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Supporting Information

69451 Weinheim, Germany

From Aryl Bromides to Enantioenriched Benzylic Alcohols in a Single Flask:

Catalytic Asymmetric Arylation of Aldehydes

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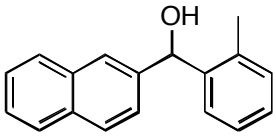
Contents

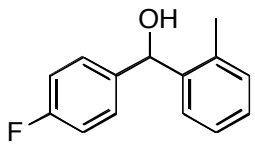
General Methods. All reactions were carried out under nitrogen using standard Schlenk techniques. NMR spectra were obtained on Brüker 500 MHz, 360 MHz, or 300 MHz Fourier transform spectrometer at the University of Pennsylvania NMR facility. ^{1}H NMR spectra were referenced to tetramethylsilane in $CDCl_3$; $^{13}C\{^{1}H\}$ NMR spectra were referenced to residual solvent. The infrared spectra were obtained using a Perkin-Elmer 1600 series spectrometer. Thin-layer chromatography was performed on Whatman precoated silica gel 60 F-254 plates and visualized by ultraviolet light or by staining with ceric ammonium molybdate stain, phosphomolybdic acid hydrate stain, or potassium permanganate. Silica gel (230-400 mesh, Silicycle) was used for flash column chromatography. All reagents were purchased from Aldrich, Acros or Strem. $ZnCl_2$ was dried at 150 ^{o}C under vacuum for 12 h and stored under nitrogen. All liquid aldehydes, aryl bromides were distilled prior to use and stored in inert atmosphere. Solid aldehydes were sublimed and stored under an inert atmosphere. Tetraethylethylenediamine (TEEDA) was used as received. Alkyl lithium reagents were titrated with diphenylacetic acid prior to use. *t*-Butyl methyl ether (*t*-BuOMe) was distilled from Na/benzophenone, Toluene and hexanes were dried via activated alumina column.

Asymmetric 2-Tolylation of Aldehydes from 2-Bromotoluene.

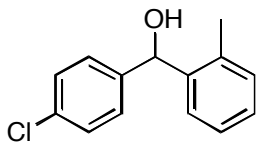


Preparation of Naphthalen-2-yl-*o*-tolyl-methanol (General Procedure A). A nitrogen purged Schlenk flask was charged with *2*-bromotoluene (216.5 μL, 1.8 mmol) and cooled to –78 ^{o}C. *n*-BuLi (0.64 mL, 2.5 M in hexanes, 1.6 mmol) was added dropwise and the solution was stirred for 10 min. The dry ice bath was removed and the flask was allowed to warm to rt for an additional hour. $ZnCl_2$ (114.5 mg, 0.84 mmol) was quickly weighed into the reaction and followed by *t*-BuOMe (1 mL). The reaction was stirred at rt for 5 h. A fine white powder was precipitated during stirring. Hexanes (5 mL) were syringed into the flask, TEEDA (68 μL, 0.32 mmol) was added, and the solution was stirred for 1 h. After the addition of (–)-MIB (4.8 mg, 0.02 mmol, 5 mol%), the reaction cooled to 0 ^{o}C for 30 min, and 2-naphthylaldehyde (62.4 mg, 0.4 mmol) was added. The reaction was stirred at 0 ^{o}C and monitored by tlc. After completion, the reaction mixture was quenched

with H_2O (20 mL) and extracted with ethyl acetate (3 x 20 mL). The organic layer was dried over $MgSO_4$, filtered, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel (hexanes:EtOAc, 95:5) to give the product (84.5 mg, 90% yield, 90% ee) as an oil. $[\alpha]_D^{20}$ = +13.171 (*c* = 0.205, THF); ^{1}H NMR ($CDCl_3$, 300 MHz): 2.32 (s, 3H), 2.37 (d, *J* = 3.9 Hz, 1H), 6.18 (d, *J* = 3.9 Hz, 1H), 7.16-7.32 (m, 3H), 7.41-7.59 (m, 4H), 7.79-7.89 (m, 4H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz): 19.9, 73.9, 125.7, 126.1, 126.5, 126.6, 126.7, 126.9, 128.09, 128.10, 128.5, 128.7, 131.0, 133.2, 133.6, 136.0, 140.6, 141.7 ppm; IR (neat): 741, 1022, 1462, 1487, 1506, 1601, 1714, 1920, 2923, 3054, 3364 cm^{-1}; HRMS calcd for $C_{18}H_{16}O$ $(M)^+$: 248.1201, found: 248.1194; ee determination condition: Chiralcel OD-H, Hexanes:IPA = 90:10, flow = 1.0 mL/min, t = 14.0 min, 17.9 min.

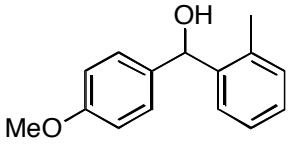


Preparation of (4-Fluoro-phenyl)-2-tolyl-methanol. General procedure A was applied to 4-fluorobenzaldehyde (43 μL, 0.4 mmol). The crude product was purified by column chromatography on silica gel (hexanes:EtOAc, 95:5) to give the product (79.2 mg, 92% yield, 80% ee) as an oil. $[\alpha]_D^{20}$ = +8.070 (*c* = 0.285, THF); ^{1}H NMR ($CDCl_3$, 500 MHz): 2.17 (s, 3H), 2.36 (d, *J* = 3.7 Hz, 1H), 5.88 (d, *J* = 4.0 Hz, 1H), 6.93-6.98 (m, 2H), 7.09-7.12 (m, 1H), 7.16-7.24 (m, 4H), 7.43 (dd, *J* = 7.4, 1.7 Hz, 1H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): 19.6, 73.0, 115.5 (d, *J* = 21.2 Hz), 126.4, 126.5, 127.9, 129.1 (d, *J* = 8.1 Hz), 130.9, 135.6, 138.9 (d, *J* = 2.8 Hz), 141.6, 162.4 (d, *J* = 244 Hz) ppm; IR (neat): 831, 1016, 1157, 1508, 1604, 2926, 3330 cm^{-1}; HRMS calcd for $C_{14}H_{13}FO$ $(M)^+$: 216.0950, found: 216.0946; ee determination condition: Chiralcel AD-H, Hexanes:IPA = 97:3, flow = 0.5 mL/min, t = 29.7 min, 31.0 min.



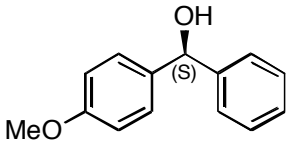
Preparation of (4-Chloro-phenyl)-2-tolyl-methanol. General procedure A was applied to 4-chlorobenzaldehyde (56 mg, 0.4 mmol). The crude product was purified by column chromatography on silica gel (hexanes:EtOAc, 95:5) to give the product (80.5 mg, 86% yield, 80% ee) as a white crystal. m.p. = 68 ^oC; $[\alpha]_D^{20}$ = +34.848 (*c* = 0.33, THF); ^{1}H NMR ($CDCl_3$, 300 MHz): 2.25 (d, *J* = 3.5 Hz, 1H), 2.27 (s, 3H), 5.98 (s, 1H), 7.14-7.35 (m, 7H), 7.43-7.50 (m, 1H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz): 19.8, 73.2, 126.7, 126.8, 128.2, 128.8, 129.0,

131.1, 133.7, 135.8, 141.5, 141.8 ppm; IR (neat): 752, 1013, 1090, 1461, 1488, 2925, 3352 cm^{-1}; HRMS calcd for $C_{14}H_{13}ClO$ $(M)^+$: 232.0655, found: 232.0652; ee determination condition: Chiralcel OD-H, Hexanes:IPA = 97:3, flow = 0.5 mL/min, t = 47.3 min, 52.2 min.

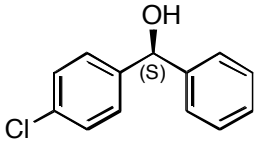


Preparation of (4-Methoxy-phenyl)-2-tolyl-methanol. General procedure A was applied to *p*-anisaldehyde (48.6 μL, 0.4 mmol). The crude product was purified by column chromatography on silica gel (hexanes:EtOAc, 95:5) to give the product (71.6 mg, 78% yield, 87% ee) as a crystal. m.p. = 54 °C; $[\alpha]_D^{20}$ = -12.340 (*c* = 0.235, THF); ^1H NMR ($CDCl_3$, 500 MHz): 2.05 (d, *J* = 3.7 Hz, 1H), 2.16 (s, 3H), 3.73 (s, 3H), 5.90 (d, *J* = 3.7 Hz, 1H), 6.80 (d, *J* = 8.7 Hz, 2H), 7.08 (d, *J* = 7.4 Hz, 1H), 7.12-7.22 (m, 4H), 7.51 (d, *J* = 7.9 Hz, 1H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): 19.6, 55.5, 73.2, 114.1, 126.2, 126.3, 127.6, 128.7, 130.7, 135.37, 135.43, 141.9, 159.3 ppm; IR (neat): 749, 778, 831, 1171, 1246, 1303, 1462, 1514, 1584, 1612, 2835, 2954, 3414 cm^{-1}; HRMS calcd for $C_{15}H_{16}O_2$ $(M)^+$: 228.1150, found: 228.1150; ee determination condition: Chiralcel AS-H, Hexanes:IPA = 95:5, flow = 0.5 mL/min, t = 27.0 min, 33.7 min.

Asymmetric Phenylation of Aldehydes from Bromobenzene.



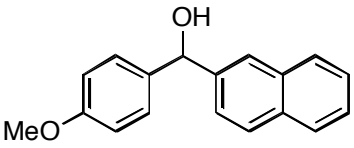
Preparation of (*S*)-(4-Methoxy-phenyl)-phenyl-methanol. General procedure A with bromobenzene (190 μL, 1.8 mmol) was applied to *p*-anisaldehyde on a 48.6 μL (0.4 mmol) scale. The crude product was purified by column chromatography on silica gel (hexanes:EtOAc, 95:5) to give the product (77.5 mg, 90% yield, 90% ee) as an oil. $[\alpha]_D^{20}$ = -26.522 (*c* = 0.23, $CHCl_3$), Absolute configuration = (*S*); Other Spectral data are consistent with previously reported data.[1]



Preparation of (*S*)-(4-Chloro-phenyl)-phenyl-methanol. General procedure A with bromobenzene (190 μL, 1.8 mmol) was applied to 4-chlorobenzaldehyde on

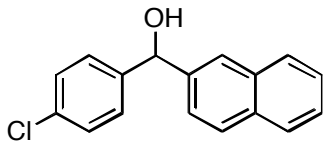
a 56 mg (0.4 mmol) scale. The crude product was purified by column chromatography on silica gel (hexanes:EtOAc, 95:5) to give the product (74.7 mg, 85% yield, 90% ee) as an oil. $[\alpha]_D^{20}$ = +12.9 (*c* = 0.24, $CHCl_3$); Absolute configuration = (*S*); Other Spectral data are consistent with previously reported data.[1]

Asymmetric 2-Naphthylation of Aldehydes from 2-Bromonaphthalene.

