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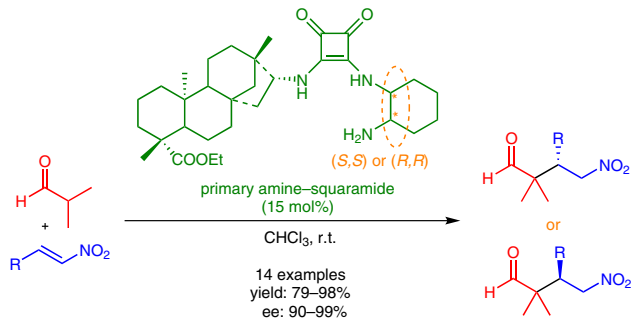
Chiral Primary Amine–Squaramide Catalyzed Highly Enantioselective Michael Addition of Isobutyraldehyde to Nitroolefins

Zhi-Wei Ma[*a]
Xiao-Feng Liu[b]
Bin Sun[b]
Xian-Hui Huang[b]
Jing-Chao Tao[*b]

[a] Department of Fundamental Courses, Henan University of Animal Husbandry and Economy, No. 2 Yingcai Street, Huiji District, Zhengzhou 450044, Henan, P. R. of China
mazhiwei1986@126.com
[b] College of Chemistry and Molecular Engineering, Zhengzhou University, No. 100 Science Avenue, High-Tech Zone, Zhengzhou 450001, Henan, P. R. of China
jctao@zzu.edu.cn



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Abstract Chiral primary amine–squaramides have not been extensively studied to date in the field of organocatalysis. In this paper, novel chiral squaramides derived from natural product stevioside were developed. Both enantiomers of a series of γ-nitroaldehydes were generated by using these squaramide catalysts for the Michael addition reaction of isobutyraldehyde to nitroolefins. This asymmetric reaction proceeded well to afford the desired products in high yields (up to 98%) with high to excellent enantioselectivities (up to 99% ee).

Key words primary amine–squaramide, isobutyraldehyde, nitroolefin, Michael addition, enantiomers

The Michael reaction promoted by organocatalysts is one of the most efficient and broadly applicable C–C bond forming reactions due to the value of the Michael adducts used as synthetic building blocks.[1] Since the pioneering work of List and Barbas in 2001,[2] there has been dramatic advance in developing more selective and efficient organocatalysts for this cornerstone transformation, and much significant progress has been made in recent years.[3]

Organocatalytic asymmetric Michael addition of unmodified aldehydes/ketones with nitroolefins to produce enantiomerically enriched Michael products has been explored extensively,[4] but only a few examples have been reported that use α,α-disubstituted aldehydes as Michael donors. It is therefore of great interest to develop new catalytic methods for this relatively underexplored transformation. On the other hand, many organocatalysts have been successfully used in the asymmetric Michael reaction of isobutyraldehyde to nitroalkenes,[4g,5] such as thioureas,[4g,5a–c] sulfamides,[5d] guanidines,[5e] and proline derivatives,[5f–i] but no similar enantioselective Michael reactions employing squaramide catalysts have been reported.

In 2008, the first report on employing a chiral squaramide in the conjugate addition reactions of 1,3-dicarbonyl compounds to β-nitrostyrenes by Rawal's group emerged.[6] After the Rawal's seminal work, chiral amine-squaramides have emerged as powerful hydrogen-bonding bifunctional organocatalysts not only for promoting simple carbon–carbon and carbon–heteroatom bond formation, but also for assisting various domino reactions, thus providing a rapid access to highly valuable enantioenriched molecules.[7]

As part of our ongoing interest in asymmetric organocatalysis,[4g,8] we have developed a highly enantioselective Michael addition of isobutyraldehyde to nitroolefins using isosteviol-derived chiral primary amine–thiourea **1** as catalyst (Figure 1).[4g] Considering that squaramides has become another complementary or even superior H-bond donor catalyst in asymmetric organocatalysis and encouraged by the rapid development in the field of asymmetric reactions using squaramides as catalysts, we envisioned that the newly designed isosteviol-derived squaramide catalysts, which were obtained by means of the replacement of the thiourea moiety with a squaramide moiety, could facilitate the Michael addition of isobutyraldehyde to nitroolefins, affording the expected optically active products.

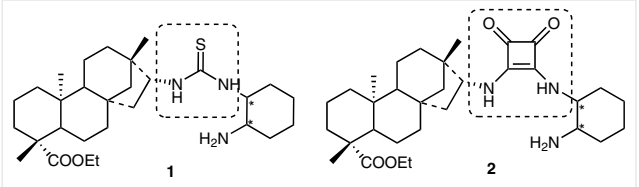
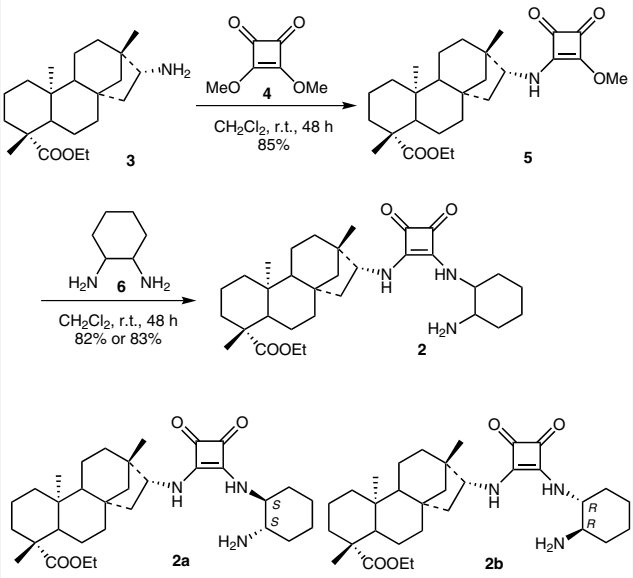


Figure 1 Isosteviol-derived thiourea **1** and squaramide **2**

Starting from commercially available natural product stevioside, amine **3** was readily prepared via hydrolyzation, esterification, oximation, and reduction reactions.[4g] Treatment of amine **3** with dimethyl squarate (**4**) in CH_2Cl_2 af-

forded mono-squaramide **5** in 85% yield. Consequently, chiral 1,2-cyclohexyldiamines (**6**) were then used in the second displacement reaction with mono-squaramide **5** to generate desired bifunctional squaramide catalysts **2a** or **2b** in good yields (82% for **2a** and 83% for **2b**) (Scheme 1).



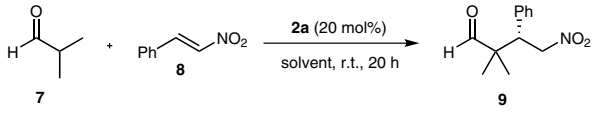
Scheme 1 Preparation of squaramides **2a** and **2b**

With these novel catalysts in hand, the effects of the squaramide catalysts were investigated. A model reaction of isobutyraldehyde to *trans*-β-nitrostyrene was performed in CH_2Cl_2 at room temperature in the presence of 20 mol% of squaramide catalysts (Table 1).

Gratifyingly, and as expected, the catalysts **2a** and **2b** were efficient and exhibited reversed senses of asymmetric induction, providing *S*-enriched and *R*-enriched adduct respectively (Table 1, entry 1 vs 2). These results indicate that both of the *S*,*S*-configuration of 1,2-diaminocyclohexane moiety and the *R*,*R*-configuration can well match the isosteviol scaffold of **2**, resulting in high yields (*S*-adduct, 90%; *R*-adduct, 90%) with high enantioselectivities (*S*-adduct, 92% ee; *R*-adduct, 93% ee). We then simply examined the effects of other conditions on the reaction using squaramide **2a**.

