Enantioselective α-Arylation of Aldehydes via the Productive Merger of Iodonium Salts and Organocatalysis

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Supporting Information

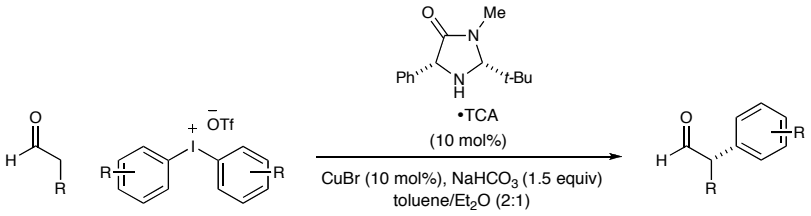
I. General Information. Commercial reagents were purified prior to use following the guidelines of Perrin and Armarego.[1] All solvents were purified according to the method of Grubbs.[2] Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator. Chromatographic purification of products was accomplished using force-flow chromatography on Silicycle or Davisil silica gel according to the method of Still.[3] Thin-layer chromatography (TLC) was performed on Silicycle 250 μm silica gel plates. TLC visualization was performed by fluorescence quenching or $KMnO_4$, ceric ammonium molybdate, or anisaldehyde stains. All yields reported are averages of at least two experimental runs.

^1H spectra were recorded on a Bruker 500 (500 MHz) and are referenced relative to residual $CDCl_3$ proton signals at δ 7.27 ppm or Acetone-D_6 at δ 2.05 ppm. ^{19}F NMR spectra were recorded on a Varian Inova 400 (376 MHz) and are referenced relative to $CFCl_3$ (δ 0.0 ppm). Data for ^1H and ^{19}F NMR are reported as follows: chemical shift (δ

(1) Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals*; 3rd ed., Pergamon Press, Oxford, 1988.
(2) Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518.
(3) Still, W. C.; Kahn, M.; Mitra, A. J. *J. Org. Chem.* **1978**, *43*, 2923.

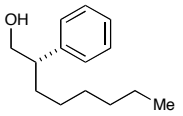
ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, h = heptet, m = multiplet, ap = apparent), integration, coupling constant (Hz) and assignment. ^{13}C spectra were recorded on a Bruker 500 (125 MHz) and are referenced relative to $CDCl_3$ at δ 77.00 ppm or Acetone-D_6 at 206.26 ppm. Data for ^{13}C NMR are reported in terms of chemical shift and multiplicity where appropriate. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in terms of frequency of absorption (cm^{-1}). High Resolution Mass spectra were obtained from the Princeton University Mass Spectral Facility. Supercritical fluid chromatography (SFC) was performed on a Berger Minigram equipped with a diode array UV detector (λ = 214–258 nm) using a chiral column (25 cm) and guard column (5 cm) as noted for each compound. High pressure liquid chromatography (HPLC) was performed on Hewlett-Packard 1100 Series chromatographs using a chiral column (25 cm) and guard column (5 cm) as noted for each compound. Optical rotations were measured on a Jasco P-1010 polarimeter with $[\alpha]_D$ values reported in degrees; concentration (c) is in g/100 mL.

II. Enantioselective Arylation of Aldehydes.



General procedure for the enantioselective arylation of aldehydes: To an oven-dried 8 mL vial equipped with a magnetic stir bar and Teflon septum was added (2*R*,5*R*)-2-*tert*-butyl-3-methyl-5-phenyl-4-imidazolidinone trichloroacetic acid salt (39.6 mg, 0.10 equiv), copper(I) bromide (14.3 mg, 0.10 equiv), sodium bicarbonate (136.0 mg, 1.50 equiv), and the diaryliodonium trifluoromethanesulfonate salt (1.00 equiv). The vial was sealed and purged with a stream of argon. Toluene (2.0 mL) and diethyl ether (1.0 mL) were added, followed by the aldehyde (1.20 mmol, 1.20 equiv). After 2-12 hours, the vial was diluted with CH_2Cl_2 (6.0 mL) and cooled to –78 °C. $NaBH_4$ (378.3 mg, 10.0 equiv) was then added, followed by cold MeOH (2.0 mL, –78 °C). The reaction was stirred for

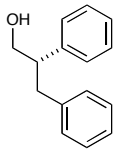
one hour at –78 °C then transferred to a flask containing saturated aqueous ammonium chloride solution (20 mL). The aqueous phase was extracted with CH_2Cl_2 (20 mL, ×3), and the combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The crude oil was then purified by column chromatography on silica gel using the noted solvent mixture to furnish the desired alcohol product.



(*S*)-2-Phenyl-1-octanol (Table 2, entry 1). Prepared following the general procedure outlined above using octanal (187 μL, 1.20 mmol), (2*R*,5*R*)-2-*tert*-butyl-3-methyl-5-phenyl-4-imidazolidinone·TCA (39.6 mg, 0.10 mmol), CuBr (14.3 mg, 0.10 mmol), $NaHCO_3$ (126 mg, 1.50 mmol), diphenyliodonium trifluoromethanesulfonate (430 mg, 1.00 mmol), toluene (2.00 mL), and Et_2O (1.00 mL). After 3 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography on silica gel using 3% EtOAc in toluene to provide the title compound (185 mg, 90% yield, 92% ee) as a colorless oil. IR (thin film) 3339, 2955, 2925, 2856, 1494, 1466, 1453, 1378, 1056, 1026, 758, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.34 (t, 2H, *J* = 7.5 Hz, Ar**H**), 7.24 (t, 1H, *J* = 7.4 Hz, Ar**H**), 7.21 (d, 2H, *J* = 7.1 Hz, Ar**H**), 3.73 (m, 2H, C**H**$_2$OH), 2.77 (m, 1H, C**H**Ar), 1.69 (m, 1H, CHArC**H**$_2$), 1.56 (m, 1H, CHArC**H**$_2$), 1.37 (br s, 1H, O**H**), 1.34-1.11 (m, 8H, (C**H**$_2$)$_4$), 0.85 (t, 3H, *J* = 7.0 Hz, C**H**$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 142.5, 128.7, 128.1, 126.7, 67.7, 48,7, 32.1, 31.7, 29.4, 27.4, 22.7, 14.1; HRMS (ESI-TOF) calculated for $C_{14}H_{22}O$ [M] m/z 206.16707, found 206.16712. $[\alpha]_D^{21}$ = +15.1 (c = 0.99, $CHCl_3$); HPLC analysis (OJ, 5% *i*-PrOH/hexanes, 1.0 mL/min, 254 nm) indicated 92% ee: t_R(minor) = 6.3 minutes, t_R (major) = 7.0 minutes.

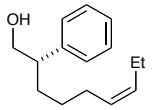
The enantiopure aldehyde can also be isolated via direct flash chromatography of the reaction mixture on Davisil silica gel using 100% toluene to provide 2-phenyloctanal (91%

yield, 90% ee) as a colorless oil, which was identical to the reported literature compound.[4] The enantiopurity of the isolated aldehyde was determined after reduction to the corresponding alcohol. HPLC analysis (OJ, 5% *i*-PrOH/hexanes, 1.0 mL/min, 220 nm) indicated 90% ee: t_R(minor) = 6.9 minutes, t_R (major) = 7.9 minutes.

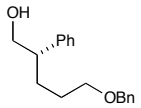


(*S*)-2,3-Diphenyl-1-propanol (Table 2, entry 2). Prepared following the general procedure outlined above using 3-phenylpropanal (158 μL, 1.20 mmol), (2*R*,5*R*)-2-*tert*-butyl-3-methyl-5-phenyl-4-imidazolidinone·TCA (39.6 mg, 0.10 mmol), CuBr (14.3 mg, 0.10 mmol), $NaHCO_3$ (126 mg, 1.50 mmol), diphenyliodonium trifluoromethanesulfonate (430 mg, 1.00 mmol), toluene (2.00 mL), and Et_2O (1.00 mL). After 3 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography on silica gel using 20% EtOAc in hexanes to provide the title compound (185 mg, 87% yield, 94% ee) as a colorless oil. IR (thin film) 3352, 3027, 2927, 1602, 1495, 1452, 1276, 1261, 1061, 1029, 757, 696 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.24 (t, 2H, *J* = 7.4 Hz, Ar**H**), 7.20-7.11 (m, 5H, Ar**H**), 7.08 (t, 1H, *J* = 7.3 Hz, Ar**H**), 7.02 (d, 2H, *J* = 7.0 Hz), 3.72 (m, 2H, C**H**$_2$OH), 3.02 (m, 1H, C**H**Ar), 2.95 (dd, 1H, *J* = 13.5, 7.5 Hz, CHArC**H**$_2$Ar), 2.84 (dd, 1H, *J* = 13.5, 7.5 Hz, CHArC**H**$_2$Ar), 1.25 (br s, 1H, O**H**); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 141.9, 139.9, 129.1, 128.7, 128.3, 128.1, 126.9, 126.1, 66.4, 50.2, 38.7; HRMS (ESI-TOF) calculated for $C_{15}H_{16}O$ [M] m/z 212.12012, found 212.12019. $[\alpha]_D^{21}$ = +70.9 (c = 1.10, $CHCl_3$); literature: $[\alpha]_D^{25}$ = +87 (c = 1.0, $CHCl_3$).[5] HPLC analysis (AD, 3% *i*-PrOH/hexanes, 1.0 mL/min, 254 nm) indicated 94% ee: t_R(minor) = 17.8 minutes, t_R (major) = 23.6 minutes.

(4) Terao, Y.; Fukuoka, Y.; Satoh, T.; Miura, M.; Nomura, M. *Tetrahedron* **2002**, *43*, 101.
(5) Absolute stereochemical correlation made by comparison, see: Senanayake, C. H.; Larsen, R. D.; Bill, T. J.; Liu, J.; Corley, E. G.; Reider, P. *Synlett* **1994**, 199.

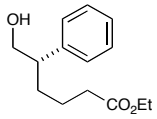


(*S*,*Z*)-2-Phenylnon-6-en-1-ol (Table 2, entry 3). Prepared following the general procedure outlined above using (*Z*)-6-nonenal (200 μL, 1.20 mmol), (2*R*,5*R*)-2-*tert*-butyl-3-methyl-5-phenyl-4-imidazolidinone·TCA (39.6 mg, 0.10 mmol), CuBr (14.3 mg, 0.10 mmol), $NaHCO_3$ (126 mg, 1.50 mmol), diphenyliodonium trifluoromethanesulfonate (430 mg, 1.00 mmol), toluene (1.50 mL), and Et_2O (1.50 mL). After 3 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography on silica gel using 3% EtOAc in toluene to provide the title compound (220 mg, 84% yield, 94% ee) as a colorless oil. IR (thin film) 3357, 3005, 2961, 2931, 2860, 1602, 1494, 1453, 1276, 1261, 1068, 1027, 758, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.33 (t, 2H, *J* = 7.5 Hz, Ar**H**), 7.24 (t, 1H, *J* = 7.5 Hz, Ar**H**), 7.20 (d, 2H, *J* = 7.8 Hz, Ar**H**), 5.35 (m, 1H, C**H**=CH), 5.26 (m, 1H, C**H**=CH), 3.75 (dd, 1H, *J* = 10.8, 5.8 Hz, C$\mathbf{H}_2$OH), 3.70 (dd, 1H, *J* = 10.8, 7.9 Hz, C$\mathbf{H}_2$OH), 2.77 (m, 1H, C**H**Ar), 2.01 (m, 4H, CH=CHC$\mathbf{H}_2$), 1.71 (m, 1H, CHArC$\mathbf{H}_2$) 1.56 (m, 1H, CHArC$\mathbf{H}_2$), 1.37 (br s, 1H, O**H**), 1.26 (m, 2H, CHArCH$_2$C$\mathbf{H}_2$), 0.94 (t, 3H, *J* = 7.8 Hz, C$\mathbf{H}_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 142.3, 131.9, 128.7, 128.6, 128.0, 126.7, 67.6, 48.6, 31.5, 27.4, 27.0, 20.5, 14.3; HRMS (ESI-TOF) calculated for $C_{15}H_{22}O$ [M] m/z 218.16707, found 218.16703. $[\alpha]_D^{21}$ = +9.1 (c = 1.27, $CHCl_3$); HPLC analysis (AS, 3% *i*-PrOH/hexanes, 1.0 mL/min, 254 nm) indicated 94% ee: t_R(major) = 7.1 minutes, t_R (minor) = 7.8 minutes.



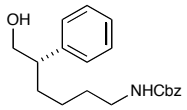
(*S*)-4-(Benzyloxy)-2-phenylpentan-1-ol (Table 2, entry 4). Prepared following the general procedure outlined above using 4-(benzyoxy)pentanal (231 mg, 1.20 mmol), (2*R*,5*R*)-2-*tert*-butyl-3-methyl-5-phenyl-4-imidazolidinone·TCA (79.1 mg, 0.20 mmol), CuBr (28.7 mg, 0.20 mmol), $NaHCO_3$ (126 mg, 1.50 mmol), diphenyliodonium trifluoromethanesulfonate (430 mg, 1.00 mmol), toluene (2.00 mL), and Et_2O (1.00 mL).

After 8 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography on silica gel using 10% EtOAc in toluene to provide the title compound (208 mg, 77% yield, 91% ee) as a pale yellow oil. IR (thin film) 3395, 3061, 3028, 2939, 2860, 1690, 1602, 1494, 1453, 1362, 1276, 1261, 1204, 1093, 1076, 1047, 1028, 908, 749, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.41-7.09 (m, 10H, Ar**H**), 4.45 (s, 2H, OC$\mathbf{H}_2$Ph), 3.74 (m, 2H, C$\mathbf{H}_2$OH), 3.42 (td, 2H, 6.4, 2.7 Hz, C$\mathbf{H}_2$OBn), 2.78 (m, 1H, C**H**Ar), 1.82 (m, 1H, CHArC$\mathbf{H}_2$), 1.64 (m, 1H, CHArC$\mathbf{H}_2$), 1.52 (m, 2H, CHArCH_2C$\mathbf{H}_2$), 1.35 (br s, 1H, O**H**); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 142.0, 138.4, 128.7, 128.3, 128.0, 127.6, 127.5, 126.8, 72.8, 70.1, 67.5, 48.4, 28.6, 27.5; HRMS (ESI-TOF) calculated for $C_{18}H_{22}O_2$ [M] m/z 270.16198, found 270.16196. $[\alpha]_D^{21}$ = –6.3 (c = 1.00, $CHCl_3$); HPLC analysis (AS, 3% *i*-PrOH/hexanes, 1.0 mL/min, 254 nm) indicated 91% ee: t_R(minor) = 19.1 minutes, t_R (major) = 20.6 minutes.

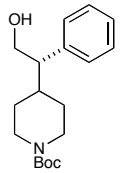


(*S*)-Ethyl 6-hydroxy-5-phenylhexanoate (Table 2, entry 5). Prepared following the general procedure outlined above using ethyl 6-oxohexanoate (190 mg, 1.20 mmol), (2*R*,5*R*)-2-*tert*-butyl-3-methyl-5-phenyl-4-imidazolidinone·TCA (39.6 mg, 0.10 mmol), CuBr (14.3 mg, 0.10 mmol), $NaHCO_3$ (126 mg, 1.50 mmol), diphenyliodonium trifluoromethanesulfonate (430 mg, 1.00 mmol), toluene (2.00 mL), and Et_2O (1.00 mL). After 6 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography on silica gel using 15% EtOAc in hexanes to provide the title compound (189 mg, 80% yield, 93% ee) as a colorless oil. IR (thin film) 3423, 2981, 2871, 2936, 1731, 1603, 1495, 1453, 1373, 1275, 1261, 1183, 1148, 1086, 1071, 1028, 763, 700 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.34 (t, 2H, *J* = 7.5 Hz, Ar**H**), 7.24 (t, 1H, *J* = 7.4 Hz, Ar**H**), 7.22 (d, 2H, *J* = 7.3 Hz, Ar**H**), 4.10 (q, 2H, *J* = 7.1 Hz, $CO_2C\mathbf{H}_2CH_3$), 3.74 (m, 2H, C$\mathbf{H}_2$OH), 2.80 (m, 1H, C**H**Ar), 2.27 (td, 2H, *J* = 7.3, 2.2 Hz, C$\mathbf{H}_2CO_2$Et), 1.75 (m, 1H, CHArC$\mathbf{H}_2$), 1.62 (m, 1H, CHArC$\mathbf{H}_2$), 1.55 (m, 2H,

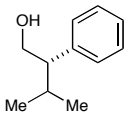
$CHArCH_2C\mathbf{H}_2$), 1.41 (br s, 1H, O**H**), 1.24 (t, 3H, J = 7.1 Hz, $CO_2CH_2C\mathbf{H}_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 173.5, 141.8, 128.7, 128.0, 126.8, 67.4, 60.2, 48.4, 34.7, 31.3, 22.7, 14.2; HRMS (ESI-TOF) calculated for $C_{14}H_{20}O_3$ [M] m/z 236.14124, found 236.14135. $[\alpha]_D^2$ = +11.3 (c = 1.05, $CHCl_3$); HPLC analysis (AS, 2% EtOH/hexanes, 1.0 mL/min, 254 nm) indicated 93% ee: t_R(major) = 24.7 minutes, t_R (minor) = 27.6 minutes.



(*S*)-Benzyl 6-hydroxy-5-phenylhexylcarbamate (Table 2, entry 6). Prepared following the general procedure outlined above using benzyl 6-oxohexylcarbamate (299 mg, 1.20 mmol), (2*R*,5*R*)-2-*tert*-butyl-3-methyl-5-phenyl-4-imidazolidinone·TCA (39.6 mg, 0.10 mmol), CuBr (14.3 mg, 0.10 mmol), $NaHCO_3$ (126 mg, 1.50 mmol), diphenyliodonium trifluoromethanesulfonate (430 mg, 1.00 mmol), toluene (2.00 mL), and Et_2O (1.00 mL). After 6 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography on silica gel using 30% EtOAc in toluene to provide the title compound (291 mg, 74% yield, 93% ee) as a colorless oil. IR (thin film) 3321, 3061, 3029, 2933, 2861, 1693, 1525, 1495, 1453, 1259, 1135, 1025, 910, 751, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.39-7.28 (m, 7H, Ar**H**), 7.24 (t, 1H, J = 7.4 Hz, Ar**H**), 7.19 (d, 2H, J = 7.4 Hz, Ar**H**), 5.07 (s, 2H, $NHC\mathbf{H}_2Ph$), 4.70 (br s, 1H, N**H**), 3.73 (m, 2H, $C\mathbf{H}_2OH$), 3.13 (m, 2H, $C\mathbf{H}_2NH$), 2.76 (m, 1H, C**H**Ar), 1.73 (m, 1H, $CHArC\mathbf{H}_2$), 1.58 (m, 1H, $CHArC\mathbf{H}_2$), 1.48 (m, 2H, $C\mathbf{H}_2CH_2NH$), 1.42 (br s, 1H, O**H**), 1.24 (m, 2H, $CHArCH_2C\mathbf{H}_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ:156.3, 142.1, 136.5, 128.7, 128.5, 128.11, 128.09, 128.0, 126.8, 67.4, 66.6, 48.5, 40.7, 31.5, 29.9, 24.3; HRMS (ESI-TOF) calculated for $C_{20}H_{25}NO_3$ [M] m/z 327.18344, found 327.18341. $[\alpha]_D^{22}$ = +13.4 (c = 1.04, $CHCl_3$); HPLC analysis (AD, 10% *i*-PrOH/hexanes, 1.0 mL/min, 220 nm) indicated 93% ee: t_R(minor) = 33.3 minutes, t_R (major) = 38.2 minutes.

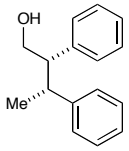


(*S*)-*tert*-Butyl 4-(2-hydroxy-1-phenylethyl)pipperdine-1-carboxylate (Table 2, entry 7). Prepared following the general procedure outlined above using *tert*-butyl 4-(2-oxoethyl)piperidine-1-carboxylate (227.3 mg, 1.00 mmol), (2*R*,5*R*)-2-*tert*-butyl-3-methyl-5-phenyl-4-imidazolidinone·TCA (39.6 mg, 0.10 mmol), CuBr (7.2 mg, 0.10 mmol), $NaHCO_3$ (63.0 mg, 0.75 mmol), diphenyliodonium trifluoromethanesulfonate (215 mg, 0.50 mmol), toluene (1.00 mL), and Et_2O (0.50 mL). After 6 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography on silica gel using 30% EtOAc in toluene to provide the title compound (124 mg, 81% yield, 93% ee) as a colorless oil that solidifies upon standing. IR (thin film) 3437, 2976, 2933, 2854, 1667, 1468, 1424, 1365, 1277, 1249, 1163, 1130, 1081, 1055, 1021, 981, 913, 867, 817, 763, 732, 701 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.34 (t, 2H, *J* = 7.3 Hz, Ar**H**), 7.26 (t, 1H, *J* = 7.6 Hz, Ar**H**), 7.19 (d, 2H, *J* = 7.4 Hz, Ar**H**), 4.12 (br s, 2H C**H**$_2$NBoc), 3.92 (m, 1H, C**H**$_2$OH), 3.86 (m, 1H, C**H**$_2$OH), 2.69 (br s, 1H, C**H**Ar), 2.57 (m, 2H, C**H**$_2$NBoc), 1.84 (m, 1H, C**H**$_2$CH$_2$NBoc), 1.77 (m, 1H, C**H**$_2$CH$_2$NBoc), 1.43 (s, 9H, C(C**H**$_3$)$_3$), 1.33 (m, 1H, C**H**$_2$CH$_2$NBoc), 1.24 (m, 1H, C**H**$_2$CH$_2$NBoc), 0.97 (m, 1H, CH$_2$CHArC**H**); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 154.7, 140.8, 128.64, 128.58, 126.9, 79.2, 64.3, 53.9, 37.9, 30.4 (2)(broad singlet, rotamers), 28.4; HRMS (ESI-TOF) calculated for $C_{18}H_{27}NO_3$ [M] m/z 305.19909, found 305.1993. $[\alpha]_D^{22}$ = +33.9 (c = 0.99, $CHCl_3$); HPLC analysis (AS, 2% EtOH/hexanes, 1.0 mL/min, 220 nm) indicated 93% ee: t_R(minor) = 17.6 minutes, t_R (major) = 18.8 minutes.



