SUPPORTING INFORMATION

Catalytic (5+1) Cycloaddition of Diazooxindoles with Imidazolidines to Access Novel Piperazine-Spirooxindole Frameworks

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Supporting Infomation

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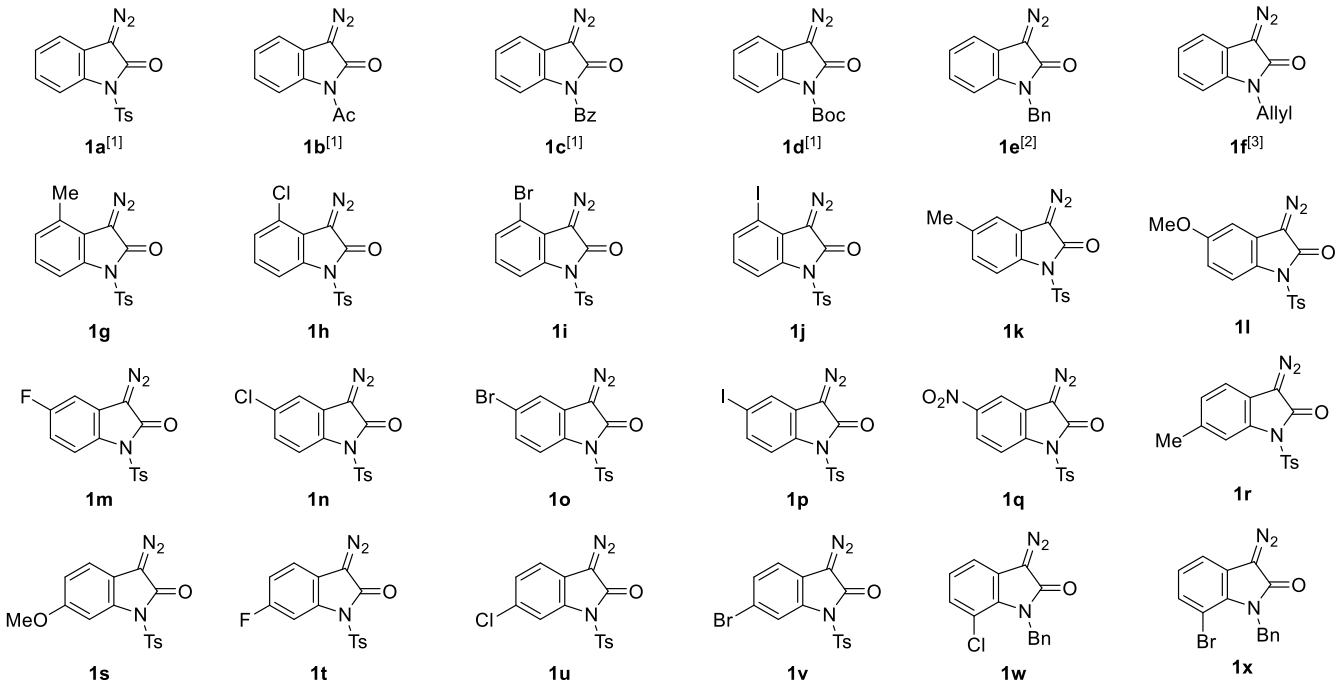
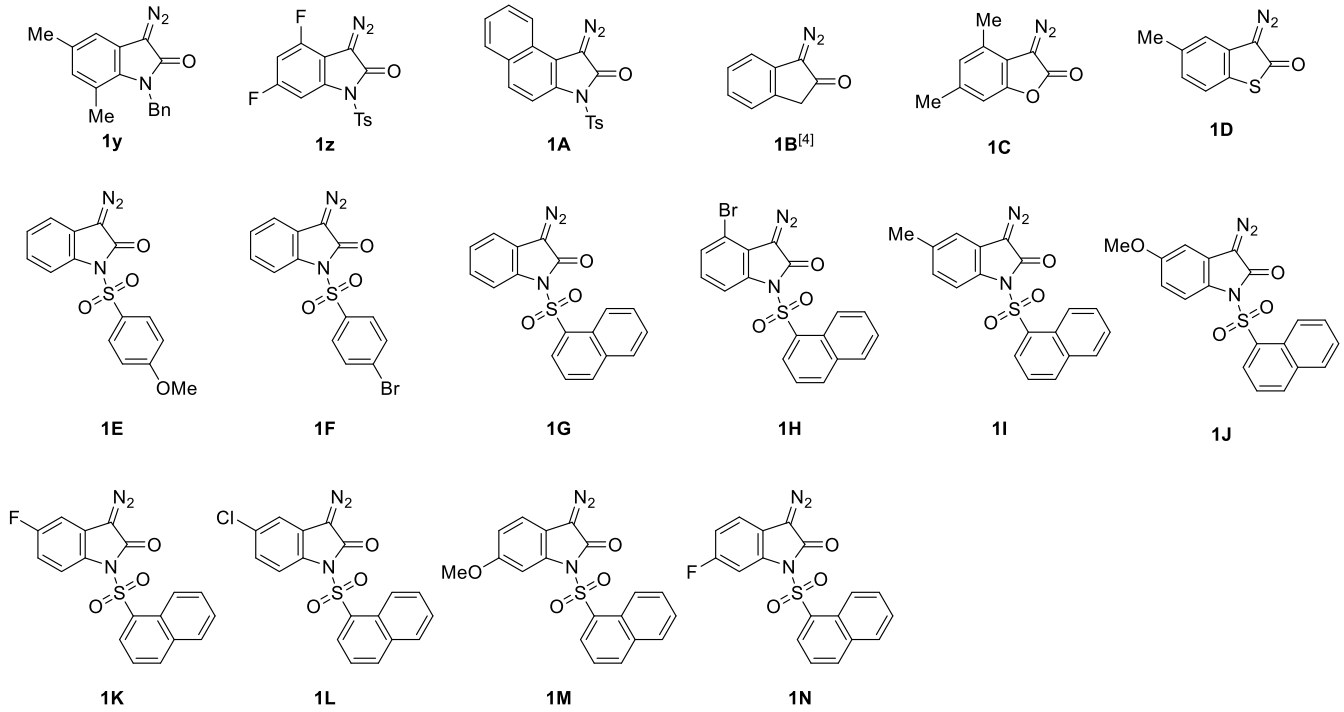
1. General Information

All available chemicals and solvents were purchased from chemical supplier and directly used without further purification. Thin layer chromatography (TLC) was carried out using precoated silica gel plates (0.25 mm, F254) and visualization was accomplished under UV light (254 nm). Flash column chromatography was performed on silica gel (200–300 mesh). Melting points were obtained uncorrected from an OptiMelt MPA100 melting point apparatus. ^{1}H NMR spectra were recorded in $CDCl_3$ on a Bruker Ascend 400 or 500 spectrometer (400 MHz or 500MHz), and chemical shifts (δ values) were reported in parts per million (ppm) relative to internal tetramethylsilane standard (TMS, 0 ppm). Multiplicity was indicated as follows: s (singlet), d (doublet), dd (doublet of doublet), t (triplet), q (quartet), and m (multiple or unresolved). The number of protons (n) for a given resonance is reported as nH. Coupling constants (*J*) were given in Hertz (Hz). ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker Ascend 400 or 500 spectrometer (100 MHz or 125 HMz) relative to internal $CDCl_3$ standard (77.16 ppm). All high-resolution mass spectra (HRMS) were obtained on a Thermo Scientific Q Exactive UHMR (Ultra-High Mass Range) Hybrid Quadrupole-Orbitrap mass spectrometer. Enantiomer excess (e.r.) values were determined by HPLC [Daicel Chiralpak Amylose (4.6 mm × 250 mm) and Chiralpak Cellulose (4.6 mm × 250 mm) in comparison with authentic materials on a Waters Breeze HPLC]. Specific rotation values were recorded on an Anton Paar MCP 200 Modular Circular Polarimeter (Specific rotation values reported are on an average of 5−6 runs).

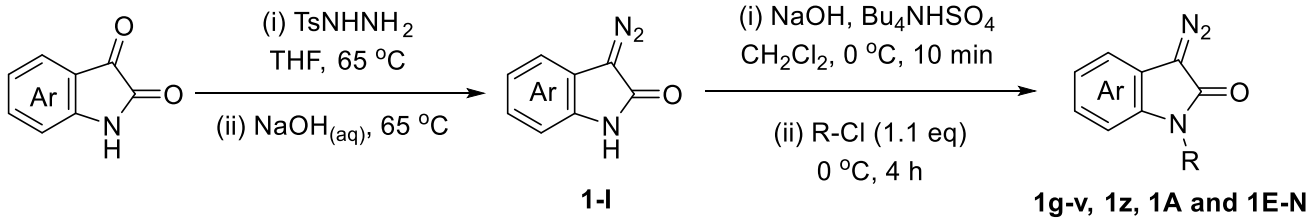
2. Preparation of Diazo Substrates

The diazo substrates (**1a-f** and **1B**) were known compounds and synthesized according to the related procedures.[1-4]





General Procedure for Diazo Substrates ***1g-v, 1z, 1A and 1E-N***

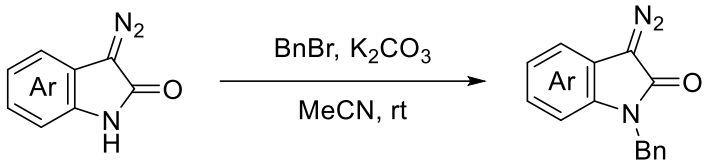


Isatin (10.0 mmol, 1.0 equiv.) and *p*-toluenesulfonylhydrazide (2.0 g, 11.0 mmol, 1.1 equiv.) were added into THF (c = 0.2 M) in a round bottom flask. The mixture was stirred at 65 °C in an oil bath for 1 h. A portion of solvent was removed under vacuum. The reaction mixture was then filtered to get precipitated solid cake. The obtained filter cake was stirred in 0.2 N NaOH aqueous solution (c = 0.2 M) at 65 °C in an oil bath for 1 h. The reaction mixture was cooled down to rt and extracted with EtOAc for three times. The combined organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated. The obtained residue was purified by flash column chromatography (hexanes/EtOAc) on silical gel to afford diazooxindole **1-I**.

A mixture of diazooxindole **1-I** (5.0 mmol, 1.0 equiv.), NaOH (600.0 mg, 15.0 mmol, 3.0 equiv.) and Bu_4NHSO_4 (84.9 mg, 0.25 mmol, 5 mol%) in CH_2Cl_2 (c = 0.2 M) was stirred at 0 °C for 10 min. R-Cl (5.5 mmol, 1.1 equiv.) was added into the mixture and continued for 4 h at 0 °C. The resulting mixture was extracted with CH_2Cl_2 for three times. The combined organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated. The obtained residue was purified by flash column

chromatography (hexanes/EtOAc) on silical gel to afford the corresponding diazooxindole substrates **1g-v**, **1z**, **1A** and **1E-N**.

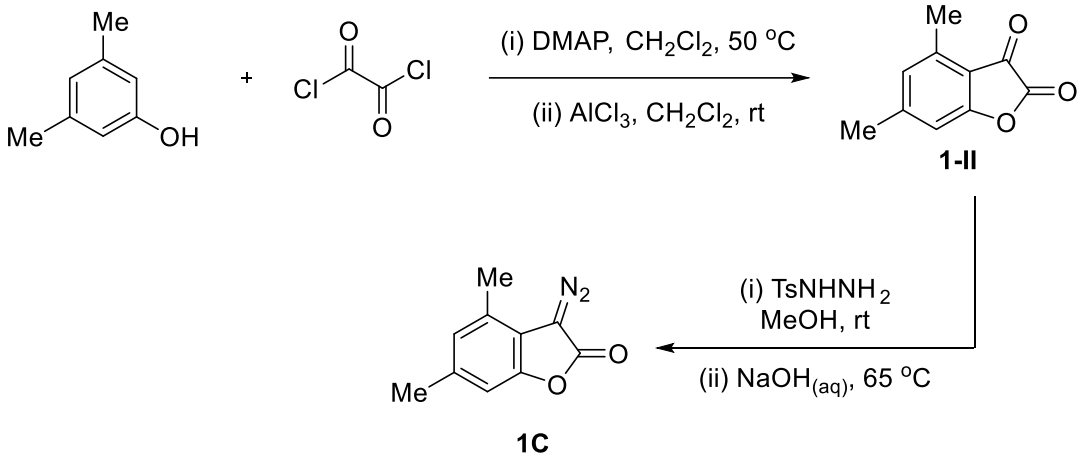
*General Procedure for Diazo Substrates **1w-y***



1-I **1w-1y**

In a round bottom flask, a mixture of **1-I** (5.0 mmol, 1.0 equiv.), K_2CO_3 (1.4 g, 10.0 mmol, 2.0 equiv.) and BnBr (1.7 g, 10.0 mmol, 2.0 equiv.) in MeCN (10 mL) was stirred at rt for 15 h. Then, the reaction mixture was diluted with water and extracted with DCM for three times. The combined organic phase was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was further purified by flash column chromatography (hexanes/EtOAc) on silical gel to afford the corresponding diazooxindole substrates **1w-y**.

*General Procedure for Diazo Substrate **1C***

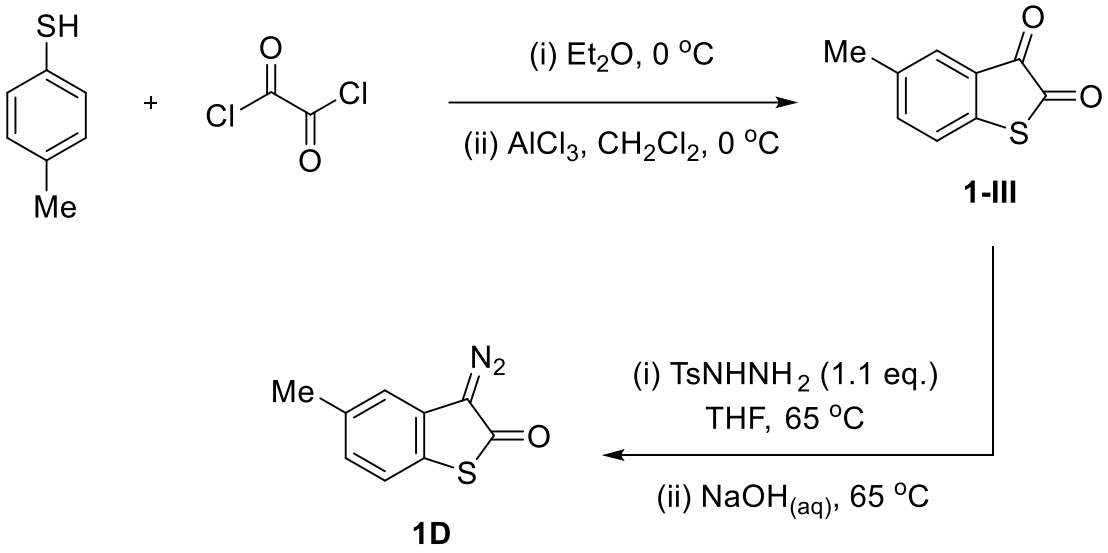


1C

The phenol (2.4 g, 20.0 mmol, 1.0 equiv.) was dissolved in CH_2Cl_2 (20 mL). Oxalyl chloride (2.7 mL, 31.88 mmol, 1.6 equiv.) and DMAP (649.1 mg, 5.31 mmol, 0.3 equiv.) were added. The solution was refluxed in an oil bath for 3 h, cooled down to rt and concentrated. Afterwards, the obtained residue was dissolved in CH_2Cl_2 (20 mL). $AlCl_3$ (5.7 g, 42.5 mmol, 2.1 equiv.) was added portionwise over 30 min at rt, and the reaction was continued to stir for 30 min at rt. Then, the reaction mixture was poured into ice carefully. The color turned from dark to yellow, and the organic phase was separated. The aqueous layer was extracted with CH_2Cl_2 twice, and the combine organic phase was washed with water, brine and dried over Na_2SO_4. The solvent was removed under reduced pressure to obtain **1-II**.

The obtained **1-II** (5.0 mmol, 1.0 equiv.) and *p*-toluenesulfonylhydrazide (1.0 g, 5.5 mmol, 1.1 equiv.) were added into MeOH in a round bottom flask. The mixture was stirred at rt. After completion, a portion of solvent was removed under vacuum. The mixture was then filtered to get precipitated solid cake. The obtained filter cake was stirred in 0.2 N NaOH aqueous solution (c = 0.2 M) at 65 °C in an oil bath for 1 h. The reaction mixture was cooled down to rt and extracted with EtOAc for three times. The combined organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated. The obtained residue was purified by flash column chromatography (hexanes/EtOAc) on silical gel to afford the corresponding diazooxindole substrate **1C.**

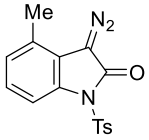
*General Procedure for Diazo Substrate **1D***



4-Methylbenzenethiol (1.2 g, 10.0 mmol, 1.0 equiv.) was dissolved in anhydrous Et_2O (20 mL). At 0 °C under Ar, oxalyl chloride (1.0 mL, 11.0 mmol, 1.1 equiv.) was added. The solution was stirred at 0 °C for 2 h and warmed to rt. The reaction mixture was concentrated in vacuo, and the residue was dissolved in anhydrous CH_2Cl_2 (20 mL). At 0 °C, $AlCl_3$ (5.7 g, 42.5 mmol, 2.1 equiv.) was added portionwise, and the reaction was continued to stir at 0 °C for 16 h. The reaction was quenched dropwise by an ice/1 M HCl mixture. The organic phase was separated. The aqueous layer was extracted with CH_2Cl_2 twice. The combine organic phase was washed with water, brine and dried over Na_2SO_4. The solvent was removed under reduced pressure to obtain **1-III**.

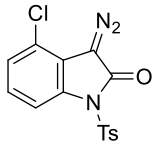
The obtaine **1-III** (891.1 mg, 5.0 mmol, 1.0 equiv.) and *p*-toluenesulfonylhydrazide (1.0 g, 5.5 mmol, 1.1 equiv.) were added into THF (c = 0.2 M) in a round bottom flask. The mixture was stirred at 65 °C in an oil bath for 1 h. A portion of solvent was removed under vacuum. The reaction mixture was then filtered to get precipitated solid cake. The obtained filter cake was stirred in 0.2 N NaOH aqueous solution (c = 0.2 M) at 65 °C in an oil bath for 1 h. The reaction mixture was cooled down to rt and extracted with EtOAc for three times. The combined organic layer was washed with brine, dried over Na_2SO_4, filtered,

and concentrated. The obtained residue was purified by flash column chromatography (hexanes/EtOAc) on silical gel to obtain the corresponding diazooxindole substrate **1D.**



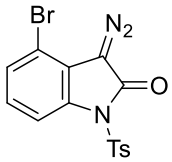
1g

The title compound **1g** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a brown solid; > 166 °C decomposition; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.97 (d, *J* = 8.5 Hz, 2H), 7.87 (d, *J* = 8.2 Hz, 1H), 7.31 (d, *J* = 8.1 Hz, 2H), 7.19–7.13 (m, 1H), 6.97–6.93 (m, 1H), 2.42 (s, 3H), 2.36 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 165.7, 145.9, 135.4, 130.1, 129.9, 129.4, 128.1, 126.6, 126.5, 114.2, 112.1, 21.9, 18.1; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{16}H_{14}N_3O_3S$ 328.0750; found 328.0744.



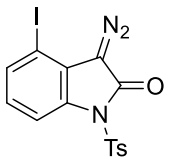
1h

The title compound **1h** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a brown solid; > 186 °C decomposition; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.96 (d, *J* = 8.5 Hz, 2H), 7.93 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.33 (d, *J* = 8.1 Hz, 2H), 7.21–7.16 (m, 1H), 7.13 (dd, *J* = 8.2, 1.0 Hz, 1H), 2.42 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 164.3, 146.2, 135.0, 131.2, 130.0, 128.1, 127.1, 125.7, 125.1, 114.4, 112.6, 21.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{15}H_{11}ClN_3O_3S$ 348.0204; found 348.0197.



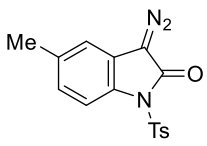
1i

The title compound **1i** was purified by flash chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as a yellow solid; > 192 °C decomposition; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.01–7.94 (m, 3H), 7.33 (d, *J* = 8.1 Hz, 2H), 7.29 (dd, *J* = 8.2, 0.8 Hz, 1H), 7.14–7.09 (m, 1H), 2.43 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 164.5, 146.2, 135.1, 131.4, 130.0, 128.2, 127.3, 116.0, 113.7, 113.1, 21.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{15}H_{11}BrN_3O_3S$ 391.9699; found 391.9688.



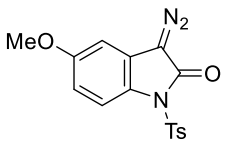
1j

The title compound **1j** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a red solid; > 165 °C decomposition; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.03 (dd, *J* = 8.3, 0.9 Hz, 1H), 7.97 (d, *J* = 8.4 Hz, 2H), 7.52 (dd, *J* = 8.1, 0.8 Hz, 1H), 7.33 (d, *J* = 8.2 Hz, 2H), 6.96 (t, *J* = 8.2 Hz, 1H), 2.43 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 164.7, 146.2, 135.1, 134.6, 131.0, 130.0, 128.2, 127.5, 118.8, 113.8, 84.6, 21.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{15}H_{11}IN_3O_3S$ 439.9560; found 439.9553.



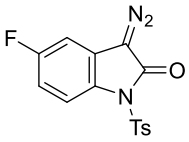
1k

The title compound **1k** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as an orange solid; > 177 °C decomposition; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.98–7.93 (m, 2H), 7.87 (d, *J* = 8.4 Hz, 1H), 7.30 (d, *J* = 8.1 Hz, 2H), 7.08–7.04 (m, 1H), 6.95–6.92 (m, 1H), 2.41 (s, 3H), 2.36 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 164.8, 145.8, 135.4, 134.9, 129.9, 128.2, 128.0, 127.4, 118.6, 116.2, 114.2, 21.9, 21.3; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{16}H_{14}N_3O_3S$ 328.0750; found 328.0746.



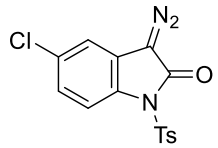
1l

The title compound **1l** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a brown solid; > 162 °C decomposition; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.94 (d, *J* = 8.4 Hz, 2H), 7.87 (d, *J* = 9.0 Hz, 1H), 7.30 (d, *J* = 8.1 Hz, 2H), 6.77 (dd, *J* = 9.0, 2.6 Hz, 1H), 6.65 (d, *J* = 2.6 Hz, 1H), 3.80 (s, 3H), 2.40 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 164.7, 157.3, 145.8, 135.3, 129.9, 128.0, 123.9, 117.5, 115.3, 112.1, 103.9, 55.9, 21.8; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{16}H_{14}N_3O_4S$ 344.0700; found 344.0694.



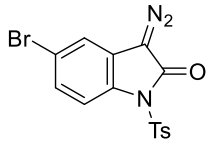
1m

The title compound **1m** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a red solid; > 182 °C decomposition; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.00–7.92 (m, 3H), 7.33 (d, *J* = 8.1 Hz, 2H), 6.95 (td, *J* = 9.1, 2.7 Hz, 1H), 6.87 (dd, *J* = 7.6, 2.6 Hz, 1H), 2.42 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 164.2, 160.1 (d, *J* = 244.4 Hz), 146.1, 135.0, 130.0, 128.0, 126.2 (d, *J* = 2.7 Hz), 117.9 (d, *J* = 10.2 Hz), 115.5 (d, *J* = 8.4 Hz), 113.3 (d, *J* = 23.7 Hz), 105.5 (d, *J* = 27.3 Hz), 21.8; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{15}H_{11}FN_3O_3S$ 332.0500; found 332.0494.



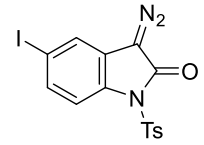
1n

The title compound **1n** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a yellow solid; > 189 °C decomposition; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.95 (d, *J* = 8.3 Hz, 2H), 7.92 (d, *J* = 8.8 Hz, 1H), 7.33 (d, *J* = 8.1 Hz, 2H), 7.21 (dd, *J* = 8.7, 2.2 Hz, 1H), 7.12 (d, *J* = 2.1 Hz, 1H), 2.42 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 163.9, 146.2, 135.0, 130.5, 130.0, 128.7, 128.1, 126.5, 118.02, 117.97, 115.3, 21.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{15}H_{11}ClN_3O_3S$ 348.0204; found 348.0197.



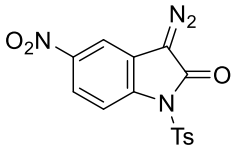
1o

The title compound **1o** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a yellow solid; > 164 °C decomposition; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.96 (d, *J* = 8.4 Hz, 2H), 7.88 (d, *J* = 8.8 Hz, 1H), 7.37 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.33 (d, *J* = 8.1 Hz, 2H), 7.27 (d, *J* = 2.1 Hz, 1H), 2.43 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 163.8, 146.2, 135.0, 130.0, 129.5, 129.2, 128.1, 120.8, 118.4, 117.9, 115.7, 21.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{15}H_{11}BrNO_3S_3$ 391.9699; found 391.9691.



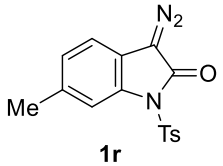
1p

The title compound **1p** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a yellow solid; > 179 °C decomposition; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.95 (d, *J* = 8.5 Hz, 2H), 7.76 (d, *J* = 8.6 Hz, 1H), 7.56 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.43 (d, *J* = 1.7 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 2H), 2.42 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 163.7, 146.2, 135.3, 135.0, 130.0, 129.9, 128.1, 126.5, 118.6, 116.0, 87.9, 21.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{15}H_{11}IN_3O_3S$ 439.9560; found 439.9550.



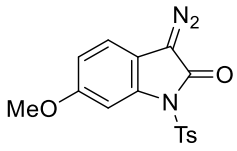
1q

The title compound **1q** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a yellow solid; > 197 °C decomposition; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.19–8.13 (m, 2H), 8.07–8.03 (m, 1H), 7.98 (d, *J* = 8.2 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 2.44 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 163.3, 146.8, 144.8, 134.6, 134.5, 130.2, 128.4, 122.3, 117.8, 114.2, 113.3, 21.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{15}H_{11}N_4O_5S$ 359.0445; found 359.0437.



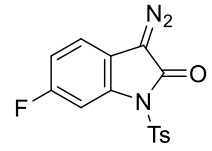
1r

The title compound **1r** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a yellow solid; > 187 °C decomposition; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.98 (d, *J* = 8.2 Hz, 2H), 7.86 (s, 1H), 7.32 (d, *J* = 8.1 Hz, 2H), 7.07–6.97 (m, 2H), 2.44 (s, 3H), 2.42 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 165.1, 145.9, 137.0, 135.4, 130.5, 129.9, 128.1, 125.7, 117.9, 115.1, 113.1, 22.1, 21.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{16}H_{14}N_3O_3S$ 328.0750; found 328.0743.



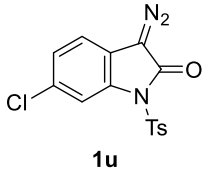
1s

The title compound **1s** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a red solid; > 191 °C decomposition; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.98 (d, *J* = 8.4 Hz, 2H), 7.69 (d, *J* = 2.4 Hz, 1H), 7.32 (d, *J* = 8.1 Hz, 2H), 7.01 (d, *J* = 8.5 Hz, 1H), 6.78 (dd, *J* = 8.5, 2.3 Hz, 1H), 3.87 (s, 3H), 2.42 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 165.5, 159.2, 145.9, 135.3, 131.2, 129.9, 128.1, 118.8, 111.0, 107.8, 101.7, 55.9, 21.8; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{16}H_{14}N_3O_4S$ 344.0700; found 344.0694.



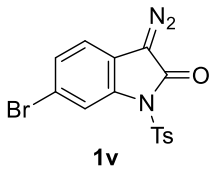
1t

The title compound **1t** was purified by flash chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as a yellow solid; > 174 °C decomposition; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.01–7.94 (m, 2H), 7.82 (dd, *J* = 8.3, 0.7 Hz, 1H), 7.33 (d, *J* = 7.9 Hz, 2H), 7.25–7.18 (m, 1H), 6.98–6.90 (m, 1H), 2.43 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 164.0, 155.3 (d, *J* = 245.8 Hz), 146.2, 135.0, 131.7 (d, *J* = 6.8 Hz), 130.0, 128.2, 127.3 (d, *J* = 7.5 Hz), 111.5 (d, *J* = 17.6 Hz), 110.5 (d, *J* = 3.4 Hz), 104.3 (d, *J* = 20.2 Hz), 21.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{15}H_{11}FN_3O_3S$ 332.0500; found 332.0494.



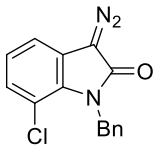
1u

The title compound **1u** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a yellow solid; > 181 °C decomposition; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.06 (d, *J* = 1.8 Hz, 1H), 7.99 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 7.21 (dd, *J* = 8.2, 1.9 Hz, 1H), 7.05 (d, *J* = 8.2 Hz, 1H), 2.43 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 164.2, 146.3, 135.0, 132.4, 130.8, 130.0, 128.2, 125.1, 118.7, 114.9, 114.7, 21.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{15}H_{11}ClN_3O_3S$ 348.0204; found 348.0199.



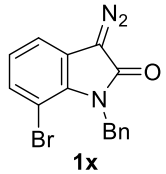
1v

The title compound **1v** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a yellow solid; > 191 °C decomposition; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.17 (d, *J* = 1.6 Hz, 1H), 7.97 (d, *J* = 8.4 Hz, 2H), 7.38–7.30 (m, 3H), 7.01 (d, *J* = 8.2 Hz, 1H), 2.43 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 164.0, 146.3, 134.9, 130.9, 130.0, 128.2, 127.9, 119.8, 119.0, 117.5, 115.2, 21.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{15}H_{11}BrN_3O_3S$ 391.9699; found 391.9692.



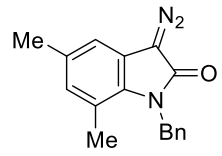
1w

The title compound **1w** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a red solid; > 181 °C decomposition; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.34–7.17 (m, 5H), 7.13–7.02 (m, 2H), 7.02–6.95 (m, 1H), 5.45 (s, 2H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 167.0, 137.8, 129.7, 128.7, 127.6, 127.3, 126.6, 123.0, 119.5, 116.7, 116.3, 45.5; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{15}H_{11}ClN_3O$ 284.0585; found 284.0578.



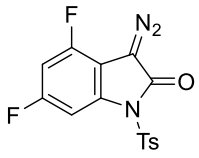
1x

The title compound **1x** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a red solid; > 191 °C decomposition; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.32–7.23 (m, 4H), 7.23–7.18 (m, 2H), 7.15 (dd, *J* = 7.6, 1.0 Hz, 1H), 6.97–6.91 (m, 1H), 5.52 (s, 2H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 167.2, 137.7, 131.12, 131.06, 128.7, 127.3, 126.5, 123.4, 119.7, 117.3, 103.4, 45.1; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{15}H_{11}BrN_3O$ 328.0080; found 328.0074.



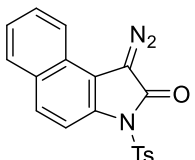
1y

The title compound **1y** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as an orange solid; > 188 °C decomposition; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.32–7.26 (m, 2H), 7.25–7.19 (m, 1H), 7.14–7.08 (m, 2H), 6.89 (s, 1H), 6.67 (s, 1H), 5.27 (s, 2H), 2.30 (s, 3H), 2.25 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 167.8, 138.1, 132.0, 130.3, 129.9, 128.9, 127.3, 125.8, 120.6, 117.4, 116.9, 45.6, 21.0, 18.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{17}H_{16}N_3O$ 278.1288; found 278.1280.



1z

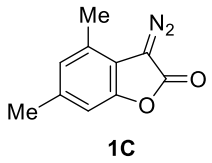
The title compound **1z** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as an orange solid; > 154 °C decomposition; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.95 (d, *J* = 8.3 Hz, 2H), 7.68–7.60 (m, 1H), 7.34 (d, *J* = 8.2 Hz, 2H), 6.72 (td, *J* = 9.4, 2.0 Hz, 1H), 2.43 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 163.9, 161.5 (dd, *J* = 246.2, 11.9 Hz), 154.7 (dd, *J* = 247.1, 14.1 Hz), 146.5, 134.6, 131.5 (dd, *J* = 14.3, 9.5 Hz), 130.0, 128.1, 100.3 (dd, *J* = 27.7, 22.2 Hz), 99.9 (dd, *J* = 20.3, 3.4 Hz), 99.5 (dd, *J* = 30.5, 4.0 Hz), 21.8; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{15}H_{10}F_2N_3O_3S$ 350.0405; found 350.0399.



1A

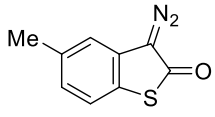
The title compound **1A** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a pink solid; > 174 °C decomposition; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.26 (d, *J* = 9.1 Hz, 1H), 8.00 (d, *J* = 8.3 Hz, 2H), 7.92–7.87 (m, 1H), 7.74 (d, *J* = 9.1 Hz, 1H), 7.61–7.55 (m, 1H), 7.53–7.44 (m, 2H), 7.31 (d, *J* = 8.2 Hz, 2H),

2.41 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 166.4, 146.0, 135.3, 131.1, 130.0, 129.8, 128.1, 127.4, 127.3, 127.0, 125.73, 125.65, 120.9, 114.1, 108.9, 21.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{19}H_{14}N_3O_3S$ 364.0750; found 364.0742.



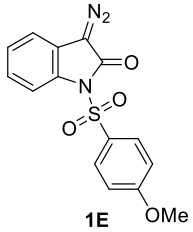
1C

The title compound **1C** was purified by flash chromatography (hexanes/EtOAc = 15:1) on silica gel and obtained as an orange solid; > 134 °C decomposition; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 6.82 (s, 1H), 6.77 (s, 1H), 2.35 (s, 6H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 168.6, 145.3, 137.1, 129.3, 126.8, 112.2, 109.6, 21.7, 17.6; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{10}H_9N_2O_2$ 189.0659; found 189.0660.



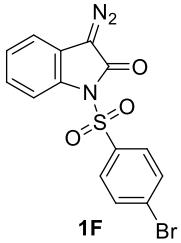
1D

The title compound **1D** was purified by flash chromatography (hexanes/EtOAc = 10:1) on silical gel and obtained as a brown solid; > 162 °C decomposition; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.27 (d, *J* = 8.0 Hz, 1H), 7.05 (d, *J* = 8.0 Hz, 1H), 6.98 (s, 1H), 2.39 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 188.1, 136.6, 127.4, 124.8, 123.8, 123.5, 119.0, 21.5; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_9H_7N_2OS$ 191.0274; found 191.0275.



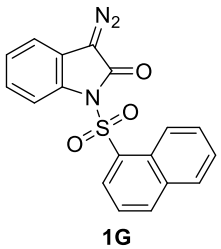
1E

The title compound **1E** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a red solid; > 182 °C decomposition; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.06–7.97 (m, 3H), 7.25 (td, *J* = 7.9, 1.5 Hz, 1H), 7.20 (td, *J* = 7.6, 1.1 Hz, 1H), 7.13 (dd, *J* = 7.6, 1.5 Hz, 1H), 6.99–6.94 (m, 2H), 3.85 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 164.5, 130.5, 130.4, 129.6, 126.5, 124.9, 118.1, 116.3, 114.4, 114.3, 55.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{15}H_{12}N_3O_4S$ 330.0543; found 330.0551.



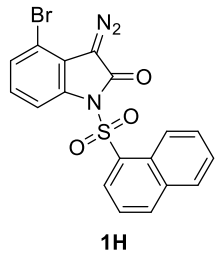
1F

The title compound **1F** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a red solid; > 182 °C decomposition; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.00–7.94 (m, 3H), 7.69–7.65 (m, 2H), 7.27 (td, *J* = 7.8, 1.5 Hz, 1H), 7.23 (td, *J* = 7.6, 1.3 Hz, 1H), 7.15 (dd, *J* = 7.4, 1.4 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 164.4, 137.1, 132.7, 130.2, 130.1, 129.6, 126.7, 125.2, 118.2, 116.3, 114.3; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{14}H_9BrN_3O_3S$ 377.9543; found 377.9550.



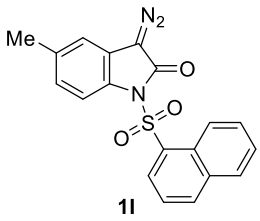
1G

The title compound **1G** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as an orange solid; > 191 °C decomposition; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.63 (dd, *J* = 7.5, 1.2 Hz, 1H), 8.53–8.48 (m, 1H), 8.17–8.12 (m, 2H), 7.95–7.91 (m, 1H), 7.67–7.62 (m, 1H), 7.57–7.50 (m, 2H), 7.37–7.31 (m, 1H), 7.26–7.22 (m, 1H), 7.14 (dd, *J* = 7.6, 1.2 Hz, 1H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 164.2, 136.2, 134.2, 133.1, 132.9, 130.8, 129.4, 129.1, 128.6, 127.2, 126.6, 124.9, 124.2, 123.6, 118.3, 116.3, 114.6; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{18}H_{12}N_3O_3S$ 350.0594; found 350.0597.



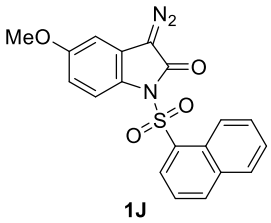
1H

The title compound **1H** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as an orange solid; > 168 °C decomposition; **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.65 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.51–8.46 (m, 1H), 8.19 (d, *J* = 8.3 Hz, 1H), 8.15 (d, *J* = 8.2 Hz, 1H), 7.99–7.95 (m, 1H), 7.70–7.65 (m, 1H), 7.61–7.54 (m, 2H), 7.35 (d, *J* = 8.2 Hz, 1H), 7.24–7.19 (m, 1H); **^{13}C NMR (125 MHz, CDCl$_3$):** δ 164.1, 136.5, 134.2, 133.2, 132.8, 131.7, 129.5, 129.2, 128.5, 128.2, 127.3, 127.2, 124.2, 123.4, 115.9, 113.8, 113.3; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{18}H_{11}BrN_3O_3S$ 427.9699; found 427.9689.



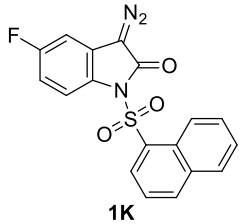
1I

The title compound **1I** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as an orange solid; > 187 °C decomposition; **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.61 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.53–8.47 (m, 1H), 8.13 (d, *J* = 8.2 Hz, 1H), 7.99 (d, *J* = 8.4 Hz, 1H), 7.94–7.90 (m, 1H), 7.66–7.60 (m, 1H), 7.56–7.50 (m, 2H), 7.12 (d, *J* = 8.3 Hz, 1H), 6.94 (s, 1H), 2.38 (s, 3H); **^{13}C NMR (125 MHz, CDCl$_3$):** δ 164.4, 136.1, 134.9, 134.2, 133.2, 132.8, 129.4, 129.0, 128.60, 128.56, 127.4, 127.1, 124.2, 123.7, 118.8, 116.2, 114.4, 21.3; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{19}H_{14}N_3O_3S$ 364.0750; found 364.0742.



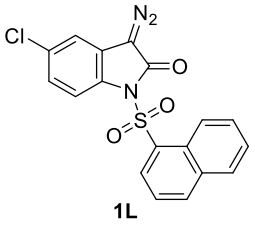
1J

The title compound **1J** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a brown solid; > 189 °C decomposition; **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.60 (d, *J* = 7.4 Hz, 1H), 8.51–8.45 (m, 1H), 8.13 (d, *J* = 8.2 Hz, 1H), 8.01 (d, *J* = 8.9 Hz, 1H), 7.95–7.90 (m, 1H), 7.66–7.60 (m, 1H), 7.57–7.50 (m, 2H), 6.85 (dd, *J* = 9.0, 2.6 Hz, 1H), 6.67 (d, *J* = 2.6 Hz, 1H), 3.83 (s, 3H); **^{13}C NMR (125 MHz, CDCl$_3$):** δ 164.3, 157.3, 136.1, 134.2, 133.1, 132.8, 129.4, 129.0, 128.6, 127.1, 124.4, 124.2, 123.6, 117.4, 115.5, 112.2, 104.2, 55.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{19}H_{14}N_3O_4S$ 380.0700; found 380.0690.



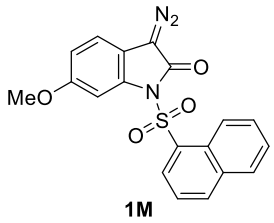
1K

The title compound **1K** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as an orange solid; > 193 °C decomposition; **^{1}H NMR (400 MHz, CDCl$_3$):** δ 8.61 (dd, *J* = 7.5, 1.3 Hz, 1H), 8.47–8.42 (m, 1H), 8.17–8.13 (m, 1H), 8.08 (dd, *J* = 9.0, 4.4 Hz, 1H), 7.96–7.91 (m, 1H), 7.67–7.61 (m, 1H), 7.58–7.50 (m, 2H), 7.03 (td, *J* = 9.1, 2.6 Hz, 1H), 6.88 (dd, *J* = 7.6, 2.6 Hz, 1H); **^{13}C NMR (125 MHz, CDCl$_3$):** δ 163.8, 160.1 (d, *J* = 244.4 Hz), 136.3, 134.2, 133.1, 132.8, 129.5, 129.1, 128.5, 127.2, 126.7 (d, *J* = 2.0 Hz), 124.2, 123.4, 117.9 (d, *J* = 10.2 Hz), 115.7 (d, *J* = 8.7 Hz), 113.4 (d, *J* = 23.8 Hz), 105.7 (d, *J* = 27.5 Hz); **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{18}H_{11}FN_3O_3S$ 368.0500; found 368.0491.



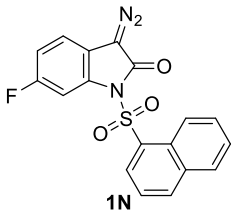
1L

The title compound **1L** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a yellow solid; > 190 °C decomposition; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.61 (dd, *J* = 7.5, 1.3 Hz, 1H), 8.46–8.41 (m, 1H), 8.15 (d, *J* = 8.2 Hz, 1H), 8.06 (d, *J* = 8.8 Hz, 1H), 7.95–7.92 (m, 1H), 7.66–7.62 (m, 1H), 7.58–7.51 (m, 2H), 7.29 (dd, *J* = 8.8, 2.1 Hz, 1H), 7.13 (d, *J* = 2.1 Hz, 1H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 163.5, 136.4, 134.2, 133.1, 132.7, 130.6, 129.5, 129.20, 129.15, 128.5, 127.2, 126.6, 124.2, 123.4, 118.2, 118.0, 115.5; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{18}H_{11}ClN_3O_3S$ 384.0204; found 384.0194.



1M

The title compound **1M** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a red solid; > 177 °C decomposition; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.61 (d, *J* = 7.4 Hz, 1H), 8.53–8.46 (m, 1H), 8.14 (d, *J* = 8.2 Hz, 1H), 7.96–7.90 (m, 1H), 7.79 (d, *J* = 2.3 Hz, 1H), 7.66–7.60 (m, 1H), 7.58–7.51 (m, 2H), 7.01 (d, *J* = 8.5 Hz, 1H), 6.80 (dd, *J* = 8.4, 2.3 Hz, 1H), 3.91 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 165.2, 159.2, 136.2, 134.2, 133.0, 132.9, 131.6, 129.4, 129.1, 128.6, 127.1, 124.2, 123.5, 119.0, 111.0, 107.7, 101.9, 56.0; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{19}H_{14}N_3O_4S$ 380.0700; found 380.0691.

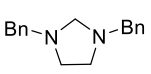


1N

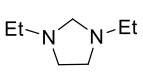
The title compound **1N** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a yellow solid; > 190 °C decomposition; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.61 (dd, *J* = 7.5, 1.3 Hz, 1H), 8.49–8.43 (m, 1H), 8.16 (d, *J* = 8.2 Hz, 1H), 7.98–7.91 (m, 2H), 7.67–7.62 (m, 1H), 7.59–7.53 (m, 2H), 7.07 (dd, *J* = 8.5, 5.1 Hz, 1H), 7.01–6.94 (m, 1H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 164.4, 161.7 (d, *J* = 244.6 Hz), 136.5, 134.2, 133.2, 132.7, 131.2 (d, *J* = 12.0 Hz), 129.5, 129.2, 128.5, 127.2, 124.2, 123.4, 119.0 (d, *J* = 9.2 Hz), 112.0 (d, *J* = 23.8 Hz), 111.8 (d, *J* = 3.4 Hz), 103.6 (d, *J* = 30.4 Hz); **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{18}H_{11}FN_3O_3S$ 368.0500; found 368.0492.

