Enantioselective α-Arylation of Ketones with Aryl Triflates Catalyzed by Difluorphos Complexes of Palladium and Nickel

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Supporting Information

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General Method. All catalytic reactions were conducted in sealed vials, and the reactions were assembled in a nitrogen-filled glovebox. The synthesis of arylpalladium halide and arylnickel halide complexes was conducted in a nitrogen-filled glovebox. $\{Pd[P(o\text{-}Tol)_3](Br)(p\text{-}Tol)\}_2$ (95.4 mg, 0.0820 mmol) was prepared according to a literature procedure.[1] Aryl triflates were prepared as described previously.[2] All other chemicals were used as received from commercial sources. $Pd(dba)_2$, segphos, BINAP, P-phos and difluorphos were purchased from Strem Chemical Co. and used as received. Toluene were distilled under argon from sodium / benzophenone prior to use. ^1H NMR spectra were obtained on a 400- or 500-MHz spectrometer, and chemical shifts were recorded relative to residual protiated solvent. ^{13}C NMR spectra were obtained at 100.6 or 125.8 MHz on a 400- or 500-MHz instrument, and chemical shifts were recorded relative to the solvent resonance. Both ^1H NMR and ^{13}C NMR chemical shifts are reported in parts per million downfield from tetramethylsilane. Chromatographic purifications were performed by flash chromatography using silica gel (200-400 mesh) or preparative TLC. The yields of the coupled products included in all tables refer to isolated yields. Enantioselectivities were measured by HPLC using the indicated columns and conditions.

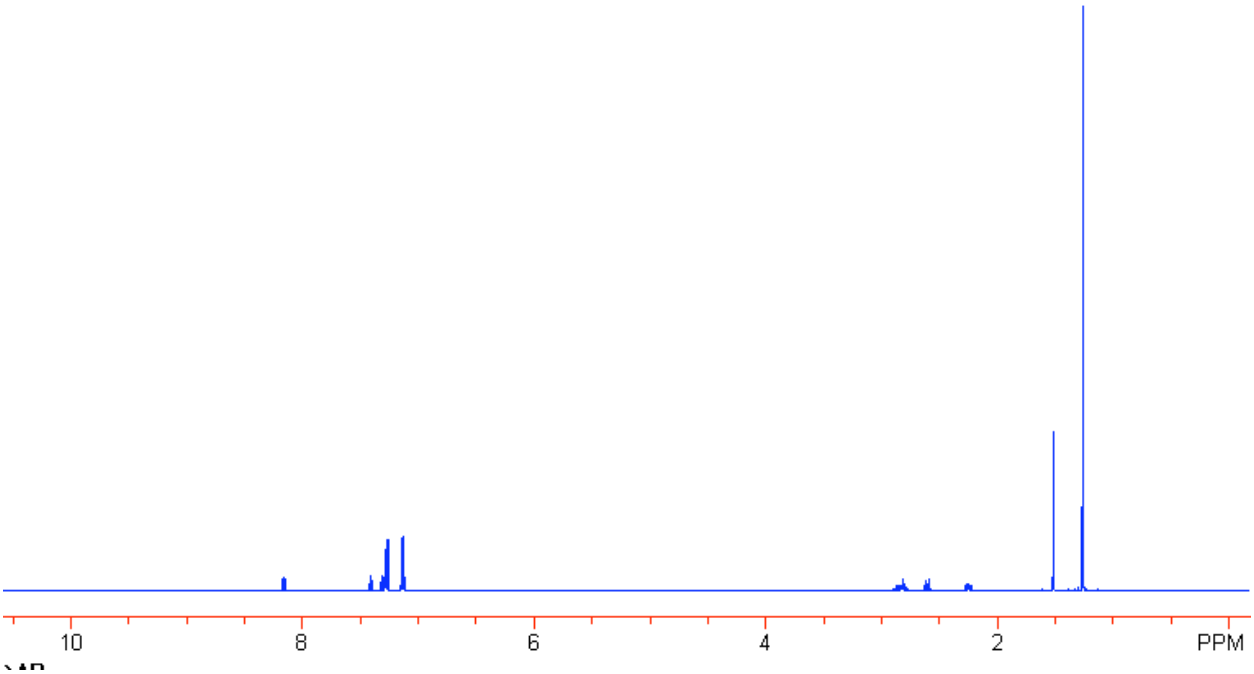
Representative Procedure for the Asymmetric Arylation of Ketones with Aryl Triflates using Pd(0)/Difluorphos (Method A). To a screw-capped vial containing (*R*)-difluorphos (8.2 mg, 0.012 mmol), $Pd(dba)_2$ (5.8 mg, 0.010 mmol), NaO^tBu (19.2 mg, 0.200 mmol) and the ketone (0.100 mmol) in toluene (2.0 mL) was added the aryl triflate (0.200 mmol). The vial was sealed with a cap containing a PTFE septum and removed from the drybox. The reaction mixture was stirred at 60 °C for 48-72 h. The crude reaction was then cooled to room temperature and quenched with ice water. The resulting solution was then diluted with ethyl acetate (15 mL) and washed with brine. The organic phase with dried over Na_2SO_4, filtered, and concentrated at

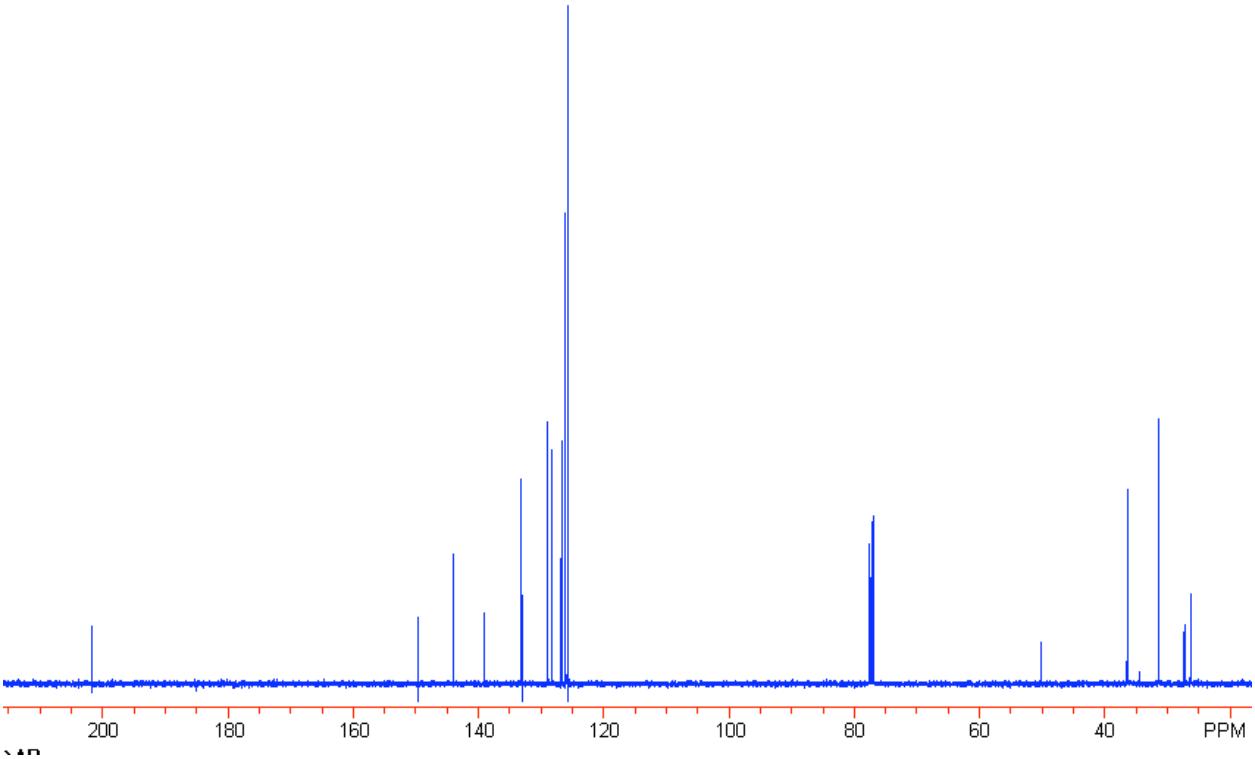
reduced pressure. Pure product was obtained from the residue by preparative TLC with the eluent described.

Representative Procedure for the Asymmetric Arylation of Ketones with Aryl Triflates Using Ni(0)/Difluorphos (Method B). To a screw-capped vial containing (*R*)-difluorphos (10.3 mg, 0.0150 mmol), $Ni(COD)_2$ (3.5 mg, 0.016mmol), NaO^tBu (48.0 mg, 0.500mmol) and the ketone (0.250 mmol) in toluene (2.0 mL) was added the aryl triflate (0.750 mmol). The vial was sealed with a cap containing a PTFE septum and removed from drybox. The reaction mixture was stirred at 80 ^oC for 60 h. The crude reaction was then cooled to room temperature and quenched with ice water. The resulting solution was then diluted with ethyl acetate (20 mL) and washed with brine. The organic phase was dried over Na_2SO_4, filtered, and concentrated at reduced pressure. The residue was then purified by chromatography on silica gel, eluting with hexane/ether to provide the product as indicated.

