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ARTICLE TYPE

Organocatalytic Asymmetric Michael Addition of Aldehydes and Ketones to Nitroalkenes Catalyzed by Adamantoyl *L*-Prolinamide

Yongchao Wang,[‡] Dong Li,[‡] Jun Lin[*] and Kun Wei[*]

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A series of Adamantoyl *L*-prolinamides have been synthesized. These compounds have been found to be highly efficient organocatalysts for the Michael addition of aldehydes and ketones to nitroalkenes. Under the optimized reaction conditions, the corresponding Michael adducts were obtained in good yields (up to 95%), excellent enantioselectivities (up to 99% *ee*) and moderate diastereoselectivities.

Introduction

The organocatalytic asymmetric Michael addition of ketones or aldehydes to nitroalkenes, as carbon-carbon bond-forming reactions in organic synthesis, is one of the most powerful and effective methods for preparation of chiral γ-nitro carbonyl compounds. The nitro group can be easily transformed into various useful functional groups, such as amines, nitrile oxides, ketones, and carboxylic acids, etc.[1,2] These Michael adducts were used as important starting materials in the enantioselective synthesis of chiral biologically active compounds and natural products, such as alkaloids (-)-Rolipram,[3] (+)-cryptopleurine,[4] (+)-ipalbidine,[5] (-)-pancracine,[6] and (-)-botryodiplodin.[7]

The Michael addition can be classified into covalent (enamine,[8] iminium,[9] or dienamine activation catalysis[10]) or noncovalent (hydrogen-bonding and Brønsted acid,[11] Brønsted base and bifunctional activation catalysis,[12] or phase-transfer catalysis[13]) depending on characteristics of the chemical structure of the catalyst and the substrate-catalyst interaction. As one of the most widely used modern organocatalysis based on covalent character, proline and proline derivatives, such as diarylprolinol silyl ethers, prolinamides, and pyrrolidines, play an important role in asymmetric catalysis.[14] Among a variety of different catalysts, prolinamide derivatives have been demonstrated as an excellent reagent in asymmetric enamine organocatalysis.[15] Although these organocatalysts give good results in the process of asymmetric Michael addition reactions, discovery of environment-friendly nonmetal-catalyzed asymmetric organocatalyst in Michael addition reaction is still needed. To the best of our knowledge, except for several adamantanamine-derived catalysts,[16] there is no report to date of adamantoyl *L*-prolinamides as organocatalyst used in asymmetric Michael addition reactions. Thus, adamantanamine-derived catalysts 2–11 (Figure 1) were designed and tested. It was demonstrated that compound 5 (3,5-dimethyl-1-adamantanamine-prolinamide) had improved effect in catalyzing the asymmetric Michael addition of aldehydes and ketones to nitroalkenes, and the preliminary experiment results were reported here.

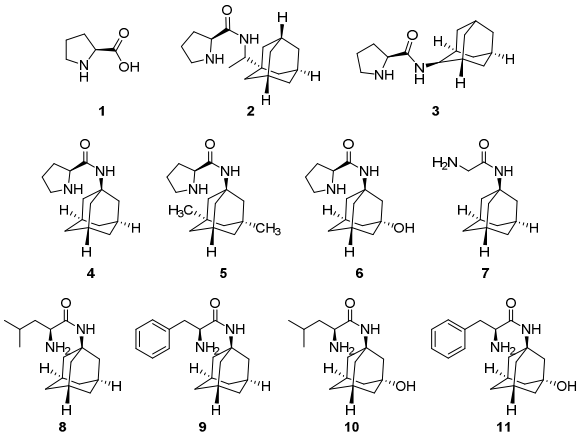
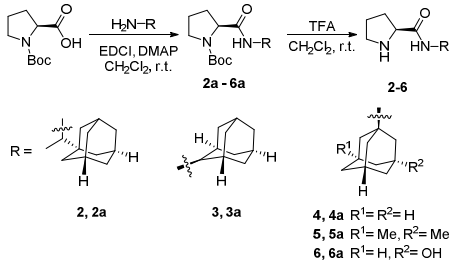


Figure 1. *L*-proline adamantoyl *L*-prolinamide catalysts.

Results and discussion

N-Boc-*L*-proline, rimantadine, 2-aminoadamantane, 1-aminoadamantane, 1-amino-3,5-dimethyl-adamantane, 3-aminoadamantan-1-ol, *N*-Boc-glycine, *N*-Boc-*L*-leucine, *N*-Boc-*L*-phenylalanine are commercially available. With these compounds as starting materials, ten amides (**2-11**) were easily prepared in two steps in 84–91% overall yield (Scheme 1 and Scheme 2, for the general procedure see experimental section).



Scheme 1. Synthetic routes to adamantoyl *L*-prolinamides **2-6**.

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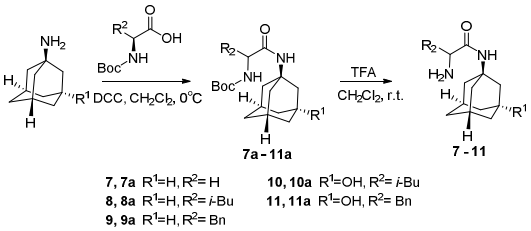
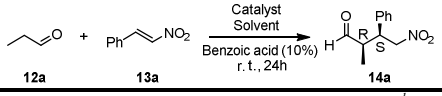


Scheme 2. Synthetic routes to catalysts **7-11**.

Initially, the model reaction of propanal (**12a**) with nitrostyrene (**13a**) was carried out in the presence of 10 mol % of catalyst and 10 mol % of benzoic acid as an additive in toluene under room temperature (Table 1). As shown in Table 1, catalysts **1**-**11** exhibited significantly different catalytic activity and enantioselectivity toward the process. *L*-proline (**1**) could catalyze this reaction, but rather poor yield and stereoselectivity were observed (Table1, entry 1). Although prolinamide **2** could efficiently promote the process with high yields (90%), poor enantioselectivity (24% *ee*, entry 2) was obtained. Among the organocatalysts surveyed, prolinamides **3** and **4** showed good catalytic activity with moderate to good enantioselectivity (entries 3 and 4). To our delight, when prolinamide **5** was used, the best result was observed with an excellent yield (92%) and enantioselectivity (93% *ee*, entry 5). In addition, prolinamide **6** was also evaluated (entry 6). Although excellent enantioselectivity (90% *ee*) was obtained, the yield (57%) was moderate. To further investigate the role of catalysts, several adamantanamine-derived chiral catalysts (**7-11**) were synthesized and tested in the model Michael reaction. The experiment result exhibited a moderate performance on both yield and stereoselectivity (entries 7-11). According to the above results, 3,5-dimethyl-1-adamantanamine-prolinamide (**5**) was confirmed to be the most effective catalyst in terms of both the yield and enantioselectivity of the reaction.

Table 1. Screening of catalysts and solvents.[a]



12a 13a 14a

entry	catalyst	solvent	time (h)	yield[b](%)	*syn*/*anti*[c]	ee(*syn*)[d](%)
1	**1**	toluene	24	36	66:34	40
2	**2**	toluene	12	90	65:35	24
3	**3**	toluene	12	94	61:39	63
4	**4**	toluene	12	93	70:30	84
5	**5**	**toluene**	**12**	**92**	**62:38**	**93**
6	**6**	toluene	12	57	64:36	90
7	**7**	toluene	12	81	58:42	28
8	**8**	toluene	12	72	60:40	41
9	**9**	toluene	12	77	59:41	53
10	**10**	toluene	12	45	64:36	54
11	**11**	toluene	12	38	66:34	61
12	**5**	CH_2Cl_2	12	86	79:21	88
13	**5**	$CHCl_3$	12	92	65:35	90
14	**5**	THF	12	79	68:32	89
15	**5**	n-hexane	12	77	69:31	82
16	**5**	methanol	12	82	68:32	62
17	**5**	acetonitrile	12	43	70:30	72
18	**5**	isopropanol	12	59	67:33	72
19[e]	**5**	toluene	48	79	67:33	91

[a]All reactions were carried out with **12a** (3.0 mmol), **13a** (1.0 mmol), and benzoic acid (10 mol%) in the presence of catalyst (10 mol%) in solvent (2.0 mL) at room temprature. [b]Yield of the isolated product. [c]Determined by ^{1}H NMR analysis of the crude products. [d]Determined by chiral HPLC, the absolute configuration was established by comparison with literature data.[17, 18, 20] [e]5 mol% of catalyst **5** was used.

To further optimize the reaction conditions, some reaction parameters, including solvents, additives, temperatures, and amounts of catalyst were examined, and the results are shown in Tables 1 and 2. A range of typical solvents were first screened in the presence of benzoic acid (10 mol%) and catalyst **5** (10 mol%) at room temperature. Some nonpolar and aprotic solvents, such as hexane, THF, toluene, $CHCl_3$, and CH_2Cl_2, were investigated for this reaction (Table 1, entries 5 and 12-15). The excellent yields and enantioselectivity (92% yield, and 93% *ee*) were obtained when the reaction was carried out in toluene (Table 1, entry 5). However, some polar solvents, such as methanol, acetonitrile, and isopropanol, gave moderate enantioselectivities (Table 1, entries 16-18), which were unsatisfactory. Moreover, we examined the influence of catalyst loading on the reaction. When the catalyst **5** was reduced to 5 mol%, the prolonged reaction time was required (Table 1, entry 19). Next, the effect of a series of different additives was tested and the results are summarized in Table 2. Apparently, the reaction proceeded very slowly in the absence of acid additives and provided poor yield after 48 h (Table 2, entries 1-3). When benzoic acid was used as an acid additive, the best result was observed with an excellent yield (92%) and enantioselectivity (93% *ee*) (Table 2, entry 8). Although the other acid additives, such as *p*-TSA, HCOOH, CH_3COOH, CF_3COOH, were also beneficial for this reaction, their yields and enantioselectivities were slightly lower than the result with PhCOOH (Table 2, entries 4-7). In addition, three chiral acids, tartaric acid, *N*-Boc-glycine and mandelic acid, were also employed and gave moderate yield and enantioselectivities (Table 2, entries 9-11). It was implied that the acid additives only provide the proton in the Michael addition. The influence of acid

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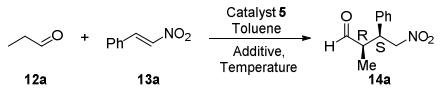
loading on the Michael addition was also examined (Table 2, entries 8, 12, and 13). It was observed that 10mol% of PhCOOH gave the optimal results. We also investigated the effect of reaction temperature (Table 2, entries 8 and 14–16). The results showed that yields and enantioselectivities have not changed significantly except for the increase of diastereoselectivity (82:18 *dr*) (Table 2, entry 14) at 0 °C by decreasing the reaction temperature from room temperature to –40 °C. Based on the overall evaluation, 0 °C was selected to be the optimal reaction temperature.