3. Preparation of Imidazolidine Substrates

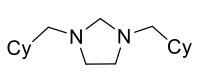
The imidazolidines (**2a, 2b, 2e, 2f, 2k** and **2l**) were known compounds and synthesized according to the related procedures.[5]



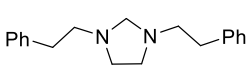
2a[5]



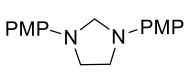
2b[5]



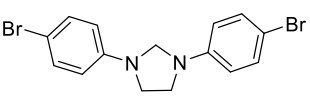
2c



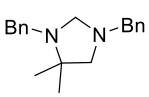
2d



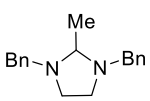
2e[5]



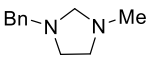
2f[5]



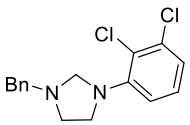
2g



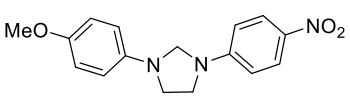
2h



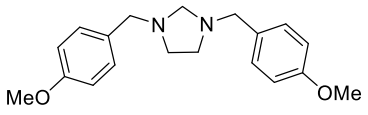
2i



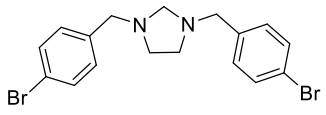
2j



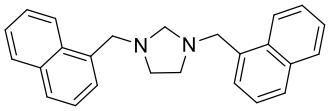
2k[5]



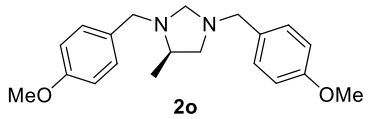
2l[5]



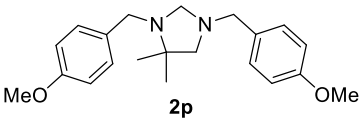
2m



2n

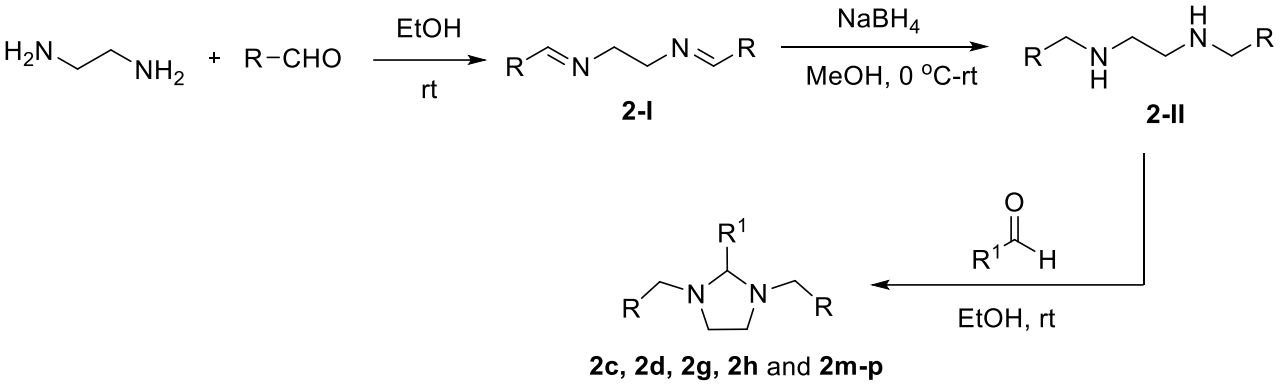


2o



2p

*General Procedure for Imidazolidines **2c, 2d, 2g, 2h** and **2m-p***



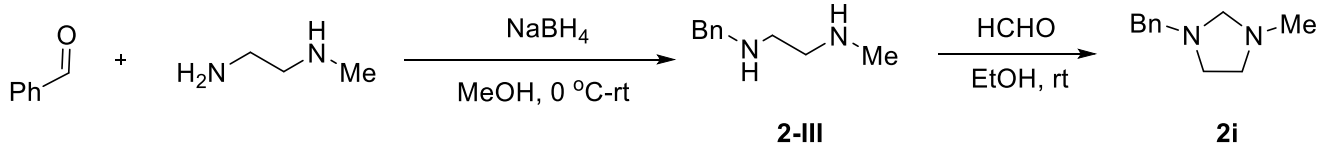
2c, **2d**, **2g**, **2h** and **2m-p**

In a round bottom flask equipped with a magnetic stir bar, a mixture of diamine (10.0 mmol, 1.00 equiv.) and aldehyde (20.0 mmol, 2.00 equiv.) in EtOH (20 mL) was stirred at rt for 3 h. Evaporate solvent to obtain the crude **2-I**.

In an oven-dried round bottom flask equipped with a magnetic stir bar, **2-I** (10.0 mmol, 1.00 equiv.) was dissolved in MeOH (20 mL). The reaction was cooled down to 0 ℃, and $NaBH_4$ (1.10 g, 30.0 mmol, 3.00 equiv.) was added portionwise. The reaction mixture was moved to rt and stirred for 3 h. The resulting mixture was quenched by water and extracted with EtOAc (30 mL*3). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure to afford **2-II**.

In a round bottom flask equipped with a magnetic stir bar, a solution of **2-II** (5.0 mmol, 1.00 equiv.) and R-CHO (5.0 mmol, 1.00 equiv.) in EtOH (10 mL) was stirred at rt until completion. The reaction was diluted by H_2O and extracted with EtOAc (15 mL*3). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel to obtain the corresponding imidazolidines **2c**, **2d**, **2g**, **2h** and **2m-p**.

*General Procedure for Imidazolidine **2i***

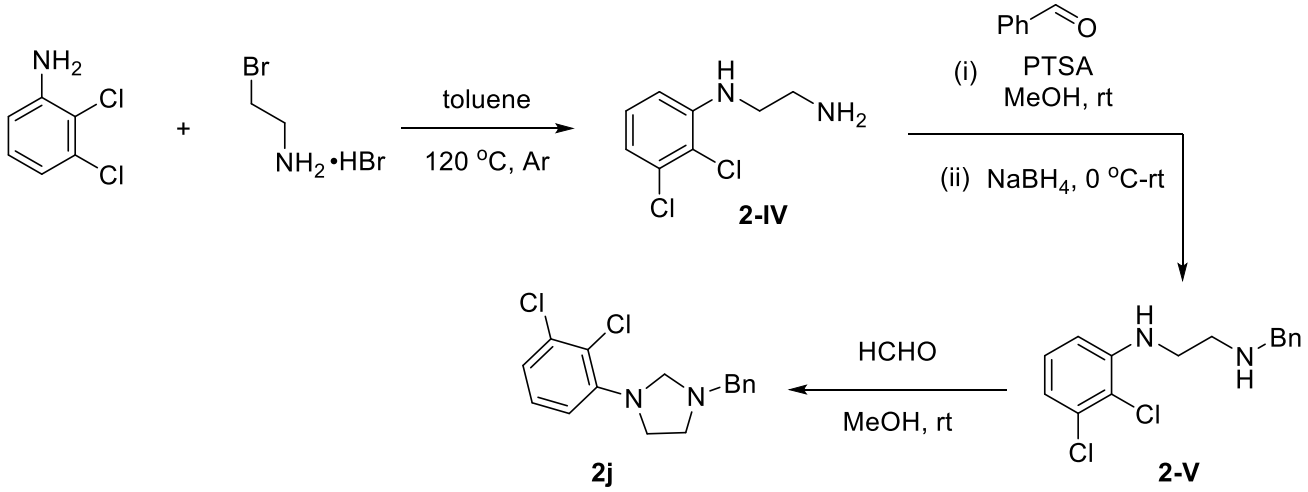


In a round bottom flask, a mixture of benzaldehyde (1.1 g, 10.0 mmol, 1.0 equiv.) and diamine (741.3 mg, 10.0 mmol, 1.0 equiv.) in MeOH (20 mL) was stirred at rt for 1 h.

The reaction was cooled down to 0 °C, and $NaBH_4$ (756.6 mg, 20.0 mmol, 2.0 equiv.) was added portionwise. The reaction mixture was moved to rt and stirred for 12 h. The resulting mixture was quenched by water and extracted with EtOAc (30 mL*3). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure to afford **2-III**.

In a round bottom flask equipped with a magnetic stir bar, a solution of **2-III** (5.0 mmol, 1.00 equiv.) and HCHO (405.8 mg, 5 mmol, 1.0 equiv., 37% in water) in EtOH (10 mL) was stirred at rt until completion. The reaction was diluted by H_2O and extracted with EtOAc (15 mL*3). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexanes/EtOAc = 10:1) to obtain to obtain the corresponding imidazolidine **2i**.

*General Procedure for Imidazolidine **2j***

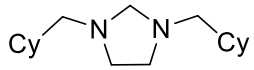


In a round bottom flask, 2,3-dichloroaniline (3.2 g, 20.0 mmol, 6.0 equiv.) and 2-bromoethylamine hydrobromide (683.0 mg, 3.33 mmol, 1.0 equiv.) were added in toluene (20 mL). The reaction was heated to 120 °C in an oil bath and refluxed for 20 h under Ar. The reaction was cooled down to rt and quenched by 20% $NaOH_{(aq)}$. The resulting mixture was extracted with EtOAc for three times. The combined organic layer was washed with water, brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexanes/EtOAc = 5:1 to 100% MeOH) to obtain **2-IV**.

The obtained **2-IV** (406.1 mg, 1.98 mmol, 1.0 equiv.) benzaldehyde (252.1 mg, 2.376 mmol, 1.2 equiv.) and a catalytic amount of PTSA (1.1 mg, 0.00594 mmol, 0.003 equiv.) were added in MeOH (10 mL). The reaction was stirred at rt until completion. At 0 °C, $NaBH_4$ (299.6 mg, 7.92 mmol, 4.0 equiv.) was added to the reaction in portions. The reaction mixture was moved to rt and stirred for 12 h. The resulting

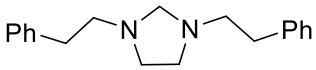
mixture was quenched by water and extracted with EtOAc (30 mL*3). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure to afford **2-V**.

In a round bottom flask equipped with a magnetic stir bar, a solution of **2-V** (5.0 mmol, 1.00 equiv.) and HCHO (405.8 mg, 5 mmol, 1.0 equiv., 37% in water) in EtOH (10 mL) was stirred at rt until completion. The reaction was diluted by H_2O and extracted with EtOAc (15 mL*3). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexanes/EtOAc = 5:1) to obtain to obtain the corresponding imidazolidine **2j**.



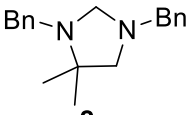
2c

The title compound **2c** was purified by flash chromatography (hexanes/EtOAc = 10:1) on silica gel and obtained as a colorless oil; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 3.31 (s, 2H), 2.74 (s, 4H), 2.31 (d, *J* = 7.1 Hz, 4H), 1.84–1.77 (m, 4H), 1.73–1.62 (m, 6H), 1.43–1.31 (m, 2H), 1.28–1.09 (m, 6H), 0.93–0.82 (m, 4H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 77.8, 62.9, 52.9, 37.4, 31.9, 26.8, 26.2; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{17}H_{33}N_2$ 265.2638; found 265.2642.



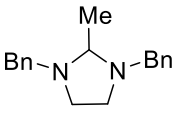
2d

The title compound **2d** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a yellow oil; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.31–7.24 (m, 4H), 7.23–7.16 (m, 6H), 3.49 (s, 2H), 2.86 (s, 4H), 2.83–2.73 (m, 8H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 140.2, 128.7, 128.5, 126.2, 76.8, 57.4, 52.6, 35.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{19}H_{25}N_2$ 281.2012; found 281.2013.



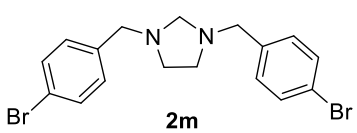
2g

The title compound **2g** was purified by flash chromatography (hexanes/EtOAc = 10:1) on silica gel and obtained as a colorless oil; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.36–7.32 (m, 2H), 7.32–7.24 (m, 6H), 7.23–7.17 (m, 2H), 3.69 (s, 2H), 3.57 (s, 2H), 3.48 (s, 2H), 2.73 (s, 2H), 1.18 (s, 6H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 140.5, 139.6, 128.6, 128.39, 128.32, 128.28, 126.9, 126.8, 74.8, 67.1, 60.3, 59.8, 51.0, 23.5; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{19}H_{25}N_2$ 281.2012; found 281.2010.



2h

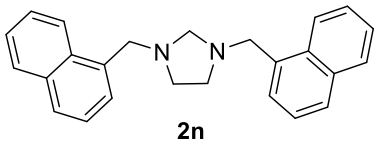
The title compound **2h** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a colorless oil; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.39–7.33 (m, 4H), 7.32–7.26 (m, 4H), 7.25–7.20 (m, 2H), 4.02 (d, *J* = 13.0 Hz, 2H), 3.30 (d, *J* = 13.0 Hz, 2H), 3.08 (q, *J* = 5.3 Hz, 1H), 3.03–2.93 (m, 2H), 2.42–2.32 (m, 2H), 1.31 (d, *J* = 5.3 Hz, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 139.3, 128.9, 128.3, 127.0, 80.9, 57.8, 50.5, 18.3; **HRMS (ESI):** calcd. for [M + H]+ $C_{18}H_{23}N_2$ 267.1856; found 267.1859.



2m

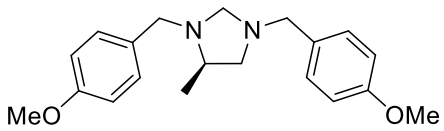
The title compound **2m** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a colorless oil; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.44–7.40 (m, 4H), 7.24–7.19 (m, 4H), 3.64

(s, 4H), 3.37 (s, 2H), 2.81 (s, 4H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 138.1, 131.3, 130.2, 120.7, 76.3, 58.6, 52.2; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{17}H_{19}Br_2N_2$ 408.9910; found 408.9918.



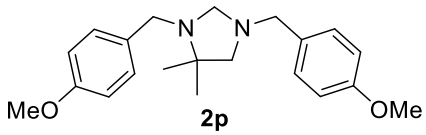
2n

The title compound **2n** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a yellow oil; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.28 (d, *J* = 8.2 Hz, 2H), 7.86 (d, *J* = 8.1 Hz, 2H), 7.77 (d, *J* = 8.1 Hz, 2H), 7.55–7.45 (m, 6H), 7.42–7.37 (m, 2H), 4.16 (s, 4H), 3.58 (s, 2H), 2.95 (s, 4H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 135.1, 133.9, 132.3, 128.6, 127.9, 126.7, 126.0, 125.7, 125.4, 124.5, 76.7, 57.7, 52.7; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{25}H_{25}N_2$ 353.2012; found 353.2016.



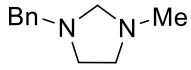
2o

The title compound **2o** was purified by flash chromatography (hexanes/EtOAc = 10:1) on silica gel and obtained as a colorless oil; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.27–7.20 (m, 4H), 6.86–6.80 (m, 4H), 3.86 (d, *J* = 12.9 Hz, 1H), 3.79 (s, 3H), 3.78 (s, 3H), 3.62 (d, *J* = 12.8 Hz, 1H), 3.57 (d, *J* = 5.8 Hz, 1H), 3.53 (d, *J* = 12.8 Hz, 1H), 3.37 (d, *J* = 12.9 Hz, 1H), 3.22 (d, *J* = 5.8 Hz, 1H), 2.97 (dd, *J* = 9.2, 7.2 Hz, 1H), 2.89–2.81 (m, 1H), 2.39 (dd, *J* = 9.2, 7.6 Hz, 1H), 1.11 (d, *J* = 6.2 Hz, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 158.6, 131.5, 131.1, 129.8, 129.7, 113.6, 113.5, 76.6, 60.3, 58.8, 58.7, 57.2, 55.1, 18.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{20}H_{27}N_2O_2$ 327.2067; found 327.2068.



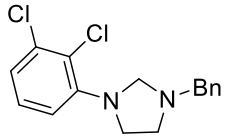
2p

The title compound **2p** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a yellow oil; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.27–7.23 (m, 2H), 7.23–7.19 (m, 2H), 6.85–6.78 (m, 4H), 3.78 (s, 3H), 3.77 (s, 3H), 3.62 (s, 2H), 3.51 (s, 2H), 3.44 (s, 2H), 2.70 (s, 2H), 1.16 (s, 6H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 158.63, 158.58, 132.5, 131.7, 129.8, 129.5, 113.70, 113.66, 74.7, 67.0, 59.61, 59.59, 55.4, 55.3, 50.3, 23.5; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{21}H_{29}N_2O_2$ 341.2224; found 341.2224.



2i

The title compound **2i** was purified by flash column chromatography (hexanes/EtOAc = 10:1) on silica gel and obtained as a colorless oil; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.37–7.33 (m, 2H), 7.32–7.27 (m, 2H), 7.25–7.20 (m, 1H), 3.71 (s, 2H), 3.36 (s, 2H), 2.86–2.82 (m, 2H), 2.80–2.75 (m, 2H), 2.36 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 139.4, 128.5, 128.3, 126.9, 78.1, 59.8, 54.4, 52.8, 41.3; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{11}H_{17}N_2$ 177.1386; found 177.1386.



2j

The title compound **2j** was purified by flash column chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a yellow oil; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.42–7.33 (m, 4H), 7.33–7.27 (m, 1H), 7.08–7.02 (m, 1H), 6.98 (dd, *J* = 7.9, 1.5 Hz, 1H), 6.73 (dd, *J* = 8.3, 1.6 Hz, 1H), 4.15 (s, 2H), 3.76 (s, 2H), 3.57 (t, *J* = 6.3 Hz, 2H), 2.97

(t, *J* = 6.3 Hz, 2H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 147.9, 138.4, 134.5, 128.8, 128.6, 127.4, 127.3, 121.34, 121.28, 114.6, 73.6, 58.6, 52.6, 49.3; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{16}H_{17}Cl_2N_2$ 307.0763; found 307.0764.

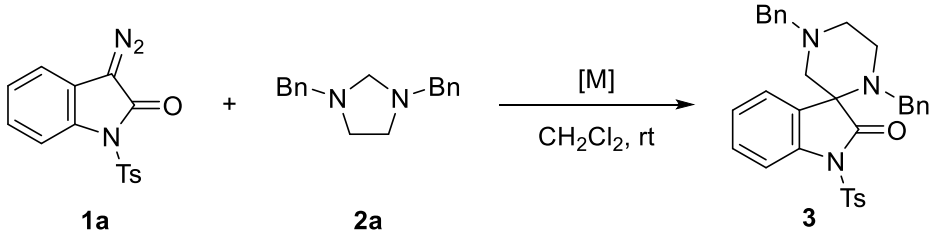
4. Exploration of the Racemic (5+1) Cycloaddition

4.1 Optimization Studies

Condition A

We first utilized diazooxindole **1a** and imidazolidine **2a** as model substrates to optimize various catalysts with CH_2Cl_2 as the solvent at rt (Table S1). Among them, $Rh_2(esp)_2$ provided the best result (Table S1, entry 23).

Table S1. Screening catalysts.[a]

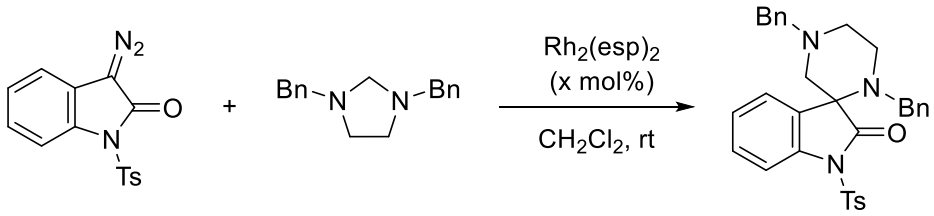


entry	catalyst	additive	yield (%)[b]
1	CuCl		20
2	CuBr		-
3	$Cu(PPh_3)_3Br$		-
4	CuI		-
5	CuOTf		-
6	$Cu(MeCN)_4NTf_2$		25
7	IPrCuCl	$NaBAr_F$	18
8	$CuCl_2$		-
9	Cu(1,10-Phen)Cl_2		-
10	$CuBr_2$		-
11	$Cu(OAc)_2$		14
12	$Cu(OTf)_2$		60
13	$FeBr_2$		-
14	$FeCl_3$•$6H_2O$		-
15	$CoBr_2$		-
16	$NiBr_2$		-

17	$ZnBr_2$		-
18	$Pd(OAc)_2$		-
19	$PdCl_2$		-
20	AgOTf		-
21	Ph_3PAuCl	$NaBAr_F$	-
22	$Rh_2(OAc)_4$		35
23	$Rh_2(esp)_2$		90
24	$Rh_2(Oct)_4$		48
25	$Rh_2(OPiv)_4$		46
26	$Rh_2(Cap)_4$		-
27	$Rh_2(TFA)_4$		-
28	$Rh_2(pfb)_4$		-
29	$Rh_2(TPA)_4$		-

[a] Reaction conditions: **1a** (0.24 mmol) in CH_2Cl_2 (2.0 mL) was injected into a solution of **2a** (0.2 mmol), catalyst ([Rh] 2 mol%, [Au] 5 mol%, [Pd]/[Ag] 10 mol%, others 20 mol%) and additive (10 mol%) in CH_2Cl_2 (2.0 mL) via a syringe pump over 1 h. The reaction was continued at rt for 12 h. [b] Isolated yields.

Table S2. Screening catalyst equiv.alents.[a]

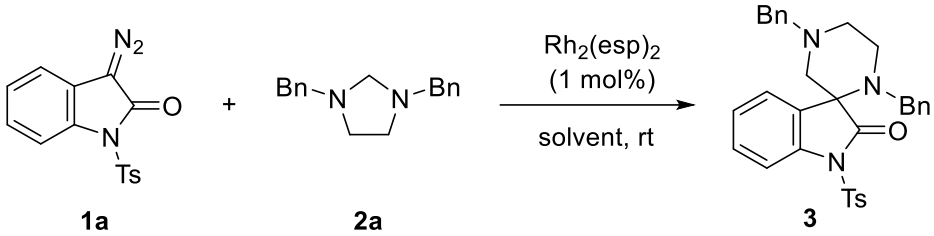


1a **2a** **3**

entry	x	yield (%)[b]
1	0.2	47
2	0.5	70
3	1.0	90
4	2.0	90

[a] Reaction conditions: **1a** (0.24 mmol) in CH_2Cl_2 (2.0 mL) was injected into a solution of **2a** (0.2 mmol) and $Rh_2(esp)_2$ (x mol%) in CH_2Cl_2 (2.0 mL) via a syringe pump over 1 h. The reaction was continued at rt for another 12 h. [b] Isolated yields.

Table S3. Screening solvents.[a]



1a **2a** **3**

entry	solvent	yield (%)[b]
1	benzene	40
2	MeCN	38
3	THF	38
4	MeOH	-
5	HFIP	38
6	CH_2Cl_2	90

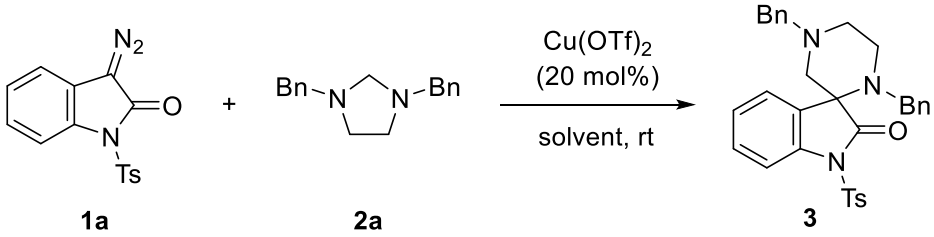
[a] Reaction conditions: **1a** (0.24 mmol) in solvent (2.0 mL) was injected into a solution of **2a** (0.2 mmol) and $Rh_2(esp)_2$ (1 mol%) in solvent (2.0 mL) via a syringe pump over 1 h. The reaction was continued at rt for another 12 h. [b] Isolated yields.

Condition A: the optimal reaction conditions were established as 1 mol% of $Rh_2(esp)_2$ as the catalyst in CH_2Cl_2 at rt for 12 h.

Condition B

In Table S1, we noticed that $Cu(OTf)_2$ was a competent catalyst, providing product **3** in 60% yield in CH_2Cl_2 at rt, while other copper salts and base-metal catalysts resulted in very slow or no reaction. So we further optimized the reaction conditions by using $Cu(OTf)_2$ as the catalyst.

Table S4. Screening solvents.[a]



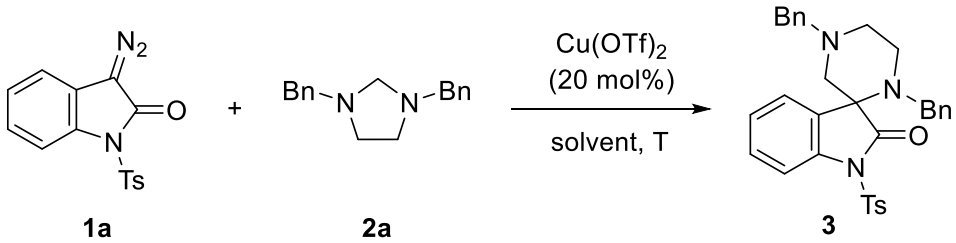
1a **2a** **3**

entry	solvent	yield (%)[b]
1	toluene	-
2	MeCN	-
3	THF	-

4	MeOH	-
5	DMF	19
6	EA	-
7	1,4-dioxane	42
8	HFIP	59
9	CH_2Cl_2	60

[a] Reaction conditions: **1a** (0.24 mmol) in solvent (2.0 mL) was injected into a solution of **1a** (0.2 mmol) and $Cu(OTf)_2$ (20 mol%) in solvent (2.0 mL) via a syringe pump over 1 h. The reaction was continued at rt for another 12 h. [b] Isolated yields.

Table S5. Screening temperature.[a]

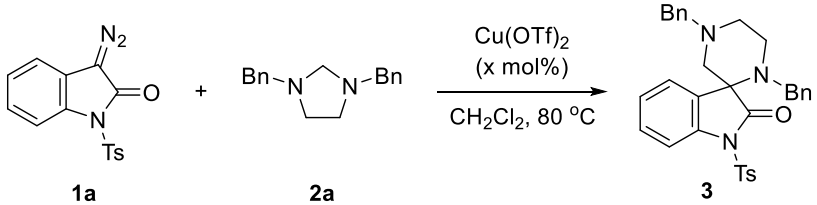


1a **2a** **3**

entry	solvent	T (°C)	time (h)	yield (%)[b]
1	CH_2Cl_2	0	24	-
2	CH_2Cl_2	25	12	60
3	CH_2Cl_2	40	12	68
4	CH_2Cl_2	80	6	85
5[c]	CH_2Cl_2	80	6	83
6	DCE	80	6	45
7	toluene	80	6	33
8	PhCl	80	6	70

[a] Reaction conditions: **1a** (0.24 mmol) in solvent (2.0 mL) was injected into a solution of **2a** (0.2 mmol) and $Cu(OTf)_2$ (20 mol%) in solvent (2.0 mL) via a syringe pump over 1 h. The reaction was continued at the corresponding temperature. [b] Isolated yields. [c] 4Å MS (100 mg) was added.

Table S6. Screening catalyst loading.[a]



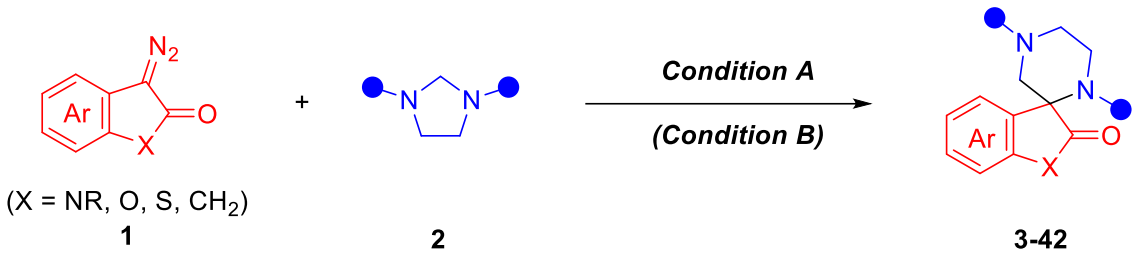
1a **2a** **3**

entry	x	yield (%)[b]
1	10	81
2	20	85
3	30	60

[a] Reaction conditions: **1a** (0.24 mmol) in CH_2Cl_2 (2 mL) was injected into a solution of **2a** (0.2 mmol) and $Cu(OTf)_2$ (x mol%) in CH_2Cl_2 (2 mL) via a syringe pump over 1 h. The reaction was continued at 80 °C for another 6 h. [b] Isolated yields.

Condition B: the optimal reaction conditions were established as 20 mol% of $Cu(OTf)_2$ as the catalyst in CH_2Cl_2 at 80 °C for 6 h. ***Note: there is a risk of explosion even though the reaction was performed in high pressure reaction tube.***

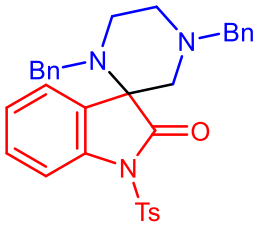
4.2 Substrate Scope



Condition A: in a reaction vial equipped with a magnetic stir bar, **2** (0.2 mmol, 1.0 equiv.) and $Rh_2(esp)_2$ (1.5 mg, 0.002 mmol, 1 mol%) were added into CH_2Cl_2 (2 mL). Then, a solution of **1** (0.24 mmol, 1.2 equiv.) in CH_2Cl_2 (2 mL) was slowly injected via an automatic syringe pump over 1 h. The reaction was continued at rt for 12 h. The resulting mixture was concentrated under reduced pressure, and the residue was purified by flash column chromatography (hexanes/EtOAc) on silica gel to afford the corresponding products.

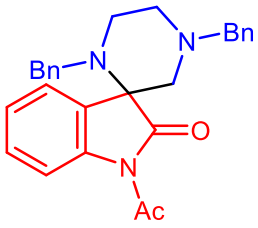
Condition B: in a high pressure reaction tube equipped with a magnetic stir bar, **2** (0.2 mmol, 1.0 equiv.) and $Cu(OTf)_2$ (14.5 mg, 0.04 mmol, 20 mol%) were added into CH_2Cl_2 (2.0 mL). Then, a solution of **1** (0.24 mmol, 1.2 equiv.) in CH_2Cl_2 (2.0 mL) was slowly injected via an automatic syringe pump over 4 h. The reaction tube was sealed and continued at 80 °C in an oil bath for 6 h. The resulting mixture cooled down to rt and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexanes/EtOAc) on silica gel to afford the corresponding products.

Compound 3



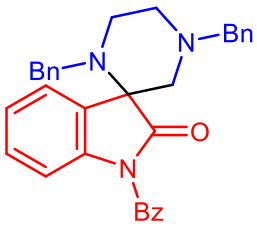
The title compound **3** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid (**Condition A:** 90% yield, 96.8 mg; **Condition B:** 85% yield, 91.4 mg); **mp:** 166–167 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.98–7.90 (m, 3H), 7.54 (d, *J* = 7.5 Hz, 1H), 7.39–7.33 (m, 1H), 7.28–7.14 (m, 11H), 7.06–7.00 (m, 2H), 3.54 (d, *J* = 13.5 Hz, 1H), 3.38 (d, *J* = 13.5 Hz, 1H), 3.17–3.07 (m, 1H), 2.95 (d, *J* = 13.2 Hz, 1H), 2.75–2.65 (m, 2H), 2.61–2.53 (m, 2H), 2.45–2.28 (m, 5H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 174.8, 145.6, 139.0, 138.2, 137.7, 135.4, 129.8, 129.7, 129.3, 128.6, 128.4, 128.2, 128.0, 127.2, 127.1, 125.1, 124.9, 114.0, 65.9, 62.2, 60.3, 55.2, 52.9, 45.8, 21.7; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{32}H_{32}N_3O_3S$ 538.2159; found 538.2169.

Compound 4



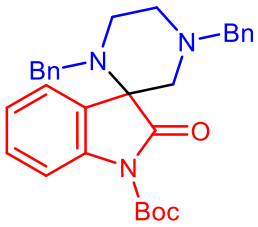
The title compound **4** was purified by flash chromatography (hexanes/EtOAc = 10:1 to 5:1) on silica gel and obtained as a white solid (**Condition A:** 85% yield, 72.3 mg; **Condition B:** 70% yield, 59.6 mg); **mp:** 64–65 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.21 (d, *J* = 8.1 Hz, 1H), 7.61 (d, *J* = 7.5 Hz, 1H), 7.35–7.31 (m, 1H), 7.30–7.18 (m, 11H), 3.67 (d, *J* = 13.5 Hz, 1H), 3.47–3.29 (m, 3H), 3.24 (d, *J* = 13.2 Hz, 1H), 2.86 (d, *J* = 11.1 Hz, 1H), 2.81–2.72 (m, 2H), 2.66 (s, 3H), 2.58–2.50 (m, 1H), 2.47 (d, *J* = 11.9 Hz, 1H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 177.2, 171.0, 139.8, 138.3, 137.8, 129.4, 129.2, 128.7, 128.4, 128.3, 127.3, 125.4, 124.3, 116.6, 66.1, 62.4, 60.8, 55.9, 53.4, 46.3, 26.8; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{27}H_{28}N_3O_2$ 426.2176; found 426.2185.

Compound 5



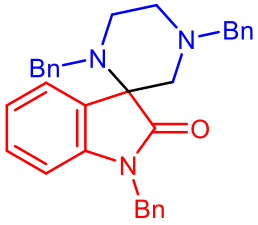
The title compound **5** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a colorless oil (**Condition A:** 88% yield, 85.8 mg; **Condition B:** 76% yield, 74.1 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.86 (d, *J* = 8.0 Hz, 1H), 7.67–7.55 (m, 4H), 7.53–7.46 (m, 2H), 7.39–7.31 (m, 5H), 7.30–7.16 (m, 7H), 3.77 (d, *J* = 13.3 Hz, 1H), 3.48 (d, *J* = 13.2 Hz, 1H), 3.42–3.29 (m, 2H), 3.27 (d, *J* = 13.2 Hz, 1H), 2.97–2.83 (m, 2H), 2.74–2.66 (m, 1H), 2.54–2.40 (m, 2H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 176.5, 169.4, 139.9, 138.5, 138.0, 134.5, 132.9, 129.7, 129.42, 129.37, 129.0, 128.6, 128.42, 128.35, 127.4, 127.2, 125.3, 124.2, 115.3, 66.5, 62.7, 60.9, 55.8, 53.9, 45.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{32}H_{30}N_3O_2$ 488.2333; found 488.2341.

Compound 6



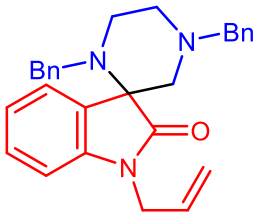
The title compound **6** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a colorless oil (**Condition A:** 90% yield, 87.0 mg; **Condition B:** 80% yield, 77.4 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.82 (d, *J* = 8.1 Hz, 1H), 7.61 (d, *J* = 7.4 Hz, 1H), 7.33–7.28 (m, 3H), 7.28–7.23 (m, 6H), 7.23–7.16 (m, 3H), 3.66 (d, *J* = 13.6 Hz, 1H), 3.43 (d, *J* = 13.6 Hz, 1H), 3.40–3.25 (m, 3H), 2.86–2.70 (m, 3H), 2.56–2.48 (m, 1H), 2.45 (d, *J* = 11.7 Hz, 1H), 1.65 (s, 9H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 174.6, 149.5, 139.5, 138.6, 138.0, 129.2, 129.0, 128.8, 128.7, 128.4, 128.3, 127.1, 124.6, 124.5, 115.0, 84.3, 66.2, 62.4, 60.7, 55.9, 53.4, 46.1, 28.3; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{30}H_{34}N_3O_3$ 484.2595; found 484.2605.

Compound 7



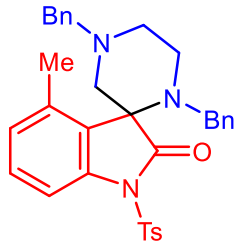
The title compound **7** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a yellow oil (**Condition A:** 90% yield, 85.3 mg; **Condition B:** 79% yield, 74.8 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.64 (s, 1H), 7.39–7.11 (m, 16H), 7.04 (t, *J* = 7.5 Hz, 1H), 6.65 (d, *J* = 7.8 Hz, 1H), 5.01 (d, *J* = 15.6 Hz, 1H), 4.79 (d, *J* = 15.6 Hz, 1H), 3.72 (d, *J* = 13.5 Hz, 1H), 3.39 (d, *J* = 13.5 Hz, 1H), 3.36–3.12 (m, 3H), 2.87–2.70 (m, 3H), 2.67–2.57 (m, 1H), 2.53 (d, *J* = 11.5 Hz, 1H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 176.6, 142.5, 138.8, 138.2, 136.2, 129.8, 129.0, 128.9, 128.80, 128.76, 128.4, 128.3, 127.6, 127.3, 127.1, 127.0, 125.2, 122.5, 109.1, 66.5, 62.6, 60.3, 56.1, 53.5, 46.2, 43.6; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{32}H_{32}N_3O$ 474.2540; found 474.2550.

Compound 8



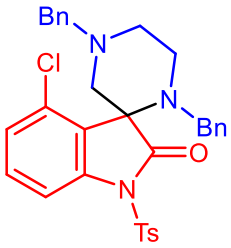
The title compound **8** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a colorless oil (**Condition A:** 84% yield, 71.2 mg; **Condition B:** 73% yield, 61.8 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.71 (s, 1H), 7.32–7.22 (m, 9H), 7.21–7.15 (m, 2H), 7.12–7.06 (m, 1H), 6.80 (d, *J* = 7.7 Hz, 1H), 5.85–5.74 (m, 1H), 5.19–5.11 (m, 2H), 4.33 (d, *J* = 5.3 Hz, 2H), 3.63 (d, *J* = 13.5 Hz, 1H), 3.44 (d, *J* = 13.5 Hz, 1H), 3.29 (d, *J* = 13.0 Hz, 1H), 3.23–3.01 (m, 2H), 2.83–2.73 (m, 2H), 2.73–2.58 (m, 2H), 2.53 (d, *J* = 11.4 Hz, 1H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 176.1, 142.6, 138.7, 138.2, 131.7, 129.7, 129.1, 128.8, 128.7, 128.34, 128.25, 127.1, 127.0, 125.6, 122.4, 117.6, 109.0, 66.5, 62.6, 60.3, 56.1, 53.3, 46.3, 42.2; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{28}H_{30}N_3O$ 424.2383; found 424.2393.

Compound 9



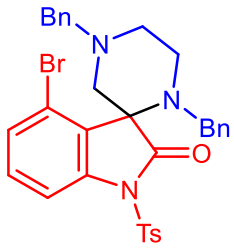
The title compound **9** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid (**Condition A:** 76% yield, 83.9 mg; **Condition B:** 62% yield, 68.4 mg); **mp:** 190–191 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.96 (d, *J* = 8.3 Hz, 2H), 7.77 (d, *J* = 8.1 Hz, 1H), 7.32–7.14 (m, 11H), 7.02 (d, *J* = 7.0 Hz, 2H), 6.93 (d, *J* = 7.7 Hz, 1H), 3.59 (d, *J* = 13.6 Hz, 1H), 3.39–3.30 (m, 2H), 3.23 (d, *J* = 13.0 Hz, 1H), 2.84 (d, *J* = 11.1 Hz, 1H), 2.71–2.61 (m, 6H), 2.57 (dt, *J* = 11.3, 2.8 Hz, 1H), 2.40 (s, 3H), 2.26 (td, *J* = 11.7, 3.2 Hz, 1H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 174.1, 145.5, 139.6, 138.0, 137.8, 136.5, 135.9, 129.8, 129.6, 128.7, 128.6, 128.44, 128.36, 128.2, 128.1, 127.1, 125.7, 111.5, 67.0, 62.2, 56.5, 55.3, 52.8, 45.7, 21.8, 18.2; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{33}H_{34}N_3O_3S$ 552.2315; found 552.2307.

Compound 10



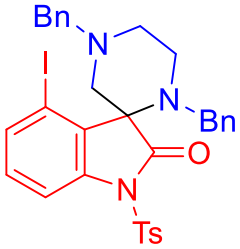
The title compound **10** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid (**Condition A:** 70% yield, 80.1 mg; **Condition B:** 56% yield, 64.1 mg); **mp:** 204–205 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.96 (d, *J* = 8.0 Hz, 2H), 7.87 (d, *J* = 8.2 Hz, 1H), 7.38–7.07 (m, 14H), 3.63 (d, *J* = 13.6 Hz, 1H), 3.36 (d, *J* = 13.6 Hz, 1H), 3.25 (t, *J* = 10.5 Hz, 1H), 3.18 (d, *J* = 12.9 Hz, 1H), 3.07 (d, *J* = 12.0 Hz, 1H), 2.81 (d, *J* = 11.0 Hz, 1H), 2.67–2.58 (m, 2H), 2.55 (d, *J* = 11.3 Hz, 1H), 2.43 (s, 3H), 2.34 (t, *J* = 10.5 Hz, 1H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 173.1, 145.9, 141.0, 138.0, 137.9, 135.6, 131.7, 130.9, 129.9, 128.9, 128.6, 128.4, 128.3, 128.2, 127.4, 127.14, 127.08, 125.0, 112.6, 67.1, 62.1, 55.5, 54.8, 52.6, 45.6, 21.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{32}H_{31}ClN_3O_3S$ 572.1769; found 572.1783.

Compound 11



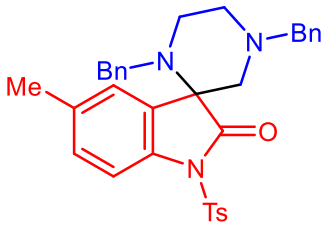
The title compound **11** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid (**Condition A:** 46% yield, 56.7 mg; **Condition B:** 37% yield 45.6 mg); **mp:** 203–204 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.02–7.88 (m, 3H), 7.37–7.12 (m, 14H), 3.63 (d, *J* = 13.6 Hz, 1H), 3.37 (d, *J* = 13.6 Hz, 1H), 3.30–3.21 (m, 1H), 3.20–3.10 (m, 2H), 2.80 (d, *J* = 10.5 Hz, 1H), 2.64–2.52 (m, 3H), 2.47–2.34 (m, 4H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 173.2, 145.9, 141.1, 137.9, 137.8, 135.6, 131.1, 130.8, 129.9, 129.1, 128.6, 128.4, 128.3, 128.2, 127.14, 127.08, 126.2, 119.6, 113.2, 67.3, 62.1, 55.5, 54.6, 52.4, 45.6, 21.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{32}H_{31}BrN_3O_3S$ 616.1264; found 616.1274.

Compound 12



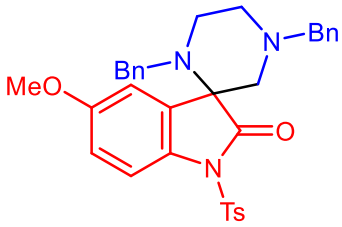
The title compound **12** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid (**Condition A:** 45% yield, 59.7 mg; **Condition B:** 38% yield, 50.4 mg); **mp:** 207–208 °C; **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.03–7.88 (m, 3H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.35–7.14 (m, 12H), 7.01 (t, *J* = 8.1 Hz, 1H), 3.64 (d, *J* = 13.6 Hz, 1H), 3.40 (d, *J* = 13.6 Hz, 1H), 3.33–3.22 (m, 1H), 3.14 (d, *J* = 12.4 Hz, 2H), 2.78 (d, *J* = 11.1 Hz, 1H), 2.63 (d, *J* = 11.5 Hz, 1H), 2.60–2.45 (m, 3H), 2.41 (s, 3H); **^{13}C NMR (125 MHz, CDCl$_3$):** δ 173.8, 145.9, 140.7, 137.8, 137.6, 137.4, 135.5, 131.3, 129.9, 129.6, 128.7, 128.5, 128.23, 128.18, 127.2, 127.1, 114.1, 91.2, 66.8, 62.1, 55.6, 54.7, 52.1, 45.5, 21.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{32}H_{31}IN_3O_3S$ 664.1125; found 664.1115.

