H, 2-propanol/hexane =15/85, flow rate 1.0 mL/min, λ = 254 nm): t_{major} = 14.8 min, t_{minor} = 18.4 min. HRMS: calcd for $C_{17}H_{14}F_3NO_3$[M + Na]$^+$ 360.0823, found 360.0828.

*(S)-1-(4-Bromophenyl)-4-nitro-3-phenylbutan-1-one (**13f**).* Amorphous solid, 55.7 mg, 80% yield. $[\alpha]^{20}_D$ = −32.6 (c = 1.0 M, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.75−7.78 (d, J = 8.4 Hz, 2H), 7.57−7.60 (d, J = 8.7 Hz, 2H), 7.26−7.36 (m, 5H), 4.78−4.84 (dd, J = 6.9, 6.9 Hz, 1H), 4.65−4.71 (dd, J = 7.8, 7.8 Hz, 1H), 4.16−4.25 (m, 1H), 3.34−3.49 (m, 2H). ^{13}C NMR (75 Hz, $CDCl_3$): δ = 195.9, 138.9, 132.1, 129.5, 129.1, 128.8, 128.0, 127.4, 79.5, 41.5, 39.2. HPLC (Chiralpak AD-H, 2-propanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 254 nm): t_{major} = 18.6 min, t_{minor} = 24.4 min.

*(S)-4-Nitro-1-phenyl-3-p-tolylbutan-1-one (**13g**).*[10c] 42.5 mg, 75% yield. $[\alpha]^{20}_D$ = −22.0 (c = 0.8 M, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.89−7.92 (d, J = 7.2 Hz, 2H), 7.53−7.58 (t, J = 8.1 Hz, 1H), 7.41−7.46 (t, J = 7.8 Hz 2H), 7.10−7.18 (dd, J = 8.4, 8.4 Hz, 4H), 4.76−4.83 (dd, J = 6.6, 6.6 Hz, 1H), 4.16−4.68 (dd, J = 7.8, 8.1 Hz, 1H), 4.13−4.22 (m, 1H), 3.34−3.50 (m, 2H), 2.30 (s, 1H). HPLC (Chiralpak AD-H, 2-propanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 254 nm): t_{major} = 11.0 min, t_{minor} (not found).

*(S)-3-(4-Methoxyphenyl)-4-nitro-1-phenylbutan-1-one (**13h**).*[10d] 43.0 mg, 72% yield. $[\alpha]^{20}_D$ = −22.7 (c = 1.0 M, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.90−7.92 (d, J = 8.4 Hz, 2H), 7.54−7.59 (t, J = 6.9 Hz 1H), 7.42−7.47 (t, J = 7.2 Hz, 2H), 7.18−7.21 (d, J = 8.4 Hz, 2H), 6.83−6.86 (d, J = 8.4 Hz, 2H), 4.76−4.82 (dd, J = 6.9, 6.3 Hz, 1H), 4.60−4.67 (dd, J = 8.1, 8.1 Hz, 1H), 4.08−4.22 (m, 1H), 3.76 (s, 3H), 3.34−3.52 (m, 2H). HPLC (Chiralpak AD-H, 2-propanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 254 nm): t_{major} = 16.7 min, t_{minor} (not found).

*(S)-3-(4-Chlorophenyl)-4-nitro-1-phenylbutan-1-one (**13i**).*[10d] 43.0 mg, 71% yield. $[\alpha]^{20}_D$ = −24.7 (c = 0.9 M, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.89−7.92 (d, J = 8.4 Hz, 2H), 7.56−7.61 (t, J = 7.2 Hz, 1H), 7.44−7.49 (t, J = 7.2 Hz, 2H), 7.21−7.32 (m, 4H), 4.78−4.85 (dd, J = 6.6, 6.6 Hz, 1H), 4.63−4.69 (dd, J = 8.1, 8.1 Hz, 1H), 4.17−4.26 (m, 1H), 3.35−3.50 (m, 2H). HPLC (Chiralpak AD-H, 2-propanol/hexane =10/90, flow rate 1.0 mL/min, λ = 254 nm): t_{major} = 18.5 min, t_{minor} (not found).

