Supporting Information

Chiral bifunctional phase transfer catalysts for asymmetric fluorination of β-keto esters

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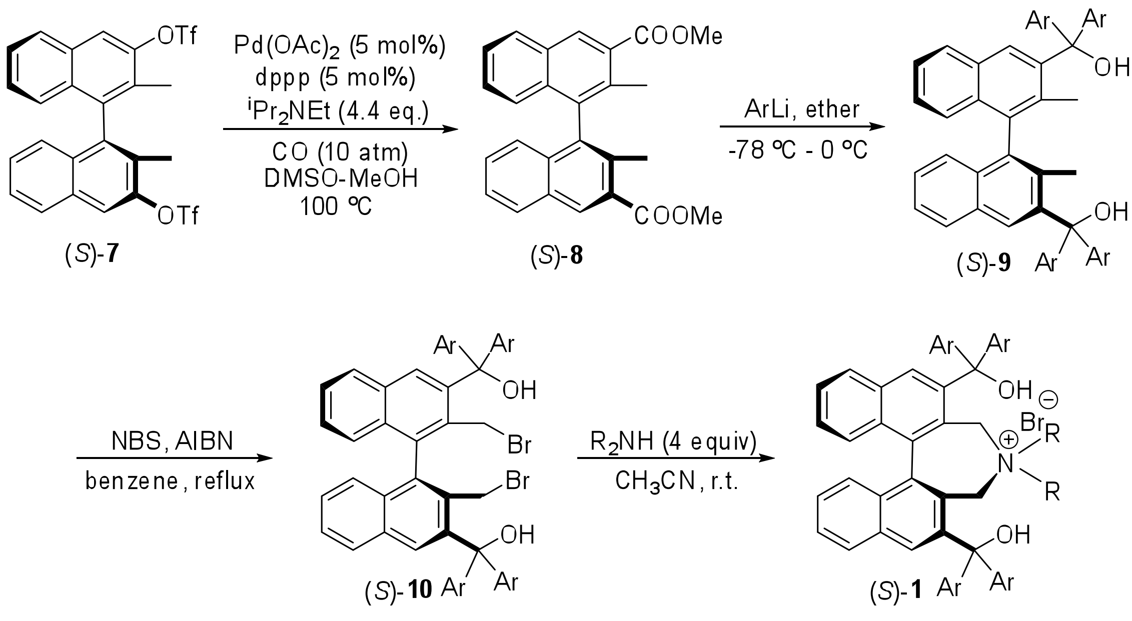
General Information:

Infrared (IR) spetra were recorded on a Shimadzu IRPrestige-21 spectrometer. ^{1}H NMR spectra were measured on a JEOL JNM-FX400 (400 MHz) spectrometer. Chemical shifts were reported in ppm from tetramethylsilane as an internal standard. Data were reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, m = multiplet, br = broad), coupling constants (Hz), and assignment. ^{13}C NMR spectra were recorded on a JEOL JNM-FX400 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts were reported in ppm from the residual solvent as an internal standard. ^{19}F NMR spectra were recorded on a JEOL JNM-FX400 (376 MHz). Chemical shifts are reported in ppm from fluorobenzene resonance (–113 ppm) as an external standard. High performed liquid chromatography (HPLC) was performed on Shimadzu 10A instruments using a Daicel CHIRALPAK OD, AD-H, OJ-H or AS-H, 4.6 mm × 25 mm column. High-resolution mass spectra (HRMS) were performed on BRUKER micrOTOF focus–KR. Optical rotations were measured on a JASCO DIP-1000 digital polarimeter. All reactions were monitored by thin-layer chromatography carried out on Merck precoated TLC plates (silica gel 60GF-254, 0.25 mm), visualization by using UV (254 nm), or dyes such as $KMnO_4$, PMA. The products were purified by flash column chromatography on silica gel 60 (Merck 1.09386.9025, 230~400 mesh). In experiments requiring dry solvents, ether and tetrahydrofuran (THF) were purchased from Kanto Chemical Co. Inc. as "dehydrated". Toluene was dried over sodium metal. Dichloromethane (CH_2Cl_2) was stored over 4 Å molecular sieves. Other simple chemicals were purchased and used as received.

Representative Procedure for the Synthesis of Chiral Ammonium Salts:



The key intermediate (*S*)-**7** was prepared according to literatures.[1]

Synthesis of (*S*)-8: Key intermediate (*S*)-**7** (1.0 g, 1.7 mmol), $Pd(OAc)_2$ (19.4 mg, 0.09 mmol), bis(diphenylphosphino)propane (dppp) (35.7 mg, 0.09 mmol) and $^{i}Pr_2NEt$

(1.26 mL, 7.6 mmol) in DMSO (8 mL) and MeOH (8 mL) were charged into autoclave under argon atmosphere. After pressurized with CO (10 atm), the mixture was heated to 105 °C with stirring for 36 h. After cooling to room temperature, the reaction mixture was poured into water and extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4, and then concentrated. The residue was purified by flash column chromatography on silica gel (ethyl acetate/hexane = 1:10 as eluant) to afford (*S*)-**8** (688 mg, quant). $[\alpha]_D^{22}$ -71.3° [*c* = 1.30, $CHCl_3$]; ^1H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 2H), 7.96 (d, *J* = 8.4 Hz, 2H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.28 (t, *J* = 7.6 Hz, 2H), 6.96 (d, *J* = 8.4 Hz, 2H), 3.99 (s, 6H) 2.23 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.6, 136.7, 134.0, 133.7, 131.3, 131.0, 129.3, 129.0, 128.4, 125.8, 125.6, 52.1, 17.8; IR (neat) 3059, 2949, 2359, 1719, 1622, 1437, 1273, 1198, 1138, 1057, 910, 750 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{26}H_{23}O_4$ ($[M+1]^+$): 399.1591, Found: 399.1579.

Synthesis of (*S*)-9: To a solution of ArBr (6 mmol) in ether (10 mL) was added a 1.6 M hexane solution of *n*-BuLi (3.75 mL, 6 mmol) dropwise at -78 °C under argon atmosphere. The reaction mixture was allowed to warm to 0 °C and stirred for 1 h, then cooled back to -78 °C. A solution of (*S*)-**8** (398 mg, 1 mmol) in ether (10 mL) was added dropwise with stirring. After the addition was completed, the mixture was again allowed to warm to 0 °C and stirred there for 2 h. The resulting mixture was poured into water and extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by flash column chromatography on silica gel (ethyl acetate/hexane as eluant) to afford (*S*)-**9**.

(*S*)-**9a** (Ar = Ph): ethyl acetate/hexane = 1:8 as eluant, 647 mg, quant.; $[\alpha]_D^{28}$ -91.2° [*c* = 0.80, $CHCl_3$]; ^1H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.0 Hz, 2H), 7.35-7.27 (m, 24H), 7.18 (t, *J* = 8.4 Hz, 2H), 6.96 (d, *J* = 8.4 Hz, 2H), 3.15 (s, 2H) 1.75 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.8, 143.1, 138.6, 134.6, 132.0, 131.0, 129.1, 128.5, 128.0, 127.9, 127.7, 127.6, 127.2, 126.6, 125.3, 125.2, 83.5, 19.0; IR (neat) 3466, 3057, 2924, 1705, 1597, 1491, 1447, 1362, 1221, 1022, 891, 750, 700 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{48}H_{38}NaO_2$ ($[M+Na]^+$): 669.2764, Found: 669.2742.

(*S*)-**9b** [Ar = 3,5-$(CF_3)_2$-Ph]: ethyl acetate/hexane = 1:15 as eluant, 1.19 g, quant.; $[\alpha]_D^{30}$ -47.6° [*c* = 0.98, $CHCl_3$]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 11.2 Hz, 4H), 7.88 (s, 4H), 7.81 (s, 4H), 7.70 (d, *J* = 8.4 Hz, 2H), 7.46 (t, *J* = 7.2 Hz, 2H), 7.32 (t, *J* = 7.2 Hz, 2H), 7.23 (s, 2H), 6.95 (d, *J* = 8.4 Hz, 2H), 3.45 (s, 2H), 1.59 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.1, 147.8, 140.0, 139.6, 132.3, 132.2, 132.0 (dq, *J* = 33.8, 1.7 Hz), 131.0, 129.6, 129.0, 128.3, 127.5 (br), 127.2 (br), 126.7, 124.8, 123.0 (dq, *J* = 274.0, 9.0 Hz), 122.1-122.0 (m), 82.2, 18.8; IR (neat) 3429, 3065, 3003, 1744, 1711, 1368, 1277, 1171, 1130, 901, 748, 683 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{56}H_{29}F_{24}O$ ($[M-OH]^+$): 1173.1830, Found: 1173.1780.

Synthesis of (*S*)-10: A mixture of (*S*)-**9** (1 mmol), *N*-bromosuccinimide (NBS) (392 mg, 2.2 mmol), and 2,2'-azobis(isobutyronitrile) (AIBN) (16.4 mg, 0.1 mmol) in benzene (5 mL) was heated and refluxed for 3 h. After being cooled to room temperature, this mixture was poured into water and extracted with ethyl acetate. The organic extracts were dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (ethyl acetate/hexane as eluant) to give (*S*)-**10**.

(*S*)-**10a** (Ar = Ph): ethyl acetate/hexane = 1:6-1:4 as eluant, 805 mg, quant.; $[\alpha]_D^{30}$ -42.1° [*c* = 0.89, $CHCl_3$]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.0 Hz, 2H), 7.42-7.26 (m, 24H), 7.21 (t, *J* = 8.0 Hz, 2H), 6.96 (d, *J* = 8.4 Hz, 2H), 4.26 (s, 4H) 3.93 (s, 2H); ^{13}C

NMR (100 MHz, $CDCl_3$) δ 146.7, 146.5, 142.6, 139.5, 133.0, 132.2, 132.1, 131.9, 128.5, 128.2, 128.1, 127.9, 127.7, 127.5, 127.4, 127.3, 127.2, 126.8, 83.5, 33.0; IR (neat) 3561, 3059, 3024, 1587, 1491, 1447, 1215, 1018, 893, 750, 700 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{48}H_{36}Br_2NaO_2$ ($[M+Na]^+$): 825.0974, Found: 825.0975.

(*S*)-**10b** [Ar = 3,5-$(CF_3)_2$-Ph]: ethyl acetate/hexane = 1:15 as eluant, 1.29 g, 96% yield; $[\alpha]_D^{29}$ -30.6° [*c* = 0.62, $CHCl_3$]; ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 10.4 Hz, 4H), 7.86 (s, 4H), 7.85 (s, 4H), 7.72 (d, *J* = 8.0 Hz, 2H), 7.56 (t, *J* = 7.6 Hz, 2H), 7.36 (t, *J* = 7.6 Hz, 2H), 7.26 (s, 2H), 6.99 (d, *J* = 8.4 Hz, 2H), 4.52 (s, 2H), 4.04 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.0, 147.9, 140.2, 139.0, 132.4, 132.3 (dq, *J* = 33.8, 8.2 Hz), 132.2, 131.4, 129.0, 128.8, 128.5, 127.7 (br), 127.3 (br), 127.2, 123.0 (dq, *J* = 274.5, 9.9 Hz), 122.7-122.5 (m), 82.4, 31.8; IR (neat) 3447, 3069, 3005, 1738; 1707, 1368, 1275, 1169, 1125, 901, 845, 750, 681 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{56}H_{27}Br_2F_{24}O$ ($[M-OH]^+$): 1329.0040, Found: 1329.0001.

Synthesis of Chiral Ammonium Salts (*S*)-1b, (*S*)-2a-b, (*S*)-2d: A mixture of (*S*)-**10** (0.5 mmol), amine (2.5 mmol) in acetonitrile (10 mL) was stirred for 1-2 days at room temperature. The mixture was concentrated and then purified by column chromatography on silica gel ($MeOH/CH_2Cl_2$ = 1/30-1/10 as eluant) to give chiral ammonium salts (*S*)-**1**-**2**.

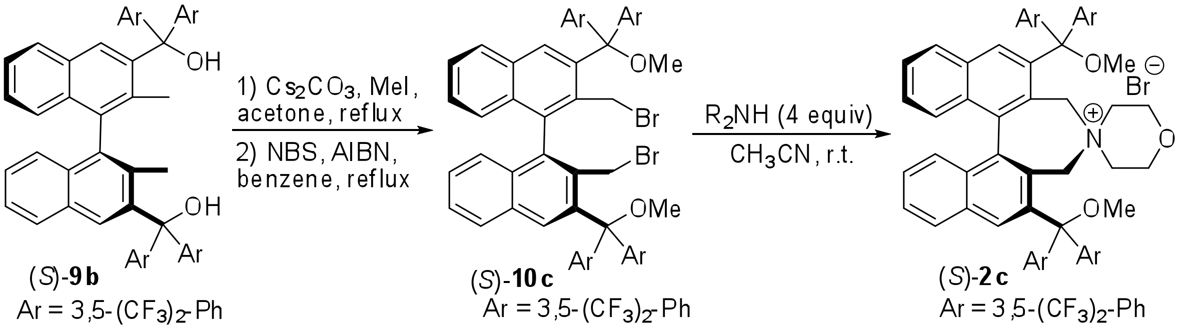
(*S*)-**1b**: 57% yield; $[\alpha]_D^{30}$ -52.6° [*c* = 0.40, $CHCl_3$]; ^1H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.4 Hz, 2H), 7.56 (d, *J* = 8.4 Hz, 4H), 7.48-7.34 (m, 10H), 7.26-7.16 (m, 12H), 6.90 (d, *J* = 8.8 Hz, 2H), 5.49 (s, 2H), 5.11 (d, *J* = 13.6 Hz, 2H), 3.37 (d, *J* = 13.6 Hz, 2H), 3.26 (t, *J* = 12.8 Hz, 2H), 3.03 (t, *J* = 12.8 Hz, 2H), 1.43-1.08 (m, 8H), 0.84 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.9, 145.3, 143.0, 139.4, 132.3, 131.1, 128.9, 128.4, 128.2, 128.1, 127.7, 127.4, 127.3, 127.2, 127.0, 126.7, 126.4, 82.6, 60.3, 60.2, 24.2, 19.9, 13.8; IR (neat) 3217, 3059, 2959, 1595, 1491, 1447, 1371, 1217, 1049, 895, 750, 702 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{56}H_{54}NO_2$ ($[M]^+$): 772.4149, Found: 772.4141.

(*S*)-**2a**: 84% yield; $[\alpha]_D^{30}$ -88.0° [*c* = 0.36, CH_3OH]; ^{1}H NMR (400 MHz, $CDCl_3$ + CD_3OD) δ 7.71 (d, *J* = 8.4 Hz, 2H), 7.50-7.38 (m, 14H), 7.29-7.20 (m, 12H), 6.90 (d, *J* = 8.4 Hz, 2H), 5.30 (d, *J* = 14.0 Hz, 2H), 3.99 (br, 2H), 3.65 (br, 2H), 3.56 (br, 2H), 3.48 (d, *J* = 14.0 Hz, 2H), 2.84 (br, 2H); ^{13}C NMR (100 MHz, $CDCl_3$+ CD_3OD) δ 147.4, 145.2, 142.7, 139.6, 132.1, 130.9, 130.8, 128.6, 128.1, 128.0, 127.9, 127.6, 127.5, 127.3, 127.2, 126.7, 126.3, 125.1, 82.1, 61.3, 60.0, 59.7; IR (neat) 3250, 3059, 1593, 1491, 1447, 1362, 1261, 1125, 1032, 887, 750, 702 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{52}H_{44}NO_3$ ($[M]^+$): 730.3316, Found: 730.3313.

(*S*)-**2b**: 78% yield; $[\alpha]_D^{30}$ -141.5° [*c* = 0.43, CH_3OH]; ^{1}H NMR (400 MHz, CD_3OD) δ 8.14 (s, 2H), 7.97 (s, 6H), 7.87 (d, *J* = 7.2 Hz, 2H), 7.86 (s, 4 H), 7.60 (t, *J* = 7.6 Hz, 2H), 7.42 (s, 2H), 7.38 (t, *J* = 7.6 Hz, 2H), 6.98 (d, *J* = 8.4 Hz, 2H), 4.98 (d, *J* = 13.6 Hz, 2H), 4.14 (br, 2H), 3.94 (br, 2H), 3.68 (br, 2H), 3.67 (d, *J* = 13.6 Hz, 2H), 3.22 (br, 2H); ^{13}C NMR (100 MHz, CD_3OD) δ 151.0, 149.1, 142.4, 141.1, 134.0, 133.4 (quint, *J* = 33.7 Hz), 132.8, 132.5, 130.3, 130.0, 129.9, 129.8, 128.4 (br), 127.7, 125.6, 124.5 (dq, *J* = 273.3, 24.7 Hz), 123.8 (br), 123.5 (br), 83.1, 62.9, 61.2, 60.9; IR (neat) 3146, 3073, 1743, 1622, 1369, 1277, 1173, 1132, 903, 770, 750, 682 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{60}H_{36}F_{24}NO_3$ ($[M]^+$): 1274.2306, Found: 1274.2280.

(*S*)-**2d**: 70% yield; $[\alpha]_D^{30}$ -121.6° [*c* = 0.53, CH_3OH]; ^{1}H NMR (400 MHz, CD_3OD) δ 8.15 (s, 2H), 7.97 (s, 6H), 7.87 (d, *J* = 9.2 Hz, 2H), 7.86 (s, 4H), 7.60 (t, *J* = 7.6 Hz, 2H), 7.42 (s, 2H), 7.38 (t, *J* = 7.6 Hz, 2H), 6.95 (d, *J* = 8.4 Hz, 2H), 4.88 (d, *J* = 13.6 Hz, 2H), 3.95 (br, 2H), 3.62 (d, *J* = 13.6, 2H), 3.35 (br, 2H), 3.27 (br, 2H), 2.61 (br, 2H); ^{13}C NMR (100 MHz, CD_3OD) δ 151.0, 149.0, 142.2, 141.1, 134.1, 133.4 (quint, *J* = 33.7 Hz), 132.8, 132.6, 130.2, 129.9, 129.8, 129.7, 128.3 (br), 127.8, 125.7, 124.5 (dq, *J* = 273.5, 25.5 Hz), 123.8 (br), 123.5 (br), 83.0, 63.2, 61.1, 23.0; IR (neat) 3125, 3005, 2970, 1738, 1371, 1279, 1173, 1136, 1032, 903, 845, 772, 683 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{60}H_{36}F_{24}NO_2S$ ($[M]^+$): 1290.2078, Found: 1290.2048.

