Asymmetric Suzuki Cross-Couplings of Activated Secondary Alkyl Electrophiles: Arylations of α-Chloroamides

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Supporting Information

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I. General Information

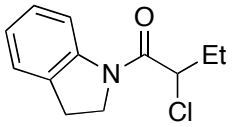
The following reagents were purchased and used without purification: $NiBr_2$·diglyme (Strem), (–)-(*S*,*S*)-**1**, (+)-(*R*,*R*)-**1** (Acros), KO*t*-Bu (Alfa), *i*-BuOH (Aldrich), toluene (Aldrich; anhydrous), and *B*-methoxy-(9-BBN) (Aldrich; 1.0 M solution in hexanes). Indoline (Alfa) was distilled prior to use.

All reactions were carried out in oven-dried glassware under an atmosphere of argon or nitrogen.

HPLC analyses were carried out on an Agilent 1100 series system with Daicel Chiralpak® columns.

II. Preparation of α-Chloroamides

The procedures and yields have not been optimized.



2-Chloro-1-(indolin-1-yl)butan-1-one. 2-Chlorobutyric acid (2.06 mL, 20.0 mmol) and anhydrous CH_2Cl_2 (45 mL) were added to an oven-dried flask under argon. This solution was cooled to 0 °C, and then oxalyl chloride (2.5 mL, 30 mmol, 1.5 equiv) and dimethylformamide

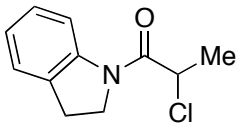
(0.15 mL, 1.9 mmol, 0.097 equiv) were added. The reaction mixture was stirred at 0 °C for 1.5 h, and then it was transferred via cannula to an oven-dried flask that contained a solution of indoline (3.4 mL, 30 mmol, 1.5 equiv) and triethylamine (4.18 mL, 30 mmol, 1.5 equiv) in anhydrous CH_2Cl_2 (30 mL) at 0 °C. The reaction mixture was stirred for 1.5 h as it was allowed to warm to room temperature. The reaction was then quenched by the addition of aqueous HCl (1 M; 45 mL), and the resulting mixture was extracted with CH_2Cl_2 (50 mL × 2). The combined organic layers were washed with brine (30 mL), dried over Na_2SO_4, and concentrated. The residue was purified by flash chromatography (5%→10% EtOAc in pentane), which furnished the product as a white crystalline solid (1.5 g, 34%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.26 (d, 1H, *J* = 8.0 Hz), 7.25-7.19 (m, 2H), 7.09-7.04 (m, 1H), 4.41-4.30 (m, 2H), 4.11 (dt, 1H, *J* = 7.1, 9.9 Hz), 3.32-3.17 (m, 2H), 2.27-2.16 (m, 1H), 2.10-1.99 (m, 1H), 1.08 (t, 3H, *J* = 7.3 Hz);

^{13}C NMR (100 MHz, $CDCl_3$): δ 166.5, 142.8, 131.6, 127.9, 124.8, 124.6, 117.8, 58.4, 48.0, 28.3, 27.7, 11.3;

IR (film): 1655, 1598, 1484, 1423, 1342, 1310, 761 cm^{-1};

LRMS (EI) for $C_{12}H_{15}ClNO$ (M+H): calcd 224, found 224.



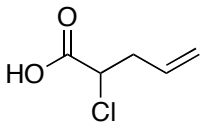
2-Chloro-1-(indolin-1-yl)propan-1-one [107236-27-1]. 2-Chloropropionyl chloride (3.17 g, 25.0 mmol) was added to a flask that contained indoline (3.08 mL, 27.5 mmol, 1.1 equiv), triethylamine (3.83 mL, 27.5 mmol, 1.1 equiv), and THF (30 mL). The solution immediately turned into a thick slurry, which was stirred for 45 min before the reaction was quenched by the addition of HCl (1 M; 30 mL). EtOAc (30 mL) was added, and the phases were separated. The aqueous layer was extracted EtOAc (30 mL × 2), and the combined organic layers, washed with brine (30 mL), dried over Na_2SO_4, and concentrated. The residue was purified by flash chromatography (10% EtOAc in pentane), which furnished the product as a white crystalline solid (2.32 g, 44%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.24 (d, 1H, *J* = 8.0 Hz), 7.25-7.18 (m, 2H), 7.07 (t, 1H, *J* = 7.4 Hz), 4.59 (q, 1H, *J* = 6.5 Hz), 4.48-4.36 (m, 1H), 4.14-4.05 (m, 1H), 3.32-3.16 (m, 2H), 1.75 (d, 3H, *J* = 6.6 Hz);

^{13}C NMR (100 MHz, $CDCl_3$): δ 166.8, 142.8, 131.6, 127.9, 124.8, 124.6, 117.7, 52.2, 47.9 28.3, 20.7;

IR (film): 1652, 1595, 1482, 1417, 1060, 1004, 755 cm^{-1};

LRMS (EI) for $C_{11}H_{13}ClNO$ (M+H): calcd 210, found 210.

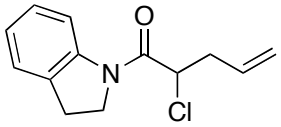


2-Chloropent-4-enoic acid [909778-25-2]. A solution of sodium nitrite (1.30 g, 18.9 mmol, 1.6 equiv) in water (3.5 mL) was added to a solution of D,L-allylglycine (1.36 g, 11.8 mmol, 1.0 equiv) in HCl (5 N; 20 mL) at 0 °C under argon. The reaction mixture was stirred at 0 °C for 5 h, and then it was allowed to warm to room temperature overnight. Sodium carbonate (800 mg) was added, and then the reaction mixture was extracted with Et_2O (10 mL × 4). The organic layers were combined and washed with brine (10 mL). The brine was extracted with Et_2O (10 mL × 3). The organic layers were combined, dried over Na_2SO_4, and concentrated to give a yellow oil (683 mg, 62%), which was used in the next step without further purification.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (br s, 1H), 5.81 (tdd, 1H, *J* = 6.9, 10.2, 17.1 Hz), 5.25-5.18 (m, 2H), 4.39-4.34 (m, 1H), 2.86-2.77 (m, 1H), 2.75-2.66 (m, 1H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 174.6, 131.6, 119.8, 56.0, 38.9;

IR (film): 1734, 1653, 1559, 1507, 1436, 1279, 668 cm^{-1}.



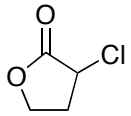
2-Chloro-1-(indolin-1-yl)pent-4-en-1-one. Oxalyl chloride (0.46 mL, 5.42 mmol, 1.1 equiv) and DMF (0.1 mL) were added to a solution of 2-chloropent-4-enoic acid (663 mg, 4.93 mmol) in CH_2Cl_2 (10 mL) at 0 °C. The solution was stirred for 2 h as it warmed to room temperature. Then, it was added via cannula to a solution of indoline (0.61 mL, 5.42 mmol, 1.1 equiv) and triethylamine (0.71 mL, 5.42 mmol, 1.1 equiv) in CH_2Cl_2 (10 mL) at 0 °C. The reaction mixture was stirred for 15 min, and then the reaction was quenched with HCl (1 M; 20 mL) and the phases were separated. The aqueous layer was extracted with CH_2Cl_2 (20 mL × 2). The organic layers were combined, washed with brine (10 mL), dried over Na_2SO_4, and concentrated. The residue was purified by flash chromatography (5% EtOAc in pentane), which furnished 2-chloro-1-(indolin-1-yl)pent-4-en-1-one (360 mg, 31%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (d, 1H, *J* = 8.0 Hz), 7.25-7.19 (m, 2H), 7.10-7.04 (m, 1H), 5.86 (tdd, 1H, *J* = 6.9, 10.2, 17.1 Hz), 5.25 (dd, 1H, *J* = 1.4, 17.1 Hz), 5.17 (d, 1H, *J* = 10.1 Hz), 4.38-4.31 (m, 2H), 4.15-4.06 (m, 1H), 3.31-3.16 (m, 2H), 2.96 (td, 1H, *J* = 6.8, 13.7 Hz), 2.75 (td, 1H, *J* = 7.3, 14.5 Hz);

^{13}C NMR (100 MHz, $CDCl_3$): δ 166.0, 142.7, 133.3, 131.7, 127.9, 124.8, 124.7, 119.3, 117.8, 55.7, 48.0, 38.5, 28.3;

IR (film): 1664, 1600, 1483, 1418, 1341, 1318, 924, 756 cm^{-1};

LRMS (EI) for $C_{13}H_{15}ClNO$ (M+H): calcd 236, found 236.

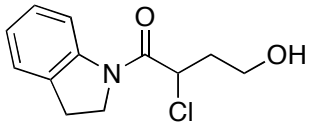


α-Chloro-γ-butyrolactone [31167-90-5]. A cold solution of $NaNO_2$ (3.45 g, 50 mmol, 1.63 equiv) was added by pipette over 5 min to a solution of D,L-homoserine (3.64 g, 30.6 mmol) in HCl (5 N; 50 mL) at 0 °C. The reaction mixture was allowed to warm to room temperature overnight. Next, Na_2CO_3 (1.33 g) was added, and the reaction mixture was extracted with Et_2O (75 mL × 3). The combined organic layers were washed with brine (50 mL), which was then extracted with Et_2O (75 mL × 4). The organic layers were combined, dried over Na_2SO_4, and concentrated. The residue was purified by flash chromatography (30% EtOAc in pentane), which furnished the product (1.82 g, 50%) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.53 (td, 1H, *J* = 6.9, 9.1 Hz), 4.49-4.36 (m, 2H), 2.78 (dt, 1H, *J* = 7.2, 14.3 Hz), 2.48 (tdd, 1H, *J* = 5.1, 6.9 Hz, 13.9 Hz);

^{13}C NMR (100 MHz, $CDCl_3$): δ 66.6, 50.4, 33.4;

IR (film): 1785, 1376, 1213, 1168, 1020, 896 cm^{-1}.



