Rh(I)-Catalyzed Enantioselective Intramolecular Hydroarylation of Unactivated Ketones with Aryl Pinacolboronic Esters

Supporting Information

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Table of Contents

Experimental

General: Unless otherwise stated, reactions were performed in flame-dried glassware or dried in an oven overnight. All reaction vessels were fitted with rubber septa or Teflon screw caps and kept under an atmosphere of nitrogen. Liquid reagents and solvents were transferred via syringe under nitrogen using standard Schlenk techniques. Tetrahydrofuran, toluene, and benzene were sparged with argon and passed through an alumina column. Dichloromethane was distilled over calcium hydride. All other solvents were used as received unless otherwise noted. Reaction temperatures above 23 °C refer to oil bath temperature which was controlled by an IKA® temperature modulator. Reactions were monitored by thin layer chromatography using SiliCycle silica gel 60 F254 precoated plates (0.25 mm), which were visualized using UV irradiation, *p*-anisaldehyde stain or $KMnO_4$ stain. Sorbent Technologies silica gel (particle size 40-63 μm) was used for column chromatography. ^{1}H and ^{13}C NMR were recorded on Bruker AVB-400, AVQ-400, DRX-500 or AV-600 spectrometers with ^{13}C operating frequencies at 100, 125 and 150 MHz, respectively, in deuterated chloroform at 23 °C. Chemical shifts are reported relative to residual solvent signal (δ = 7.26 for ^{1}H NMR and 77.00 for ^{13}C NMR). Data for ^{1}H NMR are reported as follows: chemical shift (multiplicity, coupling constant, number of hydrogens). Multiplicity is abbreviated as follows: s (singlet), br s (broad singlet), d (doublet), dd (doublet of doublets), t (triplet), tt (triplet of triplets), q (quartet), aq (apparent quartet), ap (apparent pentent), hept (heptet), m (multiplet). IR spectra were recorded on a Nicolet MAGNA-IR 850 spectrometer and are reported in frequency of absorption (cm^{-1}). Only selected IR absorbencies are reported. Enantiomeric excess (ee) was determenined by HPLC analysis on a Waters

chromatography system (1525 binary pump, 717+ autosampler, 2487 dual wavelength detector) using a Chiralcel OD-H (0.46 cm x 25 cm)(from Daicel Chemical Ind., Ltd.) stationary phase and 97:3 hexanes/isopropanol mobile phase (1 mL/min) at 220 nm. Mass spectra were recorded on an LTQ Orbitrap XL (ThermoFisher Scientific) for ESI and AutoSpec Premier (Waters) for EI through the mass spectral facility at the University of California, Berkeley.

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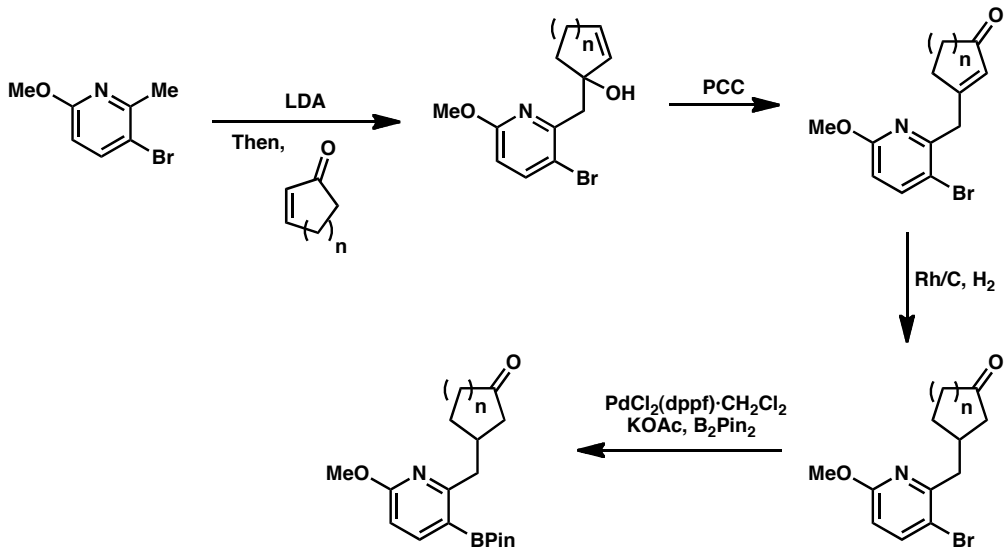
*General synthetic route for the preparation of substrates **3a-3c**:*



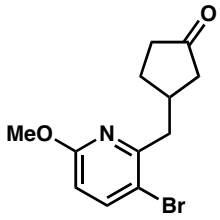
Representative Experimental Procedure for the Picoline Alkylation: 1-((3-Bromo-6-methoxypyridin-2-yl)methyl)cyclopent-2-enol: LDA was generated over 1 h in a 250-mL, flame-dried round-bottom flask by the slow addition of *n*-BuLi (2.5 M, 3.47 mL, 8.69 mmol, 2.3 equiv) to diisopropylamine (1.25 mL, 8.87 mmol, 2.35 equiv) in 20 mL of THF at -78 °C. 3-Bromo-6-methoxy-2-methylpyridine (763 mg, 3.78 mmol, 1.0 equiv) in 10 mL of THF was then added to the LDA and the resulting

mixture was allowed to stir for 1 h at -78 °C. In a separate, flame-dried 50-mL pear-shaped flask, cyclopentenone (372 mg, 4.53 mmol, 1.2 equiv) in 8 mL of THF was cooled to -78 °C and transferred via cannula into the reaction mixture, which was stirred for 1 h at that temperature. The reaction mixture was quenched with 2 mL saturated NH_4Cl solution and extracted with Et_2O (2 x 50 mL). The combined organic phases were dried over $MgSO_4$, filtered and concentrated. The crude product was purified via silica gel column chromatography (10:1 hexanes/EtOAc) to deliver 1-((3-Bromo-6-methoxypyridin-2-yl)methyl)cyclopent-2-enol (545 mg, 1.92 mmol, 51% yield). R_f 0.40 (4:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, J = 8.7 Hz, 1H), 6.56 (d, J = 8.7 Hz, 1H), 5.90 (d, J = 2.5 Hz, 1H), 5.72 (br s, 2H), 3.88 (s, 3H), 3.17 (s, 2H), 2.53 (br s, 1H), 2.38 – 2.30 (m, 1H), 2.04 – 1.92 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.2, 155.1, 143.3, 136.0, 133.5, 112.8, 110.9, 85.5, 54.1, 44.7, 38.2, 31.2; IR (film) ν_{max} 3412, 1579, 1462, 1057 cm^{-1}; HRMS (EI) calcd for $[C_{12}H_{14}NO_2Br]^+$ *m/z* 283.0208, found 283.0206.

Representative Experimental Procedure for Oxidative Allylic Transposition: 3-((3-Bromo-6-methoxypyridin-2-yl)methyl)cyclopent-2-enone: An oven-dried 25 mL round-bottom flask equipped with a stir bar was purged with nitrogen and charged with 1-((3-bromo-6-methoxypyridin-2-yl)methyl)cyclopent-2-enol (531 mg, 1.87 mmol, 1.0 equiv) followed by dichloromethane (19 mL), celite (805 mg) and PCC (806 mg, 3.74 mmol, 2.0 equiv) to yield a dark colored solution. The reaction flask was then sealed and allowed to stir at ambient temperature for 3.5 h, after which time it was passed through a plug of silica, which was washed with dichloromethane (5 mL), and concentrated under reduced pressure. The crude product was purified via silica gel column chromatography (gradient of 10:1 hexanes/EtOAc → 6:1 hexanes/EtOAc → 4:1 hexanes/EtOAc) to deliver 3-((3-bromo-6-methoxypyridin-2-yl)methyl)cyclopent-2-enone (125 mg, 441 μmol 24% yield). Rf

0.31 (2:1 hexanes/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.7 Hz, 1H), 6.55 (d, *J* = 8.7, 1H), 5.91 (t, *J* = 1.4 Hz, 1H), 3.97 (s, 2H), 3.86 (s, 3H), 2.70 – 2.67 (m, 2H), 2.44 – 2.41 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.9, 178.4, 162.9, 152.8, 142.9, 131.4, 112.1, 111.3, 53.9, 41.4, 35.7, 31.8; IR (film) ν_{max} 1708, 1617, 1462, 1016 cm^{-1}; HRMS (EI) calcd for $[C_{12}H_{12}NO_2Br]^+$ *m/z* 281.0051, found 281.0043.

Representative Experimental Procedure for Oxidative Enone Reduction: 3-((3-Bromo-6-methoxypyridin-2-yl)methyl)cyclopentanone:



3-((3-Bromo-6-methoxypyridin-2-yl)methyl)cyclopent-2-enone (124 mg, 440 μmol, 1.0 equiv) was added to a 25-mL round-bottom flask equipped with a stir bar and was diluted with 7.30 mL of THF. Rh/C (5% Rh by weight, 109 mg, 52.7 μmol, 0.12 equiv) was then added and the reaction vessel was purged with hydrogen gas for 10 min. The reaction mixture was allowed to stir under an atmosphere of hydrogen gas for 7 h, after which it was filtered through Celite and concentrated under reduced pressure. The crude residue was purified by column chromatography (gradient of 10:1 hexanes/EtOAc → 5:1 hexanes/EtOAc → 4:1 hexanes/EtOAc) to deliver 3-((3-bromo-6-methoxypyridin-2-yl)methyl)cyclopentanone (89.0 mg, 313 μmol, 71% yield). R_f 0.43 (3:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.6 Hz, 1H), 6.49 (d, *J* = 8.6 Hz, 1H), 3.88 (s, 3H), 3.02 (dd, *J* = 14.2, 6.8 Hz, 1H), 2.94 (dd, *J* = 14.2, 7.7 Hz, 1H), 2.83 – 2.74 (m, 1H), 2.42 (dd, *J* = 18.4, 7.4 Hz, 1H), 2.37 – 2.30 (m, 1H), 2.22 – 2.17 (m, 2H), 2.03 (dd, *J* = 18.4, 9.9 Hz, 1H), 1.77 – 1.67 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 219.8, 162.6, 155.6, 142.6, 112.0, 110.3, 53.8, 45.1, 42.0, 38.5, 36.2, 29.4; IR (film) ν_{max} 1740, 1460, 1298 cm^{-1}; HRMS (EI) calcd for $[C_{12}H_{14}NO_2Br]^+$ *m/z* 283.0208, found 283.0202.

Representative Experimental Procedure for Borylation: 3-((6-Methoxy-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-2-yl)methyl) Cyclopentanone (3a): Potassium acetate (154 mg, 1.57 mmol, 5.0 equiv) was added to a 25-mL Schlenk tube equipped with a stir bar. The reaction vessel was then placed under vacuum and flame-dried. Once cool, [1,1-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (dichloromethane adduct, 25.6 mg, 31.3 μmol, 0.10 equiv) was added followed by bis(pinacolato)diboron (398 mg, 1.56 mmol, 5.0 equiv). 3-((3-Bromo-6-methoxypyridin-2-yl)methyl)cyclopentanone (89.0 mg, 313 μmol, 1.0 equiv) in 3.2 mL of DMF was then transferred from a screw cap vial to the Schlenk tube via cannula. The reaction mixture was sparged with nitrogen for 10 min, sealed with a Teflon stopper and heated at 80 °C for 22 h. After this time, the reaction mixture was diluted with 3 mL of Et_2O and washed with 3 mL of water. The organic layer was isolated and the aqueous layer was extracted with Et_2O (2 mL). The combined organic phase was washed with water (2 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was first purified via column chromatography (13:1 hexanes/EtOAc → 6:1 hexanes/EtOAc) to remove bulk impurities followed by a second purification via column chromatography using slower elution conditions (13:1 hexanes/EtOAc → 10:1 hexanes/EtOAc) to yield 3-((6-Methoxy-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-2-yl)methyl)cyclopentanone (44.8 mg, 135 μmol 43% yield). R_f 0.54 (2:1 hexanes/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.3 Hz, 1H), 6.54 (d, J = 8.3 Hz, 1H), 3.92 (s, 3H), 3.12 (d, J = 7.2 Hz, 2H), 2.73 – 2.64 (m, 1H), 2.38 – 2.25 (m, 2H), 2.18 – 1.99 (m, 3H), 1.78 – 1.66 (m, 1H), 1.31 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 220.4, 165.5, 164.9, 146.5, 107.2, 83.6, 53.2, 44.8, 42.0, 38.3, 37.9, 29.0, 24.9,

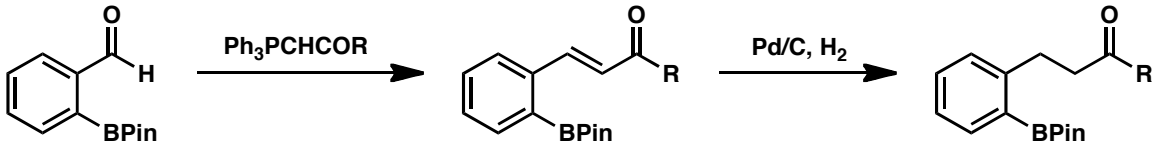
24.8. The boron-bound carbon was not detected likely due to quadropolar relaxation; IR (film) ν_{max} 1742, 1589, 1344, 1305, 1145, 1026 cm^{-1}; HRMS calcd for $[C_{18}H_{27}O_4NB]^+$: *m/z* 332.2028, found 332.2031.

3-((6-Methoxy-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-2-yl)methyl)cyclohexanone (3b) was prepared using the representative synthetic route. Bulb-to-bulb distillation (120 °C, 0.1 torr, 1 h) was necessary to purify final product. R_f 0.35 (4:1 hexanes/EtOAc); ^1H NMR (600 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.3 Hz, 1H), 6.53 (d, *J* = 8.3 Hz, 1H), 3.91 (s, 3H), 3.07 - 3.02 (m, 1H), 3.01 - 2.97 (m, 1H), 2.40 - 2.31 (m, 2H), 2.30 - 2.22 (m, 2H), 2.19 - 2.13 (m, 1H), 2.08 - 2.02 (m, 1H), 1.88 (d, *J* = 11.5 Hz, 1H), 1.66 - 1.54 (m, 1H), 1.50 - 1.39 (m, 1H), 1.32 (s, 12H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 212.2, 165.3, 164.9, 146.5, 107.1, 83.6, 53.2, 48.0, 43.8, 41.5, 40.5, 31.2, 25.3, 24.89, 24.86. The boron-bound carbon was not detected likely due to quadrupolar relaxation; IR (film) υ_{max} 2977, 1710, 1588, 1345, 1308, 1145, 1023 cm^{-1}; HRMS (ESI) calcd for $[C_{19}H_{29}O_4NB]^+$: *m/z* 346.2184, found 346.2184.

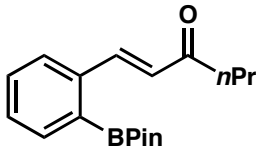
3-((6-Methoxy-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-2-yl)methyl)cycloheptanone (3c) was prepared using the representative synthetic route. Bulb-to-bulb distillation (120 °C, 0.1 torr, 1 h) was necessary to purify final product. R_f 0.37 (4:1 hexanes/EtOAc); ^1H NMR (600 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.3 Hz, 1H), 6.53 (d, *J* = 8.3 Hz, 1H), 3.91 (s, 3H), 3.01 - 2.91 (m, 2H), 2.55 - 2.50 (m, 1H), 2.49 - 2.44 (m, 3H), 2.31 - 2.23 (m, 1H), 1.95 - 1.81 (m, 3H), 1.65 - 1.55 (m, 1H), 1.44 - 1.27 (m, 14H); ^{13}C

NMR (150 MHz, $CDCl_3$) δ 214.6, 165.6, 164.8, 146.5, 107.1, 83.6, 53.2, 49.8, 44.2, 44.0, 37.1, 36.4, 28.8, 24.9, 24.6. The boron-bound carbon was not detected likely due to quadrupolar relaxation; IR (film) υ_{max} 1700, 1344, 1267, 1145 cm^{-1}; HRMS (ESI) calcd for $[C_{20}H_{31}NO_4B]^+$: *m/z* 360.2341, found 360.2341.

General synthetic route for the preparation of substrates ***5a, 5b, 9 & 10:***



Representative Experimental Procedure for the Wittig Homologation: 1-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)hex-1-en-3-one: In a 20 mL screw cap vial, 1-(triphenylphosphoranylidene)pentan-2-one[1] (430 mg, 1.2 mmol, 1.3 equiv) was diluted with 2-formylphenylboronic acid pinacol ester[2] (220 mg, 0.96 mmol, 1.0 equiv) in toluene (7 mL). The vial was then purged with nitrogen, sealed with a Teflon cap and heated to 90 °C for 20 h. The reaction mixture was then allowed to cool to room temperature and concentrated under reduced pressure. The resulting solids were suspended in Et_2O and filtered through celite to remove excess triphenylphosphine oxide and concentrated. The crude product was purified via column chromatography (4:1 hexanes/EtOAc) to deliver 1-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)hex-1-en-3-one (170 mg, 0.56 mmol, 59%). R_f 0.41 (4:1 hexanes/EtOAc); ^1H NMR (600 MHz, $CDCl_3$) δ



[1] Phosphoranes were prepared according to known methods, see: E. Ruijter, H. Schultingkemper, L. A. Wessjohan, *J. Org. Chem.,* 2005, **70**, 2820.
[2] Prepared according to known methods, see: M. Lautens, S. Mancuso, *J. Org. Chem.,* 2004, **69**, 3478.

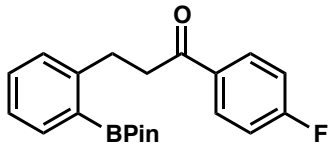
8.52 (d, *J* = 16.5 Hz, 1H), 7.87 (d, *J* = 7.4 Hz, 1H), 7.68 (d, *J* = 7.9 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 1H), 7.35 (t, *J* = 7.4 Hz, 1H), 6.58 (d, *J* = 16.5 Hz, 1H), 2.71 (t, *J* = 7.5 Hz, 2H), 1.74 (h, *J* = 7.5 Hz, 2H), 1.37 (s, 12H), 1.00 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 201.6, 144.2, 140.6, 136.4, 131.2, 129.0, 128.0, 125.4, 84.0, 41.2, 24.8, 18.2, 13.9. The boron-bound carbon was not detected likely due to quadrupolar relaxation; IR (film) υ_{max} 1668, 1612, 1347 cm^{-1}; HRMS (ESI) calcd for $[C_{18}H_{25}O_3BNa]^+$: *m/z* 323.1789, found 323.1788.

Representative Experimental Procedure for the Reduction of Enones: 1-(2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)hexan-3-one (5a): 1-(2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)hex-1-en-3-one (160 mg, 0.54 mmol, 1.0 equiv) was diluted with EtOAc (5.4 mL) in a 20 mL screw cap vial equipped with a magnetic stir bar. Pd/C (10%, 58 mg, 54 μmol, 0.1 equiv) was then added and the vial was fitted with a rubber septum and purged with hydrogen. The reaction mixture was stirred under a balloon of hydrogen at ambient temperature for 2 h at which time it was filtered through celite and concentrated. The crude product was purified via column chromatography (4:1 hexanes/EtOAc) to deliver 1-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)hexan-3-one (130 mg, 0.44 mmol, 81%). R_f 0.50 (4:1 hexanes/EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.4 Hz, 1H), 7.34 (td, *J* = 7.5, 1.6 Hz, 1H), 7.21 - 7.16 (m, 2H), 3.16 – 3.09 (m, 2H), 2.71 - 2.65 (m, 2H), 2.39 (t, *J* = 7.3 Hz, 2H), 1.61 (h, *J* = 7.4 Hz, 2H), 1.34 (s, 12H), 0.91 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 210.7, 148.2, 136.3, 131.1, 129.3, 125.4, 83.5, 46.1, 44.6, 30.5, 24.8, 17.3, 13.8. The boron-bound carbon was not detected likely due to quadrupolar relaxation; IR (film) υ_{max} 2976, 1713, 1348, 1315, 1145 cm^{-1}; HRMS (ESI) calcd for $[C_{18}H_{27}O_3BNa]^+$: *m/z* 325.1945, found 325.1944.

1-(2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)heptan-3-one (5b) was prepared using the representative synthetic route. R_f 0.50 (4:1 hexanes/EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.79 (dd, *J* = 7.4, 1.5 Hz, 1H), 7.34 (td, *J* = 7.5, 1.5 Hz, 1H), 7.21 - 7.16 (m, 2H), 3.15 – 3.09 (m, 2H), 2.73 - 2.63 (m, 2H), 2.40 (t, *J* = 7.5 Hz, 2H), 1.56 (dt, *J* = 15.1, 7.5 Hz, 2H), 1.34 (s, 12H), 1.34 - 1.26 (m, 2H), 0.90 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 210.9, 148.2, 136.3, 131.1, 129.3, 125.4, 83.5, 46.1, 42.4, 30.5, 26.0, 24.9, 22.4, 13.8. The boron-bound carbon was not detected likely due to quadrupolar relaxation; IR (film) υ_{max} 1711, 1348 cm^{-1}; HRMS (ESI) calcd for $[C_{19}H_{29}O_3BNa]^+$: *m/z* 339.2102, found 339.2100.

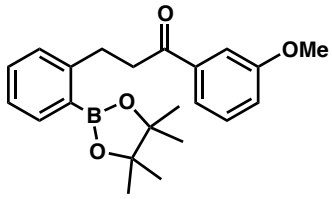
1-phenyl-3-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl) propan-1-one (9) was prepared using the representative synthetic route but employing PtO_2 (10 mol%) in the presence of Na_2CO_3 (5.0 equiv) at 0 °C for the reduction of the enone. R_f 0.50 (4:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.83 (dd, *J* = 7.4, 1.5 Hz, 1H), 7.58 - 7.52 (m, 1H), 7.49 - 7.42 (m, 2H), 7.38 (td, *J* = 7.5, 1.6 Hz, 1H), 7.27 (d, *J* = 6.1 Hz, 1H), 7.23 (td, *J* = 7.4, 1.2 Hz, 1H), 3.35 - 3.23 (m, 4H), 1.31 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.8, 148.4, 137.1, 136.3, 132.8, 131.18, 129.4, 128.5, 128.1, 125.5, 83.5, 42.2, 30.8, 24.8. The boron-bound carbon was not detected likely due to quadrupolar relaxation; IR (film) υ_{max} 1686, 1348, 743 cm^{-1}; HRMS (ESI) calcd for $[C_{21}H_{25}O_3BNa]^+$: *m/z* 359.1789, found 359.1787.

1-(4-fluorophenyl)-3-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)propan-1-one



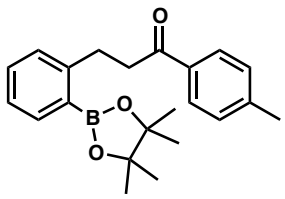
(10) was prepared using the representative synthetic route but employing PtO_2 (10 mol%) in the presence of Na_2CO_3 (5.0 equiv) at 0 °C for the reduction of the enone. R_f 0.59 (4:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (dd, *J* = 8.6, 5.6 Hz, 2H), 7.82 (dd, *J* = 7.4, 1.6 Hz, 1H), 7.40 - 7.34 (m, 1H), 7.28 - 7.19 (m, 2H), 7.11 (t, *J* = 8.6 Hz, 2H), 3.60 - 3.02 (m, 4H), 1.30 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.2, 165.6 (d, *J* = 254.2 Hz), 148.2, 136.4, 133.5 (d, *J* = 3.0 Hz), 131.2, 130.7 (d, *J* = 9.2 Hz), 129.4, 125.5, 115.5 (d, *J* = 21.8 Hz), 83.6, 42.1, 30.8, 24.8. The boron-bound carbon was not detected likely due to quadrupolar relaxation; IR (film) υ_{max} 2978, 1687, 1348, 1145 cm^{-1}; HRMS (ESI) calcd for $[C_{21}H_{25}O_3BF]^+$: *m/z* 355.1875, found 355.1880.

1-(3-methoxyphenyl)-3-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)propan-1-one (15b) was prepared using the representative synthetic route but employing PtO_2 (10 mol%) in the presence of Na_2CO_3 (5.0 equiv) at 0 °C for the reduction of the enone. R_f 0.71 (4:1 hexanes/EtOAc; buffered with 1% triethylamine; eluted twice); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 7.4, 1.5 Hz, 1H), 7.57 (d, *J* = 7.7 Hz, 1H), 7.51 (dd, *J* = 2.5, 1.6 Hz, 1H), 7.39 – 7.32 (m, 2H), 7.29 - 7.17 (m, 2H), 7.14 - 7.06 (m, 1H), 3.85 (s, 3H), 3.44 - 3.14 (m, 4H), 1.30 (s, 12H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 199.4, 159.7, 148.3, 138.4, 136.3, 131.1, 129.4, 125.4, 120.7, 119.3, 112.1, 83.5, 55.3, 42.2, 30.7, 24.7 (one sp^2 carbon was not observed, likely due to signal overlap). The boron-bound carbon was not detected likely due to quadrupolar



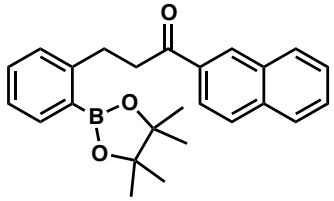
relaxation; IR (film) υ_{max} 2997, 1687, 1348 cm^{-1}; HRMS (ESI) calcd for $[C_{22}H_{27}O_4BNa]^+$: *m/z* 389.1895, found 389.1896.

3-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-1-(*p*-tolyl)propan-1-one (15c) was



prepared using the representative synthetic route but employing PtO_2 (10 mol%) in the presence of Na_2CO_3 (5.0 equiv) at 0 °C for the reduction of the enone. R_f 0.59 (4:1 hexanes/EtOAc; buffered with 1% triethylamine); ^1H NMR (600 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.9 Hz, 2H), 7.85 (d, *J* = 7.4 Hz, 1H), 7.39 (t, *J* = 7.5 Hz, 1H), 7.31 - 7.19 (m, 4H), 3.35 - 3.30 (m, 2H), 3.29 - 3.24 (m, 2H), 2.43 (s, 3H), 1.33 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.4, 148.4, 143.4, 136.3, 134.6, 131.1, 129.4, 129.1, 128.2, 125.4, 83.5, 42.1, 30.9, 24.8, 21.5. The boron-bound carbon was not detected likely due to quadrupolar relaxation; IR (film) υ_{max} 2978, 1684, 1348 cm^{-1}; HRMS (ESI) calcd for $[C_{22}H_{27}O_3BNa]^+$: *m/z* 373.1945, found 373.1947.

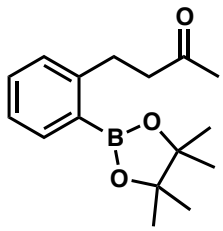
1-(naphthalen-2-yl)-3-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)propan-1-one



(15d) was prepared using the representative synthetic route but employing PtO_2 (10 mol%) in the presence of Na_2CO_3 (5.0 equiv) at 0 °C for the reduction of the enone. R_f 0.52 (4:1 hexanes/EtOAc); ^1H NMR (600 MHz, $CDCl_3$) δ 8.46 (s, 1H), 8.07 (d, *J* = 8.6 Hz, 1H), 7.92 (d, *J* = 8.1 Hz, 1H), 7.88 (t, *J* = 9.3 Hz, 2H), 7.83 (d, *J* = 7.3 Hz, 1H), 7.62 - 7.57 (m, 1H), 7.56 - 7.51 (m, 1H), 7.39 (t, *J* = 7.5 Hz, 1H), 7.29 (d, *J* = 7.6 Hz, 1H), 7.24 (t, *J* = 7.3 Hz, 1H), 3.45 - 3.39 (m, 2H), 3.39 - 3.34 (m, 2H), 1.29 (s, 12H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 199.6, 148.5, 136.3, 135.5, 134.4, 132.6, 131.2, 129.6, 129.5, 128.31, 128.26, 127.7, 126.7, 125.5, 124.0, 83.6, 42.2, 30.7, 24.8.

The boron-bound carbon was not detected likely due to quadrupolar relaxation; IR (film) υ_{max} 1680, 1348 cm^{-1}; HRMS (ESI) calcd for $[C_{25}H_{27}O_3BNa]^+$: *m/z* 409.1945, found 409.1945.

4-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)butan-2-one (15f) was prepared



using the representative synthetic route. R_f 0.60 (2:1 hexanes/EtOAc); ^1H NMR (400 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 7.2, 1.4 Hz, 1H), 7.35 (td, *J* = 7.5, 1.6 Hz, 1H), 7.19 (ddd, *J* = 12.8, 7.1, 1.1 Hz, 2H), 3.28 - 3.01 (m, 2H), 2.80 - 2.56 (m, 2H), 2.15 (s, 3H), 1.34 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.7, 148.0, 136.4, 131.2, 129.3, 125.5, 83.5, 47.1, 30.5, 29.8, 24.9. The boron-bound carbon was not detected likely due to quadrupolar relaxation; IR (film) υ_{max} 2978, 1712, 1348 cm^{-1}; HRMS (ESI) calcd for $[C_{16}H_{23}O_3BNa]^+$: *m/z* 297.1632, found 297.1632.

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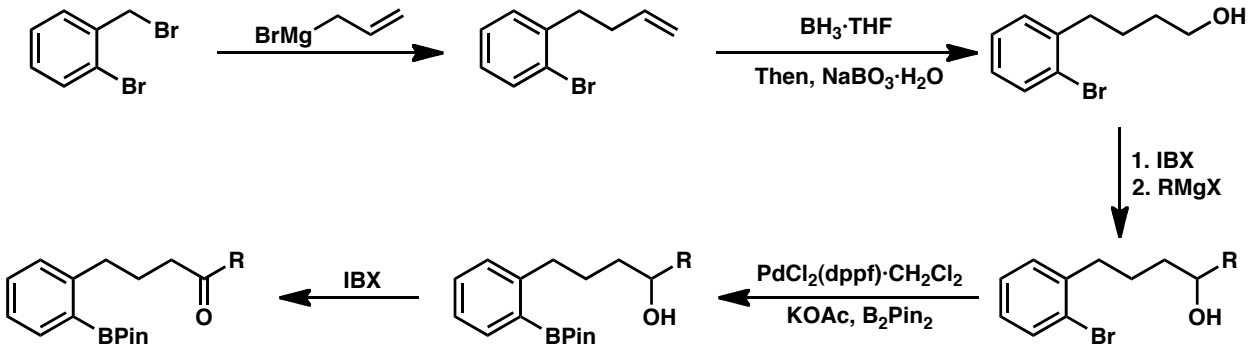
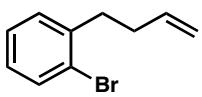
*General synthetic route for the preparation of substrates **5d-5f & 11**:*



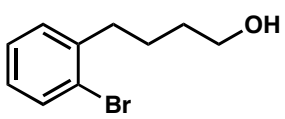
1-Bromo-2-(but-3-en-1-yl)benzene: In a flame-dried 100 mL round-bottom flask, equipped



with a magnetic stir bar and rubber septum under nitrogen, was placed 2-bromobenzyl bromide (2.0 g, 8.0 mmol, 1 equiv) and dry THF (30 mL). The flask was placed in an ice water bath and allylmagnesium bromide (1.0 M in diethyl ether, 12

mL, 12 mmol, 1.5 equiv) was added dropwise via syringe. The reaction vessel was then fitted with a reflux condenser and heated to reflux temperature in an oil bath for 2 h. The reaction was then cooled to 0 °C and quenched by the addition of saturated NH_4Cl solution. The resulting solution was extracted with EtOAc (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under vacuum to yield 1-bromo-2-(but-3-en-1-yl)benzene (1.63 g, 7.7 mmol, 97%). ^{1}H NMR spectral data were fully consistent with previously reported values.[3]

4-(2-Bromophenyl)butan-1-ol: Two flame-dried 500 mL round-bottom flasks were each



charged with 1-bromo-2-(but-3-en-1-yl)benzene (1.5 g, 7.1 mmol, 1.0 equiv) and THF (70 mL) in tandem. The vessels were then submerged in an ice water bath and borane-THF complex was added (1.0 M in THF, 28 mL, 28 mmol, 4.0 equiv) dropwise via syringe. Reactions were allowed to warm to room temperature over 5 h before being cooled to 0 °C and slowly quenched with water (120 mL). The vessels were then warmed to room temperature and sodium perborate monohydrate (5.7 g, 57 mmol, 8.0 equiv) was added portion-wise. The quenched reaction mixtures were stirred rapidly at ambient temperature for 15 h before being combined and poured into ice water and extracted with Et_2O (3 x 100 mL). The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (2:1 hexanes/EtOAc) to provide 4-(2-bromophenyl)butan-1-ol (2.3 g, 9.9 mmol, 70%). ^{1}H NMR spectral data were consistent with previously reported values.[4]

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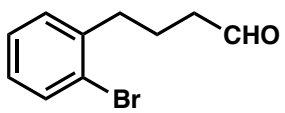
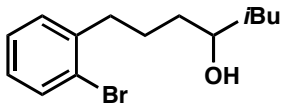
[3] I. D.G. Watson, S. Ritter, F. D. Toste, *J. Am. Chem. Soc.,* 2009, **131**, 2056.
[4] K .E. Torraca, S. I. Kuwabe, S. L. Buchwald, *J. Am. Chem. Soc.,* 2000, **122**, 12907.

4-(2-Bromophenyl)butanal: A 250 mL round-bottom flask equipped with a magnetic stir bar



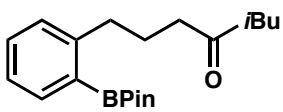
was charged with (2-bromophenyl)butan-1-ol (2.3 g, 9.9 mmol, 1.0 equiv) in wet EtOAc (99 mL) followed by IBX (5.5 g, 20.0 mmol, 2.0 equiv). The reaction vessel was then fitted with a condenser, purged with nitrogen, and heated to reflux temperature with vigorous stirring for 3 h at which time the mixture was allowed to cool to ambient temperature, filtered through a pad of silica and concentrated under reduced pressure. The crude product was purified by column chromatography (4:1 hexanes/EtOAc) to deliver 4-(2-bromophenyl)butanal (1.9 g, 8.4 mmol, 83%), which was found to be sensitive to oxidation upon standing. R_f 0.47 (4:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.78 (s, 1H), 7.53 (d, J = 8.0 Hz, 1H), 7.27 - 7.19 (m, 2H), 7.07 (td, J = 7.6, 2.0 Hz, 1H). 2.78 (t, J = 7.6 Hz, 2H), 2.50 (td, J = 7.3, 1.6 Hz, 2H), 2.06 (ap, J = 15.0, 7.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 202.0, 140.5, 132.9, 130.4, 127.8, 127.5, 124.4, 43.0, 35.2, 22.2; IR (film) υ_{max} 3427, 3059, 2918, 1725, 1020 cm^{-1}; HRMS (EI) calcd for $[C_{10}H_{11}OBr]^+$: *m/z* 225.9993, found 225.9991.

Representative Experimental Procedure for Grignard Addition: 1-(2-Bromophenyl)-6-methylheptan-4-ol: 4-(2-Bromophenyl)butanal (670 mg, 3.0 mmol, 1.0 equiv) was diluted with dry THF (30 mL) in a 100 mL, flame-dried round bottom flask equipped with a magnetic stir bar and rubber septum. The reaction vessel was then submerged in an ice water bath and isobutylmagnesium chloride (2.0 M in Et_2O, 1.9 mL, 3.8 mmol 1.3 equiv) was added dropwise via syringe. The reaction mixture was stirred at this temperature for 45 min before being quenched with saturated NH_4Cl solution (2 mL), poured into water (15 mL) and extracted with EtOAc (3 x 15 mL). The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The



crude product was purified by column chromatography (4:1 hexanes/EtOAc) to deliver 1-(2-bromophenyl)-6-methylheptan-4-ol (400 mg, 1.4 mmol, 48%). R_f 0.37 (4:1 hexanes/EtOAc); ^{1}H NMR (125 MHz, $CDCl_3$) δ 7.52 (d, J = 7.5 Hz, 1H), 7.24 - 7.20 (m, 2H), 7.08 - 7.02 (m, 1H), 3.75 - 3.69 (m, 1H), 2.81 - 2.70 (m, 2H), 1.81 - 1.71 (m, 2H), 1.72 - 1.61 (m, 1H), 1.58 - 1.47 (m, 2H), 1.46 – 1.42 (m, 1H) 1.41 -1.34 (m, 1H), 1.28 - 1.21 (m, 1H), 0.991 (t, J = 7.0 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.6, 132.7, 130.3, 127.5, 127.4, 124.4, 69.7, 46.7, 37.6, 36.1, 26.0, 24.6, 23.5, 22.0; IR (film) υ_{max} 3347, 2953, 1470, 1022, 749 cm^{-1}; HRMS (EI) calcd for $[C_{14}H_{21}OBr]^+$: *m/z* 284.0776, found 284.0779.

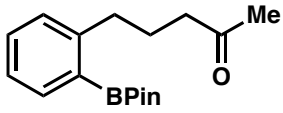
Representative Experimental Procedure for the Borylation and Oxidation of Haloarenes:



6-Methyl-1-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl) heptan-4-one (5e): A 25 mL Schlenk flask equipped with a magnetic stir bar and charged with potassium acetate (344 mg, 3.51 mmol, 5.0 equiv) was dried by flame under vacuum and cooled under a nitrogen atmosphere. Bis(pinacolato)diboron (355 mg, 1.40 mmol, 2.0 equiv) and [1,1′-Bis(diphenylphosphino)ferrocene]dichloropalladium(II) (dichloromethane adduct, 57.2 mg, 0.70 mmol, 0.10 equiv) were added and the flask was evacuated/backfilled (3X) with nitrogen. 1-(2-bromophenyl)-6-methylheptan-4-ol (200 mg, 0.70 mmol, 1.0 equiv) was then added in DMF (7 mL) and the resulting mixture was sparged with nitrogen for 5 minutes before being sealed and heated to 80 °C for 12 h. After this time, the mixture was cooled to room temperature, poured into water (10 mL) and extracted with Et_2O (2 x 10 mL). The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated. The crude residue was passed through a short column of silica (4:1 hexanes/EtOAc) and concentrated under reduced pressure. The resulting material was then diluted with wet EtOAc (10 mL) in a 20 mL screw cap vial equipped with a stir bar. IBX (566

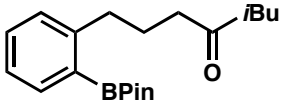
mg, 2.02 mmol, 2.9 equiv) was added and the vial was purged with nitrogen, sealed with a Teflon cap and heated to 80 °C for 2 h while stirring rapidly. The heterogeneous mixture was then cooled to room temperature, filtered through a plug of silica and concentrated under reduced pressure. The crude product was purified by column chromatography (10:1 hexanes/EtOAc) to deliver 6-methyl-1-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)heptan-4-one (148 mg, 0.45 mmol, 64%).

