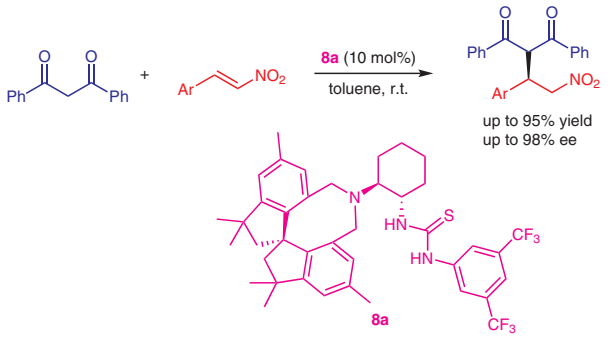
Synthesis Z. Han, X. Lin Paper

Synthesis of Chiral Tertiary Amine–Thioureas Based on Spirobiindane and Application in Catalytic Asymmetric Michael Addition Reaction

Zhao Han
Xufeng Lin*

Department of Chemistry, Zhejiang University, Hangzhou 310027, P. R. of China
lxfok@zju.edu.cn



Received: 19.11.2019
Accepted after revision: 18.12.2019
Published online: 04.02.2020
DOI: 10.1055/s-0039-1691643; Art ID: ss-2019-h0642-op

Abstract A series of novel chiral bifunctional tertiary amine–thioureas based on spirobiindane were designed and synthesized as organocatalysts. One of these catalysts was shown to promote the asymmetric Michael addition reaction of 1,3-diphenylpropane-1,3-dione to nitroolefins, affording the desired products in good yields (up to 95%) and enantioselectivities (up to 98% ee).

Key words organocatalysis, Michael addition, nitroolefins, spiro skeleton, thiourea

Over the past decade, enantioselective organocatalysis has become a fruitful catalytic strategy, offering environmentally benign and highly efficient methodologies for asymmetric synthesis.[1] Consequently, the development of effective chiral organocatalysts has become one of the most important and challenging goals of research in asymmetric organocatalysis. Chiral urea and thiourea derivatives have been recognized as privileged organocatalysts for a variety of enantioselective transformations.[2] The catalytic performance of chiral organocatalysts usually depends on their frameworks. Alongside new organocatalytic reactions, a variety of structurally diverse chiral urea and thiourea organocatalysts have been developed and widely used in many asymmetric reactions,[3] mainly including the most popular Takemoto's amine–thioureas, Jacobsen's ureas/thioureas, cinchona alkaloid based thioureas, and other types of thiourea catalysts such as imidazole–thioureas, guanidinethioureas, pyrrolidine–thioureas, and oxazoline–thioureas. Notably, Shao and Kim developed novel chiral bifunctional amine–thiourea organocatalysts bearing both central and axial chiral elements, which proved to be highly efficient in some asymmetric transformations.[4] Despite a growing focus on efforts toward new catalytic asymmetric reactions and new synthetic strategies, the development of chiral bifunctional amine–thiourea organocatalysts bearing novel backbone structures is still highly desirable and challenging in a diverse range of asymmetric catalysis. Herein, we describe our development of a new series of chiral bifunctional tertiary amine–thioureas based on spirobiindane as organocatalysts that can effectively catalyze asymmetric Michael addition of 1,3-diphenylpropane-1,3-dione to nitroolefins.

In the course of our work on the design and application of novel chiral ligands and catalysts (Figure 1), we have reported the first synthesis and application of SPINOL-derived phosphoric acids (SPAs),[5] which were shown to be highly efficient in asymmetric synthesis and widely appli-

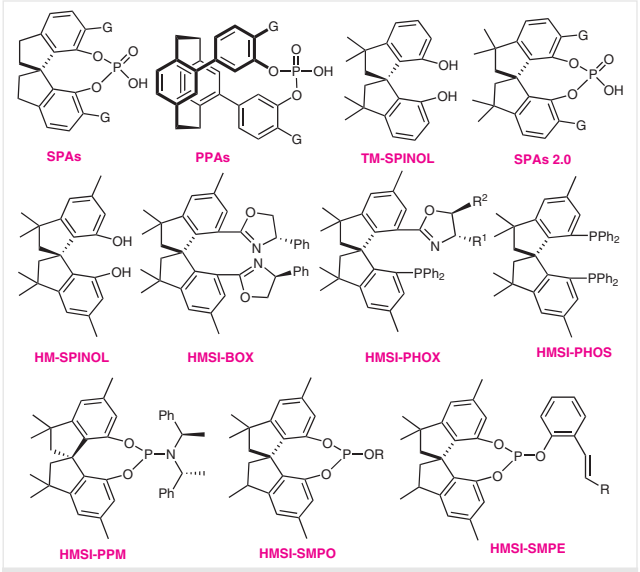
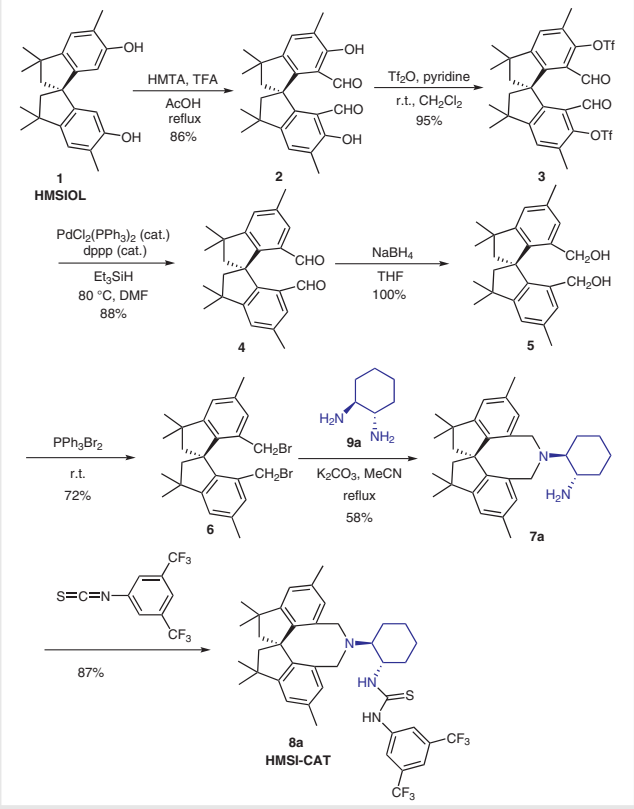


Figure 1 Chiral ligands and catalysts used by Lin's group (G = Group)

cable in over 150 asymmetric reactions.[6] Recently, we developed a novel class of planar chiral phosphoric acids (PPAs) with a [2.2]paracyclophanyl backbone as organocatalysts and demonstrated their application in an asymmetric aza-Friedel–Crafts reaction.[7] Also recently, we disclosed our successful design of a new exciting class of compounds with the axially chiral 3,3,3′,3′-tetramethyl-1,1′-spirobiindane-7,7′-diol (TM-SPINOL) core structure, and the corresponding new axially chiral ligands and new, second generation of SPAs.[8] With this innovative design principle in mind, we prepared the new hexamethyl-1,1′-spirobiindane-based chiral tertiary amine–thiourea organocatalysts (HMSI-CAT), bearing both central and axial chiral elements.

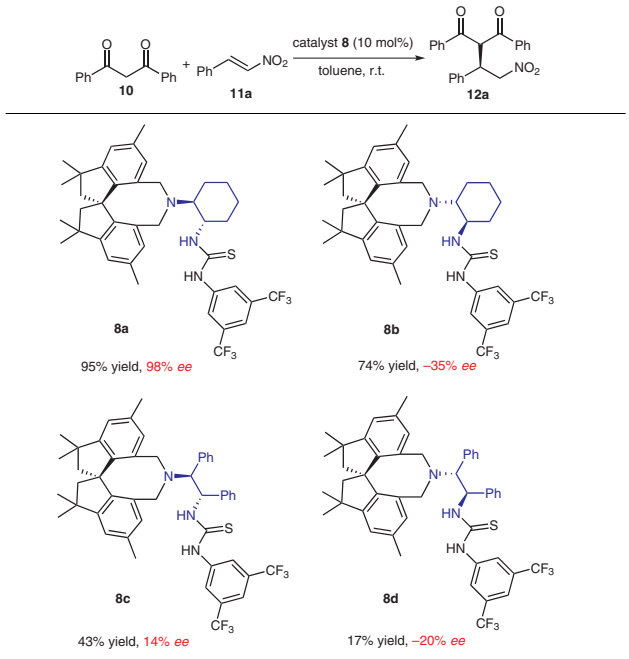
We started the synthesis of HMSI-CAT from the axially chiral (*S*)-**1** (HMSIOL) (Scheme 1), which was prepared by acid-catalyzed rearrangement of bisphenol C according to our previously published procedure.[8c] The Duff reaction of HMSIOL with hexamethylenetetramine (HMTA) afforded the corresponding product **2** in 86% yield. The subsequent esterification with trifluoromethanesulfonic anhydride (Tf_2O) afforded diester **3** in 95% yield. Then, Pd-catalyzed selective reduction with triethylsilane furnished spiro dialdehyde **4** in 96% yield. Bis-bromide **6** was obtained in 72% yield over two steps by reduction and subsequent bromination. Finally, the target hexamethyl-1,1′-spirobiindane-based chiral tertiary amine–thiourea (HMSI-CAT) **8a** was obtained in 50% yield over two steps by cyclization of **6** with (*S*,*S*)-1,2-diaminocyclohexane **9a**, followed by addition of **7a** with 3,5-bis(trifluoromethyl)phenyl isothiocyanate.