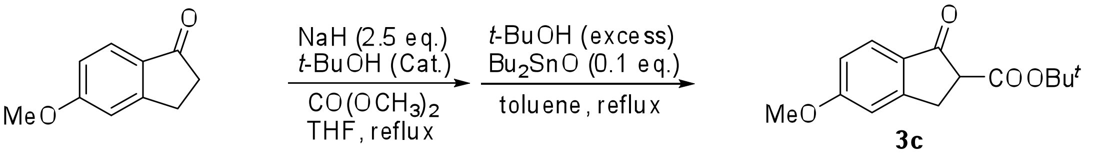
Synthesis of Methyl-protected Chiral Ammonium Salt (*S*)-2c:



A mixture of (*S*)-**9b** (190 mg, 0.16 mmol), Cs_2CO_3 (521 mg, 1.6 mmol) and methyl iodide (198 μL, 3.2 mmol) in acetone (6 mL) was heated and refluxed for 2 h. The resulting mixture was poured into water and extracted with ethyl acetate. The organic extracts were washed with brine and dried over Na_2SO_4. Evaporation of solvents gave the crude (*S*)-3,3’-bis{di[3,5-bis(trifluoromethyl)-phenyl]-hydroxymethyl}-2,2’-bismethyl-1,1’-binaphthyl, which was directly used for radical bromination as described before. The residual crude product was purified by column chromatography on silica gel (ethyl acetate/hexane = 1:100-1:10 as eluant) to afford (*S*)-**10c** (178 mg, 81% yield for two steps). $[\alpha]_D^{29}$ +3.48° [*c* = 0.81, $CHCl_3$]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (s, 2H), 7.98 (s, 4H), 7.93 (s, 4H), 7.82 (d, *J* = 9.2 Hz, 2H), 7.79 (d, *J* = 9.2 Hz, 4H), 7.58 (t, *J* = 7.6 Hz, 2H), 7.36 (t, *J* = 8.0 Hz, 2H), 7.00 (d, *J* = 8.8 Hz, 2H), 4.20 (d, *J* = 11.2 Hz, 2H), 4.02 (d, *J* = 11.2 Hz, 2H), 3.41 (s, 6H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 147.2, 146.6, 140.9, 134.3, 133.1, 132.4 (q, *J* = 33.8 Hz),132.0, 131.8, 128.6, 128.4, 128.2, 127.4 (br), 127.2, 127.0 (br), 123.0 (dq, *J* = 274.1, 11.5 Hz), 121.9-121.7 (m), 87.6, 54.2, 29.1; IR (neat) 2995, 1744, 1364, 1277, 1172, 1132, 770, 750, 682 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{58}H_{32}BrF_{24}O_2$ ([M-Br]$^+$): 1295.1197, Found: 1295.1138.

Chiral Ammonium Salt (*S*)-**2c**. (*S*)-**2c** was prepared following representative procedure for the synthesis of chiral ammonium salts (45 % yield). $[\alpha]_D^{29}$ -85.7° [*c* = 0.44, CHCl$_3$]; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.98-7.72 (m, 10H), 7.81 (s, 4H), 7.74 (s, 2H), 7.72 (t, *J* = 8.0 Hz, 2H), 7.54 (t, *J* = 8.0 Hz, 2H), 7.03 (d, *J* = 8.4 Hz, 2H), 4.85 (d, *J* = 13.6 Hz, 2H), 4.35 (br, 2H), 3.79 (br, 2H), 3.63 (s, 6H), 3.51 (br, 4H), 3.39 (d, *J* = 13.6 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 149.3, 143.7, 141.3, 134.2, 133.7, 133.0 (dq, J_1 = 33.8, 12.3 Hz), 132.1, 131.4, 130.0, 129.8, 129.1, 128.4 (br), 126.2, 125.5 (br), 123.9, 122.7 (dq, J_1 = 274.9, 26.0 Hz), 122.5 (br), 87.2, 61.1, 60.2, 59.9, 55.0; IR (neat) 2970, 1744, 1364, 1279, 1173, 1136, 903, 843, 770, 682 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{62}H_{40}F_{24}NO_3$ ([M]$^+$): 1302.2619, Found: 1302.2568.

Synthesis of Substrate 3c:[2]



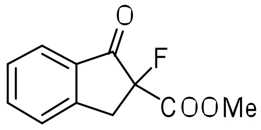
A three-neck flask was charged with NaH (60% suspension in mineral oil, 1.5 g, 37.5 mmol) and dry THF (10 mL) under Ar. The suspension was stirred at room temperature for 5 min and stood for another 5 min. The liquid phase was removed by a syringe and the residue was subjected to vacuum for 15 min. The resulting fine white powder was then suspended in THF (40 mL). To this suspension dimethyl carbonate (12.9 mL, 150 mmol) was added via a syringe. The resulting mixture was heated at reflux while a solution of 5-Methoxy-1-indanone (2.43 g, 15 mmol) in THF (20 mL) was introduced dropwise through a dropping funnel. The resulting brown mixture was heated at reflux for an additional 15 min. The resulting green mixture was cooled to 0℃, to which acetic acid (4.5 mL) was added dropwise via a syringe. The resulting mixture was further acidified by addition of an aqueous solution of HCl (1.0 *N*, 20 mL). The mixture was extracted with ethyl acetate (50 mL × 3). The combined organic phase was washed with water, saturated aqueous $NaHCO_3$, brine, dried over Na_2SO_4 and concentrated. Purification of the residue by column chromatography on silica gel (hexane/ethyl acetate = 20:1 as eluant) afforded β-keto methyl ester.

An oven-dried flask was charged with β-keto methyl ester (15 mmol), Bu_2SnO (373 mg, 1.5 mmol), *t*-BuOH (5 mL) and toluene (45 mL). The resulting mixture was heated and refluxed in a flask connected to a Dean-Star trap. Methanol and *t*-butanol collected in the Dean-Star trap were released every hour, after which a portion of *t*-BuOH (2 mL) was added. The mixture was refluxed for a total of 4 hours. The resulting yellow solution was concentrated and purified by column chromatography on silica gel (hexane/ethyl acetate = 20:1 as eluant) afforded β-keto *t*-butyl ester **3c** (3.70g, 94% yield) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 9.2 Hz, 1H), 6.91 (s, 2H), 3.89 (s, 3H), 3.60 (dd, J = 8.0, 4.0 Hz, 1H), 3.44 (dd, J = 17.2, 4.0 Hz, 1H), 3.26

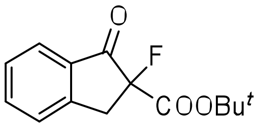
(dd, *J* = 17.2, 8.0 Hz, 1H), 1.49 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.0, 168.6, 165.6, 156.7, 128.6, 126.1, 115.7, 109.4, 81.8, 55.6, 54.5, 30.2, 27.9; IR (neat) 2978, 1728, 1701, 1597, 1489, 1368, 1256, 1142, 1088, 1024, 986, 843, 750 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{15}H_{18}NaO_4$ ([M+Na]$^+$): 285.1097, Found: 285.1096.

General Procedure of Catalytic Enantioselective Fluorination of β-Keto Esters 3 under Phase Transfer Condition.

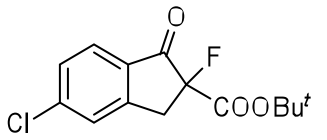
To a reaction vessel containing β-keto ester **3** (0.1 mmol) and chiral ammonium salt (*S*)-**2d** (0.002 mmol, 2 mol %) were added diethyl ether (4.0 mL). After the reaction system was cooled to –20 °C, aqueous K_2CO_3 (0.5 M in water, 1.0 mL) was added dropwise. After the reaction mixture was stirred for 10 min at –20 °C, *N*-fluorobis(benzenesulfonimide) (NFSI) (36 mg, 0.11 mmol, 1.1 equiv) was added in a single portion. The reaction mixture was then stirred vigorously at the same temperature for 1 h, quenched with saturated NH_4Cl solution (10 mL), extracted with diethyl ether (10 mL), dried over Na_2SO_4 and concentrated. Purification of the residue by column chromatography on silica gel with hexane-ethyl acetate as eluant afforded the fluorination product **4**. The product was identified by NMR spectroscopy. The enantiomeric excess of the product was determined by chiral HPLC using a chiral column.



4a': $[\alpha]_D^{27}$ +15.7° [*c* = 1.20, $CHCl_3$ (68% *ee*)]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 7.6 Hz, 1H), 7.71 (t, *J* = 7.6 Hz, 1H), 7.52-7.45 (m, 2H), 3.81 (s, 3H), 3.84-3.77 (m, 1H), 3.44 (dd, *J* = 23.6, 18.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.1 (d, *J* = 18.1 Hz), 167.7 (d, *J* = 28.0 Hz), 150.8 (d, *J* = 4.1 Hz), 136.7, 133.1, 128.6, 126.6 (d, *J* = 1.7 Hz), 125.6, 94.5 (d, *J* = 201.6 Hz), 53.2, 38.2 (d, *J* = 23.9 Hz); HRMS (ESI-TOF) calcd for $C_{11}H_9FNaO_3$ ($[M+Na]^+$): 231.0428, Found: 231.0430. HPLC analysis: DAICEL Chiralpak OD, 2-propanol/hexane = 1:10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: 10.3 min (minor) and 12.1 min (major).

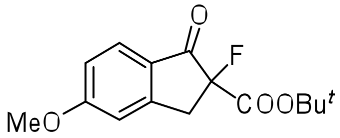


4a: $[\alpha]_D^{29}$ -3.34° [*c* = 0.35, $CHCl_3$ (96% *ee*)] [Lit[3]: $[\alpha]_D^{34}$ +3.8° (*c* = 0.86, $CHCl_3$) (83% *ee*, *R* enantiomer)]; ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 7.6 Hz, 1H), 7.69 (t, *J* = 7.6 Hz, 1H), 7.51-7.44 (m, 2H), 3.73 (dd, *J* = 18.0, 11.2 Hz, 1H), 3.40 (dd, *J* = 22.8, 17.6 Hz, 1H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.7 (d, *J* = 17.3 Hz), 166.2 (d, *J* = 27.9 Hz), 150.9 (d, *J* = 3.3 Hz), 136.4, 133.6, 128.4, 126.4 (d, *J* = 1.6 Hz), 125.4, 94.3 (d, *J* = 202.4 Hz), 84.1, 38.3 (d, *J* = 23.8 Hz), 27.8; HRMS (ESI-TOF) calcd for $C_{14}H_{15}FNaO_3$ ($[M+Na]^+$): 273.0897, Found: 273.0888. HPLC analysis: DAICEL Chiralpak AD-H, 2-propanol/hexane = 1:100, flow rate = 1.0 mL/min, λ = 254 nm, retention time: 12.0 min (major) and 14.4 min (minor).

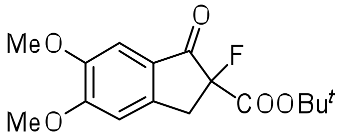


4b: $[\alpha]_D^{29}$ +41.2° [*c* = 0.51, $CHCl_3$ (94% *ee*)]; ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.4 Hz, 1H), 7.50 (s, 1H), 7.44 (d, *J* = 8.4 Hz, 1H), 3.71 (dd, *J* = 18.0, 10.8 Hz, 1H), 3.38 (dd, *J* = 22.4, 17.6 Hz, 1H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.3 (d, *J* = 18.1 Hz), 165.8 (d, *J* = 26.3 Hz), 152.3 (d, *J* = 4.1 Hz), 143.1, 132.0, 129.4, 126.7 (d, *J* = 1.7 Hz), 126.5, 94.2 (d, *J* = 202.5 Hz), 84.4, 38.0 (d, *J* = 24.7 Hz), 27.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ -161.2 (dd, *J* = 22.6, 10.5 Hz); IR (neat) 2982, 1759, 1728, 1599, 1578, 1371, 1265, 1209, 1153, 1070, 924, 746 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{14}H_{14}ClFNaO_3$ ($[M+Na]^+$): 307.0508, Found: 307.0503. HPLC analysis: DAICEL Chiralpak AD-H, 2-propanol/hexane = 1:100, flow rate = 1.0 mL/min, λ = 254 nm, retention time: 13.9 min (major) and 19.8

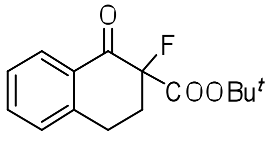
min (minor).



4c: $[\alpha]_D^{29}$ +72.5° [*c* = 1.28, $CHCl_3$ (98% *ee*)]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.8 Hz, 1H), 6.97 (d, *J* = 8.8 Hz, 1H), 6.92 (s, 1H), 3.92 (s, 3H), 3.68 (dd, *J* = 17.6, 10.8 Hz, 1H), 3.33 (dd, *J* = 23.2, 18.0 Hz, 1H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.6 (d, *J* = 18.1 Hz), 166.5 (d, *J* = 27.0 Hz), 154.1 (d, *J* = 4.2 Hz), 127.2, 126.6 (d, *J* = 1.6 Hz), 116.4, 109.7, 109.5, 94.7 (d, *J* = 202.5 Hz), 83.9, 55.8, 38.3 (d, *J* = 23.9 Hz), 27.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ -161.1 (dd, *J* = 19.6, 11.3 Hz); IR (neat) 2974, 1744, 1713, 1593, 1491, 1449, 1369, 1260, 1153, 1092, 1020, 916, 750 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{15}H_{17}FNaO_4$ ($[M+Na]^+$): 303.1003, Found: 303.1001. HPLC analysis: DAICEL Chiralpak AS-H, 2-propanol/hexane = 1:10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: 12.6 min (minor) and 18.7 min (major).

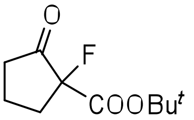


4d: $[\alpha]_D^{29}$ +65.6° [*c* = 0.91, $CHCl_3$ (97% *ee*)]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (s, 1H), 6.89 (s, 1H), 4.01 (s, 3H), 3.93 (s, 3H), 3.64 (dd, *J* = 17.6, 10.4 Hz, 1H), 3.30 (dd, *J* = 22.4, 17.2 Hz, 1H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.1 (d, *J* = 18.9 Hz), 166.7 (d, *J* = 27.0 Hz), 156.9, 150.1, 146.9 (d, *J* = 4.9 Hz), 126.3 (d, *J* = 1.7 Hz), 107.2, 105.4, 94.8 (d, *J* = 202.5 Hz), 83.9, 56.4, 56.1, 38.0 (d, *J* = 23.8 Hz), 27.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ -161.0 (dd, *J* = 22.2, 10.9 Hz); IR (neat) 2978, 1755, 1711, 1589, 1503, 1458, 1369, 1321, 1273, 1155, 777 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{16}H_{19}FNaO_5$ ($[M+Na]^+$): 333.1109, Found: 333.1110. HPLC analysis: DAICEL Chiralpak OJ-H, ethanol/hexane = 1:5, flow rate = 1.0 mL/min, λ = 254 nm, retention time: 21.7 min (minor) and 36.8 min (major).

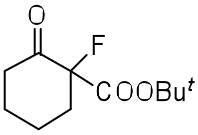


4e: $[\alpha]_D^{28}$ -8.69° [*c* = 1.18, $CHCl_3$ (90% *ee*)]; ^{1}H NMR (400 MHz,

$CDCl_3$) δ 8.07 (d, *J* = 8.0 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 1H), 3.21-3.03 (m, 2H), 2.75-2.63 (m, 1H), 2.55-2.46 (m, 1H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.2 (d, *J* = 18.1 Hz), 166.2 (d, *J* = 26.3 Hz), 142.8, 134.2, 131.0, 128.6, 128.1 (d, *J* = 1.6 Hz), 127.1, 93.0 (d, *J* = 195.1 Hz), 83.9, 31.8 (d, *J* = 22.3 Hz), 27.7, 25.1 (d, *J* = 7.4 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -161.1 (dd, *J* = 19.6, 11.3 Hz); IR (neat) 2980, 1755, 1695, 1602, 1456, 1310, 1227, 1157, 1086, 916, 839, 741 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{15}H_{17}FNaO_3$ ($[M+Na]^+$): 287.1054, Found: 287.1042. HPLC analysis: DAICEL Chiralpak AD-H, 2-propanol/hexane = 1:200, flow rate = 1.0 mL/min, λ = 254 nm, retention time: 18.0 min (minor) and 19.6 min (major).

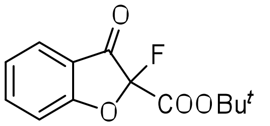


4f: $[\alpha]_D^{28}$ -64.1° [*c* = 0.54, $CHCl_3$ (98% *ee*)]; ^1H NMR (400 MHz, $CDCl_3$) δ 2.57-2.44 (m, 1H), 2.46 (t, *J* = 8.0 Hz, 2H), 2.34-2.21 (m, 1H),.2.15-2.07 (m, 2H), 1.50 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.1 (d, *J* = 17.3 Hz), 166.4 (d, *J* = 27.1 Hz), 94.4 (d, *J* = 200.8 Hz), 84.0, 35.7, 33.8 (d, *J* = 20.6 Hz), 27.9, 18.0 (d, *J* = 4.1 Hz); HRMS (ESI-TOF) calcd for $C_{10}H_{15}FNaO_3$ ($[M+Na]^+$): 225.0897, Found: 225.0893. HPLC analysis: DAICEL Chiralpak AD-H, 2-propanol/hexane = 1:99, flow rate = 0.4 mL/min, λ = 290 nm, retention time: 20.9 min (major) and 25.9 min (minor).



4g: $[\alpha]_D^{27}$ -89.2° [*c* = 0.95, $CHCl_3$ (95% *ee*)]; ^1H NMR (400 MHz, $CDCl_3$) δ 2.74-2.41 (m, 3H), 2.12-1.80 (m, 5H), 1.52 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.2 (d, *J* = 19.7 Hz), 165.8 (d, *J* = 24.7 Hz), 96.3 (d, *J* = 197.5 Hz), 83.9, 39.9, 36.0 (d, *J* = 22.2 Hz), 27.9, 26.5, 21.2 (d, *J* = 6.6 Hz); HRMS (ESI-TOF) calcd for $C_{11}H_{17}FNaO_3$ ($[M+Na]^+$): 239.1054, Found: 239.1061. HPLC analysis: DAICEL Chiralpak AD-H, 2-propanol/hexane = 1:200, flow rate = 0.4

mL/min, λ = 290 nm, retention time: 11.7 min (major) and 14.8 min (minor).



4h: $[\alpha]_D^{29}$ -65.7° [*c* = 0.76, $CHCl_3$ (90% *ee*)]; ^1H NMR (400 MHz, $CDCl_3$) δ 7.74-7.70 (m, 2H), 7.25-7.20 (m, 2H), 1.50 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.3 (d, *J* = 19.1 Hz), 171.3 (d, *J* = 1.6 Hz), 161.1 (d, *J* = 36.1 Hz), 139.4, 125.7, 124.2, 117.7, 113.5, 103.2 (d, *J* = 253.3 Hz), 85.6, 27.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -125.4 (s); IR (neat) 2984, 1769, 1744, 1614, 1462, 1371, 1302, 1165, 1148, 1098, 908, 756 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{13}H_{13}FNaO_4$ ($[M+Na]^+$): 275.0690, Found: 275.0689. HPLC analysis: DAICEL Chiralpak AD-H, 2-propanol/hexane = 1:200, flow rate = 1.0 mL/min, λ = 254 nm, retention time: 7.9 min (major) and 8.8 min (minor).

Lowing the catalyst loading (0.2 mol%).

