Catalytic Enantioselective Synthesis of Difluorinated Alkyl Bromides

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Experimental Supporting Information

General Considerations:

General:
All reactions for the preparation of substrates were performed in standard, dry glassware fitted with rubber septa under an inert atmosphere of nitrogen unless otherwise described. All difluorination reactions were performed in low density polyethylene tubes sealed with a low-density polyethylene cap under an atmosphere of air. Reported concentrations refer to solution volumes at room temperature. Concentration of organic solutions under reduced pressure was performed using house vacuum (ca. 40 mm Hg) at 30 °C. Column chromatography was performed with SiliaFlash P60 (230–400 mesh, SiliCycle). Thin layer chromatography (TLC) was used for reaction monitoring and product detection was performed using pre-coated glass plates covered with 0.20 mm silica gel with fluorescent indicator; plates were visualized by exposure to UV light (λ_{ex} = 254 nm) or by staining with potassium permanganate or ninhydrin.

CAUTION: Pyridine•9HF is a corrosive and toxic substance that will etch glassware. Safe handling can be conducted with plastic syringes and metal needles, with $NaHCO_3$ (aq.) or NaOH (aq.) employed to quench excess HF. Though

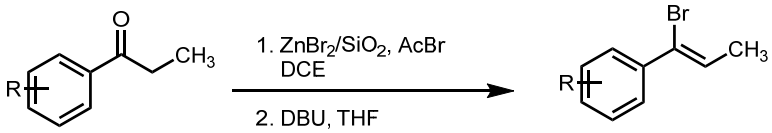
reactions should not be conducted in glassware when employing pyridine•9HF, glassware may be used to quench reactions provided sufficient quantities of base are present. Always handle pyridine•9HF while wearing gloves and in a fumehood. As a precautionary measure, have calcium gluconate gel nearby and apply immediately and liberally on skin exposed to HF.

Materials. Reagents were purchased in reagent grade from commercial suppliers and used as received, unless otherwise described. Anhydrous solvents (dioxane, dichloromethane, N,N-dimethylformamide, and tetrahydrofuran) were prepared by passing the solvent through an activated alumina column.

Instrumentation. Proton nuclear magnetic resonance (1H NMR) spectra were recorded on a Varian Mercury-400 or an Inova-500 spectrometer, are reported in parts per million downfield from tetramethylsilane, and are referenced to the residual protium resonances of the NMR solvent (CDCl3: 7.26 [$CHCl_3$]). Proton-decoupled carbon-13 nuclear magnetic resonance (13C {1 H} NMR) spectra were recorded on an Inova-500 spectrometer, are reported in parts per million downfield from tetramethylsilane, and are referenced to the carbon resonances of the NMR solvent ($CDCl_3$: 77.3). Chemical shifts for fluorine-19 nuclear magnetic resonance (19F NMR) were recorded on an Inova-500 spectrometer and are reported in parts per million downfield from chlorotrifluoromethane and are referenced to the fluorine resonance of chlorotrifluoromethane ($\delta = 0$). Data are represented as follows: chemical shift, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, sext = sextet, sept = septet, m = multiplet), coupling constants in Hertz (Hz), integration. High resolution mass spectrometric data were obtained on a Thermo q-Exactive Plus coupled with an Ultimate 3000 uHPLC (ESI) or GC (EI). GC analysis was performed using an Agilent 7890A GC system using commercially available columns. Chiral HPLC analysis was performed using an Agilent 1200 series quaternary HPLC system using commercially available CHIRALCEL analytical columns (4.6 x 250 mm).

Synthesis of Vinyl Bromide Substrates and Their Precursors

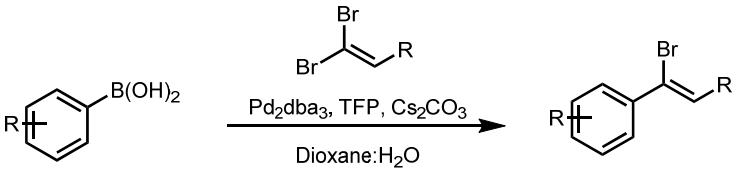
General Procedure A



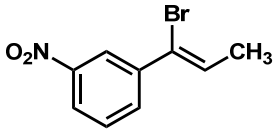
The following procedure was adapted from one reported by Legault and coworker.[1] To a 2-dram vial equipped with a septum cap and stir bar was added the propiophenone (1 equiv) and dichloroethane (0.5M). Acetyl bromide (8 equiv) was added all at once via syringe, followed by $ZnBr/SiO_2$ (1g/mmol substrate) while vigorously stirring. The reaction was allowed to proceed overnight. After this time, the reaction was filtered, washing with DCM, and quenched with $NaHCO_3$. The solution was then transferred to a separatory funnel, diluted with DCM and additional bicarbonate. The organic layer was separated and the aqueous layer extracted with DCM thrice. The combined organics were then washed with $NaHCO_3$, H_2O, and brine, and subsequently dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude material was then purified by column chromatography (Hexanes:Et_2O) to afford a mixture of the vinyl bromide and the *gem*-dibromoalkane.

In a vial equipped with a stir bar and septum cap was added the material from the previous step and THF (1M). To the stirred solution was added DBU (1.5 equiv relative to *gem*-dibromoalkane), and the reaction was allowed to proceed overnight. After this time, the mixture was diluted with Et_2O and H_2O. The organic layer was separated and the aqueous layer extracted with Et_2O. The combined organics were then washed with H_2O and brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude material was then purified by column chromatography (Hexanes:Et_2O) to afford the desired product.

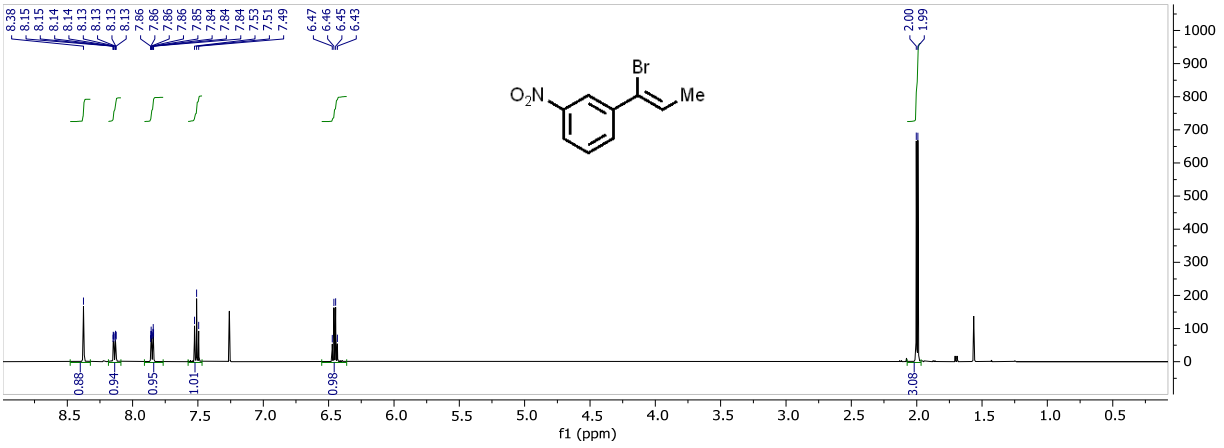
General Procedure B

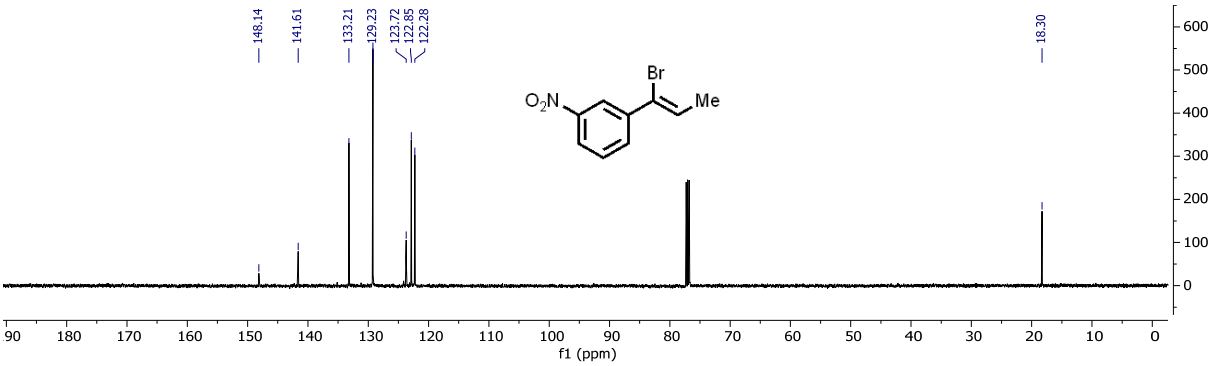


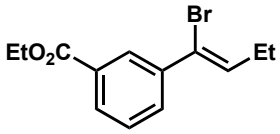
The following procedure was adapted from one reported by Paraja, *et. al.*[2] To a vial equipped with a stir var and septum cap was added the boronic acid (1 equiv), Pd_2dba_3 (0.025 equiv), and tri(2-furyl)phosphine (0.15 equiv). The vial was evacuated and backfilled thrice with N_2. To a separate vial equipped with a septum cap was added the *gem*-dibromoalkene (1.2 equiv). This was evacuated and backfilled thrice with N_2, followed by addition of dioxane (0.25M in boronic acid). The solution was then sparged with N_2 for 5 minutes. To a third vial equipped with a septum cap was added Cs_2CO_3. This vial was evacuated and backfilled thrice with N_2, followed by addition of H_2O (1M in boronic acid). The solution was then sparged with N_2 for 5 minutes. After this time, the alkene in dioxane and the aqueous Cs_2CO_3 were added simultaneously dropwise to the vial containing the boronic acid. This mixture was allowed to stir vigorously overnight. After this time, the mixture was filtered through celite, washing with EtOAc. The organic layer was then washed with brine thrice, dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude material was then purified by column chromatography (Hexanes:Et_2O) to afford the desired product.



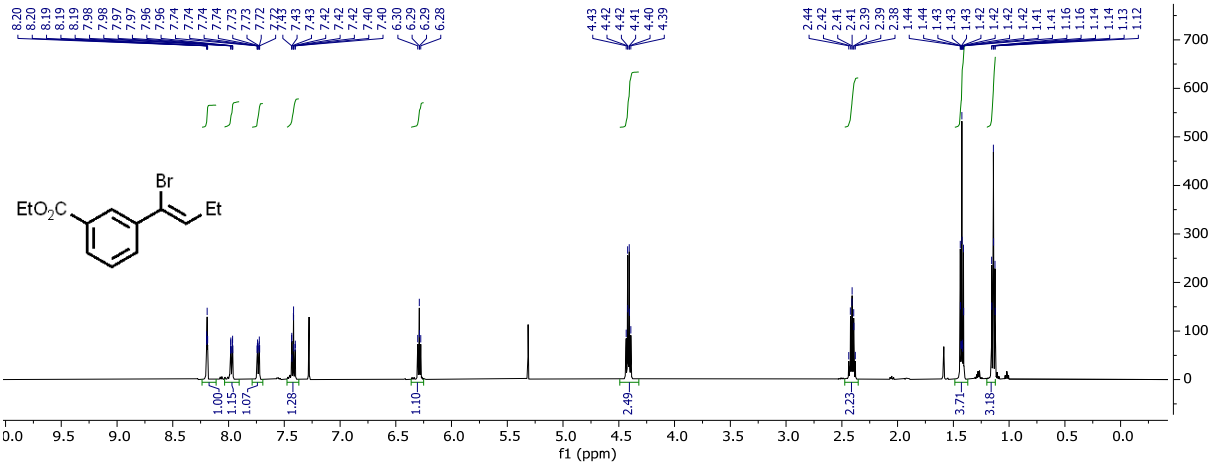
2a, (Z)-1-(1-bromoprop-1-en-1-yl)-3-nitrobenzene. Prepared according to General Procedure A from 3'-nitropropiophenone (896 mg, 5 mmol) as a clear, colorless oil, which solidified upon storage (900 mg, 74% yield).
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38 (s, 0H), 8.14 (ddd, J = 8.2, 2.4, 1.0 Hz, 1H), 7.85 (ddd, J = 7.8, 1.9, 1.0 Hz, 1H), 7.51 (t, J = 8.0 Hz, 1H), 6.45 (q, J = 6.6 Hz, 1H), 2.00 (d, J = 6.6 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 148.14, 141.61, 133.21, 129.23, 123.72, 122.85, 122.28, 18.30.
HRMS (ESI): for $C_9H_9BrNO_2$, $[M+H]^+$ calculated m/z = 241.9810 and 243.9791, found m/z = 241.9811 and 243.9790.

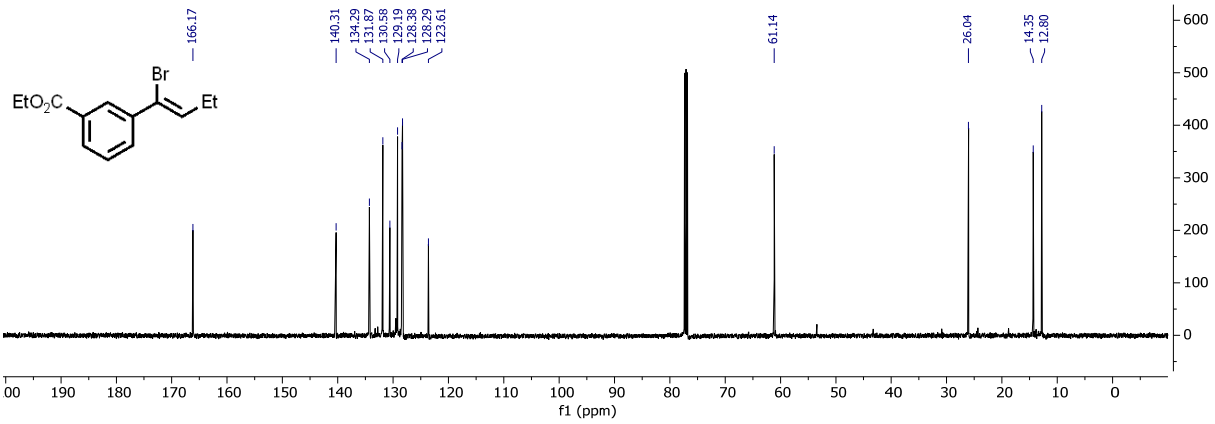


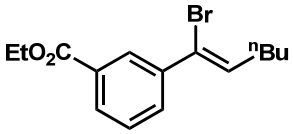




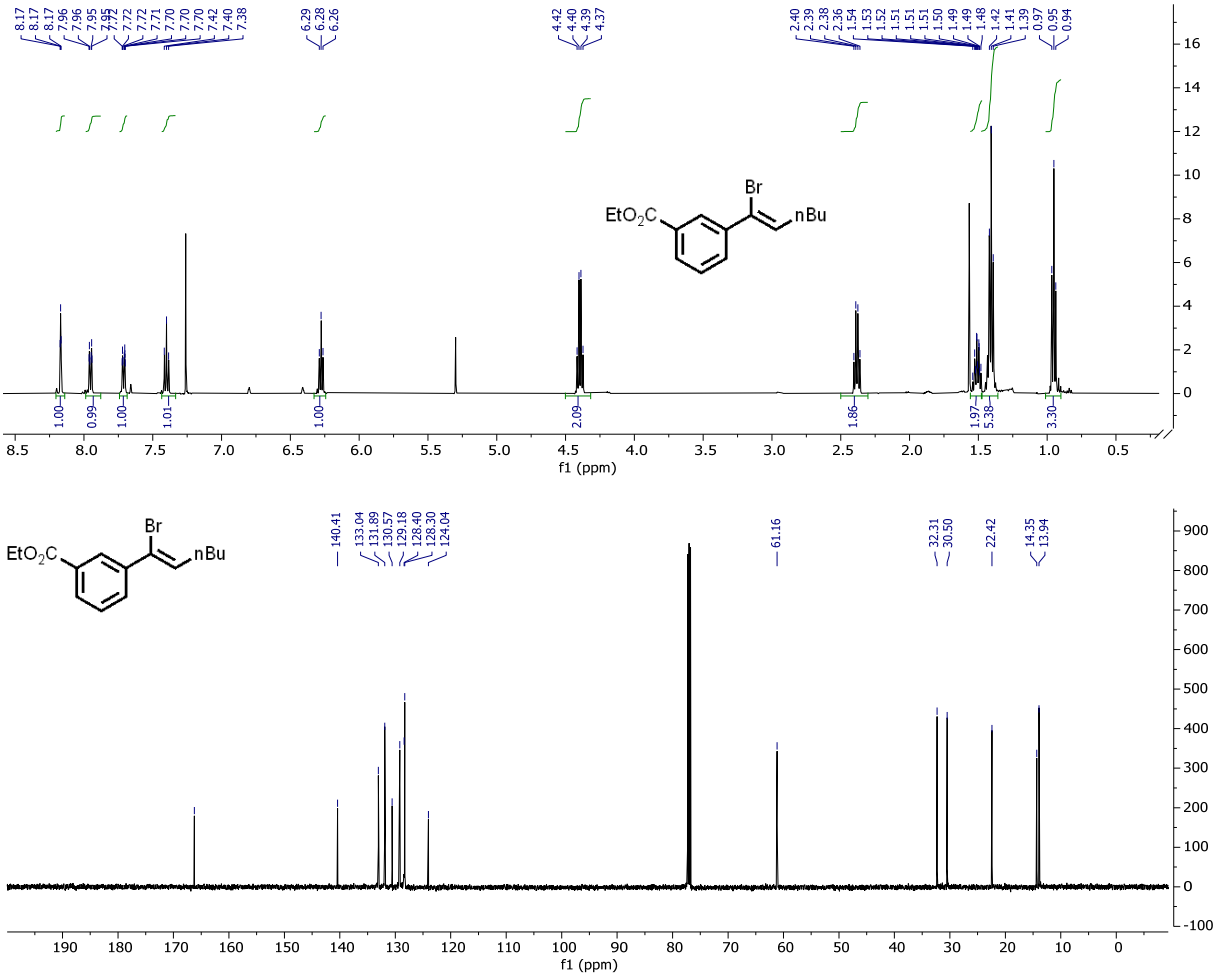
2c, (Z)-ethyl 3-(1-bromobut-1-en-1-yl)benzoate. Prepared according to General Procedure B from 3-(ethoxycarbonyl)phenylboronic acid (970 mg, 5 mmol) as a clear, orange oil (396 mg, 28% yield).
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 – 8.18 (m, 1H), 7.97 (ddd, *J* = 7.7, 1.7, 1.1 Hz, 1H), 7.73 (ddd, *J* = 7.8, 2.0, 1.1 Hz, 1H), 7.42 (td, *J* = 7.8, 0.6 Hz, 1H), 6.29 (t, *J* = 6.8 Hz, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 2.46 – 2.36 (m, 2H), 1.42 (td, *J* = 7.1, 0.7 Hz, 3H), 1.14 (td, *J* = 7.6, 0.7 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 166.17, 140.31, 134.29, 131.87, 130.58, 129.19, 128.38, 128.29, 123.61, 61.14, 26.04, 14.35, 12.80.
HRMS (ESI): for $C_{13}H_{16}BrO_2$, $[M+H]^+$ calculated *m/z* = 283.0328 and 285.0308, found *m/z* = 283.0327 and 285.0305.

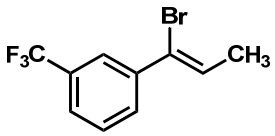




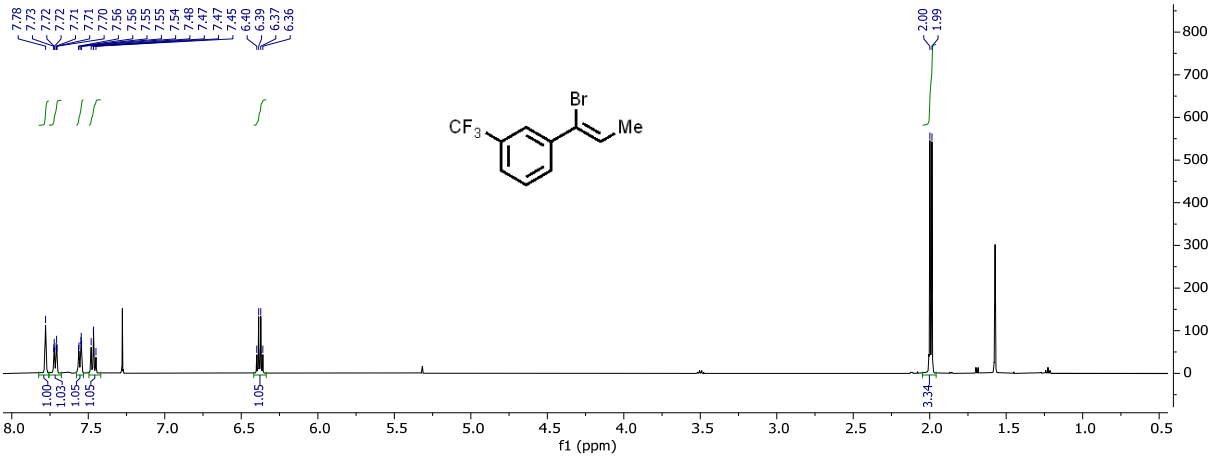


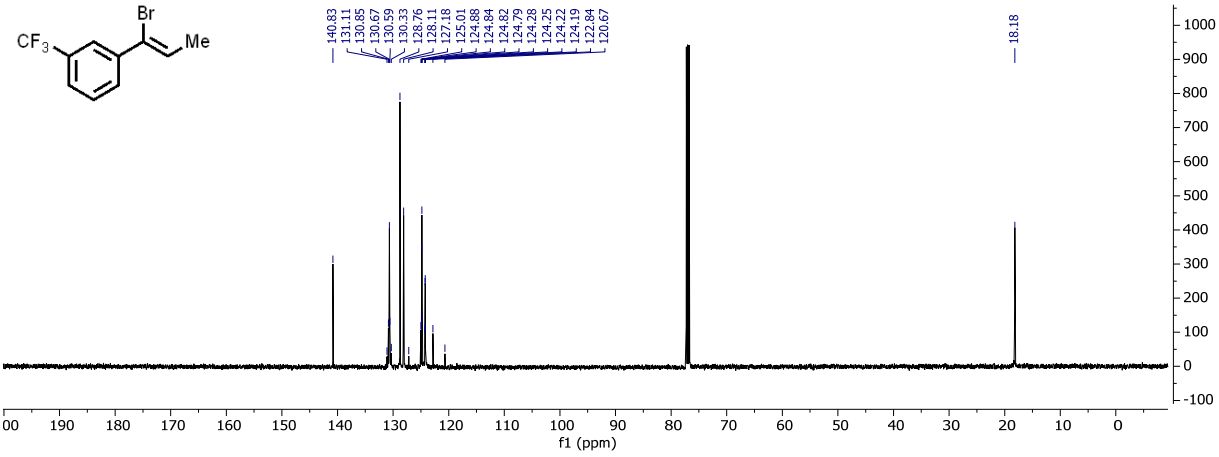
2d, (Z)-ethyl 3-(1-bromohex-1-en-1-yl)benzoate. Prepared according to General Procedure B from 3-(ethoxycarbonyl)phenylboronic acid (194 mg, 1 mmol) as a clear, yellow oil (155 mg, 49% yield).
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (t, J = 1.9 Hz, 1H), 7.95 (dt, J = 7.7, 1.3 Hz, 1H), 7.73 – 7.70 (m, 1H), 7.40 (t, J = 7.8 Hz, 1H), 6.28 (t, J = 6.9 Hz, 1H), 4.40 (q, J = 7.2 Hz, 2H), 2.38 (q, J = 7.2 Hz, 2H), 1.55 – 1.47 (m, 2H), 1.41 (t, J = 7.1 Hz, 5H), 0.95 (t, J = 7.2 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 166.23, 140.41, 133.04, 131.89, 130.57, 129.18, 128.40, 128.30, 124.04, 61.16, 32.31, 30.50, 22.42, 14.35, 13.94.
HRMS (ESI): for $C_{15}H_{20}BrO_2$, $[M+H]^+$ calculated m/z = 311.0641 and 313.0621, found m/z = 311.0640 and 313.0618.

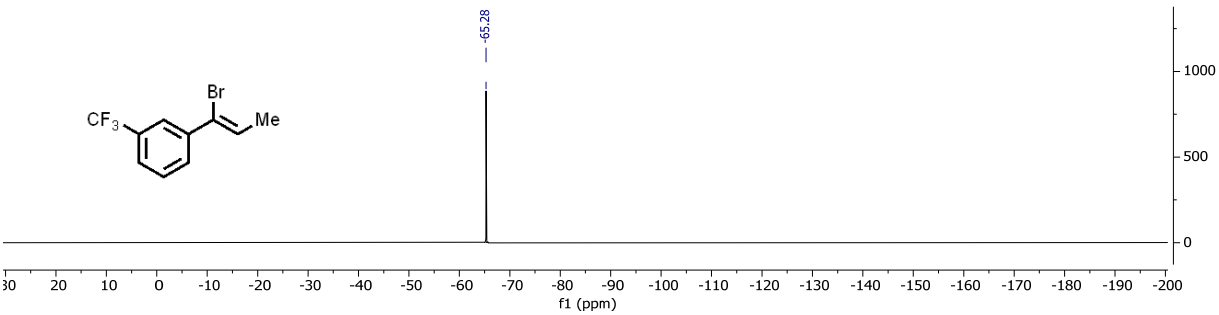


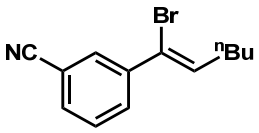


2e, (Z)-1-(1-bromoprop-1-en-1-yl)-3-(trifluoromethyl)benzene. Prepared according to General Procedure A from 3'-(trifluoromethyl)propiophenone (606 mg, 3 mmol) as a clear, colorless oil (580 mg, 73%).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.72 (dt, *J* = 7.8, 1.5 Hz, 1H), 7.58 – 7.53 (m, 1H), 7.49 – 7.44 (m, 1H), 6.38 (q, *J* = 6.6 Hz, 1H), 1.99 (d, *J* = 6.6 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 140.83, 130.98 (d, *J* = 32.6 Hz), 130.67, 128.76, 128.11, 124.83 (q, *J* = 4.1 Hz), 124.23 (q, *J* = 3.9 Hz), 121.76 (d, *J* = 272.4 Hz), 18.18.
^{19}F NMR (471 MHz, Chloroform-*d*) δ -65.28.
HRMS (EI): for $C_{10}H_8BrF_3$, $[M]^+$ calculated *m/z* = 263.9756 and 265.9736, found *m/z* = 263.9750 and 265.9729.

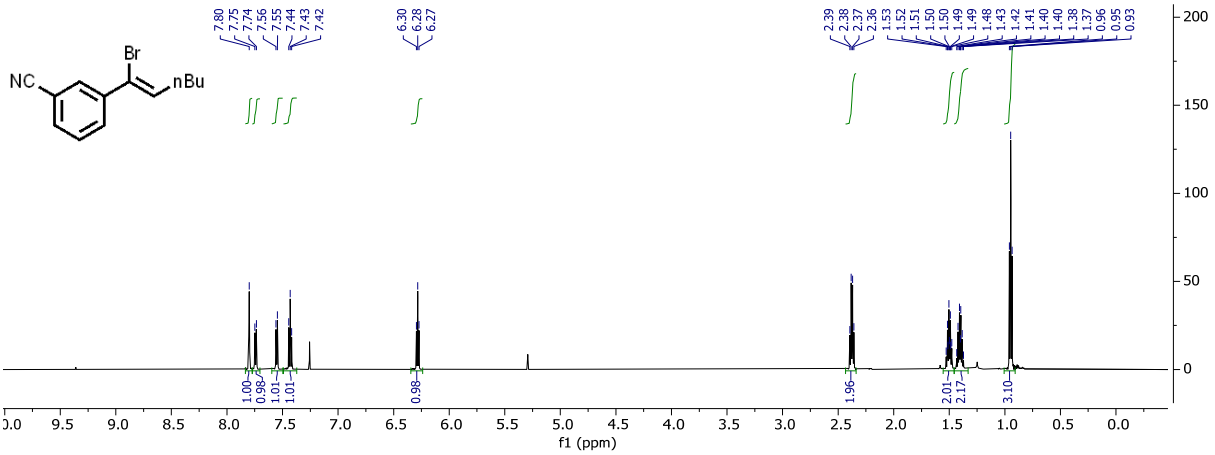


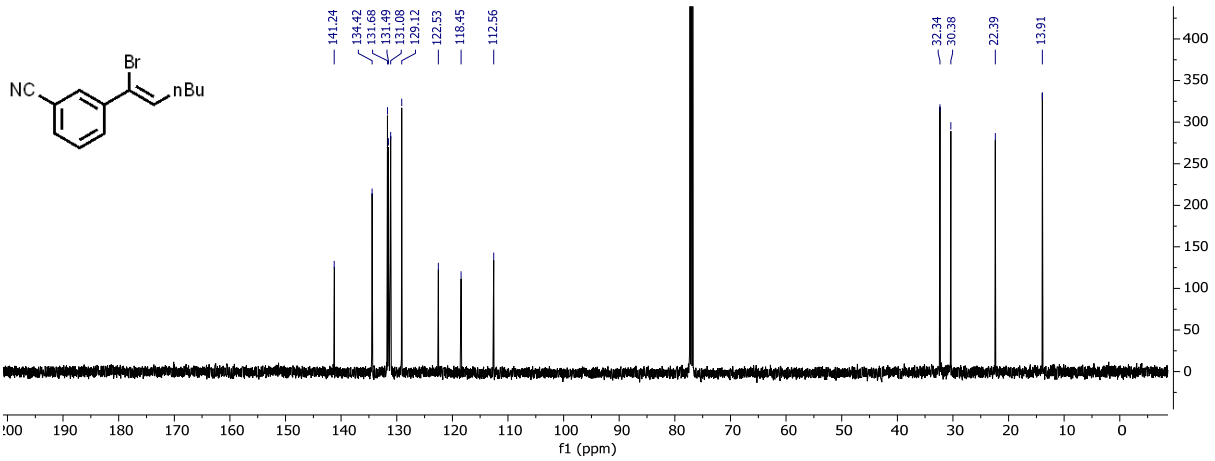


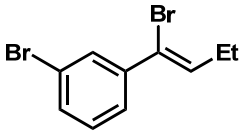




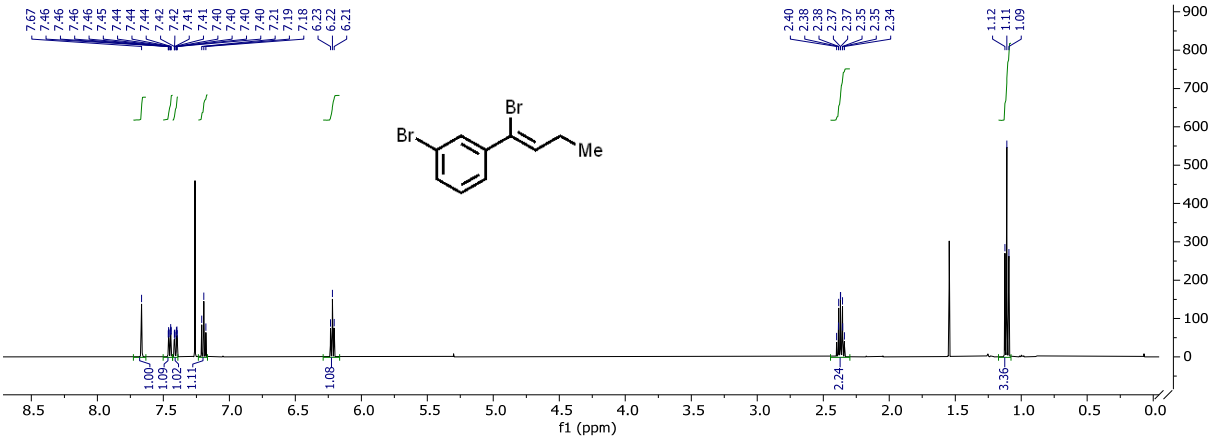
2f, (Z)-3-(1-bromohex-1-en-1-yl)benzonitrile. Prepared according to General Procedure B from 3-cyanophenylboronic acid (441 mg, 3 mmol) as a clear, orange oil (446 mg, 56% yield).
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.80 (s, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.55 (d, J = 7.7 Hz, 1H), 7.43 (t, J = 7.8 Hz, 1H), 6.28 (t, J = 6.9 Hz, 1H), 2.38 (q, J = 7.2 Hz, 3H), 1.50 (p, J = 7.5 Hz, 3H), 1.45 – 1.36 (m, 3H), 0.95 (t, J = 7.3 Hz, 5H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 141.24, 134.42, 131.68, 131.49, 129.12, 122.53, 118.45, 112.56, 32.34, 30.38, 22.39, 13.91.
HRMS (ESI): for $C_{13}H_{15}BrN$, $[M+H]^+$ calculated m/z = 264.0382 and 266.0362, found m/z = 264.0381 and 266.0360.

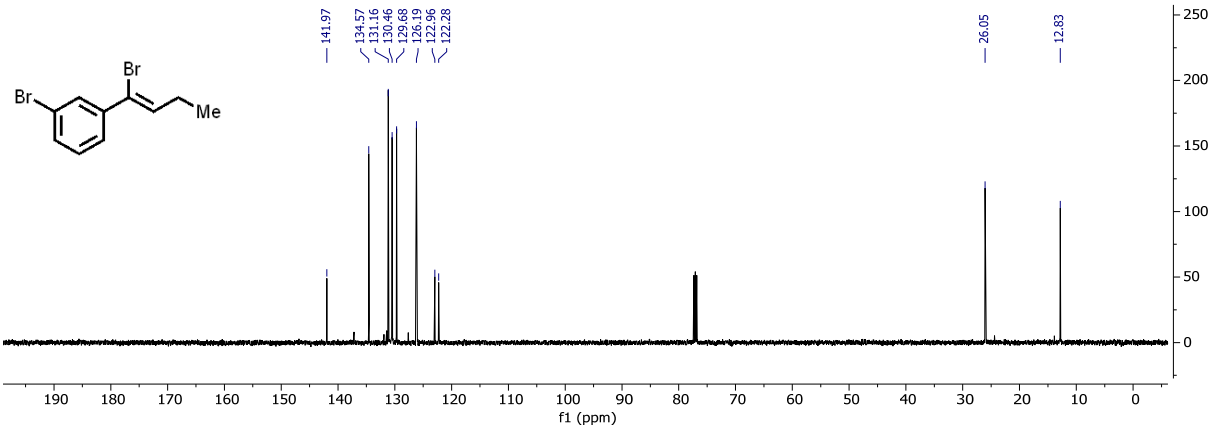


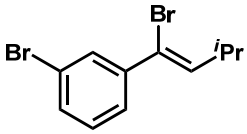




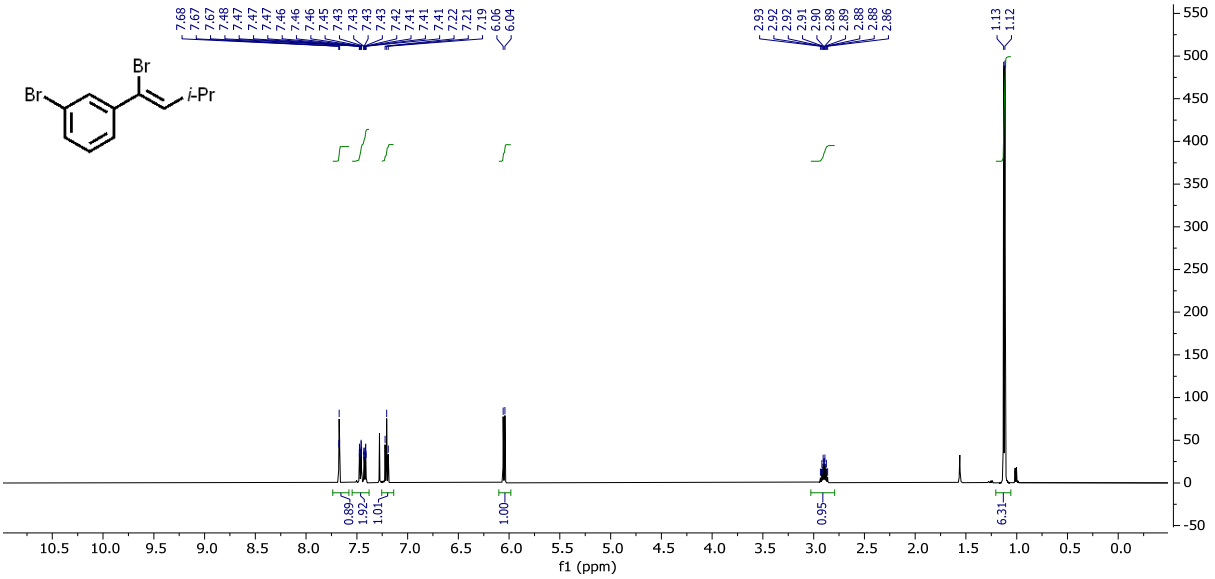
2g, (Z)-1-bromo-3-(1-bromobut-1-en-1-yl)benzene. Prepared according to General Procedure A from 1-(3-bromophenyl)butan-1-one (227 mg, 1 mmol) as a clear, colorless oil (220 mg, 76%).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (s, 0H), 7.45 (ddd, *J* = 7.9, 1.8, 1.0 Hz, 1H), 7.41 (ddd, *J* = 8.0, 1.9, 1.0 Hz, 1H), 7.19 (t, *J* = 7.9 Hz, 1H), 6.22 (t, *J* = 6.9 Hz, 1H), 2.37 (qd, *J* = 7.6, 6.9 Hz, 2H), 1.11 (t, *J* = 7.6 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 141.97, 134.57, 131.16, 130.46, 129.68, 126.19, 122.96, 122.28, 26.05, 12.83.
HRMS (EI): for $C_{10}H_{10}Br_2$, $[M]^+$ calculated *m/z* = 287.9144 and 289.9123 and 291.9103, found *m/z* = 287.9143 and 289.9121 and 291.9102.

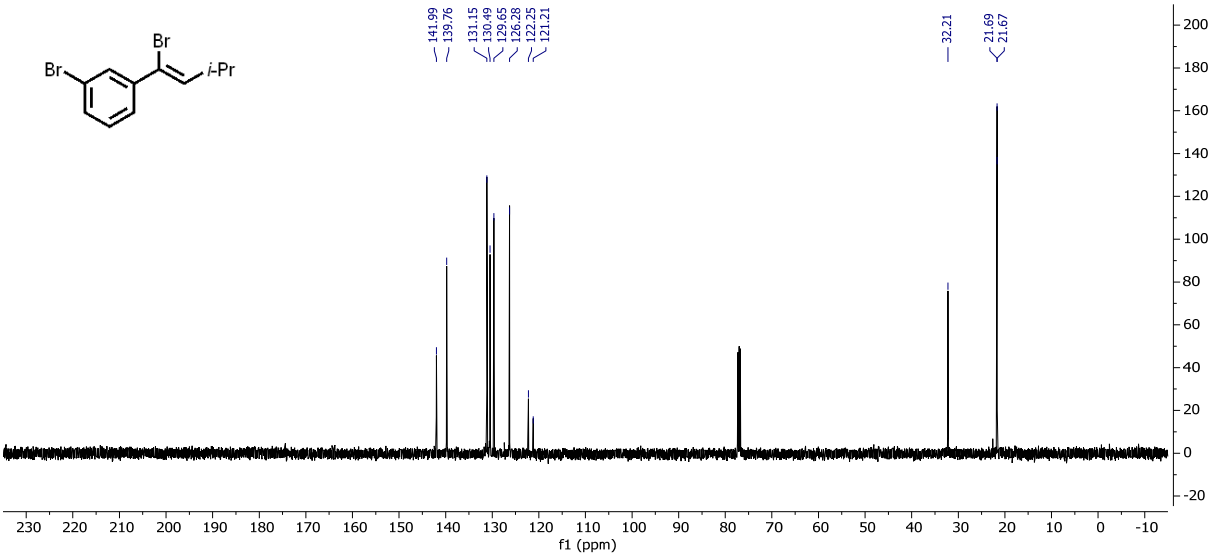


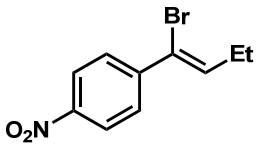




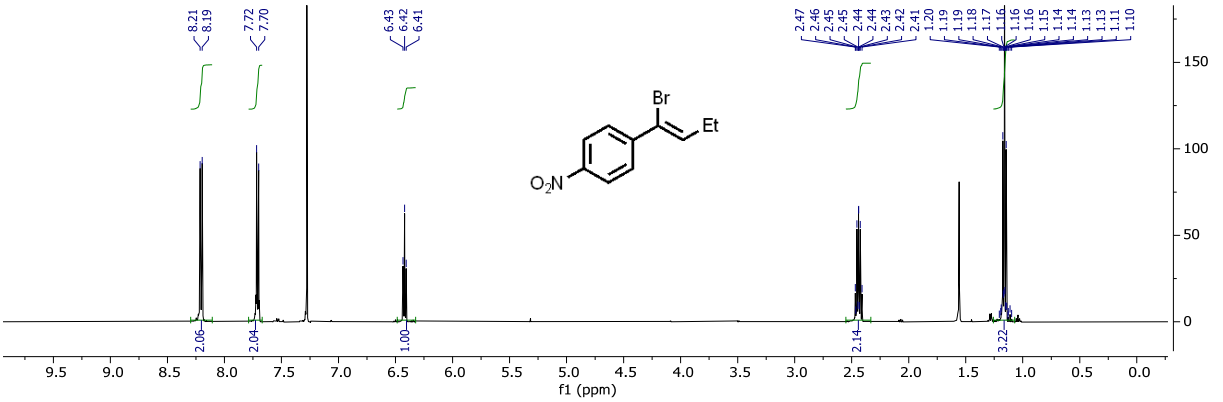
2h, (Z)-1-bromo-3-(1-bromo-3-methylbut-1-en-1-yl)benzene. Prepared according to General Procedure A from 1-(3-bromophenyl)-3-methylbutan-1-one (241 mg, 1 mmol) as a clear, colorless oil (240 mg, 79%).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (t, J = 1.9 Hz, 1H), 7.43 (dddd, J = 22.0, 8.0, 1.9, 1.0 Hz, 2H), 7.19 (t, J = 7.9 Hz, 1H), 6.03 (d, J = 8.7 Hz, 1H), 2.88 (dp, J = 8.8, 6.7 Hz, 1H), 1.10 (d, J = 6.7 Hz, 6H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 141.99, 139.76, 131.15, 130.49, 129.65, 126.28, 122.25, 121.21, 32.21, 21.68 (d, J = 2.1 Hz).
HRMS (EI): for $C_{11}H_{12}Br_2$, $[M]^+$ calculated m/z = 301.9300 and 303.9280 and 305.9259, found m/z = 301.9290 and 303.9268 and 305.9249.

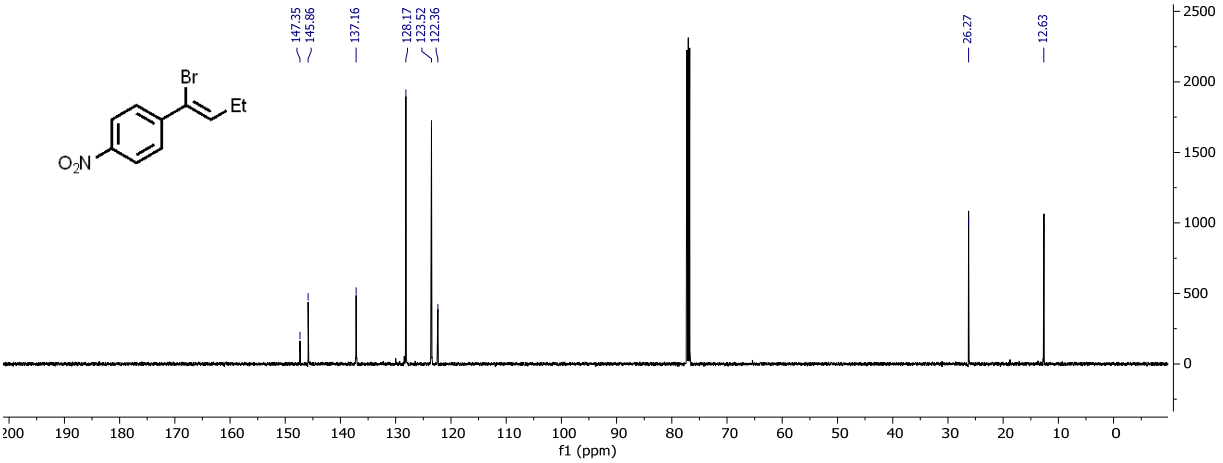


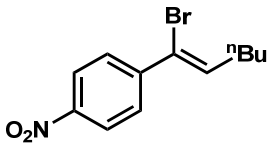




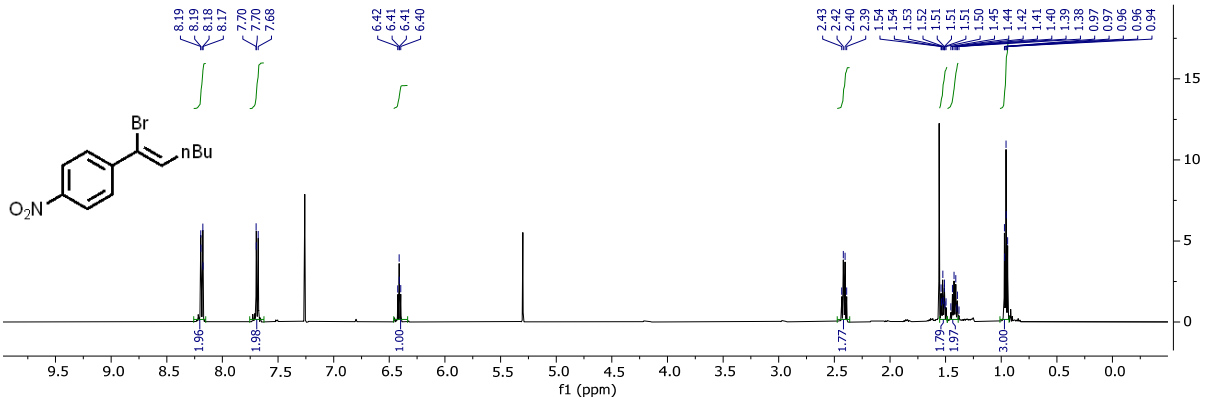
2i, (Z)-1-(1-bromobut-1-en-1-yl)-4-nitrobenzene. Prepared according to General Procedure B from 4-nitrophenylboronic acid (166 mg, 1 mmol) as an orange solid (80 mg, 31% yield).
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.9 Hz, 2H), 7.71 (d, *J* = 8.9 Hz, 2H), 6.42 (t, *J* = 6.9 Hz, 1H), 2.51 – 2.36 (m, 2H), 1.16 (t, *J* = 7.6 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 147.35, 145.86, 137.16, 128.17, 123.52, 122.36, 26.27, 12.63.
HRMS (ESI): for $C_{10}H_{11}BrNO_2$, $[M+H]^+$ calculated *m/z* = 255.9968 and 257.9947, found *m/z* = 255.9967 and 257.9946.

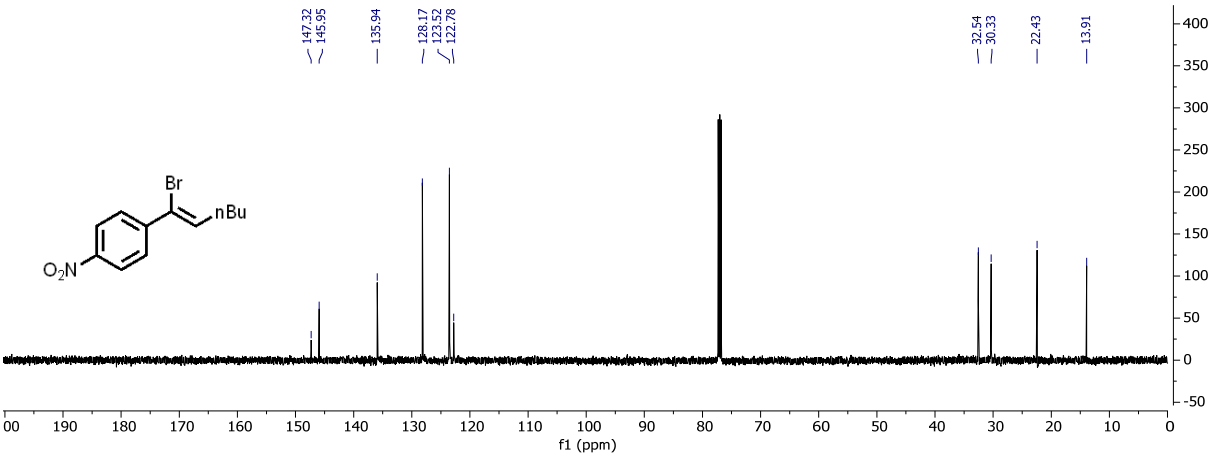


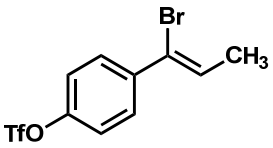




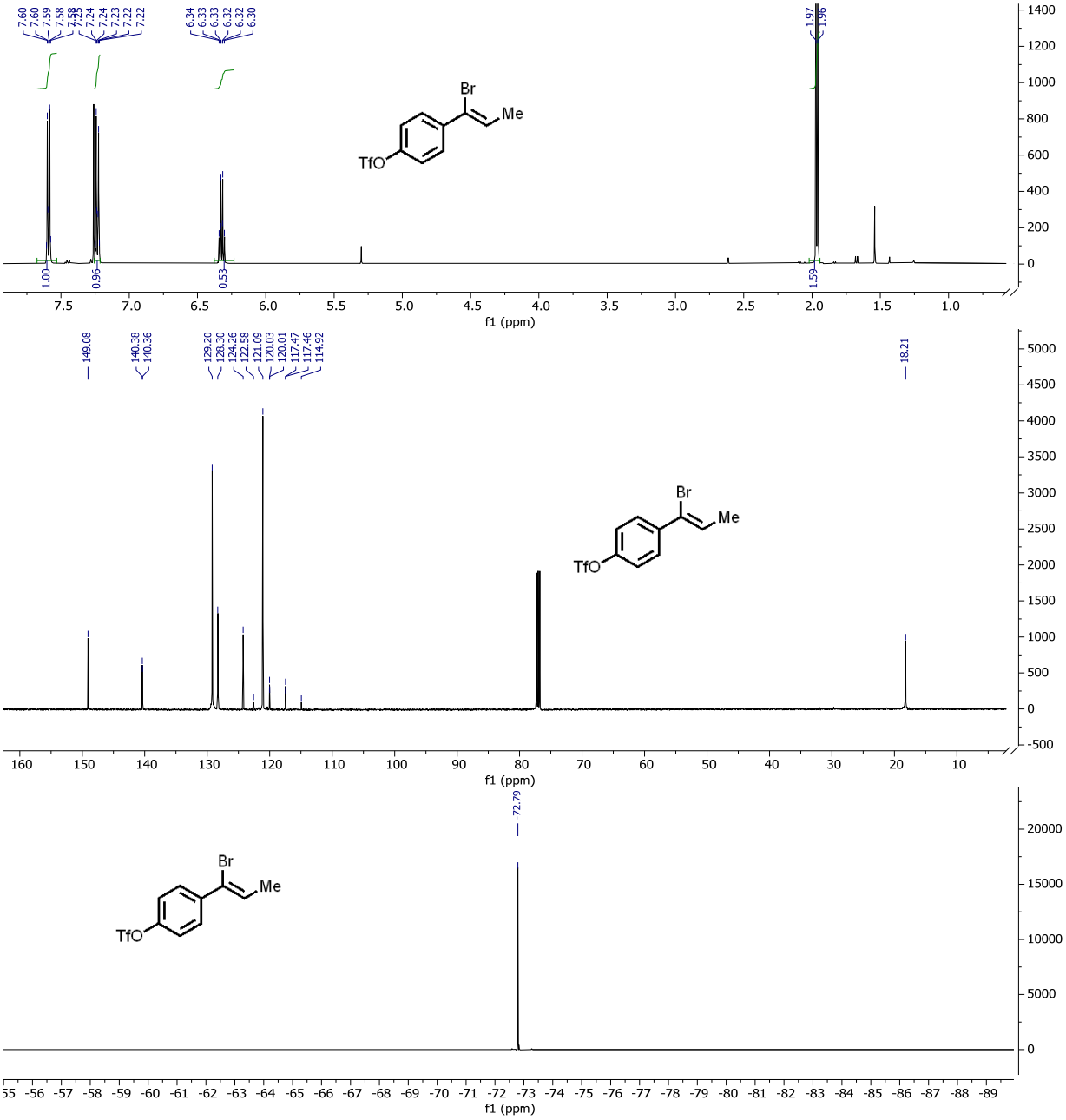
2j, (Z)-1-(1-bromohex-1-en-1-yl)-4-nitrobenzene. Prepared according to General Procedure B from 4-nitrophenylboronic acid (167 mg, 1 mmol) as an orange oil (140 mg, 50% yield).
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 – 8.17 (m, 2H), 7.71 – 7.67 (m, 2H), 6.41 (t, *J* = 6.9 Hz, 1H), 2.41 (q, *J* = 7.2 Hz, 2H), 1.55 – 1.49 (m, 2H), 1.42 (h, *J* = 7.2 Hz, 2H), 0.96 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 147.32, 145.95, 135.94, 128.17, 123.52, 122.78, 32.54, 30.33, 22.43, 13.91.
HRMS (EI): for $C_{12}H_{14}BrNO_2$, $[M]^+$ calculated *m/z* = 283.0202 and 285.0182, found *m/z* = 283.0200 and 285.0179.

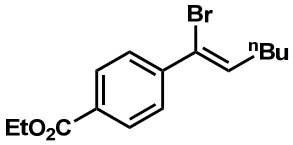




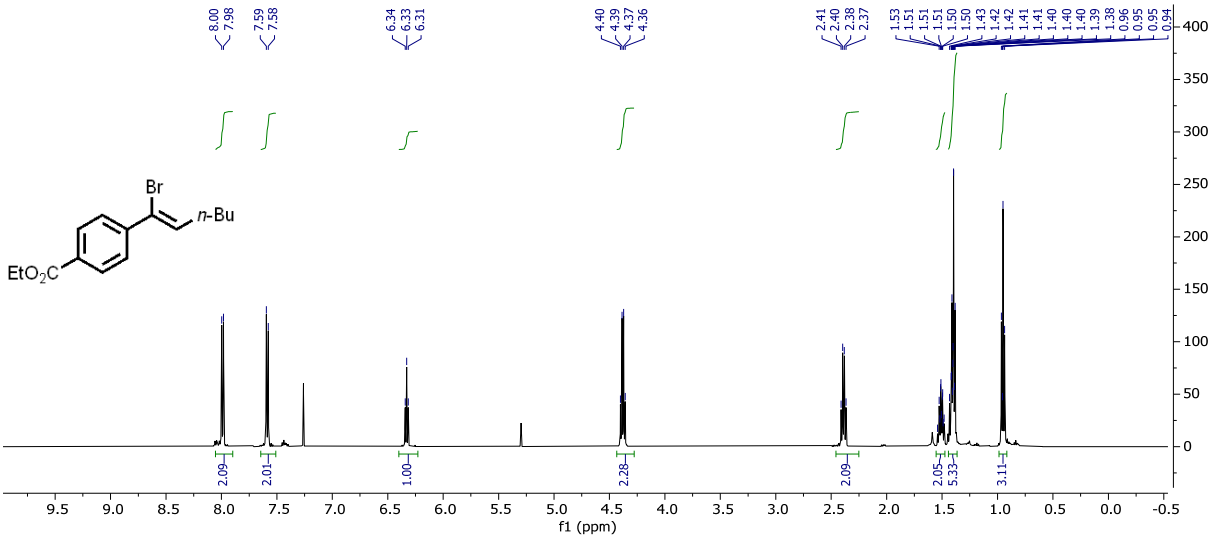


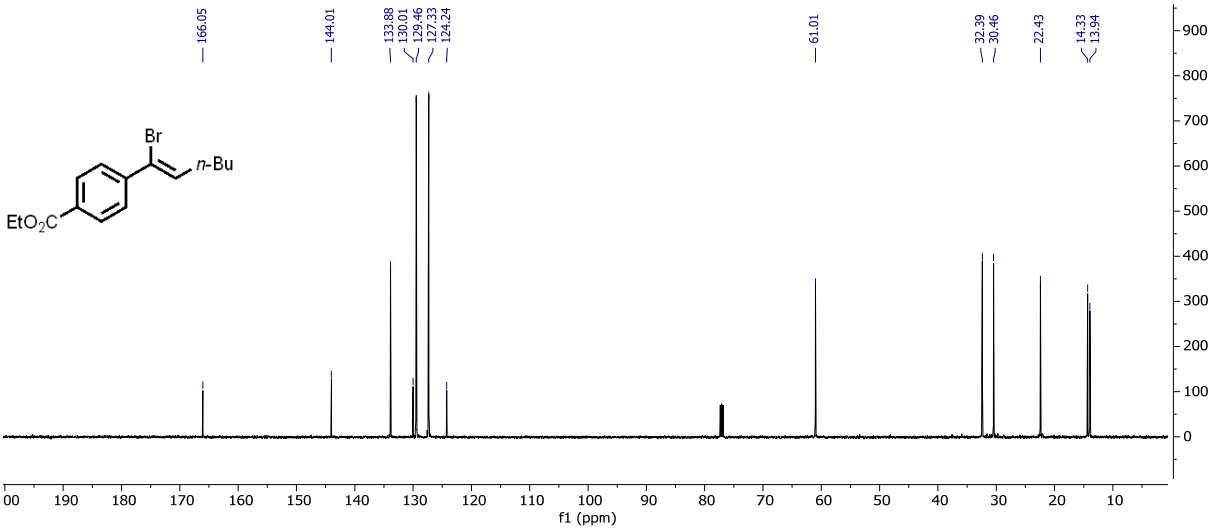
2k, (Z)-4-(1-bromoprop-1-en-1-yl)phenyl trifluoromethanesulfonate. Prepared according to General Procedure A from 4-propionylphenyl trifluoromethanesulfonate (282 mg, 1 mmol) as a clear, colorless oil (228 mg, 66%).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 – 7.56 (m, 2H), 7.25 – 7.21 (m, 2H), 6.32 (q, *J* = 6.6 Hz, 1H), 1.97 (d, *J* = 6.6 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 149.08, 140.38, 129.20, 128.30, 124.26, 121.09, 118.75 (q, *J* = 320.7 Hz), 18.21.
^{19}F NMR (471 MHz, $CDCl_3$) δ -72.79.
HRMS (EI): for $C_{10}H_8BrF_3O_3S$, $[M]^+$ calculated *m/z* = 343.9324 and 345.9304, found *m/z* = 343.9219 and 345.9297.

