Highly enantioselective Michael addition of 3-arylthio- and 3-alkylthiooxindoles to nitroolefins catalyzed by a simple cinchona alkaloid derived phosphoramide

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(Part I)

^{1}H, ^{13}C, ^{19}F, ^{31}P NMR and HPLC spectra are provided in Part II and III

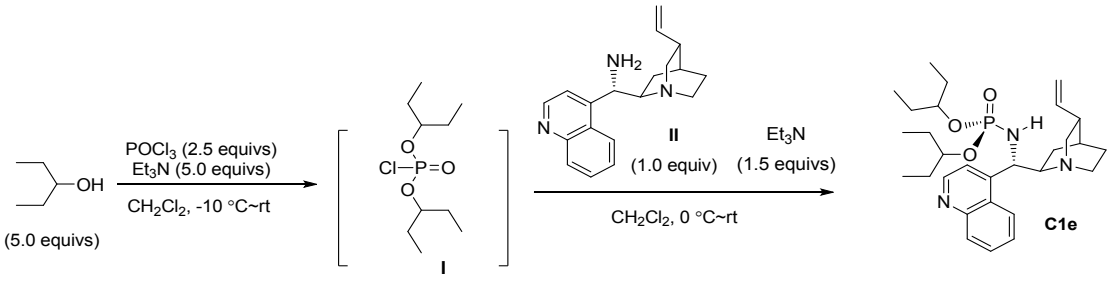
1. General information:

Reactions were monitored by thin layer chromatography using UV light to visualize the course of reaction. Purification of reaction products was carried out by flash chromatography on silica gel. Chemical yields refered to pure isolated substances. ^{1}H and ^{13}C NMR spectra were obtained using a Bruker DPX-400 spectrometer. The $[\alpha]_D$ was recored using PolAAr 3005 High Accuracy Polarimeter. Chemical shifts were reported in ppm from $CDCl_3$ with the solvent resonance as the internal standard. The following abbreviations were used to designate chemical shift multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, h = heptet, m = multiplet, br = broad.

All reactions were carried out in air except noted. Anhydrous CH_2Cl_2 was prepared by first distillation over P_2O_5 and then from CaH_2. Anhydrous Et_2O was distilled by distillation over sodium-benzophenone ketyl prior to use. Powerered MS 5Å was purchased from Aldrich and dried under vacuum at 120 ^{o}C for 12 hours, and then stored under nitrogen. Cinchonidine, quinine and cinchonine were puchased from Aldrich and used as received. Cinchona alkaloid derived primary amine was prepared according to literature method[1].

[1] (a) X. Liu, H. Li and L. Deng, *Org. Lett.,* 2005, **7**, 167; (b) B.Vakulya, S. Varga, A. Csámpai and T. Soós, *Org. Lett.,* 2005, **7**, 1967.

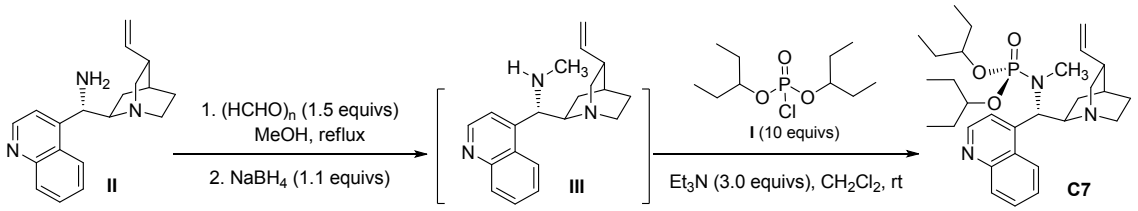
2. Synthesis of cinchonidine-derived bifunctional phosphoramide C1e



Under an atmosphere of N_2, to a flame-dried three-necked 25 mL flask were added $POCl_3$ (0.5 mL, 5.0 mmol) and 3.0 mL of anhydrous CH_2Cl_2. Then a solution of 3-pentanol (1.1 mL, 10.0 mmol) and Et_3N (1.5 mL, 10.0 mmol) in 6.0 mL of CH_2Cl_2 was added dropwise at -10 °C.The mixture was allowed to warm to room temperature. After being stirred for 12 h, the reaction mixture containing phosphorochloridate intermediate **I** was concentrated under reduced pressure, and was directly used for the next step.

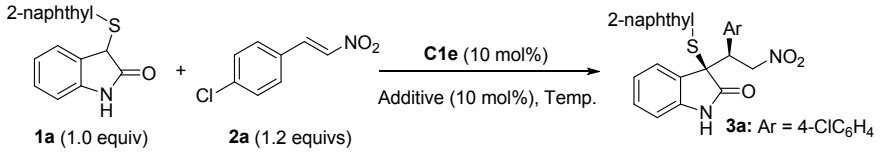
Under an atmosphere of N_2, to a three-necked flask were added cinchonidine-derived primary amine **II** (587.6 mg, 2.0 mmol) and 8.0 mL of anhydrous CH_2Cl_2, followed by the addition of Et_3N (0.5 mL, 3.0 mmol). And then the pre-prepared phosphorochloridate **I** was added dropwise to the reaction mixture at 0 °C. After 30 minutes, the resulting mixture was stirred at room temperature until the complete consumption of **II** by TLC analysis (about 5 h). Then 10.0 mL of saturated $NaHCO_3$ (aq.) was added to the reaction mixture, followed by an extraction using dichoromethane (10.0 mL × 4). The combined organic layer was washed with water and brine, dried over anhydrous Na_2SO_4, filtered and concentrated on a rotary evaporator. The residue was purified by flash chromatography on silica gel using EtOAc:$NH_3 \cdot H_2O$ (200:1, v/v) as eluent to furnish desired chiral phosphoramide catalyst **C1e** as yellowish oil (505 mg, 49% yield). (Due to the distinct presence of rotameric isomers, the ^1H NMR and ^{13}C NMR, ^{31}P NMR spectra seemed complex, so we did not designate the date, and attached the spectrum behind), ^1H NMR (400 MHz, $CDCl_3$): see below; ^{13}C NMR (100 MHz, $CDCl_3$): see below; ^{31}P NMR (161.9 MHz, $CDCl_3$): see below; IR (neat): 2937, 1459, 1382, 1341, 1236, 975, 761, 669; HRMS (ESI): Exact mass calcd for $C_{29}H_{45}N_3O_3P$ $[M+H]^+$: 514.3193, Found: 514.3199.

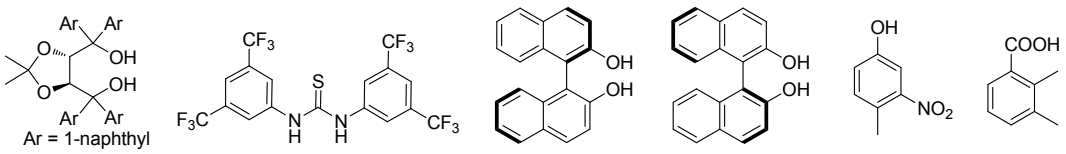
3. Synthesis of cinchonidine-derived *N*-methylated phosphoramide C7