Scheme 1 Synthesis of the spirobiindane-based chiral bifunctional amine–thiourea organocatalyst HMSI-CAT (**8a**)

Next, the efficiency and catalytic potential of the design of new organocatalyst HMSI-CAT was tested in the Michael addition[9] of 1,3-diphenylpropane-1,3-dione (**10**) to nitroolefins (Table 1). We first examined the use of chiral organocatalyst **8a** in the asymmetric reaction of **10** and *trans*-alkene **11a** in toluene at room temperature; this gave the desired adduct **12a** in 95% yield and 98% ee. The absolute configuration of (*S*)-**12a** was confirmed by comparison with known data.[4g] We also designed and synthesized catalyst **8b**, which has the same absolute configuration of the spirobiindane unit, but differs in the two stereogenic centers of the cyclohexyl scaffold, by following the procedure described in Scheme 1. Similarly, organocatalysts **8c** and **8d** were derived from bis-bromide **6** and chiral 1,2-diamino-1,2-diphenylethane. However, organocatalysts **8b–d** exhibited completely different catalytic properties when compared to **8a**, leading to the corresponding product **12a** in low to moderate yields (17–74%) with poor stereochemical control (14–35% ee). In addition, the absolute configuration of product **12a** is determined by the central chiral element of the organocatalyst, as shown in Table 1. The performances of **8a–d** clearly indicate that the two chiral elements in

Table 1 Evaluation of Catalysts in the Michael Addition Reaction[a–c]



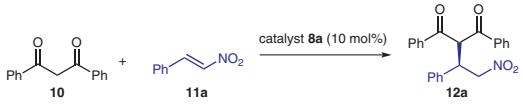
[a] Reaction conditions: **10** (0.2 mmol), **11a** (0.1 mmol), catalyst **8** (10 mol%), toluene (1 mL), 16 h.
[b] Yields are of isolated products.
[c] Enantioselectivity was determined by chiral HPLC.

chiral tertiary amine–thiourea catalyst **8a** based on the spirobiindane backbone and 1,2-diaminocyclohexane are matched, which is essential for obtaining high catalytic activity and excellent stereochemical control. Thus, the chiral tertiary amine–thiourea **8a** was chosen as the ideal catalyst for further study.

Further reaction optimization was performed by using the bifunctional organocatalyst **8a** (Table 2); the effect of temperature was first investigated. We tried lower temperatures (–40 °C and –10 °C) in toluene, but although excellent enantioselectivities resulted, the yield was reduced, despite prolonged reaction times (entries 1–3). Next, the influence of the solvent was examined; the reaction could be carried out in other solvents, including dichloromethane, chloroform, acetonitrile, ethyl acetate, tetrahydrofuran, dimethyl sulfoxide, and diethyl ether, with all providing the corresponding product **12a** in good to excellent yields (84–96%), but with only moderate enantioselectivities (54–75%; entries 4–10). Therefore, toluene was still the best reaction solvent at room temperature (entry 1).

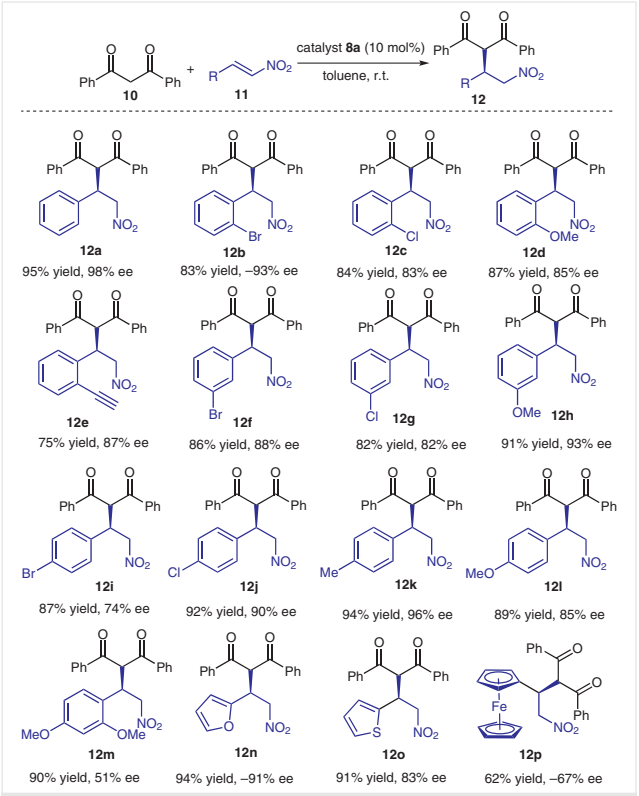
With the optimal conditions in hand, we turned our attention to investigating the reaction substrate scope when using **8a** as the chiral organocatalyst (Scheme 2). Substituents with different electronic properties, such as Br, Cl, OMe, and ethynyl on the aromatic ring of nitroolefin **11**, were all tolerated, to give the corresponding products **12a–e** in good yields and enantioselectivities. Nitroolefin reagents **11** in which the aromatic rings were substituted at different positions (*ortho*, *meta*, and *para*) were also successfully employed, with the substitution position not appearing to affect the reactivity and enantioselectivity of the reaction. The reaction with the nitroolefin bearing 2,4-dimethoxyphenyl proceeded efficiently to give the desired product **12m** in 90% yield, but only with 51% ee. Nitroolefins bearing heterocyclic groups were also successfully employed in the asymmetric Michael addition reaction, providing the desired products **12n** and **12o** in excellent yields and good enantioselectivities. The nitroolefin bearing ferrocene was also examined. Interestingly, the transformation proceeded smoothly, giving **12p** in moderate yield and enantioselectivity.

Table 2 Reaction Optimization[a–c]



Entry	Temp	Solvent	Time (h)	Yield (%)	ee (%)
1	r.t.	toluene	16	95	98
2	–40 °C	toluene	36	87	96
3	–10 °C	toluene	24	89	94
4	r.t.	CH_2Cl_2	16	90	71
5	r.t.	$CHCl_3$	16	84	69
6	r.t.	MeCN	16	92	64
7	r.t.	EtOAc	16	96	59
8	r.t.	THF	16	89	75
9	r.t.	DMSO	16	93	54
10	r.t.	Et_2O	16	90	70

[a] Reaction conditions: **10** (0.2 mmol), **11a** (0.1 mmol), catalyst **8a** (10 mol%) solvent (1 mL).
[b] Yields are of isolated products.
[c] Enantioselectivity was determined by chiral HPLC.



Scheme 2 Substrate scope for the asymmetric Michael addition

According to the dual activation model of chiral amine–thiourea,[3,4] we propose the catalytic interaction shown in Figure 2. The organocatalyst simultaneously activates the

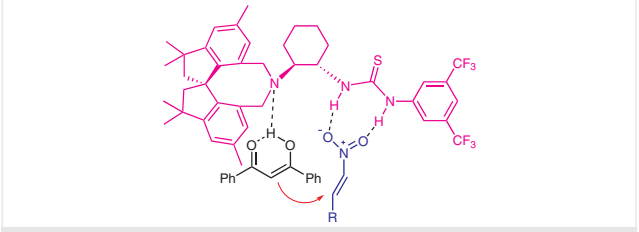


Figure 2 Proposed action of organocatalyst

two substrates, 1,3-diphenylpropane-1,3-dione and the nitroolefin, involved in the Michael reaction through hydrogen bonding.

In summary, we have developed a novel class of chiral bifunctional tertiary amine–thiourea organocatalysts, bearing both axial and central elements, based on a spirobiindane backbone. The organocatalysts were employed in the catalytic asymmetric Michael addition of 1,3-diphenylpropane-1,3-dione to nitroolefins. The performances of the newly developed organocatalysts **8** clearly indicated that the two chiral elements in chiral amine–thiourea catalyst **8a** are matched, which is essential for affording the desired products in high yields (up to 95%) and excellent enantioselectivities (up to 98% ee).

All reagents and solvents were purchased from commercial sources. NMR spectra were recorded on a Bruker DPX 400 NMR spectrometer at 400 MHz for ^{1}H NMR, 100 MHz for ^{13}C, and 376 MHz for ^{19}F NMR. The samples were prepared in $CDCl_3$ or DMSO-d_6 with tetramethylsilane (TMS) as internal standard. IR spectra were recorded on a Nicolet NEXUS 470 spectrophotometer. HRMS data were collected on Waters GCT Premier and Bruker Ultraflex mass spectrometers. Optical rotations were measured on a Perkin Elmer Model 341 polarimeter. The ee values were determined on the basis of separations done by chiral high-performance liquid chromatography. HPLC analysis was performed using Chiralcel columns (Chiralcel AS-H, AD-H).