A substantial change of the solvent has an impact effect on the catalytic activity and the stereoselection. We were delighted to observe that both the chemical yield and stereoselectivity increased with $CHCl_3$ as the solvent (94% yield, 94% ee) (Table 1, entry 3). The Michael product was obtained with poor results when the reaction was carried out in Et_2O and MeCN (entries 4 and 5). The reaction did not occur in DMF, DMSO and MeOH (entries 6, 7, and 8). Although 80% yield of the product was obtained when water was used as reaction medium, the enantioselectivity was low (entry 9). The reaction in brine also gave low conversion and enantioselectivity (34% yield, 42% ee) (entry 10).

Table 1 Screening of Catalysts and Solvents[a]

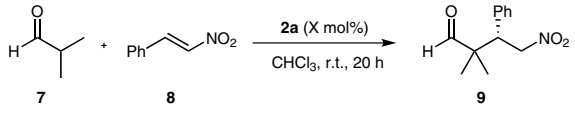


Entry	Catalyst	Solvent	Yield (%)[b]	ee (%)[c]
1	**2a**	CH_2Cl_2	90	92 (*S*)
2	**2b**	CH_2Cl_2	90	93 (*R*)
3	**2a**	$CHCl_3$	94	94 (*S*)
4	**2a**	Et_2O	32	43 (*S*)
5	**2a**	MeCN	57	67 (*S*)
6	**2a**	DMF	nr[d]	nd[e]
7	**2a**	DMSO	nr[d]	nd[e]
8	**2a**	MeOH	nr[d]	nd[e]
9	**2a**	H_2O	80	39 (*S*)
10	**2a**	brine	34	42 (*S*)

[a] Unless otherwise specified, all reactions were carried out using isobutyraldehyde (**7**; 0.40 mmol), *trans*-β-nitrostyrene (**8**; 0.20 mmol) and 20 mol% catalyst in 1.0 mL solvent at r.t. for 20 h.
[b] Isolated yield.
[c] Determined by chiral HPLC analysis.
[d] No reaction.
[e] Not determined.

Decreasing the catalyst loading from 20 mol% to 15 mol% afforded higher yield and enantioselectivity (Table 2, entries 1 vs. 2). However, a further decrease in the catalyst loading to 10 mol% resulted in an obvious decrease in the yield of the reaction (entry 3). It should be noted that decreasing isobutyraldehyde dosage resulted in decreased yield (entry 4). Moreover, when the reaction was conducted

Table 2 Optimization of the Reaction Conditions[a]



Entry	X (mol%)	Yield (%)[b]	ee (%)[c]
1	20	94	94 (*S*)
2	15	96	95 (*S*)
3	10	59	93 (*S*)
4[d]	15	87	93 (*S*)
5[e]	15	61	95 (*S*)
6[f]	15	95	98 (*R*)

[a] Unless otherwise specified, all reactions were carried out using isobutyraldehyde (**7**; 0.40 mmol), *trans*-β-nitrostyrene (**8**; 0.20 mmol) and X mol% **2a** in 1.0 mL $CHCl_3$ at r.t. for 20 h.
[b] Isolated yield.
[c] Determined by chiral HPLC analysis.
[d] Isobutyraldehyde used: 0.30 mmol.
[e] The reaction was conducted at 0 °C.
[f] Catalyst **2b** was used.

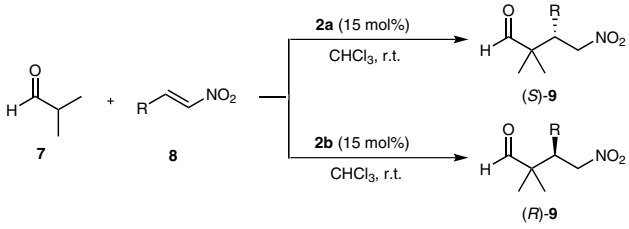
at 0 °C, though the enantioselectivity was still 95% ee, only moderate yield could be obtained (entry 5). With optimal reaction conditions established, the conjugate reaction with squaramide **2b** was carried out. The use of squaramide catalyst **2b** provided product with still high yield (95%) and better enantioselectivity (98% ee), as well as a reversal of the absolute configuration of **9a** (entry 6).

Under the optimized conditions, we further studied the generality of the asymmetric Michael addition of isobutyraldehyde **7** to a variety of nitroolefins **8a–i** in the presence of squaramide catalyst **2a** and **2b**, and the results are summarized in Table 3. Both catalysts afforded the products in high yields with high to excellent enantioselectivity in the asymmetric conjugate addition reaction. Generally, both enantiomers of the corresponding products could be achieved in almost the same yield and enantiomeric excess with catalyst **2a** and **2b**, respectively. The use of catalyst **2a** gave the conjugate adducts **9a–i** with *S*-configuration, whereas catalyst **2b** afforded the *R*-configuration. It appears that higher enantioselectivities were obtained using catalyst **2b**. This is probably due to the more appropriate match of the *R*,*R*-configuration of 1,2-diaminocyclohexane moiety and the isosteviol scaffold, although both configurations can well match the isosteviol scaffold. These results indicated that the position and the electronic property of the substituent on the aromatic ring had a limited effect on both yield and enantioselectivity (entries 1–10). Heteroaromatic nitroolefins were also suitable substrates, and the desired products were obtained with excellent yields and enantioselectivities (entries 11–13). Conjugated nitroalkene **8n** as an acceptor worked well with isobutyraldehyde to give good to high yields and enantioselectivities (entry 14). However, these catalysts could not catalyze the asymmetric addition of isobutyraldehyde to aliphatic nitroolefins. It is worth mentioning that the results promoted by squaramide **2a** and **2b** are better than those by thiourea catalyst **1**.[4g]

To further explore the scope of the reaction, the Michael addition of isobutyraldehyde to *N*-phenylmaleimide was tested and the results are displayed in Scheme 2. *N*-Phenylmaleimide also proved a good substrate and furnished the corresponding adducts in excellent yields and enantioselectivities.

On the basis of the experimental results described above, taking squaramide **2a** as an example, we propose the plausible transition state model, which reasonably explains the absolute configuration of the Michael adducts. As depicted in Figure 2, similar to the action of primary amine–thiourea catalyst, the isobutyraldehyde is activated by the primary amine through the enamine intermediate, and the nitrostyrene is directed and activated by the squaramide moiety of the catalyst **2a** through H-bond interactions simultaneously. The nitrostyrene is attacked from the *Re*-face leading to the formation of addition product **9** *S*-configuration.