Under an atmosphere of N_2, cinchonidine-derived primary amine **II** (526.9 mg, 1.8 mmol) and triformol (81 mg, 2.7 mmol) were dissolved in 10.0 mL of anhydrous CH_3OH. The reaction mixture was refluxed for 2.5 h, and then cooled to 0 ^oC, followed by the addition of $NaBH_4$ (81.2 mg, 2.0 mmol). The resulting mixture was stirred overnight, and then 2.0 mL of water was added. After concentrated under reduced pressure, the residue was extracted with CH_2Cl_2 (10.0 mL×4). The combined organic phase was then dried and concentrated, and column chromatography on silical gel afforded the *N*-Me protected product **III** as a white solid, which was directly used for the next step of phosphoramide formation, according to the procedure described in section 2. The *N*-methylated bifunctional phosphoramide catalyst **C7** was obtained by flash chromatography on silica gel, using EtOAc: petroleum ether (1:4, v/v) as eluent, as white solid in 173.5 mg (66% yield). ^1H NMR (400 MHz, $CDCl_3$): δ 8.93 (d, J = 8.4 Hz, 1H), 8.89 (d, J = 4.4 Hz, 1H), 8.12-8.10 (m, 1H), 7.74-7.70 (m, 1H), 7.66-7.62 (m, 1H), 7.22 (d, J = 4.8 Hz, 1H), 5.98-5.89 (m, 1H), 5.80 (t, J = 10.8 Hz, 1H), 5.08-5.03 (m, 2H), 4.50-4.42 (m, 1H), 3.68-3.58 (m, 2H), 3.53-3.46 (m, 1H), 3.27-3.21 (m, 1H), 2.83-2.78 (m, 1H), 2.70-2.63 (m, 1H), 2.38 (d, J = 9.2 Hz, 3H), 2.29 (brs, 1H), 1.75-1.66 (m, 6H), 1.63-1.47 (m, 2H), 1.43-1.34 (m, 2H), 1.07-1.01 (m, 1H), 0.96-0.90 (m, 7H), 0.71 (t, J = 7.6 Hz, 3H), 0.53-0.48 (m, 1H), 0.26 (t, J = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.19, 143.40, 143.37, 142.34, 129.91, 129.27, 128.13, 127.00, 125.33, 119.32, 114.09, 79.47, 79.42, 79.06, 79.00, 56.62, 54.95, 54.89, 53.00, 52.98, 41.11, 39.96, 27.97, 27.87, 27.79, 27.28, 26.86, 26.82, 26.77, 26.62, 26.57, 9.19, 9.13, 9.10, 8.61. ^{31}P NMR (161.9 MHz, $CDCl_3$): δ 6.90. IR (neat): 2926, 1251, 1222, 1045, 1013, 975, 921, 880, 762. HRMS (ESI): Exact mass calcd for $C_{30}H_{47}N_3O_3P$ $[M+H]^+$: 528.3350, Found: 528.3354.

4. **The evaluation of different additives for the reaction of 1a and 2a.**





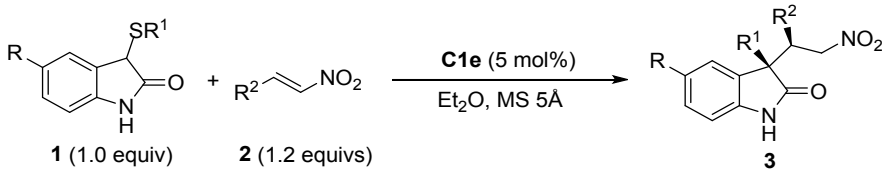
Entry [a]	Temp. (°C)	Additive	Time (h)	Yield[b] (%)	Dr[c]	Ee[d] (%)
1	-10	-	17	95	5.4:1	94
2[e]	-10	MS 3Å	21	92	6.4:1	95
3[e]	-10	MS 4Å	21	90	5.7:1	94
4[e]	-10	MS 13X	21	93	6.4:1	96
5[e]	-10	MS 5Å	21	91	6.5:1	96
6	-20	-	36	94	6.2:1	95
7	-20	**A1**	24	97	6.1:1	94
8	-20	**A2**	24	94	3.0:1	81
9	-20	**A3**	24	99	5.1:1	92
10	-20	**A4**	24	99	4.8:1	93
11	-20	**A5**	24	99	5.3:1	94
12	-20	**A6**	36	92	5.5:1	94
13	-20	$PhCO_2H$	36	98	5.7:1	94
14	-20	*o*-$OHC_6H_4CO_2H$	36	77	5.2:1	93
15	-20	*o*-$ClC_6H_4CO_2H$	96	97	6.1:1	95

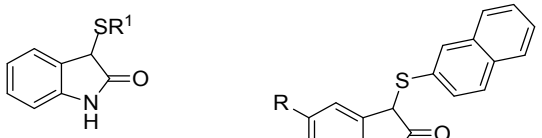
[a] Run on a 0.10 mmol scale. [b] Isolated yield. [c] Determined by ^1H NMR analysis of the crude reaction mixtures. [d] Determined by chiral HPLC analysis, for major diastereomer. [e] 50 mg powdered MS added.

To further improve the stereoselectivities of the reaction, we tried a variety of additives in the reaction of 3-thiooxindoles **1a** to nitroolefin **2a** in Et_2O, in the presence of 10 mol% catalyst **C1e**. First, different types of powdered molecular sieves (MS) were attempted, and it was found that several types of MS we examined all improved stereoselectivities to some extent, but MS 5Å as additive afforded the best result (entry 1 vs entries 4-5). Based on our previous finding that the addition of Brønsted acids could benefit on the enantioselectivity in the tertiary amine catalyzed Morita-Baylis-Hillman reaction,[2] a variety of Brønsted acids were then tried, including hydrogen-bond donors **A1-A5** and a variety of carboxylic acids. Unfortunately**,** none of them could improve the stereoselectivities (entries 7-15 vs entry 6).

[2] X.-P. Zeng, Y.-L. Liu, C.-B. Ji and J. Zhou, *Chin. J. Chem.,* 2012, **30**, 2631.

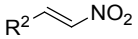
5. General procedure for the asymmetric Michael addition





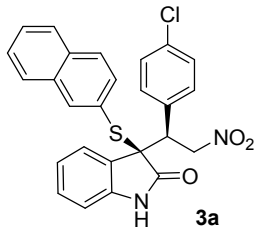
1a: R^1 = 2-naphtyl
1b: R^1 = Ph
1c: R^1 = *p*-ClC_6H_4
1d: R^1 = *p*-$MeOC_6H_4$
1e: R^1 = Bn
1f: R^1 = allyl

1g: R = F
1h: R = Cl
1i: R = Et
1j: R = MeO



2a: R^2 = *p*-ClC_6H_4
2b: R^2 = *p*-$CF_3C_6H_4$
2c: R^2 = *p*-FC_6H_4
2d: R^2 = *p*-BrC_6H_4
2e: R^2 = Ph
2f: R^2 = *p*-MeC_6H_4
2g: R = 2-thienyl
2h: R = *n*-Pr
2i: R = *i*-Pr
2j: R = $BnCH_2$

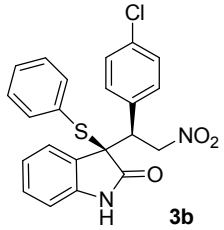
To a 5.0 mL vial were added catalyst **C1e** (6.4 mg, 0.0125 mmol), 3-thiooxindoles **1** (0.25 mmol) and MS 5Å (125.0 mg), followed by the addition of 2.5 mL anhydrous Et_2O. The reaction mixture was stirred vigorously at room temperature until full dissolution of 3-thiooxindoles **1**, and then cooled to -20 ^oC and kept stirring for about 30 min before nitroolefin **2** (0.30 mmol) was added. After the full conversion of 3-thiooxindoles **1** by TLC analysis, The solvent was carefully removed under reduced pressure, and then the residue was directly subjected to column chromatography to afford the desired product **3** using DCM as eluent.



3a

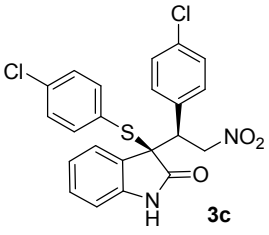
The reaction was run at -20 ^oC for 1.5 days, with 5 mol% of **C1e**, affording product **3a** in 95% yield as white solid (m.p. 170-173 ^oC); ^1H NMR analysis revealed that the dr vlues is 8:1. HPLC analysis [Chiralcel AD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; major diastereomer: t_r (major) = 15.02 min, t_r (minor) = 20.99 min, minor diastereomer: t_r (major) 24.92 min, t_r (minor) = 11.87 min] gave the isomeric composition of major diastereomer: 96% ee; $[\alpha]^{25}_D$ = -11.1 (c = 0.51, CH_2Cl_2); ^1H NMR for the major diastereomer (400 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.62-7.57 (m, 3H), 7.49-7.41 (m, 2H), 7.34 (d, *J* = 7.2 Hz, 1H), 7.27-7.25 (m, 1H), 7.23-7.13 (m, 2H), 7.08-7.04 (m, 2H), 6.84 (d, *J* = 8.8 Hz, 2H), 6.49 (d, *J*= 8.0 Hz, 1H), 5.79 (dd, *J* = 12.8, 3.6 Hz, 1H), 5.16 (t, *J* = 12.8 Hz, 1H), 4.26 (dd, *J* = 12.0, 3.2 Hz, 1H). ^{13}C NMR for the major diastereomer (100 MHz, $CDCl_3$): δ 175.24, 140.44, 137.38, 134.49, 133.48, 133.13, 132.49, 132.32, 130.46, 129.99, 128.57, 128.22, 128.08, 127.56, 127.45, 126.79, 126.48,

125.40, 124.92, 122.91, 110.41, 76.34, 60.60, 47.27. IR (neat): 3067, 1710, 1555, 1472, 1014, 753, 685; HRMS (ESI): Exact mass calcd for $C_{26}H_{23}ClN_3O_3S$ $[M+NH_4]^+$: 492.1143, Found: 492.1147.