5-(2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2yl)phenyl)



pentan-2-one (5d) was prepared using the representative synthetic route. R_f 0.48 (4:1 hexanes/EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78 (dd, *J* = 7.4, 1.5 Hz, 1H), 7.35 (td, *J* = 7.5, 1.5 Hz, 1H), 7.21 - 7.14 (m, 2H), 2.89 (t, *J* = 7.6 Hz, 2H), 2.44 (t, *J* = 7.5 Hz, 2H), 2.12 (s, 3H), 1.86 (dt, *J* = 15.1, 7.7 Hz, 2H), 1.34 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.21, 148.66, 136.20, 130.91, 129.25, 125.22, 83.44, 43.42, 34.85, 29.79, 27.14, 24.85 The boron-bound carbon was not detected likely due to quadrupolar relaxation; IR (film) υ_{max} 2977, 1712, 1348, 1145 cm^{-1}; HRMS (ESI) calcd for [$C_{17}H_{25}O_3BNa$] : *m/z* 311.1789, found 311.1789.

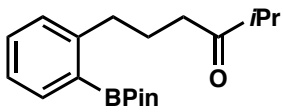
6-Methyl-1-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)heptan-4-one (5e) was



prepared using the representative synthetic route. R_f 0.37 (10:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.4 Hz, 1H), 7.34 (td, *J* = 7.5, 1.6 Hz, 1H), 7.20 - 7.15 (m, 2H), 2.89 (t, *J* = 7.6 Hz, 2H), 2.40 (t, *J* = 7.5 Hz, 2H), 2.26 (d, *J* = 7.0 Hz, 2H), 2.16 – 2.09 (m, 1H), 1.85 (pent, *J* = 7.7 Hz, 2H), 1.34 (s, 12H), 0.90 (d, *J* = 6.6 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 210.9, 148.8, 136.2, 130.9, 129.2,

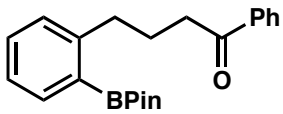
125.2, 83.4, 51.7, 43.0, 35.01, 27.1, 24.8, 24.5, 22.6. The boron-bound carbon was not detected likely due to quadrupolar relaxation; IR (film) υ_{max} 1712, 1348 cm^{-1}; HRMS (ESI) calcd for $[C_{20}H_{31}O_3BNa]^+$: *m/z* 353.2258, found 353.2256.

2-Methyl-6-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)



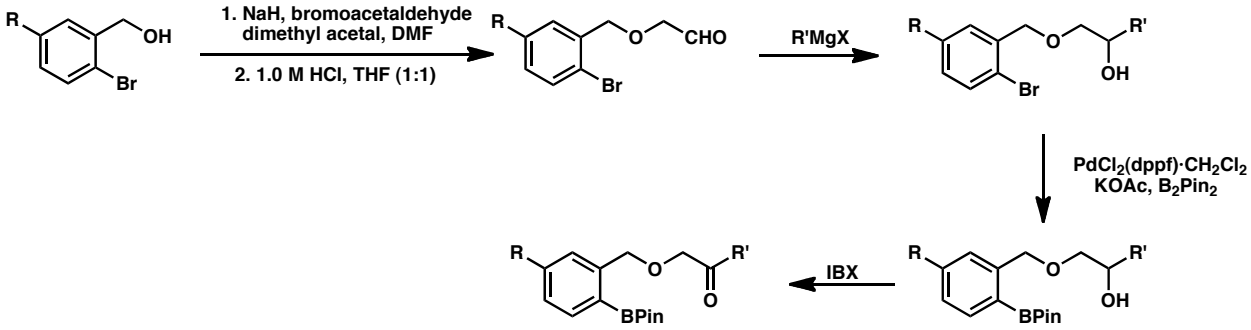
phenyl)hexan-3-one (5f) was prepared using the representative synthetic route. R_f 0.38 (4:1 hexanes/EtOAc); ^1H NMR (600 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.5 Hz, 1H), 7.34 (td, *J* = 7.5, 1.5 Hz, 1H), 7.21 - 7.14 (m, 2H), 2.89 (t, *J* = 7.6 Hz, 2H), 2.58 (hept, *J* = 6.9 Hz, 1H), 2.47 (t, *J* = 7.5 Hz, 2H), 1.85 (ap, *J* = 7.7 Hz, 2H), 1.34 (s, 12H), 1.08 (d, *J* = 7.0 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 214.7, 148.8, 136.2, 130.9, 129.2, 125.2, 83.4, 40.7, 40.0, 35.0, 27.1, 24.9, 18.2. The boron-bound carbon was not detected likely due to quadrupolar relaxation; IR (film) υ_{max} 2975, 1712, 1348, 1145 cm^{-1}; HRMS (ESI) calcd for $[C_{19}H_{29}O_3BNa]^+$: *m/z* 339.2102, found 339.2100.

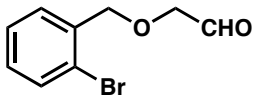
1-phenyl-4-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)



butan-1-one (11) was prepared using the representative synthetic route. R_f 0.48 (4:1 hexanes/EtOAc); ^1H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.0 Hz, 2H), 7.80 (d, *J* = 6.8 Hz, 1H), 7.54 (t, *J* = 7.3 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 1H), 7.36 (td, *J* = 7.5, 1.6 Hz, 1H), 7.21 (d, *J* = 7.4 Hz, 2H), 3.00 (q, *J* = 7.4 Hz, 4H), 2.04 (dt, *J* = 15.0, 7.5 Hz, 2H), 1.33 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.4, 148.8, 137.0, 136.2, 132.8, 130.9, 129.3, 128.5, 128.0, 125.2, 83.4, 38.2, 35.0, 27.6, 24.8 The boron-bound carbon was not detected likely due to quadrupolar relaxation; IR (film) υ_{max} 2977, 1688, 1348 cm^{-1}; HRMS (ESI) calcd for $[C_{22}H_{27}O_3BNa]^+$: *m/z* 373.1945, found 373.1944.

*General synthetic route for the preparation of substrates **7a-7c**:*

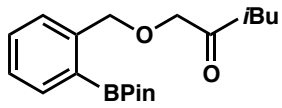


Representative Experimental Procedure for the Alkylation of Benzyl Alcohols: 2-((2-Bromobenzyl)oxy)acetaldehyde: 

In a 100 mL flame-dried round-bottom flask, NaH (60% dispersion in mineral oil, 1.07g, 26.7 mmol, 5.0 equiv) was suspended in dry DMF (24 mL). The reaction vessel, which was under a nitrogen atmosphere, was then submerged into an ice water bath and 2-bromobenzyl alcohol (1.00 g, 5.35 mmol, 1.0 equiv) was added in dry DMF (24 mL) via cannula. After 10 min at that temperature, the reaction mixture was allowed to warm to ambient temperature and stir for 1 h before being cooled back down to 0 °C. Bromoacetaldehyde dimethyl acetal (4.52 g, 3.16 mL, 26.7 mmol, 5.0 equiv.) was added dropwise via syringe and the resulting peach-colored solution was warmed to ambient temperature for 7 h at which time it was poured into ice water and extracted with Et_2O (3 x 30 mL). The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude mixture was evacuated for 12 h then dissolved in THF (50 mL) and aqueous HCl (1.0 M, 50 mL). The combined mixture was heated to 50 °C for 4 h. The mixture was then cooled, poured into water (50 mL) and extracted

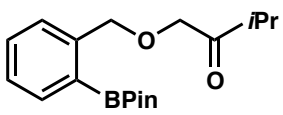
with EtOAc (3 x 50 mL). The combined organic phases were washed with saturated $NaHCO_3$ solution (50 mL), water (50 mL) dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (4:1 hexanes/EtOAc) to furnish 2-((2-bromobenzyl)oxy)acetaldehyde (920 mg, 4.02 mmol, 75%). R_f 0.18 (4:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.79 (s, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.50 (d, *J* = 1.8 Hz, 1H), 7.34 (t, *J* = 7.6 Hz, 1H), 7.19 (t, *J* = 7.6 Hz, 1H), 4.71 (s, 2H), 4.20 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 200.2, 136.4, 132.7, 129.5, 129.4, 127.6, 123.0, 75.82, 72.9; IR (film) υ_{max} 2870, 1738, 752 cm^{-1}; HRMS (ESI) calcd for $[C_9H_9O_2BrNa]^+$: *m/z* 250.9678, found 250.9678.

4-Methyl-1-((2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)



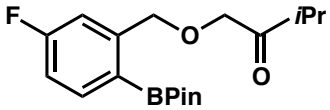
benzyl)oxy)pentan-2-one (7a) was prepared following the representative synthetic route and procedure for Grignard addition and borylation/oxidation sequence described above. R_f 0.50 (4:1 hexanes/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 1.2 Hz, 1H), 7.51 - 7.42 (m, 2H), 7.30 (td, *J* = 7.2, 1.5 Hz, 1H), 4.84 (s, 2H), 4.06 (s, 2H), 2.35 (d, *J* = 6.9 Hz, 2H), 2.22 - 2.11 (m, 1H), 1.34 (s, 12H), 0.92 (d, *J* = 6.6 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 209.1, 143.6, 135.8, 131.0, 127.8, 127.0 83.7, 75.8, 72.5, 47.8, 24.9, 24.2, 22.6. The boron-bound carbon was not detected likely due to quadrupolar relaxation; IR (film) υ_{max} 2977, 1718, 1349, 1146 cm^{-1}; HRMS (ESI) calcd for $[C_{19}H_{29}O_4BNa]^+$: *m/z* 355.2051, found 355.2049.

3-Methyl-1-((2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)



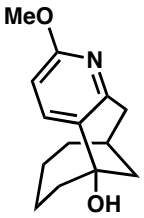
benzyl)oxy)butan-2-one (7b) was prepared following the representative synthetic route and procedure for Grignard addition and borylation/oxidation sequence described above. R_f 0.41 (4:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, *J* = 5.9 Hz, 1H), 7.48 (d, *J* = 7.2 Hz, 1H), 7.44 (td, *J* = 7.4, 1.4 Hz, 1H), 7.29 (t, *J* = 7.3 Hz, 1H), 4.85 (s, 2H), 4.16 (s, 2H), 2.84 (hept, *J* = 6.9 Hz, 1H), 1.34 (m, 12H), 1.09 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 212.5, 143.7, 135.8, 131.0, 127.9, 126.9, 83.7, 73.9, 72.5, 36.9, 24.9, 17.9. The boron-bound carbon was not detected likely due to quadropular relaxation; IR (film) υ_{max} 2976, 1712, 1349, 1146 cm^{-1}; HRMS (ESI) calcd for $[C_{18}H_{27}O_4BNa]^+$: *m/z* 341.1895, found 341.1894.

1-((5-fluoro-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)



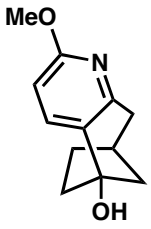
benzyl)oxy)-3-methylbutan-2-one (7c) was prepared following the representative synthetic route and procedure for alkylation of benzyl alcohols, Grignard addition and borylation/oxidation sequence above. R_f 0.50 (4:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 8.3, 6.5 Hz, 1H), 7.28 - 7.20 (m, 1H), 6.96 (td, *J* = 8.4, 2.5 Hz, 1H), 4.84 (s, 2H), 4.20 (s, 2H), 2.84 (hept, *J* = 6.8 Hz, 1H), 1.32 (s, 12H), 1.11 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 212.2, 165.0 (d, *J* = 250.6 Hz), 147.4 (d, *J* = 7.5 Hz), 138.2 (d, *J* = 8.3 Hz), 114.3 (d, *J* = 21.4 Hz), 113.7 (d, *J* = 20.1 Hz), 83.7, 74.1, 71.8 (d, *J* = 1.6 Hz), 37.0, 24.8, 17.9. The boron-bound carbon was not detected likely due to quadrupolar relaxation; IR (film) υ_{max} 2977, 1716, 1348, 1145 cm^{-1}; HRMS (EI) calcd for $[C_{18}H_{27}O_4FB]^+$: *m/z* 336.2023, found 336.2011.

Representative Experimental Procedure For Hydroarylation of Ketones 1a-1c (A): 2-methoxy-6,7,8,9,10,11-hexahydro-5*H*-5,10-methanocyclonona[*b*]pyridin-5-ol (4c):



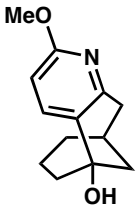
Inside a glove box, 3-((6-methoxy-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-2-yl)methyl)cycloheptanone (20.0 mg, 55 µmol, 1.0 equiv) was weighed into a 4 mL screw cap vial, equipped with a magnetic stir bar, and diluted with toluene (0.56 mL). DABCO (12.6 mg, 112 µmol, 2.0 equiv) and $[Rh(cod)(MeCN)_2]BF_4$ (2.1 mg, 5.6 µmol, 10 mol%) were then added and the vial was sealed with a Teflon cap and heated at 80 °C for 24 h at which time it was cooled to room temperature. The reaction mixture was then poured into water (1 mL) and extracted with EtOAc (3 x 1 mL) and the combined organic phases were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (2:1 hexanes/EtOAc) to provide 2-methoxy-6,7,8,9,10,11-hexahydro-5*H*-5,10-methanocyclonona[*b*]pyridin-5-ol (11.3 mg, 48.4 µmol, 87% yield).

2-Methoxy-6,7,8,9-tetrahydro-5*H*-5,8-methanocyclohepta[*b*]pyridin-5-ol (4a) was prepared following the representative experimental procedure A to yield the product (96%) after column chromatography (4:1 hexanes/EtOAc).

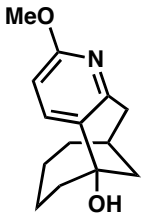


R_f 0.13 (5:1 hexanes/EtOAc); ^1H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, J = 8.5 Hz, 1H), 6.56 (d, J = 8.5 Hz, 1H), 3.89 (s, 3H), 3.08 (dd, J = 17.6, 4.1 Hz, 1H), 2.69 (d, J = 17.7 Hz, 1H), 2.63 (d, J = 5.6 Hz, 1H), 2.22 – 2.13 (m, 1H), 2.02 (dd, J = 10.7, 6.1 Hz, 1H), 1.98 – 1.92 (m, 2H), 1.84 (t, J = 13.5 Hz, 2H), 1.53 – 1.46 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.9, 152.1, 134.0, 133.4, 107.6, 78.7, 53.4, 43.3, 42.8, 42.6, 32.6, 28.9; IR (film) ν_{max} 3384, 1593, 1304, 1246 cm^{-1}; HRMS (ESI) calcd for $[C_{12}H_{16}O_2N]^+$: *m/z* 206.1176, found 206.1181.

2-Methoxy-5,6,7,8,9,10-hexahydro-5,9-methanocycloocta[*b*]pyridin-5-ol (4b) was prepared following representative experimental procedure A to yield the product (90%) after column chromatography (4:1 hexanes/EtOAc). R_f 0.19 (4:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.4 Hz, 1H), 6.56 (d, *J* = 8.5 Hz, 1H), 3.90 (s, 3H), 3.11 (dd, *J* = 18.6, 7.2 Hz, 1H), 2.63 (d, *J* = 18.5 Hz, 1H), 2.49 (br s, 1H), 1.91 (d, *J* = 12.5 Hz, 1H), 1.82 (dd, *J* = 11.5, 2.1 Hz, 1H), 1.78 - 1.49 (m, 6H), 1.14 - 1.01 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.6, 154.7, 135.1, 130.9, 107.9, 70.9, 53.3, 41.0, 40.8, 38.0, 32.4, 29.4, 20.8; IR (film) υ_{max} 3385, 2931, 1580, 1478, 1310, 1023, 824 cm^{-1}; HRMS (ESI) calcd for $[C_{13}H_{18}O_2N]^+$: *m/z* 220.1332, found 220.1331.



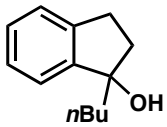
2-methoxy-6,7,8,9,10,11-hexahydro-5*H*-5,10-methanocyclonona[*b*]pyridin-5-ol (4c) was prepared following representative experimental procedure A to yield the product (87%) after column chromatography (2:1 hexanes/EtOAc). R_f 0.34 (2:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.5 Hz, 1H), 6.61 (d, *J* = 8.5 Hz, 1H), 3.92 (s, 3H), 2.99 (dd, *J* = 16.9, 5.2 Hz, 1H), 2.60 (d, *J* = 17.4 Hz, 1H), 2.47 – 2.39 (m, 1H), 2.34 (dt, *J* = 13.6, 2.7 Hz, 1H), 2.18 - 2.07 (m, 2H), 1.94 (dt, *J* = 13.5, 3.2 Hz, 1H), 1.76 (dd, *J* = 12.5, 4.9 Hz, 1H), 1.73 - 1.63 (m, 2H), 1.55 - 1.46 (m, 1H), 1.43 - 1.33 (m, 1H), 1.09 - 0.99 (m, 1H), 0.84 - 0.72 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.5, 154.1, 137.1, 129.6, 108.6, 73.1, 53.1, 44.2, 42.3, 40.8, 33.5, 28.3, 25.6, 24.1; IR (film) υ_{max} 3363, 2923, 1598, 1478, 1032, 830 cm^{-1}; HRMS (ESI) calcd for $[C_{14}H_{20}NO_2]^+$: *m/z* 234.1489, found 234.1487.



Representative Experimental Procedure For Hydroarylation of Ketones 6a-8c (B): **1-Isobutyl-1,2,3,4-tetrahydronaphthalen-1-ol (6e)**: Inside a glove box, 6-methyl-1-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)heptan-4-one (30 mg, 91 μmol, 1.0 equiv) was weighed into a 4 mL screw cap vial, equipped with a magnetic stir bar, and diluted with benzene (0.91 mL). DABCO (20 mg, 0.18 mmol, 2.0 equiv) and $[Rh(cod)(MeCN)_2]BF_4$ (3.5 mg, 9.1 μmol, 10 mol%) were then added and the vial was sealed with a Teflon cap and heated at 80 °C for 24 h at which time it was cooled to room temperature. The reaction mixture was then poured into water (1 mL) and extracted with EtOAc (3 x 1 mL) and the combined organic phases were dried over sodium sulfate, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (4:1 hexanes/EtOAc; buffered with 1% triethylamine) to provide 1-Isobutyl-1,2,3,4-tetrahydronaphthalen-1-ol (15.4 mg, 75 μmol, 83% yield).

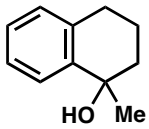
1-Propyl-2,3-dihydro-1*H*-inden-1-ol (6a) was prepared following the representative experimental procedure B to yield the product (81%) after column chromatography (10:1 hexanes/EtOAc). R_f 0.33 (4:1 hexanes/EtOAc); ^1H NMR (600 MHz, $CDCl_3$) δ 7.34 - 7.31 (m, 1H), 7.26 - 7.21 (m, 3H), 3.00 (ddd, J = 16.0, 8.6, 4.8 Hz, 1H), 2.86 - 2.79 (m, 1H), 2.36 - 2.27 (m, 1H), 2.12 - 2.06 (m, 1H), 1.89 (td, J = 13.0, 4.6 Hz, 1H), 1.76 - 1.68 (m, 2H), 1.52 - 1.43 (m, 1H), 1.40 - 1.30 (m, 1H), 0.93 (t, J = 7.3 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 147.7, 143.1, 128.2, 126.6, 124.9, 122.8, 83.8, 42.8, 40.0, 29.5, 17.6, 14.6; IR (film) υ_{max} 3362, 2957, 1172 cm^{-1}; HRMS (EI) calcd for dehydrated compound $[C_{12}H_{14}]^+$: *m/z* 158.1096, found 158.1098.

1-Butyl-2,3-dihydro-1*H*-inden-1-ol (6b) was prepared following the representative



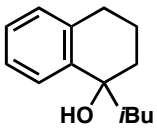
experimental procedure B to yield the product (58%) after column chromatography (10:1 hexanes/EtOAc). R_f 0.34 (4:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 - 7.30 (m, 1H), 7.26 - 7.20 (m, 3H), 3.01 3(ddd, *J* = 16.1, 8.5, 4.9 Hz, 1H), 2.83 (ap, *J* = 7.9 Hz, 1H), 2.31 (ddd, *J* = 13.2, 8.3, 4.9 Hz, 1H), 2.09 (ddd, *J* = 13.2, 8.6, 6.4 Hz, 1H), 1.95 -1.87 (m, 1H), 1.76 (dd, *J* = 11.9, 4.1 Hz, 1H), 1.77 -1.67 (m, 1H), 1.46 - 1.38 (m, 1H), 1.37 - 1.27 (m, 3H), 0.90 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.6, 143.1, 128.2, 126.6, 124.9, 122.8, 83.8, 40.2, 40.0, 29.5, 26.4, 23.2, 14.1; IR (film) υ_{max} 3364, 2956, 1169 cm^{-1}; HRMS (EI) calcd for $[C_{13}H_{18}O]^+$: *m/z* 190.1358, found 190.1354.

1-Methyl-1,2,3,4-tetrahydronaphthalen-1-ol (6d) was prepared following the representative



experimental procedure B to yield the product (78%) after column chromatography (10:1 hexanes/EtOAc). ^{1}H NMR Spectral data are fully consistent with previously reported values.[5]

1-Isobutyl-1,2,3,4-tetrahydronaphthalen-1-ol (6e) was prepared following the representative

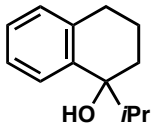


experimental procedure B to yield the product (83%) after column chromatography (4:1 hexanes/EtOAc; buffered with 1% triethylamine). R_f 0.48 (4:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.6 Hz, 1H), 7.21 (t, *J* = 7.1 Hz, 1H), 7.15 (td, *J* = 7.4, 1.5 Hz, 1H), 7.06 (d, *J* = 6.2 Hz, 1H), 2.89 - 2.66 (m, 2H), 2.17 - 2.00 (m, 1H), 1.98 - 1.70 (m, 6H), 1.68 (s, 1H), 1.08 (d, *J* = 6.1 Hz, 3H), 0.81 (d, *J* = 6.1 Hz, 3H); ^{13}C

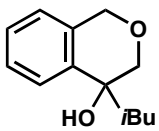
[5] M. Hatano, O. Ito, S. Suzuki, K. Ishihara, *J. Org. Chem.,* 2010, **75**, 5008.

NMR (125 MHz, CDCl3) δ 143.3, 136.4, 128.9, 127.0, 126.4, 126.1, 73.1, 50.8, 36.2, 29.9, 24.7, 24.5, 24.5, 19.9; IR (film) υ_{max} 3416, 2951, 1450, 757; HRMS (EI) calcd for $[C_{14}H_{20}O]^+$: *m/z* 204.1514, found 204.1512.

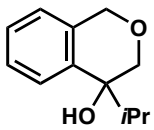
1-Isopropyl-1,2,3,4-tetrahydronaphthalen-1-ol (6f) was prepared following the representative experimental procedure B to yield the product (94%) after column chromatography (4:1 hexanes/EtOAc; buffered with 1% triethylamine). ^{1}H NMR spectral data are fully consistent with previously reported values.[5]



4-Isobutylisochroman-4-ol (8a) was prepared following the representative experimental procedure B to yield the product (62%) after column chromatography (4:1 hexanes/EtOAc; buffered with 1% triethylamine). R_f 0.33 (4:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.7 Hz, 1H), 7.32 - 7.26 (m, 1H), 7.23 (td, *J* = 7.3, 1.2 Hz, 1H), 6.99 (d, *J* = 7.4 Hz, 1H), 4.79 (d, *J* = 14.9 Hz, 1H), 4.74 (d, *J* = 15.0 Hz, 1H), 3.92 (d, *J* = 14.6 Hz, 1H), 3.83 (d, *J* = 11.5 Hz, 1H), 2.16 (s, 1H), 1.86 - 1.84 (m, 2H), 1.81 - 1.77 (m, 1H), 1.57 (br s, 1H), 0.99 (d, *J* = 6.5 Hz, 3H), 0.87 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.6, 133.8, 127.4, 127.1, 126.0, 123.9, 74.4, 69.9, 68.7, 47.1, 24.59, 24.56, 24.0; IR (film) υ_{max} 3435, 2954, 1100, 946 cm^{-1}; HRMS (EI) calcd for $[C_{13}H_{18}O_2]^+$: *m/z* 206.1307, found 206.1302.

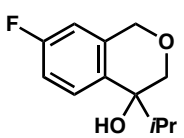


4-Isopropylisochroman-4-ol (8b) was prepared by following the representative experimental procedure B to yield the product (67%) after column chromatography (4:1



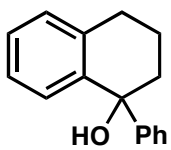
hexanes/EtOAc; buffered with 1% triethylamine). R_f 0.28 (4:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.7 Hz, 1H), 7.29 (t, *J* = 7.5 Hz, 1H), 7.23 (td, *J* = 7.4, 1.2 Hz, 1H), 6.99 (d, *J* = 7.5 Hz, 1H), 4.68 (aq, *J* = 14.8 Hz, 2H), 4.94 (d, *J* = 11.3 Hz, 1H), 3.85 (d, *J* = 11.3 Hz, 1H), 2.43 (hept, *J* = 7.1 Hz, 1H), 2.27 (s, 1H), 1.11 (d, *J* = 6.9 Hz, 3H), 0.79 (d, *J* = 7.0 Hz, 1H); ^{13}C NMR (125 MHz, CDCl3) δ 138.7, 134.7, 127.2, 125.9, 124.0, 71.5, 71.3, 68.6, 35.1, 18.3, 16.3 (one sp^2 carbon was not observed, likely due to signal overlap); IR (film) υ_{max} 3435, 2962, 1450, 1383, 1102, 760 cm^{-1}; HRMS (EI) calcd for $[C_{12}H_{16}O_2]^+$: *m/z* 192.1150, found 192.1144.

7-fluoro-4-isopropylisochroman-4-ol (8c) was prepared by following the representative



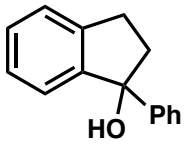
experimental procedure B to yield the product (80%) after column chromatography (4:1 hexanes/EtOAc; buffered with 1% triethylamine). R_f 0.29 (4:1 hexanes/EtOAc, 1% triethylamine); R_f 0.25 (4:1 hexanes/EtOAc, 1% triethylamine); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (dd, *J* = 8.7, 5.5 Hz, 1H), 6.98 (td, *J* = 8.6, 2.7 Hz, 1H), 6.69 (dd, *J* = 9.1, 2.4 Hz, 1H), 4.69 (aq, *J* = 15.1 Hz, 2H), 3.91 (d, *J* = 11.8 Hz, 1H), 3.83 (d, *J* = 11.8 Hz, 1H), 2.4 (hept, *J* = 7.0 Hz, 1H), 2.26 (br s, 1H), 1.09 (d, *J* = 6.9 Hz, 3H), 0.78 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.6 (d, *J* = 246.8 Hz), 136.9 (d, *J* = 7.0 Hz), 134.5 (d, *J* = 3.1 Hz), 128.2 (d, *J* = 8.2 Hz), 114.5 (d, *J* = 21.5 Hz), 110.4 (d, *J* = 21.5 Hz), 71.5, 71.1 , 68.4 (d, *J* = 2.1 Hz), 35.2, 18.2, 16.3; IR (film) υ_{max} 3434, 2964, 1250, 1110 cm^{-1}; HRMS (EI) calcd for $[C_{12}H_{15}O_2F]$: *m/z* 210.1056, found 210.1051.

Representative Experimental Procedure For Hydroarylation of Ketones 9-11 (C): 1-phenyl-1,2,3,4-tetrahydronaphthalen-1-ol (14): Inside a glove box, 1-phenyl-4-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)butan-1-one (30 mg,

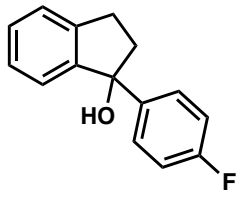


86 μmol, 1.0 equiv) was weighed into a 4 mL screw cap vial, equipped with a magnetic stir bar, and diluted with benzene (0.86 mL). 1,2-Bis(diphenylphosphino)ethane (3.4 mg, 8.6 μmol, 10 mol%) and $[Rh(cod)(OH)]_2$ (2.0 mg, 4.3 μmol, 5.0 mol%) were then added and the vial was sealed with a Teflon cap and heated at 80 °C for 24 h at which time it was cooled to room temperature. The reaction mixture was then poured into water (1 mL) and extracted with EtOAc (3 x 1 mL) and the combined organic phases were dried over sodium sulfate, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (10:1 hexanes/EtOAc; buffered with 1% triethylamine) to provide 1-phenyl-1,2,3,4-tetrahydronaphthalen-1-ol (13.8 mg, 61.5 μmol, 72% yield). ^{1}H NMR spectral data agree are fully consistent with previously reported values.[6]

1-phenyl-2,3-dihydro-1*H*-inden-1-ol (12) was prepared by following representative experimental procedure C to yield the product (85%) after column chromatography (10:1 hexanes/EtOAc; buffered with 1% triethylamine). ^{1}H NMR spectral data are fully consistent with previously reported values.[6]



1-(4-fluorophenyl)-2,3-dihydro-1*H*-inden-1-ol (13) was prepared by following the representative experimental procedure C to yield the product (74%) after column chromatography (10:1 hexanes/EtOAc; buffered with 1% triethylamine). R_f 0.36 (4:1 hexanes/EtOAc). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 - 7.28 (m, 4H), 7.23 (td, J = 7.5, 1.6 Hz, 1H), 7.09 (d, J = 7.6 Hz, 1H),



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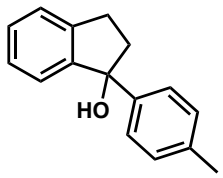
[6] M. Hatano, T. Miyamoto, K. Ishihara, *Org. lett.,* 2007, **9**, 4535.

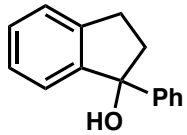
7.04 - 6.96 (m, 2H), 3.17 (dt, J = 16.2, 7.3 Hz, 1H), 2.94 (dt, J = 16.0, 6.4 Hz, 1H), 2.47 (dd, J = 7.4, 6.3 Hz, 2H), 2.07 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.8 (d, J = 245.1 Hz), 147.7, 144.0, 142.1 (d, J = 3.1 Hz), 128.6, 127.4 (d, J = 8.0 Hz), 127.1, 125.0, 123.9, 114.7 (d, J = 21.2 Hz), 85.2, 44.9, 29.8; IR (film) υ_{max} 3395, 1223, 1158 cm^{-1}; HRMS (EI) calcd for $[C_{15}H_{13}OF]^+$: *m/z* 228.0950, found 228.0949.

Representative Experimental Procedure For The Asymmetric Hydroarylation of Ketones



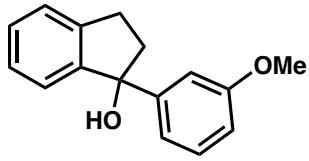
16a-16f (D): On the bench, 3-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-1-(*p*-tolyl)propan-1-one (50 mg, 0.14 mmol, 1.0 equiv), Josiphos SL-J002-1 (8.6 mg, 16 μmol, 11 mol%), and $[Rh(cod)(OH)]_2$ (3.3 mg, 7.2 μmol, 10 mol%) were weighed into a 5 mL conical vial, equipped with a magnetic stir bar,. The vial was sealed with a Teflon septum, diluted with toluene (1.4 mL) and stirred at rt for 1 h. It was then heated to 85 °C and held at this temperature for 22 h at which time it was cooled to room temperature. The reaction mixture was then poured into water (2 mL) and extracted with EtOAc (3 x 2 mL). The combined organic phases were dried over sodium sulfate, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (4:1 hexanes/EtOAc; buffered with 1% triethylamine) to give 1-(*p*-tolyl)-2,3-dihydro-1*H*-inden-1-ol (29. mg, 13 µmol, 90% yield).

1-phenyl-2,3-dihydro-1*H*-inden-1-ol (16a) was prepared in enantio-enriched form using the representative experimental procedure D over 72 h to yield the product (78%)



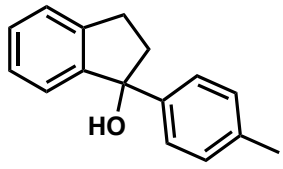
after column chromatography (4:1 hexanes/EtOAc; buffered with 1% triethylamine). ^{1}H NMR spectral data are fully consistent with previously reported values.[6] The enantiomeric excess was determined to be 94% by chiral HPLC. The retention times for the enatiomers were 10.24 and 15.50 min.

1-(3-methoxyphenyl)-2,3-dihydro-1*H*-inden-1-ol (16b) was prepared in enantio-enriched form



using representative experimental procedure D over 48 h to yield the product (85%) after column chromatography (10:1 → 4:1 hexanes/EtOAc; buffered with 1% triethylamine). R_f 0.30 (4:1 hexanes/EtOAc, 1% triethylamine). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 - 7.27 (m, 2H), 7.27 - 7.18 (m, 2H), 7.11 (d, *J* = 7.5 Hz, 1H), 7.02 (t, *J* = 1.2 Hz, 1H), 6.91 (d, *J* = 7.7 Hz, 1H), 6.81 (dd, *J* = 8.1, 2.8 Hz, 1H), 3.80 (s, 3H), 3.17 (dt, *J* = 15.2, 7.2 Hz, 1H), 3.96 (ddd, *J* = 15.9, 7.9, 5.2 Hz, 1H), 2.63 - 2.36 (m, 2H), 2.08 (br s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.4, 148.1, 147.8, 144.1, 129.1, 128.5, 127.1, 125.0, 124.0, 118.2, 112.1, 111.6, 85.5, 55.2, 44.7, 29.9; IR (film) υ_{max} 3431, 1600, 1045 cm^{-1}; HRMS (EI) calcd for $[C_{16}H_{15}O_2]^+$: *m/z* 240.1150, found 240.1154. The enantiomeric excess was determined to be 95% by chiral HPLC. The retention times for the enatiomers were 15.24 and 25.22 min.

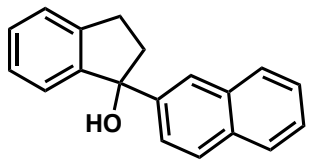
1-(*p*-tolyl)-2,3-dihydro-1*H*-inden-1-ol (16c) was prepared in enantio-enriched form using



representative experimental procedure D over 22 h to yield the product (90%) after column chromatography (10:1 → 4:1 hexanes/EtOAc; buffered with 1% triethylamine). R_f 0.41 (4:1 hexanes/EtOAc). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 - 7.27 (m, 4H), 7.23 (t, *J* = 7.3 Hz, 1H), 7.15 (d, *J* = 8.0 Hz,

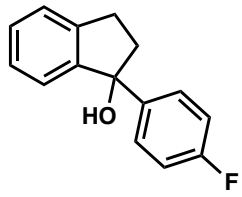
2H), 7.11 (d, *J* = 7.5 Hz, 1H), 3.17 (dt, *J* = 15.1, 7.2 Hz, 1H), 3.94 (ddd, *J* = 15.9, 7.8, 5.1 Hz, 1H), 2.62 - 2.42 (m, 2H), 2.36 (s, 3H), 2.10 (br s, 1H).^{13}C NMR (125 MHz, $CDCl_3$) δ 148.0, 144.1, 143.4, 136.5, 128.7, 128.4, 127.0, 125.6, 124.9, 123.9, 85.4, 44.8, 29.9, 21.0; IR (film) υ_{max} 3406, 817, 761 cm^{-1}; HRMS (EI) calcd for $[C_{16}H_{16}O]^+$: *m/z* 224.1201, found 224.1206. The enantiomeric excess was determined to be 94% by chiral HPLC. The retention times for the enatiomers were 8.93 and 13.81 min.

1-(naphthalen-2-yl)-2,3-dihydro-1*H*-inden-1-ol (16d) was prepared in enantio-enriched form

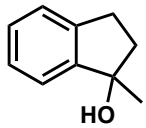


using representative experimental procedure D over 98 h to yield the product (50%) after column chromatography (10:1 → 4:1 hexanes/EtOAc; buffered with 1% triethylamine). R_f 0.39 (4:1 hexanes/EtOAc, 1% triethylamine). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.84 - 7.79 (m, 3H), 7.48 - 7.43 (m, 3H), 7.35 (dt, *J* = 14.6, 7.5 Hz, 2H), 7.25 (m, 1H), 7.11 (d, *J* = 7.5 Hz, 1H), 3.24 (dt, *J* = 15.3, 7.4 Hz, 1H), 3.02 (ddd, *J* = 16.0, 8.1, 4.5 Hz, 1H), 2.66 - 2.58 (m, 1H), 2.58 - 2.50 (m, 1H), 2.20 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.9, 144.2, 143.6, 132.9, 132.4, 128.6, 128.2, 127.8, 127.5, 127.1, 126.1, 125.8, 125.0, 124.6, 124.1, 124.0, 85.7, 44.6, 30.0; IR (film) υ_{max} 3394, 2941 cm^{-1}; HRMS (EI) calcd for $[C_{19}H_{16}O]^+$: *m/z* 260.1201, found 260.1205. The enantiomeric excess was determined to be 93% by chiral HPLC. The retention times for the enatiomers were 17.62 and 24.73 min.