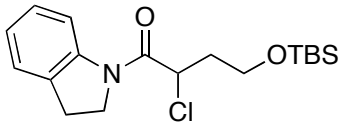
2-Chloro-4-hydroxy-1-(indolin-1-yl)butan-1-one. Indoline (4.1 mL, 36.4 mmol, 2.6 equiv) was added to an oven-dried flask containing $AlCl_3$ (2.43 g, 18.2 mmol, 1.3 equiv) in anhydrous CH_2Cl_2 (15 mL) at 0 °C. The solution was stirred for 5 min at 0 °C, and then α-chloro-γ-butyrolactone (1.68 g, 13.9 mmol, 1.0 equiv) was added. The solution was stirred for 2 h at room temperature, and then the reaction was quenched with water and stirred overnight. The reaction mixture was filtered through celite and concentrated. CH_2Cl_2 and water were added to the residue, and the organic layer was separated and concentrated. The residue was purified by flash chromatography (2:3→2:1 EtOAc:pentane, followed by 1:3→1:1 EtOAc:pentane), which provided the product (750 mg, 20%) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (d, 1H, *J* = 7.9 Hz), 7.25-7.20 (m, 2H), 7.10-7.05 (m, 1H), 4.80-4.74 (m, 1H), 4.39 (dt, 1H, *J* = 7.3, 9.8 Hz), 4.17 (dt, 1H, *J* = 7.2, 10.0 Hz), 3.88 (dd, 2H, *J* = 4.9, 11.0 Hz), 3.32-3.17 (m, 2H), 2.47-2.38 (m, 1H), 2.31-2.22 (m, 1H), 1.80 (t, 1H, *J* = 4.9 Hz);

^{13}C NMR (100 MHz, $CDCl_3$): δ 166.7, 142.5, 131.7, 127.6, 124.73, 124.66, 117.6, 58.7, 53.8, 47.9, 36.7, 28.0;

IR (film): 1660, 1598, 1483, 1418, 1263, 1054, 756 cm^{-1};

LRMS (EI) for $C_{12}H_{15}ClNO_2$ (M+H): calcd 240, found 240.



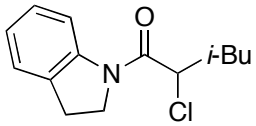
4-(*tert*-Butyldimethylsilyloxy)-2-chloro-1-(indolin-1-yl)butan-1-one. TBSCl (0.82 g, 5.33 mmol, 1.25 equiv), imidazole (732 mg, 10.7 mmol, 2.5 equiv), and DMAP (60 mg) were added in turn to a solution of 2-chloro-4-hydroxy-1-(indolin-1-yl)butan-1-one (1.02 g, 4.26 mmol) in DMF (5 mL) at 0 °C. The resulting solution was allowed to warm to room temperature with stirring overnight. Next, the reaction mixture was diluted with EtOAc (15 mL) and poured into saturated $NaHCO_3$ (20 mL). The phases were separated, and the aqueous layer was extracted with EtOAc (15 mL × 2). The organic layers were combined and washed with brine (20 mL), dried over Na_2SO_4, and concentrated. The residue was purified by flash chromatography (7% EtOAc in pentane), followed by recrystallization from EtOAc, which furnished the product as a white solid (720 mg, 43%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.26 (d, 1H, *J* = 8.0 Hz), 7.25-7.19 (m, 2H), 7.09-7.04 (m, 1H), 4.77 (dd, 1H, *J* = 5.6, 8.2 Hz), 4.36 (dt, 1H, *J* = 7.2, 9.9 Hz), 4.12 (dt, 1H, *J* = 7.0, 10.0 Hz), 3.84 (ddd, 1H, *J* = 3.8, 8.0, 11.7 Hz), 3.76 (ddd, 1H, *J* = 4.6, 5.3, 10.3 Hz), 3.32-3.17 (m, 2H), 2.34 (dddd, 1H, *J* = 4.5, 5.5, 8.0, 12.5 Hz), 2.19 (dddd, 1H, *J* = 3.8, 5.6, 9.3, 11.0 Hz), 0.89 (s, 9H), 0.06 (d, 6H, *J* = 11.6 Hz);

^{13}C NMR (100 MHz, $CDCl_3$): δ 166.7, 142.8, 131.7, 127.8, 124.8, 124.6, 117.8, 59.2, 53.6, 47.9, 37.3, 28.2, 26.1, 18.4 –5.2 –5.3;

IR (film): 1668, 1600, 1483, 1413, 1257, 1103, 937, 834, 778, 755 cm^{-1};

LRMS (EI) for $C_{18}H_{28}ClNO_2Si$: calcd 353, found 353.



2-Chloro-1-(indolin-1-yl)-4-methylpentan-1-one. Oxalyl chloride (1.18 mL, 13.4 mmol, 1.1 equiv) and DMF (0.1 mL, 1.3 mmol, 0.11 equiv) were added to a 0 °C solution of α-chloroisocaproic acid[1] (1.84 g, 12.2 mmol) in anhydrous CH_2Cl_2 (36 mL) in an oven-dried flask under argon. The reaction mixture was allowed to warm to room temperature with stirring overnight. The solution was then transferred by cannula to a solution of indoline (1.50 mL, 13.4 mmol, 1.1 equiv) and triethylamine (1.87 mL, 13.4 mmol, 1.1 equiv) in anhydrous CH_2Cl_2 (30 mL) at 0 °C under argon. The suspension was stirred for 4 h, and then the reaction was quenched by the addition of HCl (1 M; 20 mL). The reaction mixture was extracted with CH_2Cl_2 (20 mL × 2), and the combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, and concentrated. The residue was purified by flash chromatography (5% EtOAc in hexanes), which furnished the product (2.20 g, 72%) as a white solid.

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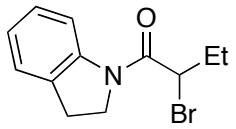
(1) Koppenhoefer, B.; Schurig, V. *Org. Syntheses* **1988**, *66*, 151–155.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (d, 1H, *J* = 8.0 Hz), 7.27-7.19 (m, 2H), 7.06 (t, 1H, *J* = 7.4 Hz), 4.49 (t, 1H, *J* = 7.2 Hz), 4.42-4.34 (m, 1H), 4.16-4.07 (m, 1H), 3.32-3.17 (m, 2H), 2.01-1.95 (m, 2H), 1.91-1.80 (m, 1H), 1.00-0.94 (m, 6H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 166.7, 142.9, 131.6, 127.9, 124.8, 124.6, 117.8, 55.2, 48.0, 42.8, 28.3, 25.3, 22.9, 22.1;

IR (film): 1668, 1600, 1482, 1413, 1262, 1107, 755 cm^{-1};

LRMS (EI) for $C_{14}H_{19}ClNO$ (M+H): calcd 252, found 252.



2-Bromo-1-(indolin-1-yl)butan-1-one. Triethylamine (2.77 g, 27.5 mmol, 1.1 equiv) and then 2-bromo-*n*-butyryl bromide were added to an oven-dried flask under argon that contained a solution of indoline (3.28 g, 27.5 mmol, 1.1 equiv) in THF (50 mL) at 0 ºC. The reaction mixture was stirred at 0 ºC for 1 h, and then the reaction was quenched by the addition of HCl (1 M; 30 mL) and EtOAc (30 mL). The phases were separated, and the aqueous layer was extracted EtOAc (2 × 30 mL). The organic layers were combined, washed with brine (30 mL), and dried over Na_2SO_4. The residue was purified by flash chromatography (10% EtOAc in pentane), which furnished the product (4.22 g, 63%) as a white crystalline solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.27 (d, 1H, *J* = 8.0 Hz), 7.24-7.17 (m, 2H), 7.09-7.03 (m, 1H), 4.37-4.29 (m, 2H), 4.07 (dt, 1H, *J* = 7.1, 10.0 Hz), 3.30-3.15 (m, 2H), 2.27 (pentet d, 1H, *J* = 7.2, 14.3 Hz), 2.12 (pentet d, 1H, *J* = 7.4, 14.7 Hz), 1.06 (t, 3H, *J* = 7.3 Hz);

^{13}C NMR (400 MHz, $CDCl_3$): δ 166.6, 142.7, 131.5, 127.7, 124.7, 124.4, 117.6, 48.3, 47.9, 28.1, 27.9, 12.3;

IR (film): 1653, 1576, 1457, 1419, 1161, 755, 668 cm^{-1};

LRMS (EI) for $C_{12}H_{14}BrNO$: calcd 267, found 267 .