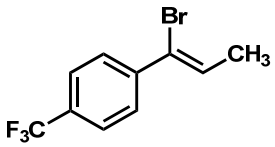




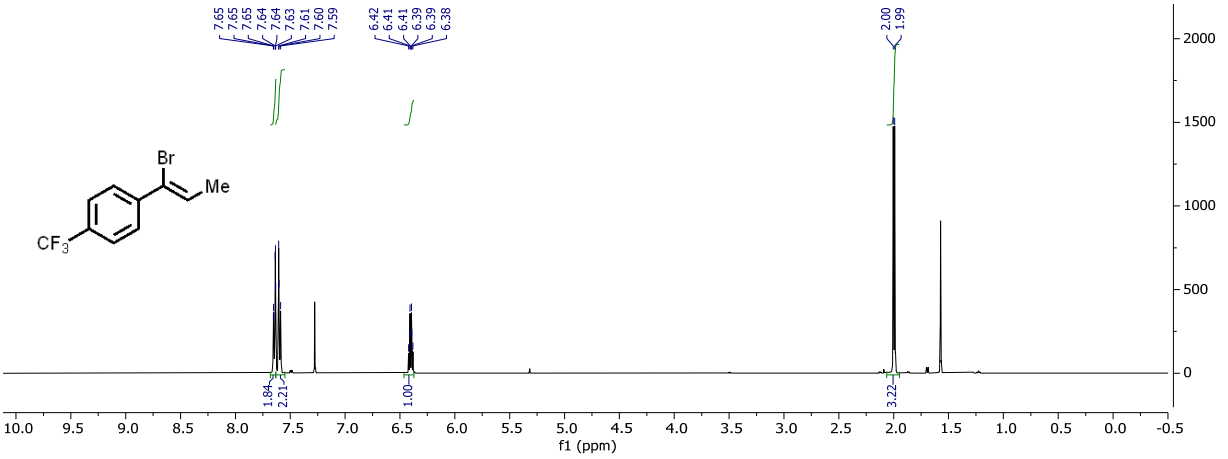
2l, (Z)-ethyl 4-(1-bromohex-1-en-1-yl)benzoate. Prepared according to General Procedure B from 4-(ethoxycarbonyl)phenylboronic acid (194 mg, 1 mmol) as a clear, orange oil (129 mg, 41% yield).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, J = 8.4 Hz, 2H), 7.59 (d, J = 8.5 Hz, 2H), 6.33 (t, J = 6.9 Hz, 1H), 4.38 (q, J = 7.1 Hz, 2H), 2.39 (q, J = 7.2 Hz, 2H), 1.55 – 1.46 (m, 2H), 1.44 – 1.34 (m, 5H), 0.95 (t, J = 7.3 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 166.05, 144.01, 133.88, 130.01, 129.46, 127.33, 124.24, 61.01, 32.39, 30.46, 22.43, 14.33, 13.94.
HRMS (ESI): for $C_{15}H_{20}BrO_2$, $[M+H]^+$ calculated m/z = 311.0642 and 313.0619, found m/z = 311.0641 and 313.0621.

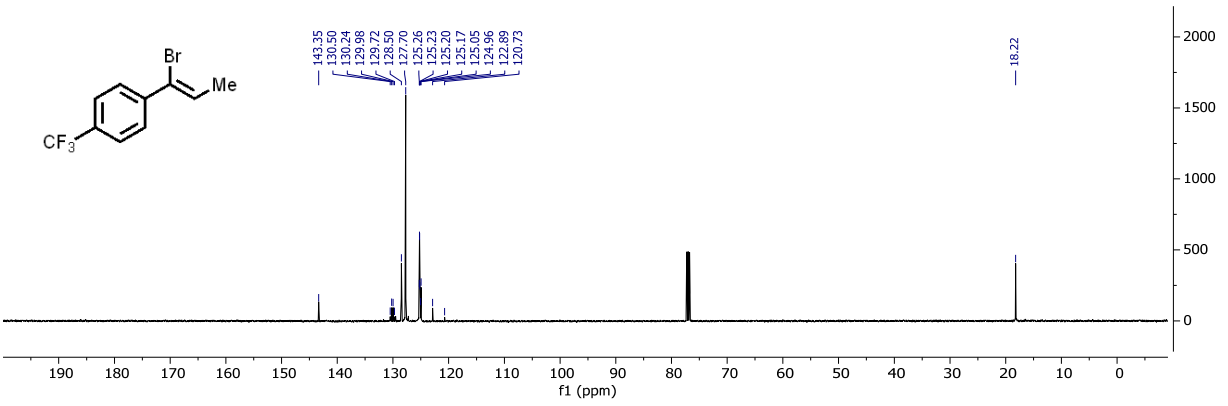


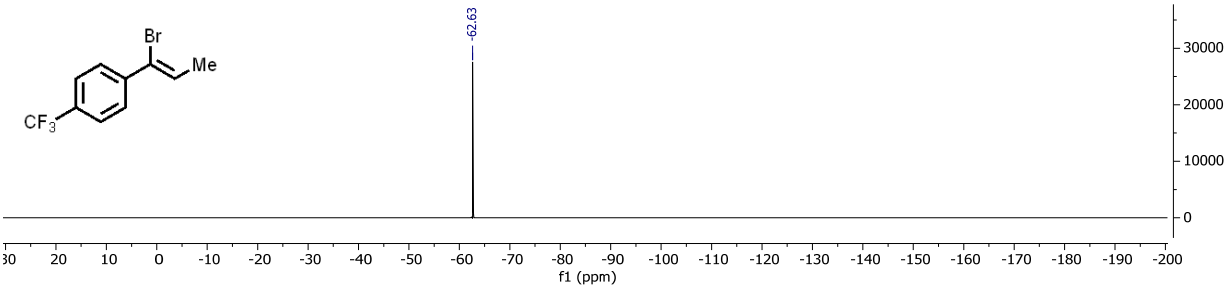


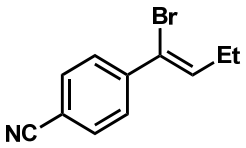


2m, (Z)-1-(1-bromoprop-1-en-1-yl)-4-(trifluoromethyl)benzene. Prepared according to General Procedure A from 4'-(trifluoromethyl)propiophenone (606 mg, 3 mmol) as a clear, colorless oil (700 mg, 88% yield).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 – 7.62 (m, 2H), 7.62 – 7.57 (m, 2H), 6.43 – 6.37 (m, 1H), 2.00 (d, J = 6.6 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 143.35, 130.11 (q, J = 32.6 Hz), 128.50, 127.70, 125.22 (q, J = 3.8 Hz), 124.96, 121.81 (d, J = 271.8 Hz), 18.22.
^{19}F NMR (471 MHz, $CDCl_3$) δ -62.63.
HRMS (EI): for $C_{10}H_8BrF_3$, $[M]^+$ calculated m/z = 263.9756 and 265.9736, found m/z = 263.9753 and 265.9732.

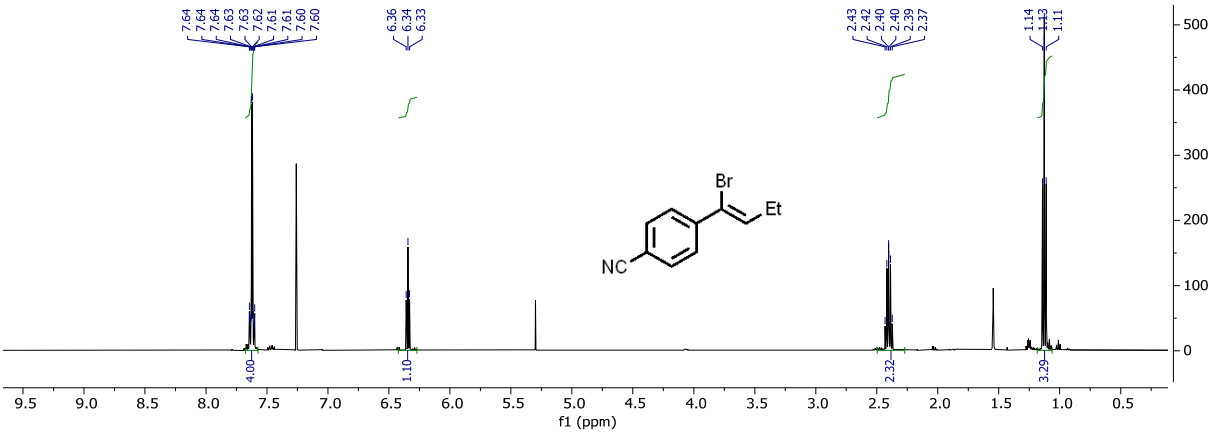


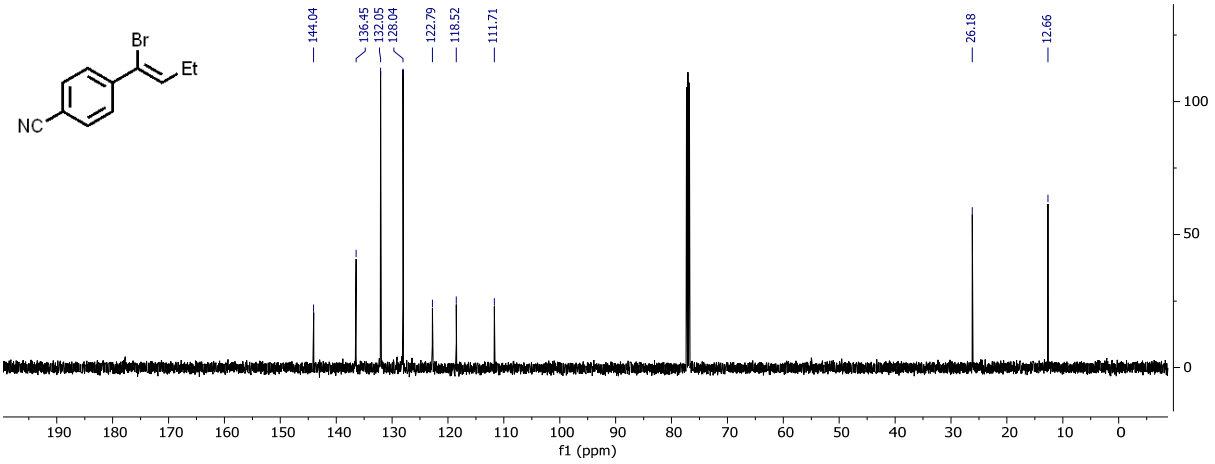


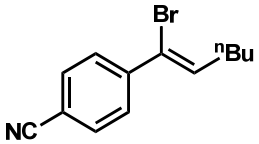




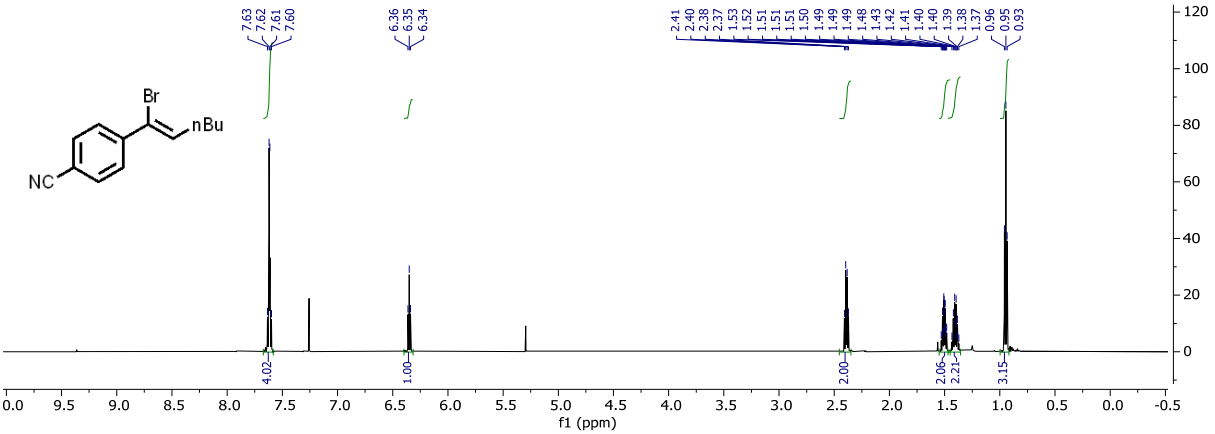
2n, (Z)-4-(1-bromobut-1-en-1-yl)benzonitrile. Prepared according to General Procedure B from 4-cyanophenylboronic acid (441 mg, 3 mmol) as a clear, yellow oil (153 mg, 21% yield).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 – 7.59 (m, 4H), 6.34 (t, J = 6.9 Hz, 1H), 2.45 – 2.33 (m, 2H), 1.13 (t, J = 7.6 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 144.04, 136.45, 132.05, 128.04, 122.79, 118.52, 111.71, 26.18, 12.66.
HRMS (ESI): for $C_{11}H_1BrN$, $[M+H]^+$ calculated m/z = 236.0069 and 238.0049, found m/z = 236.0070 and 238.0049.

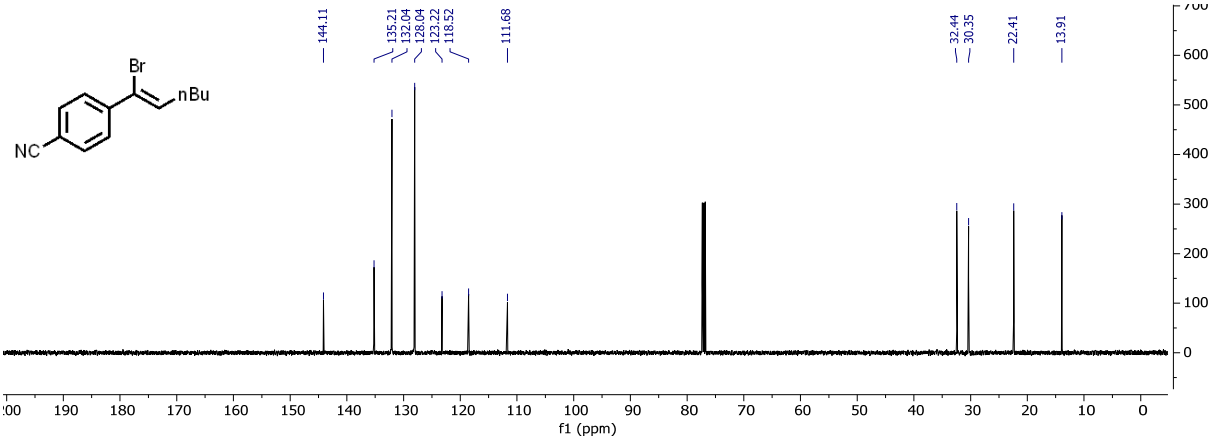


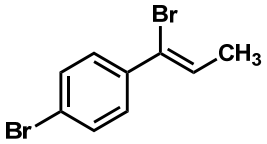




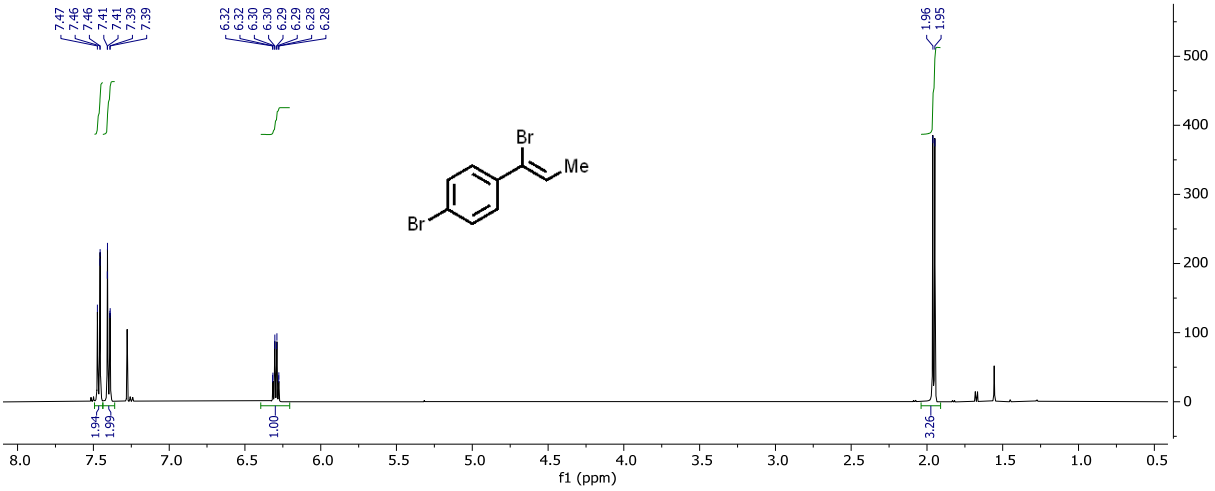
2o, (Z)-4-(1-bromohex-1-en-1-yl)benzonitrile. Prepared according to General Procedure B from 4-cyanophenylboronic acid (441 mg, 3 mmol) as a clear, yellow oil (357 mg, 45% yield).
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.64 – 7.59 (m, 4H), 6.35 (t, *J* = 6.9 Hz, 1H), 2.39 (q, *J* = 7.2 Hz, 2H), 1.54 – 1.48 (m, 2H), 1.44 – 1.36 (m, 2H), 0.95 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 144.11, 135.21, 132.04, 128.04, 123.22, 118.52, 111.68, 32.44, 30.35, 22.41, 13.91.
HRMS (ESI): for $C_{13}H_{15}BrN$, $[M+H]^+$ calculated *m/z* = 264.0382 and 266.0362, found *m/z* = 264.0382 and 266.0361.

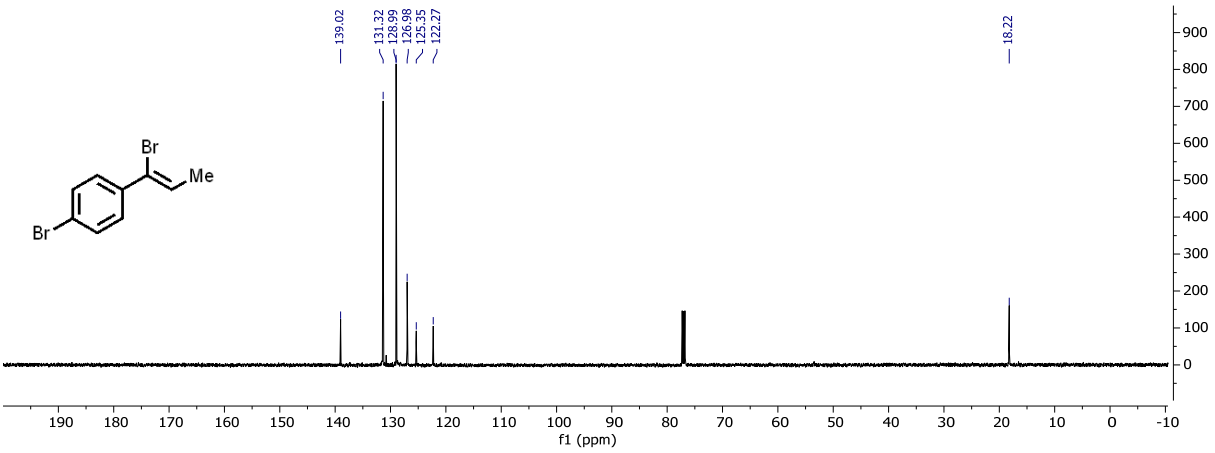


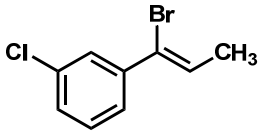




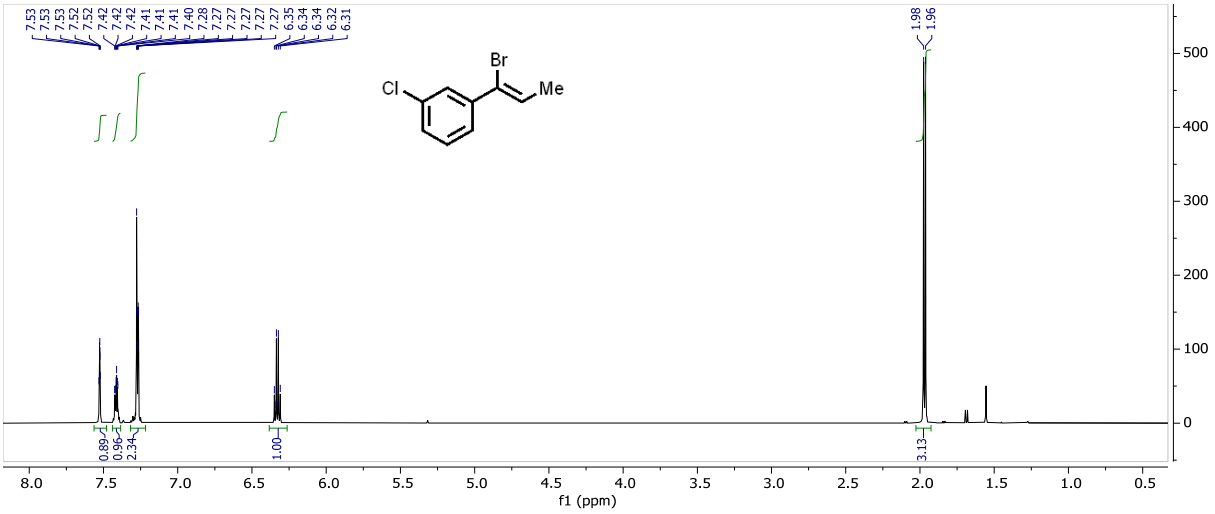
2p, (Z)-1-bromo-4-(1-bromoprop-1-en-1-yl)benzene. Prepared according to General Procedure A from 3'-bromopropiophenone (213 mg, 1 mmol) as a clear, colorless oil (160 mg, 57% yield).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (d, J = 9.1 Hz, 2H), 7.40 (d, J = 7.9 Hz, 2H), 6.30 (qd, J = 6.5, 0.9 Hz, 1H), 1.95 (d, J = 6.6 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 139.02, 131.32, 128.99, 126.98, 125.35, 122.27, 18.22.
HRMS (EI): for $C_9H_8Br_2$, $[M]^+$ calculated m/z = 273.8987 and 275.8967 and 277.8946, found m/z = 273.8986 and 275.8962 and 277.8943.

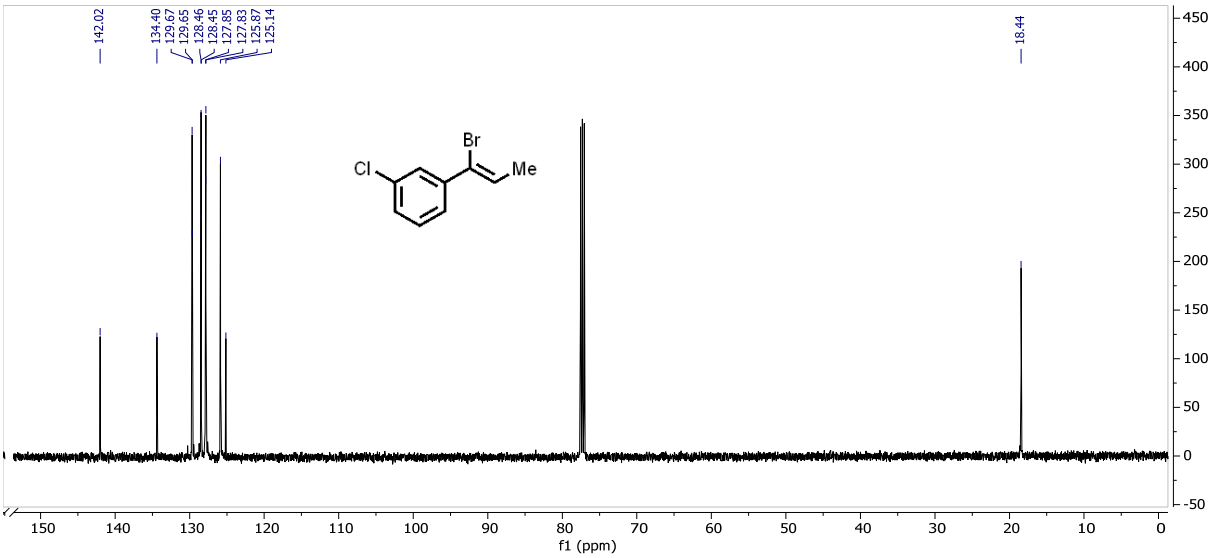


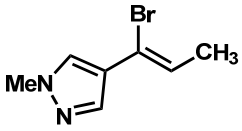




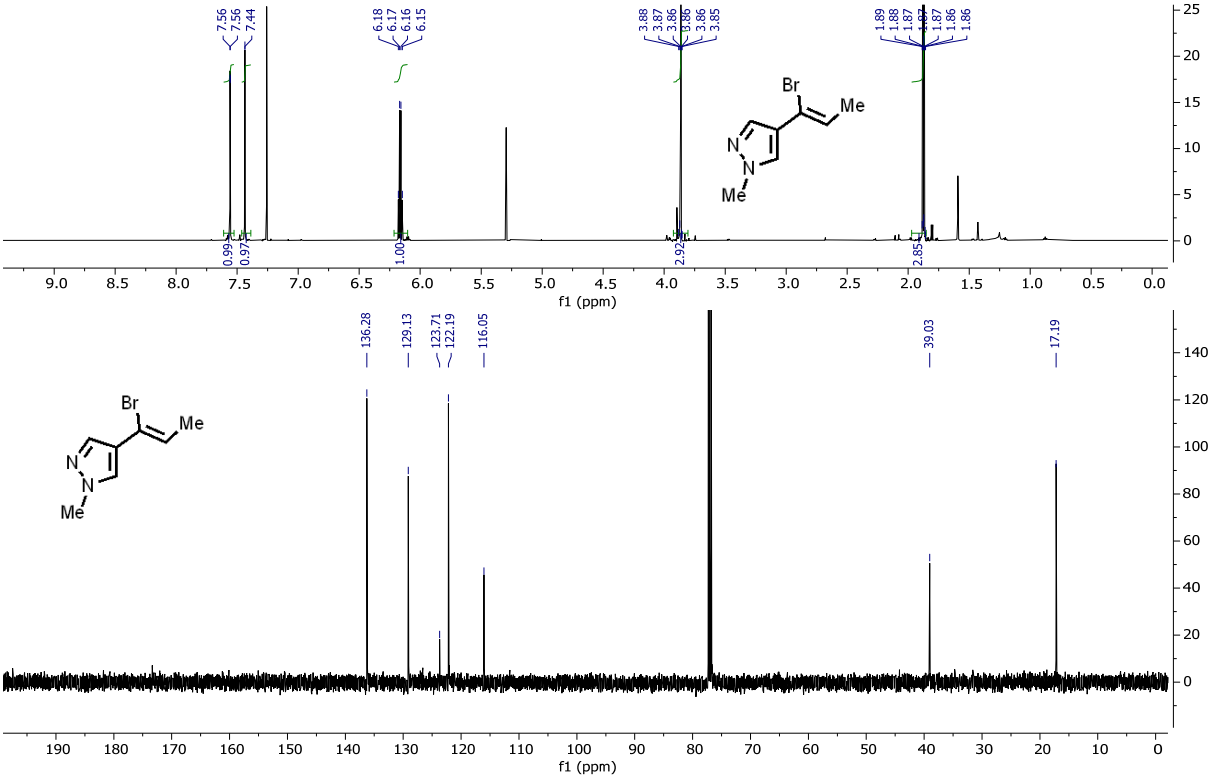
2q, (Z)-1-(1-bromoprop-1-en-1-yl)-3-chlorobenzene. Prepared according to General Procedure A from 3'-chloropropiophenone (169 mg, 1 mmol) as a clear, colorless oil (209 mg, 85%).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 – 7.50 (m, 1H), 7.44 – 7.38 (m, 1H), 7.30 – 7.23 (m, 2H), 6.33 (q, *J* = 6.7 Hz, 1H), 1.97 (d, *J* = 6.6 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 142.02, 134.40, 129.66, 128.15, 125.87, 125.14, 18.44.
HRMS (EI): for C_9H_8BrCl, $[M]^+$ calculated *m/z* = 229.9492 and 231.9472, found *m/z* = 229.9492 and 231.9468.

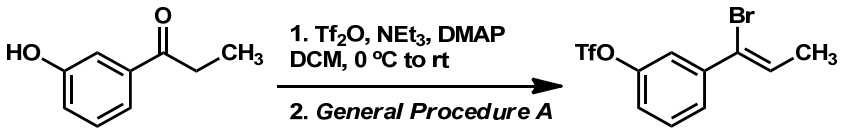






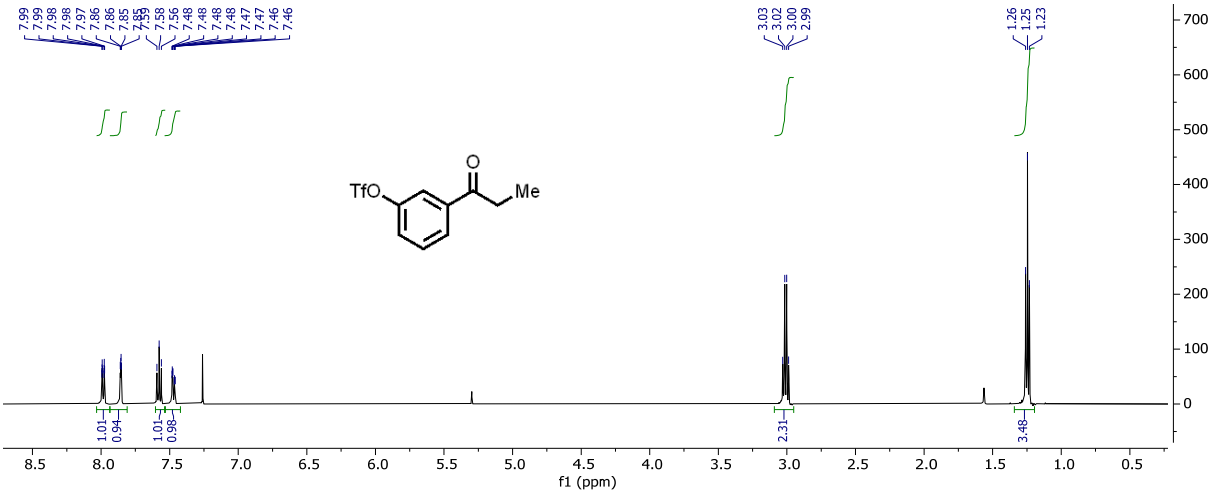
2r, (Z)-4-(1-bromoprop-1-en-1-yl)-1-methyl-1H-pyrazole. Prepared according to General Procedure A from 1-(1-methyl-1H-pyrazol-4-yl)propan-1-one (138 mg, 1 mmol) as a clear, colorless oil (45 mg, 23% yield).
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.56 (s, 1H), 7.44 (s, 1H), 6.16 (q, J = 6.6 Hz, 1H), 3.86 (s, 3H), 1.87 (d, J = 6.6 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 136.28, 129.13, 123.71, 122.19, 116.05, 39.03, 17.19.
HRMS (ESI): for $C_7H_{10}BrN_2$, $[M+H]^+$ calculated m/z = 201.0022 and 203.0001, found m/z = 201.0022 and 202.9999.

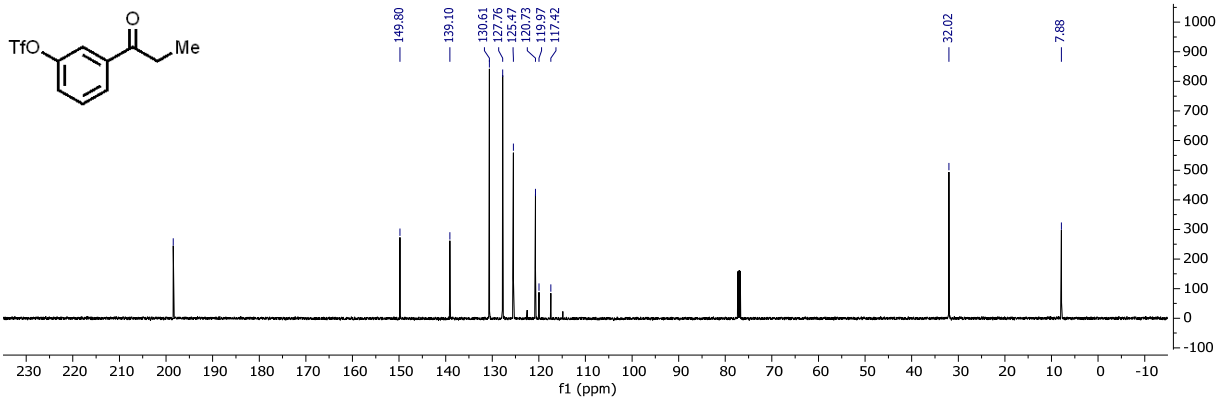


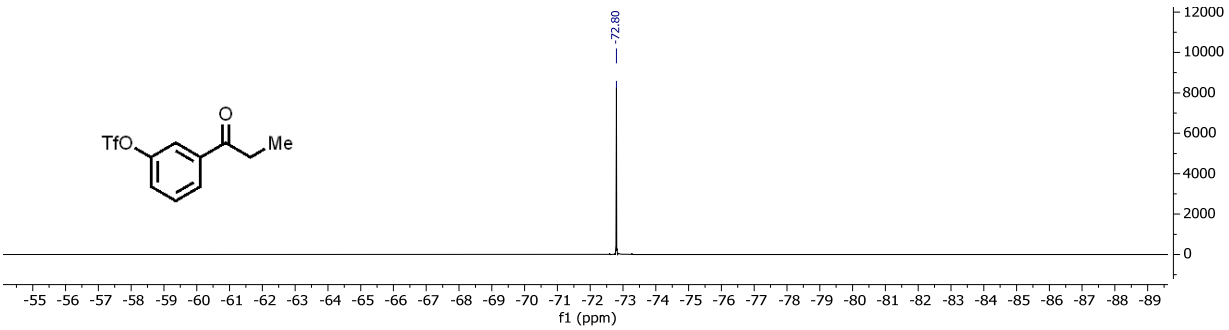


To a solution of 3'-hydroxypropiophene (750 mg, 5 mmol, 1 equiv) in DCM (10 mL, 0.5M) was added NEt_3 (2.1 mL, 15 mmol, 3 equiv) and DMAP (61 mg, 0.5 mmol, 0.1 equiv). The solution was cooled to 0 ºC and Tf_2O (5.5 mL, 1M in DCM, 1.1 equiv) was added dropwise via syringe. The solution was stirred at 0 ºC for 30 minutes and was then warmed to room temperature and stirred for an additional 3 hours. After this time, 1M HCl was added carefully, and the solution was diluted with Et_2O. The layers were separated, and the organic layer washed with 1M HCl (2x), water, $NaHCO_3$ (sat. aqueous), and brine. The organic layer was then dried over Na_2SO_4, concentrated in vacuo, and purified by column chromatography to afford 3-propionylphenyl trifluoromethanesulfonate (**S1**) as a clear, colorless oil (1.02 g, 72% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (ddd, J = 7.6, 1.5, 0.9 Hz, 1H), 7.86 (dd, J = 2.6, 1.5 Hz, 1H), 7.58 (t, J = 8.0 Hz, 1H), 7.47 (ddd, J = 8.2, 2.5, 1.0 Hz, 1H), 3.01 (q, J = 7.2 Hz, 2H), 1.25 (t, J = 7.2 Hz, 2H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 198.45, 149.80, 139.10, 130.61, 127.76, 125.47, 120.73, 118.69 (q, J = 320.8 Hz), 32.02, 7.88.
^{19}F NMR (471 MHz, $CDCl_3$) δ -72.80.
HRMS (ESI): for $C_{10}H_{10}F_3O_4S$, $[M+H]^+$ calculated m/z = 283.0246, found m/z = 283.0246.

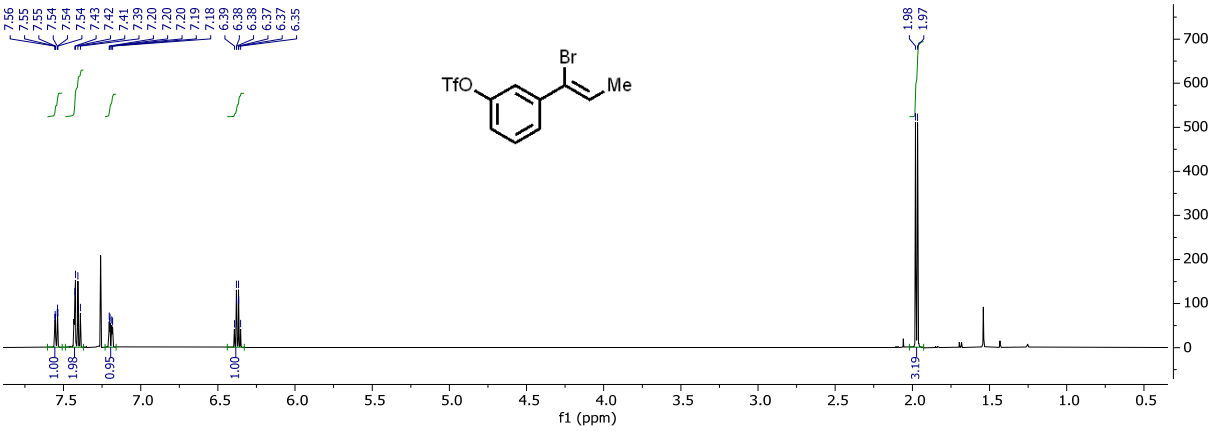


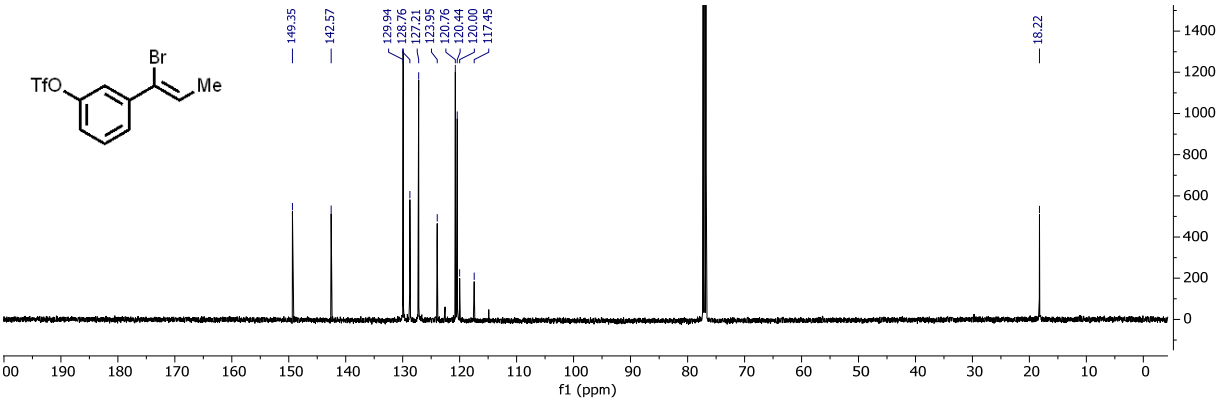


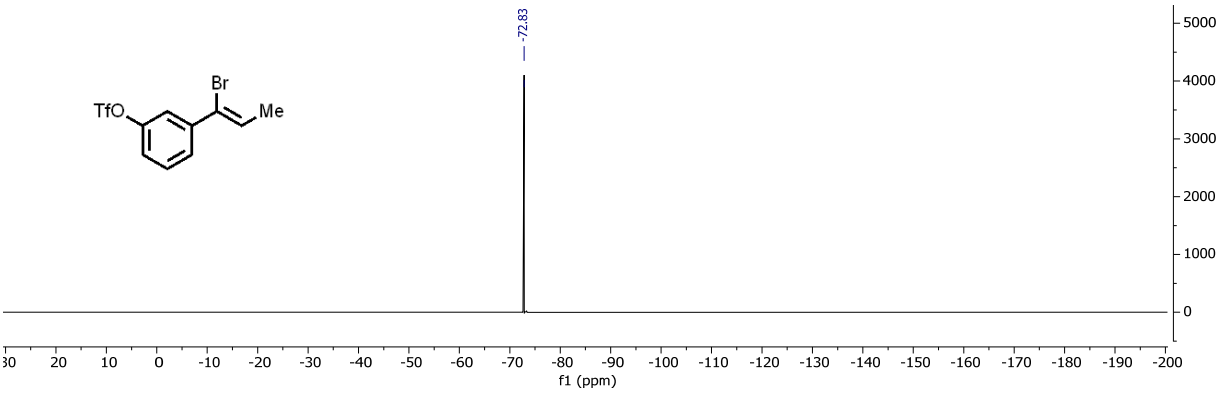


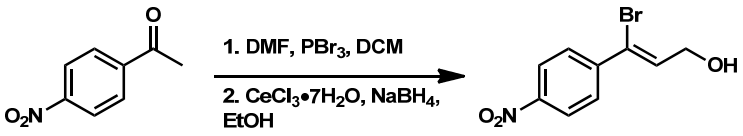
2b, (Z)-3-(1-bromoprop-1-en-1-yl)phenyl trifluoromethanesulfonate was then prepared according to General Procedure A from **S1** (282 mg, 1 mmol) as a clear, colorless oil (214 mg, 62%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 – 7.53 (m, 1H), 7.44 – 7.38 (m, 2H), 7.19 (dd, *J* = 8.3, 2.5 Hz, 1H), 6.37 (q, *J* = 6.6 Hz, 1H), 1.97 (d, *J* = 6.6 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 149.35, 142.57, 129.94, 128.76, 127.21, 123.95, 120.76, 120.44, 118.73 (d, *J* = 320.7 Hz), 18.22.
^{19}F NMR (471 MHz, $CDCl_3$) δ -72.83.
HRMS (EI): for $C_{10}H_8BrF_3O_3S$, $[M]^+$ calculated *m/z* = 343.9324 and 345.9304, found *m/z* = 343.9325 and 345.9302.





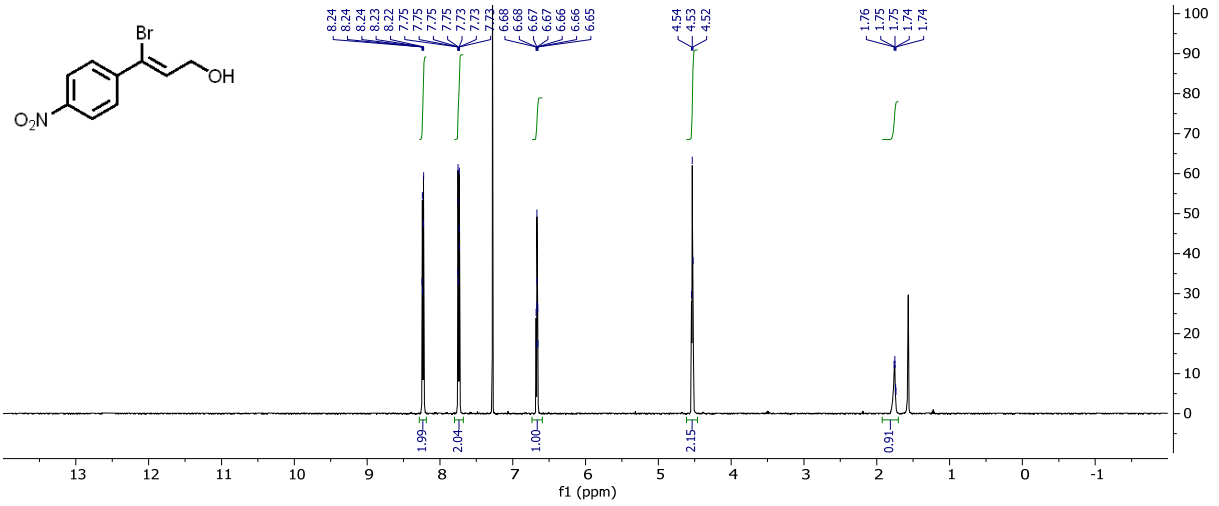


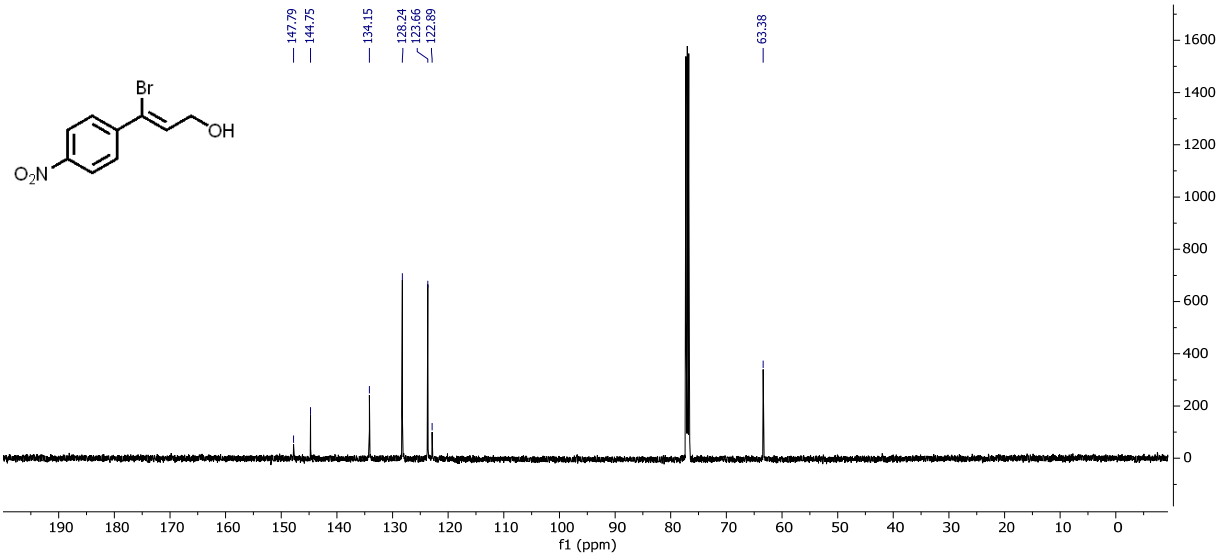


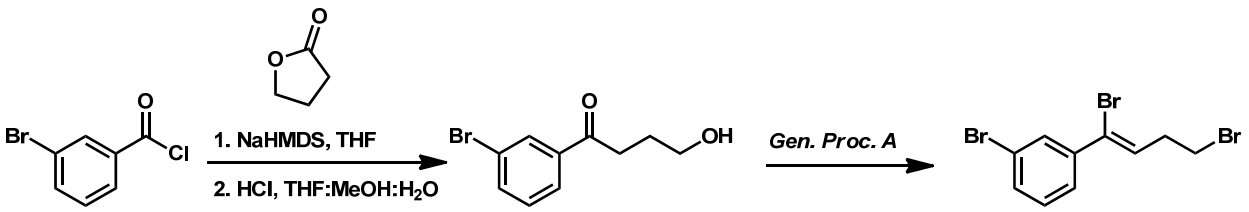
(Z)-3-bromo-3-(4-nitrophenyl)prop-2-en-1-ol. **2s** was prepared according to a modified procedure by Shunatona, *et. al*.[3] *N,N*-Dimethylformamide (7.7 mL, 100 mmol, 5 equiv) was cooled to 0 °C in dichloromethane (100 mL, 0.2M). Phosphorus tribromide (8.2 mL, 86 mmol, 4.3 equiv) was added dropwise and the mixture was stirred at 0 °C for 2 h. 4-nitroacetophenone (3.3 g, 20 mmol) was dissolved in dichloromethane and was added via canula to the stirring mixture. The reaction mixture was heated at reflux at 40 °C for 12 h. The reaction mixture was poured over cold $NaHCO_3$, extracted with Et_2O, and dried over Na_2SO_4. The solvent was removed in vacuo to give aldehyde, which was taken directly to the next step.

A portion of the crude aldehyde was dissolved in EtOH (10 mL) at 0 °C. Cerium(III) chloride heptahydrate (1.3 g, 1.2 equiv) was then added all at once. Sodium borohydride (0.441 g, 12 mmol, 4 equiv) was carefully added. The reaction mixture was warmed to ambient temperature and stirred for 30 min. Upon completion the mixture was quenched with acetone and was stirred for 1 h. Saturated NH_4Cl was added to the reaction, and the solvent was removed under vacuum. The mixture was extracted with Et_2O, dried over Na_2SO_4, and the solvent was removed in vacuo. The crude product was filtered through a short pad of silica to give alcohol **2s** (686 mg, 91%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 (dt, *J* = 9.4, 1.7 Hz, 2H), 7.74 (dt, *J* = 7.8, 0.9 Hz, 2H), 6.67 (td, *J* = 5.6, 1.1 Hz, 1H), 4.53 (t, *J* = 5.3 Hz, 2H), 1.85 – 1.71 (m, 1H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 147.79, 144.75, 134.15, 128.24, 123.66, 122.89, 63.38.
HRMS (ESI): for $C_9H_7BrNO_3$, $[M-H]^+$ calculated *m/z* = 255.9615 and 257.9594, found *m/z* = 255.9616 and 257.9595.


Br
OH
O_2N
8.24
8.24
8.24
8.23
8.22
7.75
7.75
7.75
7.73
7.73
7.72
6.68
6.68
6.67
6.67
6.66
6.66
6.65
4.54
4.53
4.52
1.76
1.75
1.75
1.74
1.74
1.99
2.04
1.00
2.15
0.91
f1 (ppm)


Br
OH
O_2N
147.79
144.75
134.15
128.24
123.66
122.89
63.38
f1 (ppm)

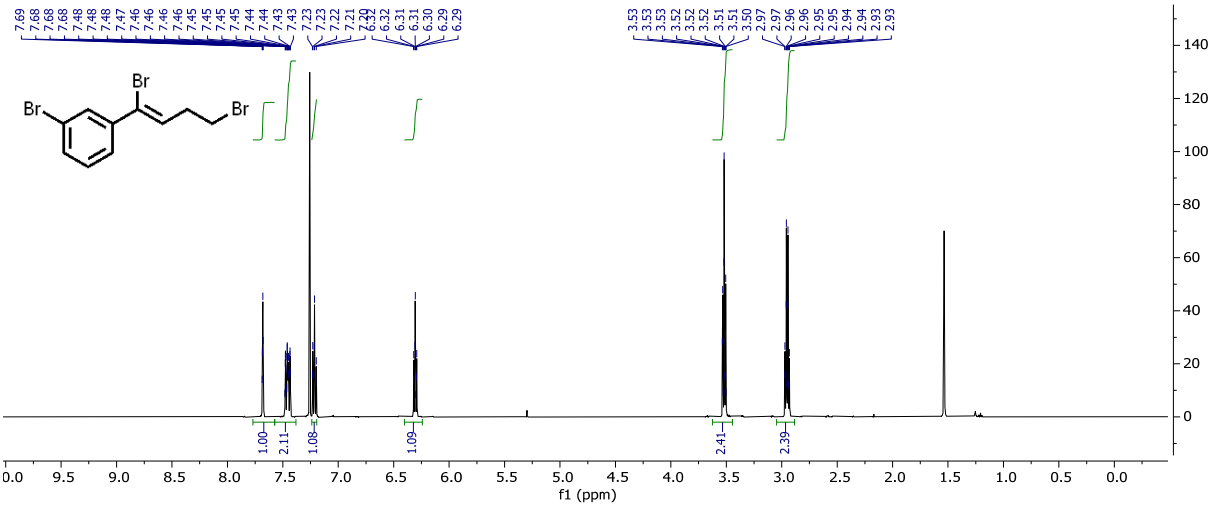


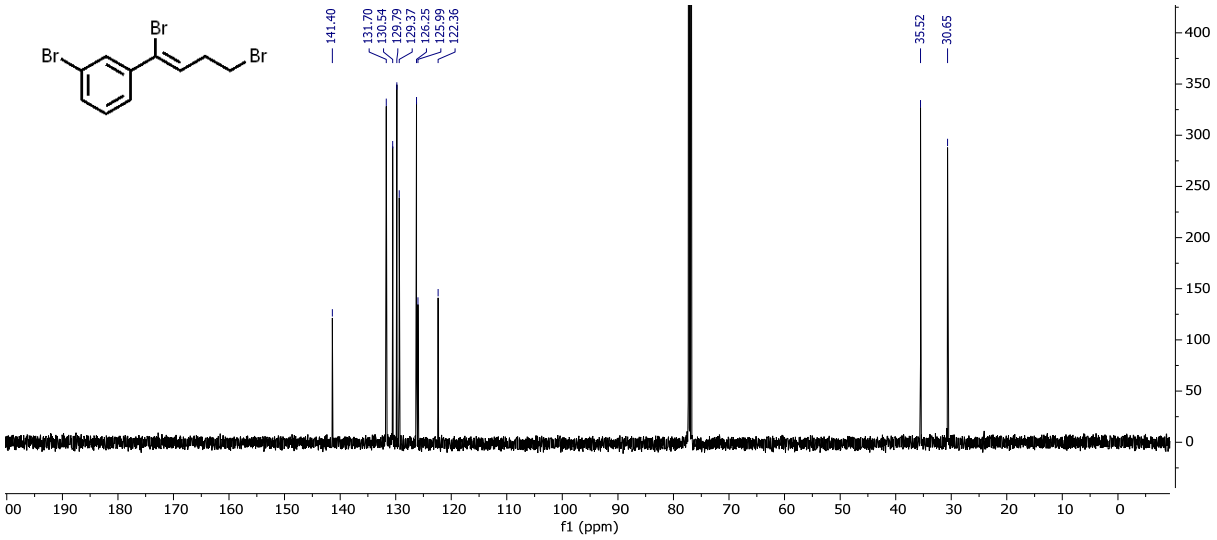
(Z)-1-bromo-3-(1,4-dibromobut-1-en-1-yl)benzene. **2t** was prepared according to a modified procedure by Murphy and coworker.[4] To a flame-dried round-bottom flask equipped with a stir bar was added THF (40 mL, 0.1M) and NaHMDS (10.5 mL, 1M in THF, 2.1 equiv). The flask was then cooled to -78 °C and γ-butyrolactone (0.38 mL, 5 mmol, 1 equiv) was added dropwise via syringe. The reaction mixture was then stirred for 1 h. After this time, 3-bromobenzoylchloride (0.66 mL, 5 mmol, 1 equiv) was added via syringe, and the solution was stirred for 30 minutes. After this time, the reaction was quenched with 1M HCl and diluted with EtOAc. The organic layers were then washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo to give the β -ketoester, which was used without further purification.

The crude β-ketoester was then dissolved in 1:1:1 THF:MeOH:H_2O (8 mL each) in a vial equipped with a stir bar and septum cap. Conc. HCl (~0.1 mL) was then added, and the vial sealed and heated to 65 °C. Upon completion by TLC, the mixture was cooled to room temperature, diluted with EtOAc, and washed with water and brine. The organic layer was then dried over Na_2SO_4 and concentrated in vacuo. The crude γ-hydroxyketone was then used without further purification.

The vinyl bromide was then synthesized according to General Procedure A without the DBU elimination as a clear, colorless oil (387 mg, 21% yield over 3 steps).