1-(4-fluorophenyl)-2,3-dihydro-1*H*-inden-1-ol (16e) was prepared in enantio-enriched form using general experimental procedure D over 70 h to yield the product (54%) after column chromatography (10:1 hexanes/EtOAc; buffered with 1% triethylamine). The enantiomeric excess was determined to be 92% by chiral HPLC. The retention times for the enatiomers were 8.87 and 14.11 min.



1-methyl-2,3-dihydro-1*H*-inden-1-ol (16f) was prepared in enantio-enriched form using representative experimental procedure D over 17 h to yield the product (90%) after column chromatography (10:1 → 4:1 hexanes/EtOAc; buffered with 1% triethylamine). R_f 0.43 (2:1 hexanes/EtOAc,) ^{1}H NMR spectral data were fully consistent with previously reported values.[7] The enantiomeric excess was determined to be 95% by chiral HPLC. The retention times for the enatiomers were 8.92 and 10.59 min.



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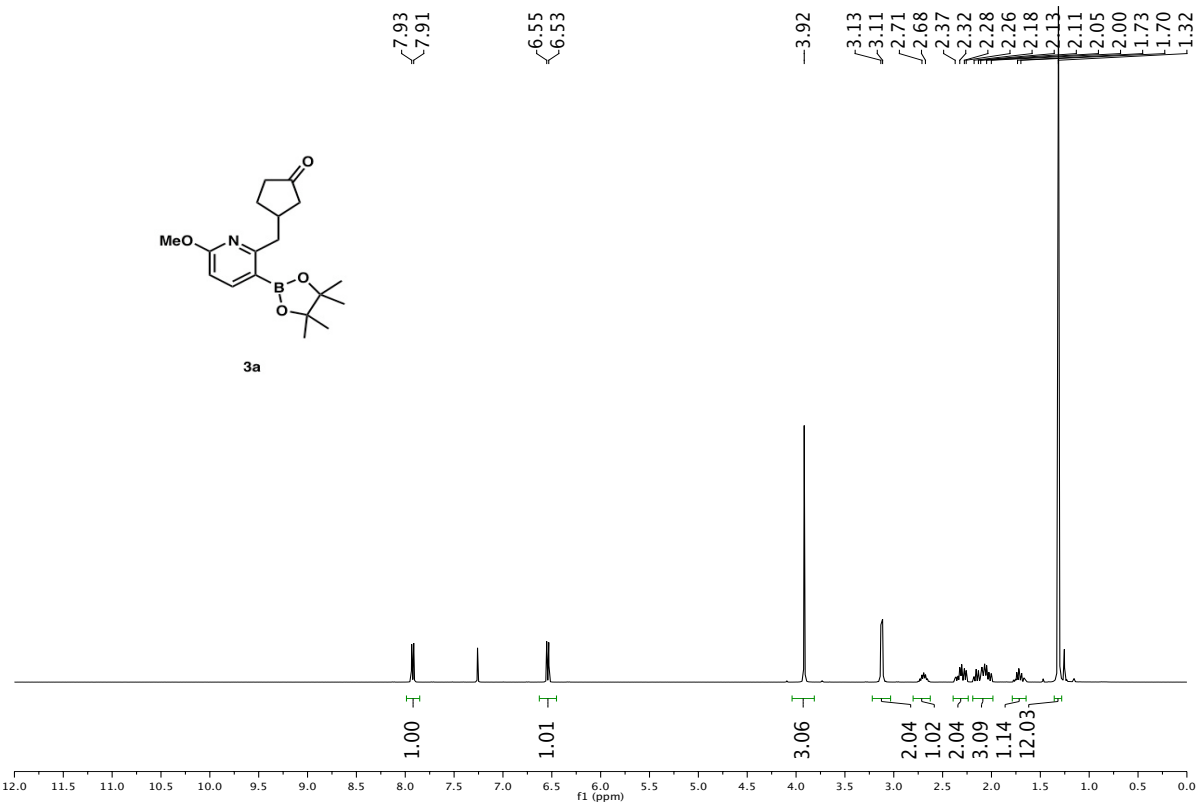
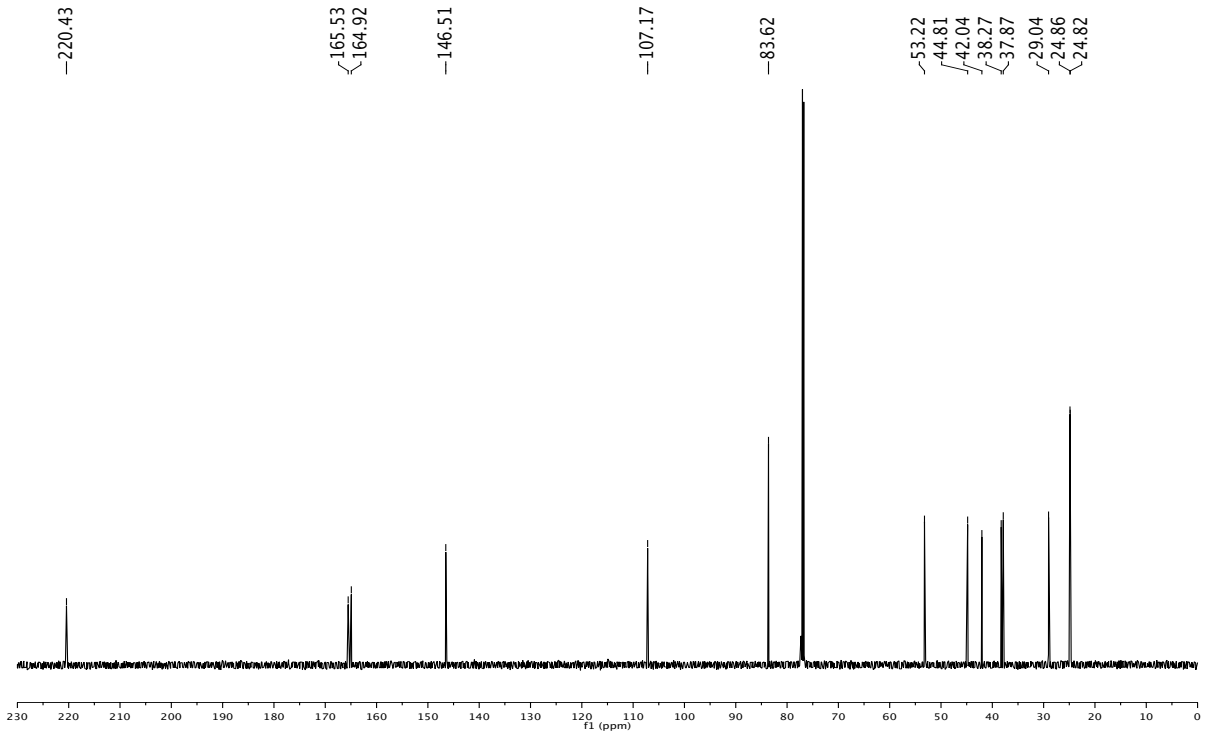
[7] M. Bietti, O. Lanzalunga, M. Salamone, *J. Org. Chem.,* 2005, **70**, 1417.


7.93
7.91
6.55
6.53
3.92
3.13
3.11
2.71
2.68
2.37
2.32
2.28
2.26
2.18
2.13
2.11
2.05
2.00
1.73
1.70
1.32
MeO
N
O
B
O
O
3a
1.00
1.01
3.06
2.04
1.02
2.04
3.09
1.14
12.03
f1 (ppm)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165.53
164.92
146.51
107.17
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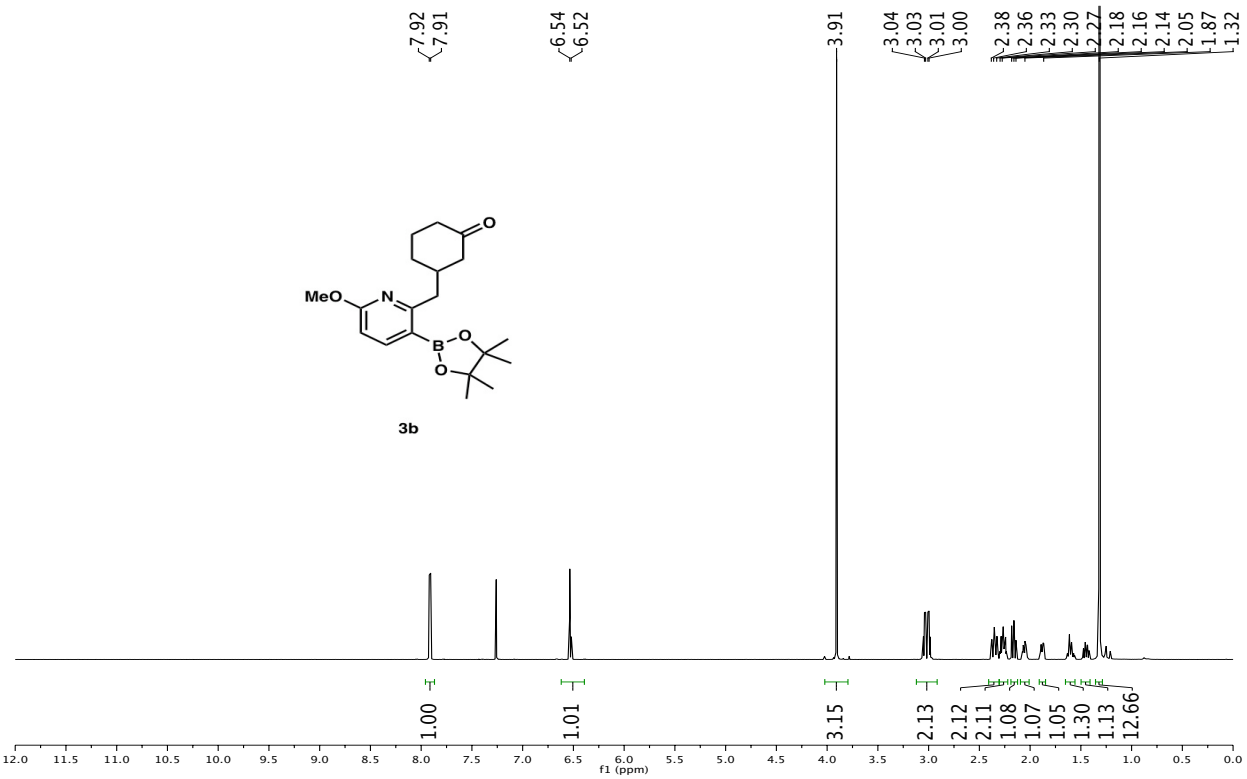
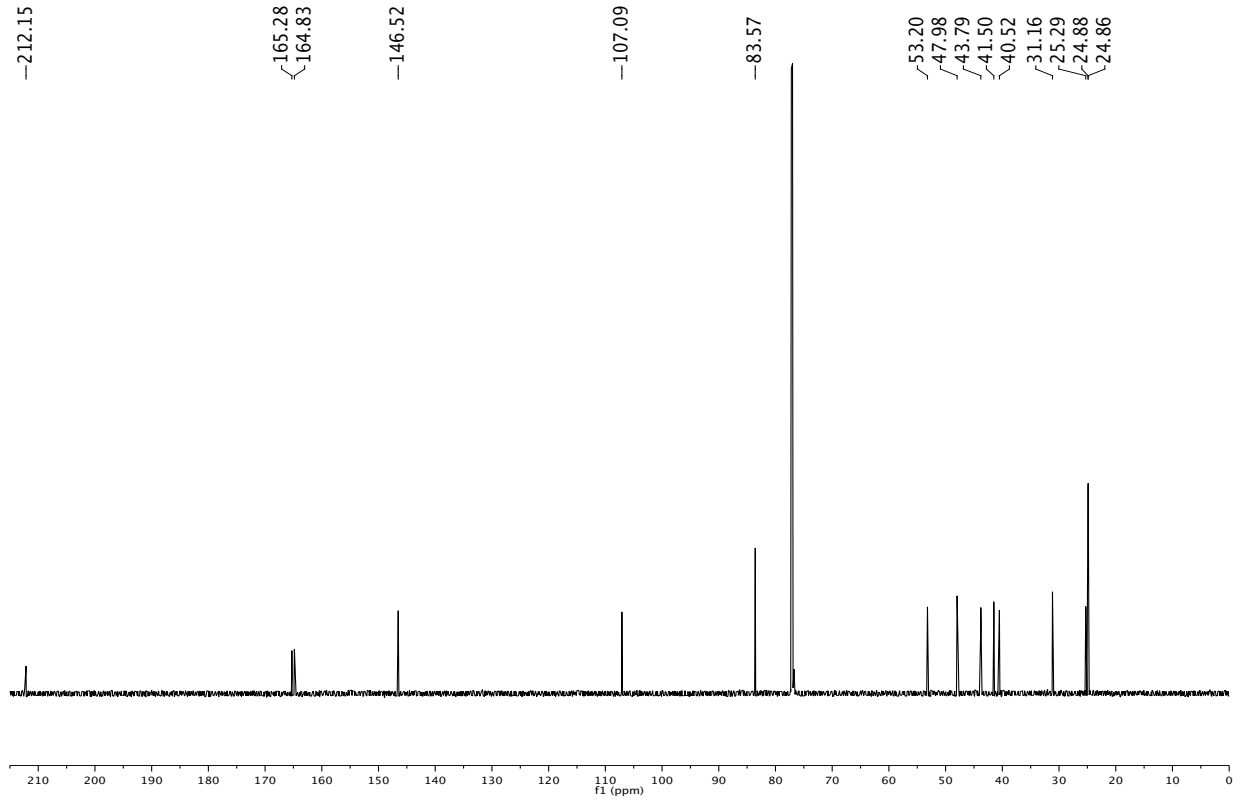
53.22
44.81
42.04
38.27
37.87
29.04
24.86
24.82
f1 (ppm)


7.92
7.91
6.54
6.52
3.91
3.04
3.03
3.01
3.00
2.38
2.36
2.33
2.30
2.27
2.18
2.16
2.14
2.05
1.87
1.32
MeO
N
O
B
O
O
3b
1.00
1.01
3.15
2.13
2.12
2.11
1.08
1.07
1.05
1.30
1.13
12.66
f1 (ppm)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165.28
164.83
146.52
107.09
83.57
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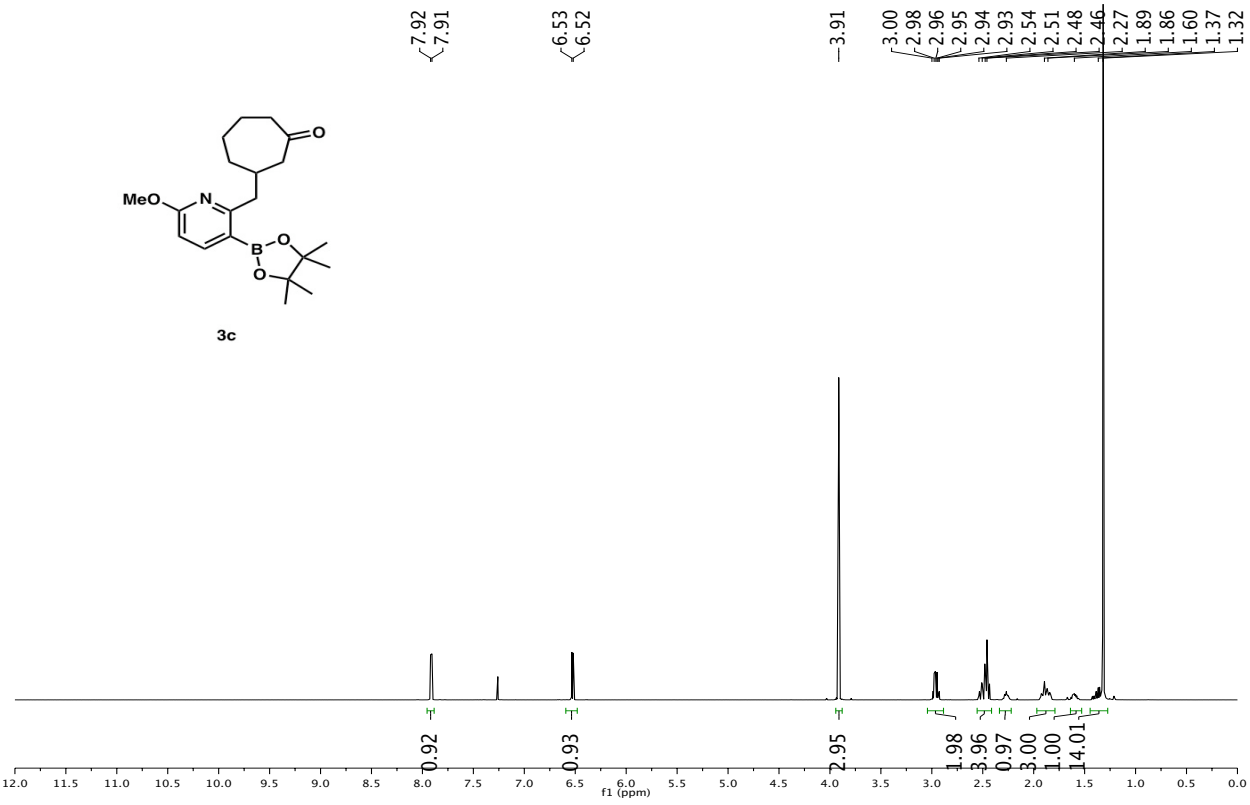
47.98
43.79
41.50
40.52
31.16
25.29
24.88
24.86
f1 (ppm)


7.92
7.91
6.53
6.52
3.91
3.00
2.98
2.96
2.95
2.94
2.93
2.54
2.51
2.48
2.46
2.27
1.89
1.86
1.60
1.37
1.32
MeO
N
O
B
O
O
3c
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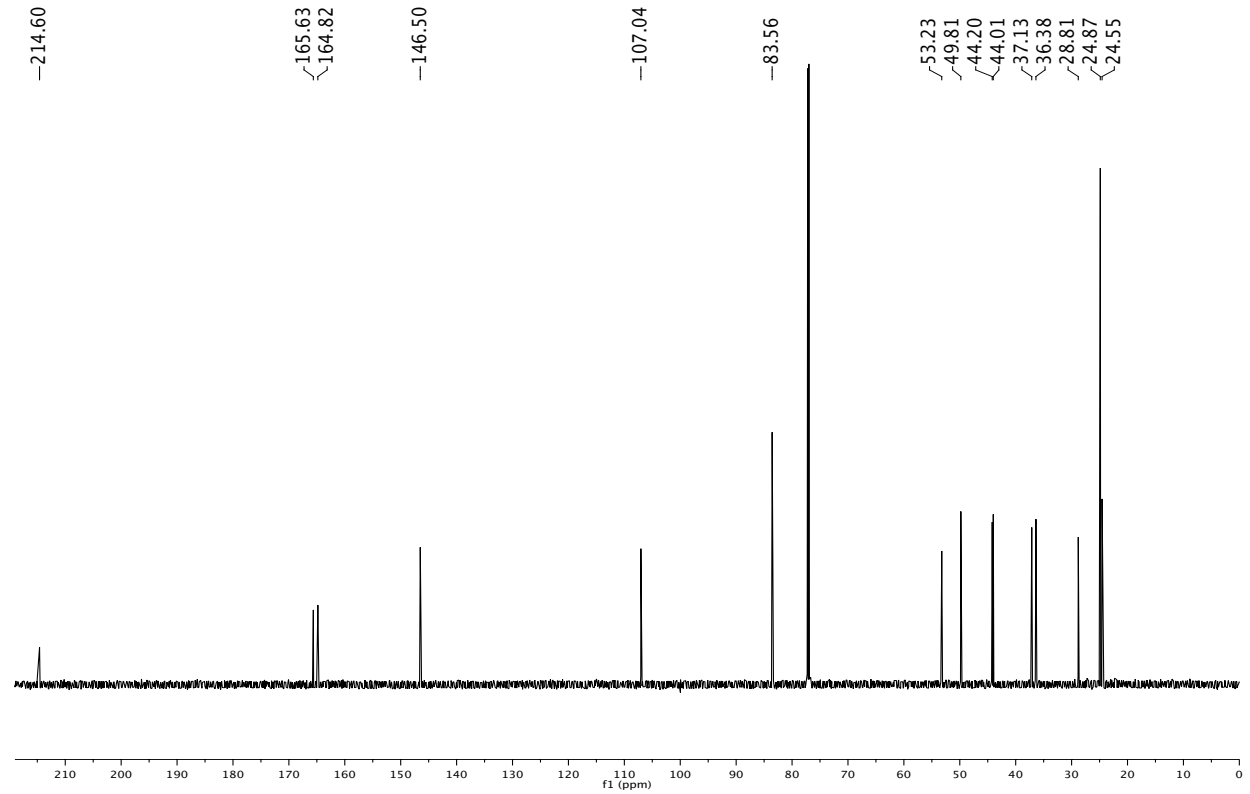
0.93
2.95
1.98
3.96
0.97
3.00
1.00
14.01
f1 (ppm)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49.81
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44.01
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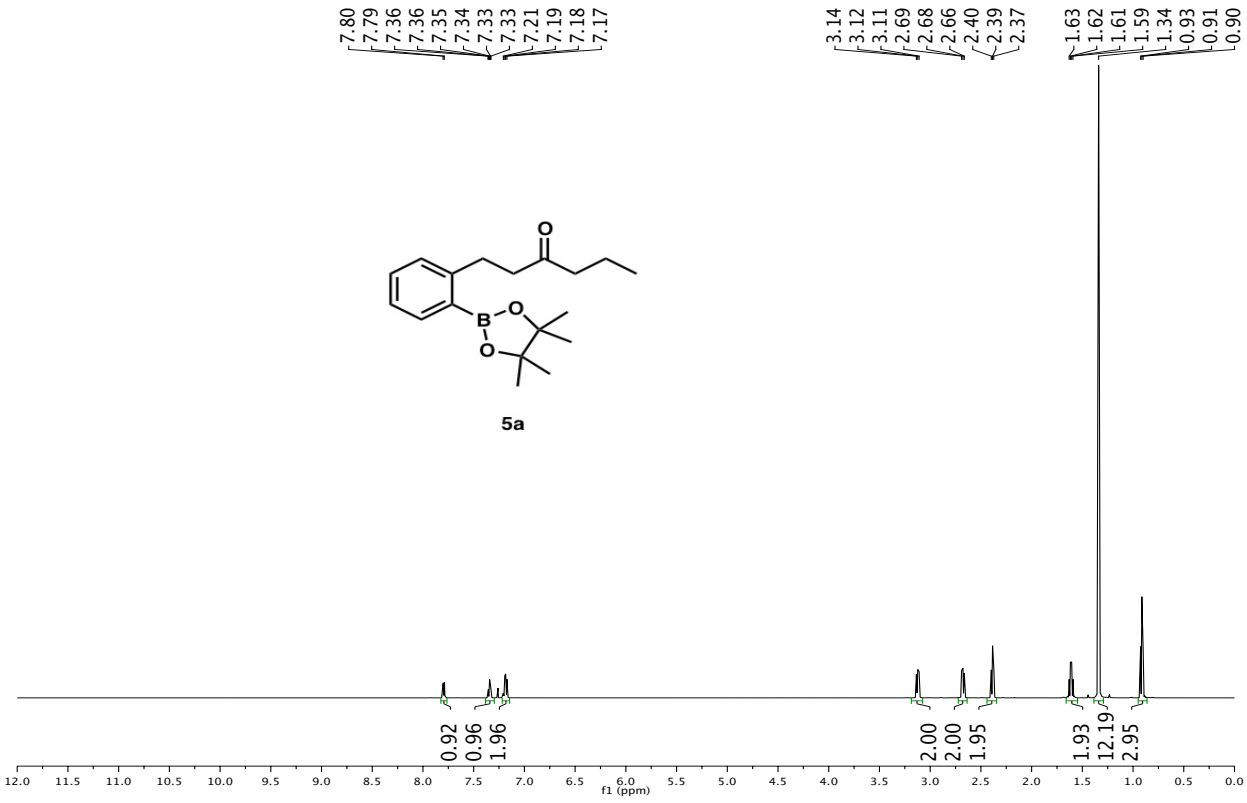
28.81
24.87
24.55
f1 (ppm)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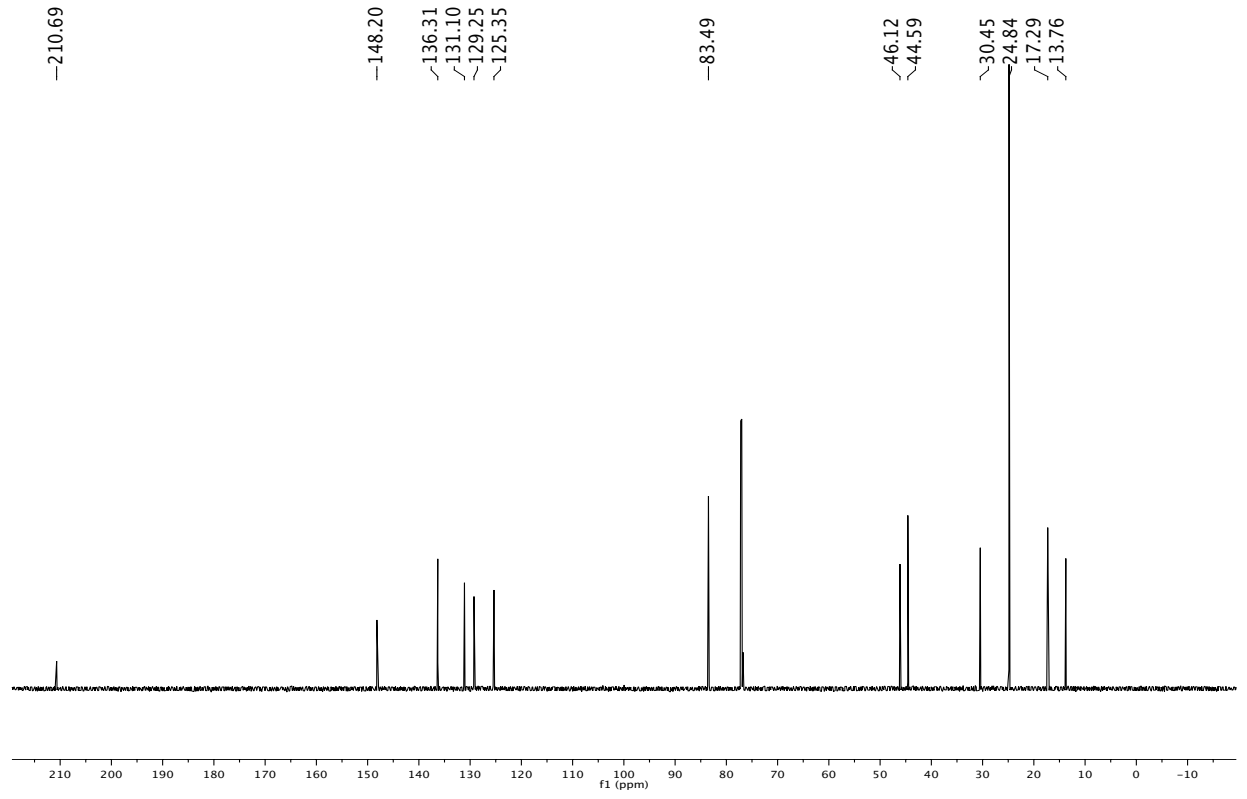
7.79
7.36
7.36
7.35
7.34
7.33
7.33
7.21
7.19
7.18
7.17
3.14
3.12
3.11
2.69
2.68
2.66
2.40
2.39
2.37
1.63
1.62
1.61
1.59
1.34
0.93
0.91
0.90
O
B
O
O
0.92
0.96
1.96
2.00
2.00
1.95
1.93
12.19
2.95
f1 (ppm)

5a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148.20
136.31
131.10
129.25
125.35
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46.12
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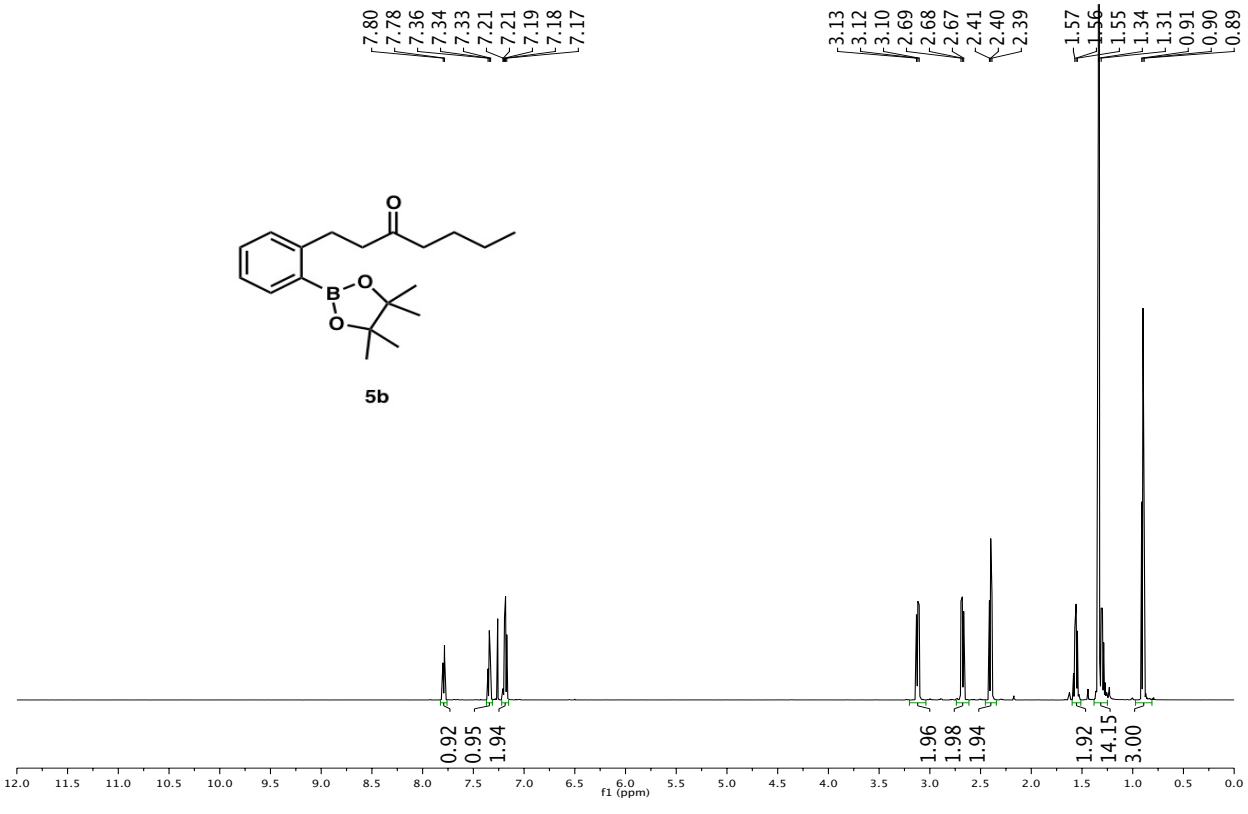
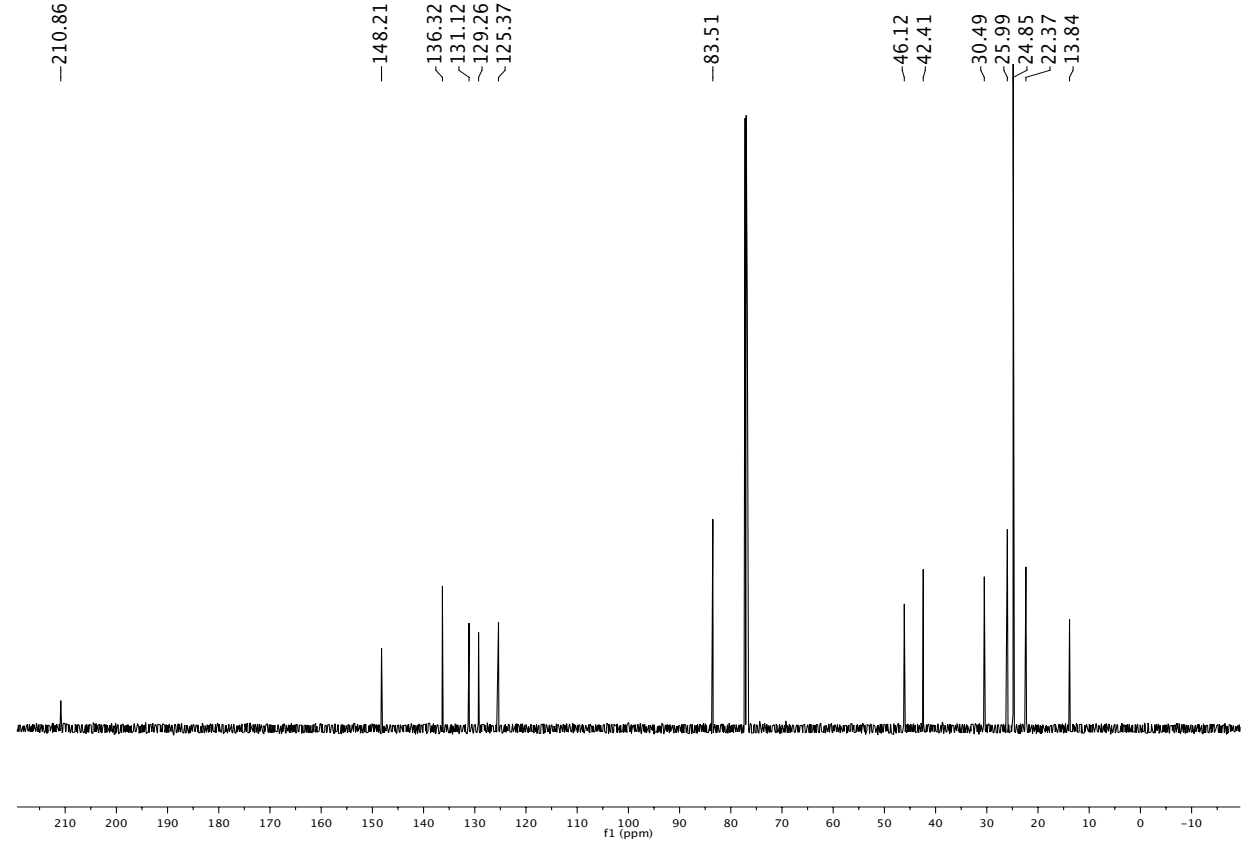
30.45
24.84
17.29
13.76
f1 (ppm)


7.80
7.78
7.36
7.34
7.33
7.21
7.21
7.19
7.18
7.17
3.13
3.12
3.10
2.69
2.68
2.67
2.41
2.40
2.39
1.57
1.56
1.55
1.34
1.31
0.91
0.90
0.89
O
B
O
O
0.92
0.95
1.94
1.96
1.98
1.94
1.92
14.15
3.00
f1 (ppm)