The solution of chiral ammonium salt (*S*)-**2d** [100μl, (*S*)-**2d** (1.4 mg, 0.002 mmol) in $MeOH/CH_2Cl_2$ (1:3, 1 mL), 0.0002 mmol] was added to a reaction vessel and the solvent was removed at 50 °C under vacuo for 2 h. β-Keto ester **3a** (23.2 mg, 0.1 mmol) and diethyl ether (4.0 mL) were added in the stated order. After the reaction system was cooled to –20 °C, aqueous K_2CO_3 (0.5 M in water, 1.0 mL) was added dropwise. After the reaction mixture was stirred for 10 min at –20 °C, *N*-fluorobis(benzenesulfonimide) (NFSI) (36 mg, 0.11 mmol, 1.1 equiv) was added in a single portion. The reaction mixture was then stirred vigorously at the same temperature for 1.5 h, quenched with saturated NH_4Cl solution (10 mL), extracted with diethyl ether（10 mL), dried over Na_2SO_4 and concentrated. Purification of the residue by column chromatography on silica gel with hexane-ethyl acetate as eluant afforded the fluorination product **4a** (25.0 mg, 99% yield, 95% *ee*).

References:

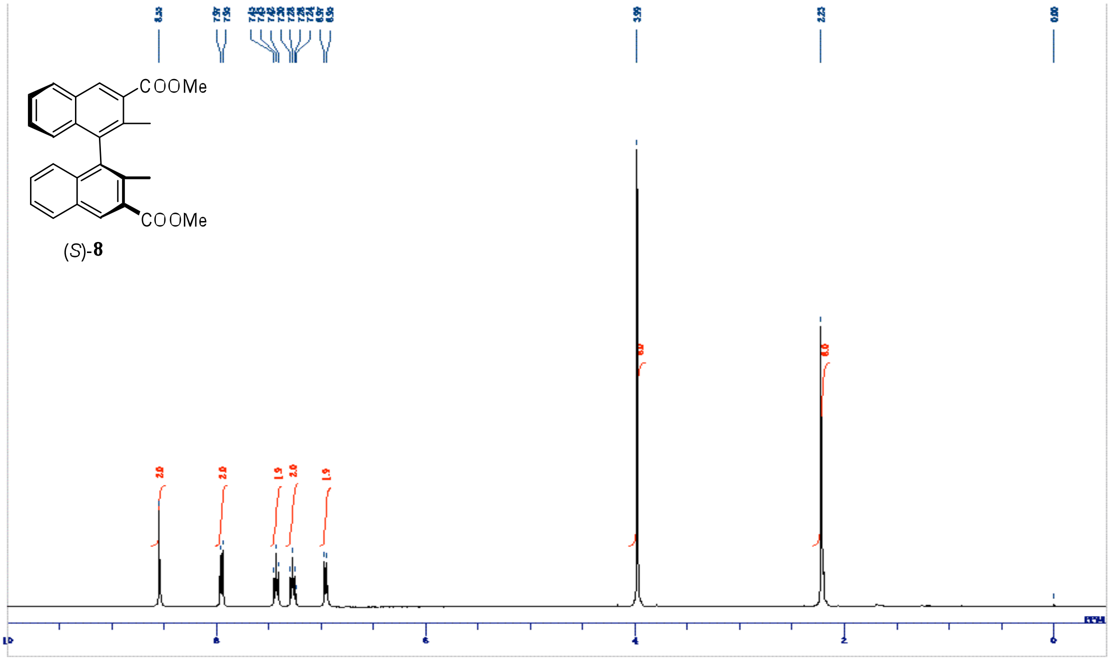
(1) T. Ooi, M. Kameda and K. Maruoka, *J. Am. Chem. Soc.*, 2003, **125**, 5139.

(2) F. Wu, H. Li, R. Hong and L. Deng, *Angew. Chem., Int. Ed.*, 2006, **45**, 947.

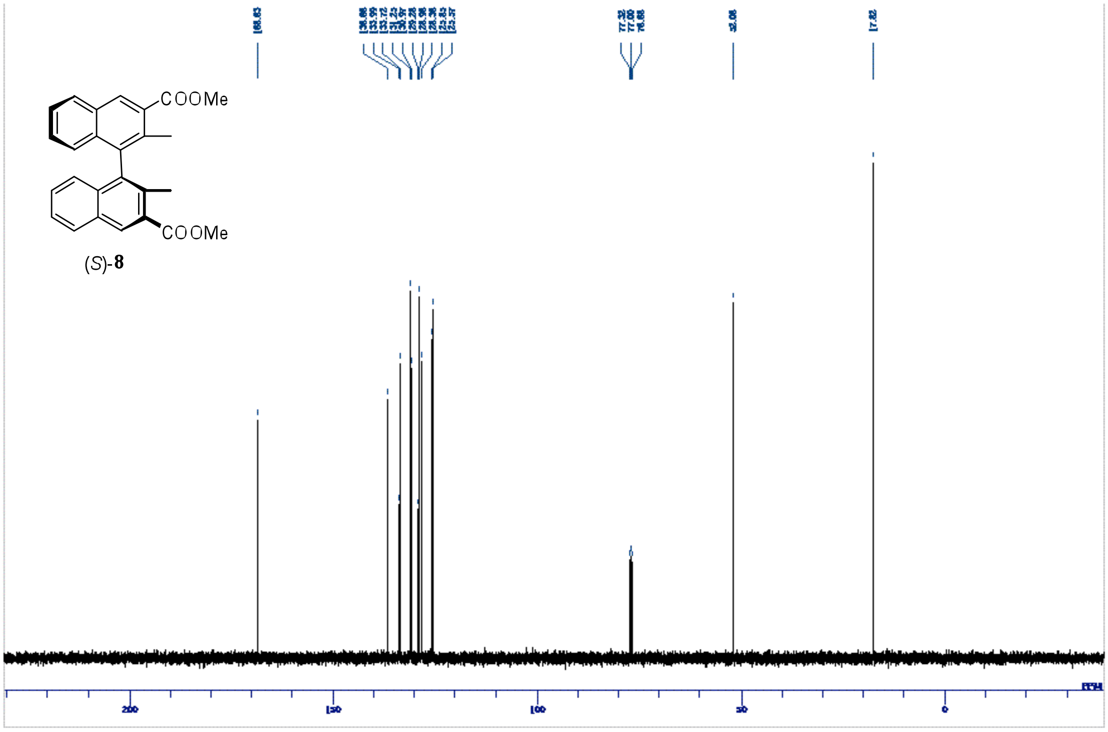
(3) Y. Hamashima, K. Yagi, H. Takano, L. Tamás and M. Sodeoka, *J. Am. Chem. Soc.*, 2002, **124**, 14530.

Copies of ^{1}H and ^{13}C NMR Spectra of Catalysts and Fluorination Products:

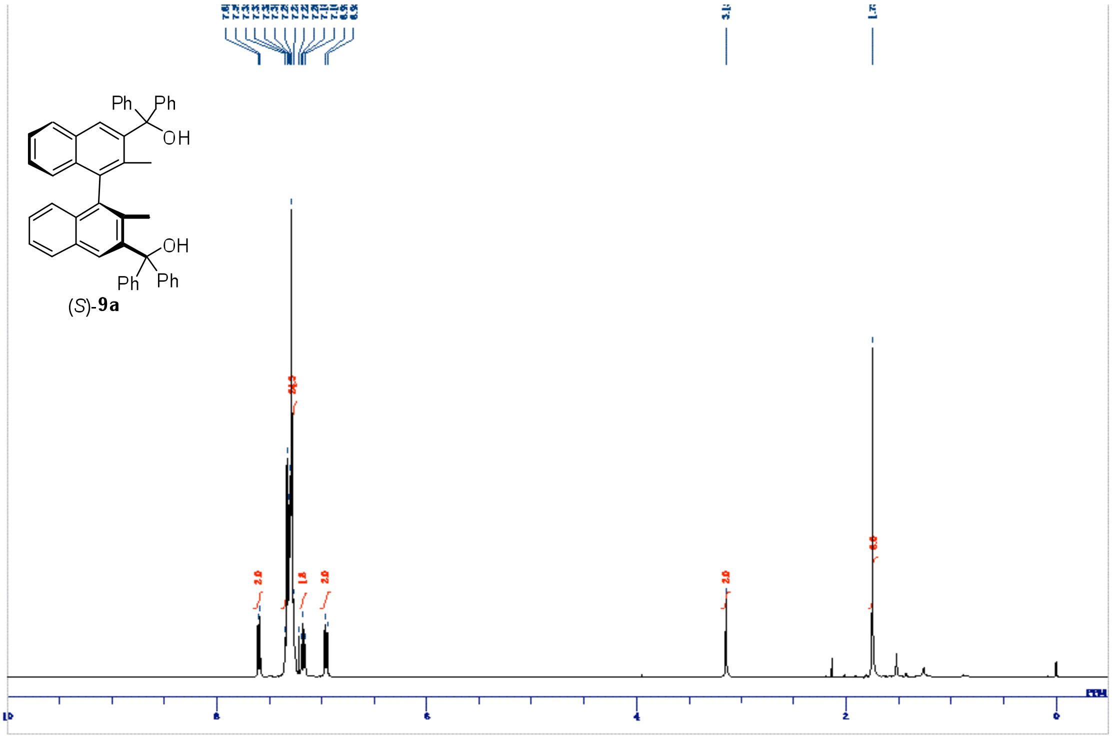
^{1}H NMR: Compound (*S*)-**8**



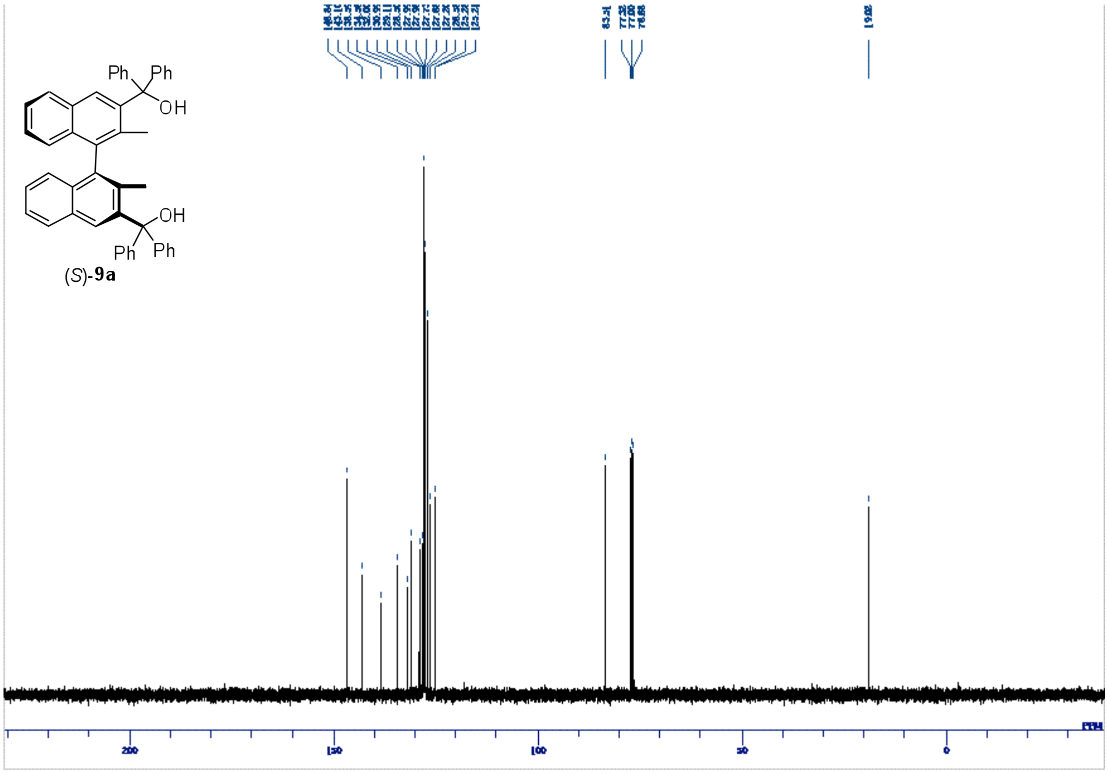
^{13}C NMR: Compound (*S*)-**8**



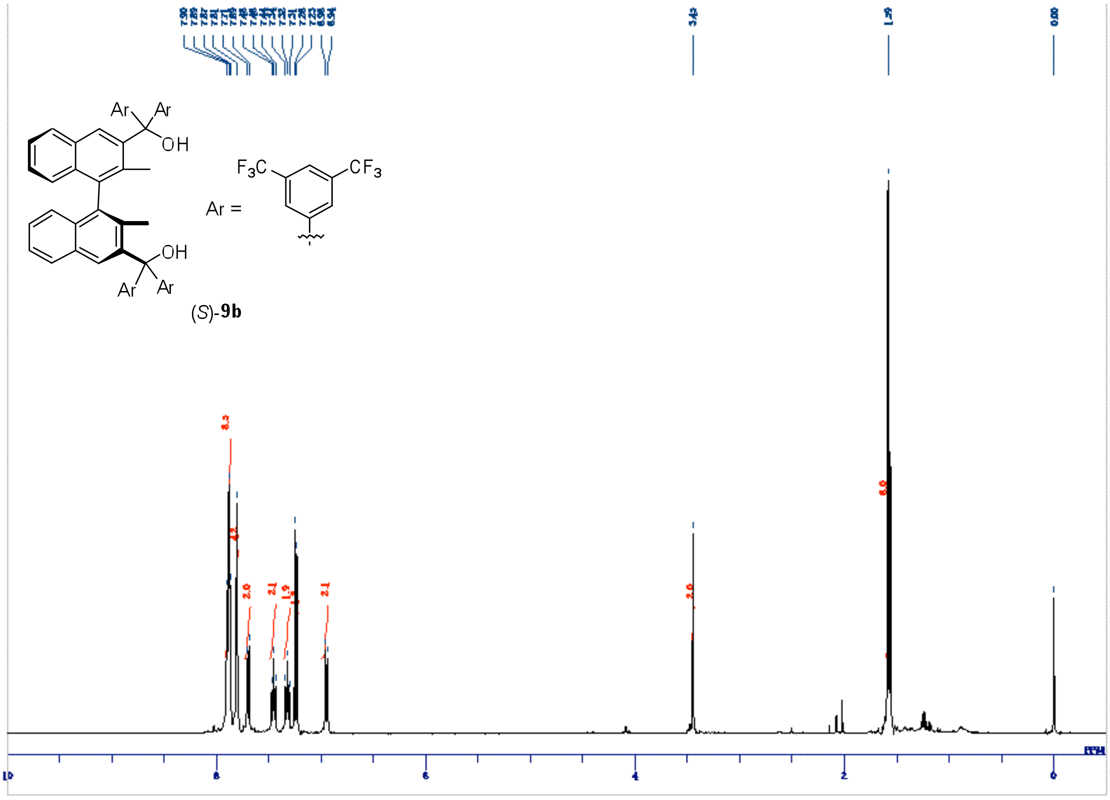
^{1}H NMR: Compound (*S*)-**9a**



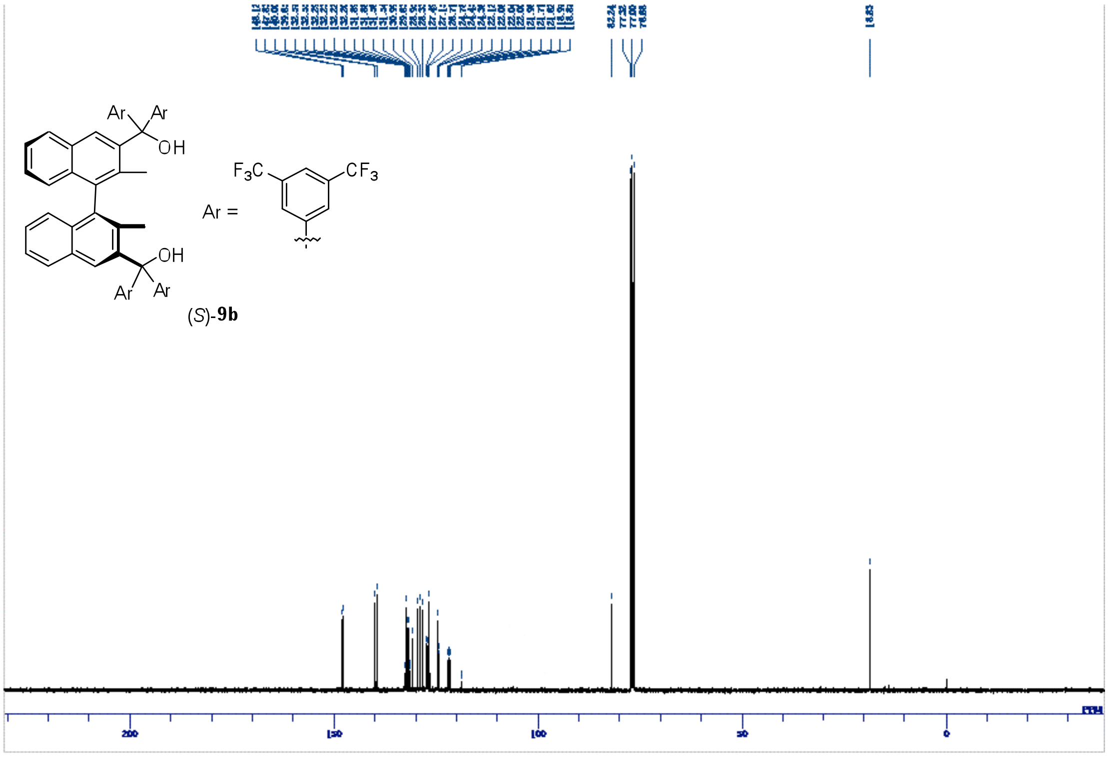
^{13}C NMR: Compound (*S*)-**9a**



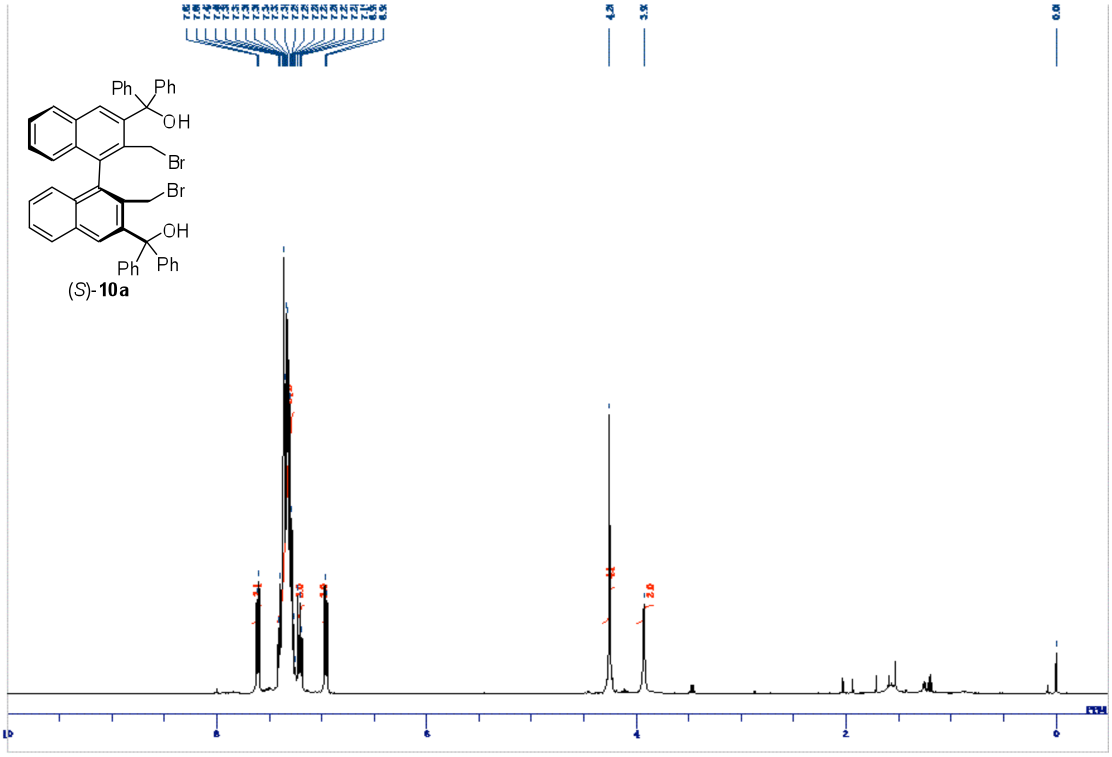
^{1}H NMR: Compound (*S*)-**9b**



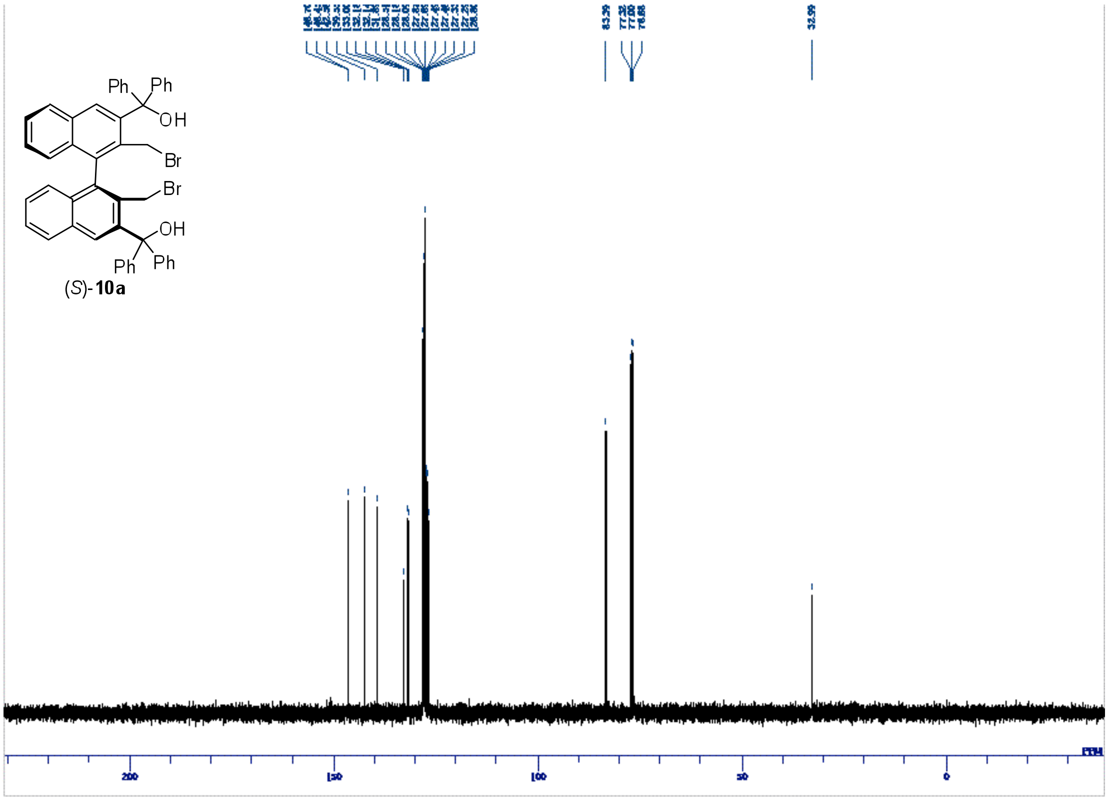
^{13}C NMR: Compound (*S*)-**9b**



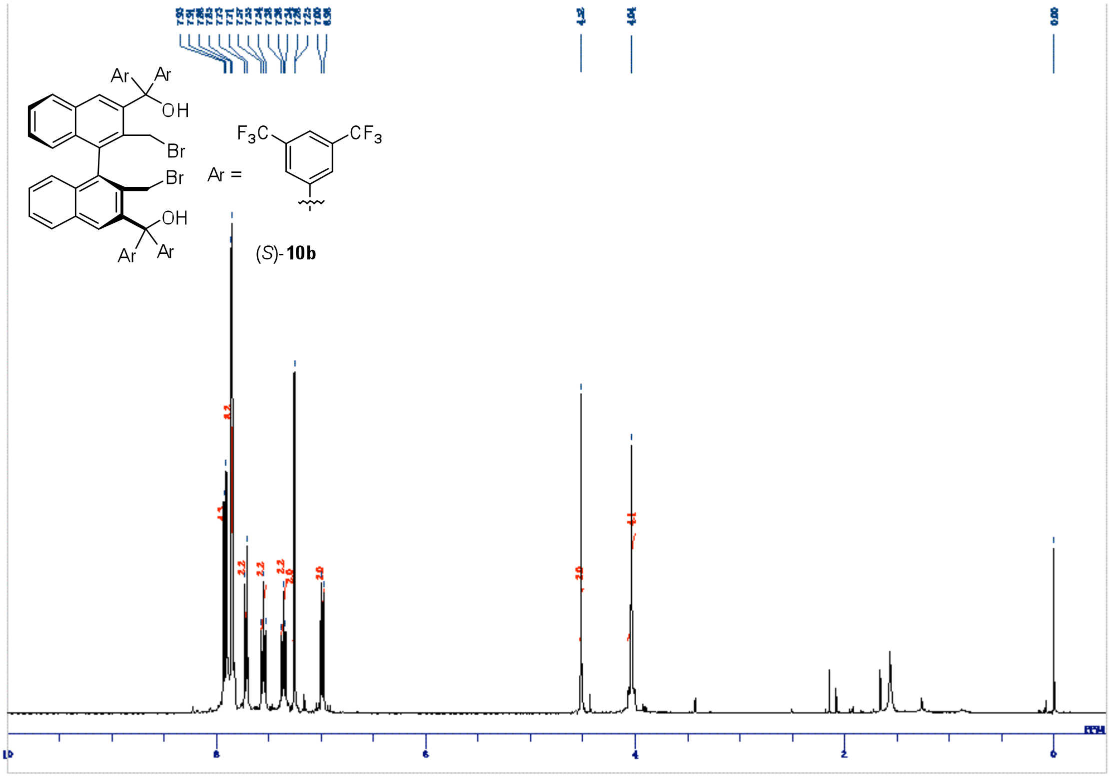
^{1}H NMR: Compound (*S*)-**10a**



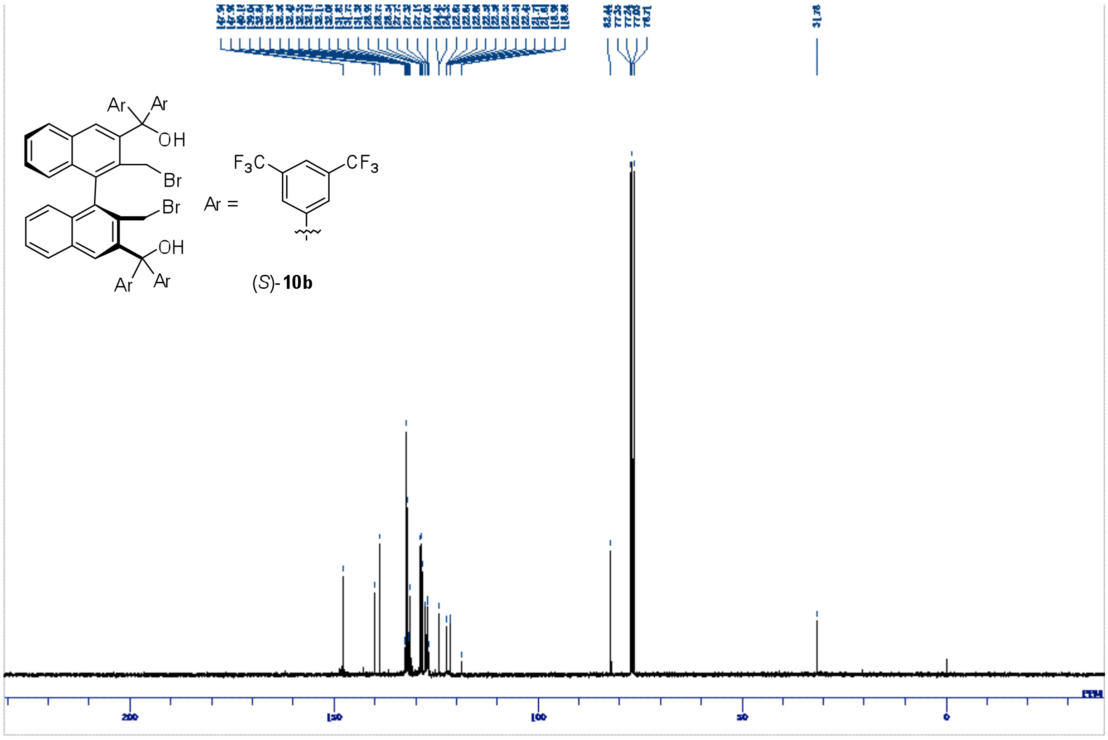
^{13}C NMR: Compound (*S*)-**10a**



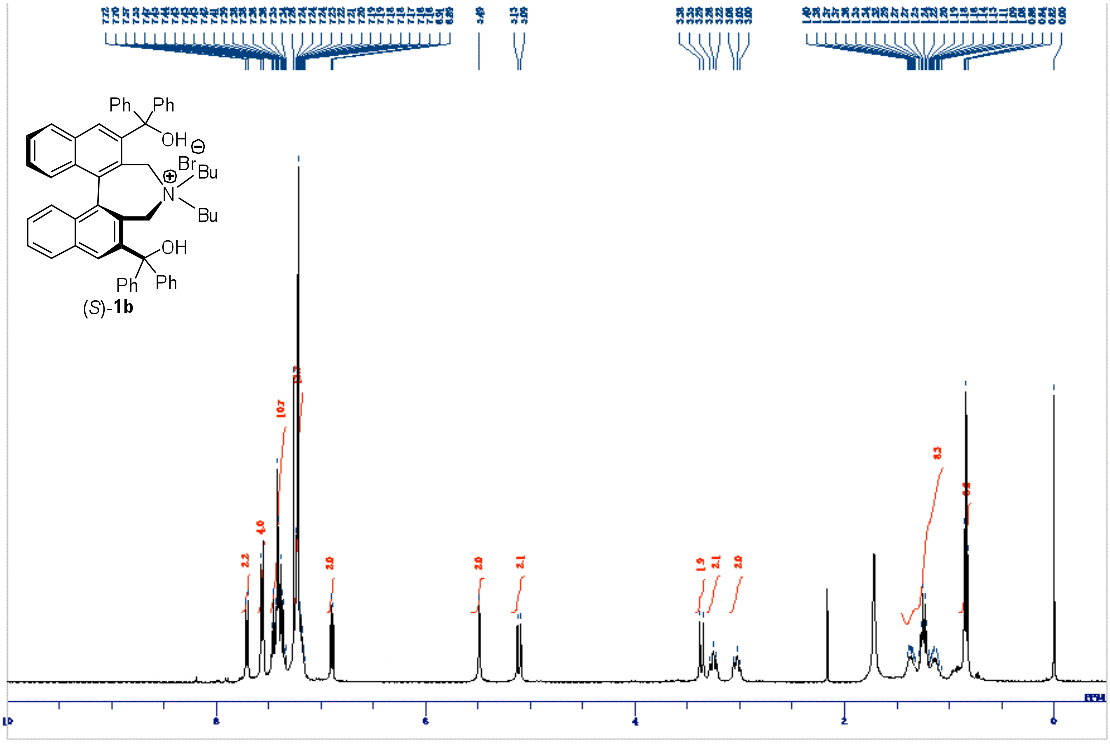
^{1}H NMR: Compound (*S*)-**10b**



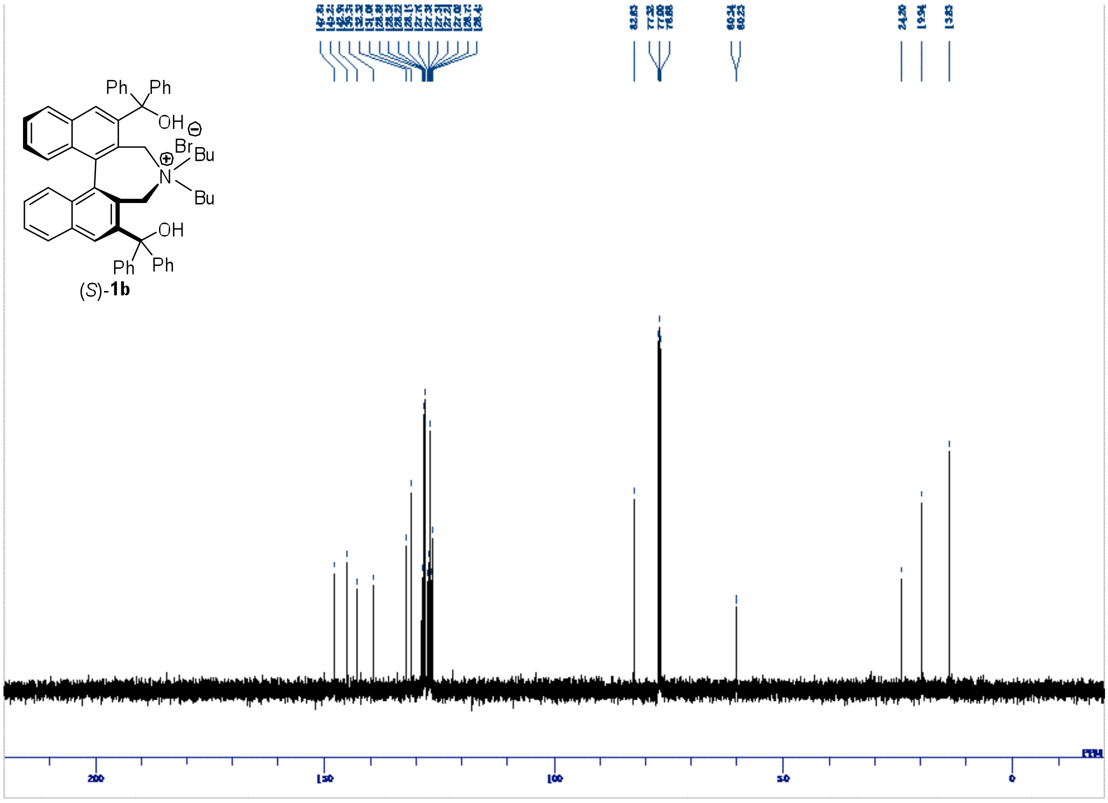
^{13}C NMR: Compound (*S*)-**10b**



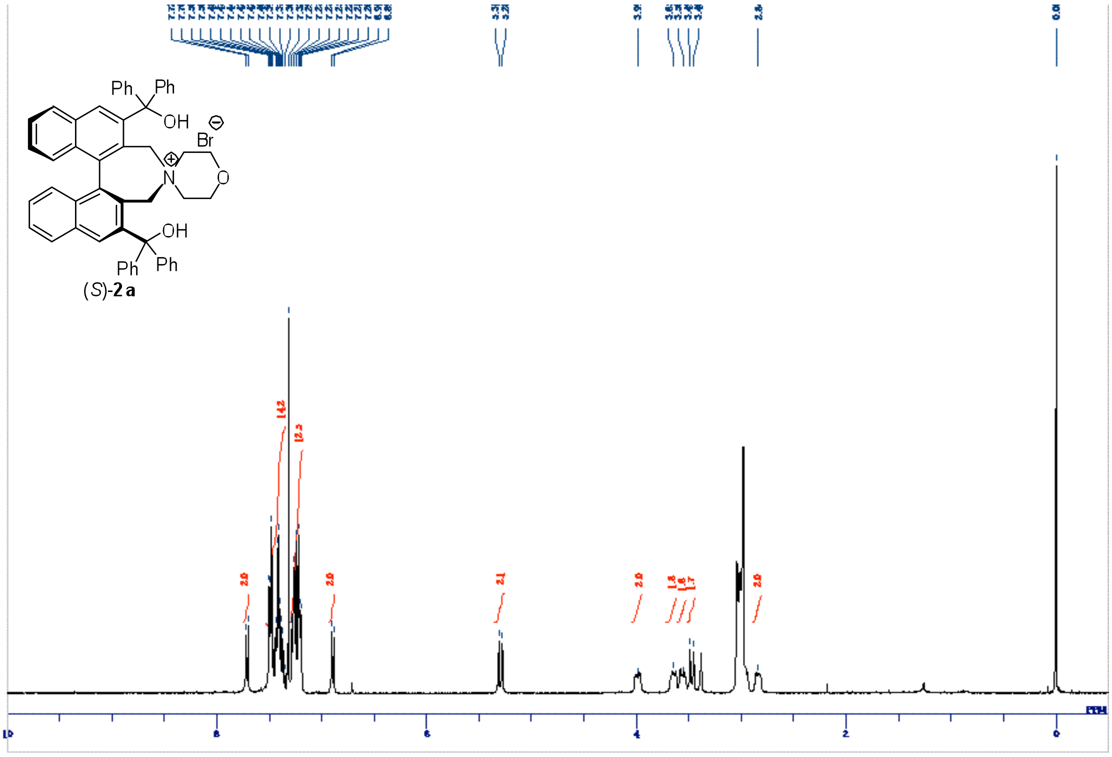
^{1}H NMR: Chiral Ammonium Salts (*S*)-**1b**