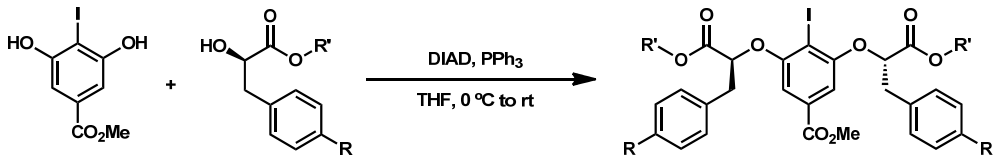
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (q, J = 1.9, 1.4 Hz, 1H), 7.46 (two overlapping dt, J = 12.5, 8.0, 2.1, 1.0 Hz, 2H), 7.22 (td, J = 7.9, 1.0 Hz, 1H), 6.31 (td, J = 6.7, 1.0 Hz, 1H), 3.52 (td, J = 6.8, 1.0 Hz, 2H), 2.95 (qd, J = 6.7, 1.0 Hz, 2H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 141.40, 131.70, 130.54, 129.79, 129.37, 126.25, 125.99, 122.36, 35.52, 30.65.
HRMS (EI): for $C_{10}H_9Br_3$, $[M]^+$ calculated m/z = 365.8249 and 367.8228 and 369.8208 and 371.8187, found m/z = 365.8247 and 367.8225 and 369.8204 and 371.8184.



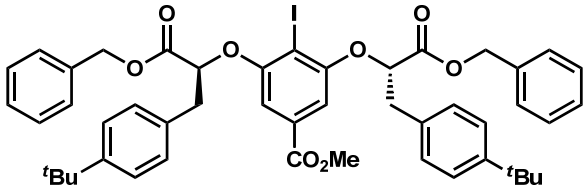

Br
Br
Br
141.40
131.70
130.54
129.79
129.37
126.25
125.99
122.36
35.52
30.65
400
350
300
250
200
150
100
50
0
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

Synthesis of Chiral Catalysts

General catalyst synthesis procedure:



The following procedure was modified from one reported by Banik, *et. al.*[5] Diisopropyl azodicarboxylate (7.66 mL, 46.0 mmol, 2.30 equiv) was added dropwise via syringe over 10 minutes to a stirred suspension of methyl 3,5-dihydroxy-4-iodobenzoate (1 equiv), triphenylphosphine (2.70 equiv), and the appropriate α-hydroxy ester (2.10 equiv) in tetrahydrofuran (0.1M) at 0 °C. The reaction mixture was warmed to room temperature. After 12 hours, the reaction mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography (DCM), followed by an additional flash column chromatography purification (Hexanes:Et_2O).

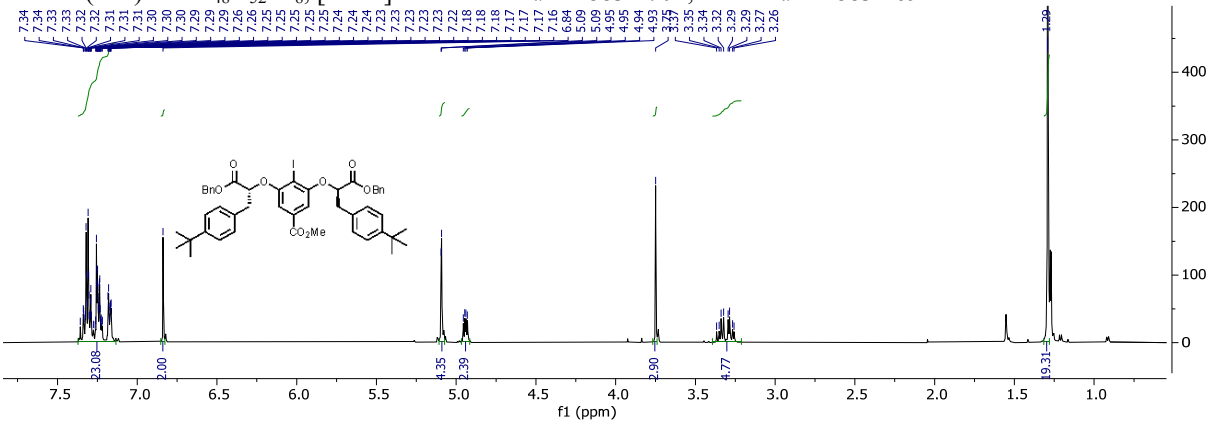


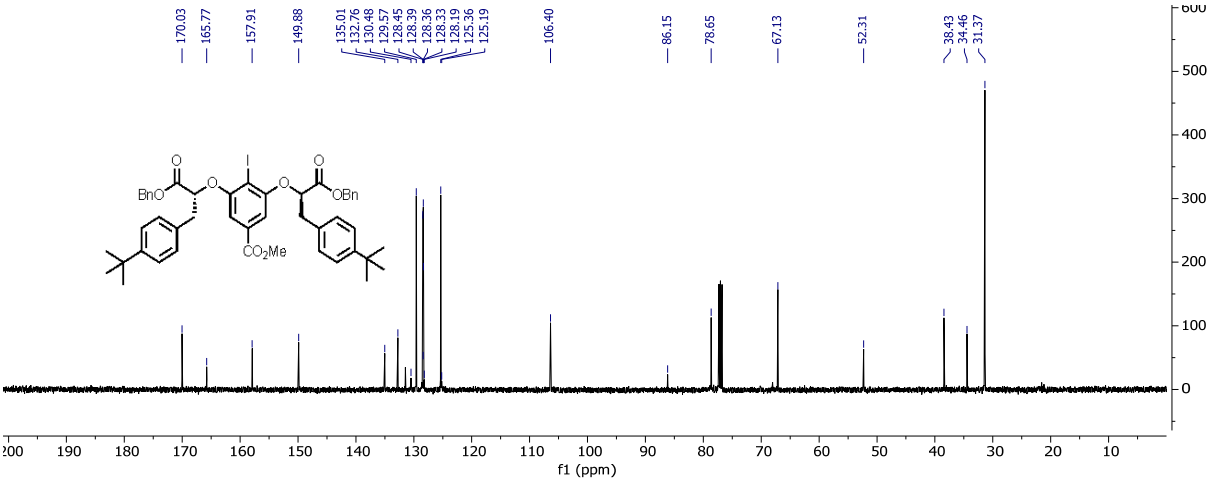
dibenzyl 2,2'-((2-iodo-5-(methoxycarbonyl)-1,3-phenylene)bis(oxy))(2R,2'R)-bis(3-(4-(tert-butyl)phenyl)propanoate). **3b** was isolated as a crystalline, white powder.

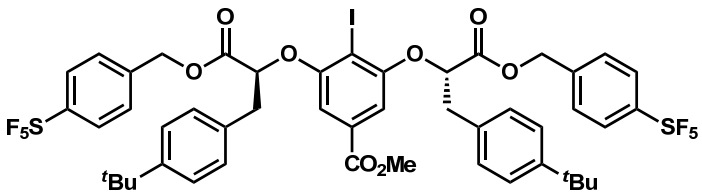
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.11 (m, 28H), 6.84 (s, 2H), 5.09 (d, J = 1.5 Hz, 5H), 4.94 (dd, J = 8.0, 4.6 Hz, 2H), 3.75 (s, 3H), 3.39 – 3.21 (m, 6H), 1.29 (s, 16H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 170.03, 165.77, 157.91, 149.88, 135.01, 132.76, 130.48, 129.57, 129.31 – 128.07 (m), 125.36, 106.40, 86.15, 78.65, 67.13, 52.31, 38.43, 34.46, 31.37.

HRMS (ESI): for $C_{48}H_{52}IO_8$, $[M+H]^+$ calculated m/z = 883.2701, found m/z = 883.2691.







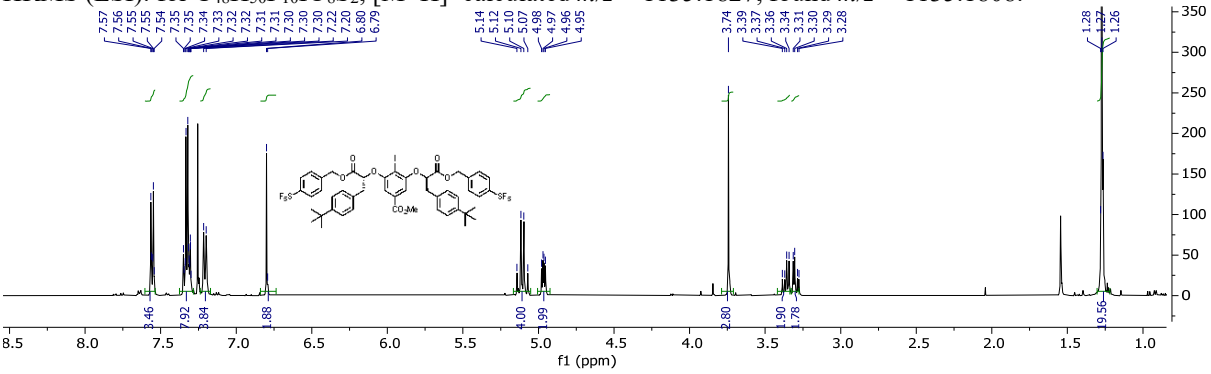
bis(4-(pentafluoro-λ^6-sulfanyl)benzyl) 2,2'-((2-iodo-5-(methoxycarbonyl)-1,3-phenylene)bis(oxy))(2R,2'R)-bis(3-(4-(tert-butyl)phenyl)propanoate). **3c** was isolated as a crystalline, white powder.

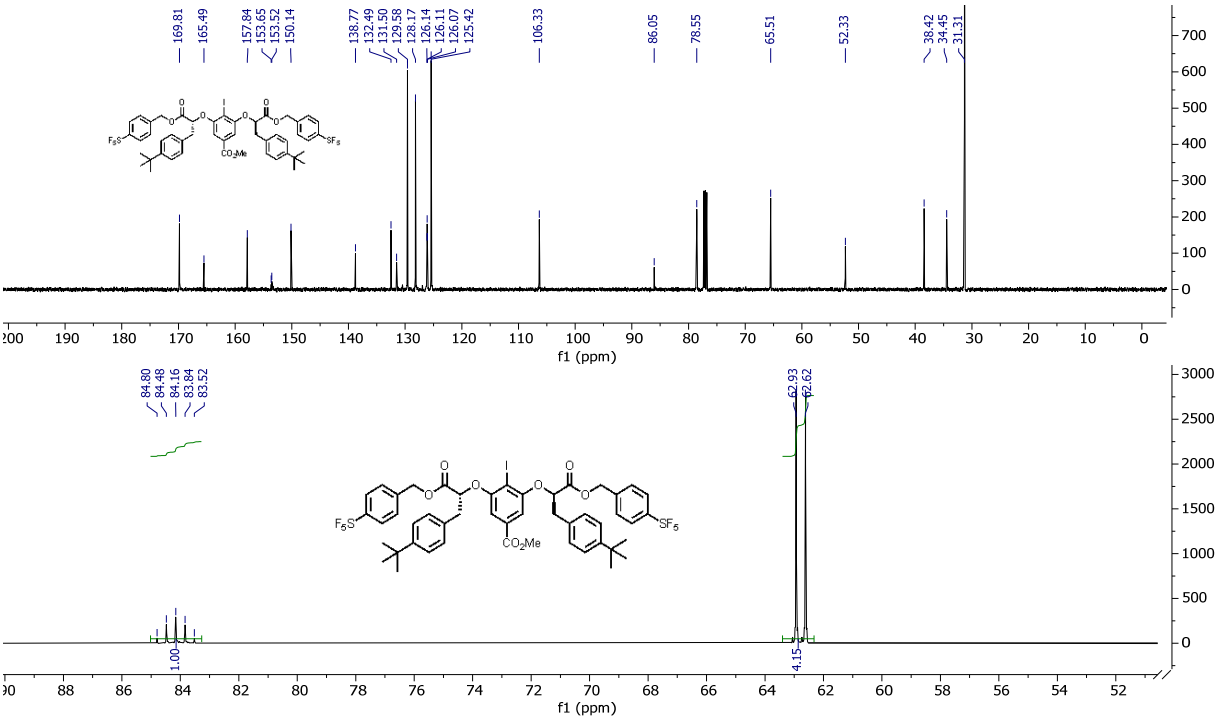
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 – 7.53 (m, 4H), 7.40 – 7.29 (m, 8H), 7.21 (d, *J* = 8.3 Hz, 4H), 6.80 (s, 2H), 5.15 – 5.05 (m, 4H), 4.97 (dd, *J* = 7.9, 4.6 Hz, 2H), 3.74 (s, 3H), 3.36 (dd, *J* = 14.0, 7.9 Hz, 2H), 3.30 (dd, *J* = 14.0, 4.6 Hz, 2H), 1.27 (s, 18H).

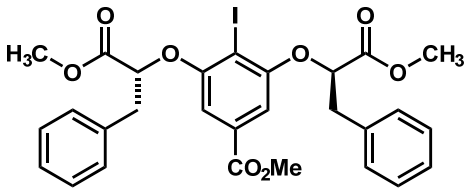
^{13}C NMR (126 MHz, $CDCl_3$) δ 169.81, 165.49, 157.84, 153.58 (d, *J* = 17.0 Hz), 150.14, 138.77, 132.49, 131.50, 129.58, 128.17, 126.31 – 125.82 (m), 125.42, 106.33, 86.05, 78.55, 65.51, 52.33, 38.42, 34.45, 31.31.

^{19}F NMR (471 MHz, $CDCl_3$) δ 84.16 (p, *J* = 150.3, 149.8 Hz, 1F), 62.77 (d, *J* = 149.6 Hz, 4F).

HRMS (ESI): for $C_{48}H_{50}F_{10}IO_8S_2$, $[M+H]^+$ calculated *m/z* = 1135.1827, found *m/z* = 1135.1808.





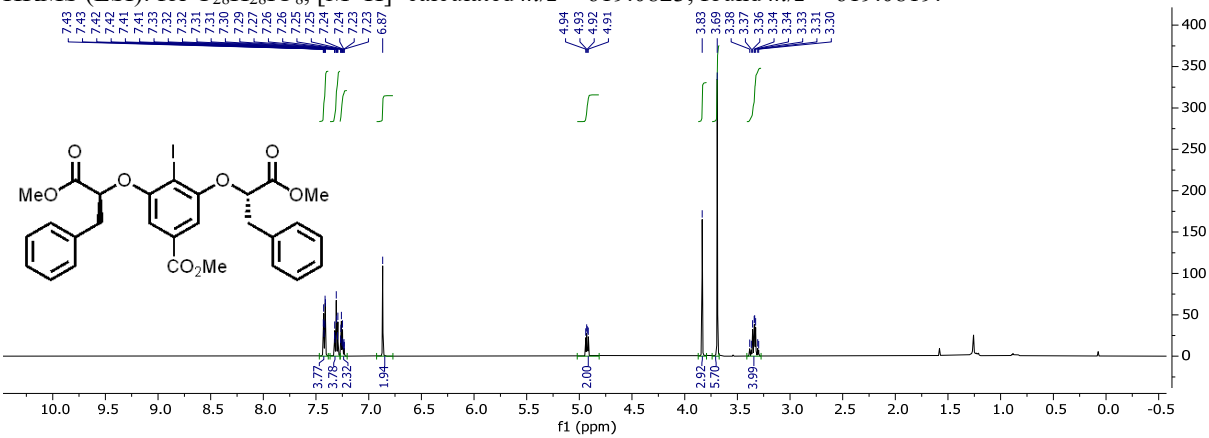


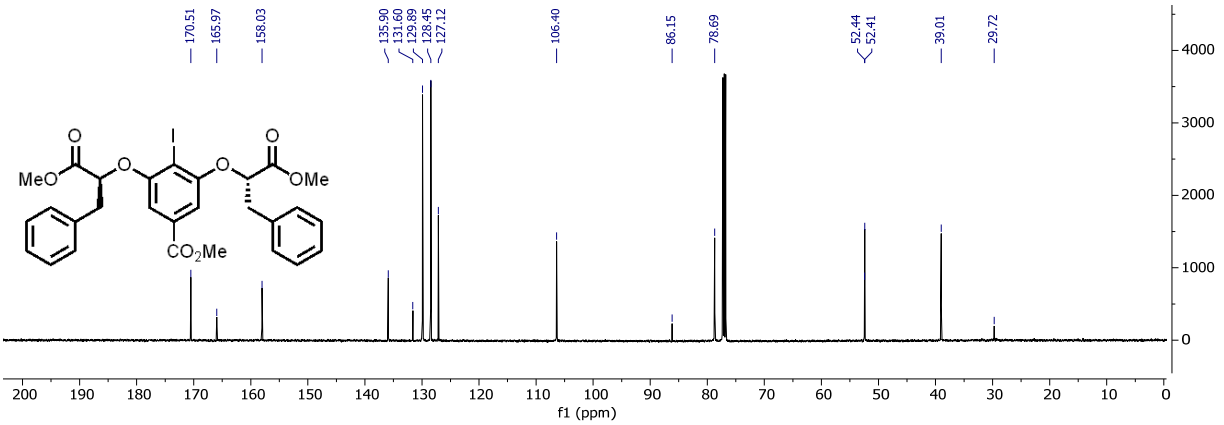
dimethyl 2,2'-((2-iodo-5-(methoxycarbonyl)-1,3-phenylene)bis(oxy))(2R,2'R)-bis(3-phenylpropanoate)

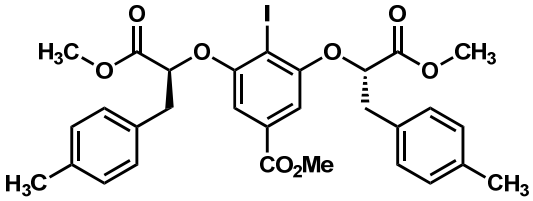
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 – 7.39 (m, 4H), 7.36 – 7.28 (m, 4H), 7.28 – 7.22 (m, 2H), 6.87 (s, 2H), 4.93 (dd, *J* = 7.8, 4.6 Hz, 2H), 3.83 (s, 3H), 3.69 (s, 6H), 3.39 – 3.28 (m, 4H). **3d** was isolated as a crystalline, white powder.

^{13}C NMR (126 MHz, $CDCl_3$) δ 170.51, 165.97, 158.03, 135.90, 131.60, 129.89, 128.45, 127.12, 106.40, 86.15, 78.69, 52.42, 39.01, 29.72.

HRMS (ESI): for $C_{28}H_{28}IO_8$, $[M+H]^+$ calculated *m/z* = 619.0823, found *m/z* = 619.0819.





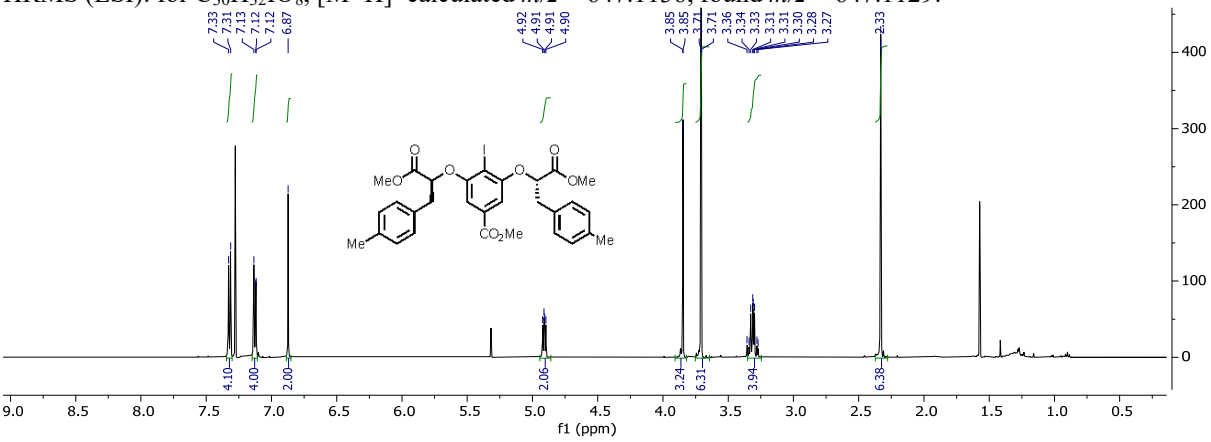


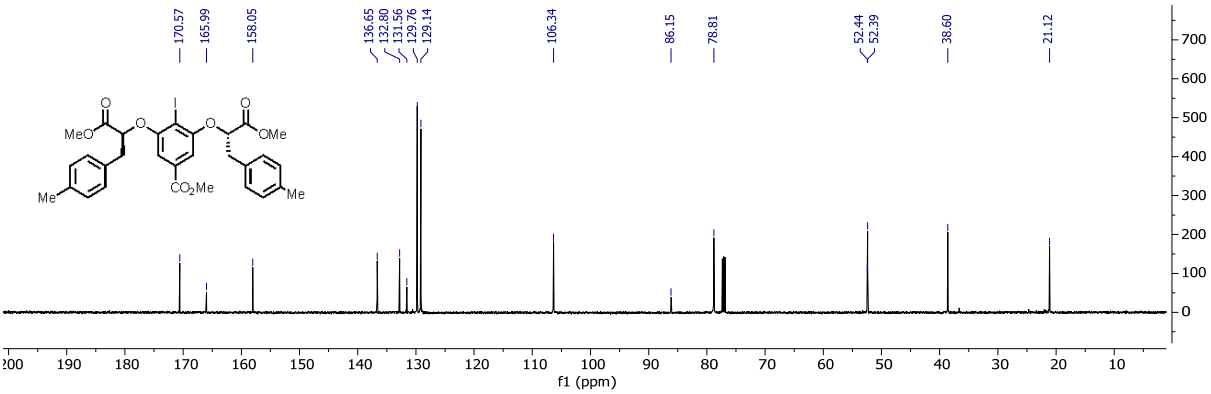
dimethyl 2,2'-((2-iodo-5-(methoxycarbonyl)-1,3-phenylene)bis(oxy))(2S,2'S)-bis(3-(p-tolyl)propanoate). **3e** was isolated as a crystalline, white powder.

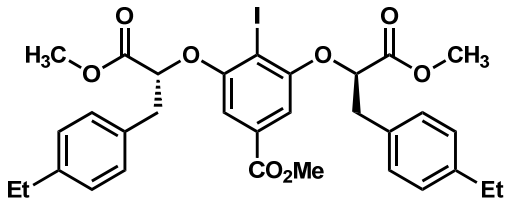
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.0 Hz, 4H), 7.15 – 7.10 (m, 4H), 6.87 (s, 2H), 4.91 (dd, *J* = 7.7, 4.6 Hz, 2H), 3.85 (d, *J* = 0.5 Hz, 3H), 3.71 (d, *J* = 0.5 Hz, 6H), 3.39 – 3.22 (m, 5H), 2.33 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 170.57, 165.99, 158.05, 136.65, 132.80, 131.56, 129.76, 129.14, 106.34, 86.15, 78.81, 52.44, 52.39, 38.60, 21.12.

HRMS (ESI): for $C_{30}H_{32}IO_8$, $[M+H]^+$ calculated *m/z* = 647.1136, found *m/z* = 647.1129.





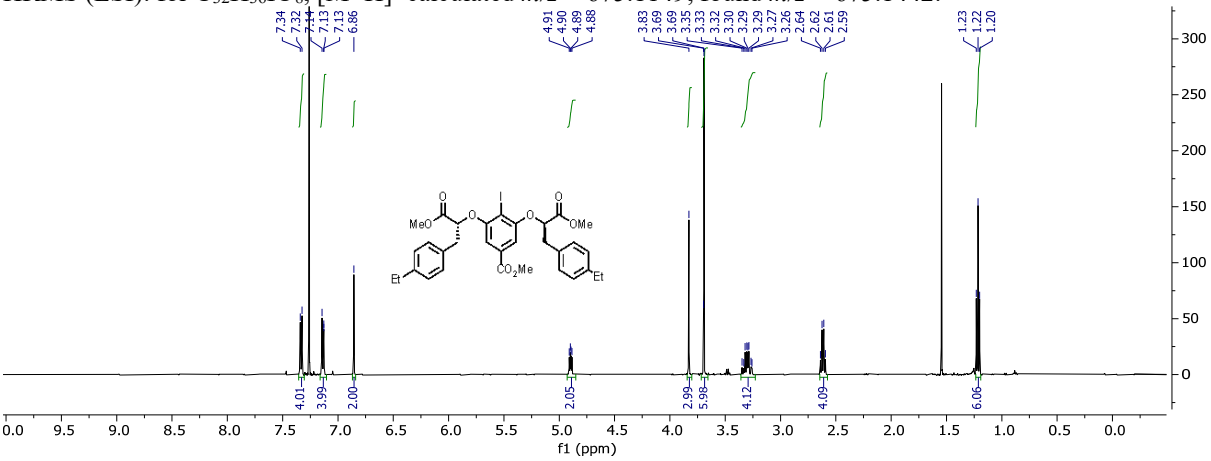


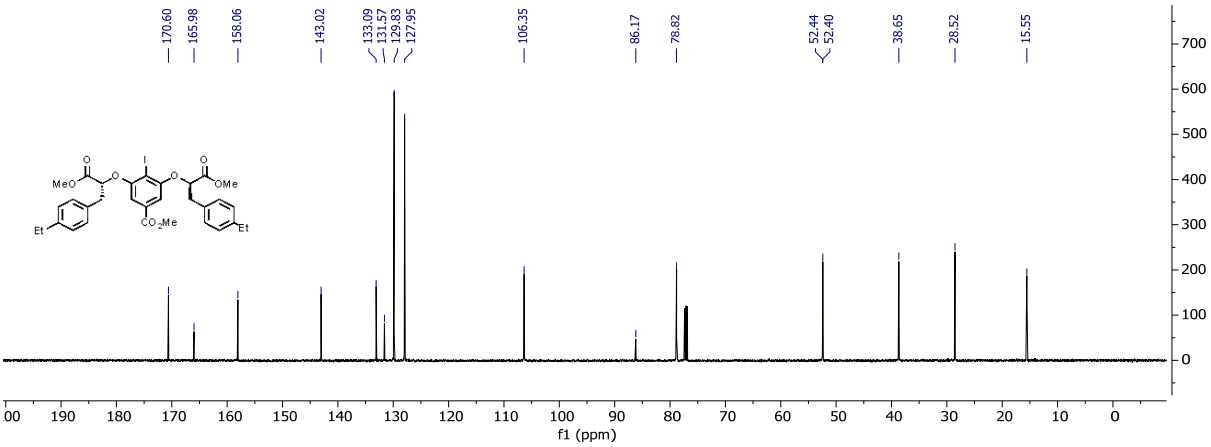
dimethyl 2,2'-((2-iodo-5-(methoxycarbonyl)-1,3-phenylene)bis(oxy))(2R,2'R)-bis(3-(4-ethylphenyl)propanoate). **3e** was isolated as a crystalline, white powder.

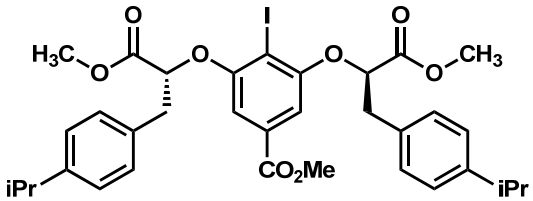
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (d, *J* = 8.1 Hz, 3H), 7.14 (d, *J* = 7.8 Hz, 4H), 6.86 (s, 2H), 4.90 (dd, *J* = 7.9, 4.5 Hz, 2H), 3.83 (s, 2H), 3.69 (s, 6H), 3.36 – 3.23 (m, 4H), 2.62 (q, *J* = 7.6 Hz, 5H), 1.22 (t, *J* = 7.6 Hz, 5H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 170.60, 165.98, 158.06, 143.02, 133.09, 131.57, 129.83, 127.95, 106.35, 86.17, 78.82, 52.44, 52.40, 38.65, 28.52, 15.55.

HRMS (ESI): for $C_{32}H_{36}IO_8$, $[M+H]^+$ calculated *m/z* = 675.1149, found *m/z* = 675.1442.





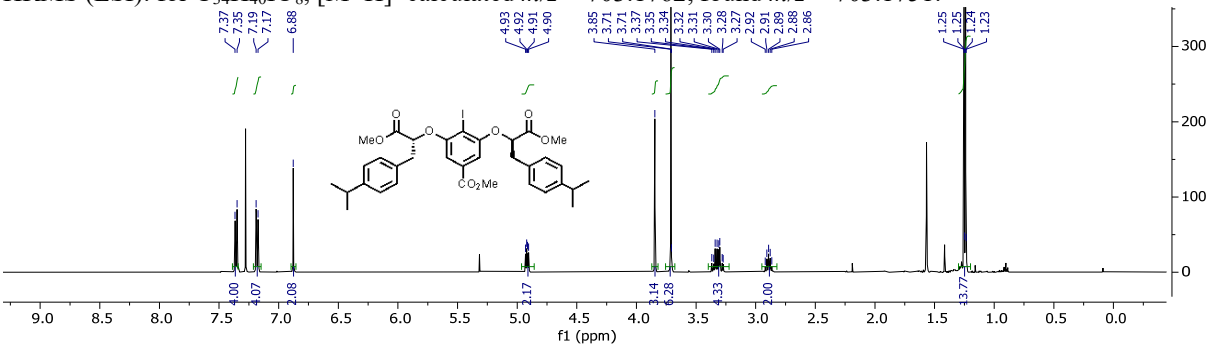


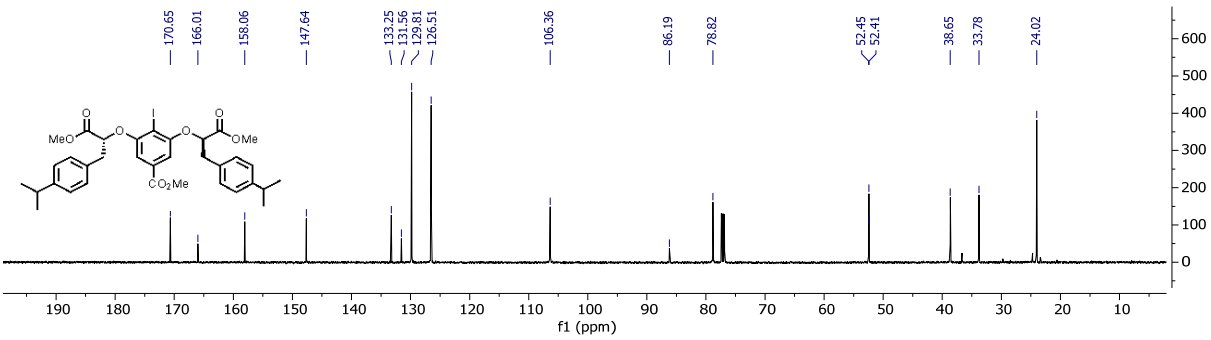
dimethyl 2,2'-((2-iodo-5-(methoxycarbonyl)-1,3-phenylene)bis(oxy))(2R,2'R)-bis(3-(4-isopropylphenyl)propanoate). **3f** was isolated as a crystalline, white powder.

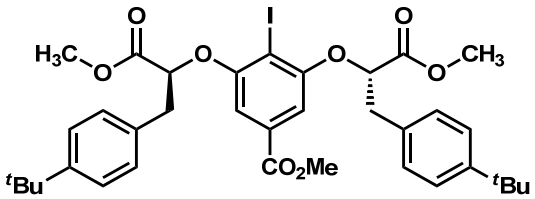
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (d, J = 8.1 Hz, 4H), 7.18 (d, J = 8.1 Hz, 4H), 6.88 (s, 2H), 4.92 (dd, J = 8.0, 4.4 Hz, 2H), 3.85 (s, 3H), 3.71 (s, 6H), 3.32 (qd, J = 14.1, 6.2 Hz, 4H), 2.89 (p, J = 6.9 Hz, 2H), 1.25 (d, J = 6.9 Hz, 12H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 170.65, 166.01, 158.06, 147.64, 133.25, 131.56, 129.81, 126.51, 106.36, 86.19, 78.82, 52.45, 52.41, 38.65, 33.78, 24.02.

HRMS (ESI): for $C_{34}H_{40}IO_8$, $[M+H]^+$ calculated m/z = 703.1762, found m/z = 703.1751.





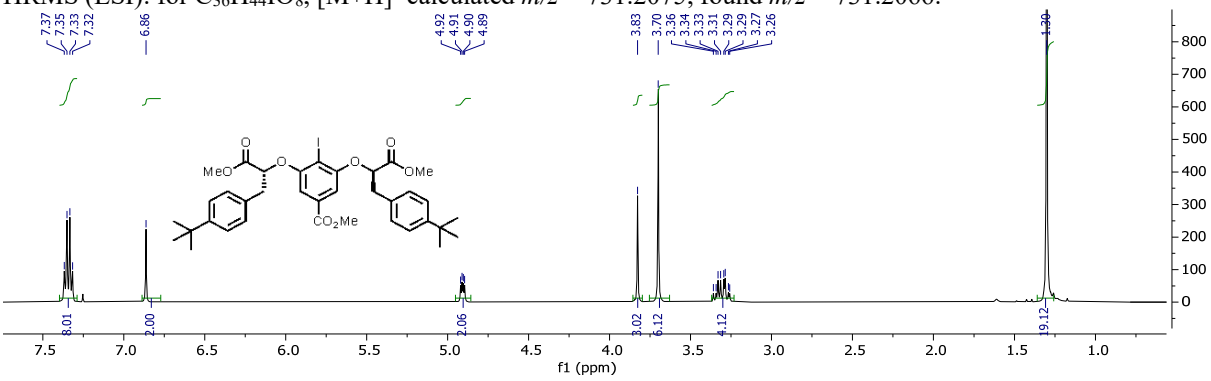


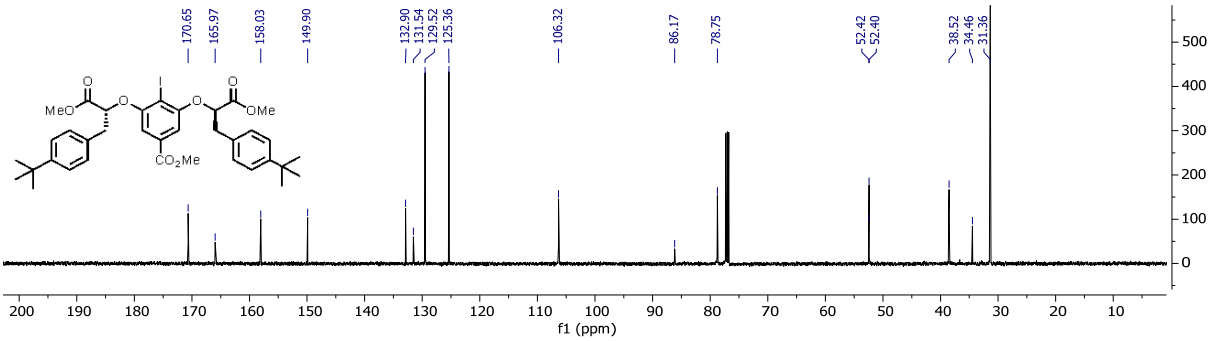
dimethyl 2,2'-((2-iodo-5-(methoxycarbonyl)-1,3-phenylene)bis(oxy))(2R,2'R)-bis(3-(4-(tert-butyl)phenyl)propanoate). **3g** was isolated as a crystalline, white powder.

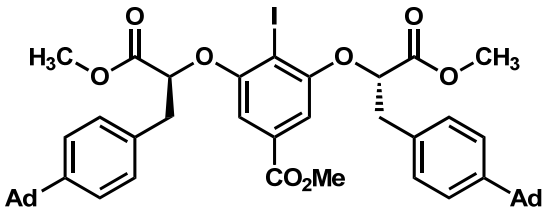
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (q, J = 8.3 Hz, 8H), 6.86 (s, 2H), 4.91 (dd, J = 8.2, 4.3 Hz, 2H), 3.83 (s, 3H), 3.70 (s, 6H), 3.31 (qd, J = 14.1, 6.2 Hz, 4H), 1.30 (s, 18H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 170.65, 165.97, 158.03, 149.90, 132.90, 131.54, 129.52, 125.36, 106.32, 86.17, 78.75, 52.42, 52.40, 38.52, 34.46, 31.36.

HRMS (ESI): for $C_{36}H_{44}IO_8$, $[M+H]^+$ calculated m/z = 731.2075, found m/z = 731.2066.





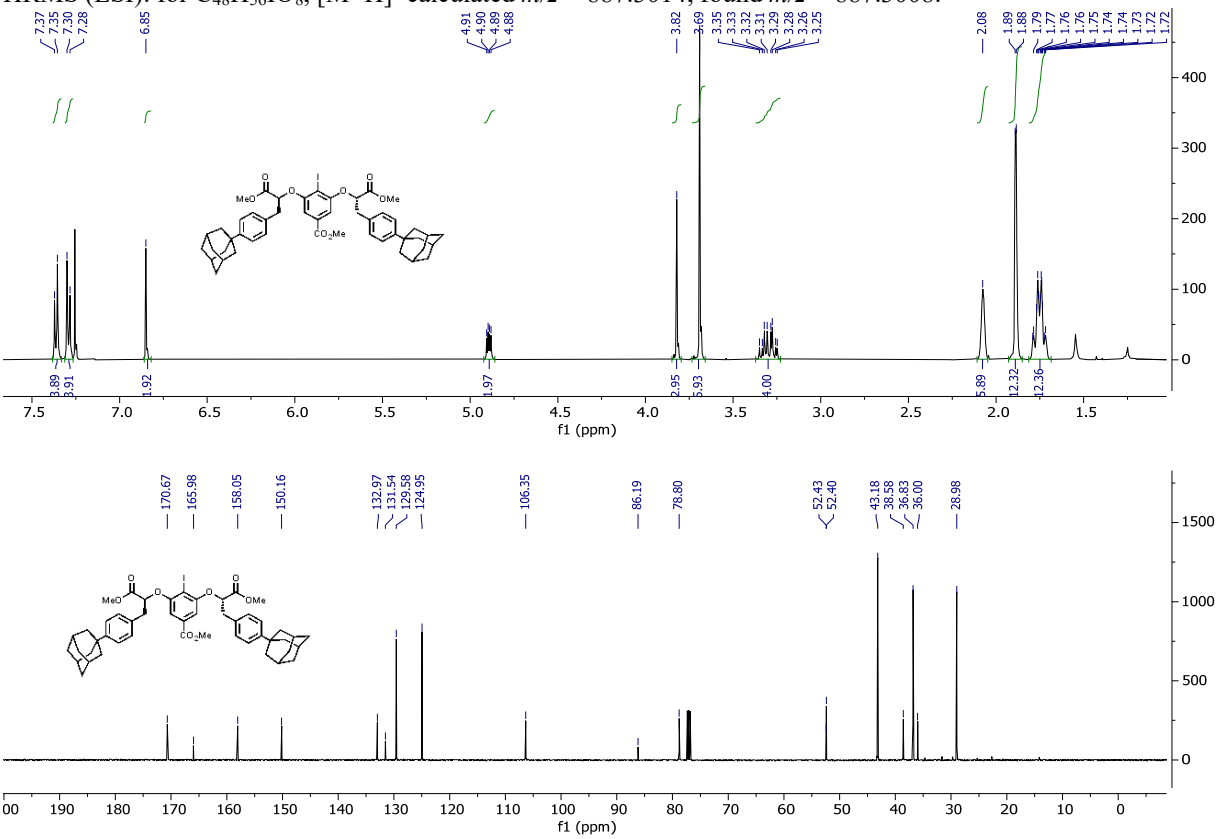


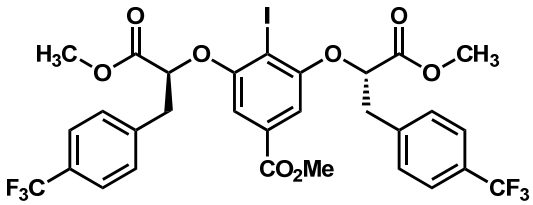
dimethyl 2,2'-((2-iodo-5-(methoxycarbonyl)-1,3-phenylene)bis(oxy))(2S,2'S)-bis(3-(4-adamantylphenyl)propanoate. **3h** was isolated as a crystalline, white powder.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (d, J = 8.3 Hz, 4H), 7.29 (d, J = 8.3 Hz, 4H), 6.85 (s, 2H), 4.89 (dd, J = 8.2, 4.3 Hz, 2H), 3.82 (s, 3H), 3.69 (s, 5H), 3.36 – 3.23 (m, 5H), 2.08 (s, 3H), 1.89 (d, J = 3.0 Hz, 14H), 1.81 – 1.69 (m, 16H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 170.67, 165.98, 158.05, 150.16, 132.97, 131.54, 129.58, 124.95, 106.35, 86.19, 78.80, 52.43, 52.40, 43.18, 38.58, 36.83, 36.00, 28.98.

HRMS (ESI): for $C_{48}H_{56}IO_8$, $[M+H]^+$ calculated *m/z* = 887.3014, found *m/z* = 887.3008.





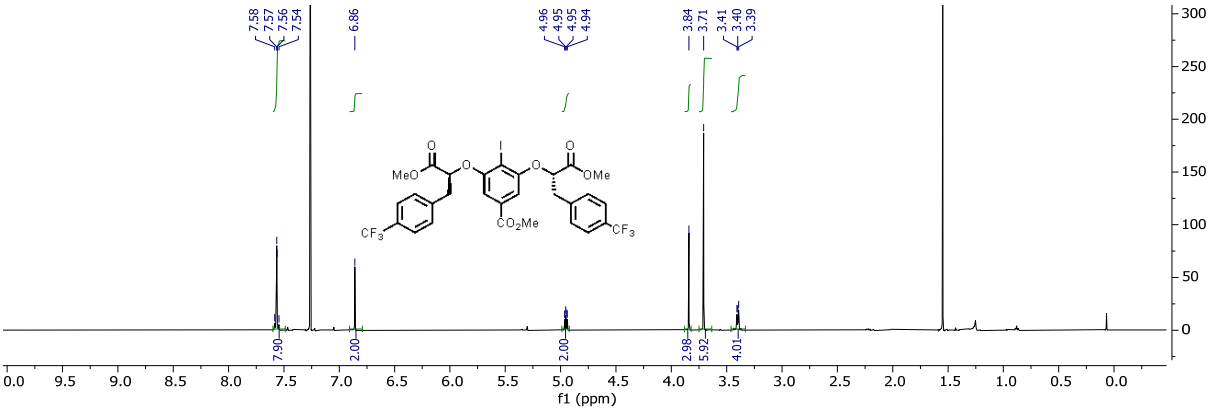
dimethyl 2,2'-((2-iodo-5-(methoxycarbonyl)-1,3-phenylene)bis(oxy))(2S,2'S)-bis(3-(4-(trifluoromethyl)phenyl)propanoate). **3i** was isolated as a crystalline, white powder.

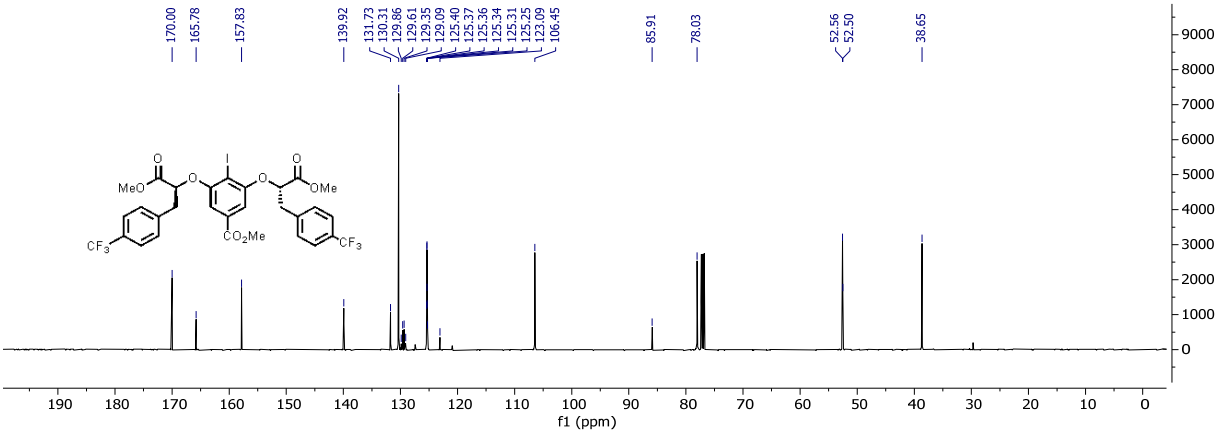
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 1.6 Hz, 7H), 6.86 (s, 2H), 4.95 (dd, *J* = 7.2, 4.9 Hz, 2H), 3.84 (s, 3H), 3.71 (s, 6H), 3.47 – 3.35 (m, 3H).

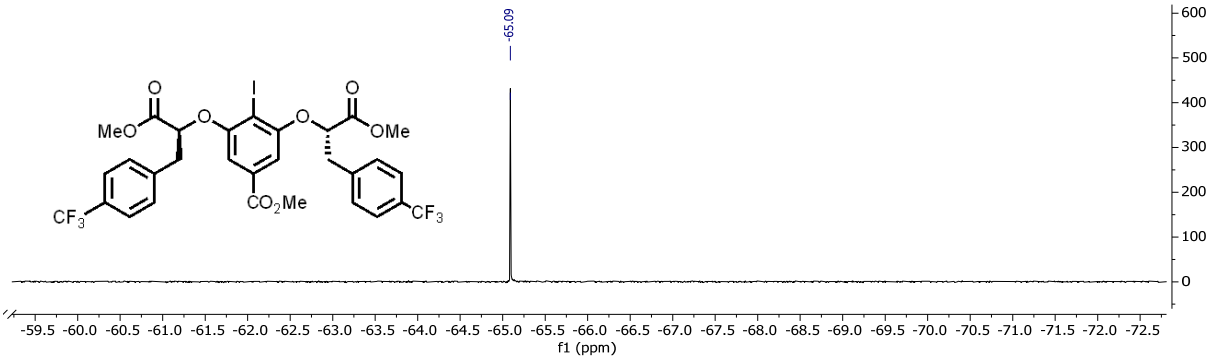
^{13}C NMR (126 MHz, $CDCl_3$) δ 170.00, 165.78, 157.83, 139.92, 131.73, 130.31, 129.48 (q, *J* = 32.3 Hz), 125.36 (q, *J* = 3.8 Hz), 124.17 (q, *J* = 272.6, 272.0, 271.2 Hz), 106.45, 85.91, 78.03, 52.56, 52.50, 38.65.

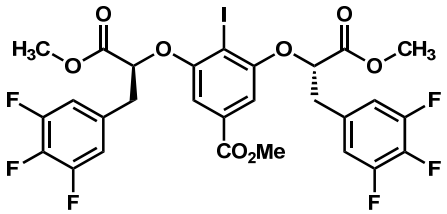
^{19}F NMR (471 MHz, $CDCl_3$) δ -65.09.

HRMS (ESI): for $C_{30}H_{26}F_6IO_8$, $[M+H]^+$ calculated *m/z* = 755.0571, found *m/z* = 755.0561.



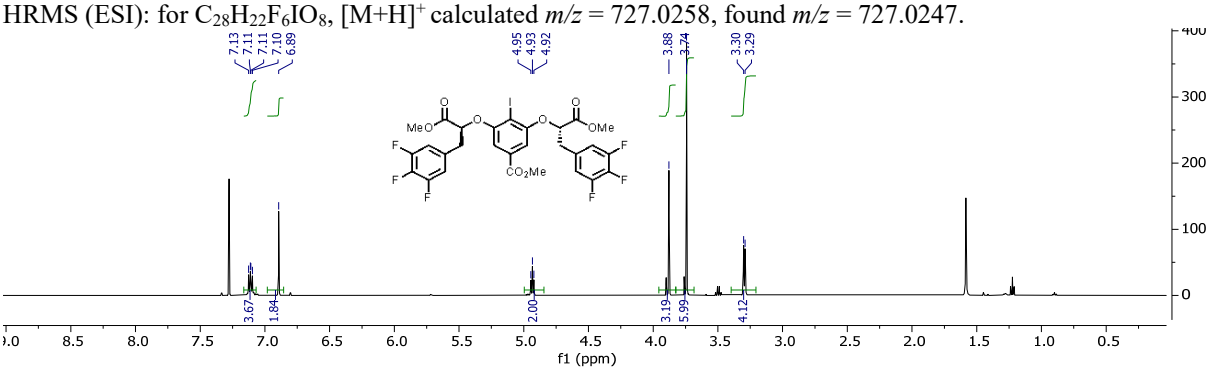


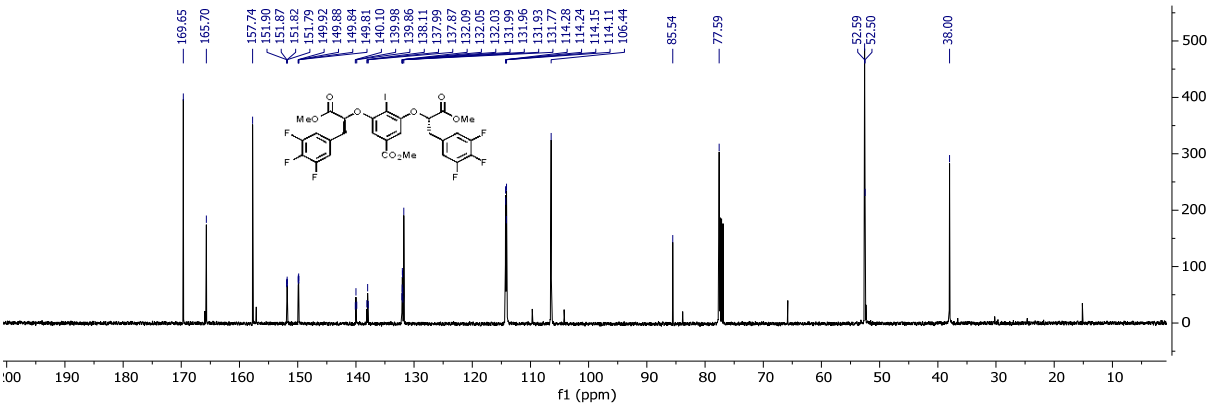


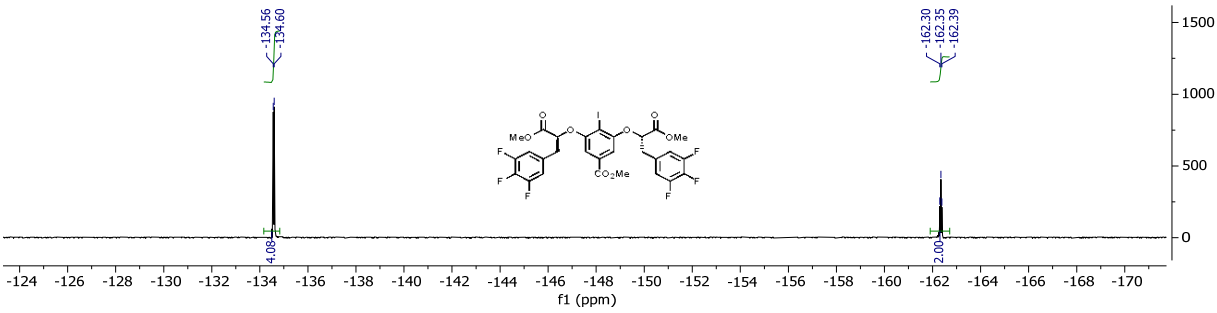


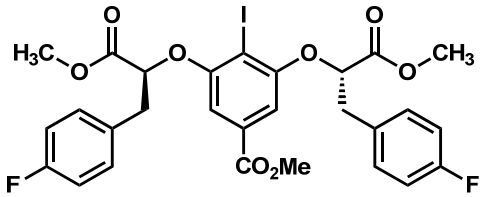
dimethyl 2,2'-((2-iodo-5-(methoxycarbonyl)-1,3-phenylene)bis(oxy))(2S,2'S)-bis(3-(3,4,5-trifluorophenyl)propanoate). **3j** was isolated as a crystalline, white powder.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11 (dd, J = 8.2, 6.4 Hz, 4H), 6.89 (s, 2H), 4.93 (t, J = 5.9 Hz, 2H), 3.88 (s, 3H), 3.74 (s, 6H), 3.30 (d, J = 5.8 Hz, 4H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 169.65, 165.70, 157.74, 150.85 (ddd, J = 249.5, 9.7, 3.8 Hz), 138.98 (dt, J = 250.6, 15.3 Hz), 132.01 (td, J = 7.8, 4.6 Hz), 131.77, 114.43 – 113.77 (m), 106.44, 85.54, 77.59, 52.59, 52.50, 38.00.
^{19}F NMR (471 MHz, $CDCl_3$) δ -134.58 (d, J = 20.5 Hz, 4F), -162.35 (t, J = 20.6 Hz, 2F).
HRMS (ESI): for $C_{28}H_{22}F_6IO_8$, $[M+H]^+$ calculated m/z = 727.0258, found m/z = 727.0247.



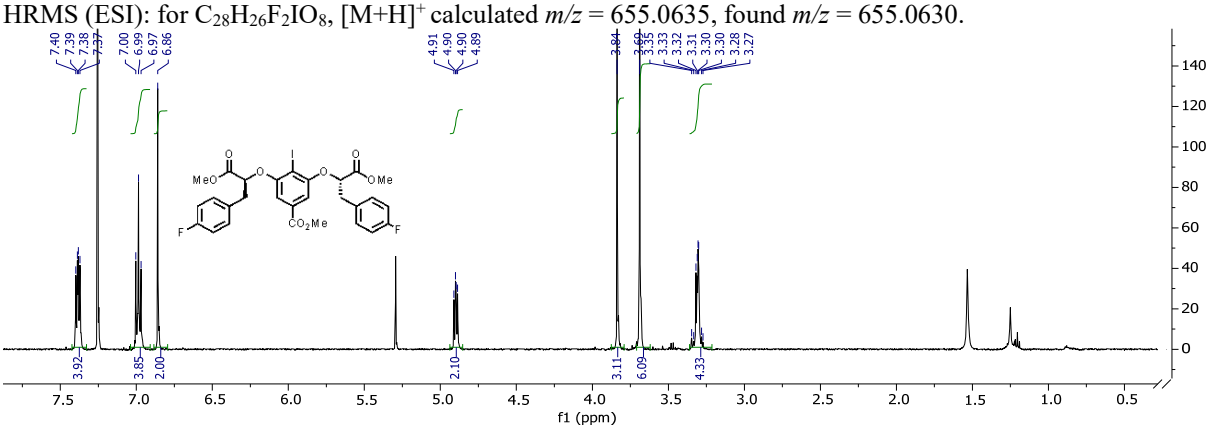


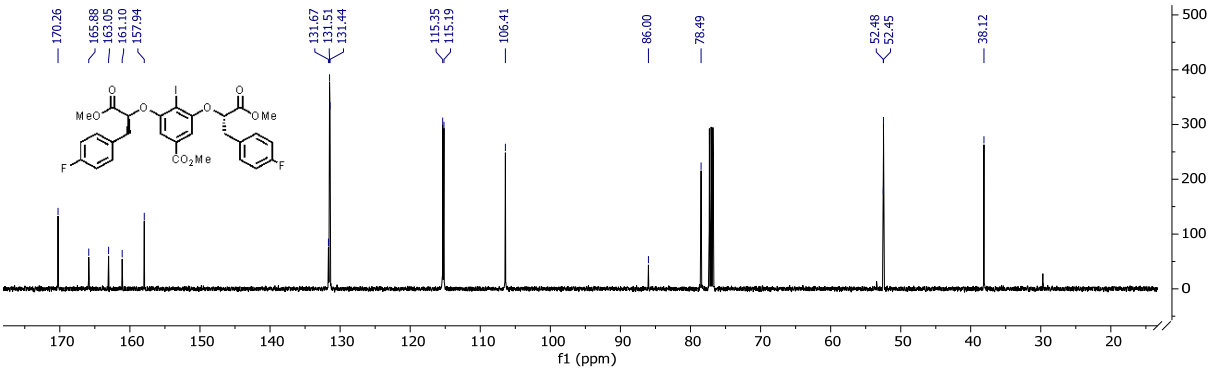


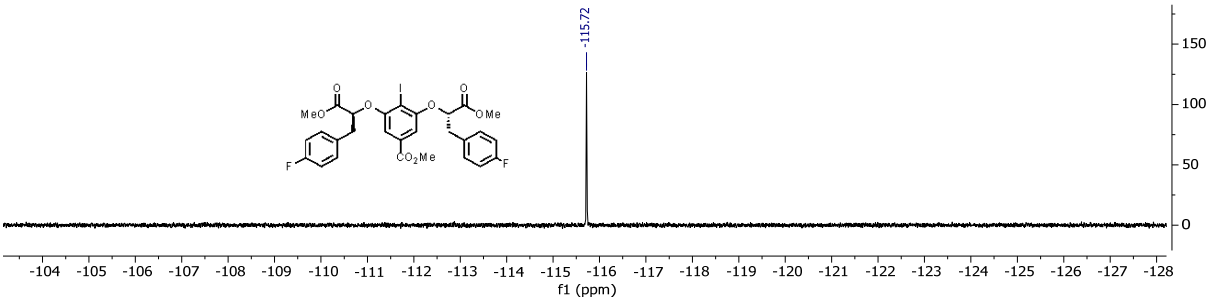


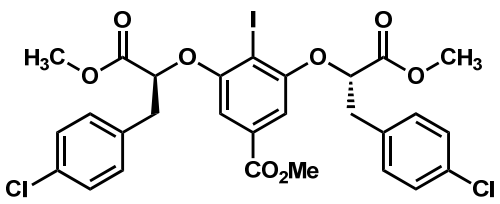
dimethyl 2,2'-((2-iodo-5-(methoxycarbonyl)-1,3-phenylene)bis(oxy))(2S,2'S)-bis(3-(4-fluorophenyl)propanoate). **3k** was isolated as a crystalline, white powder.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (dd, J = 8.6, 5.4 Hz, 4H), 6.99 (t, J = 8.7 Hz, 3H), 6.86 (s, 2H), 4.90 (dd, J = 7.2, 4.9 Hz, 3H), 3.84 (s, 3H), 3.69 (s, 6H), 3.38 – 3.24 (m, 4H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 170.26, 165.88, 163.05, 161.10, 157.94, 131.67, 131.47 (d, *J* = 8.0 Hz), 115.27 (d, *J* = 21.2 Hz), 106.41, 86.00, 78.49, 52.48, 52.45, 38.12.
^{19}F NMR (471 MHz, $CDCl_3$) δ -115.72.
HRMS (ESI): for $C_{28}H_{26}F_2IO_8$, $[M+H]^+$ calculated *m/z* = 655.0635, found *m/z* = 655.0630.