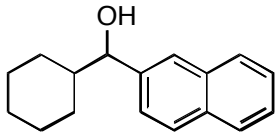


Preparation of (4-Methoxy-phenyl)-naphthalen-2-yl-methanol (General Procedure B). A nitrogen purged Schlenk flask was charged with 2-bromonaphthalene (280 mg, 1.35 mmol) and *t*-BuOMe (1 mL) and cooled to –78 °C. *n*-BuLi (0.48 mL, 2.5 M in hexanes, 1.2 mmol) was added dropwise and the solution was stirred for 10 min. The dry ice bath was replaced with 0 °C ice bath and the flask was remained for an additional hour. A thick light yellow precipitation was formed. The ice bath was removed then $ZnCl_2$ (86 mg, 0.63 mmol) was quickly weighed into the flask. The mixture was stirred for 5 h. The light yellow precipitation was changed into the white. The solution was placed under vacuum to evaporate *t*-BuOMe for 1 h. Toluene (4 mL) was syringed into the flask, TEEDA (51 μL, 0.24 mmol) was added, and the solution was stirred for 1 h. After the addition of (–)-MIB (3.6 mg, 0.015 mmol, 5 mol%), the reaction cooled to 0 °C for 30 min, and *p*-anisaldehyde (36.5 μL, 0.3 mmol) was added. The reaction was stirred at 0 °C and monitored by tlc. After completion, the reaction mixture was quenched with H_2O (20 mL) and extracted with ethyl acetate (3 x 20 mL). The organic layer was dried over $MgSO_4$, filtered, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel (hexanes:EtOAc, 95:5) to give the product (84.8 mg, 99% yield, 91% ee) as a white crystal. m.p. = 84 °C; $[\alpha]_D^{20}$ = -31.373 (*c* = 0.255, THF); ^{1}H NMR ($CDCl_3$, 500 MHz): 2.29 (d, *J* = 3.4 Hz, 1H), 3.74 (s, 3H), 5.90 (d, *J* = 3.1 Hz, 1H), 6.80-6.84 (m, 2H), 7.23-7.30 (m, 2H), 7.36 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.39-7.45 (m, 2H), 7.72-7.80 (m, 3H), 7.84 (s, 1H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): 55.5, 76.2, 114.2, 125.0 (2C), 126.1, 126.4, 127.9, 128.32, 128.35, 128.5, 133.1, 133.5, 136.3, 141.6, 159.4 ppm; IR (neat): 818, 1032, 1174, 1284, 1462, 1511, 1610, 2835, 3396 cm^{-1}; HRMS calcd for $C_{18}H_{16}O_2$ $(M)^+$: 264.1150, found:

248.1145; ee determination condition: Chiralcel OD-H, Hexanes:IPA = 90:10, flow = 1.0 mL/min, t = 17.5 min, 20.8 min.

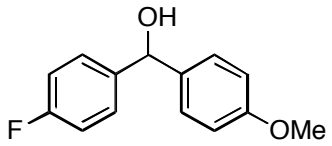


Preparation of (4-Chloro-phenyl)-naphthalen-2-yl-methanol. General procedure B was applied to 4-chlorobenzaldehyde (42.0 mg, 0.3 mmol). The substrate was added and the reaction was kept at rt instead of 0 ^{o}C. The crude product was purified by column chromatography on silica gel (hexanes:EtOAc, 95:5) to give the product (77.6 mg, 96% yield, 87% ee) as a light yellow solid. m.p. = 102 ^{o}C; $[\alpha]_D^{20}$ = +24.815 (*c* = 0.27, THF); ^{1}H NMR (C_6D_6, 500 MHz): 1.54 (d, *J* = 3.5 Hz, 1H), 5.44 (d, *J* = 2.7 Hz, 1H), 7.01-7.05 (m, 2H), 7.06-7.10 (m, 2H), 7.20-7.29 (m, 3H), 7.55 (d, *J* = 8.6 Hz, 1H), 7.57-7.60 (m, 1H), 7.62-7.65 (m, 1H), 7.66 (s, 1H) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): 75.5, 125.1, 125.6, 126.2, 126.5, 128.0, 128.3, 128.4, 128.6, 128.7, 133.37, 133.42, 133.7, 141.5, 142.9 ppm; IR (neat): 808, 1013, 1090, 1488, 3374 cm^{-1}; HRMS calcd for $C_{17}H_{13}ClO$ $(M\text{-}OH)^+$: 251.0628, found: 251.0598; ee determination condition: Chiralcel OD-H, Hexanes:IPA = 90:10, flow = 1.0 mL/min, t = 15.3 min, 17.4 min.

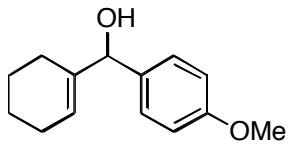


Preparation of Cyclohexyl-naphthalen-2-yl-methanol. General procedure B was applied to cyclohexylcarboxaldehyde (36.3 μL, 0.3 mmol). The crude product was purified by column chromatography on silica gel (hexanes:EtOAc, 95:5) to give the product (66.6 mg, 92% yield, 82% ee) as a white crystal. m.p. = 71 ^{o}C; $[\alpha]_D^{20}$ = +14.510 (*c* = 0.255, THF); ^{1}H NMR ($CDCl_3$, 500 MHz): 0.93 (dddd, *J* = 24.5, 12.6, 12.6, 3.4 Hz, 1H), 0.99-1.24 (m, 4H), 1.30-1.39 (m, 1H), 1.55-1.76 (m, 4H), 1.93 (d, *J* = 2.9 Hz, 1H), 1.94-2.00 (m, 1H), 4.48 (dd, *J* = 6.9, 2.8 Hz, 1H), 7.38-7.45 (m, 3H), 7.67 (s, 1H), 7.75-7.81 (m, 3H) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): 26.3, 26.4, 26.7, 29.1, 29.7, 45.2, 79.7, 125.0, 125.7, 126.0, 126.3, 127.9, 128.1, 128.2, 133.2, 133.4, 141.3 ppm; IR (neat): 747, 820, 856, 894, 1020, 1449, 1508, 2360, 2851, 2925, 3055, 3382 cm^{-1}; HRMS calcd for $C_{17}H_{20}O$ $(M)^+$: 240.1514, found: 240.1503; ee determination condition: Chiralcel OD-H, Hexanes:IPA = 90:10, flow = 1.0 mL/min, t = 8.6 min, 10.4 min.

Asymmetric 4-Methoxyphenylation of Aldehydes from 4-Bromoanisole.

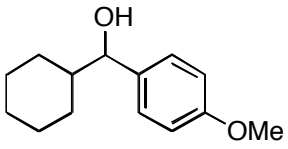


Preparation of (4-Fluoro-phenyl)-(4-methoxy-phenyl)-methanol (General Procedure C). A nitrogen purged Schlenk flask was charged with 4-bromoanisole (100.1 μL, 0.8 mmol) and *t*-BuOMe (1 mL) and cooled to –78 °C. *n*-BuLi (0.32 mL, 2.5 M in hexanes, 0.8 mmol) was added dropwise and the solution was stirred for 1 h. The dry ice bath was replaced with 0 °C ice bath. $ZnCl_2$ (114.5 mg, 0.84 mmol) was added to the reaction mixture then it was stirred for 30 min. Additional *n*-BuLi (0.32 mL, 2.5 M in hexanes, 0.8 mmol) was added to the reaction mixture and it was stirred for 4.5 h at rt. Toluene (5 mL) was syringed into the flask, TEEDA (68 μL, 0.32 mmol) was added, and the solution was stirred for 1 h. After the addition of (–)-MIB (4.8 mg, 0.02 mmol, 5 mol%), the reaction cooled to 0 °C for 30 min, and *p*-fluorobenzaldehyde (43 μL, 0.4 mmol) was added. The reaction was stirred at 0 °C and monitored by tlc. After completion, the reaction mixture was quenched with H_2O (20 mL) and extracted with ethyl acetate (3 x 20 mL). The organic layer was dried over $MgSO_4$, filtered, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel (hexanes:EtOAc, 95:5) to give the product (77.7 mg, 84% yield, 93% ee) as a white crystal. m.p. = 52 °C; $[\alpha]_D^{20}$ = +13.846 (*c* = 0.195, THF); ^{1}H NMR (C_6D_6, 300 MHz): 2.17 (s, 1H), 3.38 (s, 3H), 5.50 (s, 1H), 6.81-6.95 (m, 4H), 7.17-7.29 (m, 4H) ppm; $^{13}C\{^1H\}$ NMR (C_6D_6, 75 MHz): 55.0, 75.3, 114.3, 115.4 (d, *J* = 21.2 Hz), 128.4, 128.7 (d, *J* = 8.0 Hz), 136.9, 141.0 (d, *J* = 3.0 Hz), 159.7, 162.6 (d, *J* = 243 Hz) ppm; IR (neat): 831, 1033, 1248, 1504, 1609, 2837, 2957, 3422 cm^{-1}; HRMS calcd for $C_{14}H_{13}FO_2$ $(M)^+$: 232.0900, found: 232.0900; ee determination condition: Chiralcel AS-H, Hexanes:IPA = 95:5, flow = 0.5 mL/min, t = 20.0 min, 22.1 min.



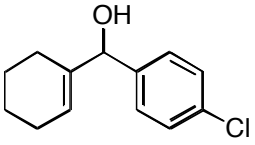
Preparation of Cyclohex-1-enyl-(4-methoxy-phenyl)-methanol. General procedure C was applied to cyclohex-1-enecarboxaldehyde (46 μL, 0.4 mmol). The crude product was purified by column chromatography on silica gel (hexanes:EtOAc, 95:5) to give the product (71.3 mg, 82% yield, 83% ee) as an oil. $[\alpha]_D^{20}$ = -32.381 (*c* = 0.21, THF); ^{1}H NMR (C_6D_6, 300 MHz): 1.46-1.62 (m, 4H), 1.83-1.97 (m, 2H), 1.99-2.14 (m, 3H), 3.42

(s, 3H), 5.02 (s, 1H), 5.90 (m, 1H), 6.90-6.96 (m, 2H), 7.39-7.45 (m, 2H) ppm; $^{13}C\{^{1}H\}$ NMR (C_6D_6, 75 MHz): 23.13, 23.14, 24.5, 25.5, 55.0, 78.0, 114.0, 122.8, 128.1, 135.8, 140.9, 159.5 ppm; IR (neat): 830, 1036, 1175, 1248, 1298, 1441, 1463, 1510, 1608, 2834, 2855, 2932, 3510 cm^{-1}; HRMS calcd for $C_{14}H_{18}O_2$ $(M\text{-}H_2O)^+$: 200.1201, found: 200.1192; ee determination condition: Chiralcel AS-H, Hexanes:IPA = 97:3, flow = 0.5 mL/min, t = 14.9 min, 20.0 min.



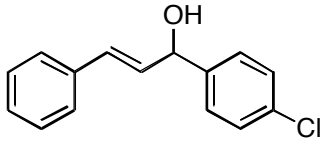
Preparation of Cyclohexyl-(4-methoxy-phenyl)-methanol. General procedure C was applied to cyclohexylcarboxaldehyde (48.5 μL, 0.4 mmol). The crude product was purified by column chromatography on silica gel (hexanes:EtOAc, 95:5) to give the product (74.0 mg, 84% yield, 78% ee) as a white crystal. m.p. = 70-72 ^{o}C; $[\alpha]_D^{20}$ = +16.889 (*c* = 0.225, THF); ^{1}H NMR (C_6D_6, 300 MHz): 0.92-1.08 (m, 1H), 1.08-1.37 (m, 4H), 1.49-1.60 (m, 1H), 1.60-1.77 (m, 4H), 1.79-1.90 (m, 1H), 2.22 (m, 1H), 3.44 (s, 3H), 4.22 (d, *J* = 7.1 Hz, 1H), 6.88-6.95 (m, 2H), 7.22-7.29 (m, 2H) ppm; $^{13}C\{^{1}H\}$ NMR (C_6D_6, 75 MHz): 26.67, 26.71, 27.1, 29.5, 29.8, 45.8, 55.0, 79.0, 114.0, 128.3, 136.9, 159.6 ppm; IR (neat): 823, 1000, 1034, 1176, 1254, 1446, 1518, 1652, 2855, 2917, 2942, 3478 cm^{-1}; HRMS calcd for $C_{14}H_{20}O_2$ $(M\text{-}H_2O)^+$: 202.1358, found: 202.1362; ee determination condition: Chiralcel AS-H, Hexanes:IPA = 97:3, flow = 0.5 mL/min, t = 12.5 min, 18.3 min.

