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Stereoselective Formation of Highly Substituted CF_3-Dihydropyrans as Versatile Building Blocks

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Contents

1. General methods

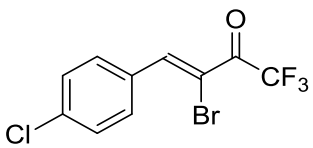
NMR spectra were acquired on a Bruker AVANCE III HD spectrometer running at 400 MHz for ^{1}H, 100 MHz for ^{13}C and 376 MHz for ^{19}F. Chemical shifts (δ) are reported in ppm relative to residual solvent signals ($CHCl_3$, 7.26 ppm for ^{1}H NMR, $CDCl_3$, 77.0 ppm for ^{13}C NMR). For ^{19}F NMR they are reported in ppm relative to $CFCl_3$ as external reference. The following abbreviations are used to indicate the multiplicity in NMR spectra: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; bs, broad signal. ^{13}C NMR spectra were acquired in broad band decoupled mode. For characterization of diastereomeric mixtures, * denotes minor diastereoisomer, $^{+}$ denotes overlap of signals from both diastereoisomers, while the major diastereomer is characterized without further denotations. Mass spectra were recorded on a Bruker Maxis Impact-TOF-MS with electrospray ionization (ESI+) or Bruker MicroTOF-Q-MS system using atmospheric pressure chemical ionization (APCI+) (both referenced to the mass of the charged species). Analytical thin layer chromatography (TLC) was performed using pre-coated aluminium-backed plates (Merck Kieselgel 60 F254) and visualized by ultraviolet radiation or $KMnO_4$ stain. For flash chromatography (FC) silica gel (Silica gel 60, 230-400 mesh, Fluka) was used. Optical rotations were measured on a Bellingham+Stanley ADP440+ polarimeter, α values are given in $deg \cdot cm^3 \cdot g^{-1} \cdot dm^{-1}$; concentration c in $g \cdot (100\ ml)^{-1}$. The diastereomeric ratio (dr) of products was evaluated by ^{1}H NMR and ^{19}F NMR analysis of the crude mixture. The enantiomeric excess (ee) of the products was determined by Ultraperformance Convergence Chromatography (ACQUITY UPC2) using Daicel Chiralpak IA, IB, IC, ID and Acquity UPC2 Trefoil CEL2 columns as chiral stationary phases. Unless otherwise noted, gradient runs were performed with 100% supercritical CO_2 for 30 s, then going from 99:1 to 60:40 CO_2/solvent over 10 min. Reference samples for UPC^2 analysis were prepared using a mixture of product obtained from reactions with **3a** and *ent*-**3a**. Unless otherwise noted, analytical grade solvents and commercially available reagents were used without further purification.

2. Starting materials

2.1. Synthesis

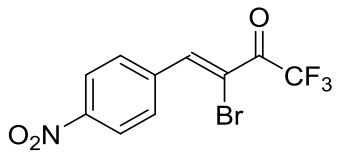
α,β-Unsaturated aldehydes **1** were obtained by a cross-metathesis reaction from the corresponding allyl benzene derivatives and crotonaldehyde.[1] α-Bromo-CF_3-enones **2** were synthesized according to a procedure described by Rulev *et al*.[2] Characterization of previously undescribed enones is presented below. Synthesis of catalyst **3a** and *ent*-**3a** was performed according to previously reported procedures.[3] Reduction of hexane-2,6-dione facilitated by yeast as described by Lieser gave (2*R*,5*S*)-hexane-2,5-diol,[4] which after mesylation, cyclization and deprotection delivered catalyst **3b** as decribed by Short *et al*.[5]

2.2. Characterization



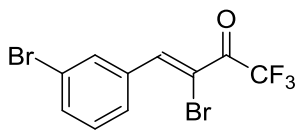
2k

2k: ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.14 (s, 1H), 7.92 (d, *J* =9 Hz, 2H), 7.48 (d, *J* = 9 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.6 (q, *J* = 35.5 Hz), 145.7, 138.2, 132.4, 131.1, 129.1, 117.1, 115.6 (q, *J* = 291.6 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ -68.58. HRMS (APCI+) *m*/*z* calcd. for $C_{10}H_5BrClF_3O$ $[M]^{+\cdot}$: 311.9159/313.9138; found: 311.9157/313.9149.



2l

2l: ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.34 (d, *J* = 8.9 Hz, 2H), 8.23 (s, 1H), 8.04 (d, *J* = 8.7 Hz, 2H). ^{13}C NMR: (100 MHz, $CDCl_3$) δ 175.6 (q, *J* = 36.2 Hz), 148.8, 144.1, 138.8, 131.4, 123.7, 120.2, 115.4 (q, *J* = 293.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ -68.95. HRMS (APCI+) *m*/*z* calcd. for $C_{10}H_5BrF_3NO_3$ $[M]^{+\cdot}$: 322.9399/324.9379; found: 322.9383/324.9379.



2o

2o: ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12 (s, 1H), 8.09 (t, *J* = 1.9 Hz, 1H), 7.86 (ddt, *J* = 7.9, 1.7, 0.7 Hz, 1H), 7.65 (ddd, *J* = 8.0, 2.0, 1.0 Hz, 1H), 7.38 (t, *J* = 7.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.7 (q, *J* = 35.6 Hz), 145.4 (q, *J* = 3.6 Hz), 134.6, 134.5, 133.5, 130.1, 129.5, 122.8, 118.0, 115.6 (q, *J* = 291.5 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ -68.70. HRMS (APCI+) *m*/*z* calcd. for $C_{10}H_5Br_2F_3O$ $[M]^{+\cdot}$: 357.8633/355.8654/359.8613; found: 359.8639/357.8637/355.8667.

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[2] A. Y. Rulev, I. A. Uchakov, V. G. Nenajdenko, E. S. Balenkova and M. G. Voronkov, *Eur. J. Org. Chem*., 2007, 6039.
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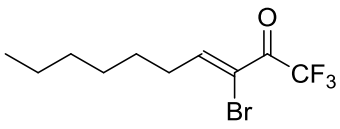
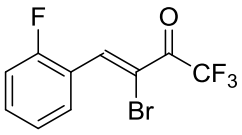


2q

2q: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (t, *J* = 6.7 Hz, 1H), 2.54 (q, *J* = 7.3 Hz, 2H), 1.54–1.62 (m, 2H), 1.29–1.42 (m, 6H), 0.9 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.8 (q, *J* = 35.7 Hz), 154.7, 121.0, 115.7 (q, *J* = 291.9 Hz), 33.8, 31.4, 29.1, 27.2, 22.4, 13.9. ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.27. HRMS (ESI+) *m/z* calcd. for $C_{10}H_{14}BrF_3O$ $[M+H]^+$: 287.0253/289.0232; found: 287.0252/289.0230.

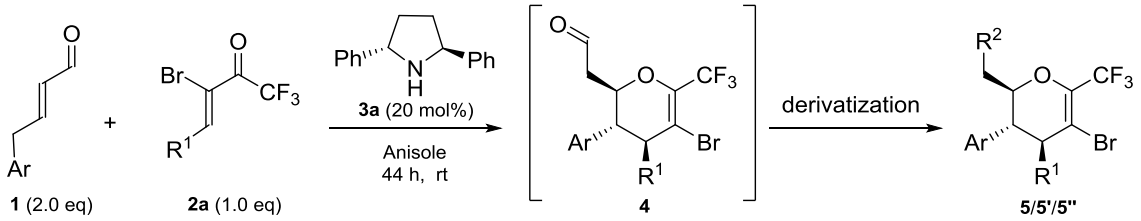


2p

2p: ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.44 (s, 1H), 8.31 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.48–7.57 (m, 1H), 7.29 (t, *J* = 7.7 Hz, 1H), 7.18 (dt, *J* = 9.3, 0.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9 (q, *J* = 35.7 Hz), 161.3 (d, *J* = 255.1 Hz), 139.6 (dq, *J* = 7.7, 3.9 Hz), 134.0 (d, *J* = 9.1 Hz), 130.3, 124.3 (d, *J* = 3.7 Hz), 121.4 (d, *J* = 10.8 Hz), 119.0, 116.1 (d, *J* = 21.7 Hz), 115.8 (q, *J* = 291.4 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ -68.81, -111.23 (ddd, *J* = 10.3, 7.2, 5.3 Hz). HRMS (APCI+) *m/z* calcd. for $C_{10}H_5BrF_4O$ $[M]^{+\cdot}$: 295.9454/297.9434; found: 295.9463/297.9442.

3. General procedure for the organocatalytic reaction

3.1. Asymmetric synthesis of chiral dihydropyrans **4**



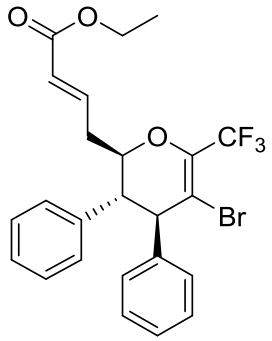
To a glass vial equipped with a magnetic stirring bar, reagents and solvent were added in the following order; enone **2** (0.10 mmol), anisole (0.2 mL), enal **1** (0.20 mmol, 2.0 eq) and catalyst **3a** (0.02 mmol, 20 mol%). The reaction mixture was stirred for 44 h at rt to afford dihydropyran **4**. After derivatization according to Method A, B or C, purification by direct submission to FC on silica gel was performed.

Method A (**5**): $NaBH_4$ (10.0 mg, 0.26 mmol, 0.26 eq) was added along with MeOH (50 µL) and stirred for 1 h at rt.

Method B (**5'**): Ph_3PCHCO_2Et (85 mg, 0.25 mmol, 2.5 eq) was added and the reaction mixture was stirred for 3 h at rt.

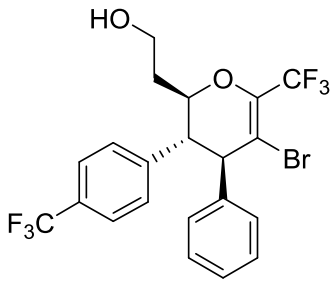
Method C (**5''**): HCl in MeOH (1 mL, 1.25 M) was added and the reaction mixture was stirred for 4 h at rt.