Compound 13



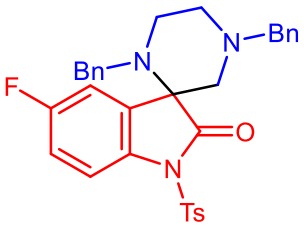
The title compound **13** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid (**Condition A:** 89% yield, 98.2 mg; **Condition B:** 67% yield, 73.9 mg); **mp:** 167–168 °C; **^{1}H NMR (500 MHz, CDCl$_3$):** δ 7.93 (d, *J* = 8.1 Hz, 2H), 7.80 (d, *J* = 8.3 Hz, 1H), 7.33 (s, 1H), 7.27–7.13 (m, 11H), 7.05–7.00 (m, 2H), 3.53 (d, *J* = 13.5 Hz, 1H), 3.38 (d, *J* = 13.5 Hz, 1H), 3.18–3.06 (m, 1H), 2.96 (d, *J* = 13.2 Hz, 1H), 2.72 (d, *J* = 11.1 Hz, 1H), 2.66 (d, *J* = 11.8 Hz, 1H), 2.59–2.51 (m, 2H), 2.42–2.34 (m, 5H), 2.32 (s, 3H); **^{13}C NMR (125 MHz, CDCl$_3$):** δ 175.0, 145.5, 138.3, 137.8, 136.7, 135.5, 134.9, 130.2, 129.7, 129.3, 128.7, 128.4, 128.2, 128.0, 127.1, 125.5, 113.8, 66.0, 62.3, 60.4, 55.2, 52.9, 45.8, 21.7, 21.3; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{33}H_{34}N_3O_3S$ 552.2315; found 552.2328.

Compound 14



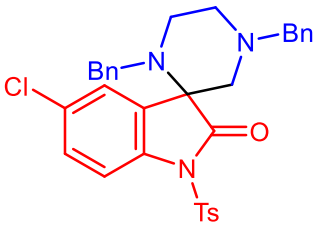
The title compound **14** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid (**Condition A:** 84% yield, 95.4 mg; **Condition B:** 73% yield, 82.9 mg); **mp:** 178–179 °C; **^{1}H NMR (500 MHz, CDCl$_3$):** δ 7.92 (d, *J* = 8.5 Hz, 2H), 7.85 (d, *J* = 8.9 Hz, 1H), 7.26–7.14 (m, 10H), 7.10 (s, 1H), 7.04–6.99 (m, 2H), 6.88 (dd, *J* = 8.9, 2.8 Hz, 1H), 3.82 (s, 3H), 3.52 (d, *J* = 13.5 Hz, 1H), 3.39 (d, *J* = 13.5 Hz, 1H), 3.14–3.04 (m, 1H), 2.92 (d, *J* = 13.3 Hz, 1H), 2.73–2.64 (m, 2H), 2.58–2.49 (m, 2H), 2.42–2.34 (m, 2H), 2.31 (s, 3H); **^{13}C NMR (125 MHz, CDCl$_3$):** δ 175.0, 157.4, 145.6, 138.2, 137.8, 135.4, 132.3, 130.8, 129.8, 128.7, 128.43, 128.41, 128.3, 128.0, 127.2, 115.1, 114.5, 111.1, 66.2, 62.3, 60.4, 55.8, 55.3, 52.8, 45.9, 21.7; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{33}H_{34}N_3O_4S$ 568.2265; found 568.2274.

Compound 15



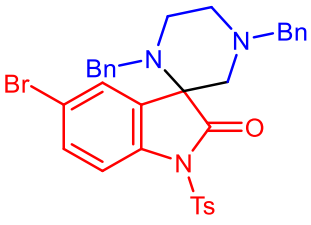
The title compound **15** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid (**Condition A:** 87% yield, 96.7 mg; **Condition B:** 61% yield 67.8 mg); **mp:** 183–184 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.97–7.88 (m, 3H), 7.32 (d, *J* = 7.2 Hz, 1H), 7.28–7.15 (m, 10H), 7.13–7.07 (m, 1H), 7.03–6.98 (m, 2H), 3.52 (d, *J* = 13.5 Hz, 1H), 3.40 (d, *J* = 13.5 Hz, 1H), 3.11–2.98 (m, 1H), 2.87 (d, *J* = 13.1 Hz, 1H), 2.71–2.62 (m, 2H), 2.60–2.50 (m, 2H), 2.46–2.36 (m, 2H), 2.30 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 174.6, 160.3 (d, *J* = 245.3 Hz), 145.9, 137.8, 137.6, 135.2, 134.9 (d, *J* = 3.0 Hz), 131.3 (d, *J* = 7.9 Hz), 129.8, 128.7, 128.5, 128.4, 128.3, 128.0, 127.31, 127.25, 116.3 (d, *J* = 23.2 Hz), 115.4 (d, *J* = 7.6 Hz), 112.8 (d, *J* = 24.2 Hz), 66.2, 62.3, 60.1, 55.5, 52.8, 45.9, 21.7; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{32}H_{31}FN_3O_3S$ 556.2065; found 556.2078.

Compound 16



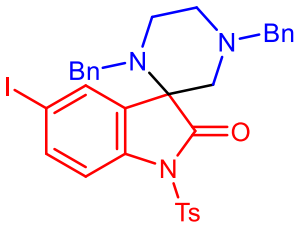
The title compound **16** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid (**Condition A:** 81% yield, 92.7 mg; **Condition B:** 50% yield 57.2 mg); **mp:** 161–162 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.95–7.85 (m, 3H), 7.58 (s, 1H), 7.34 (dd, *J* = 8.7, 2.4 Hz, 1H), 7.28–7.15 (m, 10H), 7.04–6.98 (m, 2H), 3.51 (d, *J* = 13.4 Hz, 1H), 3.41 (d, *J* = 13.4 Hz, 1H), 3.10–2.96 (m, 1H), 2.88 (d, *J* = 13.1 Hz, 1H), 2.71–2.62 (m, 2H), 2.61–2.49 (m, 2H), 2.47–2.35 (m, 2H), 2.30 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 174.2, 146.0, 137.8, 137.6, 137.4, 135.1, 131.1, 130.8, 129.9, 129.7, 128.7, 128.46, 128.45, 128.3, 128.0, 127.33, 127.26, 125.5, 115.3, 66.1, 62.2, 60.1, 55.6, 52.8, 45.9, 21.7; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{32}H_{31}ClN_3O_3S$ 572.1769; found 572.1780.

Compound 17



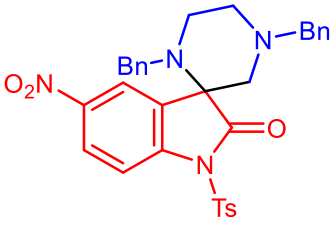
The title compound **17** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid (**Condition A:** 78% yield, 96.2 mg; **Condition B:** 46% yield, 56.7 mg); **mp:** 164–165 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.91 (d, *J* = 8.0 Hz, 2H), 7.83 (d, *J* = 8.6 Hz, 1H), 7.73 (s, 1H), 7.49 (d, *J* = 8.8 Hz, 1H), 7.32–7.14 (m, 10H), 7.00 (d, *J* = 7.2 Hz, 2H), 3.51 (d, *J* = 13.5 Hz, 1H), 3.41 (d, *J* = 13.5 Hz, 1H), 3.08–2.96 (m, 1H), 2.87 (d, *J* = 13.1 Hz, 1H), 2.71–2.62 (m, 2H), 2.61–2.50 (m, 2H), 2.46–2.36 (m, 2H), 2.30 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 174.1, 146.0, 137.9, 137.8, 137.6, 135.1, 132.6, 131.4, 129.9, 128.7, 128.5, 128.3, 128.0, 127.34, 127.26, 118.3, 115.7, 66.0, 62.2, 60.1, 55.6, 52.8, 45.9, 21.7; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{32}H_{31}BrN_3O_3S$ 616.1264; found 616.1273.

Compound 18



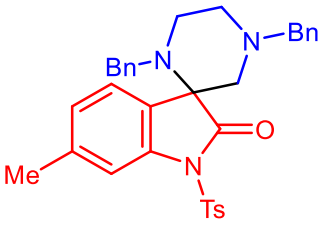
The title compound **18** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid (**Condition A:** 78% yield, 103.5 mg; **Condition B:** 46% yield, 61.0 mg); **mp:** 176–177 °C; **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.00–7.85 (m, 3H), 7.75–7.65 (m, 2H), 7.30–7.15 (m, 10H), 7.00 (d, *J* = 7.1 Hz, 2H), 3.51 (d, *J* = 13.4 Hz, 1H), 3.41 (d, *J* = 13.4 Hz, 1H), 3.02 (s, 1H), 2.87 (d, *J* = 13.1 Hz, 1H), 2.72–2.61 (m, 2H), 2.61–2.49 (m, 2H), 2.48–2.35 (m, 2H), 2.30 (s, 3H); **^{13}C NMR (125 MHz, CDCl$_3$):** δ 173.9, 146.0, 138.7, 138.5, 137.8, 137.7, 135.1, 134.2, 131.6, 129.9, 128.7, 128.48, 128.46, 128.3, 128.0, 127.33, 127.25, 116.0, 88.8, 65.9, 62.2, 60.1, 55.6, 52.8, 46.0, 21.7; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{32}H_{31}IN_3O_3S$ 664.1125; found 664.1135.

Compound 19



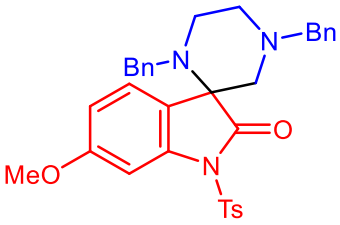
The title compound **19** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a green solid (**Condition A:** 45% yield, 52.4 mg; **Condition B:** 33% yield 38.5 mg); **mp:** 213–214 °C; **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.51 (s, 1H), 8.29 (dd, *J* = 9.0, 2.5 Hz, 1H), 8.11 (d, *J* = 9.0 Hz, 1H), 7.94 (d, *J* = 8.4 Hz, 2H), 7.28–7.15 (m, 10H), 7.02–6.94 (m, 2H), 3.53 (d, *J* = 13.4 Hz, 1H), 3.44 (d, *J* = 13.4 Hz, 1H), 3.09–2.96 (m, 1H), 2.82 (d, *J* = 13.1 Hz, 1H), 2.74–2.49 (m, 5H), 2.45 (d, *J* = 11.7 Hz, 1H), 2.31 (s, 3H); **^{13}C NMR (125 MHz, CDCl$_3$):** δ 174.0, 146.6, 144.9, 143.9, 137.5, 137.3, 134.7, 130.5, 130.1, 128.8, 128.54, 128.46, 128.40, 128.2, 127.5, 127.4, 125.9, 121.1, 114.2, 65.9, 62.2, 59.9, 55.9, 52.8, 46.2, 21.8; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{32}H_{31}N_4O_5S$ 583.2010; found 583.2018.

Compound 20



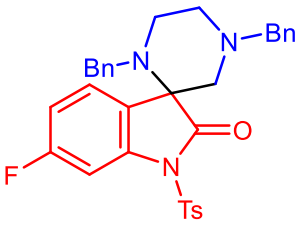
The title compound **20** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a colorless oil (**Condition A:** 83% yield, 91.6 mg; **Condition B:** 60% yield, 66.2 mg); **^{1}H NMR (500 MHz, CDCl$_3$):** δ 7.95 (d, *J* = 7.9 Hz, 2H), 7.78 (s, 1H), 7.42 (d, *J* = 7.6 Hz, 1H), 7.31–7.12 (m, 10H), 7.07–6.98 (m, 3H), 3.53 (d, *J* = 13.5 Hz, 1H), 3.37 (d, *J* = 13.5 Hz, 1H), 3.17–3.03 (m, 1H), 2.97 (d, *J* = 13.2 Hz, 1H), 2.75–2.61 (m, 2H), 2.59–2.51 (m, 2H), 2.47–2.26 (m, 8H); **^{13}C NMR (125 MHz, CDCl$_3$):** δ 175.1, 145.6, 140.1, 139.2, 138.3, 137.8, 135.6, 129.8, 128.7, 128.44, 128.40, 128.2, 128.0, 127.13, 127.12, 126.3, 125.8, 124.7, 114.6, 65.8, 62.3, 60.3, 55.2, 52.9, 45.8, 22.2, 21.8; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{33}H_{34}N_3O_3S$ 552.2315; found 552.2307.

Compound 21



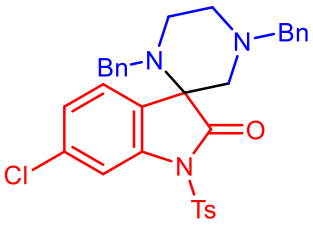
The title compound **21** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a colorless oil (**Condition A:** 91% yield, 103.3 mg; **Condition B:** 68% yield, 77.2 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.94 (d, *J* = 7.9 Hz, 2H), 7.57 (s, 1H), 7.43 (d, *J* = 8.3 Hz, 1H), 7.33–7.10 (m, 10H), 7.01 (d, *J* = 7.2 Hz, 2H), 6.74 (d, *J* = 8.4 Hz, 1H), 3.85 (s, 3H), 3.53 (d, *J* = 13.4 Hz, 1H), 3.37 (d, *J* = 13.5 Hz, 1H), 3.15–3.02 (m, 1H), 2.96 (d, *J* = 13.2 Hz, 1H), 2.74–2.60 (m, 2H), 2.59–2.46 (m, 2H), 2.44–2.25 (m, 5H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 175.1, 161.0, 145.7, 140.1, 138.3, 137.8, 135.5, 129.8, 128.7, 128.41, 128.39, 128.2, 128.0, 127.1, 125.7, 120.9, 110.5, 100.8, 65.6, 62.3, 60.4, 55.8, 55.1, 52.9, 45.8, 21.7; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{33}H_{34}N_3O_4S$ 568.2265; found 568.2255.

Compound 22



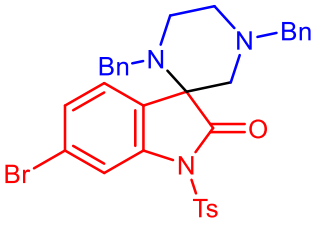
The title compound **22** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a red solid (**Condition A:** 70% yield, 77.9 mg; **Condition B:** 58% yield, 64.6 mg); **mp:** 185–186 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.95 (d, *J* = 8.0 Hz, 2H), 7.72 (d, *J* = 9.9 Hz, 1H), 7.52 (s, 1H), 7.31–7.12 (m, 10H), 7.00 (d, *J* = 7.1 Hz, 2H), 6.94–6.86 (m, 1H), 3.53 (d, *J* = 13.5 Hz, 1H), 3.39 (d, *J* = 13.5 Hz, 1H), 3.14–3.00 (m, 1H), 2.90 (d, *J* = 13.1 Hz, 1H), 2.74–2.61 (m, 2H), 2.60–2.49 (m, 2H), 2.45–2.36 (m, 2H), 2.33 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 174.6, 163.4 (d, *J* = 247.0 Hz), 146.0, 140.0 (d, *J* = 12.0 Hz), 138.0, 137.6, 135.2, 129.9, 128.7, 128.5, 128.4, 128.3, 128.1, 127.3, 127.2, 126.3 (d, *J* = 9.2 Hz), 124.7 (d, *J* = 2.6 Hz), 111.8 (d, *J* = 22.5 Hz), 102.8 (d, *J* = 29.5 Hz), 65.7, 62.3, 60.3, 55.3, 52.9, 45.9, 21.8; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{32}H_{31}FN_3O_3S$ 556.2065; found 556.2076.

Compound 23



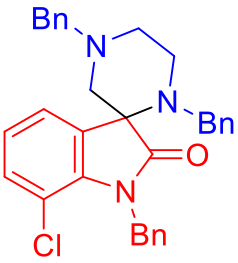
The title compound **23** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a pink solid (**Condition A:** 89% yield, 101.8 mg; **Condition B:** 66% yield, 75.5 mg); **mp:** 162–163 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.99 (d, *J* = 1.9 Hz, 1H), 7.95 (d, *J* = 8.1 Hz, 2H), 7.50 (d, *J* = 8.1 Hz, 1H), 7.28–7.15 (m, 11H), 7.00 (d, *J* = 6.9 Hz, 2H), 3.52 (d, *J* = 13.5 Hz, 1H), 3.39 (d, *J* = 13.5 Hz, 1H), 3.12–2.98 (m, 1H), 2.89 (d, *J* = 13.1 Hz, 1H), 2.72–2.61 (m, 2H), 2.60–2.50 (m, 2H), 2.45–2.36 (m, 2H), 2.33 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 174.4, 146.0, 139.9, 137.9, 137.6, 135.6, 135.2, 129.9, 128.7, 128.5, 128.4, 128.3, 128.1, 127.6, 127.30, 127.25, 126.1, 125.2, 114.6, 65.8, 62.3, 60.1, 55.4, 52.8, 45.9, 21.8; **HRMS (ESI):** calcd. for $[M + N]^+$ $C_{32}H_{31}ClN_3O_3S$ 572.1769; found 572.1760.

Compound 24



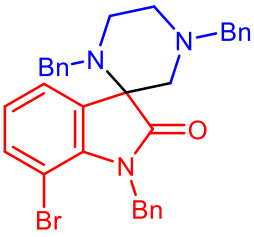
The title compound **24** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a pink solid (**Condition A:** 87% yield, 107.3 mg; **Condition B:** 75% yield, 92.5 mg); **mp:** 171–172 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.14 (d, *J* = 1.7 Hz, 1H), 7.95 (d, *J* = 8.4 Hz, 2H), 7.44 (d, *J* = 8.2 Hz, 1H), 7.36 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.28–7.14 (m, 10H), 7.02–6.96 (m, 2H), 3.52 (d, *J* = 13.5 Hz, 1H), 3.39 (d, *J* = 13.5 Hz, 1H), 3.11–2.99 (m, 1H), 2.89 (d, *J* = 13.1 Hz, 1H), 2.72–2.61 (m, 2H), 2.60–2.50 (m, 2H), 2.45–2.36 (m, 2H), 2.32 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 174.3, 146.0, 140.0, 137.9, 137.6, 135.1, 129.9, 128.7, 128.5, 128.4, 128.3, 128.2, 128.1, 127.3, 127.2, 126.4, 123.5, 117.3, 65.8, 62.3, 60.1, 55.4, 52.8, 45.9, 21.8; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{32}H_{31}BrN_3O_3S$ 616.1264; found 616.1274.

Compound 25



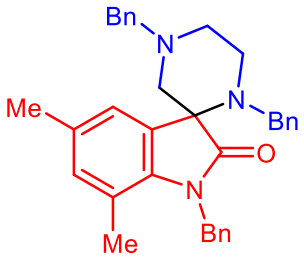
The title compound **25** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid (**Condition A:** 86% yield, 87.4 mg; **Condition B:** 75% yield, 76.2 mg); **mp:** 158–159 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.59–7.49 (m, 1H), 7.33–7.11 (m, 16H), 7.02–6.97 (m, 1H), 5.40 (d, *J* = 16.0 Hz, 1H), 5.26 (d, *J* = 16.0 Hz, 1H), 3.72 (d, *J* = 13.5 Hz, 1H), 3.44–3.18 (m, 4H), 2.89–2.69 (m, 3H), 2.62–2.52 (m, 1H), 2.47 (d, *J* = 11.7 Hz, 1H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 177.0, 138.8, 138.5, 138.03, 137.99, 132.9, 131.5, 128.8, 128.7, 128.6, 128.5, 128.3, 127.2, 127.14, 127.11, 126.7, 123.5, 115.4, 65.7, 62.6, 60.5, 56.0, 53.6, 46.1, 44.5; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{32}H_{31}ClN_3O$ 508.2150; found 508.2163.

Compound 26



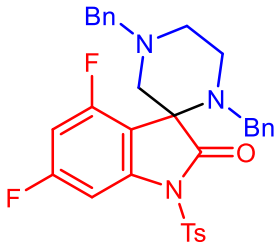
The title compound **26** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid (**Condition A:** 85% yield, 93.9 mg; **Condition B:** 60% yield, 66.3 mg); **mp:** 140–141 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.59 (d, *J* = 7.4 Hz, 1H), 7.33 (d, *J* = 8.1 Hz, 1H), 7.31–7.18 (m, 13H), 7.16–7.11 (m, 2H), 6.93 (t, *J* = 7.8 Hz, 1H), 5.43 (d, *J* = 16.3 Hz, 1H), 5.32 (d, *J* = 16.3 Hz, 1H), 3.72 (d, *J* = 13.5 Hz, 1H), 3.42–3.17 (m, 4H), 2.87–2.69 (m, 3H), 2.61–2.51 (m, 1H), 2.47 (d, *J* = 11.6 Hz, 1H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 177.2, 140.2, 138.5, 138.0, 137.9, 134.8, 133.3, 128.8, 128.7, 128.6, 128.5, 128.3, 127.2, 127.1, 127.0, 126.5, 124.0, 123.8, 102.5, 65.6, 62.5, 60.6, 56.0, 53.5, 46.0, 44.1; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{32}H_{31}BrN_3O$ 552.1645; found 552.1655.

Compound 27



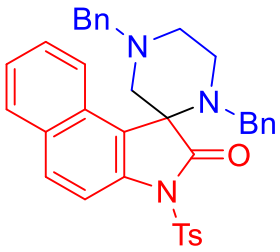
The title compound **27** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a brown solid (**Condition A:** 89% yield, 89.3 mg; **Condition B:** 70% yield, 70.2 mg); **mp:** 160–161 °C; **^{1}H NMR (500 MHz, CDCl$_3$):** δ 7.36–7.17 (m, 14H), 7.09–7.02 (m, 2H), 6.73 (s, 1H), 5.31 (d, *J* = 16.8 Hz, 1H), 4.99 (d, *J* = 16.8 Hz, 1H), 3.78 (d, *J* = 13.6 Hz, 1H), 3.50–3.27 (m, 4H), 2.92–2.80 (m, 2H), 2.78–2.71 (m, 1H), 2.59–2.50 (m, 1H), 2.47 (d, *J* = 11.6 Hz, 1H), 2.30 (s, 3H), 2.16 (s, 3H); **^{13}C NMR (125 MHz, CDCl$_3$):** δ 177.5, 139.1, 138.32, 138.27, 133.3, 132.1, 130.8, 128.90, 128.86, 128.7, 128.4, 128.3, 127.1, 127.0, 126.9, 125.8, 123.4, 119.3, 65.5, 62.6, 60.9, 55.9, 53.8, 46.0, 44.6, 21.0, 18.8; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{34}H_{36}N_3O$ 502.2853; found 502.2860.

Compound 28



The title compound **28** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid (**Condition A:** 76% yield, 87.2 mg; **Condition B:** 63% yield, 72.3 mg); **mp:** 150–151 °C; **^{1}H NMR (500 MHz, CDCl$_3$):** δ 7.96 (d, *J* = 8.0 Hz, 2H), 7.56 (dd, *J* = 9.6, 2.2 Hz, 1H), 7.32 (d, *J* = 8.1 Hz, 2H), 7.28–7.15 (m, 8H), 7.06 (d, *J* = 7.2 Hz, 2H), 6.60 (td, *J* = 9.4, 2.3 Hz, 1H), 3.60 (d, *J* = 13.5 Hz, 1H), 3.36 (d, *J* = 13.6 Hz, 1H), 3.24–3.12 (m, 2H), 2.79 (d, *J* = 10.9 Hz, 1H), 2.75–2.66 (m, 2H), 2.63 (d, *J* = 13.1 Hz, 1H), 2.57–2.50 (m, 1H), 2.43 (s, 3H), 2.36–2.28 (m, 1H); **^{13}C NMR (125 MHz, CDCl$_3$):** δ 173.0, 163.9 (dd, *J* = 249.2, 12.6 Hz), 159.4 (dd, *J* = 254.1, 14.2 Hz), 146.2, 141.3 (dd, *J* = 14.6, 10.1 Hz), 138.0, 137.8, 135.2, 130.0, 128.6, 128.47, 128.42, 128.38, 128.2, 127.3, 127.2, 111.2 (dd, *J* = 17.6, 3.5 Hz), 101.3 (t, *J* = 25.6 Hz), 99.2 (dd, *J* = 29.5, 4.1 Hz), 66.5 (d, *J* = 4.3 Hz), 62.1, 57.0, 55.4, 52.8, 45.9, 21.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{32}H_{30}F_2N_3O_3S$ 574.1970; found 574.1961.

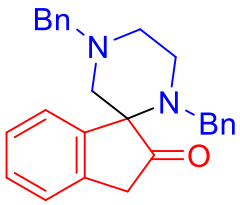
Compound 29



The title compound **29** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid (**Condition A:** 78% yield, 91.7 mg; **Condition B:** 69% yield, 81.1 mg); **mp:** 130–131 °C; **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.87 (d, *J* = 8.5 Hz, 1H), 8.21 (d, *J* = 9.0 Hz, 1H), 7.97 (d, *J* = 8.4 Hz, 2H), 7.89 (d, *J* = 9.0 Hz, 1H), 7.86 (d, *J* = 8.1 Hz, 1H), 7.62–7.55 (m, 1H), 7.49–7.42 (m, 1H), 7.32–7.08 (m, 10H), 6.97–6.91 (m, 2H), 3.58 (d, *J* = 13.6 Hz, 1H), 3.47–3.39 (m, 1H), 3.36 (d, *J* = 13.7 Hz, 1H), 3.17 (d, *J* = 12.6 Hz, 1H), 2.98 (d, *J* = 12.3 Hz, 1H), 2.92 (d, *J* = 11.3 Hz, 1H), 2.71–2.58 (m, 3H), 2.46–2.32 (m, 4H); **^{13}C NMR (125 MHz, CDCl$_3$):** δ 175.0, 145.5, 137.88, 137.85, 137.3, 135.8, 131.8, 131.0, 129.8, 129.4, 129.1, 129.0, 128.6, 128.4, 128.2, 128.1, 127.1, 126.9, 125.4, 124.3,

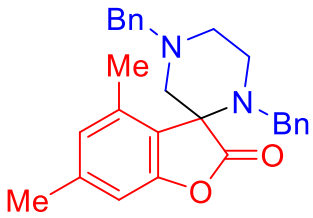
121.0, 113.9, 68.1, 62.1, 57.8, 55.6, 52.9, 45.7, 21.7; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{36}H_{34}N_3O_3S$ 588.2315; found 588.2300.

Compound 30



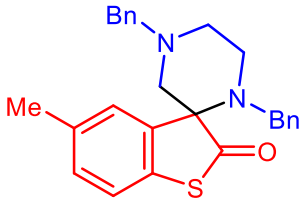
The title compound **30** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a colorless oil (**Condition A:** 90% yield, 68.9 mg; **Condition B:** 30% yield, 30.0 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.58 (d, *J* = 7.6 Hz, 1H), 7.33 (t, *J* = 7.3 Hz, 1H), 7.30–7.23 (m, 10H), 7.23–7.17 (m, 2H), 3.69 (d, *J* = 13.5 Hz, 1H), 3.57–3.41 (m, 3H), 3.41–3.31 (m, 2H), 3.27 (d, *J* = 13.4 Hz, 1H), 2.93–2.85 (m, 1H), 2.77 (dd, *J* = 12.1, 2.0 Hz, 1H), 2.71 (dt, *J* = 11.5, 3.3 Hz, 1H), 2.40 (td, *J* = 11.0, 3.4 Hz, 1H), 2.30 (d, *J* = 12.1 Hz, 1H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 217.3, 143.4, 139.3, 138.1, 136.5, 128.7, 128.6, 128.42, 128.37, 128.30, 128.0, 127.1, 127.0, 125.02, 124.95, 70.7, 62.5, 60.8, 55.6, 53.8, 46.7, 42.2; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{26}H_{27}N_2O$ 383.2118; found 383.2112.

Compound 31



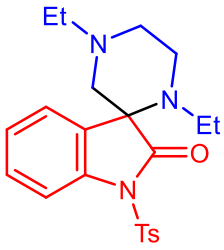
The title compound **31** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a red oil (**Condition A:** 95% yield, 78.4 mg; **Condition B:** 36% yield, 29.7 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.34–7.30 (m, 2H), 7.30–7.25 (m, 4H), 7.24–7.18 (m, 4H), 6.71 (s, 1H), 6.67 (s, 1H), 3.74 (d, *J* = 13.5 Hz, 1H), 3.65 (d, *J* = 13.0 Hz, 1H), 3.41–3.33 (m, 2H), 3.21 (d, *J* = 13.0 Hz, 1H), 2.98–2.91 (m, 1H), 2.85–2.79 (m, 1H), 2.76–2.68 (m, 2H), 2.58 (s, 3H), 2.40–2.33 (m, 1H), 2.28 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 174.0, 153.8, 140.4, 138.0, 137.7, 136.2, 128.8, 128.7, 128.51, 128.45, 127.6, 127.24, 127.18, 122.0, 109.2, 66.4, 62.4, 57.0, 56.0, 53.4, 45.7, 21.7, 17.5; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{27}H_{29}N_2O_2$ 413.2224; found 413.2213.

Compound 32



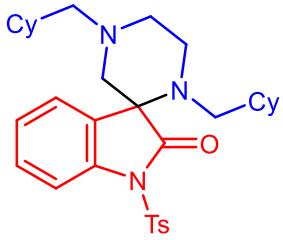
The title compound **32** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a colorless oil (**Condition A:** 87% yield, 72.1 mg; **Condition B:** 33% yield, 27.4 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.33 (s, 1H), 7.31–7.19 (m, 10H), 7.14 (d, *J* = 8.0 Hz, 1H), 7.09 (dd, *J* = 8.0, 1.8 Hz, 1H), 3.68 (d, *J* = 13.6 Hz, 1H), 3.56 (d, *J* = 13.6 Hz, 1H), 3.46–3.32 (m, 3H), 2.96–2.88 (m, 2H), 2.72–2.66 (m, 1H), 2.41–2.27 (m, 5H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 204.8, 138.8, 137.8, 137.3, 136.4, 131.4, 130.0, 128.7, 128.52, 128.46, 128.38, 127.20, 127.16, 126.6, 123.0, 75.7, 62.3, 61.4, 55.5, 53.3, 46.0, 21.5; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{26}H_{27}N_2OS$ 415.1839; found 415.1845.

Compound 33



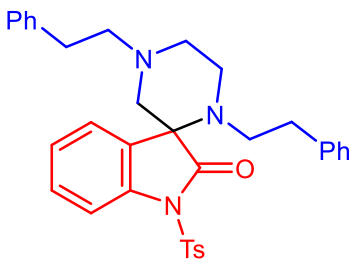
The title compound **33** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a brown oil (**Condition A:** 95% yield, 78.6 mg; **Condition B:** 78% yield, 64.5 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.01–7.91 (m, 3H), 7.41 (d, *J* = 7.5 Hz, 1H), 7.39–7.34 (m, 1H), 7.28 (d, *J* = 7.7 Hz, 2H), 7.21–7.16 (m, 1H), 3.23–3.13 (m, 1H), 2.85–2.75 (m, 2H), 2.51 (d, *J* = 11.6 Hz, 1H), 2.46–2.33 (m, 5H), 2.29–2.18 (m, 2H), 1.93–1.83 (m, 1H), 1.79–1.67 (m, 1H), 0.88 (t, *J* = 7.2 Hz, 3H), 0.73 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 175.3, 145.5, 138.8, 135.4, 129.7, 129.5, 129.4, 128.0, 125.1, 124.9, 113.8, 66.1, 60.2, 53.0, 51.9, 45.54, 45.47, 21.7, 13.0, 11.8; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{22}H_{28}N_3O_3S$ 414.1846; found 414.1839.

Compound 34



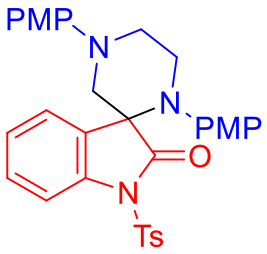
The title compound **34** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a yellow solid (**Condition A:** 91% yield, 100.1 mg; **Condition B:** 78% yield, 85.8 mg); **mp:** 163–164 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.00–7.91 (m, 3H), 7.41 (d, *J* = 6.8 Hz, 1H), 7.38–7.33 (m, 1H), 7.27 (d, *J* = 7.6 Hz, 2H), 7.19–7.14 (m, 1H), 3.12–3.01 (m, 1H), 2.74–2.61 (m, 2H), 2.50 (d, *J* = 11.5 Hz, 1H), 2.43–2.32 (m, 4H), 2.25 (d, *J* = 11.5 Hz, 1H), 2.09–2.01 (m, 1H), 2.00–1.92 (m, 1H), 1.73–1.47 (m, 9H), 1.44–1.18 (m, 5H), 1.17–0.90 (m, 6H), 0.82–0.68 (m, 2H), 0.30–0.18 (m, 2H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 174.9, 145.5, 139.0, 135.7, 129.8, 129.7, 129.3, 128.1, 125.7, 124.7, 113.7, 66.2, 65.1, 61.1, 58.2, 53.8, 46.4, 35.0, 34.6, 31.8, 31.6, 31.4, 31.0, 26.9, 26.8, 26.21, 26.16, 26.09, 26.00, 21.8; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{32}H_{44}N_3O_3S$ 550.3098; found 550.3105.

Compound 35



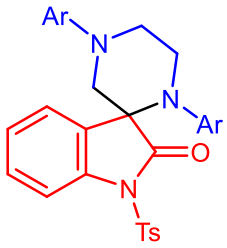
The title compound **35** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a yellow oil (**Condition A:** 94% yield, 106.36 mg; **Condition B:** 77% yield, 87.1 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.95–7.87 (m, 3H), 7.36–7.31 (m, 1H), 7.28–7.22 (m, 2H), 7.20–7.09 (m, 8H), 7.08–6.99 (m, 2H), 6.83–6.77 (m, 2H), 3.38–3.29 (m, 1H), 2.94–2.85 (m, 2H), 2.62–2.53 (m, 4H), 2.52–2.38 (m, 4H), 2.29 (d, *J* = 11.6 Hz, 1H), 2.24 (s, 3H), 2.10–1.99 (m, 2H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 175.2, 145.6, 140.2, 139.7, 138.8, 135.4, 129.7, 129.5, 129.1, 128.8, 128.5, 128.2, 128.0, 126.1, 126.0, 125.2, 124.9, 113.7, 66.1, 60.8, 59.9, 53.34, 53.32, 46.3, 34.2, 33.4, 21.7; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{34}H_{36}N_3O_3S$ 566.2472; found 566.2475.

Compound 36



The title compound **36** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid (**Condition A:** 30% yield, 34.2 mg; **Condition B:** 27% yield, 30.8 mg); **mp:** 186–187 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.92–7.76 (m, 3H), 7.58 (d, *J* = 7.5 Hz, 1H), 7.34–7.21 (m, 3H), 7.17–7.09 (m, 1H), 6.85–6.71 (m, 4H), 6.58 (d, *J* = 8.5 Hz, 2H), 6.31 (d, *J* = 8.5 Hz, 2H), 3.96–3.88 (m, 1H), 3.75 (s, 3H), 3.64 (s, 3H), 3.52–3.43 (m, 1H), 3.36–3.20 (m, 3H), 3.14 (d, *J* = 12.2 Hz, 1H), 2.46 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 174.6, 156.7, 154.4, 145.4, 145.1, 141.1, 138.5, 135.2, 129.8, 129.6, 128.9, 128.1, 127.0, 125.7, 124.7, 119.3, 114.5, 113.7, 113.6, 65.7, 60.1, 55.7, 55.2, 51.3, 49.3, 21.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{32}H_{32}N_3O_5S$ 570.2057; found 570.2072.

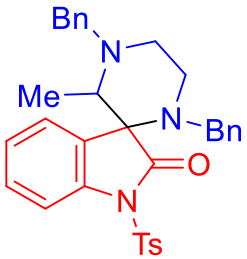
Compound 37



(Ar = 4-BrC_6H_4)

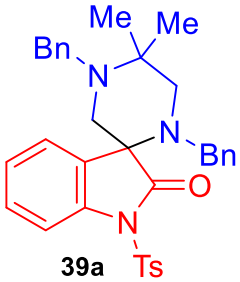
The title compound **37** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid (**Condition A:** 41% yield, 54.7 mg; **Condition B:** 35% yield, 46.7 mg); **mp:** 91–92 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.95–7.91 (m, 1H), 7.84 (d, *J* = 8.4 Hz, 2H), 7.38–7.33 (m, 2H), 7.33–7.27 (m, 4H), 7.15–7.10 (m, 1H), 6.79–6.75 (m, 2H), 6.65–6.60 (m, 2H), 6.29–6.25 (m, 2H), 4.06–3.99 (m, 1H), 3.71–3.65 (m, 1H), 3.56 (d, *J* = 12.9 Hz, 1H), 3.46–3.39 (m, 2H), 3.36 (d, *J* = 12.9 Hz, 1H), 2.50 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 174.1, 149.0, 146.9, 146.0, 138.3, 134.9, 132.1, 131.6, 130.2, 130.0, 128.4, 128.0, 125.2, 124.6, 117.5, 116.5, 114.0, 112.2, 65.7, 57.0, 49.3, 47.5, 22.0; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{30}H_{26}Br_2N_3O_3S$ 666.0056; found 666.0065.

Compound 38

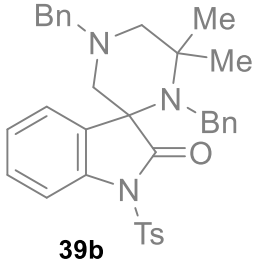


The title compound **38** was purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as an inseparable mixture of two diastereoisomers in trace amounts (< 10% dr = 1:1) under **Condition A** or **B**. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.15–7.87 (m, 4H), 7.49–7.04 (m, 12H), 7.01–6.92 (m, 2H), 4.07–3.93 (m, 1H), 3.28–2.87 (m, 3H), 2.85–2.55 (m, 2H), 2.53–2.05 (m, 6H), 0.79–0.51 (m, 3H); **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{33}H_{34}N_3O_3S$ 552.2315; found 552.2318.

Compound 39



39a

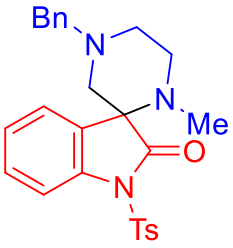


39b
(*not detected*)

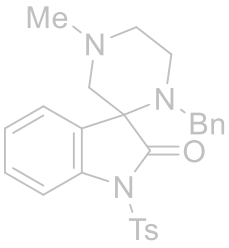
Under **Condition A** or **B**, only one regioisomer **39a** was obtained as a colorless oil by flash chromatography (hexanes/EtOAc = 5:1) on silica gel (**Condition A:** 89% yield, 100.7 mg; **Condition B:** 71% yield, 80.3 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.88 (d, *J* = 8.1 Hz, 2H), 7.83 (d, *J* = 8.2 Hz, 1H), 7.55 (d, *J* = 7.5 Hz, 1H), 7.33–7.27 (m,

3H), 7.26–7.13 (m, 9H), 7.10 (d, *J* = 7.3 Hz, 2H), 3.85 (d, *J* = 14.4 Hz, 1H), 3.22 (d, *J* = 14.4 Hz, 1H), 3.12 (d, *J* = 11.4 Hz, 1H), 3.00 (d, *J* = 13.4 Hz, 1H), 2.70 (d, *J* = 12.8 Hz, 1H), 2.64 (d, *J* = 13.4 Hz, 1H), 2.56 (d, *J* = 12.8 Hz, 1H), 2.39–2.26 (m, 4H), 1.18 (s, 3H), 1.13 (s, 3H); **^{13}C NMR (125 MHz, CDCl$_3$):** δ 174.3, 145.5, 139.9, 139.0, 138.6, 135.6, 129.8, 129.6, 129.2, 128.4, 128.3, 128.02, 127.96, 127.8, 127.1, 126.7, 125.0, 124.8, 113.8, 66.2, 57.5, 54.9, 54.0, 53.7, 52.6, 24.4, 21.8, 17.1; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{34}H_{36}N_3O_3S$ 566.2472; found 566.2462.

Compound 40



40a



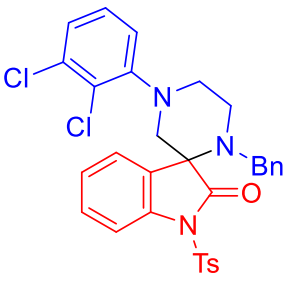
40b

Under **Condition A**, only one regioisomer **40a** was obtained by flash chromatography (hexanes/EtOAc = 5:1) on silica gel **(**85% yield, 78.5 mg, r:r > 20:1); under **Condition B,** two separable regioisomers **40a** and **40b** were obtained through PTLC (hexanes/EtOAc = 10:1; r:r = 3:1; **40a**, 55% yield, 50.7 mg; **40b**, 18% yield, 16.6 mg).

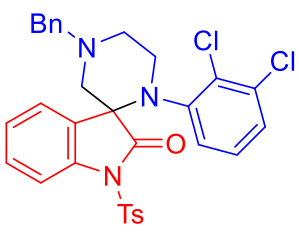
For **40a** (white solid): **mp:** 184–185 °C; **^{1}H NMR (500 MHz, CDCl$_3$):** δ 7.99–7.90 (m, 3H), 7.51 (d, *J* = 7.4 Hz, 1H), 7.39–7.33 (m, 1H), 7.30–7.17 (m, 8H), 3.53 (d, *J* = 13.4 Hz, 1H), 3.40 (d, *J* = 13.4 Hz, 1H), 3.17 (s, 1H), 2.79–2.69 (m, 2H), 2.63–2.52 (m, 2H), 2.43–2.35 (m, 4H), 1.68 (s, 3H); **^{13}C NMR (125 MHz, CDCl$_3$):** δ 174.6, 145.6, 138.9, 137.8, 135.5, 129.8, 129.6, 128.7, 128.4, 128.1, 127.2, 125.6, 124.8, 113.8, 65.9, 62.3, 59.9, 52.8, 49.7, 38.9, 21.8; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{26}H_{28}N_3O_3S$ 462.1846; found 462.1835.

For **40b** (white solid): **mp:** 178–179 °C; **^{1}H NMR (400 MHz, CDCl$_3$):** δ 8.01–7.92 (m, 3H), 7.50 (d, *J* = 7.4 Hz, 1H), 7.41–7.34 (m, 1H), 7.27 (d, *J* = 7.9 Hz, 2H), 7.24–7.15 (m, 4H), 7.07–7.01 (m, 2H), 3.20–3.09 (m, 1H), 3.03 (d, *J* = 13.1 Hz, 1H), 2.75–2.67 (m, 1H), 2.66–2.51 (m, 3H), 2.38–2.29 (m, 4H), 2.26–2.13 (m, 4H); **^{13}C NMR (100 MHz, CDCl$_3$):** δ 175.1, 145.7, 139.3, 138.3, 135.6, 129.9, 129.8, 129.4, 128.5, 128.3, 128.1, 127.2, 125.3, 124.8, 114.1, 65.8, 62.7, 55.2, 55.1, 46.2, 45.6, 21.8; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{26}H_{28}N_3O_3S$ 462.1846; found 462.1845.

Compounds 41



41a



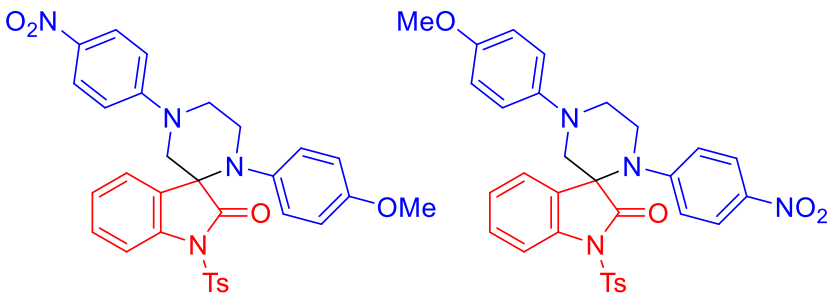
41b

Under **Condition A**, two separable regioisomers **41a** and **41b** were obtained by flash chromatography (hexanes/EtOAc = 5:1) on silica gel (r:r = 3.7:1; **41a**, 56% yield, 66.3 mg; **41b**, 15% yield, 17.8 mg); Under **Condition B**, two separable regioisomers were obtained by flash chromatography (hexanes/EtOAc = 5:1) on silica gel (r:r = 1.5:1; **41a**, 44% yield, 52.1 mg; **41b**, 29% yield, 34.3 mg).

For **41a** (white solid): **mp:** 175–176 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.03 (d, *J* = 8.2 Hz, 1H), 7.99 (d, *J* = 8.2 Hz, 2H), 7.65 (d, *J* = 7.5 Hz, 1H), 7.43–7.37 (m, 1H), 7.30–7.18 (m, 6H), 7.16–7.04 (m, 4H), 6.84 (dd, *J* = 7.8, 1.8 Hz, 1H), 3.40–3.26 (m, 2H), 3.21–3.07 (m, 3H), 2.90 (d, *J* = 12.1 Hz, 1H), 2.87–2.75 (m, 2H), 2.35 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 174.1, 150.0, 146.0, 139.2, 138.0, 135.2, 134.2, 130.0, 129.9, 128.7, 128.3, 128.2, 127.7, 127.5, 127.4, 125.2, 125.1, 118.8, 114.1, 65.8, 58.7, 55.5, 51.3, 45.6, 21.8; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{31}H_{28}Cl_2N_3O_3S$ 592.1223; found 592.1211.