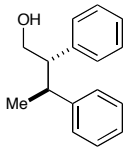
(*S*)-3-Methyl-2-phenyl-1-butanol (Table 2, entry 8). Prepared following the general procedure outlined above using isovaleraldehyde (216 μL, 2.00 mmol), (2*R*,5*R*)-2-*tert*-

butyl-3-methyl-5-phenyl-4-imidazolidinone·TCA (79.1 mg, 0.20 mmol), CuBr (14.3 mg, 0.10 mmol), $NaHCO_3$ (126 mg, 1.50 mmol), diphenyliodonium trifluoromethanesulfonate (430 mg, 1.00 mmol), toluene (2.00 mL), and Et_2O (1.00 mL). After 8 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography on silica gel using 10% EtOAc in hexanes to provide the title compound (111 mg, 68% yield, 90% ee) as a colorless oil, which was identical to the reported literature compound.[6] $[\alpha]_D^{21}$ = +9.7 (c = 1.05, $CHCl_3$); literature: $[\alpha]_D^{20}$ = +11.3 (c = 1.0, $CHCl_3$);[6] HPLC analysis (AS, 3% *i*-PrOH/hexanes, 1.0 mL/min, 254 nm) indicated 90% ee: t_R(major) = 9.4 minutes, t_R (minor) = 10.1 minutes.

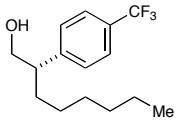


(2*S*,3*R*)-2,3-Diphenyl-1-butanol (Table 2, entry 9). Prepared following the general procedure outlined above using (*R*)-3-phenylbutanal (178 μL, 1.20 mmol), (2*R*,5*R*)-2-*tert*-butyl-3-methyl-5-phenyl-4-imidazolidinone·TCA (39.6 mg, 0.10 mmol), CuBr (14.3 mg, 0.10 mmol), $NaHCO_3$ (126 mg, 1.50 mmol), diphenyliodonium trifluoromethanesulfonate (430 mg, 1.00 mmol), toluene (2.00 mL), and Et_2O (1.00 mL). After 8 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography on silica gel using 10% EtOAc in hexanes to provide the title compound (183 mg, 81% yield, >20:1 dr determined by crude ^{1}H NMR in C_6D_6) as a white solid, which was identical to the reported literature compound.[7] $[\alpha]_D^{22}$ = –1.7 (c = 1.09, $CHCl_3$).

(6) Absolute stereochemical correlation made by comparison, see: Xie, J.-H.; Zhou, Z.-T.; Kong, W.-L.; Zhou, Q.-L. *J. Am. Chem. Soc.* **2007**, *129*, 1868.
(7) Hupe, E.; Denisenko, D.; Knochel, P. *Tetrahedron* **2003**, *59*, 9187.

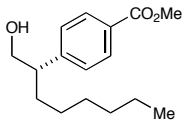


(2*S*,3*S*)-2,3-Diphenyl-1-butanol (Table 2, entry 10). Prepared following the general procedure outlined above using (*R*)-3-phenylbutanal (149 μL, 1.00 mmol), (2*R*,5*R*)-2-*tert*-butyl-3-methyl-5-phenyl-4-imidazolidinone·TCA (79.1 mg, 0.20 mmol), CuBr (14.3 mg, 0.10 mmol), $NaHCO_3$ (63.0 mg, 0.75 mmol), diphenyliodonium trifluoromethanesulfonate (215 mg, 0.50 mmol), toluene (0.75 mL), and Et_2O (0.75 mL). After 8 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography on silica gel using 3% EtOAc in toluene to provide the title compound (75.2 mg, 67% yield, 5:1 dr determined by crude ^1H NMR in C_6D_6) as a white solid, which was identical to the reported literature compound.[7] $[\alpha]_D^{22} = +38.5$ (c = 0.98, $CHCl_3$).

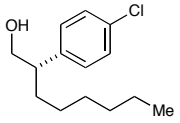


(*S*)-2-(4-(Trifluoromethyl)phenyl)-1-octanol (Table 3, entry 1). Prepared following the general procedure outlined above using octanal (187 μL, 1.20 mmol), (2*R*,5*R*)-2-*tert*-butyl-3-methyl-5-phenyl-4-imidazolidinone·TCA (39.6 mg, 0.10 mmol), CuBr (14.3 mg, 0.10 mmol), $NaHCO_3$ (126 mg, 1.50 mmol), bis(4-(trifluoromethyl)phenyl)iodonium trifluoromethanesulfonate (566 mg, 1.00 mmol), toluene (2.00 mL), and Et_2O (1.00 mL). After 2 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography on silica gel using 3% EtOAc in toluene to provide the title compound (259 mg, 95% yield, 94% ee) as a colorless oil. IR (thin film) 3314, 2928, 2859, 1619, 1468, 1420, 1323, 1163, 1120, 1068, 1017, 953, 837, 740 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.58 (d, 2H, *J* = 8.1 Hz, Ar**H**), 7.33 (d, 2H, *J* = 8.0 Hz, Ar**H**), 3.78 (m, 1H, C**H**$_2$OH), 3.73 (m, 1H, C**H**$_2$OH), 2.84 (m, 1H, C**H**Ar), 1.72 (m, 1H, CHArC**H**$_2$), 1.57 (m, 1H, CHArC**H**$_2$), 1.35 (br s, 1H, O**H**), 1.33-1.04 (m, 8H,

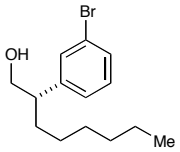
($C\mathbf{H}_2)_4$), 0.85 (t, 3H, J = 7.0 Hz, $C\mathbf{H}_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 147.0, 128.9 (q, J = 32.7 Hz), 128.4, 125.5 (q, J = 7.6 Hz), 124.2 (q, J = 272.0 Hz), 67.3, 48.6, 31.9, 31.6, 29.3, 27.2, 22.6, 14.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ: –62.8 (s); HRMS (ESI-TOF) calculated for $C_{15}H_{21}F_3O$ [M] m/z 274.15445, found 274.15444. $[\alpha]_D^{21}$ = +14.1 (c = 1.04, $CHCl_3$); HPLC analysis (AD, 3% *i*-PrOH/hexanes, 1.0 mL/min, 220 nm) indicated 94% ee: t_R(minor) = 8.8 minutes, t_R (major) = 11.9 minutes.



(*S*)-Methyl 4-(1-hydroxyoctan-2-yl)benzoate (Table 3, entry 2). Prepared following the general procedure outlined above using octanal (187 μL, 1.20 mmol), (2*R*,5*R*)-2-*tert*-butyl-3-methyl-5-phenyl-4-imidazolidinone·TCA (39.6 mg, 0.10 mmol), CuBr (14.3 mg, 0.10 mmol), $NaHCO_3$ (126 mg, 1.50 mmol), (4-(methoxycarbonyl)phenyl)(mesityl)iodonium trifluoromethanesulfonate (530 mg, 1.00 mmol), toluene (2.00 mL), and Et_2O (1.00 mL). After 5 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography on silica gel using 20% EtOAc in hexanes to provide the title compound (237 mg, 90% yield, 91% ee) as a light yellow oil. IR (thin film) 3425, 2953, 2926, 2856, 1721, 1610, 1458, 1436, 1418, 1312, 1275, 1180, 1111, 1056, 1019, 967, 854, 773, 750, 708 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.99 (d, 2H, J = 8.2 Hz, Ar**H**), 7.28 (d, 2H, J = 8.3 Hz, Ar**H**), 3.90 (s, 3H, $CO_2C\mathbf{H}_3$), 3.78 (dd, 1H, J = 10.8, 5.8 Hz, $C\mathbf{H}_2$OH), 3.73 (dd, 1H, J = 10.8, 7.8 Hz, $C\mathbf{H}_2$OH), 2.84 (m, 1H, C**H**Ar), 1.71 (m, 1H, CHArC$\mathbf{H}_2$), 1.55 (m, 1H, CHArC$\mathbf{H}_2$), 1.41 (br s, 1H, O**H**), 1.35-1.07 (m, 8H, ($C\mathbf{H}_2)_4$), 0.83 (t, 3H, J = 7.0 Hz, $C\mathbf{H}_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 167.0, 148.3, 129.9, 128.5, 128.1, 67.3, 52.1, 48.7, 31.9, 31.6, 29.2, 27.2, 22.5, 14.0; HRMS (ESI-TOF) calculated for $C_{16}H_{24}O_3$ [M] m/z 264.17254, found 264.17275. $[\alpha]_D^{22}$ = +12.5 (c = 1.09, $CHCl_3$); HPLC analysis (OD, 5% *i*-PrOH/hexanes, 1.0 mL/min, 254 nm) indicated 91% ee: t_R(major) = 14.0 minutes, t_R (minor) = 22.0 minutes.

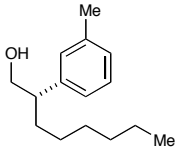


(*S*)-2-(4-Chlorophenyl)-1-octanol (Table 3, entry 3). Prepared following the general procedure outlined above using octanal (187 μL, 1.20 mmol), (2*R*,5*R*)-2-*tert*-butyl-3-methyl-5-phenyl-4-imidazolidinone·TCA (39.6 mg, 0.10 mmol), CuBr (14.3 mg, 0.10 mmol), $NaHCO_3$ (126 mg, 1.50 mmol), (4-chlorophenyl)(mesityl)iodonium trifluoromethanesulfonate (507 mg, 1.00 mmol), toluene (2.00 mL), and Et_2O (1.00 mL). After 5 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography on silica gel using 3% EtOAc in toluene to provide the title compound (227 mg, 86% yield, 93% ee) as a colorless oil. IR (thin film) 3314, 2955, 2926, 2856, 1594, 1492, 1466, 1411, 1378, 1275, 1262, 1180, 1092, 1055, 1029, 1014, 824, 767, 750, 720 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.29 (d, 2H, *J* = 8.5 Hz, Ar**H**), 7.15 (d, 2H, *J* = 8.5 Hz, Ar**H**), 3.74 (dd, 1H, *J* = 10.8, 5.6 Hz, C**H**$_2$OH), 3.67 (dd, 1H, *J* = 10.8, 8.0 Hz, C**H**$_2$OH), 2.75 (m, 1H, C**H**Ar), 1.67 (m, 1H, CHArC**H**$_2$), 1.50 (m, 1H, CHArC**H**$_2$), 1.34 (br s, 1H, O**H**), 1.30-1.06 (m, 8H, (C**H**$_2$)$_4$), 0.85 (t, 3H, *J* = 7.0 Hz, C**H**$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 141.0, 132.3, 129.40, 129.35, 128.7, 67.5, 48.1, 31.9, 31.6, 29.3, 27.2, 22.6, 14.0; HRMS (ESI-TOF) calculated for $C_{14}H_{21}ClO$ [M] m/z 240.12809, found 240.1283. $[\alpha]_D^{22}$ = +18.1 (c = 1.07, $CHCl_3$); HPLC analysis (AD, 3% *i*-PrOH/hexanes, 1.0 mL/min, 220 nm) indicated 93% ee: t_R(minor) = 10.0 minutes, t_R (major) = 10.9 minutes.



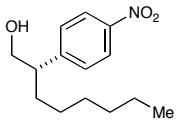
(*S*)-2-(3-Bromophenyl)-1-octanol (Table 3, entry 4). Prepared following the general procedure outlined above using octanal (187 μL, 1.20 mmol), (2*R*,5*R*)-2-*tert*-butyl-3-methyl-5-phenyl-4-imidazolidinone·TCA (39.6 mg, 0.10 mmol), CuBr (14.3 mg, 0.10

mmol), $NaHCO_3$ (126 mg, 1.50 mmol), (3-bromophenyl)(mesityl)iodonium trifluoromethanesulfonate (551 mg, 1.00 mmol), toluene (2.00 mL), and Et_2O (1.00 mL). After 3 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography on silica gel using 10% EtOAc in hexanes to provide the title compound (260 mg, 91% yield, 92% ee) as a colorless oil. IR (thin film) 3315, 2955, 2925, 2855, 1594, 1566, 1467, 1427, 1378, 1276, 1193, 1071, 997, 878, 780, 724, 695, 667 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.37 (m, 2H, Ar**H**), 7.20 (t, 1H, *J* = 7.7 Hz, Ar**H**), 7.14 (d, 1H, *J* = 7.7 Hz, Ar**H**), 3.74 (m, 1H, C**H**$_2$OH), 3.69 (m, 1H, C**H**$_2$OH), 2.73 (m, 1H, C**H**Ar), 1.67 (m, 1H, CHArC**H**$_2$), 1.52 (m, 1H, CHArC**H**$_2$), 1.35 (br s, 1H, O**H**), 1.31-1.09 (m, 8H, (C**H**$_2$)$_4$), 0.85 (t, 3H, *J* = 7.0 Hz, C**H**$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 145.2, 131.0, 130.1, 129.8, 126.8, 122.7, 67.3, 48.5, 31.9, 31.6, 29.3, 27.2, 22.6, 14.1; HRMS (ESI-TOF) calculated for $C_{14}H_{21}BrO$ [M] m/z 284.07758, found 284.07761. $[\alpha]_D^{21}$ = +15.9 (c = 1.09, $CHCl_3$); HPLC analysis (OD, 2% *i*-PrOH/hexanes, 1.0 mL/min, 230 nm) indicated 92% ee: t_R(minor) = 15.6 minutes, t_R (major) = 17.0 minutes.



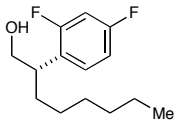
(*S*)-2-*m*-Tolyl-1-octanol (Table 3, entry 5). Prepared following the general procedure outlined above using octanal (187 μL, 1.20 mmol), (2*R*,5*R*)-2-*tert*-butyl-3-methyl-5-phenyl-4-imidazolidinone·TCA (39.6 mg, 0.10 mmol), CuBr (14.3 mg, 0.10 mmol), $NaHCO_3$ (126 mg, 1.50 mmol), (*m*-tolyl)(mesityl)iodonium trifluoromethanesulfonate (486 mg, 1.00 mmol), toluene (2.00 mL), and Et_2O (1.00 mL). After 3 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography on silica gel using 3% EtOAc in toluene to provide the title compound (203 mg, 92% yield, 91% ee) as a light yellow oil. IR (thin film) 3315, 3018, 2955, 2924, 2856, 1607, 1589, 1489, 1465, 1378, 1028, 880, 782, 765, 750, 703 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.22 (t, 1H, *J* = 7.5 Hz, Ar**H**), 7.06 (d, 1H, *J* = 7.4 Hz, Ar**H**), 7.02 (s, 1H, Ar**H**), 7.01 (d, 1H, *J* = 7.9 Hz, Ar**H**), 3.75 (dd, 1H, *J* = 10.7, 5.7

Hz, C**H**$_2$OH), 3.69 (dd, 1H, *J* = 10.7, 8.2 Hz, C**H**$_2$OH), 2.73 (m, 1H, C**H**Ar), 2.35 (s, 3H, ArC**H**$_3$), 1.66 (m, 1H, CHArC**H**$_2$), 1.55 (m, 1H, CHArC**H**$_2$), 1.34 (br s, 1H, O**H**), 1.32-1.13 (m, 8H, (C**H**$_2$)$_4$), 0.86 (t, 3H, *J* = 7.0 Hz, C**H**$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 142.4, 138.1, 128.8, 128.5, 127.4, 125.0, 67.6, 48.6, 32.0, 31.7, 29.3, 27.3, 22.6, 21.5, 14.1; HRMS (ESI-TOF) calculated for $C_{15}H_{24}O$ [M] m/z 220.18272, found 220.18281. $[\alpha]_D^{22}$ = +13.4 (c = 1.02, $CHCl_3$); HPLC analysis (OJ, 3% *i*-PrOH/hexanes, 1.0 mL/min, 220 nm) indicated 91% ee: t_R(minor) = 6.1 minutes, t_R (major) = 6.8 minutes.

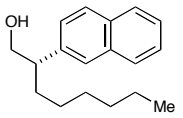


(*S*)-2-(4-Nitrophenyl)-1-octanol (Table 3, entry 6). Prepared following the general procedure outlined above using octanal (93.6 μL, 0.60 mmol), (2*R*,5*R*)-2-*tert*-butyl-3-methyl-5-phenyl-4-imidazolidinone·TCA (39.6 mg, 0.10 mmol), CuBr (7.2 mg, 0.05 mmol), $NaHCO_3$ (63.0 mg, 0.75 mmol), (4-nitrophenyl)(mesityl)iodonium trifluoromethanesulfonate (259 mg, 0.50 mmol), toluene (1.00 mL), and Et_2O (0.50 mL). After 5 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure, with the following reduction modifications: 4 equivalents of $NaBH_4$ was used and the reaction was quenched in a 0 ºC ice bath after 30 minutes. The crude material was purified by flash chromatography on silica gel using 20% EtOAc in hexanes to provide the title compound (176 mg, 70% yield, 93% ee) as an orange oil. IR (thin film) 3356, 2927, 2857, 1596, 1515, 1466, 1343, 1276, 1261, 1182, 1110, 1050, 1014, 852, 764, 752, 700 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.18 (d, 2H, *J* = 8.7 Hz, Ar**H**), 7.38 (d, 2H, *J* = 8.7 Hz, Ar**H**), 3.82 (dd, 1H, *J* = 10.7, 5.5 Hz, C**H**$_2$OH), 3.76 (dd, 1H, *J* = 10.7, 7.8 Hz, C**H**$_2$OH), 2.91 (m, 1H, C**H**Ar), 1.74 (m, 1H, CHArC**H**$_2$), 1.58 (m, 1H, CHArC**H**$_2$), 1.45 (br s, 1H, O**H**), 1.33-1.08 (m, 8H, (C**H**$_2$)$_4$), 0.84 (t, 3H, *J* = 7.0 Hz, C**H**$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 151.0, 146.7, 128.9, 123.7, 67.0, 48.6, 31.8, 31.6, 29.2, 27.2, 22.5, 14.0; HRMS (ESI-TOF) calculated for $C_{14}H_{21}NO_3$ [M] m/z 251.15214, found 251.15239. $[\alpha]_D^{21}$ = +15.6 (c = 1.03, $CHCl_3$); HPLC analysis (AD, 5% *i*-

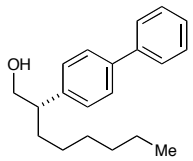
PrOH/hexanes, 1.0 mL/min, 254 nm) indicated 93% ee: t_R(minor) = 17.3 minutes, t_R (major) = 22.3 minutes.



(*S*)-2-(2,4-Difluorophenyl)-1-octanol (Table 3, entry 7). Prepared following the general procedure outlined above using octanal (156 μL, 1.00 mmol), (2*R*,5*R*)-2-*tert*-butyl-3-methyl-5-phenyl-4-imidazolidinone·TCA (79.1 mg, 0.20 mmol), CuBr (14.3 mg, 0.10 mmol), $NaHCO_3$ (63.0 mg, 0.75 mmol), bis(2,4-difluorophenyl)iodonium trifluoromethanesulfonate (251 mg, 0.50 mmol), toluene (2.00 mL), and Et_2O (1.00 mL). After 12 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography on silica gel using 2% EtOAc in toluene to provide the title compound (80.7 mg, 67% yield, 91% ee) as a colorless oil. IR (thin film) 3314, 2927, 2858, 1615, 1602, 1503, 1467, 1427, 1379, 1275, 1140, 1118, 1087, 1058, 1029, 964, 848, 812, 764, 750 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.19 (td, 1H, *J* = 8.4, 6.5 Hz, Ar**H**), 6.85 (ddd, 1H, *J* = 10.5, 8.5, 2.5 Hz, Ar**H**), 6.70 (ddd, 1H, *J* = 10.5, 9.0, 2.5 Hz, Ar**H**), 3.76 (m, 2H, C**H**$_2$OH), 3.12 (m, 1H, C**H**Ar), 1.72 (m, 1H, CHArC**H**$_2$), 1.56 (m, 1H, CHArC**H**$_2$), 1.39 (br s, 1H, O**H**), 1.33-1.10 (m, 8H, (C**H**$_2$)$_4$), 0.85 (t, 3H, *J* = 7.0 Hz, C**H**$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 161.5 (dd, *J* = 246.6, 12.2 Hz), 161.4 (dd, *J* = 247.9, 11.7 Hz), 130.0 (dd, *J* = 9.4, 6.8 Hz), 125.2 (dd, *J* = 14.9, 3.8 Hz), 111.3 (dd, *J* = 20.8, 3.7 Hz), 103.9 (dd, *J* = 27.2, 25.0 Hz), 66.4, 41.0, 31.7, 31.1, 29.3, 27.3, 22.6, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ: –113.7 (dt, *J* = 15.8, 7.5 Hz), –114.6 (dd, *J* = 16.9, 7.9 Hz); HRMS (ESI-TOF) calculated for $C_{14}H_{20}F_2O$ [M] m/z 242.14822, found 242.14804. $[\alpha]_D^{22}$ = +11.2 (c = 1.00, $CHCl_3$); HPLC analysis (AS, 3% *i*-PrOH/hexanes, 1.0 mL/min, 254 nm) indicated 91% ee: t_R(major) = 6.8 minutes, t_R (minor) = 7.9 minutes.