3.2. Characterization of chiral dihydropyrans **5/5'/5''**



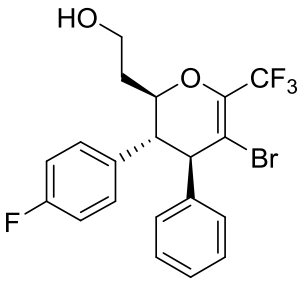
5a'

Following method B compound **5a'** was isolated as a pale brown solid by FC on silica using Et_2O:pentane 5:95 to 7.5:92.5 as eluent. $[\alpha]_D^{22}$ = -60.0 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28–7.22 (m, 3H), 7.22–7.17 (m, 3H), 6.95–6.79 (m, 5H), 5.69 (d, *J* = 15.8 Hz, 1H), 4.39 (ddd, *J* = 10.7, 7.0, 3.6 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.84 (dq, *J* = 9.4, 2.9 Hz, 1H), 2.95 (t, *J* = 10.5 Hz, 1H), 2.41–2.23 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.0, 142.5 (q, *J* = 34.8 Hz), 142.3, 139.6, 138.0, 129.0 (2C), 128.3 (2C), 128.2 (2C), 128.0 (2C), 127.7, 127.4, 124.4, 119.7 (q, *J* = 275.3 Hz) 106.8 (q, *J* = 2.4 Hz), 79.5, 60.3, 55.8, 55.1, 34.8, 14.2. ^{19}F NMR (376 MHz, $CDCl_3$): δ -65.71 (d, *J* = 2.8 Hz). HRMS (ESI+) *m/z* calcd. for $C_{24}H_{22}BrF_3O_3$ $[M+H]^+$: 495.0777/497.0757; found: 495.0779/497.0761. UPC^2: IA, 98:2 CO_2/MeOH, 3.0 mL·min^{-1}; t_{major} = 4.52 min; t_{minor} = 5.12 min.



5b

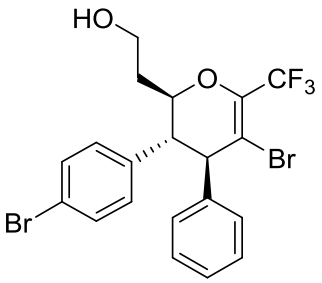
Following method A compound **5b** was isolated as a white solid by FC on silica using Et_2O:pentane 30:70 to 40:60 as eluent. $[\alpha]_D^{22}$ = -75.6 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (t, *J* = 7.8 Hz, 2H), 7.22 (bs, 3H), 7.02 (t, *J* = 7.7 Hz, 2H), 6.85–6.84 (m, 2H), 4.51 (t, *J* = 9.5, 1H), 3.83–3.74 (m, 3H), 3.08 (t, *J* = 10.4 Hz, 1H), 1.69–1.53 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.7, 142.4 (q, *J* = 34.8 Hz), 139.2, 129.9 (q, *J* = 32.4 Hz), 128.6 (2C), 128.4 (2C), 128.2 (2C), 127.6, 125.9 (q, *J* = 3.7 Hz, 2C), 123.9 (q, *J* = 272.1 Hz), 119.8 (q, *J* = 275.2 Hz), 106.7 (q, *J* = 2.4 Hz), 78.7, 58.9, 55.9, 55.8, 34.9. ^{19}F NMR (376 MHz, $CDCl_3$): δ -65.84 (d, *J* = 2.3 Hz), -62.62. HRMS (ESI+) *m/z* calcd. for $C_{21}H_{17}BrF_6O_2$ $[M+Na]^+$: 517.0208/519.0188; found: 517.0213/519.0193. UPC^2: IA, 95:5 CO_2/i-PrOH, 3.0 mL·min^{-1}; t_{major} = 4.25 min; t_{minor} = 2.76 min.



5c

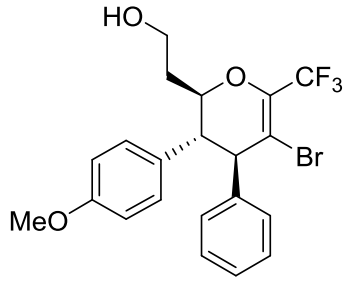
Following method A compound **5c** was isolated as a white solid by FC on silica using Et_2O:pentane 10:30 as eluent. $[\alpha]_D^{22}$ = -76.8 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21–7.20 (m, 3H), 6.94 (t, *J* = 8.5 Hz, 2H), 6.87–6.83 (m, 4H), 4.44 (td, *J* = 10.5, 2.6 Hz, 1H), 3.79–3.74 (m, 3H), 2.97 (t, *J* = 10.4 Hz, 1H), 1.69–1.57 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.0 (d, *J* = 246.7 Hz),

142.3 (q, *J* = 34.6 Hz), 139.5, 134.3 (d, *J* = 3.4 Hz), 129.5 (d, *J* = 8.0 Hz, 2C), 128.4 (2C), 128.2, 127.5 (2C), 119.8 (q, *J* = 273.5 Hz), 115.9 (d, *J* = 21.4 Hz, 2C), 106.9 (q, *J* = 2.3 Hz), 79.2, 59.1, 55.1, 55.2, 34.9. ^{19}F NMR (376 MHz, $CDCl_3$): δ -65.78 (d, *J* = 3.1 Hz), -114.24–-114.32 (m). HRMS (ESI+) *m/z* calcd. for $C_{20}H_{17}BrF_4O_2$ $[M+Na]^+$: 467.0240/469.0220; found: 467.0243/469.0226. UPC^2: IA, 98:2 CO_2/MeOH, 3.0 mL·min^{-1}; t_{major} = 8.38 min; t_{minor} = 6.67 min.



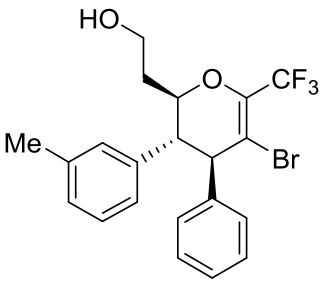
5d

Following method A compound **5d** was isolated as a white solid by FC on silica using CH_2Cl_2:pentane 70:30 to 90:10 as eluent. $[\alpha]_D^{22}$ = -94.8 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (t, *J* = 8.4 Hz, 2H), 7.22–7.20 (m, 3H), 6.86–6.84 (m, 2H), 6.77 (d, *J* = 8.3 Hz, 2H), 4.44 (ddd, *J* = 10.5, 9.7, 2.9 Hz, 1H), 3.81–3.71 (m, 3H), 2.96 (t, *J* = 10.4 Hz, 1H), 1.69–1.53 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.3 (q, *J* = 34.7 Hz), 139.4, 137.5, 132.1 (2C), 129.6 (2C), 128.5 (2C), 128.2, 127.5 (2C), 121.5, 119.7 (q, *J* = 281.3 Hz), 106.8 (q, *J* = 2.3 Hz), 78.9, 59.0, 55.8, 55.5, 35.0. ^{19}F NMR (376 MHz, $CDCl_3$): δ -65.80 (d, *J* = 2.9 Hz). HRMS (ESI+) *m/z* calcd. for $C_{20}H_{17}Br_2F_3O_2$ $[M+Na]^+$: 528.9419/526.9440/530.9399; found: 528.2422/526.9440/530.9408. UPC^2: IA, CO_2/MeOH gradient, 3.0 mL·min^{-1}; t_{major} = 3.29 min; t_{minor} = 3.06 min.



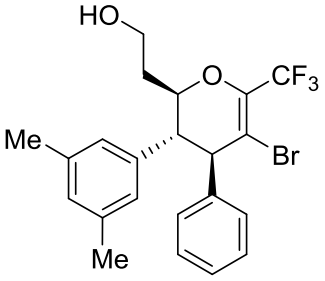
5e

Following method A compound **5e** was isolated as a white solid by FC on silica (x2) using EtOAc:pentane 10:40 and Et_2O:CH_2Cl_2 3:97 as eluent. $[\alpha]_D^{22}$ = -98.8 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.19 (bs, 3H), 6.85 (bs, 2H), 6.81-6.75 (m, 4H), 4.41 (t, *J* = 9.4, 1H), 3.81–3.74 (m, 6H), 2.92 (t, *J* = 10.4 Hz, 1H), 1.67–1.62 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.9, 142.3 (q, *J* = 34.5 Hz), 139.9, 130.4, 128.9 (2C), 128.3 (2C), 128.3, 127.3 (2C), 119.9 (q, *J* = 275.0 Hz), 114.3 (2C), 107.1 (q, *J* = 2.4 Hz), 79.8, 59.4, 56.1, 55.3, 55.2, 35.0. ^{19}F NMR (376 MHz, $CDCl_3$): δ -65.80 (d, *J* = 3.0 Hz). HRMS (ESI+) *m/z* calcd. for $C_{21}H_{20}BrF_3O_3$ $[M+Na]^+$: 479.0440/481.0420; found: 479.0444/481.0426. UPC^2: IA, CO_2/MeCN gradient, 3.0 mL·min^{-1}; t_{major} = 2.96 min; t_{minor} = 2.85 min.



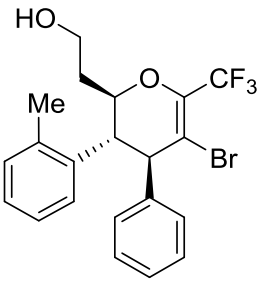
5f

Following method A compound **5f** was isolated as a white solid by FC on silica using CH_2Cl_2:pentane 70:30 to 80:20 as eluent. $[\alpha]_D^{22}$ = -98.0 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20–7.19 (m, 3H), 7.11 (t, *J* = 7.6 Hz, 1H), 7.01 (t, *J* = 7.6 Hz, 1H), 6.87-6.85 (m, 2H), 6.70–6.66 (m, 2H), 4.44 (ddd, *J* = 10.6, 9.6, 3.1 Hz, 1H), 3.87–3.82 (m, 1H), 3.79–3.71 (m, 2H), 2.93 (t, *J* = 10.4 Hz, 1H), 2.26 (s, 3H), 1.71–1.56 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.3 (q, *J* = 34.5 Hz), 139.8, 138.6, 138.3, 128.7, 128.5, 128.3 (4C), 128.2, 127.3, 125.1, 119.8 (q, *J* = 275.1 Hz), 107.3 (q, *J* = 2.4 Hz), 79.8, 59.4, 56.0, 55.8, 35.1, 21.4. ^{19}F NMR (376 MHz, $CDCl_3$): δ -65.77 (d, *J* = 3.0 Hz). HRMS (ESI+) *m/z* calcd. for $C_{21}H_{20}BrF_3O_2$ $[M+Na]^+$: 463.0491/465.0471; found: 463.0493/465.0476. UPC^2: IA, 95:5 CO_2/i-PrOH, 3.0 mL·min^{-1}; t_{major} = 4.91 min; t_{minor} = 3.77 min.