III. Preparation of Aryl-(9-BBN) Reagents

General Procedure. All aryl-(9-BBN) reagents were prepared by following a literature procedure for the synthesis of Ph-(9-BBN) via the reaction of phenylmagnesium chloride with *B*-methoxy-(9-BBN).[2] Although we routinely purified the aryl-(9-BBN) reagents by distillation, we have obtained comparable results when the aryl-(9-BBN) reagent (1.8 equiv) was not distilled prior to use in the asymmetric Suzuki reaction.

9-Phenyl-9-borabicyclo[3.3.1]nonane [23418-91-9]. Prepared from *B*-methoxy-(9-BBN) and phenylmagnesium bromide. Distilled at 95 °C at 240 mTorr.

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(2) Fang, G. Y.; Wallner, O. A.; Di Blasio, N.; Ginesta, X.; Harvey, J. N.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2007**, *129*, 14632–14639.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, 2H, *J* = 7.0 Hz), 7.58-7.53 (m, 1H), 7.50-7.45 (m, 2H), 2.29-2.24 (m, 2H), 2.06-1.96 (m, 6H), 1.87-1.76 (m, 4H), 1.31 (ddd, 2H);

9-(3-Chlorophenyl)-9-borabicyclo[3.3.1]nonane. Prepared from *B*-methoxy-(9-BBN) and 3-chlorophenylmagnesium bromide. Distilled at 150 °C at 400 mTorr.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91-7.89 (m, 1H), 7.84-7.80 (m, 1H), 7.52 (ddd, 1H, *J* = 1.2, 2.3, 8.0 Hz), 7.43-7.38 (m, 1H), 2.29-2.22 (m, 2H), 2.06-1.96 (m, 6H), 1.85-1.75 (m, 4H), 1.35-1.25 (m, 2H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 134.7, 134.5, 132.72, 132.67, 129.7, 34.3, 29.8, 23.6;

^{11}B NMR (128 MHz, $CDCl_3$): δ 61.

9-(3-Methylphenyl)-9-borabicyclo[3.3.1]nonane. Prepared from *B*-methoxy-(9-BBN) and 3-methylphenylmagnesium bromide. Distilled at 110 °C at 290 mTorr.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85-7.80 (m, 2H), 7.44-7.40 (m, 2H), 2.46 (s, 3H), 2.35-2.30 (m, 2H), 2.09-2.00 (m, 6H), 1.92-1.81 (m, 4H), 1.40-1.29 (m, 2H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 138.7, 137.5, 135.5, 133.8, 131.9, 128.2, 34.3, 29.3, 23.7, 21.7;

^{11}B NMR (128 MHz, $CDCl_3$): δ 81.

9-(4-Methoxyphenyl)-9-borabicyclo[3.3.1]nonane. Prepared from *B*-methoxy-(9-BBN) and 4-methoxyphenylmagnesium bromide. After filtration and concentration, the aryl-(9-BBN) reagent was used without further purification.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01-7.96 (m, 2H), 7.03-6.98 (m, 2H), 3.89 (s, 3H), 2.27 (br s, 2H), 2.05-1.95 (m, 6H), 1.86-1.74 (m, 4H), 1.37-1.27 (m, 2H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 163.7, 137.0, 130.9, 113.5, 55.2, 34.1, 28.4, 23.5;

^{11}B NMR (128 MHz, $CDCl_3$): δ 78.

9-(4-Fluorophenyl)-9-borabicyclo[3.3.1]nonane. Prepared from *B*-methoxy-(9-BBN) and 4-fluorophenylmagnesium bromide. Distilled at 76 °C at 200 mTorr.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01-7.95 (m, 2H), 7.17-7.10 (m, 2H), 2.29-2.22 (m, 2H), 2.05-1.91 (m, 6H), 1.85-1.74 (m, 4H), 1.35-1.25 (m, 2H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7, 165.2, 137.4, 115.3, 34.3, 29.2 23.6;

^{11}B NMR (128 MHz, $CDCl_3$): δ 80.

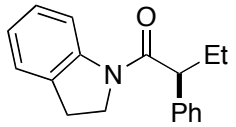
IV. Asymmetric Suzuki Arylations of α-Chloroamides

General Procedure. In a nitrogen-filled glovebox, $NiBr_2$·diglyme (8.8 mg, 0.040 mmol, 8.0%), ligand **1** (18.8 mg, 0.050 mmol, 10%; Run 1: (*S*,*S*)-**1**; Run 2: (*R*,*R*)-**1**), the electrophile (0.50 mmol), and toluene (2.5 mL) were added to a 10-mL flask. The following materials were added in turn to a 4-mL vial: KO*t*-Bu (73 mg, 0.65 mmol, 1.3 equiv), *i*-BuOH (69 μL, 0.75 mmol, 1.5 equiv), the aryl-(9-BBN) reagent (0.75 mmol, 1.5 equiv), and toluene (2.5 mL). The flask and the vial were each capped with a rubber septum, and the two mixtures were stirred for 10 min. Next, the vessels were removed from the glovebox and placed in a –5 °C bath, and the mixtures

were stirred for 10 min. The solution in the vial was then transferred by syringe to the slurry in the 10-mL flask, which was attached to a nitrogen-filled balloon. The reaction mixture was stirred at –5 °C for 24 h (it turned orange after a few min). Next, the mixture was poured into a separatory funnel and washed with a saturated solution of sodium carbonate (5 mL; if the aqueous layer is very viscous, then distilled water (3 mL) was added). The aqueous phase was extracted with EtOAc (5 mL × 2), and the organic layers were combined and washed with brine (5 mL), dried over Na_2SO_4, and concentrated. The resulting residue was purified by flash chromatography.

Run 1: (*S,S*)-**1**. Run 2: (*R,R*)-**1**.

Practical note: For the cross-couplings illustrated in Table 2, flash chromatography was used to purify the products. However, it was sometimes difficult to remove a 9-BBN-derived impurity by flash chromatography, necessitating the use of more than one chromatography. It is more practical to run a preliminary flash chromatography and then a recrystallization; this effectively removes the impurity and simultaneously enriches the ee of the product.



1-(Indolin-1-yl)-2-phenylbutan-1-one (Table 2, entry 1). 2-Chloro-1-(indolin-1-yl)butan-1-one (112 mg, 0.50 mmol) and 9-phenyl-9-borabicyclo[3.3.1]nonane (149 mg, 0.75 mmol) were used. Solvent system for chromatography: 7.5% EtOAc in pentane, then 1:1 CH_2Cl_2:pentane→CH_2Cl_2. The product was isolated as a white solid.

Run 1: 108 mg (81% yield, 93% ee). Run 2: 101 mg (76% yield, 90% ee).

The ee was determined on an AS-H column (hexanes:isopropanol 99:1, flow 1.0 mL/min), with enantiomers eluting at 8.5 (major) and 10.1 (minor) min.

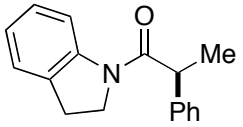
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.33 (d, 1H, *J* = 8.1 Hz), 7.38-7.29 (m, 4H), 7.26-7.21 (m, 1H), 7.19 (t, 1H, *J* = 7.8 Hz), 7.12 (d, 1H, *J* = 7.3 Hz), 6.99 (t, 1H, *J* = 7.4 Hz), 4.15 (dt, 1H, *J* = 6.6, 10.3 Hz), 3.84 (dt, 1H, *J* = 6.6, 10.3 Hz), 3.58 (t, 1H, *J* = 7.2 Hz), 3.19-3.09 (m, 1H), 3.07-2.96 (m, 1H), 2.28-2.16 (m, 1H), 1.87-1.74 (m, 1H), 0.93 (t, 3H, *J* = 7.3 Hz);

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.7, 143.5, 139.6, 131.3, 129.0, 128.3, 127.7, 127.3, 124.7, 123.8, 117.4, 54.1, 47.9, 28.22, 28.16, 12.7;

IR (film): 1646, 1559, 1540, 1457, 1406, 757, 668 cm^{-1};

LRMS (EI) for $C_{18}H_{20}NO$ (M+H): calcd 266, found 266;

$[\alpha]^{23}_D$ +123 (*c* 1.20, $CHCl_3$); 93% ee, from (*S,S*)-**1**.



1-(Indolin-1-yl)-2-phenylpropan-1-one (Table 2, entry 2). 2-Chloro-1-(indolin-1-yl)propan-1-one (105 mg, 0.50 mmol) and 9-phenyl-9-borabicyclo[3.3.1]nonane (149 mg, 0.75 mmol) were used. Solvent system for chromatography: (1) 10% EtOAc in pentane; (2) 1:1 CH_2Cl_2:pentane→CH_2Cl_2. The product was isolated as a white solid.

Run 1: 113 mg (90% yield, 88% ee). Run 2: 109 mg (87% yield, 86% ee).