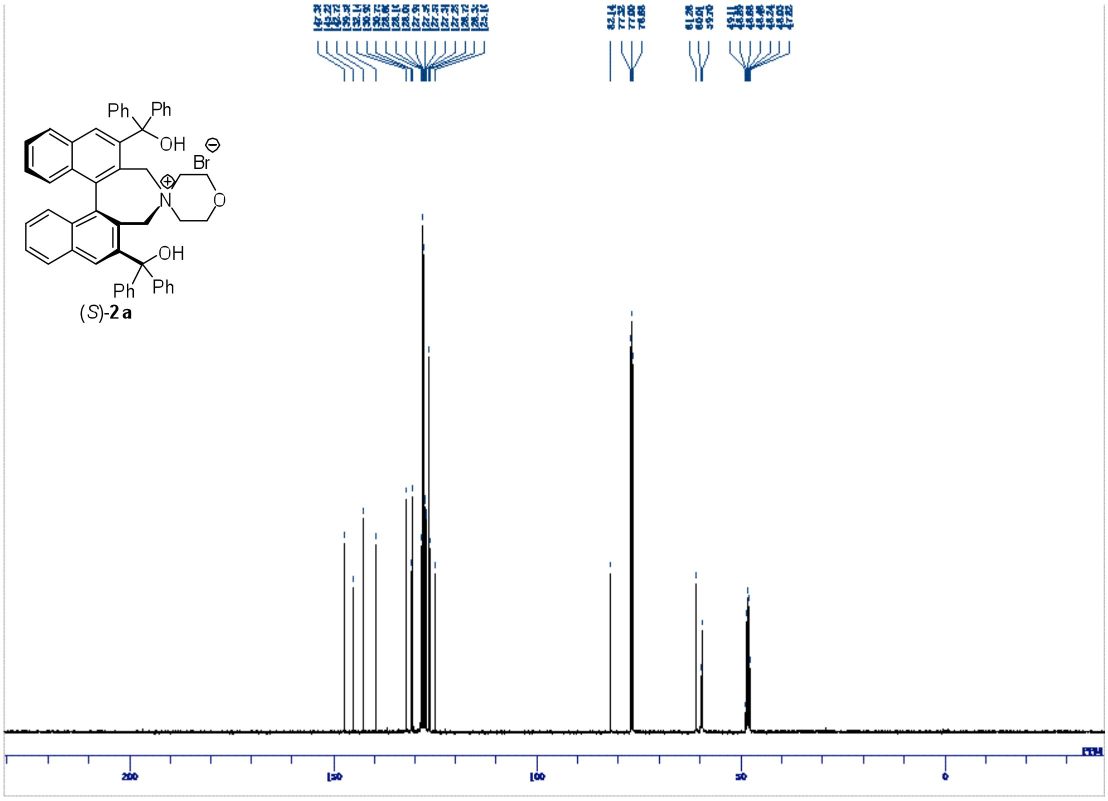
^{13}C NMR: Chiral Ammonium Salts (*S*)-**1b**



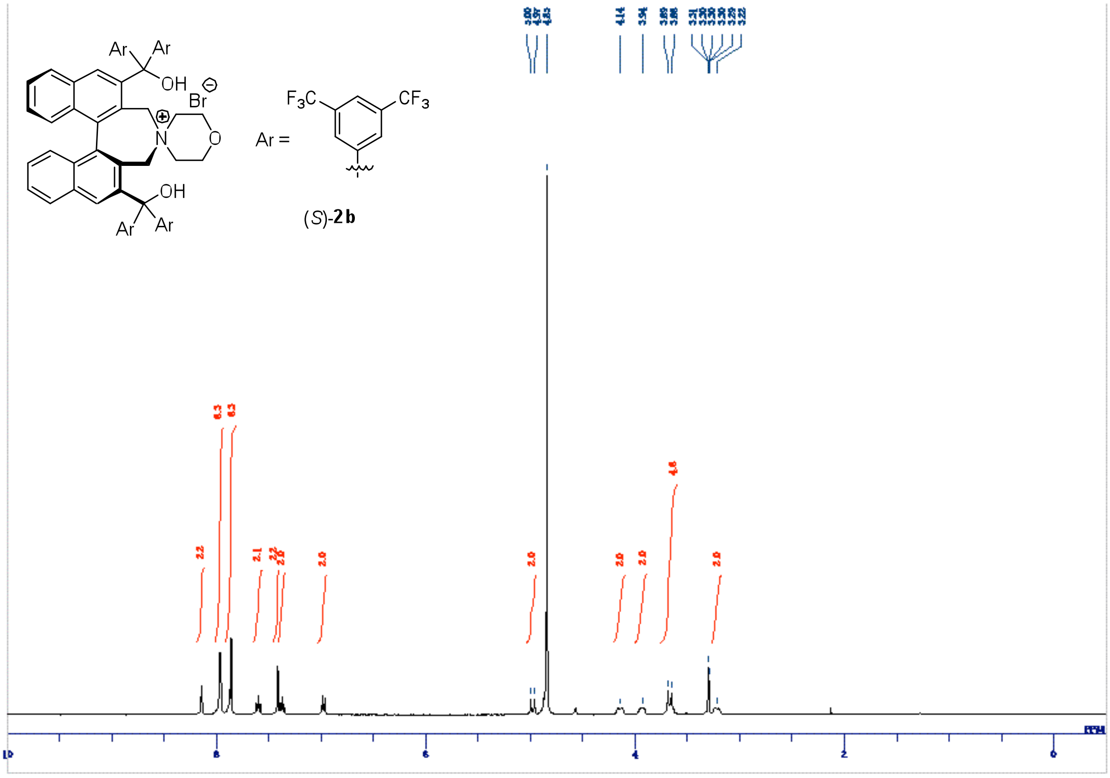
^{1}H NMR: Chiral Ammonium Salts (*S*)-**2a**



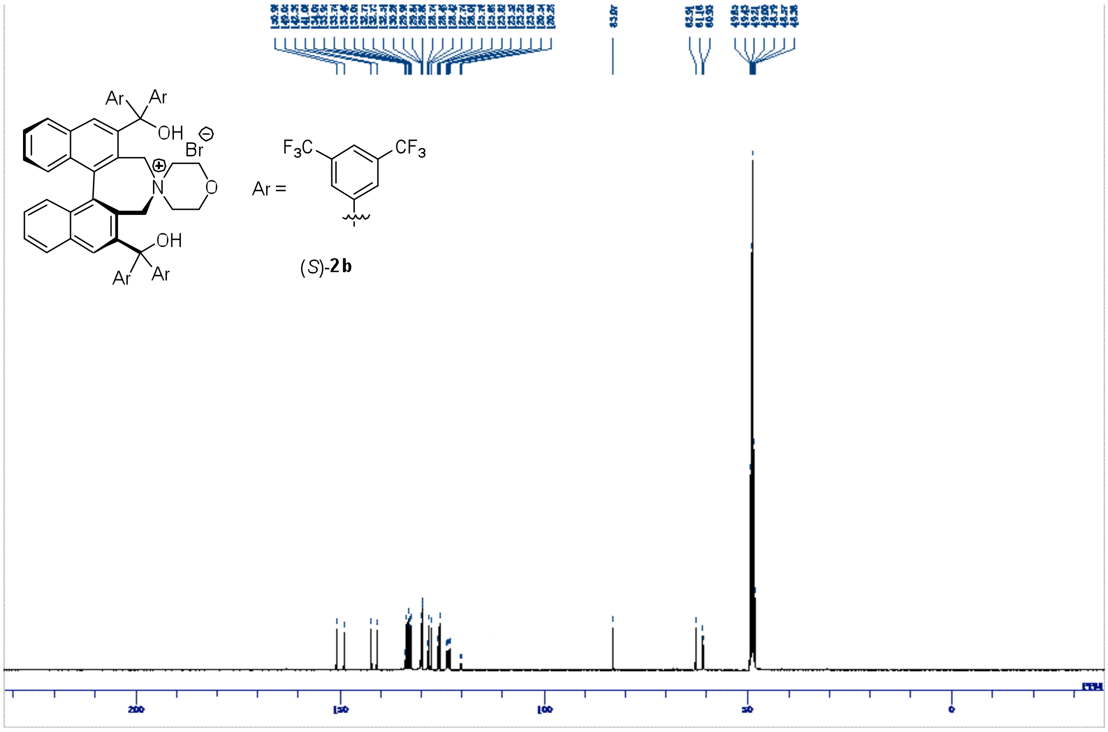
^{13}C NMR: Chiral Ammonium Salts (*S*)-**2a**



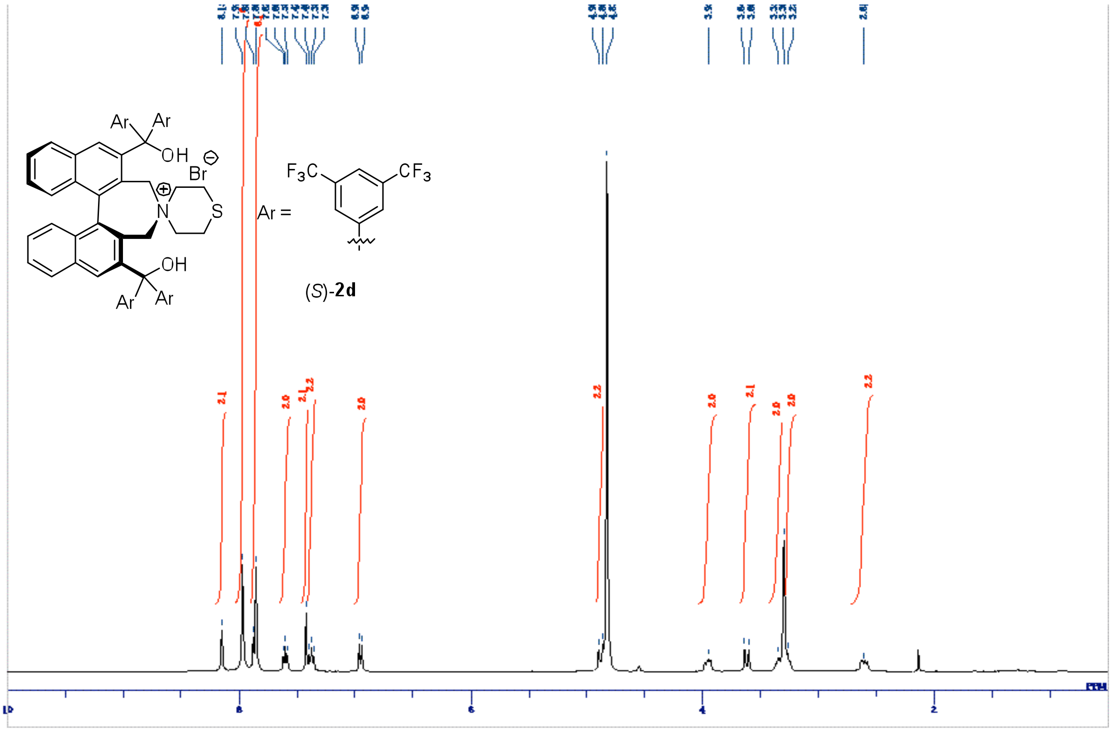
^{1}H NMR: Chiral Ammonium Salts (*S*)-**2b**



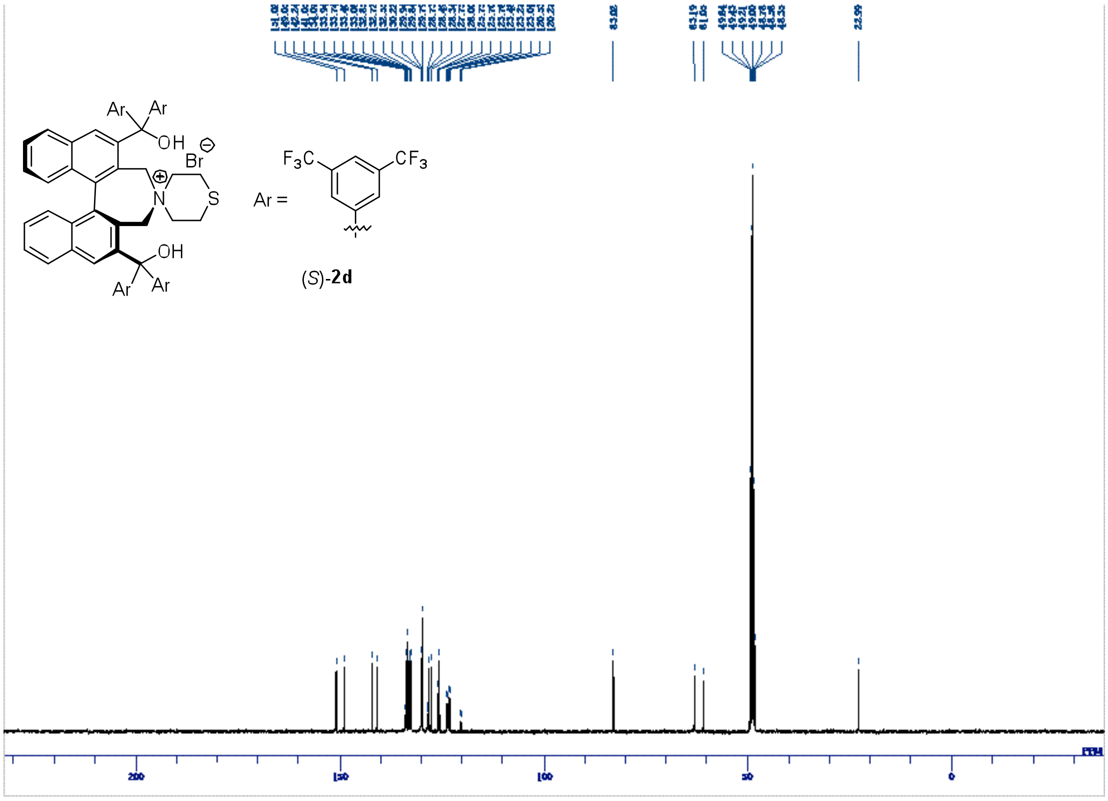
^{13}C NMR: Chiral Ammonium Salts (*S*)-**2b**



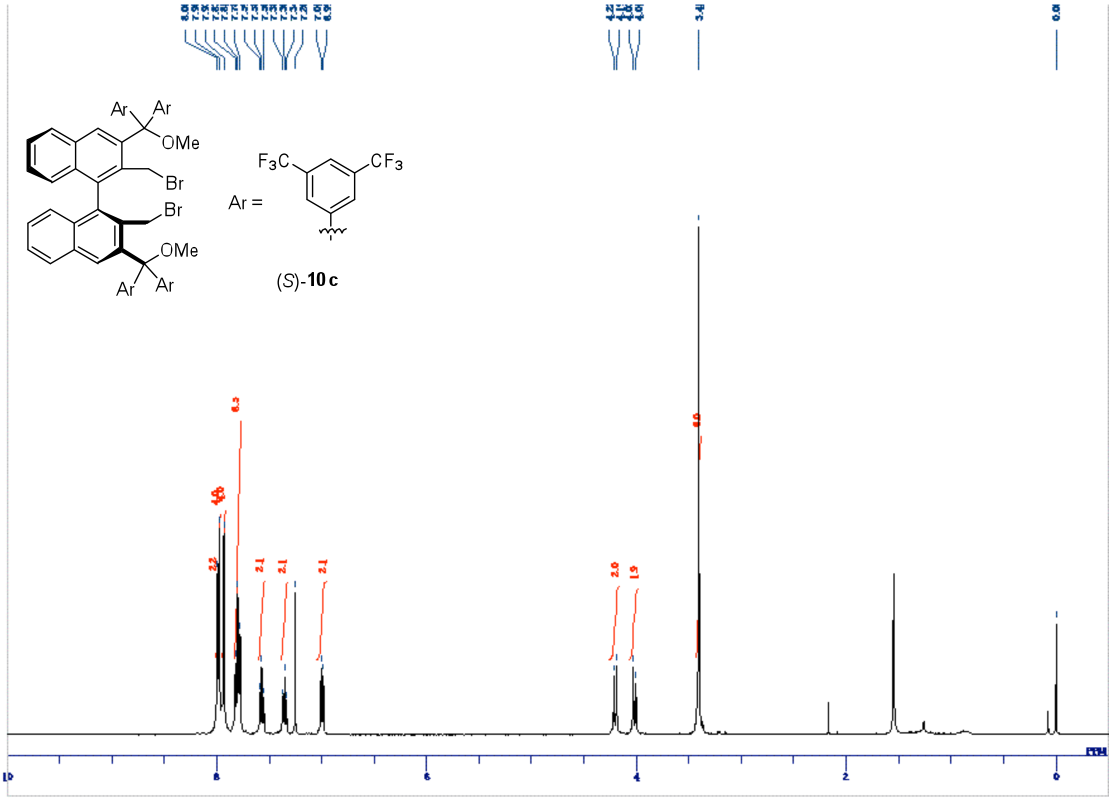
^{1}H NMR: Chiral Ammonium Salts (*S*)-**2d**



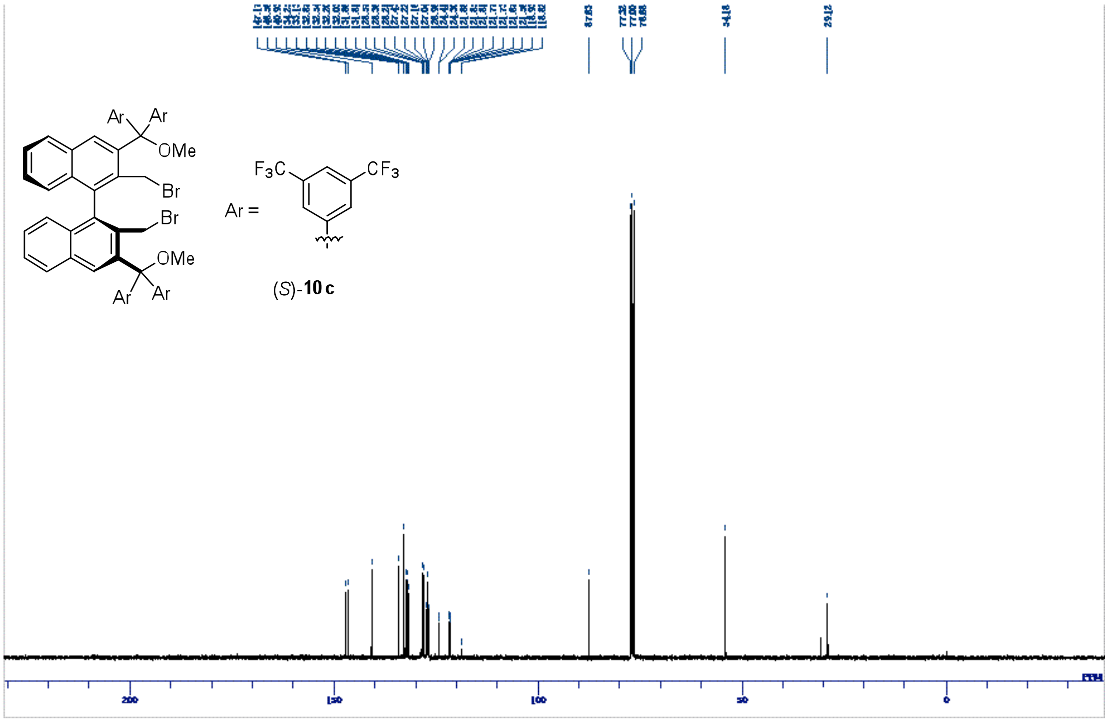
^{13}C NMR: Chiral Ammonium Salts (*S*)-**2d**