5g

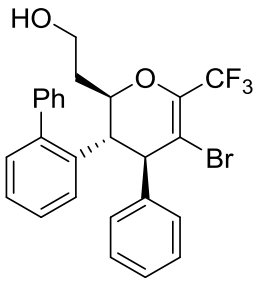
Following method A compound **5g** was isolated as a white solid by FC on silica using CH_2Cl_2:pentane 70:30 to 90:10 as eluent. $[\alpha]_D^{22}$ = –101.6 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21–7.19 (m, 3H), 6.86–6.84 (m, 3H), 6.49 (bs, 2H), 4.41 (td, *J* = 10.4, 3.2 Hz, 1H), 3.86–3.83 (m, 1H), 3.77–3.74 (m, 2H), 2.88 (t, *J* = 10.3 Hz, 1H), 2.21 (s, 6H), 1.67–1.60 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.2 (q, *J* = 34.4 Hz), 139.9, 138.3 (2C), 138.2, 129.2, 128.3 (4C), 127.2, 125.7 (2C), 119.8 (q, *J* = 275.0 Hz), 107.4 (q, *J* = 2.3 Hz), 79.9, 59.5, 56.0, 55.7, 35.1, 21.2 (2C). ^{19}F NMR (376 MHz, $CDCl_3$): δ -65.79 (d, *J* = 2.9 Hz). HRMS (ESI+) *m/z* calcd. for $C_{22}H_{22}BrF_3O_2$ $[M+Na]^+$: 477.0647/479.0627; found: 477.0649/479.0632. UPC^2: IA, CO_2/i-PrOH gradient, 3.0 mL·min^{-1}; t_{major} = 2.91 min; t_{minor} = 2.76 min.



5h

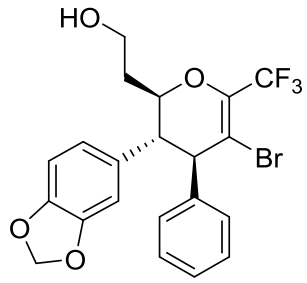
Following method A compound **5h** was isolated as a white solid by FC on silica using CH_2Cl_2:pentane 90:10 to 95:5 as eluent. $[\alpha]_D^{22}$ = -37.1 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26 (t, *J* = 7.4 Hz, 1H), 7.19–7.16 (m, 4H), 7.11 (t, *J* = 7.4 Hz, 1H), 6.95 (d, *J* = 7.5 Hz, 1H), 6.84 (d, *J* = 5.0 Hz, 2H), 4.45 (t, *J* = 10.1 Hz, 1H), 3.84 (d, *J* = 9.6 Hz, 1H), 3.74 (bs, 2H), 3.32 (t, *J* = 10.3 Hz, 1H), 1.69–1.63 (m, 2H), 1.58 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.5 (q, *J* = 34.5 Hz), 139.5, 137.3, 137.1, 130.4, 128.3 (2C), 128.1 (2C), 127.3, 127.1, 126.9, 125.9, 119.8 (q, *J* = 275.1 Hz), 107.2 (q, *J* = 2.3 Hz), 80.3, 59.5, 56.4, 50.2, 34.5, 19.5. ^{19}F NMR (376 MHz, $CDCl_3$): δ -65.71

(d, *J* = 2.9 Hz). HRMS (ESI+) *m/z* calcd. for $C_{21}H_{20}BrF_3O_2$ $[M+Na]^+$: 463.0491/465.0471; found: 463.0492/465.0474. UPC^2: IA, 95:5 CO_2/i-PrOH, 3.0 mL·min^{-1}; t_{major} = 5.92 min; t_{minor} = 4.88 min.



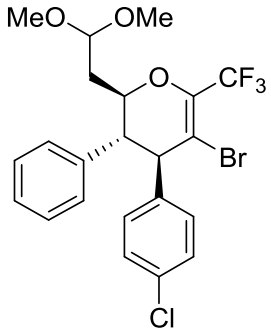
5i

Following method A compound **5i** was isolated as a pale yellow oil by FC on silica using CH_2Cl_2 as eluent. $[\alpha]_D^{22}$ = 29.6 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67–7.11 (m, 12H), 6.95–6.86 (m, 2H), 4.47 (ddd, *J* = 10.6, 8.3, 4.7 Hz, 1H), 4.13 (dq, *J* = 9.6, 2.9 Hz, 1H), 3.83 (t, *J* = 5.9 Hz, 2H), 3.28 (t, *J* = 10.3 Hz, 1H), 1.72–1.59 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.5, 142.4 (q, *J* = 34.7 Hz) 140.1, 139.5, 136.2, 130.3, 129.0 (2C), 128.5 (4C), 128.4, 127.7 (2C), 127.4, 126.8, 126.7, 126.1, 119.7 (q, *J* = 277.5 Hz), 107.4, 80.7, 59.5, 56.1, 50.2, 34.5. ^{19}F NMR (376 MHz, $CDCl_3$): δ -65.80 (d, *J* = 3.0 Hz). HRMS (ESI+) *m/z* calcd. for $C_{26}H_{22}BrF_3O_2$ $[M+Na]^+$: 525.0647/527.0627; found: 525.0654/527.0637. UPC^2: IB, CO_2/i-PrOH gradient, 3.0 mL·min^{-1}; t_{major}= 3.13 min; t_{minor} = 3.37 min.



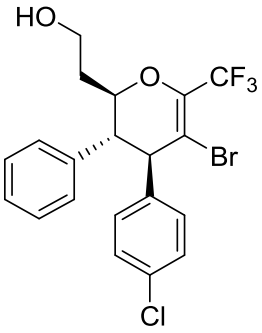
5j

Following method A compound **5j** was isolated as a pale yellow solid by FC on silica using EtOAc:pentane 10:40 as eluent. $[\alpha]_D^{22}$ = -114.4 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): 7.23–7.21 (m s, 3H), 6.90–6.88 (m, 2H), 6.65 (d, *J* = 7.9 Hz, 1H), 6.42 (d, *J* = 1.6 Hz, 1H), 6.30 (dd, *J* = 8.0, 1.6 Hz, 1H), 5.94 (d, *J* = 1.4 Hz, 1H), 5.92 (d, *J* = 1.4 Hz, 1H), 4.36 (ddd, *J* = 10.7, 8.0, 4.4 Hz, 1H), 3.80–3.75 (m, 3H), 2.89 (t, *J* = 10.4 Hz, 1H), 1.68–1.62 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.1, 146.9, 142.2 (q, *J* = 34.6 Hz), 139.8, 132.1, 128.4 (2C), 128.2 (2C), 127.4, 121.5, 119.8 (q, *J* = 273.6 Hz), 108.6, 107.8, 107.1 (q, *J* = 2.3 Hz), 101.1, 79.6, 59.3, 56.0, 55.7, 35.0. ^{19}F NMR (376 MHz, $CDCl_3$): δ -65.81 (d, *J* = 3.0 Hz). HRMS (ESI+) *m/z* calcd. for $C_{21}H_{18}BrF_3O_4$ $[M+Na]^+$: 493.0233/495.0212; found: 493.0240/495.0219. UPC^2: IB, CO_2/i-PrOH gradient, 3.0 mL·min^{-1}; t_{major} = 3.22 min; t_{minor} = 2.99 min.



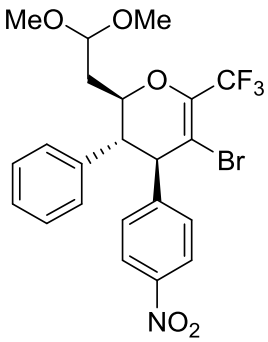
5k''

Following method C compound **5k''** was isolated as a colorless oil by FC on silica using Et_2O:pentane 1:19 as eluent. $[\alpha]_D^{22}$ = -95.2 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28–7.19 (m, 3H), 7.16 (d, *J* = 7.9 Hz, 2H), 6.88 (d, *J* = 6.8 Hz, 2H), 6.78 (d, *J* = 7.9 Hz, 2H), 4.57 (dd, *J* = 8.7, 3.3 Hz, 1H), 4.42–4.33 (m, 1H), 3.87–3.79 (m, 1H), 3.26 (d, *J* = 4.0 Hz, 6H), 2.87 (t, *J* = 10.5 Hz, 1H), 1.74–1.53 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.7 (q, *J* = 34.67 Hz), 138.4, 137.9, 133.1, 129.5 (2C), 129.0 (2C), 128.5 (2C), 127.9 (2C), 127.7, 119.7 (q, *J* = 275.8 Hz), 106.1 (q, *J* = 2.4 Hz), 101.5, 78.1, 56.0, 55.4, 53.6, 53.5, 35.9 ^{19}F NMR (376 MHz, $CDCl_3$): δ -66.97 (d, *J* = 2.7 Hz). HRMS (ESI+) *m*/*z* calcd. for $C_{22}H_{21}BrClF_3O_3$ $[M+Na]^+$: 527.0207/529.0186; found: 527.0208/529.0192.



5k

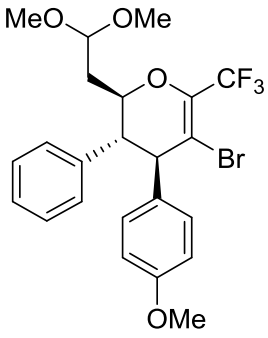
5k'' was dissolved in THF (0.5 mL)/HCl (2 M, 0.5 mL) and stirred vigorously overnight. After extraction with Et_2O, the resulting aldehyde **4k** was reduced following method A and compound **5k** was isolated as a white solid by plugging through a silica pad. $[\alpha]_D^{22}$ = -102.8 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29–7.20 (m, 3H), 7.16 (d, *J* = 8.7 Hz, 2H), 6.93–6.85 (m, 2H), 6.77 (d, *J* = 7.9 Hz, 2H), 4.46 (ddd, *J* = 10.6, 9.4, 3.0 Hz, 1H), 3.83 (dq, *J* = 10.3, 2.9 Hz, 1H), 3.80–3.68 (m, 2H), 2.91 (t, *J* = 10.4 Hz, 1H), 1.71–1.58 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.6 (q, *J* = 34.8 Hz), 138.3, 138.1, 133.1, 129.5 (2C), 129.1 (2C), 128.6 (2C), 127.9 (2C), 127.8, 119.7 (q, *J* = 275.5 Hz), 106.3 (q, *J* = 2.3 Hz), 79.4, 59.1, 55.9, 55.3, 35.0. ^{19}F NMR (376 MHz, $CDCl_3$): δ -65.84 (d, *J* = 2.8 Hz). HRMS (ESI+) *m*/*z* calcd. for $C_{20}H_{17}BrClF_3O_2$ $[M+Na]^+$: 482.9945/484.9924; found: 482.9943/484.9926. UPC^2: IA, CO_2/MeCN gradient, 3.0 mL·min^{-1}; t_{major}= 3.09 min; t_{minor} = 2.84 min.