The ee was determined on an AS-H column (hexanes:isopropanol 99:1, flow 1.0 mL/min), with enantiomers eluting at 13.0 (major) and 16.9 (minor) min.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.33 (d, 1H, *J* = 8.1 Hz), 7.34-7.30 (m, 4H), 7.26-7.22 (m, 1H), 7.20 (t, 1H, *J* = 7.8 Hz), 7.13 (d, 1H, *J* = 7.2 Hz), 7.00 (t, 1H, *J* = 7.4 Hz), 4.10 (dt, 1H, *J* = 6.6, 10.3 Hz), 3.87 (q, 1H, *J* = 6.8 Hz), 3.77 (dt, 1H, *J* = 6.6, 10.3 Hz), 3.17-3.06 (m, 1H), 3.04-2.94 (m, 1H), 1.53 (d, 3H, *J* = 6.8 Hz);

^{13}C NMR (100 MHz, $CDCl_3$): δ 172.2, 143.5, 141.3, 131.3, 129.2, 127.7 (2), 127.2, 124.7, 123.9, 117.4, 47.8, 46.5, 28.2, 20.7;

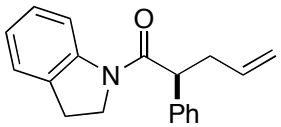
IR (film): 1653, 1599, 1482, 1403, 1286, 755, 701 cm^{-1};

LRMS (EI) for $C_{17}H_{18}NO$ (M+H): calcd 252, found 252;

$[\alpha]^{23}_D$ –160 (*c* 1.06, $CHCl_3$); 86% ee, from (*R*,*R*)-**1**.

Reaction on a gram scale (Table 2, entry 2). The reaction was carried out on a 5.0 mmol, rather than a 0.5 mmol, scale. The reaction temperature ranged from –20 °C to –5 °C for 20 h, and then it was maintained at –5 °C for the remaining 4 h.

After purification by flash chromatography (7.5% EtOAc in pentane), the product was obtained in 88% yield, as determined by ^{1}H NMR spectroscopy (vs. Ph_3CH as a standard), and 92% ee. The internal standard was removed by flash chromatography (1%→15% EtOAc in pentane), and the product was recrystallized from MTBE and hexanes to give the desired compound as white crystals (0.882 g, 70%; >99% ee).



1-(Indolin-1-yl)-2-phenylpent-4-en-1-one (Table 2, entry 3). 2-Chloro-1-(indolin-1-yl)pent-4-en-1-one (118 mg, 0.50 mmol) and 9-phenyl-9-borabicyclo[3.3.1]nonane (149 mg, 0.75 mmol) were used. Solvent system for chromatography: (1) 5% EtOAc in pentane; (2) 3:1 CH_2Cl_2:pentane→CH_2Cl_2. The product was isolated as a white solid.

Run 1: 115 mg (83% yield, 91% ee). Run 2: 105 mg (76% yield, 90% ee).

The ee was determined on an AS-H column (hexanes:isopropanol 99:1, flow 1.0 mL/min), with enantiomers eluting at 11.0 (major) and 13.2 (minor) min.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.33 (d, 1H, *J* = 8.1 Hz), 7.37-7.29 (m, 4H), 7.27-7.22 (m, 1H), 7.19 (t, 1H, *J* = 7.8 Hz), 7.13 (d, 1H, *J* = 7.3 Hz), 6.99 (dt, 1H, *J* = 0.8, 7.4 Hz), 5.81 (tdd, 1H, *J* = 6.9,

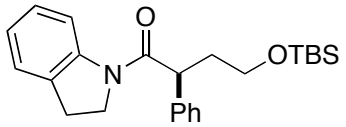
10.2, 17.1 Hz), 5.07 (ddd, 1H, *J* = 1.4, 3.1, 17.1 Hz), 5.01-4.97 (m, 1H), 4.14 (dt, 1H, *J* = 6.5, 10.3 Hz), 3.83 (dt, 1H, *J* = 6.5, 10.4 Hz), 3.78-3.73 (m, 1H), 3.14 (ddd, 1H, *J* = 6.5, 10.4, 16.6 Hz), 3.06-2.92 (m, 2H), 2.54-2.45 (td, 1H, *J* = 6.9, 14.0 Hz);

^{13}C NMR (100 MHz, $CDCl_3$): δ 170.8, 143.3, 138.8, 136.3, 131.1, 128.9, 128.1, 127.5, 127.2, 124.5, 123.7, 117.3, 116.7, 52.1, 47.7, 39.1, 28.0;

IR (film): 1646, 1597, 1479, 1407, 922, 757, 705 cm^{-1};

LRMS (EI) for $C_{19}H_{20}NO$ (M+H): calcd 278, found 278;

$[\alpha]^{23}_D$ –144 (*c* 1.03, $CHCl_3$); 90% ee, from (*R*,*R*)-**1**.



4-(*tert*-Butyldimethylsilyloxy)-1-(indolin-1-yl)-2-phenylbutan-1-one (Table 2, entry 4). 4-(*tert*-Butyldimethylsilyloxy)-2-chloro-1-(indolin-1-yl)butan-1-one (179 mg, 0.50 mmol) and 9-phenyl-9-borabicyclo[3.3.1]nonane (149 mg, 0.75 mmol) were used. Solvent system for chromatography: (1) 2%→5% EtOAc in pentane; (2) passage through a plug of reverse-phase silica with 8:2 H_2O:MeCN, followed by 2:8 H_2O:MeCN. The product was isolated as a yellow solid.

Run 1: 152 mg (77% yield, 85% ee). Run 2: 162 mg (82% yield, 83% ee).

The ee was determined on an IC column (hexanes:isopropanol 99:1, flow 1.0 mL/min), with enantiomers eluting at 18.0 (major) and 14.7 (minor) min.

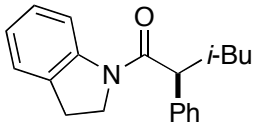
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 (d, 1H, *J* = 8.1 Hz), 7.38-7.28 (m, 4H), 7.26-7.22 (m, 1H), 7.19 (t, 1H, *J* = 7.8 Hz), 7.13 (d, 1H, *J* = 7.1 Hz), 6.99 (dt, 1H, *J* = 0.8, 7.4 Hz), 4.18 (dt, 1H, *J* = 6.4, 10.4 Hz), 4.08 (t, 1H, *J* = 7.2 Hz), 3.86 (dt, 1H, *J* = 6.6, 10.4 Hz), 3.69-3.62 (m, 1H,), 3.58-3.51 (m, 1H), 3.19-3.09 (m, 1H), 3.07-2.97 (m, 1H), 2.45-2.35 (m, 1H), 1.99-1.89 (m, 1H), 0.91 (s, 9H), 0.02 (d, 6H, *J* = 4.9 Hz);

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.6, 143.5, 139.4, 131.4, 129.0, 128.5, 127.7, 127.3, 124.6, 123.8, 117.4, 60.5, 47.9, 47.6, 37.8, 28.1, 26.1, 18.4, –5.2;

IR (film): 1654, 1482, 1401, 1258, 1101, 834, 754 cm^{-1};

LRMS (EI) for $C_{24}H_{33}NO_2Si$ (M): calcd 395, found 395;

$[\alpha]^{23}_D$ –82 (*c* 1.06, $CHCl_3$); 83% ee, from (*R*,*R*)-**1**.



1-(Indolin-1-yl)-4-methyl-2-phenylpentan-1-one (Table 2, entry 5). 2-Chloro-1-(indolin-1-yl)-4-methylpentan-1-one (112 mg, 0.50 mmol) and 9-phenyl-9-borabicyclo[3.3.1]nonane (149 mg, 0.75 mmol) were used. Solvent system for chromatography: (1) 5% EtOAc in pentane; (2) 1:1 CH_2Cl_2:pentane→CH_2Cl_2. The product was isolated as a white solid.

Run 1: 128 mg (87% yield, 86% ee). Run 2: 119 mg (81% yield, 84% ee).

The ee was determined on an AS-H column (hexanes:isopropanol 99:1, flow 1.0 mL/min), with enantiomers eluting at 8.9 (major) and 11.3 (minor) min.

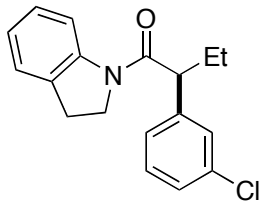
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 (d, 1H, *J* = 8.1 Hz), 7.38-7.29 (m, 4H), 7.26-7.22 (m, 1H), 7.19 (t, 1H, *J* = 7.8 Hz), 7.13 (d, 1H, *J* = 7.3 Hz), 6.99 (t, 1H, *J* = 7.4 Hz), 4.17 (dt, 1H, *J* = 6.7, 10.3 Hz), 3.90 (dt, 1H, *J* = 6.5, 10.3 Hz), 3.80 (t, 1H, *J* = 7.2 Hz), 3.21-3.11 (m, 1H), 3.09-2.99 (m, 1H), 2.13 (td, 1H, *J* = 6.7, 13.8 Hz), 1.68-1.51 (m, 2H), 0.94 (dd, 6H, *J* = 6.4, 15.7 Hz);

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.7, 143.5, 139.8, 131.3, 129.0, 128.3, 127.7, 127.2, 124.6, 123.8, 117.5, 49.8, 47.9, 44.2, 28.2, 25.9, 22.9;

IR (film): 2955, 1658, 1600, 1481, 1402, 754, 701 cm^{-1};

LRMS (EI) for $C_{20}H_{24}NO$ (M+H): calcd 294, found 294;

$[\alpha]^{23}_D$ +123 (*c* 1.00, $CHCl_3$); 86% ee, from (*S,S*)-**1**.



2-(3-Chlorophenyl)-1-(indolin-1-yl)butan-1-one (Table 2, entry 6). 2-Chloro-1-(indolin-1-yl)butan-1-one (112 mg, 0.50 mmol) and 9-(3-chlorophenyl)-9-borabicyclo[3.3.1]nonane (149 mg, 0.75 mmol) were used, as well as 10 mol% $NiBr_2$·diglyme (17.6 mg, 0.050 mmol) and 12.5 mol% diamine ligand (23.5 mg, 0.062 mmol). Solvent system for chromatography: (1) 7.5% EtOAc in pentane; (2) 2:1 CH_2Cl_2:pentane to CH_2Cl_2. The product was isolated as a white solid.