Asymmetric 4-Chlorophenylation of Aldehydes from 4-Bromochlorobenzene.



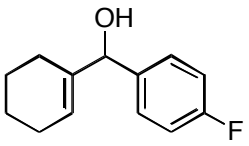
Preparation of (*p*-Chloro-phenyl)-cyclohex-1-enyl-methanol (General Procedure D). A nitrogen purged Schlenk flask was charged with 4-bromochlorobenzene (229.7 mg, 1.2 mmol) and *t*-BuOMe (1 mL) and cooled to –78 ^{o}C. *n*-BuLi (0.48 mL, 2.5 M in hexanes, 1.2 mmol) was added dropwise and the solution was stirred for 1 h. The dry ice bath was replaced with 0 ^{o}C ice bath. $ZnCl_2$ (171.8 mg, 1.26 mmol) was added to the reaction mixture then it was stirred for 30 min. Additional *n*-BuLi (0.48 mL, 2.5 M in hexanes, 1.2 mmol) was added to the reaction mixture and it was stirred for 4.5 h at rt. Toluene (5 mL) was syringed into the flask, TEEDA (102 μL, 0.48 mmol) was added, and the solution was stirred for 1 h. After the addition of

(–)-MIB (4.8 mg, 0.02 mmol, 5 mol%), the reaction cooled to 0 ^{o}C for 30 min, and cyclohex-1-enecarboxaldehyde (46 μL, 0.4 mmol) was added. The reaction was stirred at 0 ^{o}C and monitored by tlc. After completion, the reaction mixture was quenched with H_2O (20 mL) and extracted with ethyl acetate (3 x 20 mL). The organic layer was dried over $MgSO_4$, filtered, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel (hexanes:EtOAc, 97:3) to give the product (48.7 mg, 55% yield, 87% ee) as an oil. $[\alpha]_D^{20}$ = -46.939 (*c* = 0.245, THF); ^{1}H NMR (C_6D_6, 500 MHz): 1.28-1.44 (m, 4H), 1.57 (s, 1H), 1.58-1.63 (m, 1H), 1.76-1.84 (m, 1H), 1.86-1.92 (m, 2H), 4.70 (s, 1H), 5.59-5.63 (m, 1H), 7.06-7.16 (m, 4H) ppm; ^{13}C{^{1}H} NMR (C_6D_6, 125 MHz): 22.7, 22.8, 23.8, 25.5, 77.6, 123.7, 128.0, 128.4, 133.0, 140.0, 141.8 ppm; IR (neat): 834, 921, 1014, 1090, 1138, 1288, 1402, 1436, 1488, 1578, 1596, 1723, 2856, 2924, 3384 cm^{-1}; HRMS calcd for $C_{13}H_{15}ClO$ $(M)^+$: 222.0811, found: 222.0814; ee determination condition: Chiralcel AD-H, Hexanes:IPA = 95:5, flow = 0.5 mL/min, t = 15.5 min, 19.1 min.

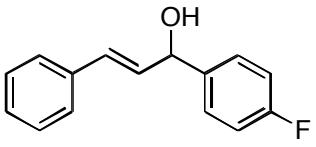


Preparation of 1-(4-Chloro-phenyl)-3-phenyl-prop-2-en-1-ol. General procedure D was applied to *trans*-cinnamaldehyde (50.4 μL, 0.4 mmol). The crude product was purified by column chromatography on silica gel (hexanes:EtOAc, 97.5:2.5) to give the product (66.6 mg, 68% yield, 81% ee) as a white crystal. m.p. = 62 ^{o}C; $[\alpha]_D^{20}$ = +4.2857 (*c* = 0.21, THF); ^{1}H NMR (C_6D_6, 360 MHz): 2.08 (s, 1H), 4.98 (d, *J* = 6.5 Hz, 1H), 6.16 (dd, *J* = 15.8, 6.5 Hz, 1H), 6.52 (d, *J* = 15.8 Hz, 1H), 7.07-7.28 (m, 9H) ppm; ^{13}C{^{1}H} NMR (C_6D_6, 90 MHz): 74.0, 126.7, 127.8 (2C), 128.56, 128.60, 130.6, 131.5, 133.2, 136.6, 141.8 ppm; IR (neat): 694, 750, 795, 826, 876, 965, 1013, 1092, 1263, 1291, 1404, 1449, 1488, 1578, 1598, 1652, 1717, 2928, 3027, 3316 cm^{-1}; HRMS calcd for $C_{15}H_{13}ClO$ $(M)^+$: 244.0655, found: 244.0654; ee determination condition: Chiralcel OD-H, Hexanes:IPA = 92:8, flow = 0.7 mL/min, t = 23.2 min, 36.7 min.

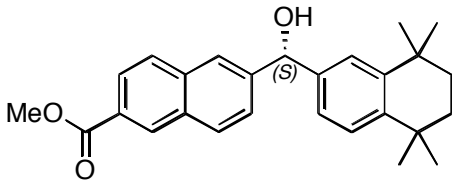
Asymmetric 4-Fluorophenylation of Aldehydes from 4-Bromofluorobenzene.



Preparation of (4-Fluoro-phenyl)-cyclohex-1-enyl-methanol. General procedure D with 4-bromofluorobenzene (131.8 μL, 1.2 mmol) was applied to cyclohex-1-enecarboxaldehyde on a 46 μL (0.4 mmol) scale. The crude product was purified by column chromatography on silica gel (hexanes:EtOAc, 97:3) to give the product (52.4 mg, 64% yield, 88% ee) as an oil. $[\alpha]_D^{20}$ = -46.800 (*c* = 0.25, THF); ^{1}H NMR (C_6D_6, 360 MHz): 1.36-1.63 (m, 4H), 1.64-1.83 (m, 2H), 1.84-2.12 (m, 3H), 4.83 (s, 1H), 5.73 (s, 1H), 6.86-7.01 (m, 2H), 7.18-7.34 (m, 2H) ppm; ^{13}C{^{1}H} NMR (C_6D_6, 90 MHz): 22.5, 22.6, 23.7, 25.0, 77.4, 114.8 (d, *J* = 21 Hz), 123.1, 128.5 (d, *J* = 7.9 Hz), 138.8 (d, *J* = 3.0 Hz), 140.0, 162.2 (d, *J* = 244 Hz) ppm; IR (neat): 837, 921, 1014, 1155, 1222, 1437, 1506, 1604, 2926, 3364 cm^{-1}; HRMS calcd for $C_{13}H_{15}FO$ $(M)^+$: 206.1107, found: 206.1100; ee determination condition: Chiralcel AD-H, Hexanes:IPA = 95:5, flow = 0.5 mL/min, t = 14.1 min, 15.8 min.



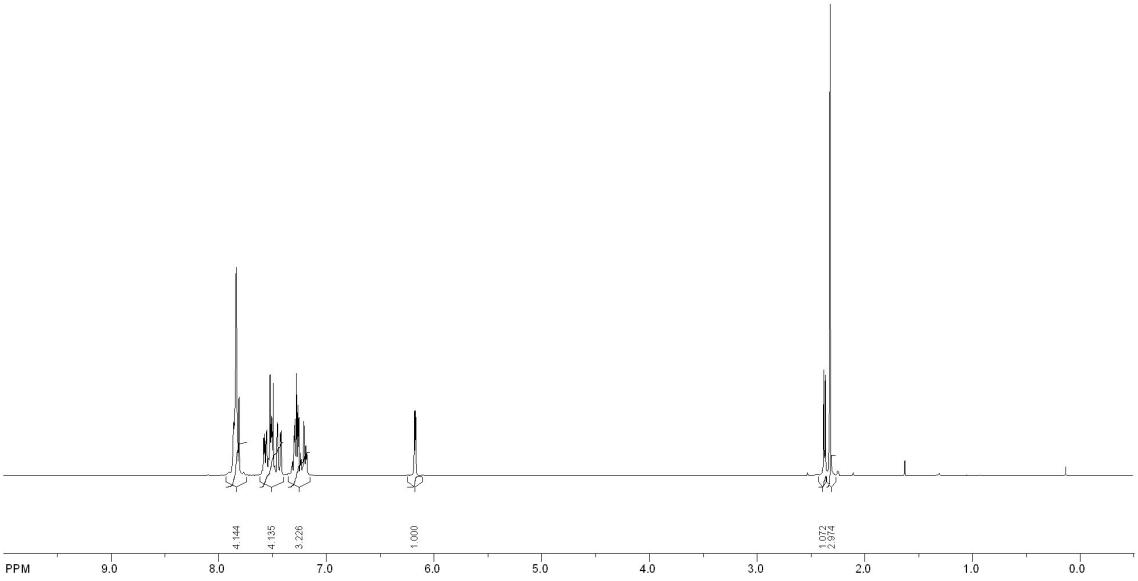
Preparation of 1-(4-Fluoro-phenyl)-3-phenyl-prop-2-en-1-ol. General procedure D with 4-bromofluorobenzene (131.8 μL, 1.2 mmol) was applied to *trans*-cinnamaldehyde on a 50.4 μL (0.4 mmol) scale. The crude product was purified by column chromatography on silica gel (hexanes:EtOAc, 97.5:2.5) to give the product (67.3 mg, 74% yield, 84% ee) as an oil. $[\alpha]_D^{20}$ = -18.286 (*c* = 0.175, THF); ^{1}H NMR (C_6D_6, 360 MHz): 1.95 (s, 1H), 5.03 (d, *J* = 6.3 Hz, 1H), 6.20 (dd, *J* = 15.9, 6.3 Hz, 1H), 6.55 (d, *J* = 15.9 Hz, 1H), 6.86-6.92 (m, 2H), 7.08-7.27 (m, 7H) ppm; ^{13}C{^{1}H} NMR (C_6D_6, 90 MHz): 74.0, 115.1 (d, *J* = 21.4 Hz), 126.7, 127.7, 128.5 (d, *J* = 8.2 Hz), 128.60, 130.3, 131.9, 136.7, 139.1 (d, *J* = 2.7 Hz), 162.3 (d, *J* = 245 Hz) ppm; IR (neat): 693, 747, 835, 967, 1090, 1156, 1225, 1295, 1449, 1507, 1602, 1649, 2854, 2925, 3027, 3424, 3550 cm^{-1}; HRMS calcd for $C_{15}H_{13}FO$ $(M)^+$: 228.0950, found: 228.0956; ee determination condition: Chiralcel OD-H, Hexanes:IPA = 92:8, flow = 0.7 mL/min, t = 22.6 min, 36.1 min.