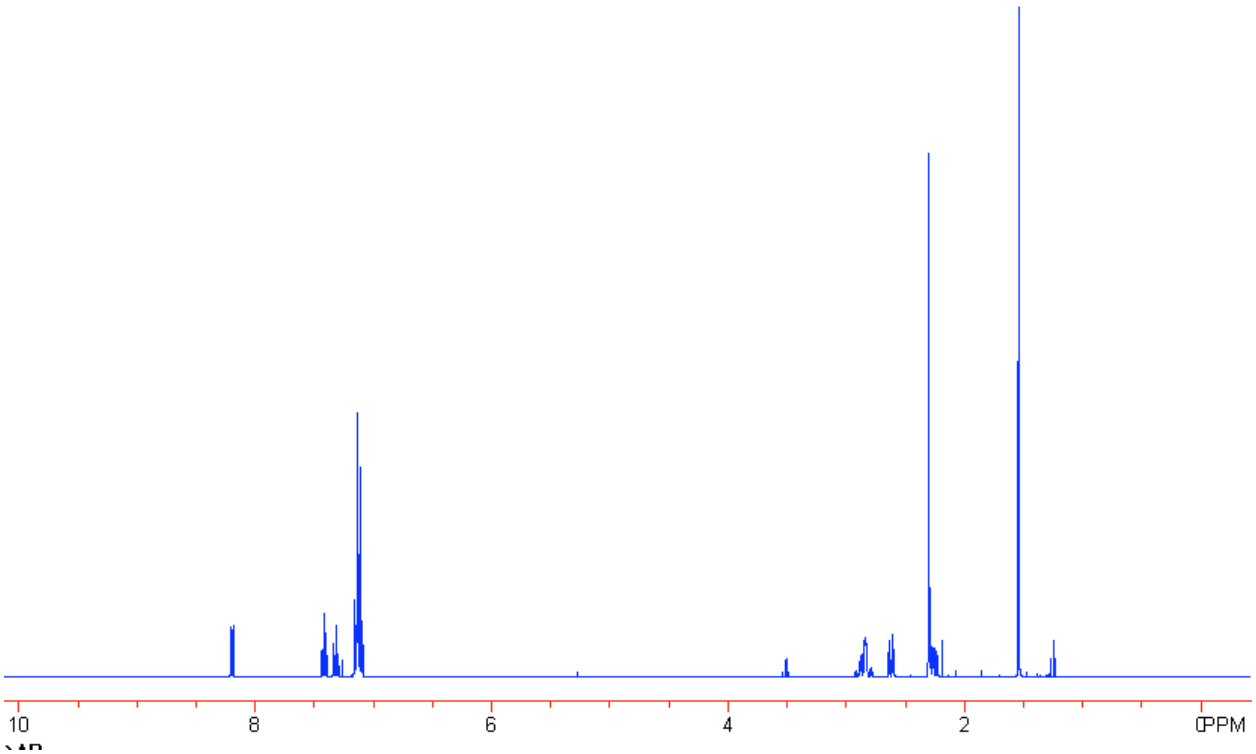
Representative Procedure for the Asymmetric Arylation of Ketones with Aryl Triflates Using Ni(0)/Difluorphos (Method C). To a screw-capped vial containing (*R*)-difluorphos (10.3 mg, 0.0150 mmol), $Ni(COD)_2$ (3.5 mg, 0.016 mmol), NaO^tBu (72.0 mg, 0.750 mmol) and ketone (0.250 mmol) in toluene (1.0 mL) was added the aryl triflate (0.100 mmol). The vial was sealed with a cap containing a PTFE septum and removed from drybox. The reaction mixture was stirred at 100 ^oC for 80 h. The crude reaction was then cooled to room temperature and quenched with ice water. The resulting solution was then diluted with ethyl acetate (20 mL) and washed with brine. The organic phase was dried over Na_2SO_4, filtered, and concentrated at reduced pressure. The residue was then purified by chromatography on silica gel, eluting with hexane/ether to provide the product as indicated yield.

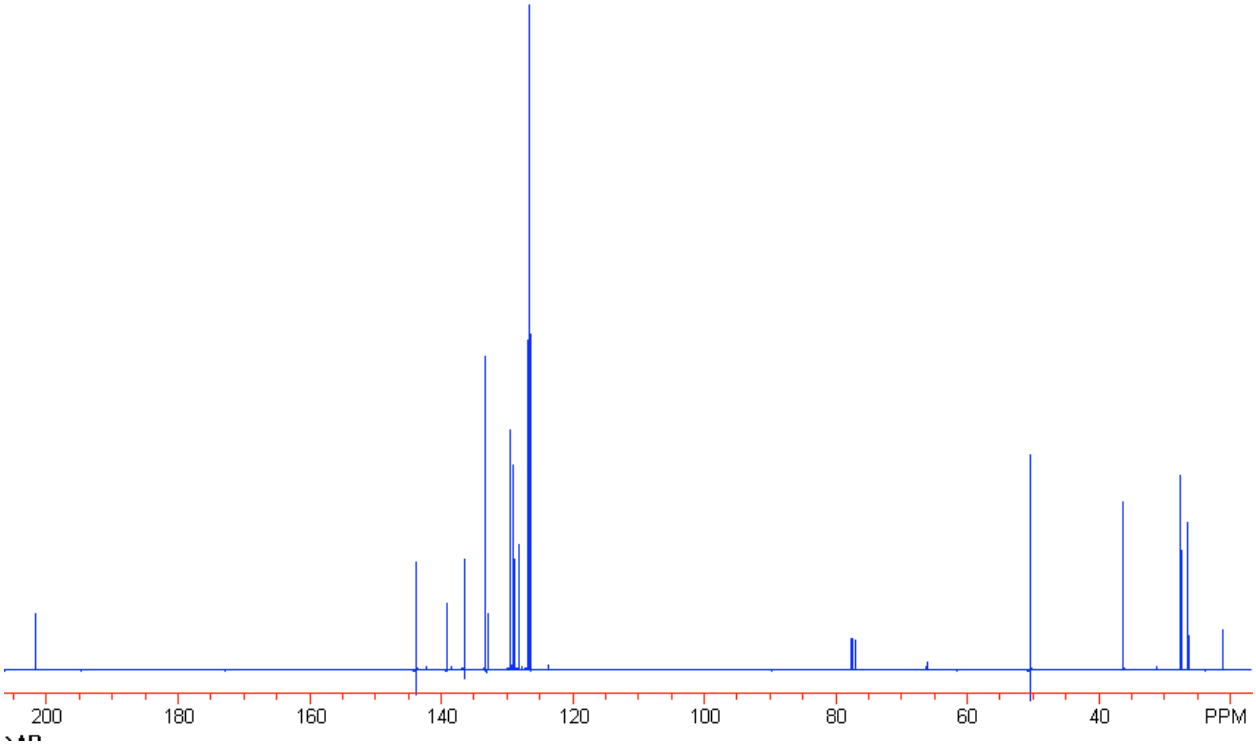
2-Methyl-2-(4-*t*-butylphenyl)-1-tetralone (Table 2, Entry 2). Method A was followed. The reaction mixture was stirred for 48 h and was purified by preparative TLC (hexane/ether = 97:3) to provide the title compound as white solid in 85% yield. The ee was determined to be 92% by chiral HPLC analysis (Chiralcel OJ-H column; solvent, hexane/isopropanol (99/1); flow rate, 0.50 mL/min; UV lamp, 254 nm). $[\alpha]^{26}_{D}$= 164 (c = 0.40, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.26 (9H, s), 1.52 (3H, s), 2.22-2.28 (1H, m), 2.60 (1H, dt, J = 13.9, 4.1 Hz), 2.77-2.89 (2H, m), 7.11-7.15 (2H, m), 7.26-7.32 (4H, m), 7.41 (1H, td, J = 7.6, 1.4 Hz), 8.16 (1H, dd, J = 7.9, 1.5 Hz) ^{13}C NMR ($CDCl_3$, 125 MHz): δ 26.4, 27.3, 31.5, 34.5, 36.5, 50.3, 125.7, 126.2, 126.8, 128.2, 128.9, 132.9, 133.3, 139.1, 144.0, 149.6, 201.7.





2-Methyl-2-(4-methylphenyl)-1-tetralone (Table 2, Entry 3). Method A was followed. The reaction mixture was stirred for 48 h and was purified by preparative TLC (hexane/ether = 97:3) to provide the title compound in 79% yield. . The ee was determined to be 92% by chiral HPLC analysis (Chiralcel AD-H column; solvent, hexane/isopropanol (98/2); flow rate, 0.50 mL/min; UV lamp, 254 nm). $[\alpha]^{26}_{D}$= 233.7 (c = 0.19, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.54 (3H, s), 2.21-2.30 (1H, m), 2.30 (3H, s), 2.62 (1H, dt, J = 14.0, 3.9 Hz), 2.82-2.89 (2H, m), 7.09-7.16 (5H, m), 7.32 (1H, t, J = 7.5 Hz), 7.42 (1H, td, J = 7.4, 1.5 Hz), 8.19 (1H, dd, J = 7.8, 1.5 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.2, 26.4, 27.5, 36.3, 50.4, 126.5, 126.8, 128.2, 128.9, 129.5, 132.9, 133.3, 136.5, 139.2, 143.8, 201.7.





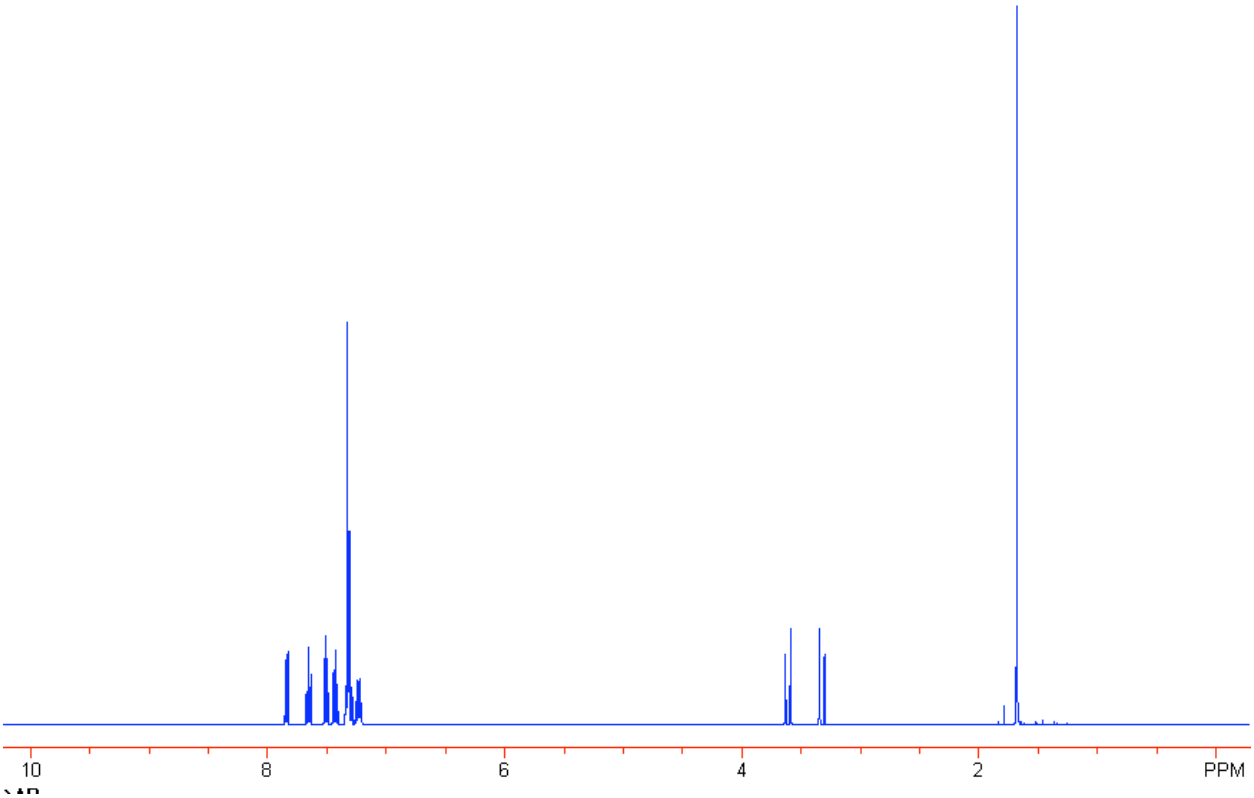
2-Methyl-2-(3,5-di-*t*-butylphenyl)-1-tetralone (Table 2, Entry 4). Method A was followed. The reaction mixture was stirred for 48 h and was purified by preparative TLC (hexane/ether =