5l''

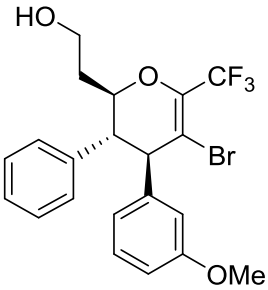
Following method C compound **5l''** was isolated as a pale yellow oil by FC on silica (x2) using CH_2Cl_2:pentane 7:3 and CH_2Cl_2:pentane 8:2 as eluent. $[\alpha]_D^{22}$ = -81.6 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (d, *J* = 8.0 Hz, 2H), 7.34–7.18 (m, 3H), 7.02 (d, *J* = 7.9 Hz, 2H), 6.93–6.84 (m, 2H), 4.65–4.52 (m, 1H), 4.49–4.37 (m, 1H), 4.08–3.97 (m, 1H), 3.32–3.23 (m, 6H), 2.90 (t, *J* = 10.5 Hz, 1H), 1.76–1.57 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.4, 147.2, 143.3 (q, *J* = 35.7 Hz), 137.2, 129.2 (2C), 129.1, 128.1 (2C), 127.8 (2C), 123.6 (2C), 119.5 (q, *J* = 275.4 Hz), 104.5, 101.4,

78.0, 55.7, 53.6, 53.5, 46.0, 36.0.^{19}F NMR (376 MHz, $CDCl_3$): δ -66.05 (d, *J* = 2.8 Hz). HRMS (ESI+) *m*/*z* calcd. for $C_{22}H_{21}BrF_3NO_5$ $[M+Na]^+$: 538.0447/540.0427; found: 538.0448/540.0430. Hydrolyzed and reduced to **5l**: UPC^2: IB, CO_2/i-PrOH gradient, 3.0 mL·min^{-1}; t_{major}= 3.56 min; t_{minor} = 3.30 min.



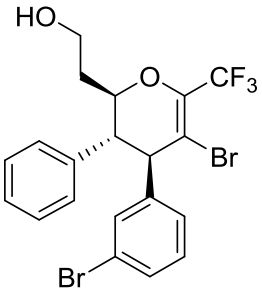
5m''

Following method C compound **5m''** was isolated as a pale yellow oil by FC on silica using 5:95 to 8:92 Et_2O:pentane as eluent. $[\alpha]_D^{22}$ = -97.6 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25–7.16 (m, 3H), 6.89 (d, *J* = 8.6 Hz, 2H), 6.76 (d, *J* = 8.5 Hz, 2H), 6.71 (d, *J* = 8.5 Hz, 2H), 4.57 (dd, *J* = 8.6, 3.2 Hz, 1H), 4.36 (td, *J* = 10.5, 2.8 Hz, 1H), 3.84–3.72 (m, 4H), 3.26 (s, 6H), 2.90 (t, *J* = 10.5 Hz, 1H), 1.73–1.53 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.6, 142.1 (q, *J* = 34.8 Hz), 138.4, 131.7, 129.2 (2C), 128.8 (2C), 128.0 (2C), 127.5 (2C), 119.9 (q, *J* = 275.2 Hz), 113.7, 107.5 (q, *J* = 2.4 Hz), 101.5, 78.1, 56.1, 55.2, 55.0, 53.6, 53.5, 36.0. ^{19}F NMR (376 MHz, $CDCl_3$): δ -65.87 (d, *J* = 3.0 Hz). HRMS (ESI+) *m*/*z* calcd. for $C_{23}H_{24}BrF_3O_4$ $[M+Na]^+$: 523.0702/525.0682; found: 523.0705/525.0690. UPC^2: CEL2, 99.5:0.5 CO_2/MeOH, 3.0 mL·min^{-1}; t_{major}= 2.65 min; t_{minor} = 4.55 min.



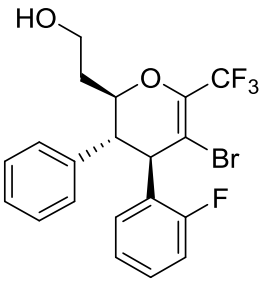
5n

Following method A compound **5n** was isolated as a white solid by FC on silica (x2) using Et_2O:pentane 80:20 and EtOAc:pentane 10:90 to 20:80 as eluent. $[\alpha]_D^{22}$ = -80.8 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25–7.21 (m, 3H), 7.11 (t, *J* = 7.9 Hz, 1H), 6.91–6.89 (m, 2H), 6.73 (dd, *J* = 8.2, 1.9 Hz, 1H), 6.45 (d, *J* = 7.5 Hz, 1H), 6.35 (s, 1H), 4.45 (td, *J* = 10.5, 2.9 Hz, 1H), 3.84–3.72 (m, 3H), 3.66 (s, 3H), 2.97 (t, *J* = 10.4 Hz, 1H), 1.71–1.55 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.4, 142.3 (q, *J* = 34.3 Hz), 141.3, 138.5, 129.3, 128.9 (2C), 128.0 (2C), 127.6, 120.6, 120.0 (q, *J* = 268.3 Hz), 114.1, 112.6, 107.0 (q, *J* = 2.3 Hz), 79.6, 59.3, 55.92, 55.87, 55.1, 35.0. ^{19}F NMR (376 MHz, $CDCl_3$): δ -65.79 (d, *J* = 2.9 Hz). HRMS (ESI+) *m*/*z* calcd. for $C_{21}H_{20}BrF_3O_3$ $[M+Na]^+$: 479.0440/481.0420; found: 479.0444/481.0426. UPC^2: IB, CO_2/i-PrOH gradient, 3.0 mL·min^{-1}; t_{major} = 3.53 min; t_{minor} = 3.32 min.



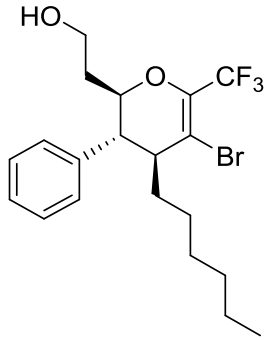
5o

Following method A compound **5o** was isolated as a white solid by FC on silica using CH_2Cl_2:pentane 80:20. $[\alpha]_D^{22}$ = -73.6 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34–7.32 (m, 1H), 7.28–7.24 (m, 3H), 7.05 (t, *J* = 7.8 Hz, 1H), 6.99 (bs, 1H), 6.90–6.88 (m, 2H), 6.76 (d, *J* = 7.6 Hz, 1H), 4.46 (td, *J* = 10.4, 3.0 Hz, 1H), 3.83–3.71 (m, 3H), 2.93 (t, *J* = 10.4 Hz, 1H), 1.71–1.55 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.7 (q, *J* = 34.6 Hz), 142.1, 137.9, 131.1, 130.6, 129.9, 129.1 (2C), 127.9 (2C), 127.8, 127.1, 122.3, 119.7 (q, *J* = 275.3 Hz), 105.9 (d, *J* = 2.3 Hz), 79.3, 59.1, 55.8, 55.6, 35.0. ^{19}F NMR (376 MHz, $CDCl_3$): δ -65.84 (d, *J* = 3.0 Hz). HRMS (ESI+) *m/z* calcd. for $C_{20}H_{17}Br_2F_3O_2$ $[M+Na]^+$: 526.9440/528.9419/530.9399; found: 526.9445/528.9426/530.9414. UPC^2: IA, 95:5 CO_2/i-PrOH gradient, 3.0 mL·min^{-1}; t_{major} = 9.91 min; t_{minor} = 7.28 min.



5p

Following method A compound **5p** was isolated as a colorless oil by FC on silica using 3:2 to 2:1 CH_2Cl_2:pentane as eluent. $[\alpha]_D^{22}$ = -81.2 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40–6.77 (m, 9H), 4.50 (td, *J* = 10.0, 2.9 Hz, 1H), 4.24 (bs, 1H), 3.84–3.68 (m, 2H), 3.16–3.02 (m, 1H), 1.75–1.55 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.9 (d, *J* = 247.4 Hz), 142.1 (bs), 138.0, 129.1 (d, *J* = 8.3 Hz), 128.9 (2C), 127.8 (2C), 127.7, 126.7 (d, *J* = 13.3 Hz), 124.2, 119.8 (q, *J* = 275.0 Hz), 115.8 (d, *J* = 21.6 Hz) 115.5 (d, *J* = 22.9 Hz), 105.8, 79.5, 59.2, 54.0 (bs, 2C), 35.0. ^{19}F NMR (376 MHz, $CDCl_3$): δ -65.87 (d, *J* = 2.7 Hz), -117.27 (bs). HRMS (ESI+) *m/z* calcd. for $C_{20}H_{17}BrF_4O_2$ $[M+Na]^+$: 467.0240/469.0220; found: 467.0242/469.0225. UPC^2: IB, 95:5 CO_2/i-PrOH, 3.0 mL·min^{-1}; t_{major}= 7.07 min; t_{minor} = 5.51 min.

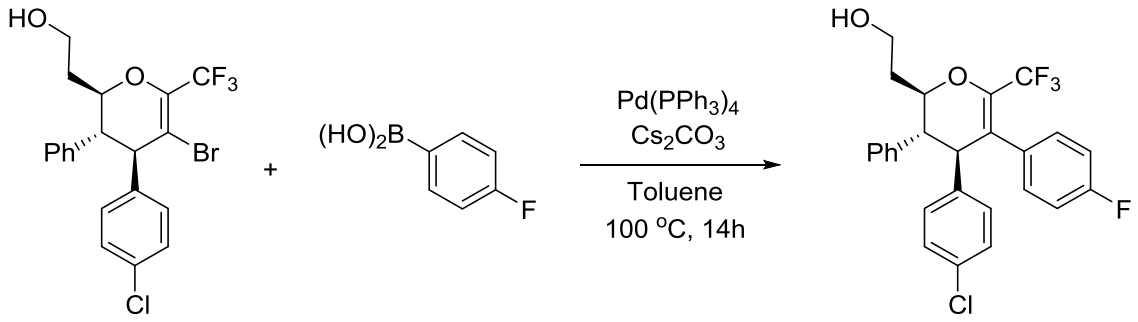


5q

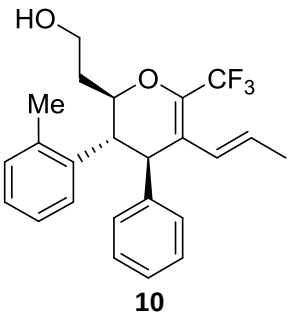
Following method A compound **5q** was isolated as a colorles oil by FC on silica using CH_2Cl_2:pentane 30:10 as eluent. $[\alpha]_D^{22}$ = -10.8 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): 7.37–7.27$^+$ (m, 3H, 3H*), 7.12–7.10$^+$ (m, 2H, 2H*), 4.36–4.32* (m, 1H), 4.18 (td, *J* = 9.8, 2.2 Hz, 1H), 3.78–3.69$^+$ (m, 2H, 2H*), 2.96* (bs, 1H), 2.89–2.84 (m, 2H), 2.47–2.45* (m, 1H), 2.09–2.03* (m, 1H), 1.75–1.22$^+$ (m, 12H, 11H*), 0.89–0.84$^+$ (m, 3H, 3H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.6 (q, *J* = 34.3 Hz), 140.5* (q, *J* = 34.3 Hz), 139.57*, 139.54, 129.2 (2C), 128.8* (2C), 128.3* (2C), 127.9 (2C), 127.7, 127.3*, 119.83 (q, *J* = 274.9 Hz), 119.80* (q, *J* = 274.8 Hz), 109.2 (q, *J* = 2.4 Hz),

107.0* (q, *J* = 2.2 Hz), 79.7, 73.4*, 59.5, 59.3*, 50.1, 47.6*, 46.93*, 46.90, 35.2, 35.0*, 34.6*, 31.7*, 31.5, 29.4, 29.1, 29.0*, 26.9*, 22.9, 22.57*, 22.55, 14.04*, 14.01. ^{19}F NMR (376 MHz, $CDCl_3$): δ -65.49 (d, *J* = 2.2 Hz)*, -65.67 (d, *J* = 2.7 Hz). HRMS (ESI^+) *m/z* calcd. for $C_{20}H_{26}BrF_3O_2$ $[M+Na]^+$: 457.0960/459.0940; found: 457.0961/459.0943. UPC^2: IB, 95:5 CO_2/i-PrOH, 3.0 mL·min^{-1}; t_{major} = 3.25 min; t_{minor} = 2.73 min.