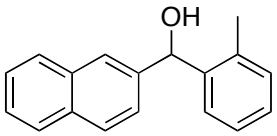


Preparation of methyl (*S*)-6-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)hydroxymethyl]-2-naphthalene carboxylate. General procedure D with 5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-bromohaphthalene (160.3 mg, 0.6 mmol) was applied to 6-carbomethoxy-2-naphthalenecarboxaldehyde (42.8 mg, 0.2 mmol). The crude product was purified by column chromatography on silica gel (hexanes:EtOAc, 92.5:7.5) to give the product (67.0 mg, 83% yield, 87% ee) as a colorless crystal. m.p. = 154 ^{o}C; $[\alpha]_D^{20}$ = -44.571 (*c* = 0.35, THF); ^{1}H NMR (C_6D_6, 500 MHz): 1.16 (d, *J* = 1.9 Hz, 6H), 1.22 (d, *J* = 1.9 Hz, 6H), 1.55 (s, 4H), 1.67 (d, *J* = 3.5 Hz, 1H), 3.54 (s, 3H), 5.64 (d, *J* = 3.5 Hz, 1H), 7.08 (dd, *J* = 8.2, 1.9 Hz, 1H), 7.19 (d, *J* = 8.2 Hz, 1H), 7.37 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.47 (d, *J* = 2.0 Hz, 1H), 7.49 (d, *J* = 3.7 Hz, 1H), 7.51 (d, *J* = 3.7 Hz, 1H), 7.81 (s, 1H), 8.17 (dd, *J* = 8.5, 1.8 Hz, 1H), 8.62 (s, 1H) ppm; ^{13}C{^{1}H} NMR (C_6D_6, 125 MHz): 31.9 (2C), 32.0 (2C), 34.2, 34.4, 35.3, 35.4, 51.6, 76.3, 124.8, 125.0, 125.2, 125.9, 126.2, 127.0, 128.3, 128.6, 129.6, 131.1, 132.3, 135.8, 141.4, 144.3, 144.8, 145.0, 166.8 ppm; IR (neat): 1288, 1633, 1722, 2965, 3428 cm^{-1}; HRMS calcd for $C_{27}H_{30}O_3$ $(M)^+$:402.2195, found: 402.2195; ee determination condition : Chiralcel OD-H, Hexanes:IPA = 92:8, flow = 1.0 mL/min, t = 10.5 min, 19.3 min.

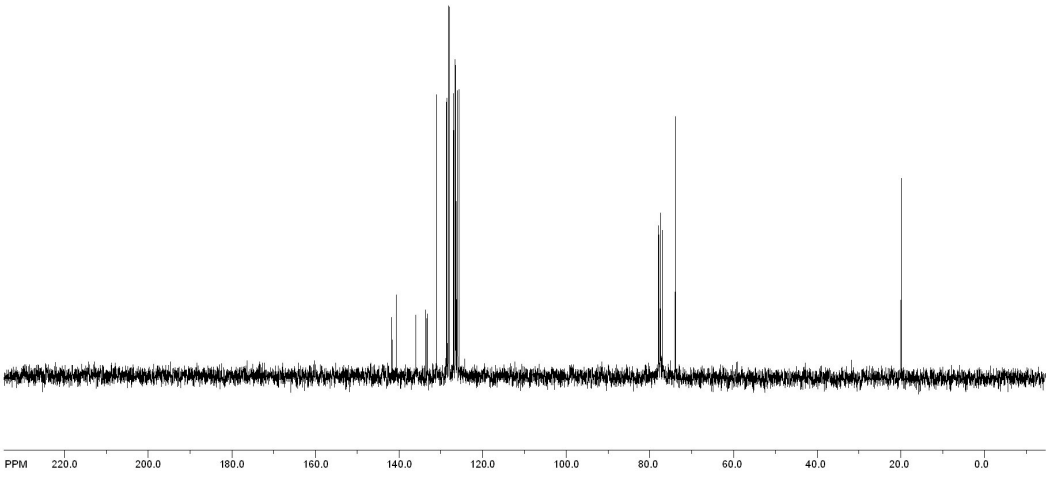
References

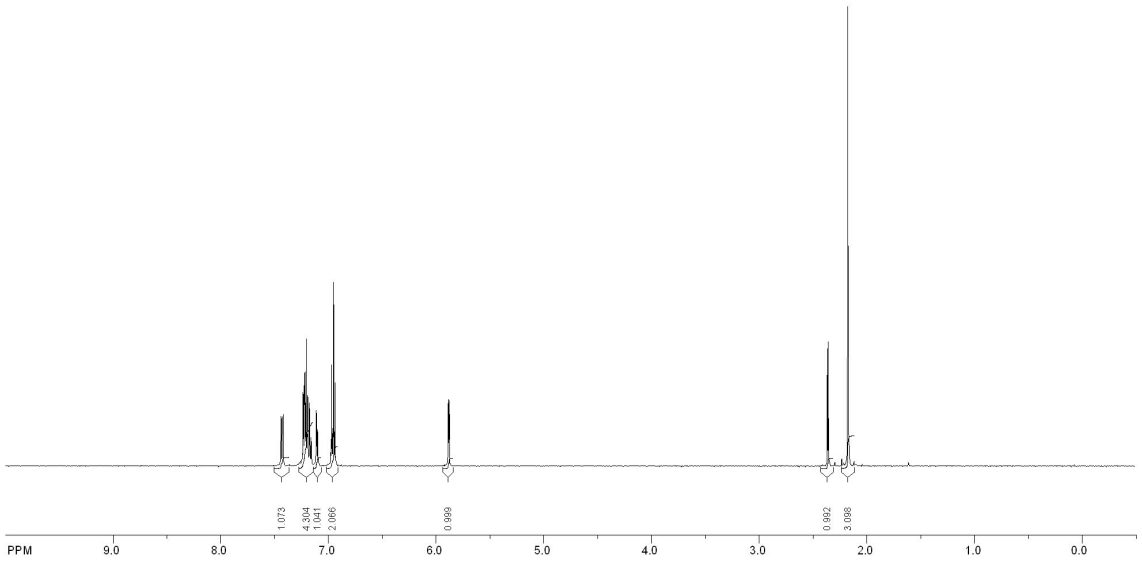
(1) Rudolph, J.; Schmidt, F.; Bolm, C. *Adv. Synth. Catal.* **2004**, *346*, 867-872.