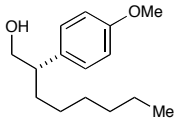


(*S*)-2-*(*2-Naphthyl)-1-octanol (Table 3, entry 8). Prepared following the general procedure outlined above using octanal (187 μL, 1.20 mmol), (2*R*,5*R*)-2-*tert*-butyl-3-methyl-5-phenyl-4-imidazolidinone·TCA (39.6 mg, 0.10 mmol), CuBr (14.3 mg, 0.10 mmol), $NaHCO_3$ (126 mg, 1.50 mmol), (2-naphthyl)(mesityl)iodonium trifluoromethanesulfonate (522 mg, 1.00 mmol), toluene (2.00 mL), and Et_2O (1.00 mL). After 3 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography on silica gel using 15% EtOAc in hexanes to provide the title compound (246 mg, 87% yield, 91% ee) as an off-white solid. IR (thin film) 3316, 3055, 2954, 2924, 2855, 1633, 1601, 1508, 1466, 1377, 1274, 1027, 960, 890, 853, 816, 764, 745 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.74 (d, 2H, *J* = 8.0 Hz, Ar**H**), 7.73 (d, 1H, *J* = 8.0 Hz, Ar**H**), 7.57 (s, 1H, Ar**H**), 7.38 (m, 2H, Ar**H**), 7.27 (dd, *J* = 8.4, 1.6 Hz, Ar**H**), 3.72 (m, 2H, C**H**$_2$OH), 2.86 (m, 1H, C**H**Ar), 1.66 (m, 1H, CHArC**H**$_2$), 1.58 (m, 1H, CHArC**H**$_2$), 1.30 (br s, 1H, O**H**), 1.29-1.03 (m, 8H, (C**H**$_2$)$_4$), 0.76 (t, 3H, *J* = 7.1 Hz, C**H**$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 140.0, 133.6, 132.6, 128.5, 127.7, 127.6, 127.2, 126.1, 125.9, 125.6, 67.6, 48.9, 32.0, 31.7, 29.4, 27.4, 22.7, 14.1; HRMS (ESI-TOF) calculated for $C_{18}H_{24}O$ [M] m/z 256.18272, found 256.18278. $[\alpha]_D^{22}$ = +15.3 (c = 1.00, $CHCl_3$); HPLC analysis (OD, 3% *i*-PrOH/hexanes, 1.0 mL/min, 254 nm) indicated 91% ee: t_R(major) = 15.3 minutes, t_R (minor) = 17.6 minutes.



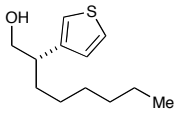
(*S*)-2-*(*Biphenyl-4-yl)-1-octanol (Table 3, entry 9). Prepared following the general procedure outlined above using octanal (187 μL, 1.20 mmol), (2*R*,5*R*)-2-*tert*-butyl-3-methyl-5-phenyl-4-imidazolidinone·TCA (39.6 mg, 0.10 mmol), CuBr (14.3 mg, 0.10 mmol), $NaHCO_3$ (126 mg, 1.50 mmol), (biphenyl-4-yl)(mesityl)iodonium

trifluoromethanesulfonate (548 mg, 1.00 mmol), toluene (2.00 mL), and Et_2O (1.00 mL). After 3 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography on silica gel using 15% EtOAc in hexanes to provide the title compound (260 mg, 87% yield, 92% ee) as a white solid. IR (thin film) 3312, 3028, 2954, 2925, 2855, 1487, 1466, 1410, 1378, 1276, 1261, 1029, 1008, 835, 764, 750, 733, 696 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.60 (d, 2H, *J* = 7.1 Hz, Ar**H**), 7.57 (d, 2H, *J* = 8.2 Hz, Ar**H**), 7.44 (t, 2H, *J* = 7.7 Hz, Ar**H**), 7.34 (t, 1H, *J* = 7.4 Hz, Ar**H**), 7.29 (d, 2H, *J* = 8.2, Ar**H**), 3.81 (m, 1H, C**H**$_2$OH), 3.75 (m, 1H, C**H**$_2$OH), 2.83 (m, 1H, C**H**Ar), 1.72 (m, 1H, CHArC**H**$_2$), 1.60 (m, 1H, CHArC**H**$_2$), 1.34 (br s, 1H, O**H**), 1.32-1.17 (m, 8H, (C**H**$_2$)$_4$), 0.86 (t, 3H, *J* = 7.1 Hz, C**H**$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 141.6, 140.9, 139.5, 128.7, 128.4, 127.3, 127.1, 127.0, 67.6, 48.3, 32.0, 31.7, 29.4, 27.3, 22.6, 14.1; HRMS (ESI-TOF) calculated for $C_{20}H_{26}O$ [M] m/z 282.19837, found 282.19855. $[\alpha]_D^{22}$ = +17.2 (c = 1.02, $CHCl_3$); HPLC analysis (OJ, 3% *i*-PrOH/hexanes, 1.0 mL/min, 254 nm) indicated 91% ee: t_R(major) = 17.8 minutes, t_R (minor) = 20.6 minutes.



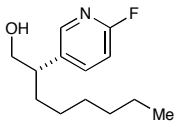
(*S*)-2-(4-Methoxyphenyl)-1-octanol (Table 3, entry 10). Prepared following the general procedure outlined above using octanal (187 μL, 1.20 mmol), (2*R*,5*R*)-2-*tert*-butyl-3-methyl-5-phenyl-4-imidazolidinone·TCA (39.6 mg, 0.10 mmol), CuBr (14.3 mg, 0.10 mmol), $NaHCO_3$ (126 mg, 1.50 mmol), bis(4-methoxyphenyl)iodonium trifluoromethanesulfonate (490 mg, 1.00 mmol), toluene (2.00 mL), and Et_2O (1.00 mL). After 6 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography on silica gel using 15% EtOAc in hexanes to provide the title compound (208 mg, 88% yield, 91% ee) as a yellow oil. IR (thin film) 3368, 2954, 2925, 2855, 1611, 1584, 1511, 1464, 1442, 1301, 1245, 1177, 1035, 750 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.12 (d, 2H, *J* = 8.6 Hz, Ar**H**), 6.87 (d,

2H, *J* = 8.6 Hz, Ar**H**), 3.80 (s, 3H, OC**H**$_3$), 3.73 (dd, 1H, *J* = 10.7, 5.6 Hz, C**H**$_2$OH), 3.65 (dd, 1H, *J* = 10.6, 8.1 Hz, C**H**$_2$OH), 2.72 (m, 1H, C**H**Ar), 1.64 (m, 1H, CHArC**H**$_2$), 1.56 (br s, 1H, O**H**), 1.51 (m, 1H, CHArC**H**$_2$), 1.38-1.10 (m, 8H, (C**H**$_2$)$_4$), 0.84 (t, 3H, *J* = 7.0 Hz, C**H**$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 158.3, 134.2, 128.9, 114.0, 67.7, 55.2, 47.8, 32.1, 31.7, 29.3, 27.3, 22.6, 14.1; HRMS (ESI-TOF) calculated for $C_{15}H_{24}O_2$ [M] m/z 236.17763, found 236.17763. $[\alpha]_D^{22}$ = +13.0 (c = 1.04, $CHCl_3$); SFC analysis (IA, 5-25% MeOH gradient over 9.0 minutes then isocratic 25% MeOH, 1.0 mL/min, 220 nm) indicated 91% ee: t_R(major) = 4.3 minutes, t_R (minor) = 5.3 minutes.



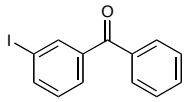
(*S*)-2-(3-Thienyl)-1-octanol (Table 3, entry 11). Prepared following the general procedure outlined above using octanal (187 μL, 1.20 mmol), (2*R*,5*R*)-2-*tert*-butyl-3-methyl-5-phenyl-4-imidazolidinone·TCA (39.6 mg, 0.10 mmol), CuBr (14.3 mg, 0.10 mmol), $NaHCO_3$ (126 mg, 1.50 mmol), (3-thienyl)(mesityl)iodonium trifluoromethanesulfonate (478 mg, 1.00 mmol), toluene (1.50 mL), and Et_2O (1.50 mL). After 3 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography on silica gel using 2% EtOAc in toluene to provide the title compound (171 mg, 81% yield, 92% ee) as a colorless oil. IR (thin film) 3354, 2955, 2924, 2856, 1465, 1412, 1378, 1336, 1276, 1261, 1027, 852, 831, 765, 750 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.31 (dd, 1H, *J* = 4.9, 2.9 Hz, Ar**H**), 7.04 (dd, 1H, *J* = 2.8, 1.1 Hz, Ar**H**), 6.98 (dd, 1H, *J* = 4.9, 1.2 Hz, Ar**H**), 3.73 (dd, 1H, *J* = 10.7, 5.4 Hz, C**H**$_2$OH), 3.65 (dd, 1H, *J* = 10.7, 7.8 Hz, C**H**$_2$OH), 2.92 (m, 1H, C**H**Ar), 1.66 (m, 1H, CHArC**H**$_2$), 1.54 (m, 1H, CHArC**H**$_2$), 1.38 (br s, 1H, O**H**), 1.33-1.15 (m, 8H, (C**H**$_2$)$_4$), 0.85 (t, 3H, *J* = 7.0 Hz, C**H**$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 143.4, 126.6, 126.0, 121.2, 67.1, 44.0, 32.0, 31.7, 29.3, 27.3, 22.6, 14.1; HRMS (ESI-TOF) calculated for $C_{12}H_{20}OS$ [M] m/z 212.12349, found 212.12334. $[\alpha]_D^{22}$ = +15.7 (c = 1.16, $CHCl_3$); HPLC analysis (OJ, 3% *i*-PrOH/hexanes, 1.0 mL/min, 220 nm) indicated 92% ee:

t_R(minor) = 8.1 minutes, t_R (major) = 8.8 minutes.

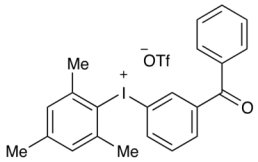


(*S*)-2-(6-Fluoropyridin-3-yl)-1-octanol (Table 3, entry 12). Prepared following the general procedure outlined above using octanal (156 μL, 1.00 mmol), (2*R*,5*R*)-2-*tert*-butyl-3-methyl-5-phenyl-4-imidazolidinone·TCA (79.1 mg, 0.20 mmol), CuBr (3.6 mg, 0.025 mmol), $NaHCO_3$ (63.0 mg, 0.750 mmol), (6-fluoropyridin-3-yl)(mesityl)iodonium trifluoromethanesulfonate (246 mg, 0.50 mmol), toluene (1.50 mL), and Et_2O (1.50 mL). After 8 hours, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography on silica gel using 15% EtOAc in toluene to provide the title compound (78.6 mg, 70% yield, 93% ee) as a light yellow oil. IR (thin film) 3370, 2956, 2926, 2857, 1596, 1483, 1401, 1275, 1253, 1126, 1058, 1026, 831, 764, 751 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 8.03 (s, 1H, Ar**H**), 7.65 (td, 1H, *J* = 8.1, 2.5 Hz, Ar**H**), 6.90 (dd, 1H, *J* = 8.4, 2.8 Hz, Ar**H**), 3.77 (m, 1H, C**H**$_2$OH), 3.72 (m, 1H, C**H**$_2$OH), 2.80 (m, 1H, C**H**Ar), 1.74 (m, 1H, CHArC**H**$_2$), 1.67 (br s, 1H, O**H**), 1.54 (m, 1H, CHArC**H**$_2$), 1.36-1.09 (m, 8H, (C**H**$_2$)$_4$), 0.84 (t, 3H, *J* = 7.0 Hz, C**H**$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) 162.6 (d, *J* = 237.8 Hz), 147.2 (d, *J* = 14.1 Hz), 140.3 (d, *J* = 7.7 Hz), 135.8 (d, *J* = 4.5 Hz), 109.4 (d, *J* = 37.2 Hz), 67.0, 45.1, 31.7, 31.6, 29.2, 27.1, 22.6, 14.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ: –71.8 (s); HRMS (ESI-TOF) calculated for $C_{13}H_{20}FNO$ [M] m/z 225.15289, found 225.15299. $[\alpha]_D^{22}$ = +4.6 (c = 1.01, $CHCl_3$); HPLC analysis (AS, 5% *i*-PrOH/hexanes, 1.0 mL/min, 254 nm) indicated 93% ee: t_R(major) = 9.5 minutes, t_R (minor) = 14.1 minutes.

III. Synthesis of (*S*)-Ketoprofen.

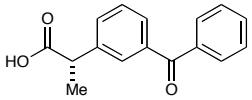


3-Iodobenzophenone. To a 250 mL round-bottom flask containing *p*-toluenesulfonic acid (8.70 g, 45.7 mmol, 3.00 equiv) was added MeCN (60.0 mL), followed by 3-aminobenzophenone (3.00 g, 15.2 mmol, 1.00 equiv). The mixture was cooled to 0 ºC and a solution of sodium nitrite (2.10 g, 30.4 mmol, 2.00 equiv) and potassium iodide (6.31 g, 38.0 mmol, 2.50 equiv) in water (9.0 mL) was added dropwise over 30 minutes. The mixture was then stirred for 1 h at 0 ºC and 1 h at room temperature. The reaction was quenched by the addition of water (150 mL) followed by sat. $NaHCO_3$ until pH 10 and 1 M $Na_2S_2O_3$ (15 mL). The aqueous phase was extracted with CH_2Cl_2 (3x) and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The crude material was purified by flash chromatography eluting with 10% EtOAc in hexanes to provide the title compound (3.76 g, 80%) as a pale yellow solid. IR (thin film) 3306, 3057, 1655, 1597, 1579, 1558, 1466, 1446, 1413, 1316, 1308, 1257, 1179, 1149, 1063, 95, 944, 810, 779, 741, 711, 694, 657, 637 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 8.13 (s, 1H, Ar**H**), 7.91 (d, 1H, *J* = 7.9 Hz, Ar**H**), 7.78 (d, 1H, *J* = 7.1 Hz, Ar**H**), 7.74 (d, 1H, *J* = 7.7 Hz, Ar**H**), 7.61 (t, 1H, *J* = 7.4 Hz, Ar**H**), 7.49 (t, 1H, *J* = 7.7 Hz, Ar**H**), 7.22 (t, 1H, *J* = 7.8 Hz, Ar**H**); ^{13}C NMR (125 MHz, $CDCl_3$) 195.1, 141.1, 139.4, 138.5, 136.8, 132.8, 130.0, 129.9, 129.2, 128.4, 94.0; HRMS (ESI-TOF) calculated for $C_{13}H_{19}IO$ [M] m/z 307.96981, found 307.96962.



(4-(Phenylcarbonyl)phenyl)(mesityl)iodonium trifluoromethylsulfonate (compound 9). To an oven-dried 250 mL round-bottom flask was added *m*-CPBA (4.73 g, 17.8

mmol, 1.10 equiv)[8] and CH_2Cl_2 (70 mL), followed by 3-iodobenzophenone (4.98 g, 16.1 mmol, 1.00 equiv) and mesitylene (2.50 mL, 17.9 mmol, 1.10 equiv). The mixture was cooled to 0 ºC and trifluoromethanesulfonic acid (2.40 mL, 27.1 mmol, 1.7 equiv) was added slowly with stirring. The reaction was stirred at 0 ºC for 1 h and at room temperature for 2 h. The solvent was removed *in vacuo* and Et_2O (~ 50 mL) was added. The heterogeneous mixture was cooled to –20 ºC for at least 30 minutes. The diaryliodonium trifluoromethansulfonate was collected via filtration, washed with Et_2O, and dried under vacuum to provide the title compound (6.71 g, 72%) as an off-white solid. IR (thin film) 1661, 1596, 1554, 1449, 1276, 1241, 1159, 1027, 994, 945, 764, 750, 718, 636 cm^{-1}; ^1H NMR (500 MHz, Acetone-D_6) δ: 8.31 (d, 1H, *J* = 8.1 Hz, Ar**H**), 8.28 (s, 1H, Ar**H**), 8.05 (d, 1H, *J* = 7.8 Hz, Ar**H**), 7.77 (t, 1H, *J* = 7.9 Hz, Ar**H**), 7.71 (m, 3H, Ar**H**), 7.55 (t, 1H, *J* = 7.8 Hz, Ar**H**), 7.30 (s, 2H, Ar**H**), 2.71 (s, 6H, ArC$\mathbf{H}_3$), 2.37 (s, 3H, ArC$\mathbf{H}_3$); ^{13}C NMR (125 MHz, Acetone-D_6) 194.1, 145.5, 143.5, 141.6, 138.2, 137.0, 135.5, 134.0, 133.6, 133.2, 131.2, 130.7, 129.5, 121.8, 113.1, 27.1, 21.0; HRMS (ESI-TOF) calculated for $C_{22}H_{20}IO$ [M] m/z 427.05588, found 427.0558.



(*S*)-Ketoprofen. To an oven-dried 8 mL vial equipped with a magnetic stir bar and Teflon septum was added (2*R*,5*R*)-2-*tert*-butyl-3-methyl-5-phenyl-4-imidazolidinone trichloroacetic acid salt (19.8 mg, 0.050 mmol, 0.10 equiv), copper(I) bromide (7.2 mg, 0.050 mmol, 0.10 equiv), sodium bicarbonate (63.0 mg, 0.75 mmol, 1.5 equiv), and the (4-(phenylcarbonyl)phenyl)(mesityl)iodonium trifluoromethylsulfonate salt (288 mg, 0.50 mmol, 1.00 equiv). The vial was sealed, purged with a stream of argon, and cooled to 0 ºC. Toluene (0.75 mL) and diethyl ether (0.75 mL) were then added, followed by propionaldehyde (44 μL, 0.60 mmol, 1.20 equiv). After 3 hours, the mixture was transferred to a 25 mL round-bottom flask and diluted with MeCN (3.75 mL). To the mixture was added (diacetoxyiodo)benzene (644 mg, 2.00 mmol, 4.00 equiv), TEMPO

(8) *m*-CPBA was dried under high-vacuum for 1 h before use, assumed 65%.

(31.2 mg, 0.20 mmol, 0.40 equiv), and water (1.25 mL). The reaction was stirred at room temperature for 3h then quenched with sat. $Na_2S_2O_8$ (10 mL) and diluted with EtOAc (10 mL). The mixture was poured into a separatory funnel and the organic layer was extracted with 1 M NaOH (4x). The aqueous extracts were then acidified with 3 M HCl (until < pH 2) and extracted with CH_2Cl_2 (3x). The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The product was purified by flash chromatography eluting with 10-20% EtOAc and 1% AcOH in hexanes to provide the title compound (89.7 mg, 71% yield over two steps, 92% ee) as a white solid, which was identical to the reported literature compound.[9] $[\alpha]_D^{22}$ = +45.7 (c = 1.03, $CHCl_3$); literature $[\alpha]_D$ = +52.6 (c = 1.03, $CHCl_3$).[9b] The enantiomeric excess was determined on the corresponding methyl ester, which was prepared by treating a solution of the acid (1.0 equiv) in EtOAc (0.20 M) with $TMSCH_2N_2$ (10.0 equiv) at 0 ºC. After 5 minutes the reaction was quenched with 1M HCl until colorless. The organic layer was separated, dried with $MgSO_4$, and concentrated *in vacuo* to provide (*S*)-ketoprofen methyl ester. HPLC analysis of the ester (AS, 5% EtOH/hexanes, 1.0 mL/min, 254 nm) indicated 92% ee: t_R(major) = 7.1 minutes, t_R (minor) = 9.6 minutes.