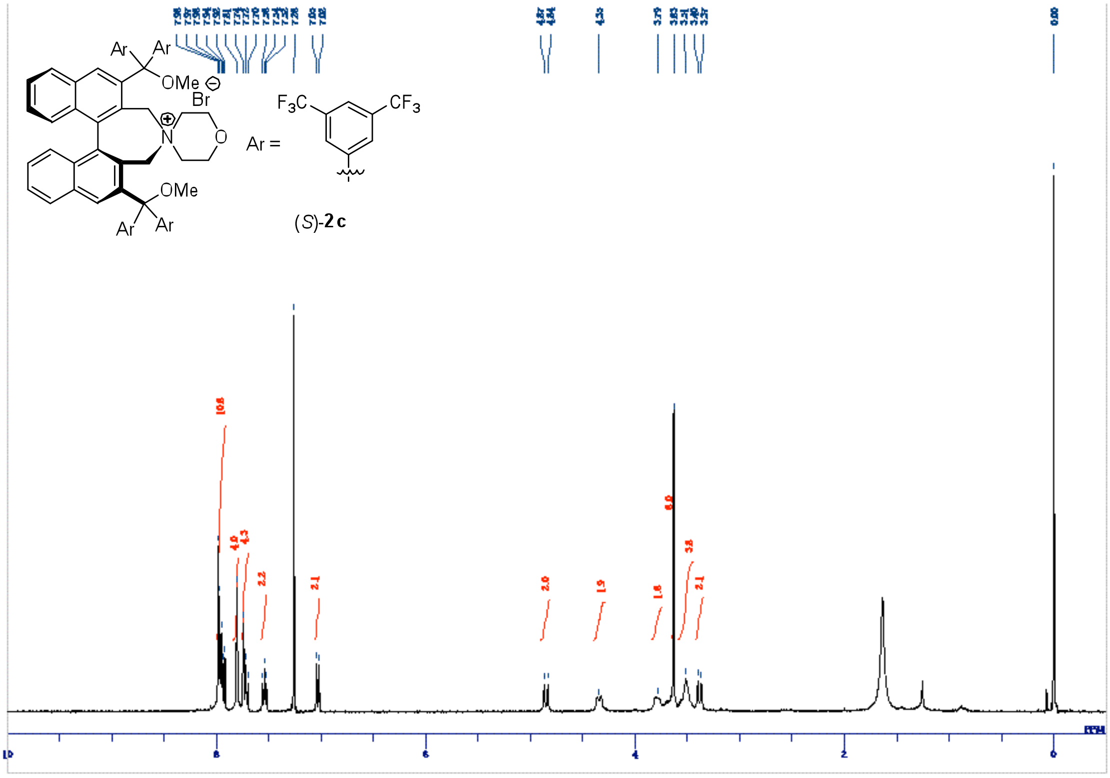
^{1}H NMR: Chiral Ammonium Salts (*S*)-**10c**



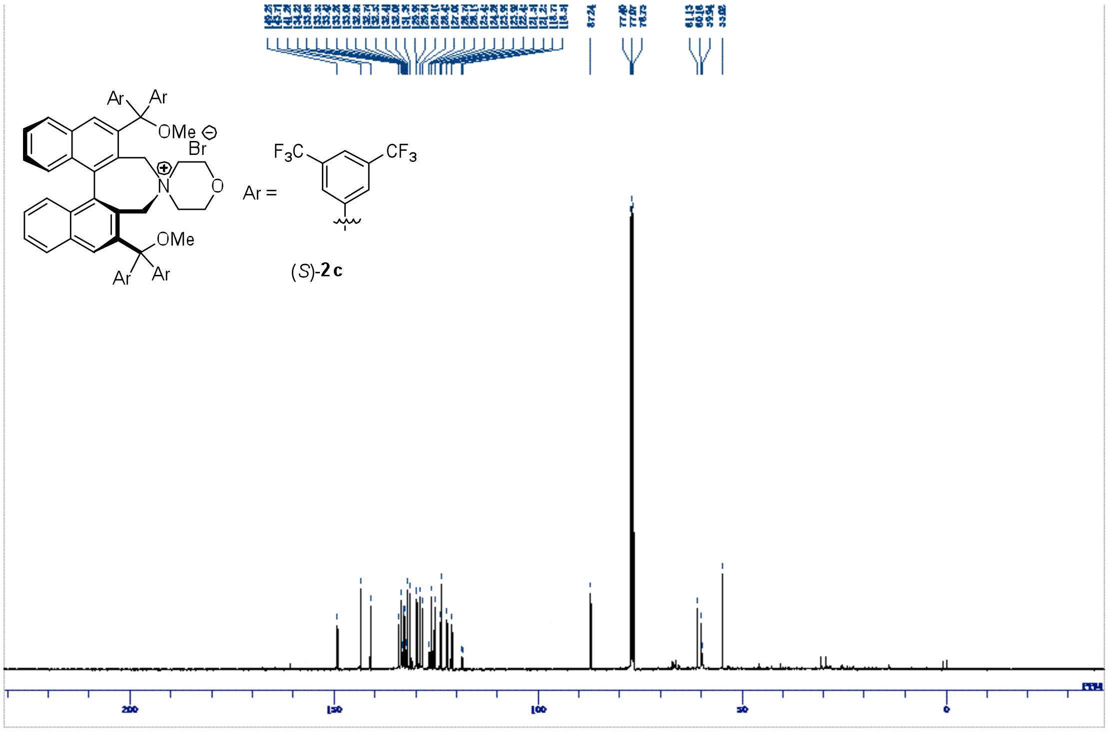
^{13}C NMR: Chiral Ammonium Salts (*S*)-**10c**



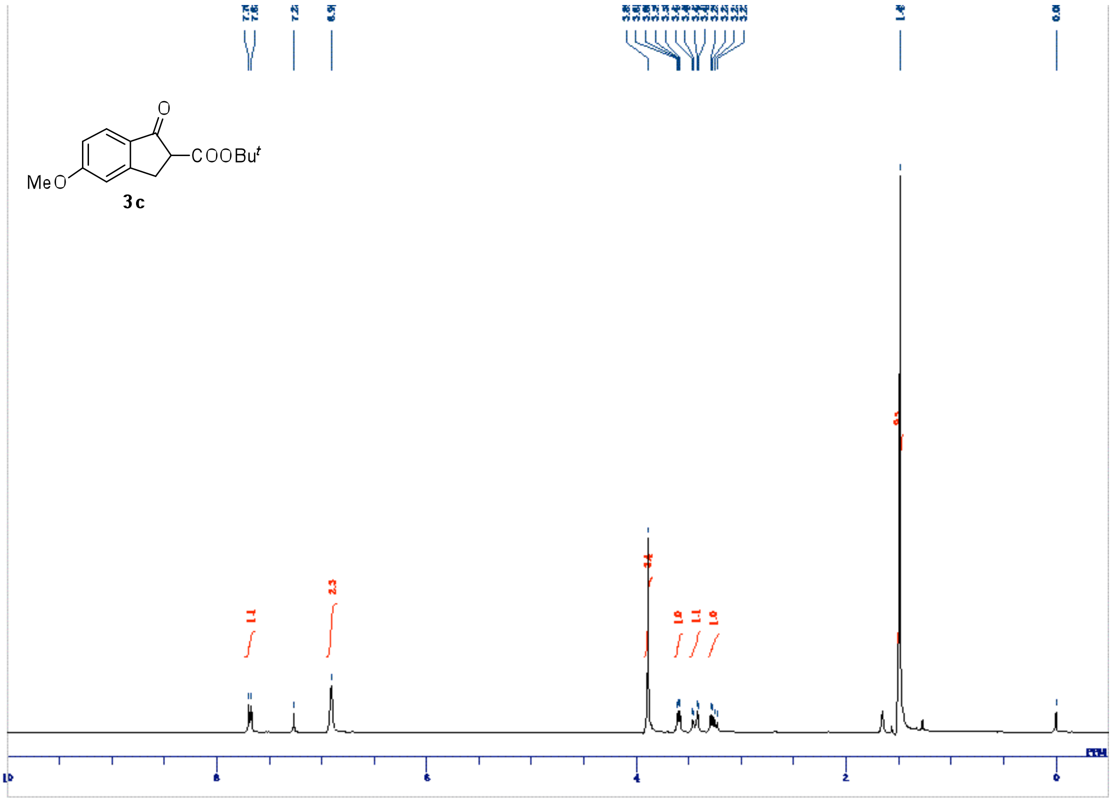
^{1}H NMR: Chiral Ammonium Salts (*S*)-**2c**



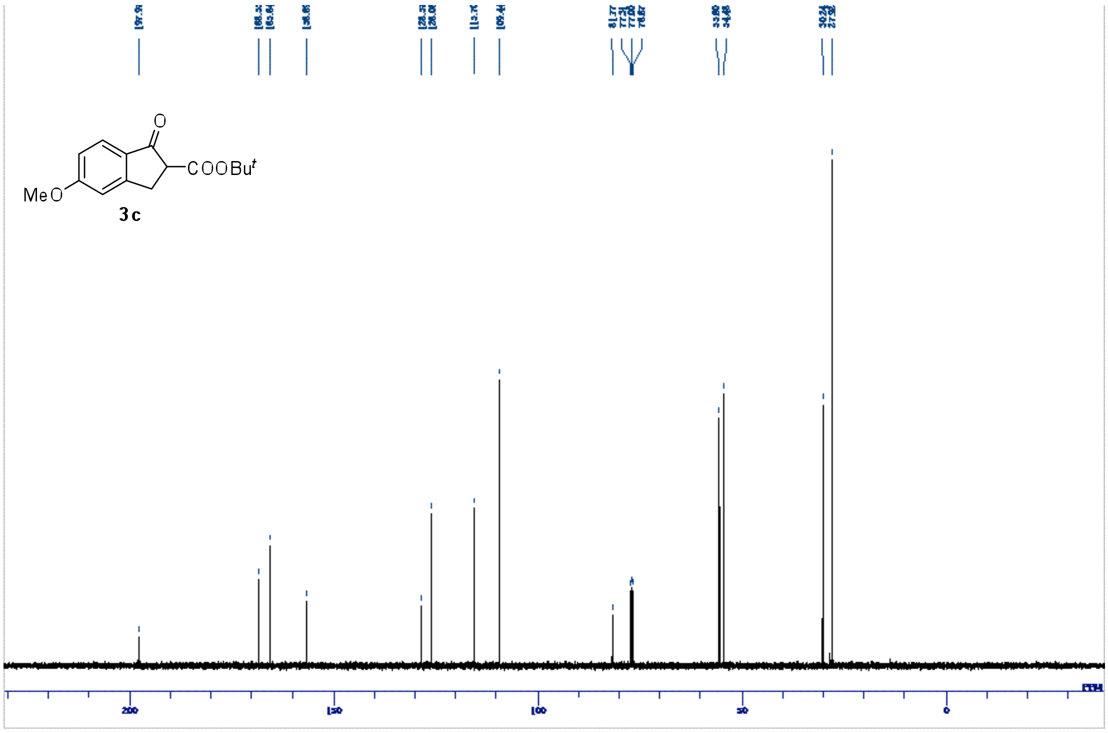
^{13}C NMR: Chiral Ammonium Salts (*S*)-**2c**