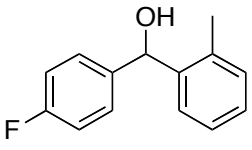




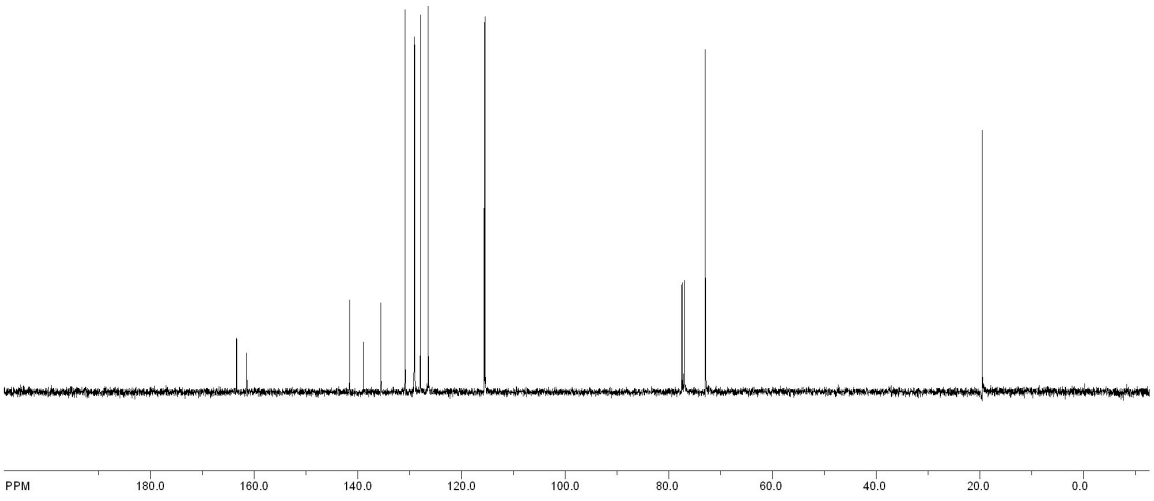
Naphthalen-2-yl-*o*-tolyl-methanol

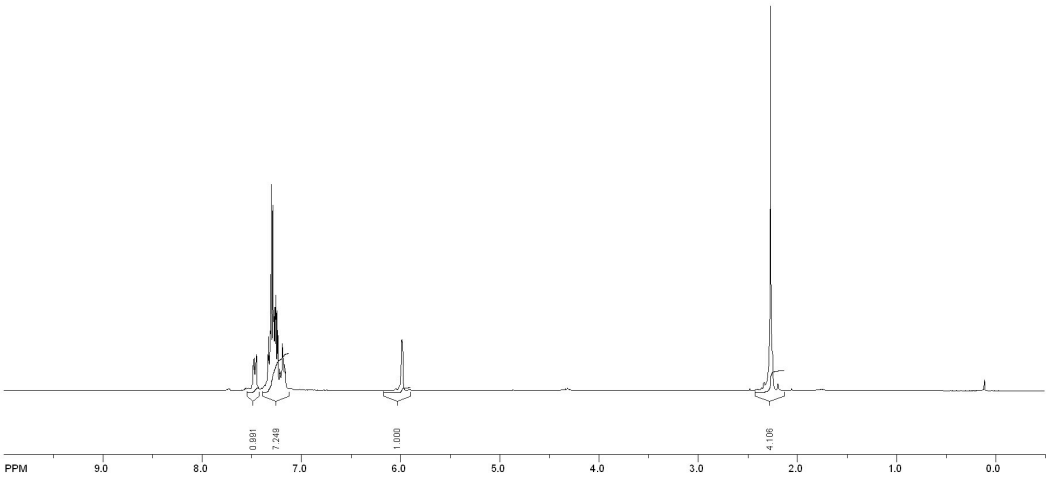


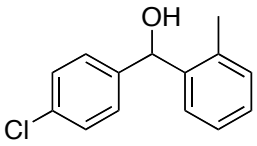




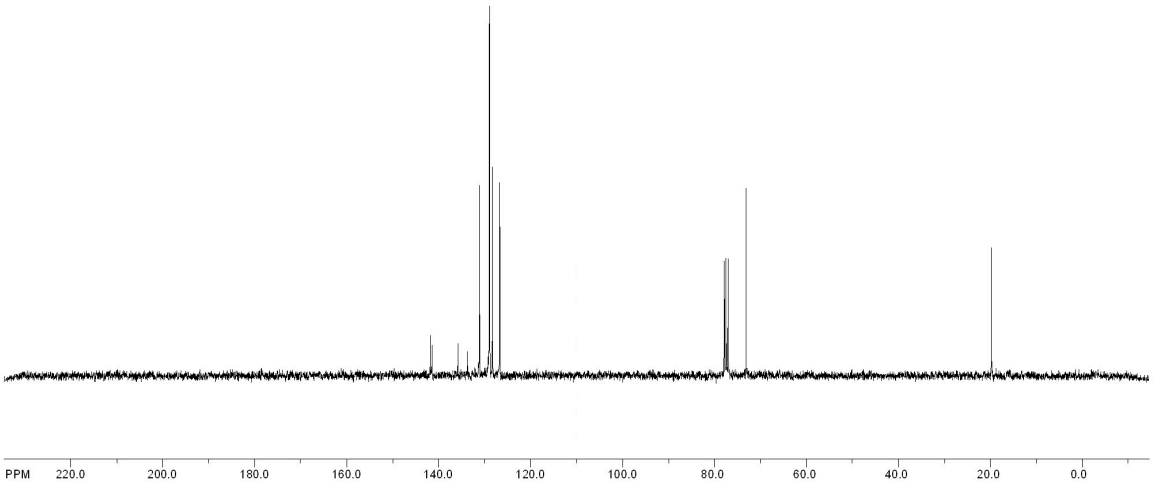
(4-Fluoro-phenyl)-2-tolyl-methanol

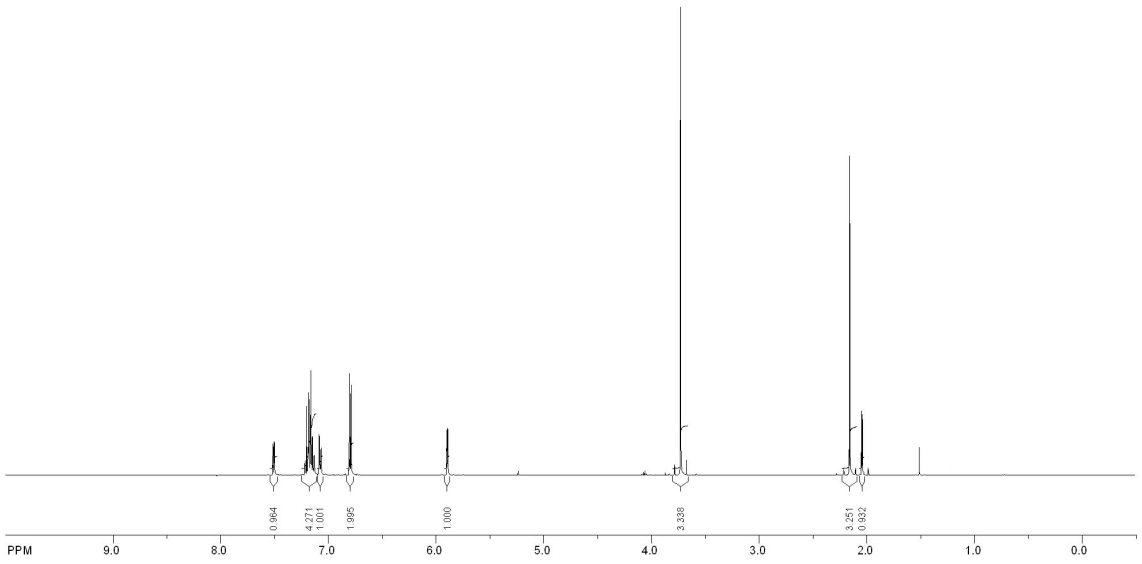


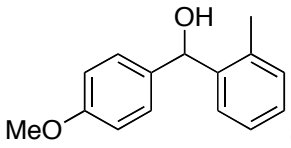




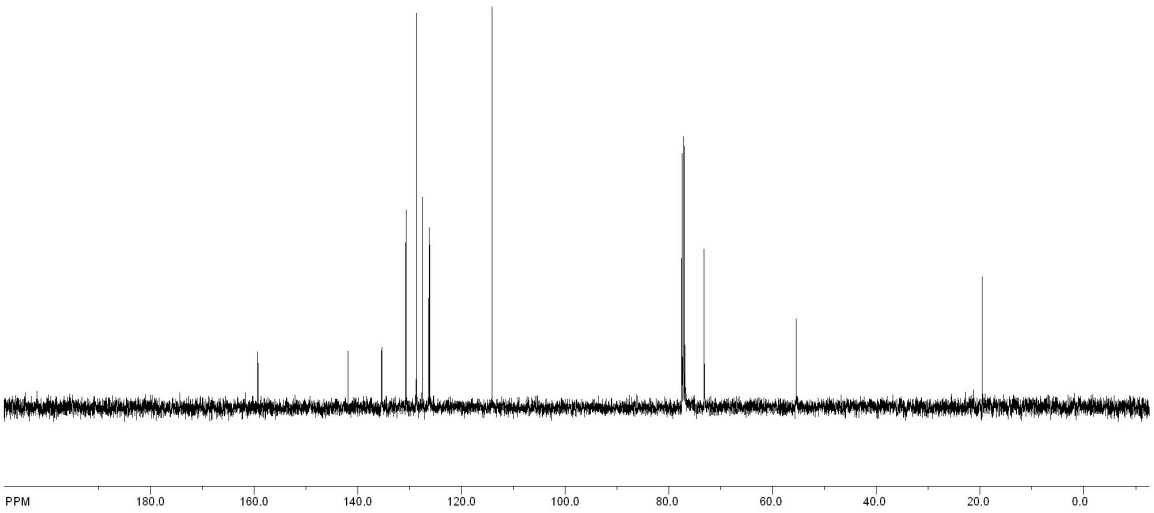
(4-Chloro-phenyl)-2-tolyl-methanol

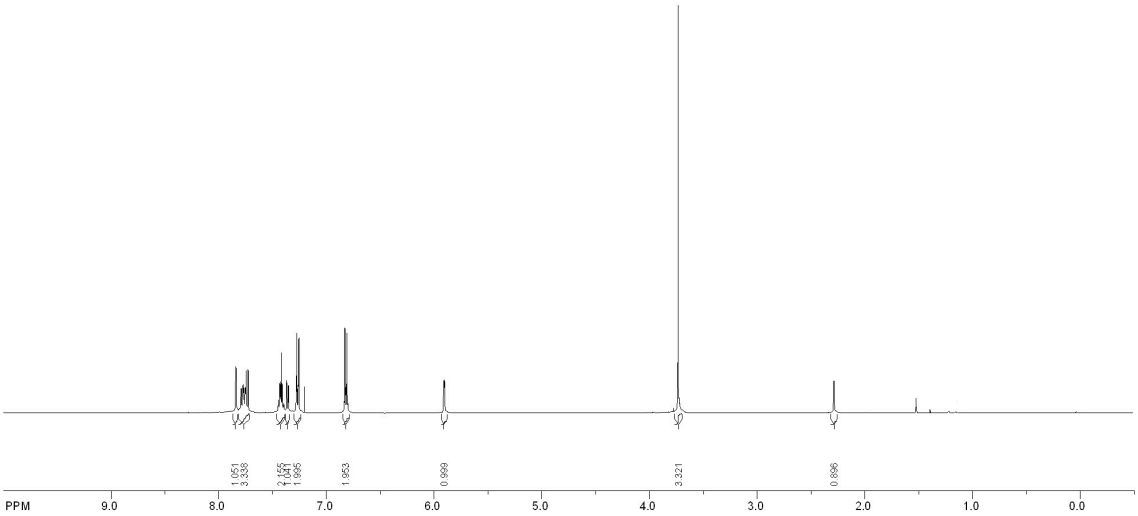


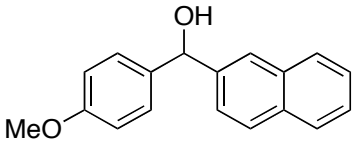




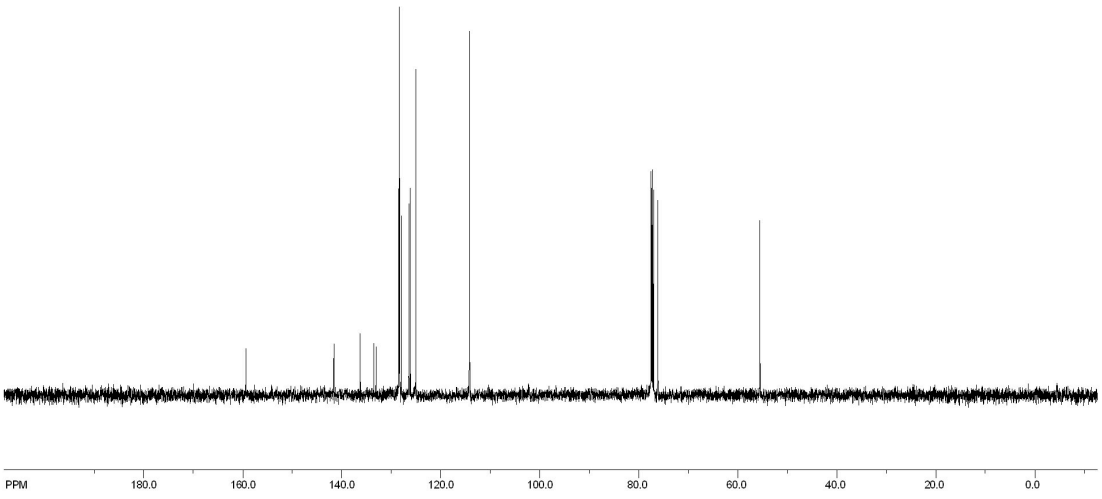
(4-Methoxy-phenyl)-2-tolyl-methanol

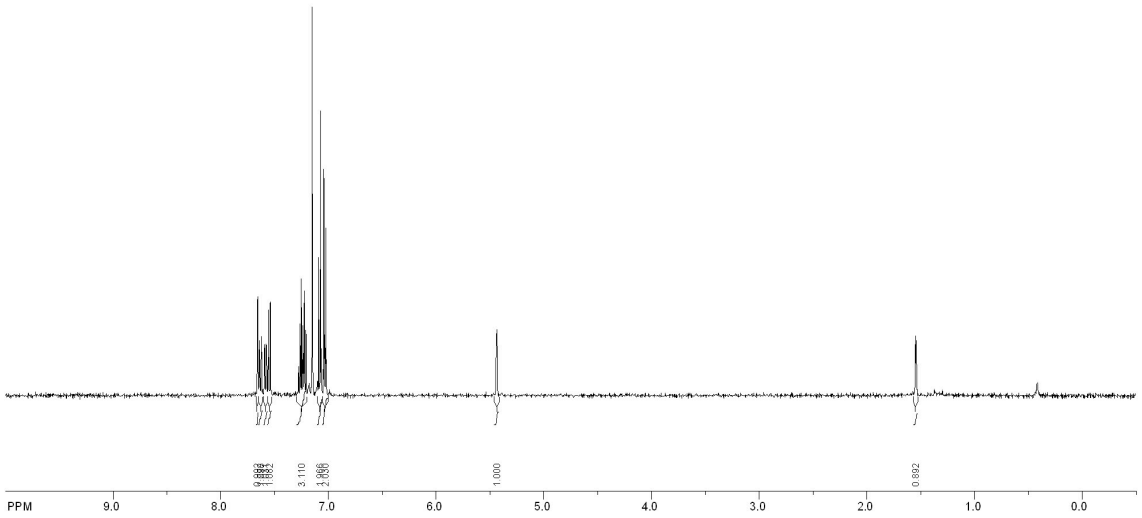


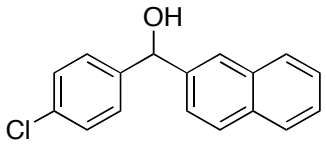




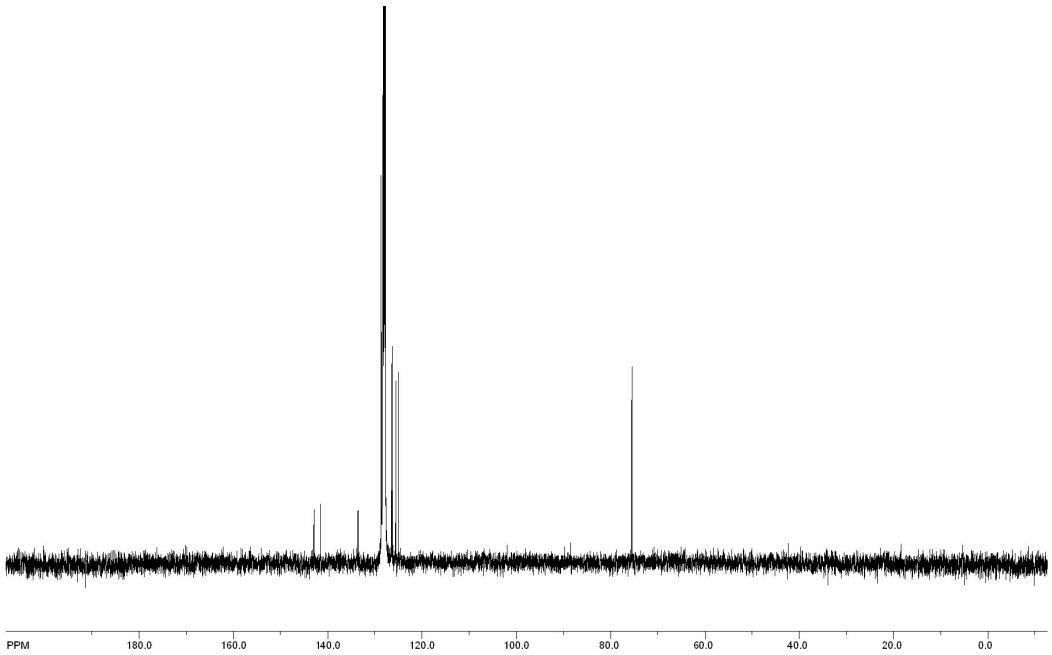
(4-Methoxy-phenyl)-naphthalen-2-yl-methanol