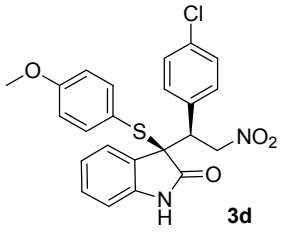
3b

The reaction was run at -30 °C for 1.5 days, with 5 mol% of **C1e**, affording product **3b** in 93% yield as white solid (m.p. 162-165 °C); ^{1}H NMR analysis revealed that the dr vlues is 7:1. HPLC analysis [Chiralcel IF, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; major diastereomer: t_r (major) = 22.44 min, t_r (minor) = 13.57 min, minor diastereomer: t_r (major) 19.47 = min, t_r (minor) = 9.57 min] gave the isomeric composition of major diastereomer: 96% ee; $[\alpha]^{25}_D$ = -68.2 (c = 0.56, CH_2Cl_2); ^{1}H NMR for the major diastereomer (400 MHz, $CDCl_3$) δ 7.41 (s, 1H), 7.32-7.26 (m, 4H), 7.24-7.07 (m, 6H), 6.84 (d, *J* = 8.4 Hz, 2H), 6.57 (d, *J* = 7.6 Hz, 1H), 5.70 (dd, *J* = 12.8, 3.2 Hz, 1H), 5.11 (t, *J* = 12.4 Hz, 1H), 4.21 (dd, *J* = 12.0, 3.2 Hz, 1H). ^{13}C NMR for the major diastereomer (100 MHz, $CDCl_3$) δ 175.19, 140.36, 136.74, 134.51, 132.35, 130.48, 130.12, 129.95, 128.79, 128.57, 127.72, 126.72, 125.49, 122.89, 110.20, 76.23, 60.55, 47.24; IR (neat): 2964, 1714, 1556, 1263, 1108, 1023, 810, 749, 691; HRMS (ESI): Exact mass calcd for $C_{22}H_{21}ClN_3O_3S$ $[M+NH_4]^+$: 442.0987, Found: 442.0990.



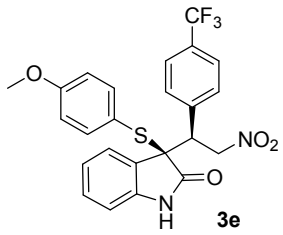
3c

The reaction was run at -30 °C for 1.5 days, with 5 mol% of **C1e**, affording product **3c** in 92% yield as white solid (m.p. 174-176 °C); ^{1}H NMR analysis revealed that the dr vlues is 7:1. HPLC analysis [Chiralcel IF, ^{i}PrOH/hexane = 10/90, 1.0 mL/min, 230 nm; major diastereomer: t_r (major) = 35.07 min, t_r (minor) = 19.15 min, minor diastereomer: t_r (major) = 21.93 min, t_r (minor) = 13.80 min] gave the isomeric composition of major diastereomer: 97% ee; $[\alpha]^{25}_D$ = -39.9 (c = 0.73, CH_2Cl_2); ^{1}H NMR for the major diastereomer (400 MHz, $CDCl_3$) δ 7.28-7.26 (m, 3H), 7.25-7.23 (m, 2H), 7.16-7.12 (m, 3H), 7.09 (d, *J* = 8.4 Hz, 2H), 6.84 (d, *J* = 8.4 Hz, 2H), 6.60 (d, *J* = 7.6 Hz, 1H), 5.65 (dd, *J* = 12.8, 3.2 Hz, 1H), 5.10 (t, *J* = 12.4 Hz, 1H), 4.20 (dd, *J* = 12.0, 3.6 Hz, 1H). ^{13}C NMR for the major diastereomer (100 MHz, $CDCl_3$) δ 174.73, 140.28, 137.96, 136.84, 134.63, 132.16, 130.45, 130.19, 129.07, 128.63, 126.51, 126.15, 125.41, 123.05, 110.33, 76.14, 60.61, 47.28. IR (neat): 3088, 2822, 1714, 1555, 1473, 1093, 1014, 823, 757, 659; HRMS (ESI): Exact mass calcd for $C_{22}H_{20}Cl_2N_3O_3S$ $[M+NH_4]^+$: 476.0597, Found: 476.0590.



3d

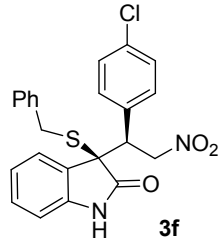
The reaction was run at 0 °C for 3.5 days, with 5 mol% of **C1e**, affording product **3d** in 90% yield as white solid (m.p. 135-137 °C); ^{1}H NMR analysis revealed that the dr vlues is 5:1. HPLC analysis [Chiralcel AD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; major diastereomer: t_r (major) = 16.37 min, t_r (minor) = 25.52 min, minor diastereomer: t_r (major) = 29.63 min, t_r (minor) = 18.56 min] gave the isomeric composition of major diastereomer: 93% ee; $[\alpha]^{25}_D$ = -28.4 (c = 0.91, CH_2Cl_2); ^{1}H NMR for the major diastereomer (400 MHz, $CDCl_3$) δ 7.52 (s, 1H), 7.29-7.22 (m, 4H), 7.13 (t, *J* = 7.6 Hz, 1H), 7.07 (d, *J* = 8.0 Hz, 2H), 6.83 (d, *J* = 8.4 Hz, 2H), 6.69 (d, *J* = 8.4 Hz, 2H), 6.60 (d, *J* = 8.0 Hz, 1H), 5.73 (dd, *J* = 13.2, 3.2 Hz, 1H), 5.11 (t, *J* = 8.4 Hz, 1H), 4.18 (dd, *J* = 12.0, 3.2 Hz, 1H), 3.73 (s, 3H). ^{13}C NMR for the major diastereomer (100 MHz, $CDCl_3$) δ 175.33, 161.21, 140.44, 138.43, 134.41, 132.53, 130.42, 129.87, 128.55, 126.84, 125.34, 122.85, 118.22, 114.32, 110.30, 76.35, 60.44, 55.22, 46.98. IR (neat): 3086, 2924, 1711, 1555, 1249, 1094, 1031, 828, 754, 683; HRMS (ESI): Exact mass calcd for $C_{23}H_{20}ClN_2O_4S$ $[M+H]^+$: 455.0827, Found: 455.0829.



3e

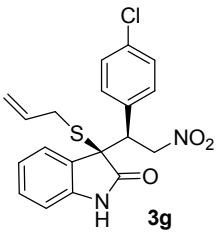
The reaction was run at -20 °C for 3.5 days, with 5 mol% of **C1e**, affording product **3e** in 91% yield as white solid (m.p. 116-118 °C); ^{1}H NMR analysis revealed that the dr vlues is 6:1. HPLC analysis [Chiralcel OZH, ^{i}PrOH/hexane = 5/95, 1.0 mL/min, 230 nm; major diastereomer: t_r (major) = 16.65 min, t_r (minor) = 22.17 min, minor diastereomer: t_r (major) = 18.64 min, t_r (minor) = 12.03 min] gave the isomeric composition of major diastereomer: 96% ee; $[\alpha]^{25}_D$ = -16.8 (c = 0.79, CH_2Cl_2); ^{1}H NMR for the major diastereomer (400 MHz, $CDCl_3$) δ 7.61 (brs, 1H), 7.36 (d, *J* = 8.4 Hz, 2H), 7.31-7.29 (m, 1H), 7.27-7.23 (m, 3H), 7.15 (t, *J* = 7.6 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 2H), 6.70 (d, *J* = 8.8 Hz, 2H), 6.62 (d, *J* = 8.0 Hz, 1H), 5.77 (dd, *J* = 13.2, 3.2 Hz, 1H), 5.16 (t, *J* = 12.4 Hz, 1H), 4.26 (dd, *J* = 12.0, 3.2 Hz, 1H), 3.73 (s, 3H). ^{13}C NMR for the major diastereomer (100 MHz, $CDCl_3$) δ 175.09, 161.29, 140.36, 138.47, 138.20, 130.53 (q, *J* = 32.6 Hz, 1C), 130.00, 129.55, 126.67, 125.31, 125.25 (q, *J* = 4 Hz, 1C), 123.72 (q, *J* = 270 Hz, 1C), 122.96, 118.07, 114.36, 110.37, 76.25, 60.25, 55.23, 47.26; ^{19}F NMR for the major diastereomer (376 MHz, $CDCl_3$): δ -62.78 (s, 3F); IR (neat): 2963, 1707, 1555, 1321, 1289, 1018,

799, 753, 699; HRMS (ESI): Exact mass calcd for $C_{24}H_{20}F_3N_2O_4S$ $[M+H]^+$: 489.1090, Found: 489.1095.