Table 3 Substrate Scope of the Catalytic Asymmetric Michael Addition of Isobutyraldehyde to Nitroolefins[a]



Entry	R	Catalyst	Product **9**	Yield (%)[b]	ee (%)[c]
1	Ph (**8a**)	**2a**	(*S*)-**9a**	96	95
		2b	(*R*)-**9a**	95	96
2	4-FC_6H_4 (**8b**)	**2a**	(*S*)-**9b**	92	95
		2b	(*R*)-**9b**	92	92
3	4-ClC_6H_4 (**8c**)	**2a**	(*S*)-**9c**	91	96
		2b	(*R*)-**9c**	92	99
4	4-BrC_6H_4 (**8d**)	**2a**	(*S*)-**9d**	89	96
		2b	(*R*)-**9d**	90	99
5	3-$O_2NC_6H_4$ (**8e**)	**2a**	(*S*)-**9e**	97	96
		2b	(*R*)-**9e**	97	99
6	4-$O_2NC_6H_4$ (**8f**)	**2a**	(*S*)-**9f**	90	96
		2b	(*R*)-**9f**	91	99
7	2-$MeOC_6H_4$ (**8g**)	**2a**	(*S*)-**9g**	88	95
		2b	(*R*)-**9g**	90	96
8	4-$MeOC_6H_4$ (**8h**)	**2a**	(*S*)-**9h**	85	94
		2b	(*R*)-**9h**	89	97
9	1-naphthyl (**8i**)	**2a**	(*S*)-**9i**	79	95
		2b	(*R*)-**9i**	82	97
10	2-naphthyl (**8j**)	**2a**	(*S*)-**9j**	81	97
		2b	(*R*)-**9j**	80	96
11	2-furyl (**8k**)	**2a**	(*S*)-**9k**	97	93
		2b	(*R*)-**9k**	98	94
12	2-thienyl (**8l**)	**2a**	(*S*)-**9l**	98	92
		2b	(*R*)-**9l**	96	95
13	5-Cl-2-thienyl (**8m**)	**2a**	(*S*)-**9m**	95	90
		2b	(*R*)-**9m**	98	97
14	PhCH=CH (**8n**)	**2a**	(*S*)-**9n**	86	95
		2b	(*R*)-**9n**	84	97

[a] Unless otherwise specified, all reactions were carried out using isobutyraldehyde (**7**; 0.40 mmol), *trans*-β-nitroalkene (**8**; 0.20 mmol) and 15 mol% **2a** or **2b** in 1.0 mL $CHCl_3$ at r.t. for 20–36 h.
[b] Isolated yield.
[c] Determined by chiral HPLC analysis.

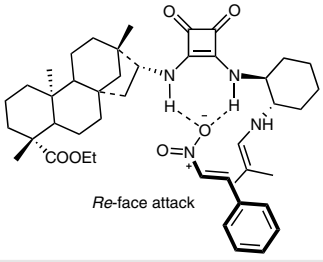
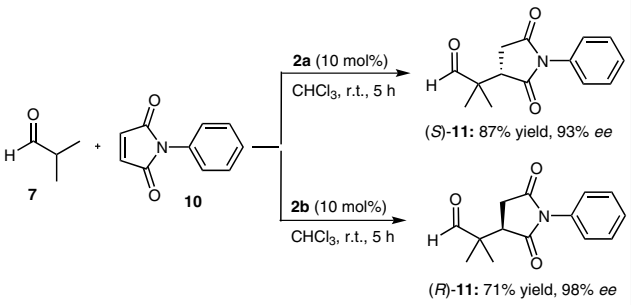


Figure 2 Proposed transition state



Scheme 2 Michael reaction of isobutyraldehyde to *N*-phenylmaleimide

In summary, we have demonstrated for the first time that novel chiral primary amine–squaramide organocatalysts derived from commercially available natural product stevioside can promote the asymmetric conjugate addition of isobutyraldehyde to various nitroolefins at room temperature in high yields (up to 98%) with high to excellent enantioselectivities (up to 99% ee). Furthermore, both enantiomers of the corresponding products can be achieved with almost the same enantiomeric excess using the chiral squaramide organocatalysts **2a** and **2b** simply by changing the configuration of 1,2-diaminocyclohexane moiety. This finding provides a novel approach to obtain both enantiomers of γ-nitroaldehydes. Further investigation of the efficacy of these organocatalysts in other catalytic asymmetric reactions is under way in our laboratory.

All chemicals were used as received unless otherwise noted. Reagent grade solvents were redistilled prior to use. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DPX 400 NMR spectrometer with TMS as internal reference. IR spectra were recorded on a Thermo Nicolet IR200 unit. ESI mass spectra were recorded on an HPLC Q-Exactive HRMS spectrometer (Thermo, USA) by using MeOH as mobile phase. Chromatography was performed on silica gel (200–300 mesh). Melting points were determined with an aXT5 A apparatus and are uncorrected. Optical rotations were determined with a PerkinElmer 341 polarimeter. Enantiomeric excesses were determined by chiral HPLC at r.t. with use of a Labtech 2006 pump, a Labtech UV600 ultra detector, and Chiralcel OD-H (4.6 mm × 250 mm) columns. The absolute configurations of the known adducts **9a–l**, **n**, and **11** were assigned by HPLC and specific rotation comparisons with the reported data, those of the unknown adduct **9m** was assigned by analogy.

Mono-Squaramide 5

Amine compound **3** (0.35 g, 1 mmol) in CH_2Cl_2 (10 mL) was added dropwise to a solution of dimethyl squarate (**4**; 0.14 g, 1 mmol) in CH_2Cl_2 (10 mmol). The reaction mixture was stirred for 48 h at r.t. TLC indicated that the reaction was complete. The solvent was removed and the residue was purified by column chromatography (silica gel, EtOAc/PE = 1:5) to afford the pure product (0.39 g, 85%) as a white solid; mp 196.7–197.8 °C; $[\alpha]_D^{20}$ –57.7 (*c* 1.0, $CHCl_3$).

IR (KBr): 713, 832, 927, 1025, 1091, 1148, 1178, 1218, 1366, 1440, 1495, 1587, 1616, 1701, 1719, 1797, 2847, 2932, 3174 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ = 0.72 (s, 3 H), 0.85–0.88 (m, 1 H), 0.91 (s, 3 H), 0.94–1.13 (m, 4 H), 1.17 (s, 3 H), 1.25 (t, *J* = 7.2 Hz, 4 H), 1.32–1.42 (m, 4 H), 1.55–1.59 (m, 2 H), 1.63–1.73 (m, 3 H), 1.76–1.93 (m, 4 H), 2.16 (d, *J* = 13.2 Hz, 1 H), 3.73 (dd, *J* = 7.2, 17.2 Hz, 1 H), 4.03–4.15 (m, 2 H), 4.40 (d, *J* = 10.4 Hz, 3 H), 5.93 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ = 13.4, 14.1, 18.9, 24.5, 29.0, 33.3, 37.9, 39.8, 41.2, 42.4, 55.4, 55.5, 56.9, 60.0, 60.5, 62.8, 63.5, 177.3, 183.2, 189.2.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{27}H_{40}NO_5$: 458.2906; found: 458.2908.

Amine-Squaramide Catalysts 2a,b

The mono-squaramide **5** (0.46 g, 1 mmol) was added to a stirred solution of (*S*,*S*)- or (*R*,*R*)-cyclohexane-1,2-diamine **6** (0.11 g, 1 mmol) in anhyd CH_2Cl_2 (25 mL). The reaction mixture was stirred at r.t. overnight. TLC indicated that the reaction was complete. The solvent was removed under reduced pressure and the crude product was purified by column chromatography (silica gel, MeOH/CH_2Cl_2 = 1:10).

Catalyst 2a

White solid; yield: 0.44 g (82%); mp 174.3–175.1 °C; $[\alpha]_D^{20}$ –255.6 (*c* 1.0, $CHCl_3$).