5b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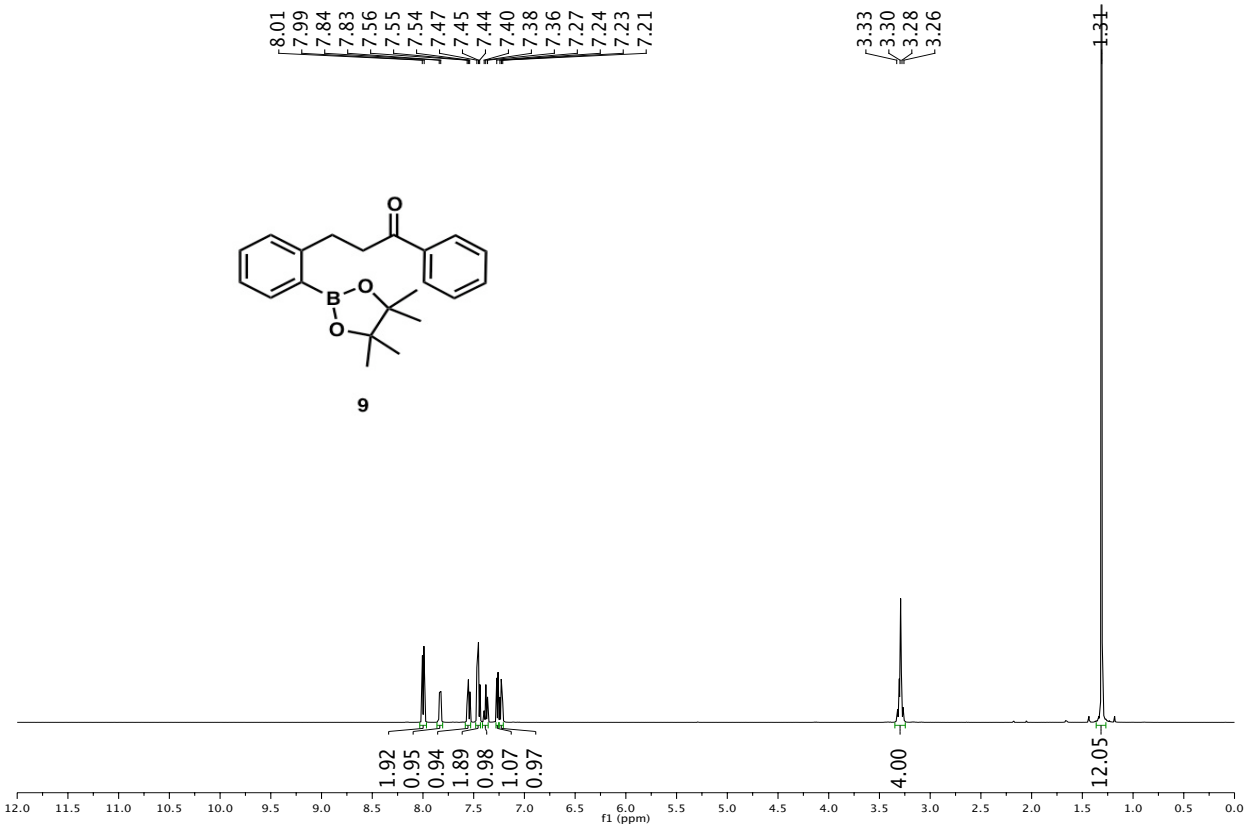
136.32
131.12
129.26
125.37
83.51
46.12
42.41
30.49
25.99
24.85
22.37
13.84
f1 (ppm)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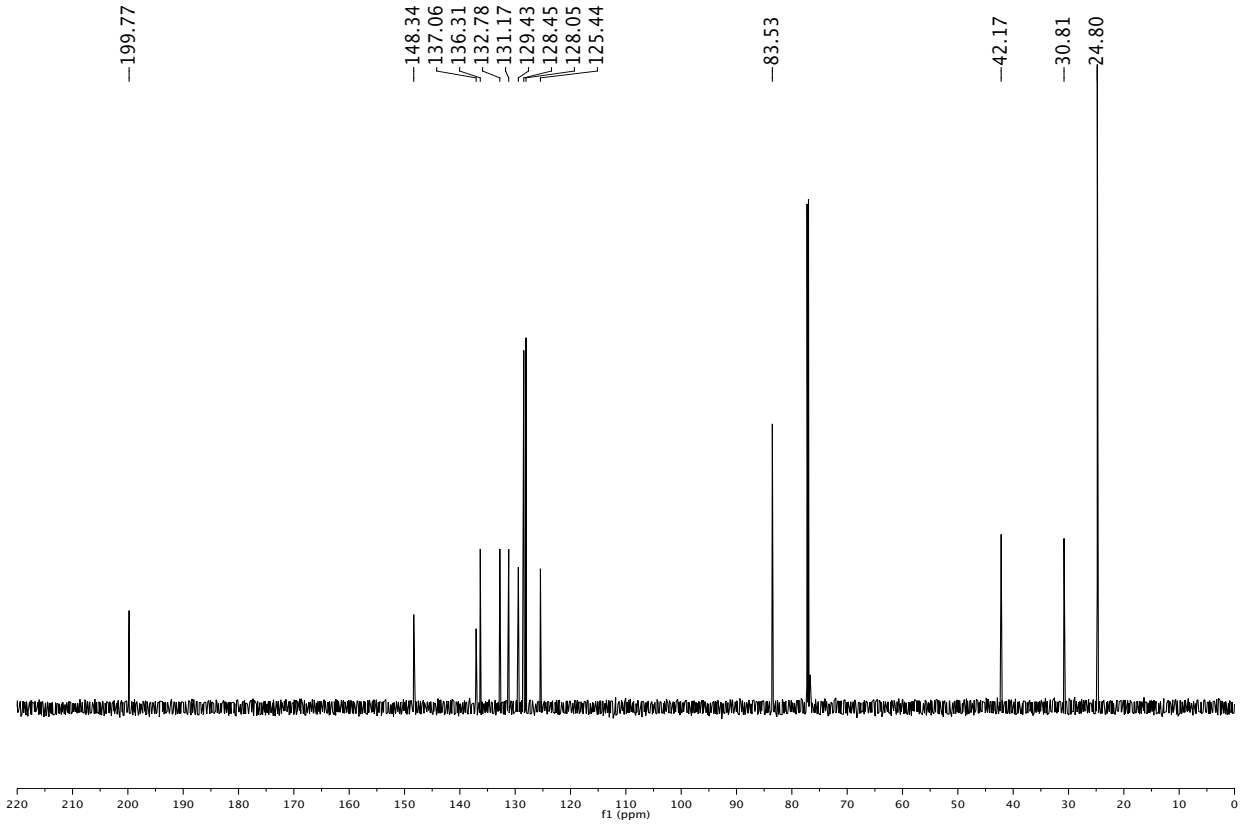
7.99
7.84
7.83
7.56
7.55
7.54
7.47
7.45
7.44
7.40
7.38
7.36
7.27
7.24
7.23
7.21
3.33
3.30
3.28
3.26
1.31
O
B
O
O
1.92
0.95
0.94
1.89
0.98
1.07
0.97
4.00
12.05
f1 (ppm)

9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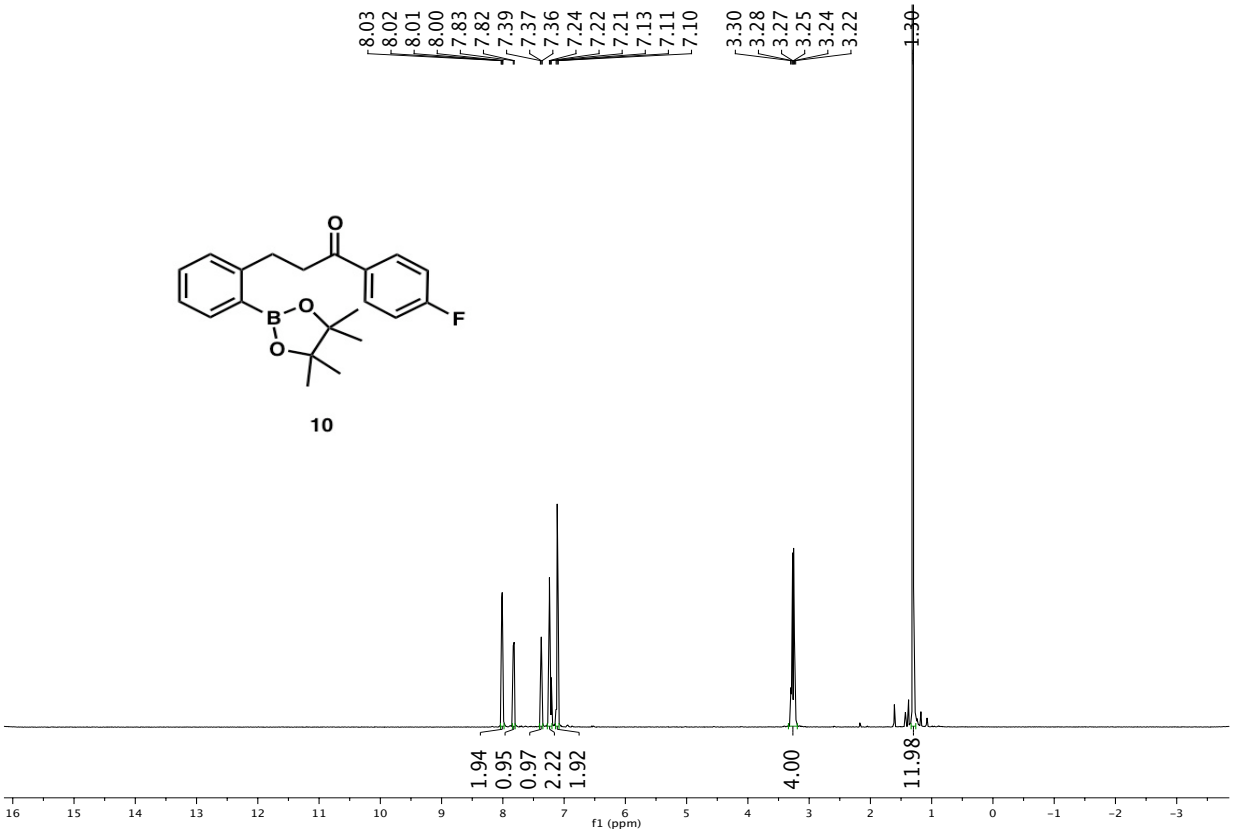
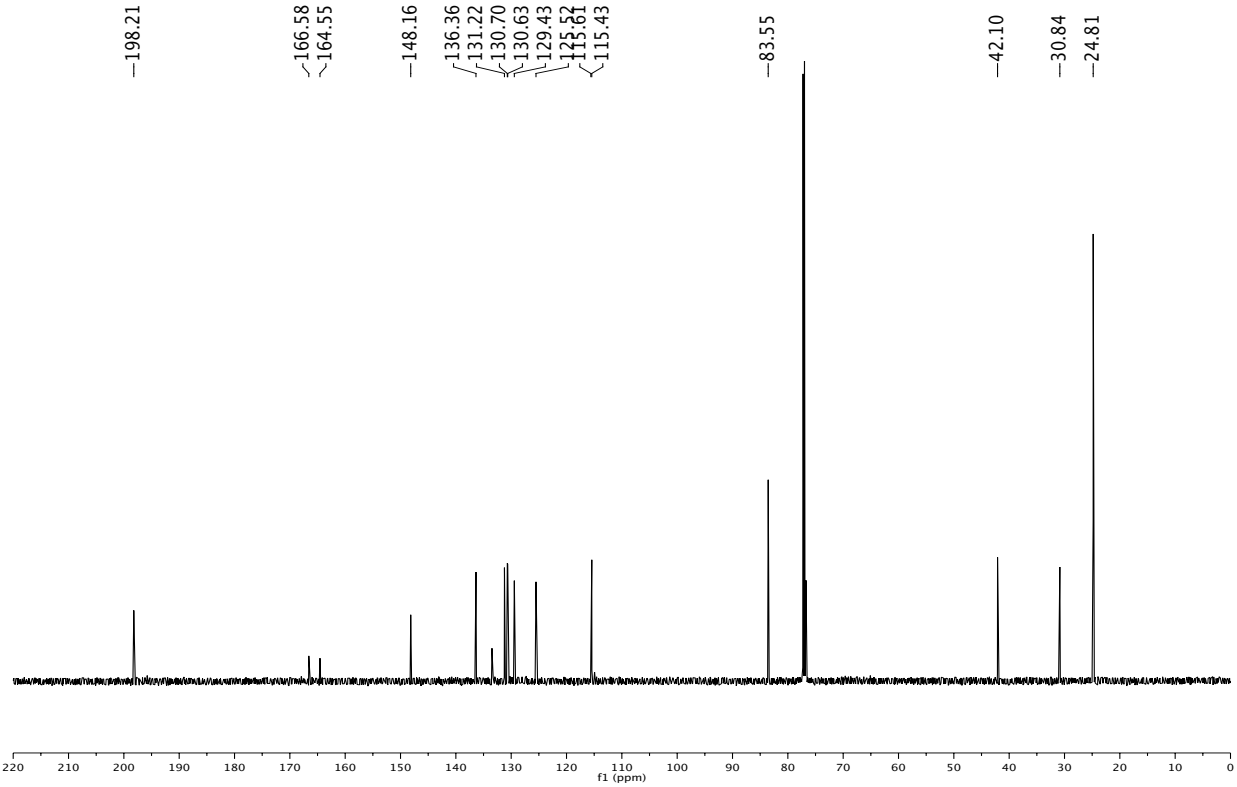
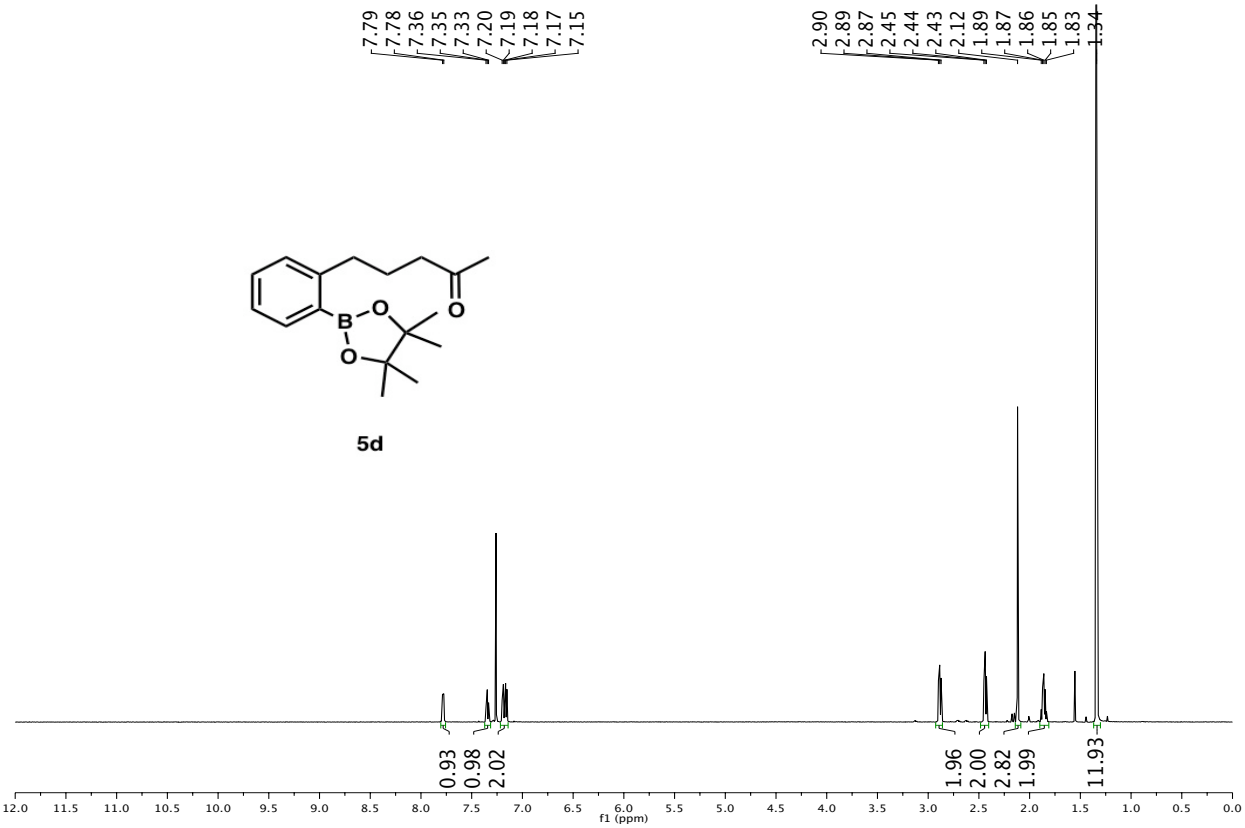
128.05
125.44
83.53
42.17
30.81
24.80
f1 (ppm)

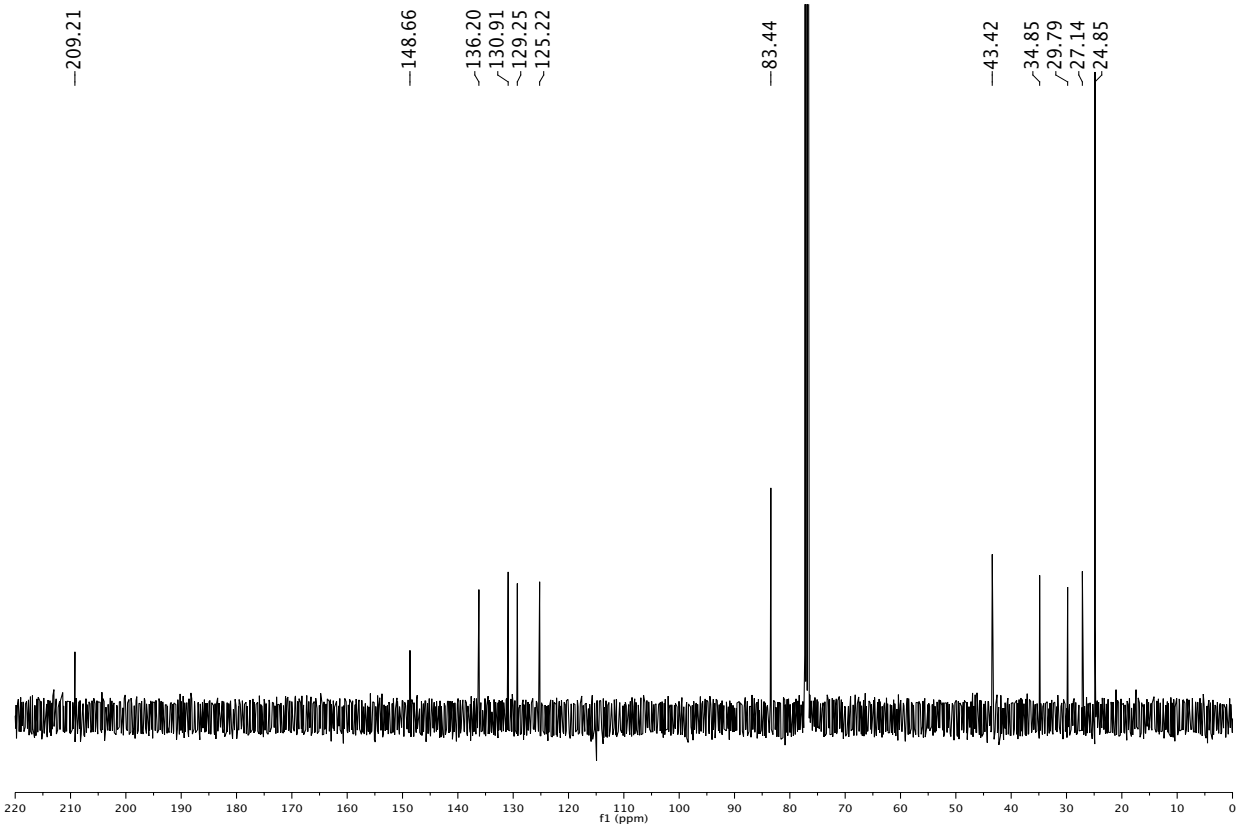


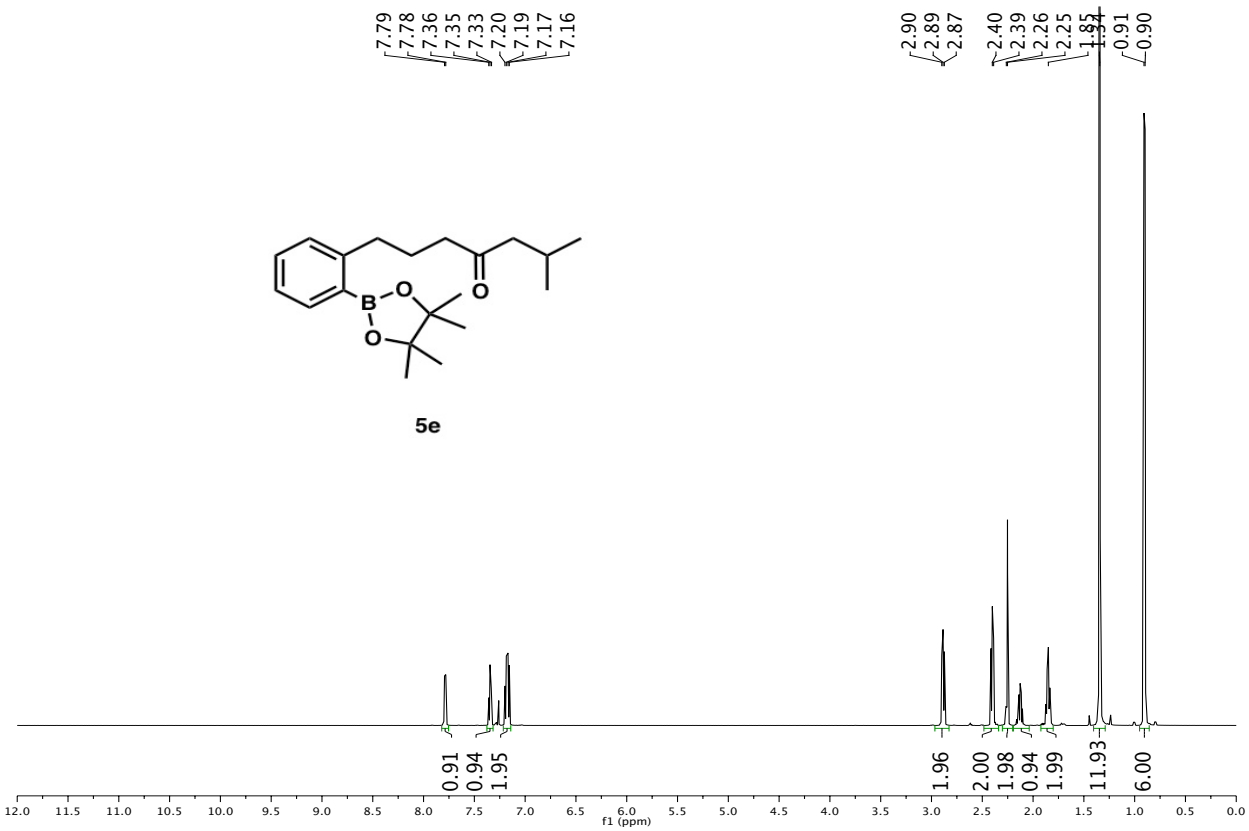
10



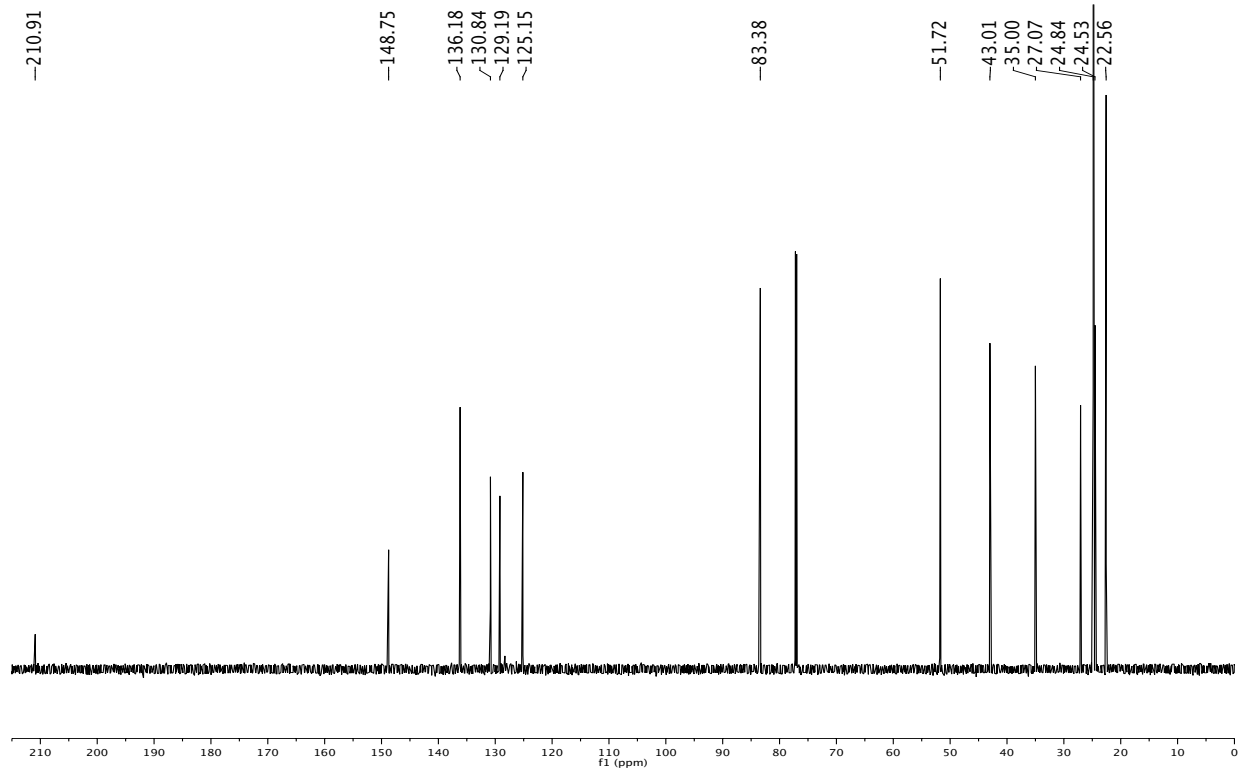


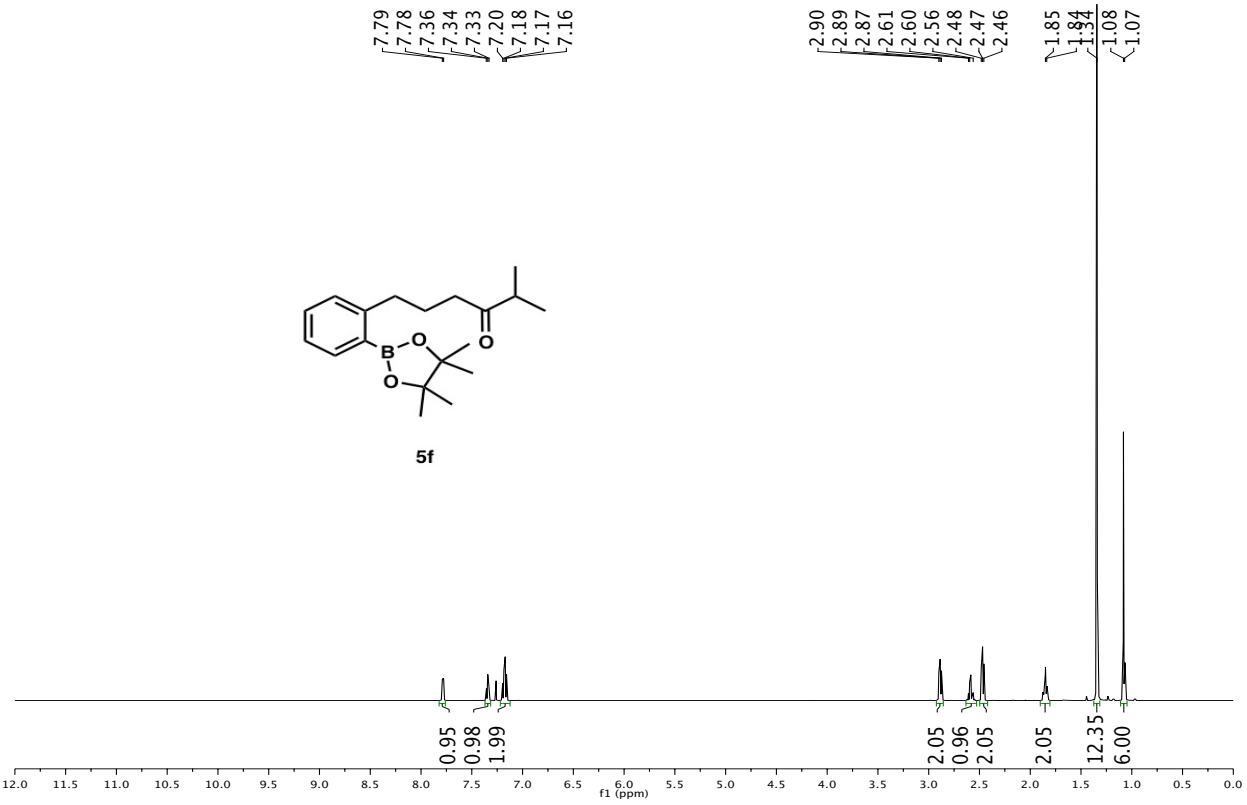
5d





5e

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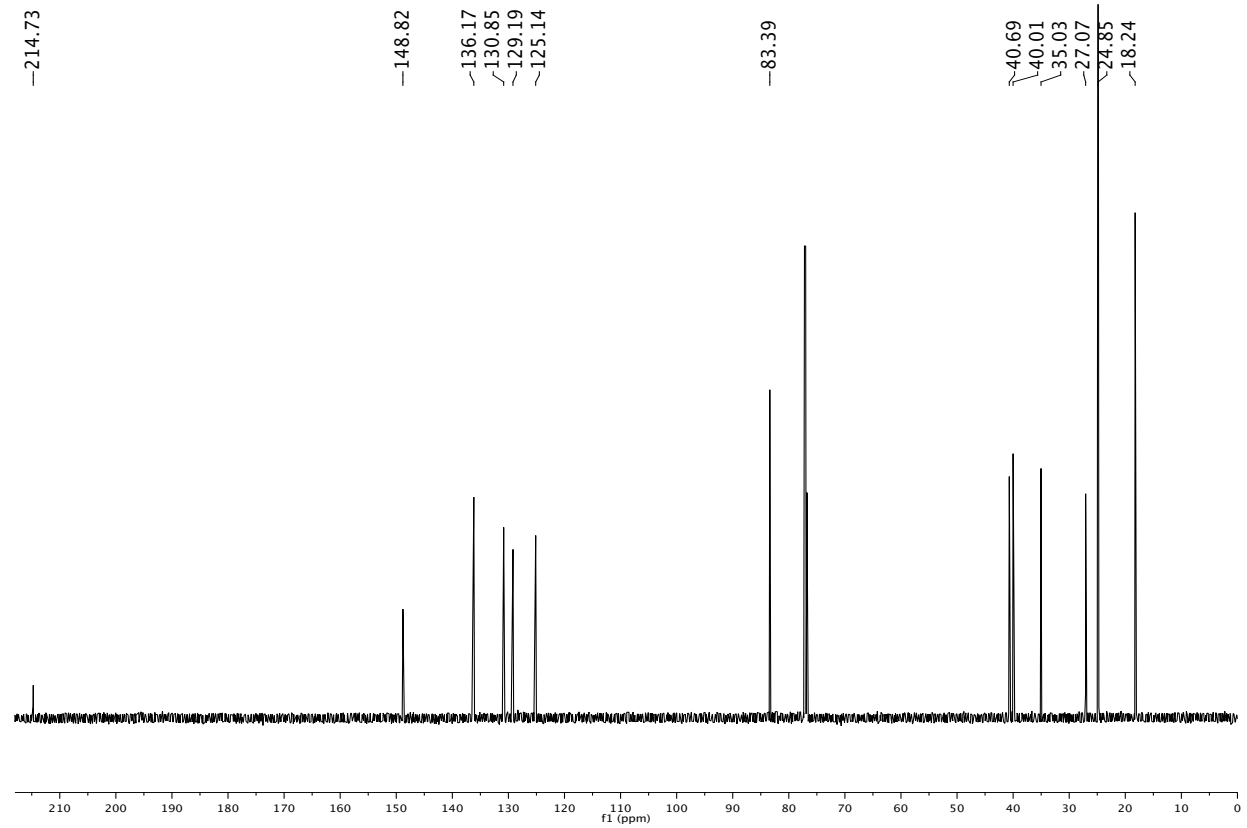
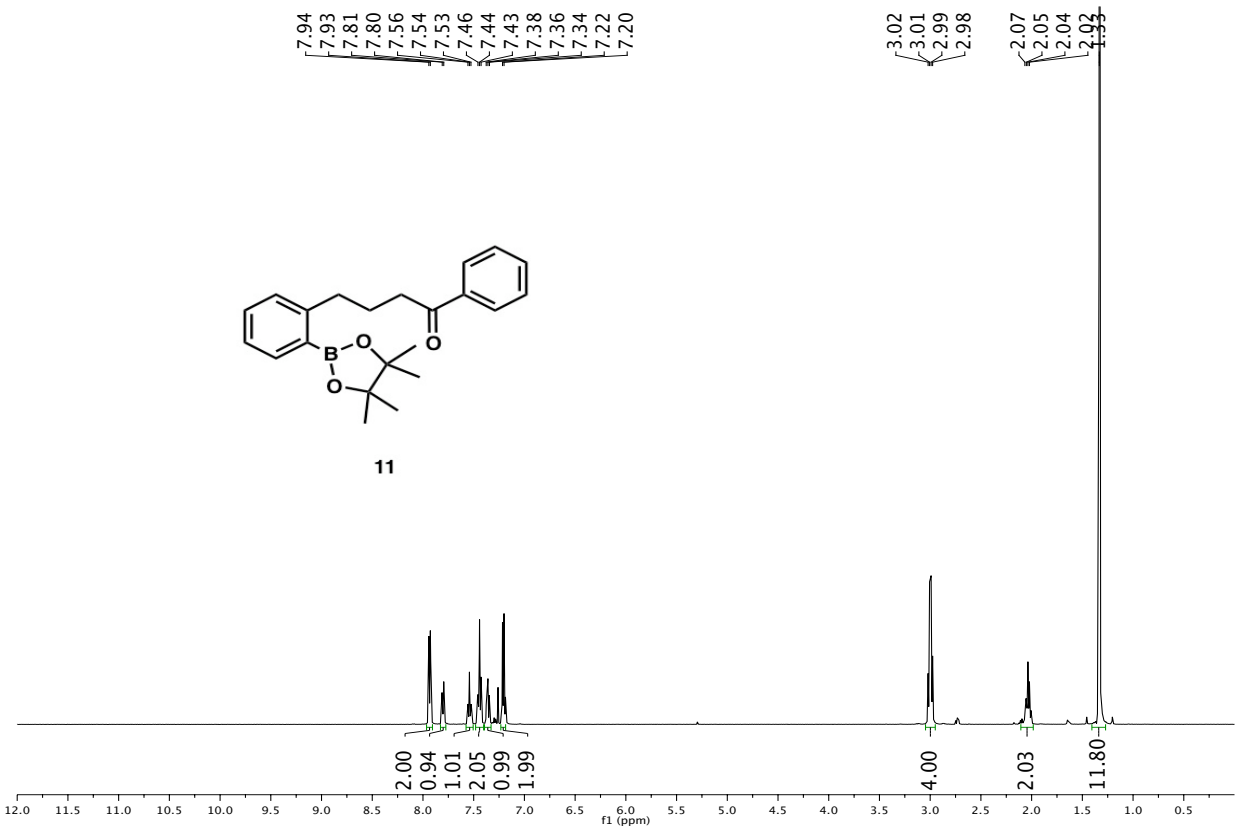
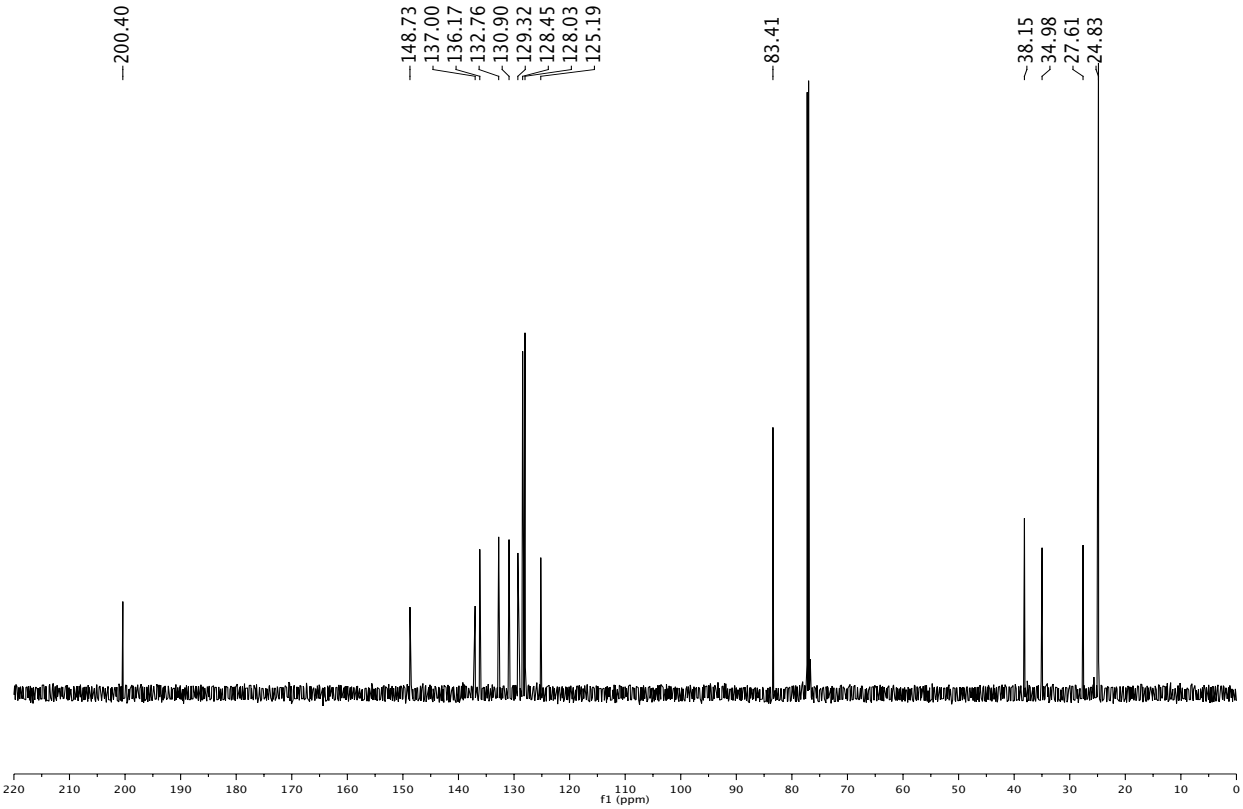
7.78
7.36
7.34
7.33
7.20
7.18
7.17
7.16
2.90
2.89
2.87
2.61
2.60
2.56
2.48
2.47
2.46
1.85
1.84
1.34
1.08
1.07
B
O
O
O
0.95
0.98
1.99
2.05
0.96
2.05
2.05
12.35
6.00
f1 (ppm)

