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4-Aminothioureaprolinal Dithioacetal as a Catalyst for Highly Enantioselective Michael Additions of Ketones and Aldehydes to Nitroolefins

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4-Aminothioureaprolinal dithioacetal **4a** is a highly efficient catalyst for the asymmetric Michael addition of ketones and aldehydes to nitroolefins requiring only 3 mol-% catalyst loading. The reactions proceeded smoothly and gave *syn* selective adducts with excellent yields (up to 98 % yield), diastereoselectivity (up to >99:1 *dr*), and enantioselectivity (up to 99 % *ee*) under solvent free conditions at room temperature. This extremely simple and practical procedure increases the attractiveness of this reaction.

Introduction

The Michael addition reaction is one of the most important C–C bond-forming reactions in organic synthesis.[1] The development of organocatalysts for asymmetric Michael reactions of carbonyl compounds with nitroalkenes is an attractive area of research.[2] Since the pioneering work of List,[3a] considerable effort has been focused on the development of organocatalytic asymmetric versions of the reaction and great advances have been made recently.[3–8] Consequently, a variety of asymmetric organocatalysts have been documented for the Michael addition of ketones or aldehydes to nitroolefins. Pyrrolidine-based organocatalysts bearing bulky groups,[4] H-bonding functionalities,[5] salt moieties,[6] or a phosphane oxide[7] functionality at the 2-position of the pyrrolidine ring have been identified as good catalysts. Thus, chiral pyrrolidine is generally considered as a "privileged" framework for asymmetric catalysis. Among the reported organocatalysts, some have shown very high efficiency, requiring only 0.5–3 mol-% catalyst loading when aldehydes were used as substrates.[3i,4a,4e,6a] In cases of less reactive donors such as ketones high catalyst loadings (5–30 mol-%) are required to effect the desired transformation in reasonable time frames and with good enantioselectivity; this is a major drawback of chiral organocatalysts. Other drawbacks include the requirements of low temperature and the use of organic solvents, which are incompatible with green chemistry. It is noteworthy that good results have been achieved in water[3j,4a–4d,5a,5b,6b–6d,8d] or under solvent-free conditions,[3g,5e,6i–6m,7] although such successes are very limited. Despite such advances, it remains a challenge to identify highly efficient organocatalysts that proceed smoothly under moderate reaction conditions and in the absence of organic solvents.

Interested in developing an efficient chiral organocatalytic system to achieve high yielding and enantioselective Michael additions, we previously developed pyrrolidine-based silyl ether **1** and homodiphenylproline methyl ether **2**[4i,4j] in which enantioselectivity was controlled primarily by steric interactions. High levels of both enantioselectivity (73–98 % *ee*) and diastereoselectivity (99:1 *dr*) were achieved with catalyst loadings of 20 mol-% for **1** and 5 mol-% for **2** in hexane (Figure 1). Catalyst **2** has shown better catalytic efficiency than catalyst **1** but its complicated synthesis has encumbered its further development and use. Subsequently, on the basis of the results obtained with **1**, we introduced an H-bond donor group into the 4-position of the pyrrolidine ring. Tuning of the H-bond donating ability localized at the 4-position by changing the electronic and steric environment through pyrrolidine modification led to the discovery of **3a** and **3b**.[8c] Catalyst **3b** was found to be superior (reaction yields >99 %) to **3a** (76 % yield) in terms of its catalytic reactivity, but similar to **3a** in terms of asymmetric

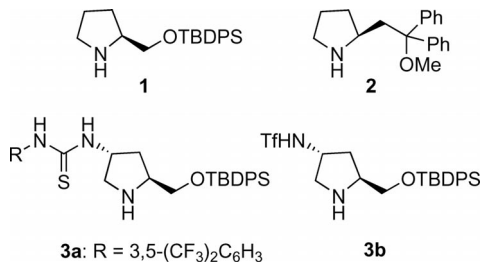

Figure 1. Previously reported pyrrolidine-based organocatalysts by our group.