(*S*)-6,6′-Dihydroxy-3,3,3′,3′,5,5′-hexamethyl-2,2′,3,3′-tetrahydro-1,1′-spirobi[indene]-7,7′-dicarbaldehyde (2)

HMSIOL [(*S*)-(–)-**1**; 3.4 g, 10 mmol) was dissolved in TFA (120 mL) under N_2, and HMTA (11.2 g, 80 mmol) was added in one portion. The yellow solution was refluxed overnight and glacial AcOH (120 mL) was added the next day. The solution then was kept refluxing for 3 d. When the starting phenols were converted, 4 M aq HCl (120 mL) was added after the mixture had cooled to 95 °C, and then the mixture was stirred for 5 h. Then, after cooling to r.t., the mixture was poured into H_2O and finally filtered to give product (*S*)-**2**.

Yield: 3.37g (86%); yellow solid; mp 256–258 °C; $[\alpha]_D^{20}$ +131.0 (*c* 1.0, CH_2Cl_2).

IR (film): 3375, 2966, 2924, 2876, 1637, 1605, 1468, 1393, 1384, 1273, 1162, 1090 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 12.01 (s, 2 H), 9.57 (s, 2 H), 7.20 (s, 2 H), 2.57 (d, *J* = 13.5 Hz, 2 H), 2.38 (d, *J* = 13.5 Hz, 2 H), 2.26 (s, 6 H), 1.37 (s, 6 H), 1.35 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.66, 162.35, 149.60, 141.77, 132.63, 127.96, 113.72, 60.29, 57.78, 43.01, 32.02, 30.12, 15.63.

HRMS (EI): *m*/*z* calcd for $C_{25}H_{28}O_4$: 392.1988; found: 392.1985.

(*S*)-7,7′-Diformyl-3,3,3′,3′,5,5′-hexamethyl-2,2′,3,3′-tetrahydro-1,1′-spirobi[indene]-6,6′-diyl Bis(trifluoromethanesulfonate) (3)

Tf_2O (3.4 mL, 20 mmol) was added dropwise to a solution of dialdehyde (*S*)-**2** (1.97 g, 5 mmol) and pyridine (3.3 mL, 40 mmol) in CH_2Cl_2 (40 mL), at 0 °C under a N_2 atmosphere. The mixture was allowed to warm to r.t. and stirred overnight. The reaction solution was diluted with CH_2Cl_2, washed with 5% aq HCl, brine, sat. aq $NaHCO_3$, and brine, and dried over anhyd Na_2SO_4. After removal of the solvent, the residue was purified by flash chromatography (silica gel, EtOAc/PE, 1:50); this gave product (*S*)-**3**.

Yield: 3.1 g (95%); white solid; mp 156–157 °C; $[\alpha]_D^{20}$ +158.5 (*c* 1.0, CH_2Cl_2).

IR (film): 2962, 2865, 1704, 1563, 1423, 1407, 1213, 1183, 1142, 1043, 990, 880, 799, 736, 621 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.79 (s, 2 H), 7.35 (s, 2 H), 2.51 (d, *J* = 12.8 Hz, 2 H), 2.45 (s, 6 H), 2.41 (d, *J* = 12.8 Hz, 2 H), 1.50 (s, 6 H), 1.40 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 186.46, 153.54, 148.31, 146.25, 130.61, 129.76, 123.53, 119.01, 115.83, 57.67, 56.54, 42.11, 31.42, 27.96, 15.85.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –73.14.

HRMS (EI): *m*/*z* calcd for $C_{27}H_{26}O_8S_2F_6$: 656.0973; found: 656.0973.

(*S*)-3,3,3′,3′,5,5′-Hexamethyl-2,2′,3,3′-tetrahydro-1,1′-spirobi[indene]-7,7′-dicarbaldehyde (4)

Under N_2, a mixture of bis-triflate (*S*)-**3** (1.97 g, 3 mmol), $Pd(OAc)_2$ (135 mg, 0.6 mmol), and 1,3-bis(diphenylphosphino)propane (248 mg, 0.6 mmol) in DMF (150 mL) was stirred to give a clear solution. Then triethylsilane (7.2 mL, 45 mmol) was added slowly. After addition was completed, the solution was warmed to 80 °C for 6 h. After cooling to r.t., the resulting mixture was diluted with Et_2O and washed sequentially with H_2O, sat. aq $NaHCO_3$, and brine. The organic layer was dried over anhyd Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography (silica gel, EtOAc/PE, 1:15) to afford product (*S*)-**4**.

Yield: 0.95 g (88%); yellow solid; mp 217–219 °C; $[\alpha]_D^{20}$ +181.2 (*c* 1.0, CH_2Cl_2).

IR (film): 3360, 2963, 2925, 2876, 1685, 1605, 1577, 1460, 1394, 1383, 1314, 1245, 1161 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.56 (s, 2 H), 7.53 (s, 2 H), 7.25 (s, 2 H), 2.56 (d, *J* = 13.3 Hz, 2 H), 2.43 (d, *J* = 17.1 Hz, 8 H), 1.45 (s, 6 H), 1.39 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 189.51, 152.38, 149.14, 137.24, 129.55, 128.42, 128.20, 58.80, 56.20, 42.40, 31.39, 28.57, 20.13.

HRMS (EI): *m*/*z* calcd for $C_{25}H_{28}O_2$: 360.2089; found: 360.2096.

(*S*)-(3,3,3′,3′,5,5′-Hexamethyl-2,2′,3,3′-tetrahydro-1,1′-spirobi[indene]-7,7′-diyl)dimethanol (5)

A portion of aldehyde (*S*)-**4** (1.14 g, 3.2 mmol) was dissolved in THF (30 mL); $NaBH_4$ (0.6 g, 16 mmol) was added at 0 °C and the mixture was stirred for 10 min. The mixture was then allowed to warm to r.t. and stirred for 3 h. After the mixture had cooled to 0 °C, H_2O (100 mL) was added and stirring continued for 8 h. The resulting mixture was diluted with Et_2O and washed sequentially with H_2O and brine. The organic layer was dried over anhyd Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography (silica gel, EtOAc/PE, 1:4) to afford product (*S*)-**5**.

Yield: 1.16 g (100%); white solid; mp 82–84 °C; $[\alpha]_D^{20}$ –10.3 (*c* 1.00, CH_2Cl_2).

IR (film): 3355, 2954, 2926, 2862, 1959, 1742, 1609, 1463, 1383, 1361, 1309, 1230, 1167, 1148, 1020, 862, 738 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.10 (s, 2 H), 6.95 (s, 2 H), 4.13 (q, *J* = 11.8 Hz, 4 H), 2.38 (d, *J* = 11.5 Hz, 8 H), 2.24 (s, 1 H), 2.16 (s, 2 H), 1.67 (s, 1 H), 1.38 (s, 6 H), 1.33 (s, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 152.38, 144.48, 137.96, 135.91, 129.95, 123.02, 60.62, 58.82, 43.13, 32.64, 30.09, 21.45.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{25}H_{32}NO_2$: 387.2300; found: 387.2292

(*S*)-7,7′-Bis(bromomethyl)-3,3,3′,3′,5,5′-hexamethyl-2,2′,3,3′-tetrahydro-1,1′-spirobi[indene] (6)

Dimethanol (*S*)-**5** (1.16 g, 3.2 mmol) and triphenylphosphine dibromide (7.1g, 16 mmol) were placed in a 100 mL flask. Then the reagents were dissolved in CH_2Cl_2 (30 mL) and stirred for 3 h under an atmosphere of N_2. Then H_2O (100 mL) was added to quench the reaction. The mixture was extracted with CH_2Cl_2, washed with H_2O and sat. aq brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash chromatography (silica gel, EtOAc/PE, 1:50) to afford product (*S*)-**6**.

Yield: 1.12 g (72%); white solid; mp 242–245 °C; $[\alpha]_D^{20}$ –117.3 (*c* 1.00, CH_2Cl_2)

IR (film): 3726, 3704, 3626, 3599, 3446, 2953, 2861, 1959, 1610, 1464, 1382, 1361, 1311, 1262, 1230, 1208, 1029, 680, 669, 656 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.99 (s, 2 H), 6.87 (s, 2 H), 3.94 (d, *J* = 10.2 Hz, 2 H), 3.81 (d, *J* = 10.2 Hz, 2 H), 2.44 (d, *J* = 13.4 Hz, 2 H), 2.28 (s, 7 H), 2.24 (s, 1 H), 1.35 (s, 6 H), 1.27 (s, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 152.71, 144.32, 138.20, 133.39, 131.86, 123.85, 57.33, 56.80, 43.26, 32.57, 30.20, 29.90, 21.25.

HRMS (EI): *m*/*z* calcd for $C_{25}H_{32}Br_2$: 488.0714; found: 488.0711

Diamines 7; General Procedure

Dibromide (*S*)-**6** (1.16 g, 3.2 mmol) was placed in a 100 mL flask followed by chiral 1,2-diaminocyclohexane or 1,2-diamino-1,2-diphenylethane (12.8 mmol) and K_2CO_3 (1.33 g, 9.6 mmol). Then the reagents were dissolved in MeCN (70 mL) under an atmosphere of N_2 and the mixture was heated under reflux overnight. After cooling of the mixture to r.t., the solvent was removed under reduced pressure. Then the resulting mixture was diluted with Et_2O and washed sequentially with H_2O, sat. aq $NaHCO_3$, and brine. The organic layer was dried over anhyd Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography (silica gel, EtOAc/PE, 1:6 + 5% Et_3N) to give the desired product **7**.