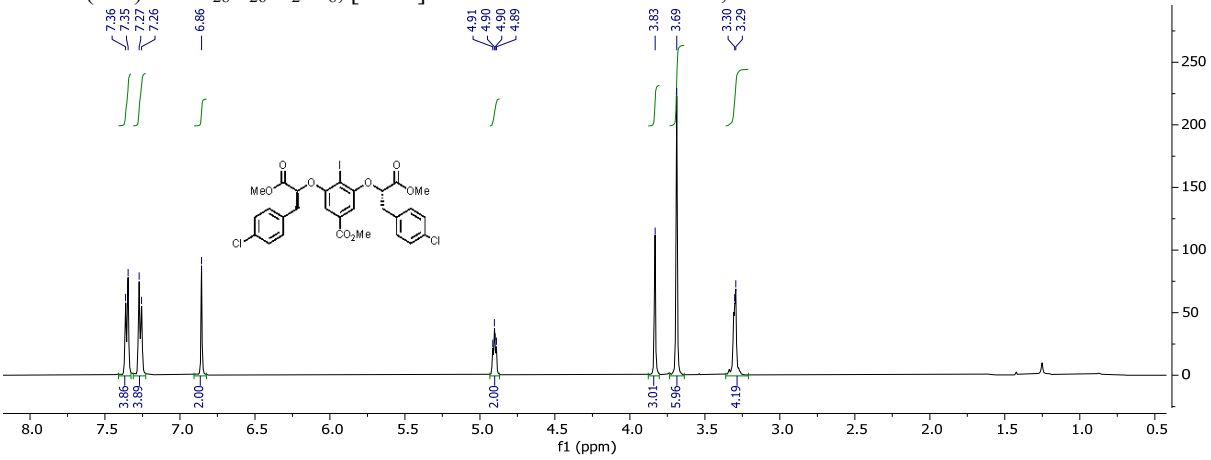


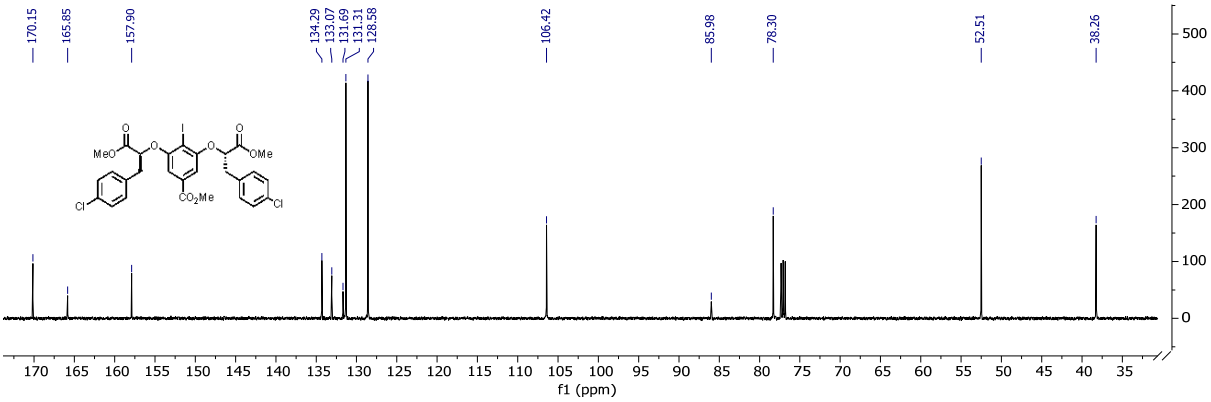


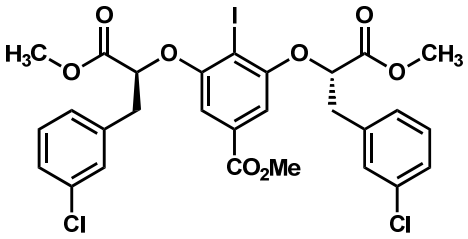
dimethyl 2,2'-((2-iodo-5-(methoxycarbonyl)-1,3-phenylene)bis(oxy))(2S,2'S)-bis(3-(4-chlorophenyl)propanoate). **3l** was isolated as a crystalline, white powder.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (d, *J* = 8.4 Hz, 4H), 7.26 (d, *J* = 8.0 Hz, 6H), 6.86 (s, 2H), 4.90 (t, *J* = 6.2 Hz, 3H), 3.83 (s, 3H), 3.69 (s, 6H), 3.35 – 3.25 (m, 4H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 170.15, 165.85, 157.90, 134.29, 133.07, 131.69, 131.31, 128.58, 106.42, 85.98, 78.30, 52.51, 38.26.

HRMS (ESI): for $C_{28}H_{26}Cl_2IO_8$, $[M+H]^+$ calculated *m/z* = 687.0044, found *m/z* = 687.0037.







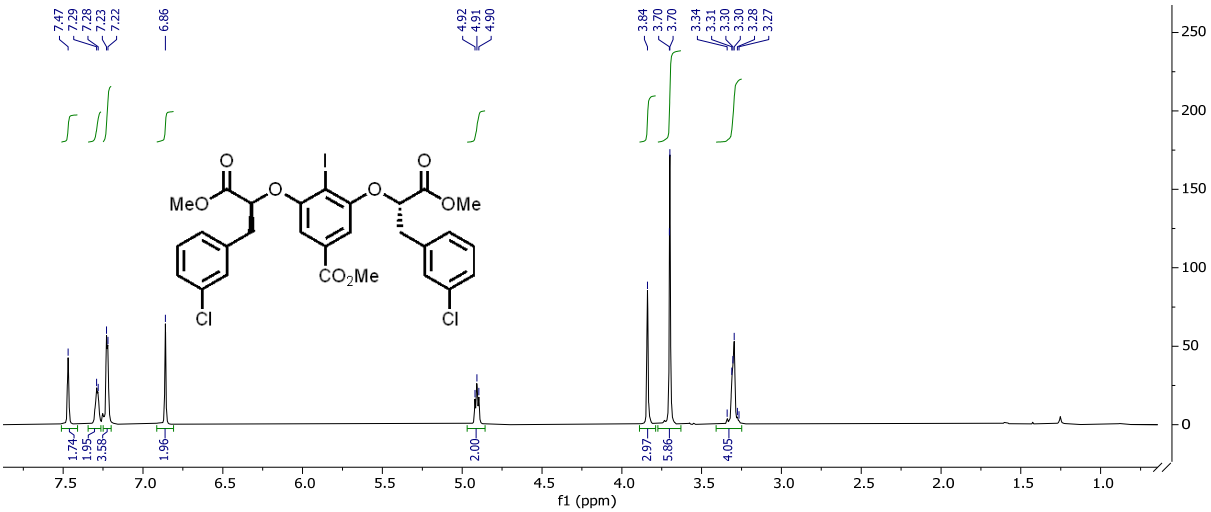
dimethyl 2,2'-((2-iodo-5-(methoxycarbonyl)-1,3-phenylene)bis(oxy))(2S,2'S)-bis(3-(3-chlorophenyl)propanoate).

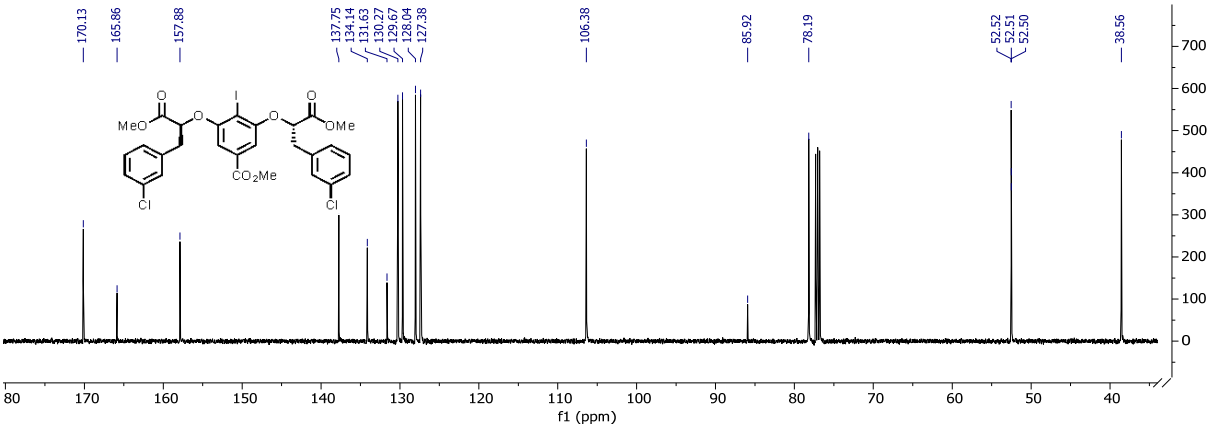
3m was isolated as a crystalline, white powder.

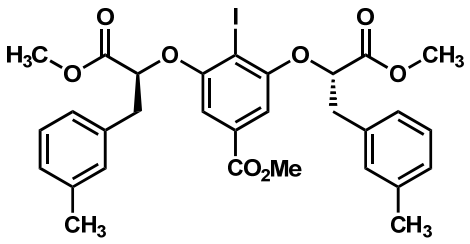
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (s, 2H), 7.29 (d, *J* = 4.7 Hz, 2H), 7.22 (d, *J* = 4.4 Hz, 4H), 6.86 (s, 2H), 4.91 (t, *J* = 6.0 Hz, 2H), 3.84 (s, 3H), 3.70 (s, 6H), 3.35 – 3.25 (m, 4H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 170.13, 165.86, 157.88, 137.75, 134.14, 131.63, 130.27, 129.67, 128.04, 127.38, 106.38, 85.92, 78.19, 52.52, 38.56.

HRMS (ESI): for $C_{28}H_{26}Cl_2IO_8$, $[M+H]^+$ calculated *m/z* = 687.0044, found *m/z* = 687.0040.





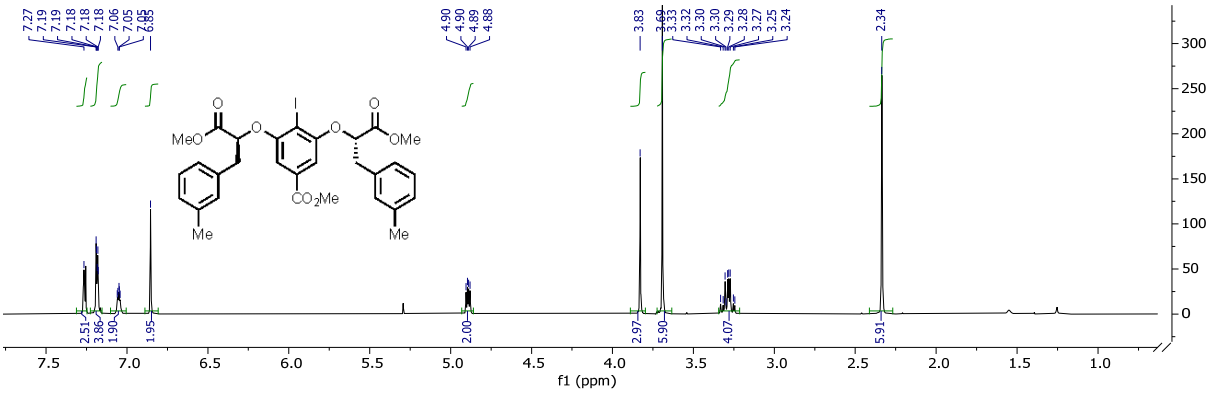


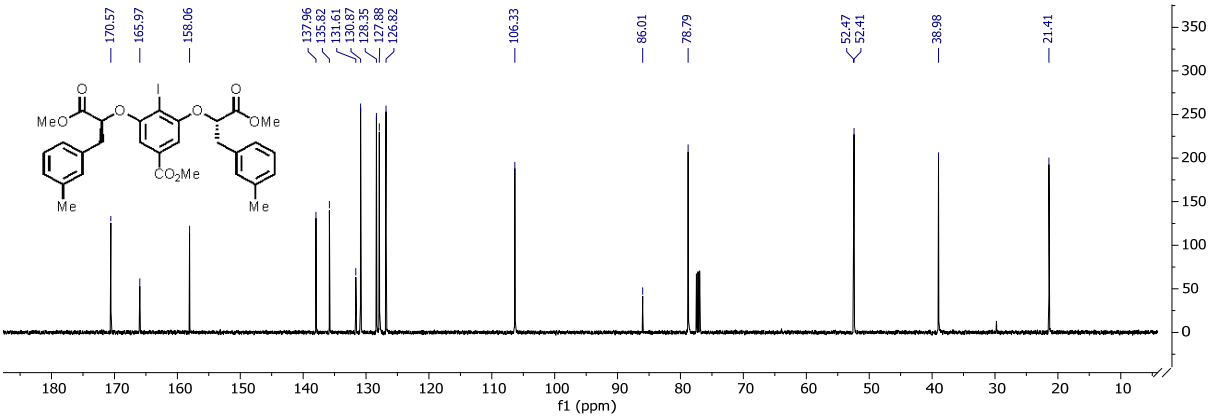
dimethyl 2,2'-((2-iodo-5-(methoxycarbonyl)-1,3-phenylene)bis(oxy))(2S,2'S)-bis(3-(m-tolyl)propanoate). **3n** was isolated as a crystalline, white powder.

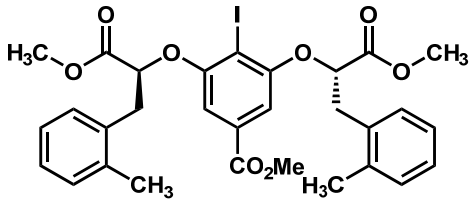
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (s, 2H), 7.21 – 7.15 (m, 4H), 7.08 – 7.03 (m, 2H), 6.85 (s, 2H), 4.89 (dd, J = 7.9, 4.5 Hz, 2H), 3.83 (s, 3H), 3.69 (s, 6H), 3.34 – 3.23 (m, 5H), 2.34 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 170.57, 165.97, 158.06, 137.96, 135.82, 131.61, 130.87, 128.35, 127.88, 126.82, 106.33, 86.01, 78.79, 52.47, 52.41, 38.98, 21.41.

HRMS (ESI): for $C_{30}H_{32}IO_8$, $[M+H]^+$ calculated m/z = 647.1136, found m/z = 647.1132.





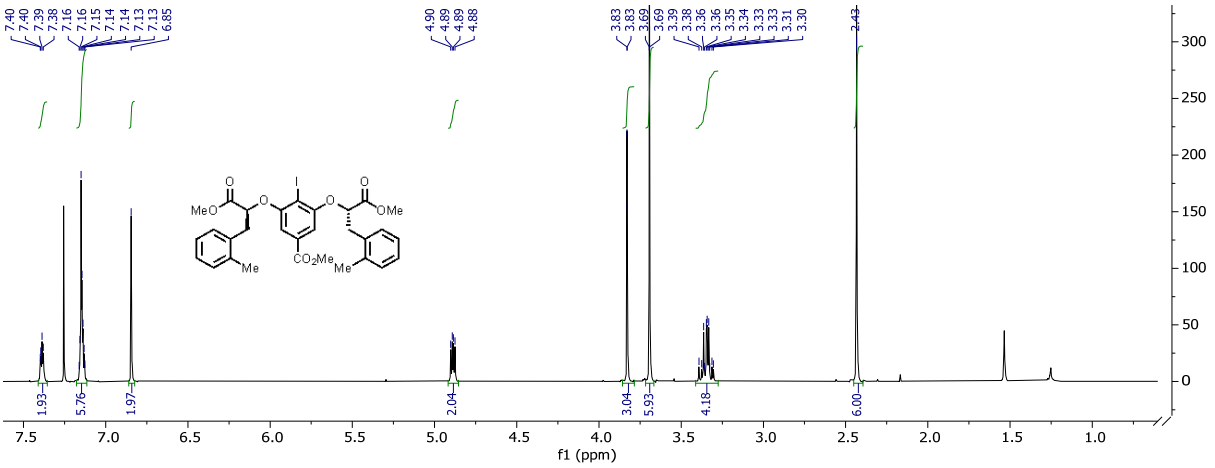


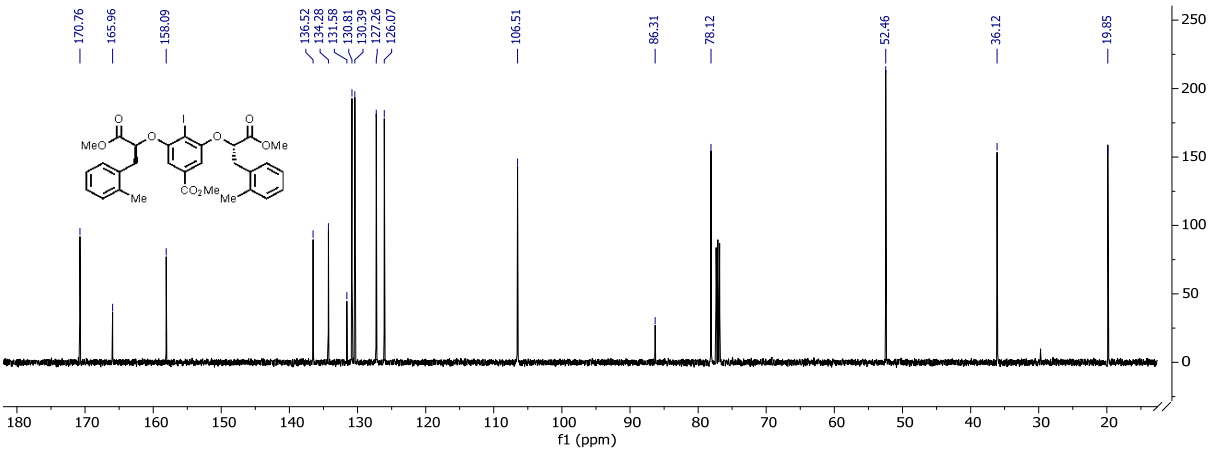
dimethyl 2,2'-((2-iodo-5-(methoxycarbonyl)-1,3-phenylene)bis(oxy))(2S,2'S)-bis(3-(o-tolyl)propanoate). **3o** was isolated as a crystalline, white powder.

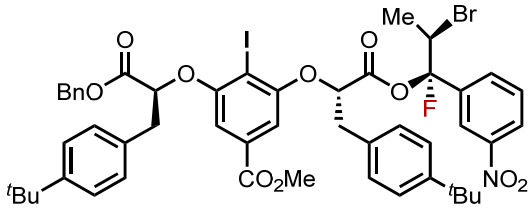
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.36 (m, 3H), 7.17 – 7.11 (m, 7H), 6.85 (s, 2H), 4.89 (dd, *J* = 8.4, 4.8 Hz, 3H), 3.83 (s, 3H), 3.69 (s, 6H), 3.40 – 3.27 (m, 5H), 2.43 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 170.76, 165.96, 158.09, 136.52, 134.28, 131.58, 130.81, 130.39, 127.26, 126.07, 106.51, 86.31, 78.12, 52.46, 36.12, 19.85.

HRMS (ESI): for $C_{30}H_{32}IO_8$, $[M+H]^+$ calculated *m/z* = 647.1136, found *m/z* = 647.1132.





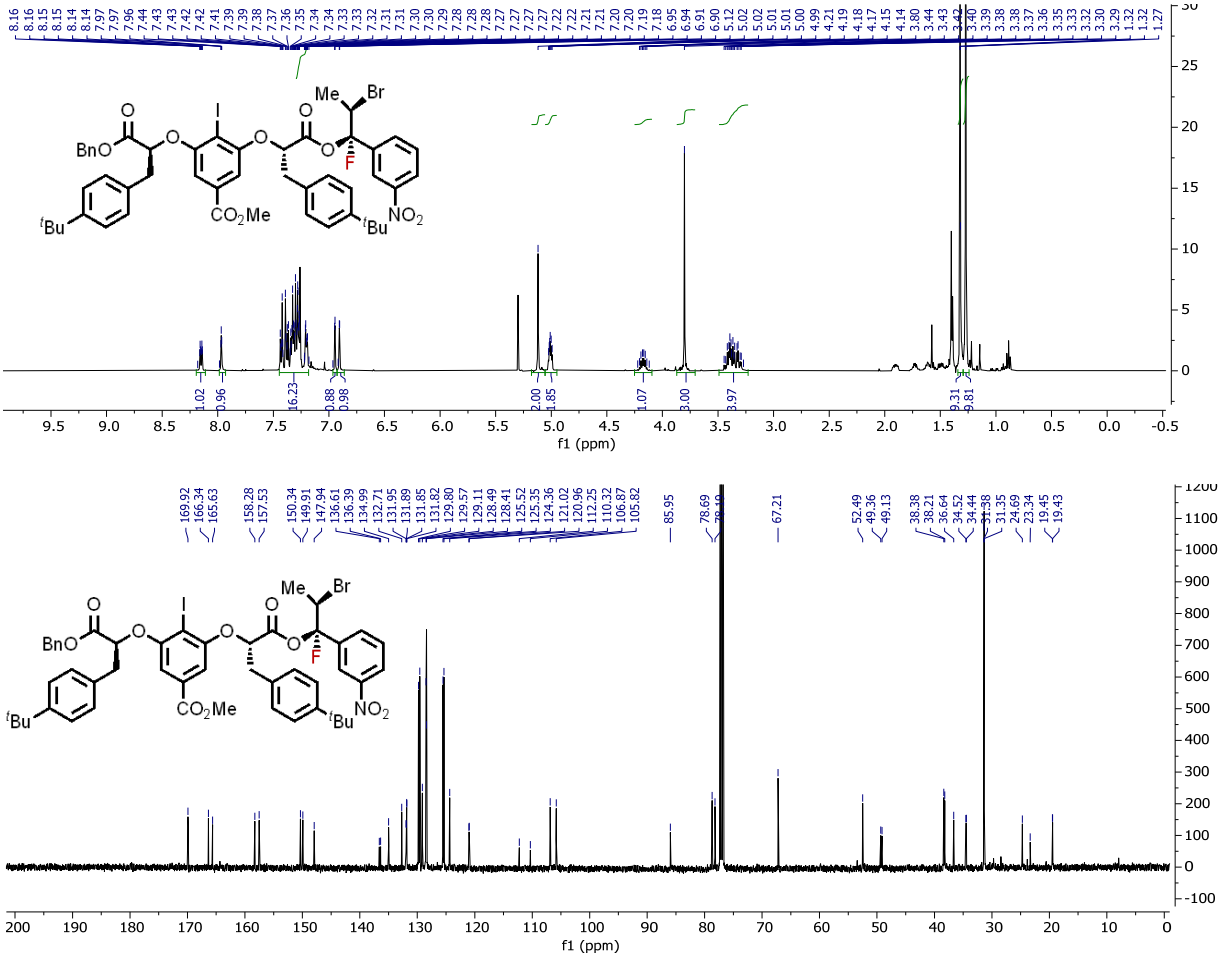


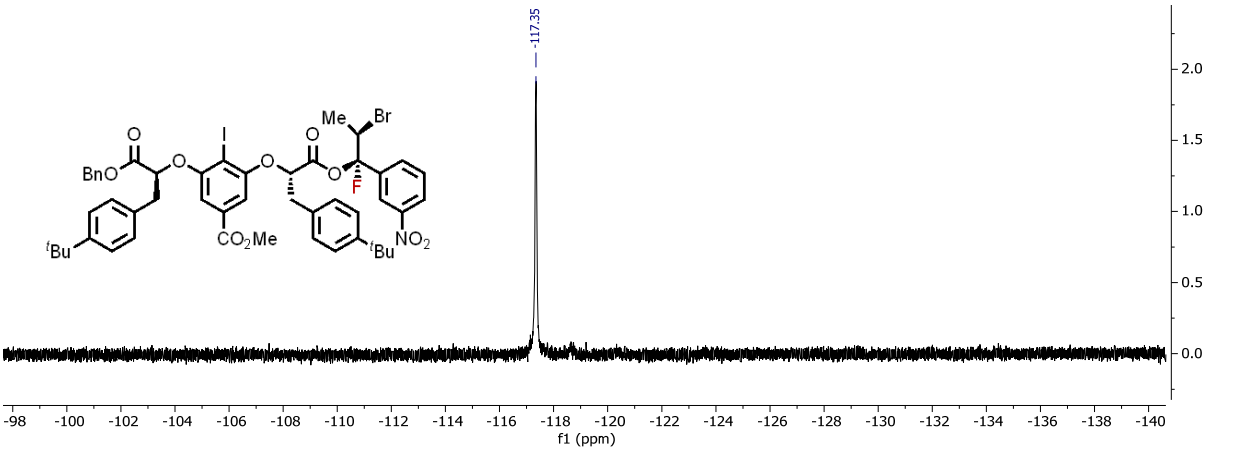
methyl 3-(((S)-1-(benzyloxy)-3-(4-(tert-butyl)phenyl)-1-oxopropan-2-yl)oxy)-5-(((S)-1-((1S,2R)-2-bromo-1-fluoro-1-(3-nitrophenyl)propoxy)-3-(4-(tert-butyl)phenyl)-1-oxopropan-2-yl)oxy)-4-iodobenzoate (**4**)

Isolated from crude reaction mixture as a minor component of the recovered catalyst, purified by repeated chromatography on SiO_2 with Hexanes/Et_2O and Hexanes/DCM. For characterization purposes, a modified reaction protocol was conducted to obtain larger quantities (30 mg, 28% yield):
242 mg substrate
88 mg catalyst
250 mg mCPBA (unpurified)
577 uL pyHF
2.3 mL DCM

Note: Relative stereochemistry of the bromostyrene-derived side-arm was not directly determined and is assigned on the basis of the major product enantiomer.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.15 (dt, *J* = 7.7, 2.2 Hz, 1H), 7.97 (d, *J* = 2.3 Hz, 1H), 7.43 (d, *J* = 8.2 Hz, 2H), 7.38 (d, *J* = 8.1 Hz, 2H), 7.36 – 7.24 (m, 9H), 7.24 – 7.18 (m, 2H), 6.95 (s, 1H), 6.91 (s, 1H), 5.12 (s, 2H), 5.05 – 4.98 (m, 2H), 4.17 (dq, *J* = 13.6, 6.8 Hz, 1H), 3.80 (s, 3H), 3.48 – 3.24 (m, 4H), 1.39 (d, *J* = 5.9 Hz, 3H), 1.32 (s, 9H), 1.27 (s, 9H).
^{19}F NMR (471 MHz, Chloroform-*d*) δ -117.34 (broad s).
^{13}C NMR (126 MHz, Chloroform-*d*) δ 170.05, 166.47, 165.76, 158.41, 157.65, 150.47, 150.04, 148.07, 136.63 (d, *J* = 27.7 Hz), 135.12, 132.84, 132.05 (d, *J* = 7.0 Hz), 131.98, 131.95, 129.92, 129.70, 129.24, 128.62, 128.53, 125.65, 125.48, 124.49, 121.11 (d, *J* = 7.9 Hz), 111.41 (d, *J* = 242.4 Hz), 107.00, 105.94, 86.08, 78.82, 78.32, 67.34, 52.62, 49.37 (d, *J* = 29.0 Hz), 38.51, 38.34, 36.77, 34.65, 34.57, 31.51, 31.48, 19.57 (d, *J* = 3.0 Hz).
HRMS (ESI): for $C_{50}H_{53}BrFINO_{10}$, $[M+H]^+$ calculated *m/z* = 1052.1876 and 154.1856, found *m/z* = 1052.1869 and 1054.1863.





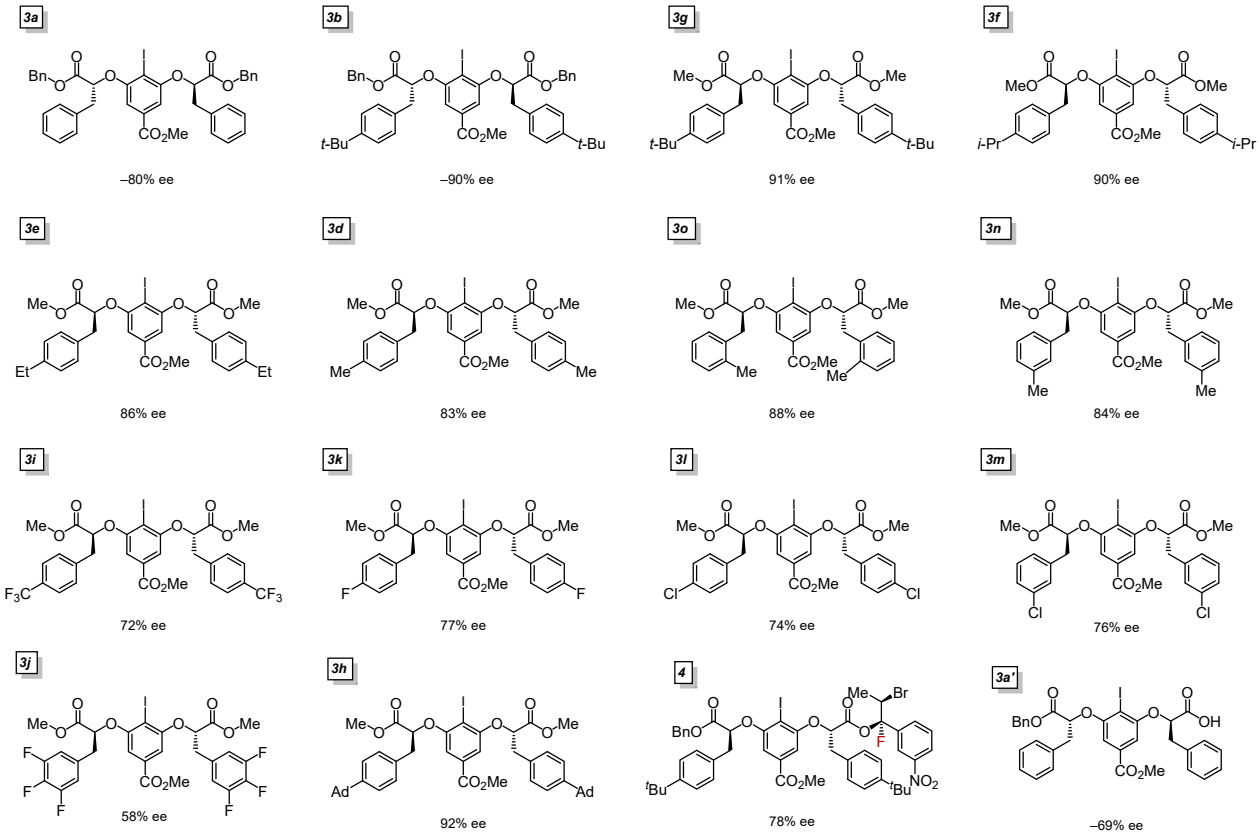
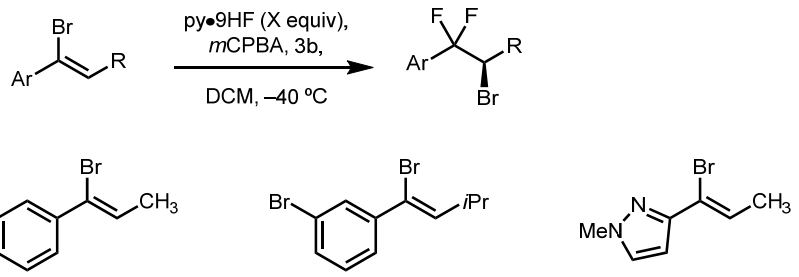
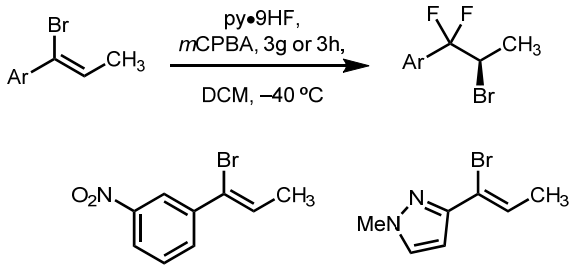


Figure S1. Catalyst structure-activity relationship study. Enantiomeric excesses were obtained using substrate **2a** under the standard conditions (*vide infra*). Methyl-ester-substituted catalysts did not undergo decomposition to iodoarenes analogous to **4**. These catalysts offered lower yields of product **1a** but with comparable enantioselectivities (cf. **3b** vs. **3g**) and were employed in the SAR study due to their simpler preparation.



X equiv	ee (%)	ee (%)	ee (%)
11	92%	70%	63%
5.5	90%		63%
2.2		30%	62%

Figure S2. 9HF·Pyridine loading optimization



catalyst	ee (%)	ee (%)
3g	91%	64%
3h	92%	71%

Figure S3. *Para*-Adamantyl Catalyst Effect

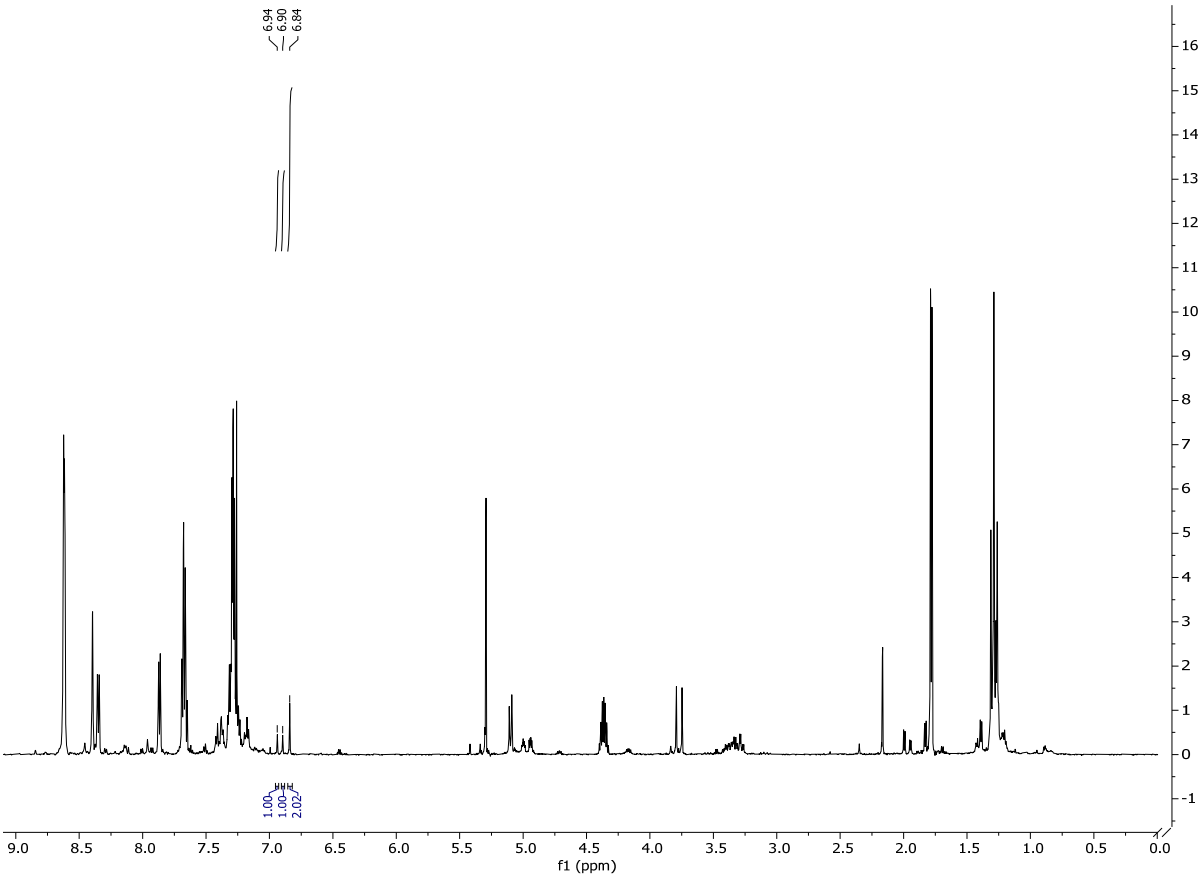


Figure S4. ^{1}H NMR spectrum of crude reaction mixture of fluorination of **2a** catalyzed by **3b** (20 mol%). Catalyst decomposition product **4** resonances can be observed at 6.94 ppm and 6.90 ppm.

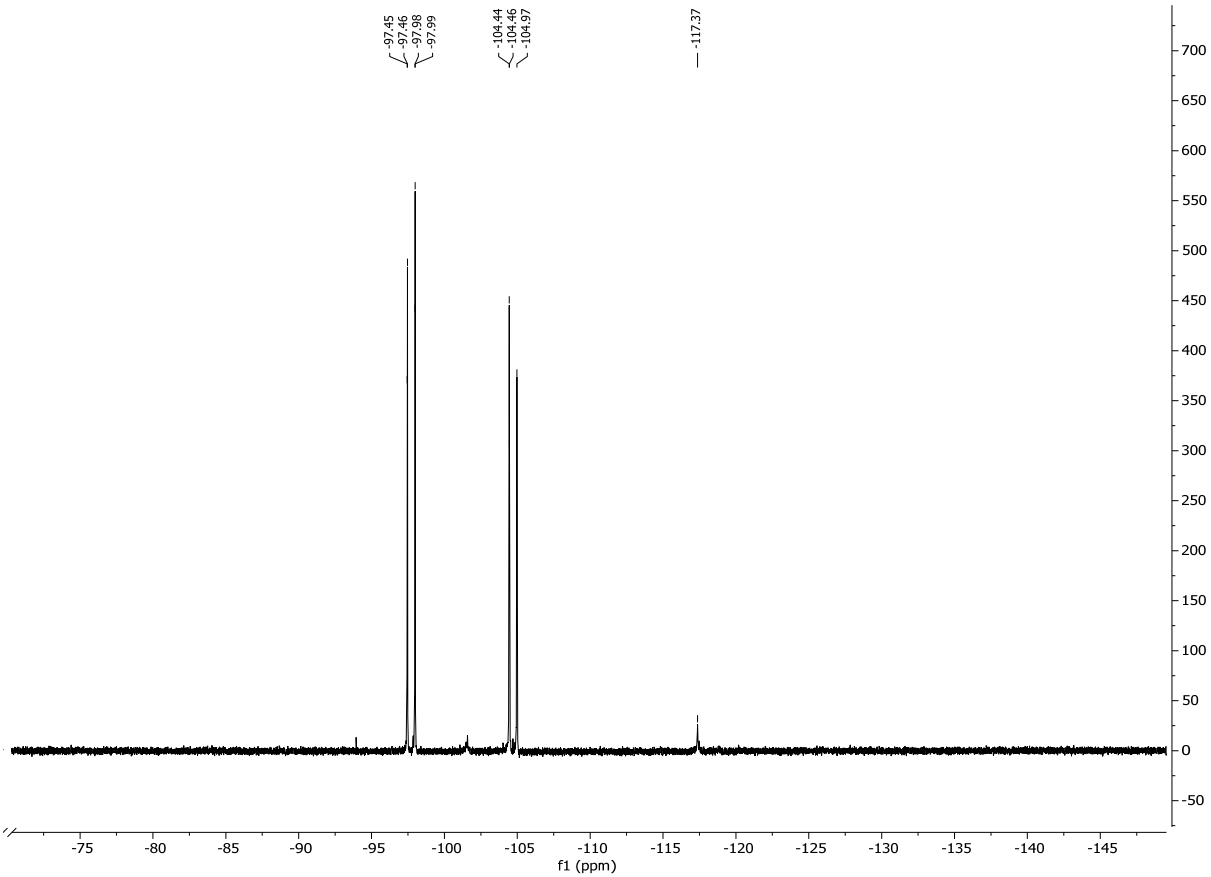


Figure S5. ^{19}F NMR spectrum of crude reaction mixture of fluorination of **2a** catalyzed by **3b** (20 mol%). Catalyst decomposition product **4** resonance can be observed at -117.37 ppm.

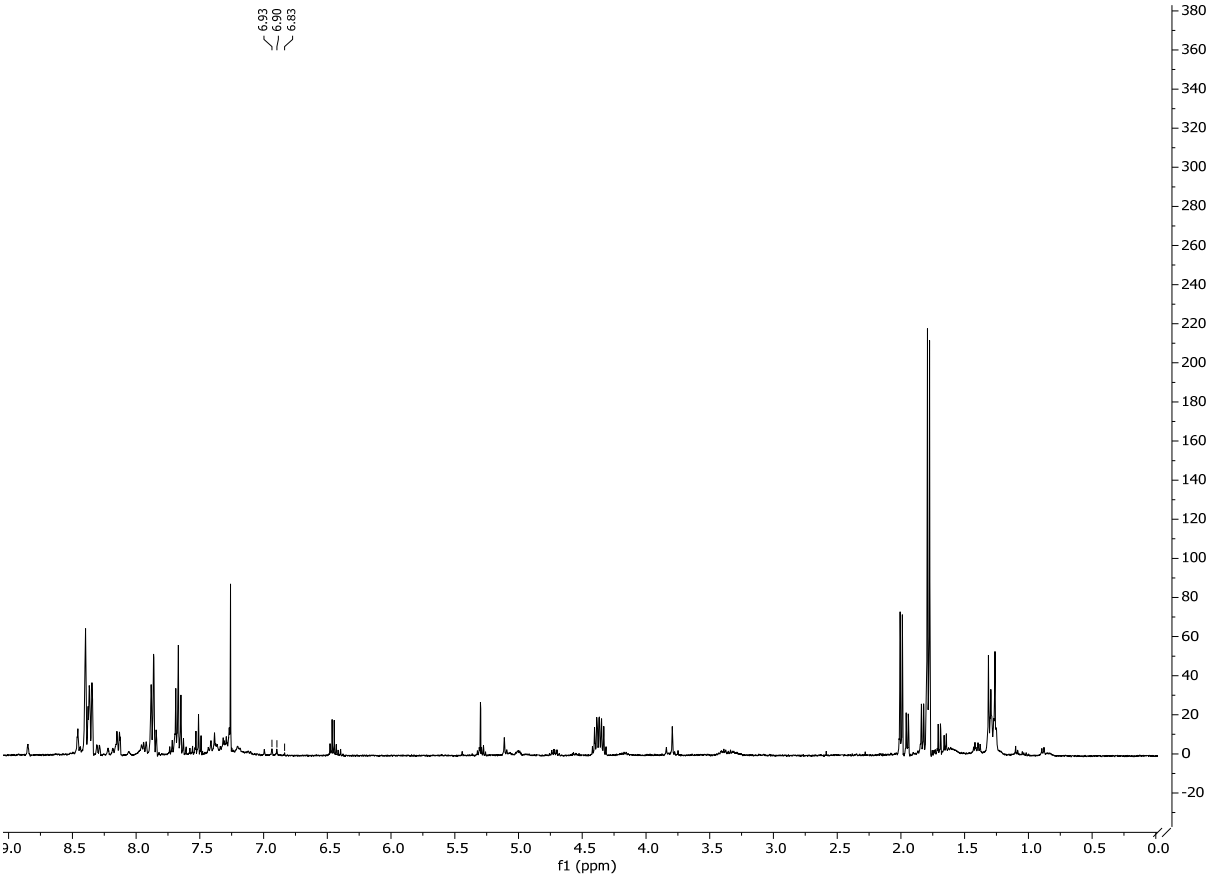


Figure S6. ^{1}H NMR spectrum of crude reaction mixture of fluorination of **2a** catalyzed by **3b** (10 mol%). Catalyst decomposition product's (**4**) diagnostic resonances can be observed at 6.94 ppm and 6.90 ppm. Parent catalyst's (**3b**) diagnostic resonance at 6.83 ppm is barely observable. Significant starting material (~6.45 ppm) remains.

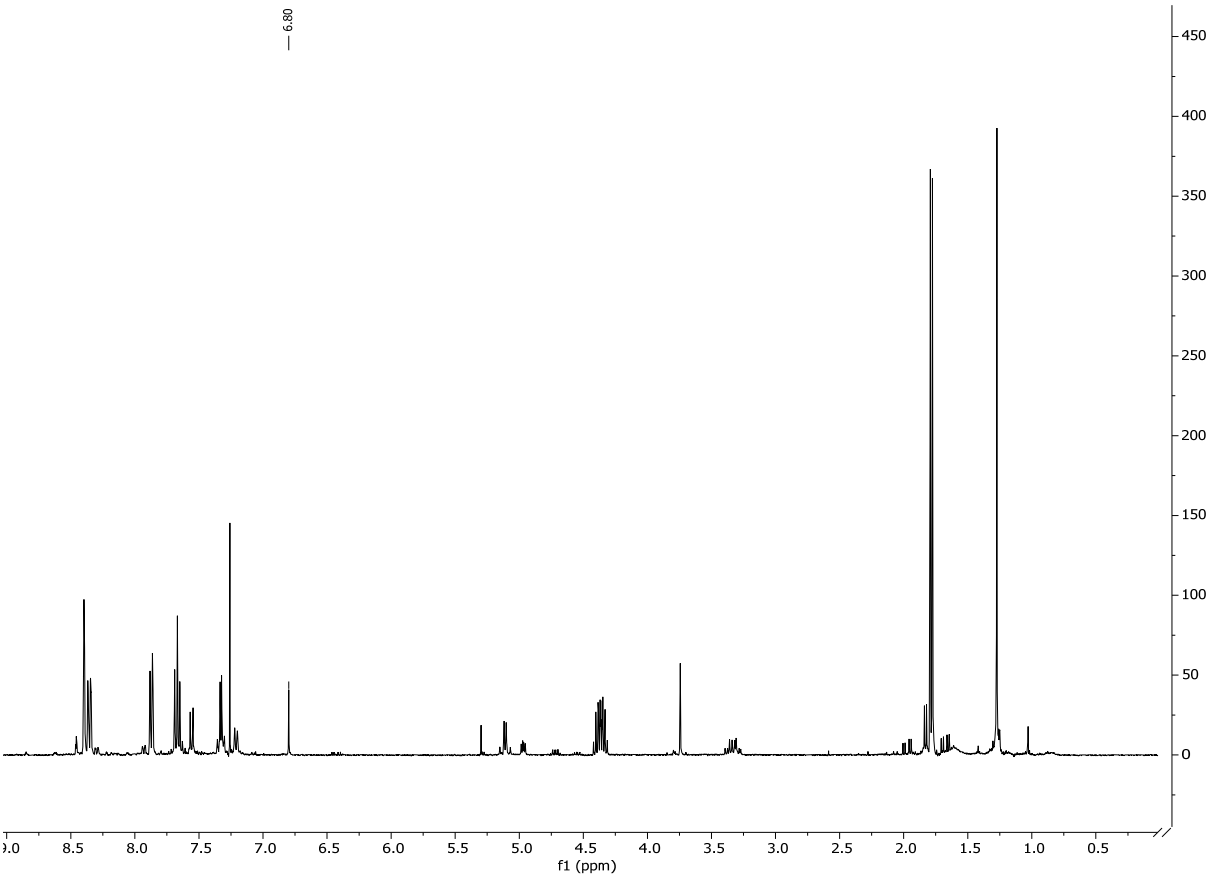


Figure S7. ^{1}H NMR spectrum of crude reaction mixture of fluorination of **2a** catalyzed by **3c** (10 mol%). No catalyst decomposition products analogous to **4** are observed.

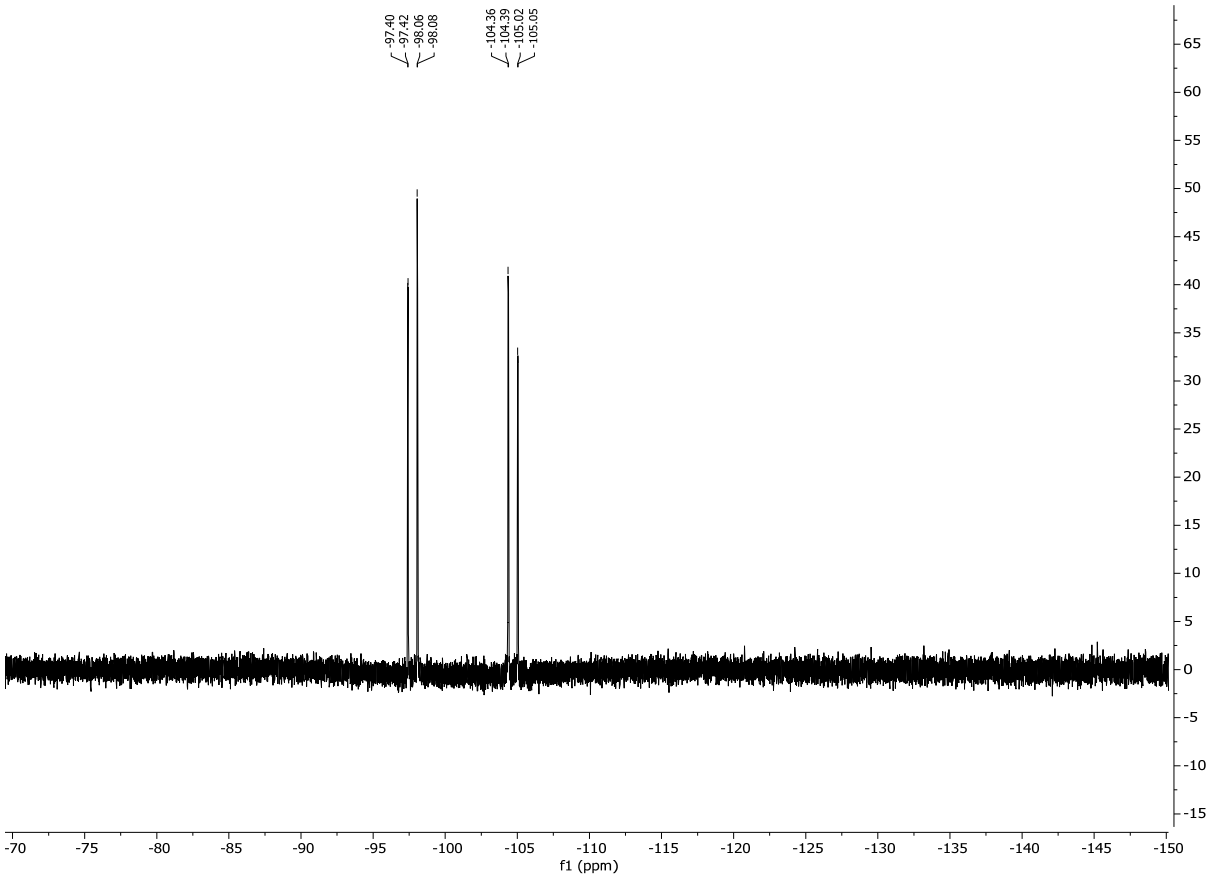
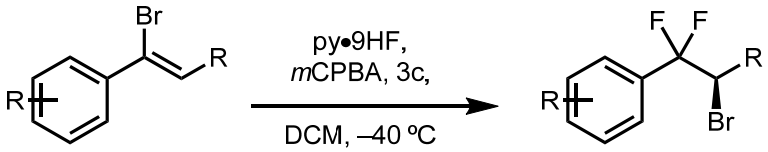


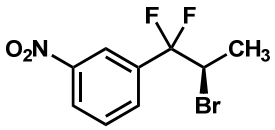
Figure S8. ^{19}F NMR spectrum of crude reaction mixture of fluorination of **2a** catalyzed by **3c** (10 mol%). No catalyst decomposition products analogous to **4** are observed.

General Procedure for Oxidative Rearrangement

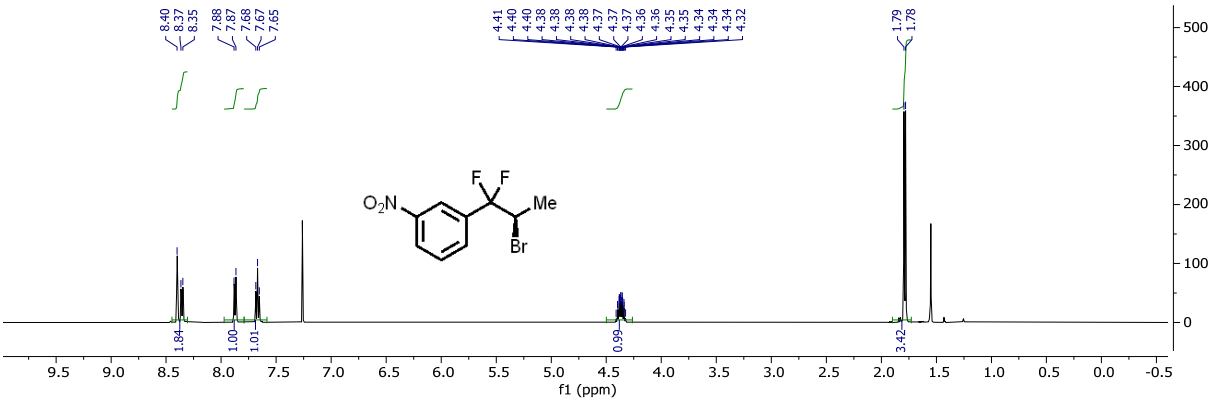


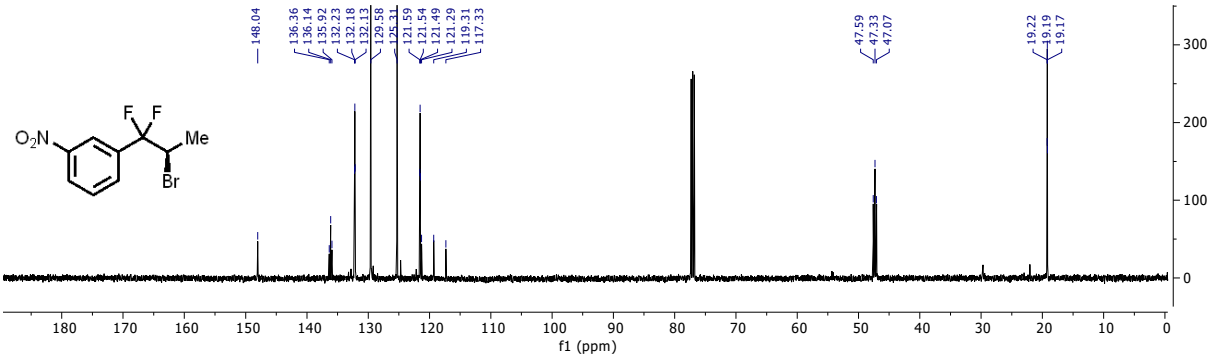
To a solution of substrate (0.2 mmol, 1 equiv) and catalyst **3c** (23 mg, 0.02 mmol, 10 mol%) in dichloromethane (2.3 mL) in a low-density polyethylene tube at –78 ºC was added HF•Pyridine (py•9HF, 70% hydrogen fluoride by weight, 577 µL, 100 equiv hydrogen fluoride) followed by *m*CPBA[6] (41.4 mg, 0.24 mmol, 1.2 equiv). The reaction was warmed to –40 ºC and stirred at that temperature for 48 hours. The heterogeneous mixture was then cooled to –78 ºC and transferred carefully into a vigorously stirred suspension of basic alumina (2.0 g) in dichloromethane at –78 ºC. The resulting suspension was allowed to warm to room temperature and was filtered through addition basic alumina, washing with 10 mL dichloromethane. The combined filtrate was concentrated in vacuo and purified by column chromatography.