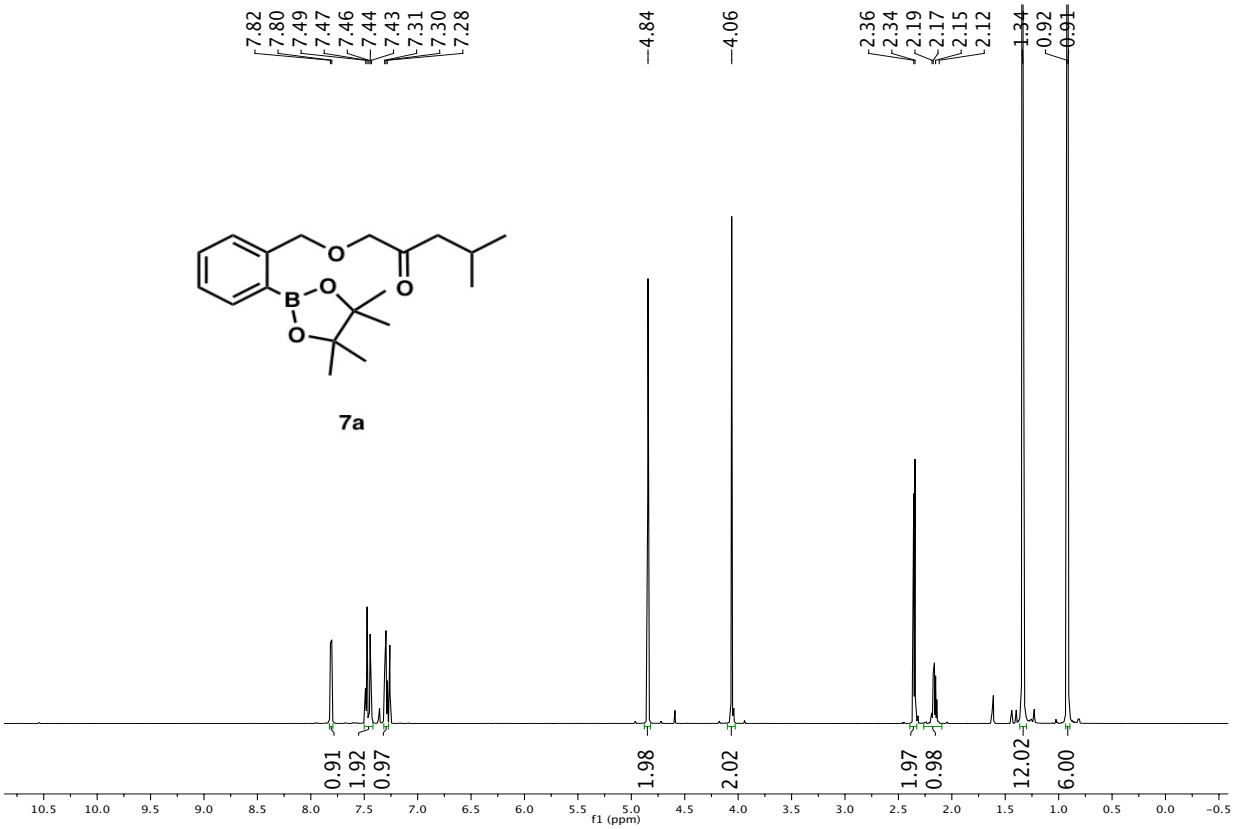
5f


214.73
148.82
136.17
130.85
129.19
125.14
83.39
40.69
40.01
35.03
27.07
24.85
18.24
f1 (ppm)



11

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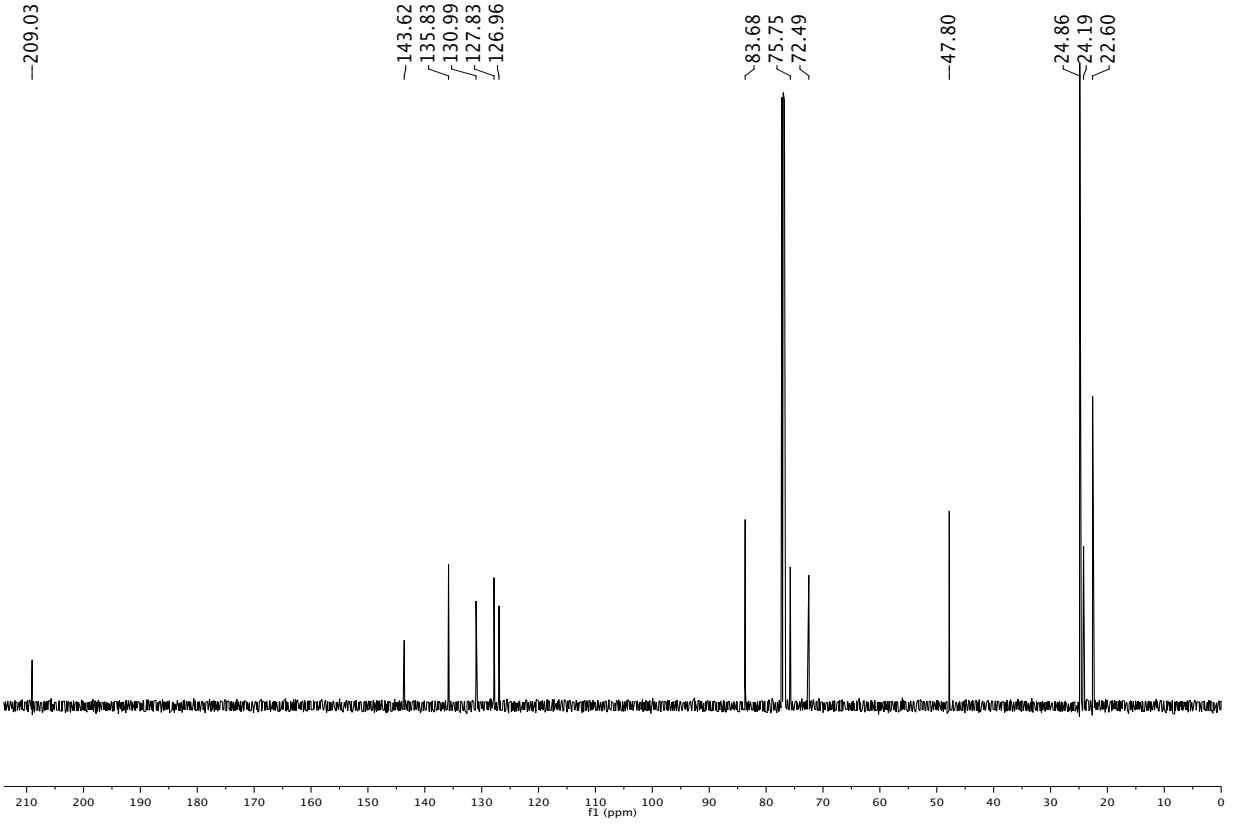
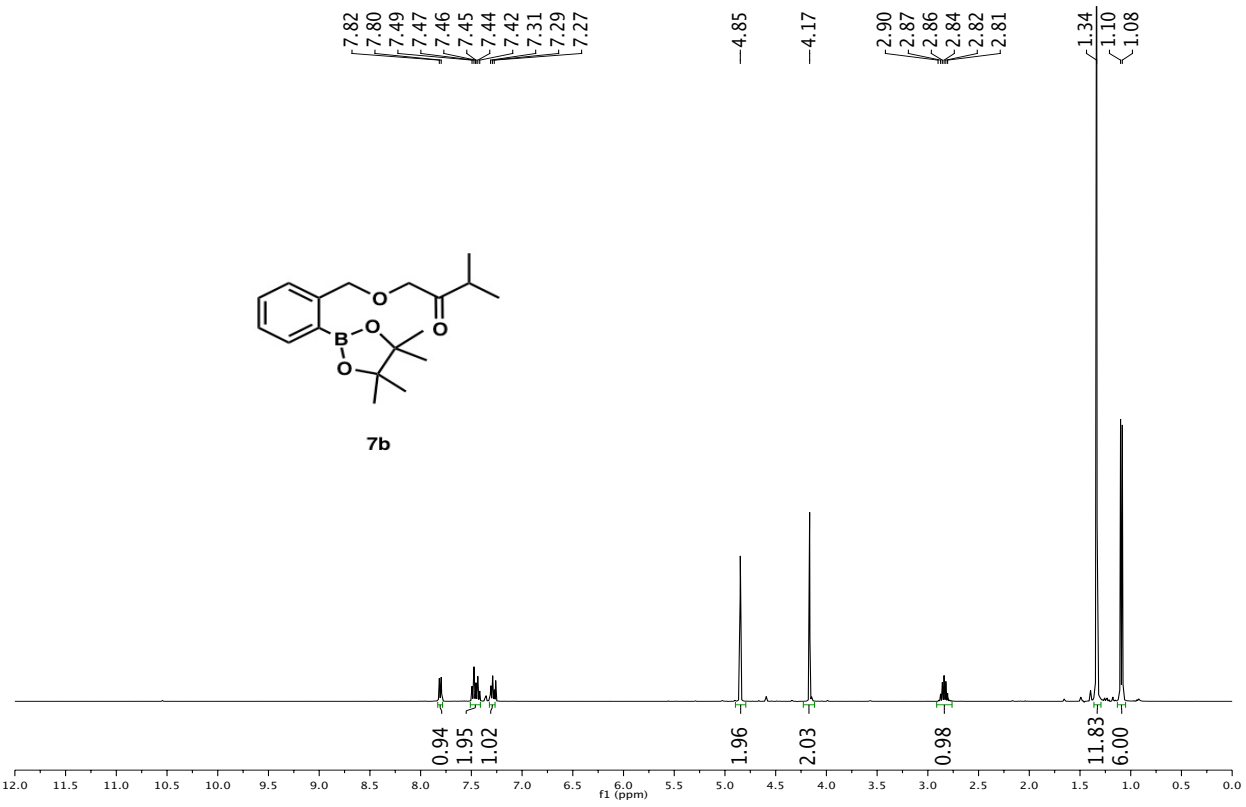
7.80
7.49
7.47
7.46
7.44
7.43
7.31
7.30
7.28
4.84
4.06
2.36
2.34
2.19
2.17
2.15
2.12
1.34
0.92
0.91
O
O
B
O
O
0.91
1.92
0.97
1.98
2.02
1.97
0.98
12.02
6.00
f1 (ppm)

7a


209.03
143.62
135.83
130.99
127.83
126.96
83.68
75.75
72.49
47.80
24.86
24.19
22.60
f1 (ppm)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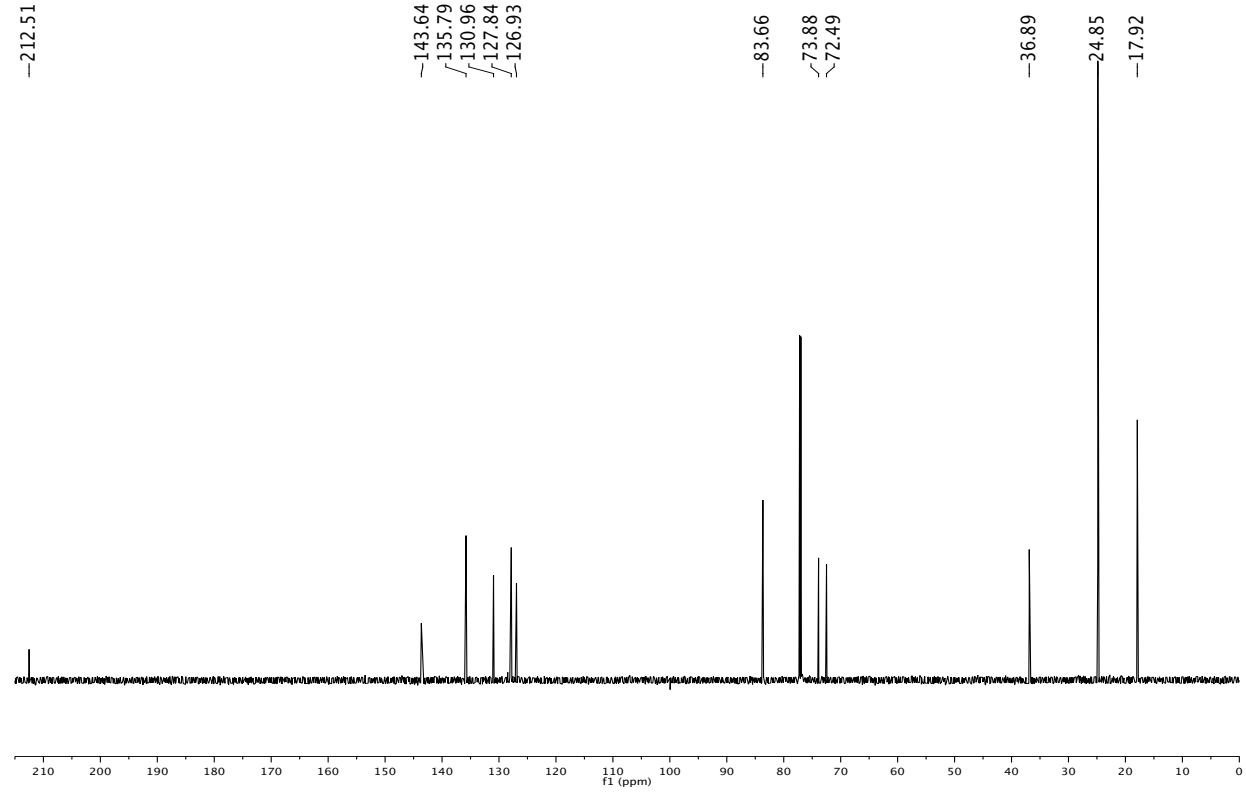
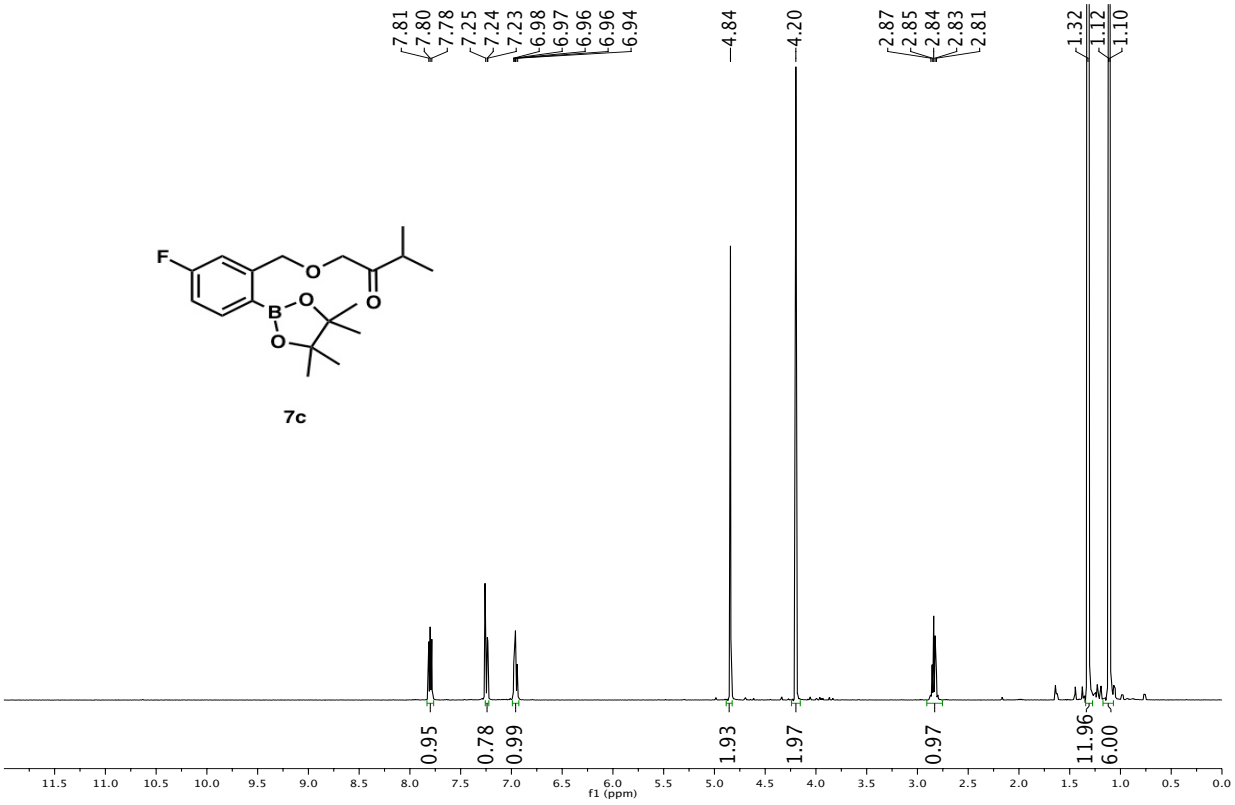
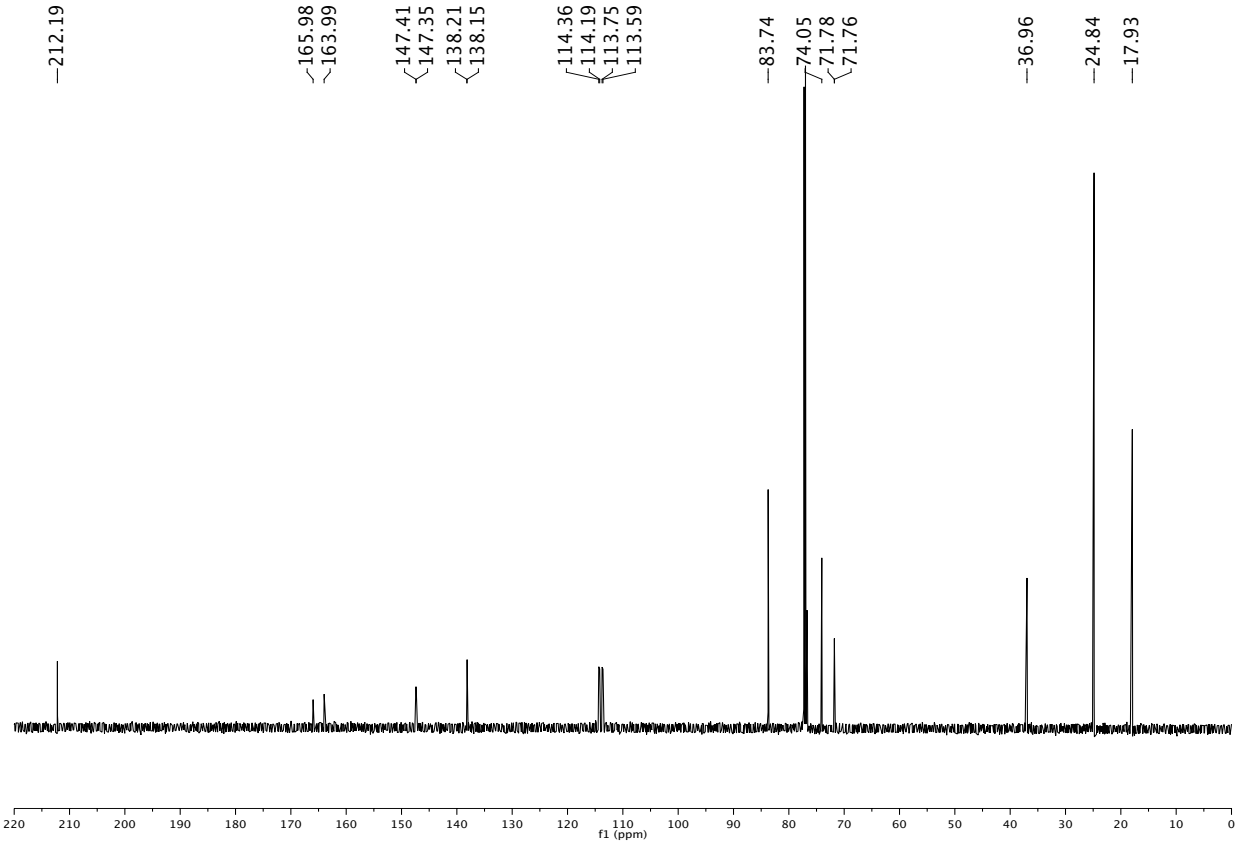
7.80
7.49
7.47
7.46
7.45
7.44
7.42
7.31
7.29
7.27
4.85
4.17
2.90
2.87
2.86
2.84
2.82
2.81
1.34
1.10
1.08
O
O
B
O
O
0.94
1.95
1.02
1.96
2.03
0.98
11.83
6.00
f1 (ppm)

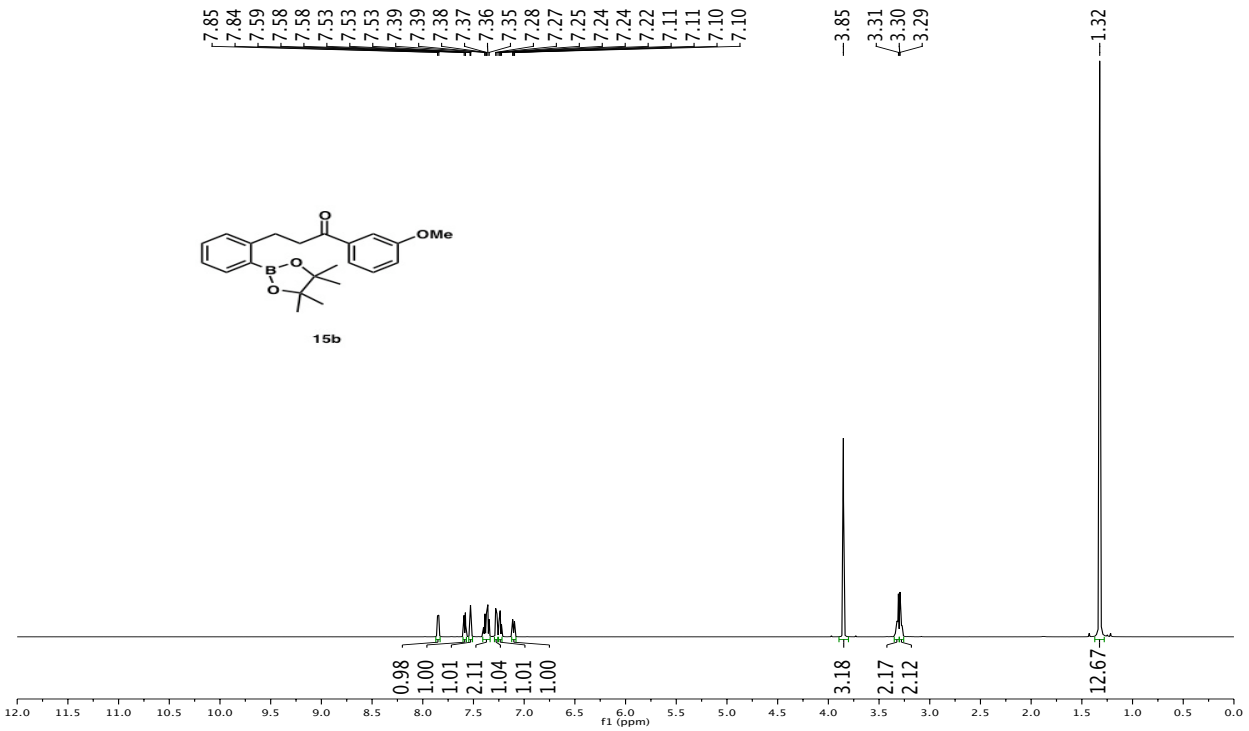
7b

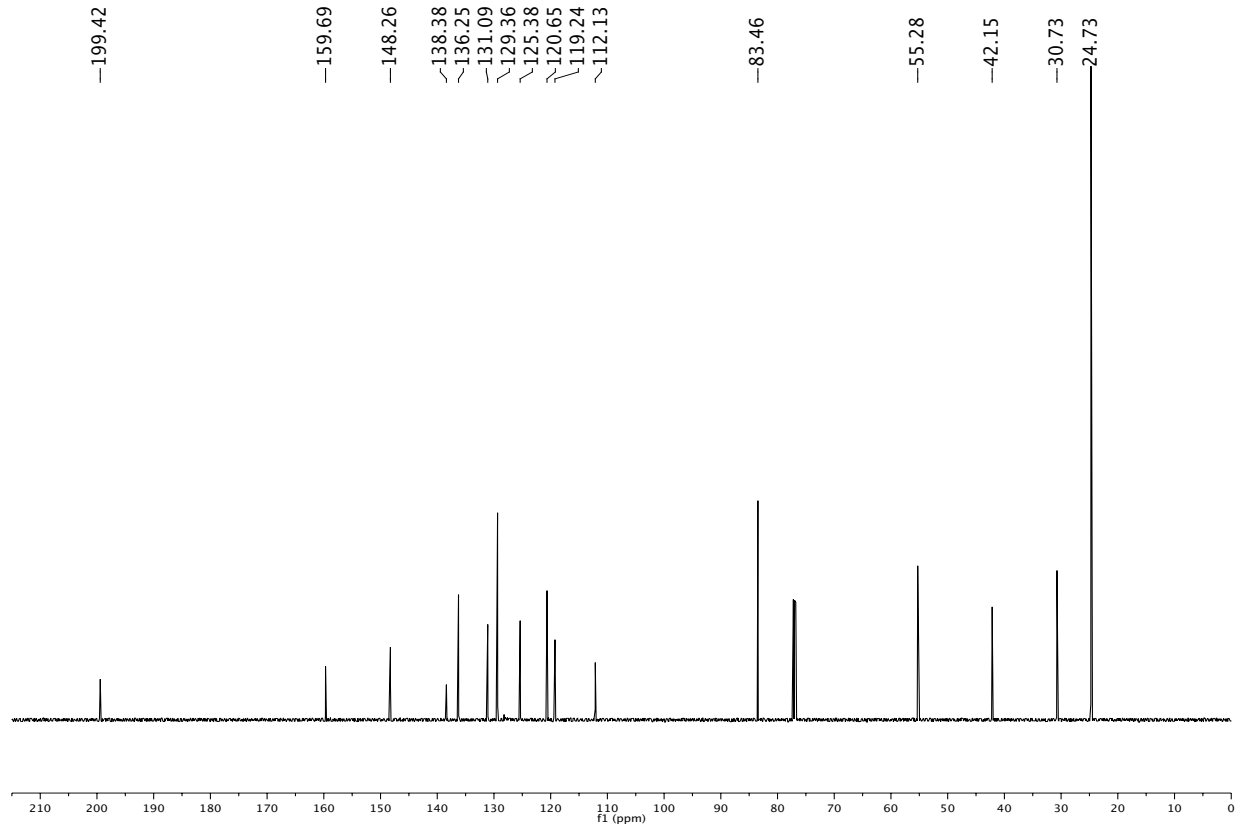

212.51
143.64
135.79
130.96
127.84
126.93
83.66
73.88
72.49
36.89
24.85
17.92
f1 (ppm)

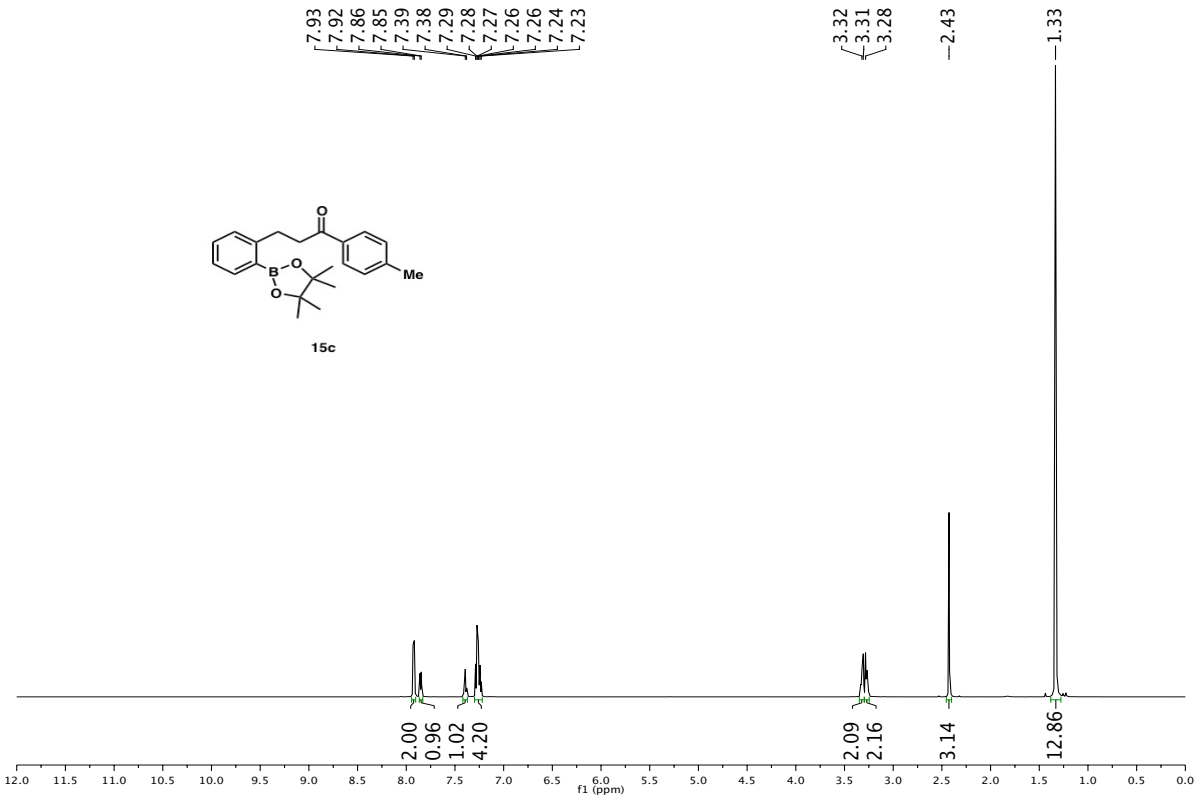


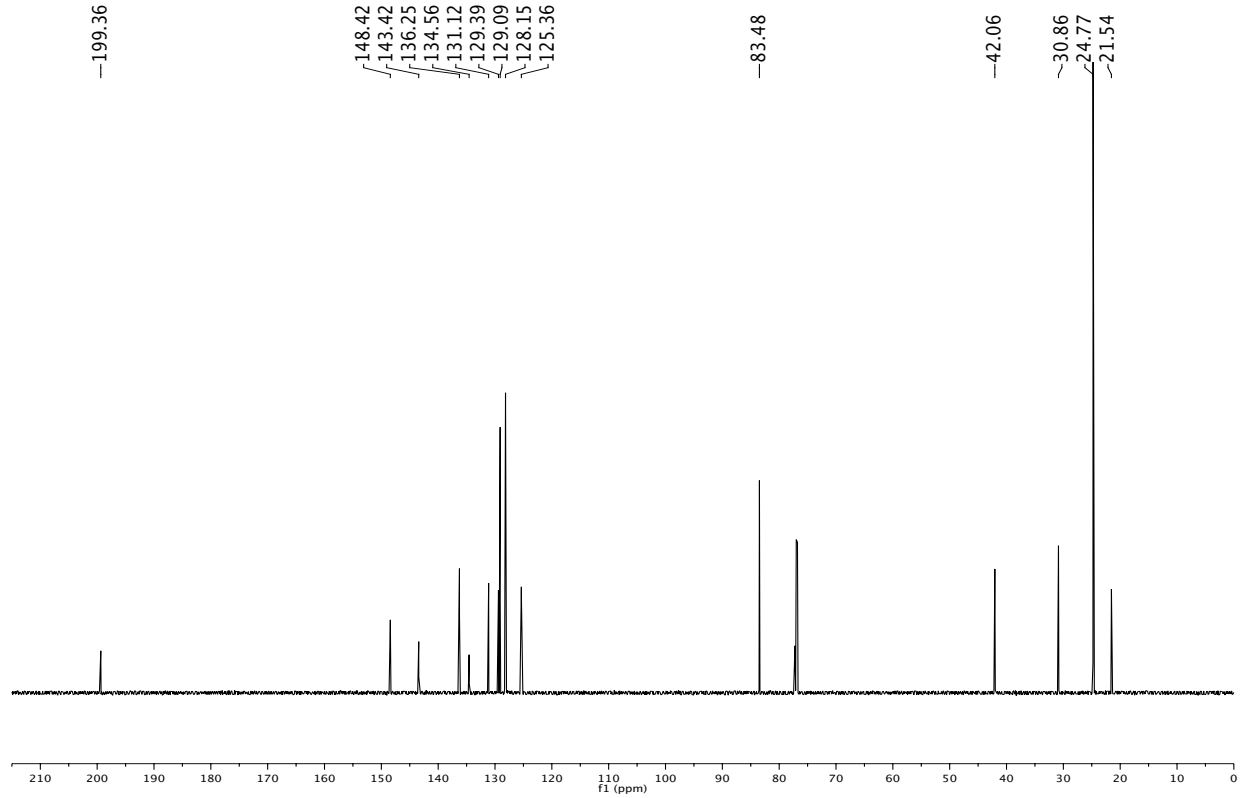
7c

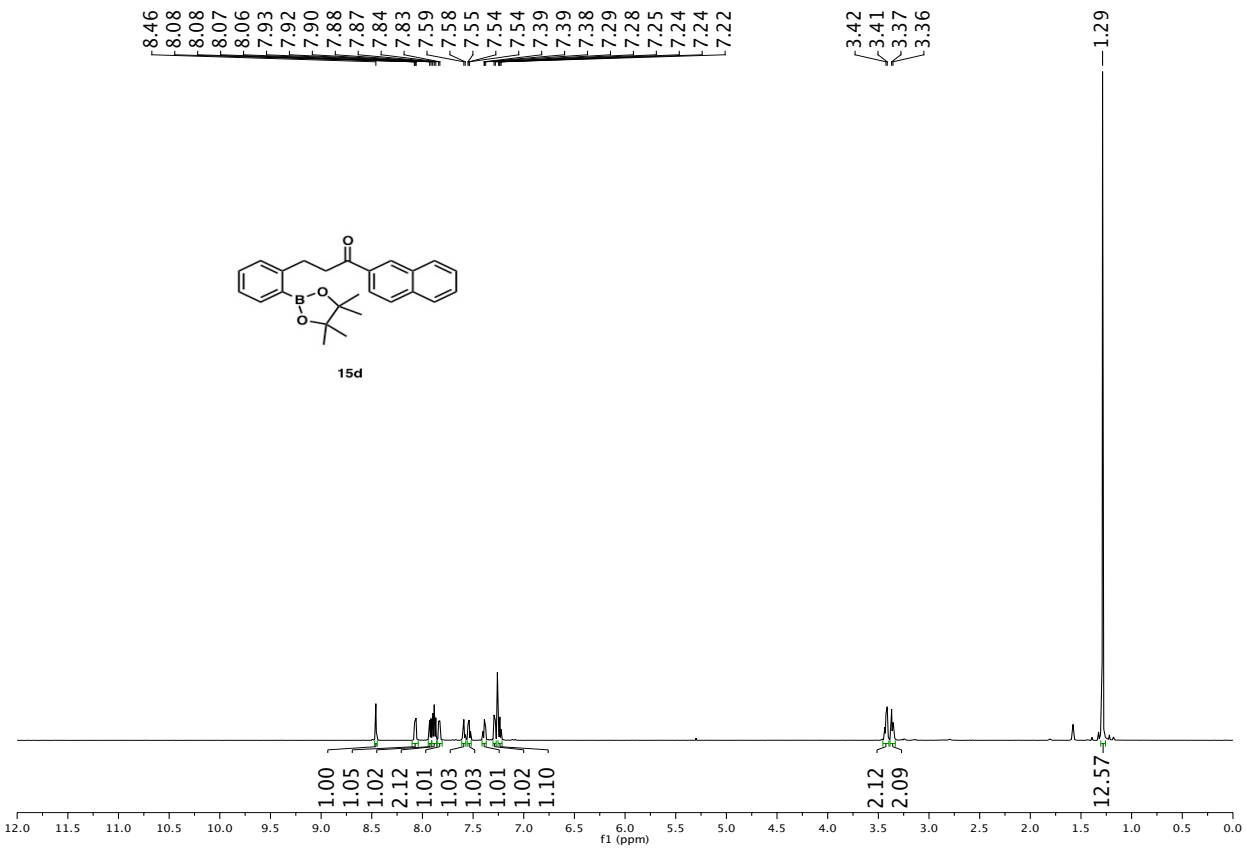


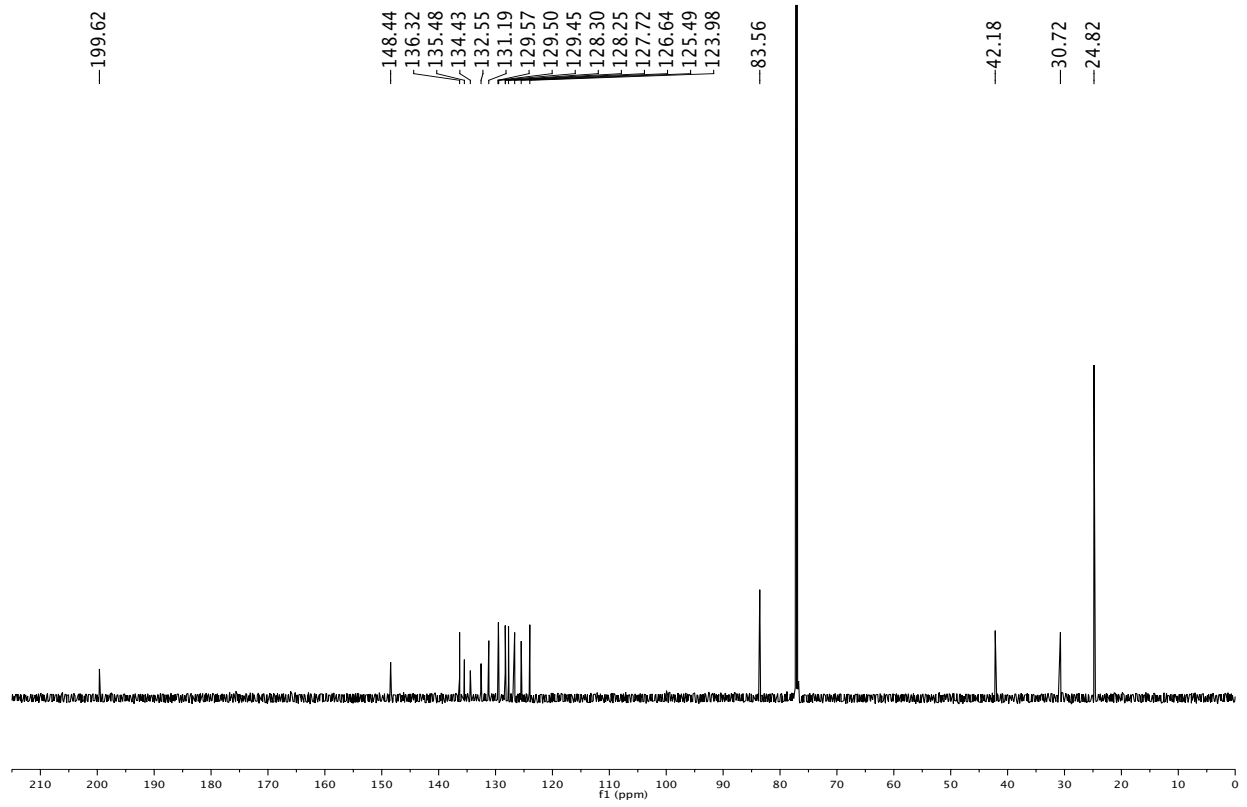

7.85
7.84
7.59
7.58
7.58
7.53
7.53
7.53
7.39
7.39
7.38
7.37
7.36
7.35
7.28
7.27
7.25
7.24
7.24
7.22
7.11
7.11
7.10
7.10
3.85
3.31
3.30
3.29
1.32
OMe
15b
0.98
1.00
1.01
2.11
1.04
1.01
1.00
3.18
2.17
2.12
12.67
f1 (ppm)