Table2 Screening of additive and temperature.[a]



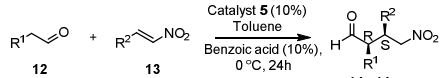
12a 13a 14a

Entry	Additive	Tem. (°C)	Time (h)	Yield[b](%)	*syn/anti*[c]	*ee*[d](%)
1	None	r.t.	48	<5	nd	nd
2	H_2O	r.t.	48	<5	nd	nd
3	Et_3N	r.t.	48	<5	nd	nd
4	*p*-TSA	r.t.	12	48	59:41	71
5	HCOOH	r.t.	12	81	60:40	84
6	CH_3COOH	r.t.	12	71	68:32	90
7	CF_3COOH	r.t.	12	88	67:33	91
8	benzoic acid	r.t.	12	92	62:38	93
9	tartaric acid	r.t.	12	81	69:31	81
10	*N*-Boc-glycine	r.t.	12	47	63:37	79
11	mandelic acid	r.t.	12	58	66:34	74
12[e]	benzoic acid	r.t.	12	93	65:35	91
13[f]	benzoic acid	r.t.	12	73	64:36	78
14	**benzoic acid**	**0**	**12**	**90**	**82:18**	**94**
15	benzoic acid	-20	36	89	65:35	95
16	benzoic acid	-40	96	91	72:28	96

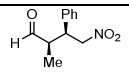
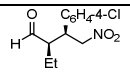
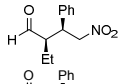
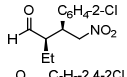
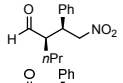
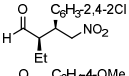
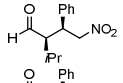
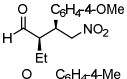
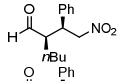
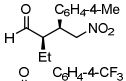
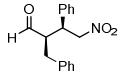
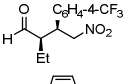
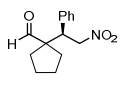
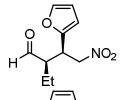
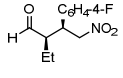
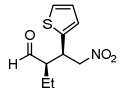
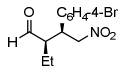
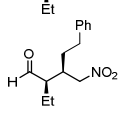
[a]All reactions were carried out with **12a** (1.0 mmol), **13a** (3.0 mmol) and additive (10 mol%)in the presence of catalyst **5** (10 mol%) in toluene (2.0 mL). [b]Yield of the isolated product. [c]Determined by ^{1}H NMR analysis of the crude products. [d]Determined by chiral HPLC. [e]20 mol% of benzoic acid was used. [f]5 mol% of benzoic acid was used.

Under the above optimized conditions, the scope of the asymmetric Michael addition reaction was investigated by applying different aldehydes and nitroalkenes in the presence of 10 mol % of catalyst **5** and 10 mol% of benzoic acid in toluene at 0 °C. The results are summarized in Table 3. The Michael addition products were obtained with good yields (81-94%) and excellent enantioselectivities (92-99% *ee*). The steric hindrance of the R^1 group for aldehydes was beneficial for the increase of diastereoselectivity to a large degree (entries 1-7). For examples, the reaction of propanal gave a moderate diastereoselectivity (64:36 *dr*) (entry 1), while that of isovaleraldehyde provided an excellent diastereoselectivity (99:1 *dr*) (entry 4). Moreover, aromatic nitroalkenes, regardless of electron-donating or electron-withdrawing substituents on the phenyl ring (entries 8-15), participated in this process in high yield (81-94%) and excellent *ee* values (95-99%). The excellent enantioselectivities (93–97% *ee*) was also observed for the Michael addition of aldehydes to nitroalkenes containing heteroaryl groups (entries 16-17). Additionally, catalyst **5** could be applied for the Michael addition of alkyl-substituted nitroalkene to aldehydes with high yield (94%) and excellent enantioselectivities (99%, entriy 18).

Table 3. Asymmetric Michael Additions of Aldehydes to nitroalkenes catalyzed by **5**[a].



12 13 14a-14r

Entry	Product	Yield[b](%)	*syn*:*anti*[c]	*ee*(*syn*)[d](%)	Entry	Product	Yield[b](%)	*syn*:*anti*[c]	*ee* (*syn*)[d](%)
1		90	64:36	95	10		91	91:9	96
2		86	86:14	98	11		82	90:10	95
3		87	89:11	92	12		81	90:10	98
4		81	99:1	98	13		83	86:14	98
5		89	77:23	93	14		93	85:15	97
6		90	81:19	96	15		89	91:9	98
7		89	97:3	97	16		83	84:16	93
8		94	92:8	99	17		85	60:40	97
9		90	86:14	98	18		94	95:5	98

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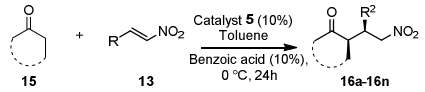
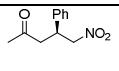
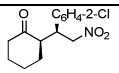
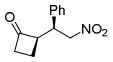
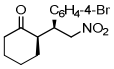
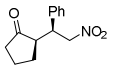
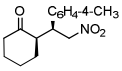
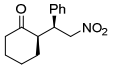
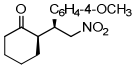
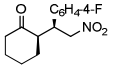
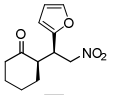
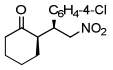
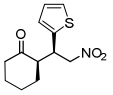
[a]All reactions were carried out with nitroalkenes (1.0 mmol) and aldehydes (3.0 mmol) in the presence of catalyst **5** (10 mol%) and benzoic acid (10 mol%) in toluene 2.0 mL) at 0 °C. [b]Yield of the isolated product. [c]Determined by ^{1}H NMR analysis of the crude products. [d]Determined by chiral HPLC, the absolute configuration was established by comparison with literature data. [17, 18, 20]

On the basis of above condition, the catalytic direct asymmetric Michael addition of ketones to nitroalkenes was also investigated, and the results are summarized in Table 4. As shown in Table 4, a dramatic lack of selectivity (55:45 *dr*, and 2% *ee*) was observed when using aliphatic ketone (Table 4, entry1). It was found that the ring size of cyclic ketones was a strong influence on the diastereoselectivity and enantioselectivity. Reaction of cyclobutanone with 13a proceeded with moderate diastereoselectivity (67:33 *dr*) and poor enantioselectivity (11% *ee*; Table 4, entry 2). The use of cyclopentanone afforded good diastereoselectivity (70:10 *dr*) and moderate enantioselectivity (40% *ee*). Notably, when cyclohexane was employed, the corresponding adduct was obtained with high yield (89%), excellent diastereoselectivity (99:1 *dr*) and excellent enantioselectivity (99% *ee*). Additionally, aromatic nitroalkenes containing electron-donating or electron-withdrawing substituents on the phenyl ring and heteroaryl groups (entries 5-12) gave high yield (81-89%) and excellent *ee* values (85-98%).

Table 4. Asymmetric Michael additions of Ketones to nitroalkenes catalyzed by 5[a].

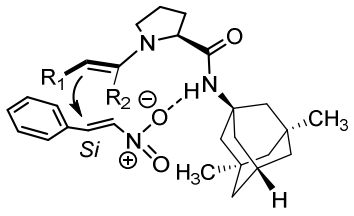


15 13 16a-16n

Entry	Product	Yield[b](%)	*syn*:*anti*[c]	*ee*(*syn*)[d](%)	Entry	Product	Yield[b](%)	*syn*:*anti*[c]	*ee*(*syn*)[d](%)
1		95	-	2	7		84	93:7	85
2		92	67:33	11	8		88	91:9	98
3		87	70:10	40	9		83	99:1	96
4		89	99:1	99	10		81	82:18	85
5		84	98:2	96	11		87	88:12	97
6		86	99:1	90	12		84	93:7	93

[a]All reactions were carried out with nitroalkenes(1.0 mmol) andketones (3.0 mmol) in the presence of catalyst **5** (10 mol%) benzoic acid (10 mol%) in toluene (1.0 mL) at 0 °C. [b]Yield of the isolated product. [c]Determined by ^{1}H NMR analysis of the crude products. [d]Determined by chiral HPLC, the absolute configuration was established by comparison with literature data. [19]

In order to account for the good enantioselectivity of the reaction, a plausible transition-state model is proposed in Scheme 3. The pyrrolidine functionality activates the aldehydeor ketones through the formation of an enamine intermediate, and the nitro group of trans-*β*-nitrostyrene is directed toward the amide group by the hydrogen bond between the *NH* group of the amide and the nitro group. The enamine formed in situ attacks the *Si* face of the nitroalkene to finish the Michael adduct. Also, the bulky aminoadamantane group is considered to be important to the high catalytic activity and enantioselectivity and diastereoselectivity of the catalyzed reactions. Our previous research[20] and some other typical literatures[21-23] could be taken as a support of the transition-state model.



Scheme 3. Possible transition state of the reaction

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Conclusions

In summary, we have developed a new prolinamide catalyst **5** for the asymmetric conjugate addition reactions of aldehydes or ketonesto nitroalkenes. This catalyst exhibited rather high catalytic efficiency and good to excellent stereoselectivity. Since the catalyst **5** can be easily prepared from commercially available Boc-*L*-proline and 1-amino-3,5-dimethyl-adamantane in two steps, we believe that catalyst **5** is an ideal candidate for laboratory or large-scale preparations. Further applications of the catalyst for a wider scope of reactions are being studied in our laboratory.