*(S)-3-(4-Bromophenyl)-4-nitro-1-phenylbutan-1-one (**13j**).*[10d] 53.6 mg, 77% yield. $[\alpha]^{20}_D$ = −25.3 (c = 1.0 M, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.82−7.84 (d, J = 7.2 Hz, 1H), 7.34−7.53 (m, 5H), 7.08−7.11 (d, J = 8.4 Hz, 2H), 4.70−4.77 (dd, J = 6.3, 6.3 Hz, 1H), 4.55−4.62 (dd, J = 8.1, 8.4 Hz, 1H), 4.08−4.17 (m, 1H), 3,28−3.42 (m, 2H). HPLC (Chiralpak AD-H, 2-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ = 254 nm): t_{major} = 19.1 min, t_{minor} = 28.4 min.

*(S)-3-(2-Bromophenyl)-4-nitro-1-phenylbutan-1-one (**13k**).*[10d] 49.4 mg, 71% yield. $[\alpha]^{20}_D$ = −33.3 (c = 1.0 M, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.93−7.96 (d, J = 7.2 Hz, 2H), 7.26−7.62 (m, 4H), 7.11−7.29 (m, 3H), 4.85−4.87 (d, J = 6.6 Hz, 2H), 4.65−4.74 (m, 1H), 3.47−3.62 (m, 2H). HPLC (Chiralpak AD-H, 2-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ = 254 nm): t_{major} = 15.8 min, t_{minor} = 19.1 min.

*(S)-4-Nitro-1-phenyl-3-(4-(trifluoromethyl)phenyl)butan-1-one (**13l**).* Amorphous solid, 54.0 mg, 80% yield. $[\alpha]^{20}_D$ = −22.2 (c = 0.3 M, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.83−7.85 (d, J = 7.2 Hz, 2H), 7.47−7.51 (t, J = 7.2 Hz, 3H), 7.34−7.41 (m, 4H), 4.75−4.82 (dd, J = 6.3, 6.3 Hz, 1H), 4.60−4.67 (dd, J = 8.4, 8.1 Hz, 1H), 4.19−4.29 (m, 1H), 3.32−3.47 (m, 2H). ^{13}C NMR (75 Hz, $CDCl_3$): δ = 196.3, 143.2, 136.2, 133.8, 130.4, 130.0, 128.8, 128.0, 126.1, 125.7, 79.1, 41.2, 39.01. HPLC (Chiralpak AD-H, 2-propanol/hexane =10/90, flow rate 0.9 mL/min, λ = 254 nm): t_{major} = 14.9 min, t_{minor} = 23.3 min. HRMS: calcd for $C_{17}H_{14}F_3NO_3$ $[M + Na]^+$ 360.0823, found 360.0828.

*(S)-4-Nitro-1-phenyl-3-(3-(trifluoromethyl)phenyl)butan-1-one (**13m**).* Amorphous solid, 53.3 mg, 79% yield. $[\alpha]^{20}_D$ = −27.8 (c = 1.0 M, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.90−7.93 (d, J = 8.1 Hz, 2H), 7.43−7.61 (m, 7H), 4.83−4.89 (dd, J = 6.3, 6.3 Hz, 1H), 4.47−4.67 (dd, J = 8.1, 8.1 Hz, 1H), 4.26−4.36 (m, 1H), 3.46−3.48 (d, J = 6.9 Hz, 2H). ^{13}C NMR (75 Hz, $CDCl_3$): δ = 196.3, 140.3, 136.2, 133.8, 131.6, 131.2, 129.6, 128.8, 128.0, 125.7, 124.9, 124.3, 79.1, 41.3, 39.0. HPLC (Chiralpak AD-H, 2-propanol/hexane = 10/90, flow rate 0.9 mL/min, λ = 254 nm): t_{major} = 12.2 min, t_{minor} = 13.8 min. HRMS: calcd for $C_{17}H_{14}F_3NO_3$ $[M + Na]^+$ 360.0823, found 360.0828.

*(S)-4-Nitro-1-phenyl-3-(2-(trifluoromethyl)phenyl)butan-1-one (**13n**).* Colorless liquid, 56.0 mg, 83% yield. $[\alpha]^{20}_D$ = −26.5 (c = 0.8 M, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.90−7.93 (d, J = 6.9 Hz,

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2H), 7.69−7.72 (d, J = 7.8 Hz, 1H), 7.36−7.60 (m, 6H), 4.77−4.91 (m, 2H), 4.63−4.69 (dd, J = 6.6, 6.9 Hz, 1H), 3.40−3.58 (m, 2H). ^{13}C NMR (75 Hz, $CDCl_3$): δ = 196.4, 138.0, 136.2, 133.7, 132.5, 128.8, 128.0, 127.9, 127.6, 126.9, 126.0, 122.4, 78.4, 41.6, 34.7. HPLC (Chiralpak AD-H, 2-propanol/hexane = 10/90, flow rate 0.9 mL/min, λ = 254 nm): t_{major} = 12.1 min, t_{minor} = 14.6 min. HRMS: calcd for $C_{17}H_{14}F_3NO_3$ $[M + Na]^+$ 360.0823, found 360.0828.