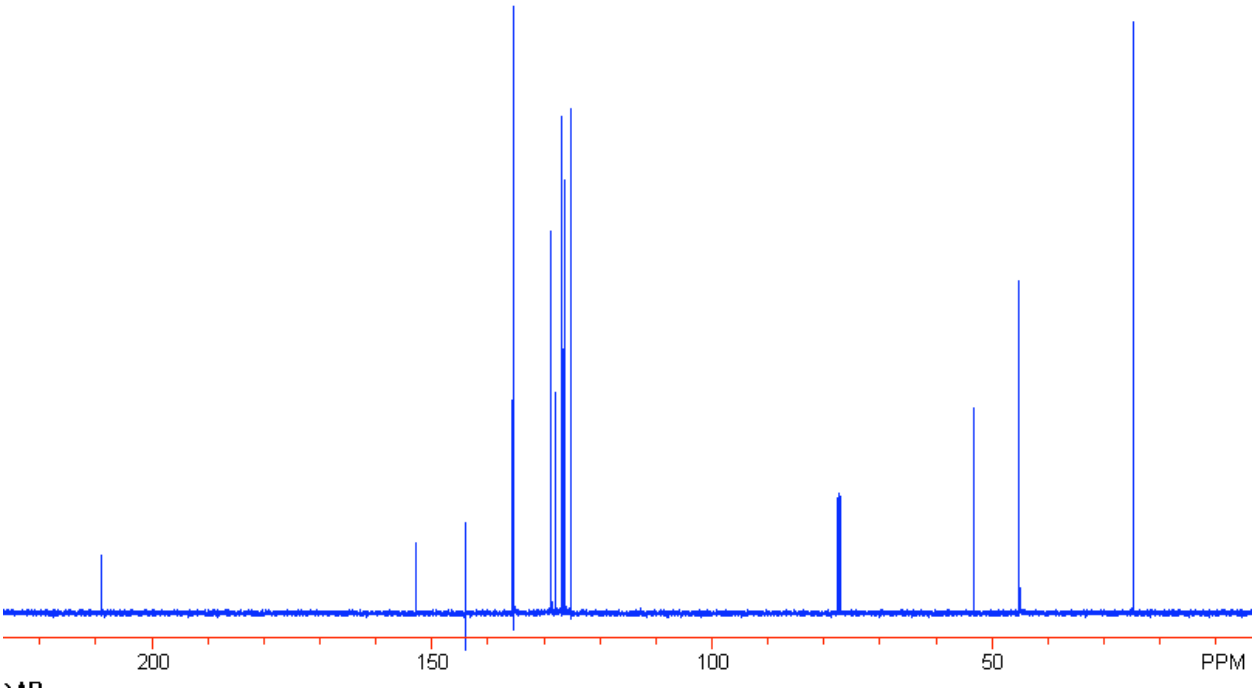
97:3) to provide the title compound as a white solid in 83% yield. . The ee was determined to be 95% by chiral HPLC analysis (Chiralcel AD-H column; solvent, hexane/isopropanol (99/1); flow rate, 0.50 mL/min; UV lamp, 254 nm). $[\alpha]^{26}_{D}$= 236 (c = 0.11, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.24 (18H, s), 1.53 (3H, s), 2.22-2.29 (1H, m), 2.63 (1H, dt, J = 14.1, 3.9 Hz), 2.70-2.90 (2H, m), 7.05 (2H, d, J = 1.7 Hz), 7.11 (1H, d, J = 6.0 Hz), 7.23 (1H, t, J = 1.7 Hz), 7.29 (1H, t, J = 7.6 Hz), 7.39 (1H, td, J = 7.3, 1.4 Hz), 8.13 (1H, dd, J = 7.8, 1.0 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 26.3, 27.5, 31.6, 35.1, 36.3, 50.8, 120.7, 120.8, 126.7, 128.0, 128.8, 133.0, 133.3, 140.9, 143.7, 150.7, 202.0. Anal. Calcd. For $C_{25}H_{32}O$: C, 86.15; H, 9.25. Found: C, 85.99; H, 9.51.

2-Methyl-2-(3,4-di-methoxylphenyl)-1-tetralone (Table 2, Entry 5). Method A was followed. The reaction mixture was stirred for 72 h and was purified by preparative TLC (hexane/ether = 80:20) to provide the title compound in 79% yield. . The ee was determined to be 91% by chiral HPLC analysis (Chiralcel AD-H column; solvent, hexane/isopropanol (90/10); flow rate, 0.5 mL/min; UV lamp, 254 nm). $[\alpha]^{26}_{D}$= 193(c = 0.24, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.50 (3H, s), 2.18-2.27 (1H, m), 2.56 (1H, dt, J = 14.2, 3.9 Hz), 2.75-2.92 (2H, m), 3.79 (6H, s), 6.72-6.74 (3H, m), 7.09 (1H, d, J = 7.6 Hz), 7.27 (1H, t, J = 7.7 Hz), 7.39 (1H, t, J = 7.0 Hz), 8.12 (1H, d, J = 7.8 Hz) ^{13}C NMR ($CDCl_3$, 100 MHz): δ 26.3, 27.4, 36.4, 50.3, 56.0, 56.1, 110.0, 111.2, 118.9, 126.8, 128.1, 128.9, 132.8, 133.3, 134.5, 143.8, 147.9, 149.1, 201.6. Anal. Calcd. For $C_{19}H_{20}O_3$: C, 77.00; H, 6.80. Found: C, 76.91; H, 6.80.

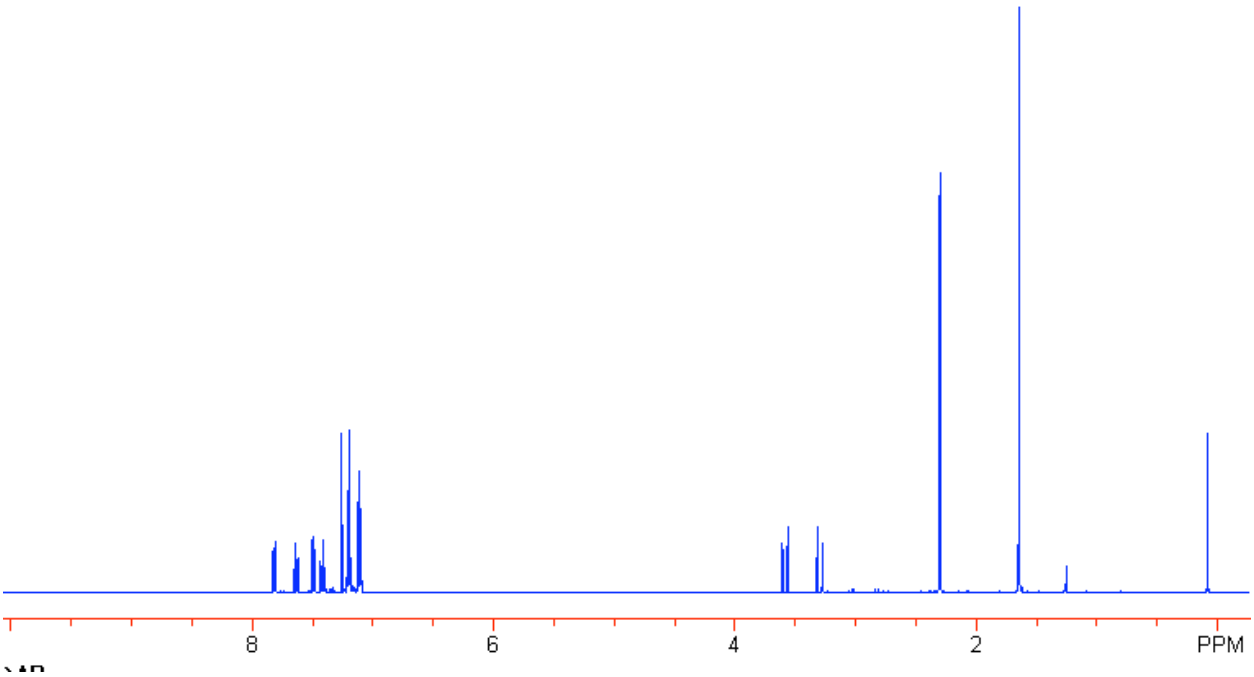
2-Methyl-2-phenyl-1-indanone (Table 2, Entry 6). Method A was followed. The reaction mixture was stirred for 40 h and was purified by preparative TLC (hexane/ether = 97:3) to provide the title compound in 77% yield. . The ee was determined to be 70% by chiral HPLC analysis (Chiralcel AD-H column; solvent, hexane/isopropanol (99/1); flow rate, 0.50 mL/min; UV lamp, 254 nm). $[\alpha]^{26}_{D}$= -34.9 (c = 0.48, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.68 (3H, s),

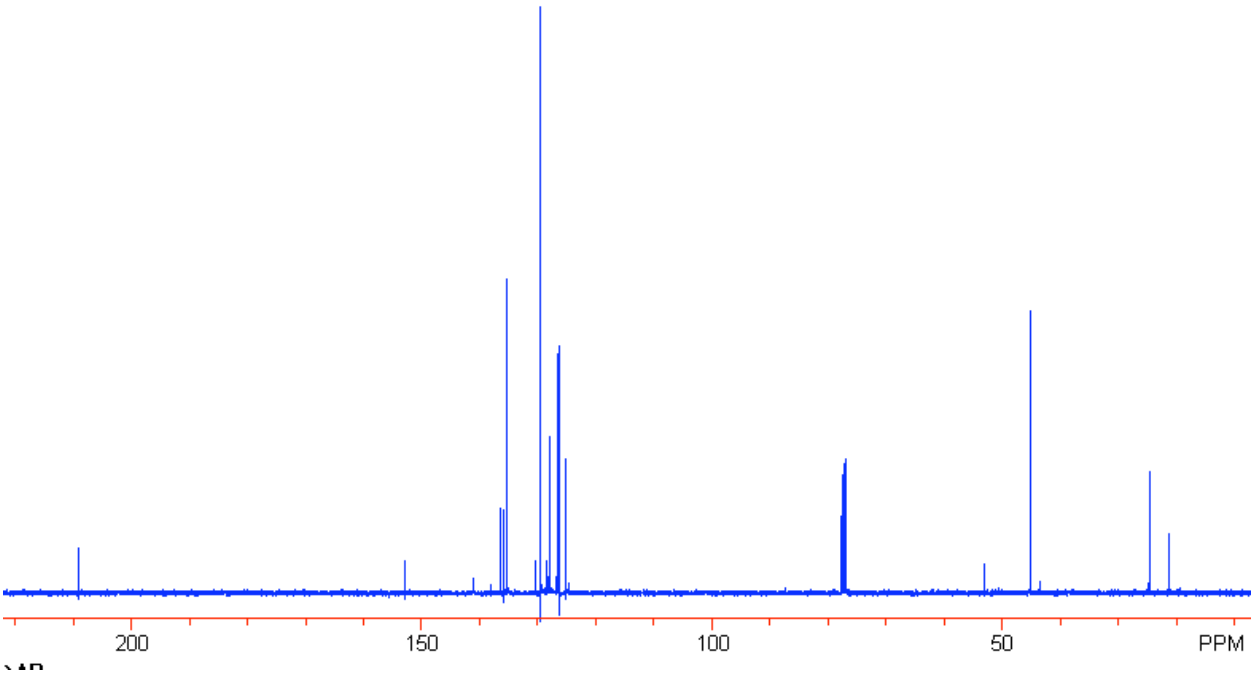
3.32 (1H, d, J = 17.6 Hz), 3.61 (1H, d, J = 17.3 Hz), 7.21-7.27 (1H, m), 7.28-7.36 (4H, m), 7.43 (1H, t, J = 7.5 Hz), 7.51 (1H, d, J = 7.7 Hz), 7.65 (1H, t, J = 7.4 Hz), 7.84 (1H, d, J = 7.6 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ □24.6, 45.1, 53.3, 125.1, 126.4, 126.6, 126.9, 128.0, 128.8, 135.4, 135.8, 144.1, 152.9, 209.0.