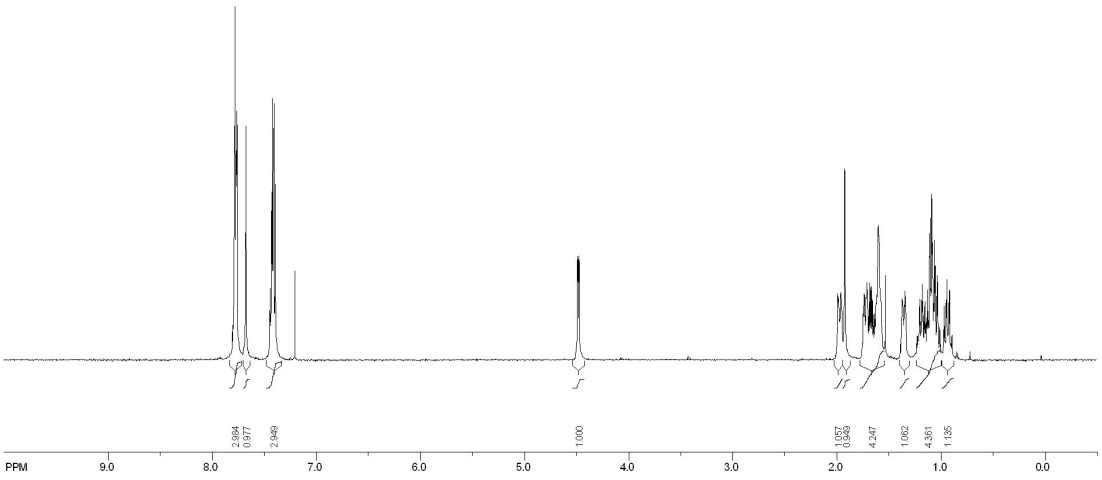


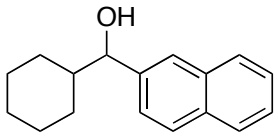




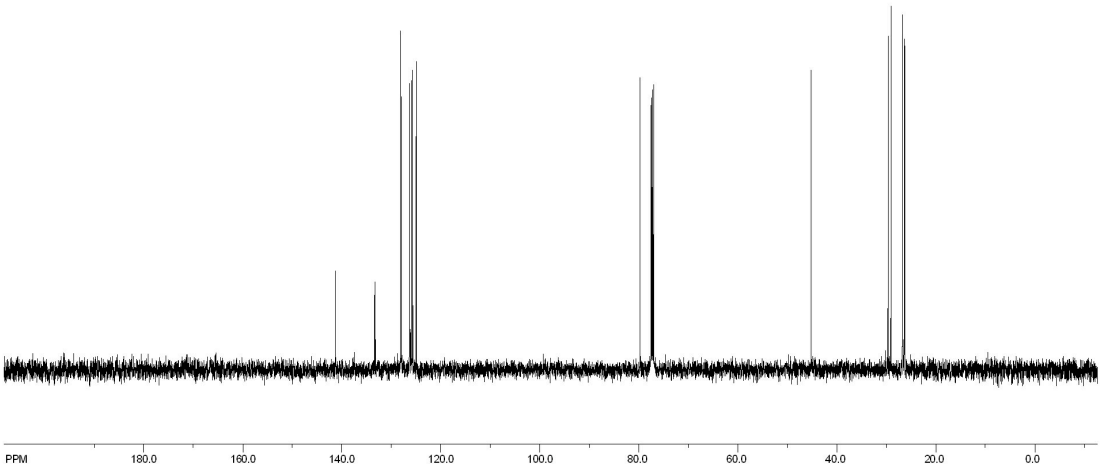
(4-Chloro-phenyl)-naphthalen-2-yl-methanol

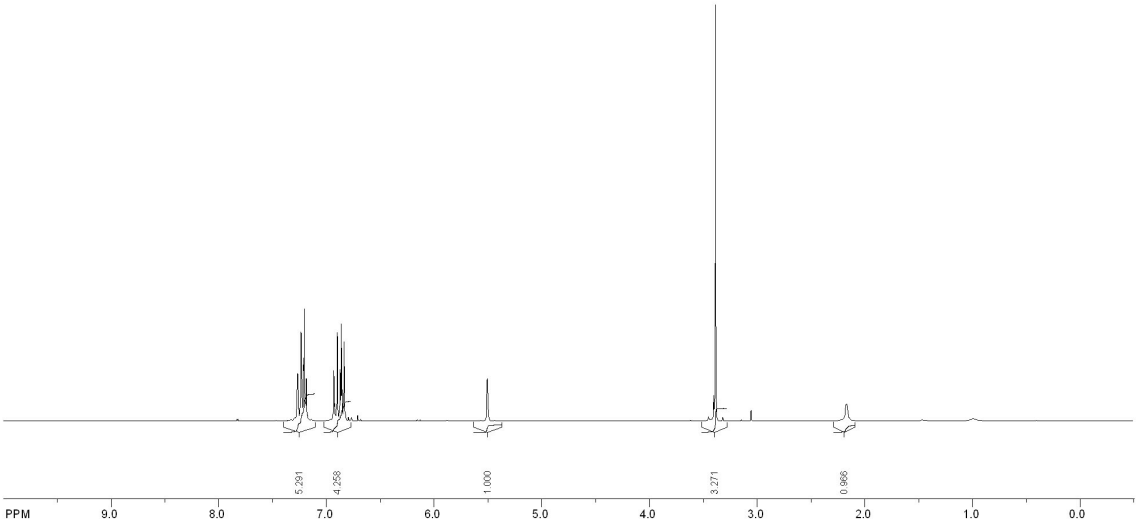


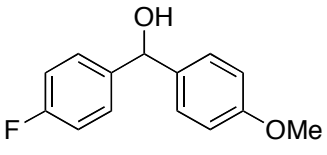




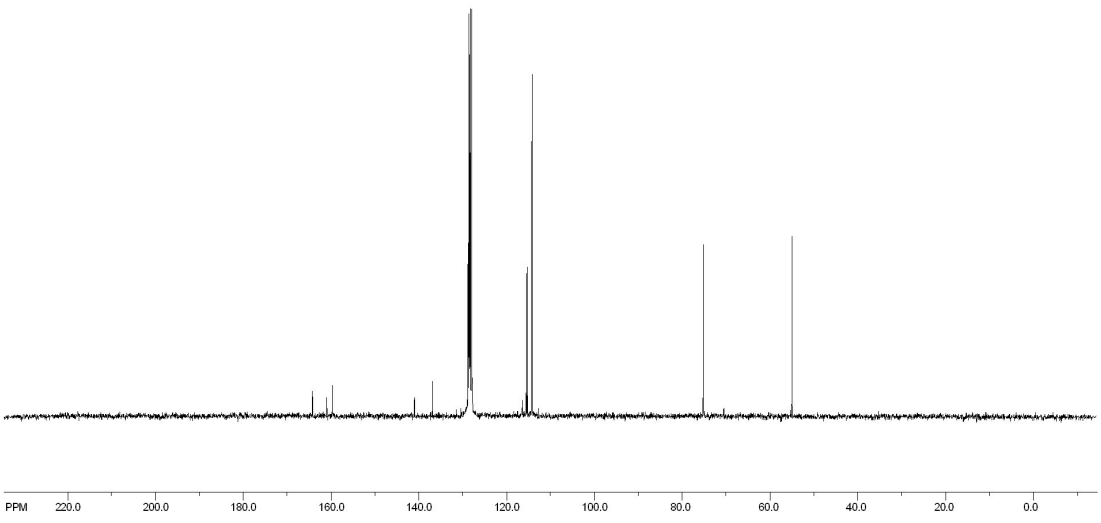
Cyclohexyl-naphthalen-2-yl-methanol

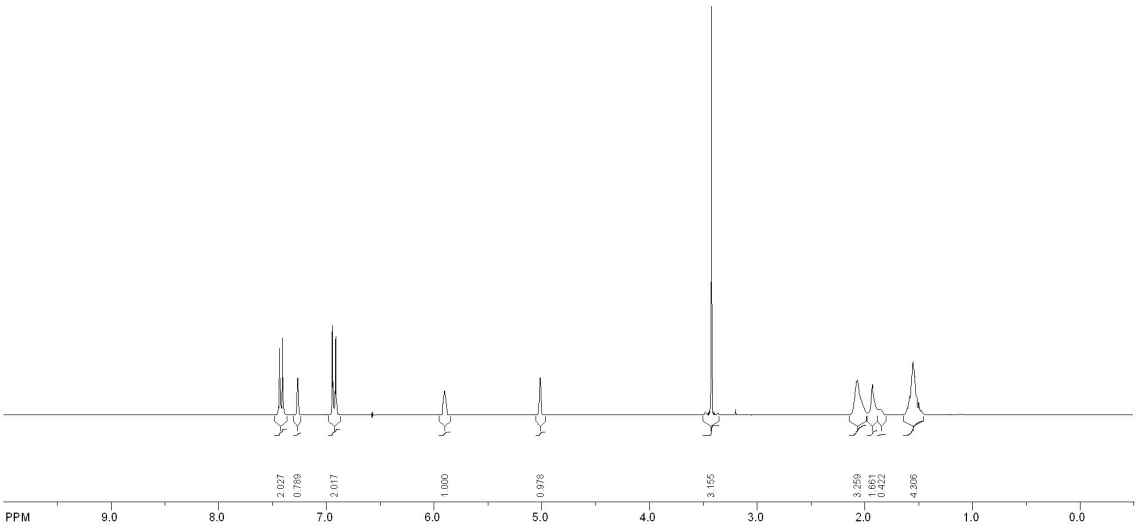


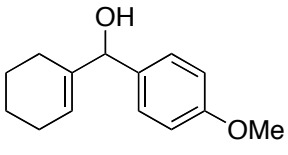




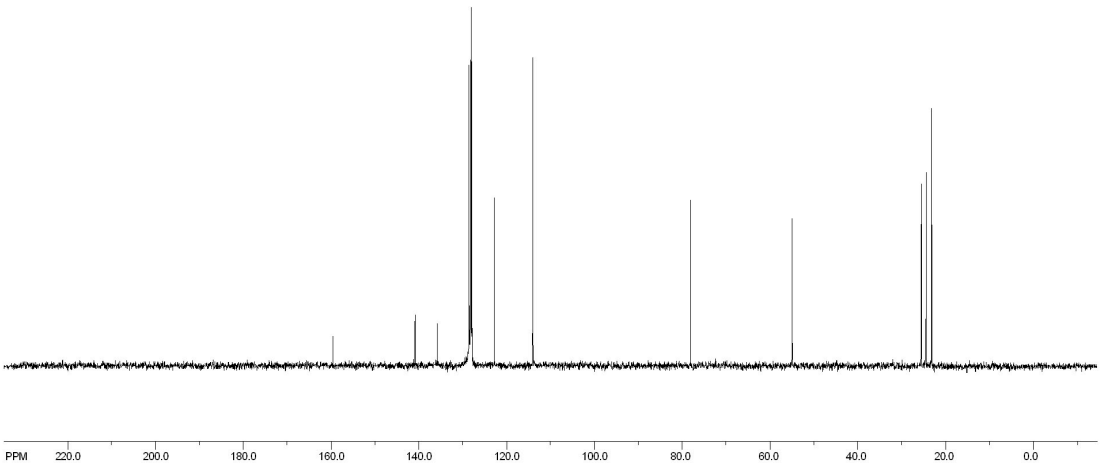
(4-Fluoro-phenyl)-(4-methoxy-phenyl)-methanol