3f

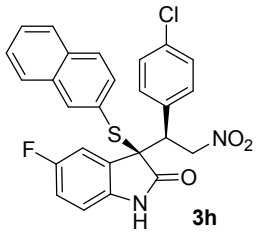
The reaction was run at 0 °C for 5 days, with 10 mol% of **C1e**, affording product **3f** in 98% yield as white solid (m.p. 92-94 °C); HPLC analysis revealed that the dr vlues is 7:1. HPLC analysis [Chiralcel AD-H, ^{i}PrOH/hexane = 5/95, 1.0 mL/min, 230 nm; major diastereomer: t_r (major) = 51.55 min, t_r (minor) = 70.11 min, minor diastereomer: t_r (major) = 45.36 min, t_r (minor) = 42.18 min] gave the isomeric composition of major diastereomer: 92% ee; $[\alpha]^{25}_D$ = -22.8 (c = 1.03, CH_2Cl_2); ^{1}H NMR for the major diastereomer (400 MHz, $CDCl_3$) δ 7.42 (s, 1H), 7.32-7.26 (m, 5H), 7.24-7.22 (m, 2H), 7.15-7.11 (m, 1H), 7.09-7.06 (m, 2H), 6.81-6.79 (m, 2H), 6.75 (d, *J* = 7.6 Hz, 1H), 5.60 (dd, *J* = 13.2, 3.6 Hz, 1H), 5.00 (t, *J* = 12.0 Hz, 1H), 4.26 (dd, *J* = 12.0, 3.2 Hz, 1H), 3.99 (ABd, *J* = 29.4, 12.4 Hz, 2H). ^{13}C NMR for the major diastereomer (100 MHz, $CDCl_3$) δ 175.32, 140.26, 135.81, 134.47, 132.10, 130.35, 130.15, 129.19, 128.67, 128.52, 127.62, 126.27, 124.87, 123.12, 110.49, 76.04, 56.79, 46.60, 33.28. IR (neat): 3068, 2827, 1706, 1552, 1471, 838, 697, 683; HRMS (ESI): Exact mass calcd for $C_{23}H_{23}ClN_3O_3S$ $[M+NH_4]^+$: 456.1143, Found: 456.1147.



3g

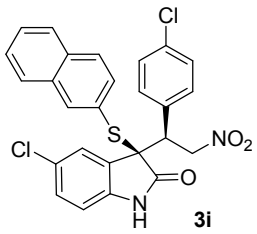
The reaction was run at 0 °C for 5 days, with 10 mol% of **C1e**, affording product **3g** in 82% yield as white solid (m.p. 139-141 °C); HPLC analysis revealed that the dr vlues is 4:1. HPLC analysis [Chiralcel AD-H, ^{i}PrOH/hexane = 5/95, 1.0 mL/min, 230 nm; major diastereomer: t_r (major) = 30.65 min, t_r (minor) = 49.81 min, minor diastereomer: t_r (major) = 36.53 min, t_r (minor) = 34.47 min] gave the isomeric composition of major diastereomer: 91% ee; $[\alpha]^{25}_D$ = -80.4 (c = 1.02, CH_2Cl_2); ^{1}H NMR for the major diastereomer (400 MHz, $CDCl_3$) δ 7.59 (s, 1H), 7.33-7.29 (m, 1H), 7.23-7.21 (m,1H), 7.16-7.12 (m, 1H), 7.08-7.06 (m, 2H), 6.82-6.76 (m, 3H), 5.82-5.71 (m, 1H), 5.65 (dd, *J* = 13.2, 3.6 Hz, 1H), 5.14-5.09 (m, 1H), 5.07-5.00 (m, 2H), 4.27-4.24 (m, 1H), 3.46-3.32 (m, 2H). ^{13}C NMR for the major diastereomer (100 MHz, $CDCl_3$) δ 175.75, 140.25, 134.49, 132.33, 131.99, 130.36, 130.16, 128.52, 126.35, 124.96, 123.12, 119.03,

110.48, 76.10, 56.40, 46.83, 31.90; IR (neat): 3070, 2964, 1714, 1555, 1262, 1092, 1016, 806, 757, 685; HRMS (ESI): Exact mass calcd for $C_{19}H_{21}ClN_3O_3S$ $[M+NH_4]^+$: 406.0987, Found: 406.0990.



3h

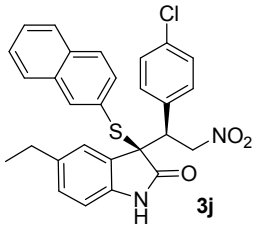
The reaction was run at -30 °C for 2.5 days, with 5 mol% of **C1e**, affording product **3h** in 90% yield as white solid (m.p. 116-118 °C); ^{1}H NMR analysis revealed that the dr vlues is 7:1. HPLC analysis [Chiralcel AD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; major diastereomer: t_r (major) = 16.71 min, t_r (minor) = 20.12 min, minor diastereomer: t_r (major) = 22.32 min, t_r (minor) = 11.92 min] gave the isomeric composition of major diastereomer: 96% ee; $[\alpha]^{25}_D$ = -2.8 (c = 0.94, CH_2Cl_2); ^{1}H NMR for the major diastereomer (400 MHz, $CDCl_3$) δ 8.07 (brs, 1H), 7.78 (s, 1H), 7.75-7.73 (m, 1H), 7.59-7.57 (m, 2H), 7.50-7.40 (m, 2H), 7.26-7.23 (m, 1H), 7.11-7.09 (m, 2H), 7.05-7.03 (m, 1H), 6.93-6.88 (m, 3H), 6.42-6.39 (m, 1H), 5.77 (dd, *J* = 13.0, 2.8 Hz, 1H), 5.14 (t, *J* = 12.4 Hz, 1H), 4.24 (dd, *J* = 11.8 Hz, 2.8 Hz, 1H). ^{13}C NMR for the major diastereomer (100 MHz, $CDCl_3$) δ 175.55, 158.82 (d, *J* = 241 Hz, 1C), 137.45, 136.37, 134.71, 133.52, 133.12, 132.33, 132.04, 130.45, 128.69, 128.50 (d, *J* = 7.7 Hz, 1C), 128.36, 128.05, 127.62, 127.58, 126.63, 124.50, 116.57 (d, *J* = 23.5 Hz, 1C), 113.15 (d, *J* = 24.9 Hz, 1C), 111.18 (d, *J* = 7.8 Hz, 1C), 75.96, 61.04, 47.21. ^{19}F NMR for the major diastereomer (376 MHz, $CDCl_3$): δ -118.41 (s, 1F). IR (neat):2964, 1716, 1556, 1482, 1261, 1098, 1024, 808, 746; HRMS (ESI): Exact mass calcd for $C_{26}H_{22}ClFN_3O_3S$ $[M+NH_4]^+$: 510.1049, Found: 510.1052.