2-Methyl-2-(4-methylphenyl)-1-indanone (Table 2, Entry 7). Method A was followed and the reaction mixture was stirred for 40 h, then purified by preparative TLC (hexane/ether = 97:3) to provide the title compound in 79% yield. . The ee was determined to be 78% by chiral HPLC analysis (Chiralcel AD-H column; solvent, hexane/isopropanol (98.5/1.5); flow rate, 1.0 mL/min; UV lamp, 254 nm). $[\alpha]^{26}_{D}$= -35.2 (c = 0.25, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.65 (3H, s), 2.30 (3H, s), 3.30 (1H, d, J = 17.3 Hz), 3.59 (1H, d, J = 17.3 Hz), 7.11 (2H, d, J = 8.5 Hz), 7.20 (2H, d, J = 8.3 Hz), 7.42 (1H, t, J = 7.4 Hz), 7.49 (1H, d, J = 7.8 Hz), 7.64 (1H, t, J = 7.5 Hz), 7.81 (1H, d, J = 7.5 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.2, 24.6, 45.1, 53.1, 125.1, 126.2, 126.6, 127.9, 129.5, 135.3, 135.9, 136.5, 141.0, 152.8, 209.1.





2-Methyl-2-(3,5-di-*t*-butylphenyl)-1-indanone (Table 2, Entry 8). Method A was followed. The reaction mixture was stirred for 40 h and was purified by preparative TLC (hexane/ether = 97:3) to provide the title compound as a white solid in 84% yield. . The ee was determined to be 89% by chiral HPLC analysis (Chiralcel AD-H column; solvent, hexane/isopropanol (98.6/1.4);

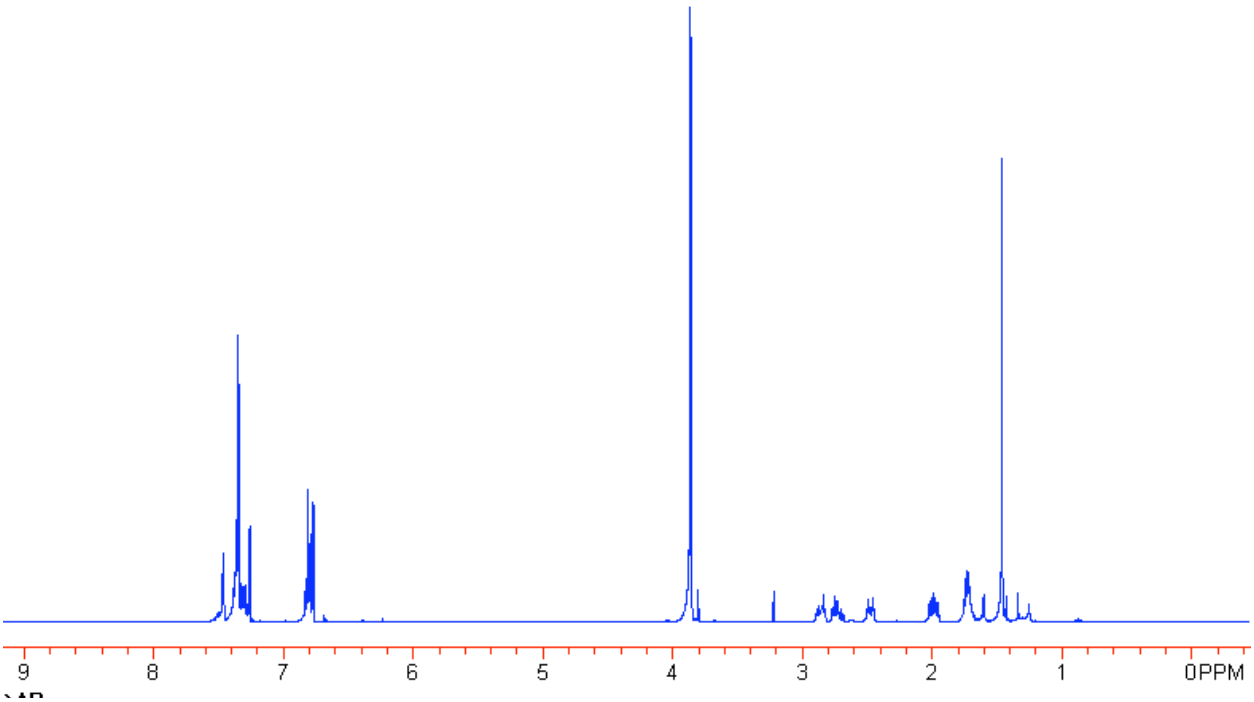
flow rate, 0.50 mL/min; UV lamp, 254 nm). $[\alpha]^{26}_{D}$= -19.3 (c = 0.15, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.30 (18H, s), 1.68 (3H, s), 3.32 (1H, d, J = 17.1 Hz), 3.63 (1H, d, J = 17.4 Hz), 7.18 (2H, d, J = 1.8 Hz), 7.31 (1H, t, J = 1.7 Hz), 7.43 (1H, t, J = 7.5 Hz), 7.50 (1H, d, J = 7.7 Hz), 7.65 (1H, td, J = 7.5, 1.1 Hz), 7.84 (1H, d, J = 7.7 Hz) ; ^{13}C NMR ($CDCl_3$, 125 MHz): δ25.2, 31.7, 35.2, 45.3, 53.8, 120.6, 121.0, 125.1, 126.5, 127.9, 135.2, 136.0, 143.0, 150.8, 152.8, 209.2. Anal. Calcd. For $C_{24}H_{30}O$: C, 86.18; H, 9.04. Found: C, 86.103; H, 9.27.

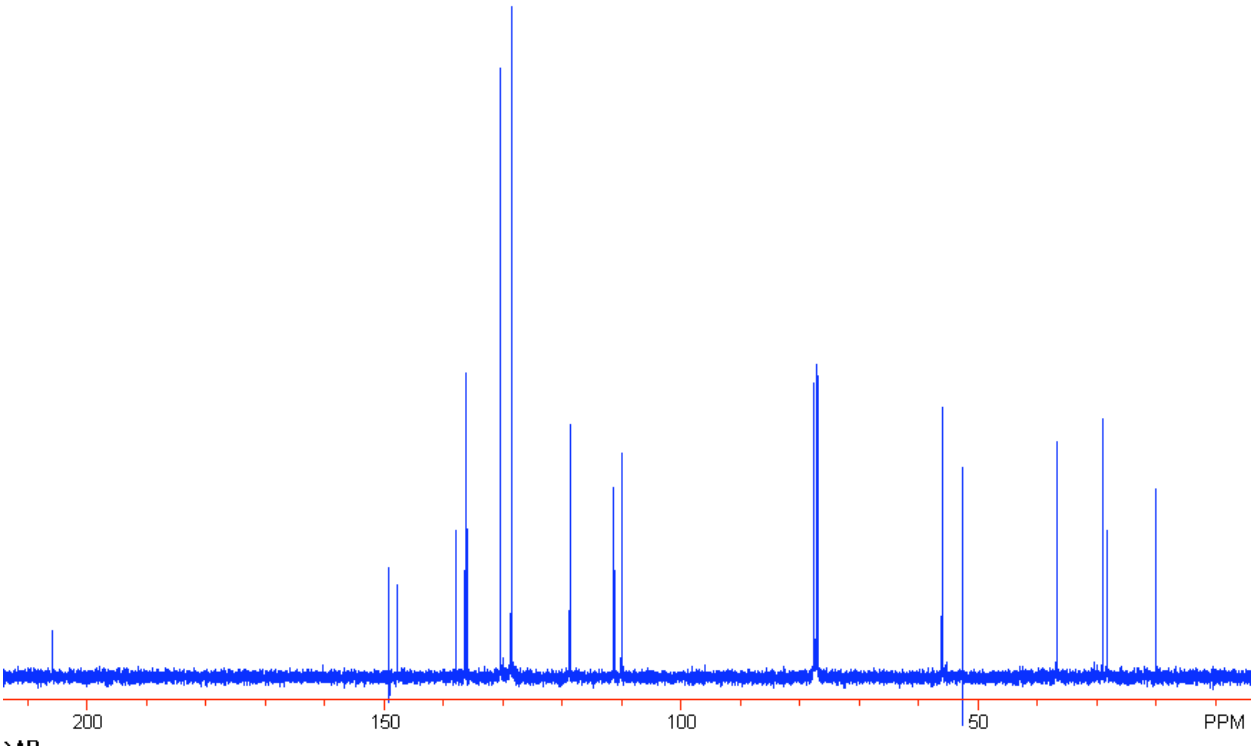
2-Methyl-2-(3,4-di-methoxylphenyl)-1-indanone (Table 2, Entry 9). Method A was followed. The reaction mixture was stirred for 50 h and was purified by preparative TLC (hexane/ether = 80:20) to provide the title compound in 78% yield. The ee was determined to be 82% by chiral HPLC analysis (Chiralcel AD-H column; solvent, hexane/isopropanol (90/10); flow rate, 0.50 mL/min; UV lamp, 254 nm). $[\alpha]^{26}_{D}$= -62.2 (c = 0.50, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.63 (3H, s), 3.28 (1H, d, J = 17.3 Hz), 3.57 (1H, d, J = 17.4 Hz), 3.820 (3H, s), 3.823 (3H, s), 6.77 (1H, d, J = 8.1 Hz), 6.83 (1H, d, J = 2.2 Hz), 6.84-6.86 (1H, m), 7.40 (1H, t, J = 7.4 Hz), 7.48 (1H, d, J = 7.5 Hz), 7.63 (1H, td, J = 7.5, 1.2 Hz), 7.80 (1H, d, J = 7.7 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 25.1, 45.0, 53.0, 56.1(2 overlapping resonances), 110.1, 111.2, 118.5, 125.1, 126.6, 128.0, 135.4, 135.7, 136.5, 148.0, 149.0, 152.7, 209.0. Anal. Calcd. For $C_{18}H_{18}O_3$: C, 76.57; H, 6.43. Found: C, 76.33; H, 6.45.