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induction. Michael additions of ketones to nitroolefins catalyzed by **3b** (5 mol-%) proceed with excellent yields (>99%) and stereoselectivities (99:1 *dr*, 99% *ee*). However, this approach is limited by the requirement of high catalyst loadings (5 mol-%), low temperatures, and the need for organic solvent.

On the basis of our experience with **3a** and **3b**, we envisioned that both the catalytic efficiency and the stereoselectivity could be further enhanced by adjusting the size of the group at the stereogenic pyrrolidine 2-position (i.e., the -CH_2OTBDPS group). Accordingly, we designed and synthesized catalysts **4a** and **4b** (Figure 2). The dithioacetal prolinals have shown better catalytic efficiency than catalyst **1**, and thus the size and/or the shape of bis(4-methylphenylthio)methyl was deemed more suitable than -OTBDPS in terms of retaining activity and exerting stereocontrol during Michael addition.[4h] Therefore, we believed that catalysts **4a** and **4b** with H-bond donors at the 4-position of the dithioacetalprolinal pyrrolidine ring would possess high catalytic efficiency; this would translate to lower catalyst concentrations necessary for highly efficient and stereocontrolled reactions. Herein, we demonstrate the effectiveness of catalysts **4a** and **4b** in catalyzing Michael addition reactions of ketones and aldehydes to nitroolefins.

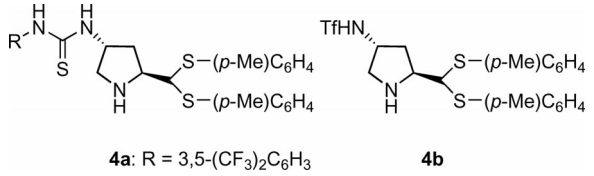
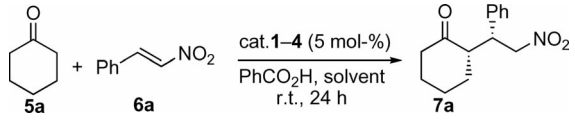


Figure 2. Designed and synthesized novel bifunctional organocatalysts.

Results and Discussion

We first examined novel catalysts **4a** and **4b** in a model reaction, the conjugate addition of cyclohexanone (**5a**) and β-nitrostyrene (**6a**), which was conducted in dichloromethane at room temperature. We also compared the results of these reactions with those of reactions using catalysts **1**–**3**, previously reported by our group. As shown in Table 1, these catalysts showed differing activities and gave the corresponding products **7a** with a range of diastereoselectivity and enantioselectivity (Table 1, Entries 1–6). Catalysts **1** and **2** displayed lower catalytic efficiency, attributable most likely to the absence of any H-bond donating group at the 4-position of pyrrolidine. The use of catalysts **2** and **4a** afforded the Michael product with excellent stereoselectivities (Table 1, Entries 2 and 5), although the use of catalyst **2** gave a slightly lower yield. In comparison to **4a**, both catalysts **3a** and **3b** gave almost the same yields but with slightly lower enantioselectivity (Table 1, Entries 3–5). This observation may be attributable to the less effective steric interaction of the -OTBDPS group with one face of the transient enamine than is possible with the bulkier bis(4-methylphenylthio)methyl moiety (Figure 3). The impaired H-bond donating ability of the sulfonamide group in **4b** relative to that of the dual H-bond donating thiourea in **4a** may be responsible for both the lower yield and the lower enantioselectivity of reactions using **4b** (Table 1, Entries 5 and 6). Predicated on these data, the thiourea appears to be far superior to the sulfonamide in terms of reactivity and ability to exert stereocontrol in this catalytic system. This is contrasted with our previous reports looking at the use of catalysts **3a** and **3b** in hexane.[8c] Consequently, these data all indicated that the catalytic performance of **4a** was superior to that of catalysts **1**–**3** and **4b**.