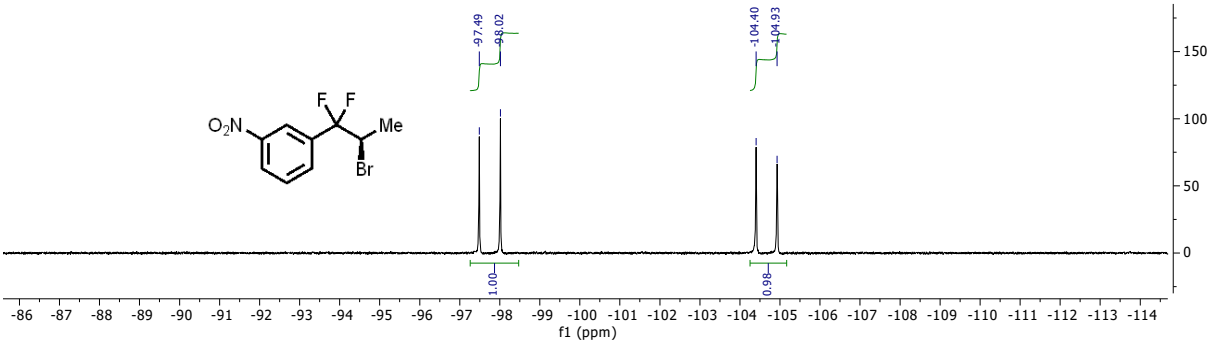
Racemic samples were prepared using the same procedure with the following modification: Iodobenzene or iodotoluene (20 mol%) were used in place of **3c**.

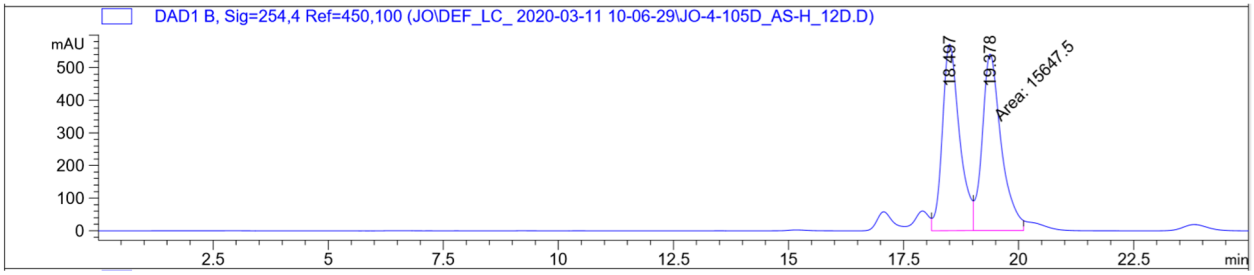


(R)-1-(2-bromo-1,1-difluoropropyl)-3-nitrobenzene. **1a** was prepared from **2a** (48.4 mg, 0.2 mmol) according to the General Procedure as a clear, colorless oil (47.1 mg, 84% yield).
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40 (s, 1H), 8.36 (d, J = 8.5 Hz, 1H), 7.87 (d, J = 8.5 Hz, 1H), 7.67 (t, J = 8.0 Hz, 1H), 4.47 – 4.27 (m, 1H), 1.79 (d, J = 6.9 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 148.04, 136.14 (t, J = 27.8 Hz), 132.18 (t, J = 5.9 Hz), 129.58, 125.31, 121.54 (t, J = 6.5 Hz), 119.31 (dd, J = 248.1, 247.1 Hz), 47.33 (t, J = 32.9 Hz), 19.19 (t, J = 3.1 Hz).
^{19}F NMR (471 MHz, $CDCl_3$) δ -97.75 (d, J = 248.0 Hz, 1F), -104.67 (d, J = 247.7 Hz, 1F).
HRMS (EI): for $C_9H_8BrF_2NO_2$, $[M]^+$ calculated m/z = 278.9701 and 280.9681, found m/z = 278.9700 and 280.9679
Chiral HPLC: Chiralpak AS-H, 1.2% isopropanol/hexanes, 0.5 ml/min; 92% ee



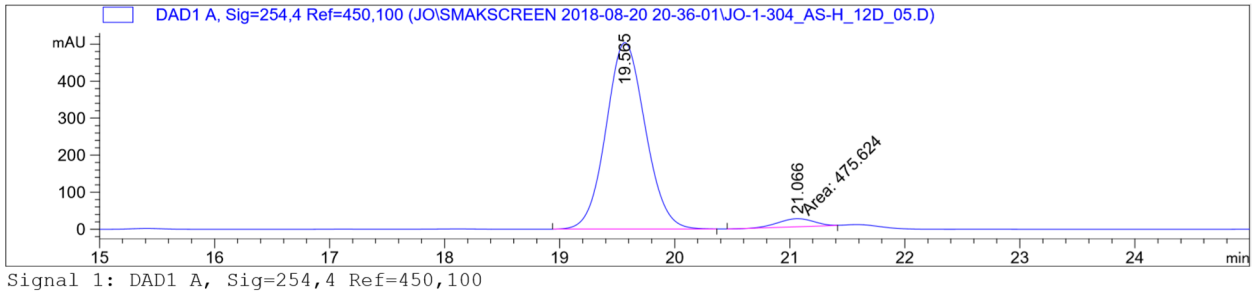






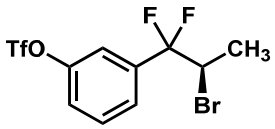
Signal 2: DAD1 B, Sig=254,4 Ref=450,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.497	VV	0.3886	1.49371e4	572.08466	48.8385
2	19.378	MF	0.4814	1.56475e4	541.74280	51.1615



Signal 1: DAD1 A, Sig=254,4 Ref=450,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.565	BB	0.3692	1.19785e4	504.06793	96.1810
2	21.066	MM	0.3614	475.62350	21.93228	3.8190



(R)-3-(2-bromo-1,1-difluoropropyl)phenyl trifluoromethanesulfonate. **1b** was prepared from **2b** (69.0 mg, 0.2 mmol) according to the General Procedure as a clear, colorless oil (62.1 mg, 81% yield).

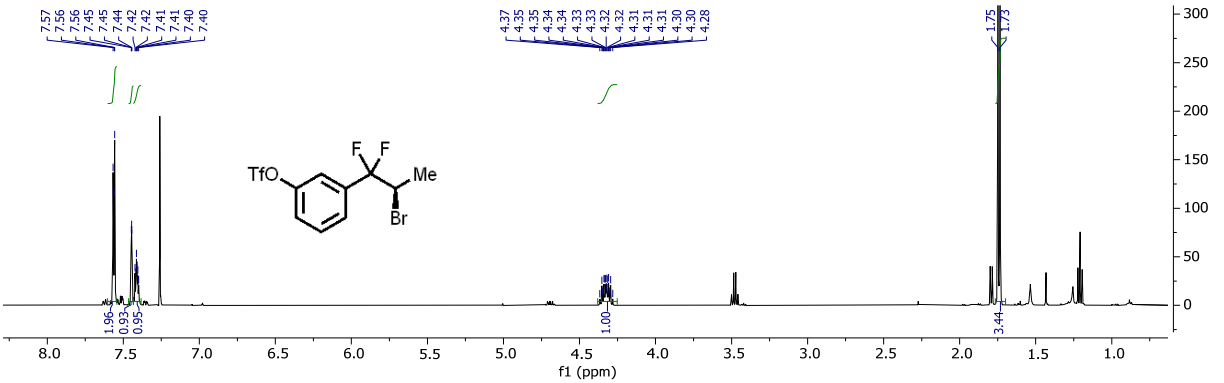
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 – 7.55 (m, 2H), 7.46 – 7.43 (m, 1H), 7.43 – 7.38 (m, 1H), 4.37 – 4.27 (m, 1H), 1.74 (d, J = 6.9 Hz, 3H).

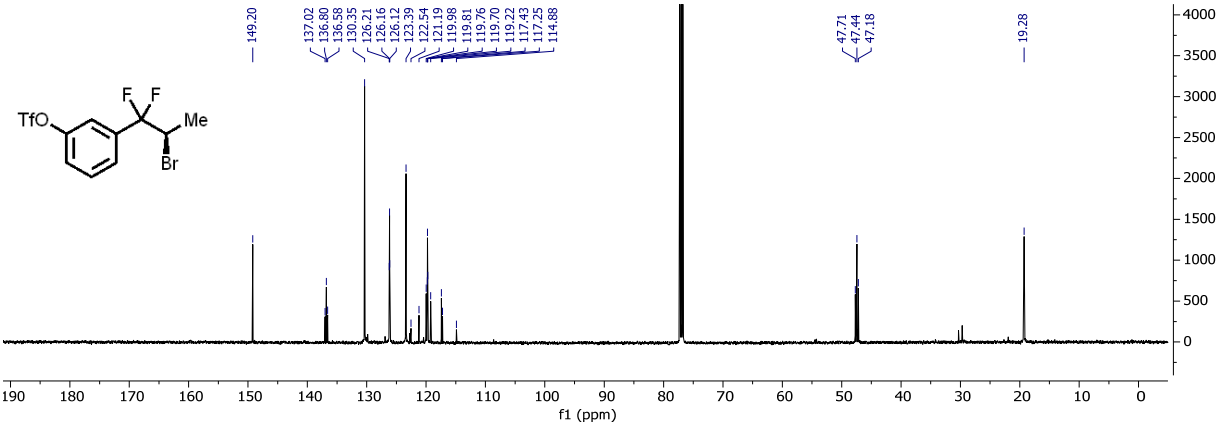
^{13}C NMR (126 MHz, $CDCl_3$) δ 149.20, 136.80 (t, J = 27.7 Hz), 130.35, 126.16 (t, J = 6.0 Hz), 123.39, 119.75 (t, J = 6.5 Hz), 119.22 (t, J = 249.7 Hz), 118.71 (q, J = 321.3 Hz) 47.44 (t, J = 32.8 Hz), 19.28 (t, J = 3.1 Hz).

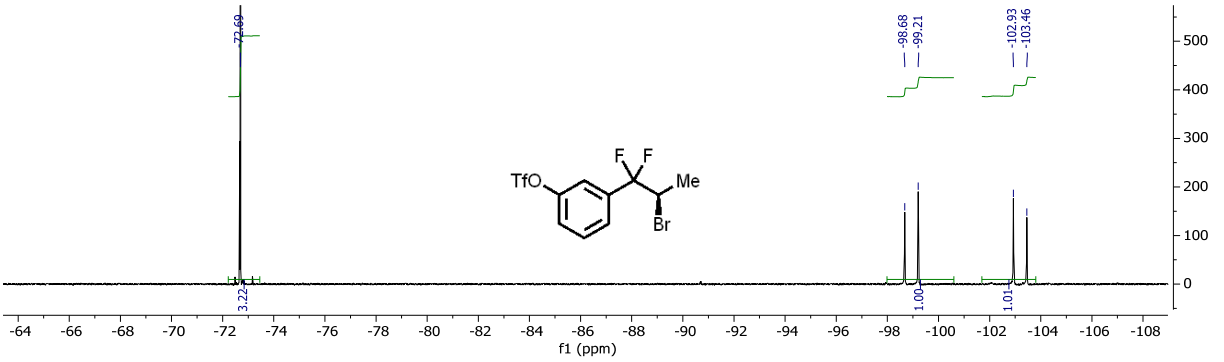
^{19}F NMR (471 MHz, $CDCl_3$) δ -72.69 (s, 3F), -98.94 (d, J = 247.2 Hz, 1F), -103.19 (d, J = 247.0 Hz, 1F).

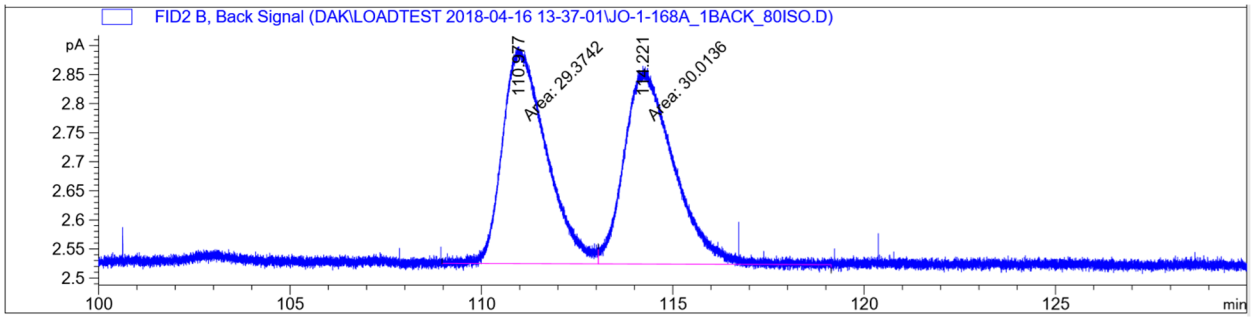
HRMS (EI): for $C_{10}H_8BrF_5O_3S$, $[M]^+$ calculated m/z = 381.9292 and 383.9272, found m/z = 381.9292 and 383.9270

Chiral GC: CP-Chirasil-Dex CB, isothermal, 14 psi, 79% ee

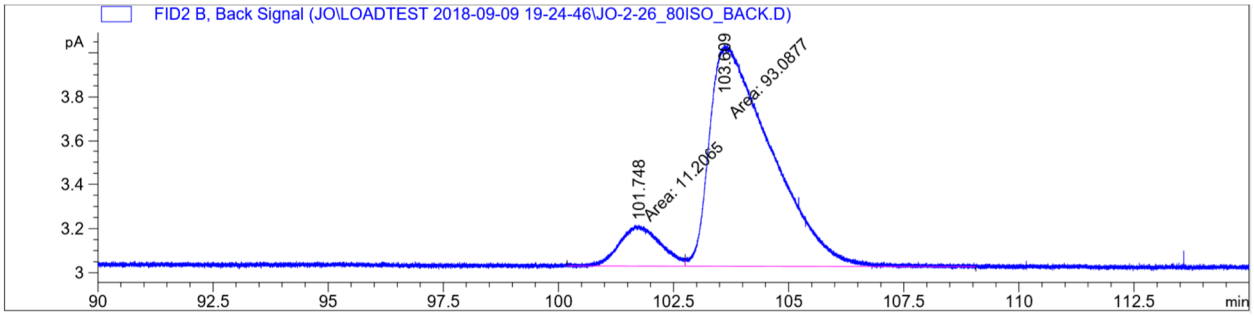




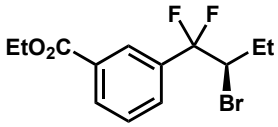




Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	110.977	MF	1.3230	29.37420	3.70059e-1	49.46166
2	114.221	FM	1.4870	30.01362	3.36397e-1	50.53834



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	101.748	MF	0.9944	11.20647	1.87827e-1	10.74506
2	103.609	FM	1.5406	93.08765	1.00703	89.25494



(R)-ethyl 3-(2-bromo-1,1-difluorobutyl)benzoate. **1c** was prepared from **2c** (56.6 mg, 0.2 mmol) according to the General Procedure as a clear, colorless oil (50.1 mg, 78% yield).

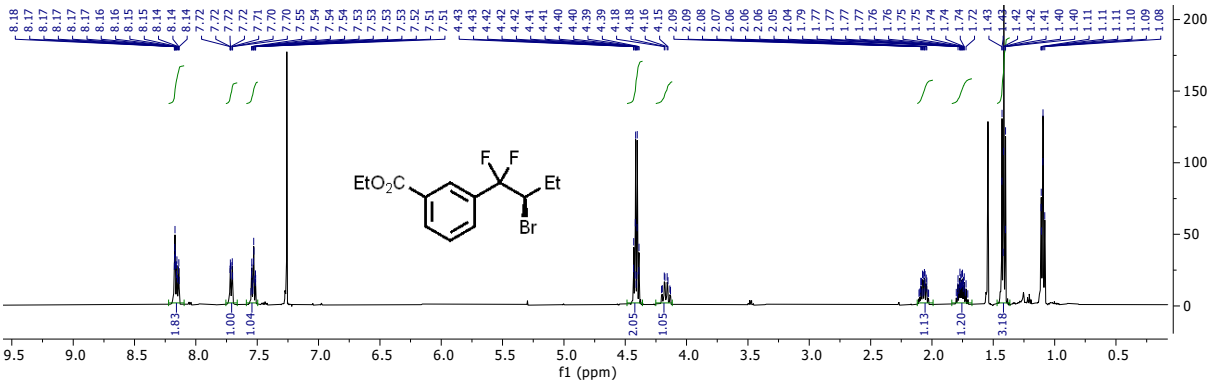
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 – 8.16 (m, 1H), 8.15 (dt, *J* = 7.5, 1.3 Hz, 1H), 7.74 – 7.68 (m, 1H), 7.53 (ddt, *J* = 7.8, 7.0, 0.8 Hz, 1H), 4.41 (q, *J* = 7.2 Hz, 2H), 4.17 (qd, *J* = 11.0, 2.8 Hz, 1H), 2.12 – 2.02 (m, 1H), 1.82 – 1.69 (m, 1H), 1.42 (td, *J* = 7.1, 0.8 Hz, 3H), 1.14 – 1.05 (m, 3H).

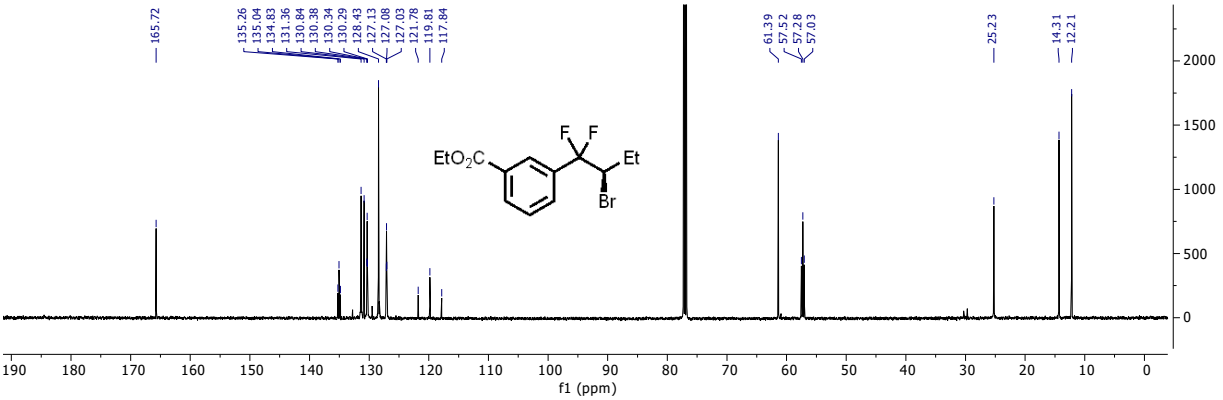
^{13}C NMR (126 MHz, $CDCl_3$) δ 165.72, 135.04 (t, *J* = 26.9 Hz), 131.36, 130.84, 130.34 (t, *J* = 6.0 Hz), 128.43, 127.08 (t, *J* = 6.3 Hz), 119.81 (t, *J* = 247.5 Hz), 61.39, 57.28 (t, *J* = 31.2 Hz), 25.23, 14.31, 12.21.

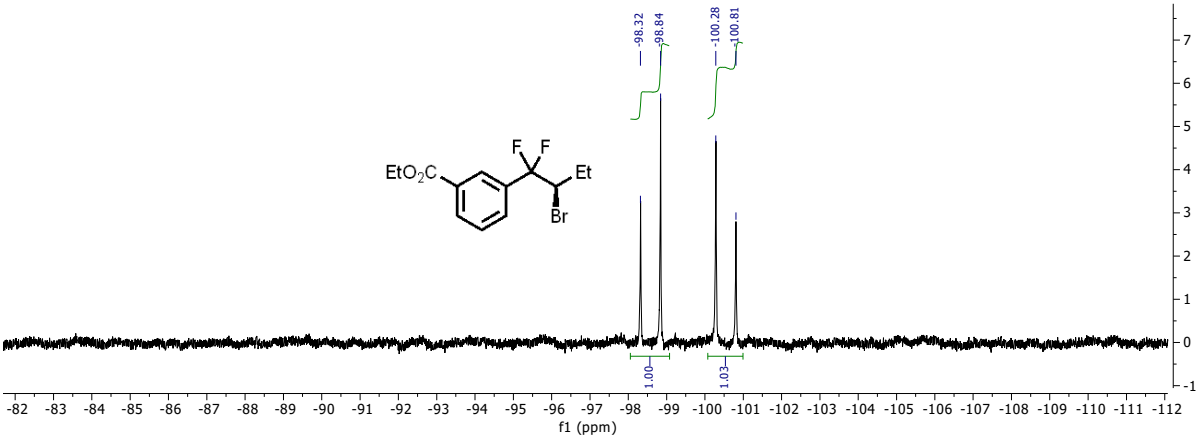
^{19}F NMR (471 MHz, $CDCl_3$) δ -98.58 (d, *J* = 246.1 Hz, 1F), -100.55 (d, *J* = 246.8 Hz, 1F).

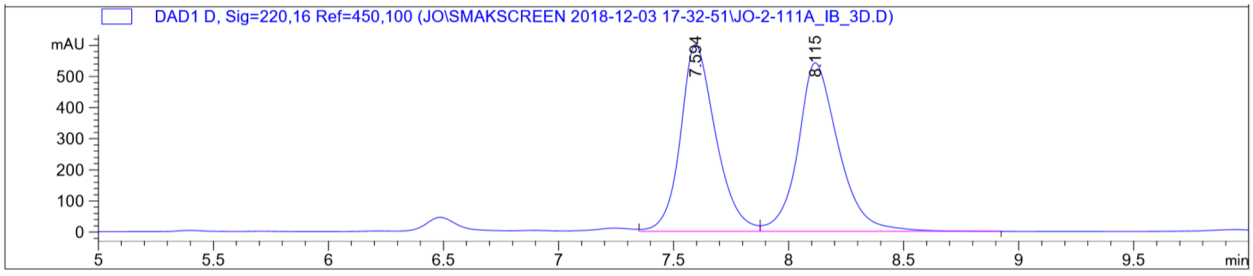
HRMS (ESI): for $C_{13}H_{16}BrF_2O_2$, $[M+H]^+$ calculated *m/z* = 321.0296 and 323.0276, found *m/z* = 321.0297 and 323.0276.

Chiral HPLC: Chiralpak IB, 0.3% isopropanol/hexanes, 1.0 ml/min, 89% ee



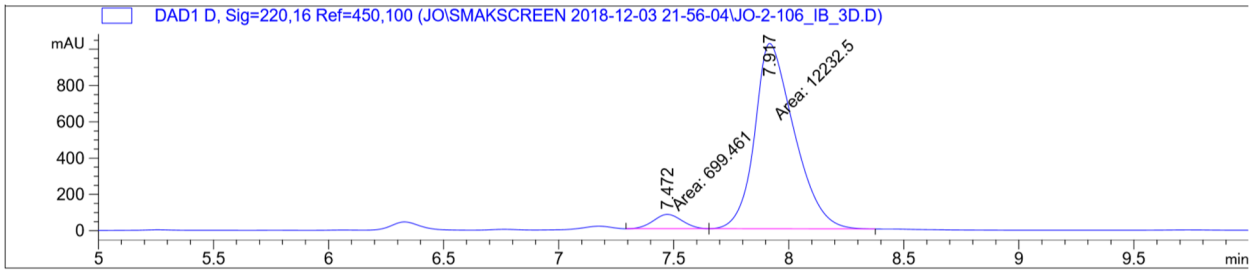






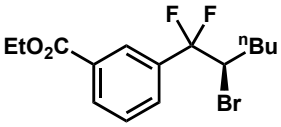
Signal 4: DAD1 D, Sig=220,16 Ref=450,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.594	VV	0.1602	6404.74365	601.51660	49.0355
2	8.115	VB	0.1813	6656.68994	542.09308	50.9645



Signal 4: DAD1 D, Sig=220,16 Ref=450,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.472	MF	0.1461	699.46063	79.77899	5.4088
2	7.917	FM	0.1993	1.22325e4	1023.16272	94.5912



(R)-ethyl 3-(2-bromo-1,1-difluorohexyl)benzoate. **1d** was prepared from **2d** (62.2 mg, 0.2 mmol) according to the General Procedure as a clear, colorless oil (58.7 mg, 84% yield).

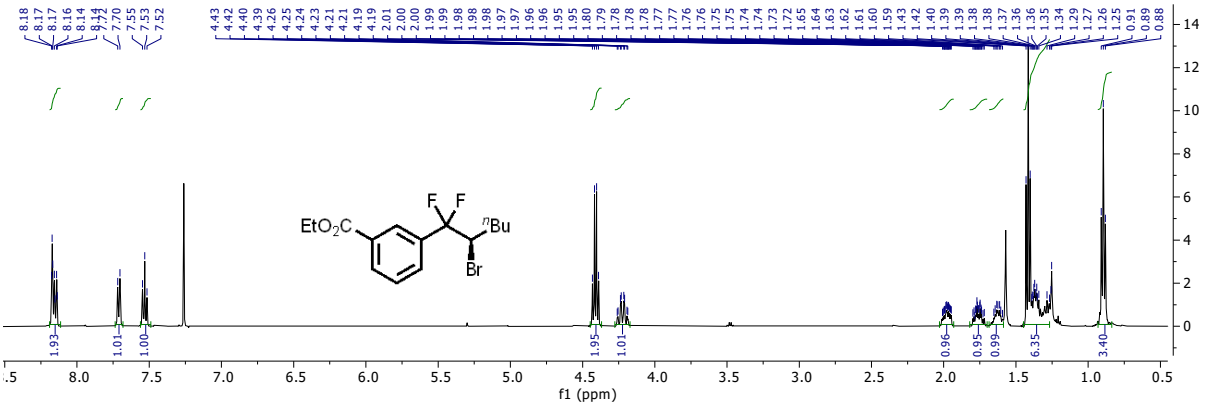
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (s, 1H), 8.15 (d, J = 7.9 Hz, 2H), 7.71 (d, J = 7.7 Hz, 1H), 7.53 (t, J = 7.8 Hz, 2H), 4.41 (q, J = 7.1 Hz, 3H), 4.22 (qd, J = 11.2, 2.8 Hz, 2H), 2.04 – 1.93 (m, 1H), 1.76 (dddd, J = 14.2, 11.0, 9.5, 4.5 Hz, 1H), 1.62 (tt, J = 9.9, 5.4 Hz, 1H), 1.42 (t, J = 7.1 Hz, 3H), 1.39 – 1.21 (m, 4H), 0.89 (t, J = 7.2 Hz, 3H).

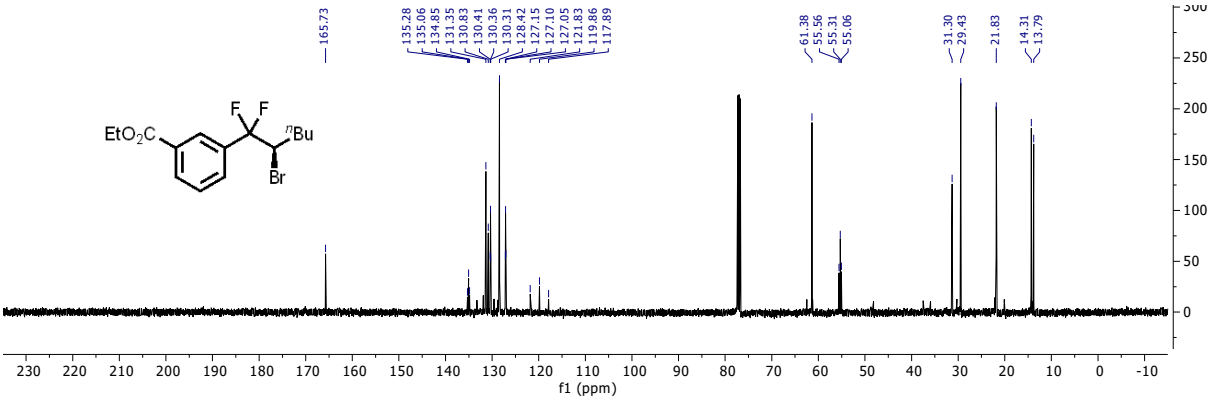
^{13}C NMR (126 MHz, $CDCl_3$) δ 165.73, 135.06 (t, J = 26.9 Hz), 131.35, 130.83, 130.36 (t, J = 6.0 Hz), 128.42, 127.10 (t, J = 6.3 Hz), 119.86 (t, J = 247.6 Hz), 61.38, 55.31 (t, J = 31.4 Hz), 31.30, 29.43, 21.83, 14.31, 13.79.

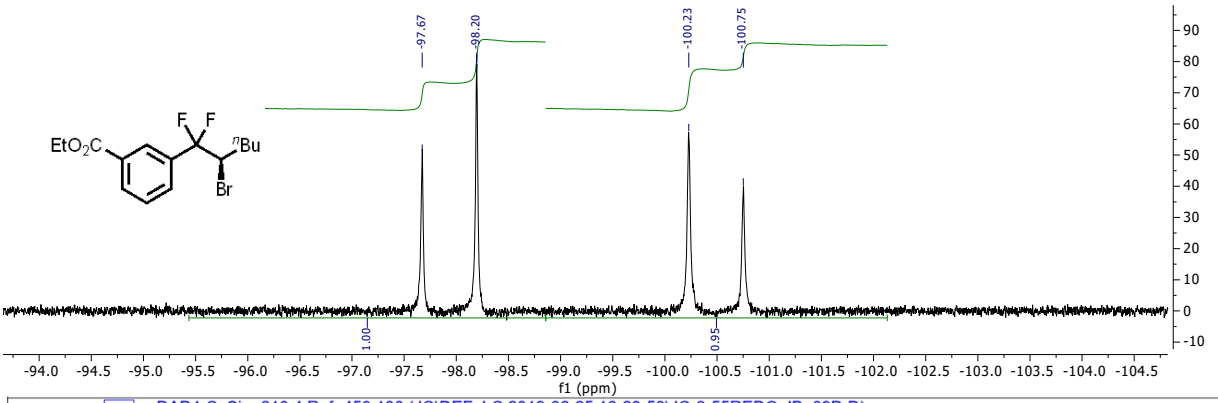
^{19}F NMR (471 MHz, $CDCl_3$) δ -97.93 (d, J = 246.3 Hz, 1F), -100.49 (d, J = 246.2 Hz, 1F).

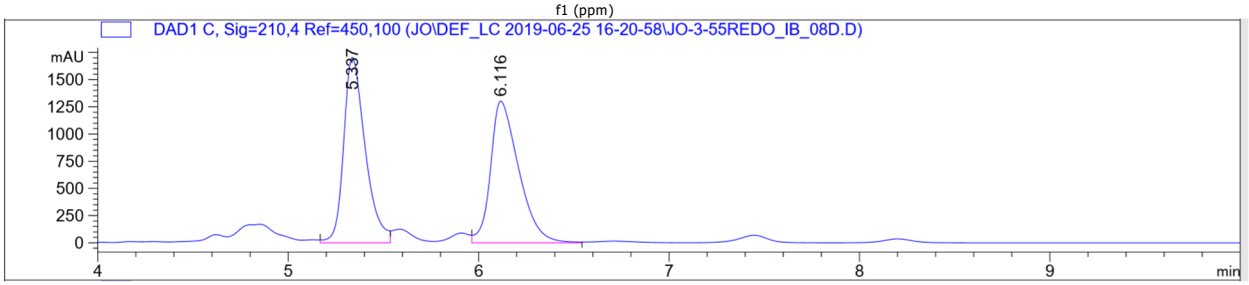
HRMS (ESI): for $C_{15}H_{20}BrF_2O_2$, $[M+H]^+$ calculated m/z = 349.0609 and 351.0589, found m/z = 349.0608 and 351.0587.

Chiral HPLC: Chiralpak IB, 0.8% isopropanol/hexanes, 1.0 ml/min, 82% ee



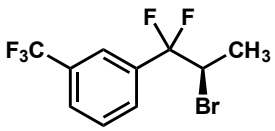






Signal 3: DAD1 C, Sig=210,4 Ref=450,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.337	VV	0.1199	1.34405e4	1705.81982	50.0102
2	6.116	VV	0.1562	1.34350e4	1303.77161	49.9898



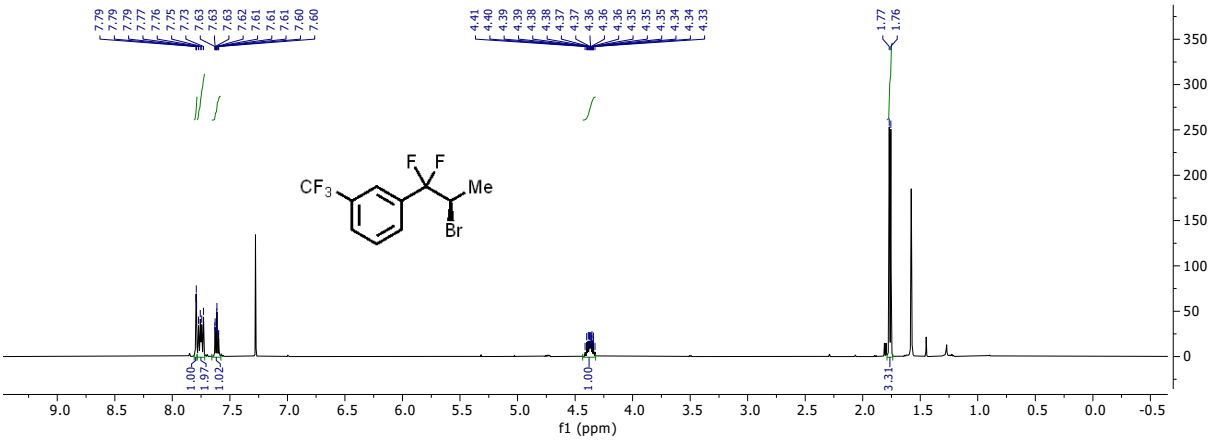
(R)-1-(2-bromo-1,1-difluoropropyl)-3-(trifluoromethyl)benzene. **1e** was prepared from **2e** (53.0 mg, 0.2 mmol) according to the General Procedure as a clear, colorless oil (36.4 mg, 60% yield).

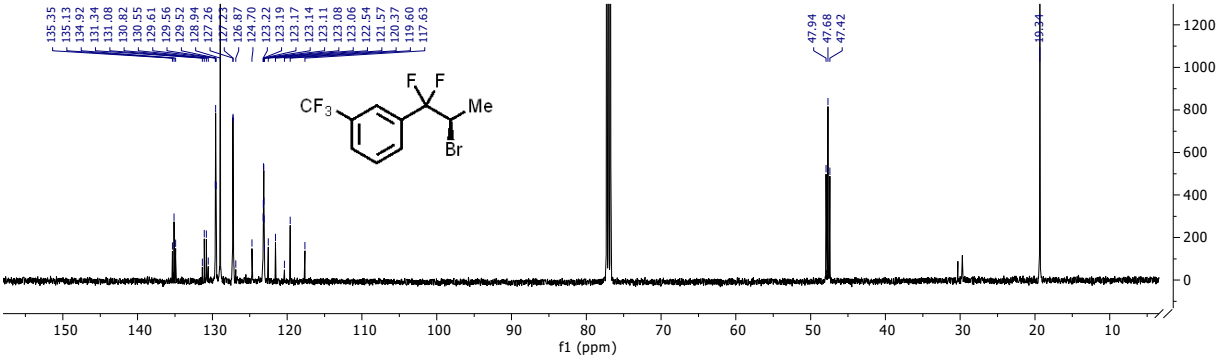
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 – 7.72 (m, 3H), 7.64 – 7.59 (m, 1H), 4.42 – 4.31 (m, 1H), 1.76 (d, J = 6.9 Hz, 3H).

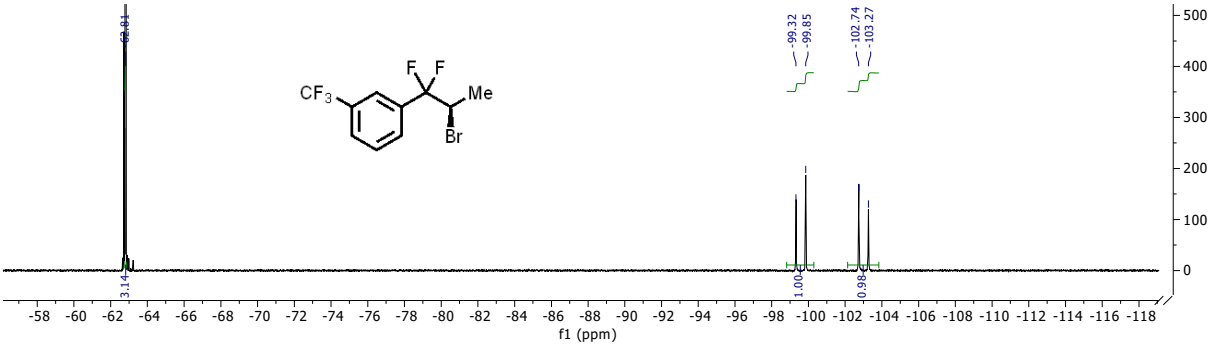
^{13}C NMR (126 MHz, $CDCl_3$) δ 135.13 (t, J = 27.2 Hz), 130.95 (q, J = 33.1 Hz), 129.56 (t, J = 6.1 Hz), 128.94, 127.24 (d, J = 4.1 Hz), 124.70 (q, J = 272.7, 271.2 Hz), 123.14 (tt, J = 7.2, 3.6 Hz), 119.80 (dd, J = 249.0, 248.4 Hz), 47.68 (t, J = 32.9 Hz), 19.34.

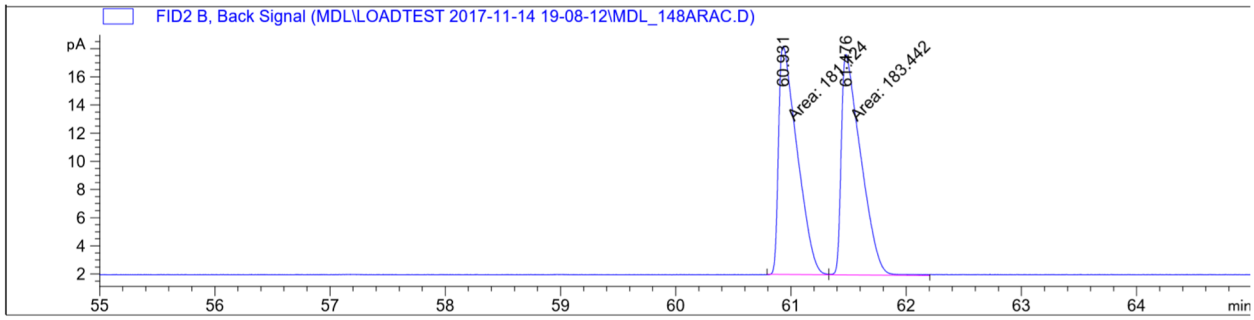
^{19}F NMR (471 MHz, $CDCl_3$) δ -62.81 (s, 3F), -99.59 (d, J = 247.5 Hz, 1F), -103.00 (d, J = 247.9 Hz, 1F).

^{19}F NMR (471 MHz, Chloroform-*d*) δ -62.81, -99.59 (d, *J* = 247.5 Hz), -103.00 (d, *J* = 247.9 Hz).
HRMS (EI): for $C_{10}H_8BrF_5$, $[M]^+$ calculated *m/z* = 301.9724 and 303.9704, found *m/z* = 301.9722 and 303.9700
Chiral GC: CP-Chirasil-Dex CB, 40 °C to 110 °C, 1 °C/min, 7 psi, 80% ee

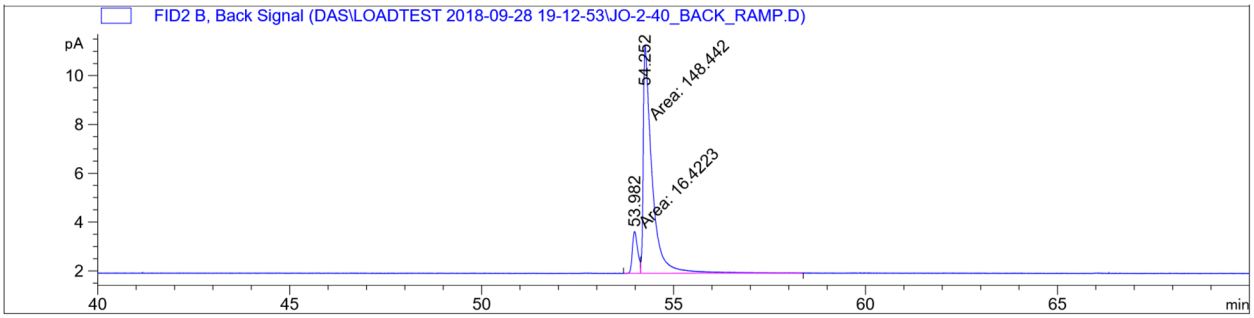




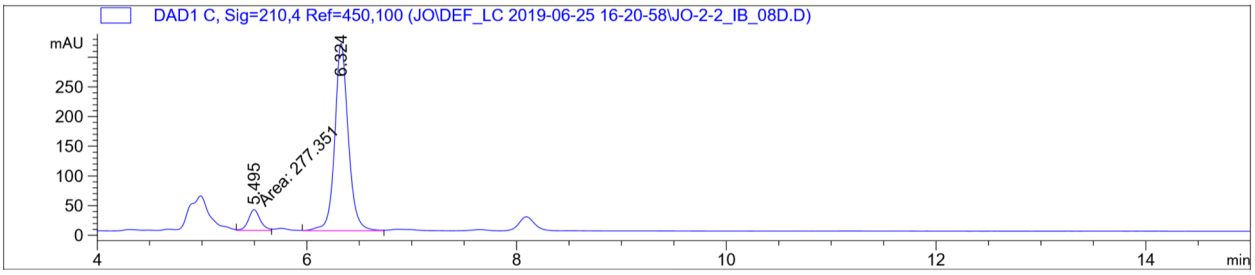




Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	60.931	MF	0.1863	181.12358	16.20064	49.68198
2	61.476	FM	0.1954	183.44238	15.64308	50.31802

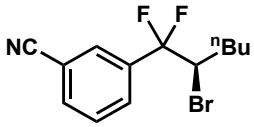


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	53.982	MF	0.1600	16.42233	1.71062	9.96114
2	54.252	FM	0.2651	148.44154	9.33304	90.03886



Signal 3: DAD1 C, Sig=210,4 Ref=450,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.495	MM	0.1316	277.35074	35.13698	8.9031
2	6.324	VB	0.1328	2837.85522	315.79031	91.0969



(R)-3-(2-bromo-1,1-difluorohexyl)benzonitrile. **1f** was prepared from **2f** (52.8 mg, 0.2 mmol) according the General Procedure as a clear, colorless oil (39.3 mg, 65% yield).

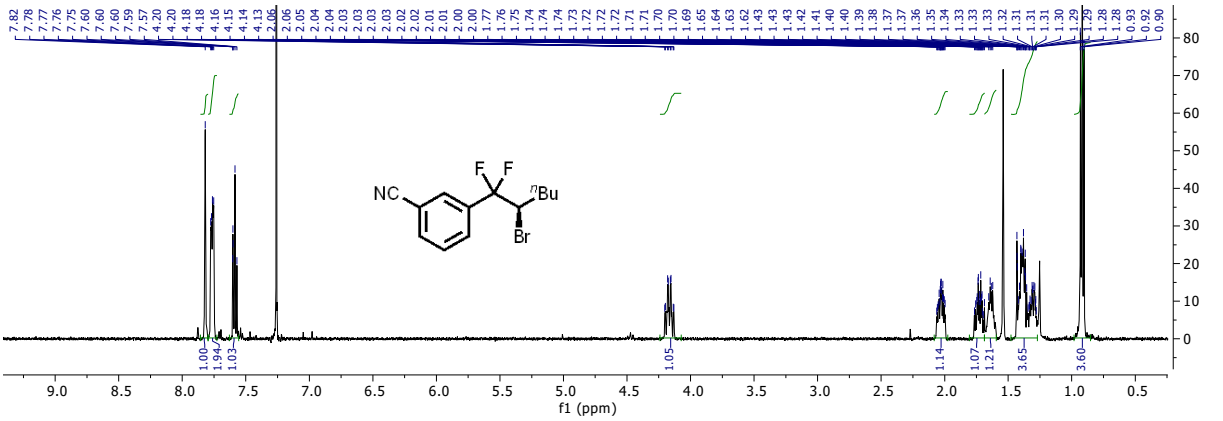
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.80 – 7.73 (m, 2H), 7.61 – 7.56 (m, 1H), 4.17 (qd, J = 11.1, 2.7 Hz, 1H), 2.08 – 1.97 (m, 1H), 1.78 – 1.58 (m, 2H), 1.47 – 1.27 (m, 3H), 0.92 (t, J = 7.2 Hz, 3H).

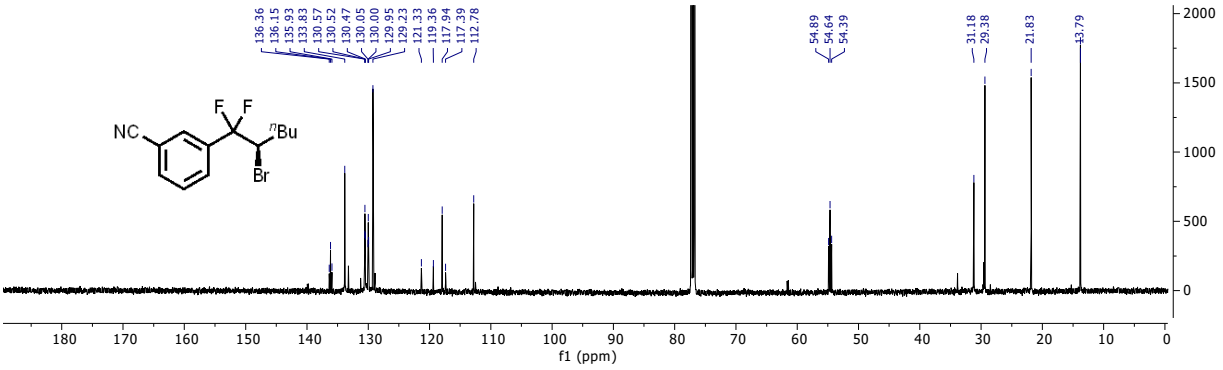
^{13}C NMR (126 MHz, $CDCl_3$) δ 136.15 (t, J = 27.5 Hz), 133.83, 130.52 (t, J = 6.1 Hz), 130.00 (t, J = 6.4 Hz), 129.23, 119.36 (t, J = 248.9 Hz), 117.94, 112.78, 54.64 (t, J = 31.5 Hz), 31.18, 29.38, 21.83, 13.79.

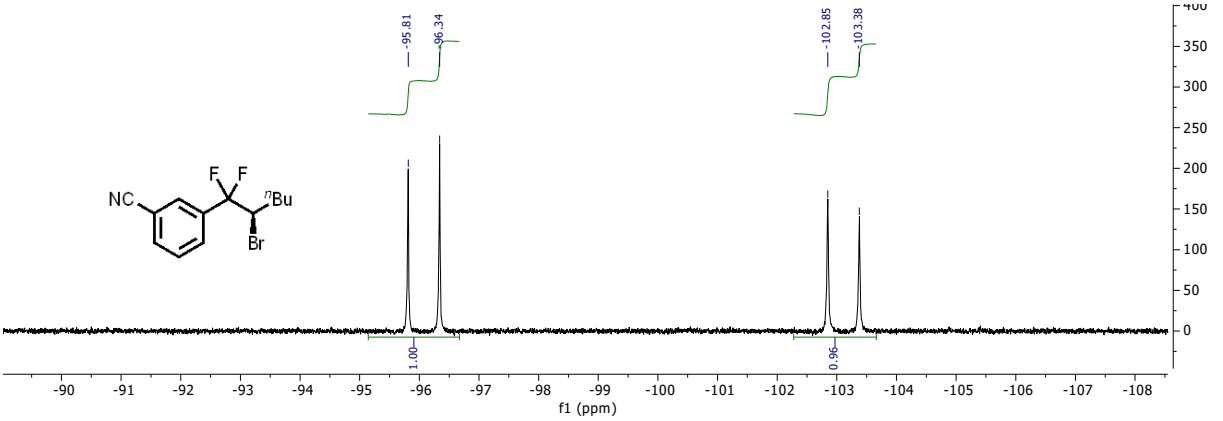
^{19}F NMR (471 MHz, $CDCl_3$) δ -96.08 (d, J = 248.2 Hz, 1F), -103.11 (d, J = 248.6 Hz, 1F).

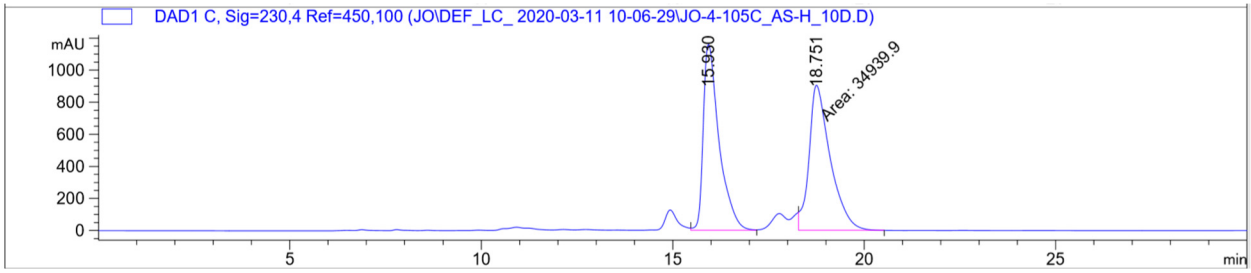
HRMS (ESI): for $C_{13}H_{15}BrF_2N$, $[M+H]^+$ calculated m/z = 302.0350 and 304.0330, found m/z = 302.0348 and 304.0327

Chiral HPLC: Chiralpak AS-H, 1.0% isopropanol/hexanes, 1.0 ml/min, 81% ee



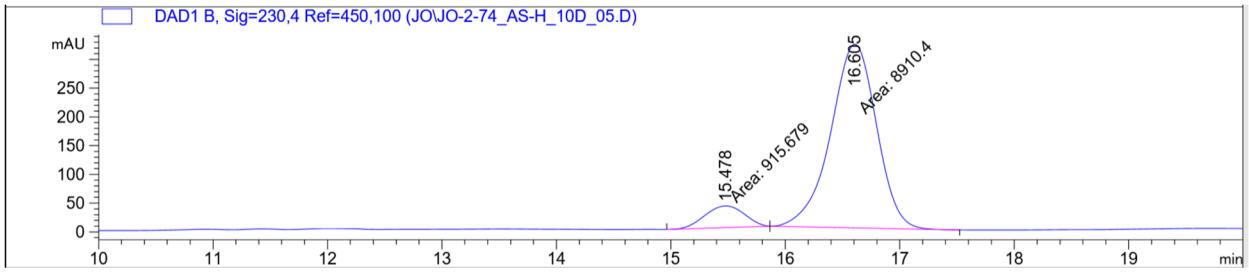






Signal 3: DAD1 C, Sig=230,4 Ref=450,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.930	VB	0.4262	3.33953e4	1159.01672	48.8698
2	18.751	FM	0.6433	3.49399e4	905.23975	51.1302



Signal 2: DAD1 B, Sig=230,4 Ref=450,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.478	MM	0.4028	915.67865	37.89011	9.3189
2	16.605	MM	0.4645	8910.40430	319.69379	90.6811

(R)-1-bromo-3-(2-bromo-1,1-difluorobutyl)benzene. **1g** was prepared from **2g** (58.0 mg, 0.2 mmol) according to the General Procedure as a clear, colorless oil (34.1 mg, 52% yield).

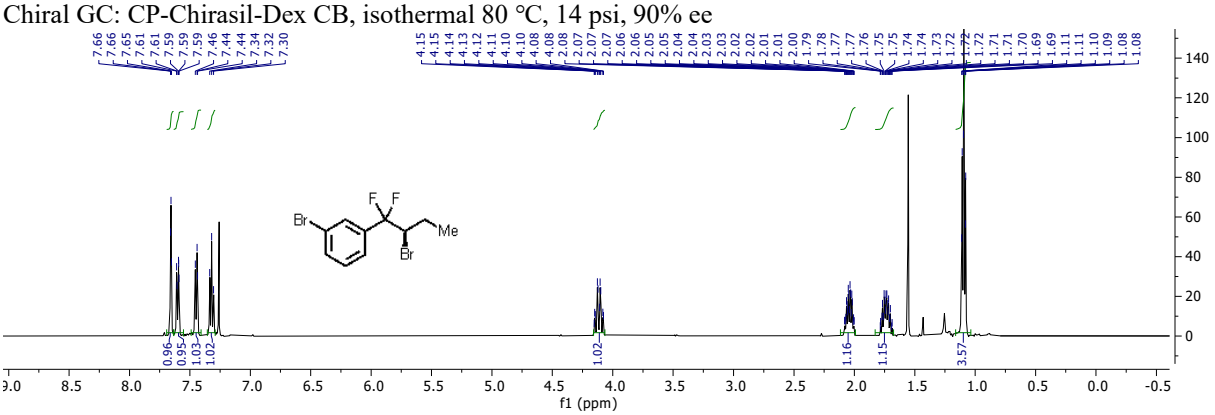
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (t, J = 1.9 Hz, 1H), 7.60 (dd, J = 7.8, 2.0 Hz, 1H), 7.45 (d, J = 7.6 Hz, 1H), 7.32 (t, J = 7.9 Hz, 1H), 4.11 (qd, J = 11.2, 2.7 Hz, 1H), 2.18 – 1.95 (m, 1H), 1.83 – 1.66 (m, 1H), 1.09 (td, J = 7.4, 1.7 Hz, 3H).

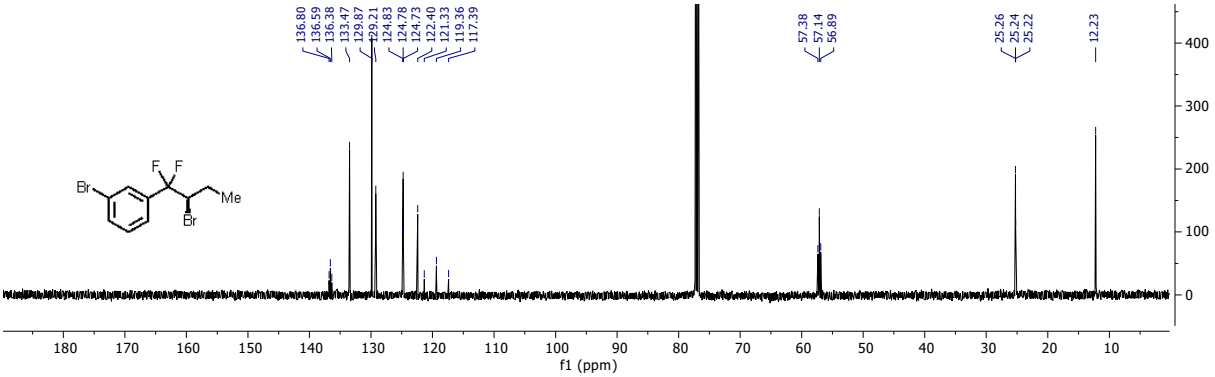
^{13}C NMR (126 MHz, $CDCl_3$) δ 136.59 (t, J = 27.0 Hz), 133.47, 129.87, 129.21, 124.78 (t, J = 6.2 Hz), 122.40, 119.36 (t, J = 247.9 Hz), 57.14 (t, J = 31.1 Hz), 25.24 (t, J = 2.5 Hz), 12.23.

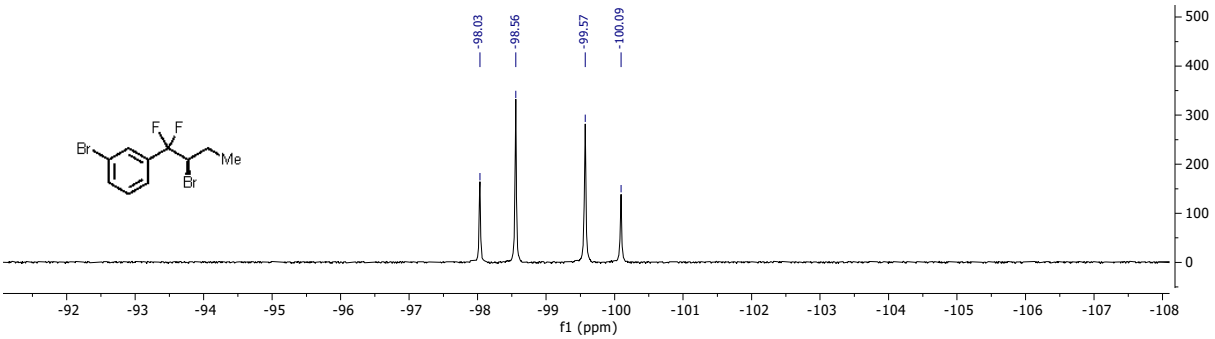
^{19}F NMR (471 MHz, $CDCl_3$) δ -98.29 (d, J = 246.3 Hz), -99.83 (d, J = 246.3 Hz).