6-Benzylidene-2-methyl-2-phenyl-cyclohexanone (Table 2, Entry 10). Method A was followed. The reaction mixture was stirred for 60 h and was purified by preparative TLC (hexane/ether = 97:3) to provide the title compound in 80% yield. . The ee was determined to be 78% by chiral HPLC analysis (Chiralcel AD-H column; solvent, hexane/isopropanol (98/2); flow rate, 0.50 mL/min; UV lamp, 254 nm). $[\alpha]^{26}_{D}$= 164 (c = 0.40, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.50 (3H, s), 1.62-1.77 (2H, m), 1.97-2.05 (1H, m), 2.48-2.55 (1H, m), 2.70-2.79 (1H,

m), 2.83-2.89 (1H, m), 7.18-7.44 (10H, m), 7.49-7.52 (1H, m). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.0, 28.2, 29.1, 36.9, 53.0, 126.6, 126.7, 128.5, 128.6, 128.9, 130.4, 136.1, 136.5, 137.7, 144.2, 205.7. Anal. Calcd. For $C_{20}H_{20}O$: C, 86.92; H, 7.2. Found: C, 86.793; H, 7.03.

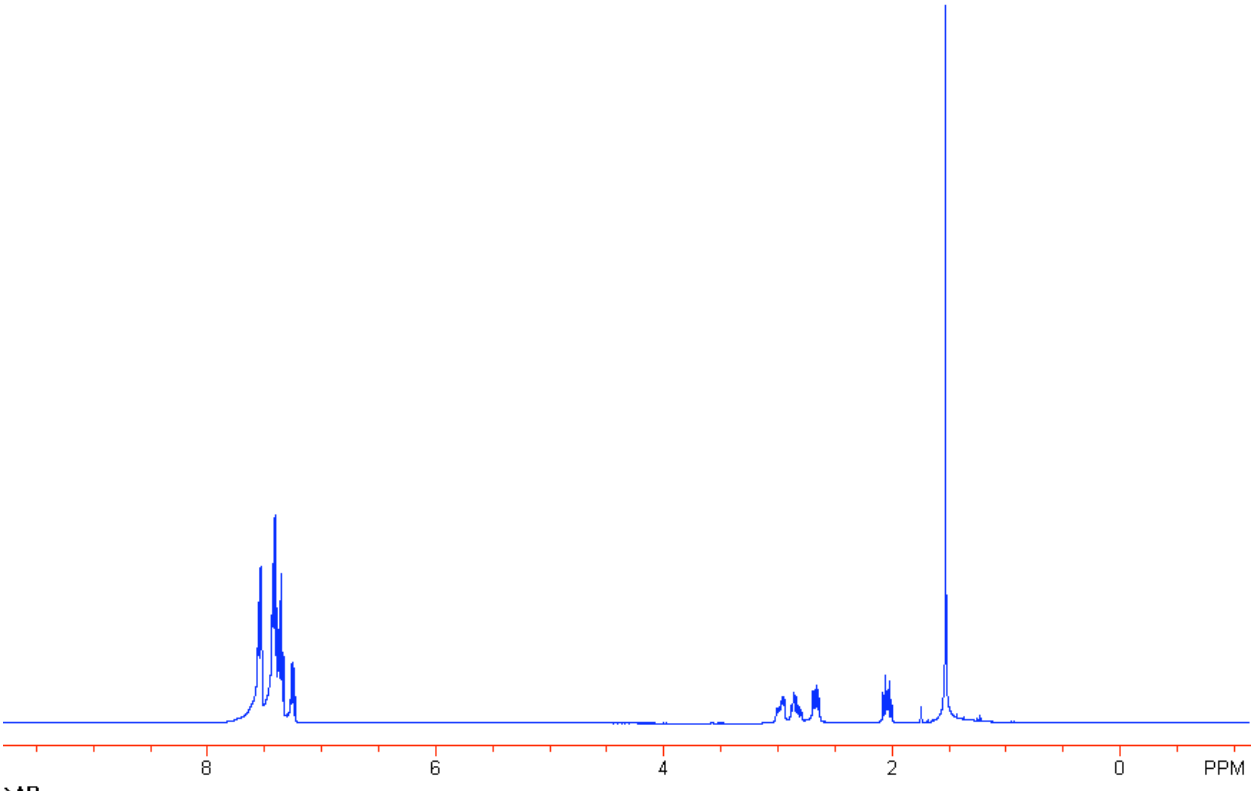
6-Benzylidene-2-methyl-2-(3,4-di-methoxyphenyl)-cyclohexanone (Table 2, Entry 11). Method A was followed. The reaction mixture was stirred for 72 h and was purified by preparative TLC (hexane/ether = 80:20) to provide the title compound in 70% yield. . The ee was determined to be 77% by chiral HPLC analysis (Chiralcel AD-H column; solvent, hexane/isopropanol (90/10); flow rate, 0.50 mL/min; UV lamp, 254 nm). $[\alpha]^{26}_D$= 84.7 (c = 0.43, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.46 (3H, s), 1.67-1.77 (2H, m), 1.94-2.05 (1H, m), 2.44-2.50 (1H, m), 2.68-2.77 (1H, m), 2.81-2.89 (1H, m), 3.86 (3H, s), 3.87 (3H, s), 6.76-6.83 (3H, m), 7.27-7.39 (5H, m), 7.46-7.49 (1H, m). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.0, 28.3, 29.1, 36.8, 50.6, 56.0, 56.1, 110.0, 111.3, 118.7, 128.5, 128.6, 130.4, 136.1, 136.30, 136.34, 138.0, 147.7, 149.1, 205.8.

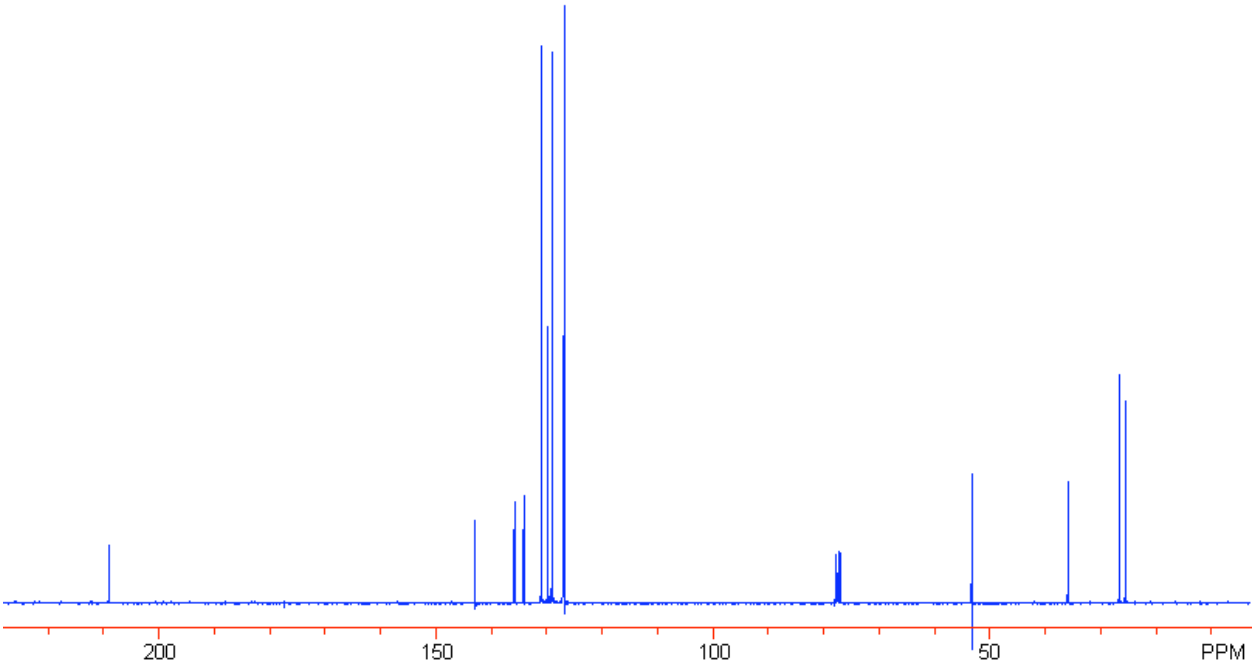




5-Benzylidene-2-methyl-2-phenyl-cyclopentanone (Table 2, Entry 12). Method A was followed. The reaction mixture was stirred for 60 h and was purified by preparative TLC (hexane/ether = 97:3) to provide the title compound in 70% yield. . The ee was determined to be

95% by chiral HPLC analysis (Chiralcel AD-H column; solvent, hexane/isopropanol (98/2); flow rate, 0.50 mL/min; UV lamp, 254 nm). $[\alpha]^{26}_{D}$= -28.3 (c = 0.12, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.53 (3H, s), 2.00-2.08 (1H, m), 2.63-2.70 (1H, m), 2.79-2.90 (1H, m), 2.93-3.02 (1H, m), 7.21-7.62 (11H, m). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 25.4, 26.5, 35.8, 53.3, 126.7, 127.0, 128.86, 128.94, 129.7, 130.9, 134.1, 135.7, 135.9, 142.8, 209.0.