*(R)-3-(Furan-2-yl)-4-nitro-1-phenylbutan-1-one (**13o**).*[10d] 36.8 mg, 71% yield. $[\alpha]^{20}_D$ = −20.2 (c = 1.0 M, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.94−7.96 (d, J = 8.4 Hz, 2H), 7.56−7.93 (m, 1H), 7.45−7.50 (m, 2H), 7.33−7.34 (m, 1H), 6.28−6.230 (d, J = 4.8 Hz, 1H), 6.18−6.19 (d, J = 5.1 Hz, 1H), 4.71−4.84 (m, 2H), 4.29−4.38 (m, 1H), 3.27−3.57 (m, 2H). HPLC (Chiralpak AD-H, 2-propanol/hexane =10/90, flow rate 1.0 mL/min, λ = 254 nm): t_{major} = 14.4 min, t_{minor} = 17.5 min.

General Procedure for 1a-Catalyzed Asymmetric Michael Addition of Acetone to Nitroolefins. The nitroolefin (0.2 mmol), $PhCO_2H$ (0.03 mmol), and catalyst **1a** (0.03 mmol) were placed in a 1.5 mL vial equipped with a Teflon-coated stir bar. Acetone (2 mmol) was added followed by $CHCl_3$ (0.2 mL) under air. The vial was capped with a white polyethylene stopper and the resulting mixture was stirred at room temperature until the reaction was complete (monitored by TLC). Then the mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate as the eluents) to afford the desired product. The enantiomeric excess of the pure product was determined by chiral HPLC analysis.

*(S)-5-Nitro-4-phenylpentan-2-one (**14a**).*[7] 38.1 mg, 92% yield. $[\alpha]^{20}_D$ = +3.6 (c = 0.8 M, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.20−7.35 (m, 5H), 4.66−4.72 (dd, J = 6.9, 6.9 Hz, 1H), 4.56−4.62 (dd, J = 7.8, 7.8 Hz, 1H), 3.95−4.05 (m, 1H), 2.90−2.92 (d, J = 7.2 Hz, 2H), 2.11 (s, 3H). HPLC (Chiralpak AD-H, 2-propanol/hexane = 10/90, flow rate 0.9 mL/min, λ = 254 nm): t_{major} = 12.8 min, t_{minor} = 13.8 min.

*(S)-5-Nitro-4-p-tolylpentan-2-one (**14b**).*[7] 39.8 mg, 90% yield. $[\alpha]^{20}_D$ = −1.7 (c = 1.0 M, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.08−7.14 (dd, J = 8.1, 8.1 Hz, 4H), 4.63−4.69 (dd, J = 6.9 Hz, 1H), 4.53−4.59 (dd, J = 7.8 Hz, 1H), 3.91−4.00 (m, 1H), 2.87−2.90 (d, J = 6.6 Hz, 2H), 2.31 (s, 3H), 2.11 (s, 3H). HPLC (Chiralpak AD-H, 2-propanol/hexane = 10/90, flow rate 0.9 mL/min, λ = 254 nm): t_{major} = 11.5 min, t_{minor} = 12.8 min.

*(S)-4-(4-Methoxyphenyl)-5-nitropentan-2-one (**14c**).*[7] 43.2 mg, 91% yield. $[\alpha]^{20}_D$ = −1.3 (c = 1.1 M, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.11−7.14 (d, J = 8.7 Hz, 2H), 6.83−6.86 (d, J = 8.7 Hz, 2H), 4.62−4.69 (dd, J = 6.9, 6.9 Hz, 1H), 4.51−4.58 (dd, J = 7.8, 7.8 Hz, 1H), 3.90−4.01 (m, 1H), 3.77 (s, 3H), 2.86−2.89 (d, J = 7.2 Hz, 2H), 2.10 (s, 3H). HPLC (Chiralpak AD-H, 2-propanol/hexane = 10/90, flow rate 0.9 mL/min, λ = 254 nm): t_{major} = 17.4 min, t_{minor} = 19.3 min.