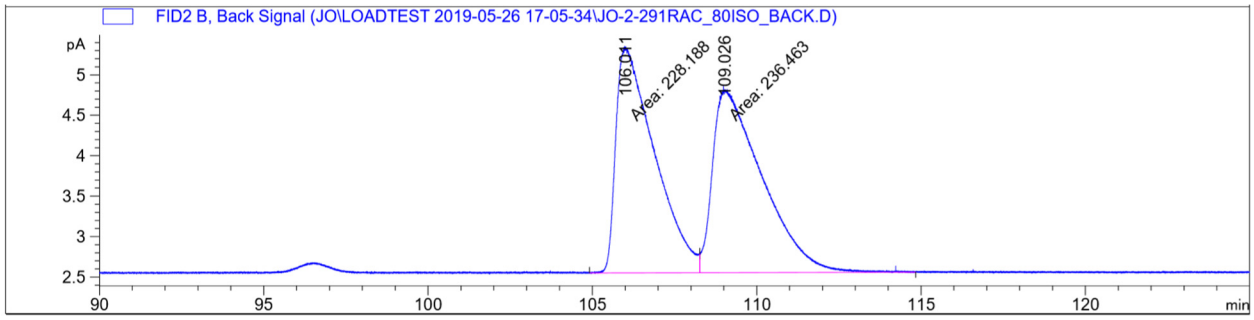
HRMS (EI): for $C_{10}H_{10}Br_2F_2$, $[M]^+$ calculated m/z = 325.9112 and 327.9091 and 329.9071, found m/z = 325.9109 and 327.9087 and 329.9066

Chiral GC: CP-Chirasil-Dex CB, isothermal 80 °C, 14 psi, 90% ee

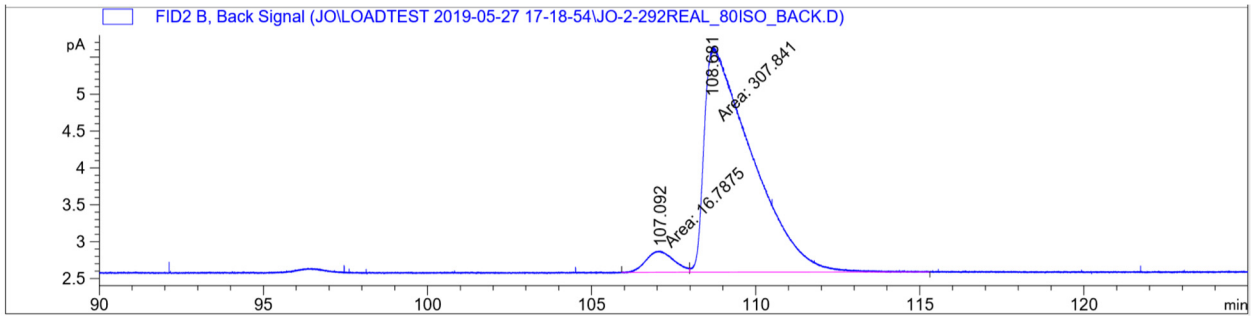




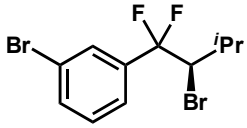




Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	106.011	MF	1.3621	228.18791	2.79211	49.10953
2	109.026	FM	1.7397	236.46307	2.26531	50.89047



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	107.092	MF	0.9568	16.78749	2.92438e-1	5.17130
2	108.681	FM	1.6785	307.84058	3.05676	94.82870

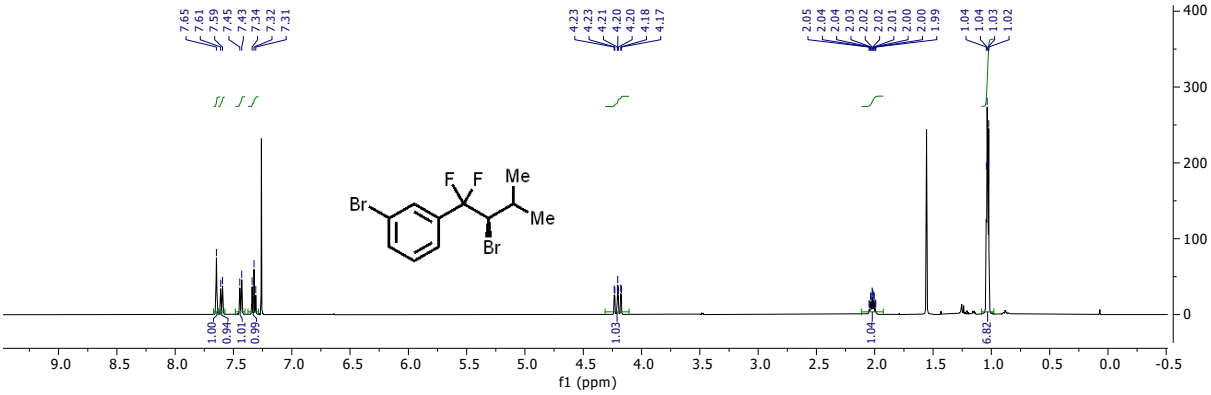


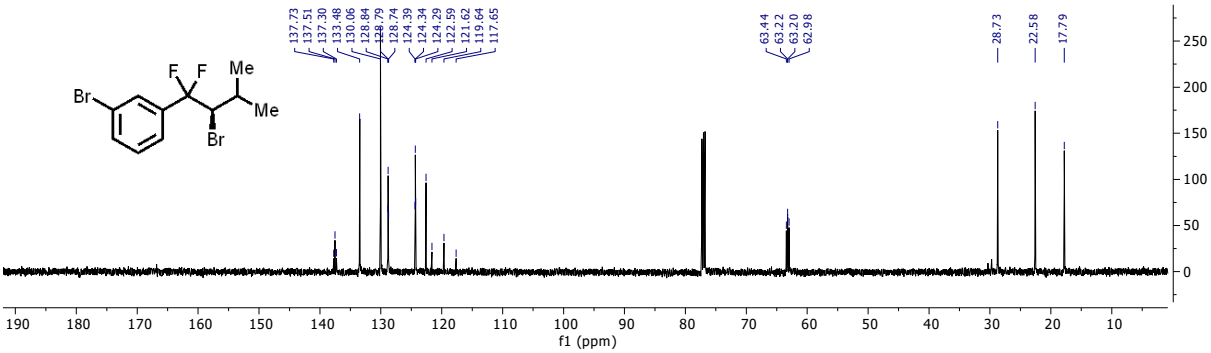
(R)-1-bromo-3-(2-bromo-1,1-difluoro-3-methylbutyl)benzene. **1h** was prepared from **2h** (60.8 mg, 0.2 mmol) according to General Procedure A as a clear, colorless oil (49.9 mg, 73% yield).

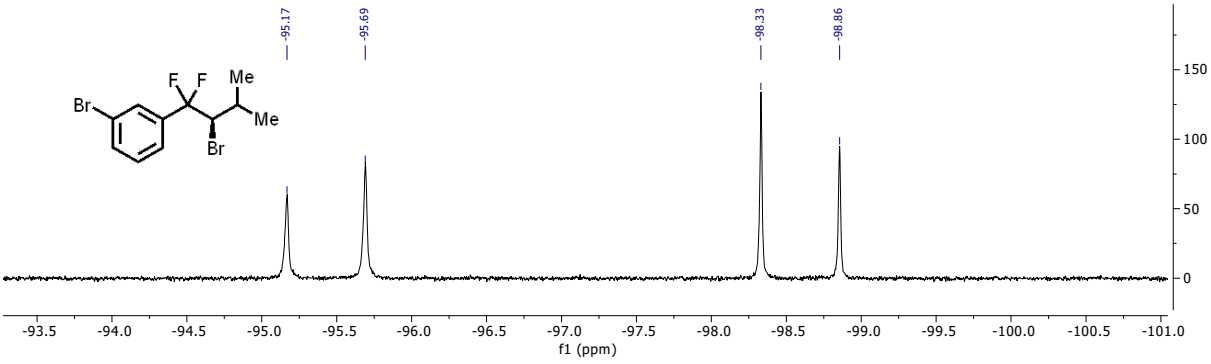
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (s, 1H), 7.60 (d, J = 8.0 Hz, 1H), 7.44 (d, J = 7.8 Hz, 1H), 7.32 (t, J = 7.9 Hz, 1H), 4.20 (ddd, J = 15.3, 13.3, 2.3 Hz, 1H), 2.02 (pd, J = 6.5, 2.2 Hz, 1H), 1.03 (dd, J = 6.6, 3.5 Hz, 6H).

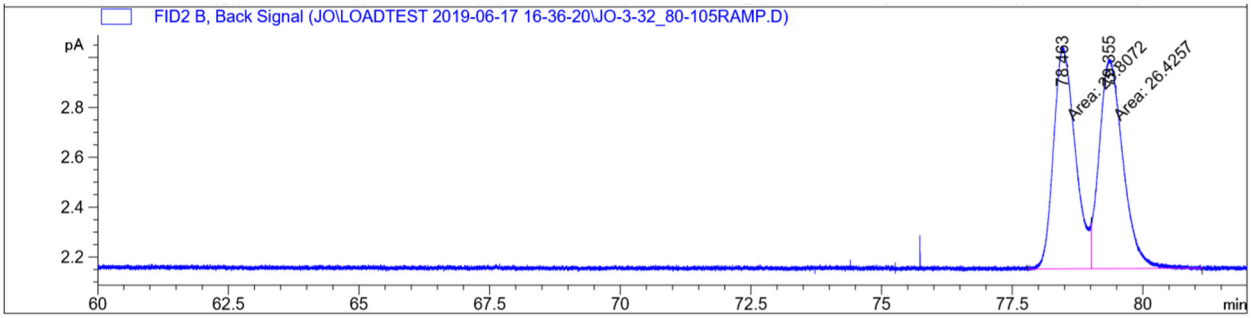
^{13}C NMR (126 MHz, $CDCl_3$) δ 137.51 (t, J = 27.0 Hz), 133.48, 130.06, 128.79 (t, J = 6.5 Hz), 124.34 (t, J = 6.0 Hz), 122.59, 119.64 (t, J = 249.0 Hz), 63.21 (dd, J = 29.9, 27.6 Hz), 28.73, 22.58, 17.79.

^{19}F NMR (471 MHz, $CDCl_3$) δ -95.43 (d, J = 245.7 Hz), -98.59 (d, J = 247.1 Hz).
HRMS (EI): for $C_{11}H_{12}Br_2F_2$, $[M]^+$ calculated m/z = 339.9268 and 341.9248 and 343.9227, found m/z = 339.9261 and 341.9240 and 343.9219
Chiral GC: CP-Chirasil-Dex CB, 80 °C to 105 °C, 0.5 °C/min, 14 psi, 70% ee

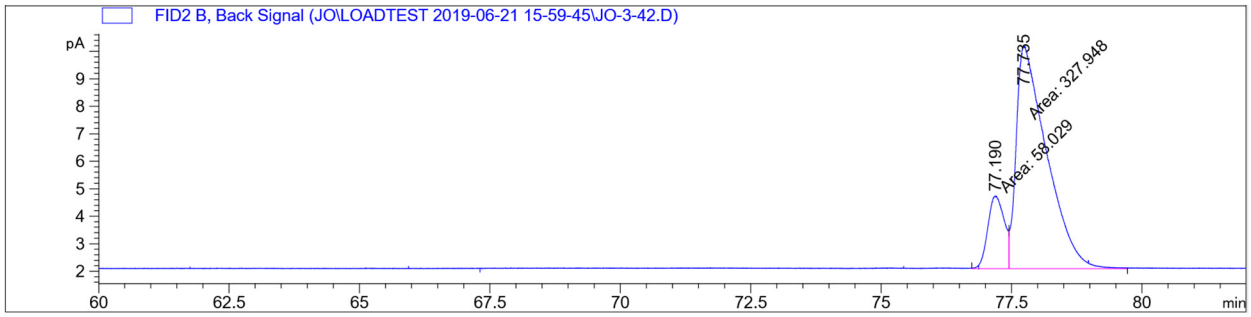








Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	78.463	MF	0.4813	25.80718	8.93741e-1	49.40790
2	79.355	FM	0.5251	26.42571	8.38796e-1	50.59210



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	77.190	MF	0.3667	58.02900	2.63769	15.03430
2	77.735	FM	0.6740	327.94830	8.10957	84.96570

(R)-1-(2-bromo-1,1-difluorobutyl)-4-nitrobenzene. **1i** was prepared from **2i** (51.2 mg, 0.2 mmol) according to the General Procedure as a white solid (48.8 mg, 83% yield).

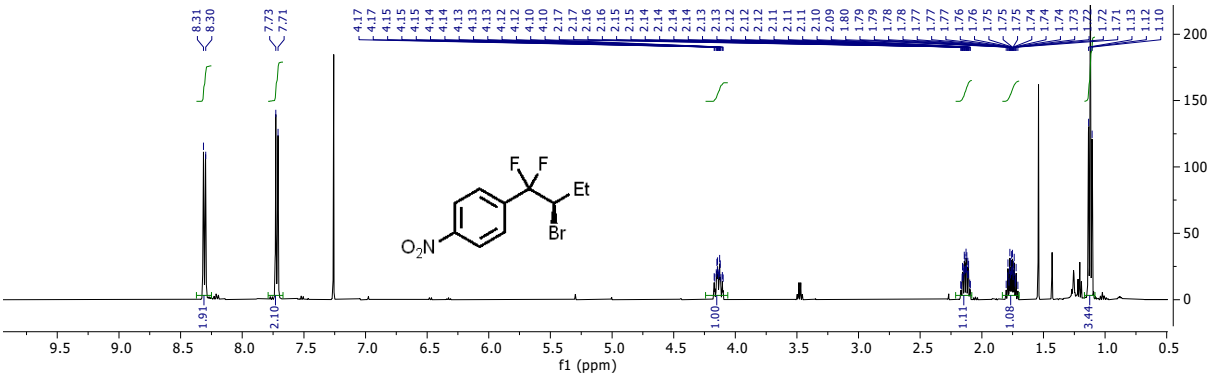
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (d, J = 8.7 Hz, 2H), 7.72 (d, J = 9.0 Hz, 2H), 4.14 (dddd, J = 13.9, 11.4, 8.7, 2.8 Hz, 1H), 2.20 – 2.07 (m, 1H), 1.76 (dddd, J = 14.6, 10.9, 7.3, 1.2 Hz, 1H), 1.12 (t, J = 7.3 Hz, 3H).

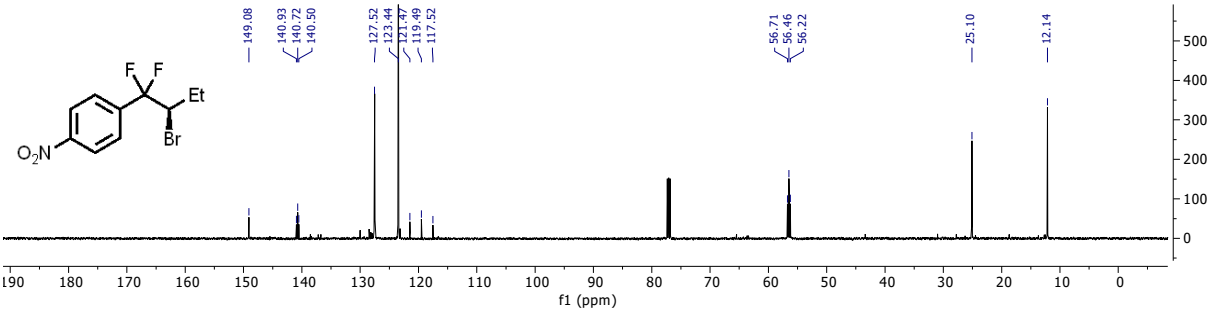
^{13}C NMR (126 MHz, $CDCl_3$) δ 149.08, 140.72 (t, J = 27.0 Hz), 127.52, 123.44, 119.49 (t, J = 247.8 Hz), 56.46 (t, J = 30.9 Hz), 25.10, 12.14.

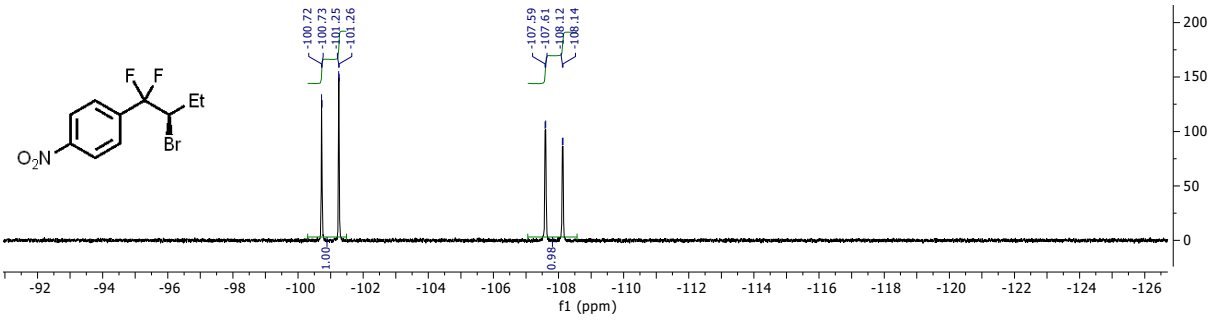
^{19}F NMR (471 MHz, $CDCl_3$) δ -100.99 (dd, J = 248.4, 6.3 Hz, 1F), -107.86 (dd, J = 248.8, 9.4 Hz, 1F).

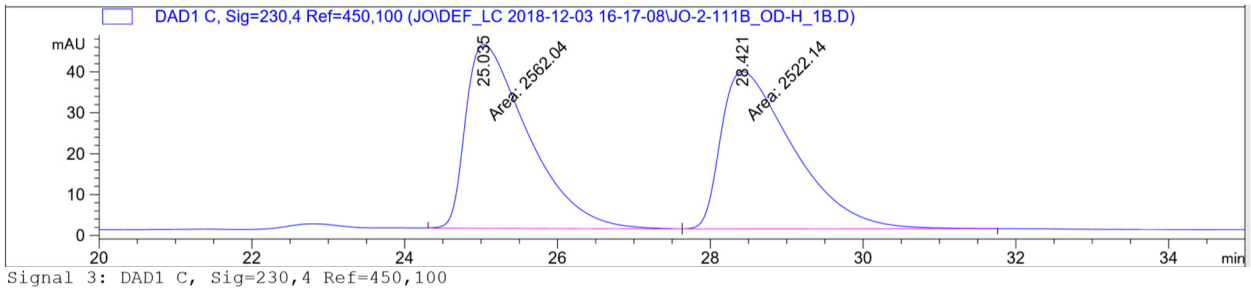
HRMS (EI): for $C_{10}H_{10}BrF_2NO_2$, $[M]^+$ calculated m/z = 292.9857 and 294.9837, found m/z = 292.9857 and 294.9835

Chiral HPLC: Chiralcel OD-H, 1.0% isopropanol/hexanes, 1.0 ml/min, 92% ee



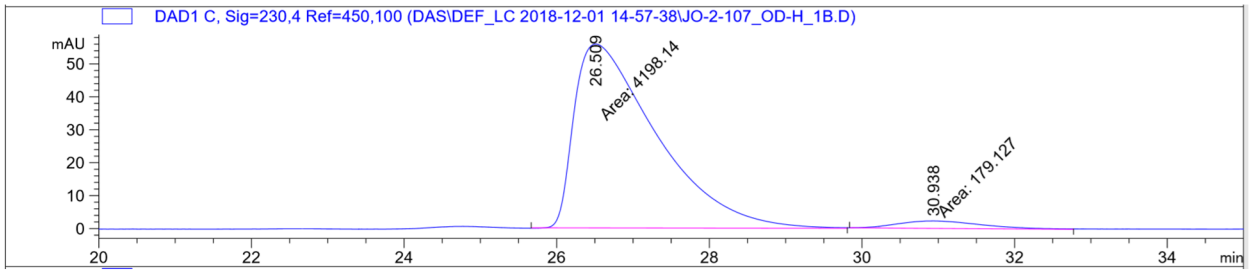






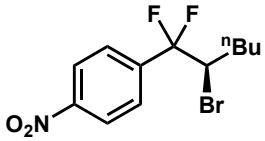
Signal 3: DAD1 C, Sig=230,4 Ref=450,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.035	MM	0.9483	2562.04492	45.03049	50.3925
2	28.421	MM	1.0922	2522.13916	38.48868	49.6075



Signal 3: DAD1 C, Sig=230,4 Ref=450,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.509	MM	1.2520	4198.13623	55.88586	95.9078
2	30.938	MM	1.2992	179.12723	2.29790	4.0922



(R)-1-(2-bromo-1,1-difluorohexyl)-4-nitrobenzene. **1j** was prepared from **2j** (56.8 mg, 0.2 mmol) according to the General Procedure as a clear, colorless oil (54.1 mg, 84% yield).

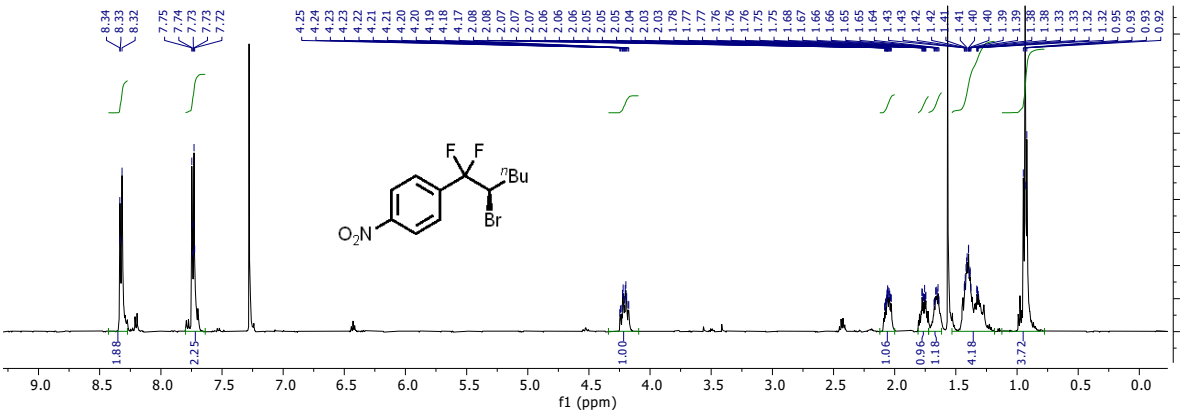
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 (d, J = 8.5 Hz, 2H), 7.74 (d, J = 8.8 Hz, 2H), 4.21 (dddd, J = 14.0, 11.3, 8.6, 2.8 Hz, 1H), 2.11 – 1.97 (m, 1H), 1.83 – 1.60 (m, 2H), 1.48 – 1.24 (m, 3H), 0.93 (t, J = 7.2 Hz, 3H).

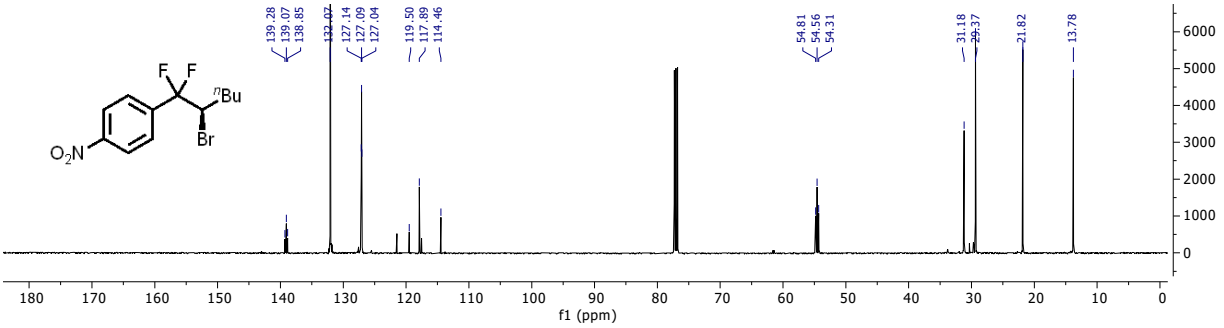
^{13}C NMR (126 MHz, $CDCl_3$) δ 139.07 (t, J = 27.1 Hz), 132.07, 127.09 (t, J = 6.2 Hz), 119.50 (t, J = 248.1 Hz), 117.89, 114.46, 54.56 (t, J = 31.3 Hz), 31.18, 29.37, 21.82, 13.78.

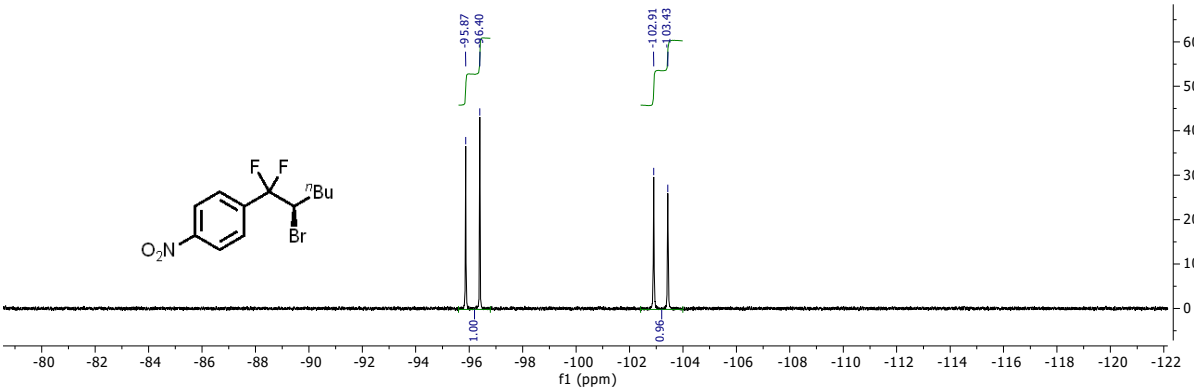
^{19}F NMR (471 MHz, $CDCl_3$) δ -96.13 (d, J = 248.2 Hz, 1F), -103.17 (d, J = 248.1 Hz, 1F).

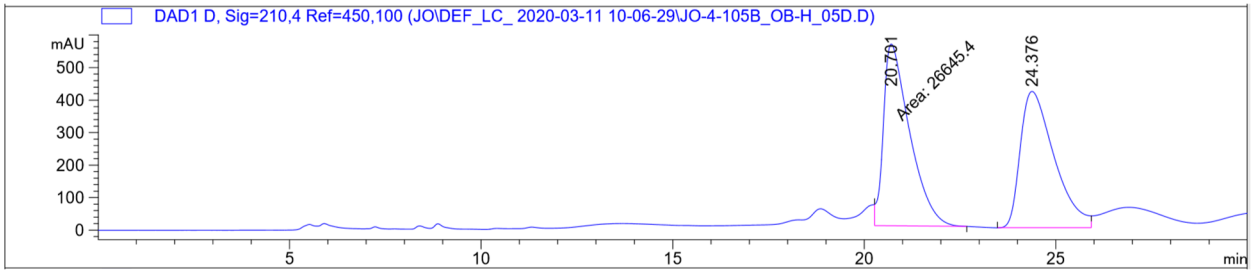
HRMS (EI): for $C_{12}H_{14}BrF_2NO_2$, $[M]^+$ calculated m/z = 321.0170 and 323.0150, found m/z = 321.0168 and 323.0147

Chiral HPLC: Chiralcel OB-H, 0.5% isopropanol/hexanes, 1.0 ml/min, 93% ee



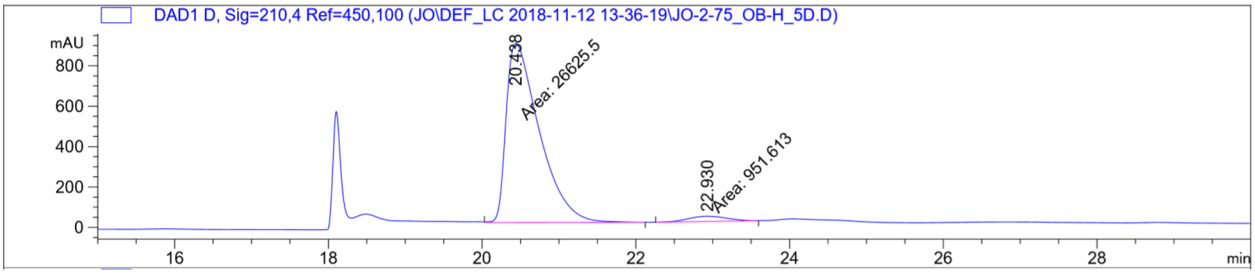






Signal 4: DAD1 D, Sig=210,4 Ref=450,100

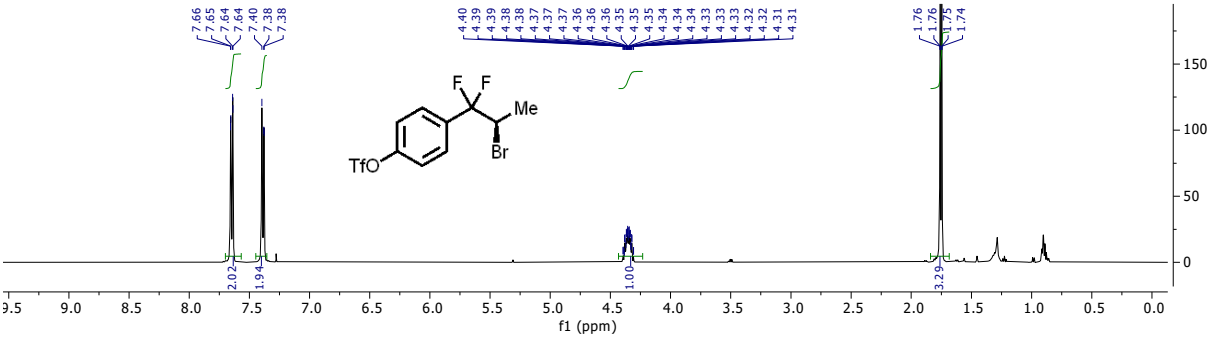
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.701	FM	0.7937	2.66454e4	559.55054	50.7911
2	24.376	BV	0.9300	2.58154e4	419.48834	49.2089

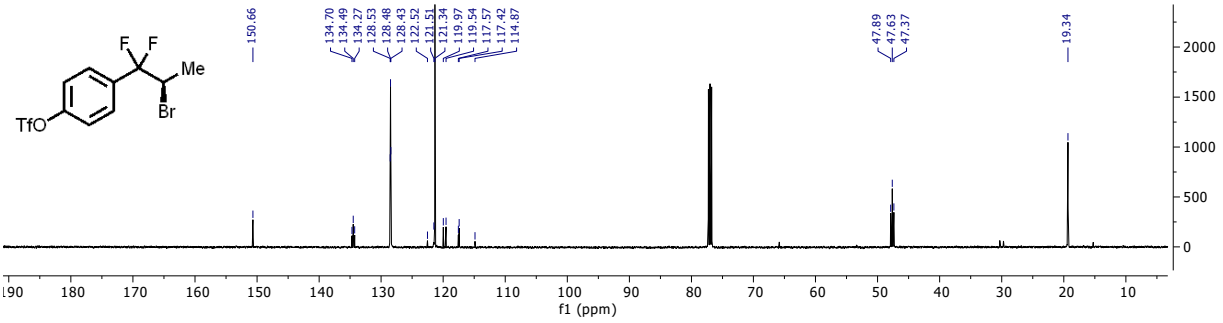


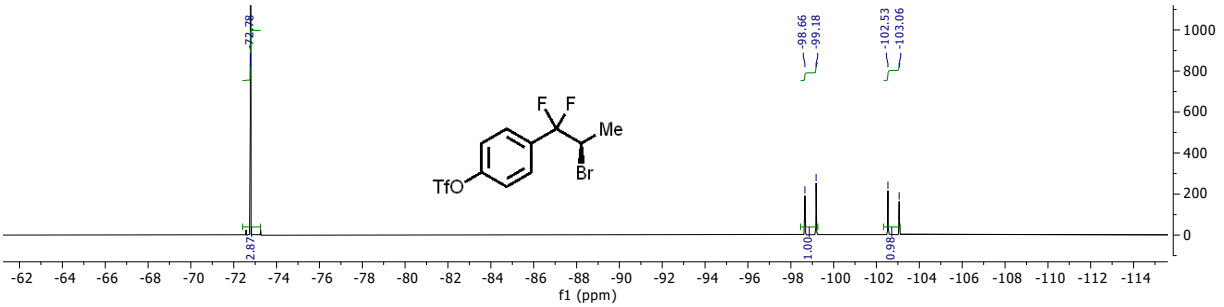
Signal 4: DAD1 D, Sig=210,4 Ref=450,100

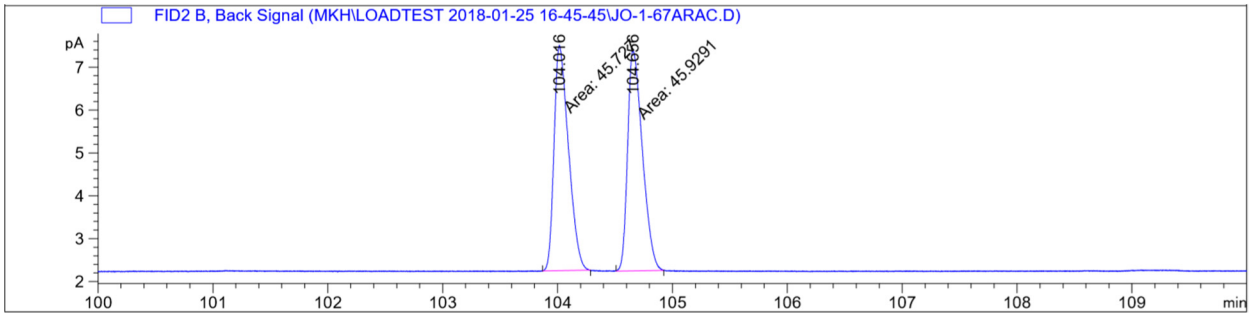
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.438	MM	0.4996	2.66255e4	888.26093	96.5493
2	22.930	MM	0.6040	951.61267	26.25781	3.4507

(R)-4-(2-bromo-1,1-difluoropropyl)phenyl trifluoromethanesulfonate. **1k** was prepared from **2k** (69.0 mg, 0.2 mmol) according to the General Procedure as a clear, colorless oil (61.3 mg, 80% yield).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, J = 8.3 Hz, 2H), 7.38 (d, J = 8.5 Hz, 2H), 4.41 – 4.30 (m, 1H), 1.75 (d, J = 7.1 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 150.66, 134.49 (t, J = 27.2 Hz), 128.48 (t, J = 6.1 Hz), 121.34, 119.54 (t, J = 248.3, 246.9 Hz), 118.32 (q, J = 321.3, 320.7, 319.9 Hz), 47.63 (t, J = 32.9 Hz), 19.34.
^{19}F NMR (471 MHz, $CDCl_3$) δ -72.78 (s, 3F), -98.92 (d, J = 247.1 Hz, 1F), -102.80 (d, J = 247.1 Hz, 1F).
HRMS (EI): for $C_{10}H_8BrF_5O_3S$, $[M]^+$ calculated m/z = 381.9292 and 383.9272, found m/z = 381.9293 and 383.9271
Chiral GC: CP-Chirasil-Dex CB, 40 °C to 200 °C, 1 °C/min, 7 psi, 80% ee

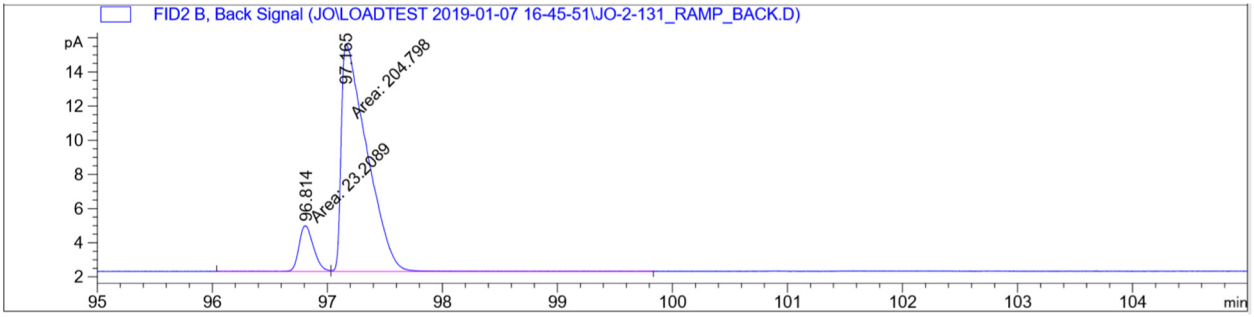




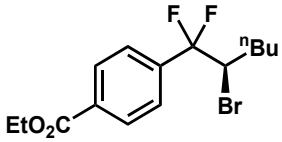




Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	104.016	MM	0.1455	45.72702	5.23653	49.88974
2	104.656	MM	0.1493	45.92914	5.12594	50.11026



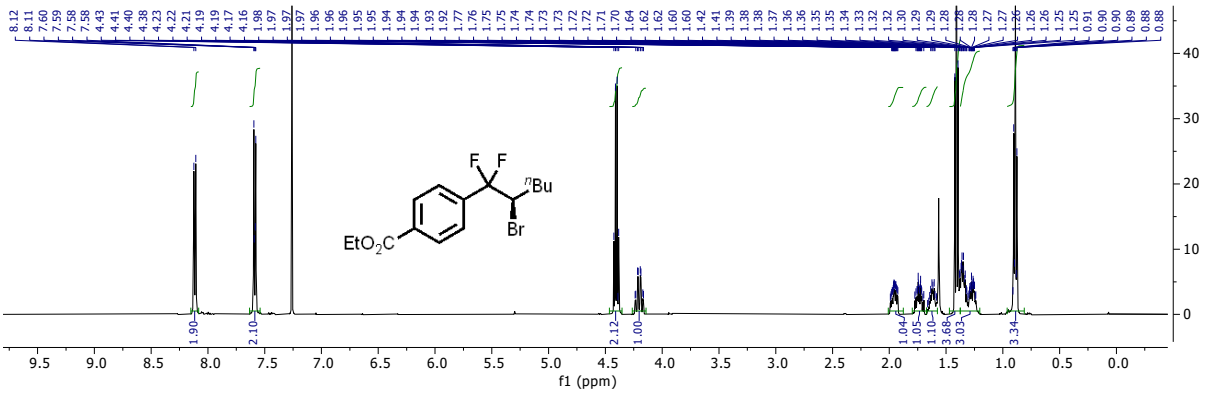
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	96.814	MF	0.1451	23.20891	2.66577	10.17903
2	97.165	FM	0.2567	204.79826	13.29851	89.82097

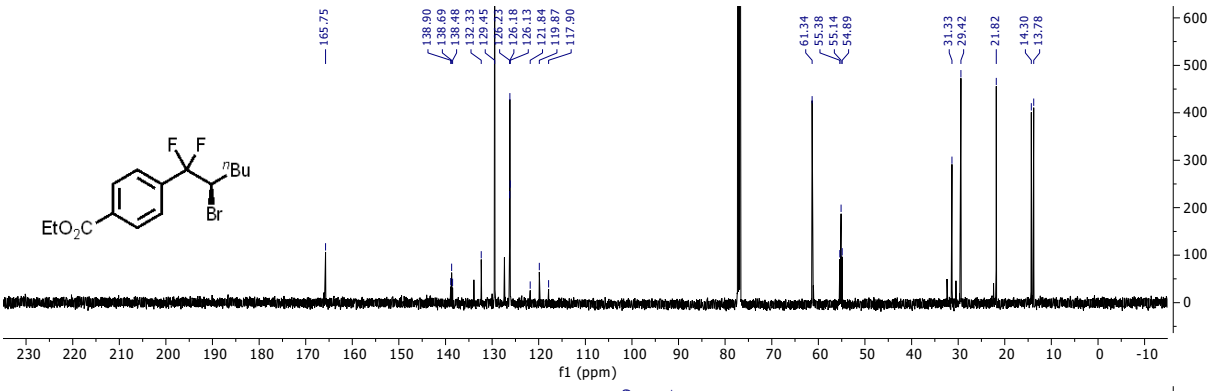


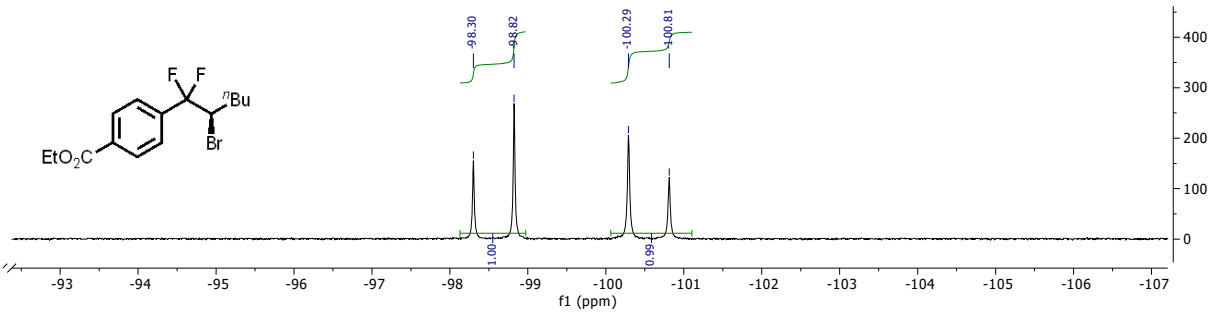
(R)-ethyl 4-(2-bromo-1,1-difluorohexyl)benzoate. **1l** was prepared from **2l** (62.2 mg, 0.2 mmol) according to the General Procedure as a clear, colorless oil (58.7 mg, 84% yield).

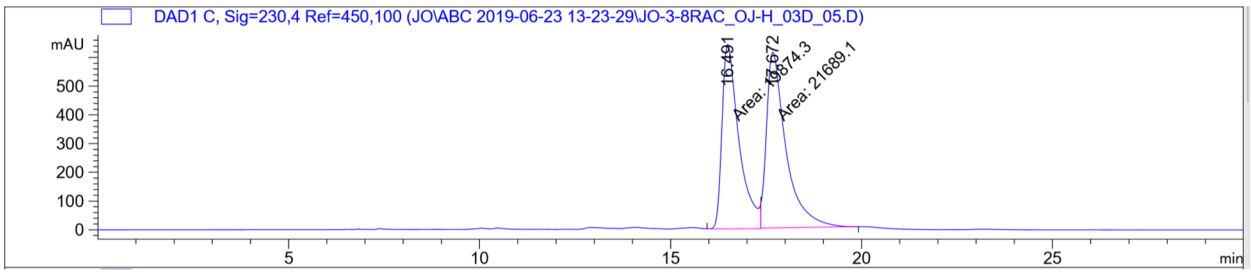
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, J = 8.1 Hz, 2H), 7.69 – 7.52 (m, 2H), 4.40 (q, J = 7.1 Hz, 2H), 4.20 (qd, J = 11.3, 2.8 Hz, 1H), 1.96 (dddd, J = 14.4, 9.9, 5.9, 2.7 Hz, 1H), 1.73 (dddd, J = 14.3, 11.1, 9.5, 4.5 Hz, 1H), 1.62 (qt, J = 9.7, 5.5 Hz, 1H), 1.41 (t, J = 7.1 Hz, 3H), 1.39 – 1.22 (m, 2H), 0.89 (t, J = 7.2 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 165.75, 138.69 (t, J = 26.5 Hz), 132.33, 129.45, 126.18 (t, J = 6.1 Hz), 119.87 (t, J = 248.1, 247.3 Hz), 61.34, 55.14 (t, J = 31.2 Hz), 31.33, 29.42, 21.82, 14.30, 13.78.
^{19}F NMR (471 MHz, $CDCl_3$) δ -98.56 (d, J = 245.7 Hz, 1F), -100.55 (d, J = 245.9 Hz, 1F).
HRMS (ESI): for $C_{15}H_{20}BrF_2O_2$, $[M+H]^+$ calculated m/z = 349.0609 and 351.0589, found m/z = 349.0607 and 351.0585.
Chiral HPLC: Chiralcel OJ-H, 0.3% isopropanol/hexanes, 0.5 ml/min, 79% ee



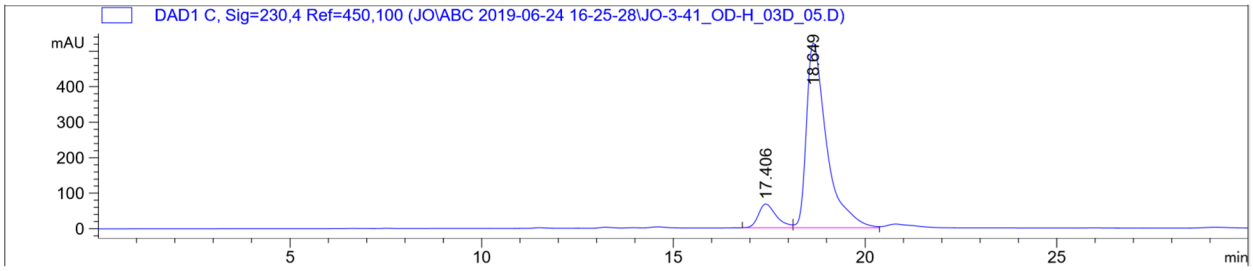






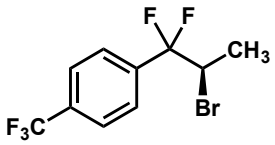
Signal 3: DAD1 C, Sig=230,4 Ref=450,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.491	MM	0.5157	1.98743e4	642.25793	47.8168
2	17.672	FM	0.5901	2.16891e4	612.54230	52.1832



Signal 3: DAD1 C, Sig=230,4 Ref=450,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.406	BV	0.4952	2196.47729	67.23141	10.3406
2	18.649	VB	0.5430	1.90449e4	520.37158	89.6594



(R)-1-(2-bromo-1,1-difluoropropyl)-4-(trifluoromethyl)benzene. **1m** was prepared from **2m** (53.0 mg, 0.2 mmol) according to the General Procedure as a clear, colorless oil (33.3 mg, 55% yield).

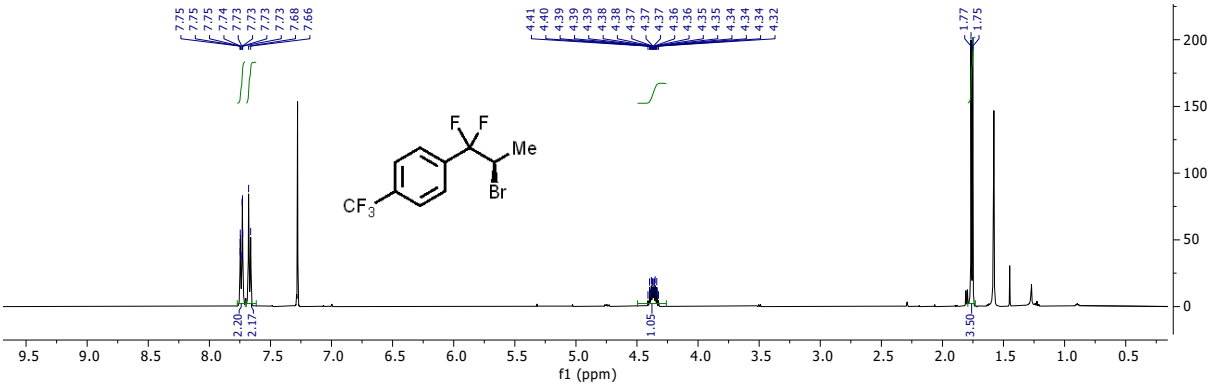
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, J = 8.3 Hz, 2H), 7.67 (d, J = 8.2 Hz, 2H), 4.37 (ddq, J = 12.2, 10.1, 6.9 Hz, 1H), 1.76 (d, J = 6.9 Hz, 3H).

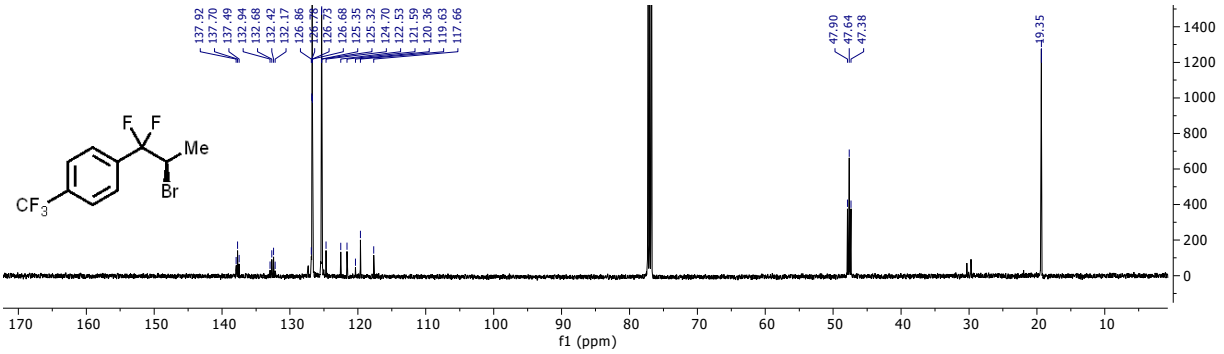
^{13}C NMR (126 MHz, $CDCl_3$) δ 137.71 (t, J = 26.8 Hz), 132.55 (q, J = 32.4, 31.7 Hz), 126.73 (t, J = 6.1 Hz), 125.34 (q, J = 3.8 Hz), 123.61 (q, J = 272.4 Hz), 119.81 (t, J = 247.9, 247.2 Hz), 47.64 (t, J = 32.8 Hz), 19.35.

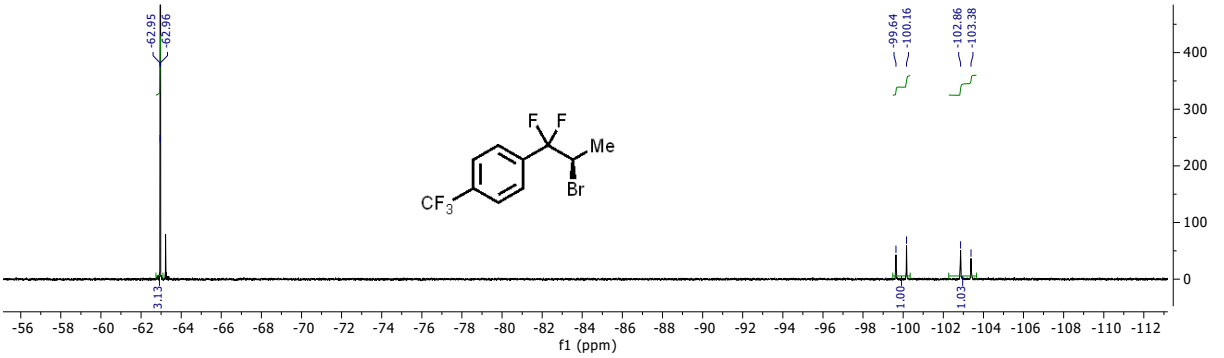
^{19}F NMR (471 MHz, $CDCl_3$) δ -62.96 (d, J = 4.9 Hz, 3F), -99.90 (d, J = 246.5 Hz, 1F), -103.12 (d, J = 246.4 Hz, 1F).

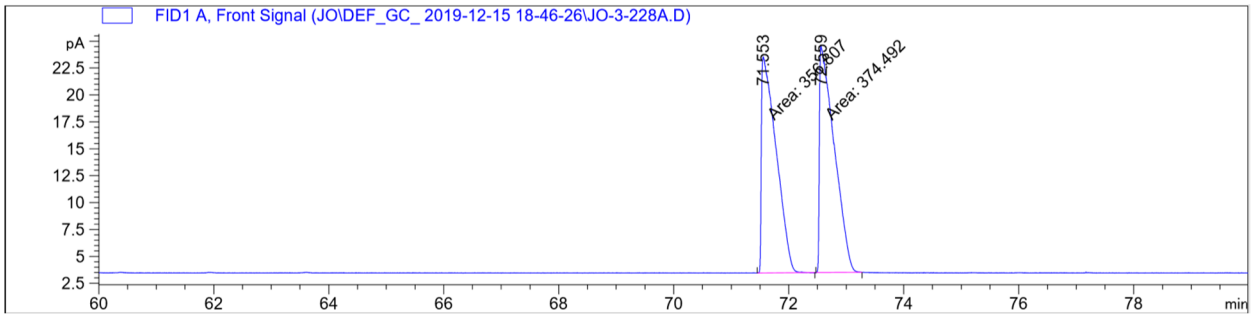
HRMS (EI): for $C_{10}H_8BrF_5$, $[M]^+$ calculated m/z = 301.9724 and 303.9704, found m/z = 301.9721 and 303.9700

Chiral GC: CP-Chirasil-Dex CB, 40 °C to 200 °C, 1 °C/min, 7 psi, 83% ee

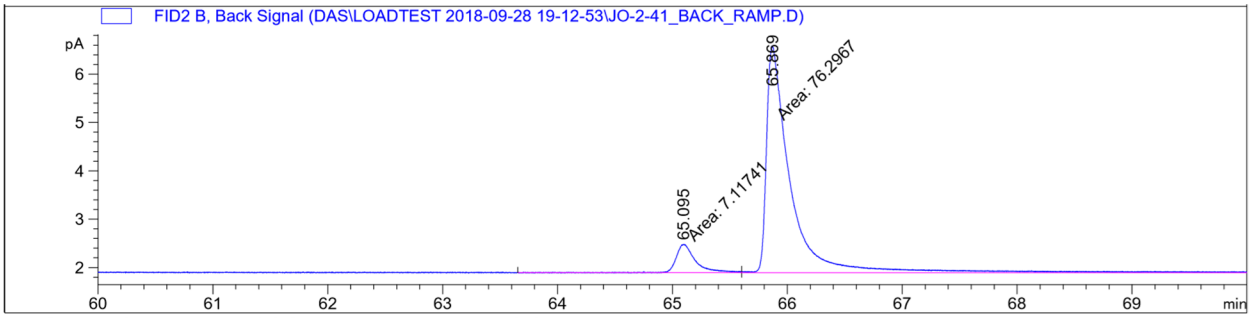




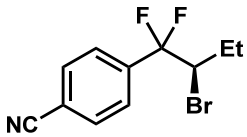




Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	71.553	MM	0.2962	356.80673	20.07510	48.79083
2	72.559	MM	0.2958	374.49207	21.10036	51.20917



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	65.095	MF	0.2025	7.11741	5.85855e-1	8.53261
2	65.869	FM	0.2713	76.29671	4.68700	91.46739



(R)-4-(2-bromo-1,1-difluorobutyl)benzonitrile. **1n** was prepared from **2n** (47.2 mg, 0.2 mmol) according to the General Procedure as a white solid (40.0 mg, 73% yield).

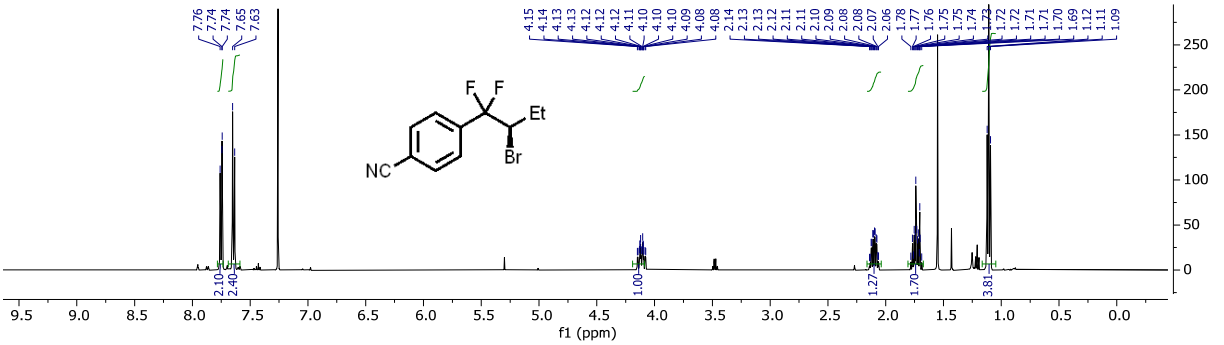
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 – 7.72 (m, 2H), 7.64 (d, *J* = 8.6 Hz, 2H), 4.11 (dddd, *J* = 13.7, 10.9, 9.0, 2.8 Hz, 1H), 2.10 (dqd, *J* = 14.5, 7.3, 2.9 Hz, 1H), 1.84 – 1.67 (m, 1H), 1.11 (t, *J* = 7.3 Hz, 3H).