IV. Preparation of Diaryliodonium Trifluoromethanesulfonates

The following diaryliodonium trifluoromethanesulfonates were prepared according to literature procedures: diphenyliodonium trifluoromethanesulfonate[10], bis(4-(trifluoromethyl)phenyl)iodonium trifluoromethanesulfonate[11], (4-(methoxycarbonyl) phenyl)(mesityl)iodonium trifluoromethanesulfonate[12], (3-bromophenyl)(mesityl) iodonium trifluoromethanesulfonate[13], (4-nitrophenyl)(mesityl)iodonium trifluoromethanesulfonate[13], and bis(4-methoxyphenyl)iodonium

(9) (a) Shiina, I.; Nakata, K.; Onda, Y.-s. *Eur. J. Org. Chem.* **2008**, 5887. (b) Fadel, A. *Synlett* **1992**, 48.
(10) Bielawski, M.; Zhu, M.; Olofsson, B. *Adv. Synth. Catal.* **2007**, *349*, 2610.
(11) Bielawski, M.; Aili, D.; Olofsson, B. *J. Org. Chem.* **2008**, *73*, 4602.
(12) Bedford, R. B.; Webster, R. L.; Mitchell, C. J. *Org. Biomol. Chem.* **2009**, 7, 4853.
(13) Phipps, R. J.; Gaunt, M. J. *Science* **2007**, *323*, 1593.

trifluoromethanesulfonate[14]. Diphenyliodonium trifluoromethanesulfonate is also commercially available (CAS: 66003-76-7).

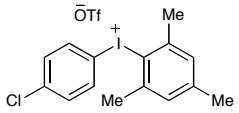
General one-pot procedure for diaryliodonium trifluoromethanesulfonates (A):[10] To an oven-dried round-bottom flask was added *m*-CPBA (1.10 equiv)[8] and CH_2Cl_2 (0.20 M), followed by the appropriate iodoarene (1.00 equiv) and mesitylene (1.10 equiv). The mixture was cooled to 0 ºC and trifluoromethanesulfonic acid (1.70 equiv) was added slowly with stirring. The reaction was allowed to warm to room temperature and stir for 2 h. The solvent was removed *in vacuo* and Et_2O was added. The heterogeneous mixture was cooled to –20 ºC for at least 30 minutes. The diaryliodonium trifluoromethansulfonate was collected via filtration, washed with Et_2O, and dried under vacuum.

General one-pot procedure for diaryliodonium trifluoromethanesulfonates *via* tetrafluoroborates (B):[11] To an oven-dried round-bottom flask was added *m*-CPBA (1.10 equiv)[8] and CH_2Cl_2 (0.25 M). The appropriate iodoarene (1.00 equiv) was then added, followed by $BF_3{\cdot}OEt_2$ (2.50 equiv). The mixture was stirred for 1h at room temperature. After cooling to 0 ºC, the boronic acid (1.10 equiv) was added in one portion. The reaction was stirred at 0 ºC for 10 minutes then room temperature for 30 minutes. The mixture was cooled back down to 0 ºC and trifluoromethanesulfonic acid (1.10 equiv) was added slowly. The mixture was warmed to room temperature and stirred an additional 15 minutes. The solvent was removed *in vacuo* and Et_2O was added to the residual solids. The heterogeneous mixture was cooled to –20 ºC for at least 30 minutes and the diaryliodonium trifluoromethanesulfonate was collected via filtration, washed with Et_2O, and dried under vacuum.

General two-pot procedure for diaryliodonium trifluoromethanesulfonates *via* tetrafluoroborates (C):[11,15] To an oven-dried round-bottom flask was added the

(14) Zhu, M.; Jalalian, N.; Olofsson, B. *Synlett* **2008**, 592.

appropriate boronic acid (1.0 equiv) and CH_2Cl_2 (0.075 M). The mixture was cooled to 0 ºC and BF_3•OEt_2 (1.10 equiv) was added. After 10 minutes, 2-(diacetoxyiodo)mesitylene (1.05 equiv) was added as a solution in CH_2Cl_2 (0.33 M). The mixture was warmed to room temperature and stirred for 2 h. The reaction was quenched by the addition of sat. $NaBF_4$ (aq). After 30 minutes of vigorous stirring, the aqueous layer was extracted with CH_2Cl_2 (2x). The combined organic layers were dried with $MgSO_4$, filtered, and concentrated. Et_2O was added to the residual solid and the diaryliodonium tetrafluoroborate was collected via filtration. The tetrafluoroborate salt was dissolved in MeCN (0.20 M) and cooled to 0 ºC. Freshly distilled trimethylsilyl trifluoromethanesulfonate (1.50 equiv) was added and the mixture was allowed to warm to room temperature and stir 12 h. The solvent was removed *in vacuo* and Et_2O was added to the residual solid and the heterogeneous mixture was cooled to –20 ºC for at least 30 mintues. The desired diaryliodonium trifluoromethanesulfonate was collected via filtration, washed with Et_2O, and dried under vacuum.



(4-Chlorophenyl)(mesityl)iodonium trifluoromethanesulfonate. Prepared following the general procedure (A) outlined above using *m*-CPBA (1.32 g, 5.00 mmol), 1-chloro-4-iodobenzene (1.07 g, 4.50 mmol), mesitylene (0.70 mL, 5.00 mmol), trifluoromethanesulfonic acid (0.66 mL, 7.50 mmol), and CH_2Cl_2 (20.0 mL). The product was obtained as a white solid (1.93 g, 85%). IR (thin film) 1474, 1245, 1171, 1088, 1029, 1001, 811 cm^{-1}; ^1H NMR (500 MHz, Acetone-D_6) δ: 8.09 (d, 2H, J = 8.8 Hz, Ar**H**), 7.61 (d, 2H, J = 8.8 Hz, Ar**H**), 7.29 (s, 2H, Ar**H**), 2.72 (s, 6H, ArC**H**$_3$), 2.36 (s, 3H, ArC**H**$_3$); ^{13}C NMR (125 MHz, Acetone-D_6) 145.4, 143.4, 139.1, 137.0, 133.1, 131.2, 122.0, 110.7, 27.0, 21.0; HRMS (ESI-TOF) calculated for $C_{15}H_{15}ICl$ [M] m/z 352.94503, found 352.94481.

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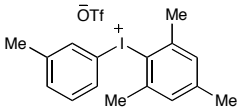
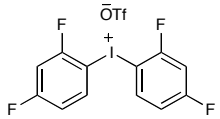
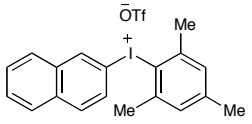
(15) Phipps, R. J.; Grimster, N. P.; Gaunt, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 8172.



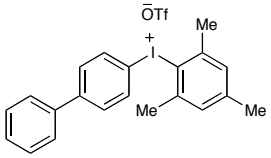
(*m*-Tolyl)(mesityl)iodonium trifluoromethanesulfonate. Prepared following the general procedure (A) outlined above using *m*-CPBA (2.64 g, 10.00 mmol), 3-iodotoluene (1.16 g, 9.00 mmol), mesitylene (1.40 mL, 10.00 mmol), trifluoromethanesulfonic acid (1.31 mL, 15.00 mmol), and CH_2Cl_2 (40.0 mL). The product was obtained as a white solid (3.55 g, 81%). IR (thin film) 1275, 1247, 1223, 1157, 1028, 766, 636 cm^{-1}; ^1H NMR (500 MHz, Acetone-D_6) δ: 7.97 (s, 1H, Ar**H**), 7.85 (d, 1H, *J* = 8.1 Hz, Ar**H**), 7.52 (d, 1H, *J* = 7.6 Hz, Ar**H**), 7.44 (t, 1H, *J* = 7.9 Hz, Ar**H**), 7.27 (s, 2H, Ar**H**), 2.72 (s, 6H, ArC$\mathbf{H}_3$), 2.37 (s, 3H, ArC$\mathbf{H}_3$); ^{13}C NMR (125 MHz, Acetone-D_6) 145.2, 143.8, 143.4, 135.5, 133.9, 132.8, 132.3, 131.1, 121.6, 113.1, 27.1, 21.2, 20.9; HRMS (ESI-TOF) calculated for $C_{16}H_{18}I$ [M] m/z 337.04532, found 337.04562.



bis(2,4-Difluorophenyl)iodonium trifluoromethanesulfonate. Prepared following the general procedure (B) outlined above using *m*-CPBA (1.44 g, 2.70 mmol), 2,4-difluoroiodobenzene (0.50 mL g, 2.50 mmol), $BF_3{\cdot}OEt_2$ (1.60 mL, 6.20 mmol), 2,4-difluorophenylboronic acid (0.86 g, 2.70 mmol), trifluoromethanesulfonic acid (0.24 mL, 2.70 mmol), and CH_2Cl_2 (20.0 mL). The product was obtained as a white solid (1.01 g, 80%). IR (thin film) 1602, 1588, 1479, 1431, 1270, 1220, 1026, 964, 855, 641 cm^{-1}; ^1H NMR (500 MHz, Acetone-D_6) δ: 8.59 (dt, 2H, *J* = 9.0, 6.9 Hz, Ar**H**), 7.51 (td, 2H, *J* = 8.8, 2.8 Hz, Ar**H**), 7.31 (td, 2H, *J* = 8.2, 2.3 Hz, Ar**H**); ^{13}C NMR (125 MHz, Acetone-D_6) 167.3 (dd, *J* = 256.2, 11.5 Hz), 162.0 (dd, *J* = 253.8, 13.5 Hz), 140.1 (d, *J* = 10.7 Hz), 116.2 (dd, *J* = 23.0, 2.8 Hz), 106.8 (t, *J* = 27.0 Hz), 97.5 (d, *J* = 21.6 Hz); ^{19}F NMR (376 MHz, Acetone-D_6) –79.5 (s), –93.5 (m), –101.4 (m); HRMS (ESI-TOF) calculated for $C_{12}H_6F_4I$ [M] m/z 352.94503, found 352.94481.

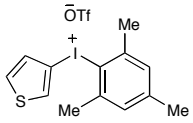


(2-Naphthyl)(mesityl)iodonium trifluoromethanesulfonate. Prepared following the general procedure (C) outlined above using 2-naphthylboronic acid (1.09 g, 6.34 mmol), BF_3•OEt_2 (0.86 mL, 6.97 mmol), 2-(diacetoxyiodo)mesitylene (2.42 g, 6.65 mmol), and CH_2Cl_2 (120 mL). The resulting tetrafluoroborate salt was directly subjected to the counterion exchange using trimethylsilyl trifluoromethanesulfonate (1.30 mL, 7.18 mmol), and MeCN (25.0 mL). The product was obtained as an off-white solid (2.20 g, 67% over two steps). IR (thin film) 1276, 1245, 1164, 1028, 750, 637 cm^{-1}; ^1H NMR (500 MHz, Acetone-D_6) δ: 8.83 (s, 1H, Ar**H**), 8.04 (m, 4H, Ar**H**), 7.71 (m, 2H, Ar**H**), 7.27 (s, 2H, Ar**H**), 2.76 (s, 6H, ArC**H**$_3$), 2.34 (s, 3H, ArC**H**$_3$); ^{13}C NMR (125 MHz, Acetone-D_6) 145.2, 143.4, 136.6, 135.5, 134.9, 132.9, 131.1, 130.1, 130.0, 129.1, 129.0, 128.9, 121.9, 110.1, 27.1, 20.1; HRMS (ESI-TOF) calculated for $C_{19}H_{18}I$ [M] m/z 373.04532, found 373.04533.

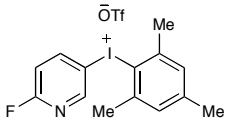


(Biphenyl-4-yl)(mesityl)iodonium trifluoromethanesulfonate. Prepared following the general procedure (A) outlined above using *m*-CPBA (2.64 g, 10.00 mmol), 4-iodobiphenyl (2.52 g, 9.00 mmol), mesitylene (1.40 mL, 10.00 mmol), trifluoromethanesulfonic acid (1.31 mL, 15.00 mmol), and CH_2Cl_2 (40.0 mL). The product was obtained as a white solid (3.86 g, 78%). IR (thin film) 1477, 1246, 1226, 1164, 1030, 768, 695, 638 cm^{-1}; ^1H NMR (500 MHz, Acetone-D_6) δ: 8.16 (d, 2H, J = 8.7 Hz, Ar**H**), 7.84 (d, 2H, J = 8.7 Hz, Ar**H**), 7.69 (d, 2H, J = 7.1 Hz, Ar**H**), 7.50 (t, 2H, J = 7.4 Hz, Ar**H**), 7.44 (t, 1H, J = 7.3 Hz, Ar**H**), 7.29 (s, 2H, Ar**H**), 2.75 (s, 6H, ArC**H**$_3$), 2.36 (s, 3H, ArC**H**$_3$); ^{13}C NMR (125 MHz, Acetone-D_6) 145.7, 145.3, 143.4, 139.3, 135.9, 131.3, 131.1, 130.0, 129.6, 128.0, 121.9, 111.6, 27.1, 21.0; HRMS (ESI-TOF) calculated

for $C_{12}H_{20}I$ [M] m/z 399.06097, found 399.06088.



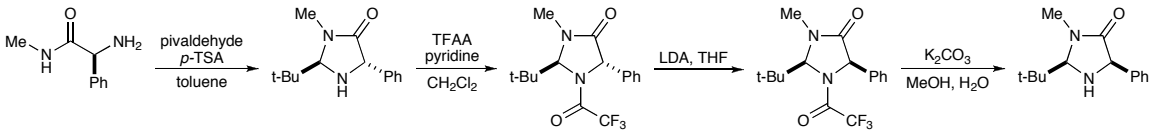
(3-Thienyl)(mesityl)iodonium trifluoromethanesulfonate. Prepared following the general procedure (C) outlined above using 3-thienylboronic acid (0.33 g, 2.58 mmol), BF_3•OEt_2 (0.35 mL, 2.85 mmol), 2-(diacetoxyiodo)mesitylene (1.03 g, 2.84 mmol), and CH_2Cl_2 (48 mL). The resulting tetrafluoroborate salt was directly subjected to the counterion exchange using trimethylsilyl trifluoromethanesulfonate (0.54 mL, 2.98 mmol), and MeCN (11.0 mL). The product was obtained as an off-white solid (0.842 g, 68% over two steps). IR (thin film) 1451, 1244, 1222, 1172, 1021, 853, 758, 765, 750, 631 cm^{-1}; ^1H NMR (500 MHz, Acetone-D_6) δ: 8.51 (dd, 1H, *J* = 2.9, 1.3 Hz, Ar**H**), 7.82 (dd, 1H, *J* = 5.2, 3.0 Hz, Ar**H**), 7.60 (dd, 1H, *J* = 5.2, 1.3 Hz, Ar**H**), 7.25 (s, 2H, Ar**H**), 2.75 (s, 6H, ArC$\mathbf{H}_3$), 2.34 (s, 3H, ArC$\mathbf{H}_3$); ^{13}C NMR (125 MHz, Acetone-D_6) 145.0, 142.9, 135.8, 131.6, 131.4, 130.9, 122.9, 96.0, 27.0, 20.8; HRMS (ESI-TOF) calculated for $C_{13}H_{14}IS$ [M] m/z 328.98609, found 328.98582.



(6-Fluoropyridin-3-yl)(mesityl)iodonium trifluoromethanesulfonate. Prepared following the general procedure (A) outlined above, with the following modifications. The *m*-CPBA (0.65 g, 2.45 mmol) and 2-fluoro-5-iodopyridine (0.50 g, 2.24 mmol) in CH_2Cl_2 (10.0 mL) were heated to 80 ºC for 2 h before the mesitylene (0.34 mL, 2.44 mmol) and trifluoromethanesulfonic acid (0.66 mL, 7.50 mmol) were added at 0 ºC and the mixture was slowly warmed to room temperature over 6 h. The product was obtained as a white solid (0.588 g, 77%). IR (thin film) 1583, 1558, 1472, 1375, 1243, 1223, 1172, 1025, 845, 750, 635 cm^{-1}; ^1H NMR (500 MHz, Acetone-D_6) δ: 8.88 (d, 1H, *J* = 2.2 Hz, Ar**H**), 8.69 (ddd, 1H, *J* = 9.3, 6.9, 2.5 Hz, Ar**H**), 7.36 (dd, 1H, *J* = 8.8, 2.8 Hz, Ar**H**), 7.28

(s, 2H, Ar**H**), 2.75 (s, 6H, ArC**H**$_3$), 2.36 (s, 3H, ArC**H**$_3$); ^{13}C NMR (125 MHz, Acetone-D_6) 165.5 (d, J = 244.3 Hz), 153.6 (d, J = 16.5 Hz), 148.6 (d, J = 9.3 Hz), 145.4, 143.4, 131.2, 122.3, 114.8 (d, J = 39.0 Hz), 107.8 (d, J = 4.5 Hz), 27.0, 20.9; HRMS (ESI-TOF) calculated for $C_{14}H_{14}FIN$ [M] m/z 342.0155, found 342.01539.

V. Synthesis of (2*R*,5*R*)-2-*tert*-butyl-3-methyl-5-phenyl-4-imidazolidinone (2).



(2*R*,5*R*)-2-*tert*-butyl-3-methyl-5-phenyl-4-imidazolidinone. To a round bottom flask containing L-phenylglycine-*N*-methylamide (21.7 g, 132 mmol, 1.00 equiv)[16] was added toluene (250 mL), followed by *p*-toluenesulfonic acid (2.51 g, 13.2 mmol, 0.10 equiv) and freshly distilled pivaldehyde (14.5 mL, 134 mmol, 1.02 equiv). The mixture was refluxed for 18 h then quenched with sat. $NaHCO_3$ solution (100 mL). The aqueous layer was extracted with EtOAc (3x) and the combined organic layers were washed with sat. $NaHCO_3$, dried with $MgSO_4$, filtered, and concentrated to provide (2*R*,5*S*)-2-*tert*-butyl-3-methyl-5-phenyl-4-imidazolidinone. The *trans* product was purified by recrystalization from EtOAc and hexanes to provide a white solid (19.1 g, 62%), which was identical to the reported literature compound.[16]

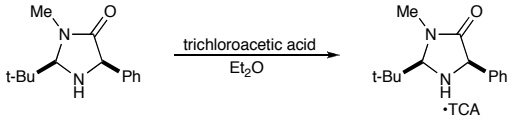
(2*R*,5*S*)-2-*tert*-butyl-3-methyl-5-phenyl-4-imidazolidinone (19.1 g, 82.3 mmol, 1.00 equiv) was dissolved in CH_2Cl_2 (330 mL) and cooled to 0 ºC. Trifluoromethylacetic anhydride (13.3 mL, 95.6 mmol, 1.20 equiv) and pyridine (82.0 mL) were added and the mixture was warmed to room temperature and stirred for 12 h. The reaction was quenched by the addition of water (200 mL) and the aqueous layer was extracted with CH_2Cl_2 (3x). The combined organic layers were dried over $MgSO_4$, filtered, and

(16) Reichard, G. A.; Stengone, C.; Paliwal, S.; Mergelsberg, I.; Majmundar, S.; Wang, C.; Tiberi, R.; McPhail, A. T.; Piwinski, J. J.; Shih, N.-Y. *Org. Lett.* **2003**, *5*, 4249.

concentrated. The crude mixture was purified by recrystalization from EtOAc and hexanes to provide (2*S*,5*S*)-2-*tert*-butyl-3-methyl-5-phenyl-1-(2,2,2-trifluoroethanoyl) imidazolidin-4-one (20.3 g, 75%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.40 (m, 3H, Ar**H**), 7.20 (br s, 2H, Ar**H**), 5.79 (s, 1H, C**H**C$(CH_3)_3$), 5.22 (s, 1H, COC**H**Ph), 3.15 (s, 3H, NC**H**$_3$), 1.07 (s, 9H, C(C**H**$_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$) 169.7, 159.5 (q, *J* = 38.8 Hz), 137.4, 129.4, 129.3 (2), 115.4 (q, *J* = 287.6 Hz), 80.7, 65.04, 65.02, 41.0, 32.5, 26.2.

To an oven-dried flask containing a solution of diisopropylamine (8.70 mL, 62.1 mmol, 1.1 equiv) in THF (150 mL) at 0 ºC was added *n*-BuLi (23.5 mL, 58.8 mmol, 1.05 equiv). The vessel was stirred for 30 minutes. (2*S*,5*S*)-2-*tert*-butyl-3-methyl-5-phenyl-1-(2,2,2-trifluoroethanoyl)imidazolidin-4-one (18.5 g, 56.3 mmol, 1.00 equiv) was dissolved in THF (150 mL) and transferred to the reaction vessel via cannula. The red mixture was stirred for 15 minutes at 0 ºC then warmed to room temperature and quenched by the addition of water. The aqueous layer was extracted with EtOAc (3x), dried over $MgSO_4$, filtered and concentrated. The crude product was dissolved in MeOH (300 mL) and K_2CO_3 (38.9 g, 252 mmol, 5.00 equiv) and water (120 mL) were added. The mixture was stirred for 3 h then diluted with water (300 mL) and CH_2Cl_2 (300 mL). The aqueous layer was extracted with CH_2Cl_2 (3x) and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by flash chromatography on silica gel using 30-50% EtOAc in hexanes followed by recrystallization using EtOAc and hexanes (repeated until 99% ee, if necessary) to give (2*R*,5*R*)-2-*tert*-butyl-3-methyl-5-phenyl-4-imidazolidinone (5.4 g, 41% over two steps, 99% ee) as a white crystalline solid. IR (thin film) 3361, 2987, 2964, 2917, 2871, 2809, 1694, 1483, 1458, 1430, 1412, 1398, 1368, 1340, 1307, 1259, 1205, 1107, 1072, 1003, 882, 851, 769, 728 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.49 (d, 2H, *J* = 7.8 Hz, Ar**H**), 7.37 (t, 2H, *J* = 7.4 Hz, Ar**H**), 7.30 (t, 1H, *J* = 7.3 Hz, Ar**H**), 4.60 (s, 1H, C**H**C$(CH_3)_3$), 4.26 (s, 1H, COC**H**Ph), 3.01 (s, 3H, NC**H**$_3$), 1.04 (s, 9H, C(C**H**$_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$) 174.0, 138.9, 128.4, 127.8, 127.7, 81.9, 61.8, 35.3, 30.8, 25.4; HRMS (ESI-TOF) calculated for $C_{14}H_{20}N_2O$ [M] m/z 232.15756, found 232.15795. $[\alpha]_D^{23}$ = –76.2 (c = 0.91, $CHCl_3$); HPLC analysis

(OJ, 10% *i*-PrOH/hexanes, 1.0 mL/min, 220 nm) indicated 99% ee: t_R(minor) = 9.5 minutes, t_R (major) = 12.2 minutes.