For **41b** (white solid): **mp:** 203–204 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.05 (d, *J* = 7.7 Hz, 2H), 7.82 (d, *J* = 7.3 Hz, 1H), 7.43–7.33 (m, 2H), 7.33–7.16 (m, 6H), 7.07–7.00 (m, 1H), 6.96 (d, *J* = 7.6 Hz, 2H), 6.26 (t, *J* = 8.0 Hz, 1H), 5.91 (dd, *J* = 8.1, 1.2 Hz, 1H), 4.09–3.93 (m, 1H), 3.64 (d, *J* = 13.5 Hz, 1H), 3.46 (d, *J* = 13.5 Hz, 1H), 3.11–2.92 (m, 2H), 2.79 (d, *J* = 11.8 Hz, 1H), 2.67–2.52 (m, 1H), 2.51–2.39 (m, 4H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 175.9, 147.0, 145.7, 138.2, 137.6, 135.1, 133.9, 131.4, 129.9, 129.7, 128.7, 128.6, 128.3, 127.3, 126.9, 126.8, 125.2, 124.0, 123.1, 113.5, 64.5, 62.2, 52.9, 48.4, 21.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{31}H_{28}Cl_2N_3O_3S$ 592.1223; found 592.1221.

Compound 42



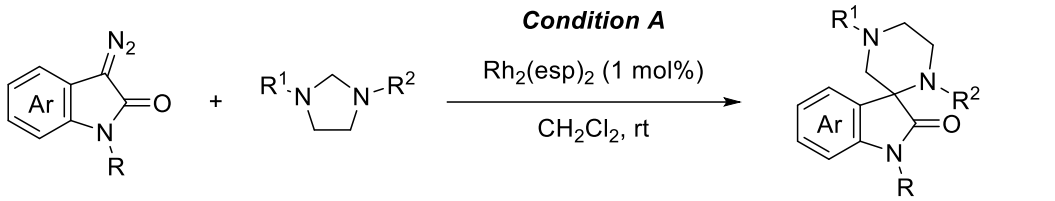
42a **42b**

Under **Condition A**, two regioisomers **42a** and **42b** were obtained as an inseparable mixture by flash chromatography (hexanes/EtOAc = 5:1) on silica gel **(**75% total yield, 87.7 mg, r.r = 5:1); under **Condition B,** the same yield and regioselectivity were obtained.

After recrystallization once in PE/EA system, the major isomer **42a** was obtained as a yellow solid in 63% yield (73.7 mg); **mp:** 206–207 °C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.04 (d, *J* = 9.3 Hz, 2H), 7.90–7.79 (m, 3H), 7.39–7.21 (m, 4H), 7.13 (t, *J* = 7.5 Hz, 1H), 6.61 (d, *J* = 9.4 Hz, 2H), 6.55 (d, *J* = 8.9 Hz, 2H), 6.34 (d, *J* = 8.9 Hz, 2H), 4.18–4.07 (m, 1H), 4.05–3.95 (m, 1H), 3.79 (d, *J* = 13.7 Hz, 1H), 3.69–3.52 (m, 5H), 3.29–3.18 (m, 1H), 2.49 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 174.7, 156.7, 153.9, 145.9, 140.5, 138.6, 135.1, 130.3, 129.9, 128.1, 127.8, 126.2, 126.1, 125.10, 125.08, 114.0, 112.5, 65.3, 55.3, 54.7, 47.9, 47.5, 21.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{31}H_{29}N_4O_6S$ 585.1802; found 585.1785.

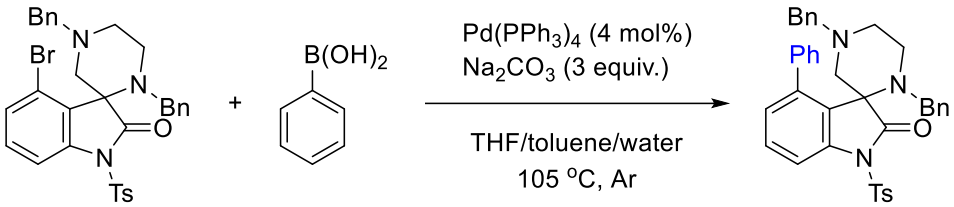
5. Transformations

5.1 Gram-Scale Synthesis

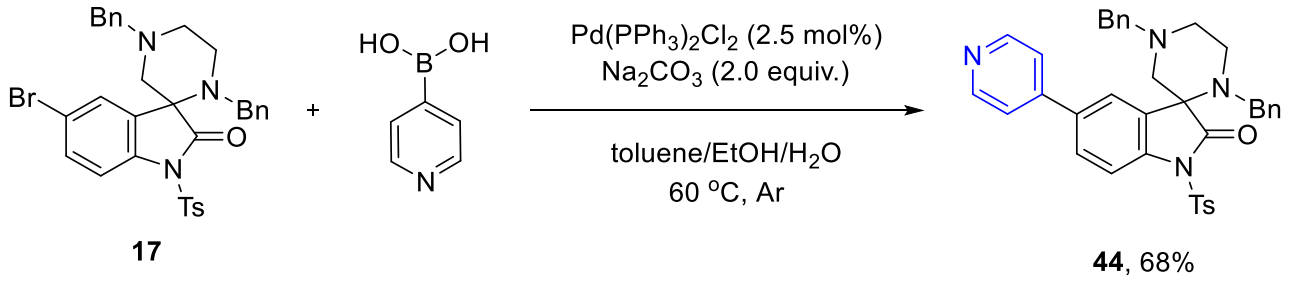


In a round bottom flask equipped with a magnetic stir bar, **2** (3.0 mmol, 1.0 equiv.) and $Rh_2(esp)_2$ (22.6 mg, 0.03 mmol, 1 mol%) were added into CH_2Cl_2 (30 mL). Then, a solution of **1** (3.6 mmol, 1.2 equiv.) in CH_2Cl_2 (30 mL) was dropwise added via a dropping funnel over 1 h. The reaction was continued at rt for 12 h. The resulting mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography (hexanes/EtOAc) on silica gel to afford the corresponding products: **3** in 86% yield (1.39 g), **40** in 80% yield (1.11 g, r:r > 20:1) and **41** in 68% total yield (1.21 g, r:r = 3.7:1).

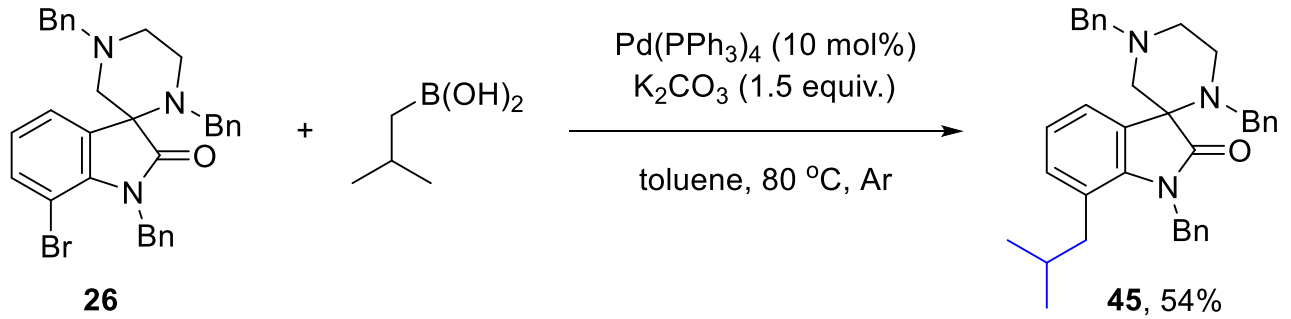
5.2 Derivatizations via Cross-Coupling Reaction



In an oven-dried Schlenk tube equipped with a magnetic stir bar, $Pd(PPh_3)_4$ (9.0 mg, 0.008 mmol, 4 mol%), Na_2CO_3 (63.6 mg, 0.6 mmol, 3.0 equiv.), phenylboronic acid (29.3 mg, 0.24 mmol, 1.2 equiv.) and **11** (123.3 mg, 0.2 mmol, 1.0 equiv.) were added in a mixed degassed solvent (2.15 mL, THF : toluene : water = 3:3:0.45) under Ar. The reaction was stirred at 105 °C in an oil bath for 12 h. The reaction was cooled down to rt, quenched with H_2O and extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash column chromatography (hexanes/EtOAc = 20:1 to 5:1) on silica gel to obtain **43** as a white solid in 83% yield (101.9 mg); **mp:** 191–192 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.07–7.99 (m, 3H), 7.46–7.42 (m, 2H), 7.40–7.28 (m, 6H), 7.23–7.13 (m, 8H), 7.02 (dd, *J* = 7.8, 1.0 Hz, 1H), 6.89–6.83 (m, 2H), 3.51 (d, *J* = 13.2 Hz, 1H), 3.43 (d, *J* = 13.7 Hz, 1H), 3.19–3.09 (m, 2H), 2.70 (d, *J* = 13.2 Hz, 1H), 2.65–2.59 (m, 1H), 2.52–2.41 (m, 6H), 1.82 (td, *J* = 11.6, 3.1 Hz, 1H); **^{13}C NMR (125 MHz, $CDCl_3$)**: δ 173.4, 145.7, 141.8, 139.8, 139.4, 137.7, 137.2, 136.0, 130.7, 129.9, 129.6, 128.80, 128.76, 128.6, 128.3, 128.2, 127.7, 127.4, 127.0, 125.1, 113.0, 67.0, 62.1, 56.1, 54.6, 52.2, 45.3, 21.9; **HRMS (ESI):** calcd. for [M + H]+ $C_{38}H_{36}N_3O_3S$ 614.2472; found 614.2458.

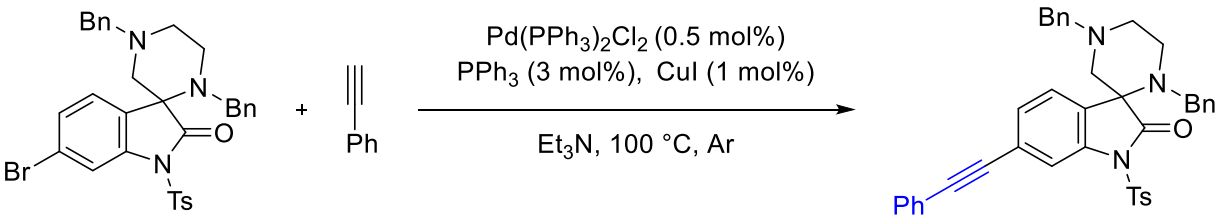


In an oven-dried Schlenk tube equipped with a magnetic stir bar, $Pd(PPh_3)_2Cl_2$ (3.5 mg, 0.005 mmol, 2.5 mol%), Na_2CO_3 (42.4 mg, 0.4 mmol, 2.0 equiv.), pyridine-4-boronic acid (24.6 mg, 0.2 mmol, 1.0 equiv.) and **17** (132.7 mg, 0.2 mmol, 1.2 equiv.) were added in a mixed degassed solvent (toluene : EtOH : water = 10:10:2) under Ar. The reaction was stirred at 60 ºC in an oil bath for 36 h. The reaction was cooled down to rt, quenched with H_2O and extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash column chromatography (hexanes/EtOAc = 3:1 to 100% EtOAc) on silica gel to obtain **44** as a colorless oil in 68% yield (83.6 mg); **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.69 (d, *J* = 5.7 Hz, 2H), 8.06 (d, *J* = 8.5 Hz, 1H), 7.97 (d, *J* = 8.3 Hz, 2H), 7.84 (s, 1H), 7.65 (dd, *J* = 8.5, 1.9 Hz, 1H), 7.55–7.44 (m, 2H), 7.29–7.14 (m, 10H), 7.06–6.99 (m, 2H), 3.55 (d, *J* = 13.5 Hz, 1H), 3.41 (d, *J* = 13.5 Hz, 1H), 3.20–3.06 (m, 1H), 2.97 (d, *J* = 13.1 Hz, 1H), 2.79–2.68 (m, 2H), 2.68–2.58 (m, 2H), 2.53–2.41 (m, 2H), 2.33 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 174.5, 150.5, 147.4, 146.0, 139.8, 138.0, 137.7, 135.3, 135.1, 130.4, 129.9, 128.7, 128.51, 128.45, 128.4, 128.3, 128.1, 127.32, 127.25, 123.6, 121.5, 114.6, 66.1, 62.2, 60.3, 55.6, 52.9, 46.1, 21.8; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{37}H_{35}N_4O_3S$ 615.2424; found 615.2423.



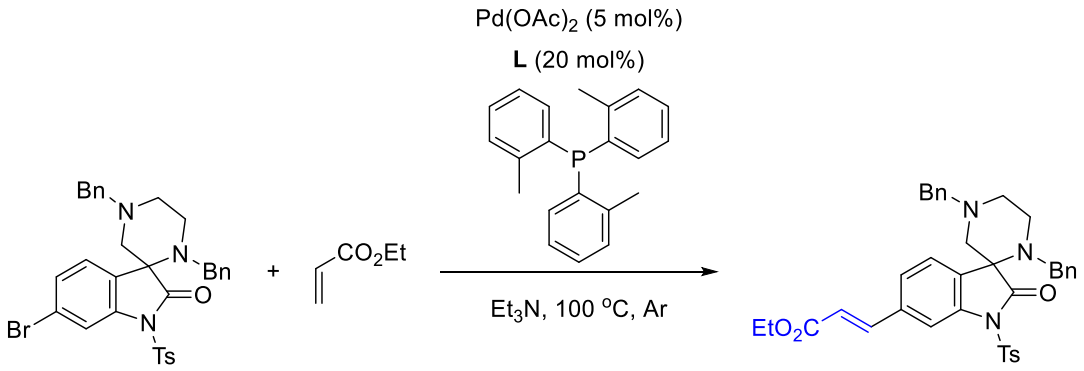
In an oven-dried Schlenk tube equipped with a magnetic stir bar, $Pd(PPh_3)_4$ (23.1 mg, 0.02 mmol, 10 mol%), K_2CO_3 (41.5 mg, 0.3 mmol, 1.5 equiv.), isobutylboronic acid (30.6 mg, 0.3 mmol, 1.5 equiv.) and **26** (110.5 mg, 0.2 mmol, 1.0 equiv.) were added in toluene under Ar. Then, the reaction was warmed to 80 ºC in an oil bath and stirred for 12 h. The reaction was cooled down to rt, filtered and concentrated under reduced pressure. The crude residue was purified by flash column chromatography (hexanes/EtOAc = 25:1 to 5:1) on silica gel to obtain **45** as a yellow oil in 54% yield (57.2 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.49 (d, *J* = 7.2 Hz, 1H), 7.35–7.31 (m, 2H), 7.30–7.18 (m, 11H), 7.06–6.97 (m, 3H), 6.93 (dd,

J = 7.8, 1.4 Hz, 1H), 5.32 (d, *J* = 16.8 Hz, 1H), 4.95 (d, *J* = 16.7 Hz, 1H), 3.76 (d, *J* = 13.6 Hz, 1H), 3.47–3.22 (m, 4H), 2.92–2.80 (m, 2H), 2.79–2.69 (m, 1H), 2.59–2.47 (m, 2H), 2.39 (dd, *J* = 14.2, 6.8 Hz, 1H), 2.27 (dd, *J* = 14.3, 7.6 Hz, 1H), 1.75–1.67 (m, 1H), 0.83 (d, *J* = 6.6 Hz, 3H), 0.77 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 177.7, 140.4, 139.0, 138.2, 137.8, 132.8, 130.9, 129.0, 128.9, 128.8, 128.4, 128.3, 127.2, 127.1, 127.0, 125.8, 123.8, 122.7, 122.3, 65.2, 62.6, 61.0, 55.8, 53.7, 46.0, 44.7, 40.4, 31.0, 22.3, 22.1; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{36}H_{40}N_3O$ 530.3166; found 530.3155.



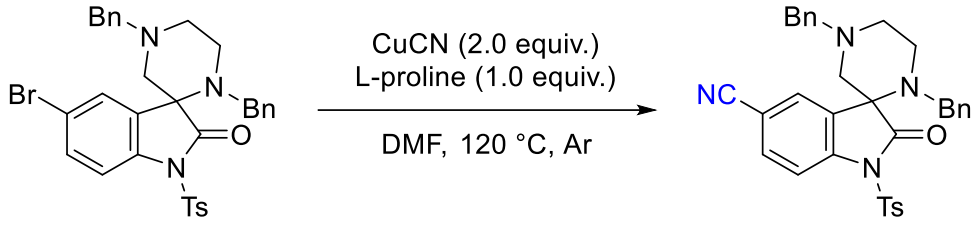
24 **46** , 88%

In an oven-dried Schlenk tube equipped with a magnetic stir bar, $Pd(PPh_3)_4Cl_2$ (0.7 mg, 0.001 mmol, 0.5 mol%), CuI (0.4 mg, 0.002 mmol, 1 mol%), PPh_3 (1.6 mg, 0.006 mmol, 3 mol%) and **26** (123.3 mg, 0.2 mmol, 1.0 equiv.) were dissolved in TEA under Ar. Then, phenylacetylene (30.6 mg, 0.3 mmol, 1.5 equiv.) was added. The reaction was warmed to 100 °C in an oil bath and stirred for 12 h. The resulting mixture was cooled down to rt, filtered and concentrated under reduced pressure. The crude residue was purified by flash column chromatography (hexanes/EtOAc = 25:1 to 5:1) on silica gel to obtain **76** as a yellow oil in 88% yield (112.3 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.13 (d, *J* = 1.3 Hz, 1H), 7.97 (d, *J* = 8.5 Hz, 2H), 7.61–7.52 (m, 3H), 7.42–7.35 (m, 4H), 7.28–7.14 (m, 10H), 7.03–6.98 (m, 2H), 3.52 (d, *J* = 13.5 Hz, 1H), 3.41 (d, *J* = 13.5 Hz, 1H), 3.15–2.99 (m, 1H), 2.90 (d, *J* = 13.1 Hz, 1H), 2.73–2.63 (m, 2H), 2.62–2.50 (m, 2H), 2.47–2.36 (m, 2H), 2.32 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 174.5, 145.9, 139.1, 138.0, 137.6, 135.3, 131.9, 129.8, 129.3, 128.73, 128.69, 128.5, 128.4, 128.2, 128.1, 127.24, 127.20, 125.1, 124.9, 122.9, 116.7, 90.6, 89.0, 65.9, 62.3, 60.1, 55.5, 52.8, 45.9, 21.7; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{40}H_{36}N_3O_3S$ 638.2472; found 638.2459.



24 **47**, 84%

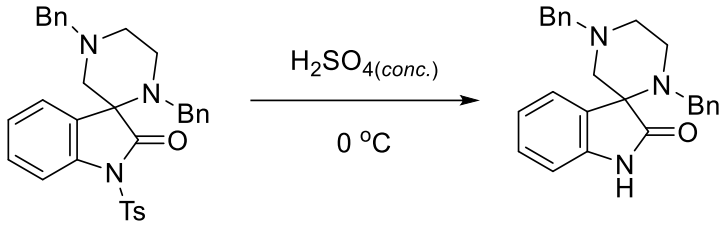
In an oven-dried Schlenk tube equipped with a magnetic stir bar, $Pd(OAc)_2$ (2.2 mg, 0.01 mmol, 5 mol%), **L** (12.1 mg, 0.04 mmol, 20 mol%), ethyl acrylate (40.0 mg, 0.4 mmol, 2.0 equiv.) and **24** (123.3 mg, 0.2 mmol, 1.0 equiv.) were dissolved in anhydrous TEA under Ar. Then, the reaction was warmed to 100 ℃ in an oil bath and stirred for 12 h. The resulting mixture was cooled down to rt, filtered and concentrated under reduced pressure. The crude residue was purified by flash column chromatography (hexanes/EtOAc = 25:1 to 5:1) on silica gel to obtain **47** as a yellow oil in 84% yield (106.8 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.13 (d, *J* = 1.5 Hz, 1H), 7.95 (d, *J* = 8.4 Hz, 2H), 7.70 (d, *J* = 16.0 Hz, 1H), 7.58 (d, *J* = 7.8 Hz, 1H), 7.36 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.29–7.14 (m, 11H), 7.04–6.99 (m, 2H), 6.52 (d, *J* = 16.0 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 3.53 (d, *J* = 13.5 Hz, 1H), 3.39 (d, *J* = 13.6 Hz, 1H), 3.15–3.01 (m, 1H), 2.92 (d, *J* = 13.1 Hz, 1H), 2.73–2.64 (m, 2H), 2.63–2.54 (m, 2H), 2.45–2.37 (m, 2H), 2.32 (s, 3H), 1.36 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 174.5, 166.8, 145.9, 143.9, 139.7, 137.9, 137.6, 136.2, 135.3, 131.4, 129.9, 128.7, 128.5, 128.4, 128.3, 128.1, 127.3, 127.2, 125.5, 125.2, 119.8, 112.8, 66.0, 62.3, 60.9, 60.1, 55.5, 52.8, 45.9, 21.8, 14.5; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{37}H_{38}N_3O_5S$ 636.2527; found 636.2512.



17 **48**, 53%

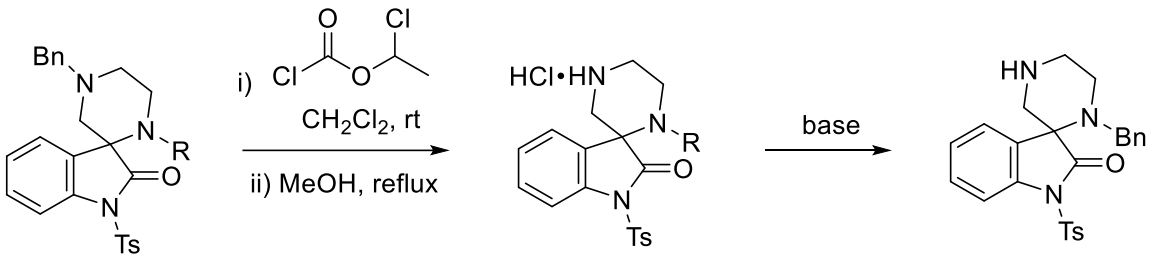
In an oven-dried Schlenk tube equipped with a magnetic stir bar, CuCN (35.8 mg, 0.4 mmol, 2.0 equiv.), L-proline (23.0 mg, 0.2 mmol, 1.0 equiv.) and **17** (132.7 mg, 0.2 mmol, 1.0 equiv.) were dissolved in DMF under Ar. Then, the reaction was warmed to 120 ℃ in an oil bath and stirred for 12 h. The resulting mixture was cooled down to rt, quenched with H_2O and extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by flash column chromatography (hexanes/EtOAc = 25:1 to 5:1) on silica gel to obtain **48** as a white solid in 53% yield (59.6 mg); **mp:** 153–154 ºC; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.07 (d, *J* = 8.5 Hz, 1H), 7.99–7.84 (m, 3H), 7.68 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.31–7.16 (m, 10H), 7.03–6.95 (m, 2H), 3.52 (d, *J* = 13.4 Hz, 1H), 3.42 (d, *J* = 13.4 Hz, 1H), 3.11–2.95 (m, 1H), 2.82 (d, *J* = 13.1 Hz, 1H), 2.71–2.55 (m, 4H), 2.54–2.45 (m, 1H), 2.40 (d, *J* = 11.7 Hz, 1H), 2.31 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 173.7, 146.5, 142.4, 137.34, 137.30, 134.7, 134.2, 130.5, 130.0, 128.9, 128.7, 128.5, 128.40, 128.38, 128.1, 127.5, 127.4, 118.5, 114.6, 108.6, 65.8, 62.2, 59.9, 55.8, 52.8, 46.0, 21.8; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{33}H_{30}N_4O_3S$ 563.2111; found 563.2101.

5.3 Derivatization via Selective N-Deprotection



3 **49**, 95%

In a reaction tube equipped with a magnetic stir bar, **3** (0.1 mmol, 1.0 equiv.) was added to the cold concentrated sulfuric acid (1 mL) at 0 ℃. The reaction mixture was stirred at 0 ℃ for 2 h and quenched with $NaHCO_3$ solution. The resulting mixture was extracted with EtOAc. The organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to obtain product **49** as a pink solid in 95% yield (36.4 mg); **mp:** 184–185 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.34 (s, 1H), 7.69 (s, 1H), 7.32–7.14 (m, 11H), 7.11–7.06 (m, 1H), 6.89 (d, *J* = 7.7 Hz, 1H), 3.63 (d, *J* = 13.5 Hz, 1H), 3.45 (d, *J* = 13.5 Hz, 1H), 3.38 (d, *J* = 13.1 Hz, 1H), 3.26–3.01 (m, 2H), 2.84–2.75 (m, 2H), 2.74–2.60 (m, 2H), 2.56 (d, *J* = 11.4 Hz, 1H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 178.8, 140.5, 138.6, 138.1, 130.2, 129.0, 128.8, 128.4, 128.2, 127.13, 127.10, 126.0, 122.5, 110.0, 66.9, 62.7, 60.0, 56.2, 53.4, 46.3; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{25}H_{26}N_3O$ 384.2070; found 384.2078.



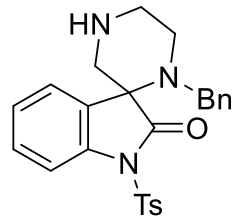
3 (R = Bn)
40a (R = Me)

50a (R = Bn)
50b (R = Me)

50a (free form)
(CCDC 2285029)

In an oven-dried reaction tube equipped with a magnetic stir bar, *α*-chloroethyl chloroformate (42.6 mg, 0.30 mmol, 1.50 equiv.) was added slowly to a solution of **3**/**40a** (0.20 mmol, 1.00 equiv.) in CH_2Cl_2 (2 mL) at rt. After the reaction was completed, solvent was removed under reduced pressure. The residue was treated with MeOH (2 mL) and refluxed in an oil bath for 40 min. The resulting mixture was cooled down to rt, and solvent was removed under reduced pressure. The residue was washed with ether to afford **50a**/**50b**. Due to the poor solubility for characterization, the free amine forms **50a** (free form) and **50b** (free form) were readily obtained quantitatively by treating **50a**/**50b** with base.

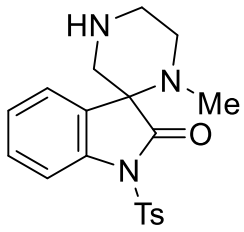
Compound 50a (free form)



50a free form
(CCDC 2285029)

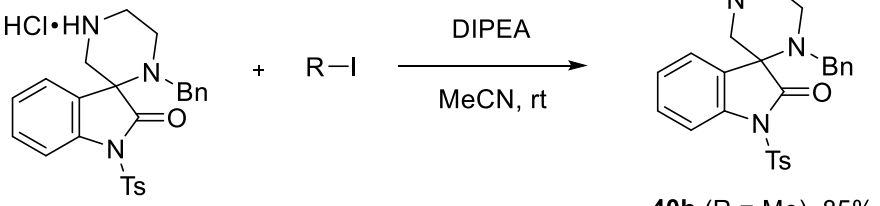
The title compound **50a** (free form) was obtained as a yellow oil in >99% yield (89.0 mg); **^{1}H NMR (500 MHz,** $CDCl_3$**):** δ 7.99–7.93 (m, 3H), 7.44 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.38 (td, *J* = 7.9, 1.4 Hz, 1H), 7.32 (d, *J* = 8.2 Hz, 2H), 7.29–7.15 (m, 4H), 7.07–7.01 (m, 2H), 3.14 (d, *J* = 13.0 Hz, 1H), 3.07–2.93 (m, 3H), 2.91–2.80 (m, 2H), 2.57 (d, *J* = 13.1 Hz, 1H), 2.47–2.40 (m, 4H); **^{13}C NMR (125 MHz,** $CDCl_3$**):** δ 176.5, 145.9, 139.3, 138.1, 135.7, 130.0, 129.8, 129.4, 128.3, 127.9, 127.3, 125.8, 123.9, 114.1, 64.7, 55.8, 54.3, 45.8, 45.5, 21.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{25}H_{26}N_3O_3S$ 448.1689; found 448.1697.

Compound 50b (free form)



50b (free form)

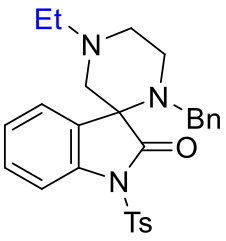
The title compound **50b** (free form) was obtained as a yellow oil in >99% yield (74.1 mg); **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.97–7.91 (m, 3H), 7.41–7.34 (m, 1H), 7.31 (d, *J* = 8.1 Hz, 2H), 7.31–7.24 (m, 1H), 7.25–7.19 (m, 1H), 3.19–3.06 (m, 2H), 3.04–2.88 (m, 2H), 2.75 (dd, *J* = 14.1, 1.2 Hz, 1H), 2.56–2.49 (m, 1H), 2.42 (s, 3H), 1.76 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 176.6, 145.9, 139.1, 135.7, 129.9, 129.7, 129.0, 127.9, 125.5, 124.0, 113.9, 64.7, 54.0, 49.1, 45.7, 39.9, 21.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{19}H_{22}N_3O_3S$ 372.1376; found 372.1369.



50a

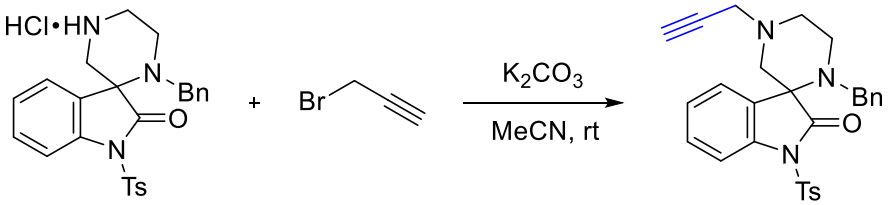
40b (R = Me), 85%
51 (R = Et), 66%

In a reaction tube equipped with a magnetic stir bar, R-I (0.3 mmol, 1.5 equiv.), DIPEA (77.6 mg, 0.6 mmol, 3.0 equiv.) and **50a** (96.8 mg, 0.2 mmol, 1.0 equiv.) were dissolved in MeCN (2 mL) and stirred at rt for 24 h. The resulting mixture was concentrated under reduced pressure. The crude residue was purified by flash column chromatography (hexanes/EtOAc) on silica gel to obtain products **40b** and **51**. Note: product **40b** was obtained as a white solid in 85% yield (78.4 mg), and its characterization data are in consistent with the minor product of **40** under Condition B.



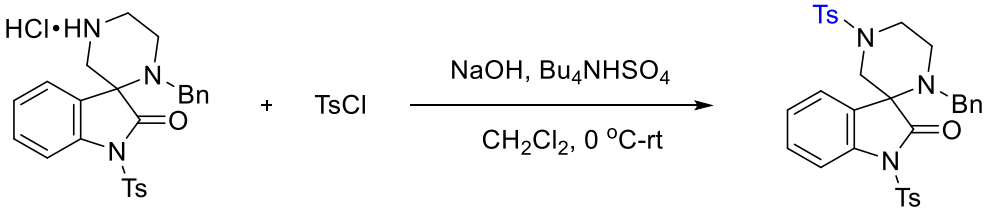
51

The title compound **51** was purified by flash chromatography (hexanes/EtOAc = 5:1 to 1:1) on silica gel and obtained as a yellow oil in 66% yield (62.8 mg); **^{1}H NMR (500 MHz,** $CDCl_3$**):** δ 8.03–7.92 (m, 3H), 7.52 (d, *J* = 7.3 Hz, 1H), 7.39 (td, *J* = 7.9, 1.4 Hz, 1H), 7.28–7.15 (m, 6H), 7.08–7.01 (m, 2H), 3.15–3.06 (m, 1H), 2.99 (d, *J* = 13.1 Hz, 1H), 2.73 (d, *J* = 11.3 Hz, 1H), 2.68–2.51 (m, 3H), 2.45–2.17 (m, 7H), 0.89 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR (100 MHz,** $CDCl_3$**):** δ 175.0, 145.7, 139.2, 138.3, 135.5, 129.8, 129.6, 128.4, 128.3, 128.1, 127.2, 125.3, 124.9, 114.1, 65.9, 60.2, 55.3, 53.0, 52.0, 45.8, 21.8, 11.8; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{27}H_{30}N_3O_3S$ 476.2002; found 476.1994.



50a **52**, 76%

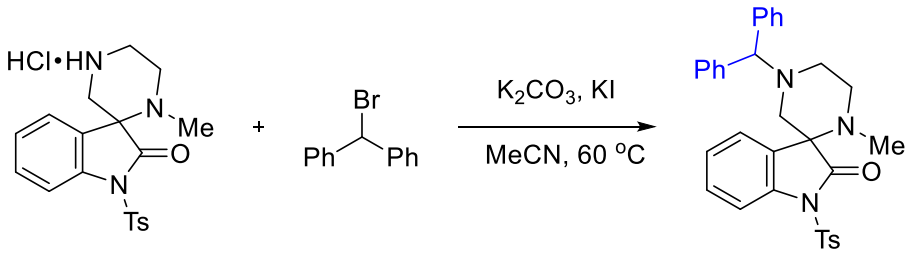
In a reaction tube equipped with a magnetic stir bar, **50a** (96.8 mg, 0.2 mmol, 1.0 equiv.), K_2CO_3 (83.0 mg, 0.6 mmol, 3.0 equiv.), and 3-bromoprop-1-yne (47.6 mg, 0.4 mmol, 2.0 equiv.) were dissolved in MeCN and stirred at rt for 24 h. The reaction was diluted with EtOAc, washed with H_2O and brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash column chromatography (hexanes/EtOAc = 5:1 to 1:1) on silica gel to obtain **52** as a white solid in 76% yield (73.8 mg); **mp:** 130–131 °C; **^{1}H NMR (400 MHz,** $CDCl_3$**):** δ 8.05–7.90 (m, 3H), 7.53 (d, *J* = 7.5 Hz, 1H), 7.39 (t, *J* = 7.9 Hz, 1H), 7.33–7.13 (m, 6H), 7.05 (d, *J* = 7.2 Hz, 2H), 3.41–3.23 (m, 2H), 3.23–3.10 (m, 1H), 3.03 (d, *J* = 13.1 Hz, 1H), 2.75–2.50 (m, 6H), 2.37 (s, 3H), 2.20 (s, 1H); **^{13}C NMR (100 MHz,** $CDCl_3$**):** δ 175.0, 145.7, 139.2, 138.1, 135.5, 130.0, 129.8, 129.2, 128.4, 128.3, 128.1, 127.3, 125.4, 124.9, 114.1, 77.6, 74.1, 65.6, 59.0, 55.0, 51.3, 46.7, 45.4, 21.8; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{27}H_{30}N_3O_3S$ 486.1846; found 486.1837.



50a **53**, 85%

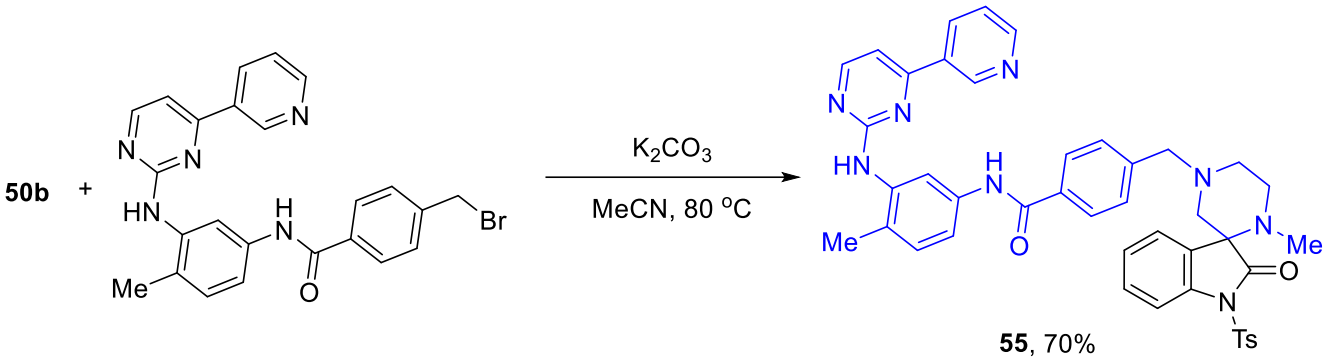
In a reaction tube equipped with a magnetic stir bar, **50a** (96.8 mg, 0.2 mmol, 1.0 equiv.), NaOH (24.0 mg, 0.6 mmol, 3.0 equiv.) and Bu_4NHSO_4 (3.4 mg, 0.01 mmol, 0.05 equiv.) were dissolved in CH_2Cl_2 at 0 °C for 10 minutes. TsCl (41.9 mg, 0.22 mmol, 1.1 equiv.) was added at 0 °C. The reaction was warmed

to rt and continued for 6 h. The reaction mixture was diluted with EtOAc, washed with H_2O and brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash column chromatography (hexanes/EtOAc = 10:1 to 3:1) on silica gel to obtain **53** as a white solid in 85% yield (102.3 mg); **mp:** 80–81 °C; **^{1}H NMR (400 MHz,** $CDCl_3$**):** δ 8.02 (d, *J* = 8.3 Hz, 1H), 7.94 (d, *J* = 8.0 Hz, 2H), 7.60–7.48 (m, 3H), 7.44 (t, *J* = 7.9 Hz, 1H), 7.36–7.09 (m, 8H), 7.01–6.88 (m, 2H), 3.23–2.93 (m, 5H), 2.86 (d, *J* = 13.1 Hz, 1H), 2.72–2.61 (m, 1H), 2.54 (d, *J* = 13.1 Hz, 1H), 2.43 (s, 3H), 2.28 (s, 3H); **^{13}C NMR (100 MHz,** $CDCl_3$**):** δ 173.5, 146.2, 144.2, 139.0, 137.2, 135.0, 132.6, 130.4, 129.94, 129.93, 128.5, 128.3, 127.9, 127.5, 127.2, 125.5, 125.3, 114.4, 64.7, 55.2, 52.3, 46.0, 44.5, 21.71, 21.66; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{32}H_{32}N_3O_5S_2$ 602.1778; found 602.1766.

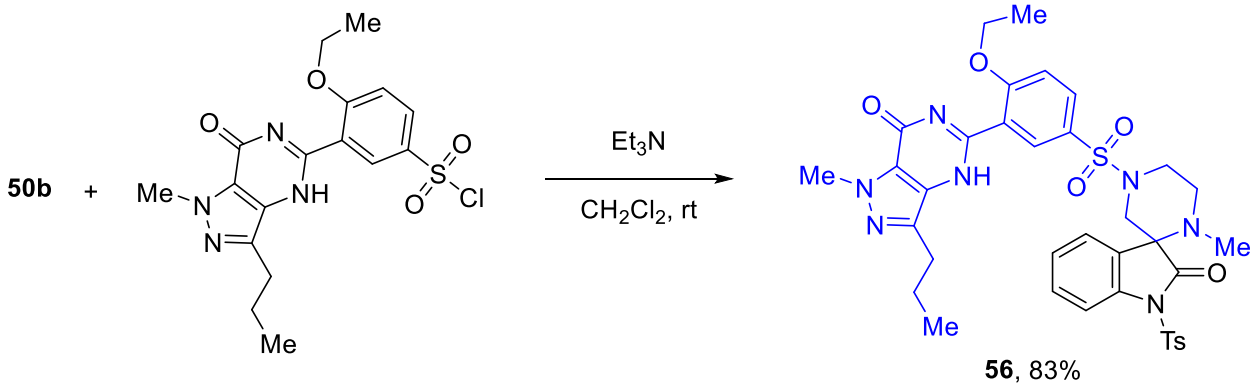


50b **54**, 72%

In a reaction tube equipped with a magnetic stir bar, **50b** (81.6 mg, 0.2 mmol, 1.0 equiv.), K_2CO_3 (83.0 mg, 0.6 mmol, 3 equiv.) and KI (49.8 mg, 0.3 mmol, 1.5 equiv.) were added in MeCN (4 mL). Then, α-bromodiphenylmethane (74.1 mg, 0.3 mmol, 1.5 equiv.) was added. The reaction tube was sealed and stirred at 60 °C in an oil bath for 24 h. The resulting mixture was cooled down to rt, filtered through a pad of celite and washed with EtOAc. The filtrate was concentrated under reduced pressure. The crude residue was purified by flash column chromatography (hexanes/EtOAc = 10:1 to 3:1) on silica gel to obtain **54** as a yellow oil in 72% yield (77.4 mg); **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.97 (d, *J* = 8.4 Hz, 2H), 7.89 (d, *J* = 8.2 Hz, 1H), 7.55–7.40 (m, 1H), 7.39–7.31 (m, 5H), 7.29 (d, *J* = 8.2 Hz, 2H), 7.23–7.16 (m, 5H), 7.16–7.09 (m, 2H), 4.20 (s, 1H), 3.40–3.11 (m, 1H), 2.82–2.61 (m, 3H), 2.49–2.29 (m, 5H), 1.70 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 174.7, 145.5, 142.3, 142.2, 138.9, 135.8, 129.8, 129.6, 128.9, 128.7, 128.6, 128.0, 127.9, 127.7, 127.19, 127.16, 125.2, 124.8, 113.7, 75.4, 66.2, 58.8, 51.5, 50.0, 38.8, 21.8; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{32}H_{32}N_3O_3S$ 538.2159; found 538.2160.

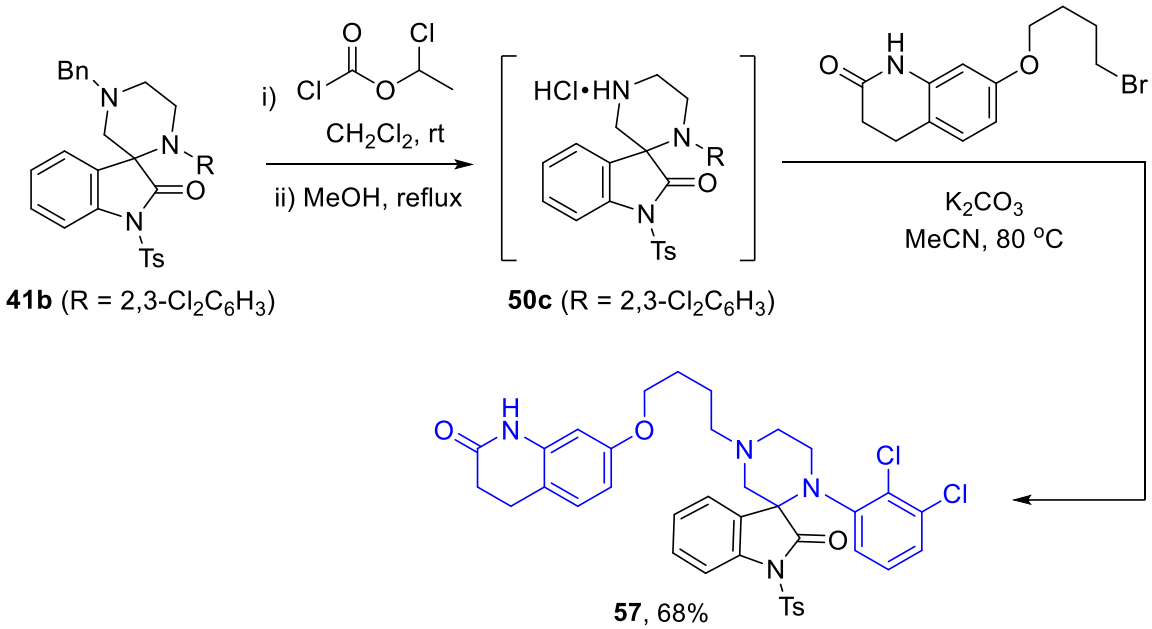


In a reaction tube equipped with a magnetic stir bar, **50b** (81.6 mg, 0.2 mmol, 1.0 equiv.), K_2CO_3 (83.0 mg, 0.6 mmol, 3.0 equiv.) and the pharmacophore (104.4 mg, 0.22 mmol, 1.1 equiv.) were dissolved in MeCN (4 mL). The reaction tube was sealed and stirred at 80 °C in an oil bath for 24 h. The resulting mixture was cooled down to rt, filtered through a pad of celite and washed with EtOAc. The filtrate was concentrated under reduced pressure. The crude residue was purified by flash column chromatography (hexanes/EtOAc = 5:1 to 100% EtOAc) on silica gel to obtain **55** as a yellow oil in 70% yield (107.1 mg); **^{1}H NMR (500 MHz,** $CDCl_3$**):** δ 9.23 (d, *J* = 2.2 Hz, 1H), 8.69 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.58 (d, *J* = 2.3 Hz, 1H), 8.54–8.48 (m, 2H), 7.99–7.94 (m, 3H), 7.92 (d, *J* = 8.2 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 2H), 7.47 (s, 1H), 7.42 (dd, *J* = 8.0, 4.8 Hz, 1H), 7.39–7.33 (m, 3H), 7.33–7.25 (m, 3H), 7.22–7.15 (m, 3H), 7.05 (s, 1H), 3.58 (d, *J* = 13.9 Hz, 1H), 3.46 (d, *J* = 13.9 Hz, 1H), 3.22 (s, 1H), 2.83–2.68 (m, 2H), 2.64–2.51 (m, 2H), 2.42–2.36 (m, 4H), 2.34 (s, 3H), 1.68 (s, 3H); **^{13}C NMR (100 MHz,** $CDCl_3$**):** δ 174.7, 165.6, 162.9, 160.7, 159.2, 151.6, 148.6, 145.8, 142.1, 138.9, 137.9, 136.8, 135.5, 135.1, 134.2, 132.8, 130.9, 129.8, 129.7, 128.9, 128.3, 128.1, 127.3, 125.3, 124.9, 124.3, 123.9, 115.5, 113.8, 113.3, 108.5, 65.9, 61.8, 59.9, 53.0, 49.7, 38.9, 21.8, 17.8; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{43}H_{41}N_8O_4S$ 765.2966; found 765.2951.