4. Transformations



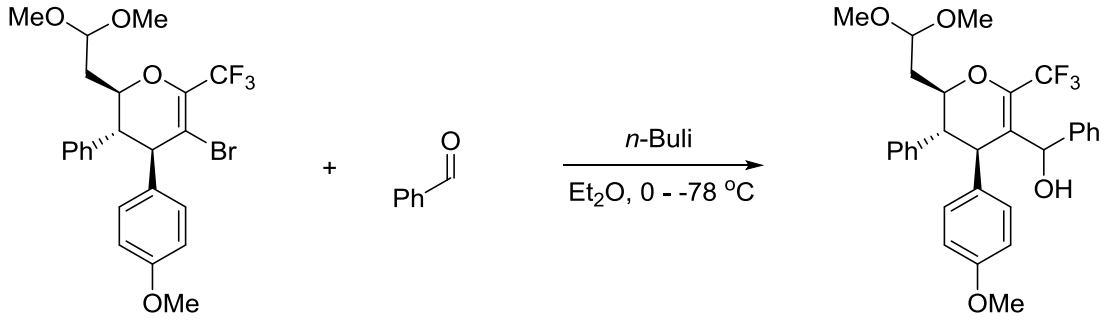
5k (16.5 mg, 0.036 mmol), (4-fluorophenyl)boronic acid (15.0 mg, 0.105 mmol, 3.0 eq) and tetrakis(triphenylphosphine)palladium (4.1 mg, 0.0036 mmol, 10 mol%) were added to a vial and flushed with argon. After addition of toluene (0.5 mL) and Cs_2CO_3 (14 µL, 0.072 mmol, 5 M in H_2O, 2.0 eq) the reaction mixture was heated to 100 °C for 14 h. The reaction mixture was directly submitted to FC on silica gel (Et_2O:pentane 1:3) and compound **9** was isolated as a colorless oil. $[\alpha]_D^{22}$ = -70.8 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25–7.16 (m, 3H), 7.03 (d, *J* = 8.6 Hz, 2H), 6.96–6.90 (m, 2H), 6.88–6.77 (m, 4H), 6.73 (d, *J* = 7.9 Hz, 2H), 4.51 (td, *J* = 10.1, 2.8 Hz, 1H), 3.90–3.76 (m, 2H), 3.73 (dq, *J* = 10.3, 2.7 Hz, 1H), 3.07 (t, *J* = 10.4 Hz, 1H), 1.80–1.67 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ161.9 (d, *J* = 246.6 Hz), 140.4 (q, *J* = 33.7 Hz), 138.8, 137.9, 132.5, 131.0–130.8 (m, 3C), 129.9 (2C), 128.9 (2C), 128.4 (2C), 127.9 (2C), 127.4, 121.9 (q, 2.2 Hz), 120.2 (q, 275.2 Hz), 114.7 (d, 21.5 Hz, 2C), 79.4, 59.6, 54.2, 54.1, 35.2. ^{19}F NMR (376 MHz, $CDCl_3$): δ -64.23 (d, *J* = 2.7 Hz), -114.51– -114.59 (m). HRMS (ESI+) *m/z* calcd. for $C_{26}H_{21}F_4O_2$ $[M+Na]^+$: 499.1058; found: 499.1063.



10

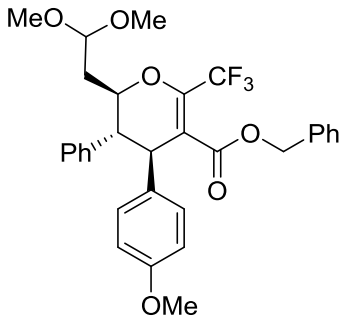
Compound **10** was synthesized according to the procedure for synthesis of compound **9** employing **5h** (15.4 mg, 0.035 mmol), *trans*-1-propen-1-ylboronic acid (9.2 mg, 0.105 mmol, 3.0 eq) and tetrakis(triphenylphosphine)palladium (4.1 mg, 0.0035 mmol, 10 mol%). The product was isolated as a pale yellow solid in 85% yield by FC on silica gel (90:10 pentane:EtOAc). $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\boldsymbol{22}}$ = -89.2 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28–7.24 (m, 1H), 7.19 (d, *J* = 7.5 Hz, 1H), 7.13–7.10 (m, 4H), 6.97 (d, *J* = 7.5 Hz, 1H), 6.75–6.73 (m, 2H), 6.25 (d, *J* = 15.7 Hz, 1H), 5.39–5.30 (m, 1H), 4.23 (td, *J* = 10.3, 2.4 Hz, 1H), 3.83–3.80 (m, 1H), 3.75–3.72 (m, 2H), 3.12 (t, *J* = 10.2 Hz, 1H), 1.67–1.52 (m, 5H), 1.49 (s, 3H). ^{13}C NMR (100

MHz, $CDCl_3$): δ 142.4, 140.8 (q, *J* = 33.4 Hz), 138.5, 137.6, 130.1, 130.0, 128.3 (2C), 127.3 (2C), 126.8, 126.7, 126.4, 126.2, 122.9 (q, *J* = 2.2 Hz), 121.0 (q, *J* = 275.2 Hz), 120.2 (q, *J* = 2.2 Hz), 80.4, 60.2, 50.3, 50.0, 34.7, 19.3, 19.0. ^{19}F NMR (376 MHz, $CDCl_3$): δ -62.88. HRMS (ESI+) *m/z* calcd. for $C_{24}H_{25}F_3O_2$ $[M+H]^+$: 403.1879; found: 403.1882.



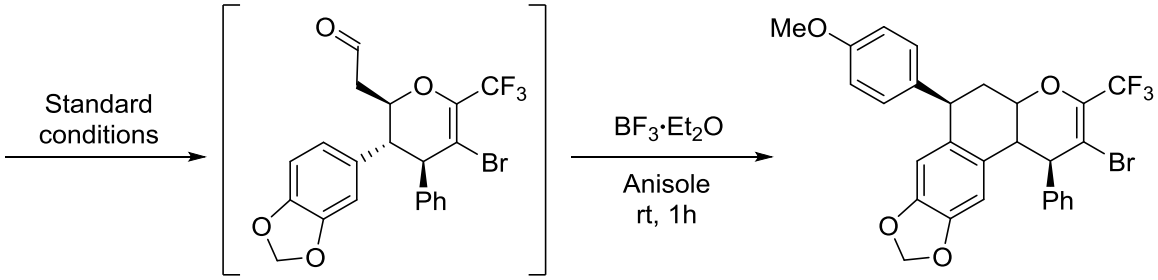
5m'' **11**

5m'' (40.0 mg, 0.080 mmol) in dry Et_2O (0.5 mL) was cooled to -78 °C and *n*-butyllithium (0.15 mL, 0.24 mmol, 0.16 M in hexane, 3.0 eq) was added. After 5 min at this temperature the reaction mixture was allowed to heat to rt and stirred for 10 min. Then the mixture was cooled to -78 °C and benzaldehyde (32 µL, 0.32 mmol, 4.0 eq) was added and the reaction mixture was allowed to slowly reach rt and stir for 1 h. The reaction mixture was diluted with Et_2O and water was added. After extraction with Et_2O (x3) the combined organic phases were dried over Na_2SO_4 and concentrated *in vacuo*. NMR-analysis showed a 4.8:1.0 mixture of diastereoisomers, and FC on silica gel (1:9 → 3:17 Et_2O:pentane) afforded compound **11** in 52% yield and >20:1.0 dr as a colorless oil. $[\alpha]_D^{22}$ = -70.4 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.32 (m, 2H), 7.32–7.27 (m, 1H), 7.23–7.15 (m, 2H), 7.14–7.04 (m, 3H), 6.77–6.54 (m, 6H), 5.86 (d, *J* = 8.5 Hz, 1H), 4.60 (dd, *J* = 8.6, 3.2 Hz, 1H), 4.02 (td, *J* = 10.5, 2.6 Hz, 1H), 3.74 (s, 3H), 3.32–3.19 (m, 7H), 2.83 (t, *J* = 10.3 Hz, 1H), 1.72–1.63 (m, 1H), 1.56–1.50 (m, 1H), 1.48 (d, *J* = 8.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.7, 143.3 (q, *J* = 33.8 Hz), 141.6, 138.9, 132.0, 129.8 (2C), 128.6 (2C), 128.2 (2C), 127.8 (2C), 127.1 (2C), 125.5 (2C), 122.6 (q, 2.0 Hz), 120.7 (q, *J* = 276.3 Hz), 114.1 (2C), 101.7, 78.3, 70.4 (q, *J* = 2.9 Hz), 56.4, 55.1, 53.6, 53.3, 47.4, 36.2. ^{19}F NMR (376 MHz, $CDCl_3$): δ -63.23 (d, *J* = 2.7 Hz). HRMS (ESI+) *m/z* calcd. for $C_{30}H_{31}F_3O_5$ $[M+Na]^+$: 551.2016; found: 551.2022.



12

Compound **12** was synthesized according to the procedure for synthesis of compound **11** employing **5m''** (35 mg, 0.070 mmol), *n*-butyllithium (0.17 mL, 0.28 mmol, 0.16 M in hexane, 4.0 eq) and benzyl chloroformate (49 µL, 0.35 mmol, 5.0 eq). The product was isolated as a pale yellow oil in 62% yield by FC on silica gel (3:17 Et_2O:pentane). $[\alpha]_D^{22}$ = -106 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26–7.13 (m, 6H), 7.00 (dd, *J* = 7.4, 2.1 Hz, 2H), 6.92–6.85 (m, 2H), 6.77 (d, *J* = 8.3 Hz, 2H), 6.59 (d, *J* = 8.8 Hz, 2H), 4.94 (d, *J* = 12.2 Hz, 1H), 4.78 (d, *J* = 12.2 Hz, 1H), 4.58 (dd, *J* = 8.5, 3.4 Hz, 1H), 4.39 (td, *J* = 10.3, 2.8 Hz, 1H), 3.93 (dq, *J* = 10.5, 2.7 Hz, 1H), 3.71 (s, 3H), 3.25 (s, 6H), 2.82 (t, *J* = 10.6 Hz, 1H), 1.69 (ddd, *J* = 14.6, 10.0, 3.5 Hz, 1H), 1.61 (ddd, *J* = 14.6, 8.6, 2.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.4, 158.5, 143.2 (q, *J* = 36.4 Hz), 138.3, 134.9, 130.2, 129.3 (2C), 128.8 (2C), 128.4 (2C), 128.3 (2C), 128.1, 128.0 (2C), 127.4, 119.5 (q, *J* = 275.2 Hz), 115.66 (q, *J* = 2.1 Hz), 113.6 (2C), 101.6, 78.2, 67.1, 55.0, 53.6, 53.5, 53.0, 48.2, 36.1. ^{19}F NMR (376 MHz, $CDCl_3$): δ -67.02 (d, *J* = 2.7 Hz). HRMS (ESI+) *m*/*z* calcd. for $C_{31}H_{31}F_3O_6$ $[M+Na]^+$: 579.1965; found: 579.1973.