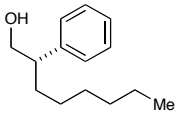
(2*R*,5*R*)-2-*tert*-butyl-3-methyl-5-phenyl-4-imidazolidinone•TCA. To a round-bottom flask was added (2*R*,5*R*)-2-*tert*-butyl-3-methyl-5-phenyl-4-imidazolidinone (1.59 g, 6.84 mmol, 1.00 equiv) in just enough Et_2O to dissolve completely (~15 mL). With stirring, trichloroacetic acid[17] (1.12 g, 6.85 mmol, 1.00 equiv) was added and the product salt began to precipitate. The vessel was cooled to 0 ºC for 15 minutes then –20 ºC for at least 30 minutes. The trichloroacetic acid salt was collected via filtration, washed with cold Et_2O, and dried under vacuum to provide (2*R*,5*R*)-2-*tert*-butyl-3-methyl-5-phenyl-4-imidazolidinone trichloroacetic acid salt (2.45 g, 90%) as a white solid.

(17) The trichloroacetic acid was recrystalized from hot $CHCl_3$ and dried on high vacuum for 12 hours before use. Use of wet trichloroacetic acid may impact the reaction efficiency.

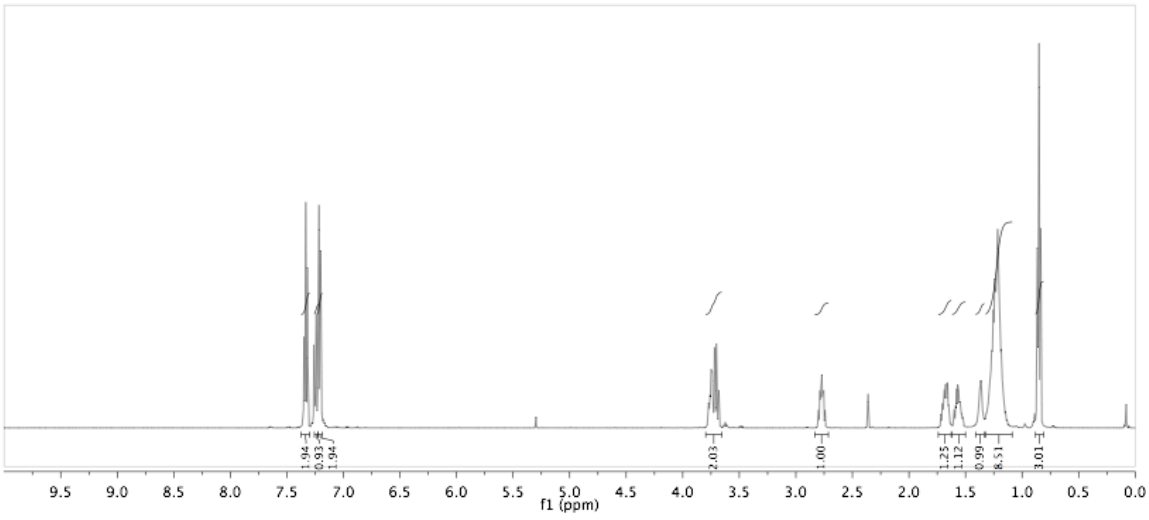
VI. Spectroscopic Data.

^{1}H, ^{13}C, and ^{19}F NMR spectra for the α-arylation products are included below.

Table 2, Entry 1:



^{1}H NMR, 500 MHz, $CDCl_3$



^{13}C NMR, 125 MHz, $CDCl_3$

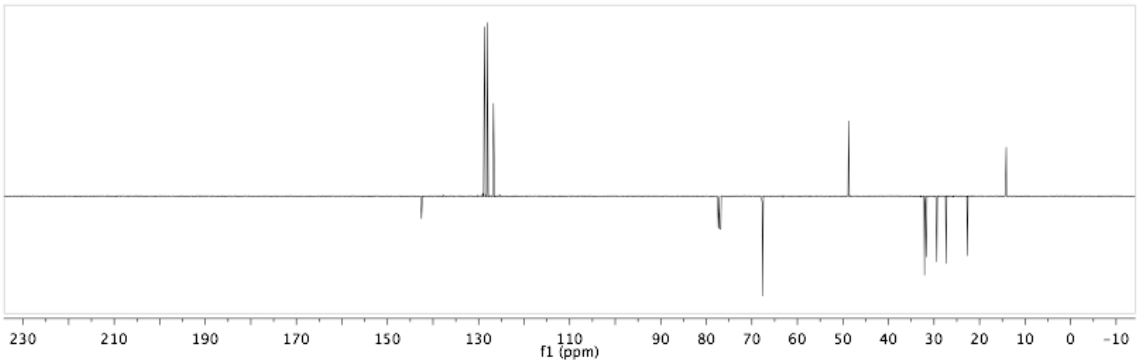
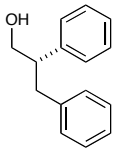
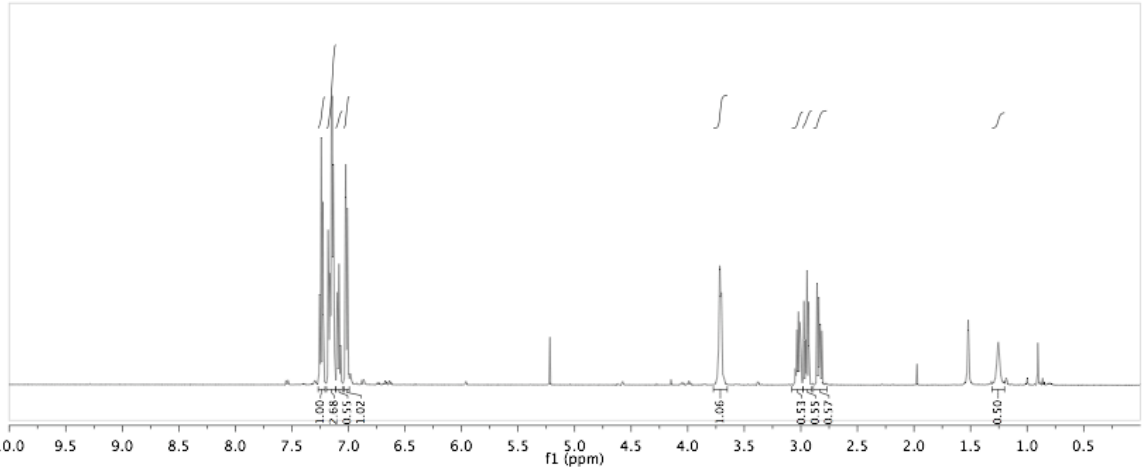


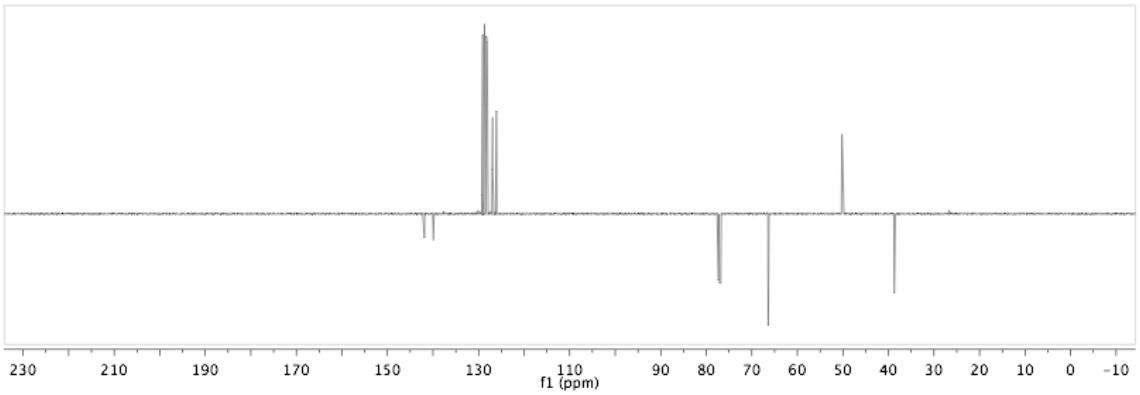
Table 2, Entry 2:



^{1}H NMR, 500 MHz, $CDCl_3$



^{13}C NMR, 125 MHz, $CDCl_3$



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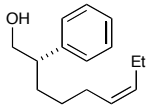
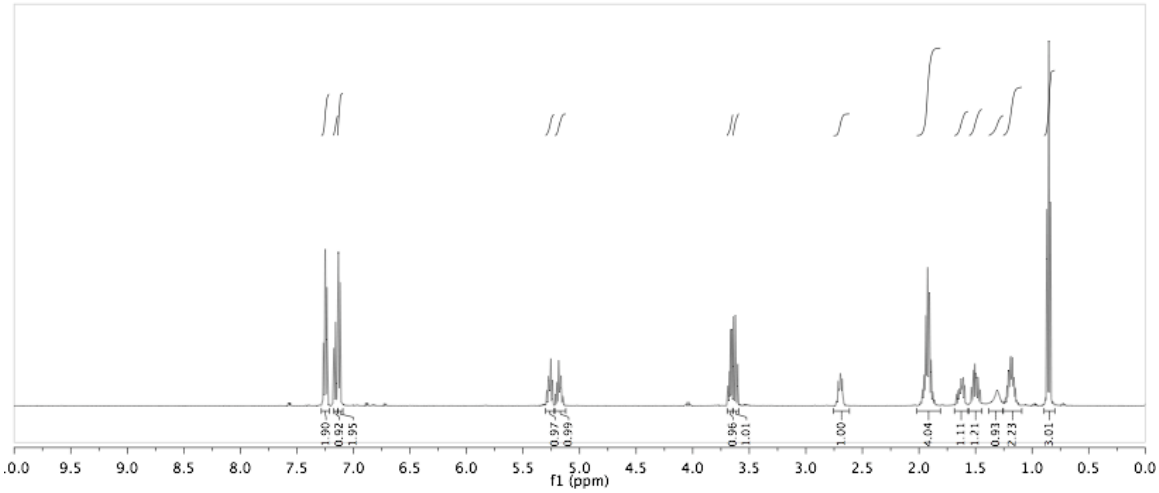
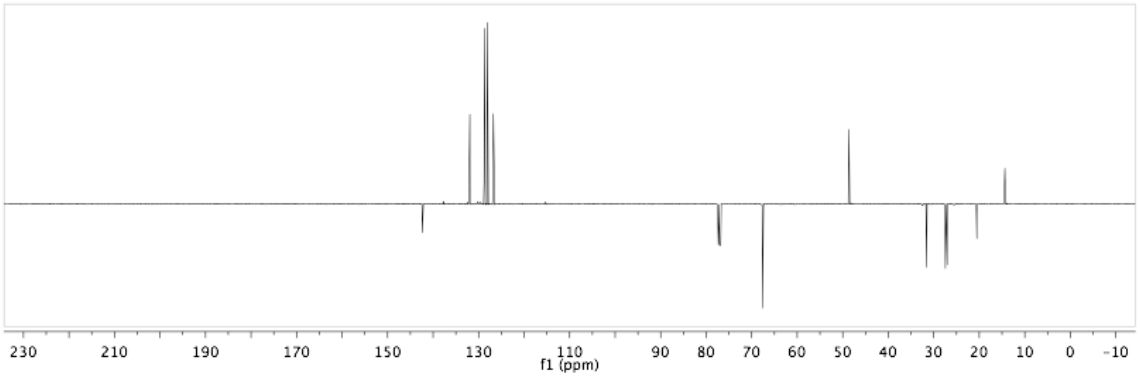


^{1}H NMR, 500 MHz, $CDCl_3$



^{13}C NMR, 125 MHz, $CDCl_3$



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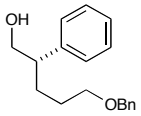
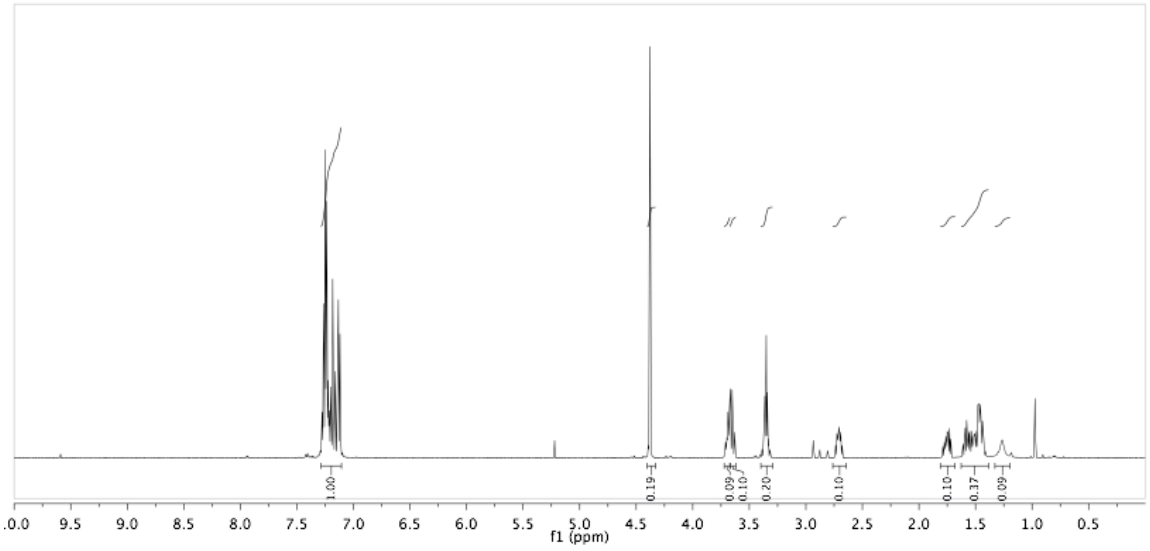
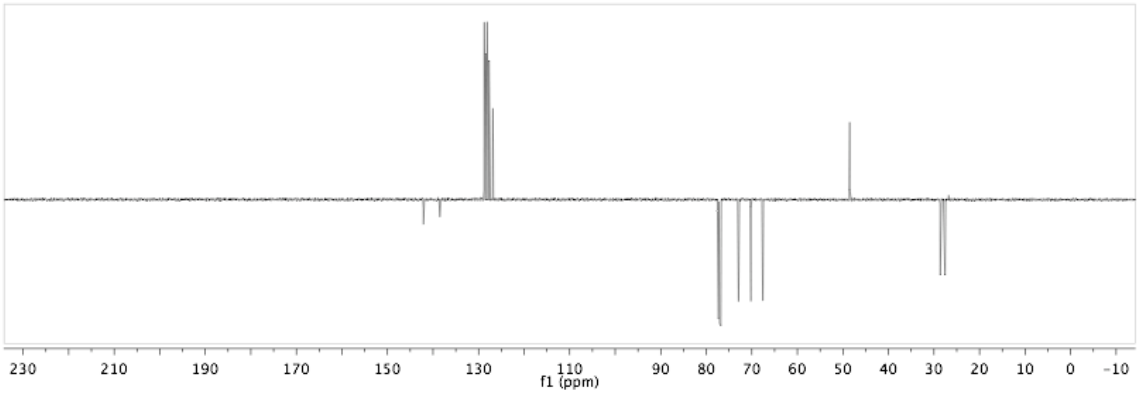


^{1}H NMR, 500 MHz, $CDCl_3$



^{13}C NMR, 125 MHz, $CDCl_3$



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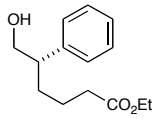
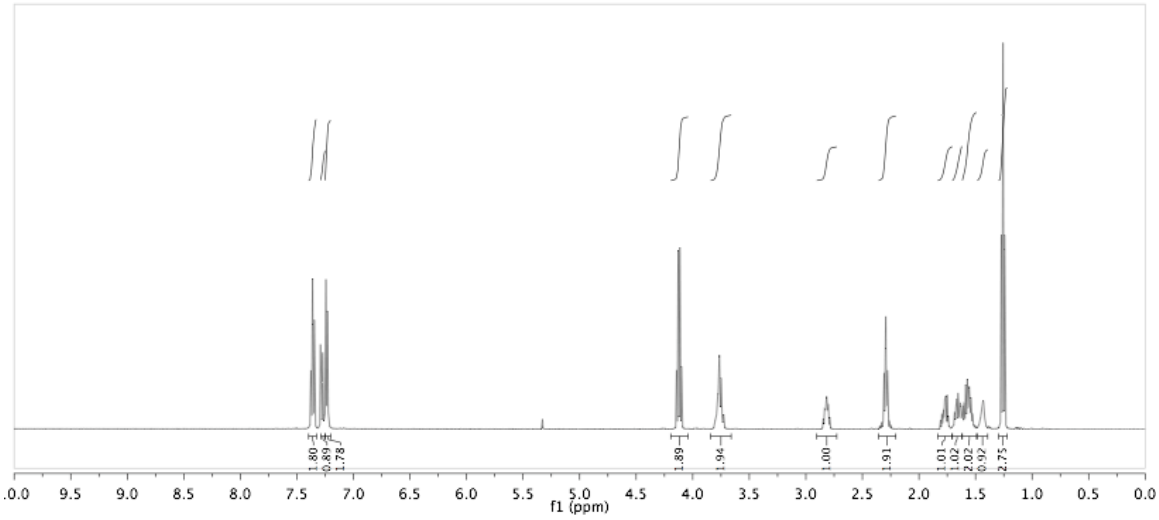
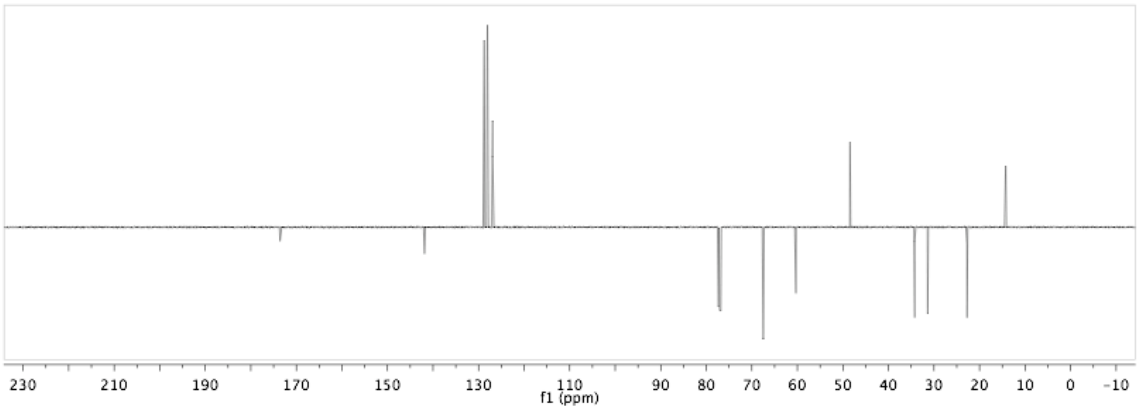