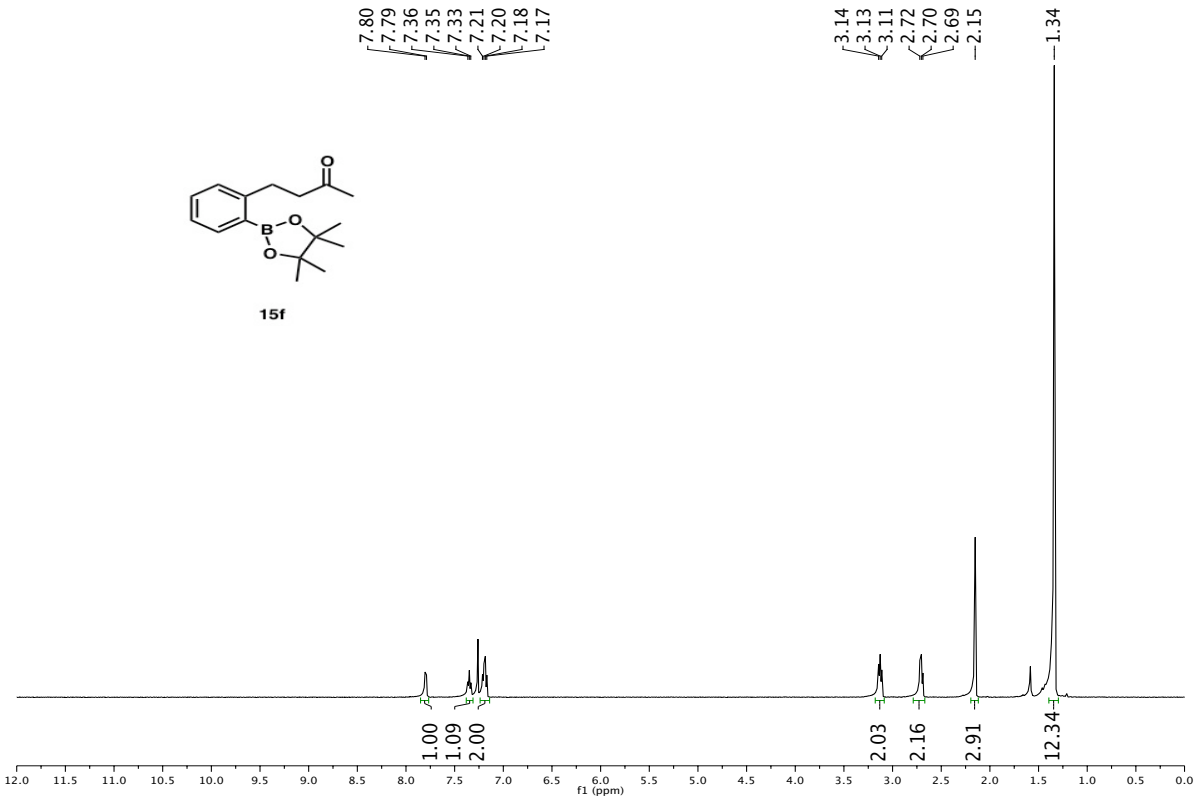

199.42
159.69
148.26
138.38
136.25
131.09
129.36
125.38
120.65
119.24
112.13
83.46
55.28
42.15
30.73
24.73
f1 (ppm)

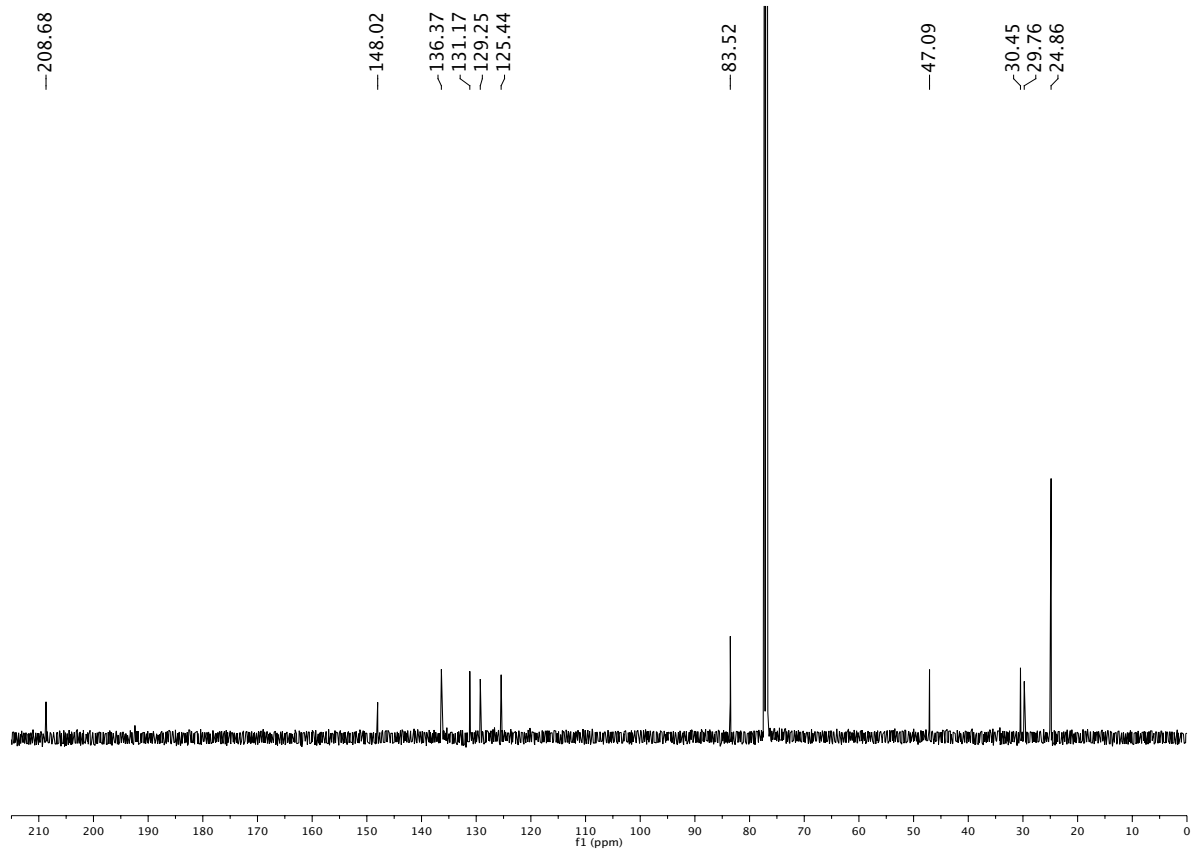


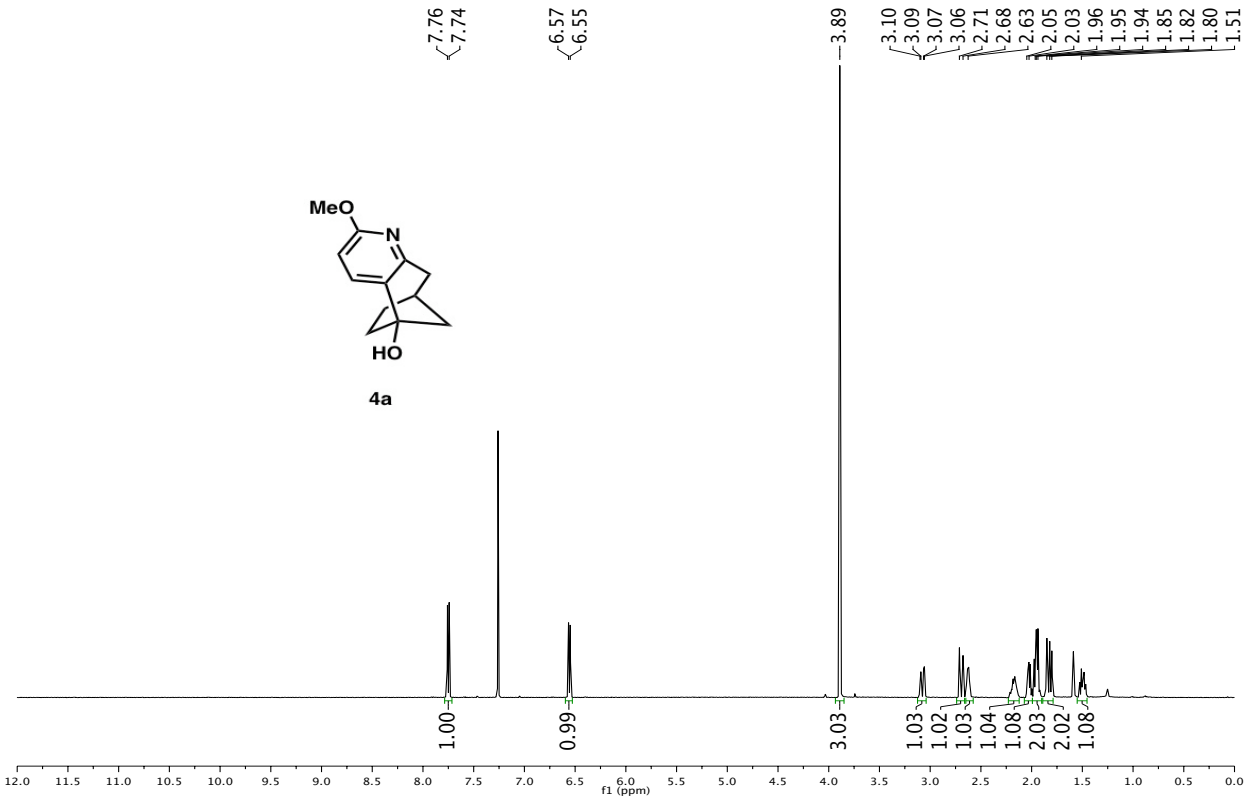


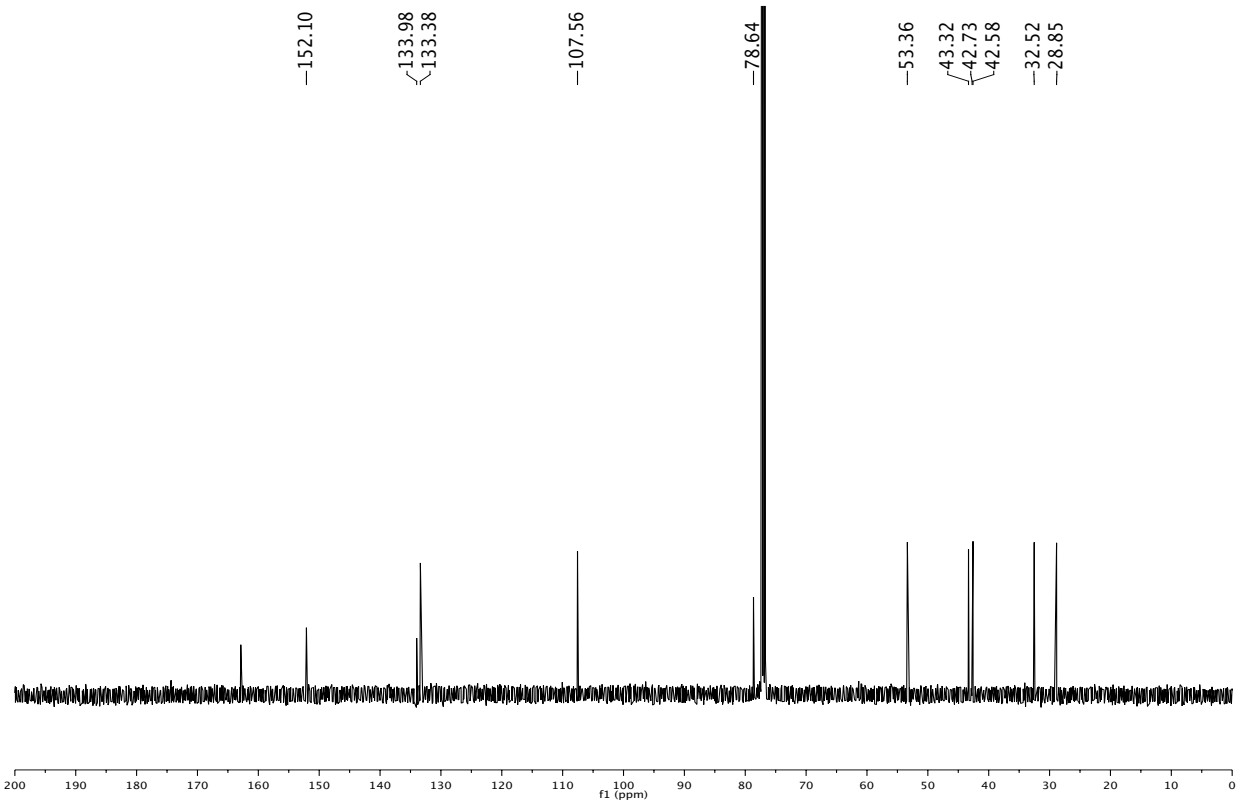


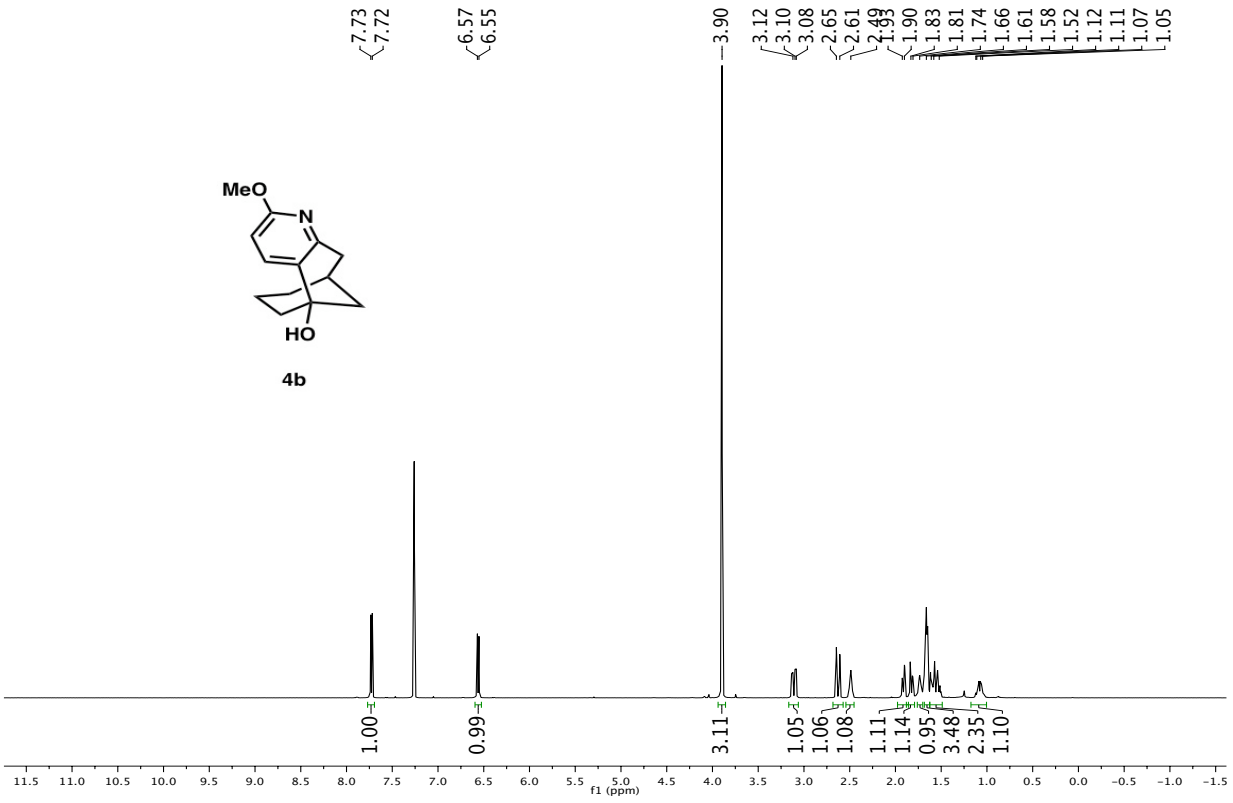


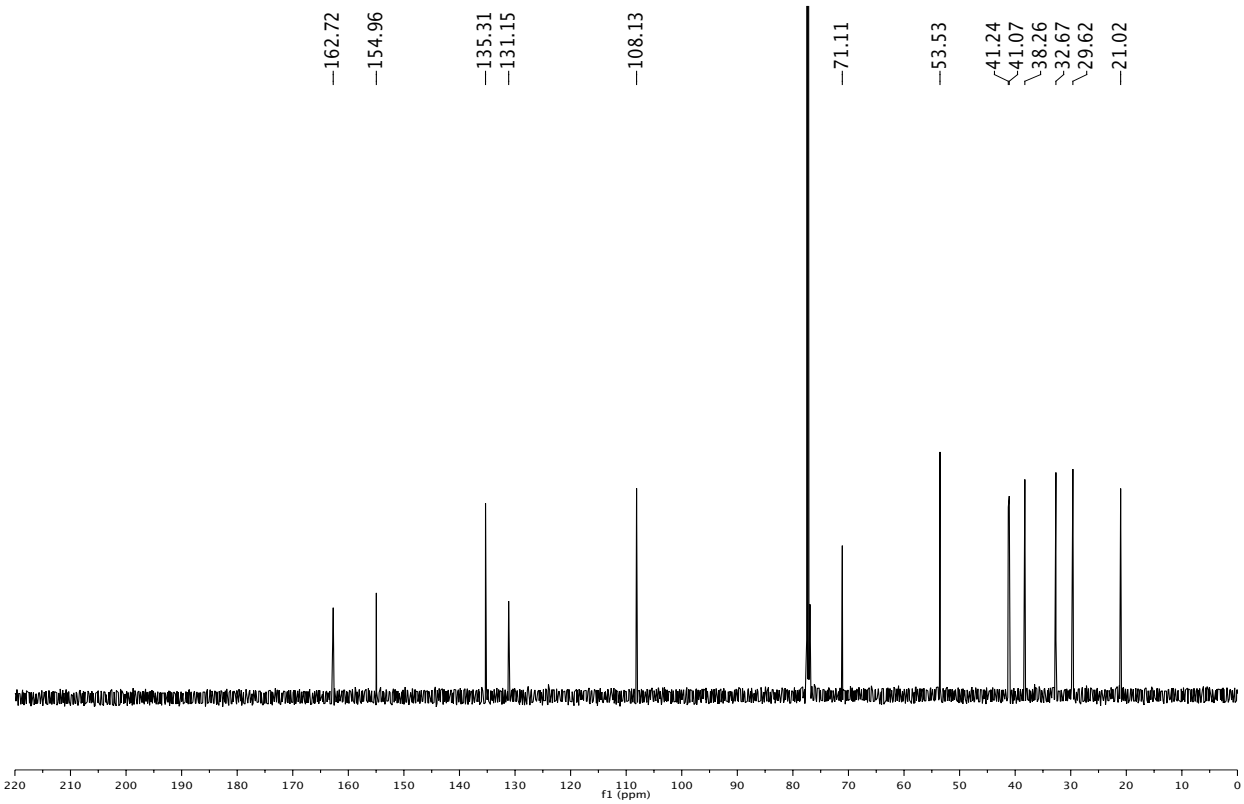


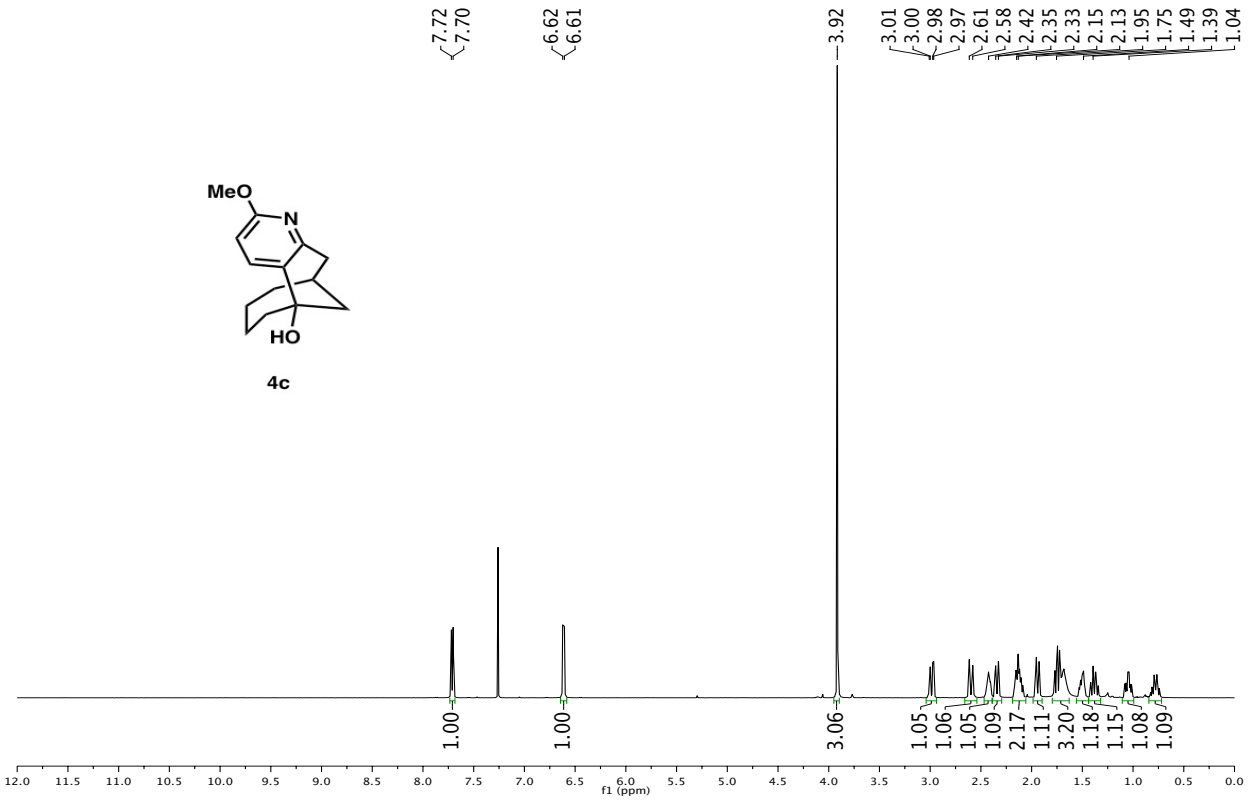




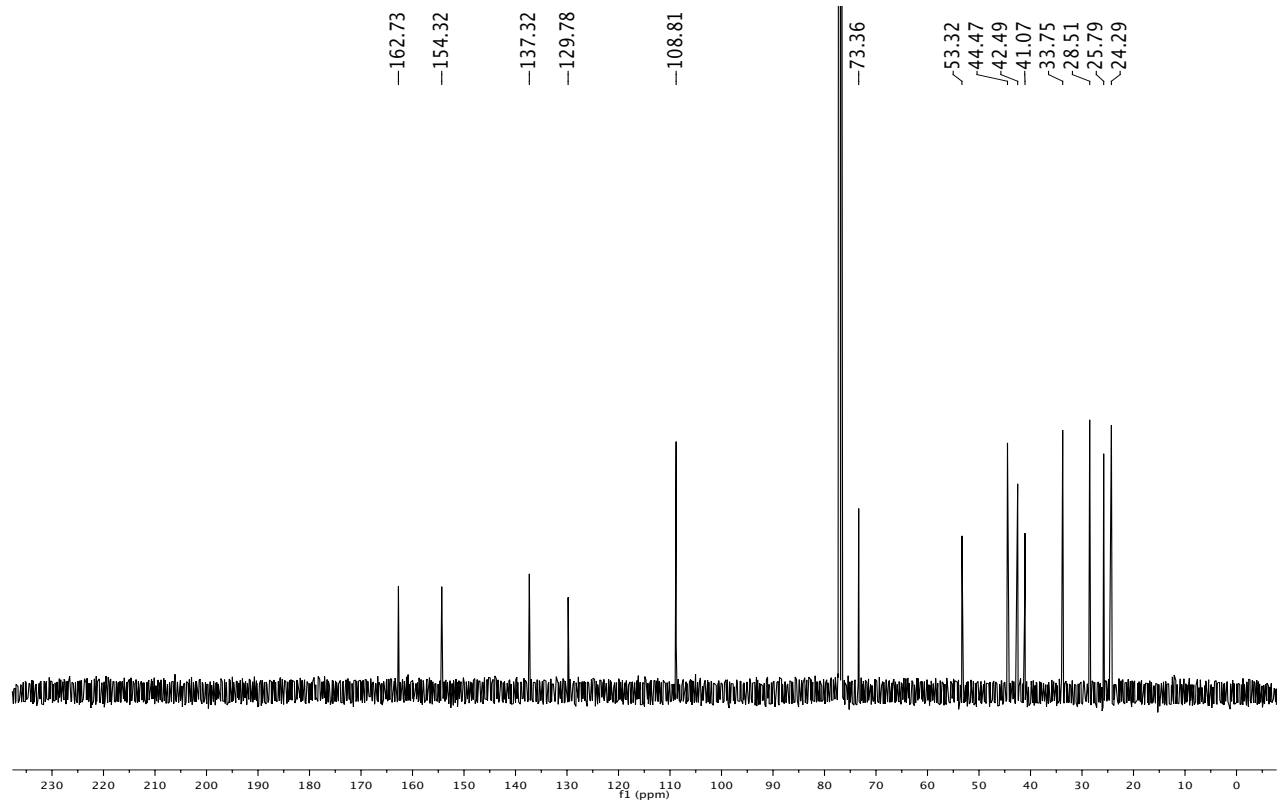


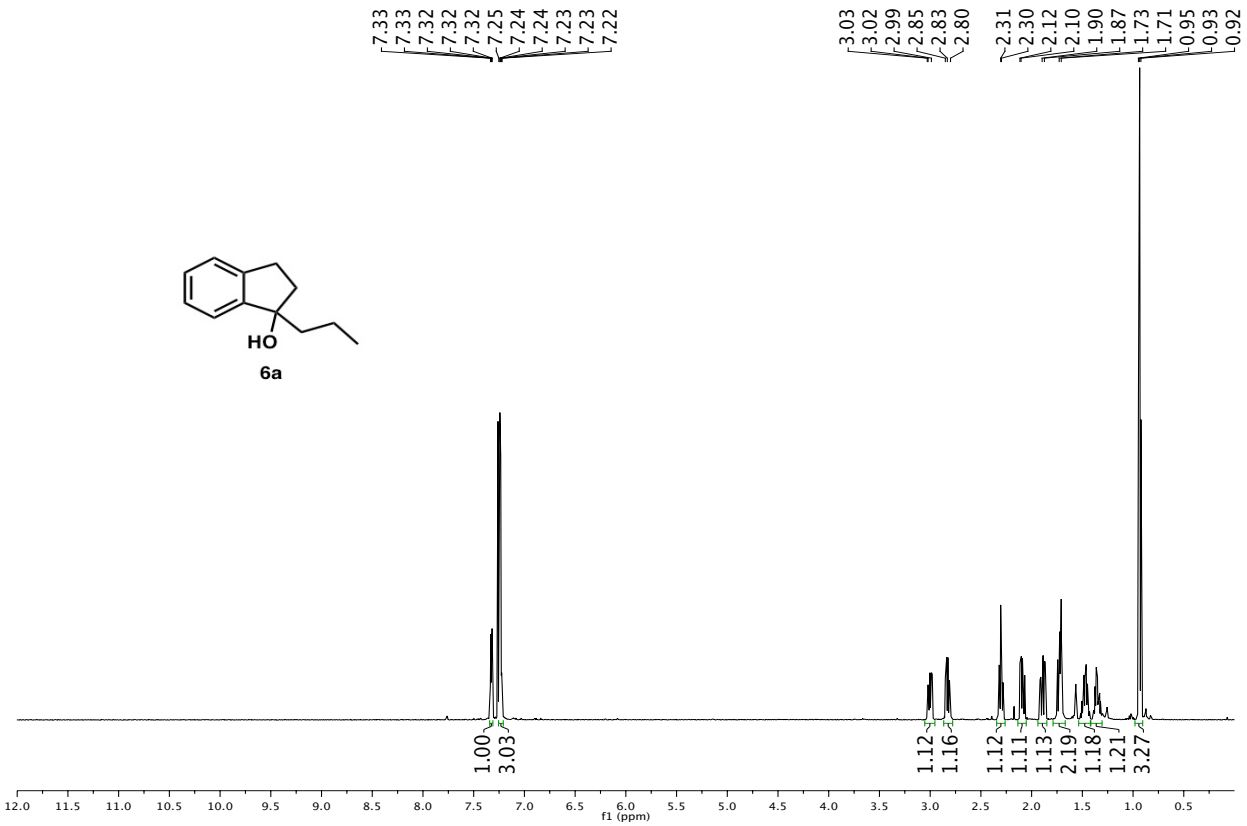

7.73
7.72
6.57
6.55
3.90
3.12
3.10
3.08
2.65
2.61
2.49
1.93
1.90
1.83
1.81
1.74
1.66
1.61
1.58
1.52
1.12
1.11
1.07
1.05
MeO
N
HO
4b
1.00
0.99
3.11
1.05
1.06
1.08
1.11
1.14
0.95
3.48
2.35
1.10
f1 (ppm)

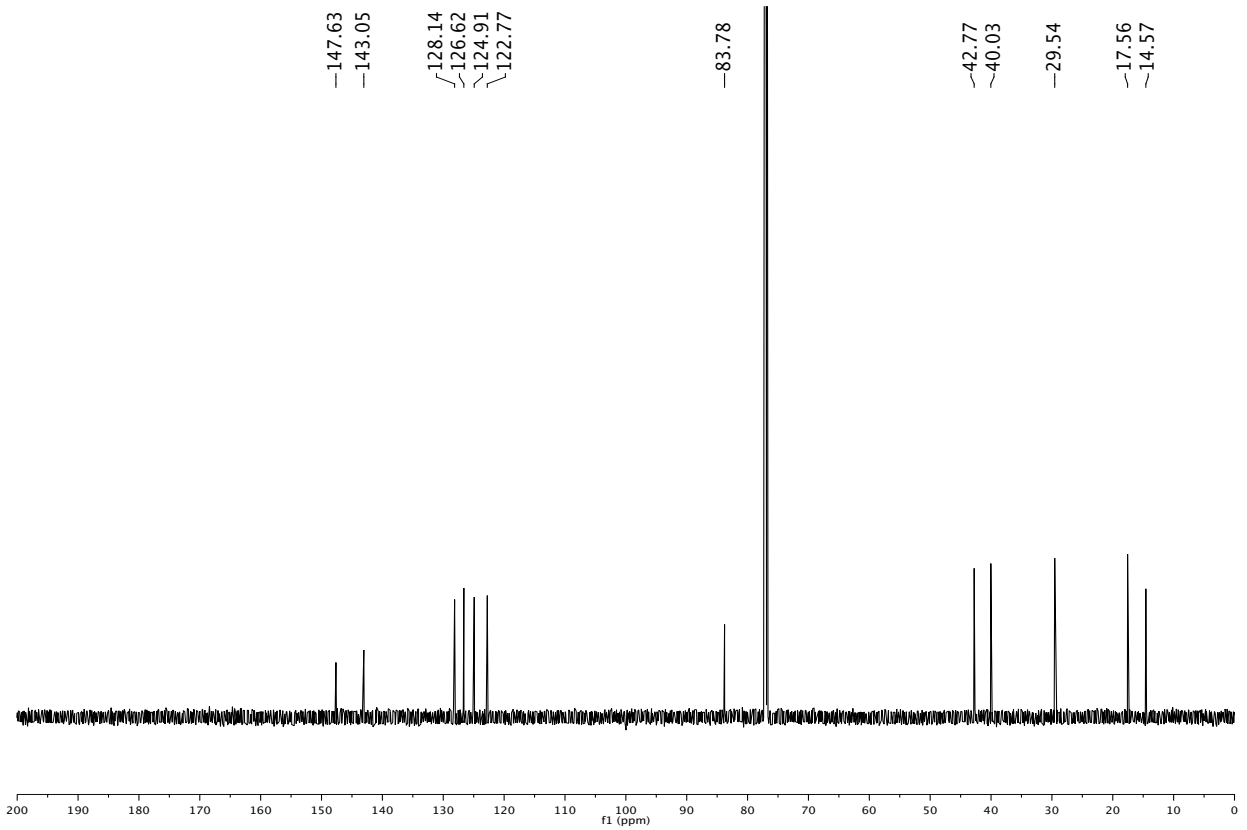

162.72
154.96
135.31
131.15
108.13
71.11
53.53
41.24
41.07
38.26
32.67
29.62
21.02
f1 (ppm)