In a reaction tube equipped with a magnetic stir bar, **50b** (81.6 mg, 0.2 mmol, 1.0 equiv.), TEA (60.7 mg, 0.6 mmol, 3.0 equiv.) and the pharmacophore (90.4 mg, 0.22 mmol, 1.1 equiv.) were dissolved in CH_2Cl_2 (4 mL). The reaction was stirred at rt for 24 h. The resulting mixture was concentrated under reduced pressure. The crude residue was purified by flash column chromatography (hexanes/EtOAc = 5:1 to 100% EtOAc) on silica gel to obtain **56** as a white solid in 83% yield (123.8 mg); **mp:** 234–235 °C; **^{1}H NMR**

(500 MHz, $CDCl_3$): δ 10.79 (s, 1H), 8.74 (d, *J* = 2.5 Hz, 1H), 8.01–7.90 (m, 3H), 7.79 (dd, *J* = 8.8, 2.5 Hz, 1H), 7.47–7.38 (m, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 7.21 (t, *J* = 7.6 Hz, 1H), 7.16 (d, *J* = 8.8 Hz, 1H), 4.38 (q, *J* = 7.1 Hz, 2H), 4.28 (s, 3H), 3.34 (s, 2H), 3.19–3.12 (m, 1H), 3.09 (s, 2H), 2.90 (t, *J* = 7.6 Hz, 2H), 2.87–2.80 (m, 1H), 2.40 (s, 3H), 1.87–1.77 (m, 2H), 1.69–1.59 (m, 6H), 0.98 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 173.5, 159.7, 153.8, 147.1, 146.6, 146.1, 138.9, 138.5, 135.1, 131.9, 131.3, 130.4, 130.0, 129.1, 128.0, 126.2, 125.5, 125.3, 124.6, 121.4, 114.1, 113.4, 66.2, 64.5, 51.8, 48.4, 45.7, 38.8, 38.4, 27.8, 22.4, 21.8, 14.7, 14.1; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{36}H_{40}N_7O_7S_2$ 746.2425; found 746.2415.



In an oven-dried reaction tube equipped with a magnetic stir bar, *α*-chloroethyl chloroformate (85.2 mg, 0.60 mmol, 3.0 equiv.) was added slowly to a solution of **41b** (118.5 mg, 0.20 mmol, 1.00 equiv.) in CH_2Cl_2 (4 mL) at rt. After the reaction was completed, solvent was removed under reduced pressure. The residue was treated with MeOH (4 mL) and refluxed in an oil bath for 40 min. The resulting mixture was cooled down to rt, and solvent was removed under reduced pressure to afford **50c** directly used for the next step.

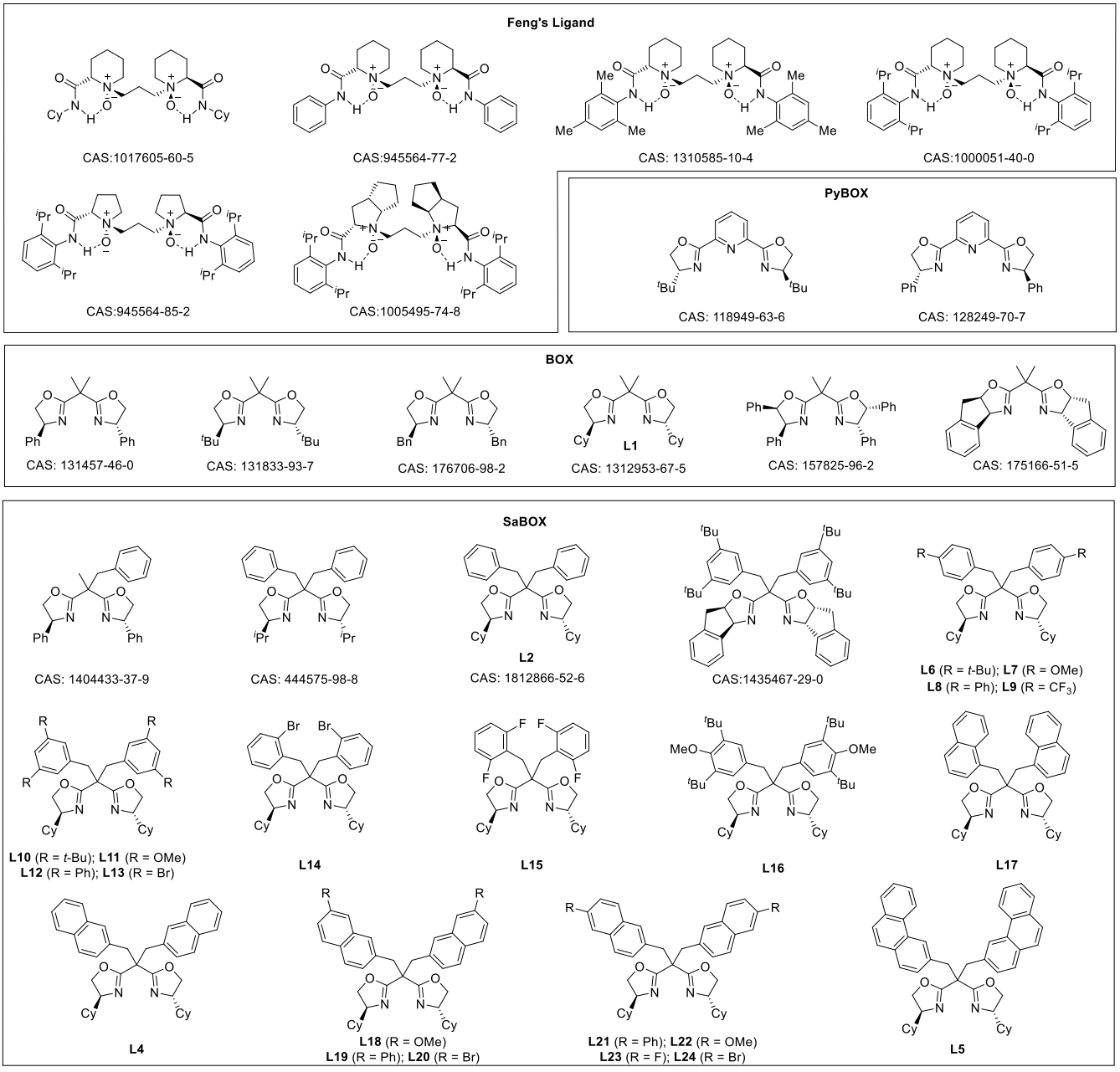
In a reaction tube equipped with a magnetic stir bar, the above obtained **50c**, K_2CO_3 (83.0 mg, 0.6 mmol, 3.0 equiv.) and the pharmacophore (69.1 mg, 0.22 mmol, 1.1 equiv.) were dissolved in MeCN (4 mL). The reaction tube was sealed and stirred at 80 °C in an oil bath for 24 h. The resulting mixture was cooled down to rt, filtered through a pad of celite and washed with EtOAc. The filtrate was concentrated under reduced pressure. The crude residue was purified by flash column chromatography (hexanes/EtOAc = 5:1 to 100% EtOAc) on silica gel to obtain **57** as a yellow oil in 68% yield (96.9 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.13 (s, 1H), 8.10–8.01 (m, 2H), 7.87 (d, *J* = 8.1 Hz, 1H), 7.37 (d, *J* = 6.6 Hz, 2H), 7.27–7.18 (m, 1H), 7.08–6.91 (m, 4H), 6.52 (dd, *J* = 8.2, 2.3 Hz, 1H), 6.41 (s, 1H), 6.20 (t, *J* = 8.0 Hz, 1H), 5.84

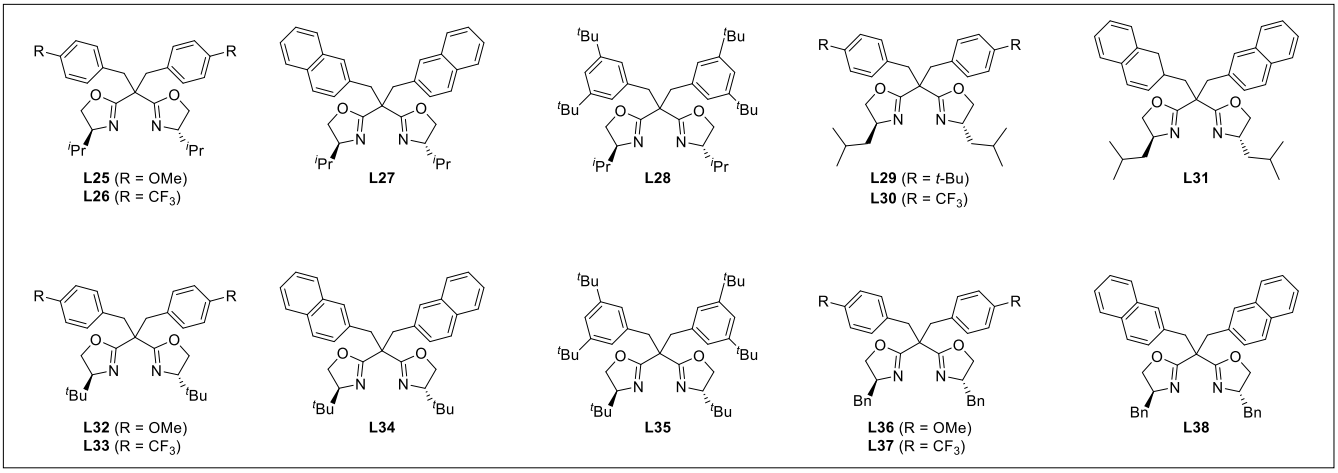
(dd, *J* = 8.1, 1.4 Hz, 1H), 4.02–3.87 (m, 3H), 3.10–2.93 (m, 2H), 2.92–2.86 (m, 2H), 2.82 (d, *J* = 11.7 Hz, 1H), 2.64–2.59 (m, 2H), 2.55–2.31 (m, 7H), 1.84–1.72 (m, 2H), 1.66–1.50 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 171.8, 158.8, 146.9, 145.8, 138.3, 138.1, 134.9, 133.9, 131.3, 130.0, 129.8, 128.7, 128.3, 126.8, 126.7, 125.3, 124.1, 123.0, 115.7, 113.5, 109.2, 102.2, 67.9, 64.5, 62.7, 57.4, 53.1, 48.4, 31.3, 27.0, 24.7, 22.9, 21.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{37}H_{37}Cl_2N_4O_5S$ 719.1856; found 719.1840.

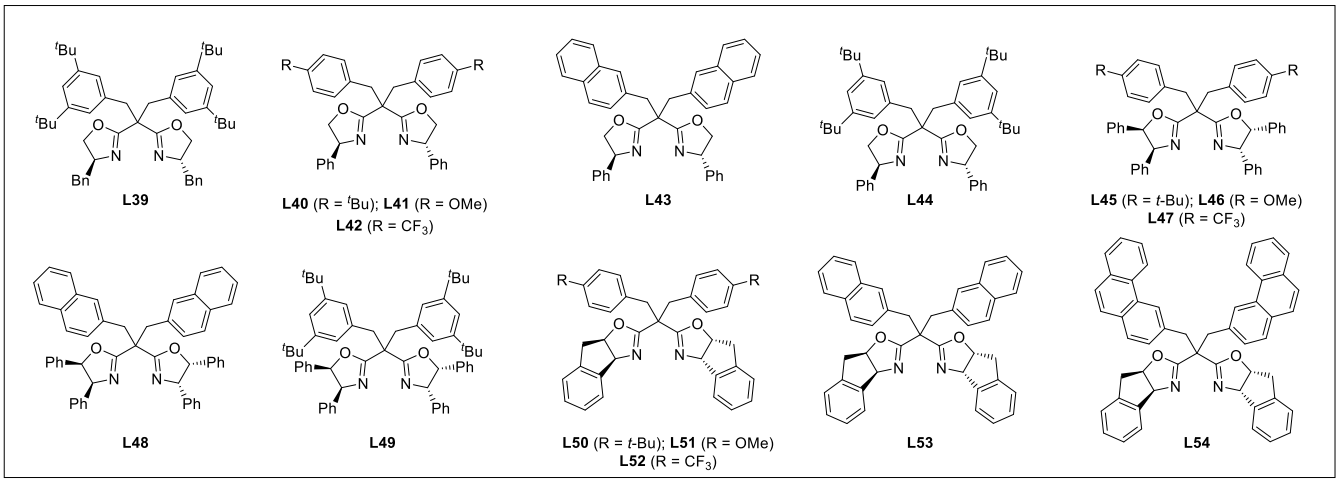
6. Exploration of the Asymmetric (5+1) Cycloaddition

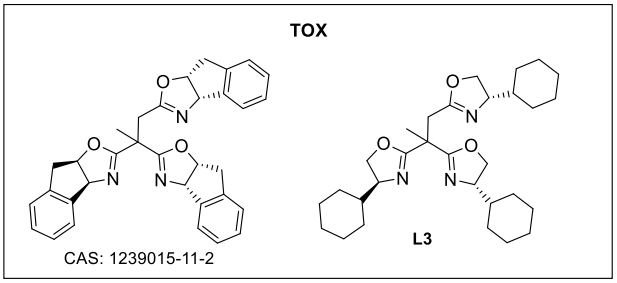
6.1 Preparation of Ligands

Ligands with CAS No. were commercially available from *Bidepharm* or *Energy Chemical*. Ligands **L3**–**L54** were synthetically available.

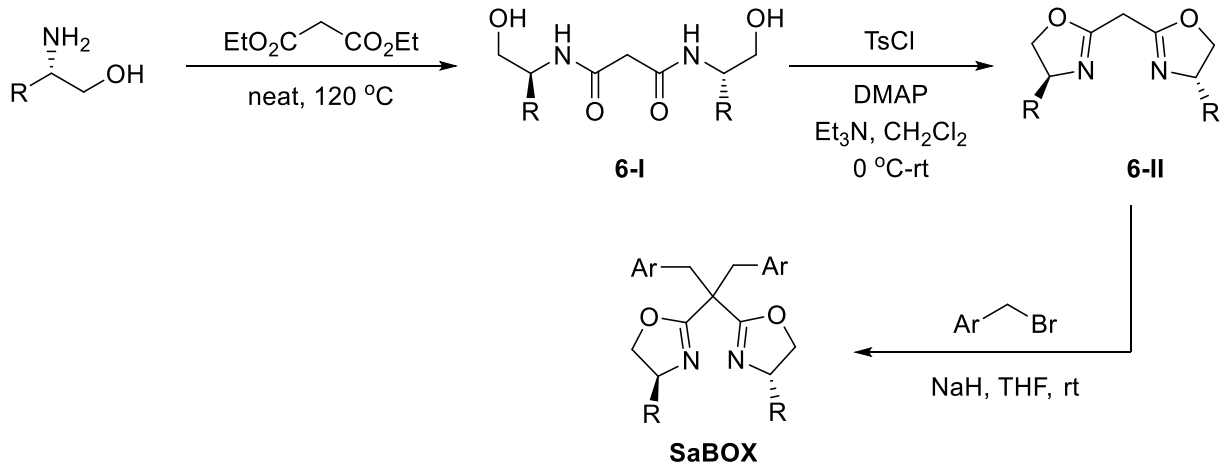








General Procedure for SaBOX ligand L4-L54

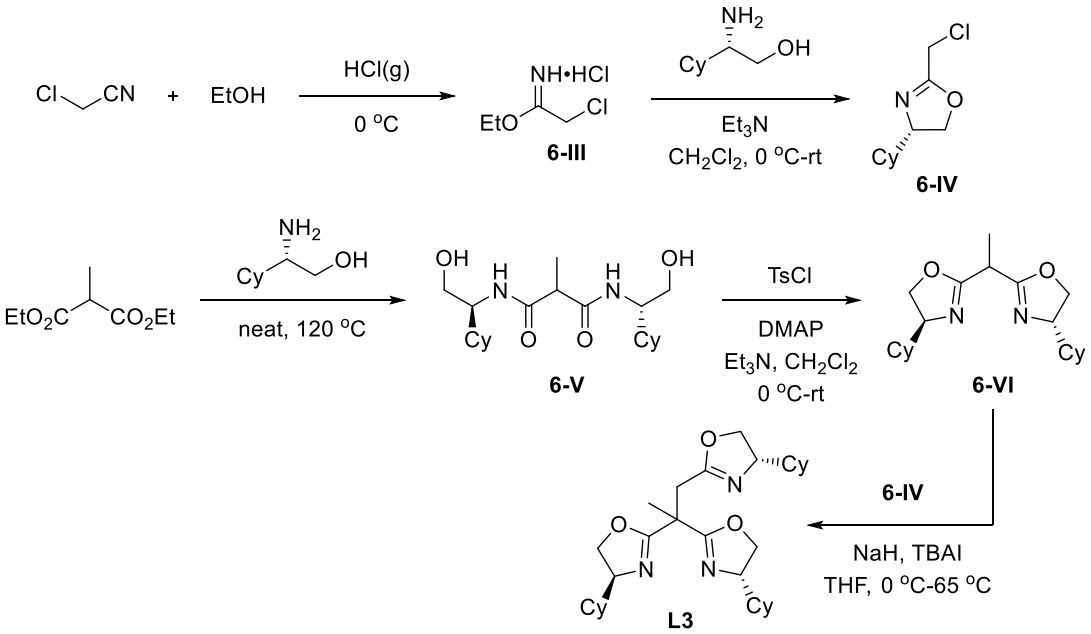


A mixture of diethyl malonate (480.5 mg, 3.0 mmol, 1.0 equiv.) and corresponding amino alcohol compounds (6.0 mmol, 2.0 equiv.) was heated at 120 °C in an oil bath for 2 h, cooled down to rt, and then ethanol produced in the reaction was removed under reduced pressure. This procedure was repeated for 4 times. The resulting crude residue was recrystallized in acetone to obtain pure **6-I**.

The obtained **6-I** (1.0 mmol, 1.0 equiv.) and DMAP (24.4 mg, 0.2 mmol, 0.2 equiv.) were dissolved in CH_2Cl_2 (5.0 mL). Et_3N (506.0 mg, 5.0 mmol, 5.0 equiv.) was added slowly. The mixture was cooled down to 0 ºC, and then a solution of TsCl (381.3 mg, 2.0 mmol, 2.0 equiv.) in CH_2Cl_2 (3.0 mL) was added within 1 h at 0 ºC. The reaction was warmed to rt and stirred for 24 h until completion. Wash the reaction with water. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexanes/EtOAc) to obtain **6-II**.

In an oven-dried round bottom flask, the obtained The obtained **6-II** (0.25 mmol, 1.0 equiv.) was dissolved in anhydrous THF (10.0 mL). NaH (60% dispersion in mineral oil; 80.0 mg, 2.0 mmol, 8.0 equiv.) was added in one portion at rt. The suspension was stirred at rt for 0.5 h. A solution of the corresponding benzyl bromide (1.25 mmol, 5.0 equiv.) in anhydrous THF (2.5 mL) was added dropwise. The resulting mixture was stirred at rt for 7 h until completion and quenched with $NH_4Cl_{(aq)}$. The aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude oil was purified by flash column chromatography on silica gel (hexanes/EtOAc) to obtain the desired SaBOX ligands **L4-L54**.

General Procedure for Cy-TOX ligand L3



In an oven-dried round bottom flask were added 2-chloroacetonitrile (3.02 g, 40.00 mmol, 1.78 equiv.) and ethanol (1.03 g, 22.38 mmol, 1.00 equiv.). The mixture was cooled down to 0 ºC, and then bubbled

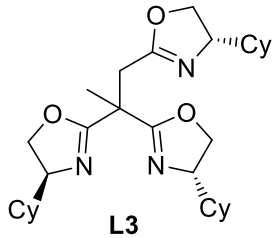
with dry $HCl_{(g)}$ (produced by NaCl and concentrated H_2SO_4) until no solid was formed. Filter and wash with hexanes to afford pure **6-III**.

The obtained **6-III** (632.0 mg, 4.00 mmol, 1.00 equiv.) was dissolved in CH_2Cl_2 (20.0 mL). At 0 ºC, (*S*)-2-amino-2-cyclohexylethan-1-ol (630.1 mg, 4.40 mmol, 1.10 equiv.) and Et_3N (485.8 mg, 4.80 mmol, 1.20 equiv.) were added. The resulting mixture was warmed to rt, stirred until the mixture turned to pink, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexanes/EtOAc = 5:1) on silical gel to afford **6-IV** as a colorless oil in.

A neat mixture of diethyl 2-methylmalonate (1.05 g, 6.00 mmol, 1.00 equiv.) and (*S*)-2-amino-2-cyclohexylethan-1-ol (1.72 g, 12.00 mmol, 2.00 equiv.) was heated at 120 °C in an oil bath for 2 h, cooled down to rt, and ethanol produced in the reaction was removed under reduced pressure. This procedure was repeated for 4 times. The resulting crude residue was recrystallized in acetone to obtain pure **6-V**.

The obtained **6-V** (737.0 mg, 2.00 mmol, 1.00 equiv.) DMAP (48.8 mg, 0.40 mmol, 0.20 equiv.), and Et_3N (1.01 g, 10.00 mmol, 5.00 equiv.) were dissolved in CH_2Cl_2 (10.0 mL). At 0 ºC, a solution of TsCl (762.6 mg, 4.00 mmol, 2.00 equiv.) in CH_2Cl_2 (6.0 mL) was added within 1 h. The resulting mixture was warmed to rt, stirred for 24 h, and washed with water. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexanes/EtOAc = 25:1) on silica gel to obtain pure **6-VI**.

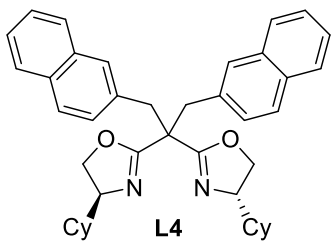
In an oven-dried vial, the obtained **6-VI** (166.3 mg, 0.50 mmol, 1.00 equiv.) was dissolved in THF (1.5 mL). NaH (60.0 mg, 60% in mineral oil, 1.50 mmol, 3.00 equiv.) was added to the solution and stirred at rt for 1 h. TBAI (27.7 mg, 0.075 mmol, 0.15 equiv.) was then added. At 0 °C, a solution of **6-IV** (201.7 mg, 1.00 mmol, 2.00 equiv.) in THF (0.5 mL) was added slowly. The resulting mixture was heated to 65 °C in an oil bath and stirred for 18 h. The reaction was cooled down to rt, quenched with $NH_4Cl_{(aq)}$, and extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude oil was purified by flash column chromatography (hexanes/EtOAc = 25:1 to 100% EtOAc) on silica gel to obtain the desired Cy-TOX ligand **L3**.



L3

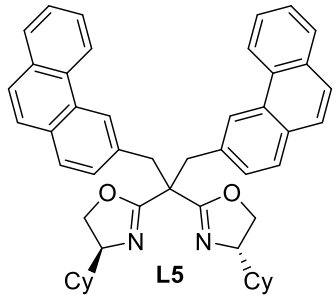
The title compound **L3** was purified by flash column chromatography (hexanes/EtOAc = 25:1 to 100% EtOAc) on silica gel and obtained as a yellow oil; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 4.27–4.10 (m, 3H), 4.07–3.97 (m, 2H), 3.95–3.86 (m, 3H), 3.86–3.79 (m, 1H), 3.05 (d, *J* = 14.6 Hz, 1H), 2.94 (d, *J* = 14.6 Hz, 1H), 1.90–1.81 (m, 2H), 1.80–1.70 (m, 7H), 1.70–1.63 (m, 3H), 1.62–1.51 (m, 6H), 1.48–1.33 (m, 3H), 1.28–1.10 (m, 9H), 1.05–0.90 (m, 6H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 166.94, 166.86, 163.6, 71.4, 71.3, 71.0, 70.7, 70.5, 70.1, 42.6, 42.5, 42.4, 40.9, 35.1, 29.6, 29.5, 29.2, 29.0, 28.7,

28.2, 26.62, 26.60, 26.2, 26.14, 26.10, 21.4; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{30}H_{48}N_3O_3$ 498.3690; found 498.3697; $[\alpha]_D^{24}$ = -260 (*c* = 1.0, $CHCl_3$, 589 nm).



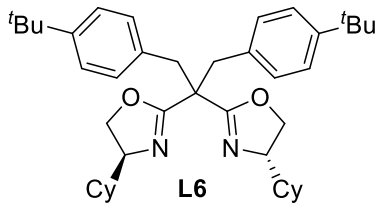
L4

The title compound **L4** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as a colorless oil; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.84–7.71 (m, 8H), 7.50–7.38 (m, 6H), 4.17 (dd, *J* = 9.7, 8.4 Hz, 2H), 3.96–3.88 (m, 2H), 3.87–3.78 (m, 2H), 3.58 (d, *J* = 14.1 Hz, 2H), 3.49 (d, *J* = 14.1 Hz, 2H), 1.68 (d, *J* = 12.9 Hz, 2H), 1.64–1.52 (m, 6H), 1.40 (d, *J* = 12.5 Hz, 2H), 1.19–0.76 (m, 12H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 166.1, 134.8, 133.4, 132.5, 129.5, 129.0, 127.8, 127.7, 127.4, 125.9, 125.6, 71.4, 70.5, 48.8, 42.7, 40.0, 29.6, 29.0, 26.6, 26.1, 26.0; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{41}H_{47}N_2O_2$ 599.3632; found 599.3626; $[\alpha]_D^{24}$ = -180 (*c* = 1.0, $CHCl_3$, 589 nm).



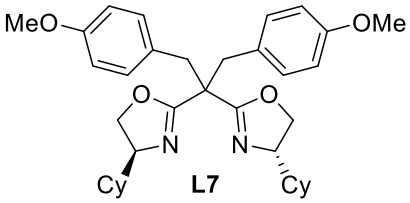
L5

The title compound **L5** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as a white solid; **mp:** 97–98 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.65–8.54 (m, 4H), 7.91–7.85 (m, 2H), 7.82 (d, *J* = 8.1 Hz, 2H), 7.76–7.69 (m, 4H), 7.62 (d, *J* = 8.1 Hz, 2H), 7.59–7.53 (m, 4H), 4.25–4.16 (m, 2H), 3.98–3.90 (m, 2H), 3.87–3.80 (m, 2H), 3.73 (d, *J* = 14.1 Hz, 2H), 3.66 (d, *J* = 14.1 Hz, 2H), 1.67 (d, *J* = 12.2 Hz, 2H), 1.56–1.44 (m, 6H), 1.33 (d, *J* = 11.3 Hz, 2H), 1.15–1.06 (m, 2H), 1.02–0.92 (m, 2H), 0.92–0.73 (m, 8H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 166.1, 135.6, 132.3, 131.0, 130.3, 130.2, 129.3, 128.7, 128.2, 126.8, 126.64, 126.61, 126.5, 124.8, 122.6, 71.5, 70.7, 48.9, 42.7, 40.5, 29.7, 29.0, 26.5, 25.9, 25.8; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{49}H_{51}N_2O_2$ 699.3945, found 699.3946; $[\alpha]_D^{24}$ = -160 (*c* = 1.0, $CHCl_3$, 589 nm).

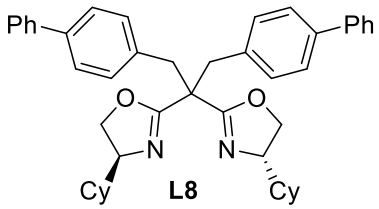


L6

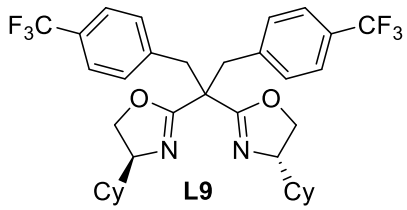
The title compound **L6** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as a colorless oil; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.29–7.25 (m, 4H), 7.21–7.16 (m, 4H), 4.19 (dd, *J* = 9.6, 8.2 Hz, 2H), 3.92 (t, *J* = 8.2 Hz, 2H), 3.88–3.81 (m, 2H), 3.30 (d, *J* = 14.2 Hz, 2H), 3.23 (d, *J* = 14.2 Hz, 2H), 1.81–1.62 (m, 7H), 1.49 (d, *J* = 12.6 Hz, 2H), 1.35–1.25 (m, 21H), 1.23–1.10 (m, 6H), 0.96–0.86 (m, 4H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 166.3, 149.2, 133.9, 130.3, 124.8, 71.4, 70.2, 48.4, 42.6, 38.1, 34.4, 31.5, 29.7, 28.9, 26.6, 26.2, 26.1; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{41}H_{59}N_2O_2$ 611.4571; found 611.4578; $[\alpha]_D^{24}$ = -90 (*c* = 1.0, $CHCl_3$, 589 nm).



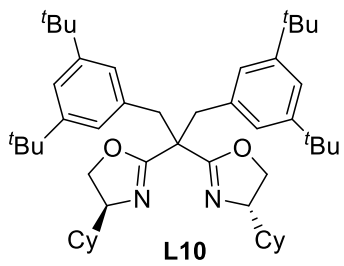
The title compound **L7** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as a colorless oil; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.23–7.13 (m, 4H), 6.85–6.75 (m, 4H), 4.16 (dd, *J* = 9.8, 8.2 Hz, 2H), 3.92 (t, *J* = 8.1 Hz, 2H), 3.88–3.75 (m, 8H), 3.28 (d, *J* = 14.2 Hz, 2H), 3.18 (d, *J* = 14.2 Hz, 2H), 1.79–1.62 (m, 7H), 1.48 (d, *J* = 12.8 Hz, 2H), 1.32–1.09 (m, 9H), 0.96–0.83 (m, 4H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 166.2, 158.4, 131.6, 129.2, 113.4, 71.3, 70.3, 55.3, 48.7, 42.7, 38.6, 29.6, 28.9, 26.7, 26.23, 26.22; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{35}H_{47}N_2O_4$ 559.3530; found 559.3536; $[\alpha]_D^{24}$ = -100 (*c* = 1.0, $CHCl_3$, 589 nm).



The title compound **L8** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as a white solid; **mp:** 72–73 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.62–7.56 (m, 4H), 7.52–7.48 (m, 4H), 7.46–7.40 (m, 4H), 7.38–7.30 (m, 6H), 4.21 (dd, *J* = 9.7, 8.2 Hz, 2H), 3.96 (t, *J* = 8.2 Hz, 2H), 3.91–3.83 (m, 2H), 3.44 (d, *J* = 14.1 Hz, 2H), 3.33 (d, *J* = 14.1 Hz, 2H), 1.78 (d, *J* = 12.8 Hz, 2H), 1.73–1.60 (m, 5H), 1.51 (d, *J* = 12.6 Hz, 2H), 1.38–1.28 (m, 2H), 1.22–1.09 (m, 6H), 1.00–0.77 (m, 5H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 166.1, 141.1, 139.6, 136.2, 131.1, 128.8, 127.2, 127.1, 126.8, 71.4, 70.4, 48.5, 42.7, 39.1, 29.7, 28.9, 26.7, 26.23, 26.19; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{45}H_{51}N_2O_2$ 651.3945; found 651.3951; $[\alpha]_D^{24}$ = -110 (*c* = 1.0, $CHCl_3$, 589 nm).

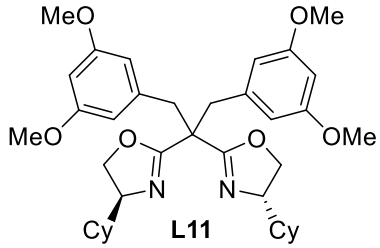


The title compound **L9** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as a white solid; **mp:** 136–137 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.51 (d, *J* = 8.0 Hz, 4H), 7.37 (d, *J* = 8.0 Hz, 4H), 4.17 (dd, *J* = 9.6, 8.2 Hz, 2H), 3.91 (t, *J* = 8.2 Hz, 2H), 3.88–3.79 (m, 2H), 3.40 (d, *J* = 14.0 Hz, 2H), 3.29 (d, *J* = 14.0 Hz, 2H), 1.79–1.62 (m, 7H), 1.47 (d, *J* = 12.5 Hz, 2H), 1.29–1.07 (m, 8H), 0.99–0.81 (m, 5H); **^{13}C NMR (125 MHz, $CDCl_3$):** 165.4, 141.1, 130.9, 129.2 (q, *J* = 31.9 Hz), 125.0 (q, *J* = 3.6 Hz), 124.4 (d, *J* = 271.6 Hz), 71.4, 70.6, 48.2, 42.8, 40.0, 29.6, 29.1, 26.6, 26.1; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{35}H_{41}F_6N_2O_2$ 635.3067; found 635.3073; $[\alpha]_D^{24}$ = -110 (*c* = 1.0, $CHCl_3$, 589 nm).



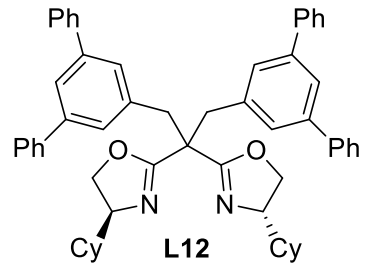
The title compound **L10** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as a white solid; **mp:** 87–88 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.27 (t, *J* = 1.6 Hz, 2H), 7.20 (d, *J* = 1.7 Hz, 4H), 4.13 (dd, *J* = 9.6, 8.0 Hz, 2H), 3.86 (t, *J* = 8.2 Hz, 2H), 3.83–3.76 (m, 2H), 3.50 (d, *J* = 14.3 Hz, 2H), 3.34 (d, *J* = 14.3 Hz, 2H), 1.73–1.58 (m, 7H), 1.40–1.26 (m, 38H), 1.24–1.04 (m, 9H), 0.88–

0.74 (m, 4H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 166.4, 150.1, 136.4, 124.9, 120.5, 71.4, 70.3, 48.2, 42.5, 39.4, 34.9, 31.7, 29.7, 28.4, 26.6, 26.2, 26.1; **HRMS (ESI):** calcd. for $[M + Na]^+$ $C_{49}H_{74}N_2NaO_2$ 745.5643; found 745.5662; $[\alpha]_D^{24}$ = -50 (*c* = 1.0, $CHCl_3$, 589 nm).



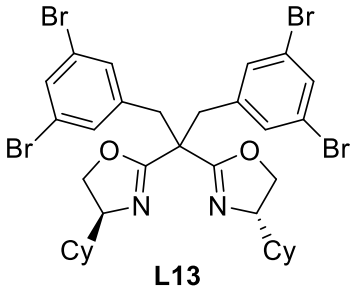
L11

The title compound **L11** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as a white solid; **mp:** 111–112 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 6.42 (d, *J* = 2.3 Hz, 4H), 6.32 (t, *J* = 2.3 Hz, 2H), 4.20 (dd, *J* = 9.7, 8.3 Hz, 2H), 3.96 (t, *J* = 8.2 Hz, 2H), 3.89–3.82 (m, 2H), 3.74 (s, 12H), 3.34 (d, *J* = 14.1 Hz, 2H), 3.22 (d, *J* = 14.2 Hz, 2H), 1.79 (d, *J* = 12.6 Hz, 2H), 1.75–1.62 (m, 6H), 1.49 (d, *J* = 12.9 Hz, 2H), 1.35–1.26 (m, 2H), 1.25–1.07 (m, 6H), 1.00–0.84 (m, 4H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 166.2, 160.4, 139.2, 108.9, 98.6, 71.5, 70.5, 55.3, 48.0, 42.7, 39.4, 29.8, 28.9, 26.7, 26.2; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{37}H_{51}N_2O_6$ 619.3742; found 619.3748; $[\alpha]_D^{24}$ = -140 (*c* = 1.0, $CHCl_3$, 589 nm).



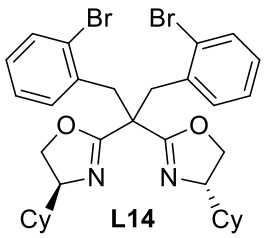
L12

The title compound **L12** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as a white solid; **mp:** 89–90 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.71–7.66 (m, 2H), 7.60 (d, *J* = 8.0 Hz, 8H), 7.52 (s, 4H), 7.46–7.37 (m, 8H), 7.37–7.31 (m, 4H), 4.25–4.14 (m, 2H), 3.94–3.76 (m, 4H), 3.64–3.44 (m, 4H), 1.73 (d, *J* = 12.3 Hz, 2H), 1.63–1.49 (m, 6H), 1.34 (d, *J* = 12.1 Hz, 2H), 1.20–1.10 (m, 2H), 1.05–0.92 (m, 5H), 0.89–0.74 (m, 5H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 166.2, 141.5, 141.3, 138.1, 128.9, 128.5, 127.4, 127.3, 124.6, 71.6, 70.7, 48.4, 42.7, 39.7, 29.7, 28.9, 26.5, 26.0, 25.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{57}H_{59}N_2O_2$ 803.4571; found 803.4561; $[\alpha]_D^{24}$ = -90 (*c* = 1.0, $CHCl_3$, 589 nm).

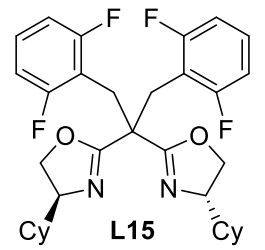


L13

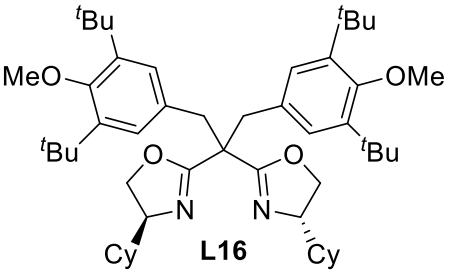
The title compound **L13** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as a white solid; **mp:** 79–80 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** 7.53 (t, *J* = 1.5 Hz, 2H), 7.34 (d, *J* = 1.4 Hz, 4H), 4.23–4.15 (m, 2H), 3.97–3.90 (m, 2H), 3.89–3.82 (m, 2H), 3.24 (d, *J* = 13.7 Hz, 2H), 3.12 (d, *J* = 13.7 Hz, 2H), 1.82 (d, *J* = 12.7 Hz, 2H), 1.73 (d, *J* = 12.8 Hz, 4H), 1.67 (d, *J* = 11.6 Hz, 2H), 1.51 (d, *J* = 12.3 Hz, 2H), 1.33–1.12 (m, 6H), 1.00–0.81 (m, 6H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 164.7, 140.7, 132.52, 132.47, 122.4, 71.5, 70.8, 48.6, 42.9, 40.6, 29.7, 29.2, 26.6, 26.2, 26.1; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{33}H_{39}Br_4N_2O_2$ 810.9740; found 810.9749; $[\alpha]_D^{24}$ = -80 (*c* = 1.0, $CHCl_3$, 589 nm).



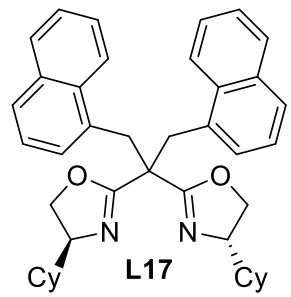
The title compound **L14** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as a colorless oil; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.57–7.47 (m, 4H), 7.19–7.11 (m, 2H), 7.08–7.00 (m, 2H), 4.15–4.06 (m, 2H), 3.92–3.81 (m, 4H), 3.70 (d, *J* = 14.5 Hz, 2H), 3.58 (d, *J* = 14.5 Hz, 2H), 1.83 (d, *J* = 12.8 Hz, 2H), 1.76–1.62 (m, 5H), 1.53 (d, *J* = 12.5 Hz, 2H), 1.37–1.27 (m, 2H), 1.27–1.08 (m, 7H), 1.00–0.89 (m, 4H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 165.7, 137.4, 132.8, 132.3, 128.2, 126.7, 126.5, 71.4, 70.6, 48.6, 42.8, 40.1, 29.8, 29.1, 26.7, 26.3, 26.2; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{33}H_{41}Br_2N_2O_2$ 655.1529; found 655.1534; $[\alpha]_D^{24}$ = -190 (*c* = 1.0, $CHCl_3$, 589 nm).



The title compound **L15** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as a colorless oil; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.21–7.12 (m, 2H), 6.87–6.77 (m, 4H), 4.14–4.06 (m, 2H), 3.90–3.81 (m, 4H), 3.56–3.46 (m, 4H), 1.82 (d, *J* = 12.8 Hz, 2H), 1.77–1.62 (m, 6H), 1.51 (d, *J* = 12.6 Hz, 2H), 1.38–1.28 (m, 2H), 1.27–1.08 (m, 6H), 1.02–0.84 (m, 4H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 165.6, 162.5 (dd, *J* = 248.4, 8.6 Hz), 128.4 (t, *J* = 10.4 Hz), 113.6 (t, *J* = 19.8 Hz), 111.0, 110.9, 110.8, 71.4, 70.6, 47.2, 42.7, 29.4, 28.9, 28.8, 26.7, 26.23, 26.21; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{33}H_{39}F_4N_2O_2$ 571.2942; found 571.2946; $[\alpha]_D^{24}$ = -130 (*c* = 1.0, $CHCl_3$, 589 nm).

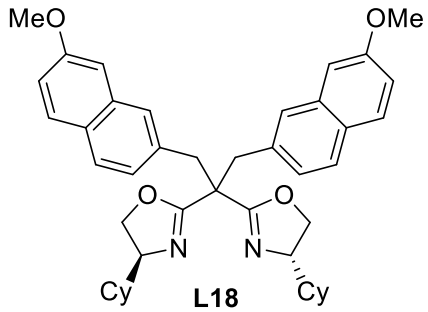


The title compound **L16** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as a white solid; **mp:** 78–79 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.16 (s, 4H), 4.15 (dd, *J* = 9.3, 8.1 Hz, 2H), 3.90–3.76 (m, 4H), 3.66 (s, 6H), 3.41 (d, *J* = 14.5 Hz, 2H), 3.25 (d, *J* = 14.5 Hz, 2H), 1.82–1.59 (m, 7H), 1.50–1.34 (m, 38H), 1.32–1.08 (m, 9H), 0.96–0.81 (m, 4H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 166.5, 158.2, 142.7, 131.3, 128.7, 71.5, 70.3, 64.3, 48.0, 42.6, 38.7, 35.7, 32.3, 29.8, 28.5, 26.6, 26.1, 26.0; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{51}H_{79}N_2O_4$ 783.6034; found 783.6028; $[\alpha]_D^{24}$ = -60 (*c* = 1.0, $CHCl_3$, 589 nm).



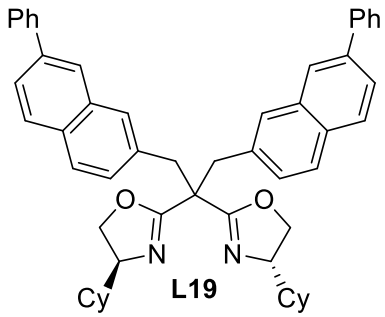
The title compound **L17** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as a colorless oil; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.23–8.16 (m, 2H), 7.86–7.79 (m, 2H), 7.72 (d, *J* = 8.1 Hz, 2H), 7.64 (d, *J* = 6.9 Hz, 2H), 7.48–7.39 (m, 4H), 7.34 (dd, *J* = 8.1, 7.2 Hz, 2H), 4.02 (d, *J* = 14.8 Hz, 2H), 3.95 (d, *J* = 14.8 Hz, 2H), 3.66–3.48 (m, 6H), 1.73–1.57 (m, 8H), 1.32 (d, *J* = 12.2 Hz, 2H), 1.18–1.04 (m, 6H), 0.97–0.70 (m, 6H) **^{13}C NMR (125 MHz, $CDCl_3$):** δ 166.2, 133.90, 133.86, 133.3, 128.7, 128.4,

127.3, 125.5, 125.3, 125.2, 124.4, 71.2, 70.2, 48.5, 42.5, 36.4, 29.7, 28.9, 26.7, 26.2, 26.1; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{41}H_{47}N_2O_2$ 599.3632; found 599.3626; $[\alpha]_D^{24}$ = -640 (*c* = 1.0, $CHCl_3$, 589 nm).