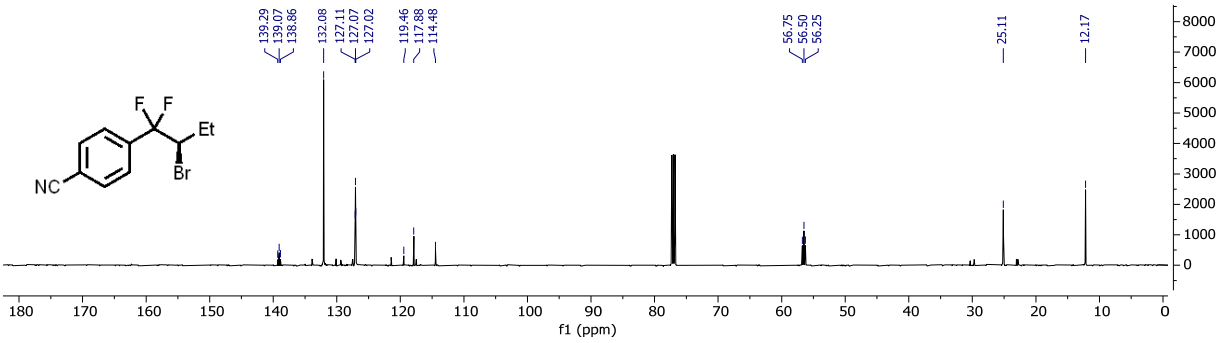
^{13}C NMR (126 MHz, $CDCl_3$) δ 139.07 (t, *J* = 27.1 Hz), 132.08, 127.07 (t, *J* = 6.2 Hz), 119.46 (dd, *J* = 249.2, 248.3 Hz), 117.88, 114.48, 56.50 (t, *J* = 31.1 Hz), 25.11, 12.17.

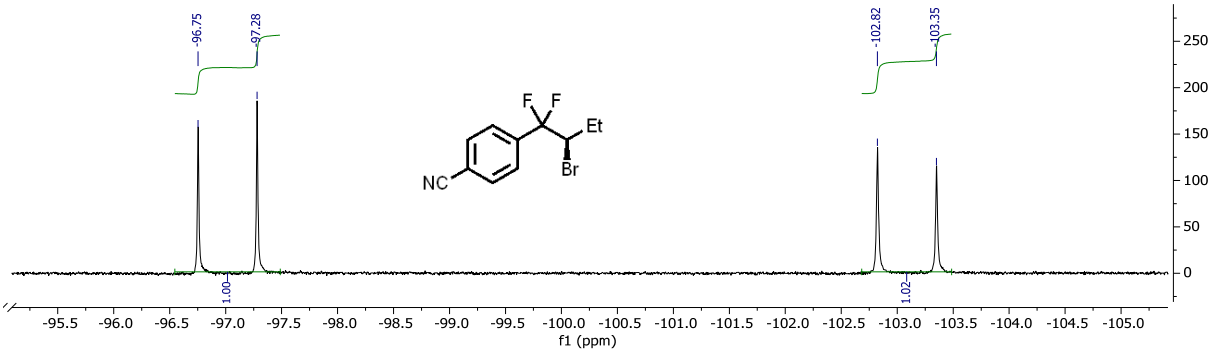
^{19}F NMR (471 MHz, $CDCl_3$) δ -97.02 (d, *J* = 248.2 Hz), -103.09 (d, *J* = 248.2 Hz).

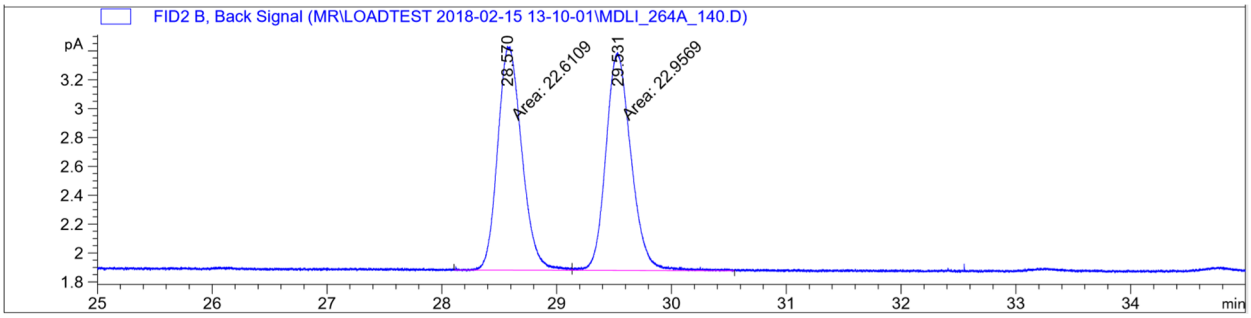
HRMS (EI): for $C_{11}H_{10}BrF_2N$, $[M]^+$ calculated *m/z* = 272.9959 and 274.9939, found *m/z* = 272.9963 and 274.9942.

Chiral GC: CP-Chirasil-Dex CB, isothermal 140 °C, 7 psi, 89% ee

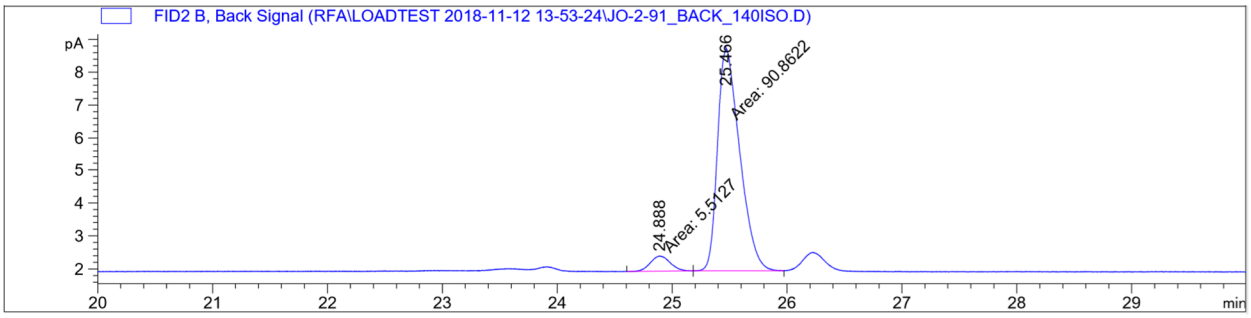




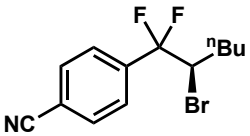




Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	28.570	MF	0.2428	22.61091	1.55190	49.62036
2	29.531	FM	0.2530	22.95690	1.51231	50.37964



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	24.888	MM	0.1976	5.51270	4.64964e-1	5.72006
2	25.466	MM	0.2223	90.86221	6.81154	94.27994



(R)-4-(2-bromo-1,1-difluorohexyl)benzonitrile. **1o** was prepared from **2o** (52.8 mg, 0.2 mmol) according to the General Procedure as a white solid (45.9 mg, 76% yield).

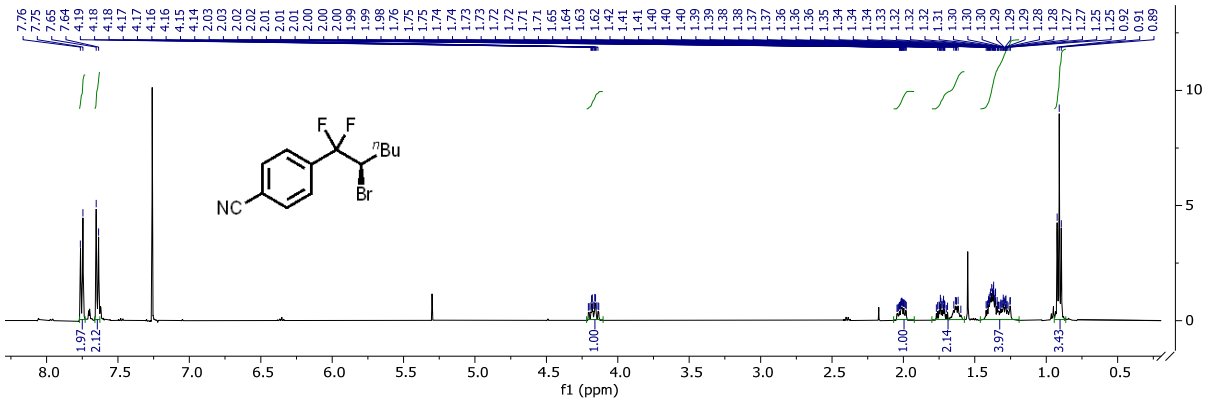
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, J = 8.8 Hz, 2H), 7.64 (d, J = 8.4 Hz, 2H), 4.17 (dddd, J = 13.7, 11.4, 8.8, 2.7 Hz, 1H), 2.01 (dddd, J = 14.3, 9.8, 5.8, 2.7 Hz, 1H), 1.79 – 1.58 (m, 2H), 1.45 – 1.18 (m, 3H), 0.91 (t, J = 7.2 Hz, 3H).

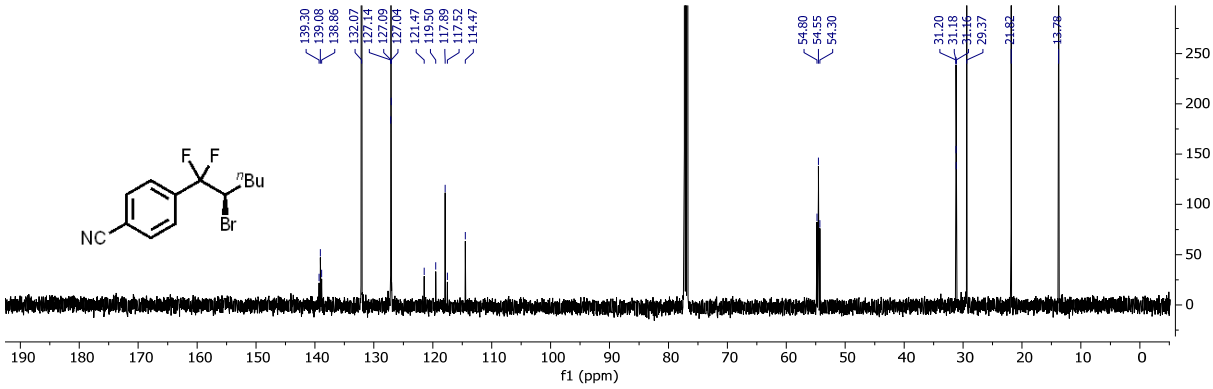
^{13}C NMR (126 MHz, $CDCl_3$) δ 139.08 (t, J = 27.3 Hz), 132.07, 127.09 (t, J = 6.2 Hz), 119.50 (t, J = 248.2 Hz), 117.89, 114.47, 54.55 (t, J = 31.3 Hz), 31.18 (t, J = 2.4 Hz), 29.37, 21.82, 13.78.

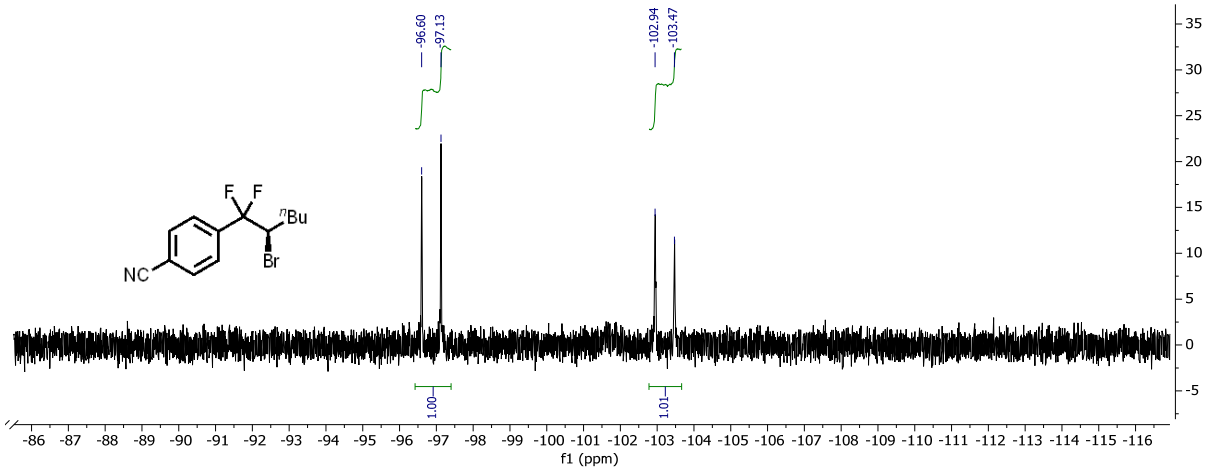
^{19}F NMR (471 MHz, $CDCl_3$) δ -96.86 (d, J = 247.8 Hz), -103.21 (d, J = 246.7 Hz).

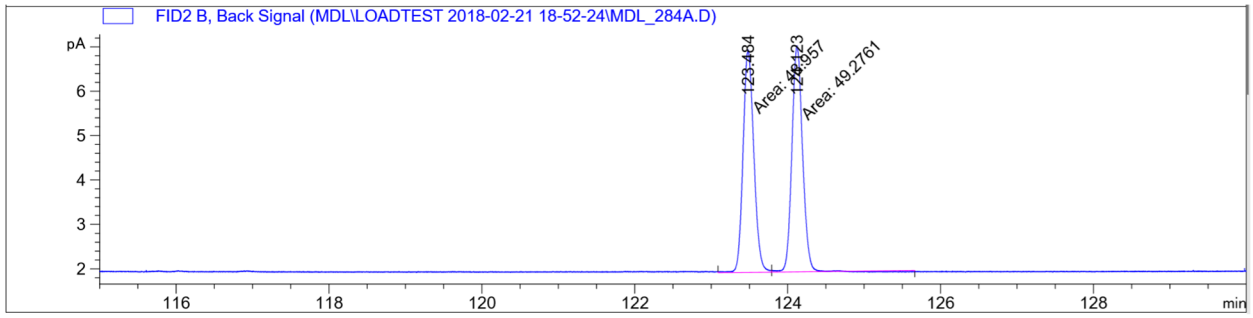
HRMS (EI): for $C_{13}H_{14}BrF_2N$, $[M]^+$ calculated m/z = 301.0272 and 303.0252, found m/z = 301.0272 and 303.0251

Chiral GC: CP-Chirasil-Dex CB, 40 °C to 200 °C, 1 °C/min, 88% ee

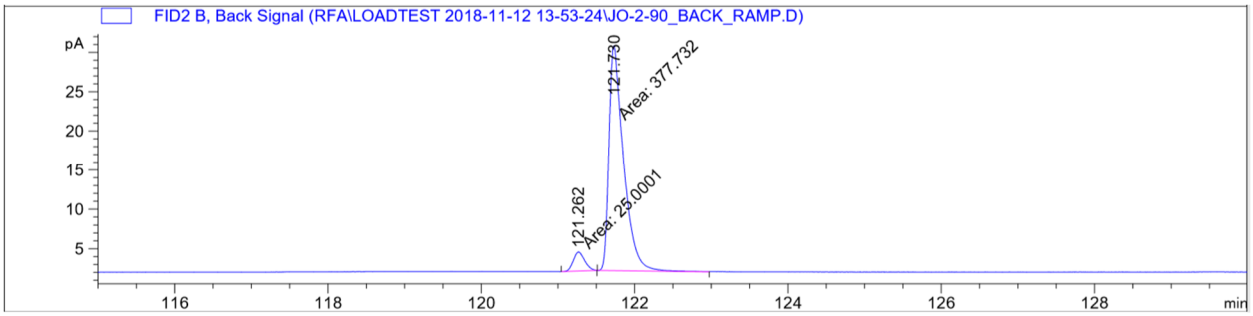

F F
nBu
NC
Br
f1 (ppm)


F F
nBu
NC
Br
f1 (ppm)

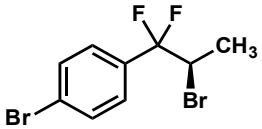

F F
nBu
NC
Br
f1 (ppm)



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	123.484	MF	0.1629	48.95699	5.00757	49.83755
2	124.123	FM	0.1613	49.27614	5.09250	50.16245



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	121.262	MM	0.1712	25.00008	2.43360	6.20762
2	121.730	MM	0.2197	377.73221	28.66029	93.79238



(R)-1-bromo-4-(2-bromo-1,1-difluoropropyl)benzene. **1p** was prepared from **2p** (55.2 mg, 0.2 mmol) according to the General Procedure as a clear, colorless oil (50.9 mg, 81% yield).

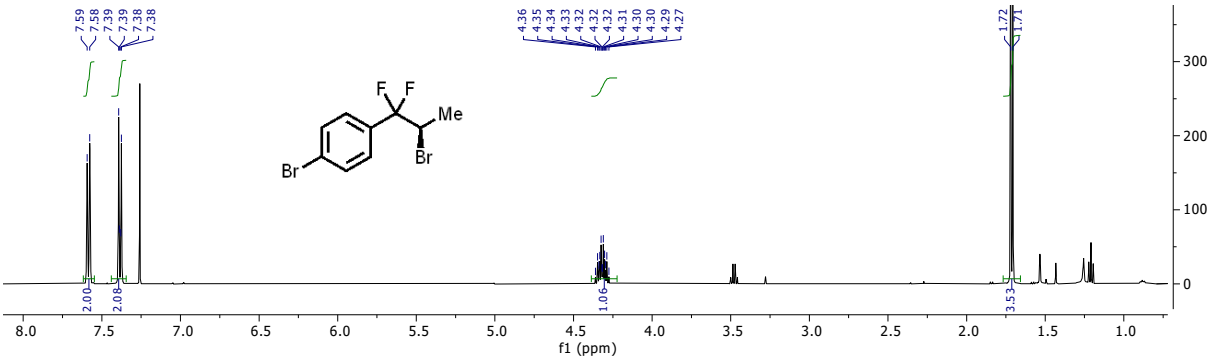
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 (d, J = 8.3 Hz, 2H), 7.41 – 7.36 (m, 2H), 4.32 (tq, J = 11.0, 6.9 Hz, 1H), 1.71 (d, J = 6.9 Hz, 3H).

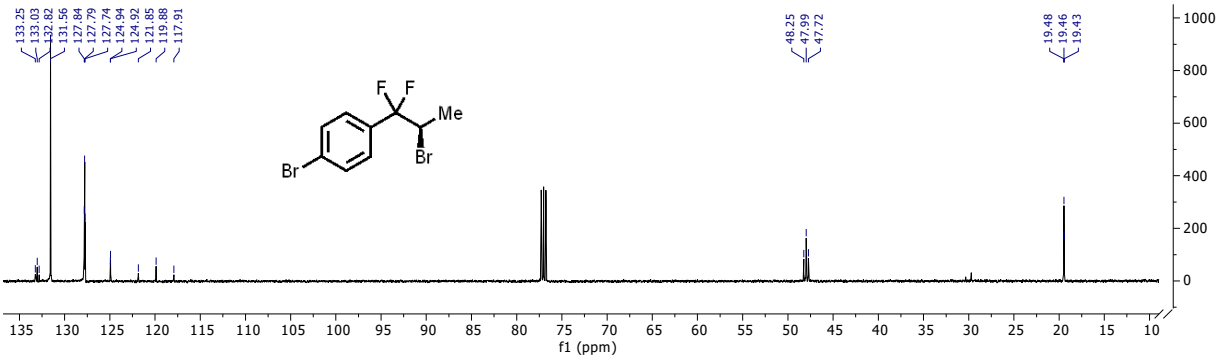
^{13}C NMR (126 MHz, $CDCl_3$) δ 133.03 (t, J = 27.1 Hz), 131.56, 127.79 (t, J = 6.1 Hz), 124.93 (d, J = 2.2 Hz), 119.88 (t, J = 247.5 Hz), 47.99 (t, J = 33.1 Hz), 19.46 (t, J = 3.1 Hz).

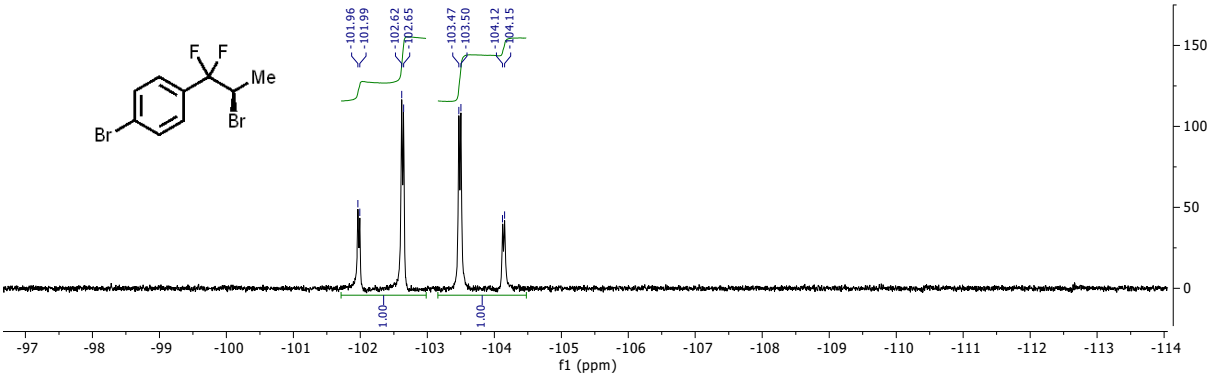
^{19}F NMR (376 MHz, $CDCl_3$) δ -102.30 (dd, J = 245.5, 10.9 Hz, 1F), -103.81 (dd, J = 245.1, 11.5 Hz, 1F).

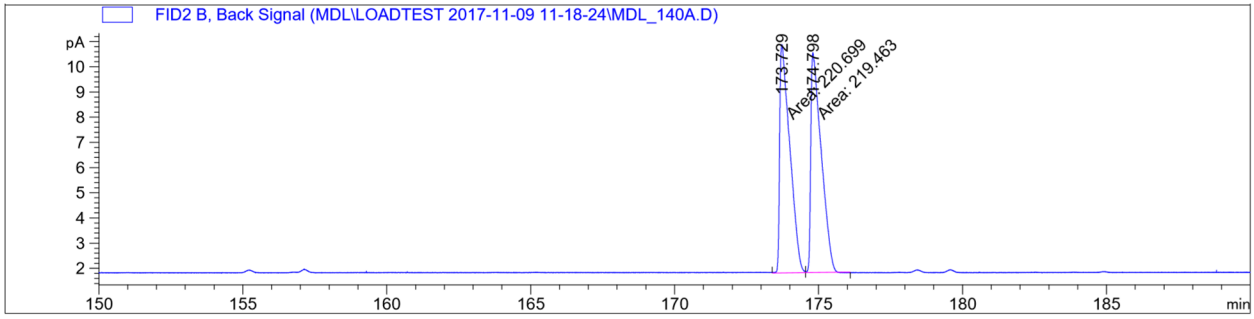
HRMS (EI): for $C_9H_8Br_2F_2$, $[M]^+$ calculated m/z = 311.8955 and 313.8935 and 315.8914, found m/z = 311.8954 and 313.8932 and 315.8911

Chiral GC: CP-Chirasil-Dex CB, 40 °C to 160 °C, 0.5 °C/min, 7 psi, 82% ee

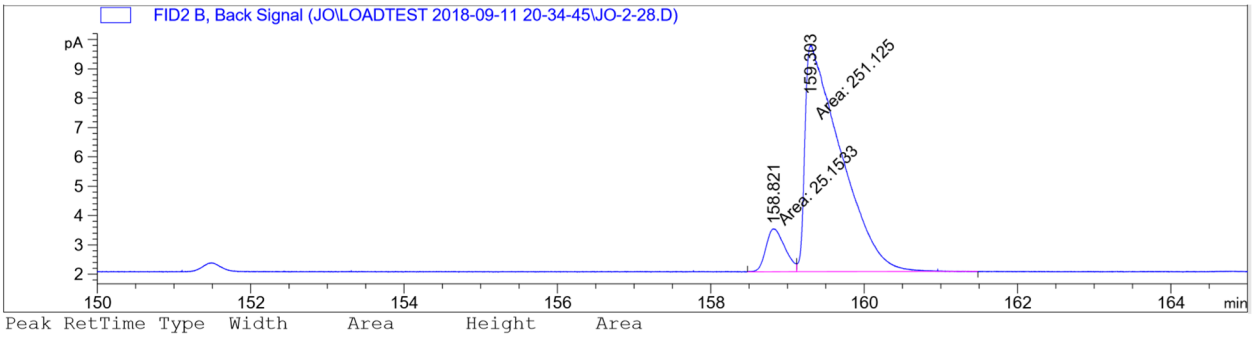




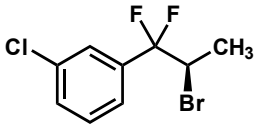




Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	173.729	MF	0.4059	220.69868	9.06238	50.14037
2	174.798	FM	0.4185	219.46294	8.74011	49.85963



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	158.821	MF	0.2846	25.15325	1.47324	9.10433
2	159.303	FM	0.5418	251.12474	7.72440	90.89567



(R)-1-(2-bromo-1,1-difluoropropyl)-3-chlorobenzene. **1q** was prepared from **2q** (46.3 mg, 0.2 mmol) according to the General Procedure as a clear, colorless oil (38.3 mg, 71% yield).

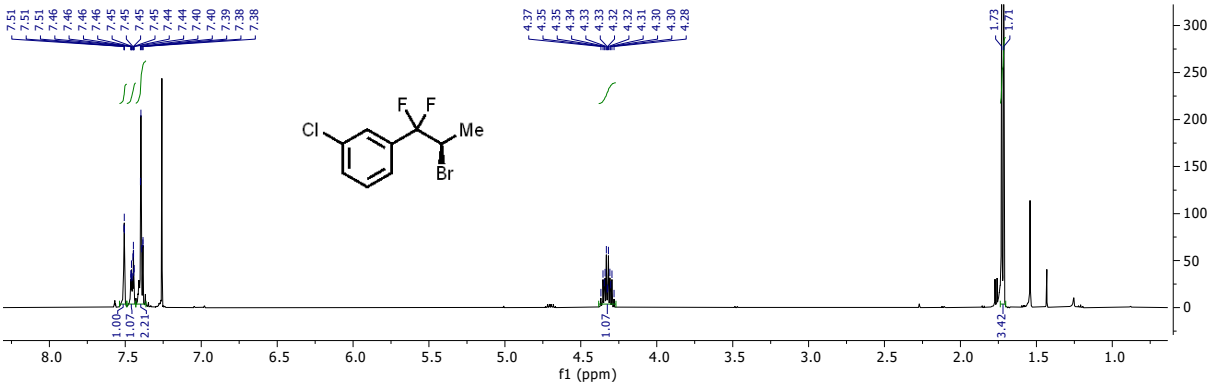
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (t, J = 0.6 Hz, 1H), 7.48 – 7.43 (m, 1H), 7.42 – 7.37 (m, 2H), 4.32 (tq, J = 11.3, 7.0 Hz, 1H), 1.72 (d, J = 7.0 Hz, 3H).

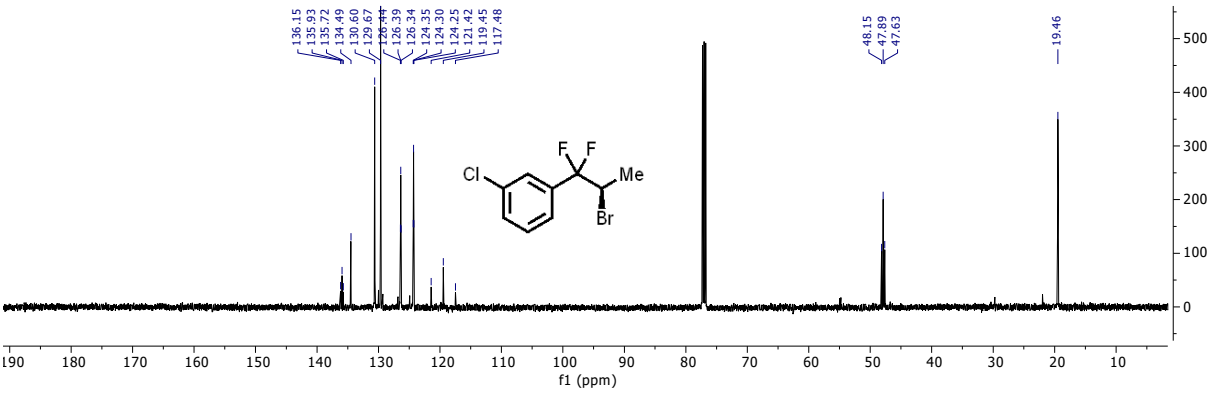
^{13}C NMR (126 MHz, $CDCl_3$) δ 135.93 (t, J = 27.1 Hz), 134.49, 130.60, 129.67, 126.39 (t, J = 6.5 Hz), 124.30 (t, J = 6.1 Hz), 119.45 (t, J = 247.7 Hz), 47.89 (t, J = 32.7 Hz), 19.46.

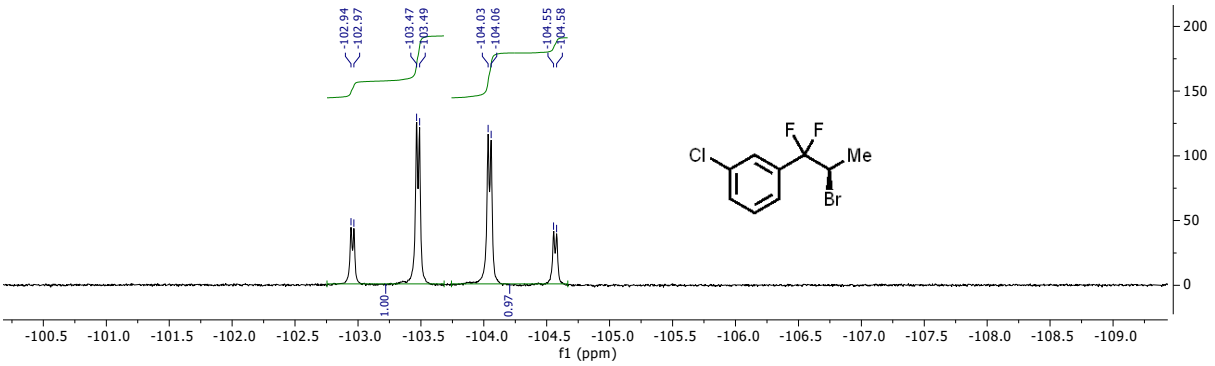
^{19}F NMR (471 MHz, $CDCl_3$) δ -103.22 (dd, J = 245.3, 11.0 Hz, 1F), -104.31 (dd, J = 245.1, 11.5 Hz, 1F).

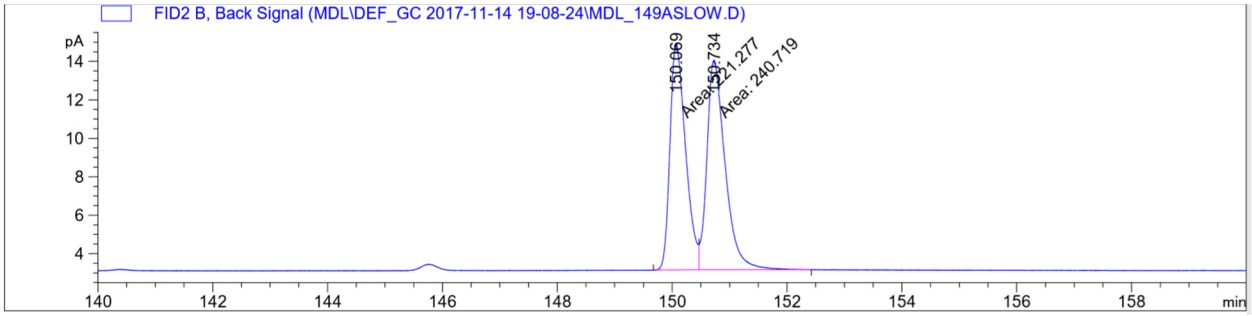
HRMS (EI): for $C_9H_8BrClF_2$, $[M]^+$ calculated m/z = 267.9460 and 269.9440, found m/z = 267.9459 and 269.9434.

Chiral GC: β-Cyclosil, 40 °C to 140 °C, 0.5 °C/min, 7 psi, 79% ee

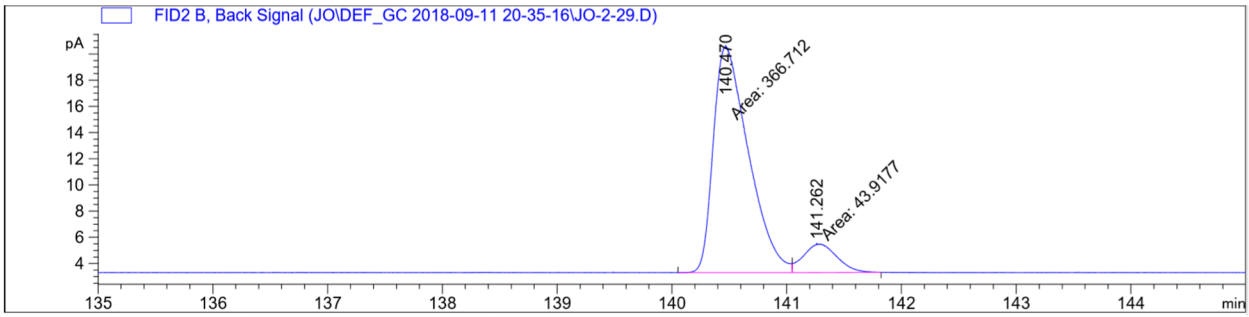




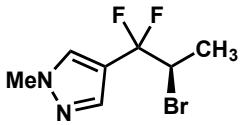




Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	150.069	MF	0.3137	221.27718	11.75755	47.89587
2	150.734	FM	0.3676	240.71915	10.91340	52.10413



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	140.470	MF	0.3521	366.71176	17.35723	89.30478
2	141.262	FM	0.3368	43.91772	2.17348	10.69522



(R)-4-(2-bromo-1,1-difluoropropyl)-1-methyl-1H-pyrazole. **1r** was prepared from **2r** (40.2 mg, 0.2 mmol) according to the General Procedure as a clear, colorless oil (39.2 mg, 82% yield).

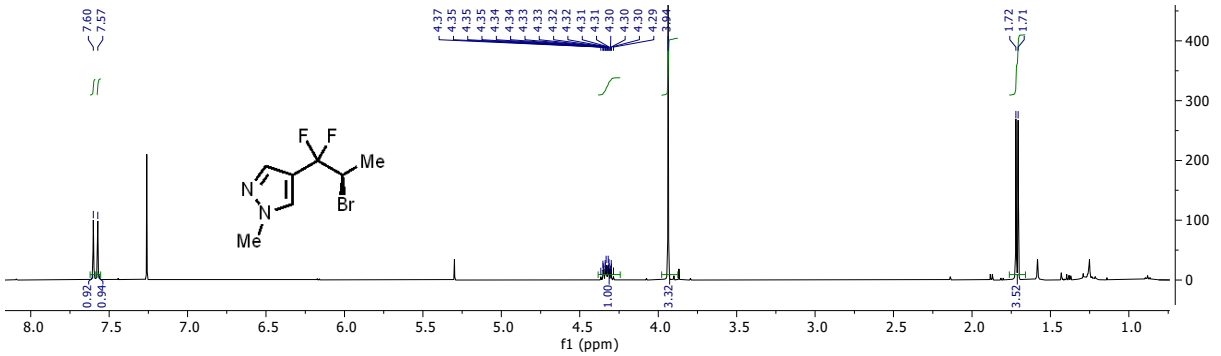
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (s, 1H), 7.57 (s, 1H), 4.39 – 4.24 (m, 1H), 3.94 (s, 3H), 1.71 (d, J = 7.0 Hz, 3H).

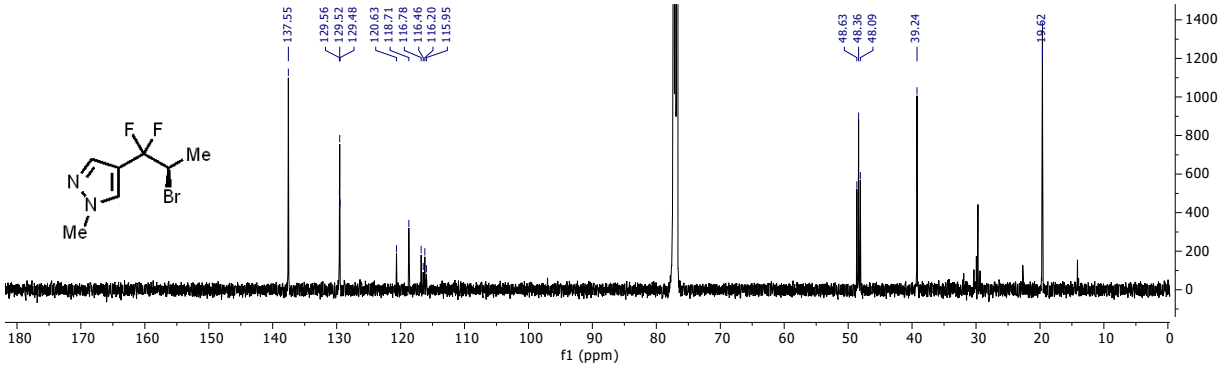
^{13}C NMR (126 MHz, $CDCl_3$) δ 137.55, 129.52 (t, J = 5.4 Hz), 118.71 (t, J = 241.9 Hz), 116.20 (t, J = 31.7 Hz), 48.36 (t, J = 34.1 Hz), 39.24, 19.62.

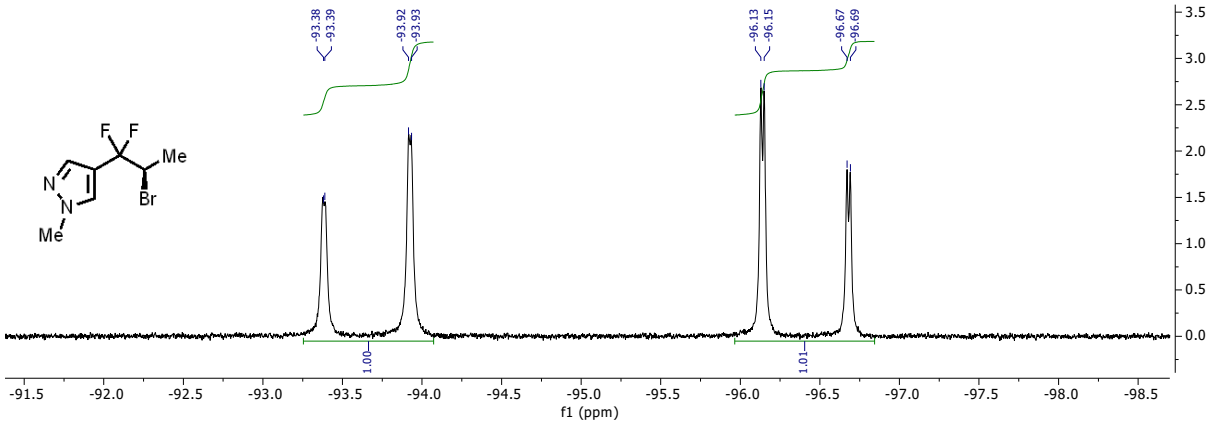
^{19}F NMR (471 MHz, CDCl3) δ -93.66 (dd, J = 253.8, 6.3 Hz, 1F), -96.41 (dd, J = 254.8, 10.0 Hz, 1F).

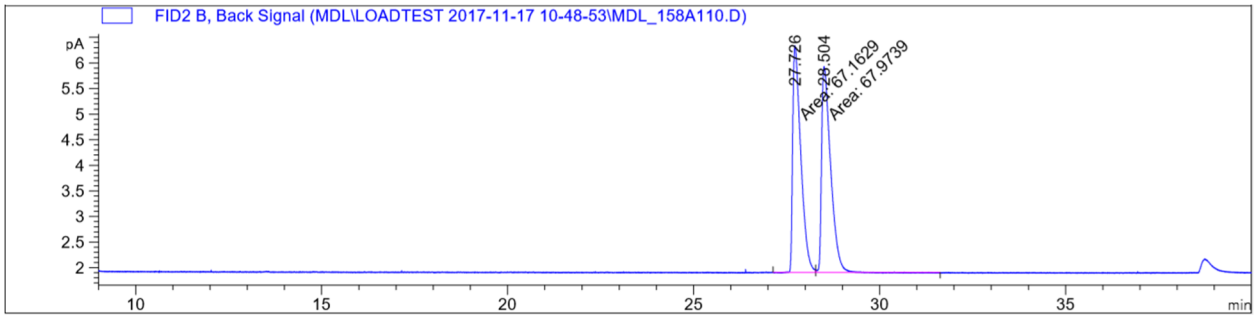
HRMS (ESI): for $C_7H_{10}BrF_2N_2$, $[M+H]^+$ calculated *m/z* = 238.9990 and 240.9969, found *m/z* = 238.9989 and 240.9965.

Chiral GC: CP-Chirasil-Dex CB, isothermal 110 °C, 7 psi, 63% ee

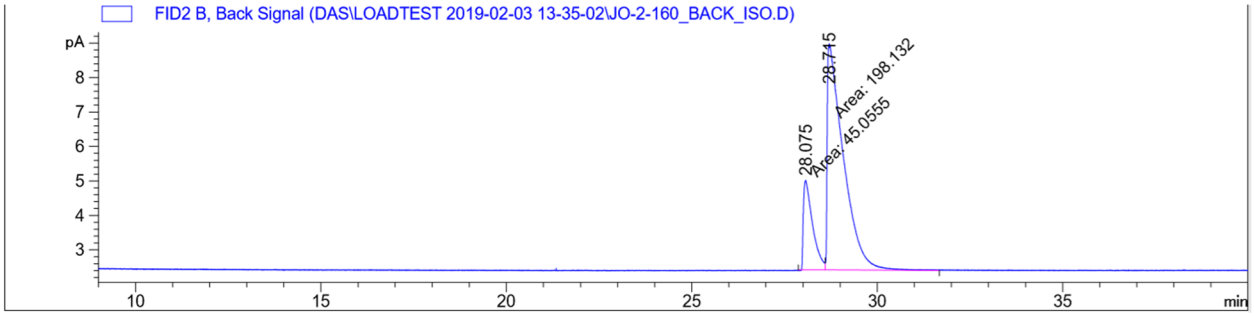




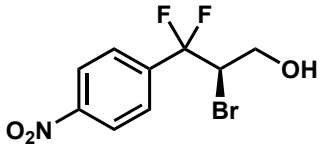




Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	27.726	MF	0.2528	67.16287	4.42854	49.69992
2	28.504	FM	0.2818	67.97392	4.02065	50.30008



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	28.075	MF	0.2886	45.05552	2.60222	18.52708
2	28.715	FM	0.5021	198.13184	6.57730	81.47292



(R)-2-bromo-3,3-difluoro-3-(4-nitrophenyl)propan-1-ol. **1s** was prepared from **2s** (51.6 mg, 0.2 mmol) according to the General Procedure as a clear, colorless oil (44.4 mg, 75% yield).

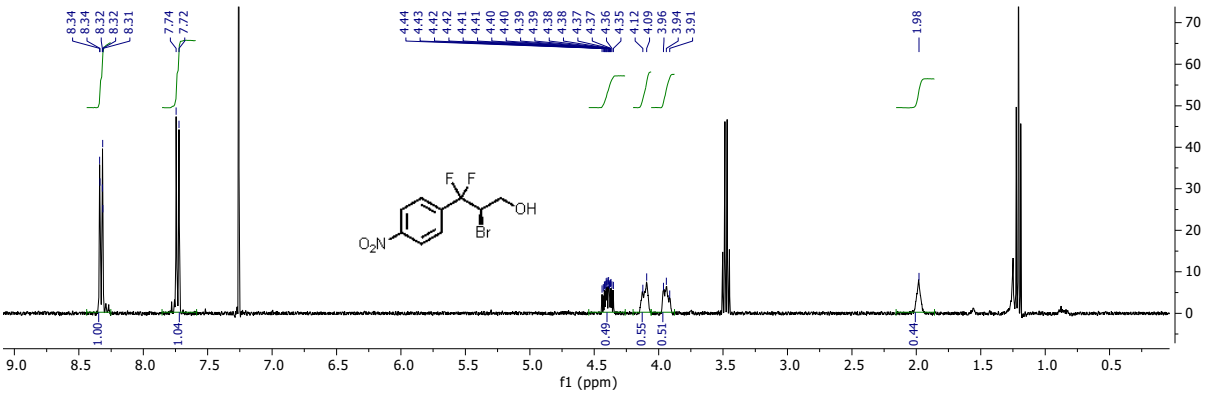
^{1}H NMR (399 MHz, $CDCl_3$) δ 8.33 (d, J = 9.1 Hz, 1H), 7.73 (d, J = 8.8 Hz, 2H), 4.40 (dddd, J = 14.8, 8.9, 7.3, 4.1 Hz, 1H), 4.19 – 4.03 (m, 1H), 3.99 – 3.83 (m, 1H), 1.98 (s, 1H).

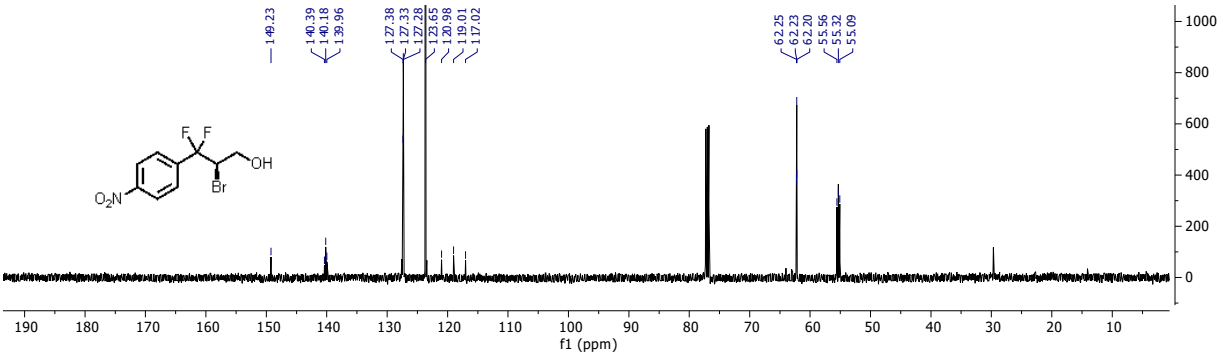
^{13}C NMR (126 MHz, $CDCl_3$) δ 149.23, 140.18 (t, J = 26.7 Hz), 127.33 (t, J = 6.2 Hz), 123.65, 119.01 (t, J = 249.9, 248.6 Hz), 62.23 (t, J = 3.2 Hz), 56.99 – 52.11 (m).

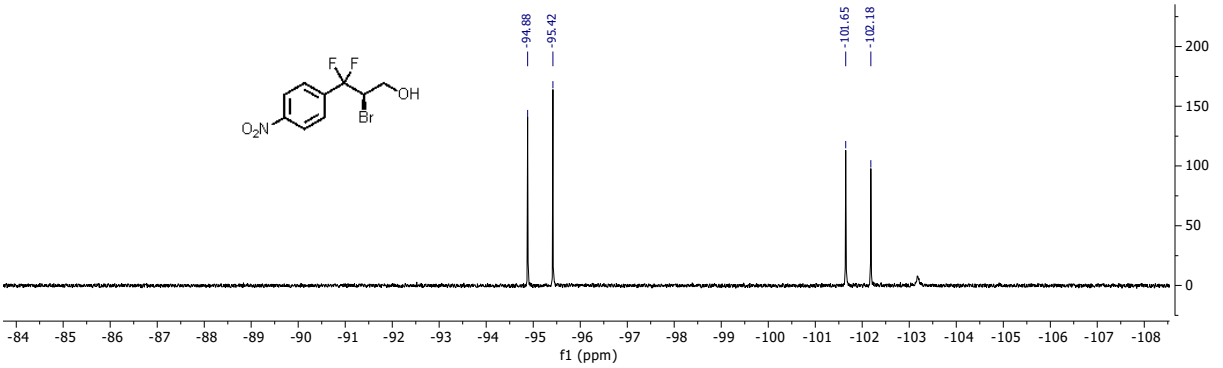
^{19}F NMR (471 MHz, $CDCl_3$) δ -95.15 (d, J = 252.0 Hz), -101.92 (d, J = 252.2 Hz).

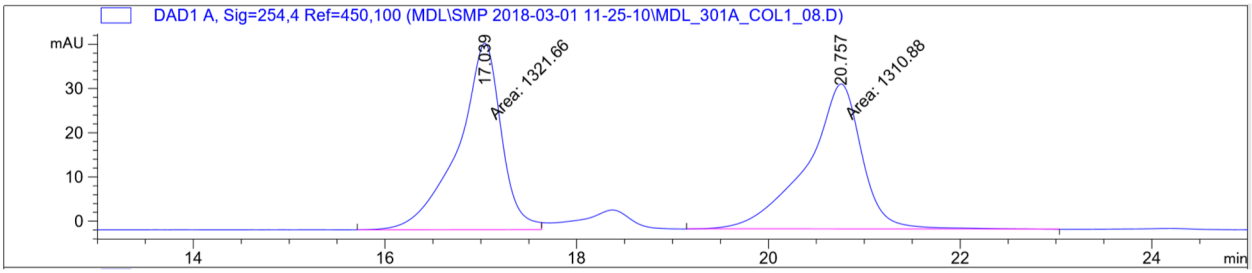
HRMS (ESI): for $C_9H_9BrF_2NO_3$, $[M+H]^+$ calculated m/z = 293.9583 and 295.9562, found m/z = 293.9583 and 295.9560.

Chiral HPLC: Chiralpak IA, 8.0% isopropanol/hexanes, 1.0 ml/min, 90% ee



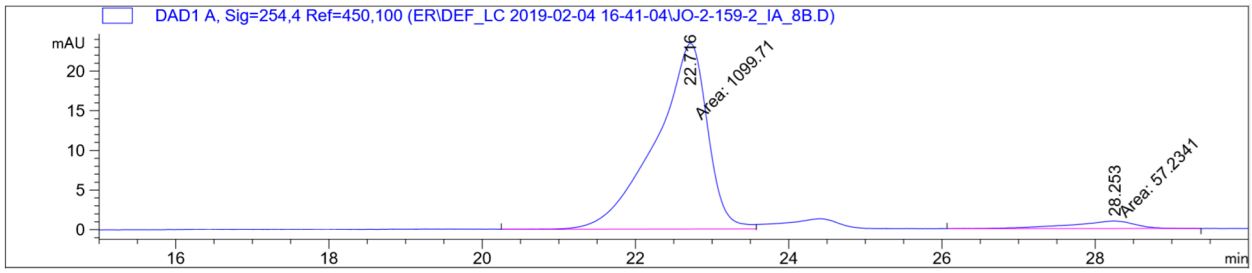






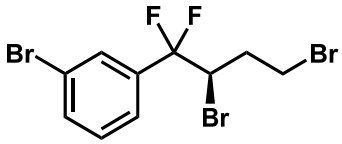
Signal 1: DAD1 A, Sig=254,4 Ref=450,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.039	MM	0.5224	1321.66040	42.16349	50.2047
2	20.757	MM	0.6664	1310.88232	32.78624	49.7953



Signal 1: DAD1 A, Sig=254,4 Ref=450,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.716	MM	0.7829	1099.70837	23.41049	95.0530
2	28.253	MM	0.9952	57.23410	9.58472e-1	4.9470



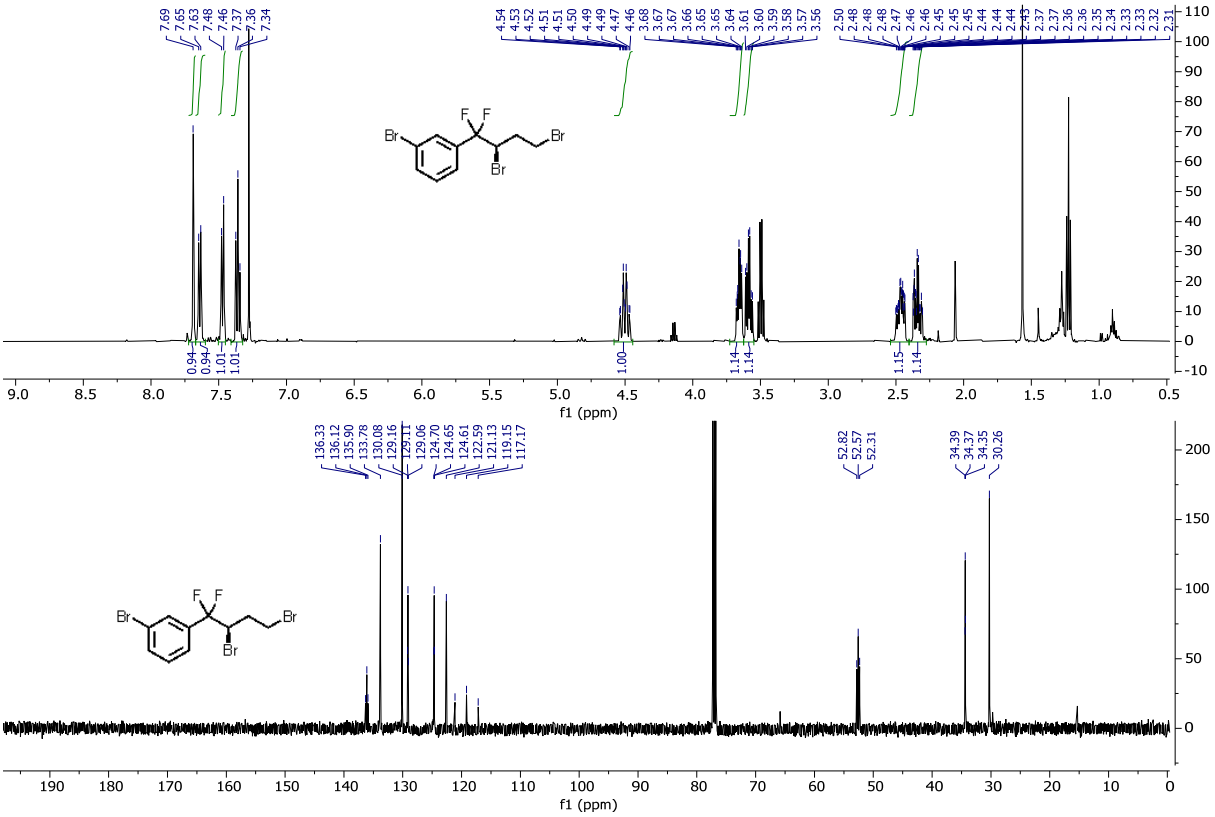
(R)-1-bromo-3-(2,4-dibromo-1,1-difluorobutyl)benzene. **1t** was prepared from **2t** (73.8 mg, 0.2 mmol) according to the General Procedure as a clear, colorless oil (79.8 mg, 98% yield). Enantiomeric excess was determined from the thioacetate substitution product. See S2 below.

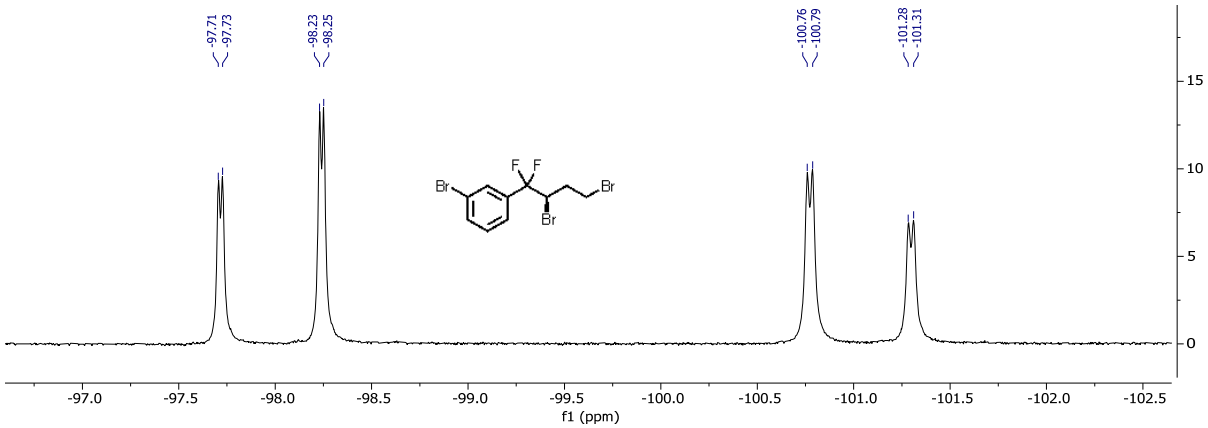
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.64 (d, J = 7.7 Hz, 1H), 7.47 (d, J = 7.8 Hz, 1H), 7.36 (t, J = 7.9 Hz, 1H), 4.50 (dtd, J = 13.3, 10.7, 2.7 Hz, 1H), 3.66 (ddd, J = 10.0, 5.8, 3.9 Hz, 1H), 3.58 (td, J = 10.3, 4.7 Hz, 1H), 2.47 (dddd, J = 15.7, 10.4, 5.8, 2.7 Hz, 1H), 2.34 (ddq, J = 15.1, 11.0, 3.9 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 136.12 (t, J = 26.6 Hz), 133.78, 130.08, 129.11 (t, J = 6.4 Hz), 124.66 (t, J = 6.1 Hz), 122.59, 119.15 (t, J = 249.8, 247.7 Hz), 53.80 – 50.59 (m), 34.37 (t, J = 2.6 Hz), 30.26.