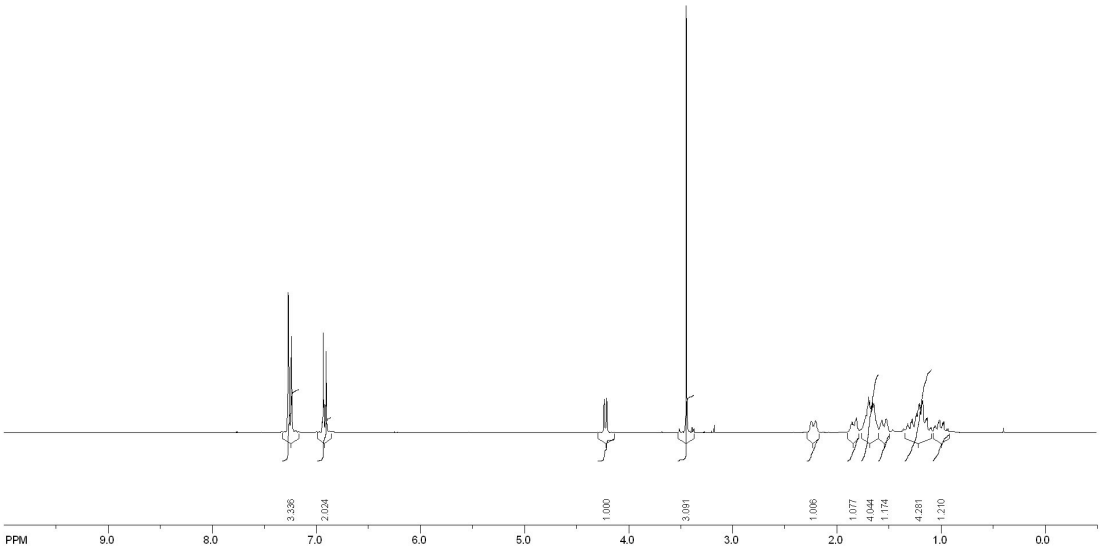


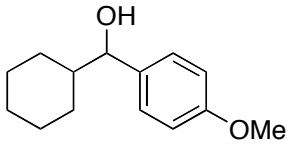




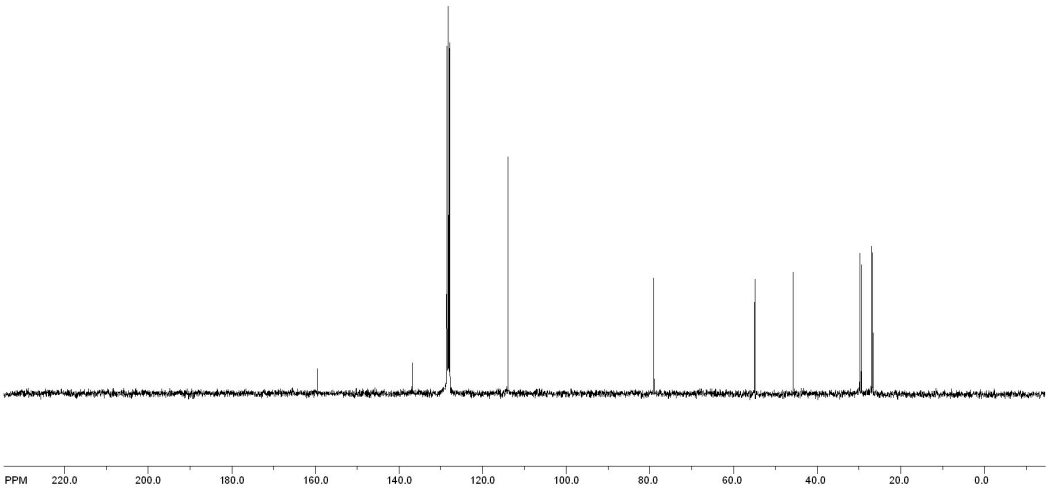
Cyclohex-1-enyl-(4-methoxy-phenyl)-methanol

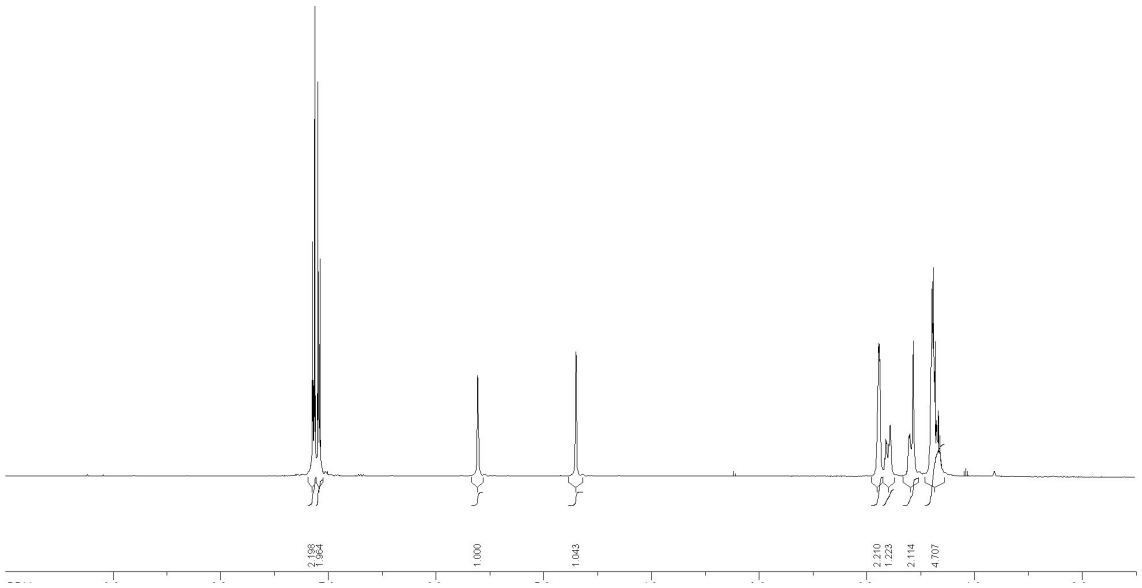


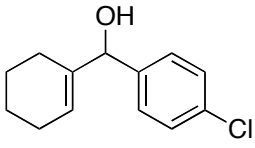




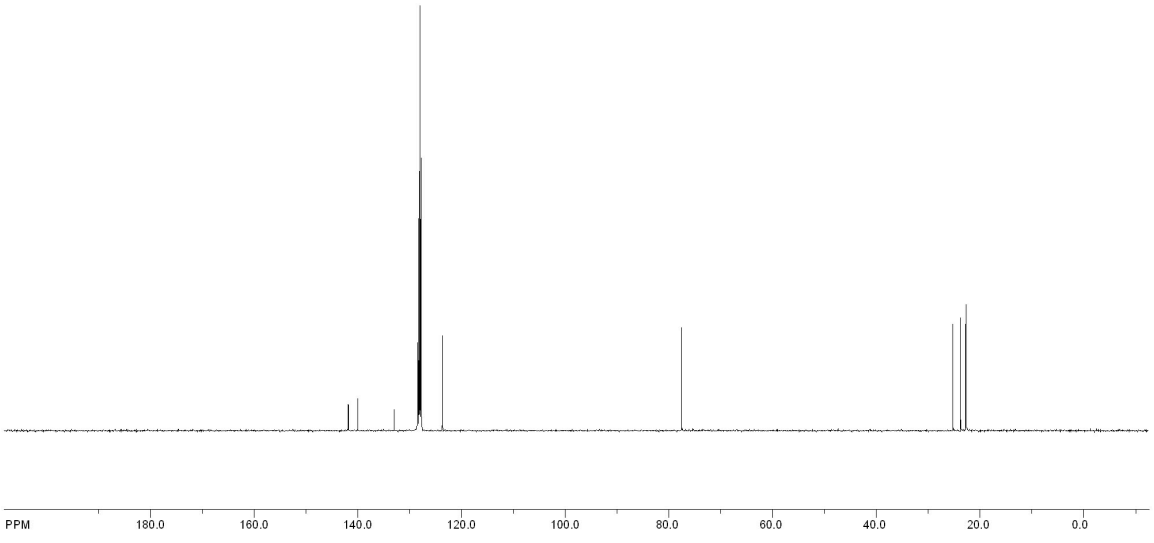
Cyclohexyl-(4-methoxy-phenyl)-methanol

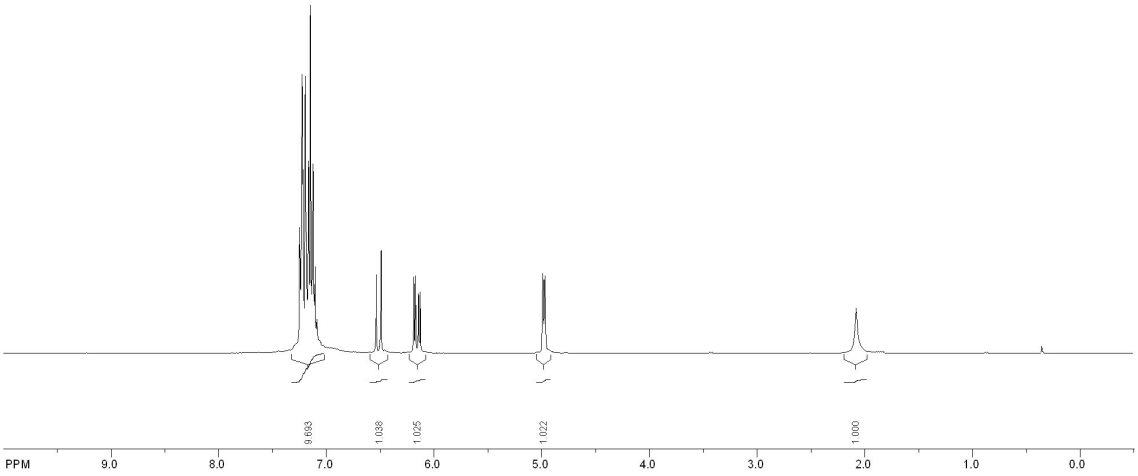


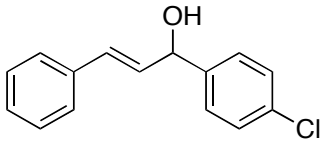




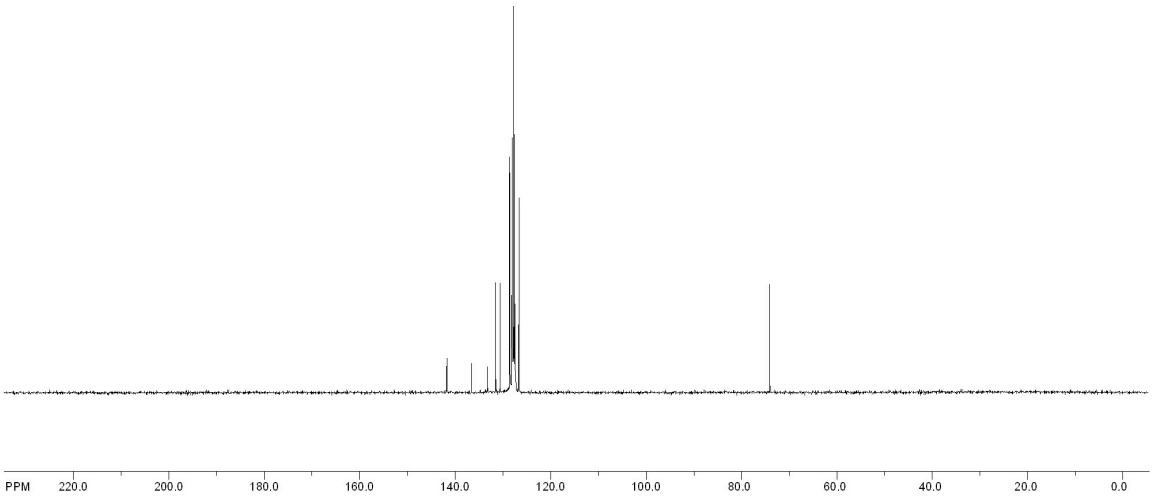
(*p*-Chloro-phenyl)-cyclohex-1-enyl-methanol