Run 1: 118 mg (79% yield, 93% ee). Run 2: 111 mg (74% yield, 91% ee).

The ee was determined on an AD-H column (hexanes:isopropanol 99:1, flow 1.0 mL/min), with enantiomers eluting at 19.8 (major) and 17.3 (minor) min.

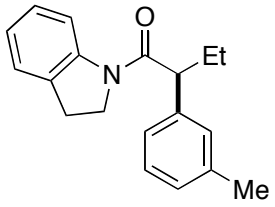
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 (d, 1H, *J* = 8.1 Hz), 7.36-7.34 (m, 1H), 7.26-7.17 (m, 4H), 7.16-7.12 (d, 1H, *J* = 7.2 Hz), 7.00 (dt, 1H, *J* = 1.0, 7.4 Hz), 4.15 (dt, 1H, *J* = 6.6, 10.3 Hz), 3.86 (dt, 1H, *J* = 6.5, 10.3 Hz), 3.56 (t, 1H, *J* = 7.3 Hz), 3.21-3.11 (m, 1H), 3.11-3.01 (m, 1H), 2.26-2.14 (m, 1H), 1.85-1.73 (m, 1H), 0.93 (t, 3H, *J* = 7.4 Hz);

^{13}C NMR (100 MHz, $CDCl_3$): δ 170.8, 143.2, 141.4, 134.6, 131.1, 130.1, 128.3, 127.6, 127.4, 126.3, 124.5, 123.9, 117.3, 53.5, 47.8, 28.04, 27.98, 12.4;

IR (film): 1646, 1596, 1479, 1407, 1258, 756, 668 cm^{-1};

LRMS (EI) for $C_{18}H_{19}ClNO$ (M+H): calcd 300, found 300;

$[\alpha]^{23}_D$ +136 (*c* 1.00, $CHCl_3$); 93% ee, from (*S,S*)-**1**.



1-(Indolin-1-yl)-2-m-tolylbutan-1-one (Table 2, entry 7). 2-Chloro-1-(indolin-1-yl)butan-1-one (112 mg, 0.50 mmol) and 9-(3-methylphenyl)-9-borabicyclo[3.3.1]nonane (159 mg, 0.75 mmol) were used. Solvent system for chromatography: (1) 7.5% EtOAc in pentane; (2) 1:1 CH_2Cl_2:pentane to CH_2Cl_2. The product was isolated as a white solid.

Run 1: 112 mg (80% yield, 93% ee). Run 2: 121 mg (87% yield, 92% ee).

The ee was determined on an AS-H column (hexanes:isopropanol 99:1, flow 1.0 mL/min), with enantiomers eluting at 9.4 (major) and 10.9 (minor) min.

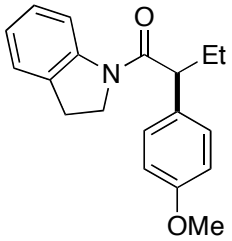
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.34 (d, 1H, *J* = 8.1 Hz), 7.23-7.17 (m, 2H), 7.17-7.10 (m, 3H), 7.05 (d, 1H, *J* = 7.4 Hz), 6.99 (t, 1H, *J* = 7.4 Hz), 4.14 (dt, 1H, *J* = 6.6, 10.3 Hz), 3.86 (dt, 1H, *J* = 6.4, 10.4 Hz), 3.54 (t, 1H, *J* = 7.3 Hz), 3.19-3.09 (m, 1H), 3.07-2.97 (m, 1H), 2.33 (s, 3H), 2.26-2.14 (m, 1H), 1.84-1.72 (m, 1H), 0.93 (t, 3H, *J* = 7.3 Hz);

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.6, 143.4, 139.3, 138.6, 131.2, 128.59, 128.57, 127.9, 127.5, 125.4, 124.5, 123.6, 117.3, 53.9, 47.7, 28.1, 28.0, 21.5, 12.6;

IR (film): 1653, 1600, 1481, 1401, 1339, 755 cm^{-1};

LRMS (EI) for $C_{19}H_{22}NO$ (M+H): calcd 280, found 280;

$[\alpha]^{23}_D$ –136 (*c* 1.11, $CHCl_3$); 92% ee, from (*R,R*)-**1**.



1-(Indolin-1-yl)-2-(4-methoxyphenyl)butan-1-one (Table 2, entry 8). 2-Chloro-1-(indolin-1-yl)butan-1-one (112 mg, 0.50 mmol) and 9-(4-methoxyphenyl)-9-borabicyclo[3.3.1]nonane (172 mg, 0.75 mmol) were used. Solvent system for chromatography: (1) 10% EtOAc in pentane; (2) 1:1 CH_2Cl_2:pentane→CH_2Cl_2 (twice). The product was isolated as a white solid.

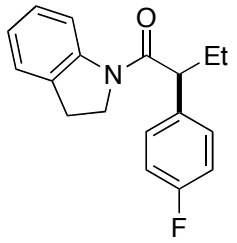
Run 1: 116 mg (79% yield, 91% ee). Run 2: 120 mg (81% yield, 90% ee).

The ee was determined on an AS-H column (hexanes:isopropanol 99:1, flow 1.0 mL/min), with enantiomers eluting at 18.8 (major) and 21.7 (minor) min.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 (m, 1H), 7.27-7.23 (m, 2H), 7.21-7.16 (m, 1H), 7.12 (d, 1H, *J* = 7.3 Hz), 6.98 (dt, 1H, *J* = 0.9, 7.4 Hz), 6.87-6.83 (m, 2H), 4.13 (dt, 1H, *J* = 6.6, 10.3 Hz), 3.90-3.82 (m, 1H), 3.78 (s, 3H), 3.52 (t, 1H, *J* = 7.3 Hz), 3.19-3.09 (m, 1H), 3.07-2.97 (m, 1H), 2.23-2.12 (m, 1H), 1.82-1.71 (m, 1H), 0.92 (t, 3H, *J* = 7.3 Hz);

^{13}C NMR (100 MHz, $CDCl_3$): δ 172.0, 158.8, 143.6, 131.6, 131.3, 129.3, 127.7, 124.6, 123.8, 117.4, 114.3, 55.5, 53.1, 47.9, 28.20, 28.16, 12.6;

IR (film): 1653, 1511, 1481, 1401, 1252, 1178, 1033, 756 cm^{-1};
LRMS (EI) for $C_{19}H_{22}NO_2$ (M+H): calcd 296, found 296;
$[\alpha]^{23}_D$ +126 (*c* 1.15, $CHCl_3$); 91% ee, from (*S,S*)-**1**.



2-(4-Fluorophenyl)-1-(indolin-1-yl)butan-1-one (Table 2, entry 9). 2-Chloro-1-(indolin-1-yl)butan-1-one (112 mg, 0.50 mmol) and 9-(4-fluorophenyl)-9-borabicyclo[3.3.1]nonane (166 mg, 0.75 mmol) were used. Solvent system for chromatography: (1) 7.5% EtOAc in pentane; (2) 1:1 CH_2Cl_2:pentane→CH_2Cl_2 (three times). The product was isolated as a white solid.

Run 1: 101 mg (71% yield, 94% ee). Run 2: 99 mg (70% yield, 93% ee).

The ee was determined on an AS-H column (hexanes:isopropanol 99:1, flow 1.0 mL/min), with enantiomers eluting at 10.7 (major) and 13.1 (minor) min.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.31 (d, 1H, *J* = 8.1 Hz), 7.34-7.28 (m, 2H), 7.23-7.17 (m, 1H), 7.15-7.11 (m, 1H), 7.04-6.97 (m, 3H), 4.15 (dt, 1H, *J* = 6.6 Hz, *J* = 10.3 Hz), 3.85 (dt, 1H, *J* = 6.5 Hz, 10.3 Hz), 3.57 (t, 1H, *J* = 7.3 Hz), 3.20-3.10 (m, 1H), 3.09-2.99 (m, 1H) 2.24-2.13 (m, 1H), 1.83-1.71 (m, 1H), 0.92 (t, 3H, *J* = 7.3 Hz);

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.4, 161.9 (d, *J* = 244 Hz), 143.2, 135.1 (d, *J* = 3.3 Hz), 131.1, 129.7, 127.6, 124.5, 123.8, 117.3, 115.7 (d, *J* = 21 Hz), 53.0, 47.7, 28.1, 28.0, 12.4;

IR (film): 1653, 1600, 1501, 1482, 1401, 1223, 756;

LRMS (EI) for $C_{18}H_{19}FNO$ (M+H): calcd 284, found 284;

$[\alpha]^{23}_D$ +131 (*c* 0.99, $CHCl_3$); 94% ee, from (*S,S*)-**1**.