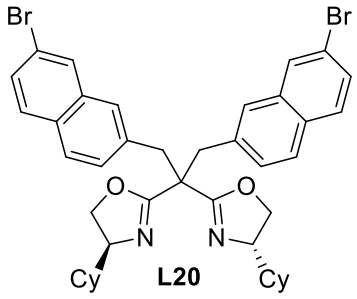
L18

The title compound **L18** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid; **mp:** 175–176 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.73–7.63 (m, 6H), 7.29 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.10 (dd, *J* = 8.9, 2.5 Hz, 2H), 7.05 (d, *J* = 2.3 Hz, 2H), 4.17 (dd, *J* = 9.7, 8.2 Hz, 2H), 3.94–3.89 (m, 8H), 3.86–3.79 (m, 2H), 3.58 (d, *J* = 14.1 Hz, 2H), 3.48 (d, *J* = 14.1 Hz, 2H), 1.69 (d, *J* = 12.4 Hz, 2H), 1.65–1.55 (m, 6H), 1.41 (d, *J* = 12.4 Hz, 2H), 1.19–0.92 (m, 8H), 0.90–0.78 (m, 4H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 166.2, 157.7, 135.4, 134.5, 129.2, 128.5, 128.0, 127.2, 126.8, 118.3, 105.7, 71.4, 70.5, 55.4, 48.7, 42.7, 40.0, 29.7, 29.0, 26.6, 26.11, 26.06; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{43}H_{51}N_2O_4$ 659.3843, found 659.3832; $[\alpha]_D^{24}$ = -150 (*c* = 1.0, $CHCl_3$, 589 nm).



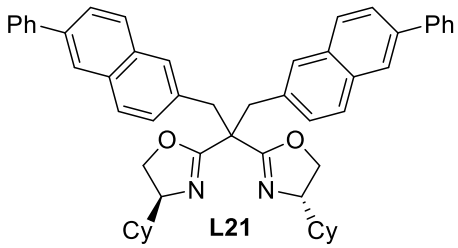
L19

The title compound **L19** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as a white solid; **mp:** 98–99 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.99 (s, 2H), 7.91 (d, *J* = 8.5 Hz, 2H), 7.84 (s, 2H), 7.80 (d, *J* = 8.4 Hz, 2H), 7.77–7.70 (m, 6H), 7.54–7.45 (m, 6H), 7.43–7.37 (m, 2H), 4.27–4.19 (m, 2H), 4.01–3.94 (m, 2H), 3.91–3.84 (m, 2H), 3.65 (d, *J* = 14.1 Hz, 2H), 3.57 (d, *J* = 14.1 Hz, 2H), 1.72 (d, *J* = 12.2 Hz, 2H), 1.65–1.55 (m, 6H), 1.44 (d, *J* = 12.2 Hz, 2H), 1.23–0.80 (m, 12H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 166.1, 141.4, 138.8, 135.3, 133.7, 131.7, 129.8, 129.2, 128.9, 128.2, 127.5, 127.4, 127.2, 125.7, 125.4, 71.4, 70.5, 48.8, 42.7, 40.0, 29.6, 29.0, 26.6, 26.03, 26.00; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{53}H_{55}N_2O_2$ 751.4258, found 751.4258; $[\alpha]_D^{24}$ = -160 (*c* = 1.0, $CHCl_3$, 589 nm).

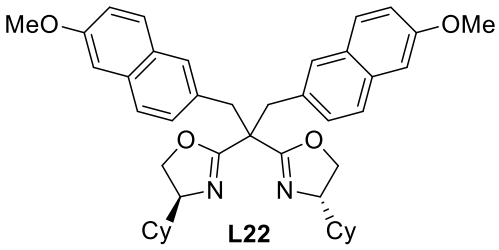


L20

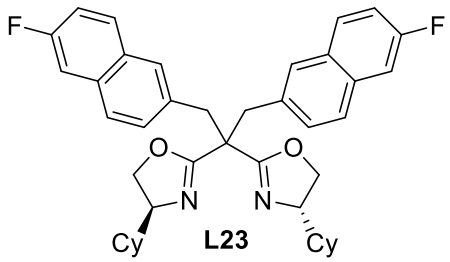
The title compound **L20** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid; **mp:** 120–121 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.91 (d, *J* = 1.7 Hz, 2H), 7.70 (d, *J* = 8.5 Hz, 2H), 7.68–7.63 (m, 4H), 7.49 (dd, *J* = 8.7, 1.9 Hz, 2H), 7.42 (dd, *J* = 8.5, 1.6 Hz, 2H), 4.16 (dd, *J* = 9.6, 8.4 Hz, 2H), 3.97–3.87 (m, 2H), 3.86–3.79 (m, 2H), 3.54 (d, *J* = 14.0 Hz, 2H), 3.47 (d, *J* = 14.1 Hz, 2H), 1.72–1.55 (m, 8H), 1.41 (d, *J* = 12.4 Hz, 2H), 1.17–0.77 (m, 12H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 165.7, 136.0, 134.4, 130.8, 129.7, 129.5, 129.4, 128.9, 128.4, 127.3, 119.9, 71.4, 70.5, 48.8, 42.8, 40.2, 29.6, 29.1, 26.6, 26.03, 25.97; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{41}H_{45}Br_2N_2O_2$ 755.1842, found 755.1840; $[\alpha]_D^{24}$ = -110 (*c* = 1.0, $CHCl_3$, 589 nm).



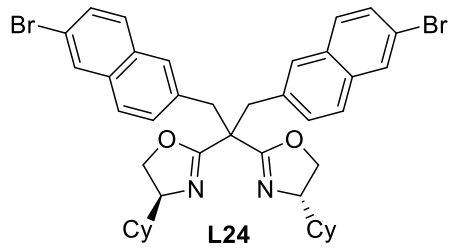
The title compound **L21** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid (163.3 mg); **mp:** 96–97 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.01 (d, *J* = 1.8 Hz, 2H), 7.84 (d, *J* = 8.6 Hz, 2H), 7.84–7.77 (m, 4H), 7.75–7.69 (m, 6H), 7.52–7.44 (m, 6H), 7.40–7.35 (m, 2H), 4.19 (dd, *J* = 9.7, 8.4 Hz, 2H), 3.97–3.90 (m, 2H), 3.88–3.81 (m, 2H), 3.61 (d, *J* = 14.1 Hz, 2H), 3.53 (d, *J* = 14.1 Hz, 2H), 1.71 (d, *J* = 11.9 Hz, 2H), 1.65–1.53 (m, 6H), 1.42 (d, *J* = 12.3 Hz, 2H), 1.17–0.93 (m, 8H), 0.91–0.79 (m, 4H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 166.0, 141.4, 138.4, 135.0, 132.8, 132.6, 129.5, 129.3, 129.0, 128.3, 127.7, 127.5, 127.4, 125.72, 125.65, 71.4, 70.5, 48.9, 42.8, 40.2, 29.7, 29.1, 26.6, 26.1, 26.0; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{53}H_{55}N_2O_2$ 751.4258, found 751.4257; $[\alpha]_D^{24}$ = -210 (*c* = 1.0, $CHCl_3$, 589 nm).



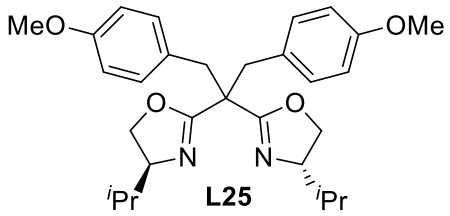
The title compound **L22** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid; **mp:** 76–77 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.69–7.60 (m, 6H), 7.39 (dd, *J* = 8.4, 1.4 Hz, 2H), 7.15–7.09 (m, 4H), 4.16 (dd, *J* = 9.8, 8.2 Hz, 2H), 3.93–3.88 (m, 8H), 3.85–3.79 (m, 2H), 3.53 (d, *J* = 14.1 Hz, 2H), 3.44 (d, *J* = 14.1 Hz, 2H), 1.70 (d, *J* = 13.1 Hz, 2H), 1.66–1.55 (m, 6H), 1.42 (d, *J* = 12.4 Hz, 2H), 1.19–0.95 (m, 8H), 0.91–0.79 (m, 4H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 166.2, 157.5, 133.5, 132.4, 129.6, 129.30, 129.25, 128.9, 126.3, 118.7, 105.7, 71.4, 70.4, 55.4, 48.9, 42.7, 39.8, 29.7, 29.0, 26.6, 26.10, 26.06; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{43}H_{51}N_2O_4$ 659.3843, found 659.3844; $[\alpha]_D^{24}$ = -140 (*c* = 1.0, $CHCl_3$, 589 nm).



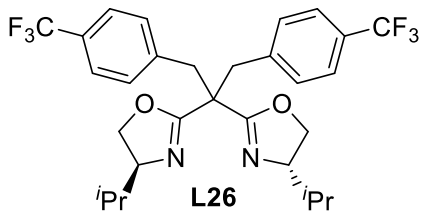
The title compound **L23** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as a white solid; **mp:** 65–66 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.76–7.71 (m, 4H), 7.68 (d, *J* = 8.5 Hz, 2H), 7.47–7.39 (m, 4H), 7.26–7.20 (m, 2H), 4.16 (dd, *J* = 9.6, 8.4 Hz, 2H), 3.94–3.88 (m, 2H), 3.87–3.79 (m, 2H), 3.55 (d, *J* = 14.1 Hz, 2H), 3.46 (d, *J* = 14.1 Hz, 2H), 1.69 (d, *J* = 12.8 Hz, 2H), 1.65–1.56 (m, 6H), 1.41 (d, *J* = 12.4 Hz, 2H), 1.19–0.93 (m, 8H), 0.92–0.77 (m, 4H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 165.9, 160.6 (d, *J* = 245.3 Hz), 134.0 (d, *J* = 2.4 Hz), 133.1 (d, *J* = 9.2 Hz), 130.4, 130.1, 130.0, 129.4, 126.8 (d, *J* = 5.2 Hz), 116.3 (d, *J* = 25.4 Hz), 110.7 (d, *J* = 20.3 Hz), 71.4, 70.5, 48.8, 42.7, 40.1, 29.6, 29.0, 26.6, 26.09, 26.05; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{41}H_{45}F_2N_2O_2$ 635.3444, found 635.3442; $[\alpha]_D^{24}$ = -140 (*c* = 1.0, $CHCl_3$, 589 nm).



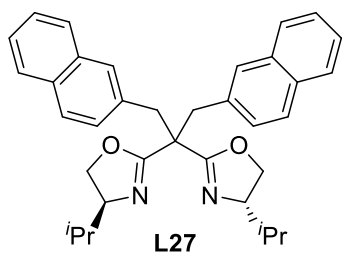
The title compound **L24** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid; **mp:** 76–77 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.96 (d, *J* = 1.6 Hz, 2H), 7.69 (s, 2H), 7.64 (d, *J* = 8.5 Hz, 2H), 7.61 (d, *J* = 8.8 Hz, 2H), 7.51 (dd, *J* = 8.7, 1.9 Hz, 2H), 7.43 (dd, *J* = 8.5, 1.5 Hz, 2H), 4.14 (dd, *J* = 9.6, 8.3 Hz, 2H), 3.92–3.86 (m, 2H), 3.85–3.79 (m, 2H), 3.54 (d, *J* = 14.0 Hz, 2H), 3.44 (d, *J* = 14.0 Hz, 2H), 1.70 (d, *J* = 12.8 Hz, 2H), 1.66–1.57 (m, 6H), 1.42 (d, *J* = 12.4 Hz, 2H), 1.20–0.95 (m, 8H), 0.92–0.78 (m, 4H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 165.8, 135.3, 133.5, 131.8, 130.0, 129.7, 129.40, 129.38, 129.32, 126.5, 119.5, 71.4, 70.5, 48.7, 42.7, 40.4, 29.6, 29.0, 26.6, 26.09, 26.06; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{41}H_{45}Br_2N_2O_2$ 755.1842, found 755.1840; $[\alpha]_D^{24}$ = -120 (*c* = 1.0, $CHCl_3$, 589 nm).



The title compound **L25** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a colorless oil; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.20–7.11 (m, 4H), 6.83–6.75 (m, 4H), 4.19–4.12 (m, 2H), 3.94–3.84 (m, 4H), 3.78 (s, 6H), 3.32 (d, *J* = 14.2 Hz, 2H), 3.14 (d, *J* = 14.2 Hz, 2H), 1.74–1.66 (m, 2H), 0.90 (d, *J* = 6.8 Hz, 6H), 0.82 (d, *J* = 6.7 Hz, 6H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 166.5, 158.4, 131.6, 129.2, 113.5, 72.1, 69.9, 55.4, 48.6, 38.6, 32.6, 19.1, 18.0; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{29}H_{39}N_2O_4$ 479.2904; found 479.2895; $[\alpha]_D^{24}$ = -20 (*c* = 1.0, $CHCl_3$, 589 nm).

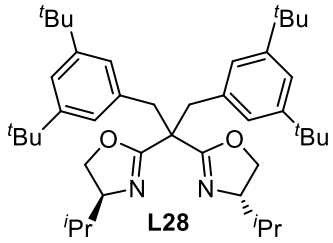


The title compound **L26** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid; **mp:** 67–68 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.52 (d, *J* = 8.0 Hz, 4H), 7.36 (d, *J* = 8.0 Hz, 4H), 4.15 (dd, *J* = 9.1, 7.7 Hz, 2H), 3.93–3.83 (m, 4H), 3.45 (d, *J* = 14.0 Hz, 2H), 3.26 (d, *J* = 14.0 Hz, 2H), 1.69–1.61 (m, 2H), 0.89 (d, *J* = 6.7 Hz, 6H), 0.83 (d, *J* = 6.7 Hz, 6H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 165.6, 141.1, 130.9, δ 129.2 (q, *J* = 32.4 Hz), 125.0 (q, *J* = 3.9 Hz), 124.4 (q, *J* = 271.7 Hz), 72.2, 70.3, 48.2, 40.1, 32.7, 18.9, 18.2; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{29}H_{33}F_6N_2O_2$ 555.2441; found 555.2431; $[\alpha]_D^{24}$ = -30 (*c* = 1.0, $CHCl_3$, 589 nm).

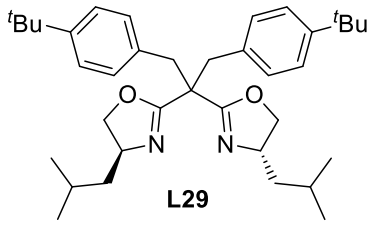


The title compound **L27** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a colorless oil; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.89–7.65 (m, 8H), 7.54–7.32 (m, 6H), 4.16 (dd, *J* = 9.3, 7.8 Hz, 2H), 4.00–3.79 (m, 4H), 3.61 (d, *J* = 14.0 Hz, 2H), 3.44 (d, *J* = 14.0 Hz, 2H), 1.75–1.63 (m, 2H), 0.88 (d, *J* = 6.7 Hz, 6H), 0.81 (d, *J* = 6.8 Hz, 6H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 166.4, 134.8,

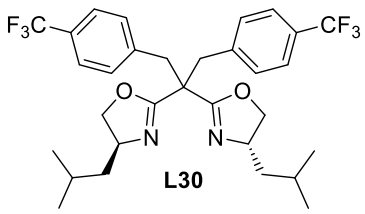
133.4, 132.5, 129.5, 129.0, 127.8, 127.7, 127.4, 125.9, 125.6, 72.2, 70.1, 48.7, 40.1, 32.7, 19.0, 18.1; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{35}H_{39}N_2O_2$ 519.3006; found 519.3003; $[\alpha]_D^{24}$ = 70 (*c* = 1.0, $CHCl_3$, 589 nm).



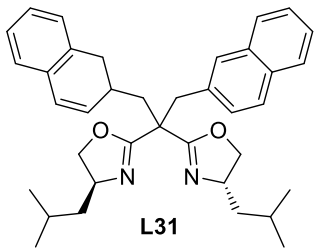
The title compound **L28** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a yellow solid; **mp:** 117–118 °C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.27–7.25(m, 2H), 7.16 (d, *J* = 1.8 Hz, 4H), 4.12 (dd, *J* = 9.4, 8.3 Hz, 2H), 3.93–3.76 (m, 4H), 3.51 (d, *J* = 14.2 Hz, 2H), 3.29 (d, *J* = 14.3 Hz, 2H), 1.59 (m, 2H), 1.29 (s, 36H), 0.85 (d, *J* = 6.7 Hz, 6H), 0.77 (d, *J* = 6.7 Hz, 6H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 166.7, 150.1, 136.4, 124.8, 120.7, 72.1, 69.8, 48.2, 39.5, 34.9, 32.6, 31.7, 19.2, 17.8; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{43}H_{67}N_2O$ 643.5197; found 643.5189; $[\alpha]_D^{24}$ = -40 (*c* = 1.0, $CHCl_3$, 589 nm).



The title compound **L29** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a colorless oil; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.37–7.27 (m, 4H), 7.27–7.18 (m, 4H), 4.39–4.27 (m, 2H), 4.15–4.05 (m, 2H), 3.79 (t, *J* = 8.0 Hz, 2H), 3.40–3.20 (m, 4H), 1.65–1.57 (m, 2H), 1.50–1.41 (m, 2H), 1.33 (s, 18H), 1.16–1.07 (m, 2H), 0.90 (dd, *J* = 12.7, 6.6 Hz, 12H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 166.3, 149.5, 133.9, 130.4, 125.0, 73.2, 64.8, 48.2, 45.2, 38.2, 34.5, 31.5, 25.6, 23.3, 22.5; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{37}H_{55}N_2O_2$ 559.4258; found 559.4250; $[\alpha]_D^{24}$ = -340 (*c* = 1.0, $CHCl_3$, 589 nm).

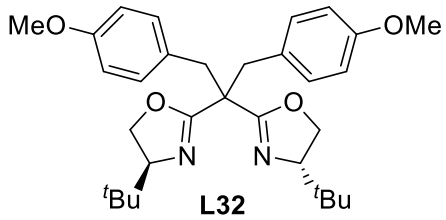


The title compound **L30** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid; **mp:** 87–88 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.53 (d, *J* = 7.9 Hz, 4H), 7.38 (d, *J* = 7.9 Hz, 4H), 4.28 (dd, *J* = 9.4, 8.2 Hz, 2H), 4.10 (dt, *J* = 15.8, 7.9 Hz, 2H), 3.75 (t, *J* = 8.0 Hz, 2H), 3.46–3.25 (m, 4H), 1.64 (dt, *J* = 13.4, 6.7 Hz, 2H), 1.43 (dt, *J* = 13.6, 6.8 Hz, 2H), 1.12 (dt, *J* = 14.0, 7.3 Hz, 2H), 0.89 (dd, *J* = 14.9, 6.6 Hz, 12H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 165.4, 141.0, 130.9, δ 129.3 (q, *J* = 32.4 Hz), 125.0 (q, *J* = 3.9 Hz), 124.4 (q, *J* = 272.1 Hz), 73.4, 64.7, 48.0, 45.4, 40.1, 25.5, 23.0, 22.6; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{31}H_{37}F_6N_2O_2$ 583.2754; found 583.2744; $[\alpha]_D^{24}$ = -20 (*c* = 1.0, $CHCl_3$, 589 nm).



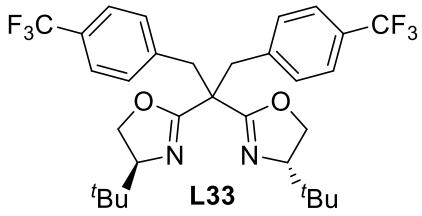
The title compound **L31** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a colorless oil; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.88–7.67 (m, 8H), 7.44 (ddt, *J* = 9.2, 4.7, 3.6 Hz, 6H), 4.29 (dd, *J* = 9.5, 8.1 Hz, 2H), 4.18–4.04 (m, 2H), 3.77 (t, *J* = 7.9 Hz, 2H), 3.65–3.41 (m, 4H), 1.62–1.52 (m, 2H), 1.44–1.33 (m, 2H),

1.04 (ddd, *J* = 13.4, 8.3, 6.5 Hz, 2H), 0.83 (d, *J* = 6.6 Hz, 6H), 0.78 (d, *J* = 6.6 Hz, 6H); **^{13}C NMR (125 MHz, $CDCl_3$)**: δ 166.1, 134.7, 133.4, 132.5, 129.4, 129.0, 127.8, 127.7, 127.5, 126.0, 125.6, 73.3, 64.7, 48.6, 45.3, 39.9, 25.4, 23.0, 22.5; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{37}H_{45}N_2O_2$ 549.3476; found 549.3479; $[\alpha]_D^{24}$ = -90 (*c* = 1.0, $CHCl_3$, 589 nm).



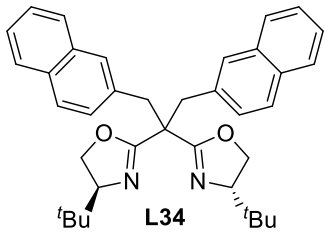
L32

The title compound **L32** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a colorless oil; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.23–7.10 (m, 4H), 6.85–6.72 (m, 4H), 4.13–4.03 (m, 2H), 4.02–3.94 (m, 2H), 3.87–3.72 (m, 8H), 3.38 (d, *J* = 14.1 Hz, 2H), 3.09 (d, *J* = 14.2 Hz, 2H), 0.84 (s, 18H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 166.4, 158.4, 131.6, 129.3, 113.5, 75.7, 68.4, 55.3, 48.6, 38.6, 34.1, 26.0; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{31}H_{43}N_2O_4$ 507.3217; found 507.3210; $[\alpha]_D^{24}$ = -130 (*c* = 1.0, $CHCl_3$, 589 nm).



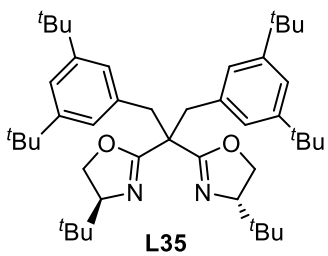
L33

The title compound **L33** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a colorless oil; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.51 (d, *J* = 8.1 Hz, 4H), 7.37 (d, *J* = 8.0 Hz, 4H), 4.08 (dd, *J* = 10.2, 8.7 Hz, 2H), 3.99 (t, *J* = 8.3 Hz, 2H), 3.83 (dd, *J* = 10.2, 7.9 Hz, 2H), 3.50 (d, *J* = 14.0 Hz, 2H), 3.21 (d, *J* = 14.0 Hz, 2H), 0.84 (s, 18H); **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 165.7, 141.2, 130.9, δ 129.2 (q, *J* = 32.3 Hz), 125.0 (q, *J* = 3.8 Hz), 124.4 (q, *J* = 272.2 Hz), 75.9, 68.8, 48.3, 40.0, 34.0, 25.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{31}H_{37}F_6N_2O_2$ 583.2754; found 583.2744; $[\alpha]_D^{24}$ = -250 (*c* = 1.0, $CHCl_3$, 589 nm).



L34

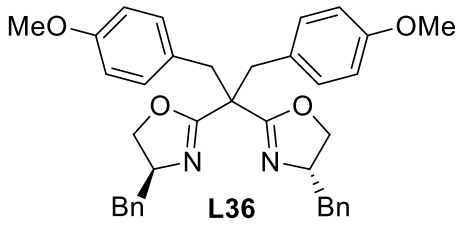
The title compound **L34** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid; **mp:** 65–66 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.83–7.77 (m, 2H), 7.77–7.70 (m, 6H), 7.48–7.37 (m, 6H), 4.08 (dd, *J* = 10.2, 8.7 Hz, 2H), 3.99 (dd, *J* = 8.7, 7.6 Hz, 2H), 3.83 (dd, *J* = 10.1, 7.7 Hz, 2H), 3.66 (d, *J* = 14.0 Hz, 2H), 3.38 (d, *J* = 14.0 Hz, 2H), 0.84 (s, 18H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 166.4, 134.9, 133.5, 132.5, 129.6, 129.1, 127.8, 127.7, 127.4, 125.9, 125.5, 75.8, 68.6, 48.8, 40.3, 34.1, 26.0; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{37}H_{43}N_2O_2$ 547.3319; found 547.3314; $[\alpha]_D^{24}$ = -40 (*c* = 1.0, $CHCl_3$, 589 nm).



L35

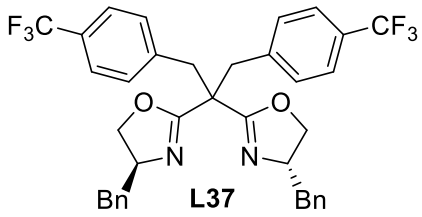
The title compound **L35** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a colorless oil; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.26–7.22 (m, 2H), 7.13 (d, *J* = 1.8 Hz, 4H), 4.07 (dd, *J* = 10.2, 8.6 Hz, 2H), 3.96 (t, *J* = 8.1 Hz, 2H), 3.77 (dd, *J* = 10.1, 7.6 Hz, 2H), 3.53 (d, *J* = 14.4 Hz, 2H), 3.25 (d, *J* = 14.4 Hz, 2H),

1.29 (s, 36H), 0.83 (s, 18H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 166.8, 150.1, 136.5, 124.7, 120.6, 75.8, 68.6, 48.1, 39.2, 34.9, 34.1, 31.8, 25.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{45}H_{71}N_2O_2$ 671.5510; found 671.5508; $[\alpha]_D^{24}$ = 50 (*c* = 1.0, $CHCl_3$, 589 nm).



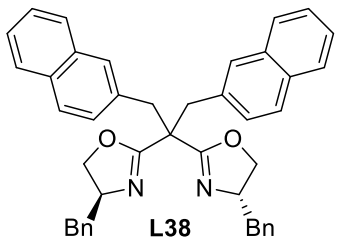
L36

The title compound **L36** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a colorless oil; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.32–7.25 (m, 4H), 7.25–7.18 (m, 6H), 7.18–7.10 (m, 4H), 6.89–6.78 (m, 4H), 4.38–4.26 (m, 2H), 4.12 (t, *J* = 8.9 Hz, 2H), 3.89 (t, *J* = 7.9 Hz, 2H), 3.78 (s, 6H), 3.36–3.20 (m, 4H), 3.03 (dd, *J* = 13.7, 5.1 Hz, 2H), 2.37 (dd, *J* = 13.7, 9.4 Hz, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 167.0, 158.6, 138.3, 131.6, 129.3, 129.0, 128.7, 126.6, 113.6, 72.0, 67.5, 55.4, 48.7, 41.7, 38.8; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{37}H_{39}N_2O_4$ 575.2904; found 575.2897; $[\alpha]_D^{24}$ = -10 (*c* = 1.0, $CHCl_3$, 589 nm).



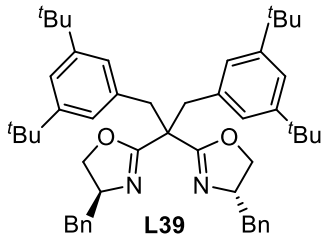
L37

The title compound **L37** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a colorless oil; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.55 (d, *J* = 8.0 Hz, 4H), 7.37 (d, *J* = 8.0 Hz, 4H), 7.30 (t, *J* = 7.4 Hz, 4H), 7.25–7.19 (m, 2H), 7.19–7.09 (m, 4H), 7.19–7.10 (m, 2H), 4.14 (t, *J* = 9.0 Hz, 2H), 3.88 (t, *J* = 8.1 Hz, 2H), 3.51–3.24 (m, 4H), 3.02 (dd, *J* = 13.7, 5.4 Hz, 2H), 2.44 (dd, *J* = 13.8, 8.9 Hz, 2H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 166.2, 140.9, 137.8, 130.9, 129.3, 128.7, 126.7,δ 125.1 (q, *J* = 4.0 Hz), δ 124.3 (q, *J* = 272.1 Hz), 72.2, 67.5, 48.3, 41.6, 40.3; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{37}H_{33}F_6N_2O_2$ 651.2441; found 651.2431; $[\alpha]_D^{24}$ = 210 (*c* = 1.0, $CHCl_3$, 589 nm).

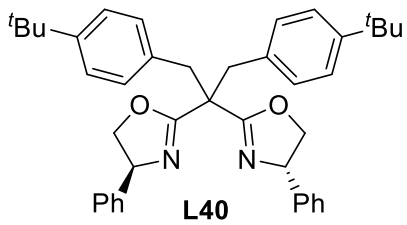


L38

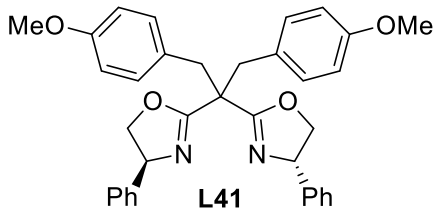
The title compound **L38** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid; **mp:** 60–61 °C;**^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.88–7.75 (m, 8H), 7.52–7.42 (m, 6H), 7.31–7.14 (m, 6H), 7.09–6.98 (m, 4H), 4.39–4.29 (m, 2H), 4.13 (dd, *J* = 9.4, 8.5 Hz, 2H), 3.88 (dd, *J* = 8.5, 7.5 Hz, 2H), 3.59 (s, 4H), 2.97 (dd, *J* = 13.7, 5.1 Hz, 2H), 2.24 (dd, *J* = 13.7, 9.5 Hz, 2H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 166.9, 138.1, 134.6, 133.4, 132.6, 129.5, 129.2, 129.0, 128.6, 127.8, 127.6, 126.6, 126.1, 125.8, 72.2, 67.5, 48.8, 41.6, 40.1; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{43}H_{39}N_2O_2$ 615.3006; found 615.3009; $[\alpha]_D^{24}$ = 20 (*c* = 1.0, $CHCl_3$, 589 nm).



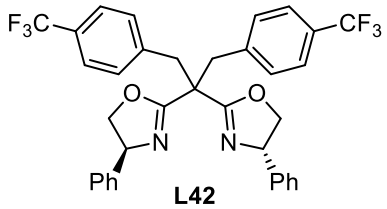
The title compound **L39** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a colorless oil; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.31–7.18 (m, 13H), 7.10 (d, *J* = 7.4 Hz, 4H), 4.36–4.22 (m, 2H), 4.11 (t, *J* = 8.9 Hz, 2H), 3.88 (t, *J* = 7.9 Hz, 2H), 3.52 (d, *J* = 14.2 Hz, 2H), 3.35 (d, *J* = 14.2 Hz, 2H), 2.97 (dd, *J* = 13.7, 5.3 Hz, 2H), 2.37 (dd, *J* = 13.7, 9.0 Hz, 2H), 1.31 (s, 36H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 167.3, 150.3, 138.3, 136.2, 129.3, 128.6, 126.5, 124.8, 120.8, 72.2, 67.5, 48.3, 42.0, 39.8, 34.9, 31.8; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{51}H_{67}N_2O_2$ 739.5197; found 739.5187; $[\alpha]_D^{24}$ = 50 (*c* = 1.0, $CHCl_3$, 589 nm).



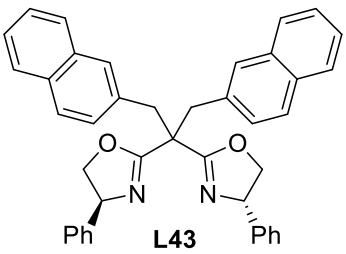
The title compound **L40** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid; **mp:** 63–64 °C;**^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.35–7.23 (m, 14H), 7.12–7.06 (m, 4H), 5.19 (t, *J* = 9.7 Hz, 2H), 4.66 (dd, *J* = 10.3, 8.3 Hz, 2H), 4.04 (t, *J* = 8.8 Hz, 2H), 3.45 (s, 4H), 1.34 (s, 18H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 168.2, 149.7, 141.9, 133.8, 130.5, 128.7, 127.6, 127.1, 125.2, 75.1, 69.9, 48.9, 38.3, 34.6, 31.6; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{41}H_{47}N_2O_2$ 599.3632; found 599.3623; $[\alpha]_D^{24}$ = -50 (*c* = 1.0, $CHCl_3$, 589 nm).



The title compound **L41** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a yellow solid; **mp:** 159–160 °C;**^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.36–7.16 (m, 10H), 7.06–6.91 (m, 4H), 6.88–6.76 (m, 4H), 5.18 (t, *J* = 9.5 Hz, 2H), 4.72–4.55 (m, 2H), 4.02 (t, *J* = 8.5 Hz, 2H), 3.80 (s, 6H), 3.43 (q, *J* = 14.2 Hz, 4H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 168.1, 158.7, 142.0, 131.8, 129.0, 128.6, 127.6, 127.0, 113.8, 75.1, 69.7, 55.3, 49.1, 38.6; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{35}H_{35}N_2O_4$ 547.2591; found 547.2581; $[\alpha]_D^{24}$ = -180 (*c* = 1.0, $CHCl_3$, 589 nm).

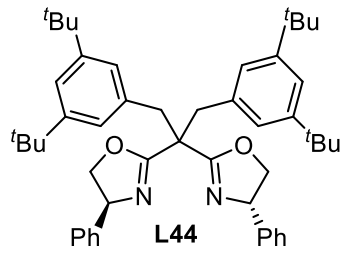


The title compound **L42** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a colorless oil; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.54 (d, *J* = 8.0 Hz, 4H), 7.45 (d, *J* = 8.0 Hz, 4H), 7.31–7.25 (m, 6H), 7.02 (dd, *J* = 7.3, 2.3 Hz, 4H), 5.20 (dd, *J* = 10.2, 8.7 Hz, 2H), 4.64 (dd, *J* = 10.3, 8.4 Hz, 2H), 4.06 (t, *J* = 8.6 Hz, 2H), 3.53 (q, *J* = 14.1 Hz, 4H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 167.1, 141.6, 140.8, 131.0, δ 129.5 (q, *J* = 32.5 Hz), 128.8, 127.9, 126.78, 126.76, 125.3 (q, *J* = 3.7 Hz), 124.4 (q, *J* = 272.0 Hz), 75.2, 69.7, 48.7, 40.1;**HRMS (ESI):** calcd. for $[M + H]^+$ $C_{35}H_{29}F_6N_2O_2$ 623.2128; found 623.2120; $[\alpha]_D^{24}$ = -140 (*c* = 1.0, $CHCl_3$, 589 nm).



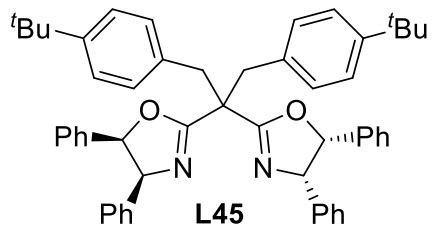
L43

The title compound **L43** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid; **mp:** 66–67 °C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.92–7.81 (m, 4H), 7.81–7.75 (m, 2H), 7.75–7.69 m, 2H), 7.56–7.41 (m, 6H), 7.19–7.11 (m, 2H), 7.11–6.98 (m, 4H), 6.95–6.80 (m, 4H), 5.18 (t, *J* = 9.6 Hz, 2H), 4.64 (dd, *J* = 10.2, 8.6 Hz, 2H), 4.02 (t, *J* = 8.8 Hz, 2H), 3.85–3.64 (m, 4H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 167.9, 141.8, 134.6, 133.6, 132.7, 129.6, 129.1, 128.6, 128.0, 127.9, 127.7, 127.5, 126.9, 126.1, 125.8, 75.3, 69.8, 49.3, 40.1; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{41}H_{35}N_2O_2$ 587.2693; found 587.2688; $[\alpha]_D^{24}$ = -50 (*c* = 1.0, $CHCl_3$, 589 nm).



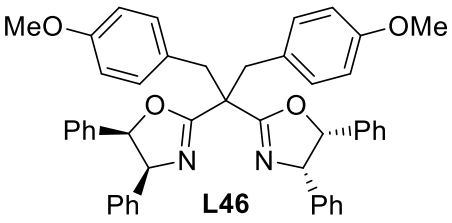
L44

The title compound **L44** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid; **mp:** 166–167 °C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.36 (dd, *J* = 13.4, 1.8 Hz, 6H), 7.22–7.11 (m, 6H), 6.79–6.66 (m, 4H), 5.15 (dd, *J* = 10.3, 8.7 Hz, 2H), 4.65 (dd, *J* = 10.3, 8.2 Hz, 2H), 3.97 (t, *J* = 8.5 Hz, 2H), 3.69 (d, *J* = 14.2 Hz, 2H), 3.55 (d, *J* = 14.2 Hz, 2H), 1.27 (s, 36H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 168.1, 150.6, 142.2, 136.1, 128.7, 127.4, 126.8, 125.2, 121.1, 75.3, 69.7, 48.7, 39.1, 34.9, 31.7; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{49}H_{63}N_2O_2$ 711.4884; found 711.4875; $[\alpha]_D^{24}$ = -60 (*c* = 1.0, $CHCl_3$, 589 nm).



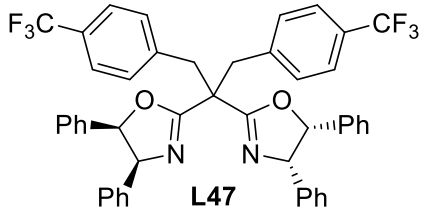
L45

The title compound **L45** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid; **mp:** 87–88 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.48–7.37 (m, 8H), 7.04–6.85 (m, 20H), 5.78 (d, *J* = 10.2 Hz, 2H), 5.46–5.39 (m, 2H), 3.83 (dd, *J* = 14.1, 1.7 Hz, 2H), 3.51 (dd, *J* = 14.2, 1.6 Hz, 2H), 1.37 (d, *J* = 1.4 Hz, 18H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 168.3, 149.9, 137.5, 135.9, 133.9, 130.6, 128.1, 127.7, 127.6, 127.5, 127.1, 125.2, 86.3, 73.7, 49.5, 39.8, 34.6, 31.6; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{53}H_{55}N_2O_2$ 751.4258; found 751.4254; $[\alpha]_D^{24}$ = 390 (*c* = 1.0, $CHCl_3$, 589 nm).

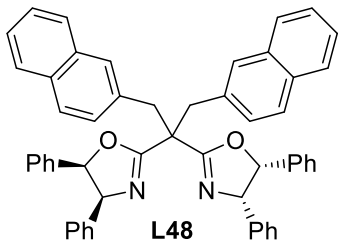


L46

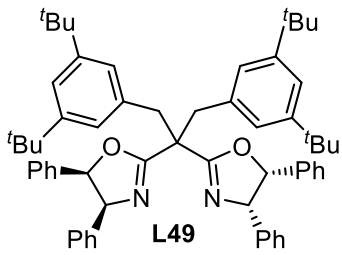
The title compound **L46** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid; **mp:** 152–153 °C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.49–7.39 (m, 4H), 7.04–6.83 (m, 24H), 5.78 (d, *J* = 10.2 Hz, 2H), 5.44 (d, *J* = 10.3 Hz, 2H), 3.87–3.76 (m, 8H), 3.49 (d, *J* = 14.1 Hz, 2H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 168.1, 158.7, 137.4, 135.9, 131.9, 129.0, 128.1, 127.62, 127.60, 127.4, 127.0, 113.7, 86.2, 73.7, 55.4, 49.8, 40.0; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{47}H_{43}N_2O_4$ 699.3217; found 699.3214; $[\alpha]_D^{24}$ = 420 (*c* = 1.0, $CHCl_3$, 589 nm).



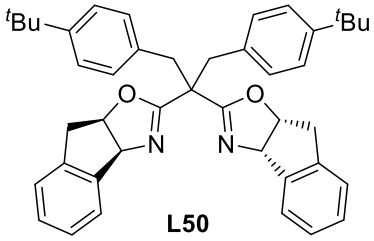
The title compound **L47** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid; **mp:** 73–74 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.83–7.44 (m, 8H), 7.25–6.48 (m, 20H), 5.74 (d, *J* = 10.3 Hz, 2H), 5.48 (d, *J* = 10.3 Hz, 2H), 3.93 (d, *J* = 13.9 Hz, 2H), 3.58 (d, *J* = 14.0 Hz, 2H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 167.38, 140.89, 137.06, 135.39, 131.20, δ 129.66 (q, *J* = 32.5 Hz), 128.03, 127.77, 127.72, 127.70, 127.29, 127.03, 125.29 (q, *J* = 3.8 Hz), 124.39 (q, *J* = 271.9 Hz), 86.60, 73.75, 49.32, 41.42; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{47}H_{37}F_6N_2O_2$ 775.2754; found 775.2746; $[\alpha]_D^{24}$ = 290 (*c* = 1.0, $CHCl_3$, 589 nm).



The title compound **L48** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid; **mp:** 90–91 °C; **^{1}H NMR (500 MHz, $CDCl_3$)**: δ 8.05 (d, *J* = 1.7 Hz, 2H), 7.95–7.87 (m, 4H), 7.87–7.80 (m, 2H), 7.70 (dd, *J* = 8.4, 1.7 Hz, 2H), 7.56–7.46 (m, 4H), 7.05–6.72 (m, 20H), 5.76 (d, *J* = 10.4 Hz, 2H), 5.45 (d, *J* = 10.4 Hz, 2H), 4.10 (d, *J* = 14.0 Hz, 2H), 3.81 (d, *J* = 14.0 Hz, 2H); **^{13}C NMR (125 MHz, $CDCl_3$)**: δ 168.1, 137.4, 135.8, 134.6, 133.6, 132.8, 129.9, 129.1, 128.1, 127.9, 127.83, 127.81, 127.7, 127.6, 127.5, 127.1, 127.0, 126.2, 125.9, 86.4, 73.8, 50.1, 41.7; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{53}H_{43}N_2O_2$ 739.3319; found 739.3322; $[\alpha]_D^{24}$ = 280 (*c* = 1.0, $CHCl_3$, 589 nm).

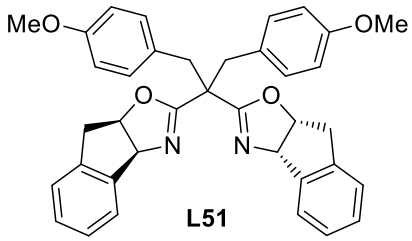


The title compound **L49** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid; **mp:** 91–92 °C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.38 (s, 6H), 7.04–6.82 (m, 20H), 5.72 (d, *J* = 10.0 Hz, 2H), 5.38 (d, *J* = 10.0 Hz, 2H), 3.92 (d, *J* = 14.3 Hz, 2H), 3.65 (d, *J* = 14.4 Hz, 2H), 1.36 (s, 36H); **^{13}C NMR (100 MHz, $CDCl_3$)** : δ 168.6, 150.5, 137.3, 136.3, 135.8, 128.1, 127.8, 127.7, 127.5, 127.0, 126.9, 124.9, 121.0, 86.4, 73.8, 49.1, 40. 7, 35.0, 31.8; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{61}H_{71}N_2O_2$ 863.5510; found 863.5504; $[\alpha]_D^{24}$ = 370 (*c* = 1.0, $CHCl_3$, 589 nm).



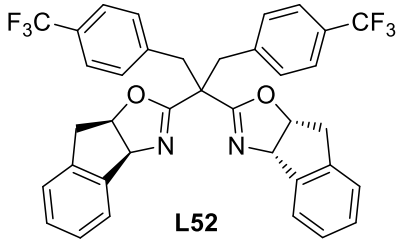
The title compound **L50** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a yellow solid; **mp:** 90–91 °C;**^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.50–7.41 (m, 2H), 7.40–7.23 (m, 6H), 6.89–6.75 (m, 4H), 6.75–6.61 (m, 4H), 5.61 (d, *J* = 7.8 Hz, 2H), 5.31 (t, *J* = 7.1 Hz, 2H), 3.35 (dd, *J* = 18.1, 6.8 Hz, 2H), 3.20 (d, *J* = 14.2 Hz, 2H), 3.07 (d, *J* = 18.0 Hz, 2H), 2.99 (d, *J* = 14.2 Hz, 2H), 1.20 (s, 18H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 167.7, 149.0, 141.7, 140.0, 133.1, 130.0, 128.5, 127.6, 126.0, 125.3,

124.6, 83.5, 76.7, 47.8, 39.5, 37.9, 34.3, 31.5; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{43}H_{47}N_2O_2$ 623.3632; found 623.3622; $[\alpha]_D^{24}$ = -480 (*c* = 1.0, $CHCl_3$, 589 nm).