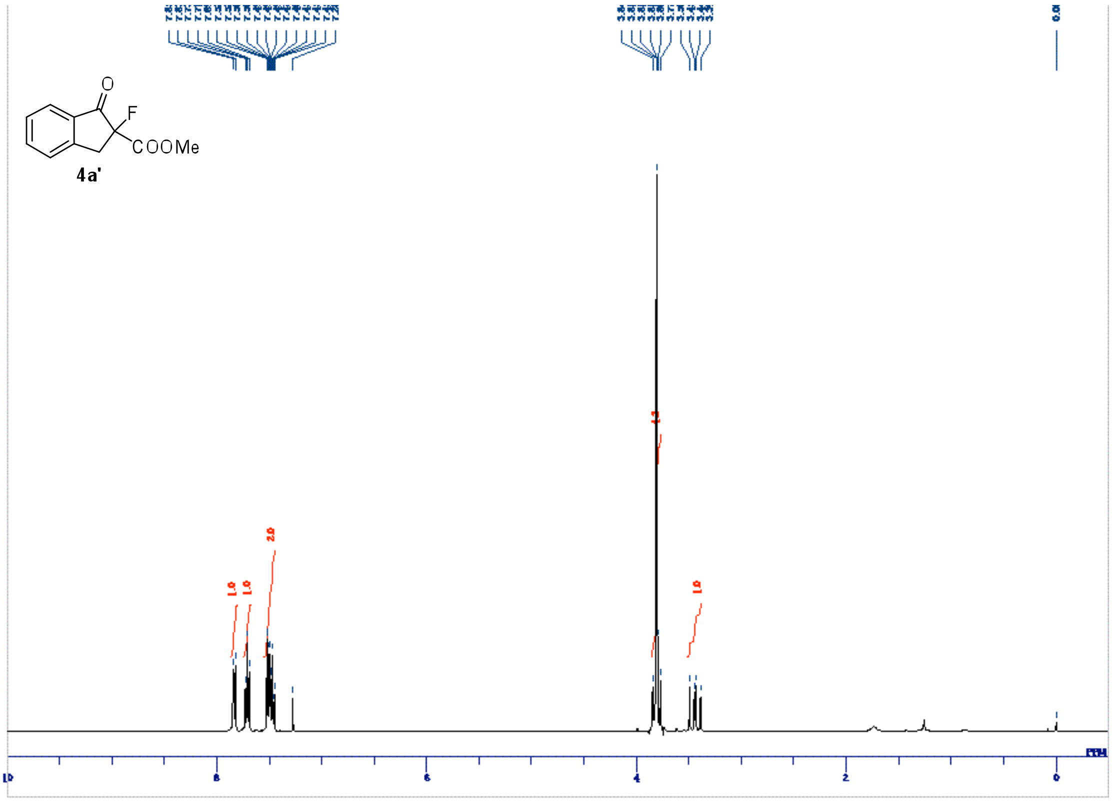
^{1}H NMR: Substrate **3c**



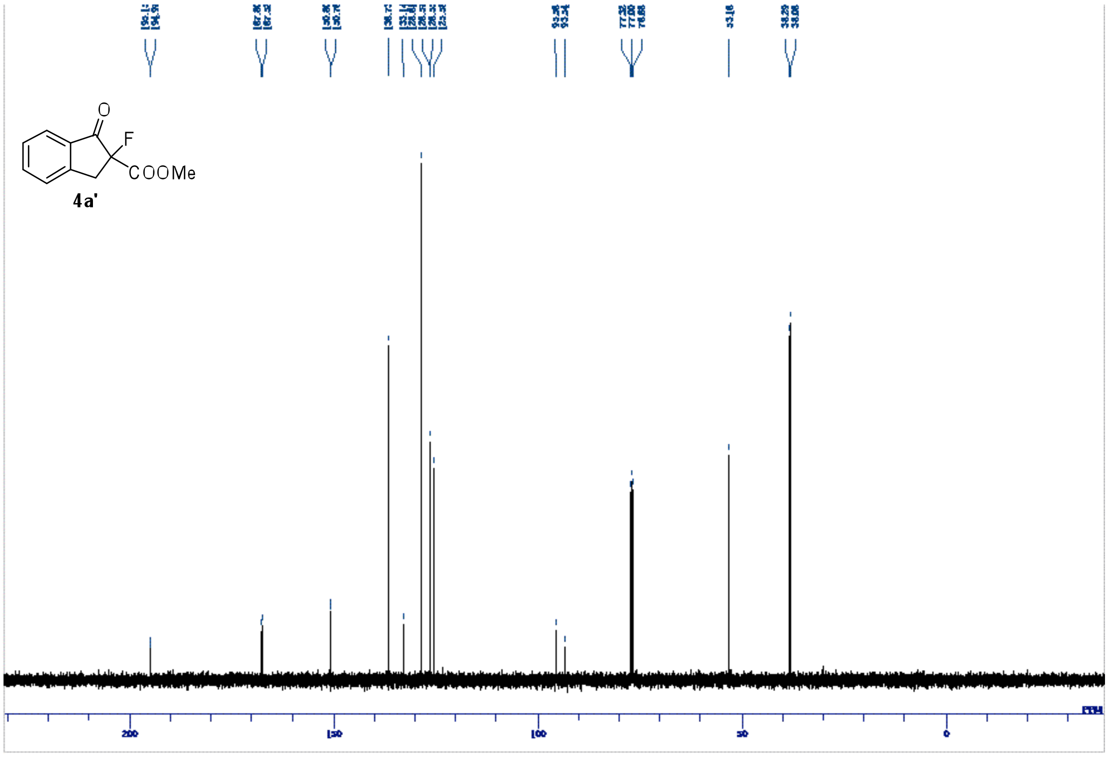
^{13}C NMR: Substrate **3c**



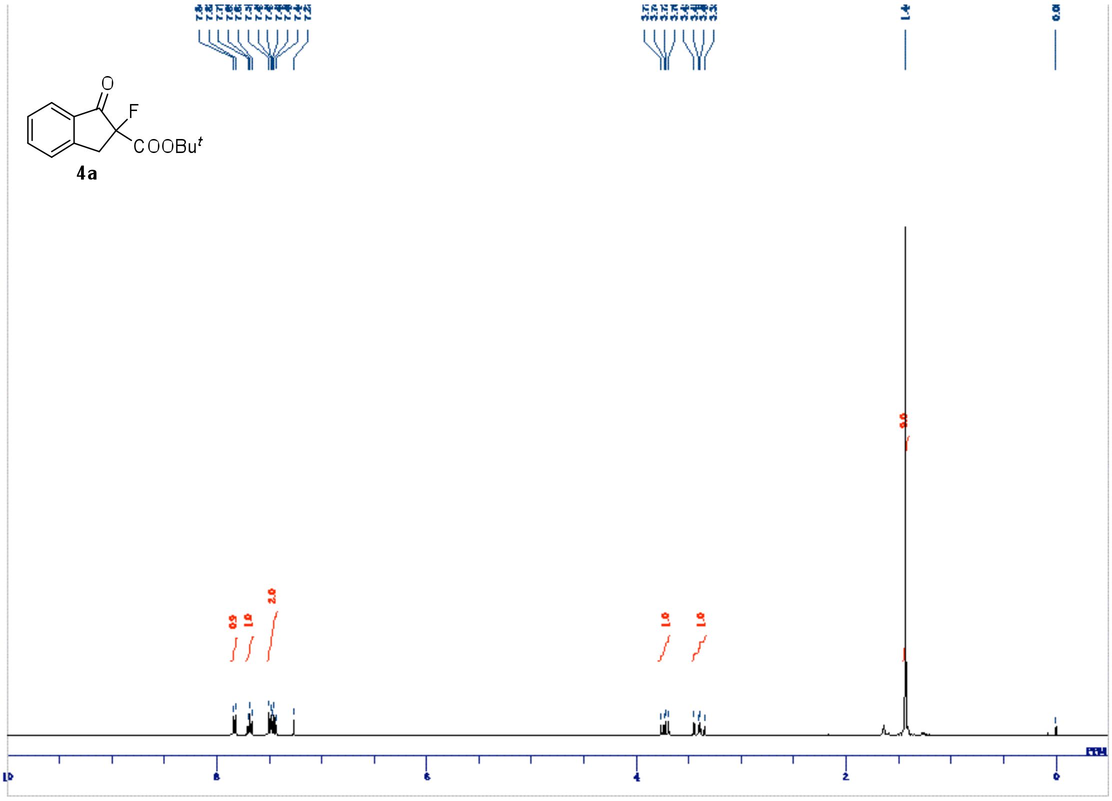
^{1}H NMR: Product **4a’**



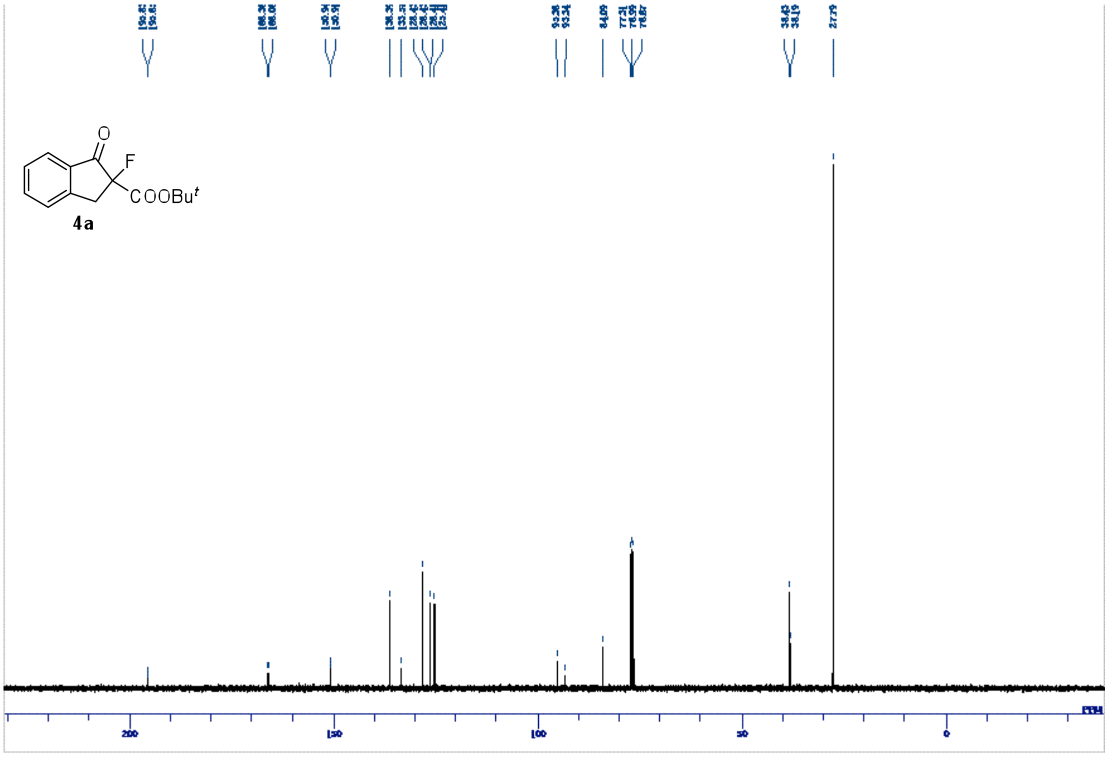
^{13}C NMR: Product **4a’**



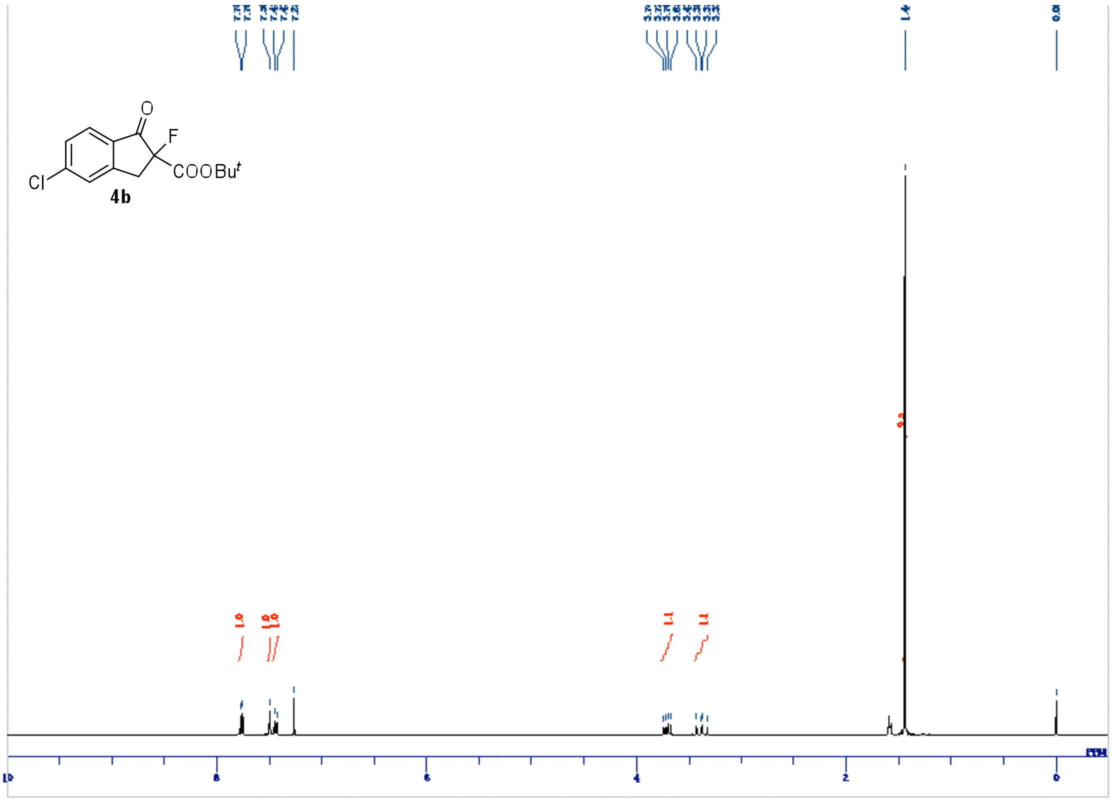
^{1}H NMR: Product **4a**



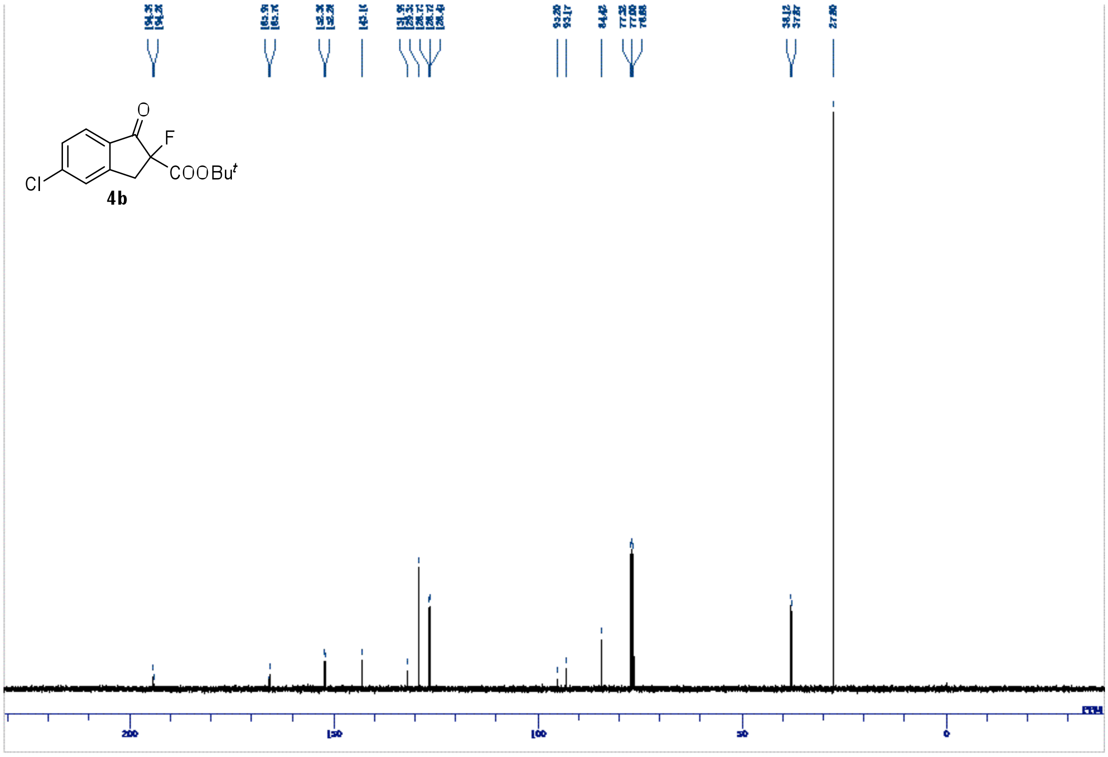
^{13}C NMR: Product **4a**



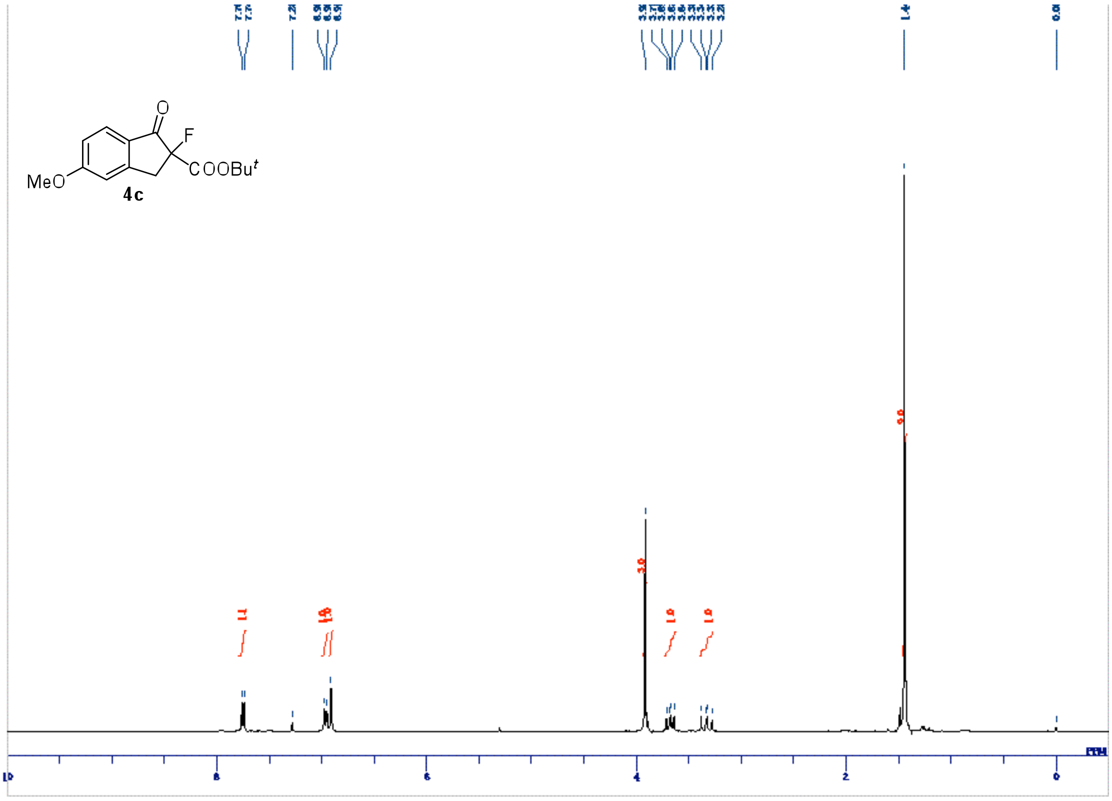
^{1}H NMR: Product **4b**



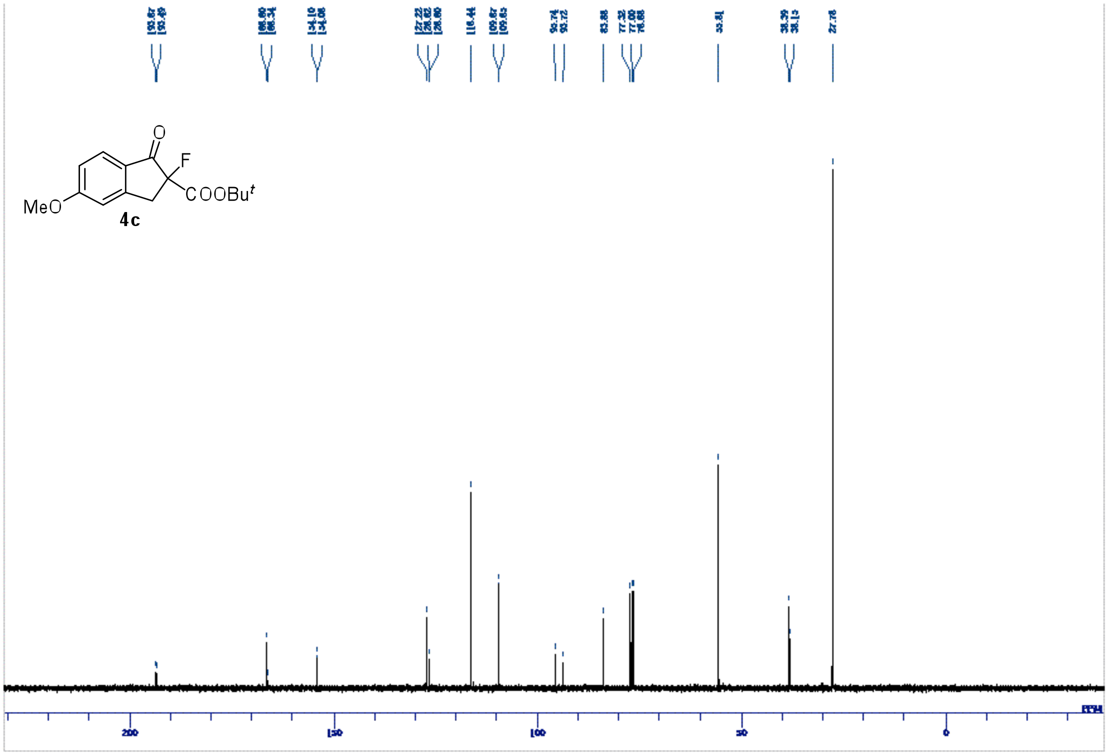
^{13}C NMR: Product **4b**



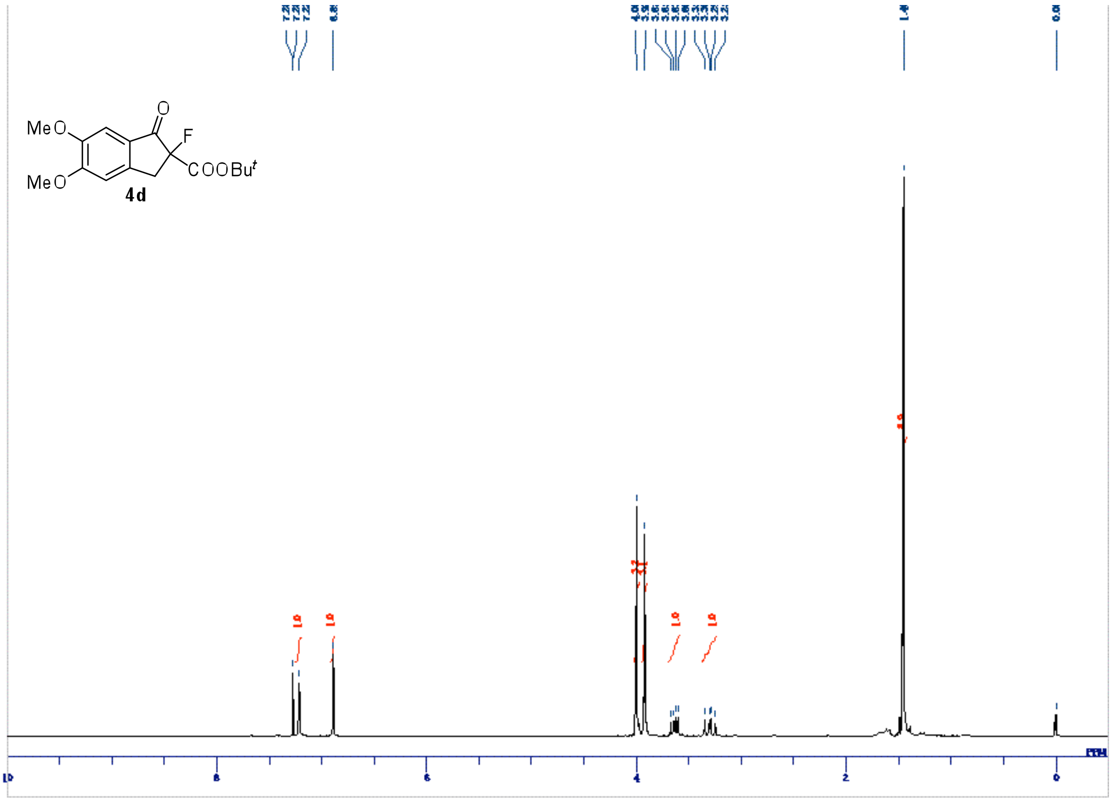
^{1}H NMR: Product **4c**