IR (KBr): 974, 1029, 1096, 1128, 1150, 1181, 1223, 1375, 1467, 1529, 1585, 1669, 1722, 1794, 2849, 2937, 3255 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ = 0.71 (s, 3 H), 0.84–0.90 (m, 1 H), 0.94 (s, 3 H), 0.97–1.05 (m, 3 H), 1.09 (d, *J* = 11.2 Hz, 1 H), 1.16 (s, 3 H), 1.24 (t, *J* = 6.8 Hz, 4 H), 1.28–1.44 (m, 8 H), 1.54–2.01 (m, 13 H), 2.05 (d, *J* = 11.2 Hz, 1 H), 2.63 (s, 1 H), 2.81 (s, 3 H), 3.62 (s, 1 H), 4.00–4.13 (m, 2 H), 4.28 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ = 13.4, 14.2, 18.9, 20.4, 21.7, 24.6, 28.9, 34.0, 38.0, 39.9, 41.3, 42.3, 43.7, 55.6, 56.9, 60.0, 62.8, 177.5, 182.1.

HRMS: *m*/*z* [M+ H]$^+$ calcd for $C_{32}H_{50}N_3O_4$: 540.3801; found: 540.3801.

Catalyst 2b

White solid; yield: 0.45 g (83%); mp 175.8–176.4 °C; $[\alpha]_D^{20}$ +52.6 (*c* 1.0, $CHCl_3$).

IR (KBr): 853, 974, 1029, 1095, 1150, 1181, 1223, 1375, 1467, 1527, 1584, 1670, 1721, 1793, 2849, 2937, 3267 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ = 0.79 (s, 3 H), 0.85–0.88 (m, 1 H), 0.92 (s, 3 H), 0.95–1.06 (m, 3 H), 1.11 (d, *J* = 11.6 Hz, 1 H), 1.17 (s, 3 H), 1.23 (t, *J* = 6.8 Hz, 4 H), 1.31–1.45 (m, 7 H), 1.56–1.63 (m, 4 H), 1.70–2.06 (m, 10 H), 2.15 (d, *J* = 13.2 Hz, 1 H), 2.71 (m, 1 H), 3.71–3.73 (m, 1 H), 4.00–4.12 (m, 3 H), 4.29–4.30 (m, 2 H), 7.72 (s, 1 H), 8.00 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ = 13.4, 14.1, 18.9, 20.4, 21.7, 24.4, 24.6, 29.0, 33.6, 38.0, 38.1, 39.8, 41.3, 42.2, 43.7, 54.8, 55.6, 59.9, 63.0, 177.5, 182.0.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{32}H_{50}N_3O_4$: 540.3801; found: 540.3803.

Asymmetric Michael Reactions; General Procedure

Isobutyraldehyde (**7**; 29 mg, 0.40 mmol) was added to a mixture of a catalyst **2a** or **2b** (15 mol%) and a nitroalkene **8** (0.20 mmol) in $CHCl_3$ (1.0 mL). The reaction mixture was stirred at r.t. for the time required. After the nitroalkene had been consumed (TLC), the mixture was subjected to TLC on silica gel (EtOAc/PE = 1:2) to afford the pure desired

Michael product **9**. The enantiomeric excesses of the products **9** were determined by chiral HPLC analysis with Chiralcel OD-H columns (Table 3).

Only the Michael addition products obtained using the catalyst **2a** are listed below. For the yields and ee values of the Michael addition products prepared using the catalyst **2b**, see Table 3.

(*S*)-2,2-Dimethyl-4-nitro-3-phenylbutanal [(*S*)-9a][5f]

Light yellow oil; yield: 42.4 mg (96%); $[\alpha]_D^{20}$ –7.8 (*c* 1.0, $CHCl_3$); 95% ee.

HPLC: Chiralcel OD-H (hexanes/*i*-PrOH = 80:20, flow rate = 0.7 mL/min, λ = 254 nm); t_R = 18.7 min (minor), 27.3 min (major).

IR (KBr): 530, 669, 721, 786, 839, 902, 1014, 1093, 1222, 1362, 1420, 1557, 1636, 1714, 2850, 2925, 2965, 3003, 3413 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$/TMS): δ = 1.02 (s, 3 H, CH_3), 1.15 (s, 3 H, CH_3), 3.78–3.82 (dd, *J* = 4.2, 11.3 Hz, 1 H, CH), 4.69–4.73 (dd, *J* = 4.2, 13.1 Hz, 1 H, CH_2), 4.84–4.91 (dd, *J* = 11.4, 12.9 Hz, 1 H, CH_2), 7.21–7.37 (m, 5 H, ArH), 9.54 (s, 1 H, CHO).

^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ = 18.9, 21.7, 48.2, 48.5, 76.3, 128.2, 128.7, 129.1, 135.4, 204.3.

HRMS: *m*/*z* [M – H]$^-$ calcd for $C_{12}H_{14}NO_3$: 220.0979; found: 220.0977.

(*S*)-3-(4-Fluorophenyl)-2,2-dimethyl-4-nitrobutanal [(*S*)-9b][5b]

Light yellow oil; yield: 44.0 mg (92%); $[\alpha]_D^{20}$ –1.6 (*c* 1.0, $CHCl_3$); 95% ee.

HPLC: Chiralcel OD-H (hexanes/*i*-PrOH = 80:20, flow rate = 0.7 mL/min, λ = 254 nm); t_R = 16.0 min (minor), 29.4 min (major).

IR (KBr): 530, 755, 845, 902, 1092, 1165, 1222, 1361, 1422, 1512, 1557, 1604, 1713, 2850, 2925, 2968, 3003, 3412 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$/TMS): δ = 1.01 (s, 3 H, CH_3), 1.13 (s, 3 H, CH_3), 3.77–3.81 (dd, *J* = 4.0, 11.6 Hz, 1 H, CH), 4.67–4.72 (dd, *J* = 4.0, 12.8 Hz, 1 H, CH_2), 4.80–4.86 (dd, *J* = 11.6, 12.8 Hz, 1 H, CH_2), 7.01–7.05 (m, 2 H, ArH), 7.17–7.21 (m, 2 H, ArH), 9.51 (s, 1 H, CHO).

^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ = 18.9, 21.7, 47.8, 48.2, 76.4, 115.7 (d, *J* = 21.8 Hz), 130.7 (d, *J* = 8.0 Hz), 131.2 (d, *J* = 3.5 Hz), 162.4 (d, *J* = 246.0 Hz), 204.1.

HRMS: *m*/*z* [M – H]$^-$ calcd for $C_{12}H_{13}FNO_3$: 238.0885; found: 238.0883.

(*S*)-3-(4-Chlorophenyl)-2,2-dimethyl-4-nitrobutanal [(*S*)-9c][5f]

Light yellow solid; yield: 46.4 mg (91%); mp 62–63 °C; $[\alpha]_D^{20}$ –2.1 (*c* 1.0, $CHCl_3$); 96% ee.

HPLC: Chiralcel OD-H (hexanes/*i*-PrOH = 80:20, flow rate = 0.7 mL/min, λ = 254 nm); t_R = 17.7 min (minor), 28.2 min (major).

IR (KBr): 530, 665, 721, 786, 839, 883, 902, 1014, 1092, 1221, 1361, 1420, 1493, 1557, 1639, 1714, 2850, 2925, 2965, 3003, 3413 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$/TMS): δ = 1.00 (s, 3 H, CH_3), 1.12 (s, 3 H, CH_3), 3.76–3.80 (dd, *J* = 4.0, 11.2 Hz, 1 H, CH), 4.67–4.72 (dd, *J* = 4.0, 12.8 Hz, 1 H, CH_2), 4.80–4.86 (dd, *J* = 11.6, 13.2 Hz, 1 H, CH_2), 7.14–7.17 (d, *J* = 8.4 Hz, 2 H, ArH), 7.30–7.32 (d, *J* = 8.4 Hz, 2 H, ArH), 9.49 (s, 1 H, CHO).