Table 1. The effect of catalysts and conditions on the asymmetric Michael addition reactions of cyclohexanone and nitrostyrene.[a]



Entry	Catalyst	Solvent	Yield[b]	*dr*[c]	*ee*[d]
1	**1**	DCM	16	98:2	87
2	**2**	DCM	70	97:2	95
3	**3a**	DCM	92	94:6	90
4	**3b**	DCM	94	97:3	88
5	**4a**	DCM	94	98:2	97
6	**4b**	DCM	75	97:3	90
7	**4a**	hexane	96	99:1	95
8	**4a**	$CHCl_3$	82	>99:1	96
9	**4a**	DCE	91	>99:1	97
10	**4a**	toluene	92	>99:1	96
11	**4a**	DMF	trace	–	–
12	**4a**	H_2O	92	99:1	97
13[e]	**4a**	neat	96	>99:1	98
14	**4a**	neat	97	99:1	98
15[f]	**4a**	neat	95	99:1	98

[a] Unless specified, all reactions were carried out with cyclohexanone (1.25 mmol, 5 equiv.) and nitrostyrene (0.25 mmol, 1 equiv.) in the presence of the catalyst (0.0125 mmol, 5 mol-%) and $PhCO_2H$ (5 mol-%) as additive in the solvent (1 mL) at room temperature (25 °C). [b] Isolated yield. [c] Determined by ^{1}H NMR spectroscopy. [d] Determined by chiral HPLC analysis. [e] With 6 mmol of cyclohexanone. [f] With 3 mol-% of catalyst **4a** was used.

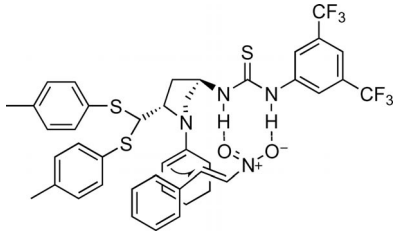


Figure 3. Proposed transition-state model of the **4a**-catalyzed Michael addition reaction.

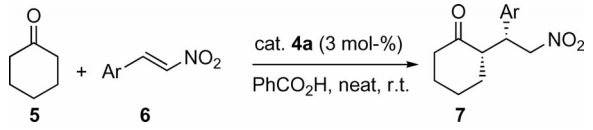
In order to refine and optimize the high reactivity and enantioselectivity of catalyst **4a**, various reaction conditions were examined. A series of solvents were screened in the presence of benzoic acid (5 mol-%) and catalyst **4a** (5 mol-%) at room temperature (Table 1, Entries 4 and 7–13). In nonpolar or less polar solvents, desired Michael product **7a** was obtained in good yield and with excellent stereocontrol (Table 1, Entries 4 and 7–10). However, the reaction pro-

ceeded sluggishly in polar solvents such as DMF, and only trace amounts of product were observed (Table 1, Entry 11). To our delight, excellent yields and stereoselectivities (92% yield, 99:1 *dr*, and 97% *ee*) could be obtained when the reaction was carried out in water (Table 1, Entry 12). The best result was achieved under neat conditions (96% yield, >99:1 *dr*, 98% *ee*; Table 1, Entry 13). We then examined the influence of catalyst loading on the reaction. Remarkably, the use of only 3 mol-% catalyst with 5 mol-% benzoic acid as an additive in 5 equiv. of cyclohexanone afforded the desired product in outstanding yield with excellent diastereoselectivity and enantioselectivity (95% yield, 99:1 *dr*, 98% *ee*; Table 1, Entry 15). To the best of our knowledge reports using such a low catalyst loading for Michael additions of cyclic ketones to nitrostyrene are exceedingly rare.

With optimized conditions in hand, a variety of nitrostyrenes bearing different substitutions were investigated, and the results are summarized in Table 2. Generally, nitrostyrenes bearing both electron-withdrawing (Table 2, Entries 2–10) and electron-donating (Table 2, Entries 11–15) aryl groups and heterocyclic groups (Table 2, Entries 16 and 17) gave the desired products in good yields (84–98% yield) with excellent selectivities (up to >99:1 *dr* and up to 99% *ee*). The position of substitution for β-nitrostyrenes in some substrates had a slight influence on the yield. For example, when the brominated position of nitrostyrene was changed from *ortho* to *meta* and *para*, the yield decreased from 94 to 90 and 86%, respectively, although the enantioselectivity was not significantly influenced by the difference in substitution pattern (Table 2, Entries 6–8). The excellent enantioselectivity (93–95% *ee*) observed for reactions involving heteroaryl substrates (Table 2, Entries 16 and 17) indicated that they also are good Michael acceptors for cyclohexanone.