(*S*$_a$,1*S*,2*S*)-2-(2,4,4,7,7,9-Hexamethyl-4,5,6,7-tetrahydro-11*H*-diindeno[7,1-*cd*:1′,7′-*ef*]azocin-12(13*H*)-yl)cyclohexan-1-amine (7a)

Prepared according to the general procedure; yield: 822 mg (58%); white solid; mp 84–86 °C; $[\alpha]_D^{20}$ –183.4 (*c* 1.00, CH_2Cl_2).

IR (film): 3384, 3303, 3060, 3027, 2956, 2920, 2858, 1958, 1736, 1603, 1452, 1361, 1309, 1263, 1073, 1028, 858, 804, 750, 698 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.88 (d, *J* = 14.0 Hz, 4 H), 3.86 (d, *J* = 13.1 Hz, 2 H), 3.29 (d, *J* = 13.1 Hz, 2 H), 2.85 (td, *J* = 10.1, 4.1 Hz, 1 H), 2.38 (d, *J* = 17.1 Hz, 8 H), 2.02 (d, *J* = 11.1 Hz, 1 H), 1.93 (d, *J* = 12.6 Hz, 2 H), 1.66 (dd, *J* = 22.7, 13.4 Hz, 4 H), 1.51 (s, 6 H), 1.44–1.31 (m, 2 H), 1.26 (s, 6 H), 1.07 (dtd, *J* = 14.5, 12.5, 2.7 Hz, 4 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 150.90, 146.17, 137.23, 131.31, 130.56, 122.00, 72.78, 57.56, 57.54, 51.69, 48.23, 41.69, 35.64, 32.51, 30.34, 28.31, 26.43, 25.17, 21.32.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{31}H_{42}N_2$: 443.3426; found: 443.3422.

(*S*$_a$,1*R*,2*R*)-2-(2,4,4,7,7,9-Hexamethyl-4,5,6,7-tetrahydro-11*H*-diindeno[7,1-*cd*:1′,7′-*ef*]azocin-12(13*H*)-yl)cyclohexan-1-amine (7b)

Prepared according to the general procedure; yield: 748 mg (53%); white solid; mp 88–90 °C; $[\alpha]_D^{20}$ –201.2 (*c* 1.00, CH_2Cl_2).

IR (film): 3361, 2923, 2855, 1743, 1669, 1608, 1463, 1361, 1261, 1086, 1026, 858, 804 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.89 (s, 2 H), 6.79 (s, 2 H), 3.72 (s, 2 H), 3.14 (d, *J* = 12.7 Hz, 2 H), 2.66–2.55 (m, 1 H), 2.38 (d, *J* = 12.7 Hz, 2 H), 2.34 (s, 6 H), 2.22 (s, 1 H), 2.04 (s, 1 H), 1.97 (dd, *J* = 9.0, 5.3 Hz, 1 H), 1.92 (d, *J* = 12.6 Hz, 2 H), 1.55 (dd, *J* = 16.2, 13.8 Hz, 2 H), 1.49 (s, 6 H), 1.24 (s, 6 H), 1.20–1.05 (m, 4 H), 0.79 (dt, *J* = 32.2, 10.9 Hz, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 151.23, 146.44, 137.53, 129.51, 122.19, 71.10, 57.67, 57.61, 52.45, 41.97, 35.17, 32.38, 30.43, 27.34, 26.15, 25.31, 21.38.

HRMS (ESI): *m*/*z* [M$^+$] calcd for $C_{31}H_{42}N_2$: 443.3426; found: 443.3424.

(*S*$_a$,1*S*,2*S*)-2-(2,4,4,7,7,9-Hexamethyl-4,5,6,7-tetrahydro-11*H*-diindeno[7,1-*cd*:1′,7′-*ef*]azocin-12(13*H*)-yl)-1,2-diphenylethan-1-amine (7c)

Prepared according to the general procedure; yield: 973 mg (56%); white solid; mp 96–99 °C; $[\alpha]_D^{20}$ –58.0(*c* 1.00, CH_2Cl_2).

IR (film): 3445, 2923, 2856, 1743, 1607, 1464, 1361, 1261, 1079, 1024, 858, 803, 669 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.23 (d, *J* = 2.6 Hz, 1 H), 7.22 (d, *J* = 1.8 Hz, 2 H), 7.18 (s, 2 H), 7.17 (d, *J* = 2.2 Hz, 2 H), 7.16 (s, 1 H), 7.15 (s, 1 H), 7.13 (d, *J* = 2.1 Hz, 1 H), 6.87 (s, 2 H), 6.56 (s, 2 H), 4.39 (d, *J* = 4.1 Hz, 1 H), 3.67 (d, *J* = 4.1 Hz, 1 H), 3.48 (dd, *J* = 30.4, 12.8 Hz, 4 H), 2.34(s, 6 H), 2.33 (d, *J* = 8.3 Hz, 2 H), 1.84 (d, *J* = 12.5 Hz, 2 H), 1.64 (br s, 2 H), 1.46 (s, 6 H), 1.20 (s, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 151.25, 146.72, 143.88, 140.61, 136.94, 130.17, 129.89, 129.69, 127.81, 127.67, 127.33, 127.19, 126.47, 122.26, 71.61, 57.59, 57.56, 56.38, 48.58, 41.99, 32.36, 30.40, 21.49.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{39}H_{44}N_2$: 541.3512; found: 541.3574.

(*S*$_a$,1*R*,2*R*)-2-(2,4,4,7,7,9-Hexamethyl-4,5,6,7-tetrahydro-11*H*-diindeno[7,1-*cd*:1′,7′-*ef*]azocin-12(13*H*)-yl)-1,2-diphenylethan-1-amine (7d)

Prepared according to the general procedure; yield: 778 mg (45%); white solid; mp 98–102 °C; $[\alpha]_D^{20}$ –17.0 (*c* 1.00, CH_2Cl_2).

IR (film): 3384 2956, 2858, 1742, 1603, 1452, 1382, 1262, 1069, 1029, 860, 804, 702 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.15 (m, 5 H), 6.96–6.89 (m, 3 H), 6.80 (s, 2 H), 6.74 (dd, *J* = 6.6, 2.9 Hz, 2 H), 6.68 (s, 2 H), 4.44 (d, *J* = 8.5 Hz, 1 H), 3.92 (d, *J* = 8.5 Hz, 1 H), 3.82 (d, *J* = 12.9 Hz, 2 H), 3.44 (d, *J* = 12.9 Hz, 2 H), 2.33 (d, *J* = 12.5 Hz, 2 H), 2.25 (s, 6 H), 1.87 (br s, 2 H), 1.46 (s, 6 H), 1.18 (s, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 150.91, 146.09, 143.83, 139.06, 137.14, 130.28, 130.16, 129.17, 127.88, 127.77, 126.97, 126.67, 126.29, 122.03, 75.32, 58.35, 57.52, 50.46, 41.77, 32.25, 30.28, 21.25.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{39}H_{44}N_2$: 541.3512; found: 541.3579.

Thioureas 8; General Procedure

Diamine **7** (1 mmol) was added to a 50 mL flask and dissolved in CH_2Cl_2 (30 mL). Then 3,5-bis(trifluoromethyl)phenyl isothiocyanate (271 mg 1 mmol) was added and the mixture was stirred for 18 h.

The resulting mixture was diluted with CH_2Cl_2 and washed sequentially with H_2O, sat. aq $NaHCO_3$, and brine. The organic layer was dried over anhyd Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography (silica gel, EtOAc/PE, 1:4) to afford the desired product **8**.

(S_a)-1-[3,5-Bis(trifluoromethyl)phenyl]-3-[(1*S*,2*S*)-2-(2,4,4,7,7,9-hexamethyl-4,5,6,7-tetrahydro-11*H*-diindeno[7,1-*cd*:1′,7′-*ef*]azocin-12(13*H*)-yl)cyclohexyl]thiourea (8a)

Prepared according to the general procedure; yield: 620 mg (87%); white solid; mp 135–137 °C; $[\alpha]_D^{20}$ –70.4 (*c* 1.00, CH_2Cl_2).

IR (film): 3294, 2924, 2855, 1741, 1466, 1382, 1277, 1138, 1097, 1024, 860, 803, 699 cm^{-1}.

^1H NMR (400 MHz, DMSO): δ = 10.03 (s, 1 H), 8.28 (s, 2 H), 7.71 (s, 1 H), 6.88 (d, *J* = 8.8 Hz, 4 H), 4.63 (s, 1 H), 3.61 (d, *J* = 13.0 Hz, 2 H), 3.30 (d, *J* = 13.1 Hz, 2 H), 2.75 (t, *J* = 8.4 Hz, 1 H), 2.29 (d, *J* = 14.5 Hz, 8 H), 2.24–2.16 (m, 1 H), 1.75 (d, *J* = 12.5 Hz, 2 H), 1.64–1.47 (m, 3 H), 1.43 (s, 6 H), 1.26–1.21 (m, 2 H), 1.18 (s, 6 H), 0.88–0.79 (m, 4 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 151.58, 146.57, 140.17, 137.57, 133.02 ($J_{F\text{-}C}$ = 33.7 Hz), 130.21, 127.19, 124.48, 122.78, 121.76, 119.05, 117.85, 68.62, 57.86, 57.37, 48.77, 41.81, 33.21, 32.48, 30.24, 28.78, 25.90, 24.66, 21.24.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –62.91 (s).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{40}H_{45}F_6N_3S$: 714.3317; found: 714.3308.