3i

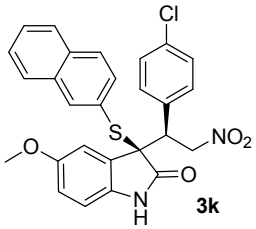
The reaction was run at -30 °C for 2.5 days, with 5 mol% of **C1e**, affording product **3i** in 91% yield as white solid (m.p. 136-138 °C); ^{1}H NMR analysis revealed that the dr vlues is 6:1. HPLC analysis [Chiralcel AD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; major diastereomer: t_r (major) = 12.19 min, t_r (minor) = 18.76 min, minor diastereomer: t_r (major) = 16.99 min, t_r (minor) = 10.77 min] gave the isomeric composition of major diastereomer: 95% ee; $[\alpha]^{25}_D$ = 34.5 (c = 0.92, CH_2Cl_2); ^{1}H NMR for the major diastereomer (400 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.80 (s, 1H), 7.75-7.73 (m, 1H), 7.60-7.58 (m, 2H), 7.51-7.42 (m, 2H), 7.29-7.23 (m, 2H), 7.18-7.15 (m, 1H), 7.10 (d, *J* = 8.4 Hz, 2H), 6.86 (d, *J* = 8.4 Hz, 2H), 6.40 (d, *J* = 8.4 Hz, 1H), 5.77 (dd, *J* = 12.8, 3.2 Hz, 1H), 5.14 (t, *J* = 12.8 Hz, 1H), 4.23 (dd, *J* = 11.8, 3.2 Hz, 1H). ^{13}C NMR for the

major diastereomer (100 MHz, $CDCl_3$) δ 175.17, 138.91, 137.59, 134.74, 133.55, 133.12, 132.37, 131.96, 130.42, 129.94, 128.71, 128.40, 128.27, 128.07, 127.67, 127.58, 126.66, 125.61, 124.43, 111.43, 76.00, 60.73, 47.13. IR (neat): 2963, 1715, 1556, 1262, 1094, 1016, 802, 746; HRMS (ESI): Exact mass calcd for $C_{26}H_{22}Cl_2N_3O_3S$ $[M+NH_4]^+$: 526.0753, Found:526.0757.



3j

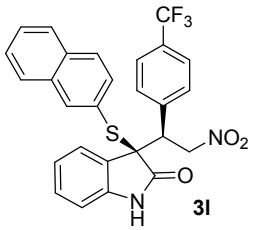
The reaction was run at -30 °C for 2.5 days, with 5 mol% of **C1e**, affording product **3j** in 99% yield as white solid (m.p. 88-90 °C); ^{1}H NMR analysis revealed that the dr vlues is 6:1. HPLC analysis [Chiralcel AD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; major diastereomer: t_r (major) = 10.39 min, t_r (minor) = 19.75 min, minor diastereomer: t_r (major) = 16.60 min, t_r (minor) = 9.36 min] gave the isomeric composition of major diastereomer: 94% ee; $[\alpha]^{25}_D$ = -9.2 (c = 0.94, CH_2Cl_2); ^{1}H NMR for the major diastereomer (400 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.74-7.72 (m, 2H), 7.60-7.56 (m, 2H), 7.49-7.42 (m, 2H), 7.28-7.25 (m, 1H), 7.10-7.07 (m, 3H), 7.01-6.99 (m, 1H), 6.87-6.85 (m, 2H), 6.39 (d, *J* = 7.6 Hz, 1H), 5.79 (dd, *J* = 13.2, 3.2 Hz, 1H), 5.15 (t, *J* = 12.4 Hz, 1H), 4.23 (dd, *J* = 12.0, 3.2 Hz, 1H), 2.69 (q, *J* = 7.6 Hz, 2H), 1.28 (t, *J* = 8.0 Hz, 3H). ^{13}C NMR for the major diastereomer (100 MHz, $CDCl_3$) δ 175.46, 139.18, 138.19, 137.32, 134.46, 133.45, 133.11, 132.49, 130.52, 129.27, 128.53, 128.16, 128.02, 127.55, 127.39, 126.74, 126.45, 125.14, 124.91, 110.17, 76.43, 60.73, 47.35, 28.69, 16.22. IR (neat): 2963, 1712, 1554, 1260, 1088, 1018, 796, 747; HRMS (ESI): Exact mass calcd for $C_{28}H_{24}ClN_2O_3S$ $[M+H]^+$: 503.1191, Found: 503.1191.



3k

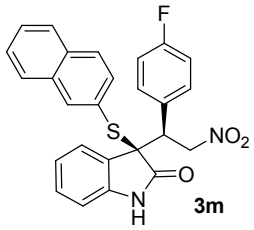
The reaction was run at -20 °C for 3 days, with 5 mol% of **C1e**, affording product **3k** in 97% yield as white solid (m.p. 96-98 °C); ^{1}H NMR analysis revealed that the dr vlues is 5:1. HPLC analysis [Chiralcel AD-H, ^{i}PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; major diastereomer: t_r (major) = 16.78 min, t_r (minor) = 24.35 min, minor diastereomer: t_r (major) = 27.89 min, t_r (minor) = 14.58 min] gave the isomeric composition of major diastereomer: 95% ee; $[\alpha]^{25}_D$ = +14.5 (c = 0.52, CH_2Cl_2); ^{1}H NMR for the major diastereomer (400 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.77-7.75 (m, 1H), 7.69-7.67 (m, 1H), 7.63-7.61 (m, 1H), 7.51-7.44 (m, 2H), 7.30-7.28 (m, 1H), 7.12-7.11 (m, 2H), 7.00-6.86 (m, 4H), 6.73-6.70 (m, 1H), 6.40 (d, *J* = 8.4 Hz, 1H), 5.75 (dd, *J* =

13.2, 3.2 Hz, 1H), 5.15 (t, *J* = 12.4 Hz, 1H), 4.25 (dd, *J* = 12.0, 3.2 Hz, 1H), 3.82 (s, 3H). ^{13}C NMR for the major diastereomer (100 MHz, $CDCl_3$) δ 175.00, 155.84, 137.30, 134.53, 133.73, 133.50, 133.17, 132.45, 132.42, 130.60, 128.58, 128.23, 128.13, 128.07, 127.57, 127.44, 126.49, 125.03, 114.47, 112.50, 110.68, 76.20, 60.98, 55.93, 47.41. IR (neat): 3051, 2835, 1709, 1553, 1489, 1204, 813, 746; HRMS (ESI): Exact mass calcd for $C_{27}H_{22}ClN_2O_4S$ $[M+H]^+$: 505.0983, Found: 505.0992.



3l

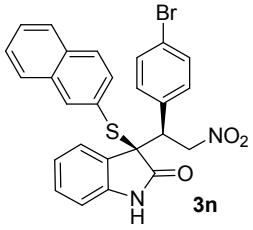
The reaction was run at -30 °C for 1.5 days, with 5 mol% of **C1e**, affording product **3l** in 95% yield as white solid (m.p. 148-150 °C); ^{1}H NMR analysis revealed that the dr vlues is 7:1. HPLC analysis [Chiralcel IC, *i*PrOH/hexane = 5/95, 1.0 mL/min, 230 nm; major diastereomer: t_r (major) = 11.82 min, t_r (minor) = 19.05 min, minor diastereomer: t_r (major) = 10.30 min, t_r (minor) = 13.34 min] gave the isomeric composition of major diastereomer: 97% ee; $[\alpha]^{25}_D$ = -4.3 (c = 1.01, CH_2Cl_2); ^{1}H NMR for the major diastereomer (400 MHz, $CDCl_3$) δ 7.84 (s, 1H), 7.76-7.74 (m, 1H), 7.64-7.59 (m, 2H), 7.50-7.42 (m, 3H), 7.37-7.35 (m, 3H), 7.29-7.26 (m, 1H), 7.23-7.15 (m, 2H), 7.06-7.04 (m, 2H), 6.49 (d, *J* = 7.6 Hz, 1H), 5.83 (dd, *J* = 13.2, 3.2 Hz, 1H), 5.21 (t, *J* = 12.4 Hz, 1H), 4.35 (dd, *J* = 11.6, 2.8 Hz, 1H). ^{13}C NMR for the major diastereomer (100 MHz, $CDCl_3$) δ 174.93, 140.36, 138.01, 137.44, 133.54, 133.15, 132.49, 130.62 (q, *J* = 32 Hz, 1C), 130.12, 129.61, 128.28, 128.10, 127.58, 127.52, 126.65, 126.54, 125.40, 125.29 (q, *J* = 3.6 Hz, 1C), 124.79, 123.71 (q, *J* = 271 Hz, 1C), 123.01, 110.43, 76.22, 60.45, 47.58. ^{19}F NMR for the major diastereomer (376 MHz, $CDCl_3$): δ -62.80 (s, 3F). IR (neat): 2963, 1707, 1554, 1322, 1261, 1112, 1067, 1017, 848, 800, 743, 682; HRMS (ESI): Exact mass calcd for $C_{27}H_{23}F_3N_3O_3S$ $[M+NH_4]^+$: 526.1407, Found: 526.1414.