4j **13**

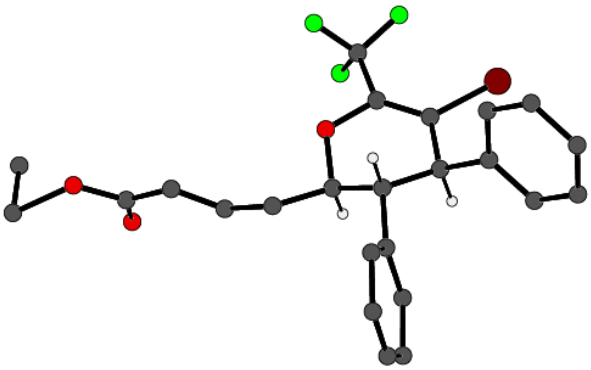
After performing the general procedure for the organocatalytic step (0.10 mmol scale), borontrifluoro etherate (25 µL, 0.20 mmol, 2.0 eq) was added at rt and the reaction mixture was stirred for 1 h. Direct submission to FC on silica gel (1:19 Et_2O:pentane) afforded compound **13** as a colorless solid in an overall yield of 44% and 20.0:5.9:2.2:<1.0<0.5 dr. $[\alpha]_D^{22}$ = -35.2 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53–7.35 (m, 5H), 7.04 (d, *J* = 8.6 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 6.53 (s, 1H), 6.22 (s, 1H), 5.81 (d, *J* = 1.4 Hz, 1H), 5.76 (d, *J* = 1.4 Hz, 1H), 4.21–4.05 (m, 2H), 3.82–3.66 (m, 5H), 2.62 (ddd, *J* = 12.5, 5.8, 3.3 Hz, 1H), 2.14 (q, *J* = 12.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.4, 146.4, 146.3, 142.0, 141.7 (q, *J* = 34.7 Hz), 137.5, 133.2, 129.5, 129.5 (2C), 129.4 (2C), 129.2 (2C), 128.0, 119.7 (q, *J* = 275.2 Hz), 114.1 (2C), 109.5 (q, *J* = 2.5 Hz), 109.3, 106.3, 100.9, 78.7, 55.3, 54.5, 48.1, 45.0, 38.4. ^{19}F NMR (376 MHz, $CDCl_3$):

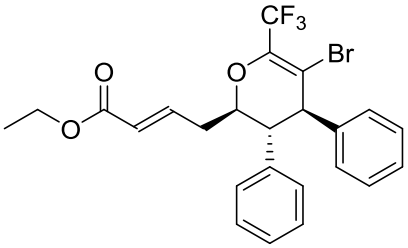
δ -66.08 (d, *J* = 2.7 Hz). HRMS (APCI+) *m*/*z* calcd. for $C_{28}H_{22}BrF_3O_4$ $[M]^{+\cdot}$: 558.0648/560.0628; found: 558.0655/560.0649.

5. Crystallographic data

Compound **5a'**

Item	Value
Molecular formula	C24H22BrF3O3
Formula weight	495.32
Crystal system	orthorhombic
Space Group	P 21 21 21
a (Å)	9.671
b (Å)	10.892
c (Å)	21.822
α (°)	90
β (°)	90
γ (°)	90
Volume (Å^3)	2298.6
Z	4
T (K)	295
ρ (g cm^{-1})	1.431
λ (Å)	0.71073
μ (mm^{-1})	1.834
# measured refl	10758
# unique refl	5412
R_{int}	0.0726
# parameters	261
R(F^2), all refl	0.1616
R_w(F^2), all refl	0.1943
Goodness of fit	1.038



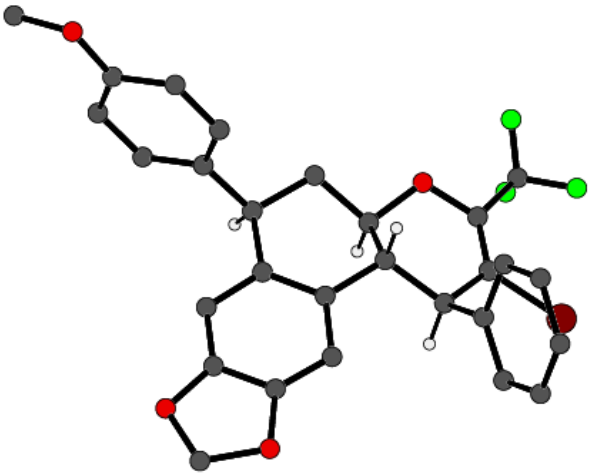


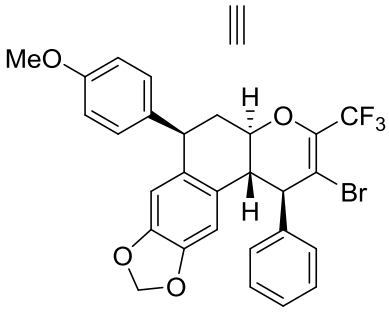
5a'

Crystal data for **5a'**: $C_{24}H_{22}BrF_3O_3$, *M* = 495.32, orthorhombic, space group P $2_12_12_1$ (no. 115), *a* = 9.671(3) Å, *b* = 10.892(3) Å, *c* = 21.822(6) Å, Flack parameter = 0.012, *V* = 2298.6(12) Å^3, *T* = 295 K, *Z* = 4, d_c = 1.431 g cm^{-3}, *μ*(Mo Kα, λ = 0.71073 Å) = 1.834 mm^{-1}, 10758 reflections collected, 5412 unique [R_{int} = 0.0726], which were used in all calculations. Refinement on F^2, final R(F) = 0.1616, R_w(F2) = 0.1943. CCDC number 1405445.

Compound **13**

Item	Value
Molecular formula	C28 H22BrF3O4
Formula weight	559.36
Crystal system	monoclinic
Space Group	P 1 21 1
a (Å)	10.6758
b (Å)	9.3185
c (Å)	25.405
α (°)	90
β (°)	99.557
γ (°)	90
Volume (Å^3)	2492.3
Z	4
T (K)	100
ρ (g cm^{-1})	1.491
λ (Å)	0.71073
μ (mm^{-1})	1.705
# measured refl	25880
# unique refl	14583
R_{int}	0.0996
# parameters	641
R(F^2), all refl	0.2437
R_w(F^2), all refl	0.2913
Goodness of fit	1.02