(S_a)-1-[3,5-Bis(trifluoromethyl)phenyl]-3-[(1*R*,2*R*)-2-(2,4,4,7,7,9-hexamethyl-4,5,6,7-tetrahydro-11*H*-diindeno[7,1-*cd*:1′,7′-*ef*]azocin-12(13*H*)-yl)cyclohexyl]thiourea (8b)

Prepared according to the general procedure; yield: 527 mg (74%); white solid; mp 221–222 °C; $[\alpha]_D^{20}$ –174.0 (*c* 1.00, CH_2Cl_2).

IR (film): 3254, 2925, 2857, 1739, 1464, 1382, 1277, 1136, 1023, 966, 862, 803, 682 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 9.45 (s, 1 H), 8.01 (s, 2 H), 7.56 (s, 1 H), 7.37 (s, 1 H), 6.80 (s, 4 H), 4.27 (s, 1 H), 3.67 (s, 2 H), 3.18 (d, *J* = 12.5 Hz, 2 H), 2.29 (d, *J* = 12.6 Hz, 2 H), 2.05 (s, 6 H), 1.93 (s, 1 H), 1.78 (d, *J* = 12.5 Hz, 2 H), 1.57–1.40 (m, 2 H), 1.37 (s, 6 H), 1.31–1.18 (m, 2 H), 1.14 (s, 6 H), 1.11–0.79 (m, 4 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 151.69, 147.21, 142.49, 137.88, 132.13, ($J_{F\text{-}C}$ = 33.3), 130.78, 128.28, 125.58, 123.56, 122.83, 120.17, 117.45, 68.47, 58.34, 58.30, 57.44, 42.42, 33.39, 32.50, 30.56, 29.81, 28.78, 26.11, 25.59, 21.12.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –58.12 (s).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{40}H_{45}F_6N_3S$: 714.3317; found: 714.3314.

(S_a)-1-[3,5-Bis(trifluoromethyl)phenyl]-3-[(1*S*,2*S*)-2-(2,4,4,7,7,9-hexamethyl-4,5,6,7-tetrahydro-11*H*-diindeno[7,1-*cd*:1′,7′-*ef*]azocin-12(13*H*)-yl)-1,2-diphenylethyl]thiourea (8c)

Prepared according to the general procedure; yield: 734 mg (90%); yellow solid; mp 136–138 °C; $[\alpha]_D^{20}$ –75.3 (*c* 1.00, CH_2Cl_2).

IR (film): 3244, 2924, 2856, 1698, 1471, 1384, 1277, 1137, 1029, 957, 861, 803, 682 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.50–7.40 (m, 3 H), 7.18–7.02 (m, 11 H), 6.79 (s, 2 H), 6.30 (s, 2 H), 3.70–3.30 (m, 4 H), 2.25 (d, *J* = 12.6 Hz, 2 H), 2.11 (s, 5 H), 1.75 (d, *J* = 12.6 Hz, 2 H), 1.37 (s, 6 H), 1.14 (d, *J* = 7.2 Hz, 1 H), 1.12 (s, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 151.21, 146.67, 139.52, 139.15, 137.08, 131.91 ($J_{F\text{-}C}$ = 33.4), 130.04, 129.33, 128.37, 128.13, 128.00, 126.85, 124.21, 123.44, 122.67, 121.50, 118.29, 77.16, 60.42, 57.54, 57.28, 48.87, 41.77, 32.10, 30.11, 21.02.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –62.85.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{40}H_{45}F_6N_3S$: 812.3473; found: 812.3467.

(S_a)-1-[3,5-Bis(trifluoromethyl)phenyl]-3-[(1*R*,2*R*)-2-(2,4,4,7,7,9-hexamethyl-4,5,6,7-tetrahydro-11*H*-diindeno[7,1-*cd*:1′,7′-*ef*]azocin-12(13*H*)-yl)-1,2-diphenylethyl]thiourea (8d)

Prepared according to the general procedure; yield: 685 mg (84%); white solid; mp 135–137 °C; $[\alpha]_D^{20}$ –36.7 (*c* 1.00, CH_2Cl_2).

IR (film): 3277, 2926, 2858, 1680, 1532, 1470, 1278, 1178, 1135, 885, 861, 804, 682 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.59 (s, 1 H), 7.55 (d, *J* = 16.7 Hz, 3 H), 7.13 (d, *J* = 16.5 Hz, 3 H), 7.02–6.84 (m, 5 H), 6.69 (s, 2 H), 6.51 (s, 4 H), 5.16 (s, 1 H), 4.12–3.98 (m, 1 H), 3.80 (d, *J* = 12.6 Hz, 2 H), 3.29 (d, *J* = 12.8 Hz, 2 H), 2.24 (d, *J* = 12.6 Hz, 2 H), 2.03 (s, 6 H), 1.75 (d, *J* = 12.6 Hz, 2 H), 1.35 (s, 6 H), 1.18 (t, *J* = 6.5 Hz, 1 H), 1.09 (s, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 151.26, 146.24, 140.32, 137.51, 137.32, 132.19 ($J_{F\text{-}C}$ = 35.4 Hz), 130.51, 129.10, 128.94, 128.79, 127.52, 124.38, 122.70, 121.67, 118.95, 73.57, 62.37, 57.65, 57.56, 50.30, 41.92, 32.27, 30.36, 21.13, 1.14.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –62.87.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{40}H_{45}F_6N_3S$: 812.3473; found: 812.3472.

Asymmetric Michael Addition of 1,3-Diphenylpropane-1,3-dione (10) to Nitroolefins 11; General Procedure

To a solution of 1,3-diphenylpropane-1,3-dione (**10**; 44.8 mg, 0.2 mmol, 2 equiv) and nitroolefin **11** (0.1 mmol, 1 equiv) in toluene (1 mL) was added catalyst **8a** (0.01 mmol, 0.1 equiv). The resulting mixture was stirred at r.t. for 16 h. After the reaction was completed, the corresponding product was isolated and purified by flash chromatography (silica gel, EtOAc/hexane, 1:10 to 1:3).

(*S*)-2-(2-Nitro-1-phenylethyl)-1,3-diphenylpropane-1,3-dione (12a)

Prepared according to the general procedure; yield: 35.4 mg (95%).

HPLC (Chiralpak AS-H, hexane/*i*-PrOH, 85:15, flow rate 1 mL/min, λ = 210 nm): t_R (major) = 27.4 min, t_R (minor) = 37.4 min; 98% ee.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.79 (d, *J* = 7.7 Hz, 2 H), 7.71 (d, *J* = 7.6 Hz, 2 H), 7.45 (dt, *J* = 15.1, 7.4 Hz, 2 H), 7.30 (dt, *J* = 15.1, 7.7 Hz, 5 H), 7.12 (dt, *J* = 9.0, 7.2 Hz, 5 H), 5.77 (d, *J* = 8.0 Hz, 1 H), 4.92 (d, *J* = 6.8 Hz, 2 H), 4.55 (dd, *J* = 14.5, 7.0 Hz, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 194.25, 193.62, 136.78, 136.18, 135.81, 134.09, 133.82, 128.98, 128.85, 128.79, 128.62, 128.26, 128.18, 77.31, 59.87, 44.03.

ESI-MS: *m*/*z* = 374.3 [M + H]$^+$.

(*S*)-2-[1-(2-Bromophenyl)-2-nitroethyl]-1,3-diphenylpropane-1,3-dione (12b)

Prepared according to the general procedure; yield: 37.4 mg (83%).

HPLC (Chiralpak AD-H, hexane/*i*-PrOH, 90:10, flow rate 1 mL/min, λ = 210 nm): t_R (minor) = 21.6 min, t_R (major) = 23.2 min; –93% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94–7.84 (m, 2 H), 7.75 (d, *J* = 7.4 Hz, 2 H), 7.61–7.56 (m, 1 H), 7.53 (t, *J* = 7.4 Hz, 2 H), 7.37 (q, *J* = 8.1 Hz, 4 H), 7.19–7.13 (m, 1 H), 7.10–7.02 (m, 2 H), 6.04 (d, *J* = 5.2 Hz, 1 H), 5.18 (s, 1 H), 5.13–5.03 (m, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 194.66, 193.59, 136.21, 135.92, 135.60, 134.13, 133.96, 133.88, 132.51, 129.59, 128.97, 128.92, 128.75, 128.73, 128.68, 127.84, 127.21, 75.42, 57.18, 42.22.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{18}BrNO_4$: 474.0371; found: 474.0308.

(*S*)-2-[1-(2-Chlorophenyl)-2-nitroethyl]-1,3-diphenylpropane-1,3-dione (12c)

Prepared according to the general procedure; yield: 34.2 mg (84%).