^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ = 18.9, 21.7, 47.8, 48.2, 76.2, 129.0, 130.4, 134.0, 134.1, 203.9.

HRMS: *m*/*z* [M – H]$^-$ calcd for $C_{12}H_{13}ClNO_3$: 254.0589; found: 254.0589.

(*S*)-3-(4-Bromophenyl)-2,2-dimethyl-4-nitrobutanal [(*S*)-9d][5f]

White solid; yield: 53.2 mg (89%); mp 89–90 °C; $[\alpha]_D^{20}$ –3.7 (*c* 1.0, $CHCl_3$); 96% ee.

HPLC: Chiralcel OD-H (hexanes/*i*-PrOH = 80:20, flow rate = 0.7 mL/min, λ = 254 nm); t_R = 20.1 min (minor), 29.5 min (major).

IR (KBr): 530, 650, 719, 757, 782, 836, 884, 1009, 1077, 1091, 1221, 1361, 1415, 1435, 1490, 1556, 1636, 1413, 2850, 2925, 2970, 3000, 3412 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$/TMS): δ = 1.00 (s, 3 H, CH_3), 1.12 (s, 3 H, CH_3), 3.74–3.78 (dd, *J* = 4.0, 11.2 Hz, 1 H, CH), 4.67–4.71 (dd, *J* = 4.0, 13.2 Hz, 1 H, CH_2), 4.79–4.85 (dd, *J* = 11.2, 13.2 Hz, 1 H, CH_2), 7.08–7.11 (d, *J* = 8.4 Hz, 2 H, ArH), 7.46–7.48 (d, *J* = 8.4 Hz, 2 H, ArH), 9.49 (s, 1 H, CHO).

^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ = 18.9, 21.8, 47.9, 48.1, 76.1, 122.3, 130.8, 131.9, 134.5, 203.9.

HRMS: *m*/*z* [M – H]$^-$ calcd for $C_{12}H_{13}BrNO_3$: 298.0084; found: 298.0085.

(*S*)-3-(3-Nitrophenyl)-2,2-dimethyl-4-nitrobutanal [(*S*)-9e][5b]

Light yellow oil; yiel: 51.6 mg (97%); $[\alpha]_D^{20}$ +3.3 (*c* 1.0, $CHCl_3$); 96% ee.

HPLC: Chiralcel OD-H (hexanes/*i*-PrOH = 80:20, flow rate = 0.7 mL/min, λ = 254 nm); t_R = 30.0 min (minor), 49.6 min (major).

IR (KBr): 530, 675, 698, 737, 758, 792, 813, 903, 1092, 1221, 1360, 1421, 1534, 1557, 1636, 1713, 2853, 2924, 2965, 3003, 3412 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$/TMS): δ = 1.06 (s, 3 H, CH_3), 1.18 (s, 3 H, CH_3), 3.94–3.98 (dd, *J* = 4.0, 11.6 Hz, 1 H, CH), 4.77–4.81 (dd, *J* = 4.0, 13.6 Hz, 1 H, CH_2), 4.92–4.98 (dd, *J* = 11.6, 13.6 Hz, 1 H, CH_2), 7.54–7.58 (t, *J* = 8.0 Hz, 1 H, ArH), 7.59–7.62 (m, 1 H, ArH), 8.14 (t, *J* = 1.6 Hz, 1 H, ArH), 8.18–8.20 (m, 1 H, ArH), 9.51 (s, 1 H, CHO).

^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ = 19.0, 21.8, 48.0, 48.3, 75.9, 123.9, 129.8, 135.4, 138.1, 148.3, 203.2.

HRMS: *m*/*z* [M – H]$^-$ calcd for $C_{12}H_{13}N_2O_5$: 265.0830; found: 265.0831.

(*S*)-3-(4-Nitrophenyl)-2,2-dimethyl-4-nitrobutanal [(*S*)-9f][5c]

Light yellow solid; yield: 47.9 mg (90%); mp 58–59 °C; $[\alpha]_D^{20}$ –10.1 (*c* 1.0, $CHCl_3$); 96% ee.

HPLC: Chiralcel OD-H (hexanes/*i*-PrOH = 80:20, flow rate = 0.7 mL/min, λ = 254 nm); t_R = 37.9 min (minor), 61.0 min (major).

IR (KBr): 530, 665, 721, 786, 839, 883, 902, 1014, 1092, 1221, 1361, 1420, 1493, 1639, 1714, 2850, 2925, 2965, 3003, 3413 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$/TMS): δ = 1.05 (s, 3 H, CH_3), 1.17 (s, 3 H, CH_3), 3.92–3.96 (dd, *J* = 4.0, 11.6 Hz, 1 H, CH), 4.76–4.81 (dd, *J* = 4.0, 13.2 Hz, 1 H, CH_2), 4.90–4.96 (dd, *J* = 11.6, 13.6 Hz, 1 H, CH_2), 7.43–7.45 (d, *J* = 8.8 Hz, 2 H, ArH), 8.20–8.22 (d, *J* = 8.8 Hz, 2 H, ArH), 9.49 (s, 1 H, CHO).

^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ = 19.1, 21.9, 48.1, 48.2, 75.8, 123.9, 130.2, 143.4, 147.7, 203.2.

HRMS: *m*/*z* [M – H]$^-$ calcd for $C_{12}H_{13}N_2O_5$: 265.0830; found: 265.0833.

(*S*)-3-(2-Methoxyphenyl)-2,2-dimethyl-4-nitrobutanal [(*S*)-9g][5f]

Light yellow oil; yield: 44.2 mg (88%); $[\alpha]_D^{20}$ +16.4 (*c* 1.0, $CHCl_3$); 95% ee.

HPLC: Chiralcel OD-H (hexanes/*i*-PrOH = 80:20, flow rate = 0.7 mL/min, λ = 254 nm); t_R = 12.0 min (minor), 19.1 min (major).

IR (KBr): 530, 733, 760, 785, 903, 982, 1027, 1092, 1222, 1362, 1420, 1556, 1636, 1714, 2850, 2923, 2965, 3004, 3410 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ = 1.05 (s, 3 H, CH_3), 1.10 (s, 3 H, CH_3), 3.82 (s, 3 H, OCH_3), 4.09–4.15 (dd, *J* = 7.2, 14.0 Hz, 1 H, CH), 4.71–4.75 (dd, *J* = 4.4, 12.8 Hz, 1 H, CH_2), 4.87–4.93 (dd, *J* = 10.8, 12.8 Hz, 1 H, CH_2), 6.88–6.95 (m, 2 H, ArH), 7.12–7.14 (dd, *J* = 1.2, 7.2 Hz, 1 H, ArH), 7.24–7.29 (m, 1 H, ArH), 9.51 (s, 1 H, CHO).

^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ = 20.0, 21.0, 48.4, 55.3, 60.4, 75.8, 111.3, 120.8, 124.0, 129.3, 157.4, 204.1.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{13}H_{17}NO_4Na$: 274.1055; found: 274.1045.

(*S*)-3-(4-Methoxyphenyl)-2,2-dimethyl-4-nitrobutanal [(*S*)-9h][5f]

Light yellow solid; yield: 42.7 mg (85%); mp 59–60 °C; $[\alpha]_D^{20}$ +2.0 (*c* 1.0, $CHCl_3$); 94% ee.