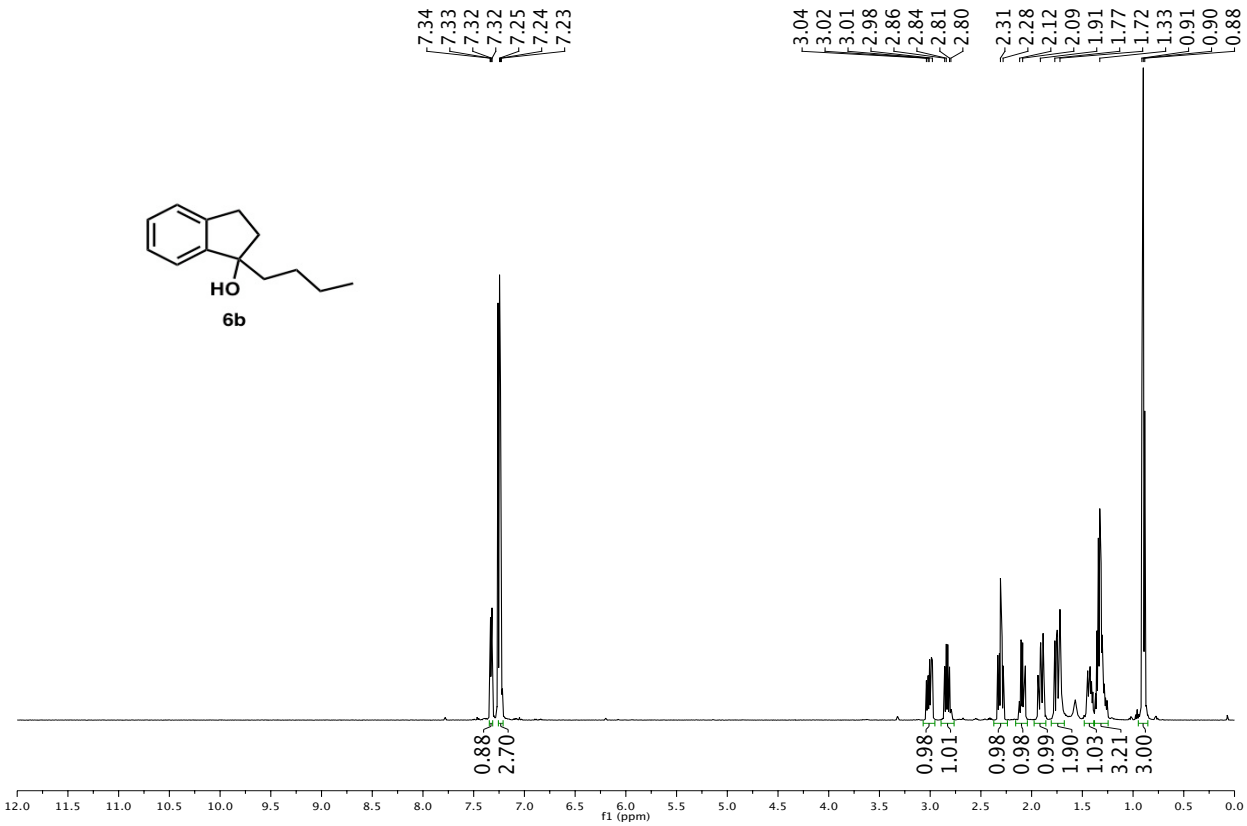


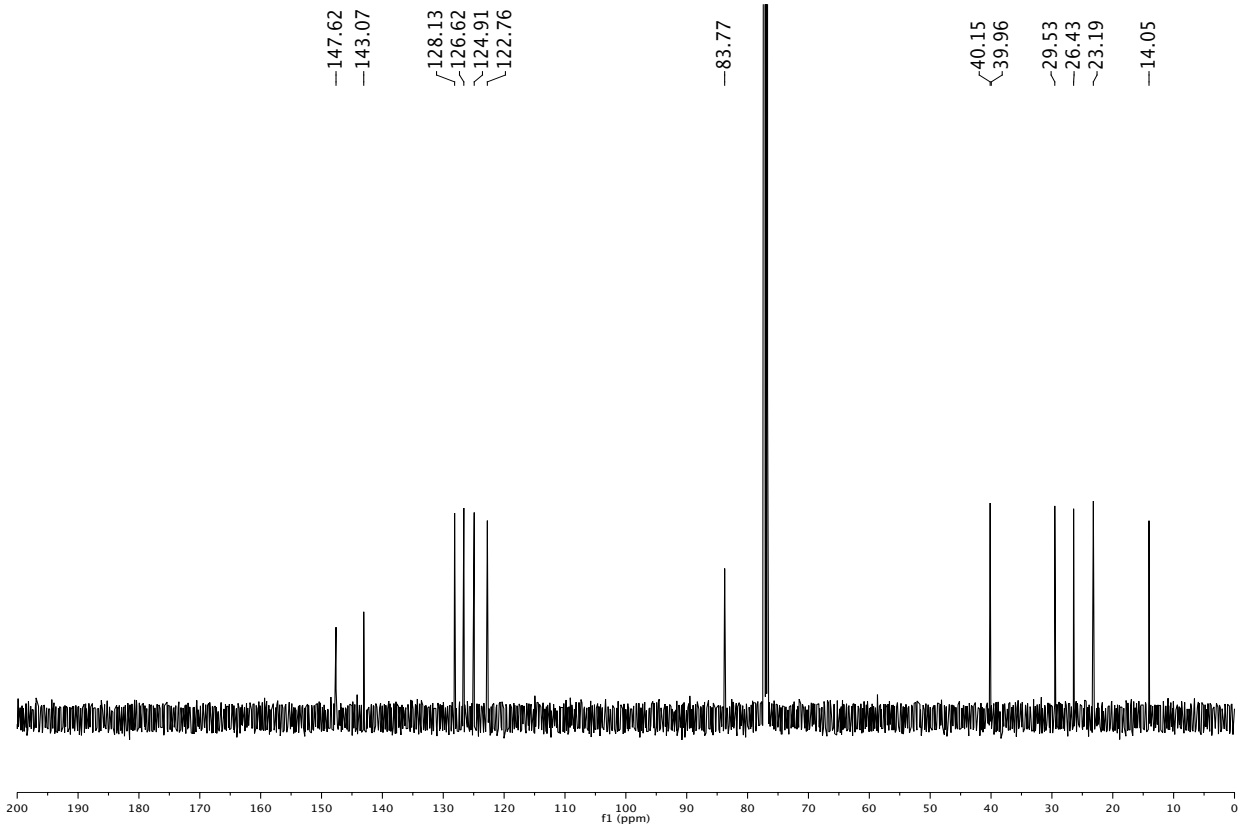
4c

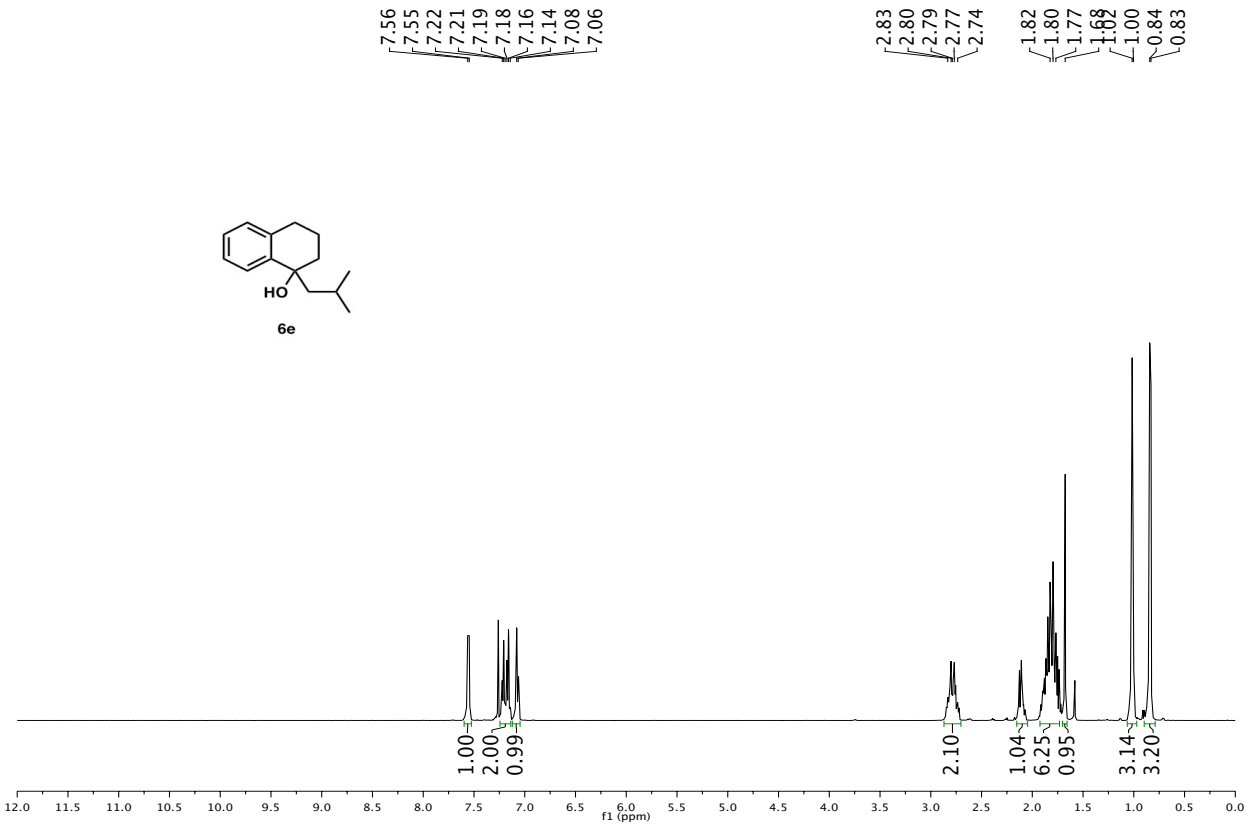


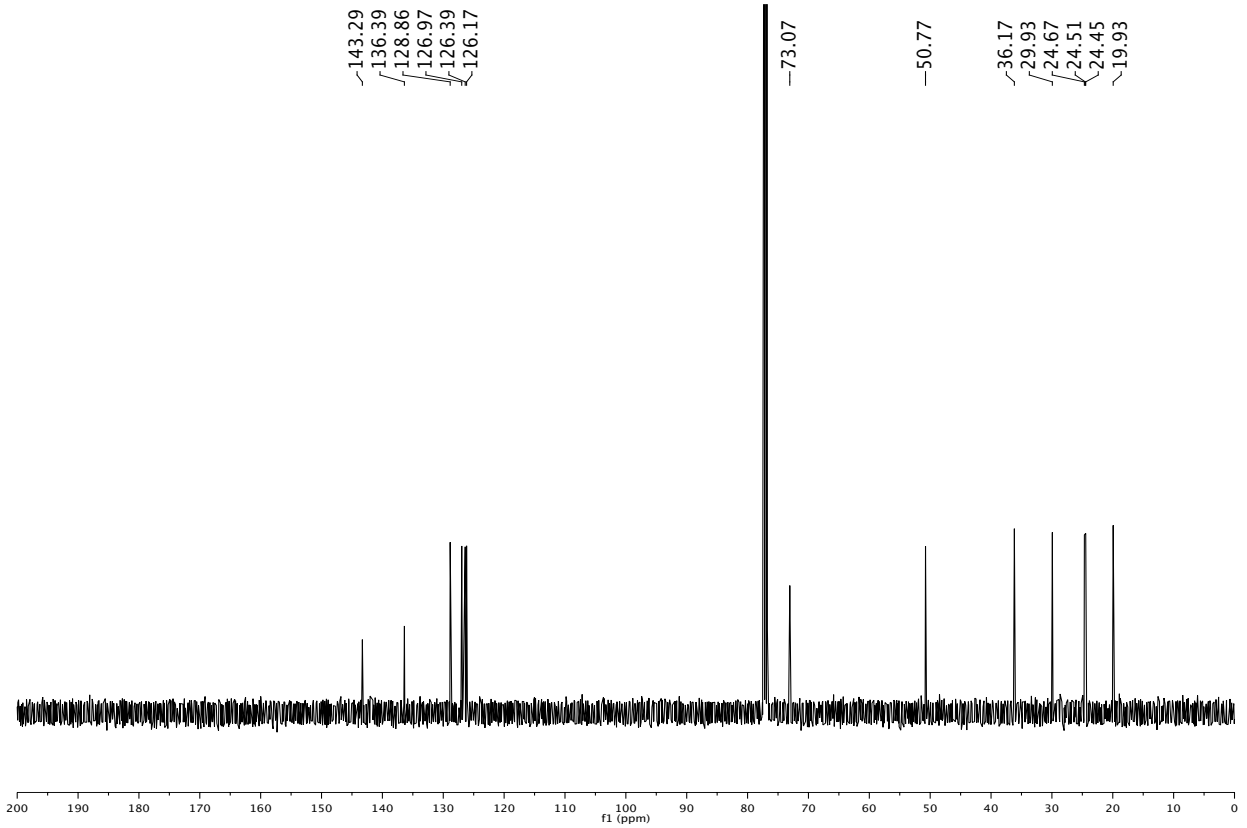


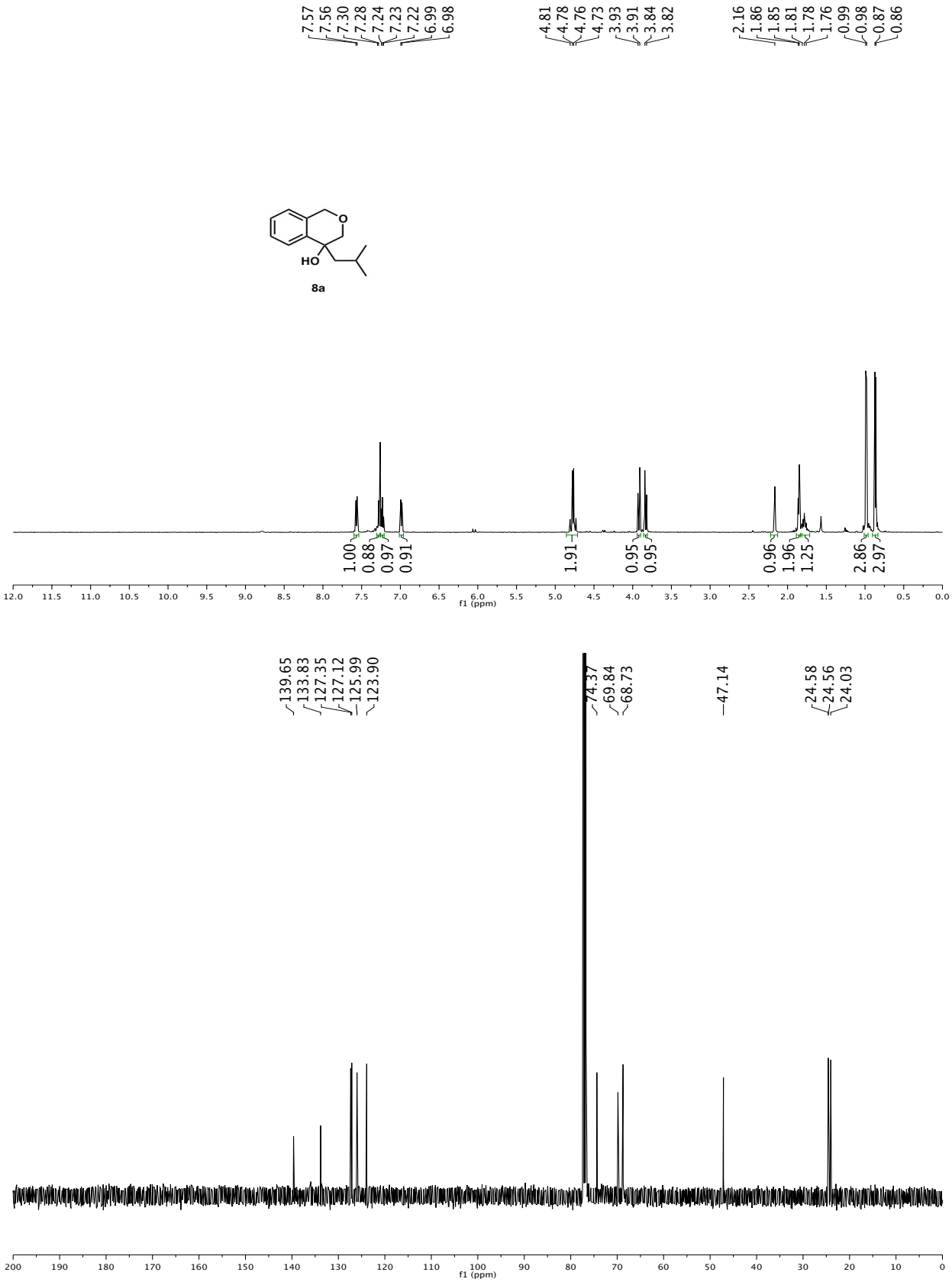


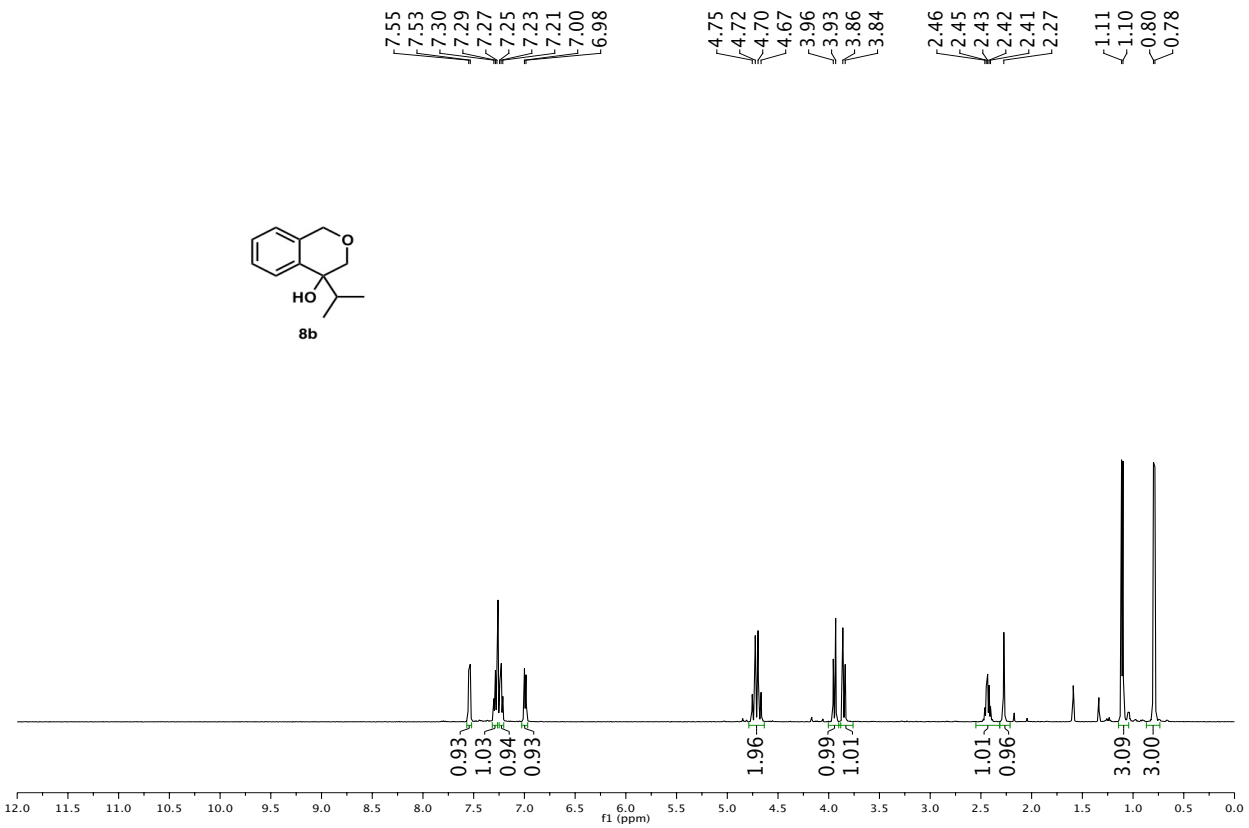


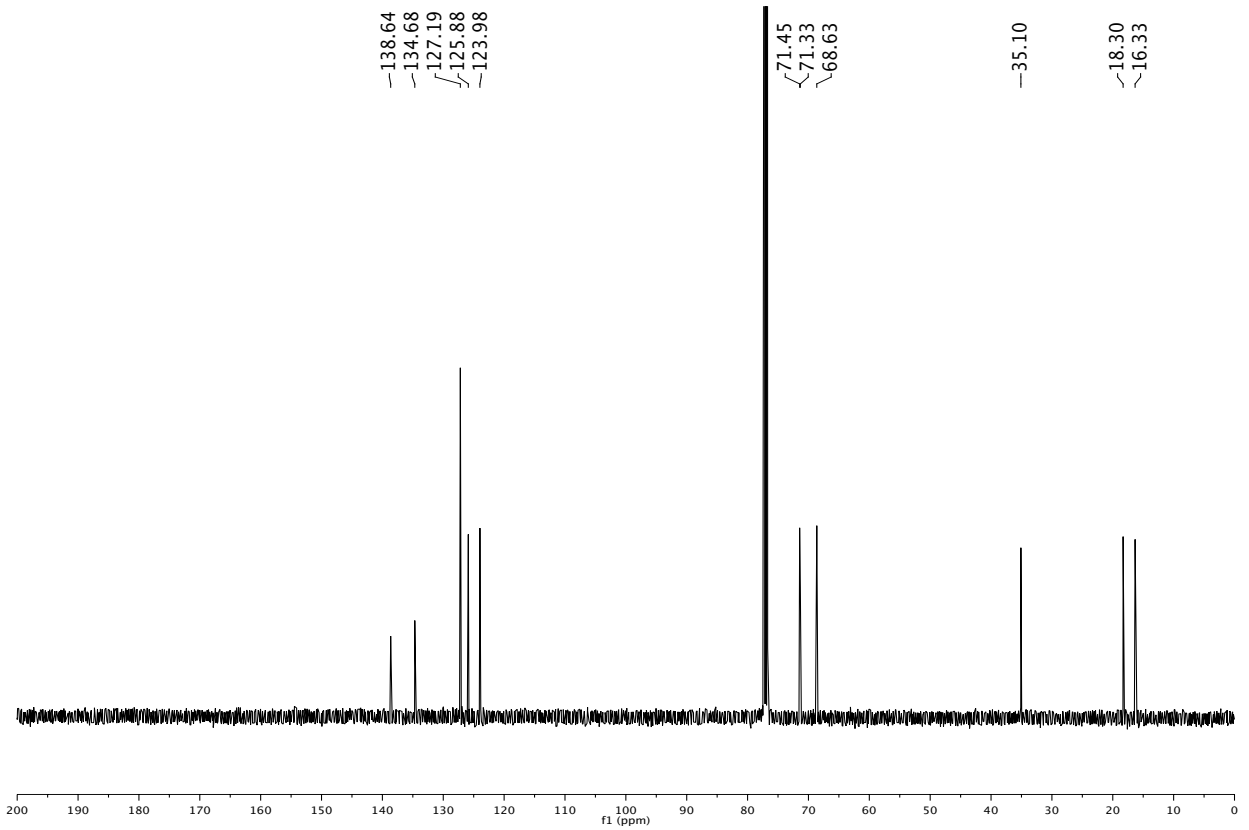


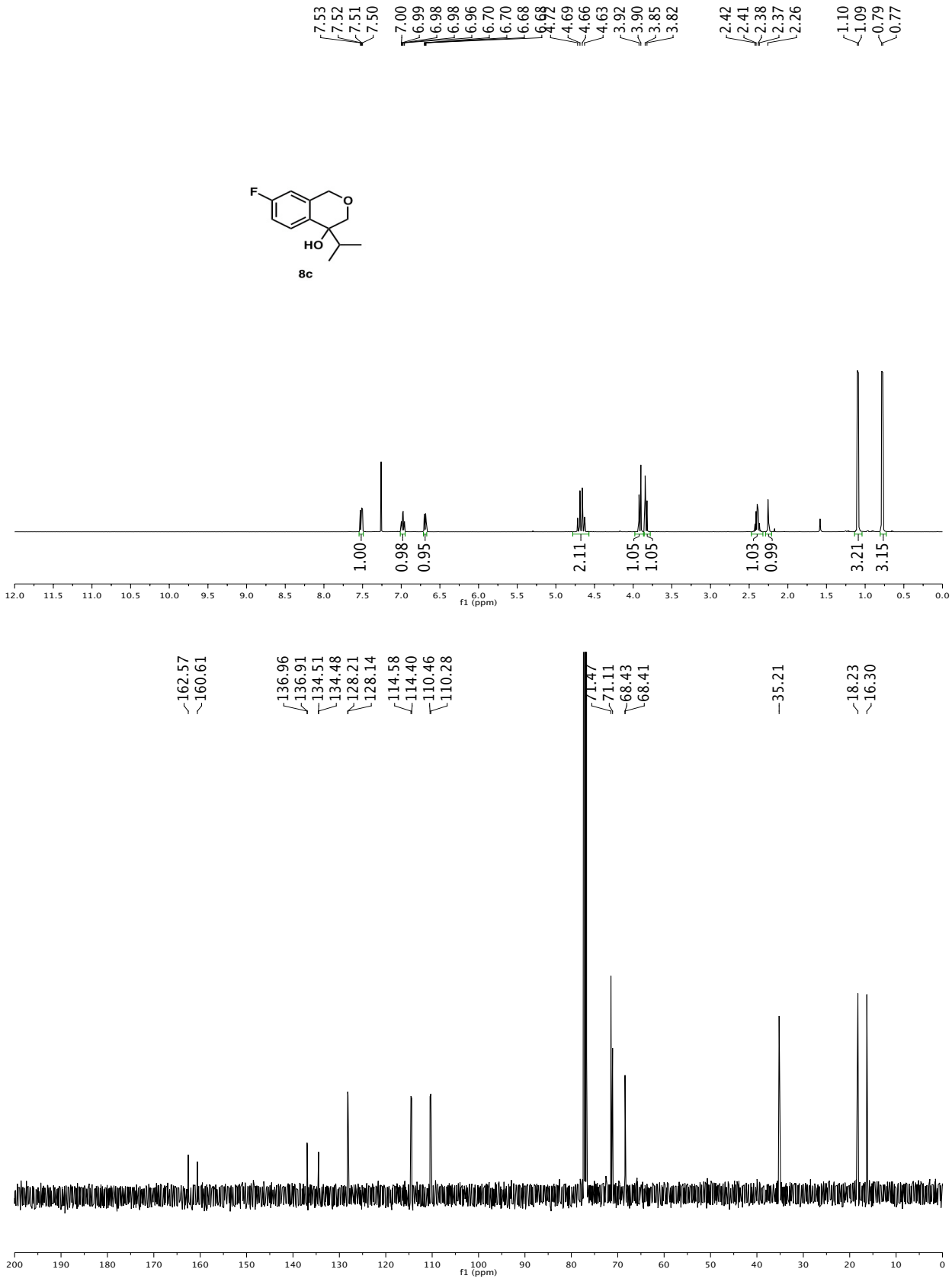

7.56
7.55
7.22
7.21
7.19
7.18
7.16
7.14
7.08
7.06
2.83
2.80
2.79
2.77
2.74
1.82
1.80
1.77
1.68
1.02
1.00
0.84
0.83
HO
6e
1.00
2.00
0.99
2.10
1.04
6.25
0.95
3.14
3.20
f1 (ppm)


143.29
136.39
128.86
126.97
126.39
126.17
73.07
50.77
36.17
29.93
24.67
24.51
24.45
19.93
f1 (ppm)





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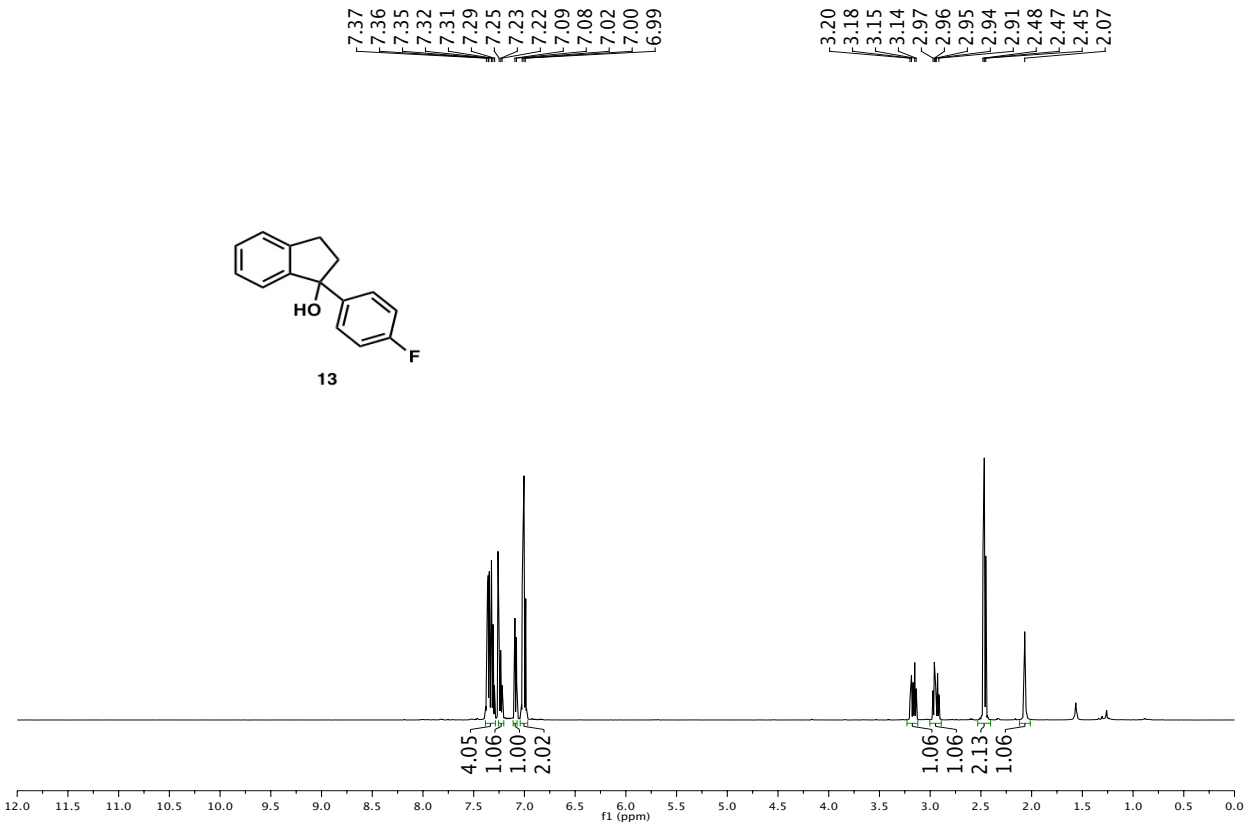
7.52
7.51
7.50
7.00
6.99
6.98
6.98
6.96
6.70
6.70
6.68
6.68
4.72
4.69
4.66
4.63
3.92
3.90
3.85
3.82
2.42
2.41
2.38
2.37
2.26
1.10
1.09
0.79
0.77
F
O
HO
8c
1.00
0.98
0.95
2.11
1.05
1.05
1.03
0.99
3.21
3.15
f1 (ppm)
162.57
160.61
136.96
136.91
134.51
134.48
128.21
128.14
114.58
114.40
110.46
110.28
71.47
71.11
68.43
68.41
35.21
18.23
16.30
f1 (ppm)


7.37
7.36
7.35
7.32
7.31
7.29
7.25
7.23
7.22
7.09
7.08
7.02
7.00
6.99
3.20
3.18
3.15
3.14
2.97
2.96
2.95
2.94
2.91
2.48
2.47
2.45
2.07
HO
F
13
4.05
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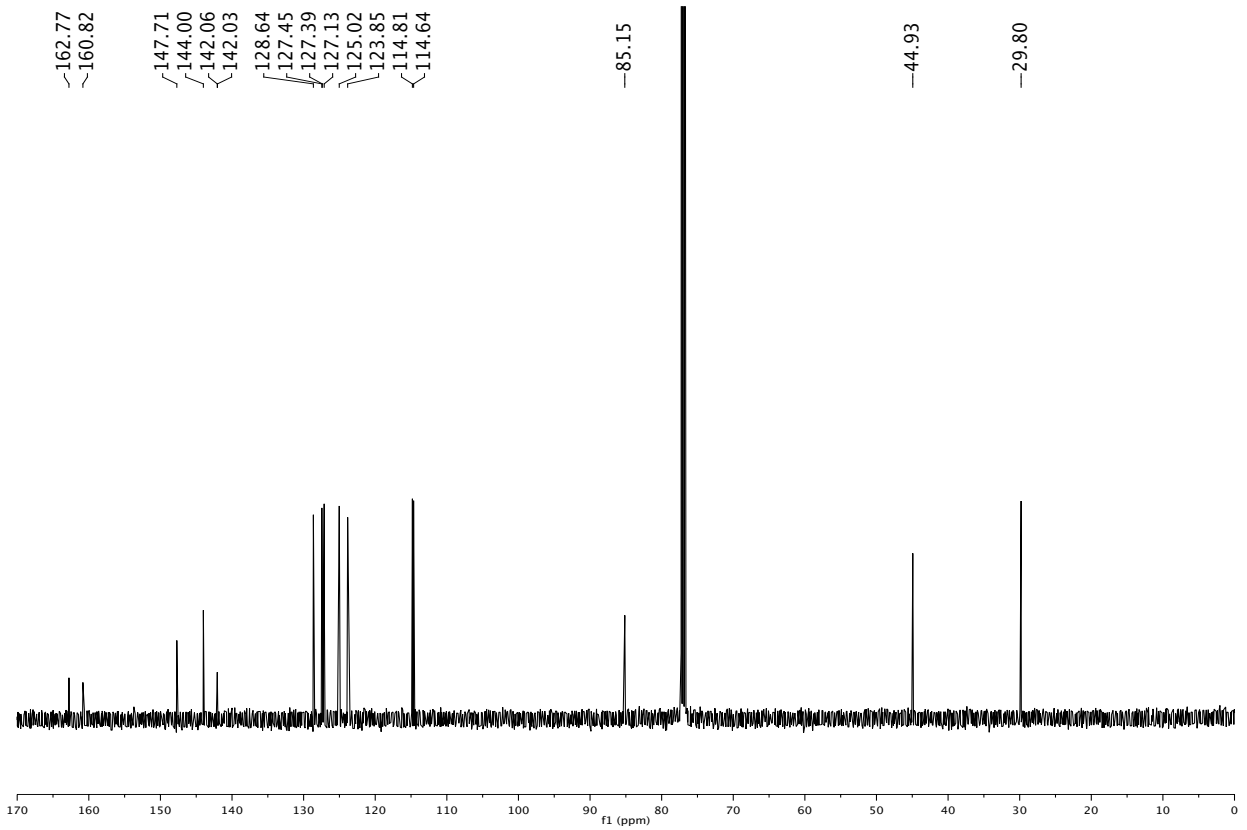
1.06
1.06
2.13
1.06
f1 (ppm)


162.77
160.82
147.71
144.00
142.06
142.03
128.64
127.45
127.39
127.13
125.02
123.85
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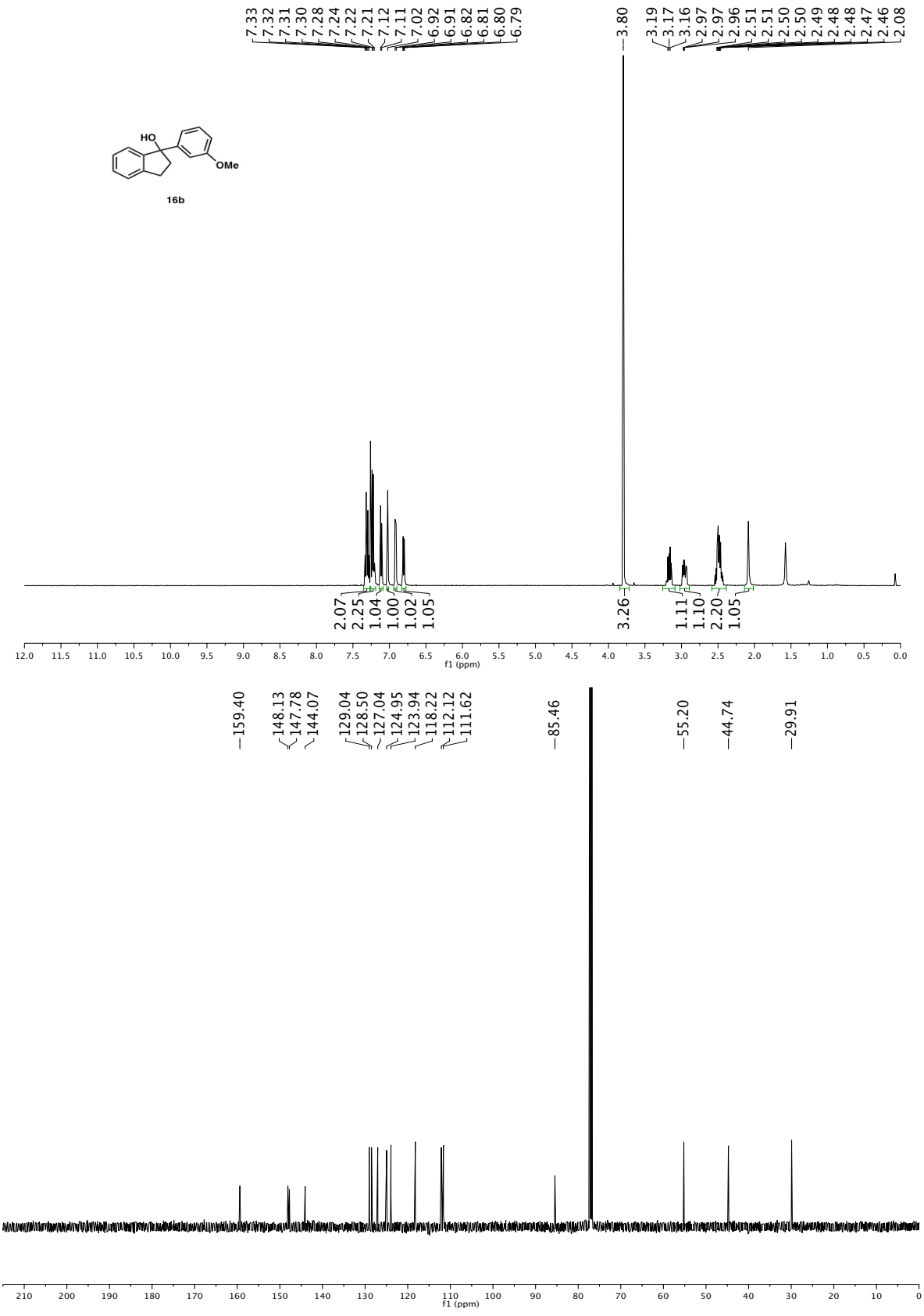
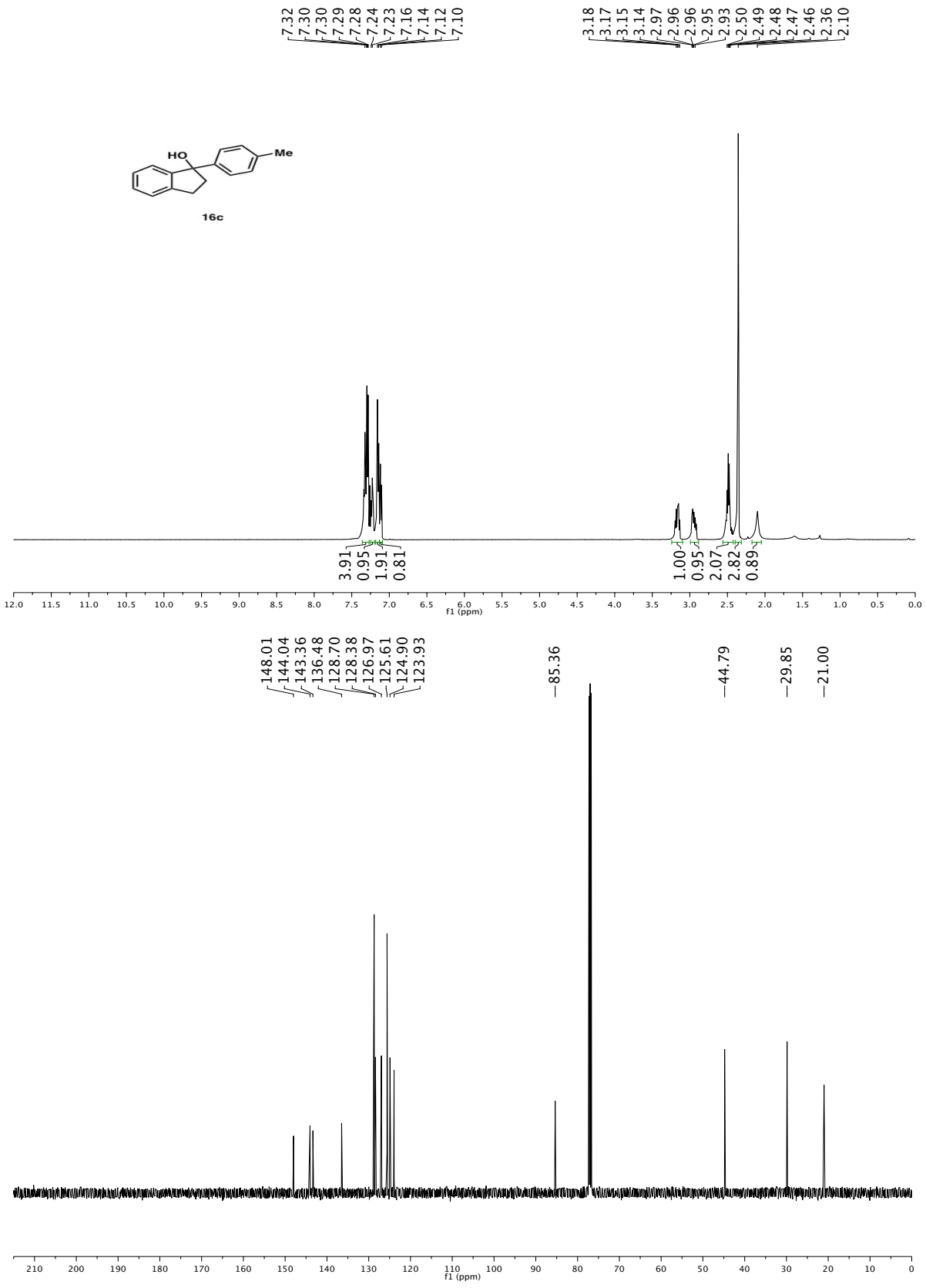
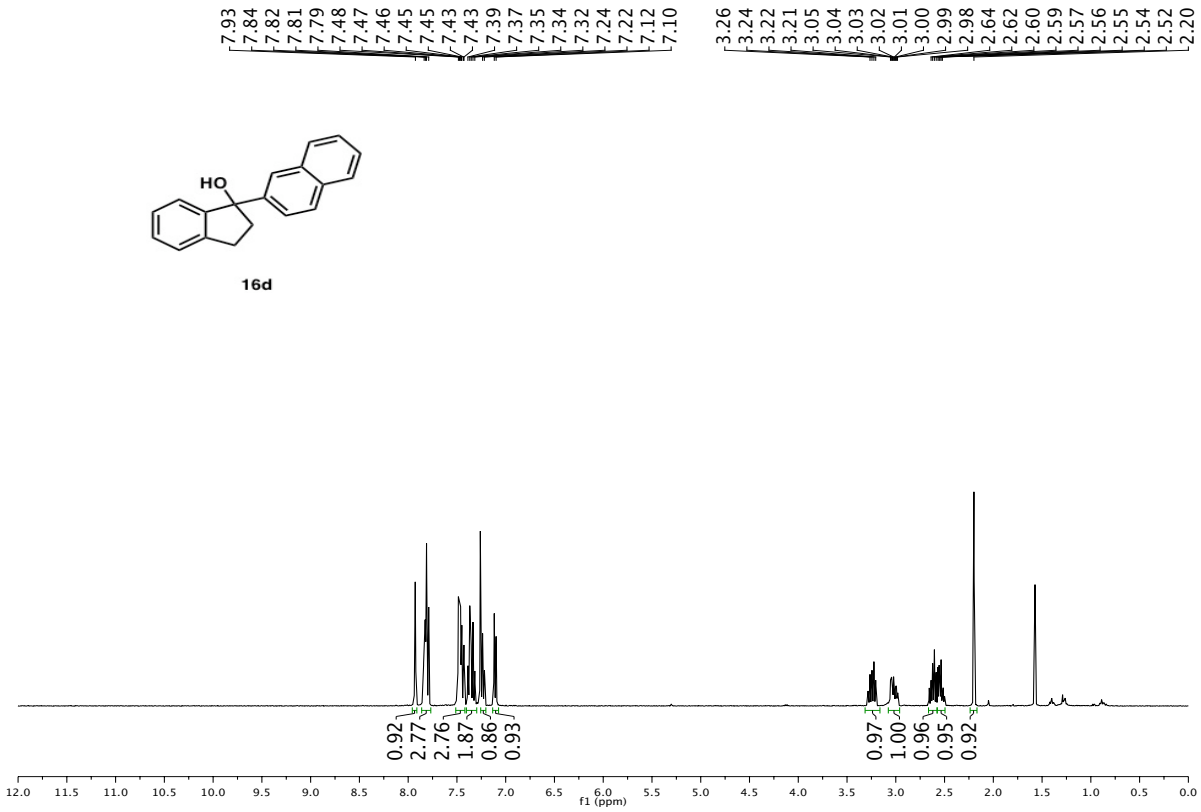
114.64
85.15
44.93
29.80
f1 (ppm)