Eq 5. In a nitrogen-filled glovebox, $NiBr_2$·diglyme (7.0 mg, 0.032 mmol, 8.0%), ligand (*R,R*)-**1** (15.1 mg, 0.040 mmol, 10%), 2-chloro-1-(indolin-1-yl)propan-1-one (83.4 mg, 0.40 mmol), *n*-tetradecane (60.9 mg, 0.31 mmol, 0.77 equiv; internal standard), and toluene (2.0 mL) were added to a 10-mL flask. The following materials were added in turn to a 4-mL vial: KO*t*-Bu (58.3 mg, 0.52 mmol, 1.3 equiv), *i*-BuOH (44.6 mg, 0.60 mmol, 1.5 equiv), Ph-(9-BBN) (119 mg, 0.60 mmol, 1.5 equiv), and toluene (2.0 mL). The flask and the vial were each capped with a rubber septum, and the two mixtures were stirred for 10 min. Next, the vessels were removed from the glovebox and placed in a –5 °C bath, and the mixtures were stirred for 10 min. The solution in the vial was then transferred by syringe to the slurry in the 10-mL flask, which was attached to an argon-filled manifold. The reaction mixture was stirred at –5 °C for 11 h, at which time an aliquot was removed and passed through a plug of silica (washed with Et_2O).

GC analysis showed 86% conversion of the starting material, and HPLC analysis showed a starting-material ee of 54% and a product ee of 90% (AS-H column (hexanes:isopropanol 99:1,

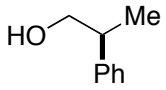
flow 1.0 mL/min); starting material: 21.5 (major) and 30.4 (minor) min; product: 14.1 (minor) and 18.2 (major) min).

Eq 6 and 7. In a nitrogen-filled glovebox, $NiBr_2$·diglyme (8.8 mg, 0.040 mmol, 8.0%), ligand (*S*,*S*)-**1** (18.8 mg, 0.050 mmol, 10%), 2-chloro-1-(indolin-1-yl)propan-1-one (105 mg; 0.50 mmol; eq 6: *R* enantiomer, 95% ee, eq 7: *S* enantiomer, 95% ee), *n*-tetradecane (99 mg, 0.50 mmol, 1.0 equiv), and toluene (2.5 mL) were added to a 10-mL flask. The following materials were added in turn to a 4-mL vial: KO*t*-Bu (73 mg, 0.65 mmol, 1.3 equiv), *i*-BuOH (55.5 mg, 0.75 mmol, 1.5 equiv), Ph-(9-BBN) (149 mg, 0.75 mmol, 1.5 equiv), and toluene (2.5 mL). The flask and the vial were each capped with a rubber septum, and the two mixtures were stirred for 10 min. Next, the vessels were removed from the glovebox and placed in a –5 °C bath, and the mixtures were stirred for 10 min. The solution in the vial was then transferred by syringe to the slurry in the 10-mL flask, which was attached to an argon-filled manifold. The reaction mixture was stirred at –5 °C for 12 h, at which time an aliquot was removed and passed through a plug of silica (washed with Et_2O).

Eq 6: GC analysis showed 67% conversion of the starting material, and HPLC analysis showed a starting-material ee of 95% and a product ee of 88% (AS-H column (hexanes:isopropanol 99:1, flow 1.0 mL/min); starting material: 20.7 (major) and 28.3 (minor) min; product: 13.6 (major) and 17.1 (minor) min).

Eq 7: GC analysis showed 67% conversion of the starting material, and HPLC analysis showed a starting-material ee of 95% and a product ee of 88% (AS-H column (hexanes:isopropanol 99:1, flow 1.0 mL/min); starting material: 20.7 (minor) and 28.3 (major) min; product: 13.6 (major) and 17.1 (minor) min).

V. Functionalization Reactions (eq 3 and eq 4) and Assignment of Absolute Configuration



(*S*)-(–)-2-Phenyl-1-propanol [37778-99-7] (eq 3).[3] A solution of *n*-BuLi (1.6 M solution in hexanes; 2.44 mL, 3.9 mmol, 3.9 equiv) was added dropwise to a solution of of diisopropylamine (580 μL, 4.1 mmol, 4.1 equiv) in THF (15 mL) at 0 °C. The mixture was stirred for 15 min, then ammonia·borane (123 mg, 4.0 mmol, 4.0 equiv) was added. The resulting mixture was stirred at 0 °C for 15 min, and then it was warmed to room temperature. A solution of (*S*)-1-(indolin-1-yl)-2-phenylpropan-1-one (recrystallized; >99% ee; 251 mg, 1.0 mmol, 1.0 equiv) in THF (15 mL) was added, and then the reaction mixture was heated to reflux

(3) Myers, A. G.; Yang, B. H.; Chen, H.; McKinstry, L.; Kopecky, D. J.; Gleason, J. L. *J. Am. Chem. Soc.* **1997**, *119*, 6496–6511.

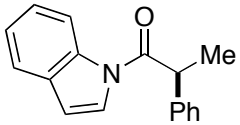
for 24 h. Next, the mixture was cooled to 0 °C, and the reaction was quenched by the addition of aqueous HCl (1 M; 20 mL). The layers were separated, and the aqueous layer was extracted with Et_2O (10 mL × 4). The combined organic layers were washed with HCl (1 M; 5 mL), NaOH (3 M; 5 mL), and brine (10 mL). The organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography (10%→80% Et_2O in hexanes), which furnished the product as a clear, colorless oil.

Run 1: 109 mg (80% yield, >99% ee); Run 2: 116 mg (85% yield, >99% ee).

The ee was determined on an AS-H column (hexanes:isopropanol 99:1, flow 1.0 mL/min), with enantiomers eluting at 17.0 (major) and 18.6 (minor) min.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36-7.31 (m, 2H), 7.25-7.22 (m, 3H), 3.74-3.69 (m, 2H), 3.01-2.91 (m, 1H), 1.28 (d, 3H, J = 7.0 Hz);

$[\alpha]^{24}_D$ –13.6 (*c* 1.00, $CHCl_3$); >99% ee. Lit.[4] $[\alpha]^{22}_D$ –12 (*c* 1.00, $CHCl_3$), 89% ee (S).



(*S*)-1-(1*H*-Indol-1-yl)-2-phenylpropan-1-one (eq 4). Toluene (7.5 mL) and DDQ (460 mg, 2.03 mmol, 1.30 equiv) were added to a Schlenk flask that contained (*S*)-1-(indolin-1-yl)-2-phenylpropan-1-one (recrystallized; >99% ee; 392 mg, 1.56 mmol) under argon. The resulting solution was heated to reflux overnight. The solution was then diluted with EtOAc (15 mL) and washed with water (10 mL). The aqueous layer was extracted with EtOAc (15 mL), and the combined organic layers were washed with brine (12 mL), dried over $MgSO_4$, and concentrated. The residue was purified by flash chromatography (2%→20% EtOAc in hexanes), which furnished the product as a white solid (351 mg, 90%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.53 (d, 1H, J = 8.3 Hz), 7.43 (d, 1H, J = 7.8 Hz), 7.34 (d, 1H, J = 3.8 Hz), 7.32-7.22 (m, 5H), 7.21-7.14 (m, 2H), 6.42 (d, 1H, J = 3.8 Hz), 4.35 (q, 1H, J = 6.9 Hz), 1.57 (d, 3H, J = 6.8 Hz);

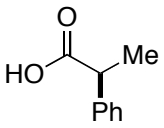
^{13}C NMR (100 MHz, $CDCl_3$): δ 172.5, 141.1, 136.1, 130.4, 129.5, 127.6, 127.4, 125.4, 125.1, 124.0, 120.9, 117.1, 109.3, 46.5, 20.5;

IR (film): 1701, 1540, 1451, 1352, 1292, 1208, 910, 750, 700 cm^{-1};

LRMS (EI) for $C_{17}H_{15}NO$ (M): calcd 249, found 249;

$[\alpha]^{18}_D$ +101 (*c* 0.87, $(CH_3)_2CO$); >99% ee, based on the ee of the acid (after hydrolysis).

(4) Dai, X.; Strotman, N. A.; Fu, G. C. *J. Am. Chem. Soc.* **2008**, *130*, 3302–3303.

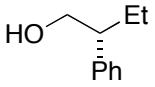


(*S*)-2-Phenylpropionic acid [7782-24-3] (eq 4). A solution of aqueous H_2O_2 (30% w/w; 1 mL) and LiOH·H_2O (192 mg, 4.58 mmol, 3.25 equiv) were added to a solution of (*S*)-1-(1*H*-indol-1-yl)-2-phenylpropan-1-one (351 mg, 1.41 mmol) in THF (14 mL) and H_2O (4 mL) at 0 °C. The resulting suspension was allowed to warm to room temperature and stirred overnight. Next, the reaction was quenched by the addition of saturated sodium thiosulfate (8 mL) and saturated sodium bicarbonate (10 mL). The mixture was stirred for 15 min, and then the THF was removed by rotary evaporation, and the aqueous layer was extracted with CH_2Cl_2 (10 mL). Next, the aqueous layer was acidified (pH<5) with HCl (1 M) and extracted with EtOAc (15 mL × 4). The combined organic layers were dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography (2%→20% EtOAc in hexanes), which furnished the product (161 mg, 76%) as a brown oil.

The ee was determined on an AD-H column (hexanes:isopropanol 97:3, flow 1.0 mL/min), with enantiomers eluting at 29.9 (minor) and 34.2 (major) min.

^{1}H NMR (400 MHz, $CDCl_3$): δ 12.01 (br s, 1H), 7.41-7.36 (m, 4H), 7.36-7.29 (m, 1H), 3.74 (q, 1H, *J* = 7.2 Hz), 1.52 (d, 3H, *J* = 7.2 Hz);

$[\alpha]^{18}_D$ +59 (*c* 1.01, $CHCl_3$); >99% ee. Lit.[5] $[\alpha]^{20}_D$ +72 (*c* 1.0, $CHCl_3$), 96% ee (S).