^{1}H NMR, 500 MHz, $CDCl_3$



^{13}C NMR, 125 MHz, $CDCl_3$



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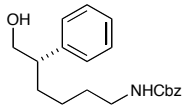
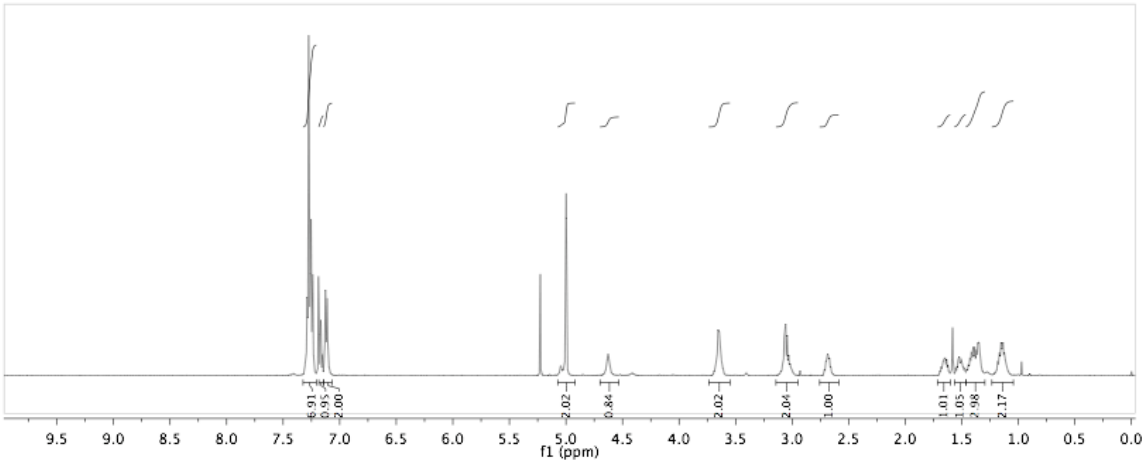
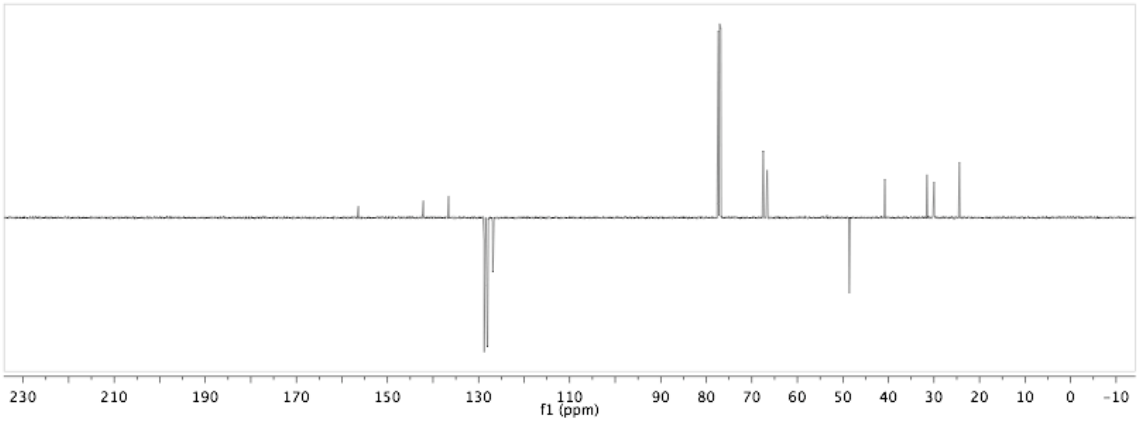


^{1}H NMR, 500 MHz, $CDCl_3$



^{13}C NMR, 125 MHz, $CDCl_3$



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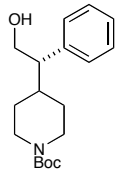
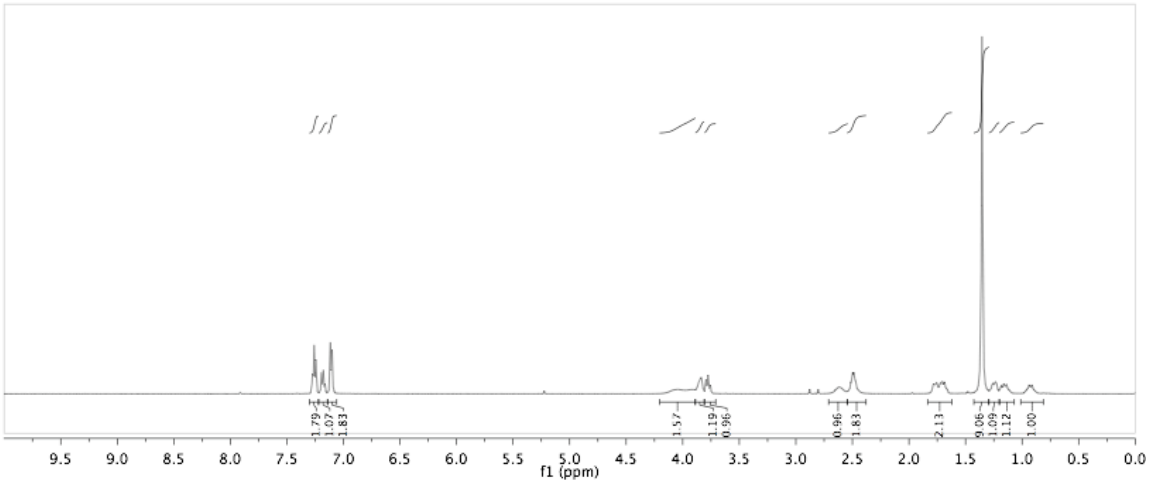
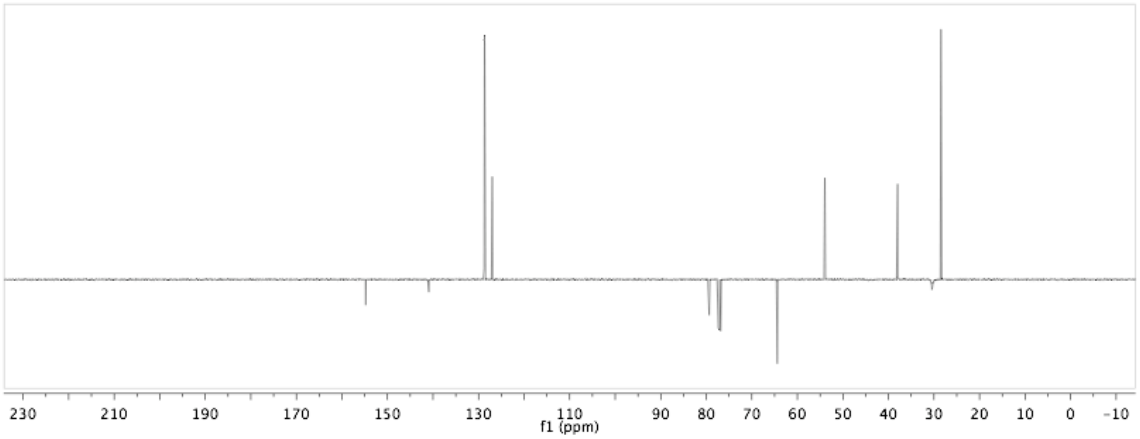


^{1}H NMR, 500 MHz, $CDCl_3$



^{13}C NMR, 125 MHz, $CDCl_3$



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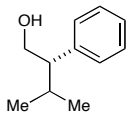
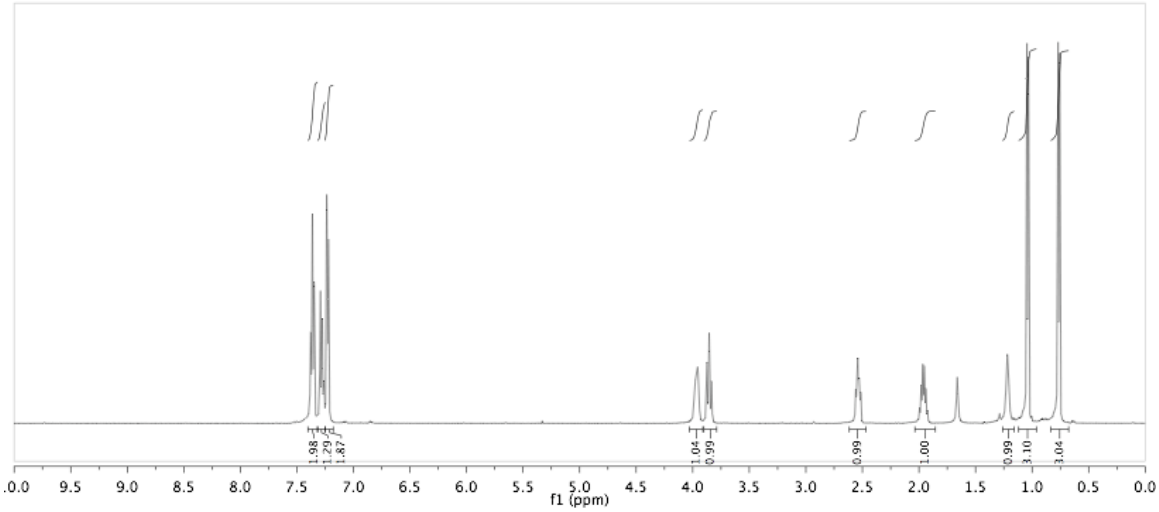
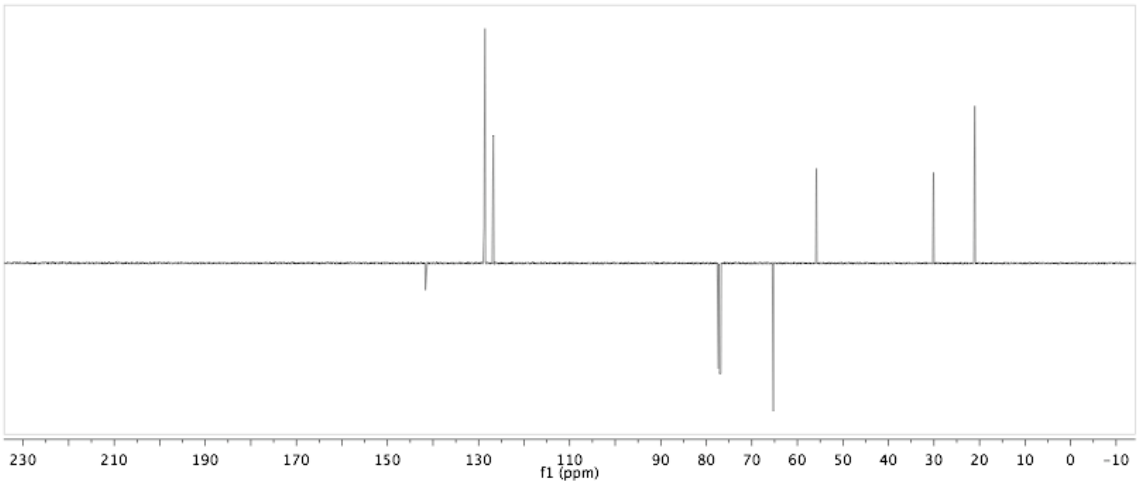


^{1}H NMR, 500 MHz, $CDCl_3$



^{13}C NMR, 125 MHz, $CDCl_3$



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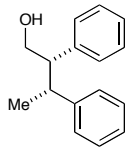
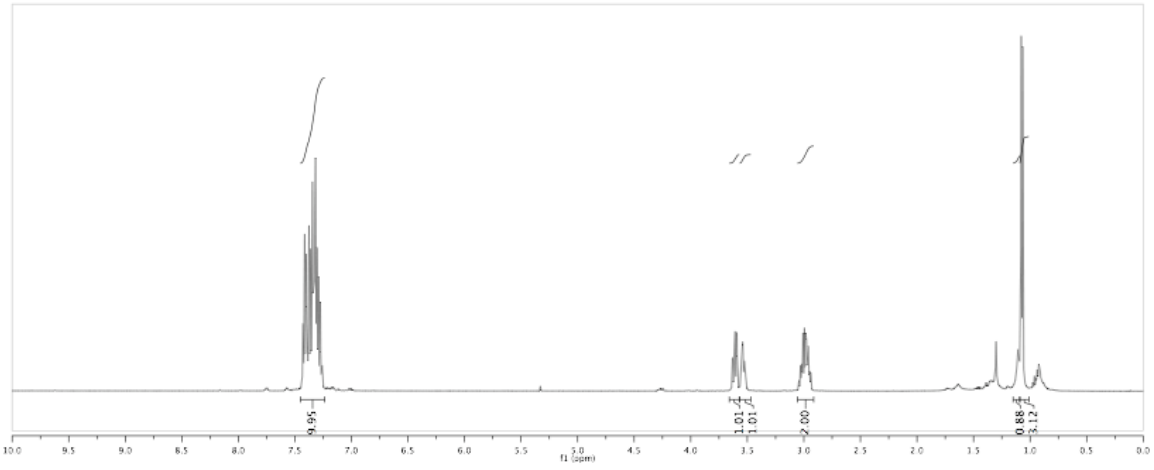


^{1}H NMR, 500 MHz, $CDCl_3$



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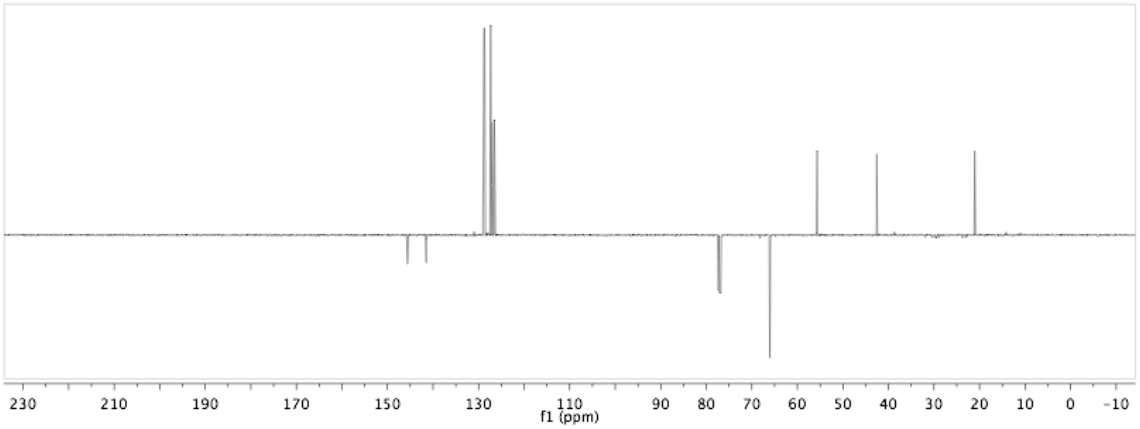

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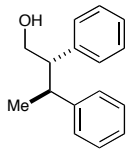
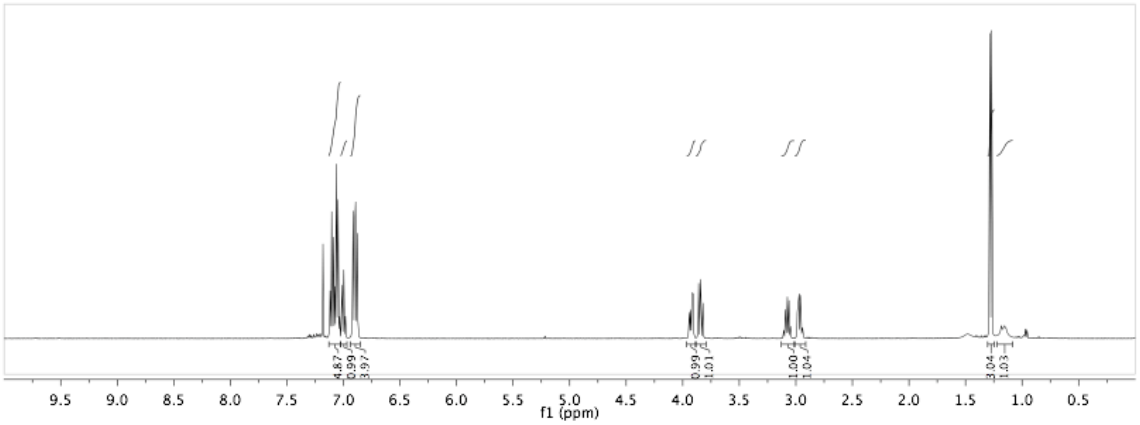


^{1}H NMR, 500 MHz, $CDCl_3$



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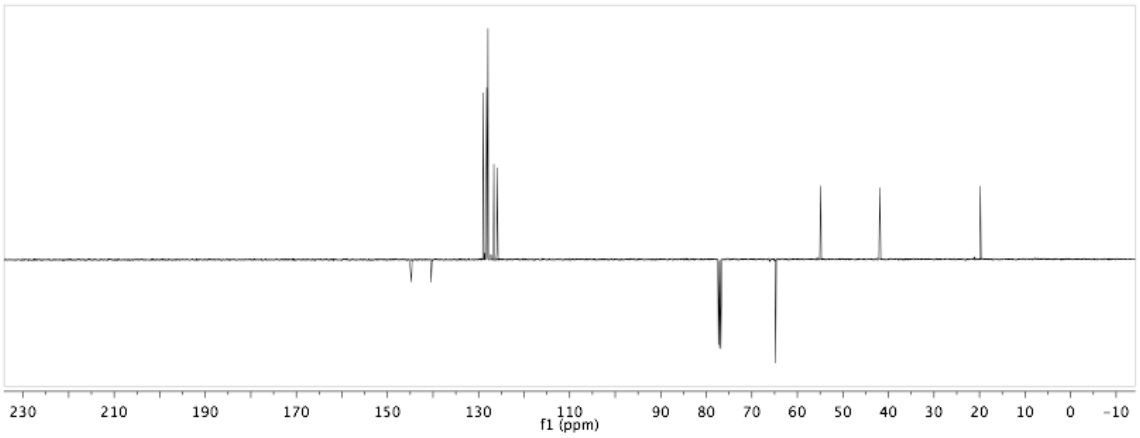

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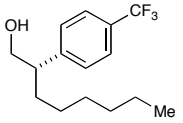
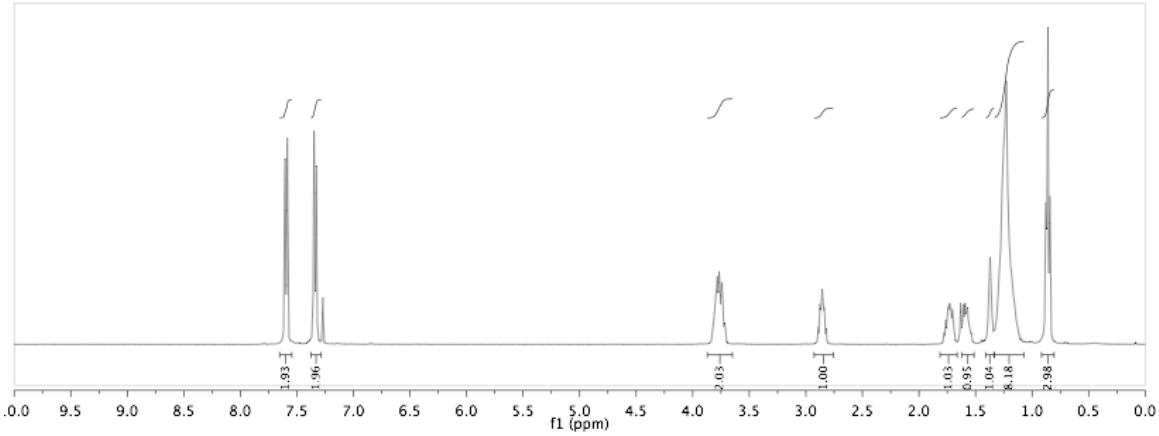
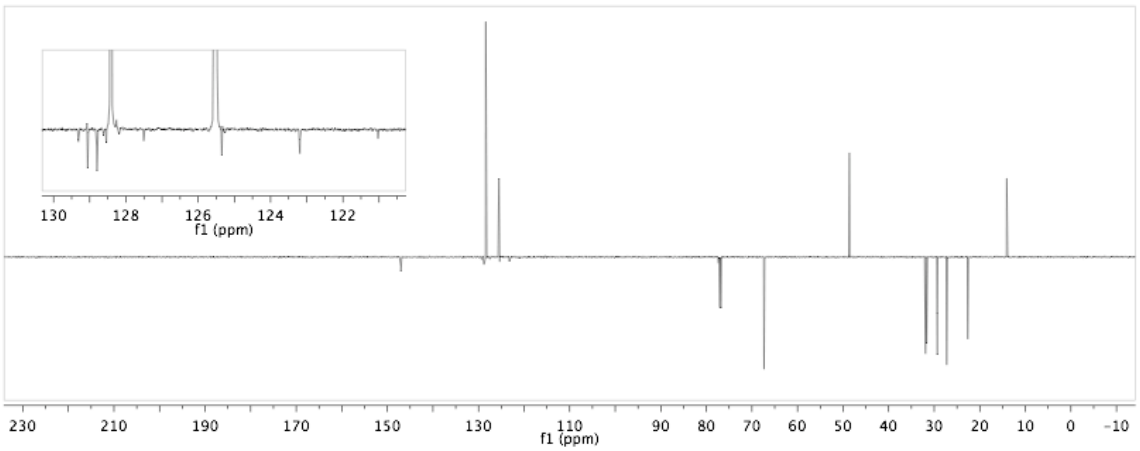