7.32
7.30
7.30
7.29
7.28
7.24
7.23
7.16
7.14
7.12
7.10
3.18
3.17
3.15
3.14
2.97
2.96
2.96
2.95
2.93
2.50
2.49
2.48
2.47
2.46
2.36
2.10
HO
Me
16c
3.91
0.95
1.91
0.81
1.00
0.95
2.07
2.82
0.89
f1 (ppm)
148.01
144.04
143.36
136.48
128.70
128.38
126.97
125.61
124.90
123.93
85.36
44.79
29.85
21.00
f1 (ppm)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7.81
7.79
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7.47
7.46
7.45
7.45
7.43
7.43
7.39
7.37
7.35
7.34
7.32
7.24
7.22
7.12
7.10
3.26
3.24
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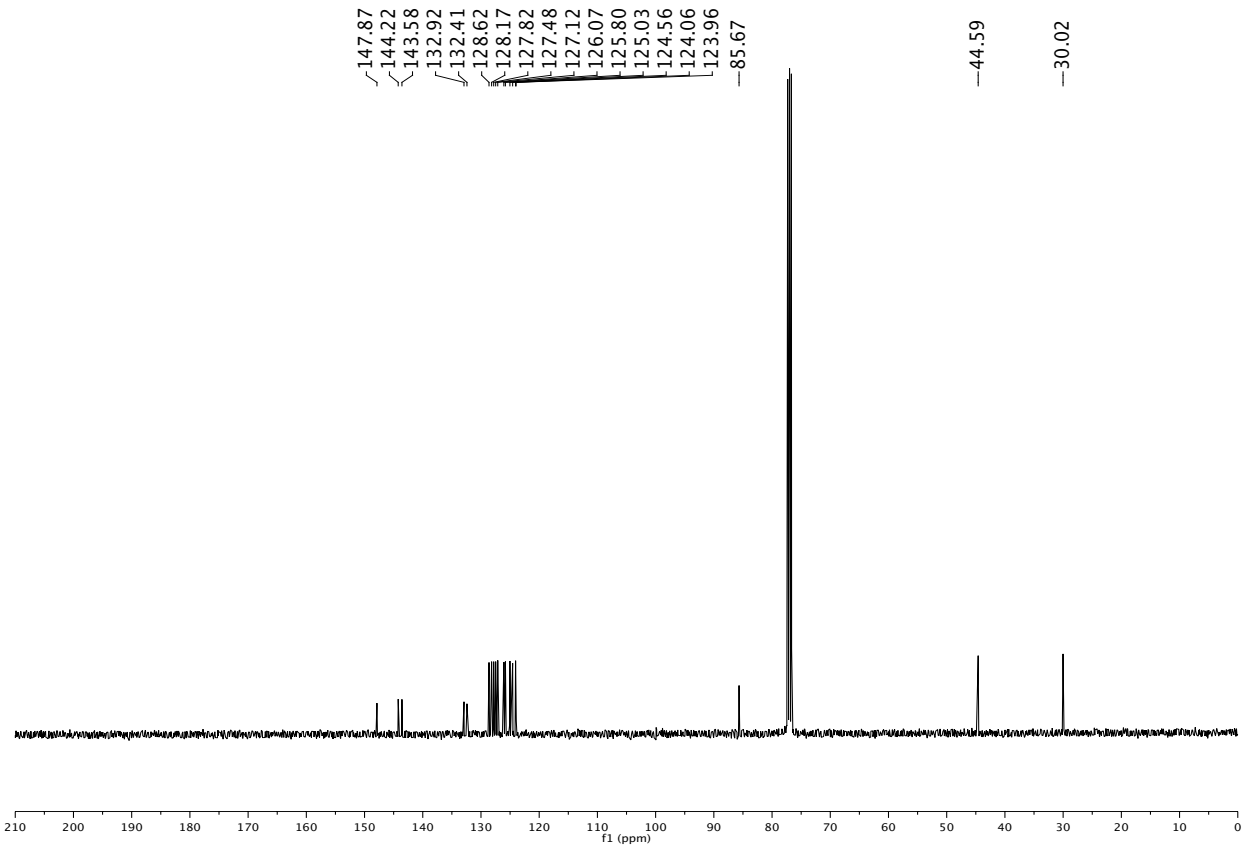
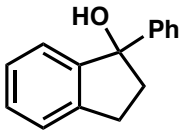
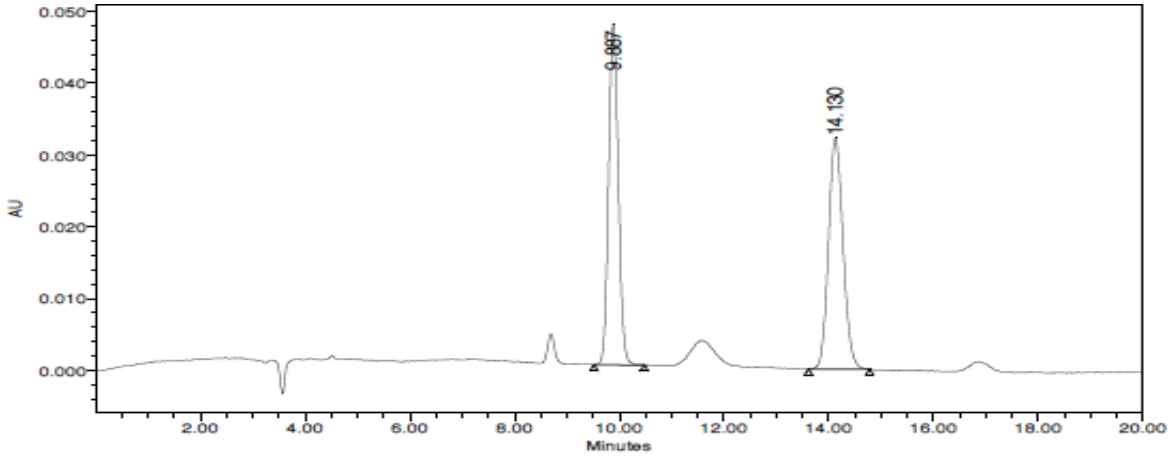
3.21
3.05
3.04
3.03
3.02
3.01
3.00
2.99
2.98
2.64
2.62
2.60
2.59
2.57
2.56
2.55
2.54
2.52
2.20
HO
16d
0.92
2.77
2.76
1.87
0.86
0.93
0.97
1.00
0.96
0.95
0.92
f1 (ppm)

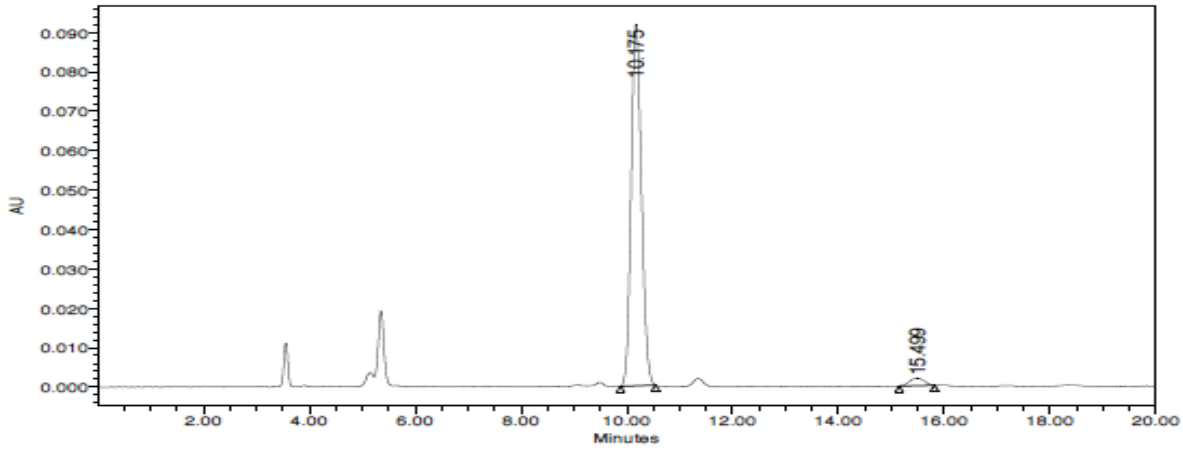

147.87
144.22
143.58
132.92
132.41
128.62
128.17
127.82
127.48
127.12
126.07
125.80
125.03
124.56
124.06
123.96
85.67
44.59
30.02
f1 (ppm)



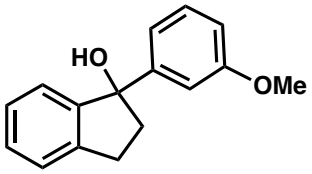
16a



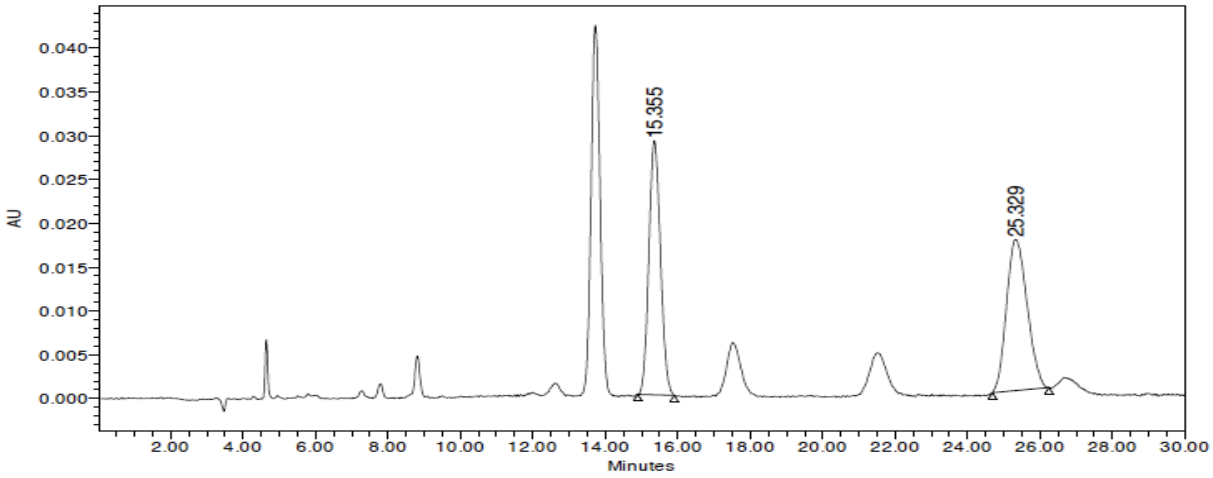
	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	9.887	611596	49.60	47612	59.61
2	14.130	621525	50.40	32255	40.39



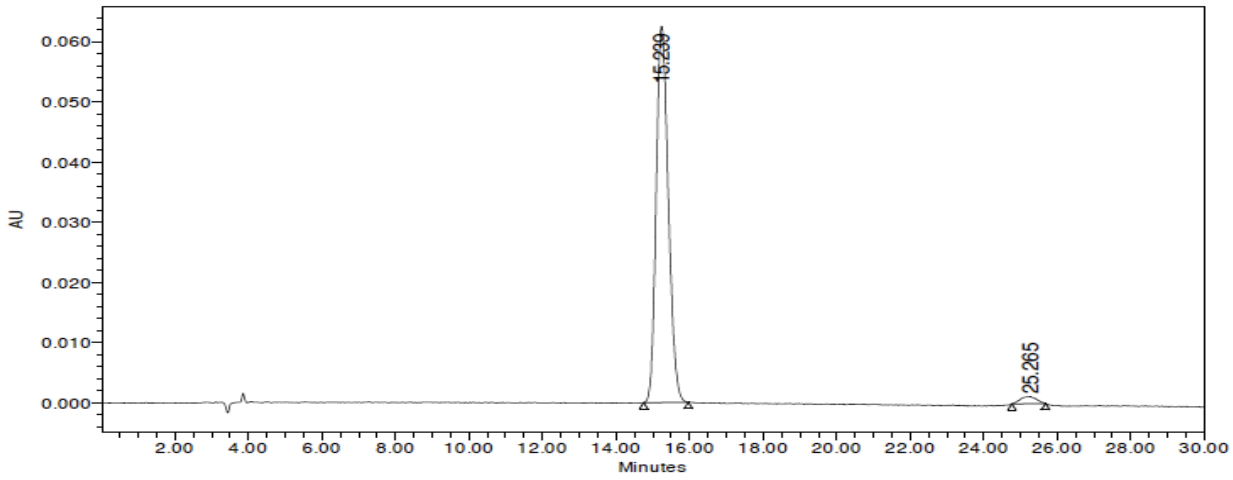
	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	10.175	1243021	97.13	92143	97.90
2	15.499	36754	2.87	1972	2.10



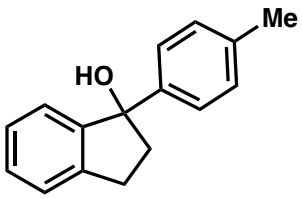
16b



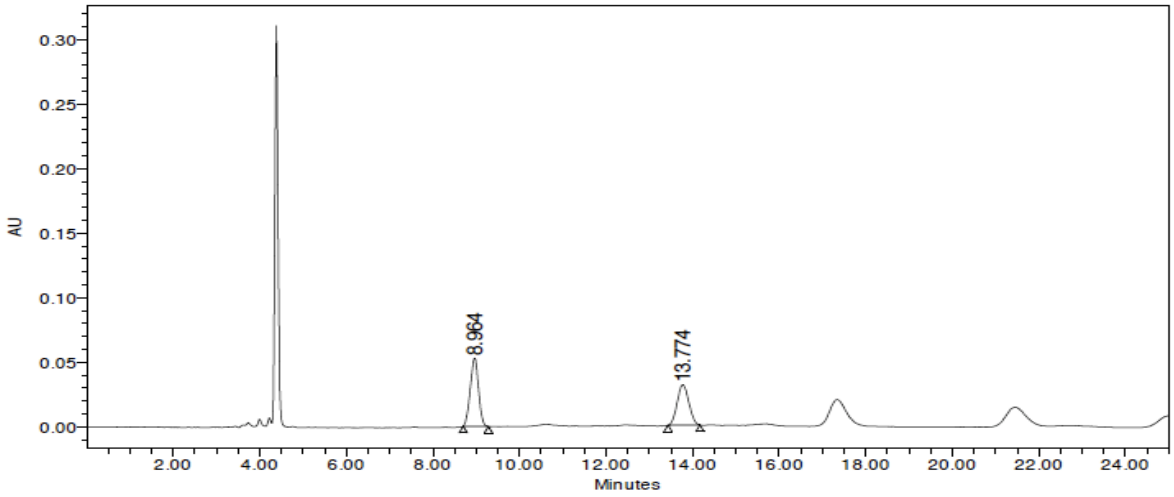
	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	15.355	645668	48.64	29039	62.76
2	25.329	681680	51.36	17233	37.24



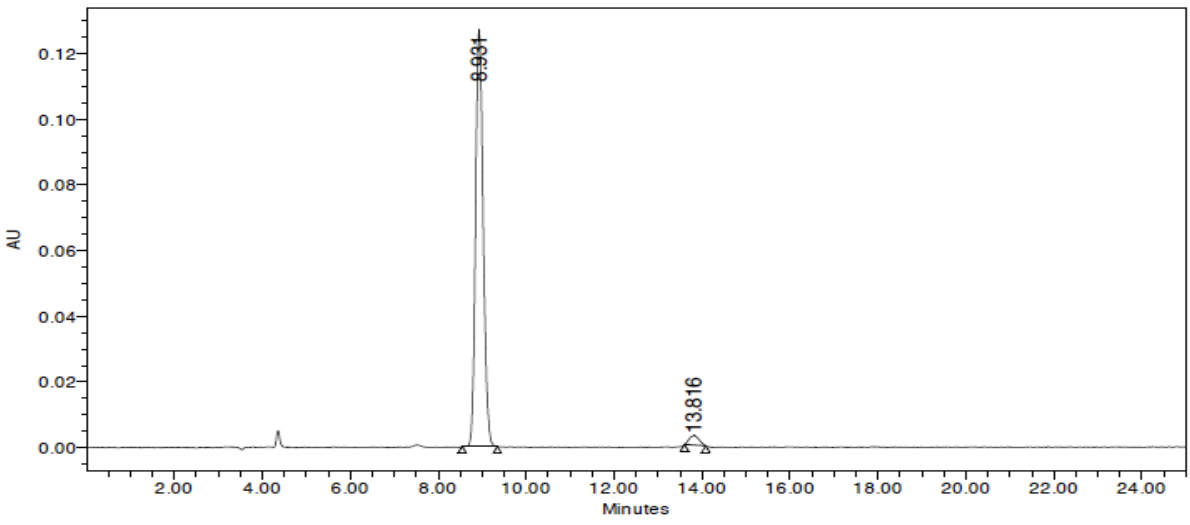
	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	15.239	1435295	97.50	62579	98.13
2	25.265	36833	2.50	1195	1.87



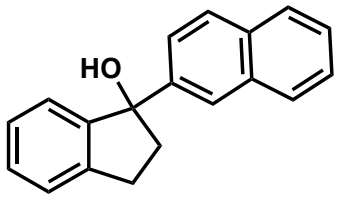
16c



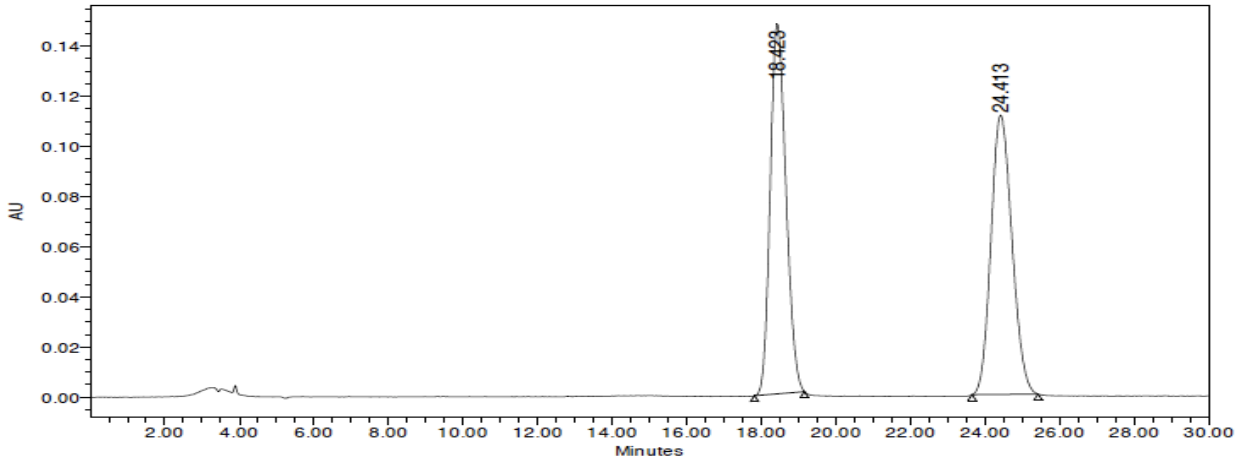
	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	8.964	699430	54.61	53046	62.95
2	13.774	581423	45.39	31225	37.05



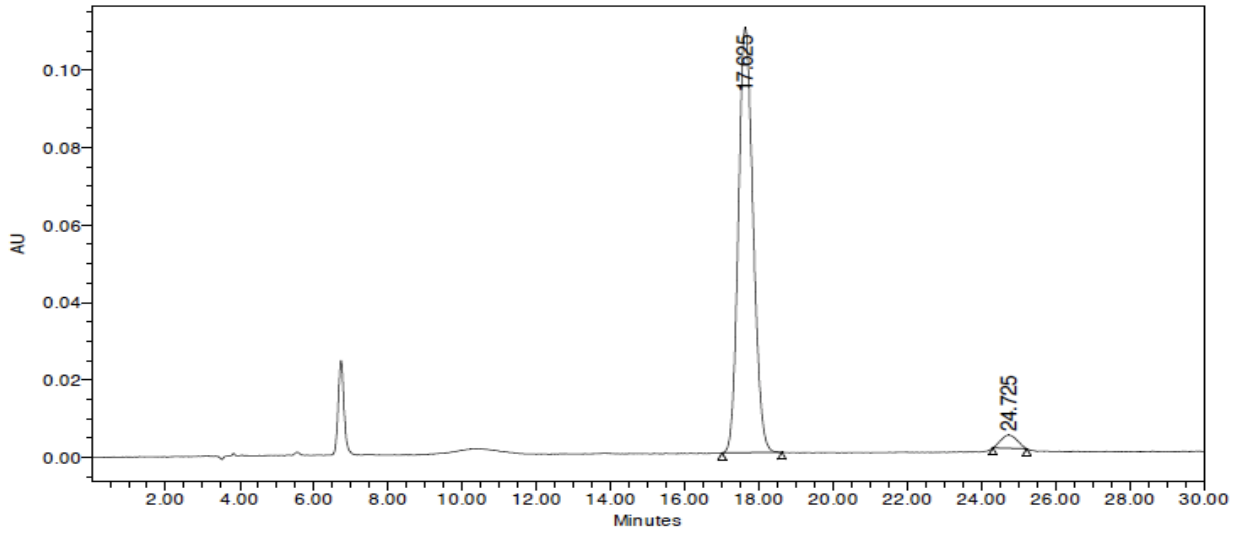
	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	8.931	1514433	97.12	127033	97.80
2	13.816	44847	2.88	2858	2.20



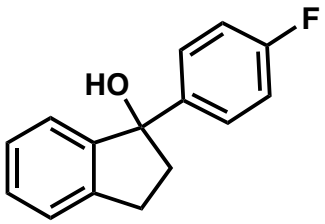
16d



	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	18.423	4331248	49.81	147519	56.99
2	24.413	4364462	50.19	111324	43.01



	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	17.625	3039061	96.71	109921	97.00
2	24.725	103330	3.29	3401	3.00



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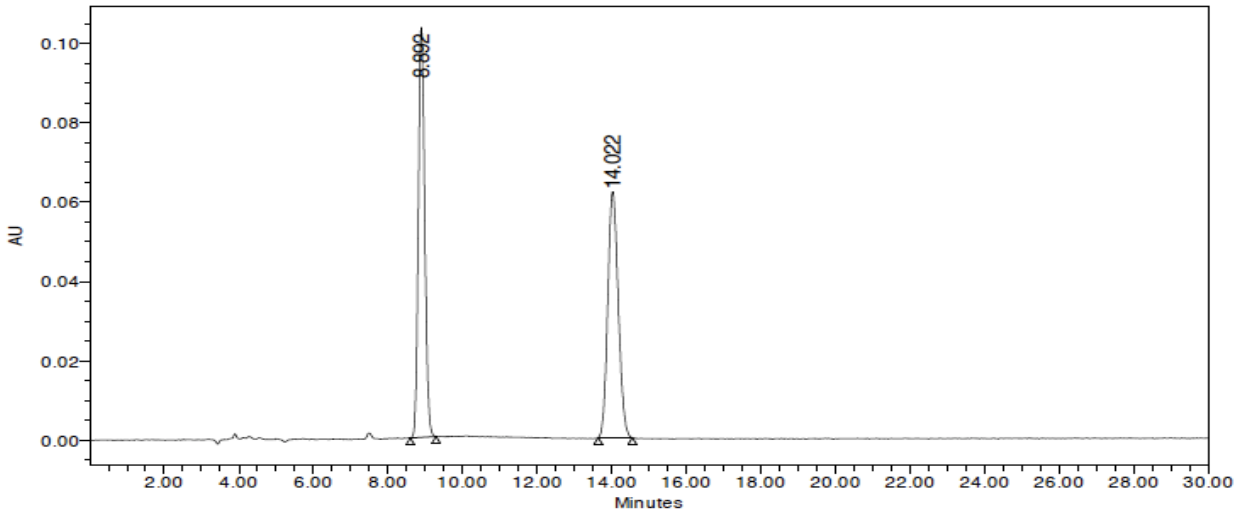
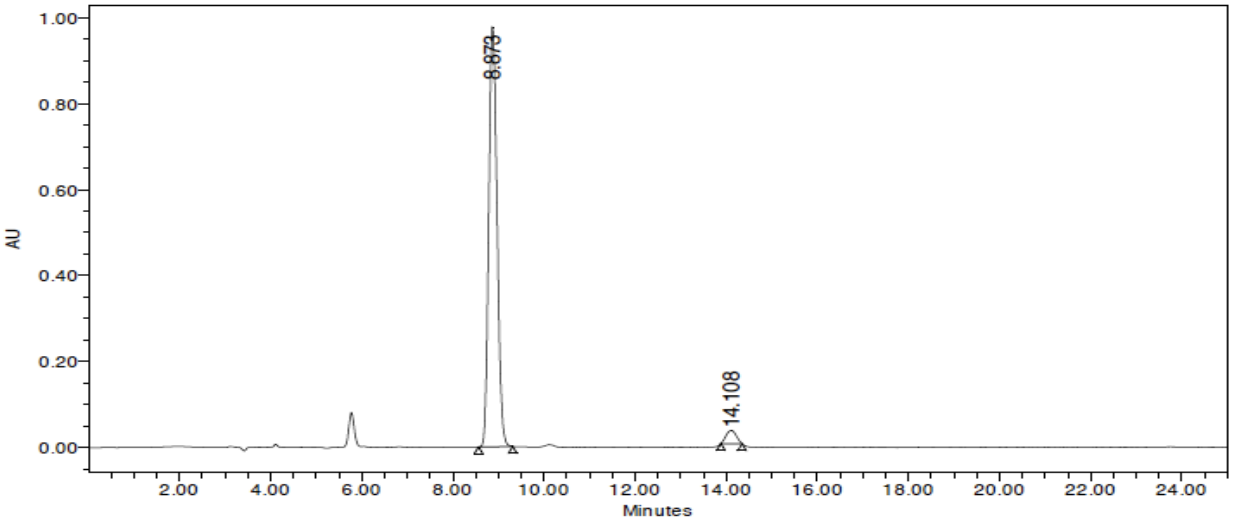
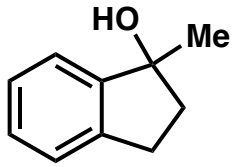


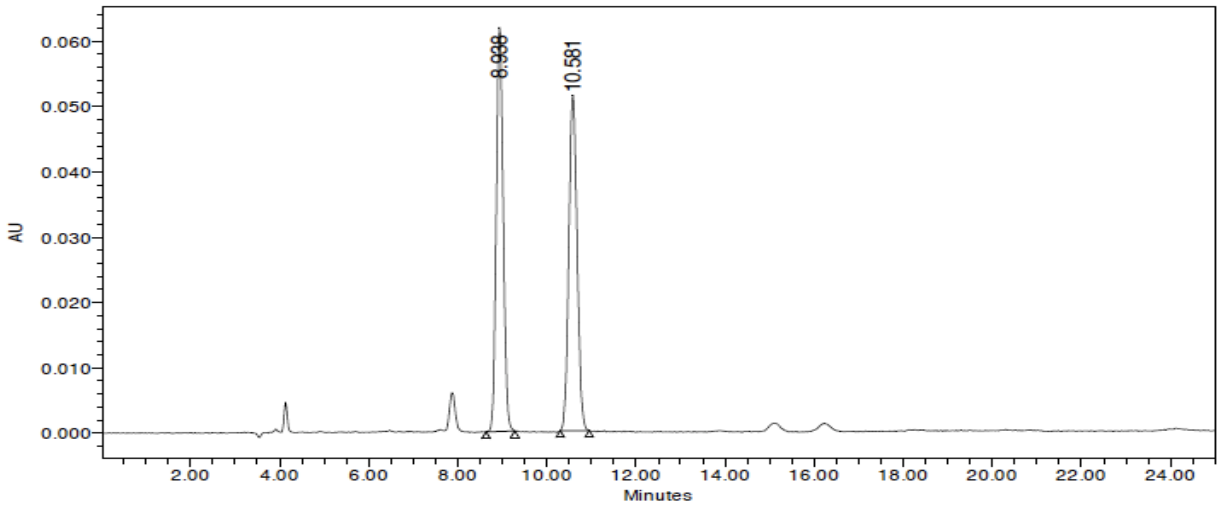
	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	8.892	1225575	50.32	103909	62.62
2	14.022	1209829	49.68	62034	37.38



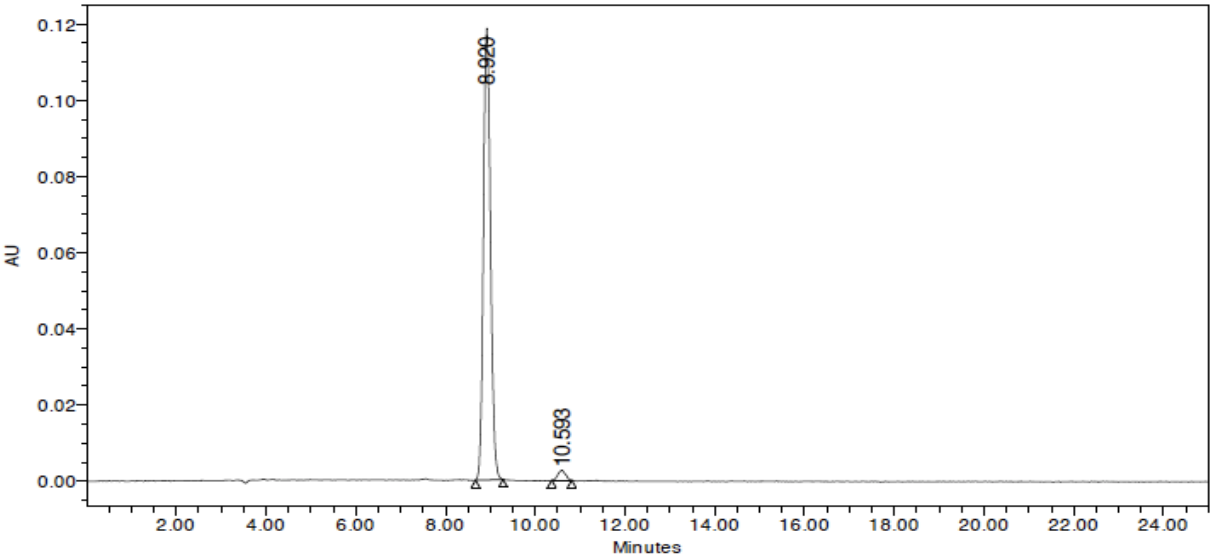
	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	8.873	12335311	96.22	979226	96.92
2	14.108	484038	3.78	31120	3.08



16e

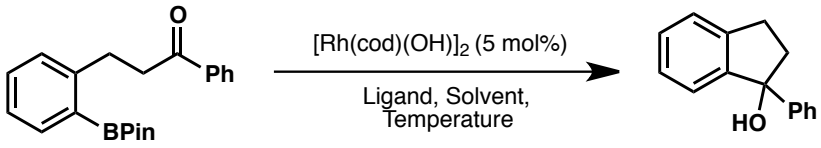


	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	8.938	668035	50.11	61958	54.67
2	10.581	664997	49.89	51377	45.33



	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	8.920	1291251	97.70	118741	97.88
2	10.593	30365	2.30	2572	2.12

Complete asymmetric optimization table:



entry	ligand (mol%)	solvent	temp (°C)	time (h)	pdt : SM[a]	% ee[b]
1	(*R,R*) - 1-Napthyl DIPAMP (10)	C_6D_6	80	24	1.0 : 0	5
2	(*R,R*) - Chiraphos (10)	C_6D_6	80	48	1.0 : 0	11 (74)[c]
3	(*R,R*) - CatASium D (10)	C_6D_6	80	120	0.6 : 1.0	12
4	(*S,S*) - DIOP (10)	C_6D_6	80	120	0.8 : 1.0	12
5	(*R*) - MEOBIPHEP SL-A116-1 (10)	C_6D_6	80	48	> 20 : 1	-15
6	(*R*) - BINAP (10)	C_6D_6	80	24	1.0 : 0	49
7	(*R,S*) - Josiphos SL-J005-1 (10)	C_6D_6	80	72	1.0 : 0	17
8	(*R,S*) - MandyPhos SL-M001-1 (10)	C_6D_6	80	72	1.0 : 0	1
9	(*R,R*) - TaniaPhos SL-T002-1 (10)	C_6D_6	80	72	>20 : 1	-3
10	(*R,R*) - WalPhos SL-W001-1 (11)	C_6D_6	80	72	0.6 : 1.0	-35
11	(*R,S*) - Josiphos SL-J003-1 (10)	C_6D_6	80	120	8.1 : 1.0	59
12	(*R,S*) - Josiphos SL-J013-1 (10)	C_6D_6	80	92	1.0 : 0	81 (92)
13	(*R,S*) - Josiphos SL-J013-1 (10)	THF	80	120	10 : 1.0	78
14	(*R,S*) - Josiphos SL-J013-1 (10)	1,2-DCE	80	24	0 : 1.0	-
15	(*R,S*) - Josiphos SL-J013-1 (10)	MeCN	80	24	0 : 1.0	-
16	(*R,S*) - Josiphos SL-J013-1 (11)	C_6D_6	80	72	3.7 : 1.0	84
17	(*R,S*) - Josiphos SL-J013-1 (11)	C_6D_6	80	88	5.4 : 1.0	91
18	(*R,S*) - Josiphos SL-J002-1 (11)	C_6D_6	80	72	1.5 : 1.0	85
19	(*R,S*) - Josiphos SL-J002-1 (12)	C_6D_6	80	72	6.6 : 1.0	88
20	(*R,S*) - Josiphos SL-J002-1 (15)	C_6D_6	80	72	4.6 : 1.0	92
21	(*R,S*) - Josiphos SL-J002-1 (15)	d^8-PhMe	80	72	7.8 : 1.0	89
22	(*R,S*) - Josiphos SL-J002-1 (15)	PhMe	80	72	5.7 : 1.0	95 (72)[d]
23	(*R,S*) - Josiphos SL-J002-1 (11)	PhMe	80	72	5.7 :1 .0	94 (69)[d]
24	*(R,S) - Josiphos SL-J002-1 (11)*	*PhMe*	*85*	*72*	*1.0 : 0*	*94 (78)*[d]
25	(*R,S*) - Josiphos SL-J002-1 (15)	d^8-PhMe	100	72	13 : 1.0	85
26	(*R,S*) - Josiphos SL-J002-1 (15)	C_6D_6	100	72	3.6 : 1.0	87
27	(*R,S*) - Josiphos SL-J011-1 (15)	d^8-PhMe	80	72	1.5 : 1.0	79
28	(*R,S*) - Josiphos SL-J011-1 (15)	d^8-PhMe	100	72	2.7 : 1.0	73
29	(*R,S*) - Josiphos SL-J011-1 (15)	d^8-PhMe	100	72	6.3 : 1.0	78
30	(*R,S*) - Josiphos SL-J002-1 (15)	PhF	80	120	8.8 : 1.0	90[d]

[a] Ratios determined by ^{1}H NMR [b] Enantiometric excess determined by chiral HPLC [c] Values in parentheses are isolated yields [d] Material stirs at rt for 1 h before being heated.