HPLC (Chiralpak AD-H, hexane/*i*-PrOH, 90:10, flow rate 0.8 mL/min, λ = 254 nm): t_R (major) = 25.8 min, t_R (minor) = 27.2 min; 83% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96–7.92 (m, 2 H), 7.87–7.81 (m, 2 H), 7.61–7.57 (m, 2 H), 7.45–7.41 (m, 5 H), 7.29–7.25 (m, 2 H), 7.19–7.17 (m, 1 H), 7.13–7.07 (m, 2 H), 6.13–6.07 (m, 1 H), 5.19–5.16 (m, 2 H), 5.15–5.08 (m, 1 H), 4.20–4.14 (m, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 193.66, 192.59, 135.21, 134.92, 134.60, 133.13, 132.96, 132.88, 131.51, 128.59, 127.97, 127.92, 127.75, 127.68, 126.84, 126.21, 74.42, 56.18, 39.17.

ESI-MS: *m*/*z* = 408.1 [M + H]$^+$.

(*S*)-2-[1-(2-Methoxyphenyl)-2-nitroethyl]-1,3-diphenylpropane-1,3-dione (12d)

Prepared according to the general procedure; yield: 35.1 mg (87%).

HPLC (Chiralpak AD-H, hexane/*i*-PrOH, 85:15, flow rate 1 mL/min, λ = 210 nm): t_R (major) = 16.9 min, t_R (minor) = 23.2 min; 85% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92–7.83 (m, 4 H), 7.52 (ddd, *J* = 7.7, 5.4, 1.2 Hz, 2 H), 7.42–7.33 (m, 4 H), 7.20–7.08 (m, 2 H), 6.81–6.71 (m, 2 H), 6.07 (d, *J* = 8.0 Hz, 1 H), 5.23 (dd, *J* = 13.1, 9.9 Hz, 1 H), 4.91 (dd, *J* = 13.1, 4.1 Hz, 1 H), 4.81 (ddd, *J* = 9.9, 8.0, 4.1 Hz, 1 H), 3.84 (d, *J* = 2.5 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 194.51, 194.35, 157.17, 136.49, 136.04, 133.84, 132.59 (s), 131.09 (s), 129.44, 128.98, 128.77, 128.67, 124.27, 121.13, 111.00, 75.93, 57.20, 55.35, 41.05.

ESI-MS: *m*/*z* = 404.1 [M + H]$^+$.

(*S*)-2-[1-(2-Ethynylphenyl)-2-nitroethyl]-1,3-diphenylpropane-1,3-dione (12e)

Prepared according to the general procedure; yield: 29.8 mg (75%).

HPLC (Chiralpak AD-H, hexane/*i*-PrOH, 85:15, flow rate 1 mL/min, λ = 254 nm): t_R (major) = 18.6 min, t_R (minor) = 21.2 min; 87% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92–7.86 (m, 2 H), 7.83–7.78 (m, 2 H), 7.55–7.48 (m, 4 H), 7.41–7.33 (m, 4 H), 7.17 (s, 1 H), 7.16–7.11 (m, 2 H), 6.19 (d, *J* = 6.9 Hz, 1 H), 5.27–5.18 (m, 1 H), 5.11 (s, 2 H), 3.49 (s, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 194.55, 193.60, 139.09, 136.29, 135.74, 134.25, 134.10, 133.87, 129.39, 128.97, 128.82, 128.77, 128.72, 127.88, 83.69, 81.84, 75.66, 57.72, 41.93.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{25}H_{19}NO_4$: 420.1212; found: 420.1204.

(*S*)-2-[1-(3-Bromophenyl)-2-nitroethyl]-1,3-diphenylpropane-1,3-dione (12f)

Prepared according to the general procedure; yield: 38.8 mg (86%).

HPLC (Chiralpak AS-H, hexane/*i*-PrOH, 85:15, flow rate 1 mL/min, λ = 210 nm): t_R (major) = 29.0 min, t_R (minor) = 53.1 min; 88% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, *J* = 7.3 Hz, 2 H), 7.84 (d, *J* = 7.6 Hz, 2 H), 7.57 (d, *J* = 7.2 Hz, 2 H), 7.43 (d, *J* = 7.8 Hz, 5 H), 7.27 (d, *J* = 6.1 Hz, 2 H), 7.18 (s, 1 H), 7.10 (t, *J* = 7.6 Hz, 1 H), 6.10 (d, *J* = 6.5 Hz, 1 H), 5.18 (d, *J* = 5.2 Hz, 1 H), 5.14 (s, 1 H), 4.17 (q, *J* = 7.0 Hz, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 192.55, 191.99), 137.48, 132.92, 132.67, 128.88, 127.71, 127.60, 127.43, 127.26, 127.19, 127.09, 125.23, 75.68, 58.08, 42.28.

ESI-MS: *m*/*z* = 453.3 [M + H]$^+$.

(*S*)-2-[1-(3-Chlorophenyl)-2-nitroethyl]-1,3-diphenylpropane-1,3-dione (12g)

Prepared according to the general procedure; yield: 33.4 mg (82%).

HPLC (Chiralpak AS-H, hexane/*i*-PrOH, 85:15, flow rate 1 mL/min, λ = 254 nm): t_R (major) = 24.9 min, t_R (minor) = 45.4 min; 82% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87–7.78 (m, 3 H), 7.77–7.69 (m, 2 H), 7.51–7.46 (m, 2 H), 7.38–7.29 (m, 6 H), 7.07 (s, 3 H), 5.78–5.70 (m, 1 H), 4.95–4.87 (m, 2 H), 4.58–4.46 (m, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 193.91, 193.34, 138.83, 135.99, 135.63, 134.81, 134.28, 134.03, 130.23, 129.07, 128.96, 128.79, 128.61, 128.54, 128.45, 126.59, 77.08, 59.44, 43.63.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{18}ClNO_4$: 430.0822; found: 430.0816.

(*S*)-2-[1-(3-Methoxyphenyl)-2-nitroethyl]-1,3-diphenylpropane-1,3-dione (12h)

Prepared according to the general procedure; yield: 36.7 mg (91%).

HPLC (Chiralpak AD-H, hexane/*i*-PrOH, 85:15, flow rate 1 mL/min, λ = 220 nm): t_R (major) = 20.0 min, t_R (minor) = 32.6 min; 93% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90–7.84 (m, 2 H), 7.82–7.76 (m, 2 H), 7.58–7.47 (m, 2 H), 7.38 (dt, *J* = 11.4, 7.8 Hz, 4 H), 7.11 (t, *J* = 7.9 Hz, 1 H), 6.82 (d, *J* = 7.7 Hz, 1 H), 6.76–6.72 (m, 1 H), 6.69 (dd, *J* = 8.2, 1.9 Hz, 1 H), 5.83 (d, *J* = 7.9 Hz, 1 H), 4.98 (dd, *J* = 6.8, 3.4 Hz, 2 H), 4.59 (td, *J* = 8.1, 5.3 Hz, 1 H), 3.67 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 194.29, 193.61, 159.83, 138.35, 136.21, 135.84, 134.12, 133.83, 130.06, 128.99, 128.87, 128.82, 128.65, 120.36, 114.28, 113.59, 77.26, 59.71, 55.20, 44.05.

ESI-MS: *m*/*z* = 404.1 [M + H]$^+$.

(*S*)-2-[1-(4-Bromophenyl)-2-nitroethyl]-1,3-diphenylpropane-1,3-dione (12i)

Prepared according to the general procedure; yield: 39.2 mg (87%).

HPLC (Chiralpak AD-H, hexane/*i*-PrOH, 85:15, flow rate 1 mL/min, λ = 220 nm): t_R (major) = 29.8 min, t_R (minor) = 40.9 min; 74% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.93–7.86 (m, 2 H), 7.82–7.76 (m, 2 H), 7.59–7.50 (m, 2 H), 7.39 (dt, *J* = 14.0, 7.8 Hz, 4 H), 7.33 (d, *J* = 8.4 Hz, 2 H), 7.12 (d, *J* = 8.5 Hz, 2 H), 5.81 (d, *J* = 8.2 Hz, 1 H), 4.94 (d, *J* = 7.1 Hz, 2 H), 4.60 (dd, *J* = 14.7, 7.2 Hz, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 194.06, 193.45, 136.08, 135.89, 135.76, 134.40, 134.14, 132.21, 130.12, 129.18, 129.07, 128.89, 128.71, 122.35, 59.69, 43.65.

ESI-MS: *m*/*z* = 453.3 [M + H]$^+$.

(*S*)-2-[1-(4-Chlorophenyl)-2-nitroethyl]-1,3-diphenylpropane-1,3-dione (12j)

Prepared according to the general procedure; yield: 37.4 mg (92%)

HPLC (Chiralpak AS-H, hexane/*i*-PrOH, 85:15, flow rate 1 mL/min, λ = 210 nm): t_R (major) = 27.6 min, t_R (minor) = 38.3 min; 90% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.93–7.86 (m, 2 H), 7.82–7.75 (m, 2 H), 7.58–7.53 (m, 2 H), 7.45–7.37 (m, 4 H), 7.18 (s, 4 H), 5.84–5.76 (m, 1 H), 4.98–4.91 (m, 2 H), 4.66–4.57 (m, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 194.0, 193.3, 136.0, 135.7, 135.2, 134.3, 134.1, 134.0, 1297, 129.2, 129.1, 129.0, 128.8, 128.68, 77.24, 59.78, 43.5.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{18}ClNO_4$: 430.0822; found: 430.0818.