^{19}F NMR (471 MHz, c_6d_6) δ -97.98 (dd, J = 246.8, 10.3 Hz), -101.04 (dd, J = 246.5, 13.3 Hz).

HRMS (EI): for $C_{10}H_9Br_3F_2$, $[M]^+$ calculated m/z = 403.8217 and 405.8196 and 407.8176 and 409.8156, found m/z = 403.8211 and 405.8190 and 407.8169 and 409.8149.




-97.71
-97.73
-98.23
-98.25
-100.76
-100.79
-101.28
-101.31
F
F
Br
Br
Br
15
10
5
0
-97.0
-97.5
-98.0
-98.5
-99.0
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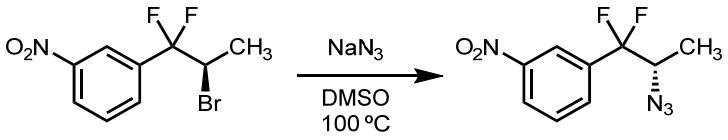
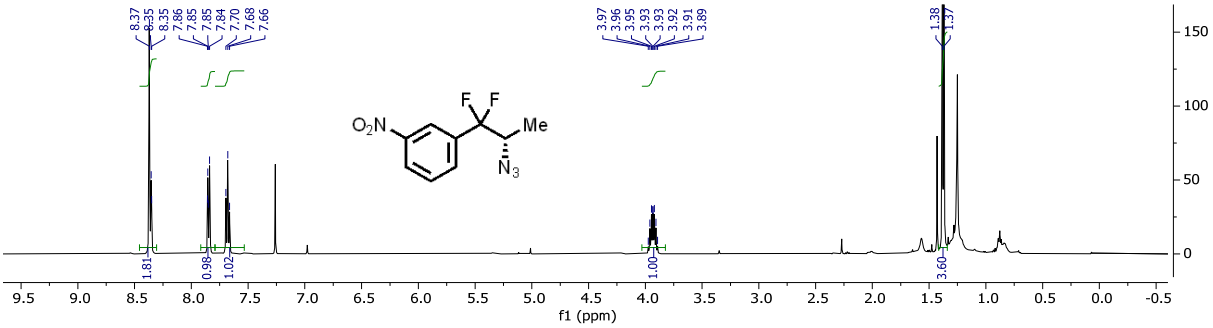
-100.0
-100.5
-101.0
-101.5
-102.0
-102.5
f1 (ppm)

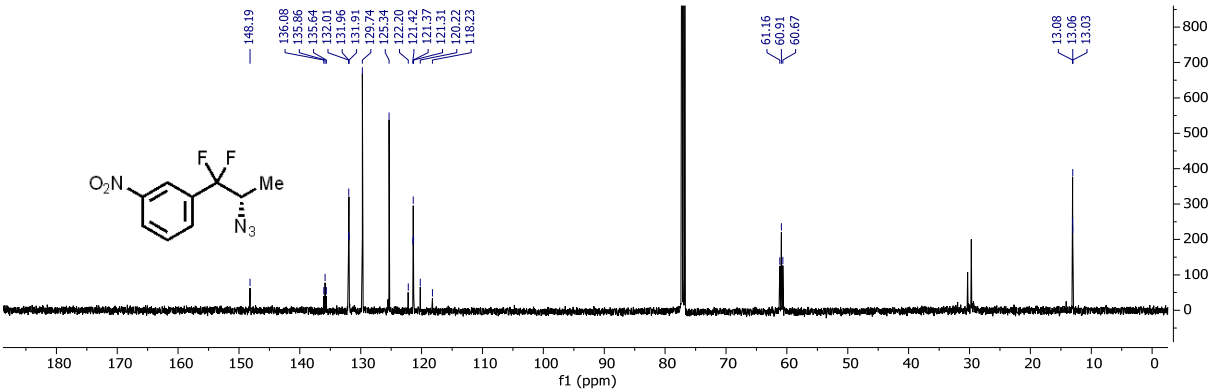
Derivatizations

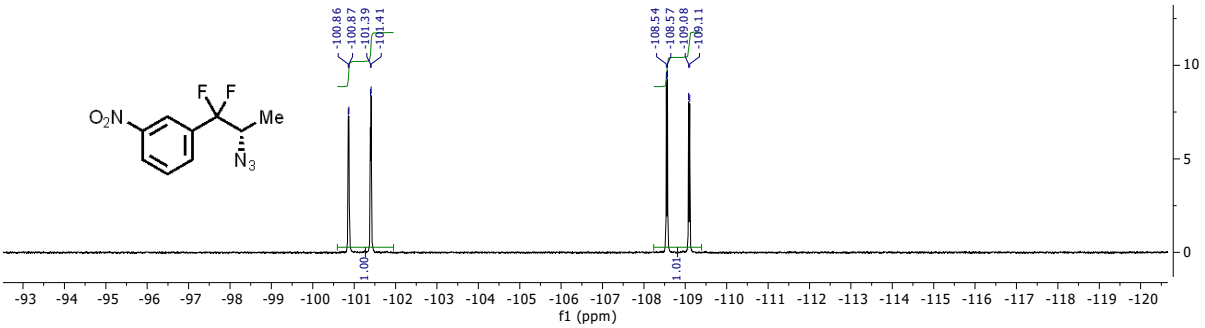


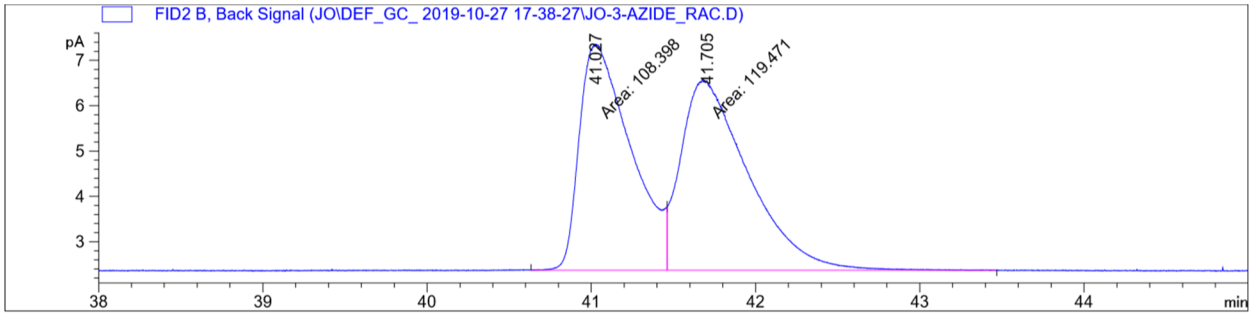
5. (S)-1-(2-azido-1,1-difluoropropyl)-3-nitrobenzene. To a solution of **1a** (28 mg, 0.1 mmol) in DMSO (0.3 mL) under N_2, was added solid NaN_3 (20 mg, 3 equiv). The mixture was briefly degassed by direct exposure to high vacuum, refilled with N_2, and sealed. The mixture was heated at 100°C for 12 hours, and upon cooling was diluted with brine. The aqueous layer was extracted 3x with Et_2O, and the combined organic layers were washed 3x with brine, dried over $MgSO_4$, filtered, and concentrated. The crude residue was purified by column chromatography eluting with Hexanes/Et_2O on a gradient from pure hexanes to 5% Et_2O, affording the title compound as a colorless oil (18 mg, 74%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40 – 8.33 (m, 1H), 7.88 – 7.82 (m, 0H), 7.68 (t, J = 7.9 Hz, 0H), 3.99 – 3.87 (m, 0H), 1.38 (d, J = 6.8 Hz, 1H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 148.19, 135.86 (t, J = 27.3 Hz), 131.96 (t, J = 6.0 Hz), 129.74, 125.34, 121.37 (t, J = 6.8 Hz), 120.22 (d, J = 249.7 Hz), 60.91 (t, J = 30.8 Hz), 13.06 (t, J = 3.2 Hz).
^{19}F NMR (471 MHz, $CDCl_3$) δ -101.13 (dd, J = 252.3, 7.8 Hz, 1F), -108.82 (dd, J = 252.5, 12.7 Hz, 1F).
HRMS (ESI): for $C_9H_8F_2O_2Na$, $[M+Na]^+$ calculated m/z = 265.0508, found m/z = 265.0508.
Chiral GC: CP-Chirasil-Dex CB, isothermal 110 °C, 14 psi, 90% ee

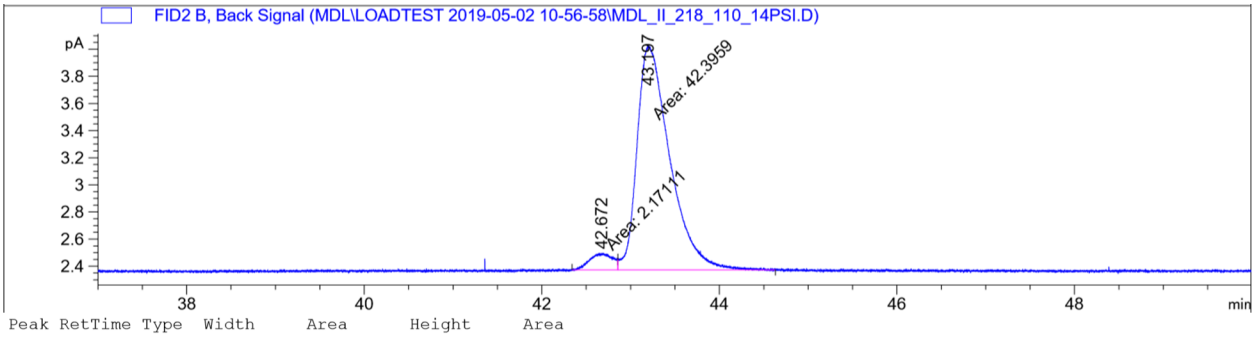








Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	41.027	MF	0.3627	108.39780	4.98073	47.57025
2	41.705	FM	0.4767	119.47111	4.17721	52.42975

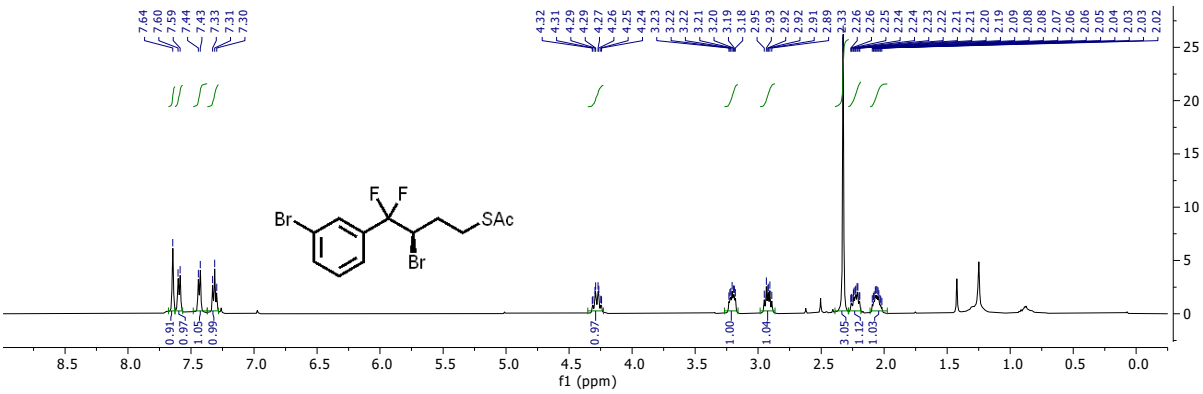


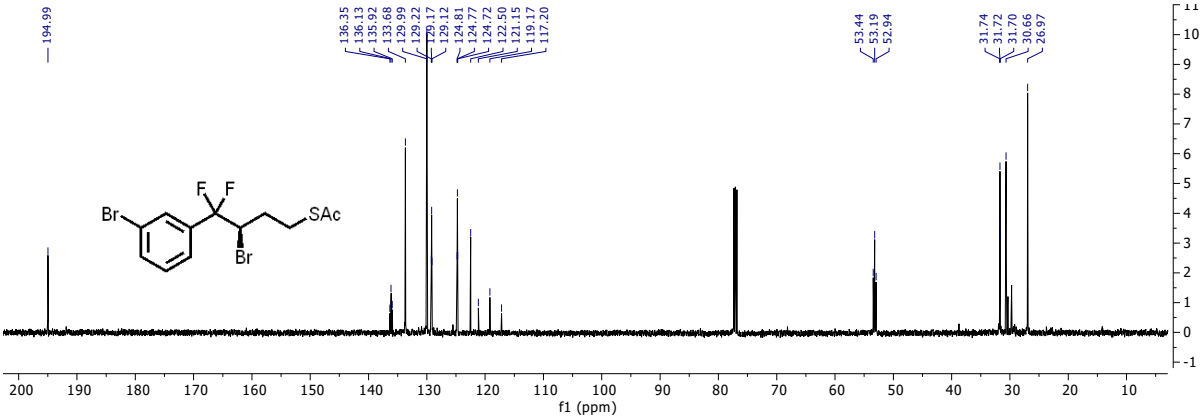
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	42.672	MF	0.3015	2.17111	1.20021e-1	4.87156
2	43.197	FM	0.4273	42.39592	1.65382	95.12844

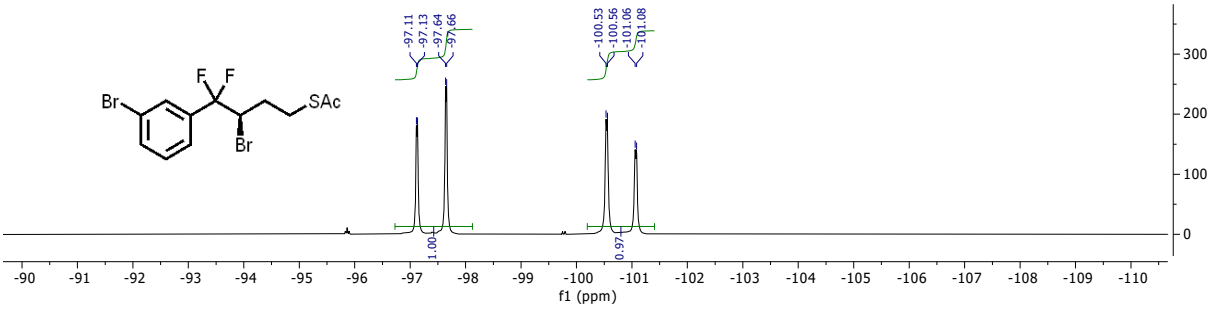
S2 (R)-S-(3-bromo-4-(3-bromophenyl)-4,4-difluorobutyl) ethanethioate. To a solution of **1t** (82 mg, 0.2 mmol) in DMSO (2 mL) under N_2, was added solid KSAc (46 mg, 2 equiv). The mixture was briefly degassed by direct exposure to high vacuum, refilled with N_2, and sealed. The mixture was stirred at room temperature for 1 hour, and upon cooling was diluted with brine. The aqueous layer was extracted 3x with Et_2O, and the combined organic layers were washed 3x with brine, dried over $MgSO_4$, filtered, and concentrated. The product was used without further purification (80 mg, 77%).

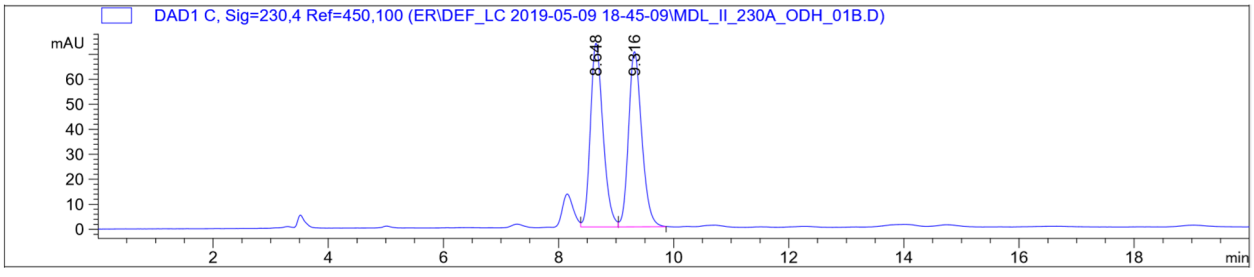
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.64 (s, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.43 (d, *J* = 7.9 Hz, 1H), 7.31 (t, *J* = 7.9 Hz, 1H), 4.28 (td, *J* = 13.3, 12.0, 9.2 Hz, 1H), 3.21 (ddd, *J* = 13.0, 7.8, 4.4 Hz, 1H), 2.92 (dt, *J* = 13.9, 8.0 Hz, 1H), 2.32 (s, 3H), 2.23 (dtd, *J* = 15.7, 8.9, 7.9, 2.4 Hz, 1H), 2.05 (dddd, *J* = 15.2, 11.7, 7.7, 4.4 Hz, 1H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 194.99, 136.13 (t, *J* = 26.9 Hz), 133.68, 129.99, 129.17 (t, *J* = 6.4 Hz), 124.77 (t, *J* = 6.2 Hz), 122.50, 119.17 (t, *J* = 248.4 Hz), 53.19 (t, *J* = 31.9 Hz), 31.72 (t, *J* = 2.4 Hz), 30.66, 26.97.
^{19}F NMR (471 MHz, Chloroform-*d*) δ -97.39 (dd, *J* = 246.7, 10.0 Hz, 1F), -100.81 (dd, *J* = 246.5, 12.7 Hz, 1F).
HRMS (EI): for $C_{12}H_{12}Br_2F_2OS$, $[M]^+$ calculated *m/z* = 399.8938 and 401.8918 and 403.8897, found *m/z* = 399.8937 and 401.8915 and 403.8893.
Chiral HPLC: Chiralcel OD-H, 1.0% isopropanol/hexanes, 1.0 ml/min, 76% ee



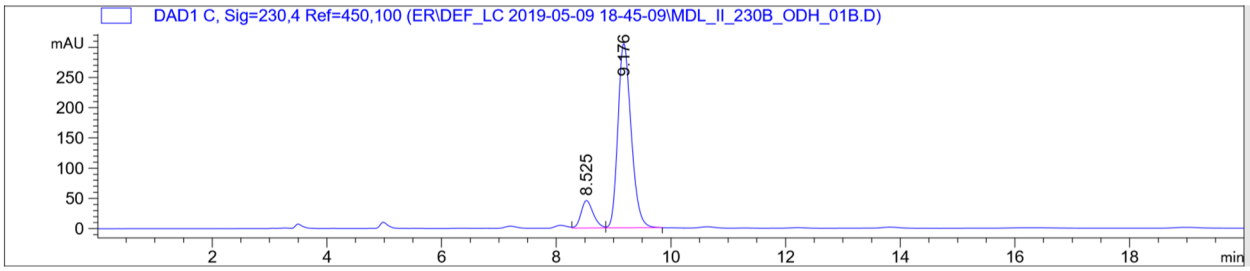






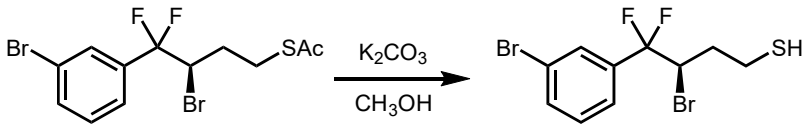
Signal 3: DAD1 C, Sig=230,4 Ref=450,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.648	VV	0.2342	1122.96265	73.51925	49.9885
2	9.316	VB	0.2448	1123.47949	70.16842	50.0115



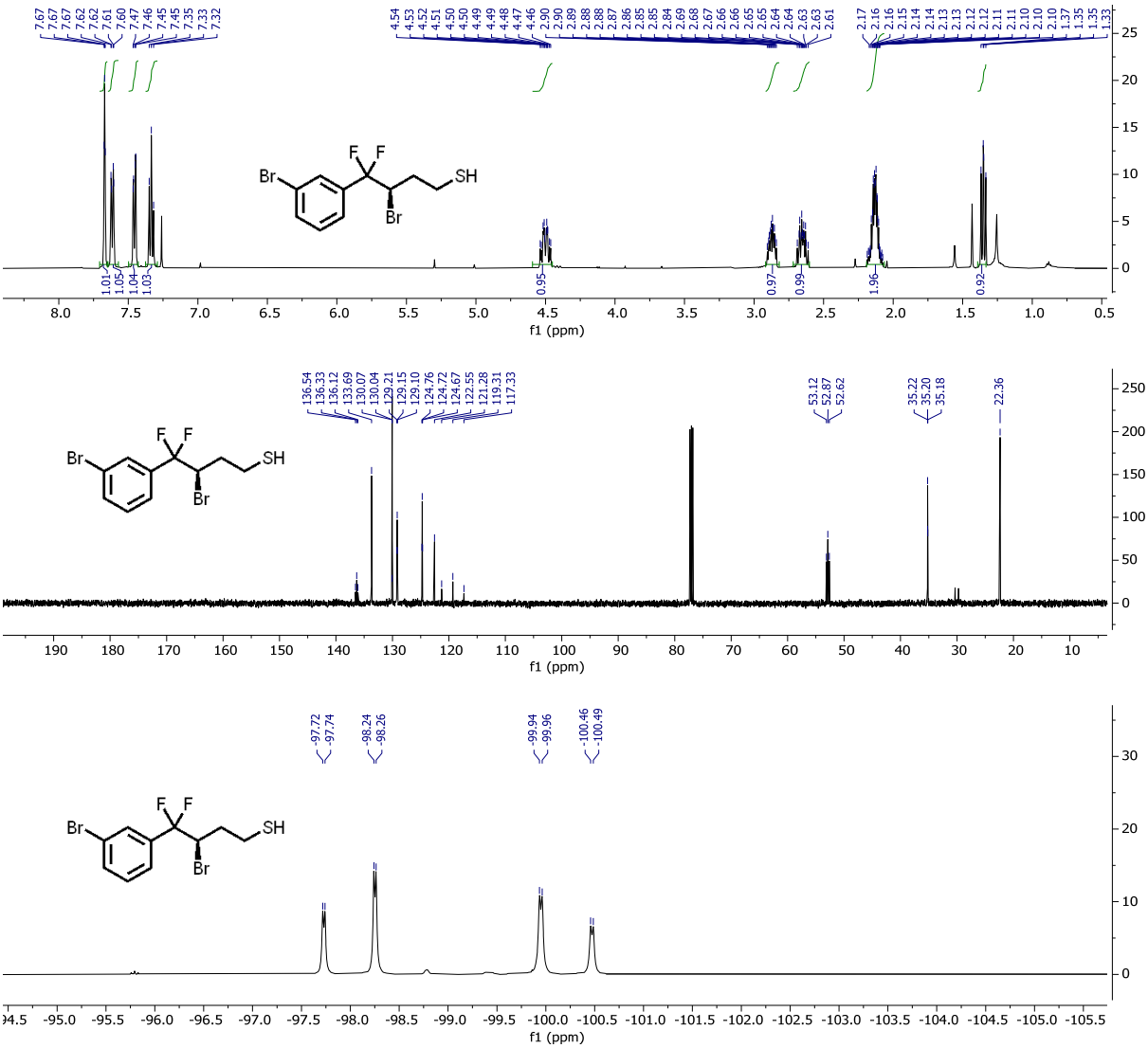
Signal 3: DAD1 C, Sig=230,4 Ref=450,100

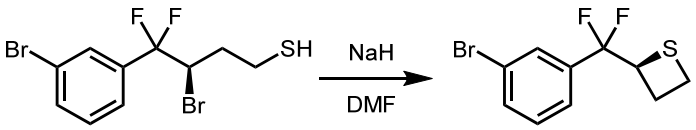
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.525	VV	0.2268	676.37372	45.67154	12.0967
2	9.176	VB	0.2478	4915.01953	305.29327	87.9033



S3. (R)-3-bromo-4-(3-bromophenyl)-4,4-difluorobutane-1-thiol. To a solution of **S2** (159 mg, 0.39 mmol) in methanol (8 mL) under N_2, was added solid K_2CO_3 (110 mg, 2 equiv). The mixture was briefly degassed by direct exposure to high vacuum, refilled with N_2, and sealed. The mixture was stirred at room temperature for 1 hour and quenched with aqueous ammonium chloride. The aqueous layer was extracted 3x with Et_2O, and the combined organics dried over $MgSO_4$, filtered, and concentrated. The residue was purified by column chromatography on SiO_2 eluting with Hexanes/Et_2O as a clear, colorless oil. (104 mg, 73%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.67 (t, *J* = 1.9 Hz, 1H), 7.61 (dd, *J* = 7.9, 2.0 Hz, 1H), 7.46 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.33 (t, *J* = 7.9 Hz, 1H), 4.56 – 4.45 (m, 1H), 2.87 (dtd, *J* = 13.7, 7.1, 4.4 Hz, 1H), 2.65 (dtd, *J* = 13.6, 9.1, 6.8 Hz, 1H), 2.13 (tdd, *J* = 9.4, 7.4, 4.5 Hz, 2H), 1.35 (dd, *J* = 9.3, 7.7 Hz, 1H).
^{13}C NMR (126 MHz, Chloroform-*d*) δ 136.33 (t, *J* = 26.8 Hz), 133.69, 130.04, 129.15 (t, *J* = 6.5 Hz), 124.72 (t, *J* = 6.1 Hz), 122.55, 119.31 (t, *J* = 247.9 Hz), 52.87 (t, *J* = 31.5 Hz), 35.21 (d, *J* = 2.3 Hz), 22.36.
^{19}F NMR (471 MHz, Chloroform-*d*) δ -97.99 (dd, *J* = 246.3, 10.7 Hz, 1F), -100.21 (dd, *J* = 246.3, 13.0 Hz, 1F).
HRMS (EI): for $C_{10}H_{10}Br_2F_2S$, $[M]^+$ calculated *m/z* = 357.8833 and 359.8812 and 361.8792, found *m/z* = 357.8835 and 359.8813 and 361.8792.

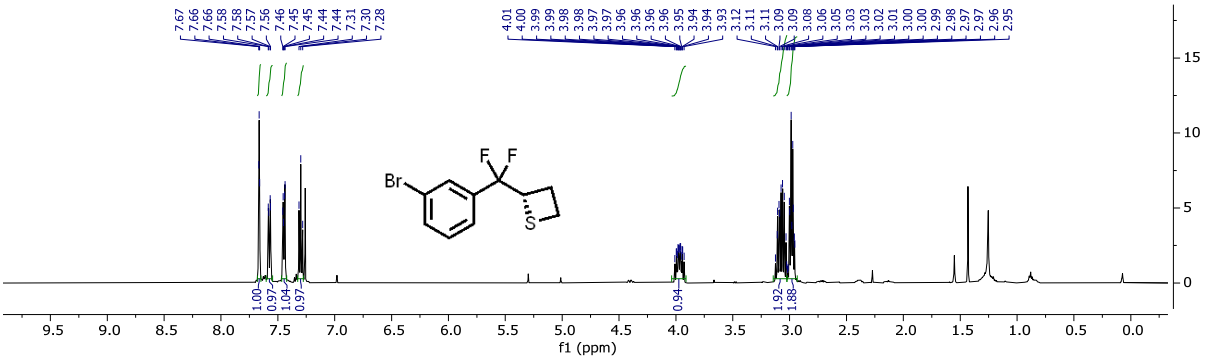


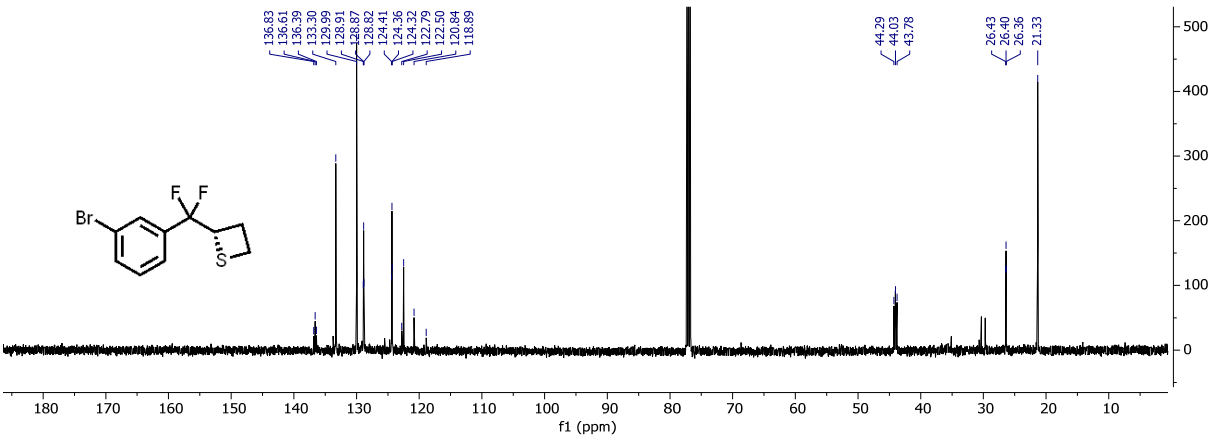


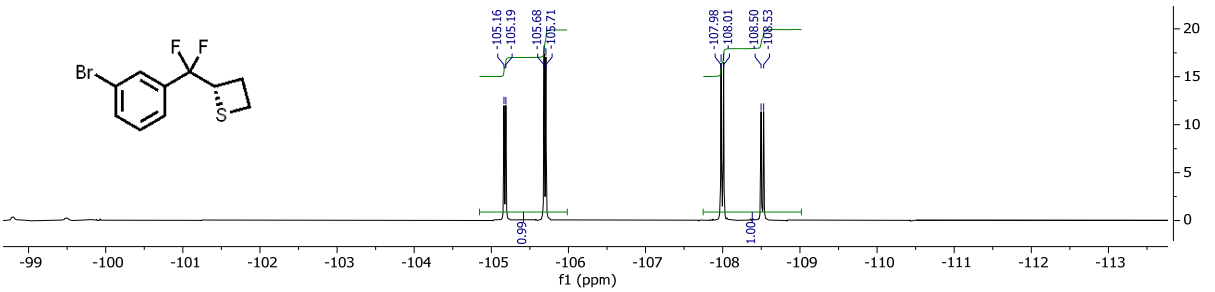
7. (S)-2-((3-bromophenyl)difluoromethyl)thietane. A solution of **S3** (53 mg, 0.147 mmol) in DMF (1.5 mL) was added under N_2 to solid NaH (95%, 4.2 mg, 1.2 equiv) [Caution! Sodium hydride in DMF can lead to runaway exothermic reactions on large scale.]. The mixture was briefly degassed by direct exposure to high vacuum, refilled with N_2, and sealed. The mixture was stirred at room 90 ºC for 9 hours, and upon cooling to room temperature was quenched with aqueous ammonium chloride. The aqueous layer was extracted 3x with Et_2O, and the combined organics were washed three times with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by column chromatography on SiO_2 eluting with Hexanes/Et_2O as a clear, colorless oil (28 mg, 68%).

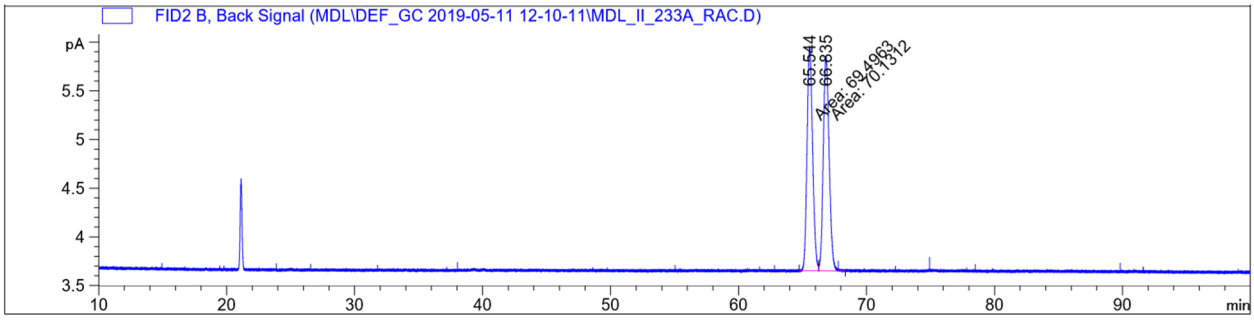
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.66 (t, *J* = 1.9 Hz, 1H), 7.61 – 7.52 (m, 1H), 7.45 (dt, *J* = 7.7, 1.3 Hz, 1H), 7.30 (t, *J* = 7.9 Hz, 1H), 3.97 (dddd, *J* = 15.4, 11.1, 7.7, 6.6 Hz, 1H), 3.14 – 3.02 (m, 2H), 3.02 – 2.94 (m, 2H).
^{13}C NMR (126 MHz, Chloroform-*d*) δ 136.61 (t, *J* = 27.5 Hz), 133.30, 129.99, 128.87 (t, *J* = 6.2 Hz), 124.36 (t, *J* = 5.9 Hz), 120.84 (t, *J* = 208.4 Hz), 44.04 (t, *J* = 31.1 Hz), 26.40 (t, *J* = 3.5 Hz), 21.33.

^{19}F NMR (471 MHz, Chloroform-*d*) δ -105.44 (dd, *J* = 244.1, 11.1 Hz, 1F), -108.25 (dd, *J* = 244.1, 15.5 Hz, 1F).
HRMS (EI): for $C_{10}H_9BrF_2S$, $[M]^+$ calculated *m/z* = 277.9571 and 279.9550, found *m/z* = 277.9568 and 279.9545.
Chiral GC: β-Cyclosil, isothermal 120 °C, 14 psi, 76% ee

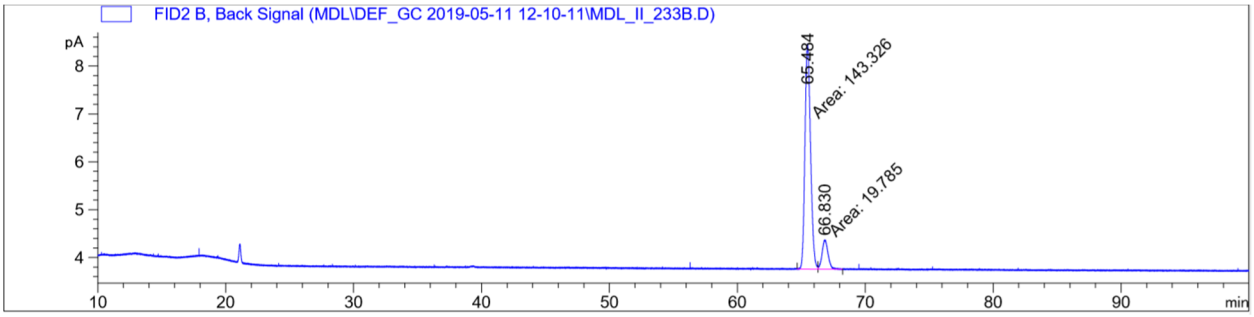




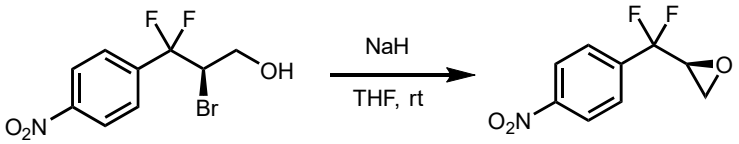




Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	65.544	MF	0.5039	69.49633	2.29857	49.77266
2	66.835	FM	0.5322	70.13118	2.19624	50.22734

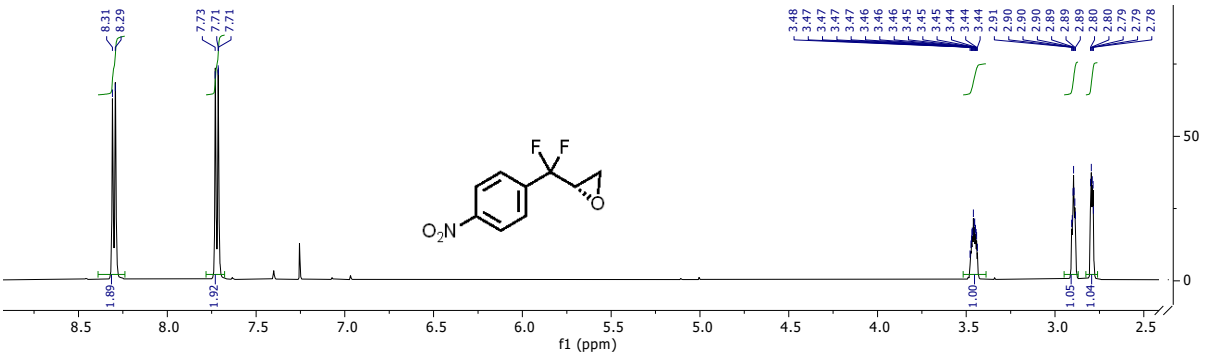


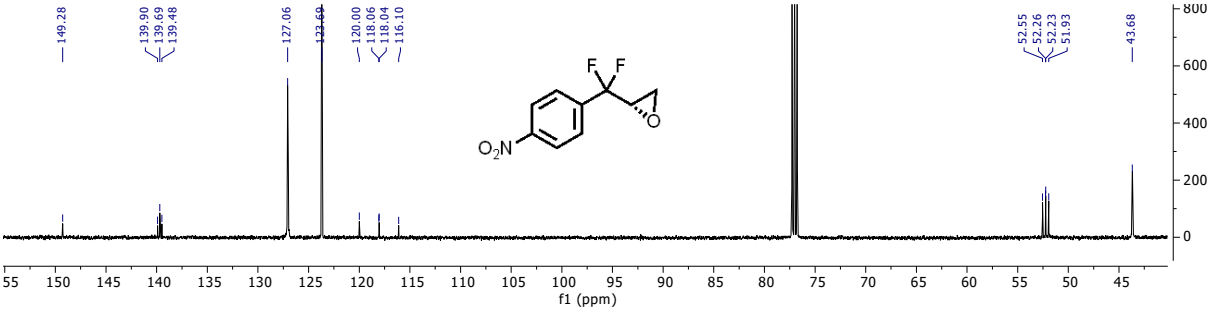
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	65.484	MF	0.5074	143.32643	4.70781	87.87026
2	66.830	FM	0.5387	19.78500	6.12102e-1	12.12974

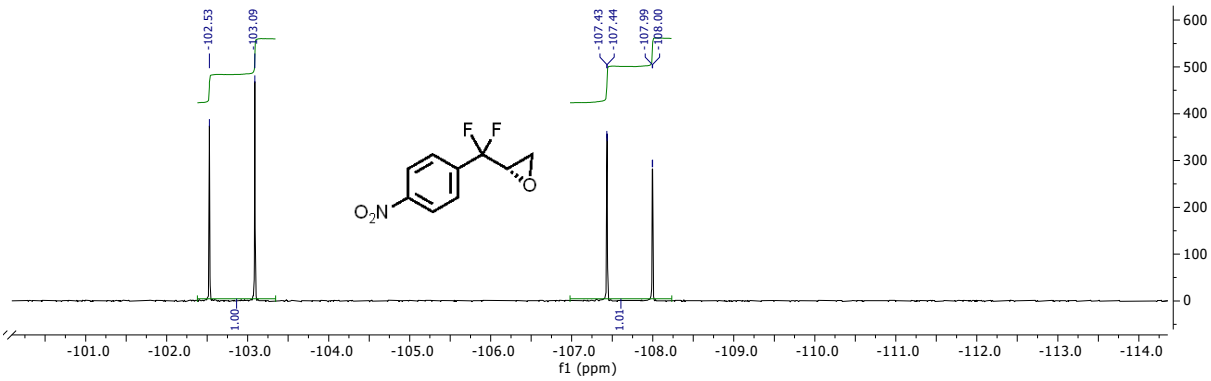


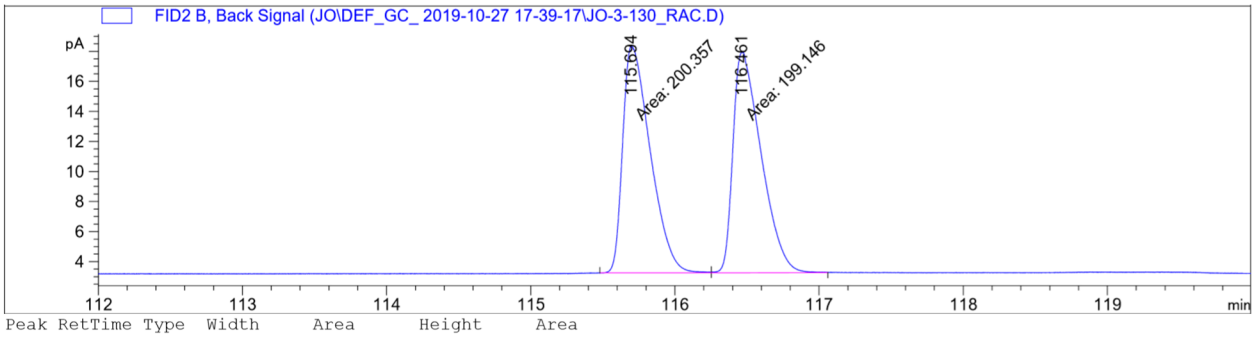
6. (S)-2-(difluoro(4-nitrophenyl)methyl)oxirane. A solution of **1s** (29.6 mg, 0.1 mmol) in THF (0.8 mL) was added under N_2 to a suspension of NaH (95%, 4.8 mg, 2 equiv) in THF (0.2 mL) at room temperature. The mixture was stirred for 15 minutes and was quenched by aqueous ammonium chloride. The aqueous layer was extracted 3x with Et_2O, and the combined organics dried over Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography on SiO_2 eluting with Hexanes/Et_2O and isolated as a white solid (13 mg, 70%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (d, J = 8.2 Hz, 2H), 7.76 – 7.63 (m, 2H), 3.46 (dddd, J = 9.2, 5.4, 3.9, 2.4 Hz, 1H), 2.90 (ddd, J = 5.3, 3.6, 1.6 Hz, 1H), 2.79 (dd, J = 5.0, 2.3 Hz, 1H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 149.28, 139.69 (t, J = 26.8 Hz), 127.06, 123.69, 118.05 (dd, J = 246.1, 243.3 Hz), 52.24 (dd, J = 40.6, 36.8 Hz), 43.68.
^{19}F NMR (471 MHz, $CDCl_3$) δ -102.81 (d, J = 263.8 Hz, 1F), -107.72 (dd, J = 263.7, 2.3 Hz, 1F).
HRMS (EI): for $C_9H_7F_2NO_3$, $[M]^+$ calculated m/z = 215.0389, found m/z = 215.038.
Chiral GC: β-Cyclosil, 40 °C to 120 °C, 1 °C/min, 14 psi, 92% ee

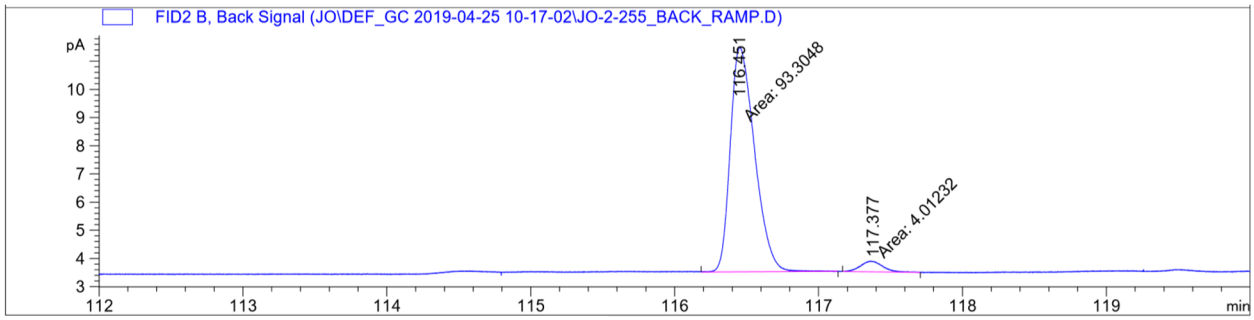






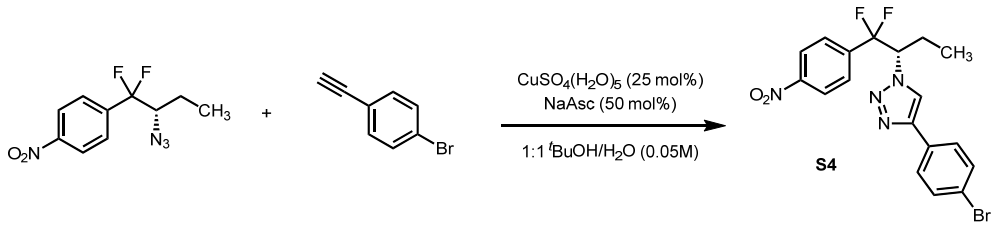


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	115.694	MF	0.2209	200.35736	15.11787	50.15162
2	116.461	FM	0.2255	199.14589	14.71975	49.84838



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	116.451	MM	0.1954	93.30479	7.95966	95.87707
2	117.377	MM	0.1785	4.01232	3.74736e-1	4.12293

X-ray Crystallography: X-ray crystallography quality crystals were obtained of the following derivative (prepared by azide displacement using the method described for **5** on **1i** followed by the standard click-chemistry technique with p-bromophenylacetylene) by vapor diffusion of pentane into MTBE:



S4. (S)-4-(4-bromophenyl)-1-(1,1-difluoro-1-(4-nitrophenyl)butan-2-yl)-1H-1,2,3-triazole. The azide product (3 mg, 0.012 mmol, 1 equiv) was dissolved in a 1:1 mixture of *t*BuOH/H_2O (0.05M overall). To this solution was added, in succession, p-bromophenylacetylene (2.5 mg, 0.014 mmol, 1.2 equiv), $CuSO_4$•$5H_2O$ (0.8 mg, 0.003 mmol, 0.25 equiv), and sodium ascorbate (1.2 mg, 0.006 mmol, 0.5 equiv). The vial was placed under an N_2 atmosphere and sealed with electrical tape. The solution was stirred overnight at room temperature. After this time, the reaction mixture was diluted with EtOAc and H_2O. The organic layers were separated and washed with brine, dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. The crude material was then purified by flash column chromatography (5% to 60% Et_2O/Hexanes) to afford **S4** as a white solid (5 mg, 95% yield).

X-ray crystallography: A crystal mounted on a diffractometer was collected data at 100 K. The intensities of the reflections were collected by means of a Bruker APEX II CCD diffractometer ($Mo_{K\alpha}$ radiation, λ=0.71073 Å), and equipped with an Oxford Cryosystems nitrogen flow apparatus. The collection method involved 0.5° scans in ω at 28° in 2θ. Data integration down to 0.78 Å resolution was carried out using SAINT V8.37A[7] with reflection spot size optimization. Absorption corrections were made with the program SADABS.[7] The structure was solved by the Intrinsic Phasing methods and refined by least-squares methods again F^2 using SHELXT-2014[8] and SHELXL-2014[9] with OLEX 2 interface.[10] Non-hydrogen atoms were refined anisotropically, and hydrogen atoms were allowed to ride on the respective atoms. Crystal data as well as details of data collection and refinement are summarized in Table 1, and geometric parameters are shown in Table 2. The Ortep plots produced with SHELXL-2014 program, and the other drawings were produced with Accelrys DS Visualizer 2.0.[11]

Table S1. Experimental details

	MLII-99-2
Crystal data	
Chemical formula	$C_{18}H_{15}BrF_2N_4O_2$
M_r	437.25

Crystal system, space group	Monoclinic, $P2_1$
Temperature (K)	100
a, b, c (Å)	12.6771 (15), 5.6603 (7), 13.2825 (15)
β (°)	112.3222 (18)
V (Å^3)	881.68 (18)
Z	2
Radiation type	Mo $K\alpha$
μ (mm^{-1})	2.37
Crystal size (mm)	0.10 × 0.04 × 0.02
Data collection	
Diffractometer	Bruker D8 goniometer with CCD area detector
Absorption correction	Multi-scan *SADABS*
T_{min}, T_{max}	0.565, 0.746
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	5582, 3654, 2999
R_{int}	0.030
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.641
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.051, 0.119, 1.03
No. of reflections	3654
No. of parameters	245
No. of restraints	1
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	1.13, -0.38
Absolute structure	Flack x determined using 1028 quotients [(I+)-(I-)]/[(I+)+(I-)] (Parsons, Flack and Wagner, Acta Cryst. B69 (2013) 249-259).
Absolute structure parameter	-0.004 (13)

Computer programs: *SAINT* 8.37A (Bruker-AXS, 2015), *SHELXT2014* (Sheldrick, 2015), *SHELXL2014* (Sheldrick, 2015), Bruker *SHELXTL* (Sheldrick, 2015).

Table S2. Geometric parameters (Å, º)

Br1—C16	1.908 (7)	C7—C8	1.518 (10)
F1—C7	1.369 (9)	C8—C9	1.529 (10)
F2—C7	1.373 (8)	C8—H8	1.0000
O1—N4	1.253 (9)	C9—C10	1.505 (10)
O2—N4	1.203 (10)	C9—H9A	0.9900
N1—N2	1.320 (7)	C9—H9B	0.9900
N1—C12	1.364 (9)	C10—H10A	0.9800
N2—N3	1.355 (8)	C10—H10B	0.9800
N3—C11	1.347 (8)	C10—H10C	0.9800
N3—C8	1.475 (8)	C11—C12	1.384 (9)
N4—C3	1.480 (8)	C11—H11	0.9500
C1—C6	1.384 (10)	C12—C13	1.473 (9)
C1—C2	1.403 (9)	C13—C14	1.393 (12)
C1—H1	0.9500	C13—C18	1.396 (9)
C2—C3	1.379 (10)	C14—C15	1.384 (9)
C2—H2	0.9500	C14—H14	0.9500
C3—C4	1.381 (9)	C15—C16	1.374 (10)
C4—C5	1.379 (9)	C15—H15	0.9500
C4—H4	0.9500	C16—C17	1.371 (10)
C5—C6	1.403 (12)	C17—C18	1.387 (9)
C5—H5	0.9500	C17—H17	0.9500
C6—C7	1.524 (10)	C18—H18	0.9500
N2—N1—C12	108.9 (6)	C9—C8—H8	107.9
N1—N2—N3	106.8 (6)	C10—C9—C8	113.9 (6)
C11—N3—N2	111.6 (5)	C10—C9—H9A	108.8
C11—N3—C8	128.7 (6)	C8—C9—H9A	108.8
N2—N3—C8	119.6 (5)	C10—C9—H9B	108.8
O2—N4—O1	124.2 (6)	C8—C9—H9B	108.8
O2—N4—C3	119.2 (7)	H9A—C9—H9B	107.7
O1—N4—C3	116.6 (8)	C9—C10—H10A	109.5
C6—C1—C2	120.0 (6)	C9—C10—H10B	109.5
C6—C1—H1	120.0	H10A—C10—H10B	109.5
C2—C1—H1	120.0	C9—C10—H10C	109.5

C3—C2—C1	117.4 (6)	H10A—C10—H10C	109.5
C3—C2—H2	121.3	H10B—C10—H10C	109.5
C1—C2—H2	121.3	N3—C11—C12	104.1 (6)
C2—C3—C4	123.5 (7)	N3—C11—H11	127.9
C2—C3—N4	119.2 (7)	C12—C11—H11	127.9
C4—C3—N4	117.3 (6)	N1—C12—C11	108.6 (6)
C5—C4—C3	119.0 (7)	N1—C12—C13	122.7 (6)
C5—C4—H4	120.5	C11—C12—C13	128.7 (6)
C3—C4—H4	120.5	C14—C13—C18	118.7 (6)
C4—C5—C6	119.1 (7)	C14—C13—C12	120.7 (6)
C4—C5—H5	120.5	C18—C13—C12	120.7 (6)
C6—C5—H5	120.5	C15—C14—C13	120.8 (7)
C1—C6—C5	121.0 (6)	C15—C14—H14	119.6
C1—C6—C7	118.5 (6)	C13—C14—H14	119.6
C5—C6—C7	120.5 (6)	C16—C15—C14	119.1 (7)
F1—C7—F2	105.1 (5)	C16—C15—H15	120.4
F1—C7—C8	109.8 (6)	C14—C15—H15	120.4
F2—C7—C8	109.4 (5)	C17—C16—C15	121.6 (6)
F1—C7—C6	108.8 (5)	C17—C16—Br1	120.5 (6)
F2—C7—C6	109.5 (6)	C15—C16—Br1	118.0 (5)
C8—C7—C6	113.8 (6)	C16—C17—C18	119.4 (7)
N3—C8—C7	108.6 (6)	C16—C17—H17	120.3
N3—C8—C9	110.9 (5)	C18—C17—H17	120.3
C7—C8—C9	113.5 (6)	C17—C18—C13	120.4 (6)
N3—C8—H8	107.9	C17—C18—H18	119.8
C7—C8—H8	107.9	C13—C18—H18	119.8
C12—N1—N2—N3	-0.3 (7)	F2—C7—C8—N3	-52.8 (7)
N1—N2—N3—C11	0.9 (7)	C6—C7—C8—N3	-175.7 (6)
N1—N2—N3—C8	179.4 (5)	F1—C7—C8—C9	-174.1 (5)
C6—C1—C2—C3	0.9 (10)	F2—C7—C8—C9	71.0 (7)
C1—C2—C3—C4	1.6 (10)	C6—C7—C8—C9	-51.9 (8)
C1—C2—C3—N4	-177.5 (6)	N3—C8—C9—C10	-59.4 (8)
O2—N4—C3—C2	169.8 (7)	C7—C8—C9—C10	177.9 (6)

O1—N4—C3—C2	-7.8 (9)	N2—N3—C11—C12	-1.1 (7)
O2—N4—C3—C4	-9.4 (9)	C8—N3—C11—C12	-179.4 (6)
O1—N4—C3—C4	172.9 (6)	N2—N1—C12—C11	-0.3 (7)
C2—C3—C4—C5	-2.4 (10)	N2—N1—C12—C13	-179.9 (6)
N4—C3—C4—C5	176.8 (6)	N3—C11—C12—N1	0.9 (7)
C3—C4—C5—C6	0.6 (10)	N3—C11—C12—C13	-179.6 (6)
C2—C1—C6—C5	-2.6 (10)	N1—C12—C13—C14	160.4 (6)
C2—C1—C6—C7	177.6 (6)	C11—C12—C13—C14	-19.1 (10)
C4—C5—C6—C1	1.9 (10)	N1—C12—C13—C18	-19.8 (10)
C4—C5—C6—C7	-178.3 (6)	C11—C12—C13—C18	160.7 (7)
C1—C6—C7—F1	52.7 (8)	C18—C13—C14—C15	1.7 (9)
C5—C6—C7—F1	-127.0 (7)	C12—C13—C14—C15	-178.5 (6)
C1—C6—C7—F2	167.2 (6)	C13—C14—C15—C16	-0.7 (10)
C5—C6—C7—F2	-12.6 (9)	C14—C15—C16—C17	-0.4 (10)
C1—C6—C7—C8	-70.0 (8)	C14—C15—C16—Br1	179.5 (5)
C5—C6—C7—C8	110.2 (7)	C15—C16—C17—C18	0.5 (10)
C11—N3—C8—C7	86.8 (8)	Br1—C16—C17—C18	-179.5 (5)
N2—N3—C8—C7	-91.4 (7)	C16—C17—C18—C13	0.6 (10)
C11—N3—C8—C9	-38.6 (10)	C14—C13—C18—C17	-1.7 (9)
N2—N3—C8—C9	143.3 (6)	C12—C13—C18—C17	178.5 (6)
F1—C7—C8—N3	62.1 (7)		

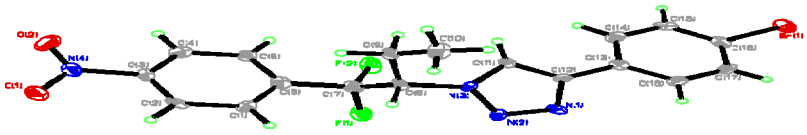


Figure S9. Perspective views showing 50% probability displacement

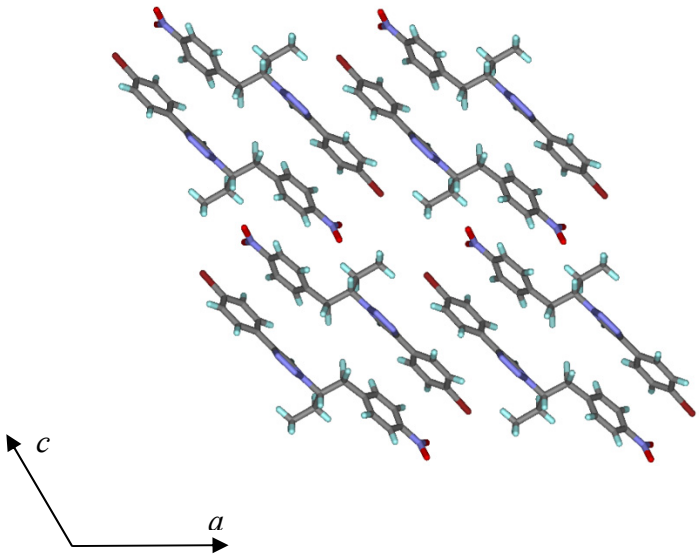


Figure S10. Three-dimensional supramolecular architecture viewed along the *b*-axis direction.

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