HPLC: Chiralcel OD-H (hexanes/*i*-PrOH = 80:20, flow rate = 0.7 mL/min, λ = 254 nm); t_R = 20.8 min (minor), 31.2 min (major).

IR (KBr): 528, 755, 845, 897, 1091, 1162, 1217, 1360, 1418, 1511, 1557, 1604, 1713, 2850, 2921, 2968, 3004, 3406 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ = 1.00 (s, 3 H, CH_3), 1.12 (s, 3 H, CH_3), 3.71–3.75 (dd, *J* = 4.0, 11.2 Hz, 1 H, CH), 3.78 (s, 3 H, OCH_3), 4.64–4.68 (dd, *J* = 4.0, 13.2 Hz, 1 H, CH_2), 4.78–4.84 (dd, *J* = 11.6, 12.8 Hz, 1 H, CH_2), 6.84–6.86 (d, *J* = 8.4 Hz, 2 H, ArH), 7.11–7.13 (d, *J* = 8.4 Hz, 2 H, ArH), 9.52 (s, 1 H, CHO).

^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ = 18.9, 21.6, 47.8, 48.4, 76.5, 114.1, 127.1, 130.1, 159.3, 204.5.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{13}H_{17}NO_4Na$: 274.1055; found: 274.1043.

(*S*)-2,2-Dimethyl-3-(naphthalene-1-yl)-4-nitrobutanal [(*S*)-9i][5c]

Light yellow solid; yield: 42.8 mg (79%); mp 105–106 °C; $[\alpha]_D^{20}$ –77.4 (*c* 1.0, $CHCl_3$); 95% ee.

HPLC: Chiralcel OD-H (hexanes/*i*-PrOH = 80:20, flow rate = 0.7 mL/min, λ = 254 nm); t_R = 30.2 min (minor), 57.6 min (major).

IR (KBr): 497, 781, 795, 876, 1108, 1377, 1432, 1468, 1550, 1599, 1716, 2715, 2814, 2969, 3438 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ = 0.94 (s, 3 H, CH_3), 1.18 (s, 3 H, CH_3), 4.83–4.87 (dd, *J* = 1.6, 10.4 Hz, 1 H, CH), 4.90–5.02 (m, 2 H, CH_2), 7.36–7.52 (m, 3 H, ArH), 7.55–7.59 (t, *J* = 8 Hz, 1 H, ArH), 7.79–7.86 (dd, *J* = 8, 21.2 Hz, 2 H, ArH), 8.21–8.24 (d, *J* = 8.8 Hz, 1 H, ArH), 9.57 (s, 1 H, CHO).

^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ = 18.9, 21.7, 40.3, 49.1, 77.0, 123.1, 124.9, 125.0, 126.0, 126.8, 128.8, 129.1, 132.3, 132.9, 134.1, 204.5.

HRMS: *m*/*z* [M – H]$^-$ calcd for $C_{16}H_{16}NO_3$: 270.1136; found: 270.1136.

(*S*)-2,2-Dimethyl-3-(naphthalene-2-yl)-4-nitrobutanal [(*S*)-9j][5a]

Light yellow oil; yield: 43.9 mg (81%); $[\alpha]_D^{20}$ +3.1 (*c* 1.0, $CHCl_3$); 97% ee.

HPLC: Chiralcel OD-H (hexanes/*i*-PrOH = 80:20, flow rate = 0.85 mL/min, λ = 254 nm); t_R = 31.3 min (minor), 63.8 min (major).

IR (KBr): 530, 752, 787, 827, 902, 1092, 1221, 1361, 1421, 1556, 1636, 1714, 2853, 2923, 2962, 3003, 3413 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ = 1.03 (s, 3 H, CH_3), 1.17 (s, 3 H, CH_3), 3.93–3.97 (dd, *J* = 4.0, 11.2 Hz, 1 H, CH), 4.74–4.79 (dd, *J* = 4.0, 12.8 Hz, 1 H, CH_2), 4.95–5.01 (dd, *J* = 11.2, 12.8 Hz, 1 H, CH_2), 7.30–7.33 (dd, *J* = 1.6 Hz, 1 H, ArH), 7.46–7.51 (m, 2 H, ArH), 7.66 (s, 1 H, ArH), 7.79–7.82 (m, 3 H, ArH), 9.55 (s, 1 H, CHO).

^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ = 19.1, 21.8, 48.5, 48.7, 76.4, 126.4, 126.6, 127.6, 127.9, 128.4, 128.5, 132.9, 133.1, 204.3.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{17}NO_3Na$: 294.1106; found: 294.1094.

(*S*)-3-(Furan-2-yl)-2,2-dimethyl-4-nitrobutanal [(*S*)-9k][5b]

Light yellow oil; yield: 40.9 mg, 97% yield; $[\alpha]_D^{20}$ +20.1 (*c* 1.0, $CHCl_3$); 93% ee.

HPLC: Chiralcel OD-H (hexanes/*i*-PrOH = 80:20, flow rate = 0.7 mL/min, λ = 254 nm); t_R = 12.5 min (minor), 20.2 min (major).

IR (KBr): 530, 665, 721, 786, 839, 883, 902, 1014, 1092, 1221, 1361, 1420, 1493, 1557, 1639, 1714, 2850, 2925, 2968, 3003, 3413 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ = 1.05 (s, 3 H, CH_3), 1.18 (s, 3 H, CH_3), 3.91–3.94 (dd, *J* = 3.8, 7.2 Hz, 1 H, CH), 4.57–4.61 (dd, *J* = 3.9, 9.0 Hz, 1 H, CH_2), 4.73–4.79 (dd, *J* = 3.1, 12.9 Hz, 1 H, CH_2), 6.22 (d, *J* = 3.2 Hz, 1 H, ArH), 6.31–6.32 (dd, *J* = 1.9, 3.2 Hz, 1 H, ArH), 7.37 (d, *J* = 1.2 Hz, 1 H, ArH), 9.52 (s, 1 H, CHO).

^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ = 19.1, 21.2, 42.3, 48.2, 74.9, 109.7, 110.4, 142.8, 149.8, 203.5.

HRMS: *m*/*z* [M – H]$^-$ calcd for $C_{10}H_{12}NO_4$: 210.0772; found: 210.0766.

(*S*)-2,2-Dimethyl-4-nitro-3-(thiophen-2-yl)butanal [(*S*)-9l][5a]

Light yellow oil; yield:44.5 mg (98%); $[\alpha]_D^{20}$ –10.2 (*c* 1.0, $CHCl_3$); 92% ee.

HPLC: Chiralcel OD-H (hexanes/*i*-PrOH = 80:20, flow rate = 0.7 mL/min, λ = 254 nm); t_R = 17.3 min (minor), 29.6 min (major).

IR (KBr): 530, 665, 758, 806, 902, 999, 1092, 1221, 1361, 1422, 1558, 1636, 1713, 2853, 2925, 2965, 3004, 3413 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ = 1.12 (s, 3 H, CH_3), 1.20 (s, 3 H, CH_3), 3.96–4.00 (dd, *J* = 4.4, 9.2 Hz, 1 H, CH), 4.61–4.70 (m, 2 H, CH_2), 6.71 (d, *J* = 4 Hz, 1 H, ArH), 6.77 (d, *J* = 4 Hz, 1 H, ArH), 9.49 (s, 1 H, CHO).

^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ = 19.1, 21.6, 44.7, 48.4, 77.4, 125.9, 127.5, 130.0, 136.8, 203.3.