3m

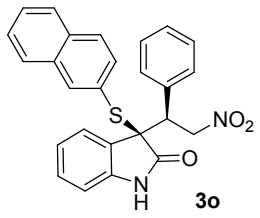
The reaction was run at -20 °C for 2.5 days, with 5 mol% of **C1e**, affording product **3m** in 98% yield as white solid (m.p. 132-135 °C); ^{1}H NMR analysis revealed that the dr vlues is 7:1. HPLC analysis [Chiralcel OZ-H, *i*PrOH/hexane = 5/95, 1.0 mL/min, 230 nm; major diastereomer: t_r (major) = 18.69 min, t_r (minor) = 22.19 min, minor diastereomer: t_r (major) = 16.29 min, t_r (minor) = 14.54 min] gave the isomeric composition of major diastereomer: 96% ee; $[\alpha]^{25}_D$ = -11.2 (c = 0.70, CH_2Cl_2); ^{1}H NMR for the major diastereomer (400 MHz, $CDCl_3$) δ 7.84 (s, 1H), 7.76-7.74 (m, 1H), 7.65-7.59 (m, 2H), 7.50-7.42 (m, 2H), 7.34-7.28 (m, 3H), 7.21-7.13 (m, 2H), 6.91-6.87 (m, 2H), 6.81-6.76 (m, 2H), 6.48 (d,

J = 7.2 Hz, 1H), 5.78 (dd, *J* = 12.8, 3.2 Hz, 1H), 5.16 (t, *J* = 12.4 Hz, 1H), 4.28 (dd, *J* = 12.0 Hz, 3.2 Hz, 1H); ^{13}C NMR for the major diastereomer (100 MHz, $CDCl_3$): δ 175.24, 162.55 (d, *J* = 246 Hz, 1C), 140.43, 137.31, 133.48, 133.14, 132.48, 130.86 (d, *J* = 8.2 Hz, 1C), 129.95, 129.56 (d, *J* = 3.5 Hz, 1C), 128.21, 128.08, 127.56, 127.42, 126.91, 126.47, 125.48, 125.02, 122.87, 115.34 (d, *J* = 21.3 Hz, 1C), 110.26, 76.48, 60.79, 47.24; ^{19}F NMR for the major diastereomer (376 MHz, $CDCl_3$): δ -112.90 (s, 1F); IR (neat): 3078, 2828, 2358, 1709, 1556, 1509, 1472, 754, 696, 679; HRMS (ESI): Exact mass calcd for $C_{26}H_{23}FN_3O_3S$ $[M+NH_4]^+$: 476.1439, Found: 476.1446.



3n

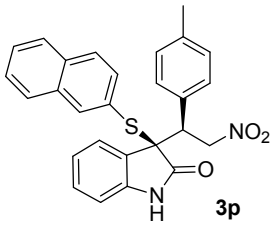
The reaction was run at -20 °C for 3 days, with 5 mol% of **C1e**, affording product **3n** in 99% yield as white solid (m.p. 144-146 °C); ^{1}H NMR analysis revealed that the dr vlues is 8:1. HPLC analysis [Chiralcel AD-H, *i*PrOH/hexane = 15/85, 1.0 mL/min, 230 nm; major diastereomer: t_r (major) = 15.55 min, t_r (minor) = 23.99 min, minor diastereomer: t_r (major) = 27.11 min, t_r (minor) = 12.55 min] gave the isomeric composition of major diastereomer: 96% ee; $[\alpha]^{25}_D$ = -13.5 (c = 0.61, CH_2Cl_2); ^{1}H NMR for the major diastereomer (400 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.75-7.73 (m, 1H), 7.63-7.56 (m, 3H), 7.49-7.41 (m, 2H), 7.35-7.33 (m, 1H), 7.28-7.13 (m, 5H), 6.78 (d, *J* = 8.4 Hz, 2H), 6.49 (d, *J* = 7.6 Hz, 1H), 5.79 (dd, *J* = 13.2, 3.2 Hz, 1H), 5.16 (t, *J* = 12.4 Hz, 1H), 4.25 (dd, *J* = 12.0, 3.2 Hz, 1H); ^{13}C NMR for the major diastereomer (100 MHz, $CDCl_3$) δ 175.08, 140.41, 137.37, 133.50, 133.14, 132.88, 132.49, 131.52, 130.79, 130.00, 128.23, 128.09, 127.57, 126.78, 126.49, 125.42, 124.93, 122.92, 122.79, 110.36, 76.27, 60.52, 47.36; IR (neat):2964, 1709, 1553, 1263, 813, 753, 683; HRMS (ESI): Exact mass calcd for $C_{26}H_{23}BrN_3O_3S$ $[M+NH_4]^+$: 536.0638, Found: 536.0638.



3o

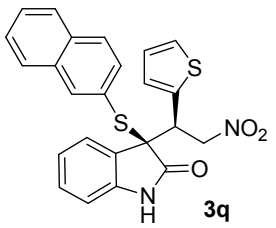
The reaction was run at -20 °C for 6 days, with 5 mol% of **C1e**, affording product **3o** in 95% yield as white solid (m.p. 85-87 °C); ^{1}H NMR analysis revealed that the dr vlues is 6:1. HPLC analysis [Chiralcel OZ-H, *i*PrOH/hexane = 10/90, 1.0 mL/min, 230 nm; major diastereomer: t_r (major) = 10.91 min, t_r (minor) = 13.51 min, minor diastereomer: t_r (major) = 9.85 min, t_r (minor) = 12.13 min] gave the isomeric composition of major diastereomer: 96% ee; ^{1}H NMR for the major diastereomer (400 MHz, $CDCl_3$) δ 7.83-7.80 (m, 2H), 7.74-7.72 (m, 1H), 7.61-7.56 (m, 2H), 7.49-7.40 (m, 2H), 7.31-7.24 (m, 2H), 7.21-7.13 (m, 3H), 7.11-7.06 (m, 2H), 6.91-6.90 (m, 2H), 6.48 (d, *J* = 7.6 Hz, 1H), 5.82 (dd, *J* = 12.8, 3.2 Hz, 1H), 5.22 (t, *J* = 12.0 Hz, 1H), 4.26 (dd, *J* = 12.0, 3.2 Hz, 1H). ^{13}C NMR for the mixture diastereomer (100 MHz, $CDCl_3$) δ

175.55, 140.51, 137.67, 137.27, 133.82, 133.43, 133.12, 132.73, 132.51, 129.79, 129.13, 128.80, 128.58, 128.45, 128.39, 128.30, 128.13, 128.07, 127.53, 127.34, 127.18, 126.48, 126.40, 125.50, 125.35, 125.19, 122.73, 110.25, 109.69, 76.54, 60.87, 47.91; IR (neat):3056, 1710, 1551, 1467, 813, 746, 696; HRMS (ESI): Exact mass calcd for $C_{26}H_{21}N_2O_3S$ $[M+H]^+$: 441.1267, Found: 441.1273.