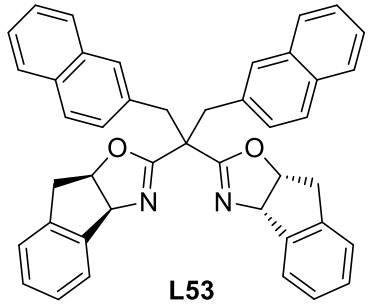
L51

The title compound **L51** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid; **mp:** 174–175 °C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.51–7.41 (m, 2H), 7.40–7.20 (m, 6H), 6.76–6.52 (m, 4H), 6.46–6.18 (m, 4H), 5.60 (d, *J* = 7.8 Hz, 2H), 5.40–5.20 (m, 2H), 3.67 (s, 6H), 3.35 (dd, *J* = 18.1, 6.7 Hz, 2H), 3.24–3.03 (m, 4H), 2.96 (d, *J* = 14.3 Hz, 2H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 167.6, 158.0, 141.7, 140.0, 131.3, 128.5, 128.2, 127.6, 126.0, 125.3, 113.1, 83.5, 76.6, 55.1, 47.9, 39.5, 37.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{37}H_{34}N_2O_2$ 571.2591; found 571.2581; $[\alpha]_D^{24}$ = -180 (*c* = 1.0, $CHCl_3$, 589 nm).



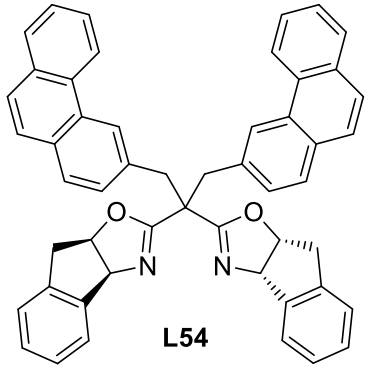
L52

The title compound **L52** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid; **mp:** 187–188 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.43–7.39 (m, 2H), 7.37 (dd, *J* = 7.3, 1.3 Hz, 2H), 7.33–7.27 (m, 4H), 6.97 (d, *J* = 8.0 Hz, 4H), 6.81 (d, *J* = 8.0 Hz, 4H), 5.62 (d, *J* = 7.8 Hz, 2H), 5.32 (ddd, *J* = 7.8, 6.7, 1.1 Hz, 2H), 3.37 (d, *J* = 6.7 Hz, 1H), 3.34 (t, *J* = 3.4 Hz, 2H), 3.31 (s, 1H), 3.03 (s, 2H), 3.00 (d, *J* = 3.9 Hz, 2H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 166.8, 141.5, 140.0, 139.8, 130.5, 128.8, δ 128.4 (q, *J* = 32.6 Hz), 127.8, 125.8, 125.4, 125.4, 124.7 (q, *J* = 3.7 Hz), 122.1 (q, *J* = 271.8 Hz), 84.0, 76.5, 47.3, 39.7, 39.3; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{37}H_{29}F_6N_2O_2$ 647.2128; found 647.2119; $[\alpha]_D^{24}$ = -220 (*c* = 1.0, $CHCl_3$, 589 nm).



L53

The title compound **L53** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid; **mp:** 105–106 °C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.70–7.62 (m, 2H), 7.48 (d, *J* = 7.4 Hz, 2H), 7.41–7.20 (m, 16H), 6.82 (dd, *J* = 8.5, 1.7 Hz, 2H), 5.64 (d, *J* = 8.0 Hz, 2H), 5.39–5.28 (m, 2H), 3.47 (d, *J* = 14.5 Hz, 2H), 3.36 (d, *J* = 6.9 Hz, 1H), 3.34–3.26 (m, 3H), 3.05 (d, *J* = 18.1 Hz, 2H); **^{13}C NMR (125 MHz, $CDCl_3$)**: δ 167.6, 141.5, 139.9, 133.9, 133.1, 132.2, 129.2, 128.7, 128.6, 127.9, 127.7, 127.5, 127.2, 126.0, 125.6, 125.41, 125.39, 83.6, 76.8, 47.7, 39.6, 39.0; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{43}H_{35}N_2O_2$ 611.2693; found 611.2686; $[\alpha]_D^{24}$ = -180 (*c* = 1.0, $CHCl_3$, 589 nm).

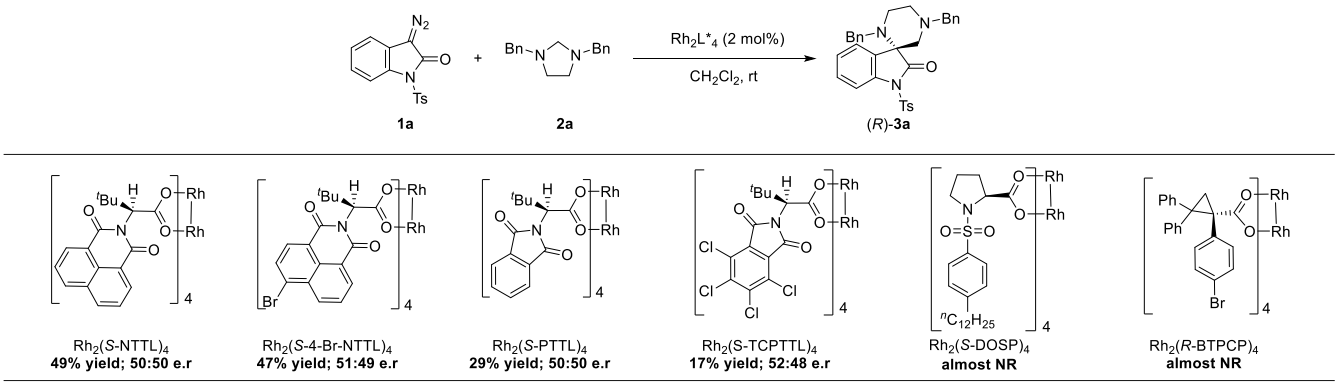


The title compound **L54** was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid; **mp:** 146–147 °C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.28 (d, *J* = 1.7 Hz, 2H), 8.19 (d, *J* = 8.3 Hz, 2H), 7.83–7.79 (m, 2H), 7.66 (d, *J* = 8.8 Hz, 2H), 7.59 (d, *J* = 8.9 Hz, 2H), 7.50–7.44 (m, 4H), 7.32–7.20 (m, 8H), 7.17–7.12 (m, 2H), 6.99 (dd, *J* = 8.2, 1.7 Hz, 2H), 5.62 (d, *J* = 7.9 Hz, 2H), 5.32 (ddd, *J* = 8.1, 6.8, 1.5 Hz, 2H), 3.64–3.49 (m, 4H), 3.30 (dd, *J* = 18.1, 6.9 Hz, 2H), 3.00 (d, *J* = 18.0 Hz, 2H); **^{13}C NMR (101 MHz, $CDCl_3$):** δ 167.6, 141.5, 139.8, 134.9, 132.1, 130.7, 130.2, 129.9, 128.6, 128.5, 128.4, 128.1, 127.6, 126.7, 126.54, 126.51, 126.4, 125.8, 125.2, 124.7, 122.7, 83.7, 76.7, 47.8, 39.7, 39.5, 27.1; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{51}H_{39}N_2O_2$ 711.3006; found 711.3000; $[\alpha]_D^{24}$ = 20 (*c* = 1.0, $CHCl_3$, 589 nm).

6.2 Optimization Studies

Initially, we utilized diazooxindole **1a** with imidazolidine **2a** as model substrates to evaluate several well-established chiral rhodium catalysts. Unfortunately, product **3** was obtained with no stereocontrol (Table S7).

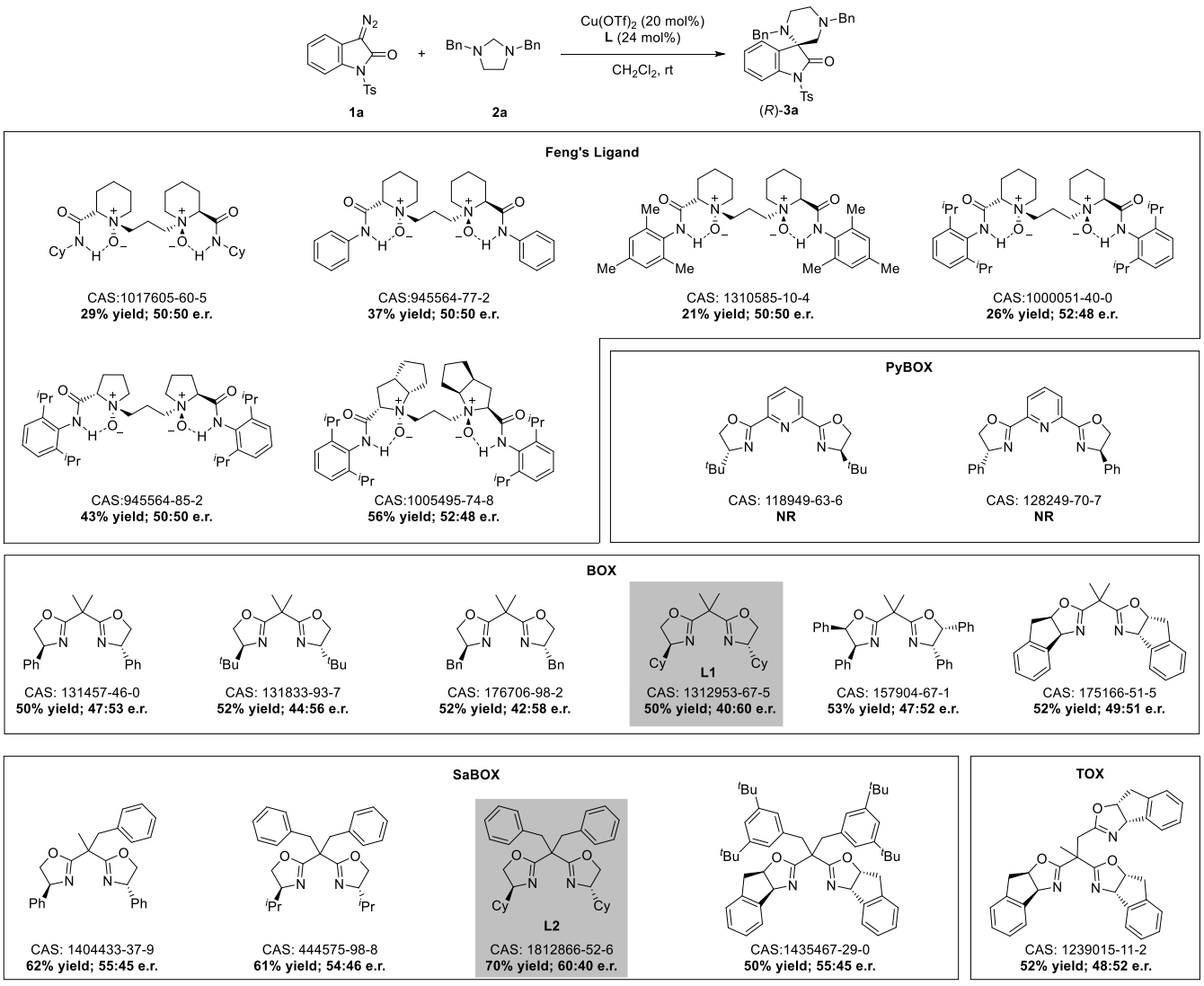
Table S7. Screening chiral rhodium catalyst.[a],[b],[c]



[a] Reaction conditions: $Rh_2L^*_4$ (2 mol%) and **L** were dissolved in CH_2Cl_2 (1.0 mL) in a vial and stirred for 1 h at rt. $Rh_2L^*_4$ (2 mol%) and **2a** (0.2 mmol) were dissolved in CH_2Cl_2 (2.0 mL). Then, a solution of **1a** (0.24 mmol) in CH_2Cl_2 (2.0 mL) was slowly injected via an automatic syringe pump over 1 h. The reaction was continued at rt for 24 h. [b] Isolated yields. [c] e.r. values were determined by chiral HPLC analysis.

We then evaluated different types of commercially available chiral ligands under $Cu(OTf)_2$ in CH_2Cl_2 at rt. Gratifyingly, Cy-BOX **L1** gave promising result (50% yield with 60:40 e.r.), and Cy-SaBOX **L2** gave better result (70% yield with 60:40 e.r.). These results were summarized in Table S8.

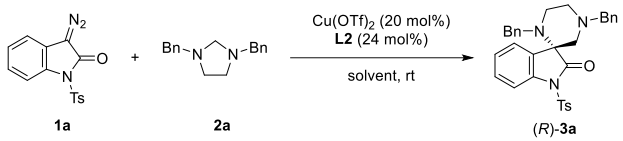
Table S8. Screening $Cu(OTf)_2$/**L*** catalytic system.[a],[b],[c]



[a] Reaction conditions: $Cu(OTf)_2$ (20 mol%) and **L** (24 mol%) were dissolved in CH_2Cl_2 (1.0 mL) in a vial and stirred for 1 h at rt. A solution of **2a** (0.2 mmol) in CH_2Cl_2 (1.0 mL) was injected in one portion. Then, a solution of **1a** (0.24 mmol) in CH_2Cl_2 (2.0 mL) was slowly injected via an automatic syringe pump over 1 h. The reaction was continued at rt for 24 h. [b] Isolated yields. [c] e.r. values were determined by chiral HPLC analysis.

Various solvents were further evaluated under $Cu(OTf)_2$/**L2** catalytic system at rt, as shown in Table S9. Although most solvents gave low e.r. values or no reaction at all (Table S9, entries 1-16), HFIP gave much improved yield and enantioselectivity (Table S9, entry 17). TFE gave almost comparable enantioselectivity but much lower yield (Table S9, entry 18). Lowering the temperature to -4 ^oC further increased the enantioselectivity (Table S9, entry 19).

Table S9. Screening solvent.[a],[b],[c]

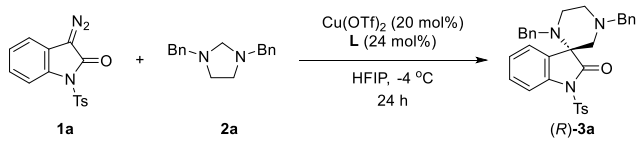


entry	solvent	yield (%)[b]	e.r.[c]
1	CH_2Cl_2	70	60:40
2	DCE	51	58:42
3	$CHCl_3$	35	57:43
4	1,4-dioxane	44	57:43
5	DME	49	59:41
6	Et_2O	33	57:43
7	THF	38	59:41
8	*n*-hexane	-	-
9	MeCN	-	-
10	MeOH	-	-
11	DMF	-	-
12	DMSO	-	-
13	benzene	45	56:44
14	toluene	43	54:46
15	PhCl	47	55:45
16	$PhCF_3$	33	55:45
17	HFIP	80	73:27
18	TFE	40	70:30
19[d]	HFIP	71	77:23

[a] Reaction conditions: $Cu(OTf)_2$ (20 mol%) and **L2** (24 mol%) were dissolved in solvent (1.0 mL) in a vial and stirred for 1 h at rt. A solution of **2a** (0.2 mmol) in solvent (1.0 mL) was injected in one portion. Then, a solution of **1a** (0.24 mmol) in solvent (2.0 mL) was slowly injected via an automatic syringe pump over 1 h. The reaction was continued at rt for 24 h. [b] Isolated yields. [c] E.r. values were determined by chiral HPLC analysis. [d] At -4 ºC.

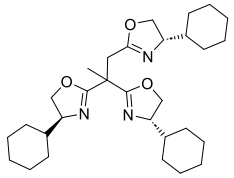
For BOX ligands, increasing the steric hindrance at the bridged methylene of the bisoxazoline is generally beneficial for the stereocontrol. Thus, a series of bulky SaBOX ligands (**L4** and **L6-17**) were synthesized and evaluated by using $Cu(OTf)_2$ in HFIP at -4 °C. Among them, the 2-naphthyl-armed Cy-SaBOX **L4** stood out as optimal, offering 84:16 e.r.. Based on the encouraging result of Cy-SaBOX **L4**, more SaBOX ligands (**L5** and **L18-24**) were further synthesized and evaluated. Among them, the 3-phenanthrenyl-armed Cy-SaBOX **L5** proved to be a bit better than **L4**, giving 86:14 e.r.. In comparison, the Cy-TOX **L3** led to almost no stereocontrol. In addition, other chiral SaBOX ligands with substituents other than Cy with different steric and electric properties were not suitable for this reaction (**L25-54**).

Table S10. Screening more SaBOX ligands.[a],[b],[c]

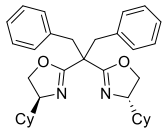


1a 2a (*R*)-3a

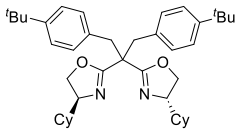
Cy-TOX



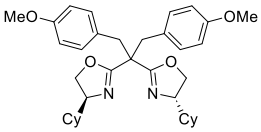
L3
54% yield; 57:43 e.r.



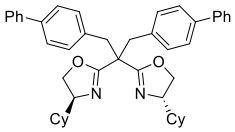
L2
71% yield; 77:23 e.r.



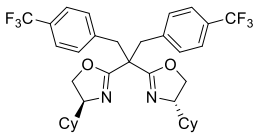
L6
77% yield; 58:42 e.r.



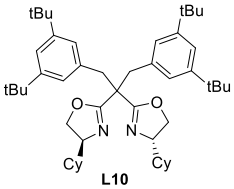
L7
76% yield; 66:34 e.r.



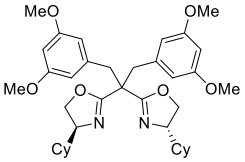
L8
78% yield; 72:28 e.r.



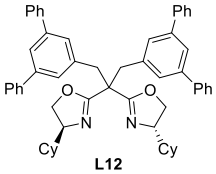
L9
73% yield; 69:31 e.r.



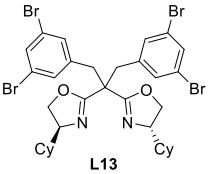
L10
NR



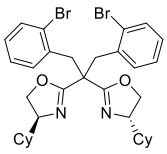
L11
76% yield; 67:33 e.r.



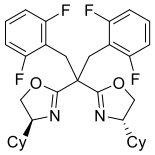
L12
74% yield; 70:30 e.r.



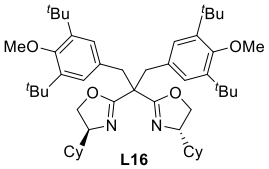
L13
65% yield; 72:28 e.r.



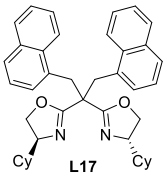
L14
67% yield; 72:28 e.r.



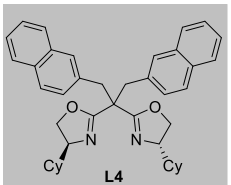
L15
75% yield; 74:26 e.r.



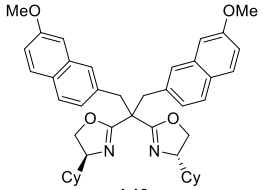
L16
54% yield; 65:35 e.r.



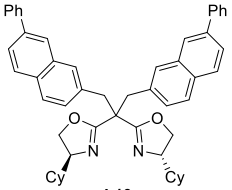
L17
72% yield; 83:17 e.r.



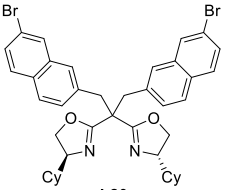
L4
82% yield; 84:16 e.r.



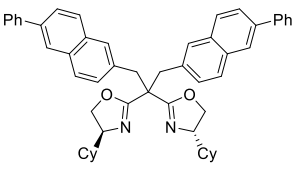
L18
55% yield; 81:19 e.r.



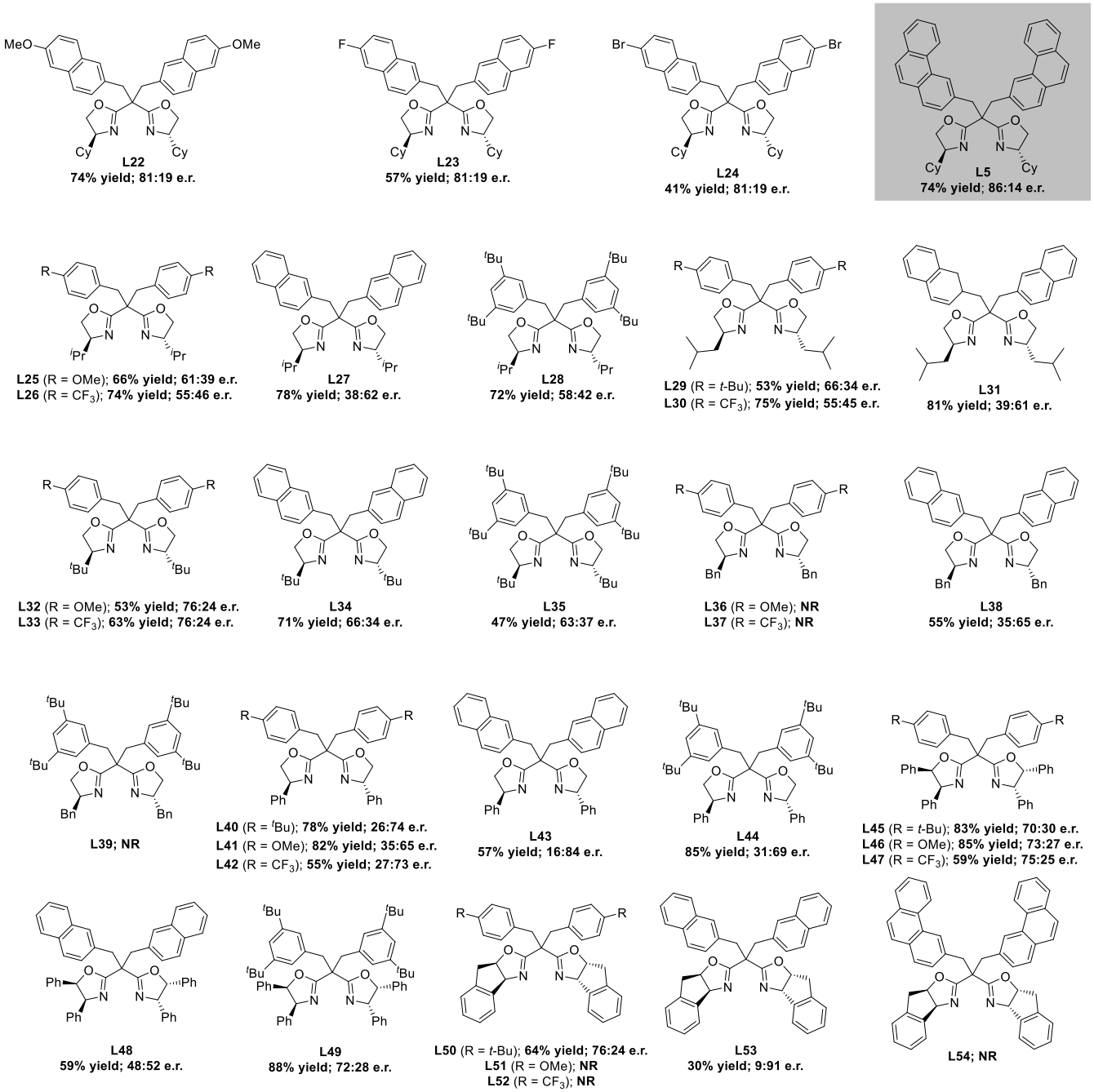
L19
80% yield; 82:18 e.r.



L20
47% yield; 77:23 e.r.



L21
65% yield; 81:19 e.r.

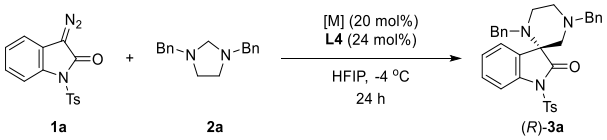


[a] Reaction conditions: $Cu(OTf)_2$ (20 mol%) and **L** (24 mol%) were dissolved in HFIP (1.0 mL) in a vial and stirred for 1 h at rt. A solution of **2a** (0.2 mmol) in HFIP (1.0 mL) was injected in one portion. The reaction mixture was cooled down to -4 °C. Then, a solution of **1a** (0.24 mmol) in HFIP (2.0 mL) was slowly injected via an automatic syringe pump over 1 h. The reaction was continued at -4 °C for 24 h. [b] Isolated yields. [c] E.r. values were determined by chiral HPLC analysis.

Next, the combinations of various transition metal catalysts with **L4** were tested in HFIP at -4 °C. Herein, **L4** rather than **L5** was utilized, mainly because the two ligands led to similar results, while the synthesis of **L4** was much more cost-effective. As summarized in Table S11, we can draw several conclusions. (i) Copper catalyst was generally suitable for this reaction (Table S11, entries 1-13), while high temperature

was necessary for other transition metals, leading to poor or no stereocontrol (Table S11, entries 14-23). (ii) The anion of copper salt plays a key role for this reaction. Copper triflate or perchlorate was suitable for this reaction (Table S11, entries 1, 5-6 and 8-10), while copper bromide was totally inert for this transformation (Table S11, entries 2 and 7). (iii) Copper(I) and copper(II) triflate gave similar result (Table S11, entry 1 vs entry 6).

Table S11. Screening transition metal catalyst.[a],[b],[c]



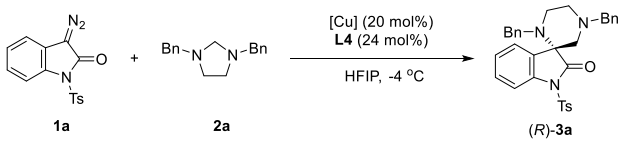
entry	[M]	yield (%)[b]	e.r.[c]
1	$Cu(OTf)_2$	82	84:16
2	$CuBr_2$	<5	
3[d]	$Cu(hfac)_2$	81	82:18
4	$Cu(H_2O)_4(OTf)_2$	58	80:20
5	$Cu(ClO_4)_2•6H_2O$	82	83:17
6	CuOTf	84	83:17
7	CuBr	<5	
8	CuOTf•1/2toluene	83	83:17
9	CuOTf•1/2benzene	78	82:18
10	$Cu(MeCN)_4OTf$	37	82:18
11	$Cu(MeCN)_4NTf_2$	39	82:18
12	$Cu(MeCN)_4PF_6$	34	81:19
13	$Cu(MeCN)_4BF_4$	36	82:18
14[e]	$FeCl_3•6H_2O$	34	50:50
15[e]	$Ni(ClO_4)_2•6H_2O$	45	59:41
16[e]	$Co(OTf)_2$	56	55:45
17[e]	$Zn(OTf)_2$	74	58:42
18[e]	$Al(OTf)_3$	54	53:47
19[e]	AgOTf	45	55:45

20[e]	$Yb(OTf)_3$	30	53:47
21[e]	$In(OTf)_3$	56	55:45
22[e]	$InCl_3$	43	49:51
23[e]	$Sc(OTf)_3$	44	53:47

[a] Reaction conditions: [M] (20 mol%) and **L4** (24 mol%) were dissolved in HFIP (1.0 mL) in a vial and stirred for 1 h at rt. A solution of **2a** (0.2 mmol) in HFIP (1.0 mL) was injected in one portion. The reaction mixture was cooled down to -4 °C. Then, a solution of **1a** (0.24 mmol) in HFIP (2.0 mL) was slowly injected via an automatic syringe pump over 4 h. The reaction was continued at -4 °C for 24 h. [b] Isolated yields. [c] E.r. values were determined by chiral HPLC analysis. [d] At rt. [e]At 80 °C.

These results promoted us to explore the subtle influence of copper salt anions as shown in Table S12. Unfortunately, the enantioselectivity could be hardly improved. Also, the addition of 4Å MS had no obvious influence for the reaction efficiency and stereocontrol.

Table S12. Evaluation of the anion influence.[a],[b],[c]



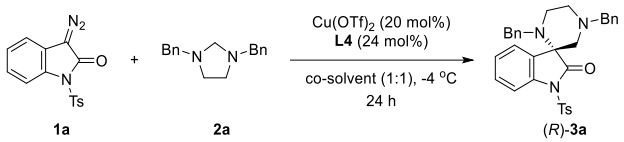
entry	[Cu]	yield (%)[b]	e.r.[c]
1	$Cu(OTf)_2$	82	84:16
2	$Cu(ClO_4)_2•6H_2O$	87	83:17
3	$Cu(BF_4)_2•xH_2O$	86	83:17
4	$CuSO_4$	43	68:32
5	$Cu(NO_3)_2•2.5H_2O$	72	83:17
6[d]	$Cu(NTf)_2$	76	82:18
7[e]	$Cu(PF_6)_2$	84	82:18
8[f]	$Cu(SbF_6)_2$	83	84:16
9[g]	$Cu(BAr_F)_2$	NR	

[a] Reaction conditions: [M] (20 mol%), **L4** (24 mol%) and 4Å MS (100 mg) were added in HFIP (1.5 mL) in a vial and stirred for 3 h at rt. A solution of **2a** (0.2 mmol) in HFIP (0.5 mL) was injected in one portion. The reaction mixture was cooled down to -4 °C. Then, a solution of **1a** (0.24 mmol) in HFIP (2.0 mL) was slowly injected via an automatic syringe pump over 1 h. The reaction was continued at -4 °C for

24 h. [b] Isolated yields. [c] E.r. values were determined by chiral HPLC analysis. [d] Generated in situ by stirring $CuBr_2$ (20 mol%) and $AgNTf_2$ (40 mol%). [e] Generated in situ by stirring $CuBr_2$ (20 mol%) and $AgPF_6$ (40 mol%). [f] Generated in situ by stirring $CuBr_2$ (20 mol%) and $AgSbF_6$ (40 mol%). [g] Generated in situ by stirring $CuBr_2$ (20 mol%) and $NaBAr_F$ (40 mol%).

In addition, we tried some co-solvent systems, while no improvement was obtained (Table S13).

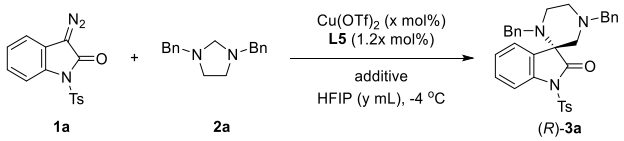
Table S13. Screening co-solvent system.[a],[b],[c]



entry	co-solvent	yield (%)[b]	e.r.[c]
1	CH_2Cl_2/HFIP	88	83:17
2	$CHCl_3$/HFIP	78	78:22
3	DCE/HFIP	68	80:20
4	toluene /HFIP	48	75:25
5	PhCl/HFIP	70	77:23
6	$PhCF_3$/HFIP	72	83:17
7	TFE/HFIP	52	82:18

[a] Reaction conditions: $Cu(OTf)_2$ (20 mol%) and **L4** (24 mol%) were dissolved in co-solvent (1.0 mL) in a vial and stirred for 1 h at rt. A solution of **2a** (0.2 mmol) in co-solvent (1.0 mL) was injected in one portion. The reaction mixture was cooled down to -4 °C. Then, a solution of **1a** (0.24 mmol) in co-solvent (2.0 mL) was slowly injected via an automatic syringe pump over 1 h. The reaction was continued at -4 °C for 24 h. [b] Isolated yields. [c] E.r. values were determined by chiral HPLC analysis.

Table S14. Screening other reaction parameters.[a],[b],[c]

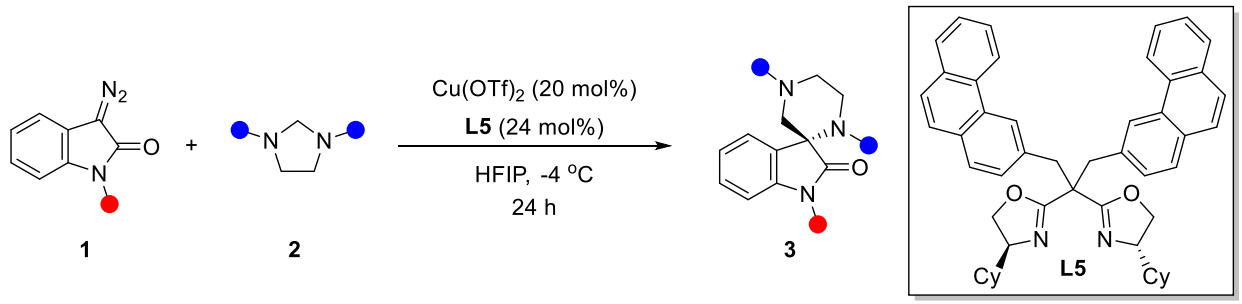


entry	x	additive	y (mL)	yield (%)[b]	e.r.[c]
1	20	-	4	81	86:14
2	10	-	4	72	86:14

3	5	-	4	70	86:14
4[d]	20	4Å MS	4	52	85:15
5	20	-	3	78	85:15
6	20	-	6	66	78:22

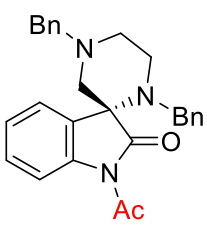
[a] Reaction conditions: $Cu(OTf)_2$ (x mol%), **L5** (1.2x mol%) and additive were added in HFIP in a vial and stirred for 1 h at rt. A solution of **2a** (0.2 mmol) in HFIP was injected in one portion. The reaction mixture was cooled down to -4 °C. Then, a solution of **1a** (0.24 mmol) in HFIP was slowly injected via an automatic syringe pump over 1 h. The reaction was continued at -4 °C for 24 h. [b] Isolated yields. [c] E.r. values were determined by chiral HPLC analysis. [d] 4Å MS (100 mg).

6.3 Protecting Group Effect and Substrate Scope



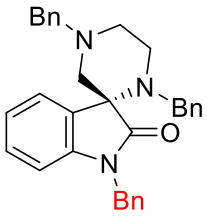
General Procedure: $Cu(OTf)_2$ (14.5 mg, 0.04 mmol, 20 mol%) and **L5** (33.5 mg, 0.048 mmol, 24 mol%) were dissolved in HFIP (1.0 mL) in a vial and stirred for 1 h at rt. A solution of **2** (0.2 mmol, 1.0 equiv.) in HFIP (1.0 mL) was injected in one portion. The reaction mixture was cooled down to -5 °C. Then, a solution of **1** (0.24 mmol, 1.2 equiv.) in HFIP (2.0 mL) was slowly injected via an automatic syringe pump over 4 h. The reaction was continued at -4 °C for 24 h. The resulting mixture was warmed to rt, concentrated under reduced pressure. The residue was purified by flash column chromatography (hexanes/EtOAc) on silica gel to afford the corresponding products.

Compound (*R*)-4



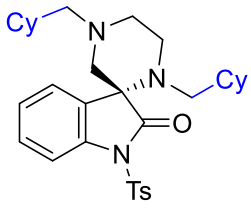
The title compound was prepared via the general procedure, purified by flash column chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid in 10% yield (8.5 mg); $[\alpha]_D^{24}$ = +10 (*c* = 1.0, $CHCl_3$, 589 nm); 55:45 e.r. was determined by HPLC analysis: Chiralpak IG-3 column (25 cm), hexanes/^{i}PrOH = 95/5, 1.0 mL/min, 240 nm; $t_{(major)}$ = 8.1 min, $t_{(minor)}$ = 7.2 min.

Compound (*R*)-7



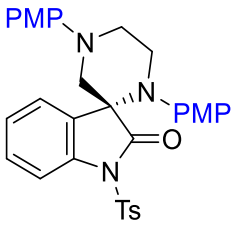
The title compound was prepared via the general procedure, purified by flash column chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a yellow oil in 68% yield (64.4 mg); $[\alpha]_D^{24}$ = +60 (*c* = 1.0, $CHCl_3$, 589 nm); 70.5:29.5 e.r. was determined by HPLC analysis: Chiralpak IE-3 column (25 cm), hexanes/^{i}PrOH = 80/20, 1.0 mL/min, 250 nm; $t_{(major)}$ = 16.7 min, $t_{(minor)}$ = 21.5 min.

Compound (*R*)-34



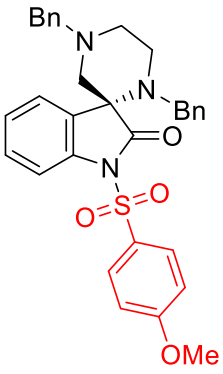
The title compound was prepared via the general procedure, purified by flash column chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a yellow solid in 18% yield (19.8 mg); $[\alpha]_D^{24}$ = -20 (*c* = 1.0, $CHCl_3$, 589 nm); 76:24 e.r. was determined by HPLC analysis: Chiralpak IA-3 column (25 cm), hexanes/^{i}PrOH =95/5, 1.0 mL/min, 270 nm; $t_{(major)}$ = 7.8 min, $t_{(minor)}$ = 6.4 min.

Compound (*R*)-36



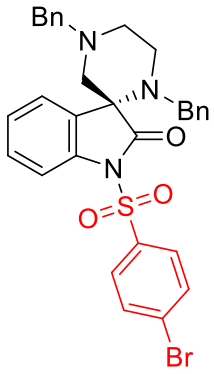
The title compound was prepared via the general procedure, purified by flash column chromatography (hexanes/EtOAc = 5:1) on silica gel and obtained as a white solid in 22% yield (25 mg); $[\alpha]_D^{24}$ = +30 (*c* = 1.0, $CHCl_3$, 589 nm); 55:45 e.r. was determined by HPLC analysis: Chiralpak IA-3 column (25 cm), hexanes/^{i}PrOH = 70/30, 1.0 mL/min, 240 nm; $t_{(major)}$ = 10.3 min, $t_{(minor)}$ = 16.2 min.

Compound (*R*)-58



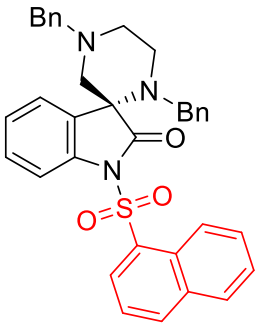
The title compound was prepared via the general procedure, purified by flash column chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as a pink solid in 70% yield (77.5 mg); **mp:** 149–150 °C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.00 (d, *J* = 8.8 Hz, 2H), 7.93 (d, *J* = 8.1 Hz, 1H), 7.55 (d, *J* = 7.5 Hz, 1H), 7.36 (t, *J* = 7.9 Hz, 1H), 7.29–7.13 (m, 9H), 7.04 (d, *J* = 7.0 Hz, 2H), 6.89 (d, *J* = 8.6 Hz, 2H), 3.76 (s, 3H), 3.55 (d, *J* = 13.5 Hz, 1H), 3.38 (d, *J* = 13.5 Hz, 1H), 3.21–3.05 (m, 1H), 2.97 (d, *J* = 13.1 Hz, 1H), 2.77–2.53 (m, 4H), 2.46–2.32 (m, 2H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 174.8, 164.4, 139.2, 138.2, 137.8, 130.4, 129.9, 129.7, 129.3, 128.7, 128.4, 128.2, 127.2, 127.1, 125.1, 125.0, 114.3, 114.0, 65.9, 62.3, 60.3, 55.7, 55.3, 53.0, 45.8; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{32}H_{32}N_3O_4S$ 554.2108, found 554.2100; $[\alpha]_D^{24}$ = +80 (*c* = 1.0, $CHCl_3$, 589 nm); 87:13 e.r. was determined by HPLC analysis: Chiralpak IA-3 column (25 cm), hexanes/^{i}PrOH = 80/20, 1.0 mL/min, 280 nm; $t_{(major)}$ = 9.0 min, $t_{(minor)}$ =7.7 min.

Compound (*R*)-59



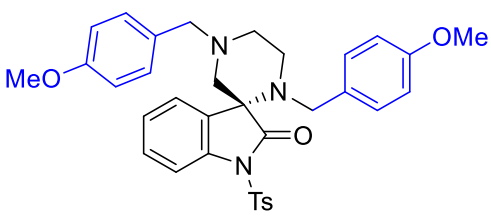
The title compound was prepared via the general procedure, purified by flash column chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as a pink solid in 89% yield (107.3 mg); **mp:** 161–162 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.97–7.86 (m, 3H), 7.61 (d, *J* = 8.6 Hz, 2H), 7.53 (d, *J* = 7.5 Hz, 1H), 7.39–7.33 (m, 1H), 7.28–7.15 (m, 9H), 7.10–7.04 (m, 2H), 3.59 (d, *J* = 13.5 Hz, 1H), 3.36 (d, *J* = 13.5 Hz, 1H), 3.22–3.10 (m, 1H), 3.04 (d, *J* = 13.1 Hz, 1H), 2.77 (d, *J* = 11.3 Hz, 1H), 2.70–2.55 (m, 3H), 2.44–2.30 (m, 2H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 174.7, 138.8, 138.0, 137.6, 137.4, 132.5, 129.90, 129.87, 129.5, 129.3, 128.7, 128.5, 128.37, 128.35, 127.3, 127.2, 125.5, 124.9, 113.9, 65.9, 62.3, 60.2, 55.2, 53.1, 45.8; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{31}H_{29}BrN_3O_3S$ 602.1108, found 602.1099; $[\alpha]_D^{24}$ = +30 (*c* = 1.0, $CHCl_3$, 589 nm); 86:14 e.r. was determined by HPLC analysis: Chiralpak IA-3 column (25 cm), hexanes/^{i}PrOH = 95/5, 1.0 mL/min, 254 nm; $t_{(major)}$ = 13.3 min, $t_{(minor)}$ = 10.0 min.

Compound (*R*)-60



The title compound was prepared via the general procedure, purified by flash column chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as a white solid in 83% yield (95.2 mg); **mp:** 176–177 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.65 (d, *J* = 7.4 Hz, 1H), 8.43 (d, *J* = 8.5 Hz, 1H), 8.09 (d, *J* = 8.2 Hz, 1H), 8.03 (d, *J* = 8.1 Hz, 1H), 7.84 (d, *J* = 8.1 Hz, 1H), 7.64 (t, *J* = 7.8 Hz, 1H), 7.52 (d, *J* = 7.5 Hz, 1H), 7.45–7.37 (m, 2H), 7.37–7.31 (m, 1H), 7.27–7.20 (m, 1H), 7.19–7.07 (m, 8H), 6.92–6.84 (m, 2H), 3.34 (d, *J* = 13.5 Hz, 1H), 3.23 (d, *J* = 13.5 Hz, 1H), 3.03–2.86 (m, 2H), 2.60 (d, *J* = 11.2 Hz, 1H), 2.53–2.41 (m, 3H), 2.32 (d, *J* = 11.8 Hz, 1H), 2.30–2.21 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 174.1, 139.5, 138.1, 137.5, 135.9, 134.1, 133.3, 133.2, 129.7, 129.3, 129.1, 128.8, 128.7, 128.4, 128.32, 128.25, 128.15, 127.12, 127.08, 127.04, 125.1, 125.0, 124.3, 123.7, 114.2, 66.0, 62.1, 60.6, 55.4, 52.5, 45.7; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{35}H_{32}N_3O_3S$ 574.2159, found 574.2149; $[\alpha]_D^{24}$ = +10 (*c* = 1.0, $CHCl_3$, 589 nm); 87.5:12.5 e.r. was determined by HPLC analysis: Chiralpak IA-3 column (25 cm), hexanes/^{i}PrOH = 95/5, 1.0 mL/min, 254 nm; $t_{(major)}$ = 14.6 min, $t_{(minor)}$ = 13.0 min.

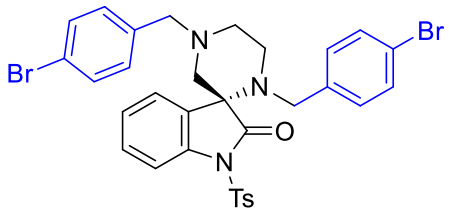
Compound (*R*)-61



The title compound was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as a red solid in 72% yield (86.1 mg); **mp:** 133–134 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.97–7.90 (m, 3H), 7.53 (d, *J* = 7.5 Hz, 1H), 7.39–7.32 (m, 1H), 7.27–7.18 (m, 3H),

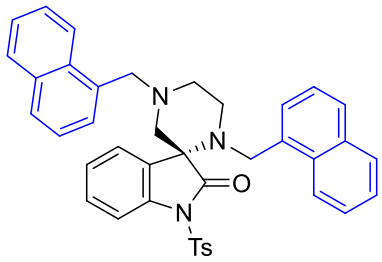
7.14 (d, *J* = 8.5 Hz, 2H), 6.93 (d, *J* = 8.3 Hz, 2H), 6.77 (d, *J* = 8.6 Hz, 2H), 6.74 (d, *J* = 8.6 Hz, 2H), 3.77 (s, 3H), 3.75 (s, 3H), 3.47 (d, *J* = 13.3 Hz, 1H), 3.31 (d, *J* = 13.3 Hz, 1H), 3.13–3.01 (m, 1H), 2.87 (d, *J* = 12.8 Hz, 1H), 2.72–2.60 (m, 2H), 2.58–2.47 (m, 2H), 2.40–2.29 (m, 5H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 174.8, 158.82, 158.79, 145.7, 139.1, 135.5, 130.2, 129.84, 129.76, 129.73, 129.6, 129.4, 128.0, 125.1, 125.0, 114.0, 113.8, 113.6, 66.0, 61.7, 60.2, 55.4, 55.3, 54.7, 52.8, 45.7, 21.8; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{34}H_{36}N_3O_5S$ 598.2370, found 598.2357; $[\alpha]_D^{24}$ = +90 (*c* = 1.0, $CHCl_3$, 589 nm); 91:9 e.r. was determined by HPLC analysis: Chiralpak IA-3 column (25 cm), hexanes/^{i}PrOH = 80/20, 1.0 mL/min, 250 nm; $t_{(major)}$ = 13.2 min, $t_{(minor)}$ = 9.0 min.