Other carbonyl compounds, including aldehydes and cyclic or acyclic ketones, were also examined in **4a**-catalyzed Michael additions with **6a**. The reactions gave the corresponding products (Table 3, Entries 1–7) in moderate to

Table 2. Asymmetric Michael addition reactions of cyclohexanone and nitroolefins catalyzed by **4a**.[a]

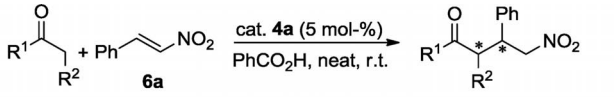


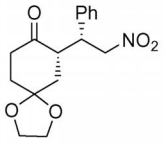
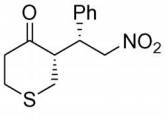
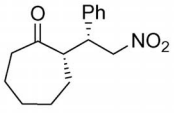
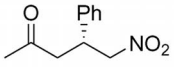
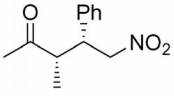
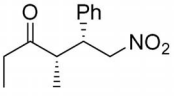
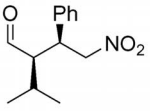
5 **6** **7**

Entry	Ar	Time [h]	Yield[b] [%]	*dr*[c] *syn*/*anti*	*ee*[d]
1	Ph	24	95	99:1	98
2	2-FPh	24	97	99:1	99
3	4-FPh	48	92	>99:1	98
4	2-ClPh	27	92	99:1	97
5	4-ClPh	48	94	99:1	98
6	2-BrPh	24	94	99:1	98
7	3-BrPh	48	90	98:2	98
8	4-BrPh	72	86	99:1	98
9	4-NO_2Ph	48	89	98:2	97
10	2,4-Cl_2Ph	72	86	99:1	98
11	4-MePh	24	92	99:1	99
12	2-MeOPh	21	97	98:2	91
13	4-MeOPh	48	98	98:2	96
14	1-naphthyl	60	86	99:1	97
15	2-naphthyl	60	90	98:2	95
16	2-furyl	22	84	98:2	93
17	2-thienyl	46	85	97:3	95

[a] All reactions were carried out with cyclohexanone (1.25 mmol, 5 equiv.) and nitrostyrene (0.25 mmol, 1 equiv.) in the presence of the catalyst (0.0075 mmol, 3 mol-%) and $PhCO_2H$ (5 mol-%) as additive in the absence of solvent at room temperature (25 °C). [b] Isolated yield. [c] Determined by ^1H NMR spectroscopy. [d] Determined by chiral HPLC analysis.

Table 3. Asymmetric Michael additions of ketones and nitrostyrene catalyzed by **4a**.[a]



Entry	Product	Time [h]	Yield[b] [%]	*dr*[c] *syn*/*anti*	*ee*[d]
1[e]		72	77	96:4	90
2[e]		72	87	99:1	98
3[f]		177	72	96:4	80
4[g]		12	97	–	55
5[h]		48	84	65:35	*syn*:84 *anti*:90
6[f]		153	75	>99:1	97
7[i]		66	85	98:2	83

[a] Unless otherwise specified, reactions were carried out with ketone (1.25 mmol, 5 equiv.) and nitrostyrene (0.25 mmol, 1 equiv.) in the presence of catalyst **4a** (5 mol-%) and benzoic acid (5 mol-%) as additive under neat conditions at room temperature (25 °C). [b] Isolated yield. [c] Determined by ^1H NMR spectroscopy. [d] Determined by chiral HPLC analysis. [e] With 1 mL of dichloromethane as solvent. [f] With ketone (5 mmol, 20 equiv.), catalyst **4a** (20 mol-%), and benzoic acid (10 mol-%). [g] With acetone (5 mmol, 20 equiv.) and benzoic acid (10 mol-%). [h] With ketone (5 mmol, 20 equiv.), catalyst **4a** (10 mol-%), and benzoic acid (10 mol-%). [i] With isovaleraldehyde (2.5 mmol, 10 equiv.), catalyst **4a** (10 mol-%), and benzoic acid (10 mol-%).