HRMS: *m*/*z* [M – H]$^-$ calcd for $C_{10}H_{12}NO_3S$: 226.0543; found: 226.0540.

(*S*)-3-(5-Chlorothiphen-2-yl)-2,2-Dimethyl-4-nitrobutanal (*S*)-9m

Light yellow oil; yield: 49.6 mg (95%); $[\alpha]_D^{20}$ +13.1 (*c* 1.0, $CHCl_3$); 90% ee.

HPLC: Chiralcel OD-H (hexanes/*i*-PrOH = 80:20, flow rate = 0.7 mL/min, λ = 254 nm); t_R = 16.8 min (minor), 29.6 min (major).

IR (KBr): 530, 665, 758, 806, 902, 999, 1092, 1221, 1361, 1422, 1558, 1636, 1713, 2853, 2925, 2965, 3004, 3413 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ = 1.12 (s, 3 H, CH_3), 1.20 (s, 3 H, CH_3), 3.96–4.00 (dd, *J* = 4.4, 9.2 Hz, 1 H, CH), 4.61–4.70 (m, 2 H, CH_2), 6.71 (d, *J* = 4 Hz, 1 H, ArH), 6.77 (d, *J* = 4 Hz, 1 H, ArH), 9.49 (s, 1 H, CHO).

^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ = 19.1, 21.6, 44.7, 48.4, 77.4, 125.9, 127.5, 130.0, 136.8, 203.3.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{10}H_{12}ClNO_3SNa$: 284.0124; found: 284.0113.

(*S*,*E*)-2,2-Dimethyl-3-(nitromethyl)-5-phenylpent-4-enal [(*S*)-9n][5c]

Light yellow oil; yield: 42.5 mg (86%); $[\alpha]_D^{20}$ +8.7 (*c* 1.0, $CHCl_3$); 95% ee.

HPLC: Chiralcel OD-H (hexanes/*i*-PrOH = 80:20, flow rate = 0.6 mL/min, λ = 254 nm); t_R = 19.3 min (minor), 22.7 min (major).

IR (KBr): 530, 696, 750, 784, 902, 975, 1092, 1221, 1361, 1421, 1556, 1636, 1714, 2850, 2925, 2965, 3003, 3413 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$/TMS): δ = 1.16 (s, 6 H, 2 × CH_3), 3.25–3.31 (dt, *J* = 4.0, 10.0 Hz, 1 H, CH), 4.42–4.48 (dd, *J* = 10.8, 12.0 Hz, 1 H, CH_2), 4.50–4.54 (dd, *J* = 4.0, 12.0 Hz, 1 H, CH_2), 5.99–6.05 (dd, *J* = 10.0, 15.6 Hz, 1 H, CH=C*H*), 6.51–6.55 (d, *J* = 15.6 Hz, 1 H, C*H*=CH), 7.24–7.35 (m, 5 H, ArH), 9.51 (s, 1 H, CHO).

^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ = 19.1, 21.0, 47.2, 47.8, 76.7, 122.8, 126.6, 128.2, 128.6, 135.9, 136.3, 203.8.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{17}NO_3Na$: 270.1106; found: 270.1096.

(*R*)-2-(2,5-Dioxo-1-phenylpyrrolidin-3-yl)-2-methylpropionaldehyde [(*R*)-11][8a]

Isobutyraldehyde (**7**; 29 mg, 0.40 mmol) was added to a mixture of the catalyst **2b** (10 mol%) and *N*-phenylmaleimide (**10**; 35 mg, 0.20 mmol) in $CHCl_3$ (1.0 mL). The reaction mixture was stirred at r.t. for 5 h. After the *N*-phenylmaleimide had been consumed (TLC), the mixture was subjected to TLC on silica gel (EtOAc/hexane) to afford the pure Michael product (*R*)-**11** (34.8 mg, 71%) as a white solid; mp 106–107 °C; $[\alpha]_D^{20}$ +5.5 (*c* 1.0, $CHCl_3$); 98% ee.

HPLC: Chiralcel OD-H (hexanes/*i*-PrOH = 80:20, flow rate = 0.7 mL/min, λ = 210 nm); t_R = 37.0 min (major), 49.2 min (minor).

IR (KBr): 499, 563, 627, 666, 703, 755, 814, 885, 1164, 1189, 1395, 1454,1471, 1490, 1500, 1705, 1773, 2730, 2822, 2932, 2989, 3459 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$/TMS): δ = 1.27 (s, 3 H, CH_3), 1.31(s, 3 H, CH_3), 2.58–2.64 (dd, *J* = 5.6, 18.2 Hz, 1 H, CH_2), 2.92–2.99 (dd, *J* = 9.6, 18.4 Hz, 1 H, CH_2), 3.12–3.16 (dd, *J* = 5.6, 9.6 Hz, 1 H, CH), 7.27 (d, *J* = 7.6 Hz, 2 H, ArH), 7.37–7.41 (t, *J* = 7.2 Hz, 1 H, ArH), 7.45–7.49 (t, *J* = 7.2 Hz, 2 H, ArH), 9.50 (s, 1 H, CHO).

^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ = 19.6, 20.3, 31.8, 45.0, 48.5, 126.5, 128.7, 129.2, 131.8, 174.8, 176.9, 202.8.

HRMS: *m*/*z* [M – H]$^-$ calcd for $C_{14}H_{14}NO_3$: 244.0979: found: 244.0978.

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Supporting Information

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References

(1) For selected reviews, see: (a) Christoffers, J.; Baro, A. *Angew. Chem. Int. Ed.* **2003**, *42*, 1688. (b) Zhang, Y.; Wang, W. *Catal. Sci. Technol.* **2012**, *2*, 42. (c) Tsogoeva, S. B. *Eur. J. Org. Chem.* **2007**, 1701. (d) Almaşi, D.; Alonso, D. A.; Nájera, C. *Tetrahedron: Asymmetry* **2007**, *18*, 299. (e) Krause, N.; Hoffmann-Röder, A. *Synthesis* **2001**, 171. (f) Berner, O. M.; Tedeschi, L.; Enders, D. *Eur. J. Org. Chem.* **2002**, 1877.

(2) (a) List, B.; Pojarliev, P.; Martin, H. J. *Org. Lett.* **2001**, *3*, 2423. (b) Betancort, J. M.; Barbas, C. F. *Org. Lett.* **2001**, *3*, 3737.

(3) For selected examples, see: (a) Moorthy, N. V. G.; Dyapa, R.; Pansare, S. V. *Org. Lett.* **2015**, *17*, 5312. (b) Gu, X.; Dai, Y.; Guo, T.; Franchino, A.; Dixon, D. J.; Ye, J. *Org. Lett.* **2015**, *17*, 1505. (c) Fu, N.; Zhang, L.; Luo, S. *Org. Lett.* **2015**, *17*, 382. (d) Rout, S.; Ray, S. K.; Unhale, R. A.; Singh, V. K. *Org. Lett.* **2014**, *16*, 5568. (e) Mukaiyama, T.; Ogata, K.; Sato, I.; Hayashi, Y. *Chem. Eur. J.* **2014**, *20*, 13410. (f) Mukaiyama, T.; Ogata, K.; Sato, I.; Hayashi, Y. *Chem. Eur. J.* **2014**, *20*, 13583. (g) Kótai, B.; Kardos, G.; Hamza, A.; Farkas, V.; Pápai, I.; Soós, T. *Chem. Eur. J.* **2014**, *20*, 5631. (h) Androvič, L.; Drabina, P.; Svobodová, M.; Sedlák, M. *Tetrahedron: Asymmetry* **2016**, *27*, 782. (i) Liu, S.; Wang, Q.; Ye, L.; Shi, Z.; Zhao, Z.; Yang, X.; Ding, K.; Li, X. *Tetrahedron* **2016**, *72*, 5115. (j) Kanberoğlu, E.; Tanyeli, C. *Asian J. Org. Chem.* **2016**, *5*, 114. (k) Guo, Q.; Fraboni, A. J.; Brenner-Moyer, S. E. *Org. Lett.* **2016**, *18*, 2628. (l) Zhao, B.-L.; Zhang, D.; Liu, L.; Du, D.-M. *Org. Biomol. Chem.* **2016**, *14*, 6337.