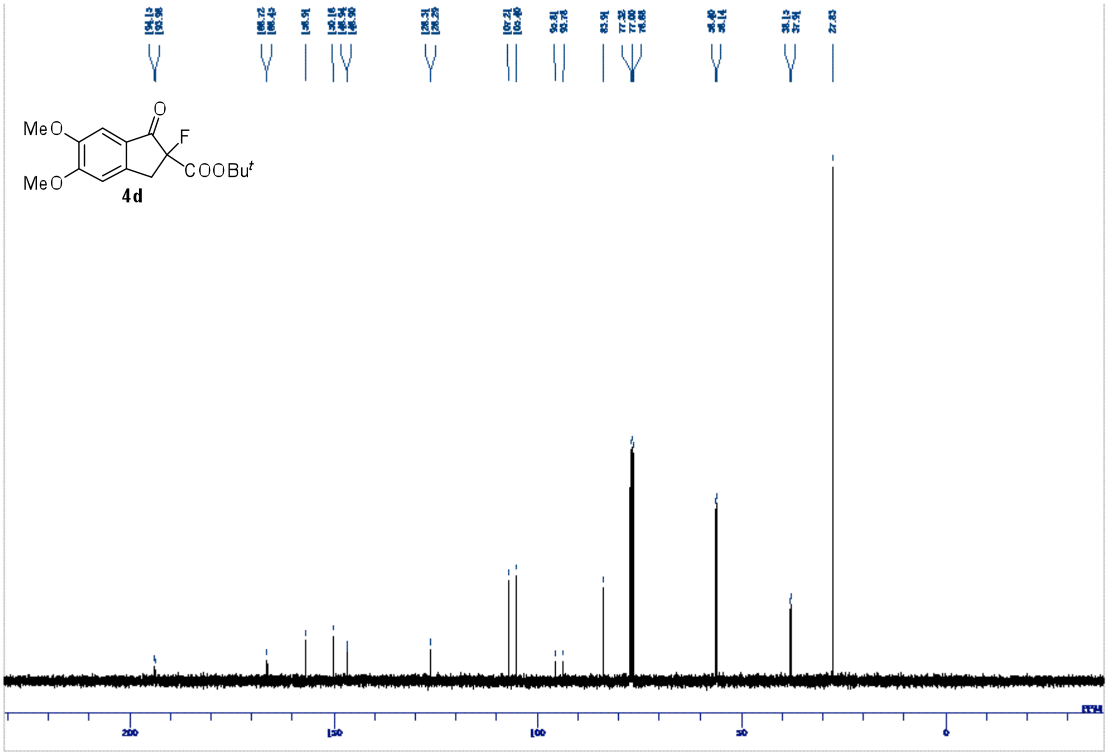
^{13}C NMR: Product **4c**



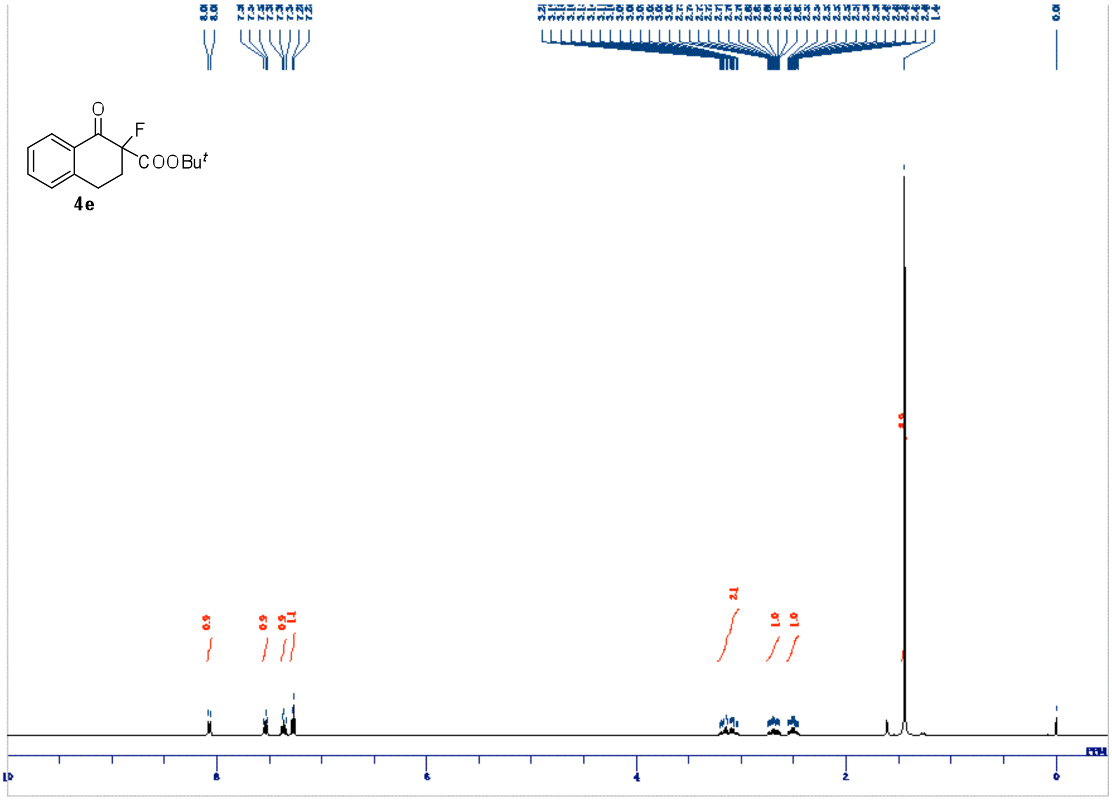
^{1}H NMR: Product **4d**



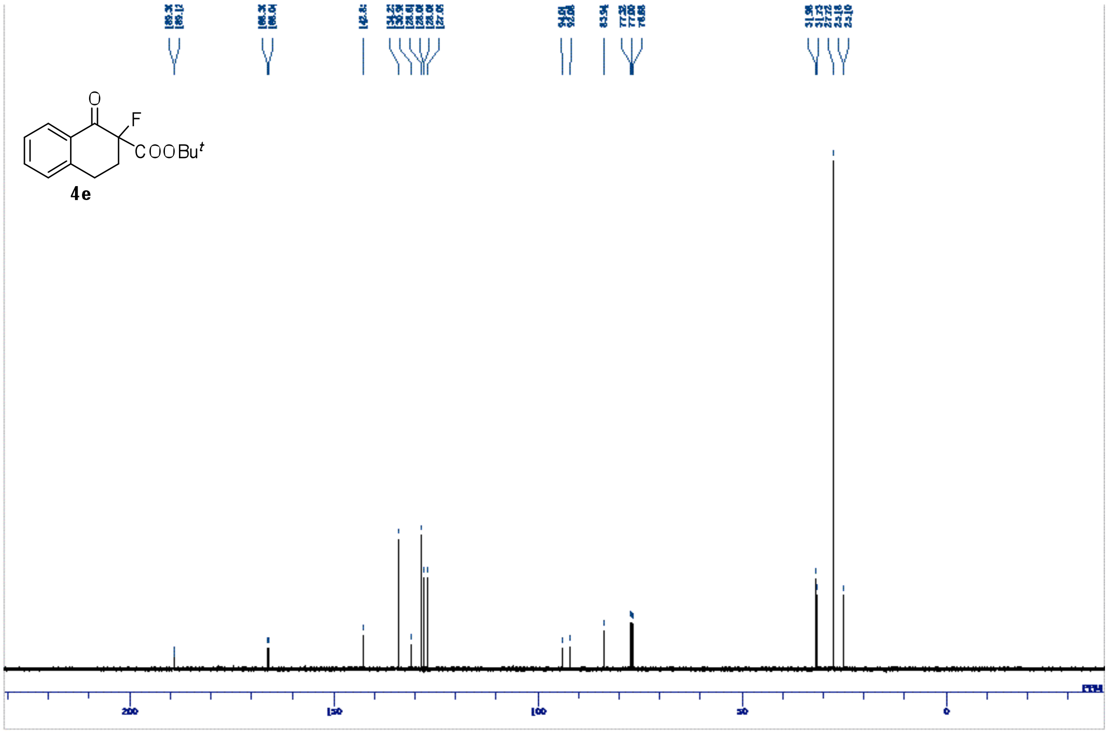
^{13}C NMR: Product **4d**



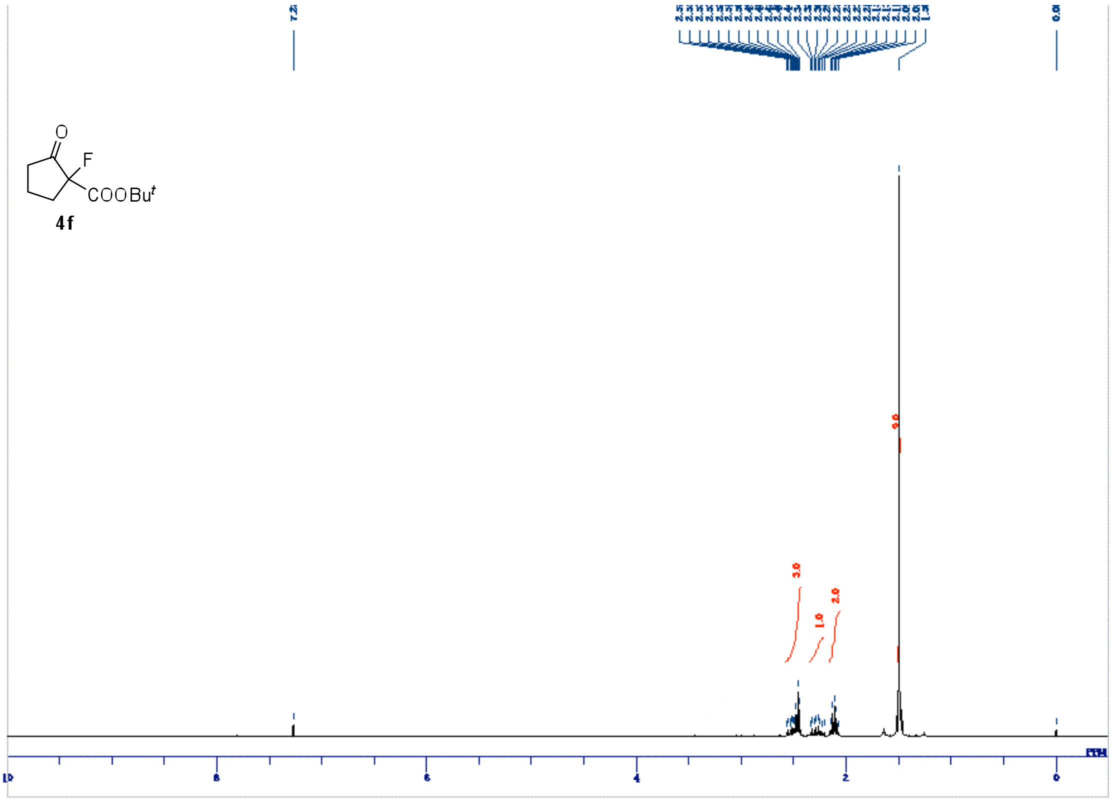
^{1}H NMR: Product **4e**



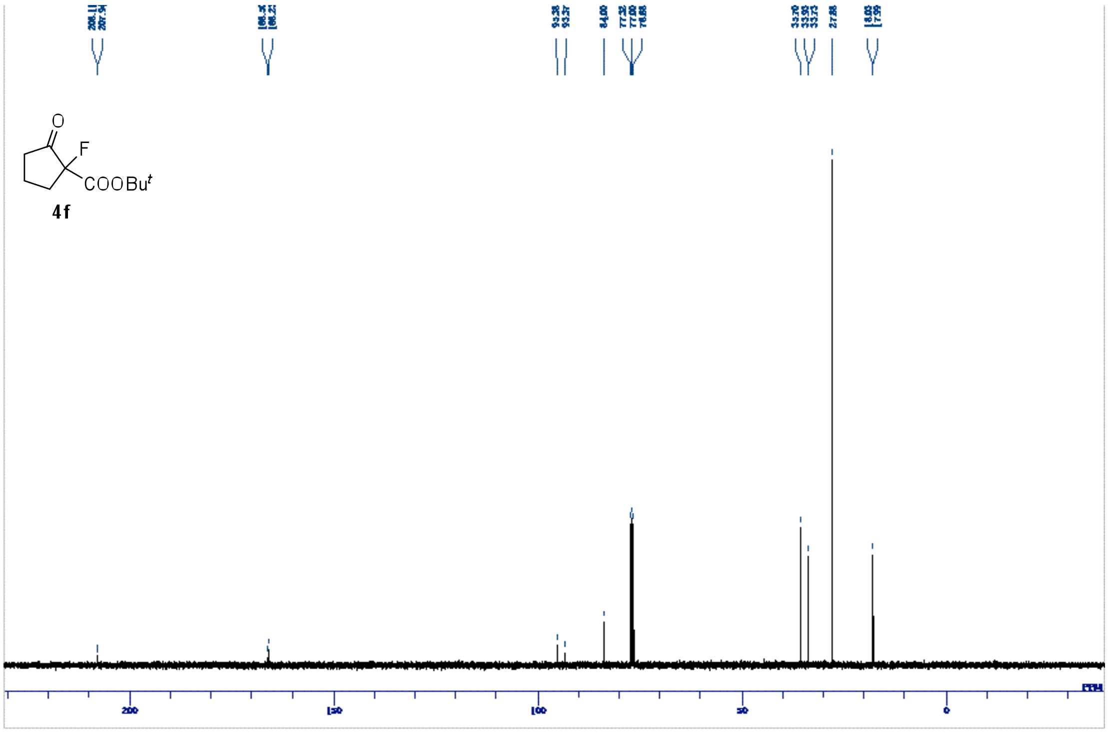
^{13}C NMR: Product **4e**



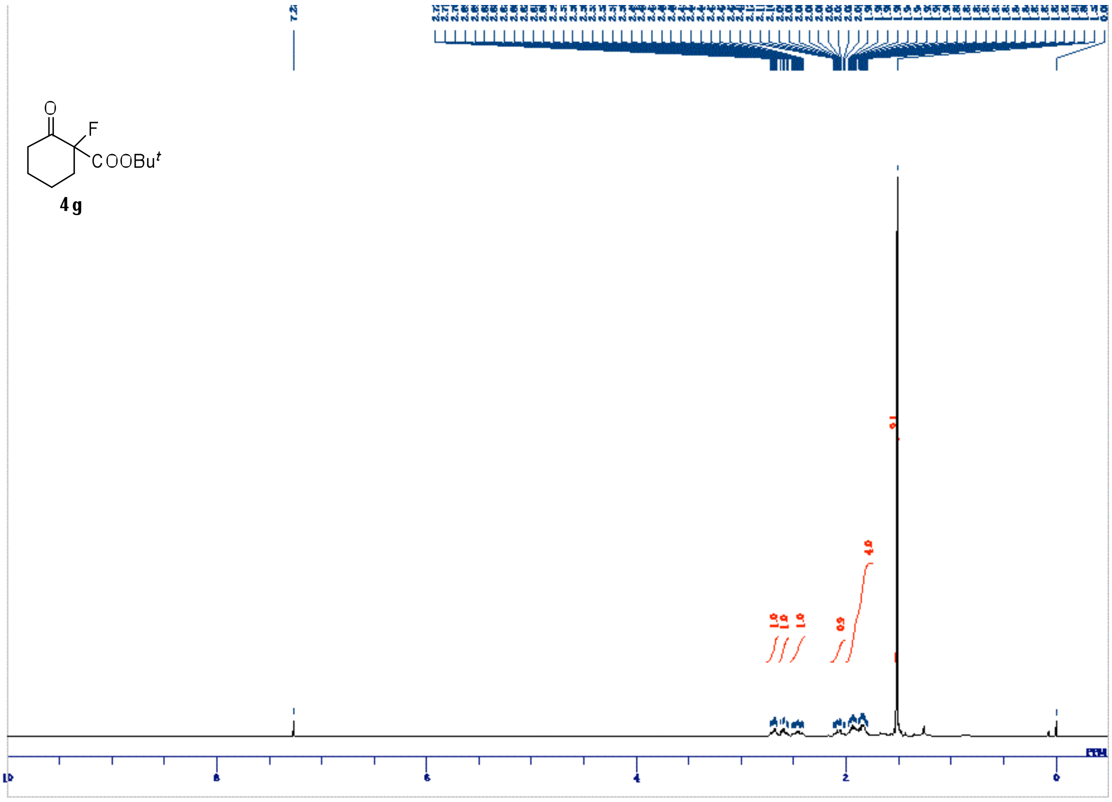
^{1}H NMR: Product **4f**



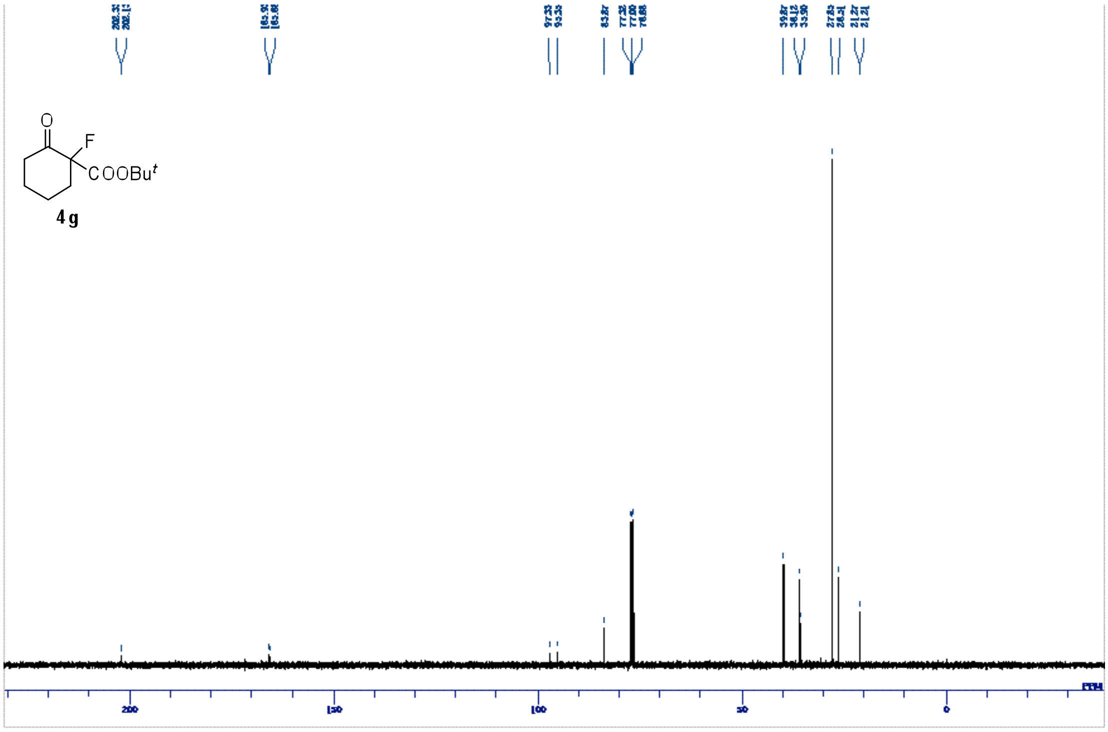
^{13}C NMR: Product **4f**



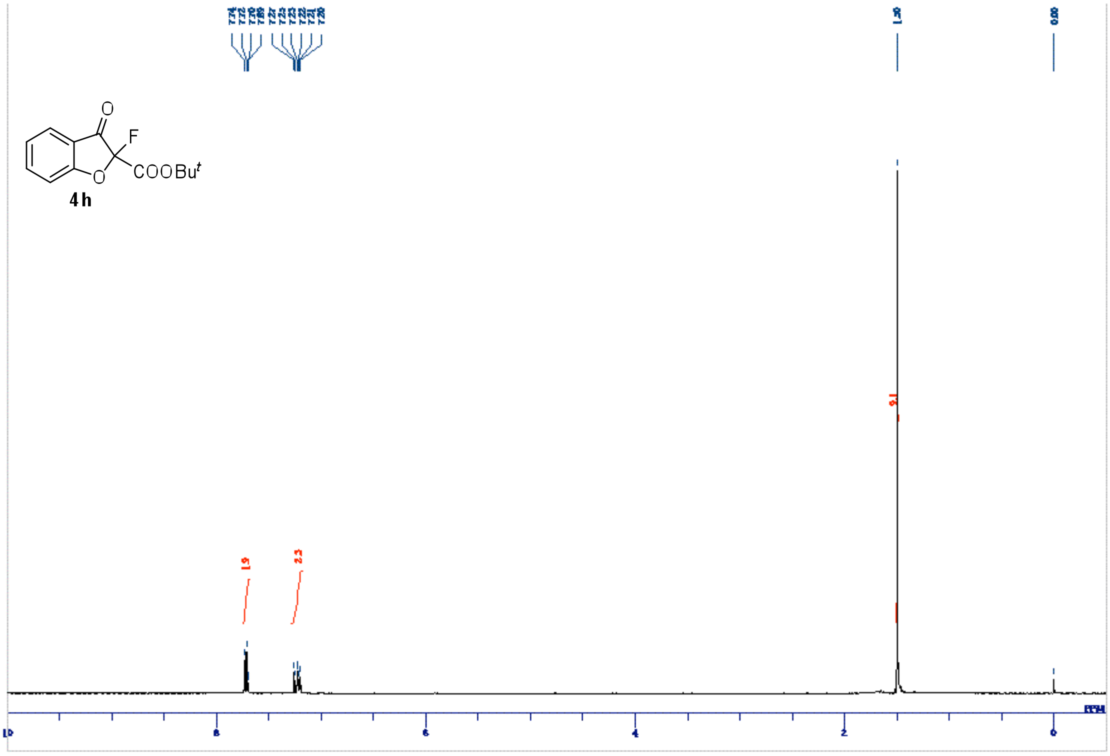
^{1}H NMR: Product **4g**



^{13}C NMR: Product **4g**



^{1}H NMR: Product **4h**



^{13}C NMR: Product **4h**