Compound (*R*)-62



The title compound was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as a white solid in 84% yield (116.8 mg); **mp:** 149–150 °C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.99–7.89 (m, 3H), 7.49 (d, *J* = 7.5 Hz, 1H), 7.40–7.30 (m, 5H), 7.26 (d, *J* = 8.1 Hz, 2H), 7.21 (td, *J* = 7.5, 1.0 Hz, 1H), 7.10 (d, *J* = 8.4 Hz, 2H), 6.93 (d, *J* = 8.4 Hz, 2H), 3.50 (d, *J* = 13.7 Hz, 1H), 3.30 (d, *J* = 13.7 Hz, 1H), 3.19–3.06 (m, 1H), 2.95 (d, *J* = 13.3 Hz, 1H), 2.76–2.66 (m, 1H), 2.65–2.51 (m, 3H), 2.45–2.30 (m, 5H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 174.5, 145.8, 139.1, 137.2, 136.8, 135.5, 131.6, 131.4, 130.3, 130.1, 130.0, 129.8, 128.9, 128.1, 125.2, 124.8, 121.04, 120.97, 114.1, 65.8, 61.5, 60.1, 54.7, 53.0, 45.9, 21.8; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{32}H_{30}Br_2N_3O_3$ 694.0369, found 694.0356; $[\alpha]_D^{24}$ = +30 (*c* = 1.0, $CHCl_3$, 589 nm); 79:21 e.r. was determined by HPLC analysis: Chiralpak IA-3 column (25 cm), hexanes/^{i}PrOH = 80/20, 1.0 mL/min, 230 nm; $t_{(major)}$ = 9.6 min, $t_{(minor)}$ = 8.0 min.

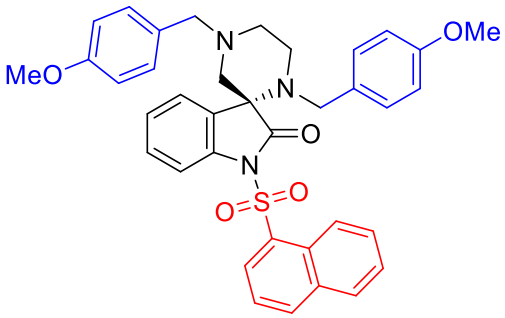
Compound (*R*)-63



The title compound was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as a white solid in 41% yield (52.3 mg); **mp:** 228–229 °C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.24–8.16 (m, 1H), 8.01 (d, *J* = 8.2 Hz, 1H), 7.94 (d, *J* = 8.1 Hz, 2H), 7.88–7.64 (m, 6H), 7.54–7.23 (m, 8H), 7.23–7.15 (m, 2H), 7.05 (d, *J* = 8.0 Hz, 2H), 3.90 (d, *J* = 13.1 Hz, 1H), 3.76 (d, *J* = 13.1 Hz, 1H), 3.17 (d, *J* = 13.0 Hz, 1H), 3.02 (d, *J* = 12.9 Hz, 1H), 2.94–2.74 (m, 2H), 2.69 (d, *J* = 11.5 Hz, 1H), 2.62–2.39 (m, 3H), 2.01 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 175.0, 145.8, 139.0, 135.2, 133.9, 133.7, 133.4, 133.1, 132.4, 132.1, 129.74, 129.72, 128.7, 128.42, 128.36, 128.2, 128.0, 127.9, 127.4, 127.2, 126.4, 125.82, 125.80, 125.77, 125.67, 125.24, 125.16, 124.8, 124.4, 114.1, 66.4, 60.9, 60.8, 53.5, 52.5, 46.1, 21.4; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{40}H_{36}N_3O_3S$ 638.2472, found 638.2463; $[\alpha]_D^{24}$ = +60 (*c* = 1.0, $CHCl_3$, 589 nm); 81.5:18.5

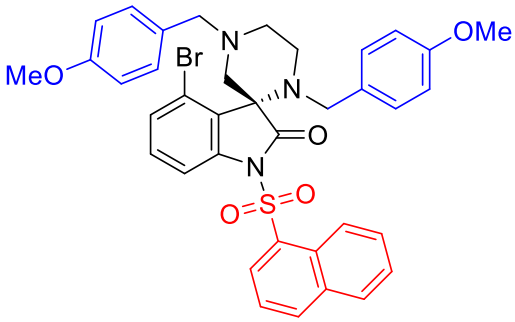
e.r. was determined by HPLC analysis: Chiralpak IA-3 column (25 cm), hexanes/^{i}PrOH = 95/5, 1.0 mL/min, 254 nm; $t_{(major)}$ = 14.5 min, $t_{(minor)}$ = 16.6 min.

Compound (*R*)-64



The title compound was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as a white solid in 77% yield (97.6 mg); **mp:** 100–101 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.64 (dd, *J* = 7.5, 1.1 Hz, 1H), 8.44 (d, *J* = 8.6 Hz, 1H), 8.10 (d, *J* = 8.2 Hz, 1H), 8.03 (d, *J* = 8.1 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.68–7.62 (m, 1H), 7.52 (d, *J* = 7.0 Hz, 1H), 7.45–7.38 (m, 2H), 7.38–7.33 (m, 1H), 7.27–7.20 (m, 1H), 7.01 (d, *J* = 8.5 Hz, 2H), 6.78 (d, *J* = 8.6 Hz, 2H), 6.76–6.66 (m, 4H), 3.77 (s, 3H), 3.73 (s, 3H), 3.27 (d, *J* = 13.3 Hz, 1H), 3.17 (d, *J* = 13.3 Hz, 1H), 2.96–2.80 (m, 2H), 2.62–2.53 (m, 1H), 2.49–2.42 (m, 2H), 2.37 (d, *J* = 13.1 Hz, 1H), 2.32–2.18 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 174.1, 158.8, 158.7, 139.5, 135.8, 134.1, 133.23, 133.20, 130.1, 129.8, 129.7, 129.5, 129.4, 129.3, 129.2, 128.8, 128.4, 127.1, 125.0, 124.3, 123.7, 114.2, 113.7, 113.5, 66.1, 61.6, 60.5, 55.4, 55.3, 54.8, 52.5, 45.5; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{37}H_{36}N_3O_5S$ 634.2370; found 634.2360; $[\alpha]_D^{24}$ = +60 (*c* = 1.0, $CHCl_3$, 589 nm); 93:7 e.r. was determined by HPLC analysis: Chiralpak IA-3 column (25 cm), hexanes/^{i}PrOH = 80/20, 1.0 mL/min, 310 nm; $t_{(major)}$ = 10.9 min, $t_{(minor)}$ = 9.3 min.

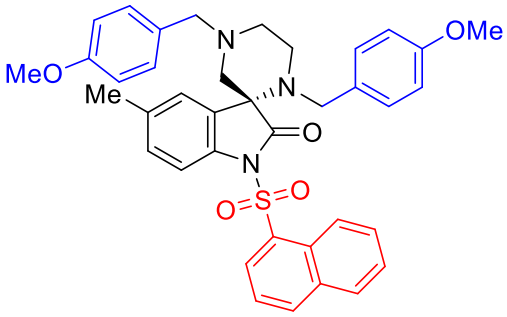
Compound (*R*)-65



The title compound was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as a pink solid in 45% yield (64.1 mg); **mp:** 167–168 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.66 (dd, *J* = 7.5, 1.3 Hz, 1H), 8.38 (d, *J* = 8.5 Hz, 1H), 8.16 (d, *J* = 8.2 Hz, 1H), 8.04 (d, *J* = 8.0 Hz, 1H), 7.91 (d, *J* = 8.0 Hz, 1H), 7.68 (t, *J* = 7.9 Hz, 1H), 7.49–7.44 (m, 1H), 7.43–7.38 (m, 1H), 7.36 (d, *J* = 7.8 Hz, 1H), 7.29–7.24 (m, 1H), 7.03 (d, *J* = 8.2 Hz, 2H), 6.95 (d, *J* = 8.6 Hz, 2H), 6.76–6.68 (m, 4H), 3.78 (s, 3H), 3.73 (s, 3H), 3.35 (d, *J* = 13.3 Hz, 1H), 3.13 (d, *J* = 13.3 Hz, 1H), 3.08–3.01 (m, 2H), 2.98 (td, *J* = 11.7, 3.3 Hz, 1H), 2.65 (d, *J* = 11.1 Hz, 1H), 2.46–2.35 (m, 2H), 2.30 (d, *J* = 12.7 Hz, 1H), 2.21 (td, *J* = 11.7, 3.2 Hz, 1H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 172.6, 158.72, 158.65, 141.5, 136.0, 134.1, 133.5, 133.2, 131.0, 130.6, 130.1, 129.7, 129.6, 129.4, 129.0, 128.4, 127.2, 126.1, 124.4, 123.6, 119.7, 113.7, 113.6, 113.4, 67.4, 61.4, 55.4, 55.3, 55.0, 54.9, 51.9, 45.1; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{37}H_{35}BrN_3O_5S$ 712.1475; found 712.1474; $[\alpha]_D^{24}$ = +10 (*c* = 1.0, $CHCl_3$, 589 nm); 74:26 e.r. was

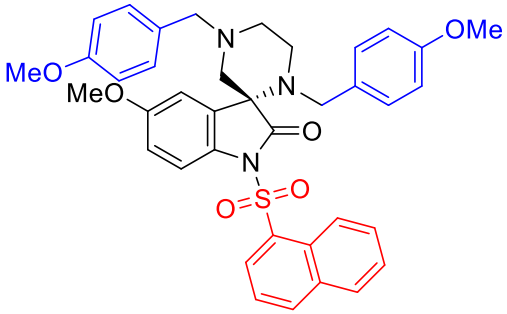
determined by HPLC analysis: Chiralpak IE-3 column (25 cm), hexanes/^{i}PrOH = 70/30, 1.0 mL/min, 310 nm; $t_{(major)}$ = 24.1 min, $t_{(minor)}$ = 18.2 min.

Compound (*R*)-66



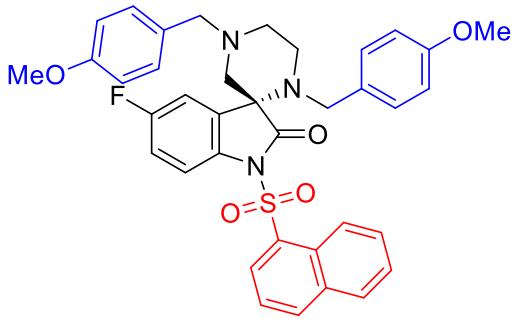
The title compound was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as a pink solid in 67% yield (86.8 mg); **mp:** 132–133 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.63 (dd, *J* = 7.5, 1.2 Hz, 1H), 8.44 (d, *J* = 8.6 Hz, 1H), 8.10 (d, *J* = 8.2 Hz, 1H), 7.89 (d, *J* = 8.3 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.64 (t, *J* = 7.9 Hz, 1H), 7.43–7.34 (m, 2H), 7.30 (s, 1H), 7.21 (dd, *J* = 8.4, 2.3 Hz, 1H), 7.02 (d, *J* = 8.1 Hz, 2H), 6.78 (d, *J* = 8.5 Hz, 2H), 6.75–6.66 (m, 4H), 3.78 (s, 3H), 3.74 (s, 3H), 3.27 (d, *J* = 13.2 Hz, 1H), 3.18 (d, *J* = 13.3 Hz, 1H), 2.97–2.82 (m, 2H), 2.59 (d, *J* = 11.0 Hz, 1H), 2.50–2.33 (m, 6H), 2.31–2.16 (m, 2H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 174.3, 158.8, 158.7, 137.1, 135.8, 134.8, 134.1, 133.3, 133.2, 130.22, 130.15, 129.9, 129.5, 129.4, 129.2, 129.1, 128.8, 128.5, 127.0, 125.6, 124.3, 123.8, 113.9, 113.7, 113.5, 66.1, 61.5, 60.5, 55.4, 55.3, 54.7, 52.5, 45.5, 21.3; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{38}H_{38}N_3O_5S$ 648.2527, found 648.2528; $[\alpha]_D^{24}$ = +40 (*c* = 1.0, $CHCl_3$, 589 nm); 92:8 e.r. was determined by HPLC analysis: Chiralpak IA-3 column (25 cm), hexanes/^{i}PrOH = 80/20, 1.0 mL/min, 280 nm; $t_{(major)}$ = 9.7 min, $t_{(minor)}$ = 8.1 min.

Compound (*R*)-67



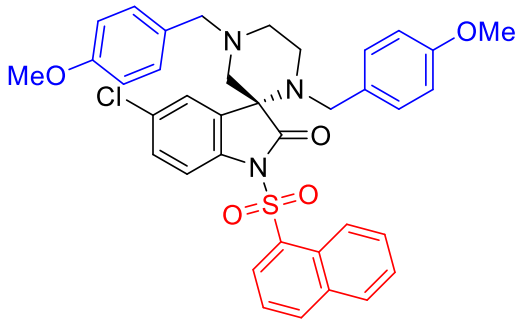
The title compound was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as a brown solid in 71% yield (94.3 mg); **mp:** 93–94 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.63 (d, *J* = 6.9 Hz, 1H), 8.43 (d, *J* = 8.4 Hz, 1H), 8.08 (d, *J* = 8.2 Hz, 1H), 7.93 (d, *J* = 8.9 Hz, 1H), 7.83 (d, *J* = 7.9 Hz, 1H), 7.63 (t, *J* = 7.8 Hz, 1H), 7.44–7.34 (m, 2H), 7.08 (s, 1H), 7.02 (d, *J* = 8.4 Hz, 2H), 6.94 (dd, *J* = 8.9, 2.7 Hz, 1H), 6.77 (d, *J* = 8.5 Hz, 2H), 6.73 (d, *J* = 8.5 Hz, 2H), 6.68 (d, *J* = 8.6 Hz, 2H), 3.84 (s, 3H), 3.78 (s, 3H), 3.73 (s, 3H), 3.27 (d, *J* = 13.2 Hz, 1H), 3.17 (d, *J* = 13.2 Hz, 1H), 2.96–2.78 (m, 2H), 2.56 (d, *J* = 9.1 Hz, 1H), 2.49–2.40 (m, 2H), 2.36 (d, *J* = 13.1 Hz, 1H), 2.31–2.18 (m, 2H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 174.2, 158.8, 158.7, 157.3, 135.7, 134.1, 133.23, 133.16, 132.7, 130.6, 130.1, 129.9, 129.4, 129.2, 128.8, 128.4, 127.0, 124.2, 123.8, 115.1, 114.4, 113.7, 113.5, 111.3, 66.3, 61.5, 60.5, 55.8, 55.4, 55.3, 54.8, 52.4, 45.5; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{38}H_{38}N_3O_6S$ 664.2476, found 664.2479; $[\alpha]_D^{24}$ = +90 (*c* = 1.0, $CHCl_3$, 589 nm); 91:9 e.r. was determined by HPLC analysis: Chiralpak IA-3 column (25 cm), hexanes/^{i}PrOH = 70/30, 1.0 mL/min, 220 nm; $t_{(major)}$ = 13.1 min, $t_{(minor)}$ = 9.7 min.

Compound (*R*)-68



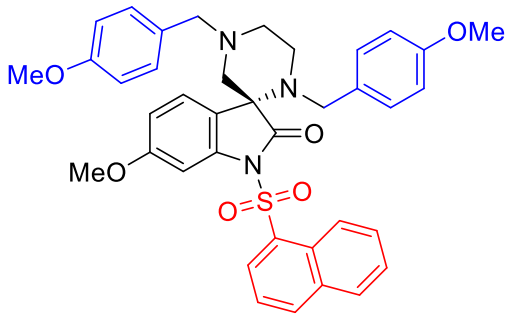
The title compound was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as a pink solid in 73% yield (95.2 mg); **mp:** 155–156 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.63 (d, *J* = 7.4 Hz, 1H), 8.38 (d, *J* = 8.5 Hz, 1H), 8.09 (d, *J* = 8.2 Hz, 1H), 8.01 (dd, *J* = 8.9, 4.3 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.65 (t, *J* = 7.8 Hz, 1H), 7.43–7.33 (m, 2H), 7.29 (d, *J* = 6.9 Hz, 1H), 7.13 (td, *J* = 8.9, 2.7 Hz, 1H), 7.01 (d, *J* = 8.3 Hz, 2H), 6.77–6.71 (m, 4H), 6.69 (d, *J* = 8.6 Hz, 2H), 3.78 (s, 3H), 3.74 (s, 3H), 3.26 (d, *J* = 13.1 Hz, 1H), 3.19 (d, *J* = 13.1 Hz, 1H), 2.89–2.80 (m, 1H), 2.76 (d, *J* = 13.0 Hz, 1H), 2.57–2.49 (m, 1H), 2.49–2.41 (m, 2H), 2.36 (d, *J* = 13.1 Hz, 1H), 2.33–2.20 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 173.9, 160.2 (d, *J* = 245.1 Hz), 158.8, 136.0, 135.3 (d, *J* = 2.1 Hz), 134.1, 133.4, 132.9, 131.2 (d, *J* = 7.6 Hz), 129.9, 129.7, 129.4, 129.3, 128.9, 128.3, 127.1, 124.2, 123.6, 116.2 (d, *J* = 23.3 Hz), 115.4 (d, *J* = 7.9 Hz), 113.7, 113.5, 112.9 (d, *J* = 25.2 Hz), 66.3, 61.5, 60.2, 55.3, 55.0, 52.4, 45.5; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{37}H_{35}FN_3O_5S$ 652.2276; found 652.2275; $[\alpha]_D^{24}$ = +40 (*c* = 1.0, $CHCl_3$, 589 nm); 90:10 e.r. was determined by HPLC analysis: Chiralpak IA-3 column (25 cm), hexanes/^{i}PrOH = 80/20, 1.0 mL/min, 230 nm; $t_{(major)}$ = 11.1 min, $t_{(minor)}$ = 8.7 min.

Compound (*R*)-69



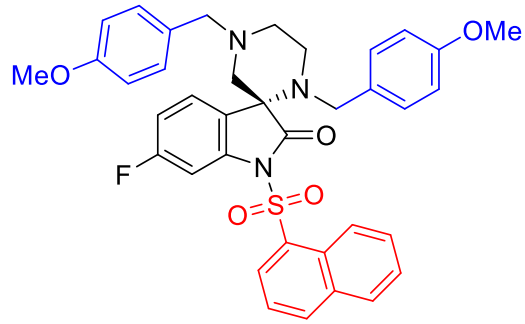
The title compound was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as a pink solid in 62% yield (82.9 mg); **mp:** 195–196 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.63 (d, *J* = 7.4 Hz, 1H), 8.37 (d, *J* = 8.5 Hz, 1H), 8.10 (d, *J* = 8.2 Hz, 1H), 7.98 (d, *J* = 8.7 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.65 (t, *J* = 7.8 Hz, 1H), 7.55 (s, 1H), 7.46–7.33 (m, 3H), 7.01 (d, *J* = 8.0 Hz, 2H), 6.84–6.60 (m, 6H), 3.78 (s, 3H), 3.74 (s, 3H), 3.32–3.14 (m, 2H), 2.91–2.69 (m, 2H), 2.59–2.19 (m, 6H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 173.6, 158.8, 137.9, 136.1, 134.1, 133.4, 132.8, 131.0, 130.7, 129.9, 129.6, 129.5, 129.4, 129.0, 128.3, 127.2, 125.6, 124.3, 123.5, 115.4, 113.8, 113.6, 66.2, 61.5, 60.2, 55.4, 55.1, 52.4, 45.6; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{37}H_{35}ClN_3O_5S$ 668.1980, found 668.1973; $[\alpha]_D^{24}$ = +10 (*c* = 1.0, $CHCl_3$, 589 nm); 87:13 e.r. was determined by HPLC analysis: Chiralpak IE-3 column (25 cm), hexanes/^{i}PrOH = 70/30, 1.0 mL/min, 310 nm; $t_{(major)}$ = 28.5 min, $t_{(minor)}$ = 20.9 min.

Compound (*R*)-70



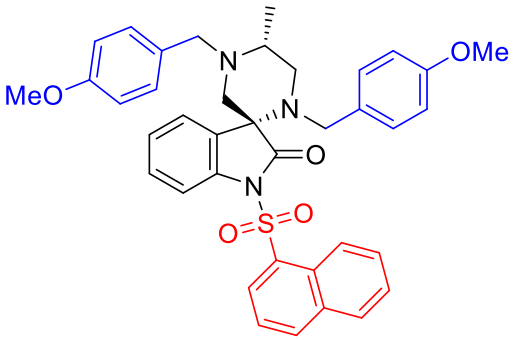
The title compound was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as a pink solid in 92% yield (122.1 mg); **mp:** 124–125 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.63 (d, *J* = 7.4 Hz, 1H), 8.45 (d, *J* = 8.3 Hz, 1H), 8.10 (d, *J* = 8.2 Hz, 1H), 7.84 (d, *J* = 7.7 Hz, 1H), 7.69–7.61 (m, 2H), 7.47–7.35 (m, 3H), 7.01 (d, *J* = 8.2 Hz, 2H), 6.81–6.66 (m, 7H), 3.89 (s, 3H), 3.78 (s, 3H), 3.73 (s, 3H), 3.27 (d, *J* = 13.2 Hz, 1H), 3.17 (d, *J* = 13.2 Hz, 1H), 2.96–2.79 (m, 2H), 2.55 (d, *J* = 11.1 Hz, 1H), 2.48–2.39 (m, 2H), 2.35 (d, *J* = 13.1 Hz, 1H), 2.31–2.16 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 174.5, 160.9, 158.74, 158.69, 140.5, 135.9, 134.1, 133.3, 133.2, 130.2, 129.8, 129.5, 129.4, 129.3, 128.9, 128.4, 127.1, 125.7, 124.2, 123.7, 120.8, 113.7, 113.5, 110.3, 101.1, 65.7, 61.6, 60.5, 55.9, 55.4, 55.3, 54.6, 52.5, 45.5; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{38}H_{38}N_3O_6S$ 664.2476, found 664.2468 $[\alpha]_D^{24}$ = +30 (*c* = 1.0, $CHCl_3$, 589 nm); 90:10 e.r. was determined by HPLC analysis: Chiralpak IE-3 column (25 cm), hexanes/^{i}PrOH = 70/30, 1.0 mL/min, 294 nm; $t_{(major)}$ = 30.7 min, $t_{(minor)}$ = 23.6 min.

Compound (*R*)-71



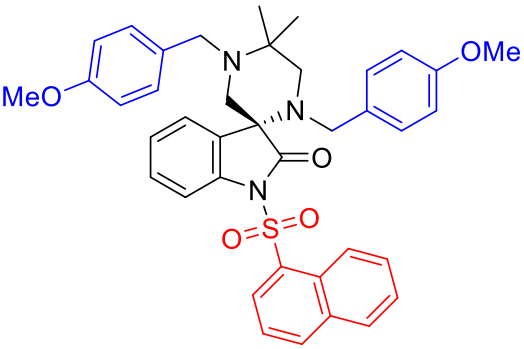
The title compound was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as an orange solid in 73% yield (95.2 mg); **mp:** 136–137 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.63 (dd, *J* = 7.5, 1.2 Hz, 1H), 8.41 (d, *J* = 8.1 Hz, 1H), 8.11 (d, *J* = 8.2 Hz, 1H), 7.90–7.77 (m, 2H), 7.65 (t, *J* = 7.8 Hz, 1H), 7.49 (t, *J* = 7.0 Hz, 1H), 7.45–7.36 (m, 2H), 7.00 (d, *J* = 8.5 Hz, 2H), 6.94 (td, *J* = 8.6, 2.4 Hz, 1H), 6.79–6.65 (m, 6H), 3.77 (s, 3H), 3.73 (s, 3H), 3.26 (d, *J* = 13.1 Hz, 1H), 3.18 (d, *J* = 13.3 Hz, 1H), 2.92–2.74 (m, 2H), 2.54 (d, *J* = 11.1 Hz, 1H), 2.49–2.39 (m, 2H), 2.34 (d, *J* = 13.1 Hz, 1H), 2.31–2.18 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 174.0, 163.3 (d, *J* = 246.9 Hz), 158.79, 158.77, 140.4 (d, *J* = 12.1 Hz), 136.1, 134.1, 133.4, 132.8, 129.83, 129.79, 129.38, 129.35, 129.0, 128.3, 127.1, 126.3 (d, *J* = 7.9 Hz), 124.6 (d, *J* = 2.2 Hz), 124.3, 123.5, 113.7, 113.5, 111.7 (d, *J* = 22.3 Hz), 103.0 (d, *J* = 29.5 Hz), 65.8, 61.5, 60.3, 55.33, 55.32, 54.7, 52.4, 45.5; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{37}H_{35}FN_3O_5S$ 652.2276, found 652.2277; $[\alpha]_D^{24}$ = +10 (*c* = 1.0, $CHCl_3$, 589 nm); 90:10 e.r. was determined by HPLC analysis: Chiralpak IE-3 column (25 cm), hexanes/^{i}PrOH = 70/30, 1.0 mL/min, 296 nm; $t_{(major)}$ = 20.1 min, $t_{(minor)}$ = 16.2 min.

Compound (*R*)-72



The title compound was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as an inseparable mixture of two diastereoisomers in 67% yield (yellow oil, 86.8 mg, d.r. = 8.3:1); **^{1}H NMR (500 MHz, $CDCl_3$) for the major isomer:** δ 8.64 (dd, *J* = 7.5, 1.2 Hz, 1H), 8.40 (d, *J* = 8.6 Hz, 1H), 8.13 (d, *J* = 8.2 Hz, 1H), 7.99 (d, *J* = 8.0 Hz, 1H), 7.88 (d, *J* = 8.1 Hz, 1H), 7.70–7.62 (m, 1H), 7.45–7.32 (m, 4H), 7.23–7.18 (m, 1H), 7.02 (d, *J* = 8.4 Hz, 2H), 6.79 (d, *J* = 8.3 Hz, 2H), 6.73–6.67 (m, 4H), 3.82 (d, *J* = 13.9 Hz, 1H), 3.78 (s, 3H), 3.74 (s, 3H), 2.99 (d, *J* = 13.9 Hz, 1H), 2.86 (d, *J* = 13.1 Hz, 1H), 2.80–2.71 (m, 1H), 2.60 (d, *J* = 12.4 Hz, 1H), 2.46–2.28 (m, 3H), 2.23 (d, *J* = 13.1 Hz, 1H), 1.00 (d, *J* = 6.1 Hz, 3H); **^{13}C NMR (125 MHz, $CDCl_3$) for the major isomer:** δ 174.0, 158.7, 158.5, 139.7, 135.8, 134.1, 133.6, 133.0, 130.3, 130.2, 129.7, 129.4, 129.3, 129.2, 128.8, 128.4, 127.0, 125.1, 124.5, 124.3, 123.8, 114.1, 113.8, 113.6, 65.9, 59.5, 56.3, 55.7, 55.34, 55.32, 54.2, 52.8, 16.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{38}H_{38}N_3O_5S$ 648.2527, found 648.2529; $[\alpha]_D^{24}$ = +50 (*c* = 1.0, $CHCl_3$, 589 nm).

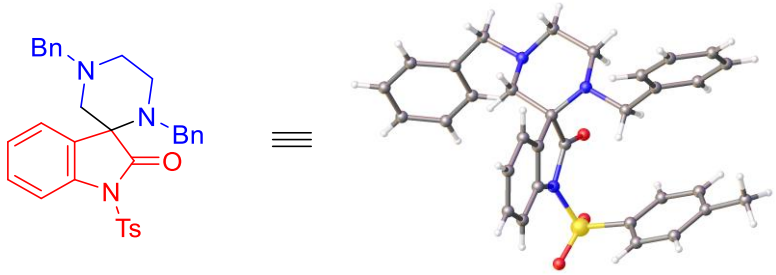
Compound (*R*)-73



The title compound was prepared via the general procedure, purified by flash chromatography (hexanes/EtOAc = 3:1) on silica gel and obtained as a yellow oil in 46% yield (60.9 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.60 (dd, *J* = 7.4, 1.3 Hz, 1H), 8.34 (dd, *J* = 8.7, 1.0 Hz, 1H), 8.08 (d, *J* = 8.1 Hz, 1H), 7.96 (d, *J* = 8.1 Hz, 1H), 7.82 (d, *J* = 8.1 Hz, 1H), 7.62 (dd, *J* = 8.2, 7.4 Hz, 1H), 7.58 (d, *J* = 7.4 Hz, 1H), 7.39–7.34 (m, 2H), 7.27–7.17 (m, 2H), 7.07 (d, *J* = 8.6 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 6.73–6.65 (m, 4H), 3.77 (s, 3H), 3.74 (s, 3H), 3.60 (d, *J* = 13.7 Hz, 1H), 3.15 (d, *J* = 13.8 Hz, 1H), 2.82 (d, *J* = 11.5 Hz, 1H), 2.76 (d, *J* = 13.3 Hz, 1H), 2.56 (d, *J* = 12.7 Hz, 1H), 2.48 (d, *J* = 12.6 Hz, 1H), 2.30 (d, *J* = 13.4 Hz, 1H), 2.20 (d, *J* = 11.5 Hz, 1H), 1.11 (s, 3H), 1.03 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 176.7, 158.7, 158.6, 138.7, 135.9, 134.1, 133.3, 132.9, 131.6, 131.5, 131.0, 130.0, 129.3, 129.17, 129.07, 128.9, 128.4, 127.1, 125.8, 125.1, 124.3, 123.7, 113.7, 113.6, 113.5, 70.4, 63.6, 63.5, 55.7, 55.4, 55.3, 55.0, 45.6, 32.2; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{39}H_{40}N_3O_5S$ 662.2683, found 662.2673; $[\alpha]_D^{24}$ = +10 (*c* = 1.0, $CHCl_3$, 589 nm); 80:20 e.r. was determined by HPLC analysis: Chiralpak IE-3 column (25 cm), hexanes/^{i}PrOH = 70/30, 1.0 mL/min, 230 nm; $t_{(major)}$ = 16.2 min, $t_{(minor)}$ = 13.1 min.

7. X-Ray Structures

All suitable crystals were obtained by interlayer diffusion of hexanes into EtOAc solution at ambient temperature. A colorless crystal of the corresponding compound was mounted on a glass fiber at a random orientation. The data were collected at 100 K by a diffractometer Rigaku Oxford Diffraction Supernova Dual Source, Cu at Zero equipped with an AtlasS2 CCD using Cu Kα radiation (1.54178 Å) by using a w scan mode.

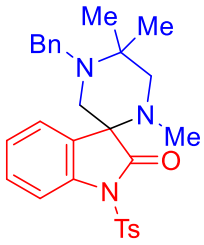


3

Table S15 Crystal data and structure refinement for 3.

CCDC	2211107
Empirical formula	$C_{32}H_{31}N_3O_3S$
Formula weight	537.66
Temperature/K	150.00(10)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	8.97690(10)
b/Å	15.76810(10)
c/Å	19.74970(10)
α/°	90
β/°	101.0220(10)
γ/°	90
Volume/Å^3	2743.98(4)
Z	4
ρ_{calc}g/cm^3	1.301
μ/mm^{-1}	1.355
F(000)	1136.0
Crystal size/mm^3	0.14 × 0.12 × 0.11

Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	7.226 to 143.192
Index ranges	-10 ≤ h ≤ 11, -19 ≤ k ≤ 15, -19 ≤ l ≤ 24
Reflections collected	13870
Independent reflections	5234 [R_{int} = 0.0163, R_{sigma} = 0.0163]
Data/restraints/parameters	5234/0/354
Goodness-of-fit on F^2	1.038
Final R indexes [I>=2σ (I)]	R_1 = 0.0344, wR_2 = 0.0908
Final R indexes [all data]	R_1 = 0.0369, wR_2 = 0.0931
Largest diff. peak/hole / e $Å^{-3}$	0.34/-0.33



39a

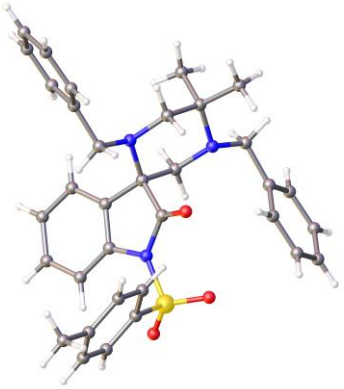
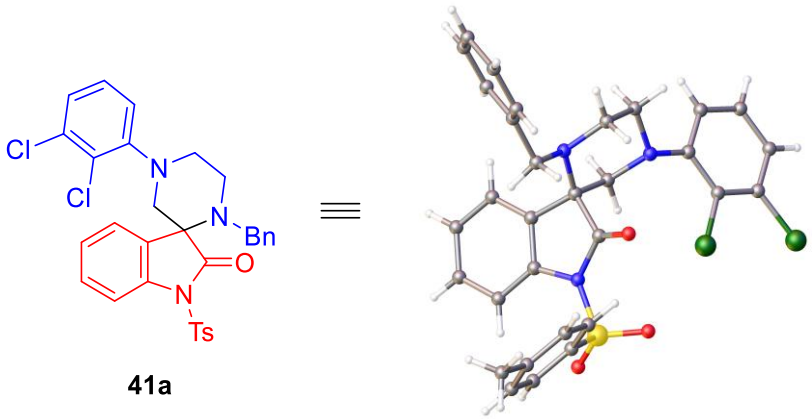


Table S16 Crystal data and structure refinement for 39a.

CCDC	2285030
Empirical formula	$C_{34}H_{35}N_3O_3S$
Formula weight	565.71
Temperature/K	150.00(10)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	12.2123(2)
b/Å	15.8408(3)

c/Å	15.5544(2)
α/°	90
β/°	96.2020(10)
γ/°	90
Volume/Å^3	2991.43(8)
Z	4
ρ_{calc}g/cm^3	1.256
μ/mm^{-1}	1.268
F(000)	1200.0
Crystal size/mm^3	0.14 × 0.12 × 0.09
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	7.99 to 148.082
Index ranges	-14 ≤ h ≤ 14, -19 ≤ k ≤ 18, -19 ≤ l ≤ 13
Reflections collected	12221
Independent reflections	5902 [R_{int} = 0.0368, R_{sigma} = 0.0398]
Data/restraints/parameters	5902/0/374
Goodness-of-fit on F^2	1.036
Final R indexes [I>=2σ (I)]	R_1 = 0.0462, wR_2 = 0.1219
Final R indexes [all data]	R_1 = 0.0498, wR_2 = 0.1257
Largest diff. peak/hole / e Å^{-3}	0.45/-0.53

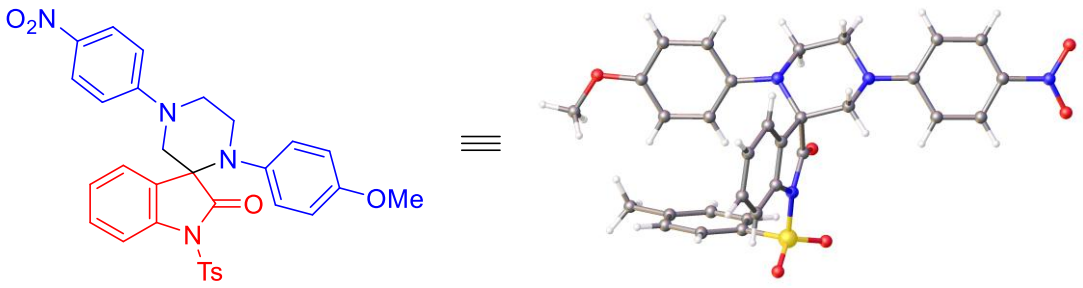


41a

Table S17 Crystal data and structure refinement for 41a.

CCDC	2285031

Empirical formula	$C_{31}H_{27}Cl_2N_3O_3S$
Formula weight	592.51
Temperature/K	150.00(10)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	9.7448(3)
b/Å	15.6659(5)
c/Å	18.4389(8)
α/°	90
β/°	99.771(4)
γ/°	90
Volume/Å^3	2774.07(18)
Z	4
ρ_{calc}g/cm^3	1.419
μ/mm^{-1}	3.127
F(000)	1232.0
Crystal size/mm^3	0.15 × 0.12 × 0.1
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	7.45 to 148.23
Index ranges	$-11 \leq h \leq 12$, $-19 \leq k \leq 13$, $-22 \leq l \leq 16$
Reflections collected	10058
Independent reflections	5453 [R_{int} = 0.0432, R_{sigma} = 0.0510]
Data/restraints/parameters	5453/0/362
Goodness-of-fit on F^2	1.041
Final R indexes [I>=2σ (I)]	R_1 = 0.0523, wR_2 = 0.1405
Final R indexes [all data]	R_1 = 0.0597, wR_2 = 0.1496
Largest diff. peak/hole / e Å^{-3}	0.42/-0.58



42a

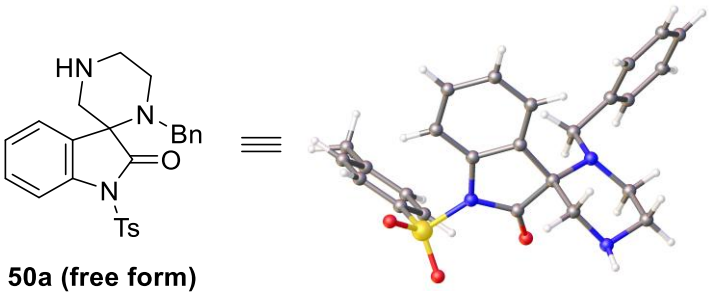
Table S18 Crystal data and structure refinement for 42a.

CCDC	2296400
Empirical formula	$C_{31}H_{28}N_4O_6S$
Formula weight	584.63
Temperature/K	150.00(10)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	14.1078(3)
b/Å	9.8109(2)
c/Å	20.5476(5)
α/°	90
β/°	105.510(3)
γ/°	90
Volume/Å^3	2740.43(11)
Z	4
ρ_{calc}g/cm^3	1.417
μ/mm^{-1}	1.502
F(000)	1224.0
Crystal size/mm^3	0.16 × 0.12 × 0.11
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	6.832 to 147.882
Index ranges	-17 ≤ h ≤ 16, -11 ≤ k ≤ 11, -25 ≤ l ≤ 18
Reflections collected	10777
Independent reflections	5407 [R_{int} = 0.0536, R_{sigma} = 0.0639]
Data/restraints/parameters	5407/0/381
Goodness-of-fit on F^2	1.049

Final R indexes [I>=2σ (I)] $R_1 = 0.0543$, $wR_2 = 0.1463$

Final R indexes [all data] $R_1 = 0.0713$, $wR_2 = 0.1627$

Largest diff. peak/hole / e $Å^{-3}$ 0.52/-0.39

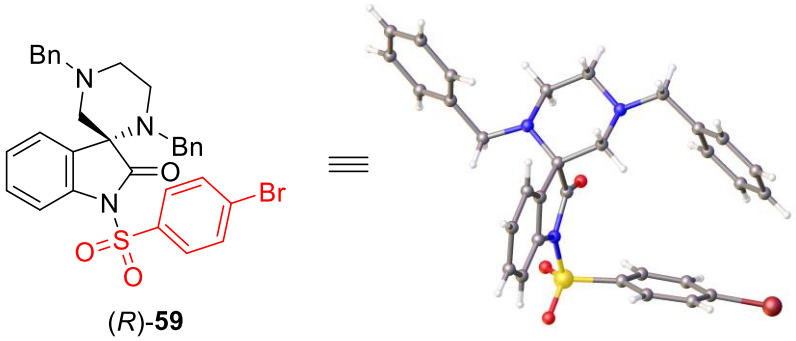


50a (free form)

Table S19 Crystal data and structure refinement for 50a (free form).

CCDC	2285029
Empirical formula	$C_{25}H_{25}N_3O_3S$
Formula weight	447.54
Temperature/K	170.00(10)
Crystal system	triclinic
Space group	P-1
a/Å	9.8264(10)
b/Å	10.1478(9)
c/Å	11.3909(10)
α/°	78.618(7)
β/°	89.893(8)
γ/°	88.457(7)
Volume/$Å^3$	1113.10(18)
Z	2
$\rho_{calc}g/cm^3$	1.335
μ/mm^{-1}	1.557
F(000)	472.0
Crystal size/mm^3	0.15 × 0.13 × 0.12
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	7.918 to 133.192
Index ranges	$-11 \le h \le 11$, $-12 \le k \le 12$, $-13 \le l \le 13$

Reflections collected	7227
Independent reflections	3891 [R_{int} = 0.0639, R_{sigma} = 0.0617]
Data/restraints/parameters	3891/0/294
Goodness-of-fit on F^2	1.076
Final R indexes [I>=2σ (I)]	R_1 = 0.0928, wR_2 = 0.2552
Final R indexes [all data]	R_1 = 0.1102, wR_2 = 0.2731
Largest diff. peak/hole / e $Å^{-3}$	1.04/-0.44

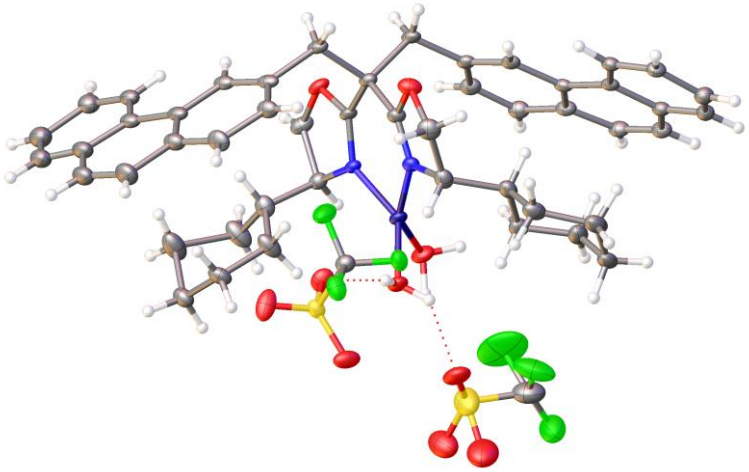


(*R*)-**59**

Table S20 Crystal data and structure refinement for (*R*)-59.

CCDC	2306191
Empirical formula	$C_{31}H_{28}BrN_3O_3S$
Formula weight	602.53
Temperature/K	248(2)
Crystal system	orthorhombic
Space group	P212121
a/Å	9.2241(4)
b/Å	16.0310(8)
c/Å	19.3480(7)
α/°	90
β/°	90
γ/°	90
Volume/Å3	2861.0(2)
Z	4

ρcalcmg/mm3	1.399
μ/mm-1	2.937
F(000)	1240.0
Crystal size/mm3	0.1 × 0.1 × 0.02
Radiation Source	Cu Kα (λ = 1.54184)
2Θ range for data collection	7.162 to 154.598°
Index ranges	-11 ≤ h ≤ 11, -19 ≤ k ≤ 19, -24 ≤ l ≤ 14
Reflections collected	17033
Independent reflections	5676[R(int) = 0.0845]
Data/restraints/parameters	5676/0/352
Goodness-of-fit on F2	1.051
Final R indexes [I>=2σ (I)]	R1 = 0.0620, wR2 = 0.1721
Final R indexes [all data]	R1 = 0.0712, wR2 = 0.1861
Largest diff. peak/hole / e Å-3	0.92/-0.75
Flack parameter	-0.04(2)



X-ray of $Cu(OTf)_2$/**L5** complex (**P602_2**)

Table S21 Crystal data and structure refinement for P602_2.

Identification code	P602_2 (CCDC 2414952)
Empirical formula	$C_{51}H_{53}CuF_6N_2O_{10}S_2$
Formula weight	1095.61

Temperature/K	220.02(10)
Crystal system	monoclinic
Space group	$P2_1$
a/Å	16.2979(4)
b/Å	15.3383(5)
c/Å	20.8584(6)
α/°	90
β/°	90.353(2)
γ/°	90
Volume/Å^3	5214.1(3)
Z	4
ρ_{calc}g/cm^3	1.396
μ/mm^{-1}	2.026
F(000)	2272.0
Crystal size/mm^3	0.12 × 0.1 × 0.08
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	5.422 to 133.194
Index ranges	-19 ≤ h ≤ 15, -18 ≤ k ≤ 18, -24 ≤ l ≤ 24
Reflections collected	33083
Independent reflections	15777 [R_{int} = 0.0558, R_{sigma} = 0.0521]
Data/restraints/parameters	15777/1307/1392
Goodness-of-fit on F^2	1.365
Final R indexes [I>=2σ (I)]	R_1 = 0.1217, wR_2 = 0.3265
Final R indexes [all data]	R_1 = 0.1371, wR_2 = 0.3445
Largest diff. peak/hole / e Å^{-3}	1.80/-0.58
Flack parameter	0.16(6)

8. References

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