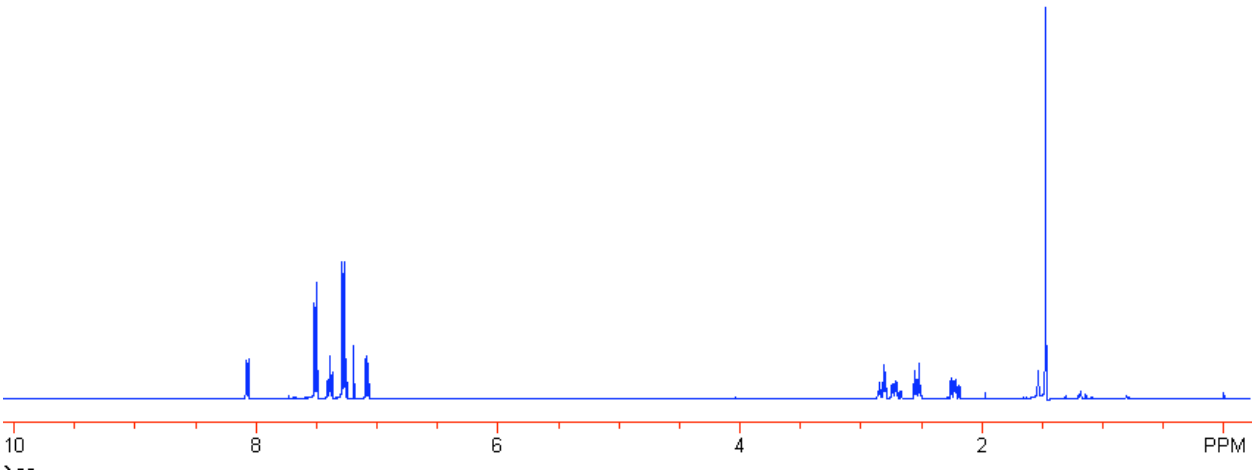
2-Methyl-2-(4-trifluoromethylphenyl)-1-indanone (Table 3, Entry 2). Method B was followed. The reaction mixture was stirred at 80 ^{o}C for 60 h and was purified by chromatography on silica gel, eluting with hexane/ether (97/3) to provide the product in 69%

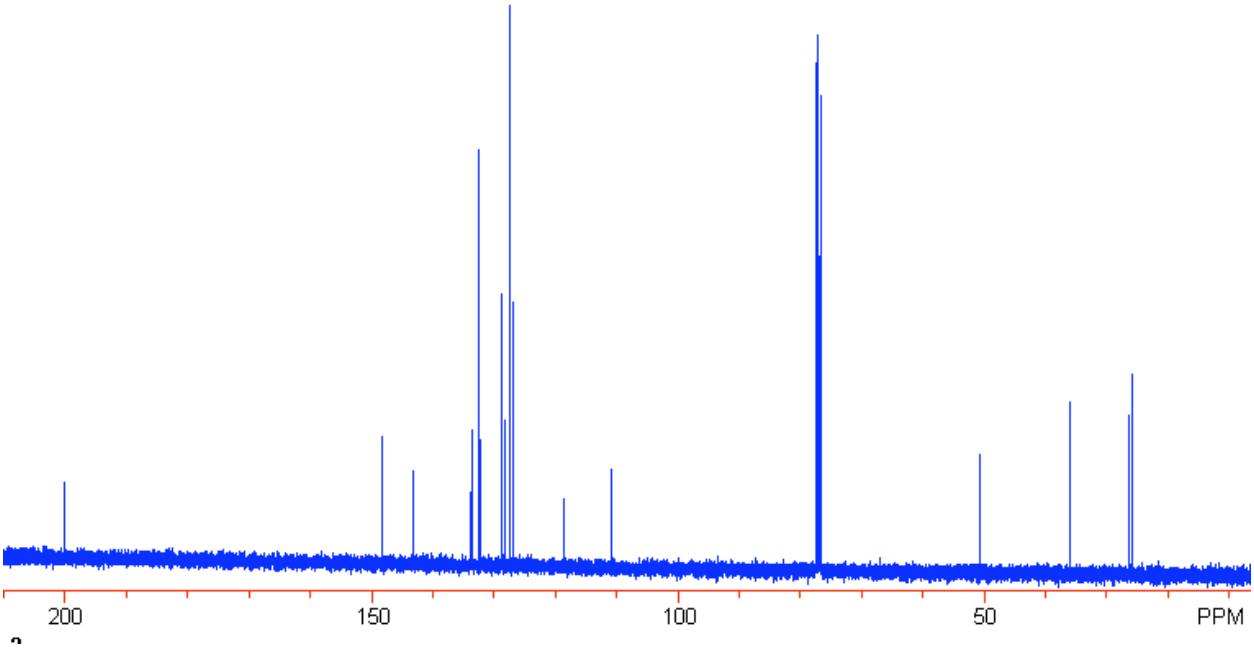
yield. The ee was determined to be 96% by chiral HPLC analysis (Chiralcel OJ column; solvent, hexane/isopropanol (98/2); flow rate, 0.50 mL/min; UV lamp, 254 nm). $[\alpha]^{26}_{D}$= -33.4 (c = 0.31, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.68 (3H, s), 3.35 (1H, d, J = 17.6 Hz), 3.58 (1H, d, J = 17.4 Hz), 7.42-7.46 (3H, m), 7.51 (1H, d, J = 7.5 Hz), 7.55 (2H, d, J = 7.1 Hz), 7.67 (1H, td, J = 7.5, 1.2 Hz), 7.83 (1H, d, J = 7.4 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 24.8, 44.8, 53.3, 124.4 (q, J = 270.3 Hz), 125.2, 125.7 (q, J = 3.8 Hz), 126.7, 126.9, 128.2, 129.1 (q, J = 32.4 Hz), 135.4, 135.7, 148.1, 152.5, 208.1 Anal. Calcd. For $C_{17}H_{13}F_3O$: C, 70.34; H, 4.51. Found: C, 69.92; H, 4.56.

2-Methyl-2-(3-trifluoromethylphenyl)-1-indanone (Table 3, Entry 3). Method B was followed. The reaction mixture was stirred at 80 ^{o}C for 70 h and was purified by chromatography on silica gel, eluting with hexane/ether (97/3) to provide the product in 70% yield. The ee was determined to be 86% by chiral HPLC analysis (Chiralcel OJ-H column; solvent, hexane/isopropanol (97/3); flow rate, 0.50 mL/min; UV lamp, 254 nm). $[\alpha]^{26}_{D}$= -30.2 (c = 0.45, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.67 (3H, s), 3.35 (1H, d, J = 17.3 Hz), 3.57 (1H, d, J = 17.3 Hz), 7.38-7.52 (5H, m), 7.61 (1H, brs), 7.66 (1H, td, J = 7.5, 1.2 Hz), 7.83 (1H, d, J = 7.8 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 25.0, 44.8, 53.2, 123.0 (q, J = 270.8 Hz), 123.2 (q, J = 3.8 Hz), 123.8 (q, J = 3.8 Hz), 125.2, 126.7, 128.2, 129.3, 130.9, 131.2 (q, J = 31.9 Hz), 135.4, 135.7, 145.1, 152.4, 208.1 Anal. Calcd. For $C_{17}H_{13}F_3O$: C, 70.34; H, 4.51. Found: C, 69.99; H, 4.46.

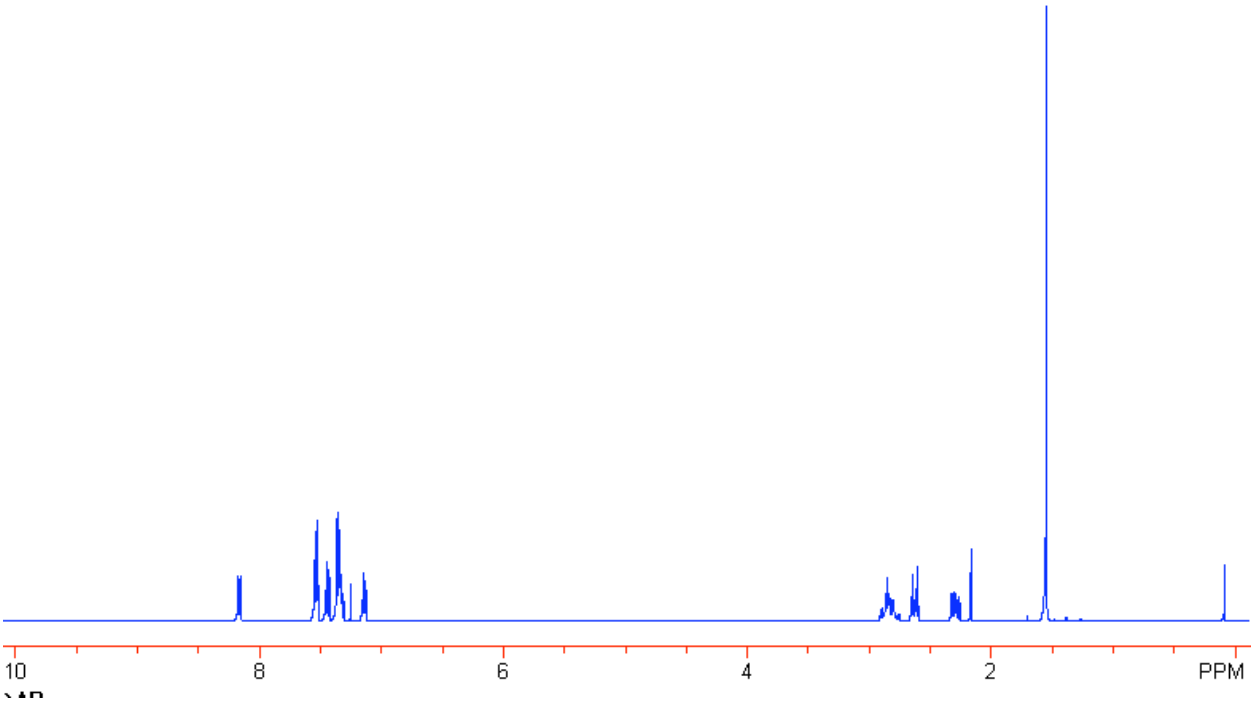
2-Methyl-2-(4-cyanophenyl)-1-tetralone (Table 3, Entry 4). Method C was followed. The reaction mixture was stirred at 100 ^{o}C for 80 h and was purified by chromatography on silica gel, eluting with hexane/ether (80/20) to provide the product in 55% yield. The ee was determined to be 97% by chiral HPLC analysis (Chiralcel OB-H column; solvent, hexane/isopropanol (80/20);

flow rate, 1.0 mL/min; UV lamp, 254 nm). $[\alpha]^{26}_{D}$= 191 (c = 0.44, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.53 (3H, s), 2.25-2.32 (1H, m), 2.60 (1H, dt, J = 14.2, 4.5 Hz), 2.73-2.80 (1H, m), 2.89 (1H, dt, J = 17.1, 4.4 Hz), 7.14 (1H, d, J = 7.8 Hz), 7.32-7.35 (3H, m), 7.45 (1H, t, J = 7.4 Hz), 7.55-7.58 (2H, m), 8.14 (1H, d, J =7.8Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 26.1, 26.5, 36.2, 50.9, 110.9, 118.9, 127.1, 127.6, 128.4, 129.0, 132.4, 132.6, 133.9, 143.4, 148.3, 200.4.