good yields (72–97% yield) and with moderate to excellent enantioselectivity (55–98%*ee*). The analogues of cyclohexanone, such as 1,4-cyclohexanedione monoethylene acetal and tetrahydro-4*H*-thiopyran-4-one, displayed good reactivity, and their use afforded the corresponding products in high yields and with good stereoselectivities (Table 3, Entries 1 and 2). The ring size of cyclic ketones was found to strongly impact the reaction rate. Cycloheptanone was minimally reactive although the inclusion of **4a** led to a moderate yield with good stereoselectivity of the α-substituted product (Table 3, Entry 3). Acyclic symmetric ketones, such as acetone and 3-pentanone, were also found to be effective Michael donors. Reaction of acetone with **6a** proceeded with excellent yield (97%) and moderate enantioselectivity (55%*ee*; Table 3, Entry 4). The use of 3-pentanone, one of the most challenging ketones, afforded excellent diastereoselectivity (>99:1 *dr*) and enantioselectivity (97%*ee*) despite requiring a high catalyst loading and long reaction time (Table 3, Entry 6). To the best of our knowledge, only two reports thus far have examined the analogous transformation of 3-pentanone to give *syn*[3c] or *anti*[3g] products with >80%*dr* and >95%*ee*.

When using unsymmetrical ketone substrates such as 2-butanone, the reaction took place at the more substituted site, presumably because the enamine intermediates were formed under thermodynamic control. Good enantioselectivity (*syn* 84%*ee*, *anti* 90%*ee*) and good yield (84% yield) were achieved with moderate diastereoselectivity (Table 3, Entry 5). Aldehydes were also found to be compatible with catalyst **4a** as evidenced by the reaction of isovaleraldehyde to nitrostyrene. This Michael addition proceeded smoothly, leading to the desired product in 85% yield with good stereoselectivities (98:2 *dr*, 83%*ee*; Table 3, Entry 7).

The stereochemistry of major product **7a** was determined to be (2*S*,3*R*) by comparison of its optical rotation with the value reported in the literature.[3g,6d] The absolute stereochemical result can be explained by an acyclic synclinal transition state, as proposed by Seebach and Golinski.[9] As shown in Figure 3, we propose that pyrrolidine-based thiourea **4a** serves as a bifunctional catalyst. The pyrrolidine reacts with carbonyl compounds to form an enamine, whereas the thiourea moiety activates the nitroolefin towards nucleophilic attack by establishing a dual H-bonding network. We envision that the transient enamine attacks the nitroolefin from the *Re* face to afford the *syn* product; this process is consistent with the data generated and may help to inform future applications of **4a** and related catalysts.

Conclusions

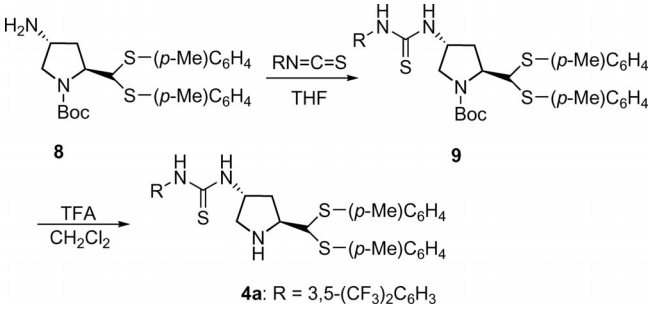
In conclusion, we have designed and synthesized novel chiral pyrrolidine-based thiourea and sulfonamide bifunctional organocatalysts and have successfully applied these catalysts to the asymmetric Michael addition reactions of ketones and aldehydes to nitroolefins. When **4a** was used as the catalyst, only 3 mol-% catalyst loading was sufficient for good yields (up to 98% yield) and excellent stereoselectivities (up to >98%*dr* and 99%*ee*) under solvent-free conditions at room temperature. This catalytic system is universal and is amenable to an exceptionally broad range of substrates including ketones (cyclic/acyclic), aldehydes, and a variety of nitroolefins.