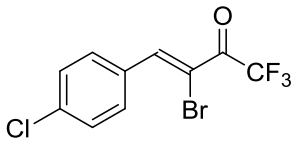




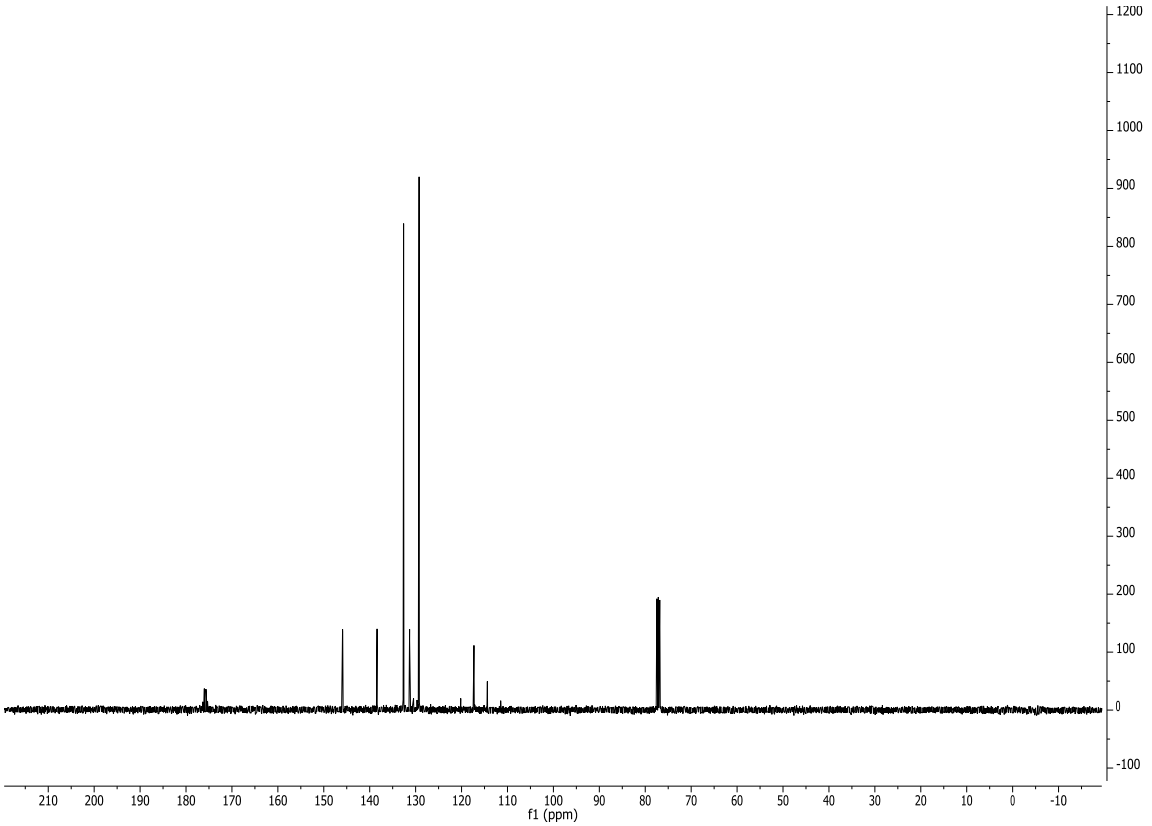
13

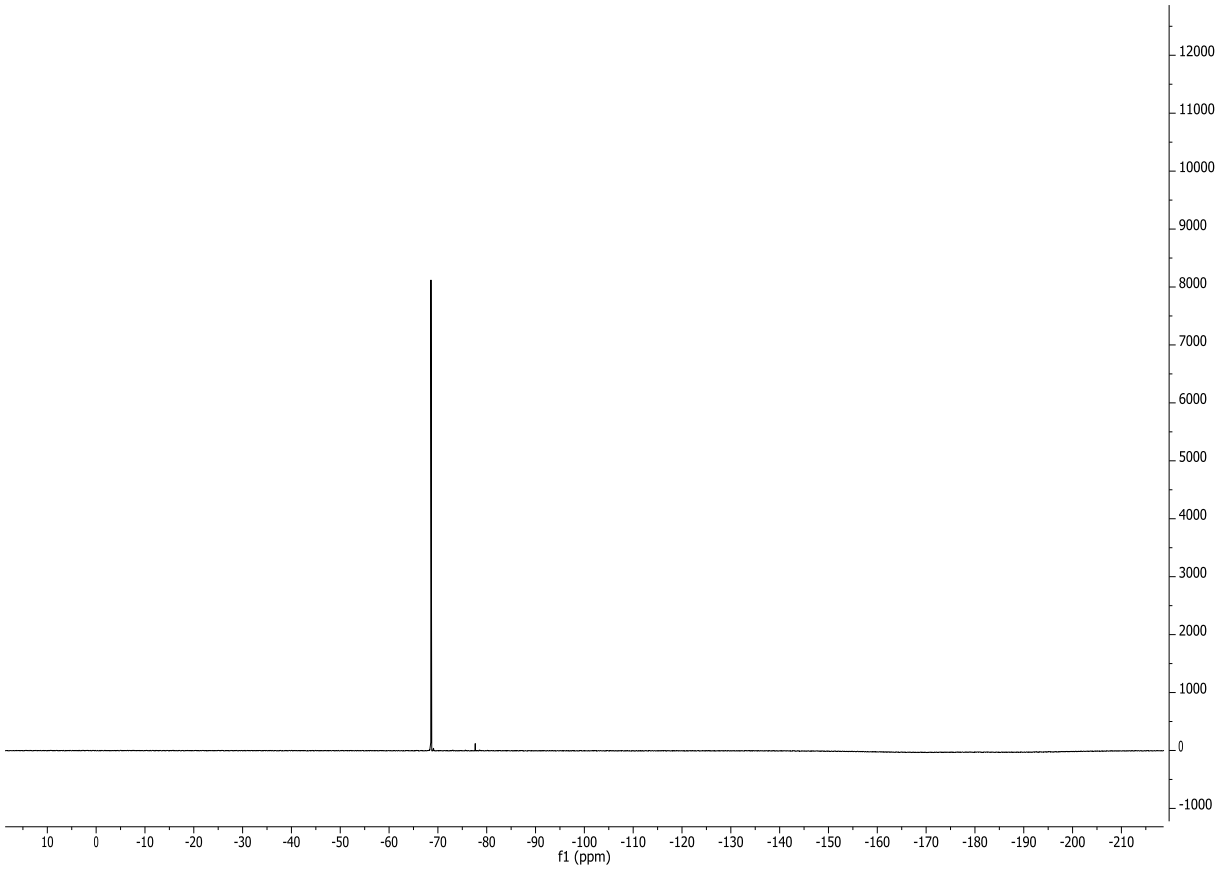
Crystal data for **13**: $C_{28}H_{22}BrF_3O_4$, M = 559.36, monoclinic, space group P 2_1 (no. 6), a = 10.6758(14) Å, b = 9.3185(8) Å, c = 25.405(3) Å, β = 99.557(13)°, Flack parameter = -0.017, V = 2492.3(5) Å^3, T = 100 K, Z = 4, d_c = 1.491 g cm^{-3}, μ(Mo Kα, λ = 0.71073 Å) = 1.705 mm^{-1}, 25880 reflections collected, 14583 unique [R_{int} = 0.0996], which were used in all calculations. Refinement on F^2, final R(F) = 0.2437, R_w(F2) = 0.2913. CCDC number 1405279.