2-Methyl-2-(4-trifluoromethylphenyl)-1-tetralone (Table 3, Entry 5). Method C was followed. The reaction mixture was stirred at 100 ^{o}C for 80 h and was purified by chromatography on silica gel, eluting with hexane/ether (97/3) or bezene/CH_2Cl_2 (4/1) to provide the product in 40% yield. The ee was determined to be 98% by chiral HPLC analysis (Chiralcel OJ-H column; solvent, hexane/isopropanol (98/2); flow rate, 0.5 mL/min; UV lamp, 254 nm). $[\alpha]^{26}_{D}$= 162 (c = 0.35, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.56 (3H, s), 2.25-2.34 (1H, m), 2.63 (1H, dt, J = 14.0, 4.3 Hz), 2.76-2.92 (2H, m), 7.14 (1H, d, J = 7.5 Hz), 7.31-7.37 (3H, m), 7.44 (1H, td, J = 7.4, 1.4 Hz), 7.53 (2H, d, J = 8.0 Hz), 8.16 (1H, dd, J = 7.8, 1.0 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 26.2, 26.8, 36.3, 50.8, 124.3 (q, J = 270.6 Hz), 125.7 (q, J = 3.8 Hz), 127.0, 127.1, 128.3, 129.0, 129.2 (q, J = 32.4 Hz), 132.5, 133.7, 143.5, 146.7, 200.8.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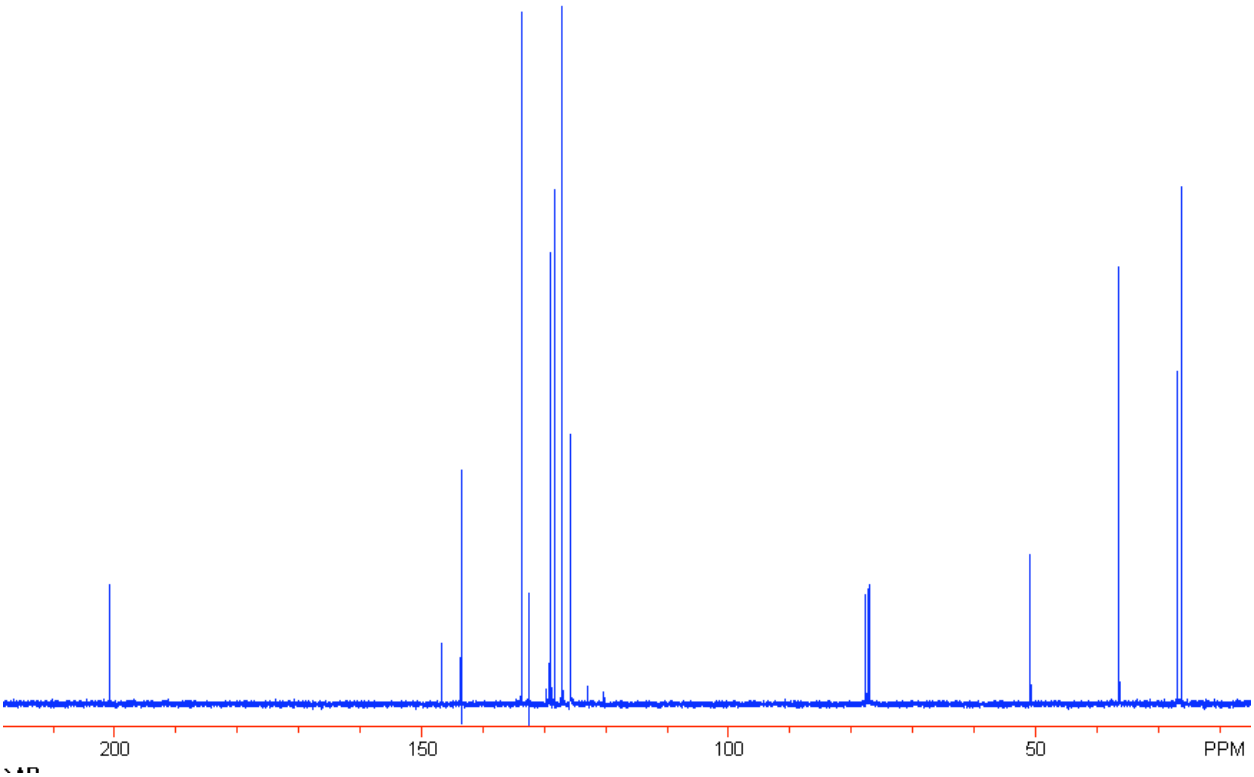
8
6
4
2
PPM


200
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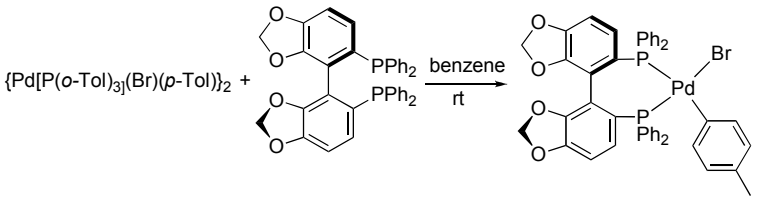
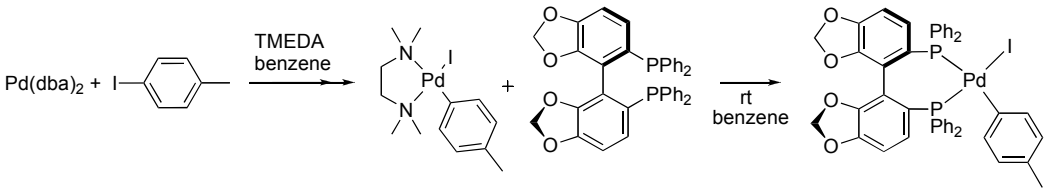
100
50
PPM



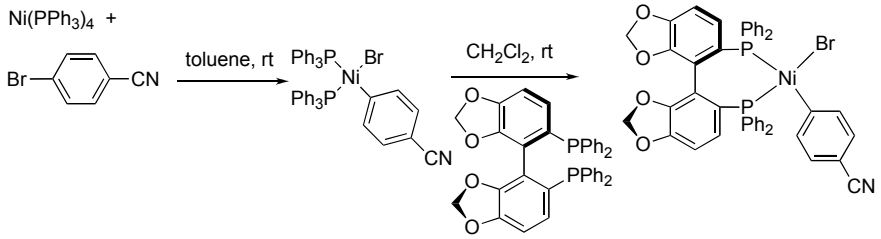
Preparation of Pd(segphos)(*p*-tol)(Br). To a solution of Segphos (100mg, 0.164mmol) in benzene (7.40 mL) was added $\{Pd[P(o\text{-}Tol)_3](Br)(p\text{-}Tol)\}_2$[1] (95.4 mg, 0.0820 mmol). The mixture was then stirred at room temperature for 1 h. The resulting solution was filtered through Celite, and the volatile materials were evaporated under vacuum to provide a yellow solid. The crude product was washed with ether and further recrystallized with by layering a CH_2Cl_2 solution of the complex with hexane and cooling at -30 °C to provide a yellow solid (72.8 mg) in 50% yield. ^{1}H NMR (C_6D_6, 400 MHz): δ 2.02 (3H, s), 4.91 (1H, s), 5.06 (1H, s), 5.22 (1H, s), 5.23 (1H, s), 5.92 (1H, d, J = 8.0 Hz), 6.13 (1H, d, J = 7.2 Hz), 6.37 (1H, t, J = 8.6 Hz), 6.67-7.15 (15H, m), 7.27-7.33 (2H, m), 7.74-7.84 (2H, m), 7.86-8.05 (4H, m), 8.19-8.25 (2H, m). ^{31}P {^{1}H} NMR (benzene) δ 9.0 (d, J = 42.6 Hz), 24.6 (d, J = 42.7 Hz). Anal. Calcd. For $C_{45}H_{35}BrO_4P_2Pd$: C, 60.86; H, 3.97. Found: C, 61.15; H, 4.29.



Preparation of Pd(segphos)(*p*-tol)(I). To a purple solution of $Pd(dba)_2$ (0.500 g, 0.880 mmol) in 25 ml of benzene was added TMEDA (0.160 mL, 1.13 mmol) and *p*-iodotoluene (273 mg, 1.25 mmol). The mixture was slowly heated to 50 ºC, during which time, the color changed to green. After filtration of the solution through Celite, the volatile materials were evaporated under reduced pressure, and the residue was washed with ether. The crude product was recrystallized by layering a CH_2Cl_2 solution of the complex with ether and cooling at -30 °C to

provide PdI(*p*-tol)(TMEDA) in 70% yield as a yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz): δ2.21 (3H, s), 2.30 (6H, s), 2.53 (2H, t, J = 5.3 Hz), 2.64 (6H, s), 2.69 (2H, t, J = 5.3 Hz), 6.75 (2H, d, J = 8.0 Hz), 7.09 (2H, d, J = 7.5 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 20.9, 50.0, 50.1, 58.5, 62.3, 127.8, 131.8, 136.3, 140.0. Anal. Calcd. For $C_{13}H_{23}N_2IPd$: C, 35.43; H, 5.26; N, 6.36. Found: C, 35.21, H, 5.17, N, 6.27.

To a solution of Segphos (61.0mg, 0.100mmol) in benzene (10 mL) was added PdI(*p*-tol)(TMEDA) (40.0 mg, 0.0907 mmol). The mixture was stirred at room temperature for 30 min, after which time 20 m of pentane was added to afford a yellow precipitate. The resulting mixture was filtered to provide the crude product as a yellow solid. This solid was then washed with ether and dried *in vacuo* (33.5 mg, 40% yield). ^{1}H NMR (C_6D_6, 400 MHz): δ 2.06 (3H, s), 4.87-4.91 (1H, m), 5.01-5.05 (1H, m), 5.23 (1H, d, J = 1.4 Hz), 5.24 (1H, d, J = 1.2 Hz), 5.96 (1H, dd, J = 8.0, 1.0 Hz), 6.19 (1H, dd, J = 8.1, 1.4 Hz), 6.50 (1H, t, J = 8.5 Hz), 6.66-7.20 (15H, m), 7.26-7.34 (2H, m), 7.80 (2H, td, J = 7.9, 2.6 Hz), 7.87-8.00 (4H, m), 8.17-8.25 (2H, m). ^{31}P {^{1}H} NMR (benzene) δ 9.9 (d, J = 43.9 Hz), 21.3 (d, J = 45.2 Hz). Anal. Calcd. For $C_{45}H_{35}IO_4P_2Pd$: C, 57.80; H, 3.77. Found: C, 57.70; H, 4.06.