Experimental Section

General: Reactions requiring anhydrous conditions were performed under a positive pressure of nitrogen by using oven-dried glassware (110 °C). All organic layers obtained from extractions were dried with anhydrous sodium sulfate. THF was distilled from sodium benzophenone ketyl, and dichloromethane was distilled from calcium hydride prior to use. Petroleum ether and ethyl acetate for flash column chromatography were distilled before use. All reactions were monitored by TLC with silica gel coated plates. Flash column chromatography was performed on silica gel H (10–40 μ). ^{1}H NMR and ^{13}C NMR spectra were recorded with a Bruker Avance 300 spectrometer. HPLC analysis was performed with a Waters 1525 HPLC with 2487 UV detector. ChiralPak columns were purchased from Daicel Chemical Industries, Ltd. Optical rotations were measured with a Perkin–Elmer-341 Polarimeter at λ = 589 nm by using a 1-mL cell with a 1-dm path length at room temperature.

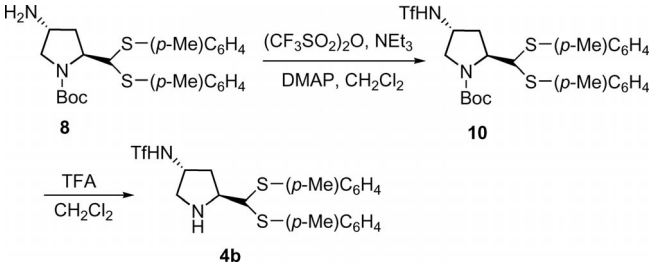
Synthesis of Catalyst 4a and 4b: The syntheses of catalysts **1**, **2**, **3a**, and **3b** have been reported previously.[4i,4j,8c] Intermediate **8**, formed en route to catalysts **4a** and **4b**, was prepared from (2*S*,4*R*)-4-hydroxyproline. For experimental details and data see the Supporting Information.

1-{(3*R*,5*S*)-5-[bis(*p*-tolylthio)methyl]pyrrolidin-3-yl}-3-[3,5-bis(trifluoromethyl)phenyl]thiourea (4a): 1-Isothiocyanato-3,5-bis(trifluoromethyl)benzene (0.623 g, 2.3 mmol) was added to a solution of **8** (0.519 g, 1.17 mmol) in THF (5 mL) at room temperature. The mixture was stirred for 3 h and then purified by silica gel column chromatography to give compound **9** (0.676 g, 81% yield). Trifluoroacetic acid (1 mL) was added to a solution of compound **9** in dichloromethane (4 mL) at 0 °C, and the mixture was stirred further for 6 h. The reaction mixture was concentrated to remove the excess amount of trifluoroacetic acid. The residue was dissolved in water, and the pH of the solution was adjusted to 8 with aqueous NH_3. The resulting aqueous solution was extracted with dichloromethane, and the combined organic layer was dried (Na_2SO_4) and concentrated. The residue was purified by flash column chromatography to give **4a** (0.469 g, 83% yield) as a yellowish foam. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.10–2.18 (m, 2 H, CH_2 pyrrolidine), 2.30–2.32 (s, 6 H, CH_3), 3.00–3.02 (m, 2 H, CH_2 pyrrolidine), 3.31–3.37



(m, 1 H, CH pyrrolidine), 3.63–3.65 (m, 1 H, CH pyrrolidine), 4.21–4.23 (m, 1 H, CH), 4.75 (br., 1 H, NH), 7.06–7.32 (m, 8 H, CH phenyl), 7.62 (s, 1 H, CH phenyl), 7.91 (s, 2 H, CH phenyl) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.0, 36.4, 51.4, 55.5, 60.0, 65.8, 117.5, 118.4, 118.5, 121.1, 123.4, 124.7, 128.3, 129.1, 129.3, 129.9, 131.9, 132.3, 132.8, 132.9, 133.4, 133.5, 138.7, 140.1, 179.8 ppm.