(*R*)-(–)-2-Phenyl-1-butanol [16460-75-6].[6] A solution of *n*-BuLi (1.6 M solution in hexanes; 0.83 mL, 1.33 mmol, 3.9 equiv) was added dropwise to a solution of diisopropylamine (200 μL, 1.43 mmol, 4.2 equiv) in THF (5 mL) at 0 °C. The mixture was stirred for 15 min, then ammonia·borane (44 mg, 1.2 mmol, 3.5 equiv) was added. The resulting mixture was stirred at 0 °C for 15 min, and then it was warmed to room temperature. A solution of (*R*)-1-(indolin-1-yl)-2-phenylbutan-1-one (90% ee; 89 mg, 0.34 mmol, 1.0 equiv) in THF (5 mL) was added, and then the reaction mixture was heated to reflux for 22 h. Next, the mixture was cooled to 0 °C, and the reaction was quenched by the addition of aqueous HCl (1 M; 5 mL). The layers were separated, and the aqueous layer was extracted with Et_2O (3 mL × 4). The combined organic layers were washed with HCl (1 M; 3 mL), NaOH (2 M; 4 mL), and brine (3 mL). The organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography (8%→60% Et_2O in hexanes), then washed with HCl (1 M; 3 mL; to remove an indoline impurity), thereby producing the alcohol as a yellow oil (25 mg, 49%).

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(5) Coulbeck, E.; Eames, J. *Tetrahedron: Asymmetry* **2008**, *19*, 2223–2233.

(6) Myers, A. G.; Yang, B. H.; Chen, H.; McKinstry, L.; Kopecky, D. J.; Gleason, J. L. *J. Am. Chem. Soc.* **1997**, *119*, 6496–6511.

The ee was determined to be 90% on an AD-H column (hexanes:isopropanol 99:1, flow 1.0 mL/min), with enantiomers eluting at 14.3 (major) and 15.7 (minor) min.

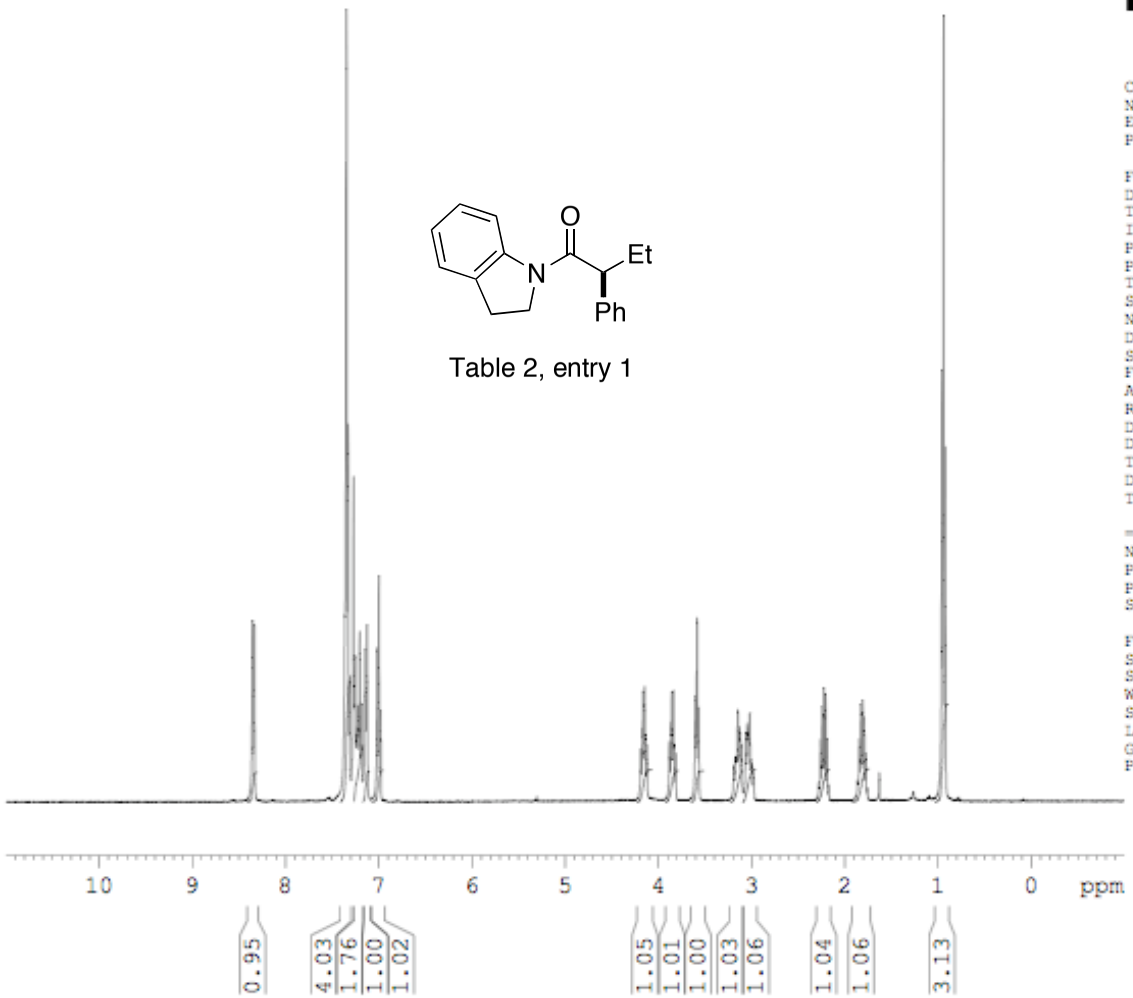
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32-7.27 (m, 2H), 7.22-7.16 (m, 3H), 3.75-3.65 (m, 2H), 2.67-2.62 (m, 1H), 1.76-1.68 (m, 1H), 1.62-1.50 (m, 2H), 0.80 (t, 3H, J = 7.4 Hz);

$[\alpha]^{23}_D$ –15.1 (*c* 0.95, $CHCl_3$); 90% ee. Lit. $[\alpha]^{23}_D$ –15.0±2.5 (*c* 1.00, $CHCl_3$), 92% ee (*R*);[7] $[\alpha]^{22}_D$ +18 (*c* 1.50, $CHCl_3$), 99% ee (*S*).[8]

VI. ^{1}H NMR Spectra

(7) Matsubara, S.; Yamamoto, H.; Oshima, K. *Angew. Chem., Int. Ed.* **2002**, *41*, 2837–2840

(8) Dai, X.; Strotman, N. A.; Fu, G. C. *J. Am. Chem. Soc.* **2008**, *130*, 3302–3303.



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BRUKER

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PROCNO                    1

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PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH               8278.146 Hz
FIDRES           0.126314 Hz
AQ               3.9584243 sec
RG                      362
DW                 60.400 usec
DE                  6.00 usec
TE                  292.2 K
D1              1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    1H
P1                  14.00 usec
PL1                  0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                    65536
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WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
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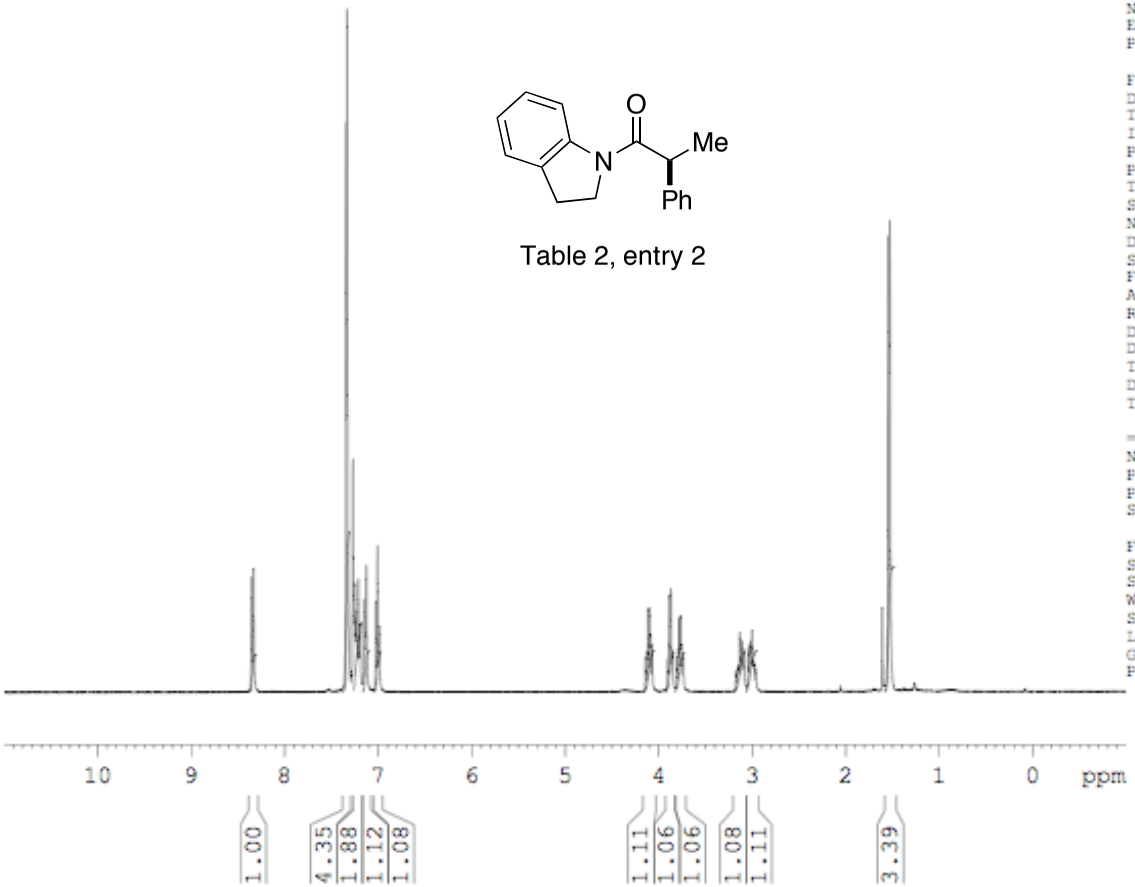