Experimental section

General information

Reagents and Materials were of the highest commercially available (Adamas) grade and used without further purification. Solvents were purified by standard procedures and distilled before use. The reactions were monitored by thin layer chromatography (TLC) using silica gel GF_{254}. Column chromatography was performed on silica gel (200 – 300 mesh). Compounds were visualized by UV and spraying with H_2SO_4 (10%) in ethanol and followed by heating. The NMR spectra were recorded on a Bruker DRX400 (^{1}H: 400 MHz, ^{13}C: 100 MHz) or Bruker DRX500 (^{1}H: 500 MHz, ^{13}C: 125 MHz) with TMS as the internal standard, chemical shifts (δ) are expressed in *ppm*, and *J* values are given in Hz, and deuterated $CDCl_3$ and was used as solvent. IR spectra were recorded on a FT-IR Thermo Nicolet Avatar 360 using KBr pellet. The mass spectroscopic data were obtained at the Agilent 1100 LC/MSD Trap LC-mass spectrometer. HPLC analysis was performed with a Shimadzu LC-10A instrument equipped with Daicel HPLC columns.

General Procedure for Preparation of adamantoyl L-prolinamide 2-6.

To a stirred solution of *N*-t-butyloxycarbonyl-*L*-proline (1.075g, 5 mmol) in dry dichloromethane (15 mL), was added DMAP (210 mg, 1.5 mmol). The mixture was allowed to stir for 15min and then cooled to 0 °C and then EDCI (1.22g, 5.5 mmol) was added. After 20 min, a solution of aminoadamantanes (4 mmol) in dichloromethane (15 mL) was added to the above reaction mixture. The resulting solution was stirred at room temperature until complete consumption of nitroalkene (monitored by TLC). The reaction was quenched with water and extracted with dichloromethane (3 × 50mL). The combined organic layers were washed with saturated brine solution (20 mL), followed by drying over Na_2SO_4 and evaporating in vacuo. The crude product was purified by column chromatography to give the pure *N*-t-butyloxycarbonyl-*L*-prolineamide (**2a**).

To a solution of **2a** (4 mmol) in CH_2Cl_2 (10 mL) was added TFA (3 mL). After stirring at 0 °C for 2.5 hour, the solution was concentrated under vacuum to leave a glutinous phase. The pH of the mixture was brought into the range of 12 by the addition of 2M NaOH. The aqueous phase was extracted with ethyl acetate. The ethyl acetate extracts were pooled, washed with brine, dried over anhydrous Na_2SO_4, filtered off and the solvent was evaporated at low pressure to give a crude residue that was purified by column chromatography to give the pure L-prolineamide (**2**).

***N*-t-butyloxycarbonyl-rimantadine-*L*-prolineamide (2a).** 95% yield; White solid, m.p. 181–183 °C; $[\alpha]_D^{20}$ = –48.5 (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 7.60 (s, 1H), 4.34 –4.24 (m, 1H), 4.00 (m, 1H), 3.49–3.32 (m, 2H), 2.45 (s, 1H), 2.15 (s, 1H), 1.91–1.73 (m, 15H), 1.63 (d, *J* = 8.0 Hz, 2H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ 170.6, 154.8, 80.3, 61.5, 59.7, 53.0, 47.1, 38.3, 37.1, 37.0, 35.8, 30.9, 28.4, 28.3, 14.4; IR (KBr): 1160, 1385, 1532, 1663, 2901, 3330 cm^{-1}; HRMS (EI) *m/z*: calcd for $C_{22}H_{36}N_2O_3$ $[M+Na]^+$ 399.2618, found 399.2618.

Rimantadine-*L*-prolineamide (2). 96% yield; White solid, m.p. 123–126 °C; $[\alpha]_D^{20}$ = –87.7 (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 7.67 (d, *J* = 9.2 Hz, 1H), 3.75–3.71 (m, 1H), 3.65–3.58 (m, 1H), 3.07–3.01 (m, 1H), 2.18–2.08 (m, 2H), 1.98–1.92 (m, 4H), 1.77–1.46 (m, 16H), 1.02 (d, *J* = 9.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ 174.1, 60.8, 52.1, 47.4, 38.4, 37.1, 36.0, 31.1, 28.3, 26.3, 14.1; IR (KBr): 1103, 1511, 1654, 2672, 2844, 2904, 3289 cm^{-1}; HRMS (EI) *m/z*: calcd for $C_{15}H_{24}N_2O$ $[M+H]^+$ 249.1961, found 249.1963.

***N*-t-butyloxycarbonyl-2-aminoadamantane-*L*-prolineamide (3a).** The method for the synthesis of **3a** was similar to that of **2a. 3a** is white solid, 93% yield; m.p. 138–141 °C; $[\alpha]_D^{20}$ = –91.4 (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS):δ 7.60 (s, 1H), 4.34–4.24 (m, 1H), 4.00 (m, 1H), 3.49–3.32 (m, 2H), 2.45 (s, 1H), 2.15 (s, 1H), 1.91–1.73 (m, 15H), 1.63 (d, *J* = 8.0 Hz, 2H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ 170.4, 156.1, 80.4, 59.8, 53.2, 47.1, 37.5, 37.1, 37.0, 31.8, 37.8, 28.4, 27.2, 24.6; IR (KBr): 1168, 1380, 1540, 1650, 1712, 2905, 3064, 3289 cm^{-1}; HRMS (EI) *m/z*: calcd for $C_{20}H_{32}N_2O_3$ $[M+Na]^+$ 371.2305, found 371.2305.

2-Aminoadamantane-*L*-prolineamide (3). The method for the synthesis of **3** was similar to that of **2**. **3** is white solid, 94% yield; m.p. 108–112 °C; $[\alpha]_D^{20}$ = –37.6 (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 8.19 (d, *J* = 5.6 Hz, 1H), 3.99 (d, *J* = 8.8 Hz, 1H), 3.76–3.73 (m, 1H), 3.07–3.01 (m, 1H), 2.96–2.90 (m, 1H), 2.18–2.09 (m, 2H), 1.97–1.70 (m, 16H), 1.68–1.62 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ 173.9, 60.8, 52.3, 47.3, 37.6, 37.1, 37.0, 32.2, 32.0, 32.0, 30.9, 27.3, 27.1, 26.2; IR (KBr): 874, 1095, 1507, 1663, 2660, 2860, 2913, 3309 cm^{-1}; HRMS (EI) *m/z*: calcd for $C_{15}H_{24}N_2O$ $[M+H]^+$ 249.1961, found 249.1963.

***N*-t-butyloxycarbonyl-1-aminoadamantane-*L*-prolineamide (4a).**The method for the synthesis of **4a** was similar to that of **2a**. **4a** is amorphous powder, 88% yield; $[\alpha]_D^{20}$ = –95.3 (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 7.28 (s, 1H), 5.66 (s, 1H), 4.19–4.07 (m, 1H), 3.43 (m, 2H), 2.33 (s, 1H), 2.13–2.07 (m, 4H), 1.98 (d, *J* = 3 Hz, 6H), 1.84 (s, 2H), 1.67 (s, 6H), 1.48 (s, *J*, 9H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ 171.5, 154.7, 80.3, 61.8, 51.5, 47.0, 41.6, 36.3, 31.1, 29.4, 28.4, 27.6, 23.7; IR (KBr): 1164, 1385, 1646, 1707, 2901, 3321 cm^{-1}; HRMS (EI) *m/z*: calcd for $C_{20}H_{32}N_2O_3$ $[M+Na]^+$ 371.2311, found 371.2315.

1-Aminoadamantane-*L*-prolineamide (4). The method for the synthesis of **4** was similar to that of **2**. **4** is white solid, 97% yield; m.p. 103–106 °C; $[\alpha]_D^{20}$ = –74.4 (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 7.35 (s, 1H), 3.61–3.58 (m, 1H), 3.02–2.96 (m, 1H), 2.91–2.85 (m, 1H), 2.23 (s, 2H), 2.01 (s, 5H), 2.00 (s, 7H), 1.89–1.83 (m, 1H), 1.68 (s, 10H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ 174.1, 61.2, 50.7, 47.2, 41.6, 36.4, 30.8, 29.4, 26.2; IR (KBr): 1102, 1511, 1650, 2668, 2852, 2909, 3285 cm^{-1};

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HRMS (EI) *m/z*: calcd for $C_{15}H_{24}N_2O$ $[M+H]^+$ 249.1966, found 249.1961.

***N*-t-butyloxycarbonyl-1-amino-3,5-dimethyl-adamantane-*L*-prolineamide (5a).** The method for the synthesis of **5a** was similar to that of **2a**. **5a** is white solid, 90% yield; m.p. 168–171 °C; $[\alpha]_D^{20}$ = –6.8 (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 7.02 (s, 1H), 5.91 (s, 1H), 4.29 (s, 2H), 3.66 (s, 2H), 3.48–3.89 (m, 4H), 2.46 (s, 1H), 2.17 (s, 2H), 1.97–1.90 (m, 10H), 1.71–1.58 (m, 12H), 1.48 (s, 9H), 1.02 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ 171.6, 156.0, 80.3, 61.7, 60.0, 53.0, 47.1, 38.3, 37.0, 35.8, 31.2, 28.4, 28.2, 27.3, 24.7, 23.8, 14.4; IR (KBr): 1168, 1389, 1646, 1712, 2931, 3326 cm^{-1}; HRMS (EI) *m/z*: calcd for $C_{20}H_{32}N_2O_4$ $[M+Na]^+$ 399.2618, found 399.2615.

1-Amino-3,5-dimethyl-adamantane-*L*-prolineamide (5). The method for the synthesis of **5** was similar to that of **2**. **5** is white solid, 95% yield; m.p. 82–85 °C; $[\alpha]_D^{20}$ = –35.4 (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 7.39 (s, 1H), 3.61–3.58 (m, 1H), 3.02–2.96 (m, 1H), 2.90–2.84 (m, 1H), 2.14–2.04 (m, 4H), 1.91–1.81 (m, 4H), 1.78–1.37 (m, 7H), 1.40–1.37 (d, *J* = 12 Hz, 2H), 1.30–1.27 (d, *J* = 12 Hz, 2H), 1.19–1.12 (m, 2H), 0.85 (s 6H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ 174.1, 61.2, 52.3, 50.7, 47.6, 47.4, 47.2, 42.7, 42.6, 40.0, 32.3, 30.7, 30.1, 26.2; IR (KBr): 866, 1516, 1642, 2848, 2901, 3281 cm^{-1}; HRMS (EI) *m/z*: calcd for $C_{17}H_{28}N_2O$ $[M+H]^+$ 277.2274, found 277.2274.