***N*-{(3*R*,5*S*)-5-[Bis(*p*-tolylthio)methyl]pyrrolidin-3-yl}-1,1,1-trifluoromethanesulfonamide (4b):** $(CF_3SO_2)_2O$ (0.25 mL, 1.48 mmol) was added dropwise to the mixture of compound **8** (0.519 g, 1.17 mmol), NEt_3 (0.25 mL, 1.8 mmol), and DMAP (0.05 g, 0.4 mmol) in freshly distilled DCM (20 mL) at –76 °C. After addition, the mixture was stirred for 30 min and then poured into saturated aqueous sodium hydrogen carbonate. The phases were separated, and the aqueous phase was extracted with CH_2Cl_2. The combined organic phase was washed with 1 N HCl and brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by silica gel column chromatography to give compound **10** (0.565 g, 84% yield). Trifluoroacetic acid (1.1 mL, 15 equiv.) was added to the solution of product **10** (0.565 g) in dichloromethane at 0 °C, and the mixture was stirred at room temperature overnight. After workup, the residue was purified by silica gel column chromatography to afford catalyst **4b** (0.427 g, 94% yield) as a yellowish foam. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.82–2.30 (m, 2 H, CH_2 pyrrolidine), 2.32–2.33 (s, 6 H, CH_3), 2.85–2.89 (d, J = 12 Hz, 1 H, CH pyrrolidine), 3.20–3.25 (m, 1 H, CH pyrrolidine), 3.38–3.45 (m, 1 H, CH), 4.19–4.24 (m, 2 H, CH_2 pyrrolidine), 5.75 (br., 1 H, NH), 7.09–7.14 (m, 4 H, CH phenyl), 7.25–7.34 (m, 4 H, CH phenyl) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.1, 37.5, 52.6, 55.2, 59.3, 65.3, 117.7, 122.0, 129.2, 129.3, 130.0, 130.0, 133.3, 133.5, 138.7, 138.7 ppm.



Representative Procedure for the Michael Addition of Ketones to Nitroolefins: Catalyst **4a** (4.6 mg, 0.0075 mmol), benzoic acid (1.5 mg, 0.0125 mmol), and cyclohexanone (0.13 mL, 1.25 mmol) were mixed at room temperature (25 °C). After stirring for 10 min, nitroolefin **6a** (37.3 mg, 0.25 mmol) was added. The resulting mixture was gently stirred at room temperature for the given time and then directly diluted with ethyl acetate (20 mL) and washed with saturated $NaHCO_3$ and NaCl solutions. The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (ethyl acetate/petroleum ether) to afford Michael adduct product **7a** (58 mg, 95% yield) as a white solid. The relative configurations of the products (*syn* or *anti*) were determined by comparison of the ^{1}H NMR spectroscopic data with those reported in the literature. The absolute configurations of each product were determined either by comparison of optical rotation values with those reported in the literature or by comparison of HPLC retention times. Spectral data for compounds are in agreement with literature reports.

(*S*)-2-[(*R*)-2-Nitro-1-phenylethyl]cyclohexanone (7a): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.21–1.58 (m, 1 H, CH_2 hexanone), 1.62–1.75 (m, 4 H, CH_2 hexanone), 2.04–2.10 (m, 1 H, CH_2 hexanone), 2.38–2.47 (m, 2 H, CH_2, hexanone), 2.68 (m, 1 H, CH hexanone), 3.72–3.80 (dt, J = 9.9, 4.5 Hz, 1 H, CH), 4.53–4.66 (dd, J = 12.3, 10 Hz, 1 H, CH_2), 4.91–4.97 (dd, J = 12.4, 4.5 Hz, 1 H, CH_2), 7.15–7.17 (d, J = 6.9 Hz, 2 H, CH phenyl), 7.23–7.34 (m, 3 H, CH phenyl) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.0, 28.5, 33.1, 42.7, 43.9, 52.5, 78.8, 127.7, 128.1, 128.9, 137.7, 211.9 ppm. HPLC (Chiralpak AS-H, 254 nm, 0.5 mL/min, hexane/*i*PrOH = 80:20): t_R = 22.8 (major), 17.2 (minor) min; 98% *ee*.

Supporting Information (see footnote on the first page of this article): Full experimental procedures and catalyst synthesis.

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