(*S*)-2-[2-Nitro-1-(*p*-tolyl)ethyl]-1,3-diphenylpropane-1,3-dione (12k)

Prepared according to the general procedure; yield: 36.4 mg (94%).

HPLC (Chiralpak AS-H, hexane/*i*-PrOH, 85:15, flow rate 1 mL/min, λ = 54 nm): t_R (major) = 20.7 min, t_R (minor) = 28.1 min; 96% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91–7.85 (m, 2 H), 7.83–7.76 (m, 2 H), 7.52 (ddd, *J* = 7.4, 5.8, 3.1 Hz, 3 H), 7.38 (dt, *J* = 12.3, 7.8 Hz, 4 H), 7.12 (d, *J* = 8.1 Hz, 2 H), 7.00 (d, *J* = 7.9 Hz, 2 H), 5.84 (d, *J* = 8.1 Hz, 1 H), 4.99–4.92 (m, 2 H), 4.63–4.55 (m, 1 H), 2.22 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 194.36, 193.68, 137.91, 136.23, 135.88, 134.07, 133.78, 133.68, 129.66, 128.97, 128.83, 128.67, 128.13, 127.21, 77.55, 60.03, 43.78, 21.03.

ESI-MS: *m*/*z* = 388.3 [M + H]$^+$.

(*S*)-2-[1-(4-Methoxyphenyl)-2-nitroethyl]-1,3-diphenylpropane-1,3-dione (12l)

Prepared according to the general procedure; yield: 35.9 mg (89%).

HPLC (Chiralpak AD-H, hexane/*i*-PrOH, 70:30, flow rate 1 mL/min, λ = 230 nm): t_R (major) = 10.7 min, t_R (minor) = 21.6 min; 85% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.89 (dd, *J* = 8.4, 1.1 Hz, 2 H), 7.79 (dd, *J* = 8.4, 1.1 Hz, 2 H), 7.58–7.47 (m, 3 H), 7.43–7.32 (m, 4 H), 7.18–7.12 (m, 2 H), 6.75–6.68 (m, 2 H), 5.81 (d, *J* = 8.2 Hz, 1 H), 4.94 (d, *J* = 6.7 Hz, 2 H), 4.65–4.52 (m, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 194.37, 193.75, 159.27, 136.22, 135.92, 134.11, 133.81, 129.44, 129.00, 128.87, 128.83, 128.66, 128.53, 114.36, 77.71, 60.13, 55.23, 43.49.

ESI-MS: *m*/*z* = 404.1 [M + H]$^+$.

(*S*)-2-[1-(2,4-Dimethoxyphenyl)-2-nitroethyl]-1,3-diphenylpropane-1,3-dione (12m)

Prepared according to the general procedure; yield: 39.0 mg (90%).

HPLC (Chiralpak AD-H, hexane/*i*-PrOH, 70:30, flow rate 1 mL/min, λ = 230 nm): t_R (major) = 11.2 min, t_R (minor) = 14.4 min; 51% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.95–7.78 (m, 4 H), 7.52 (dd, *J* = 16.0, 7.5 Hz, 2 H), 7.38 (dt, *J* = 11.6, 7.8 Hz, 4 H), 7.06 (d, *J* = 8.9 Hz, 1 H), 6.37–6.23 (m, 2 H), 6.04 (d, *J* = 8.2 Hz, 1 H), 5.18 (dd, *J* = 12.8, 10.1 Hz, 1 H), 4.84 (dd, *J* = 12.8, 4.2 Hz, 1 H), 4.73 (ddd, *J* = 10.0, 8.3, 4.2 Hz, 1 H), 3.81 (s, 3 H), 3.69 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 194.49 (s), 194.30 (s), 160.65 (s), 158.12 (s), 136.46 (s), 136.06 (s), 133.80 (s), 133.63 (s), 131.74 (s), 128.89 (s), 128.68 (s), 128.63 (s), 128.58 (s), 116.39 (s), 104.48 (s), 99.06 (s), 76.09 (s), 57.42 (s), 55.29 (d, *J* = 2.9 Hz), 40.73 (s).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{23}NO_6$: 456.1423; found: 456.1418.

(*R*)-2-[1-(2-Furyl)-2-nitroethyl]-1,3-diphenylpropane-1,3-dione (12n)

Prepared according to the general procedure; yield: 34.1 mg (94%).

HPLC (Chiralpak AS-H, hexane/*i*-PrOH, 85:15, flow rate 1 mL/min, λ = 210 nm): t_R (minor) = 20.7 min, t_R (major) = 25.1 min; –91% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90–7.81 (m, 4 H), 7.55 (t, *J* = 7.3 Hz, 2 H), 7.40 (dd, *J* = 13.2, 7.6 Hz, 4 H), 7.21 (s, 1 H), 6.11 (t, *J* = 2.9 Hz, 2 H), 6.02 (d, *J* = 7.8 Hz, 1 H), 4.94 (dd, *J* = 9.4, 6.4 Hz, 2 H), 4.72 (d, *J* = 4.2 Hz, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 193.76, 149.77, 142.49, 135.88, 135.43, 134.12, 133.95, 129.01, 128.93, 128.64, 110.71, 108.96, 75.57, 56.71, 37.80.

ESI-MS: *m*/*z* = 364.5 [M + H]$^+$.

(*R*)-2-[2-Nitro-1-(2-thienyl)ethyl]-1,3-diphenylpropane-1,3-dione (12o)

Prepared according to the general procedure; yield: 34.5 mg (91%).

HPLC (Chiralpak AS-H, hexane/*i*-PrOH, 85:15, flow rate 1 mL/min, λ = 262 nm): t_R (major) = 23.9 min, t_R (minor) = 26.8 min; 83% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91–7.83 (m, 4 H), 7.57–7.52 (m, 2 H), 7.41 (t, *J* = 7.8 Hz, 4 H), 7.12 (dd, *J* = 5.1, 0.9 Hz, 1 H), 6.87 (d, *J* = 2.8 Hz, 1 H), 6.80 (dd, *J* = 5.1, 3.6 Hz, 1 H), 5.96 (d, *J* = 7.3 Hz, 1 H), 5.00 (d, *J* = 6.0 Hz, 2 H), 4.89 (dd, *J* = 13.0, 7.0 Hz, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 194.16 (s), 193.64 (s), 139.35 (s), 136.10 (s), 135.71 (s), 134.28 (s), 134.14 (s), 129.13 (s), 129.09 (s), 128.85 (s), 128.81 (s), 127.28 (s), 127.20 (s), 125.56 (s), 78.09 (s), 60.00 (s), 39.60 (s).

ESI-MS: *m*/*z* = 380.4 [M + H]$^+$.

(*S*)-2-[1-Ferrocenyl-2-nitroethyl)-1,3-diphenylpropane-1,3-dione (12p)

Prepared according to the general procedure; yield: 29.8 mg (62%).

HPLC (Chiralpak AD-H, hexane/*i*-PrOH, 70:30, flow rate 1 mL/min, λ = 254 nm): t_R (minor) = 11.6 min, t_R (major) = 13.1 min; –67% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81–7.75 (m, 4 H), 7.57–7.47 (m, 2 H), 7.44–7.31 (m, 4 H), 5.90–5.83 (m, 1 H), 5.27–5.09 (m, 2 H), 4.28–4.19 (m, 1 H), 4.13 (s, 5 H), 4.06–3.96 (m, 4 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 194.82, 194.34, 136.01, 135.96, 133.77, 133.74, 128.86, 128.83, 128.64, 128.56, 87.13, 77.76, 69.29, 69.05, 68.41, 67.79, 66.64, 59.59, 38.60.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{27}H_{23}FeNO_4$: 504.0874; found: 504.0871.

Funding Information

This work was funded by the National Natural Science Foundation of China (21572200).

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0039-1691643.

References

(1) (a) Mohr, J. T.; Krout, M. R.; Stoltz, B. M. *Nature* **2008**, *455*, 323. (b) MacMillan, D. W. C. *Nature* **2008**, *455*, 304. (c) Tsogoeva, S. B. *Eur. J. Org. Chem.* **2007**, *11*, 1701. (d) Yang, J. W. *Science* **2006**, *313*, 1584. (e) Seayad, J.; List, B. *Org. Biomol. Chem.* **2005**, *3*, 719. (f) Dalko, P. I.; Moisan, L. *Angew. Chem. Int. Ed.* **2004**, *43*, 5138. (g) Grondal, C.; Jeanty, M.; Enders, D. *Nat. Chem.* **2010**, *2*, 167. (h) Oliveira, V. G.; Cardoso, M. F. C.; Forezi, L. S. M. *Catalysts* **2018**, *8*, 605. (i) Qin, Y.; Zhu, L.; Luo, S. *Chem. Rev.* **2017**, *117*, 9433.