*(S)-4-(4-Bromophenyl)-5-nitropentan-2-one (**14d**).*[9f] 53.8 mg, 94% yield. $[\alpha]^{20}_D$ = +2.3 (c = 1.0 M, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.44−7.46 (d, J = 8.1 Hz, 2H), 7.09−7.12 (d, J = 8.4 Hz, 2H), 4.64−4.71 (dd, J = 6.6, 6.6 Hz, 1H), 4.53−4.60 (dd, J = 7.8, 8.1 Hz, 1H), 2.87−2.90 (d, J = 6.9 Hz, 2H), 2.12 (s, 3H). HPLC (Chiralpak AD-H, 2-propanol/hexane = 10/90, flow rate 0.9 mL/min, λ = 254 nm): t_{major} = 16.4 min, t_{minor} = 18.9 min.

*(S)-4-(4-Chlorophenyl)-5-nitropentan-2-one (**14e**).*[9f] 46.1 mg, 93% yield. $[\alpha]^{20}_D$ = +2.5 (c = 1.0 M, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.29−7.31 (d, J = 8.4 Hz, 2H), 7.15−7.17 (d, J = 8.4 Hz, 2H), 4.65−4.71 (dd, J = 6.6, 6.6 Hz, 1H), 4.53−4.60 (dd, J = 8.1, 7.8 Hz, 1H), 2.88−2.90 (d, J = 7.2 Hz, 2H), 2.12 (s, 3H). HPLC (Chiralpak AD-H, 2-propanol/hexane = 10/90, flow rate 0.9 mL/min, λ = 254 nm): t_{major} = 15.0 min, t_{minor} = 17.1 min.

*(S)-4-(2-Bromophenyl)-5-nitropentan-2-one (**14f**).*[9f] 52.6 mg, 92% yield. $[\alpha]^{20}_D$ = +16.4 (c = 1.0 M, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.58−7.61 (d, J = 7.8 Hz, 1H), 7.12−7.31 (m, 3H), 4.69−4.80 (d, J = 6.6 Hz, 2H), 4.42−4.51 (m, 1H), 2.91−3.08 (m, 2H), 2.16 (s, 3H). HPLC (Chiralpak AS-H, 2-propanol/hexane = 15/85, flow rate 0.9 mL/min, λ = 254 nm): t_{major} = 16.3 min, t_{minor} = 20.1 min.

*(S)-5-Nitro-4-(3-(trifluoromethyl)phenyl)pentan-2-one (**14g**).*[9g] 50.1 mg, 91% yield. $[\alpha]^{20}_D$ = +2.0 (c = 1.0 M, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.45−7.56 (m, 4H), 4.70−4.77 (dd, J = 6.6, 6.6 Hz, 1H), 4.59−4.66 (dd, J = 8.1, 8.1 Hz, 1H), 4.05−4.14 (m, 1H), 2.94−2.96 (d, J = 6.9 Hz, 2H), 2.14 (s, 3H). ^{13}C NMR (75 Hz, $CDCl_3$): δ = 204.7, 140.1, 131.6, 131.1, 129.6, 125.6, 124.8, 124.1, 78.9, 45.8, 38.7, 30.3. HPLC (Chiralpak AS-H, 2-propanol/hexane =15/85, flow rate 0.9 mL/min, λ = 210 nm): t_{major} = 14.8 min, t_{minor} = 26.9 min.

*(R)-4-(Furan-2-yl)-5-nitropentan-2-one (**14h**).*[9f] 37.9 mg, 96% yield. $[\alpha]^{20}_D$ = +6.2 (c = 1.0 M, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.34 (s, 1H), 6.29−6.30 (d, J = 3.3 Hz, 1H), 6.14−6.15 (d, J = 3.3 Hz, 1H), 4.62−4.73 (m, 2H), 4.06−4.14 (m, 1H), 2.85−3.02 (m, 2H), 2.17 (s, 3H). HPLC (Chiralpak AD-H, 2-propanol/hexane = 10/90, flow rate 0.9 mL/min, λ = 254 nm): t_{major} = 12.4 min, t_{minor} = 14.2 min.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H NMR spectra of the compounds **1a−f**, **13a−o**, **14a−h** and ^{13}C NMR spectra of the compounds **1a−f**, **13d−f**, and **13l−n**. This material is available free of charge via the Internet at http://pubs.acs.org/.

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Notes

The authors declare no competing financial interest.

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