3p

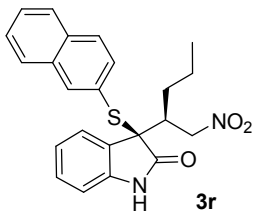
The reaction was run at -20 °C for 8 days, with 5 mol% of **C1e**, affording product **3p** in 99% yield as white solid (m.p. 101-103 °C); ^{1}H NMR analysis revealed that the dr vlues is 5:1. HPLC analysis [Chiralcel OZ-H, ^{i}PrOH/hexane = 5/95, 1.0 mL/min, 230 nm; major diastereomer: t_r (major) = 19.66 min, t_r (minor) = 22.57 min, minor diastereomer: t_r (major) = 16.73 min, t_r (minor) = 15.51 min] gave the isomeric composition of major diastereomer: 95% ee; ^{1}H NMR for the major diastereomer (400 MHz, $CDCl_3$) δ 8.17 (brs, 1H), 7.75-7.69 (m, 2H), 7.58-7.52 (m, 2H), 7.45-7.36 (m, 2H), 7.31-7.29 (m, 1H), 7.24-7.10 (m, 3H), 6.99-6.85 (m, 2H), 6.78-6.76 (m, 2H), 6.48 (d, *J* = 7.2 Hz, 1H), 5.80 (dd, *J* = 12.8, 3.2 Hz, 1H), 5.18 (t, *J* = 12.4 Hz, 1H), 4.21 (dd, *J* = 11.8, 2.8 Hz, 1H), 2.17 (s, 3H). ^{13}C NMR for the mixture diastereomer (100 MHz, $CDCl_3$) δ 175.80, 140.60, 138.16, 137.80, 137.61, 137.26, 133.39, 133.08, 132.70, 132.52, 131.27, 130.72, 129.71, 129.09, 129.02, 128.91, 128.72, 128.45, 128.08, 128.07, 127.50, 127.41, 127.30, 126.45, 126.35, 125.41, 125.25, 125.19, 122.67, 122.31, 110.36, 109.84, 76.75, 61.92, 60.83, 48.22, 47.52, 21.00, 20.93 (IR (neat): 3056, 1711, 1552, 1471, 818, 748; HRMS (ESI): Exact mass calcd for $C_{27}H_{23}N_2O_3S$ $[M+H]^+$: 455.1424, Found: 455.1431.



3q

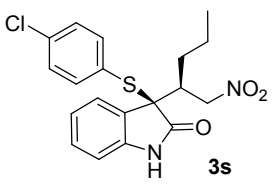
The reaction was run at -20 °C for 4.5 days, with 5 mol% of **C1e**, affording product **3q** in 95% yield as white solid (m.p. 82-84 °C); ^{1}H NMR analysis revealed that the dr vlues is 7:1. HPLC analysis [Chiralcel OZ-H, ^{i}PrOH/hexane = 5/95, 1.0 mL/min, 230 nm; major diastereomer: t_r (major) = 24.43 min, t_r (minor) = 28.39 min, minor diastereomer: t_r (major) = 21.29 min, t_r (minor) = 38.64 min] gave the isomeric composition of major diastereomer: 94% ee; ^{1}H NMR for the major diastereomer (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.83 (s, 1H), 7.75-7.73 (m, 1H), 7.62-7.58 (m, 2H), 7.50-7.41 (m, 2H), 7.32-7.27 (m, 2H), 7.24-7.22 (m, 1H), 7.17-7.13 (m,

1H), 7.04-7.03(m, 1H), 6.74-6.70 (m, 2H), 6.56 (d, *J* = 7.6 Hz, 1H), 5.88 (dd, *J* = 12.6, 2.8 Hz, 1H), 5.11 (t, *J* = 11.6 Hz, 1H), 4.60 (dd, *J* = 11.8, 2.8 Hz, 1H). ^{13}C NMR for the mixture diastereomer (100 MHz, $CDCl_3$) δ 175.51, 140.99, 137.74, 137.38, 136.01, 133.51, 133.15, 132.71, 132.54, 130.11, 129.06, 128.73, 128.24, 128.12, 127.56, 127.43, 127.07, 126.81, 126.46, 126.19, 125.62, 125.53, 125.03, 124.97, 122.88, 110.46, 109.92, 78.05, 61.78, 60.47, 43.77; IR (neat): 3195, 1711, 1552, 1471, 748, 703; HRMS (ESI): Exact mass calcd for $C_{24}H_{19}N_2O_3S_2$ $[M+H]^+$: 447.0832, Found: 447.0835.



3r

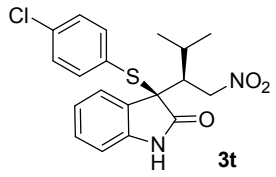
The reaction was run at 0 °C for 4.5 days, with 10 mol% of **C1e**, affording product **3r** in 96% yield as white solid (m.p. 69-72 °C); ^{1}H NMR analysis revealed that the dr vlues is 6:1. HPLC analysis [Chiralcel IF, ^{i}PrOH/hexane = 10/90, 1.0 mL/min, 230 nm; major diastereomer: t_r (major) = 17.84 min, t_r (minor) = 12.58 min, minor diastereomer: t_r (major) = 16.00 min, t_r (minor) = 11.09 min] gave the isomeric composition of major diastereomer: 97% ee; ^{1}H NMR for the major diastereomer (400 MHz, $CDCl_3$) δ 9.28 (brs, 1H), 7.72-7.70 (m, 2H), 7.52-7.49 (m, 2H), 7.45-7.35 (m, 2H), 7.29-7.28 (m, 1H), 7.21-7.18 (m, 2H), 7.13-7.10 (m, 1H), 6.63 (d, *J* = 7.6 Hz, 1H), 5.47 (dd, *J* = 13.2, 2.0 Hz, 1H), 4.65 (dd, *J* = 13.4, 8.8 Hz, 1H), 3.25-3.22 (m, 1H), 1.30-1.19 (m, 4H), 0.76 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR for the mixture diastereomer (100 MHz, $CDCl_3$) δ 177.37, 177.09, 140.53, 140.14, 137.62, 137.42, 133.40, 133.37, 133.05, 133.02, 132.76, 132.66, 129.55, 129.01, 128.07, 128.03, 128.00, 127.92, 127.56, 127.53, 127.47, 127.38, 127.30, 126.44, 126.33, 125.38, 125.15, 124.63, 124.46, 122.90, 122.82, 110.67, 110.25, 76.81, 62.03, 61.48, 41.55, 41.33, 32.65, 32.32, 20.08, 20.00, 14.04, 13.88. IR (neat): 3208, 2960, 1709, 1550, 1468, 816, 746; HRMS (ESI): Exact mass calcd for $C_{23}H_{26}N_3O_3S$ $[M+NH_4]^+$: 424.1689, Found: 424.1697.



3s

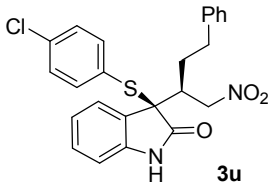
The reaction was run at 0 °C for 3.5 days, with 10 mol% of **C1e**, affording product **3s** in 96% yield as white solid (m.p. 127-130 °C); ^{1}H NMR analysis revealed that the dr vlues is 6:1. HPLC analysis [Chiralcel IF, ^{i}PrOH/hexane = 5/95, 1.0 mL/min, 230 nm; major diastereomer: t_r (major) = 23.27 min, t_r (minor) = 16.27 min, minor diastereomer: t_r (major) = 21.30 min, t_r (minor) = 15.37

min] gave the isomeric composition of major diastereomer: 98% ee; ^{1}H NMR for the major diastereomer (400 MHz, $CDCl_3$) δ 9.28-9.22 (m, 1H), 7.29-7.23 (m, 2H), 7.21-7.17 (m, 2H), 7.12-7.09 (m, 3H), 6.81 (d, *J* = 8.0 Hz, 1H), 5.33 (dd, *J* = 13.2, 2.8 Hz, 1H), 4.60 (dd, *J* = 13.4, 8.4 Hz, 1H), 3.19-3.13 (m, 1H), 1.32-1.19 (m, 4H), 0.78-0.77 (m, 3H). ^{13}C NMR for the mixture diastereomer (100 MHz, $CDCl_3$) δ 177.25, 177.01, 140.40, 138.11, 137.97, 136.66, 136.57, 129.76, 129.30, 128.80, 128.60, 127.26, 126.62, 126.43, 124.39, 123.06, 122.99, 110.69, 110.33, 76.79, 76.60, 61.93, 61.48, 41.51, 41.32, 32.50, 32.22, 21.10, 19.96, 13.97, 13.82. IR (neat): 2959, 1712, 1551, 1468, 1092, 823, 746; HRMS (ESI): Exact mass calcd for $C_{19}H_{23}ClN_3O_3S$ $[M+NH_4]^+$: 408.1143, Found: 408.1147.