***N*-t-butyloxycarbonyl-3-aminoadamantan-1-ol-*L*-prolineamide (6a).** The method for the synthesis of **6a** was similar to that of **2a**. **6a** is white solid, 91% yield; m.p. 181–183 °C; $[\alpha]_D^{20}$ = –86.6 (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 7.29 (s, 1H), 5.78 (s, 1H), 4.20–4.07 (m, 1H), 3.44–3.31 (m, 2H), 2.26 (s, 3H), 2.09 (s, 2H), 2.05–1.87 (m, 7H), 1.70 (s, 2H), 1.56 (s, 2H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ 171.2, 154.6, 80.4, 69.0, 61.7, 54.0, 49.0, 47.1, 44.0, 40.3, 34.9, 31.1, 30.6, 28.4, 23.6; IR (KBr): 1401, 1540, 1671, 2921, 3313, 3391 cm^{-1}; HRMS (EI) *m/z*: calcd for $C_{20}H_{32}N_2O_4$ $[M+Na]^+$ 387.2254, found 387.2250.

3-Aminoadamantan-1-ol-adamantane-*L*-prolineamide (6). The method for the synthesis of **6** was similar to that of **2**. **6** is white solid, 92% yield; m.p. 154–157 °C; $[\alpha]_D^{20}$ = –48.1 (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 7.49 (s, 1H), 3.61–3.58 (m, 1H), 3.01–2.90 (m, 1H), 2.88–2.84 (m, 1H), 2.43 (s, 2H), 2.25 (s, 2H), 2.14–1.74 (m, 9H), 2.72–1.63 (m, 7H), 1.59–1.51 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ 174.4, 68.9, 61.0, 53.3, 49.0, 47.2, 44.0, 40.3, 40.3, 34.0, 30.8, 30.6, 26.2;IR (KBr): 1144, 1352, 1552, 1659, 2925, 3252 cm^{-1}; HRMS (EI) *m/z*: calcd for $C_{15}H_{24}N_2O_2$ $[M+H]^+$ 265.1910, found 265.1913.

General Procedure for Preparation of Catalysts7-11.

The solution of *N-t*-butyloxycarbonyl-*L*-proline (1.052g, 5 mmol) amantadine (604.5 mg, 4 mmol) in dry dichloromethane (6 mL) was allowed to stir for 15 min and then cooled to 0 °C and then a dichloromethane (5 mL) solution of dicyclohexylcarbodiimide (1.236 g, 6 mmol) was added. After 20 min, the resulting solution was stirred at room temperature until complete consumption of amantadine (monitored by TLC). The reaction was quenched with water and extracted with dichloromethane (3 × 100mL). The combined organic layers were washed with saturated brine solution (100 mL), followed by drying over Na_2SO_4 and evaporating in vacuo. The crude product was purified by column chromatography to give the pure tert-butyl (2-(((3s,5s,7s)-adamantan-1-yl)amino)-2-oxoethyl)carbamate (**7a**).

To a solution of **7a** (4 mmol) in CH_2Cl_2 (10 mL) was added TFA (3 mL). After stirring at 0 °C for 2.5 hour, the solution was concentrated under vacuum to leave a glutinous phase. The pH of the mixture was brought into the range of 12 by the addition of 2M NaOH. The aqueous phase was extracted with ethyl acetate. The ethyl acetate extracts were pooled, washed with brine, dried over anhydrous Na_2SO_4, filtered off and the solvent was evaporated at low pressure to give a crude residue that was purified by column chromatography to give the pure *L*-prolineamide (**7**).

Tert-butyl (2-(((3*S*,5*S*,7*S*)-adamantan-1-yl)amino)-2-oxoethyl)carbamate (7a). White solid, 93% yield; m.p. 71–74 °C; $[\alpha]_D^{20}$ = –1.6 (c 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ 5.84 (s, 1H), 5.33 (s, 1H), 4.14–4.12 (m, 1H), 3.68 (s, 2H), 2.08 (s, 4H), 1.99 (d, *J* = 2.0 Hz, 1H), 1.68 (s, 6H), 1.46 (s, 10H), 1.28–1.26 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, TMS): δ 168.7, 156.5, 80.4, 60.8, 52.4, 45.4, 42.0, 36.7, 29.8, 28.7, 14.6; IR (KBr): 576, 1049, 1164, 1487, 1679, 2909, 3322, 3407 cm^{-1}; HRMS (EI) *m/z*: calcd for $C_{17}H_{28}N_2O_3$ $[M+Na]^+$ 331.1992, found 331.1990.

***N*-((3*S*,5*S*,7*S*)-adamantan-1-yl)-2-aminoacetamide (7).** White solid, 97% yield; m.p. 110–112°C; $[\alpha]_D^{20}$ = –8.9 (c 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ 6.91 (s, 1H), 3.22 (s, 2H), 2.08 (m, 3H), 2.00 (s, 6H), 1.69 (s, 6H), 1.36 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$, TMS): δ 172.0, 51.6, 45.8, 42.0, 36.8, 29.8; IR (KBr): 1075, 1383, 1464, 1515, 1649, 1727, 2861, 2931, 3342 cm^{-1}; HRMS (EI) *m/z*: calcd for $C_{12}H_{20}N_2O$ $[M+H]^+$ 209.1648, found 209.1646.

Tert-butyl (1-(((3*S*,5*S*,7*S*)-adamantan-1-yl)amino)-4-methyl-1-oxopentan-2-yl)carbamate (8a).[24] The method for the synthesis of **8a** was similar to that of **7a**. **8a** is amorphous powder, 90% yield; $[\alpha]_D^{20}$ = –10.9 (c 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ 7.70 (s, 1H), 4.96–4.95 (m, 1H), 4.43–4.42 (m, 1H), 4.17 (s, 1H), 3.70–3.68 (m, 1H), 1.95 (s, 3H), 1.84–1.61 (m, 12H), 1.56–1.18 (m, 20H), 0.93–0.89 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$, TMS): δ 156.8, 153.9, 80.7, 55.1, 52.1, 50.4, 42.5, 33.0, 32.2, 32.0, 29.6, 28.7, 26.5, 26.4, 25.9, 25.8, 25.0, 23.4, 22.2;IR (KBr) 878, 1098, 1307, 1519, 1646, 2848, 2901, 3289, 3379 cm^{-1}; HRMS (EI) *m/z*: calcd for $C_{21}H_{36}N_2O_3$ $[M+H]^+$ 365.2726, found 365.2724.

***N*-((3*S*,5*S*,7*S*)-adamantan-1-yl)-2-amino-4-methylpentanamide (8).**[24] The method for the synthesis of **8** was similar to that of **7**. **8** is amorphous powder, 96% yield; $[\alpha]_D^{20}$ = –23.5 (c 1.0, $CDCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ 6.96 (s, 1H), 3.25–3.22 (m, 1H), 2.07 (s, 3H), 2.01 (s, 6H), 1.68 (s, 9H), 1.44 (s, 2H), 1.32–1.25 (m, 1H), 0.96–0.91 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$, TMS): δ 175.1, 54.4, 51.4, 44.7, 41.9, 36.8, 34.4, 29.8, 25.3, 23.8, 21.9; IR (KBr): 653, 1095, 1356, 1450, 1523, 1658, 1704, 2852, 2917, 3322 cm^{-1}; HRMS (EI) *m/z*: calcd for $C_{16}H_{28}N_2O$ $[M+H]^+$ 265.2274, found 265.2271.

Tert-butyl (1-(((3*S*,5*S*,7*S*)-adamantan-1-yl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (9a). The method for the synthesis of **9a** was similar to that of **7a**. **9a** is white solid, 89% yield; m.p. 83–85°C; $[\alpha]_D^{20}$ = –15.1 (c 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ 7.31 (t, *J* = 14.8 Hz, 2H), 7.25 (t, *J* = 14.2 Hz, 3H), 5.29 (s, 2H), 4.19 (s, 1H), 3.10–3.08 (m, 1H), 2.95–

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2.93 (m, 1H), 2.03 (s, 2H), 1.84 (s, 6H), 1.64 (s, 6H), 1.41 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$, TMS): δ 170.2, 155.8, 137.6, 129.9, 129.0, 127.2, 80.2, 56.9, 52.3, 41.7, 39.6, 36.7, 30.1, 29.7, 28.7; IR (KBr): 1042, 1172, 1258, 1540, 1667, 2856, 2921, 3052, 3318 cm^{-1}; HRMS (EI) *m/z*: calcd for $C_{24}H_{34}N_2O_3$ $[M+Na]^+$ 421.2461, found 421.2466.

***N*-((3*S*,5*S*,7*S*)-adamantan-1-yl)-2-amino-3-phenylpropanamide (9).** The method for the synthesis of **9** was similar to that of **7**. **9** is white solid, 94% yield; m.p. 130–133°C; $[\alpha]_D^{20}$ = –68.3 (c 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ 7.34–7.29 (m, 2H), 7.27–7.22 (m, 3H), 6.94 (s, 1H), 3.48–3.46 (m, 1H), 3.22–3.19 (m, 1H), 2.75–2.70 (m, 1H), 2.08 (s, 3H), 1.99 (s, 7H), 1.69 (s, 7H), 1.29 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, TMS): δ 173.5, 138.6, 129.8, 129.0, 127.1, 57.3, 51.5, 41.9, 41.6, 36.8, 29.8; IR (KBr): 735, 894, 1111, 1348, 1516, 1662, 2851, 2917, 3309, 3383 cm^{-1}; HRMS (EI) *m/z*: calcd for $C_{19}H_{26}N_2O$ $[M+H]^+$ 299.2117, found 299.2122.