(2) (a) Zhang, Z.; Schreiner, P. R. *Chem. Soc. Rev.* **2009**, *38*, 1187. (b) Connon, S. J. *Chem. Eur. J.* **2006**, *12*, 5418. (c) Koutoulogenis, G.; Kaplaneris, N.; Kokotos, C. G. *Beilstein J. Org. Chem.* **2016**, *12*, 462. (d) Fang, X.; Wang, C.-J. *Chem. Commun.* **2015**, *51*, 1185. (e) Giacalone, F.; Gruttadauria, M.; Agrigento, P.; Noto, R. *Chem. Soc. Rev.* **2012**, *41*, 2406. (f) Palomo, C.; Oiarbide, M.; López, R. *Chem. Soc. Rev.* **2009**, *38*, 632.

(3) (a) Takemoto, Y. *Org. Biomol. Chem.* **2005**, *3*, 4299. (b) Taylor, M. S.; Jacobsen, E. N. *Angew. Chem. Int. Ed.* **2006**, *45*, 1520. (c) Vakulya, B.; Varga, S.; Csampai, A.; Soos, T. *Org. Lett.* **2005**, *7*, 1967. (d) Tsogoeva, S. B.; Yalalov, D. A.; Hateley, M. J.; Weckbecker, C.; Huthmacher, K. *Eur. J. Org. Chem.* **2005**, *23*, 4995. (e) Sohtome, Y.; Takemura, N.; Takada, K.; Takagi, R.; Iguchi, T.; Nagasawa, K. *Chem. Asian J.* **2007**, *2*, 1150. (f) Sohtome, Y.; Hashimoto, Y.; Nagasawa, K. *Adv. Synth. Catal.* **2005**, *347*, 1643. (g) Cao, C.; Ye, M.; Sun, X.; Tang, Y. *Org. Lett.* **2006**, *8*, 2901. (h) Cao, Y.; Lai, Y.; Wang, X.; Li, Y.; Xiao, W. *Tetrahedron Lett.* **2007**, *48*, 21. (i) Chang, Y.; Yang, J.; Dang, J.; Xue, Y. *Synlett* **2007**, 2283.

(4) (a) Kim, S. M.; Lee, J. H.; Kim, D. Y. *Synlett* **2008**, 2659. (b) Jung, S. H.; Kim, D. Y. *Tetrahedron Lett.* **2008**, *49*, 5527. (c) Peng, F.; Shao, Z.; Fan, B.; Song, H.; Li, G.; Zhang, H. *J. Org. Chem.* **2008**, *73*, 5202. (d) Kang, Y. K.; Kim, D. Y. *J. Org. Chem.* **2009**, *74*, 5734. (e) Li, Y.; Li, X.; Peng, F.; Li, Z.; Wu, S.; Sun, Z.; Zhang, H.; Shao, Z. *Org. Lett.* **2011**, *13*, 6200. (f) Li, X.; Li, Y.; Peng, F.; Li, Z.; Wu, S.; Sun, Z.; Zhang, H.; Shao, Z. *Org. Lett.* **2011**, *13*, 6160. (g) Tan, B.; Zhang, X.; Chua, P.; Zhong, G. *Chem. Commun.* **2009**, 779.

(5) (a) Xu, F.; Huang, D.; Han, C.; Shen, W.; Lin, X.; Wang, Y. *J. Org. Chem.* **2010**, *75*, 8677. (b) Huang, D.; Xu, F.; Lin, X.; Wang, Y. G. *Chem. Eur. J.* **2012**, *18*, 3148. (c) Li, X.; Zhao, Y.; Qu, H.; Mao, Z.; Lin, X. *Chem. Commun.* **2013**, *49*, 1401. (d) Huang, D.; Li, X.; Xu, F.; Li, L.; Lin, X. *ACS Catal.* **2013**, *3*, 2244. (e) Li, X.; Chen, D.; Gu, H.; Lin, X. *Chem. Commun.* **2014**, *50*, 7538. (f) Shen, X.; Wang, Y.; Wu, T.; Mao, Z.; Lin, X. *Chem. Eur. J.* **2015**, *21*, 9039. (g) Lou, H.; Wang, Y.; Jin, E.; Lin, X. *J. Org. Chem.* **2016**, *81*, 2019. (h) Xie, E.; Rahman, A.; Lin, X. *Org. Chem. Front.* **2017**, *4*, 1407. (i) Rahman, A.; Lin, X. *Org. Biomol. Chem.* **2018**, *16*, 4753. (j) Luo, J.; Zhang, T.; Wang, L.; Liao, G.; Yao, Q.; Wu, Y.; Zhan, B.; Lan, Y.; Lin, X.; Shi, B. *Angew. Chem. Int. Ed.* **2019**, *58*, 6708.

(6) (a) Čorić, I.; Müller, S.; List, B. *J. Am. Chem. Soc.* **2010**, *132*, 17370. (b) Xing, C.; Liao, Y.; Ng, J.; Hu, Q. *J. Org. Chem.* **2011**, *76*, 4125. (c) Xu, B.; Zhu, S.-F.; Xie, X.-L.; Shen, J.-J.; Zhou, Q.-L. *Angew. Chem. Int. Ed.* **2011**, *50*, 11483. (d) Rubush, D. M.; Morges, M. A.; Rose, B. J.; Thamm, D. H.; Rovis, T. *J. Am. Chem. Soc.* **2012**, *134*, 13554. (e) Chen, Z.; Wang, B.; Wang, Z.; Zhu, G.; Sun, J. *Angew. Chem. Int. Ed.* **2013**, *52*, 2027. (f) Wu, J.; Wang, Y.; Drljevic, A.; Rauniyar, V.; Phipps, R.; Toste, F. D. *Proc. Natl. Acad. Sci. U. S. A.* **2013**, *110*, 13729. (g) Wang, S.-G.; You, S.-L. *Angew. Chem. Int. Ed.* **2014**, *53*, 2194. (h) Zhang, Y.; Zhao, J.; Jiang, F.; Sun, S.; Shi, F. *Angew. Chem. Int. Ed.* **2014**, *53*, 13912. (i) Gobé, V.; Guinchard, X. *Chem. Eur. J.* **2015**, *21*, 8511. (j) Rong, Z.; Zhang, Y.; Chua, R. H. B.; Pan, H.; Zhao, Y. *J. Am. Chem. Soc.* **2015**, *137*, 4944. (k) Li, S.; Zhang, J.; Li, X.; Cheng, D.; Tan, B. *J. Am. Chem. Soc.* **2016**, *138*, 16561. (l) Zhang, J.; Yu, P.; Li, S.-Y.; Sun, H.; Xiang, S.-H.; Wang, J.-J.; Houk, K. N.; Tan, B. *Science* **2018**, *361*, 6407. (m) Qi, L.-W.; Mao, J. -H.; Zhang, J.; Tan, B. *Nat. Chem.* **2018**, 10. (n) Yin, Y.; Dai, Y.; Jia, H.; Li, J.; Bu, L.; Qiao, B.; Zhao, X.; Jiang, Z. *J. Am. Chem. Soc.* **2018**, *140*, 6083. (o) Qi, L.-W.; Li, S.; Xiang, S.-H.; Wang, J.; Tan, B. *Nat. Catal.* **2019**, *2*, 314. (p) Gong, W.; Chen, X.; Jiang, H.; Chu, D.; Cui, Y.; Liu, Y. *J. Am. Chem. Soc.* **2019**, *141*, 7498.

(7) Xie, E.; Huang, S.; Lin, X. *Org. Lett.* **2019**, *21*, 3682.

(8) (a) Sun, W.; Gu, H.; Lin, X. *J. Org. Chem.* **2018**, *83*, 4034. (b) Chang, S.; Wang, L.; Lin, X. *Org. Biomol. Chem.* **2018**, *16*, 2239. (c) Gu, H.; Han, Z.; Xie, H.; Lin, X. *Org. Lett.* **2018**, *20*, 6544. (d) Shan, H.; Zhou, Q.; Yu, J.; Zhuang, S.; Hong, X.; Lin, X. *J. Org. Chem.* **2018**, *83*, 11873. (e) Zhou, Q.; Pan, R.; Shan, H.; Lin, X. *Synthesis* **2018**, *51*, 557. (f) Wang, L.; Zhong, J.; Lin, X. *Angew. Chem. Int. Ed.* **2019**, *58*, 15824.

(9) (a) Mase, N.; Thayumanavan, R.; Tanaka, F.; Barbas, C. F. III. *Org. Lett.* **2004**, *6*, 2527. (b) Wang, W.; Wang, J.; Li, H. *Angew. Chem. Int. Ed.* **2005**, *44*, 1369. (c) Mase, N.; Watanabe, K.; Yoda, H.; Tanaka, F.; Barbas, C. F. III. *J. Am. Chem. Soc.* **2006**, *128*, 4966. (d) Okino, T.; Hoashi, Y.; Takemoto, Y. *J. Am. Chem. Soc.* **2003**, *125*, 12672. (e) Zhou, W.; Liu, H.; Du, D. *Org. Lett.* **2008**, *10*, 2817. (f) Tsubogo, T.; Yamashita, Y.; Kobayashi, S. *Angew. Chem. Int. Ed.* **2009**, *48*, 9117.