(4) For selected examples, see: (a) Servín, F. A.; Madrigal, D.; Romero, J. A.; Chávez, D.; Aguirre, G.; Anaya de Parrodi, C.; Somanathan, R. *Tetrahedron Lett.* **2015**, *56*, 2355. (b) Nakashima, K.; Hirashima, S.-i.; Kawada, M.; Koseki, Y.; Tada, N.; Itoh, A.; Miura, T. *Tetrahedron Lett.* **2014**, *55*, 2703. (c) Hu, X.; Wei, Y.-F.; Wu, N.; Jiang, Z.; Liu, C.; Luo, R.-S. *Tetrahedron: Asymmetry* **2016**, *27*, 420. (d) Rogozińska-Szymczak, M.; Mlynarski, J. *Eur. J. Org. Chem.* **2015**, 6047. (e) Wang, Y.; Li, D.; Lin, J.; Wei, K. *RSC Adv.* **2015**, *5*, 5863. (f) Cao, X.; Wang, G.; Zhang, R.; Wei, Y.; Wang, W.; Sun, H.; Chen, L. *Org. Biomol. Chem.* **2011**, *9*, 6487. (g) Ma, Z.-W.; Liu, Y.-X.; Zhang, W.-J.; Tao, Y.; Zhu, Y.; Tao, J.-C.; Tang, M.-S. *Eur. J. Org. Chem.* **2011**, 6747.

(5) (a) Bai, J.-F.; Xu, X.-Y.; Huang, Q.-C.; Peng, L.; Wang, L.-X. *Tetrahedron Lett.* **2010**, *51*, 2803. (b) He, T.; Gu, Q.; Wu, X.-Y. *Tetrahedron* **2010**, *66*, 3195. (c) Zhang, X.-J.; Liu, S.-P.; Lao, J.-H.; Du, G.-J.; Yan, M.; Chan, A. S. C. *Tetrahedron: Asymmetry* **2009**, *20*, 1451. (d) Zhang, X.-J.; Liu, S.-P.; Li, X.-M.; Yan, M.; Chan, A. S. C. *Chem. Commun.* **2009**, *45*, 833. (e) Avila, A.; Chinchilla, R.; Fiser, B.; Gómez-Bengoa, E.; Nájera, C. *Tetrahedron: Asymmetry* **2014**, *25*, 462. (f) Chang, C.; Li, S.-H.; Reddy, R. J.; Chen, K. *Adv. Synth. Catal.* **2009**, *351*, 1273. (g) Kumar, T. P. *Tetrahedron: Asymmetry* **2015**, *26*, 907. (h) Kumar, T. P.; Haribabu, K. *Tetrahedron: Asymmetry* **2014**, *25*, 1129. (i) He, J.; Chen, Q.; Ni, B. *Tetrahedron Lett.* **2014**, *55*, 3030. (j) Fernandes, T. de. A.; Vizcaíno-Milla, P.; Ravasco, J. M. J. M.; Ortega-Martínez, A.; Sansano, J. M.; Nájera, C.; Costa, P. R. R.; Fiser, B.; Gómez-Bengoa, E. *Tetrahedron: Asymmetry* **2016**, *27*, 118. (k) Nugent, T. C.; Shoaib, M.; Shoaib, A. *Org. Biomol. Chem.* **2011**, *9*, 52.

(6) Malerich, J. P.; Hagihara, K.; Rawal, V. H. *J. Am. Chem. Soc.* **2008**, *130*, 14416.

(7) For selected reviews and recent examples, see: (a) Chauhan, P.; Mahajan, S.; Kaya, U.; Hack, D.; Enders, D. *Adv. Synth. Catal.* **2015**, *357*, 253. (b) Alemán, J.; Parra, A.; Jiang, H.; Jørgensen, K. A. *Chem. Eur. J.* **2011**, *17*, 6890. (c) Izquierdo, J.; Landa, A.; Bastida, I.; López, R.; Oiarbide, M.; Palomo, C. *J. Am. Chem. Soc.* **2016**, *138*, 3282. (d) Sun, Q.-S.; Zhu, H.; Chen, Y.-J.; Yang, X.-D.; Sun, X.-W.; Lin, G.-Q. *Angew. Chem. Int. Ed.* **2015**, *54*, 13253. (e) Maity, S.; Parhi, B.; Ghorai, P. *Angew. Chem. Int. Ed.* **2016**, *55*, 7723. (f) Zhao, B.-L.; Du, D.-M. *Eur. J. Org. Chem.* **2015**, 5350. (g) Zhao, B.-L.; Du, D.-M. *Asian J. Org. Chem.* **2015**, *4*, 778. (h) Dong, Z.; Yan, C.; Gao, Y.; Dong, C.; Qiu, G.; Zhou, H.-B. *Adv. Synth. Catal.* **2015**, *357*, 2132. (i) Wang, Z.-H.; Wu, Z.-J.; Yue, D.-

F.; You, Y.; Xu, X.-Y.; Zhang, X.-M.; Yuan, W.-C. *Org. Biomol. Chem.* **2016**, *14*, 6568. (j) Cui, L. Y.; Wang, Y. H.; Chen, S. R.; Wang, Y. M.; Zhou, Z. H. *RSC Adv.* **2015**, *5*, 88133. (k) Zhao, B.-L.; Du, D.-M. *Chem. Commun.* **2016**, *52*, 6162. (l) Zhu, Y.; Dong, Z.; Cheng, X.; Zhong, X.; Liu, X.; Lin, L.; Shen, Z.; Yang, P.; Li, Y.; Wang, H.; Yan, W.; Wang, K.; Wang, R. *Org. Lett.* **2016**, *18*, 3546. (m) Zhao, M.-X.; Zhu, H.-K.; Dai, T.-L.; Shi, M. *J. Org. Chem.* **2015**, *80*, 11330. (n) Zhou, D.; Huang, Z.; Yu, X.; Wang, Y.; Li, J.; Wang, W.; Xie, H. *Org. Lett.* **2015**, *17*, 5554.

(8) (a) Ma, Z.-W.; Liu, Y.-X.; Li, P.-L.; Ren, H.; Zhu, Y.; Tao, J.-C. *Tetrahedron: Asymmetry* **2011**, *22*, 1740. (b) Ma, Z.-W.; Liu, Y.-X.; Huo, L.-J.; Gao, X.; Tao, J.-C. *Tetrahedron: Asymmetry* **2012**, *23*, 443. (c) Ma, Z.-W.; Wu, Y.; Sun, B.; Du, H.-L.; Shi, W.-M.; Tao, J.-C. *Tetrahedron: Asymmetry* **2013**, *24*, 7. (d) Song, Z.-T.; Zhang, T.; Du, H.-L.; Ma, Z.-W.; Zhang, C.-H.; Tao, J.-C. *Chirality* **2014**, *26*, 121.