Tert-butyl ((*S*)-1-(((1*R*,3*R*,5*R*,7*S*)-3-hydroxyadamantan-1-yl)amino)-4-methyl-1-oxopentan-2-yl)carbamate (10a). The method for the synthesis of **10a** was similar to that of **7a**. **10a** is white solid, 91% yield; m.p. 101–103°C; $[\alpha]_D^{20}$ = –30.9 (c 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ 6.29 (s, 1H), 5.23 (s, 1H), 4.00 (d, *J* = 5.8 Hz, 1H), 2.26 (s, 2H), 2.07–1.89 (m, 7H), 1.72–1.48 (m, 10H), 1.41 (s, 9H), 0.97–0.88 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$, TMS): δ 172.3, 156.2, 80.3, 69.5, 54.7, 53.9, 49.3, 44.4, 41.7, 40.6, 40.5, 35.3, 30.9, 28.7, 25.2, 23.3, 22.7; IR (KBr): 629, 1042, 1172, 1246, 1360, 1536, 1663, 2353, 2921, 3322 cm^{-1}; HRMS (EI) *m/z*: calcd for $C_{21}H_{36}N_2O_4$ $[M+Na]^+$ 403.2567, found 403.2565.

***(S)*-2-amino-*N*-((1*R*,3*R*,5*R*,7*S*)-3-hydroxyadamantan-1-yl)-4-methylpentanamide (10).** The method for the synthesis of **10** was similar to that of **7**. **10** is white solid, 95% yield; m.p. 120–122°C; $[\alpha]_D^{20}$ = –31.1 (c 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ 7.07 (m, 1H), 3.12 (d, *J* = 4.2 Hz, 1H), 2.32 (s, 3H), 2.11 (s, 2H), 1.88 (s, 2H), 1.79–1.74 (m, 4H), 1.57–1.40 (m, 8H), 1.21–1.13 (m, 1H), 0.81–0.73 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$, TMS): δ 175.1, 68.9, 60.7, 54.2, 53.8, 49.2, 44.5, 44.3, 40.5, 35.3, 30.9, 25.2, 23.7, 22.0; IR (KBr): 563, 911, 959, 1037, 1136, 1217, 1262, 1328, 1548, 1654, 2851, 2917, 3048, 3342 cm^{-1}; HRMS (EI) *m/z*: calcd for $C_{16}H_{28}N_2O_2$ $[M+H]^+$ 281.2223, found 281.2223.

Tert-butyl((*S*)-1-(((1*R*,3*R*,5*R*,7*S*)-3-hydroxyadamantan-1-yl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (11a). The method for the synthesis of **11a** was similar to that of **7a**. **11a** is white solid, 88% yield; m.p. 90–93°C; $[\alpha]_D^{20}$ = –4.4 (c 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ 7.32–7.22 (m, 5H), 5.61 (s, 3H), 5.35 (s, 2H), 4.21 (s, 1H), 3.08–3.04 (m, 1H), 2.22 (s, 1H), 1.92–1.66 (m, 14H), 1.51 (s, 2H), 1.42 (s, 6H), 1.38–1.32 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, TMS): δ 170.6, 155.8, 137.4, 129.9, 129.0, 128.8, 127.3, 80.4, 69.4, 56.8, 54.7, 49.1, 48.8, 44.4, 40.4, 40.3, 39.4, 35.2, 34.2, 30.9, 28.7, 25.3, 22.5; IR (KBr): 751, 1037, 1168, 1315, 1372, 1540, 1662, 2917, 3329 cm^{-1}; HRMS (EI) *m/z*: calcd for $C_{24}H_{34}N_2O_4$ $[M+Na]^+$ 437.2410, found 437.2408.

***(S)*-2-amino-*N*-((1*R*,3*R*,5*R*,7*S*)-3-hydroxyadamantan-1-yl)-3-phenylpropanamide (11).** The method for the synthesis of **11** was similar to that of **7**. **11** is white solid, 96% yield; m.p. 162–165°C; $[\alpha]_D^{20}$ = –52.8 (c 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ 7.33–7.23 (m, 5H), 7.07 (s, 1H), 3.48 (d, *J* = 3.8 Hz, 1H), 3.20 (d, *J* = 13.6 Hz, 1H), 2.75 (t, *J* = 22.0 Hz, 1H), 2.28 (s, 2H), 2.03 (s, 2H), 1.95–1.87 (m, 4H), 1.72 (s, 7H), 1.58–1.56 (m, 2H), 1.34 (d, *J* = 6.2, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, TMS): δ 173.7, 138.4, 129.8, 129.1, 127.2, 69.5, 57.2, 54.0, 49.3, 44.5, 41.4, 40.6, 35.3, 31.0, 22.5;IR (KBr):1049, 1348, 1450, 1540, 1650, 2852, 2909, 3064, 3269 cm^{-1}; HRMS (EI) *m/z*: calcd for $C_{19}H_{26}N_2O_2$ $[M+H]^+$315.2067, found 315.2061.

General Procedure for the Michael Addition.

To a stirred solution of corresponding freshly distilled aldehyde or ketones (3 mmol, 3.0 equiv) in indicated solvent (2 mL) were added catalyst and benzoic acid. The mixture was stirred at the indicated temperature for 30 min, then corresponding nitroolifen (1 mmol, 1.0 equiv) was added. The resulting solution was stirred at the same temperature until complete consumption of nitroalkene (monitored by TLC). The solvent was quenched with ice water (2 mL), and extracted with ethyl acetate (3 x 10mL). The combined organic phase was dried over Na_2SO_4, after removing the solvent, the crude product was purified by flash chromatography to afford the corresponding Michael adducts. Enantiomeric excess was determined by chiral HPLC analysis.

(2*R*,3*S*)-2-methyl-4-nitro-3-phenylbutanal (14a).[20] The title compound **14a** was prepared from propanal and nitrostyrene according to the general procedure of Michael addition. **14a** is pale yellow oil, 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.71 (s, 1H), 9.54 (s, 1H), 7.36–7.27 (m, 5H), 7.22–7.16 (m, 3H), 4.82–4.78 (m, 2H), 4.71–4.65 (m, 1H), 3.84–3.78 (m, 2H), 2.83–2.75 (m, 2H), 1.02 (d, *J* = 7.2 Hz, 2H), 1.00 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.4, 136.6, 129.4, 129.1, 129.1, 128.2, 128.1, 78.1, 48.7, 48.4, 44.8, 44.0, 12.1, 11.7; HPLC (Chiralcel OD-H, *n*-hexane: *i*-PrOH = 90: 10, flow rate: 1.0 mL/min, λ = 254 nm), T_{major} = 33.6, $T_{mino\ r}$ = 25.8, 94% *ee*.

(2*R*,3*S*)-2-ethyl-4-nitro-3-phenylbutanal (14b).[20] The title compound **14b** was prepared from butyraldehyde and nitrostyrene according to the general procedure of Michael addition. **14b** is pale yellow oil, 86% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.72 (s, 1H), 9.48 (s), 7.37–7.29 (m, 4H), 7.18 (d, *J* = 8.0, 2H), 4.75–4.71 (m, 1H), 4.71–4.60 (m, 1H), 3.83–3.76 (m, 1H), 2.71–2.66 (m, 1H), 1.52–1.49 (m, 2H), 0.99 (t, *J* = 7.2 Hz, 1H), 0.99 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.2, 136.8, 129.1, 128.2, 128.1, 128.0, 78.5, 55.0, 42.7, 20.4, 10.7; HPLC (Chiralcel AD-H, *n*-hexane: *i*-PrOH = 99:1, flow rate: 0.8 mL/min, λ = 254 nm), T_{major} = 31.5, T_{minor} = 40.8, 98% *ee*.

(*R*)-2-((*S*)-2-nitro-1-phenylethyl)pentanal (14c).[20] The title compound **14c** was prepared from *n*-pentanal and nitrostyrene according to the general procedure of Michael addition. **14c** is pale yellow oil, 87% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.70 (s, 1H), 9.48 (s), 7.37-7.28 (m, 4H), 7.18 (d, *J* = 7.6, 2H), 4.73-4.62 (m, 2H), 3.81-3.75 (m, 1H), 2.73-2.68 (m, 1H), 1.51-1.17(m, 5H), 0.94 (t, *J* = 6.8 Hz, 1H), 0.89 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.2, 136.8, 129.1, 128.2, 128.1, 128.0, 78.4, 53.8, 43.2, 29.5, 19.8, 13.9; HPLC (Chiralcel OD-H, *n*-hexane: *i*-PrOH = 96:4, flow rate: 1.0 mL/min, λ = 254 nm), T_{major} = 38.7, T_{minor} = 31.1, 92% *ee*.

(2*R*,3*S*)-2-isopropyl-4-nitro-3-phenylbutanal (14d).[20] The title compound **14d** was prepared from *i*-pentanal and nitrostyrene according to the general procedure of Michael addition. **14d** is

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pale yellow oil, 81% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.93 (s, 1H), 9.71 (s), 7.36–7.27 (m, 3H), 7.19 (d, J = 7.6, 2H), 4.69–4.65 (m, 1H), 4.60–4.54 (m, 1H), 3.93–3.87 (m, 1H), 2.79–2.76 (m, 1H), 1.72–1.69 (m, 1H), 1.09 (d, J = 7.2 Hz, 3H), 0.88 (d, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.3, 137.1, 129.2, 128.1, 128.0, 79.0, 58.7, 41.9, 27.9, 21.7, 17.0; HPLC (Chiralcel AD-H, *n*-hexane: *i*-PrOH = 97: 3, flow rate: 0.5 mL/min, λ = 254 nm), T_{major} = 23.7, T_{minor} = 28.1, 98% *ee*.