Table 2, entry 2

BRUKER

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EXPNO                     2
PROCNO                    1

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PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                      362
DW                   60.400 usec
DE                    6.00 usec
TE                   291.2 K
D1                1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                    14.00 usec
PL1                    0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                    65536
SF            400.1300074 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
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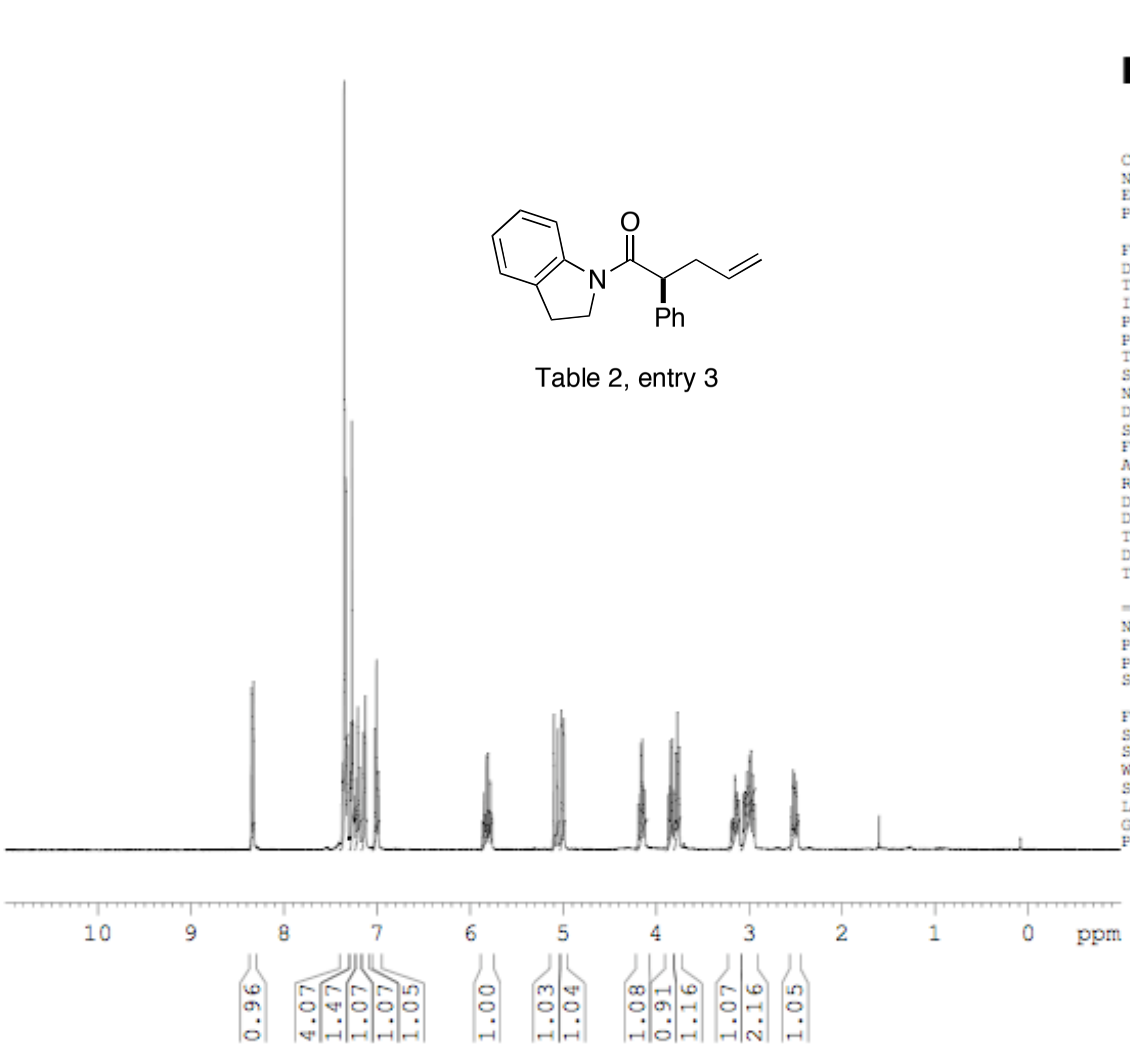

Table 2, entry 3

BRUKER

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NAME                  V-080
EXPNO                     5
PROCNO                    1

F2 - Acquisition Parameters
Date_              20100111
Time                  20.24
INSTRUM               spect
PROBHD    5 mm QNP 1H/13
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                      512
DW                   60.400 usec
DE                    6.00 usec
TE                   292.2 K
D1              1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    1H
P1                   14.00 usec
PL1                   0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                    65536
SF            400.1300074 MHz
WDW                      EM
SSB                       0
LB                    0.30 Hz
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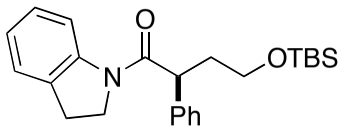

Table 2, entry 4


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EXPNO                     3
PROCNO                    1

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Time                   9.43
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PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                     203.2
DW                    60.400 usec
DE                     6.00 usec
TE                    292.2 K
D1              1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                    14.00 usec
PL1                    0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
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SF            400.1300220 MHz
WDW                      EM
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LB                     0.30 Hz
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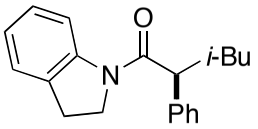

Table 2, entry 5


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EXPNO                     1
PROCNO                    1

F2 - Acquisition Parameters
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Time                  11.07
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PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                      256
DW                   60.400 usec
DE                    6.00 usec
TE                   292.2 K
D1                1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                    14.00 usec
PL1                    0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                    65536
SF            400.1300074 MHz
WDW                      EM
SSB                       0
LB                    0.30 Hz
GB                        0
PC                    1.00
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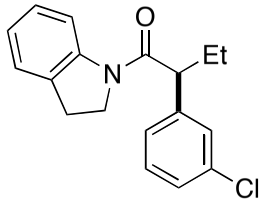

Table 2, entry 6


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Current Data Parameters
NAME                  V-107
EXPNO                     7
PROCNO                    1

F2 - Acquisition Parameters
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Time                  18.26
INSTRUM               spect
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PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                      181
DW                   60.400 usec
DE                    6.00 usec
TE                   293.2 K
D1                1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                    15.07 usec
PL1                    0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                    65536
SF                400.1300177 MHz
WDW                      EM
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LB                    0.30 Hz
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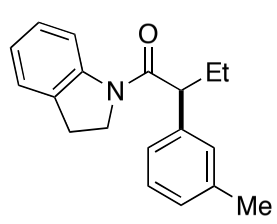

Table 2, entry 7


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Current Data Parameters
NAME                  V-067
EXPNO                     5
PROCNO                    1

F2 - Acquisition Parameters
Date_              20100107
Time                  20.03
INSTRUM               spect
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PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH               8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                    228.1
DW                   60.400 usec
DE                    6.00 usec
TE                   292.2 K
D1             1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                   14.00 usec
PL1                   0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                    65536
SF            400.1300074 MHz
WDW                      EM
SSB                       0
LB                    0.30 Hz
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PC                    1.00
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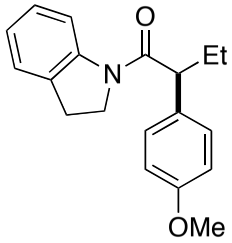

Table 2, entry 8


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EXPNO                     5
PROCNO                    1

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Time                  13.50
INSTRUM               spect
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PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH               8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                    228.1
DW                 60.400 usec
DE                  6.00 usec
TE                  293.2 K
D1             1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                   15.07 usec
PL1                   0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                    65536
SF            400.1300212 MHz
WDW                      EM
SSB                       0
LB                   0.30 Hz
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PC                     1.00
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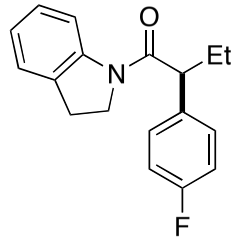

Table 2, entry 9


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PROCNO                    1

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Time                  20.19
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PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                    406.4
DW                   60.400 usec
DE                    6.00 usec
TE                   292.2 K
D1              1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                   14.00 usec
PL1                   0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                    65536
SF            400.1300074 MHz
WDW                      EM
SSB                       0
LB                    0.30 Hz
GB                        0
PC                    1.00
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