3t

The reaction was run at rt for 8 days, with 20 mol% of **C1e**, affording product **3t** in 80% yield as white solid (m.p. 115-117 ^{o}C); ^{1}H NMR analysis revealed that the dr vlues is 5:1. HPLC analysis [Chiralcel IF, ^{i}PrOH/hexane = 10/90, 1.0 mL/min, 230 nm; major diastereomer: t_r (major) = 13.08 min, t_r (minor) = 8.65 min, minor diastereomer: t_r (major) = 11.58 min, t_r (minor) = 10.01 min] gave the isomeric composition of major diastereomer: 92% ee; $[\alpha]^{25}_D$ = +17.3 (c = 0.93, CH_2Cl_2); ^{1}H NMR for the major diastereomer (400 MHz, $CDCl_3$) δ 9.11 (brs, 1H), 7.30-7.20 (m, 4H), 7.13-7.09 (m, 3H), 6.80 (d, *J* = 7.6 Hz, 1H), 5.53-5.49 (m, 1H), 4.88-4.82 (m, 1H), 3.25-3.22 (m, 1H), 1.96-1.89 (m, 1H), 0.85 (d, *J* = 6.8 Hz, 3H), 0.54 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR for the major diastereomer (100 MHz, $CDCl_3$) δ 176.66, 140.16, 138.19, 136.74, 129.79, 128.85, 127.73, 126.49, 124.89, 123.06, 110.79, 72.99, 61.97, 46.08, 29.48, 22.79, 17.13; IR (neat): 3088, 2963, 1715, 1559, 1472, 827, 752; HRMS (ESI): Exact mass calcd for $C_{19}H_{23}ClN_3O_3S$ $[M+NH_4]^+$: 408.1143, Found: 408.1156.

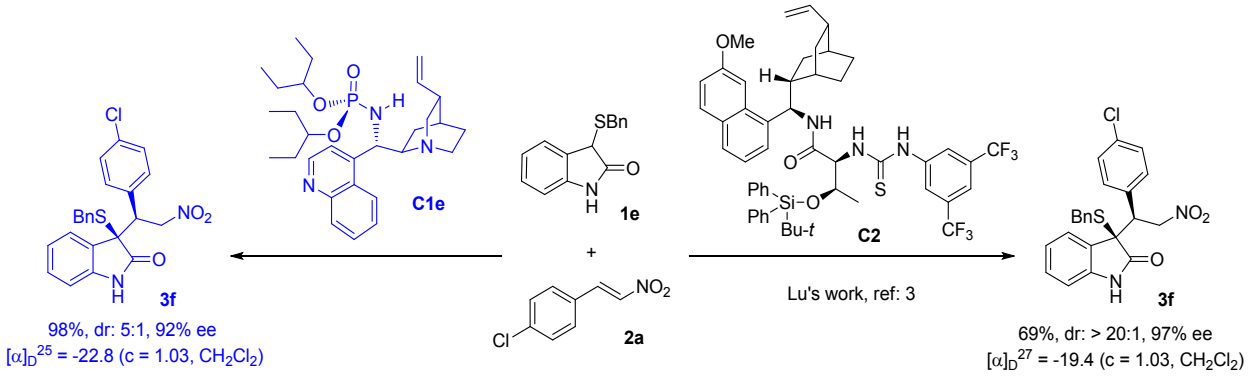


3u

The reaction was run at rt for 8 days, with 20 mol% of **C1e**, affording product **3u** in 97% yield as white solid (m.p. 53-55 ^{o}C); ^{1}H NMR analysis revealed that the dr vlues is 4:1. HPLC analysis [Chiralcel IF, ^{i}PrOH/hexane = 10/90, 1.0 mL/min, 230 nm; major diastereomer: t_r (major) = 18.14 min, t_r (minor) = 14.84 min, minor diastereomer: t_r (major) = 13.45 min, t_r (minor) = 10.99 min] gave the isomeric composition of major diastereomer: 97% ee; ^{1}H NMR for the major

diastereomer (400 MHz, $CDCl_3$) δ 8.50 (brs, 1H), 7.24-7.19 (m, 4H), 7.18-7.12 (m, 4H), 7.11-7.09 (m, 2H), 7.07-7.04 (m, 2H), 6.75 (d, *J* = 7.6 Hz, 1H), 5.25 (dd, *J* = 13.2, 3.2 Hz, 1H), 4.63 (dd, *J* = 13.2, 8.8 Hz, 1H), 3.24-3.19 (m, 1H), 2.57-2.53 (m, 2H), 1.98-1.95 (m, 1H), 1.72-1.63 (m, 1H). ^{13}C NMR for the mixture diastereomer (100 MHz, $CDCl_3$) δ 176.54, 176.25, 140.54, 140.23, 140.17, 139.95, 138.13, 136.73, 136.70, 129.86, 129.37, 128.88, 128.44, 128.27, 127.21, 126.54, 126.38, 126.23, 126.19, 124.80, 124.58, 123.14, 110.56, 110.12, 76.56, 61.71, 61.31, 41.41, 41.19, 33.33, 33.15, 32.22. IR (neat): 3210, 2927, 1710, 1551, 1469, 1090, 822, 746, 697; HRMS (ESI): Exact mass calcd for $C_{24}H_{25}ClN_3O_3S$ $[M+NH_4]^+$: 470.1300, Found: 470.1304.

6. The determination of relative and absolute configuration of compound 3f



In the Lu's work,[3] the asymmetric Michael addition of 3-thiooxindole **1e** with nitroolefin **2a** catalyzed by multifunctional catalyst **C2** afforded (*R, S*)-**3f** as the major product. By our method using catalyst **C1e**, compound **3f** was obtained in 98% yield as white solid (dr: 5:1, 92% ee for major diastereomer). Both major and minor diastereomer could be purified as pure compound for clear NMR analysis. By comparing both the ^{1}H and ^{13}C NMR of the major diastereomer with literature report data for **3f**, together with its optical rotation value, the absolute configuration of the major diastereomer of product **3f** was assigned to be (*R, S*). The absolute configuration of other products were tentatively assigned.

For the major diastereomer of **3f**, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (s, 1H), 7.32-7.26 (m, 5H), 7.24-7.22 (m, 2H), 7.15-7.11 (m, 1H), 7.09-7.06 (m, 2H), 6.81-6.79 (m, 2H), 6.75 (d, *J* = 7.6 Hz, 1H), 5.60 (dd, *J* = 13.2, 3.6 Hz, 1H), 5.00 (t, *J* = 12.0 Hz, 1H), 4.26 (dd, *J* = 12.0, 3.2 Hz, 1H), 3.99 (ABd, *J* = 29.4, 12.4 Hz, 2H). ^{13}C NMR for the major diastereomer (100 MHz, $CDCl_3$) δ 175.32, 140.26, 135.81, 134.47, 132.10, 130.35, 130.15, 129.19, 128.67, 128.52, 127.62, 126.27, 124.87, 123.12, 110.49, 76.04, 56.79, 46.60, 33.28. $[\alpha]^{25}_{D}$ = -22.8 (c = 1.03, CH_2Cl_2).

For the minor diastereomer of **3f**, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (brs, 1H), 7.38 (d, *J* = 7.6 Hz, 1H), 7.22-7.14 (m, 4H), 7.12-7.04 (m, 5H), 7.01-6.98 (m, 2H), 6.67-6.65 (m, 1H), 5.41-5.32 (m, 2H), 4.25-4.22 (m, 1H), 3.46 (ABd, *J* = 72.4, 12.0 Hz, 2H). ^{13}C NMR for the minor diastereomer (100 MHz, $CDCl_3$) δ 176.57, 139.55, 135.15, 134.21, 132.46, 132.00, 129.47, 129.04, 128.50, 128.43, 128.00, 127.59, 124.77, 123.28, 110.20, 75.17, 58.39, 48.88, 34.68. HRMS (ESI): Exact mass calcd for $C_{23}H_{23}ClN_3O_3S$ $[M+NH_4]^+$: 456.1143, Found: 456.1145. $[\alpha]^{25}_{D}$ = -17.9 (c = 0.69, CH_2Cl_2).

[3] X. Dou, B. Zhou, W. Yao, F. Zhong, C. J and Y. Lu, *Org. Lett.,* 2013, **15**, 4920.