(*R*)-2-((*S*)-2-nitro-1-phenylethyl)hexanal (14e).[20] The title compound **14e** was prepared from *n*-hexaldehyde and nitrostyrene according to the general procedure of Michael addition. **14e** is pale yellow oil, 89% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.70 (s, 1H), 9.47 (s), 7.36–7.27 (m, 3H), 7.17 (d, J = 7.2, 2H), 4.83–4.61 (m, 3H), 3.81–3.75 (m, 1H), 2.72–2.62 (m, 1H), 1.50–1.27 (m, 9H), 1.22 (t, J = 10.4 Hz, 1H), 1.17 (d, J = 17.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.3, 136.8, 129.1, 128.2, 128.1, 128.0, 78.5, 53.9, 43.1, 28.5, 27.0, 22.5, 13.7; HPLC (Chiralcel OD-H, *n*-hexane: *i*-PrOH = 97: 3, flow rate: 1.0 mL/min, λ = 254 nm), T_{major} = 40.5, T_{minor} = 30.4, 93% *ee*.

(2*R*,3*S*)-2-benzyl-4-nitro-3-phenylbutanal (14f).[25] The title compound **14f** was prepared from benzenepropanal andnitrostyrene according to the general procedure of Michael addition. **14f** is pale yellow oil, 90% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.73 (d, J = 2.0, 1H), 9.59 (s), 7.43–7.07 (m, 15H), 4.89–4.85 (m, 1H), 4.78–4.72 (m, 2H), 3.90–3.85 (m, 1H), 3.15–3.02 (m, 1H), 2.84–2.77 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 203.5, 127.8, 137.7, 129.7, 129.6, 129.3, 129.2, 128.9, 128.8, 128.5, 127.4, 78.5, 55.8, 54.9, 44.9, 43.9, 34.7, 34.0; HPLC (Chiralcel AS-H, *n*-hexane: *i*-PrOH = 97:3, flow rate: 0.7 mL/min, λ = 254 nm), T_{major} = 49.0, T_{minor} = 55.3, 96% *ee*.

(*R*)-1-(2-nitro-1-phenylethyl)cyclopentane-1-carbaldehyde (14g). The title compound **14g** was prepared from carboxaldehyde and nitrostyrene according to the general procedure of Michael addition. **14g** is pale yellow oil, 89% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.51 (s, 1H), 7.35–7.28 (m, 3H), 7.24–7.22 (m, 2H), 5.02–4.97 (m, 1H), 4.75–4.71 (m, 1H), 2.10–2.05 (m, 1H), 1.92–1.90 (m, 1H), 1.69–1.55 (m, 7H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 204.8, 139.5, 137.6, 136.8, 132.6, 129.8, 129.6, 129.2, 129.1, 128.9, 128.5, 77.8, 60.7, 49.7, 33.0, 31.9, 31.9, 25.3, 25.1; HPLC (Chiralcel OD-H, *n*-hexane: *i*-PrOH = 95:5, flow rate: 0.5 mL/min, λ = 254 nm), T_{major} = 43.5, T_{minor} = 37.3, 97% *ee*.

(2*R*,3*S*)-2-ethyl-3-(4-fluorophenyl)-4-nitrobutanal (14h).[20] The title compound **14h** was prepared from *n*-butyraldehyde and 4-fluoro-β-nitrostyrene according to the general procedure of Michael addition. **14h** is pale yellow oil, 94% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.72 (d, J = 2.4 Hz), 9.49 (d, J = 2.8 Hz, 1H), 7.19–7.15 (m, 2H), 7.07–6.99 (m, 2H), 4.82–4.70 (m, 2H), 3.84–3.79 (m, 2H), 2.61–2.55 (m, 1H), 1.78–1.57 (m, 3H),1.00 (t, J = 15.2 Hz, 3H), 0.84 (d, J = 15.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.8, 163.6, 161.1, 132.1, 129.9, 116.2, 116.0, 78.0, 55.0, 43.3, 41.8, 20.6, 11.4; HPLC (Chiralcel AD-H, *n*-hexane: *i*-PrOH = 99:1, flow rate: 1.0 mL/min, λ = 254 nm), T_{major} = 25.0, T_{minor} = 33.3, 99% *ee*.

(2*R*,3*S*)-3-(4-bromophenyl)-2-ethyl-4-nitrobutanal (14i).[20] The title compound **14i** was prepared from *n*-butyraldehyde and 4-bromo-β-nitrostyrene according to the general procedure of Michael addition. **14i** is pale yellow oil, 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.71 (s, 1H), 9.49 (s), 7.50–7.45 (t, J = 16.8, 2H), 7.01 (d, J = 8, 2H), 4.78–4.70 (m, 1H), 4.62–4.57 (m, 1H), 3.81–3.75 (m, 1H), 2.70–2.65 (m, 1H), 1.56–1.46 (m, 2H), 1.00 (t, J = 14.8 Hz, 1H), 0.83 (d, J = 14.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.7, 135.9, 132.3, 129.7, 122.2, 78.3, 54.6, 42.0, 20.3, 10.5; HPLC (Chiralcel AD-H, *n*-hexane: *i*-PrOH = 98.5:1.5, flow rate: 1.0 mL/min, λ = 254 nm), T_{major} = 32.0, T_{minor} = 50.4, 98% *ee*.

(2*R*,3*S*)-3-(4-chlorophenyl)-2-ethyl-4-nitrobutanal (14j).[20] The title compound **14j** was prepared from *n*-butyraldehyde and 4-chloro-β-nitrostyreneaccording to the general procedure of Michael addition. **14j** is pale yellow oil, 91% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.71 (s, 1H), 9.49 (s), 7.32–7.45 (t, J = 16.8, 2H), 7.13 (d, J = 7.6, 2H), 4.75–4.71 (m, 1H), 4.63–4.57 (m, 1H), 3.82–3.76 (m, 1H), 2.70–2.65 (m, 1H), 1.56–1.46 (m, 2H), 1.00 (t, J = 14.4 Hz, 1H), 0.83 (d, J = 15.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.7, 135.4, 134.0, 129.6, 129.4, 78.3, 54.7, 42.0, 20.3, 10.5; HPLC (Chiralcel AD-H, *n*-hexane: *i*-PrOH = 98.5:1.5, flow rate: 1.0 mL/min, λ = 254 nm), T_{major} = 27.9, T_{minor} = 42.0, 96% *ee*.

(2*R*,3*S*)-3-(2-chlorophenyl)-2-ethyl-4-nitrobutanal (14k).[20] The title compound **14k** was prepared from *n*-butyraldehyde and 2-chloro-β-nitrostyreneaccording to the general procedure of Michael addition. **14k** is pale yellow oil, 82% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.74 (s, 1H), 9.52 (s), 7.42–7.28 (m, 1H), 7.26–7.19 (m, 4H), 4.89–4.78 (m, 1H), 4.76–4.67 (m, 1H), 4.50–4.45 (m, 1H), 4.38–4.33 (m, 1H), 2.96 (s, 1H), 1.63–1.50 (m, 1H), 0.98 (t, J = 14.8 Hz, 1H), 0.86 (d, J = 14.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.9, 134.5, 134.4, 130.6, 129.3, 127.5, 77.4, 50.1, 39.2, 20.4, 10.7; HPLC (Chiralcel AD-H, *n*-hexane: *i*-PrOH = 98.5:1.5, flow rate: 1.0 mL/min, λ = 254 nm), T_{major} = 16.7, T_{minor} = 18.7, 95% *ee*.

(2*R*,3*S*)-3-(2,4-dichlorophenyl)-2-ethyl-4-nitrobutanal (14l).[20] The title compound **14l** was prepared from *n*-butyraldehyde and 2, 4-dichloro-β-nitrostyreneaccording to the general procedure of Michael addition. **14l** is pale yellow oil, 81% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.72 (s, 1H), 9.57 (s), 9.44 (s, 1H), 7.26 (d, J = 8.0 Hz, 1H), 7.17 (d, J = 8.4 Hz, 1H), 4.88–4.76 (m, 1H), 4.71–4.67 (m, 1H), 4.34–4.28 (m, 1H), 2.94 (d, J = 7.2 Hz, 1H), 1.61–1.53 (m, 2H), 0.99 (t, J = 14.8 Hz), 0.87 (d, J = 14.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.5, 135.1, 134.5, 133.2, 130.4, 130.0, 127.9, 53.7, 38.6, 20.4, 10.6; HPLC (Chiralcel AD-H, *n*-hexane: *i*-PrOH = 99:1, flow rate: 1.0 mL/min, λ = 254 nm), T_{major} = 19.2, T_{minor} = 21.8, 98% *ee*.

(2*R*,3*S*)-2-ethyl-3-(4-methoxyphenyl)-4-nitrobutanal (14m).[20] The title compound **14m** was prepared from *n*-butyraldehyde and 4-methoxy-β-nitrostyreneaccording to the general procedure of Michael addition. **14m** is pale yellow oil, 83% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.71 (s, 1H), 9.46 (d, J = 2.4), 7.09 (d, J = 8.0, 2H), 6.88–6.84 (m, 2H), 4.71–4.67 (m, 1H), 4.61–4.55 (m, 1H), 3.78 (m, J = 5.2, 4H), 2.66–2.61 (m, 1H), 1.70–1.64 (m, 1H), 1.52–1.45 (m, 1H), 0.96 (t, J = 14.8 Hz, 1H), 0.83 (d, J = 14.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.4, 159.3, 129.0, 128.5, 114.5, 78.8, 55.2, 42.0, 20.3, 10.7; HPLC (Chiralcel AD-H, *n*-hexane: *i*-PrOH = 96:4, flow rate: 1.0 mL/min, λ = 254 nm), T_{major} = 19.4, T_{minor} = 16.4, 95% *ee*.

(2*R*,3*S*)-2-ethyl-4-nitro-3-(*p*-tolyl)butanal (14n).[20] The title

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compound **14n** was prepared from *n*-butyraldehyde and 4-methyl-*β*-nitrostyreneaccording to the general procedure of Michael addition. **14n** is pale yellow oil, 93% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.71 (s, 1H), 9.47 (s), 7.15–7.11 (m, 2H), 7.05 (d, J = 0.8, 2H), 4.80–4.69 (m, 1H), 4.67–4.57 (m, 1H), 3.78–3.72 (m, 1H), 2.68–2.63 (m, 1H), 2.31 (d, J = 6.0, 3H),1.54–1.47 (m, 2H), 0.98 (t, J = 22 Hz, 1H), 0.82 (d, J = 14.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.4, 137.9, 133.6, 129.8, 128.1, 127.8, 78.7, 55.1, 42.4, 21.1, 20.4, 10.7; HPLC (Chiralcel OD-H, *n*-hexane: *i*-PrOH = 92:8, flow rate: 0.5 mL/min, λ = 254 nm), T_{major} = 43.5, T_{minor} = 37.3, 97% *ee*.