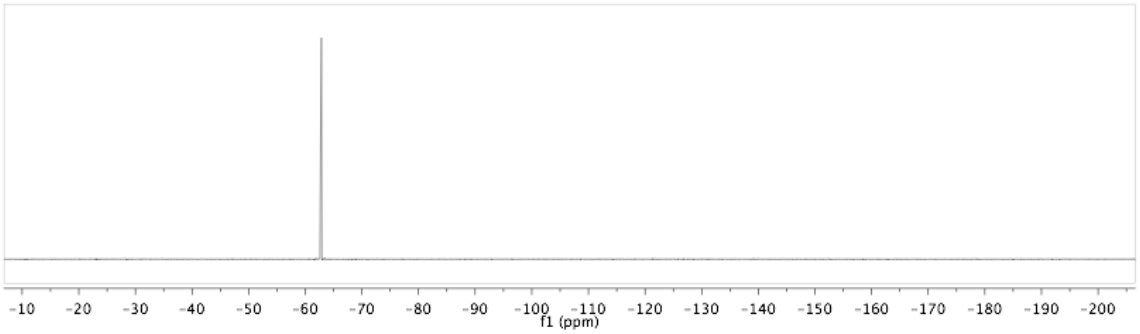
^{1}H NMR, 500 MHz, $CDCl_3$



^{13}C NMR, 125 MHz, $CDCl_3$



^{19}F NMR, 376 MHz, $CDCl_3$



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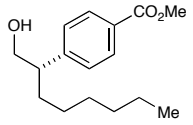
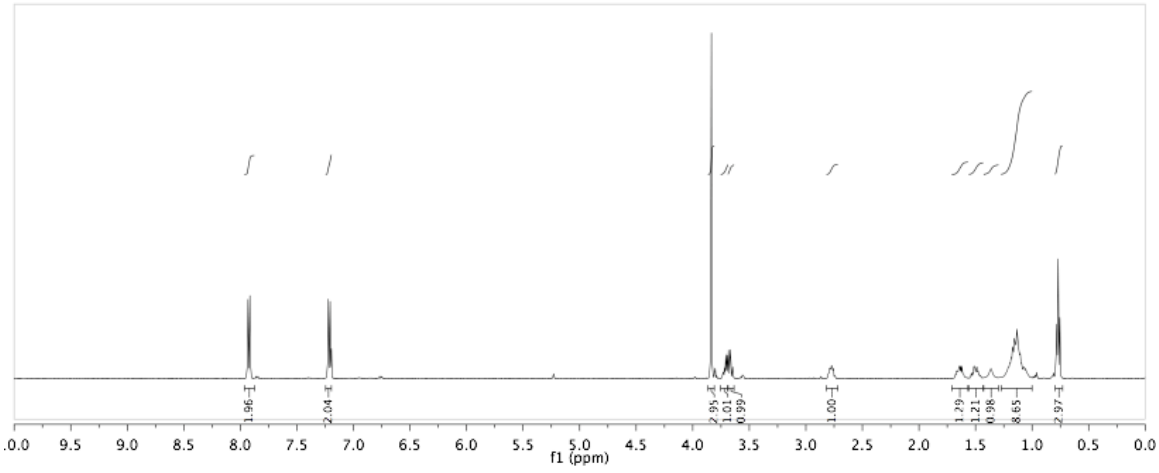


^{1}H NMR, 500 MHz, $CDCl_3$



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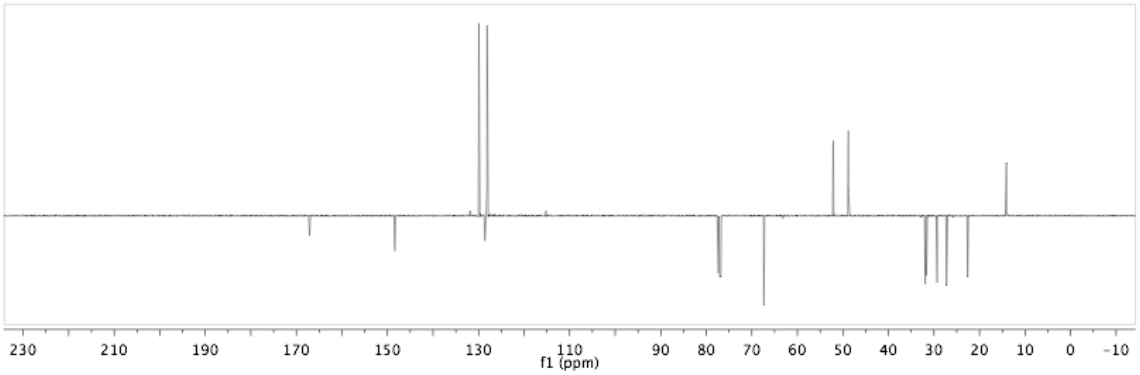

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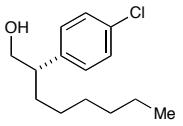
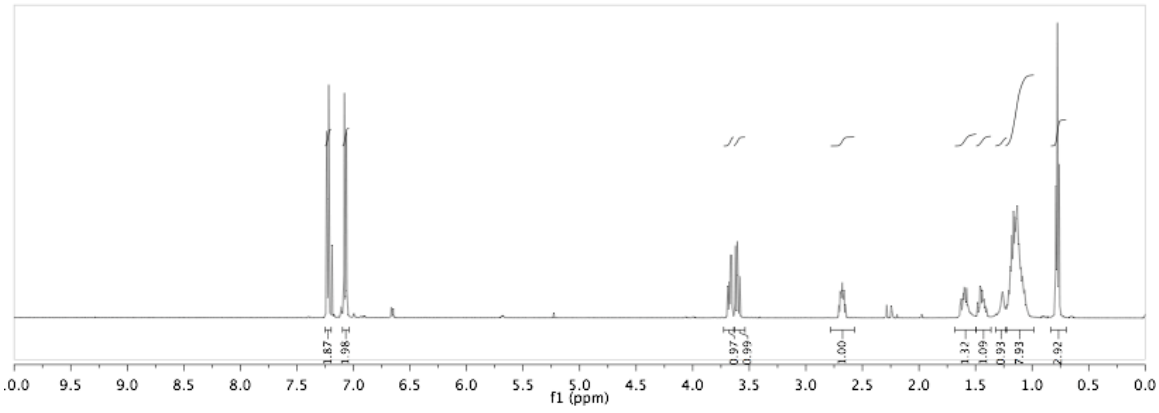


^{1}H NMR, 500 MHz, $CDCl_3$



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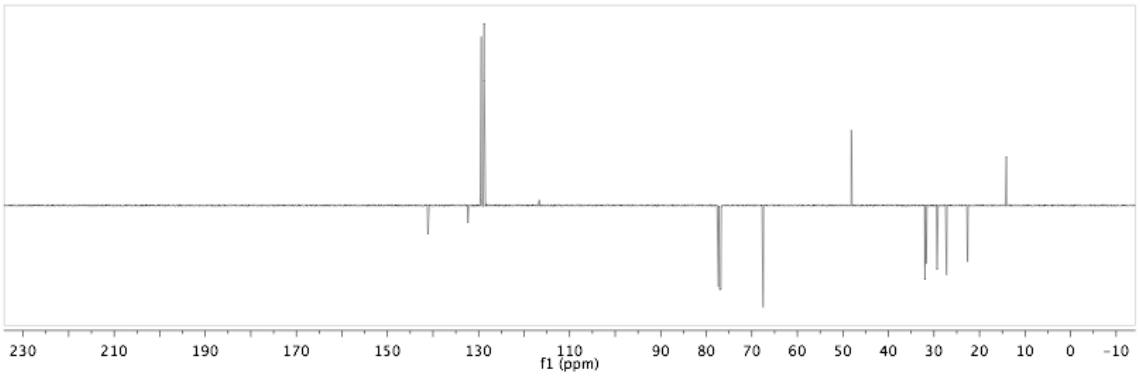

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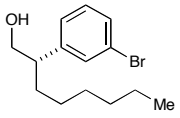

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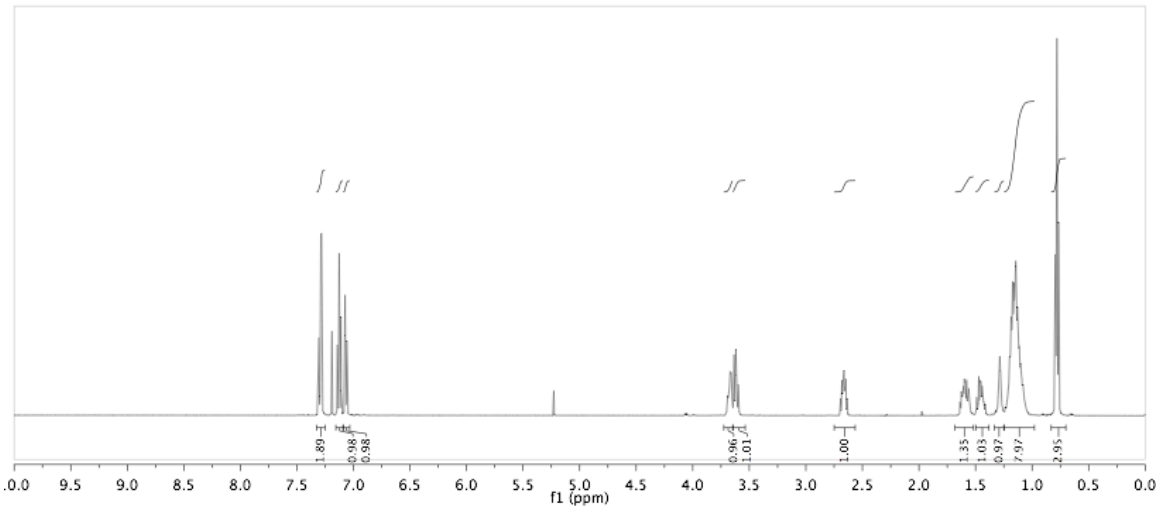

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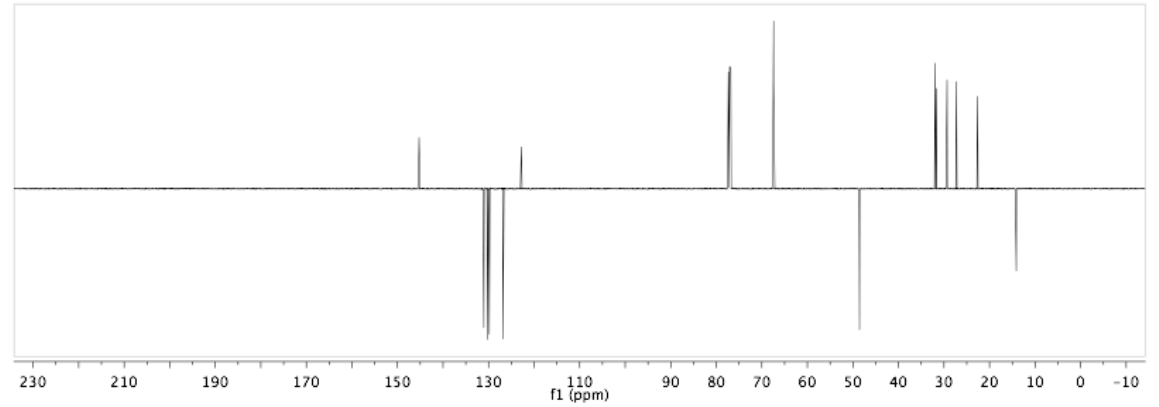

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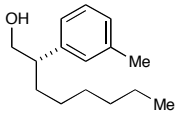

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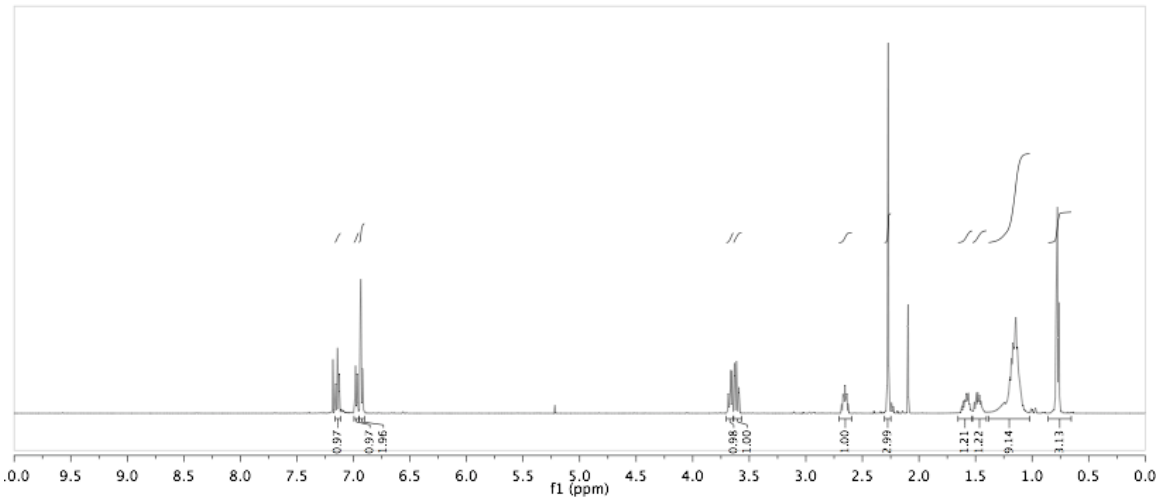
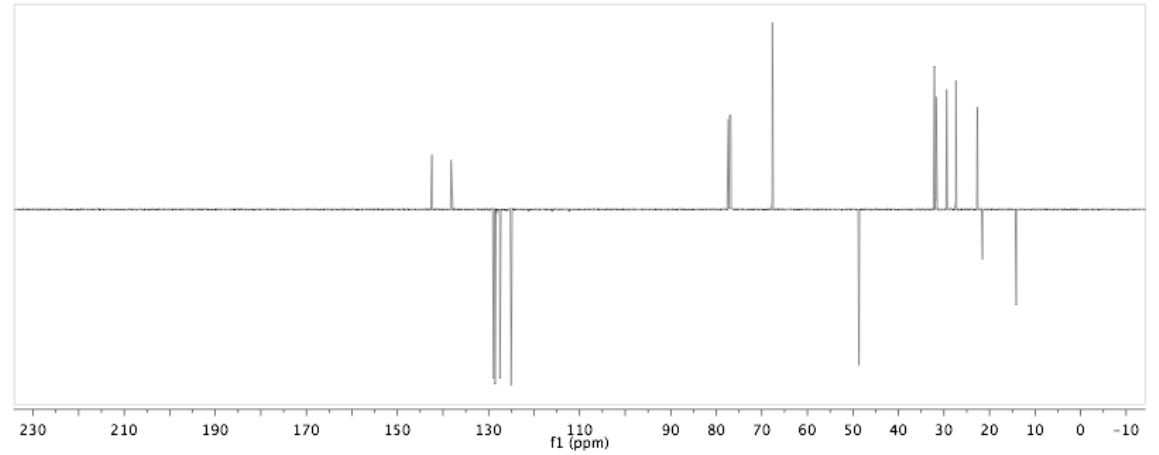


^{13}C NMR, 125 MHz, $CDCl_3$



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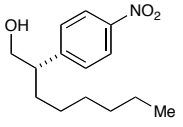
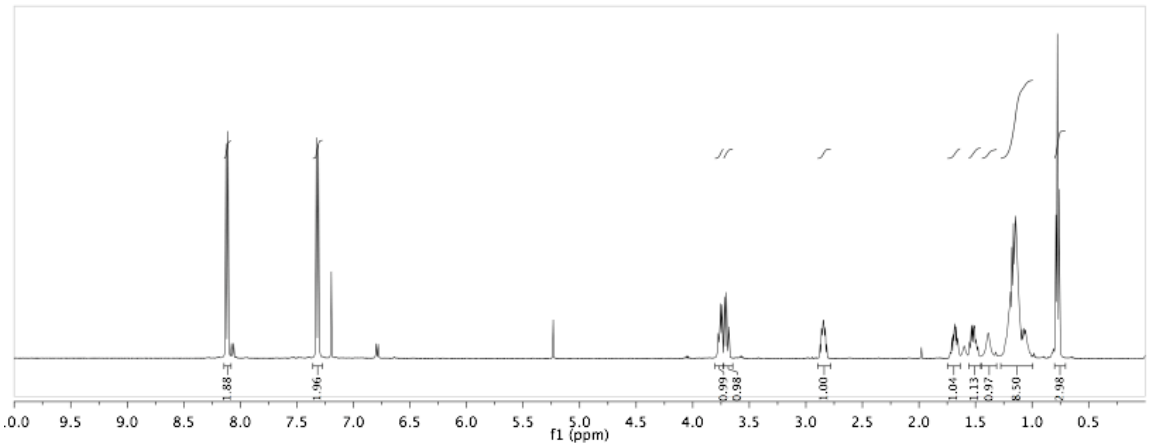


^{1}H NMR, 500 MHz, $CDCl_3$



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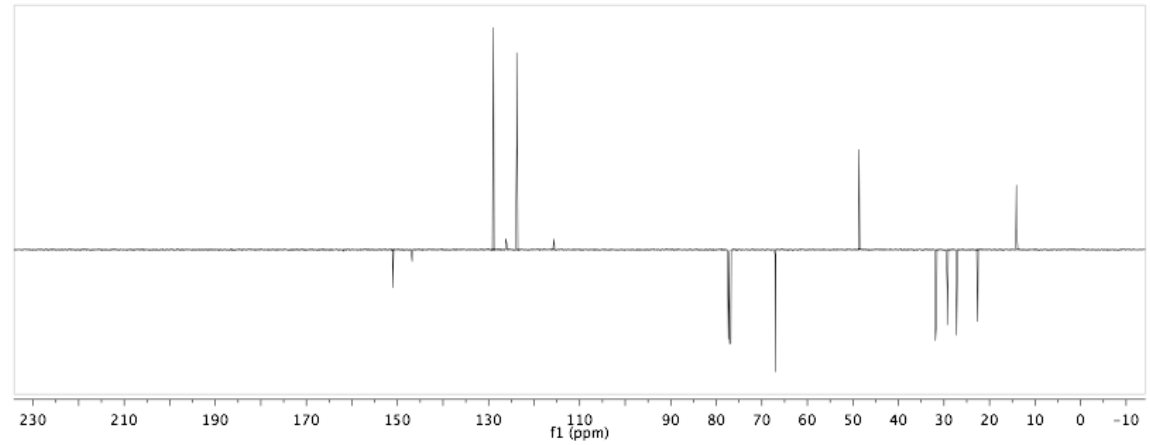

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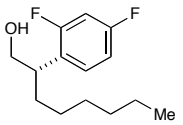
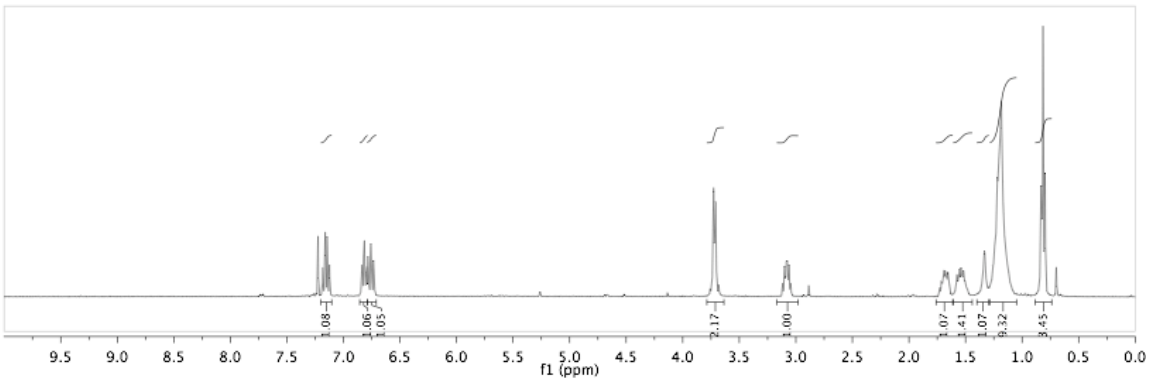


^{1}H NMR, 500 MHz, $CDCl_3$



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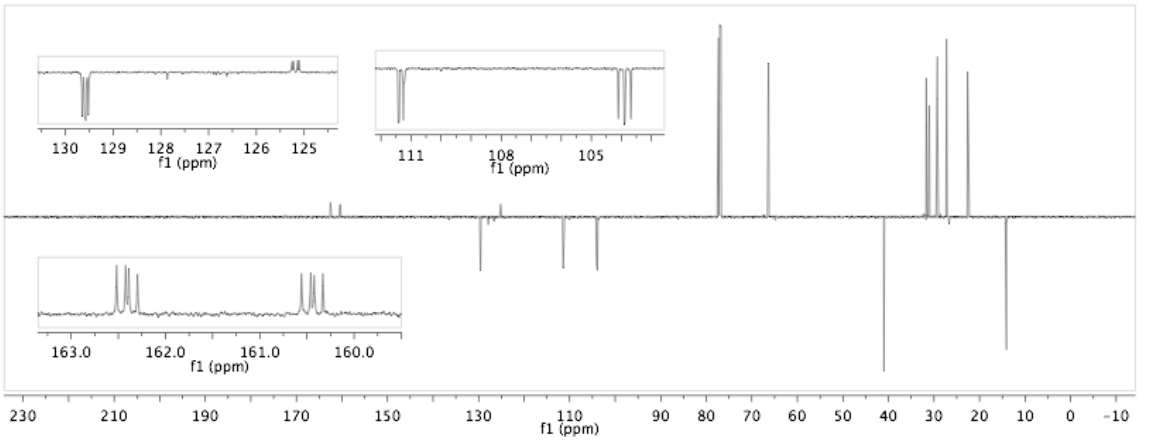
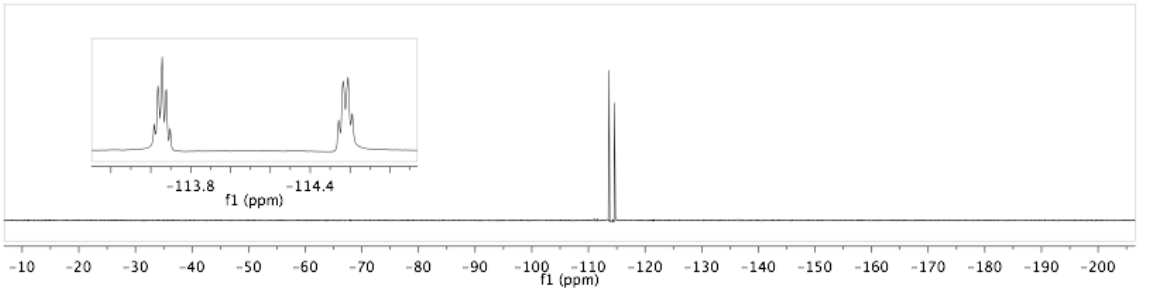