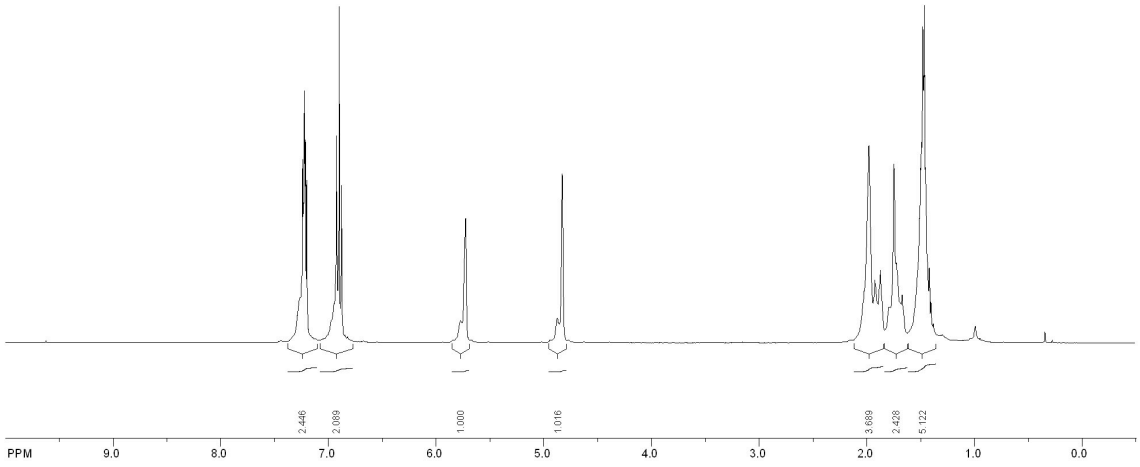


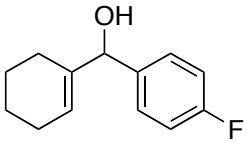




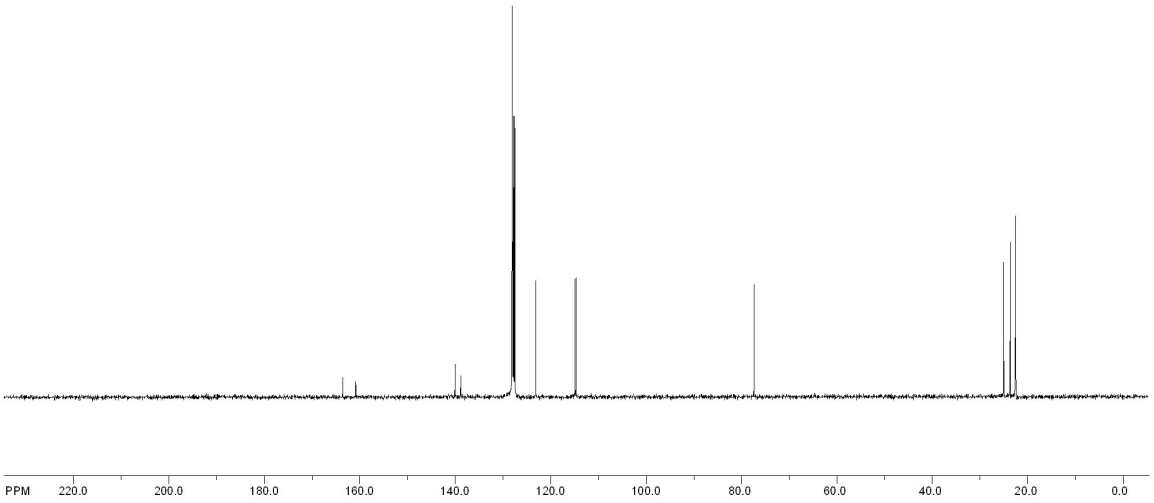
1-(4-Chloro-phenyl)-3-phenyl-prop-2-en-1-ol

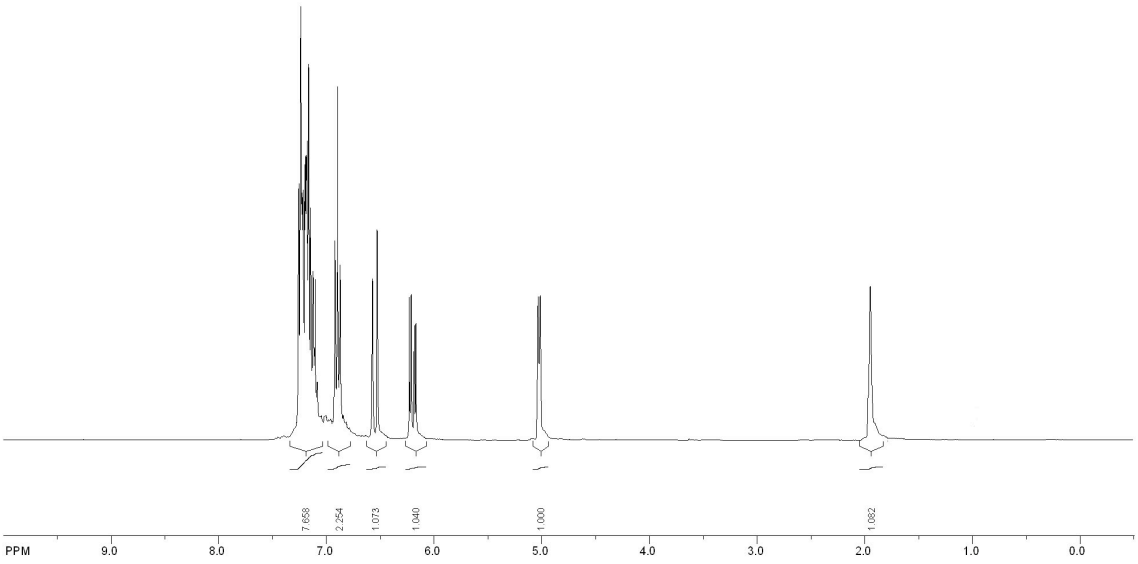


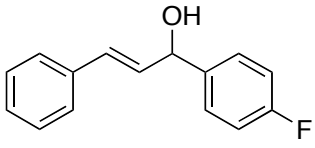




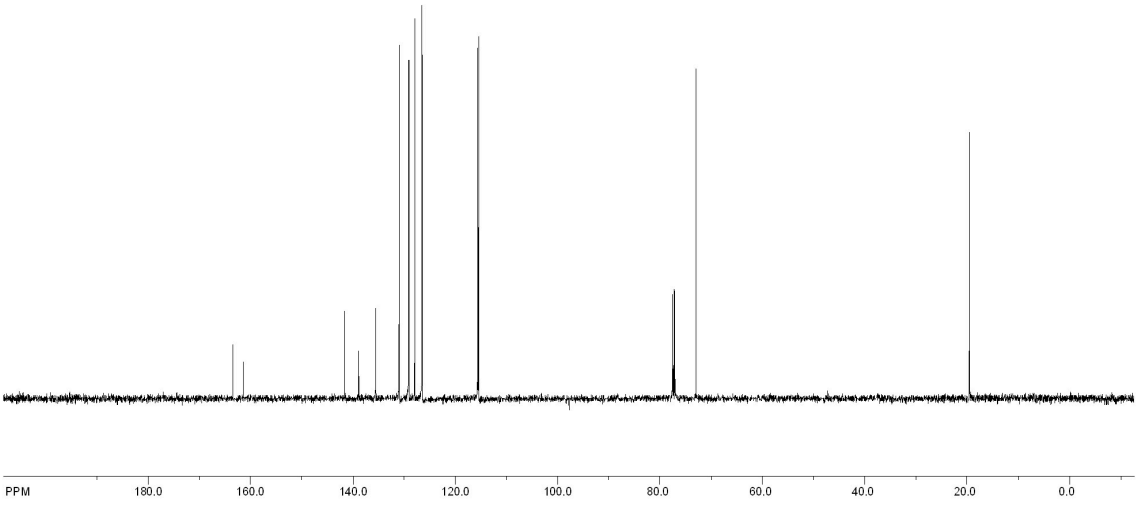
(4-Fluoro-phenyl)-cyclohex-1-enyl-methanol

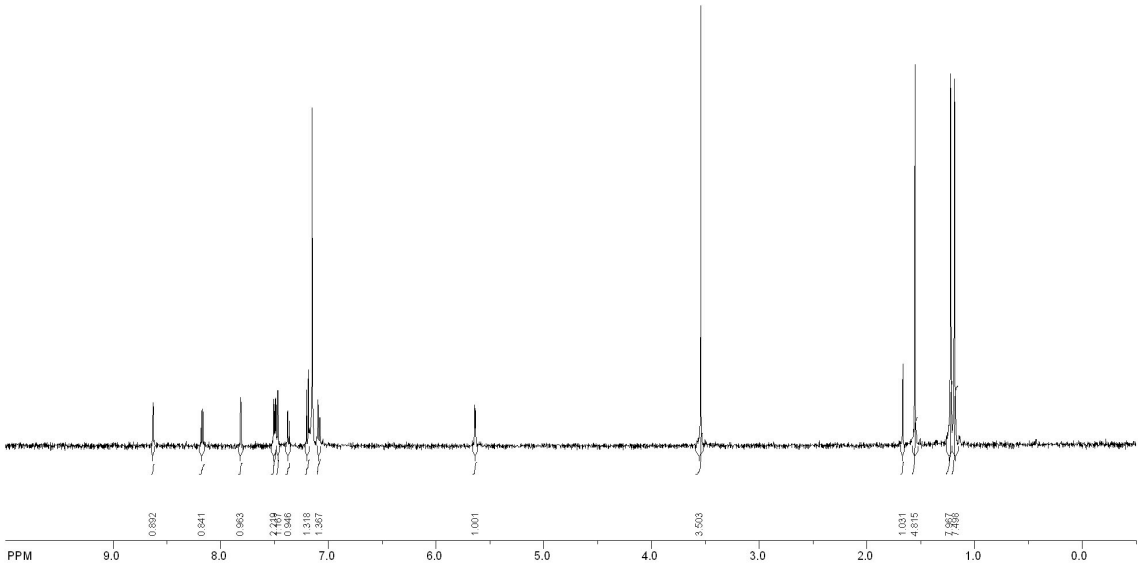


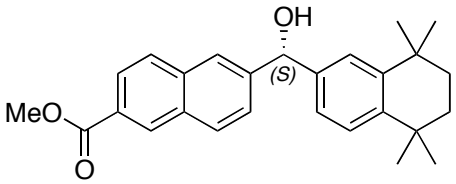




1-(4-Fluoro-phenyl)-3-phenyl-prop-2-en-1-ol







(*S*)-6-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)hydroxymethyl]-2-naphthalene carboxylate