(2*R*,3*S*)-2-ethyl-4-nitro-3-(4-(trifluoromethyl)phenyl)butanal (14o).[20] The title compound **14o** was prepared from *n*-butyraldehyde and 4-trifluoromethyl-*β*-nitrostyreneaccording to the general procedure of Michael addition. **14o** is pale yellow oil, 89% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.72 (s, 1H), 9.51 (s), 7.62 (d, J = 8.0, 2H), 7.34 (d, J = 8.0, 2H), 4.83–4.76 (m, 1H), 4.69–4.63 (m, 1H), 3.93–3.87 (m, 1H), 2.77–2.72 (m, 1H), 1.56–1.45 (m, 2H), 1.00 (t, J = 8.8 Hz), 0.84 (d, J = 8.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.5, 141.4, 128.5, 126.1, 126.0, 78.1, 54.5, 42.2, 21.1, 20.3, 10.4; HPLC (Chiralcel AS-H, *n*-hexane: *i*-PrOH = 93:7, flow rate: 0.5 mL/min, λ = 254 nm), T_{major} = 27.4, T_{minor} = 30.1, 98% *ee*.

(2*R*,3*R*)-2-ethyl-3-(furan-2-yl)-4-nitrobutanal (14p).[20] The title compound **14p** was prepared from *n*-butyraldehyde and 2-(2-nitroethenyl)furanaccording to the general procedure of Michael addition. **14p** is pale yellow oil, 83% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.71 (s, 1H), 9.60 (s), 7.37 (s, 1H), 6.31 (s, 1H), 6.20 (s, 1H), 4.75–4.65 (m, 2H), 4.05–4.00 (m, 1H), 2.79–2.74 (m, 1H), 1.57–1.53 (m, 2H), 0.99 (t, J = 8.8 Hz, 1H), 0.89 (d, J = 8.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.4, 150.1, 14.7, 110.5, 110.4, 109.0, 108.8, 76.0, 53.4, 36.5, 20.0, 10.9; HPLC (Chiralcel AS-H, *n*-hexane: *i*-PrOH = 96:4, flow rate: 0.5 mL/min, λ = 254 nm), T_{major} = 41.1, T_{minor} = 35.8, 93% *ee*.

(2*R*,3*R*)-2-ethyl-4-nitro-3-(thiophen-2-yl)butanal (14q).[20] The title compound **14q** was prepared from *n*-butyraldehyde and 1-(2-thienyl)-2-nitroethene according to the general procedure of Michael addition. **14q** is pale yellow oil, 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.70 (s, 1H), 9.52 (s), 7.34 (d, J = 4.0 Hz, 2H), 7.11 (d, J = 4.8 Hz, 2H), 4.82–4.59 (m, 4H), 4.03–3.96 (m, 2H), 2.69–2.64 (m, 1H), 2.56–2.51 (m, 1H), 1.80–1.75 (m, 1H), 1.67–1.50 (m, 3H), 1.02 (t, J = 11.2 Hz, 2H), 0.90 (t, J = 11.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.4, 203.0, 137.2, 136.6, 127.1, 126.9, 126.9, 126.0, 123.5, 123.3, 78.3, 77.9, 54.9, 54.6, 39.4, 38.2, 20.7, 20.3, 11.6, 10.9; HPLC (Chiralcel AD-H, *n*-hexane: *i*-PrOH = 98:2, flow rate: 0.7 mL/min, λ = 254 nm), T_{major} = 36.2, T_{minor} = 46.8, 97% *ee*.

(2*R*,3*R*)-2-ethyl-3-(nitromethyl)-5-phenylpentanal (14r).[26] The title compound **14q** was prepared from *n*-butylaldehyde and (4-nitrobut-3-enyl)benzene according to the general procedure of Michael addition. **14q** is pale yellow oil, 94% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.71 (1H, s), 7.35–7.18 (1H, m), 4.58–4.49 (2H, m), 2.74–2.64 (3H, m), 2.51–2.47 (2H, m), 1.86–1.69 (3H, m), 1.61–1.54 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 203.4, 140.9, 129.1, 128.7, 126.8, 54.2, 36.6, 33.4, 31.4, 19.1, 12.3; HPLC (Chiralcel OD-H, *n*-hexane: *i*-PrOH = 90:10, flow rate: 0.5 mL/min, λ = 210 nm), T_{major} = 37.4, T_{minor} = 40.1, 99% *ee*.

(*S*)-5-nitro-4-phenylpentan-2-one (16a).[27] The title compound **16a** was prepared from acetone and nitrostyrene according to the general procedure of Michael addition. **16a** is pale yellow oil, 95% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35 (d, J = 7.2, 1H), 7.30 (t, J = 6.6, 1H), 7.25 (d, J = 7.4, 1H), 4.75–4.71 (m, 1H), 4.65–4.62 (m, 1H), 4.06–4.03 (m, 1H), 2.95 (d, J = 7.0, 1H), 2.16 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 205.8, 139.2, 129.5, 128.3, 127.8, 79.9, 46.5, 39.5, 30.8; HPLC (Chiralcel AS-H, *n*-hexane: *i*-PrOH = 92:8, flow rate: 0.5 mL/min, λ = 210 nm), T_{major} = 33.6, T_{minor} = 26.4, 2% *ee*.

(*R*)-2-((*S*)-2-nitro-1-phenylethyl)cyclobutan-1-one (16b).[27] The title compound **16b** was prepared from cyclobutanone and nitrostyrene according to the general procedure of Michael addition. **16b** is pale yellow oil, 92% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36 (t, J = 14.5, 4H), 7.32 (t, J = 7.4, 3H), 5.11–5.07 (m, 1H), 4.89–4.86 (m, 1H), 4.69–4.64 (m, 1H), 3.77–3.72 (m, 2H), 3.67–3.62 (m, 1H), 3.14–3.10 (m, 1H), 3.07–3.02 (m, 1H), 3.00–2.93 (m, 1H), 2.21–2.18 (m, 1H), 2.11–2.03 (m, 1H), 1.78–1.65 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 208.9, 137.4. 136.9. 129.5. 128.6. 128.5. 128.0. 78.7. 61.9. 61.4. 45.4. 44.9. 44.7. 16.2. 14.7; HPLC (Chiralcel AS-H, *n*-hexane: *i*-PrOH = 75:25, flow rate: 0.7 mL/min, λ = 210 nm), T_{major} = 13.7, T_{minor} = 11.2, 11% *ee*.

(*R*)-2-((*S*)-2-nitro-1-phenylethyl)cyclopentan-1-one (16c).[27] The title compound **16c** was prepared from cyclopentanoneand nitrostyrene according to the general procedure of Michael addition. **16c** is pale yellow oil, 90% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34 (t, J = 14.6, 3H), 7.29 (t, J = 13.0, 2H), 7.22–7.19 (d, J = 7.3, 3H), 5.38–5.35 (m, 1H), 5.04 (d, J = 7.8, 1H), 4.77–4.72 (m, 1H), 3.79–3.69 (m, 1H), 2.45–2.43 (m, 2H), 2.20–2.11 (m, 1H), 1.97–1.88 (m, 1H), 1.79–1.64 (m, 1H), 1.55–1.46 (m, 1H), 1.35–1.28 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 218.9, 138.2, 78.7, 51.8, 50.9, 48.8, 44.6, 44.4, 42.9, 39.7, 39.1, 28.7, 27.4, 22.5, 21.0, 20.7; HPLC (Chiralcel AS-H, *n*-hexane: *i*-PrOH = 75:25, flow rate: 0.8 mL/min, λ = 210 nm), T_{major} = 14.7, T_{minor} = 10.8, 40% *ee*.

(*R*)-2-((*S*)-2-nitro-1-phenylethyl)cyclohexan-1-one (16d).[27] The title compound **16d** was prepared from cyclohexanone and nitrostyrene according to the general procedure of Michael addition. **16d** is white solid, 89% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34 (t, J = 14.6 Hz, 2H), 7.29 (t, J = 14.4 Hz, 1H), 7.19 (d, J = 7.3 Hz, 2H), 4.99–4.95 (m, 1H), 4.66 (t, J = 22.4 Hz, 1H), 3.81–3.77 (m, 1H), 2.74–2.69 (m, 1H), 2.52–2.38 (m, 1H), 2.12–2.07 (m, 1H), 1.82–1.55 (m, 1H), 1.30–1.22 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 212.3, 138.2, 129.3, 128.6, 128.2, 79.3, 52.9, 44.4, 43.2, 33.6, 28.9, 25.4; HPLC (Chiralcel AS-H, *n*-hexane: *i*-PrOH = 85:15, flow rate: 0.8 mL/min, λ = 210 nm), T_{major} = 17.6, T_{minor} = 11.9, 99% *ee*.

(*R*)-2-((*S*)-1-(4-fluorophenyl)-2-nitroethyl)cyclohexan-1-one (16e).[27] The title compound **16e** was prepared from cyclohexanone and 4-fluoro-*β*-nitrostyreneaccording to the general procedure of Michael addition. **16e** is white solid, 84% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.14 (d, J = 7.5 Hz, 1H), 7.63 (t, J = 15.4 Hz, 1H), 7.50 (t, J = 15.4 Hz, 2H), 7.19–7.16 (m, 3H), 7.05–7.02 (m, 3H), 4.97–4.94 (m, IH), 4.65–4.60 (m, 1H), 3.82–3.77 (m, 1H), 2.71–2.65 (m, 1H), 2.52–2.37 (m, 1H), 2.13–2.09 (m, 1H), 1.84–1.59 (m, 6H), 1.34–1.21 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 212.1, 172.1, 163.6, 161.6, 134.0, 133.9, 130.6, 130.2, 130.1, 128.9, 116.4, 116.2, 79.2, 52.9, 43.7, 43.1,

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33.6, 30.1, 28.9, 25.5; HPLC (Chiralcel AD-H, *n*-hexane: *i*-PrOH = 92:8, flow rate: 0.9 mL/min, λ = 210 nm), T_{major} = 20.8, T_{minor} = 24.2, 96% *ee*.