^{13}F NMR, 376 MHz, $CDCl_3$



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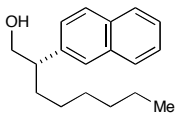
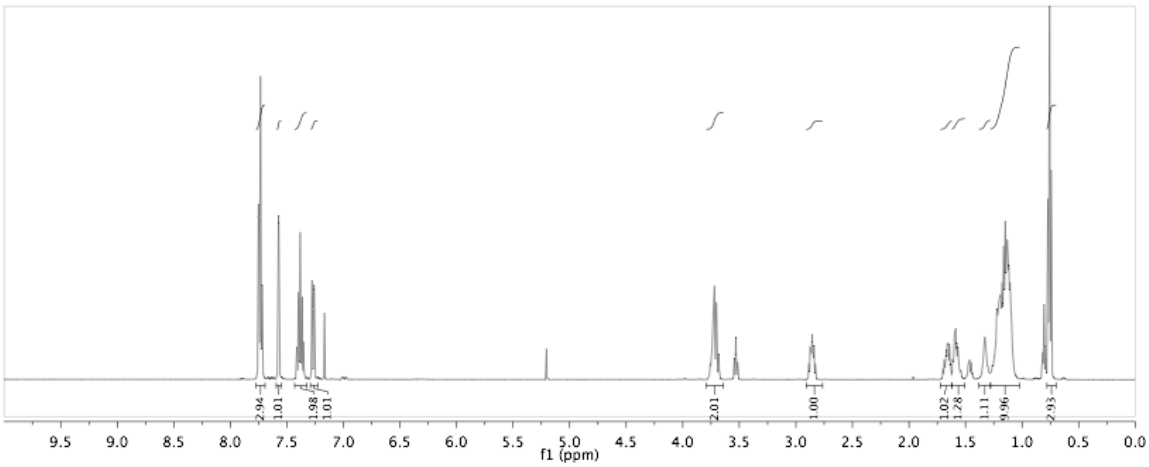


^{1}H NMR, 500 MHz, $CDCl_3$



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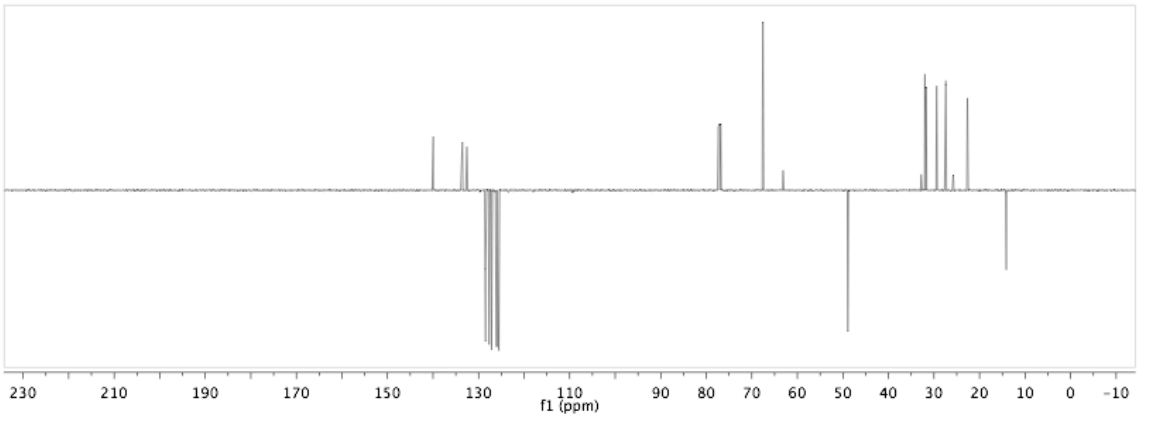

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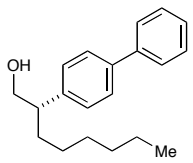

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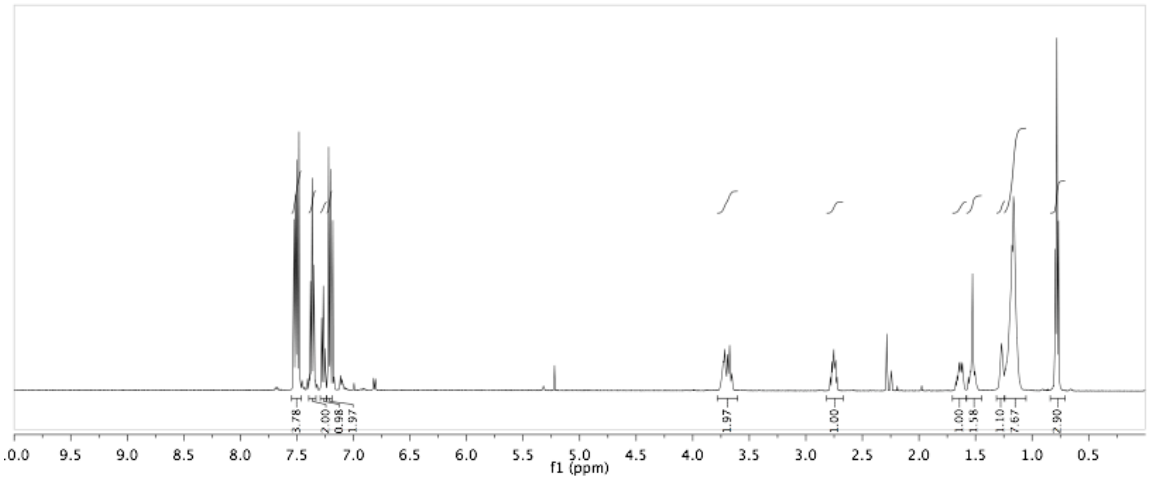

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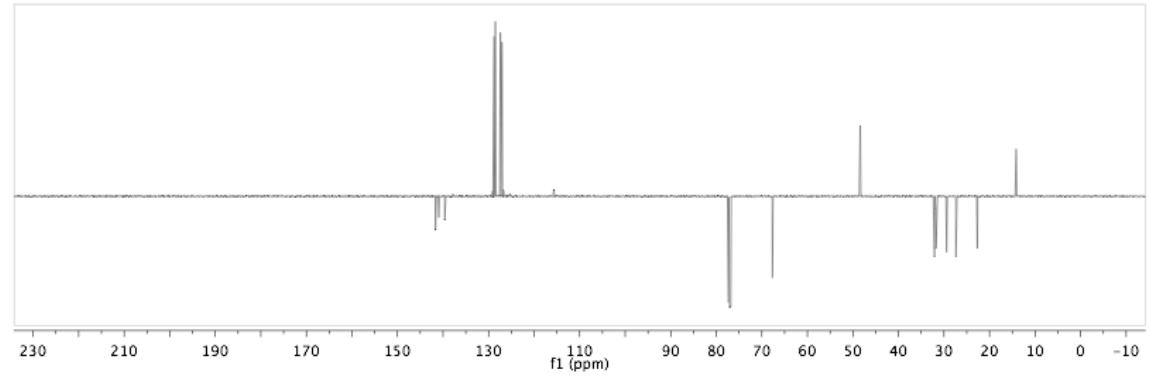

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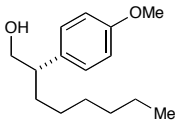
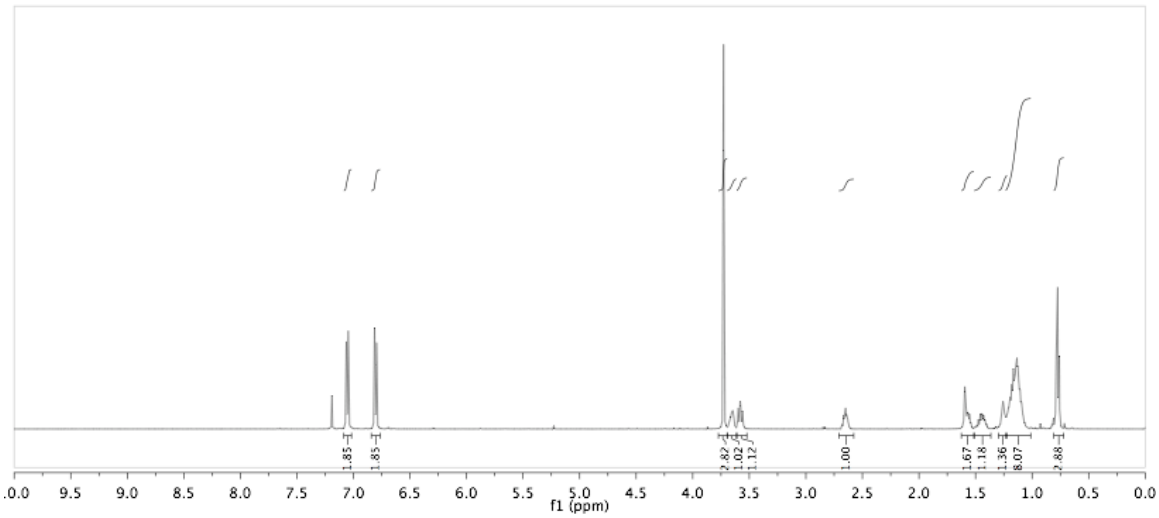


^{1}H NMR, 500 MHz, $CDCl_3$



^{13}C NMR, 125 MHz, $CDCl_3$

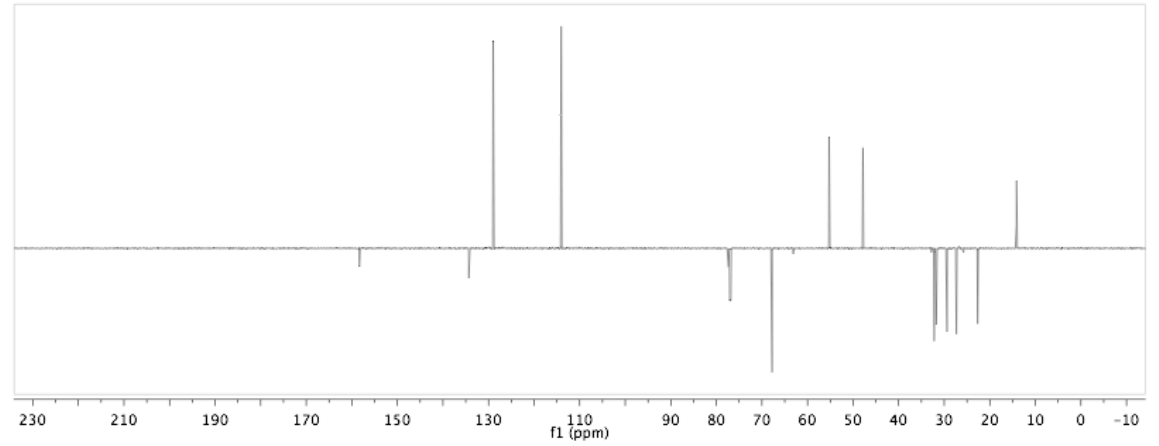
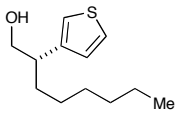
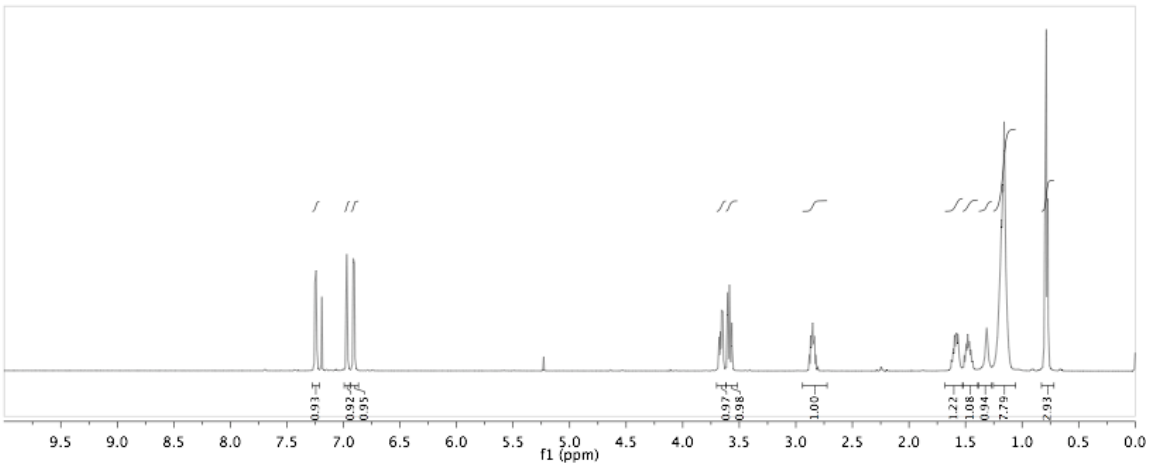


Table 3, Entry 11:



^{1}H NMR, 500 MHz, $CDCl_3$



^{13}C NMR, 125 MHz, $CDCl_3$

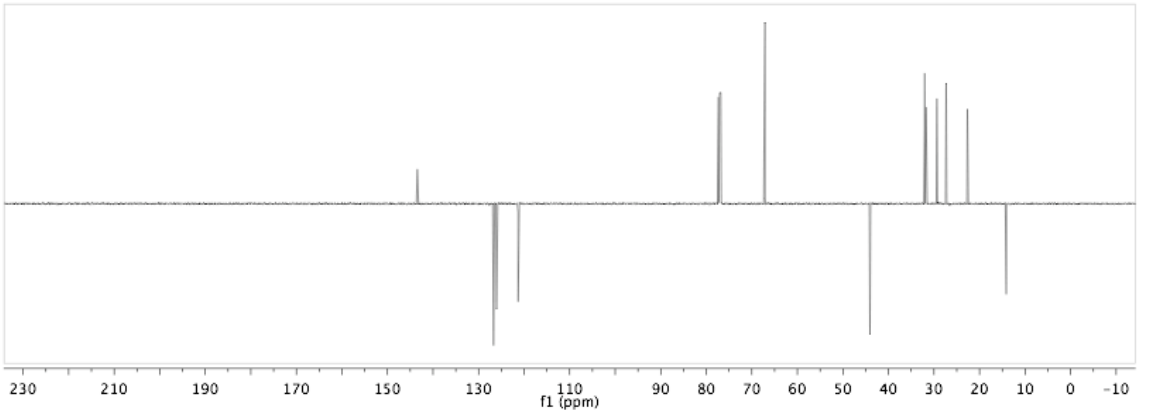
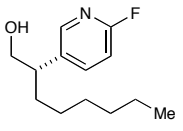
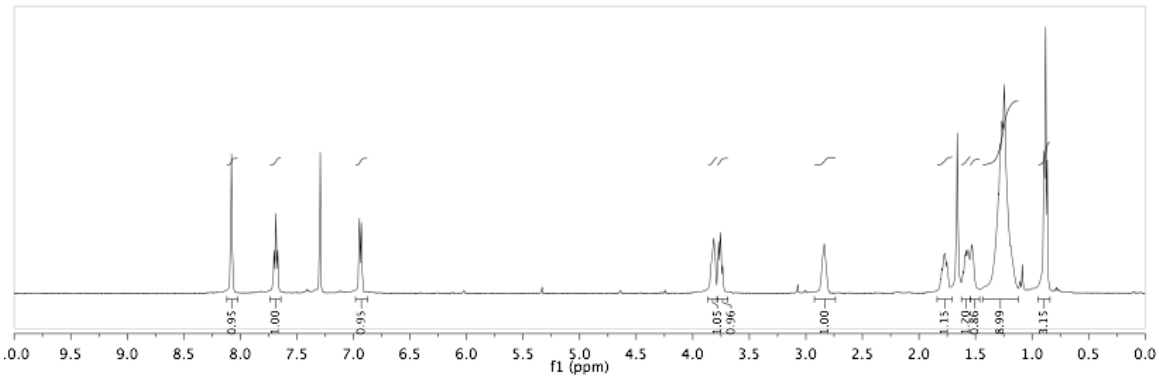


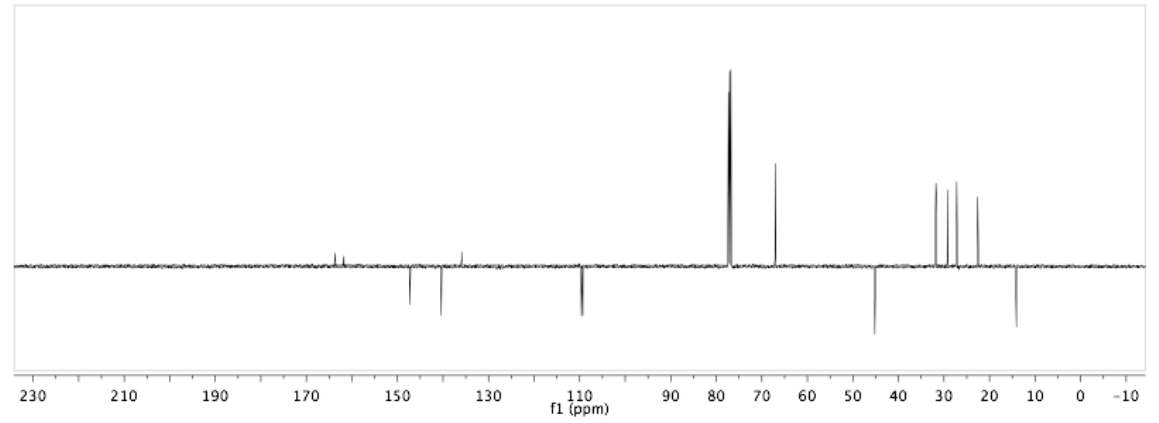
Table 3, Entry 12:



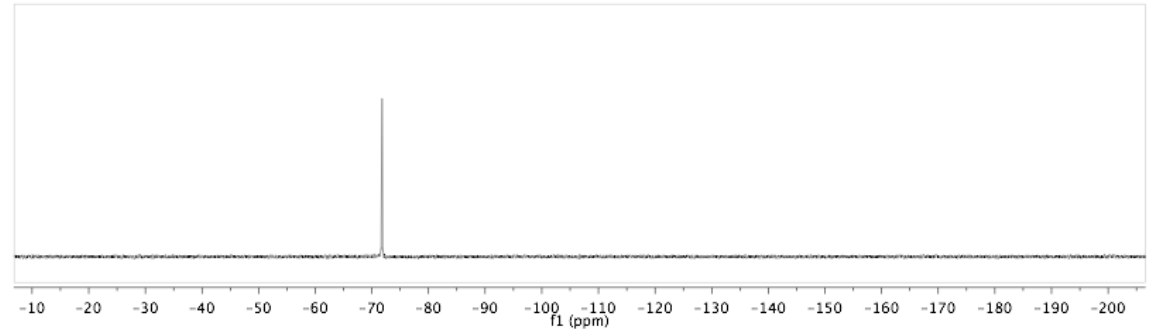
^{1}H NMR, 500 MHz, $CDCl_3$



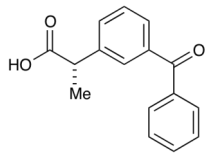
^{13}C NMR, 125 MHz, $CDCl_3$



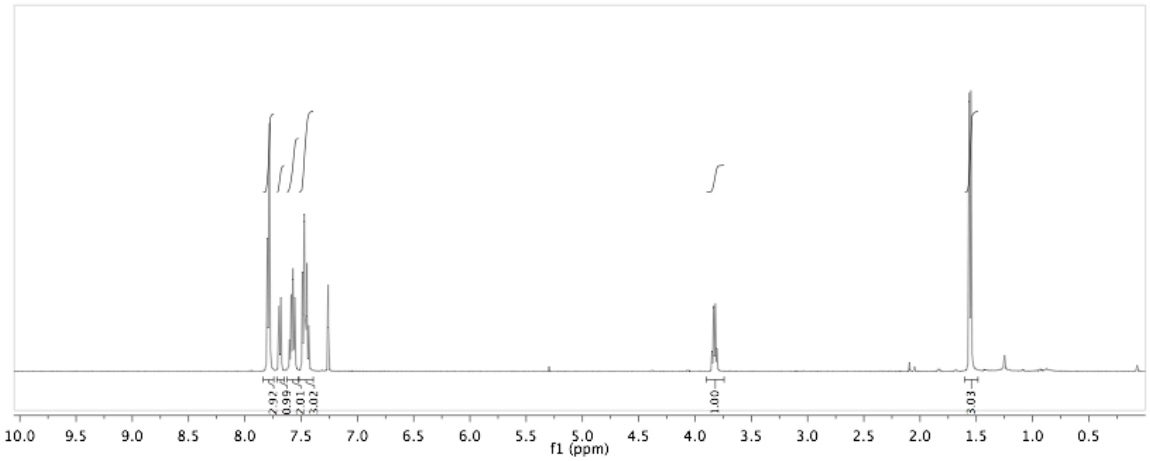
^{19}F NMR, 376 MHz, $CDCl_3$



(*S*)-Ketoprofen, Scheme 3:



^{1}H NMR, 500 MHz, $CDCl_3$



^{13}C NMR, 125 MHz, $CDCl_3$