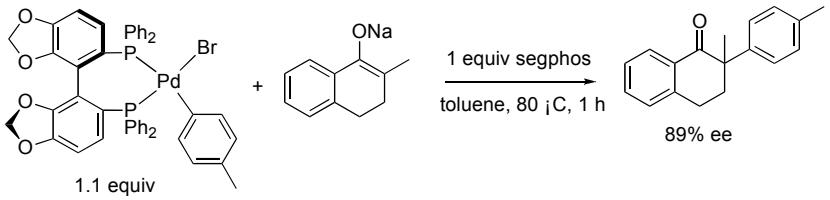


Prepapration of (segphos)Ni(C_6H_4-4-CN)Br complex. To a solution of $Ni(PPh_3)_4$ (221 mg, 0.200 mmol) in toluene (2 mL) was added 4-bromobenzonitrile (182 mg, 1.00 mmol) in toluene (2 mL). The mixture was stirred at room temperature for 2.5 h at which time full conversion was achieved, according to ^{31}P NMR spectroscopy. The resulting light-brown suspension was filtered, washed with ether and pentane, and dried *in vacuo* to provide $(PPh_3)_2Ni(C_6H_4$-4-CN)Br

as a yellow solid (115 mg, 75% yield). ^{1}H NMR (CD_2Cl_2, 500 MHz): δ 6.33 (2H, broad s), 6.90-7.05 (2H, m), 7.42-7.55 (18H, m), 7.63 (12H, broad s). ^{31}P {^{1}H} NMR (CD_2Cl_2) δ 24.0. Anal. Calcd. For $C_{43}H_{34}BrNNiP_2$: C, 67.49; H, 4.48; N, 1.83. Found: C, 67.54; H, 4.50; N, 1.93.

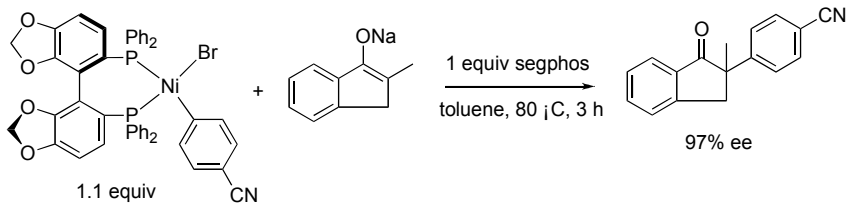
A mixture of Ni(Br)(C_6H_4CN)(PPh_3)$_2$ (62 mg, 0.081 mmol) and segphos (50 mg, 0.082 mmol) were dissolved in CH_2Cl_2 (2 mL), and the resulting solution was stirred at room temperature for 25 min. Ether (2 mL) was then added to the reaction mixture, followed by pentane (5 mL). The resulting mixture was then kept at –35 ºC for 20 h to afford (segphos)Ni(C_6H_4-4-CN)Br as dark brown crystals (34 mg, 49% yield). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 5.45 (1H, broad s), 5.52 (1H, broad s), 5.79 (2H, s), 6.48 (2H, s), 6.81 (2H, d, J = 8.0 Hz), 7.11-7.59 (18 H, m), 7.69 (2H, broad s), 7.83-8.01 (4H, m). ^{31}P {^{1}H} NMR ($CDCl_3$) δ 14.1 (d, J = 42.7 Hz), 26.1 (d, J = 45.9 Hz). Anal. Calcd. For $C_{45}H_{32}BrNNiO_4P_2$•0.5CH_2Cl_2•0.5Et_2O): C, 61.29; H, 4.11; N, 1.50. Found: C, 61.40; H, 3.98; N, 1.63. The ratio of CH_2Cl_2 and Et_2O to the nickel complex was determined by ^{1}H NMR spectroscopy.

Stoichiometric reactions of the arylmetal halide complexes:



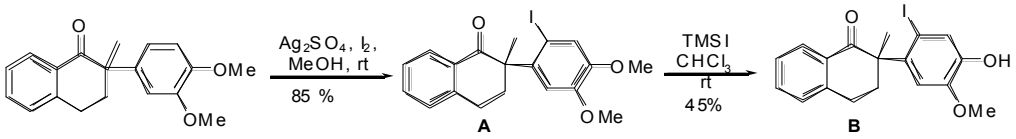
Reaction of Pd(segphos)(*p*-tol)(Br), and the sodium enolate of 2-methyl-1-tetralone: To a screw-capped vial containing segphos (20.6 mg, 0.0338 mmol), Pd(segphos)(*p*-tol)(Br) (30.0 mg, 0.0338 mmol), and the sodium enolate of 2-methyl-1-tetralone (6.2 mg, 0.0338 mmol) was added toluene (0.675 mL). The vial was sealed with a cap containing a PTFE septum and removed from drybox. The reaction mixture was stirred at 80 °C for 1 h. The same workup, purification and

Chiral HPLC conditions were then followed as for the catalytic reactions. The yield of product was 90% and ee of the product was 89%.



Reaction of (segphos)Ni(C_6H_4-4-CN)Br with the sodium enolate of 2-methyl-1-tetralone: To a screw-capped vial containing segphos (33.3 mg, 0.0546 mmol), (segphos)Ni(C_6H_4-4-CN)Br complex (46.5 mg, 0.0546 mmol) and the sodium enolate of 2-methyl-1-indanone(9.1 mg, 0.055 mmol) was added toluene (0.440 mL). The vial was sealed with a cap containing a PTFE septum and removed from drybox. The reaction mixture was stirred at 80 °C for 3 h. The same workup, purification and Chiral HPLC conditions were followed as for the catalytic reactions. The yield of the product was 90% and ee of the product was 97%.

Determination of Absolute Configuration:



Iodination: To a solution of 2-methyl-2-(3,4-di-methoxylphenyl)-1-tetralone[3] (50.0 mg, 0.168 mmol) in MeOH (5 mL) was added Ag_2SO_4 (57.5 mg, 0.185 mmol) and I_2 (47.0 mg, 0.185 mmol) at room temperature. The mixture was stirred for 4 h at room temperature. The resulting mixture was filtered through Celite to provide a clear solution. The solvent was evaporated under vacuum to provide crude product. The crude product was purified by chromatography on silica gel, eluting with hexane/ether (4/1) to provide the product **A** in 85% yield. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.70 (3H, s), 1.78-1.85 (1H, m), 2.93-3.02 (1H, m), 3.14-3.30 (2H, m), 3.84 (3H, s),

3.85 (3H, s), 6.91 (1H, s), 7.24 (1H, d, J = 7.6 Hz), 7.33 (1H, s), 7.35 (1H, t, J = 7.4 Hz), 7.49 (1H, td, J = 7.3, 1.5 Hz), 8.18 (1H, dd, J = 7.7, 1.5 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 22.8, 26.2, 35.4, 52.8, 56.1, 56.3, 86.2, 112.9, 124.9, 127.1, 128.4, 129.1, 133.3, 133.6, 139.5, 141.8, 148.1, 148.9, 200.0.

Demethylation of the Aryl Methyl Ether[4]: To a solution of iodo compound **A** (50.0 mg, 0.118 mmol) in $CHCl_3$ (0.5 mL) was added TMSI (17.7 μL) under an inert atmosphere. This mixture was stirred at room temperature for 48 h, after which time the reaction mixture was diluted with 5 mL of methanol. To this solution was added 10 mL of brine, and the resulting solution was extracted with ether (2 × 15 mL). The extract was washed with sodium bisulfate and brine, and dried with Na_2SO_4. The solvent was removed under vacuum. The crude product was purified by chromatography on silica gel, eluting with hexane/ether (4/1) to provide the product **B** in 45% yield. A single crystal of **B** that was suitable for X-ray diffraction was obtained by layering a CH_2Cl_2 solution of **B** with hexane and cooling at – 20 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.65 (3H, s), 1.75-1.83 (1H, m), 2.95-3.04 (1H, m), 3.13-3.33 (2H, m), 3.85 (3H, s), 5.60 (1H, bs), 7.05 (1H, s), 7.24 (1H, d, J = 7.4 Hz), 7.31 (1H, s), 7.34 (1H, t, J = 7.6 Hz), 7.49 (1H, td, J = 7.4, 1.5 Hz), 8.18 (1H, dd, J = 7.8, 1.5 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 22.9, 26.2, 35.5, 52.7, 56.4, 84.8, 115.9, 124.2, 127.0, 128.5, 129.1, 133.3, 133.6, 140.6, 141.7, 144.9, 145.7, 199.9.

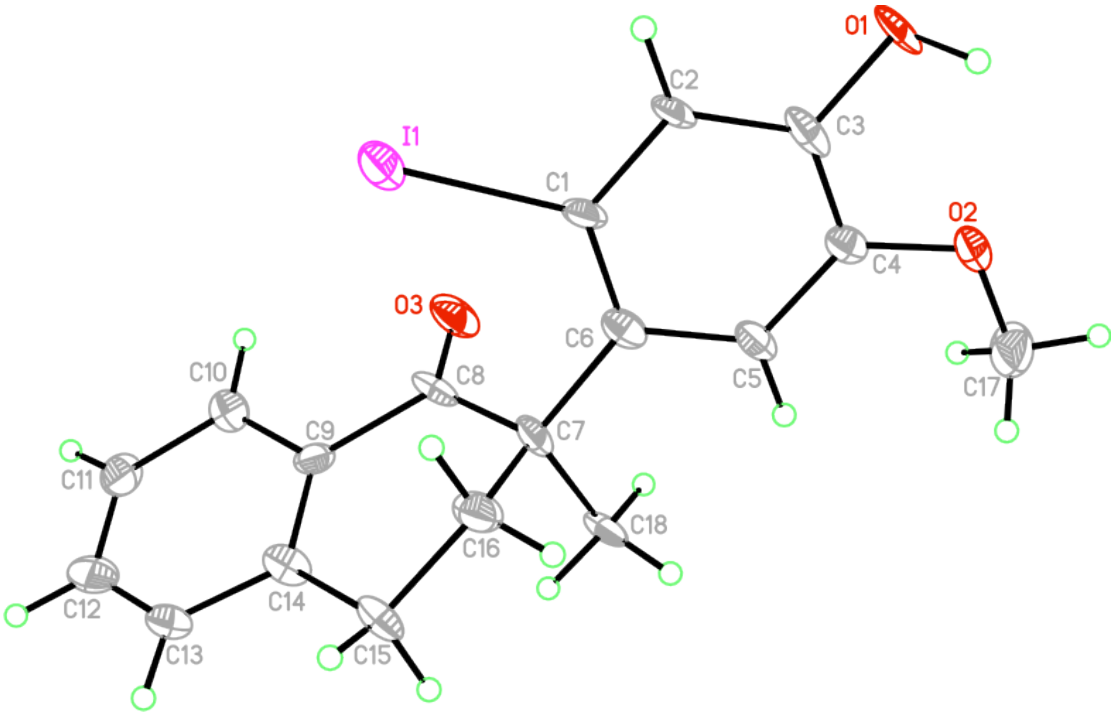


Figure S1. ORTEP digram of the des-methyl, iodo-derivative B.

References:

1. Ritter, K. *Synthesis* **1993**, 735.
2. Paul, F.; Patt, J.; Hartwig, J. F. *Organometallics* **1995**, *14*, 3030.
3. Compound A was obtained according the condition of table 2, entry 5.
4. Vickery, E. H.; Pahler, L. F.; Eisenbraun, E. J. *J. Org. Chem.* **1979**, *44*, 4444.