(*R*)-2-((*S*)-1-(4-chlorophenyl)-2-nitroethyl)cyclohexan-1-one (16f).[27] The title compound **16f** was prepared from cyclohexanone and 4-chloro-β-nitrostyreneaccording to the general procedure of Michael addition. **16f** is white solid, 86% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30 (t, *J* = 14.0 Hz, 2H), 7.14 (t, *J* = 8.2 Hz, 2H), 4.98–4.94 (m, 1H), 4.64–4.59 (m, 1H), 3.81–3.76 (m, 1H), 2.70–2.64 (m, 1H), 2.49–2.47 (m, 1H), 2.41–2.35 (m, 1H), 2.12–2.09 (m, 1H), 1.82–1.79 (m, 1H), 1.74–1.56 (m, 3H), 1.28–1.21 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 211.9, 136.8, 134.0, 130.0, 129.5, 79.0, 52.8, 43.8, 43.1, 33.6, 28.8, 25.5; HPLC (Chiralcel AD-H, *n*-hexane: *i*-PrOH = 90:10, flow rate: 0.9 mL/min, λ = 210 nm), T_{major} = 27.9, T_{minor} = 18.8, 90% *ee*.

(*R*)-2-((*S*)-1-(2-chlorophenyl)-2-nitroethyl)cyclohexan-1-one(16g).[27] The title compound **16g** was prepared from cyclohexanone and 2-chloro-β-nitrostyrene according to the general procedure of Michael addition. **16g** is white solid, 84% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39 (d, *J* = 7.6 Hz, 1H), 7.28–7.21 (m, 3H), 4.95–4.88 (m, 2H), 4.34–4.30 (m, 1H), 2.93 (s, 1H), 2.50–2.47 (m, 1H), 2.44–2.37 (m, 1H), 2.13–2.37 (m, 1H), 2.13–2.10 (m, 1H), 1.84–1.81 (m, 1H), 1.75–1.57 (m, 3H), 1.39-1.27 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 212.0, 135.9, 134.9, 130.7, 129.9, 129.3, 127.8, 77.8, 52.2, 43.2, 41.4, 33.4, 28.9, 25.7; HPLC (Chiralcel AS-H, *n*-hexane: *i*-PrOH = 90:10, flow rate: 0.8 mL/min, λ = 210 nm), T_{major} = 19.7, T_{minor} = 14.1, 85% *ee*.

(*R*)-2-((*S*)-1-(4-bromophenyl)-2-nitroethyl)cyclohexan-1-one (16h).[27] The title compound **16h** was prepared from cyclohexanone and 4-bromo-β-nitrostyreneaccording to the general procedure of Michael addition. **16h** is white solid, 88% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.46 (t, *J* = 16.4 Hz, 2H), 7.08 (t, *J* = 8.2 Hz, 2H), 4.97–4.94 (m, 1H), 4.62–4.60 (m, 1H), 3.80–3.75 (m, 1H), 2.70–2.64 (m, 1H), 2.50–2.47 (m, 1H), 2.42–2.36 (m, 1H), 2.12–2.08 (m, 1H), 1.83–1.80 (m, 1H), 1.75–1.57 (m, 3H), 1.29–1.21 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 211.9, 137.3, 132.5, 130.4, 122.1, 78.9, 52.8, 43.9, 43.1, 33.6, 28.8, 25.5; HPLC (Chiralcel AD-H, *n*-hexane: *i*-PrOH = 90:10, flow rate: 0.7 mL/min, λ = 210 nm), T_{major} = 23.7, T_{minor} = 28.1, 98% *ee*.

(*R*)-2-((*S*)-2-nitro-1-(*p*-tolyl)ethyl)cyclohexan-1-one (16i).[27] The title compound **16i** was prepared from cyclohexanone and 4-methyl-β-nitrostyreneaccording to the general procedure of Michael addition. **16i** is white solid, 83% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.14 (d, *J* = 8.0 Hz, 2H), 7.07 (d, *J* = 8.0 Hz, 2H), 4.97–4.93 (m, 1H), 4.65–4.60 (m, 1H), 3.77–3.72 (m, 1H), 2.71–2.69 (m, 1H), 2.50–2.47 (m, 1H), 2.44–2.33 (m, 4H), 2.11–2.08 (m, 1H), 1.81–1.57 (m, 4H), 1.28–1.23 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 212.5, 137.8, 135.1, 130.0, 128.4, 79.5, 52.9, 44.0, 43.1, 33.6, 28.9, 25.4, 21.5; HPLC (Chiralcel AD-H, n-hexane: *i*-PrOH = 92:8, flow rate: 0.8 mL/min, λ = 210 nm), T_{major} = 16.7, T_{minor} = 18.7, 96% *ee*.

(*R*)-2-((*S*)-1-(4-methoxyphenyl)-2-nitroethyl)cyclohexan-1-one (16j).[27] The title compound **16j** was prepared from cyclohexanone and 4-methoxy-β-nitrostyreneaccording to the general procedure of Michael addition. **16j** is white solid, 81% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.10 (d, *J* = 8.6 Hz, 2H), 6.88–6.86 (m, 2H), 4.95–4.92 (m, 1H), 4.63–4.58 (m, 1H), 3.80 (s, 3H), 3.76–3.71 (m, 1H), 2.70–2.64 (m, 1H), 2.50–2.47 (m, 1H), 2.43–2.40 (m, 1H), 2.11–2.08 (m, 1H), 1.82–1.58 (m, 4H), 1.28–1.24 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 212.5, 159.4, 129.9, 129.6, 114.7, 114.5, 79.5, 55.6, 53.1, 43.6, 53.1, 43.6, 43.1, 35.5, 28.9, 25.4; HPLC (Chiralcel AS-H, *n*-hexane: *i*-PrOH = 90:20, flow rate: 0.8 mL/min, λ = 210 nm), T_{major} = 19.7, T_{minor} = 20.0, 85% *ee*.

(*R*)-2-((*R*)-1-(furan-2-yl)-2-nitroethyl)cyclohexan-1-one (16k).[27] The title compound **16k** was prepared from cyclohexanoneand 2-(2-nitroethenyl)furanaccording to the general procedure of Michael addition. **16k** is white solid, 87% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.33 (d, *J* = 9.4 Hz, 1H), 6.28 (d, *J* = 2.2 Hz, 1H), 6.19–6.17 (m, 1H), 4.81–4.70 (m, 2H), 4.68–4.65 (m, 1H), 4.00–3.95 (m, 1H), 2.78–2.73 (m, 1H), 2.47–2.45 (m, 1H), 2.40–2.34 (m, 1H), 2.11–2.09 (m, 2H), 1.83–1.38 (m, 5H), 1.27–1.25 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 152.5, 151.4, 142.7, 142.4, 110.9, 110.7, 109.3, 107.9, 77.1, 75.6, 51.4, 51.5, 42.9, 51.5, 42.9, 42.5, 37.9, 37.1, 32.9, 30.4, 28.6, 27.7, 25.5; HPLC (Chiralcel AD-H, *n*-hexane: *i*-PrOH = 98:2, flow rate: 1.0 mL/min, λ = 210 nm), T_{major} = 36.7, T_{minor} = 30.3, 97% *ee*.

(*R*)-2-((*R*)-2-nitro-1-(thiophen-2-yl)ethyl)cyclohexan-1-one (16l).[27] The title compound **16l** was prepared from cyclohexanoneand 1-(2-thienyl)-2-nitroethene according to the general procedure of Michael addition. **16l** is white solid, 84% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37 (d, *J* = 1.0, 1H), 6.32–6.31 (m, 1H), 6.21–6.20 (m, 1H), 4.83–4.80 (m, 2H), 4.72–4.68 (m, 1H), 4.02–3.97 (m, 1H), 2.81–2.75 (m, 1H), 2.51–2.36 (m, 1H), 2.15–2.11 (m, 1H), 1.89–1.86 (m, 1H), 1.81–1.63 (m, 4H), 1.35–1.27 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 211.2, 151.4, 142.7, 110.7, 109.4, 77.7, 51.5, 43.0, 38.0, 32.9, 28.6, 25.5; HPLC (Chiralcel AS-H, *n*-hexane: *i*-PrOH = 80:20, flow rate: 0.8 mL/min, λ = 210 nm), T_{major} = 14.2, T_{minor} = 12.0, 93% *ee*.

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Notes and references

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*†Electronic Supplementary Information (ESI) available: ^{1}H and ^{13}C NMR spectra for compounds **2–11**, **2a-11a**, **14a-14r**, **16a-16n**; The spectra of chiral HPLC for compounds **14a-14r** and **16a-16n**. This material is available free of charge via the Internet at http://pubs.acs.org.*

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Organocatalytic Asymmetric Michael Addition of Aldehydes and Ketones to Nitroalkenes Catalyzed by Adamantoyl *L*-Prolinamide

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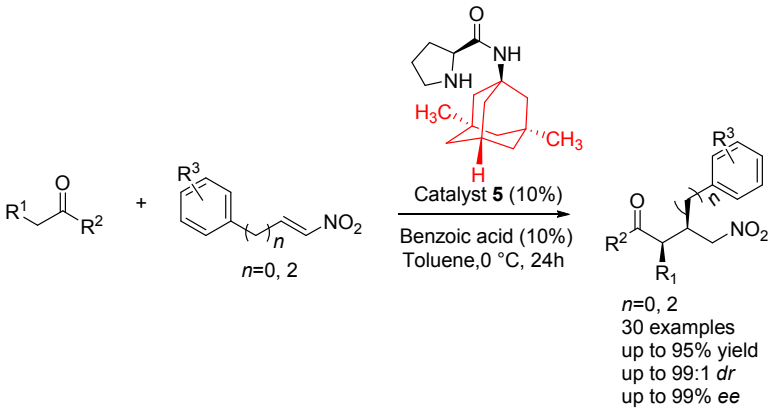

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