NMR - spectra



2k

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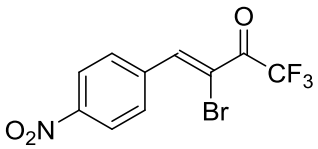
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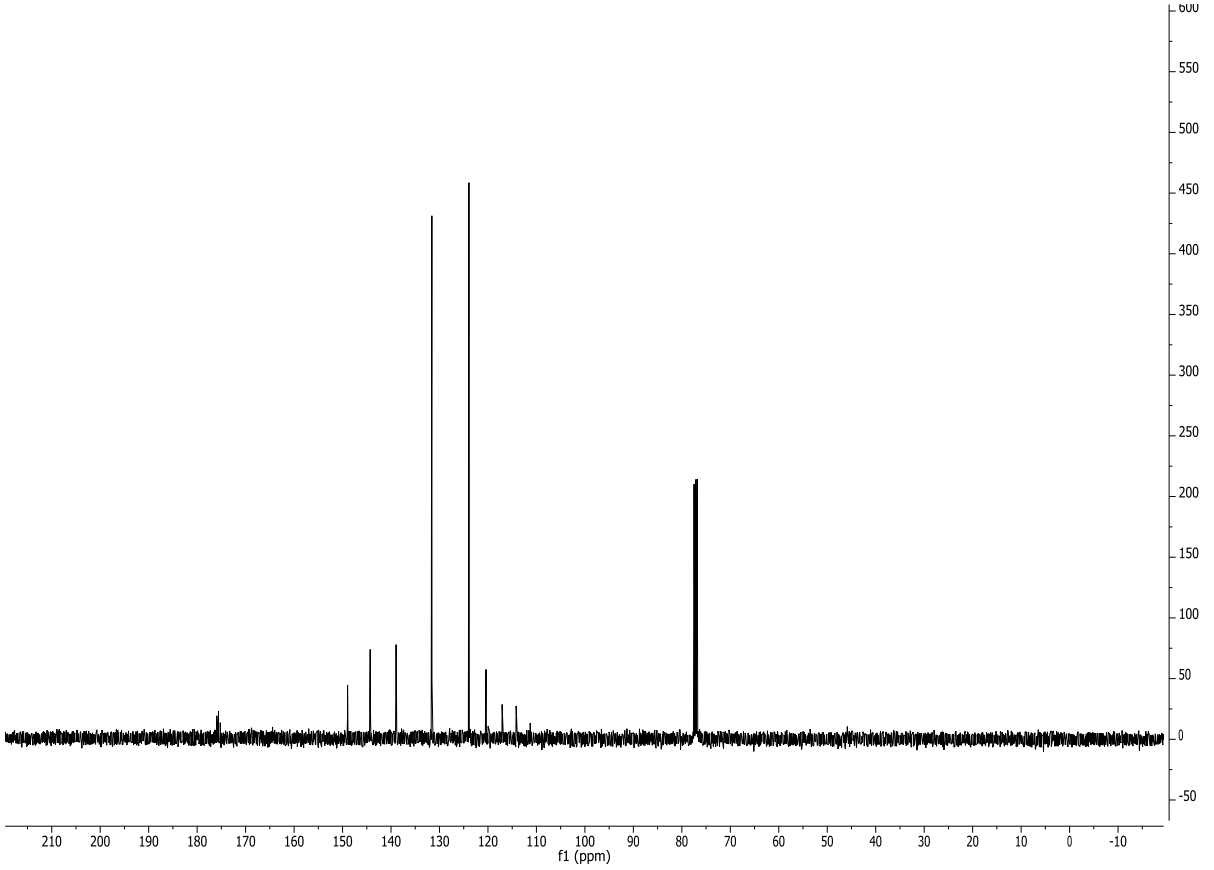
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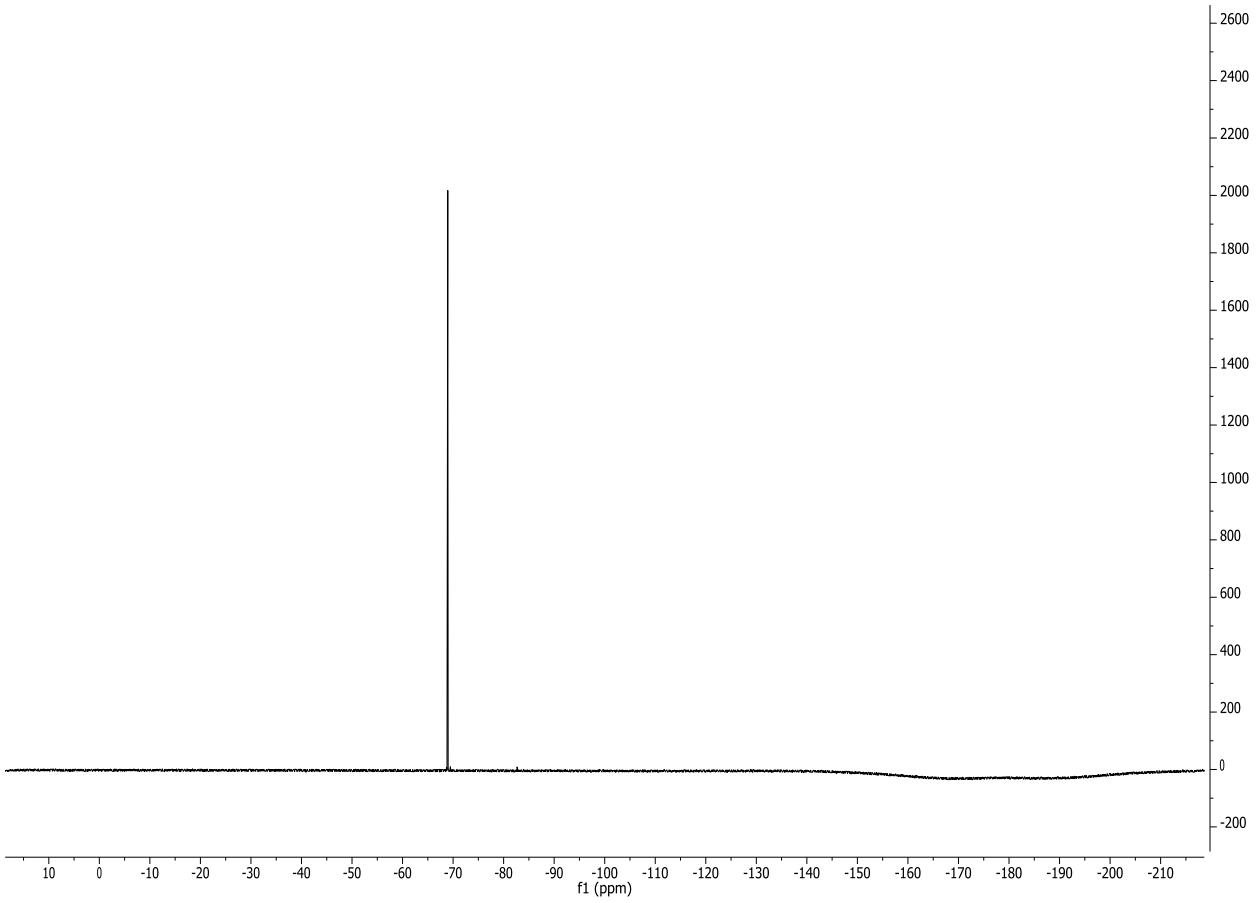
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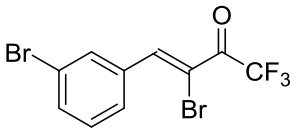
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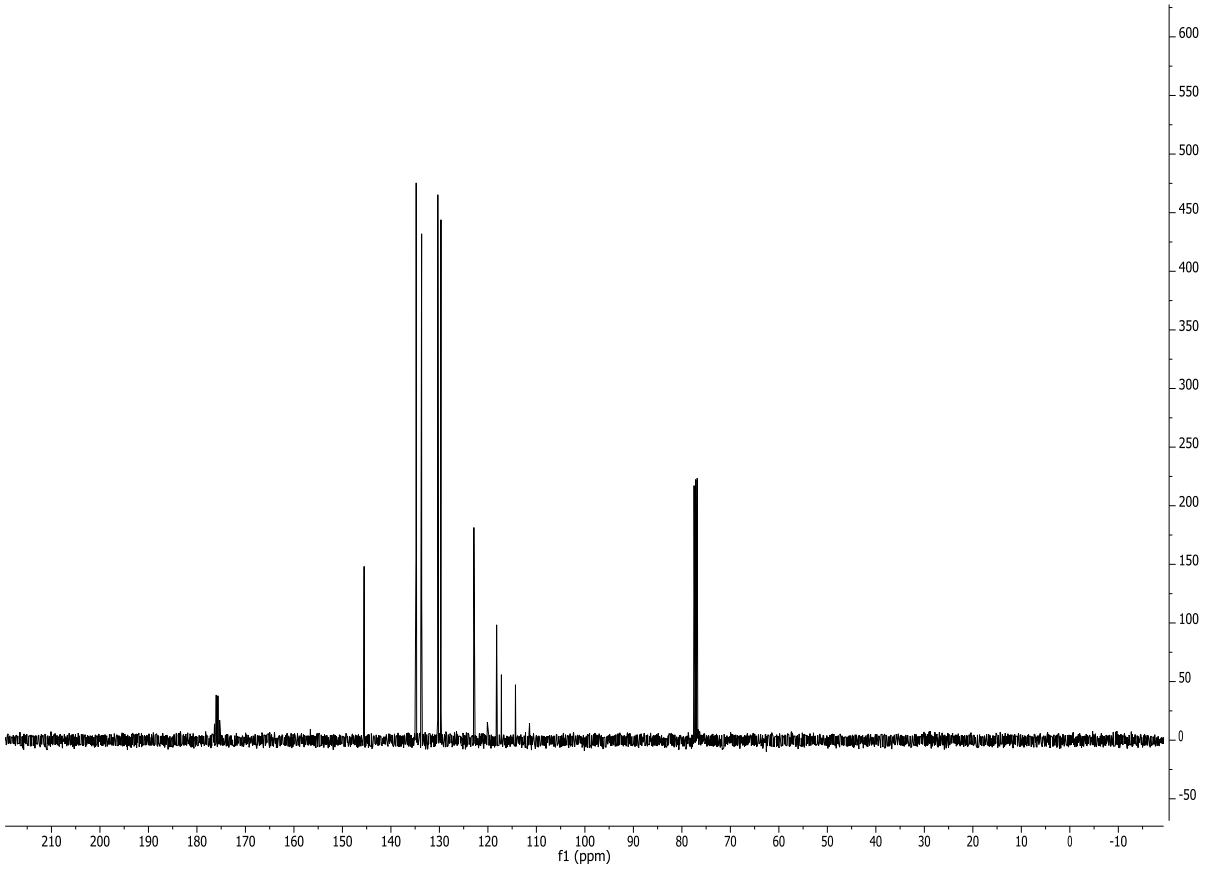
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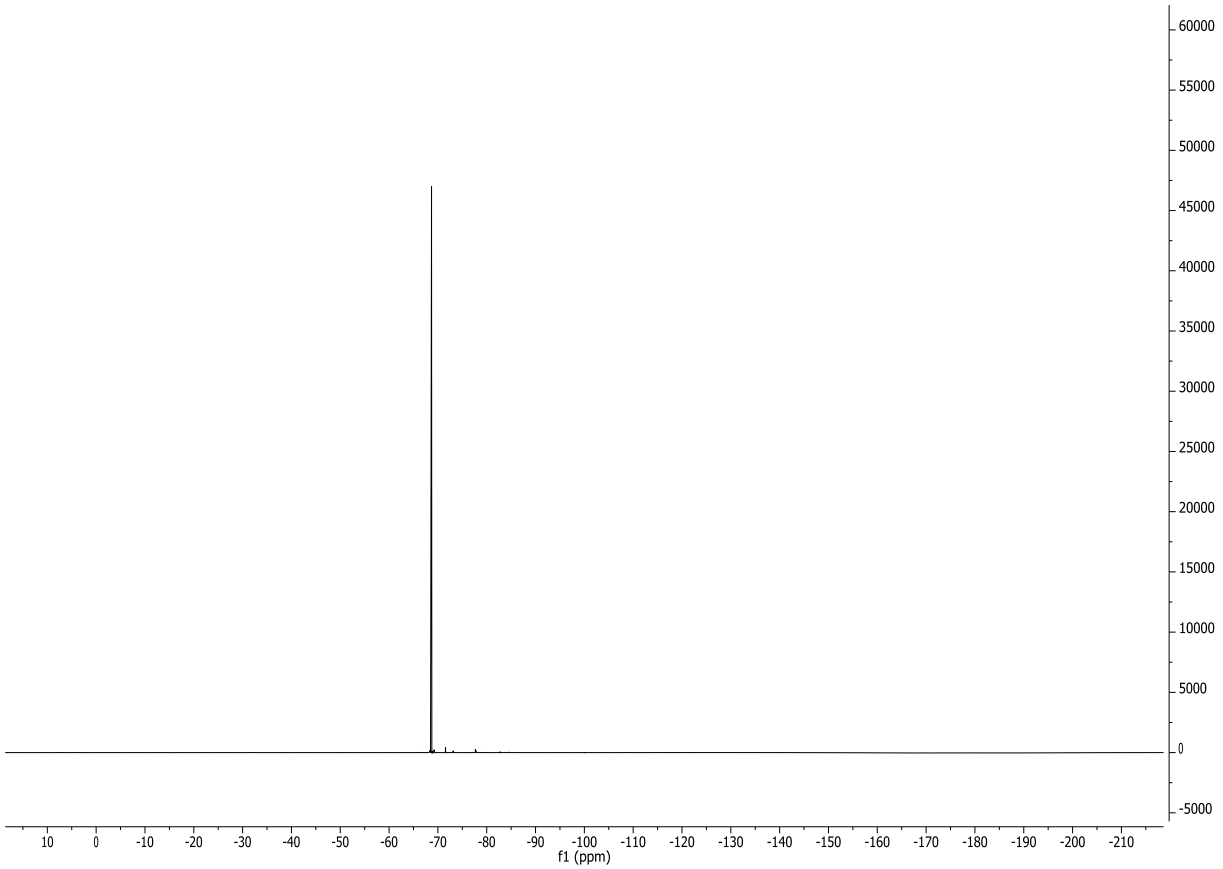
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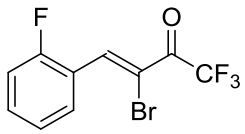
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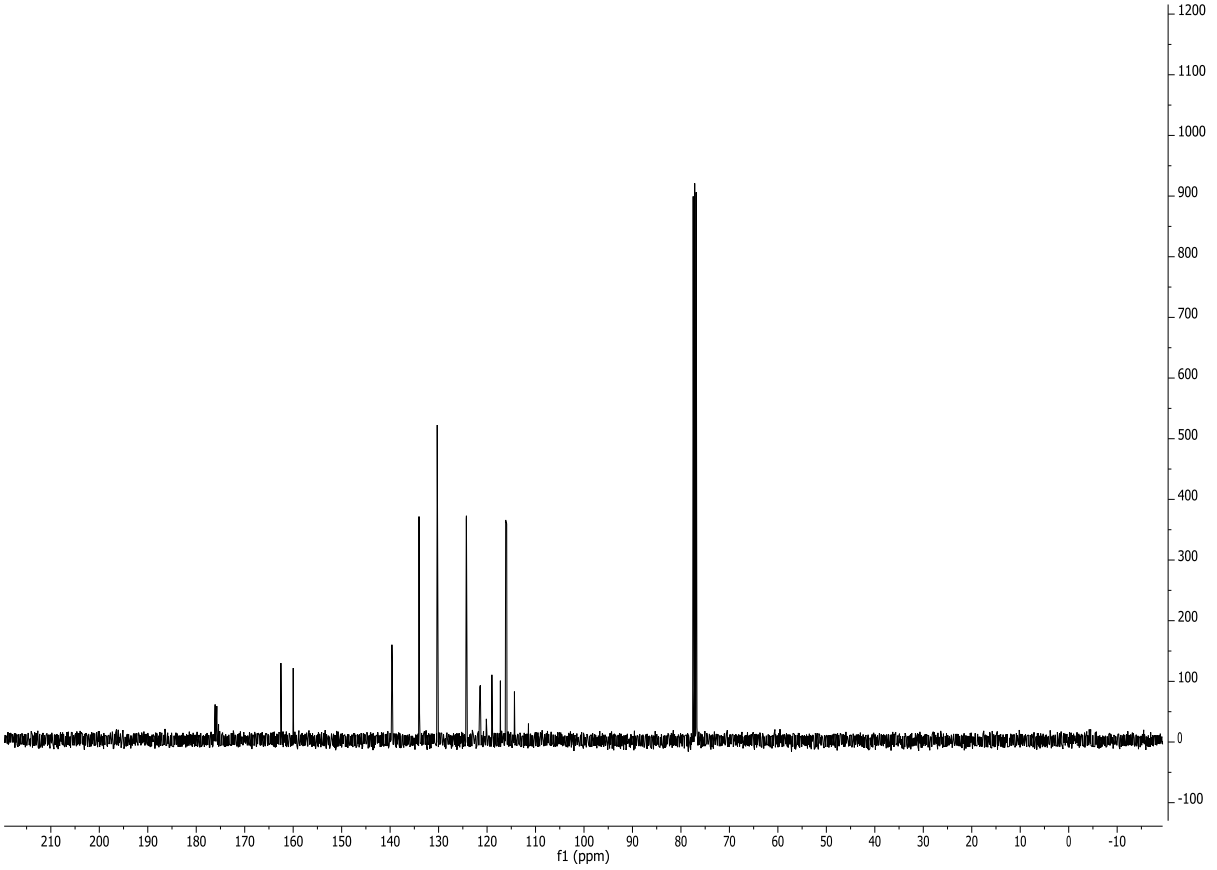
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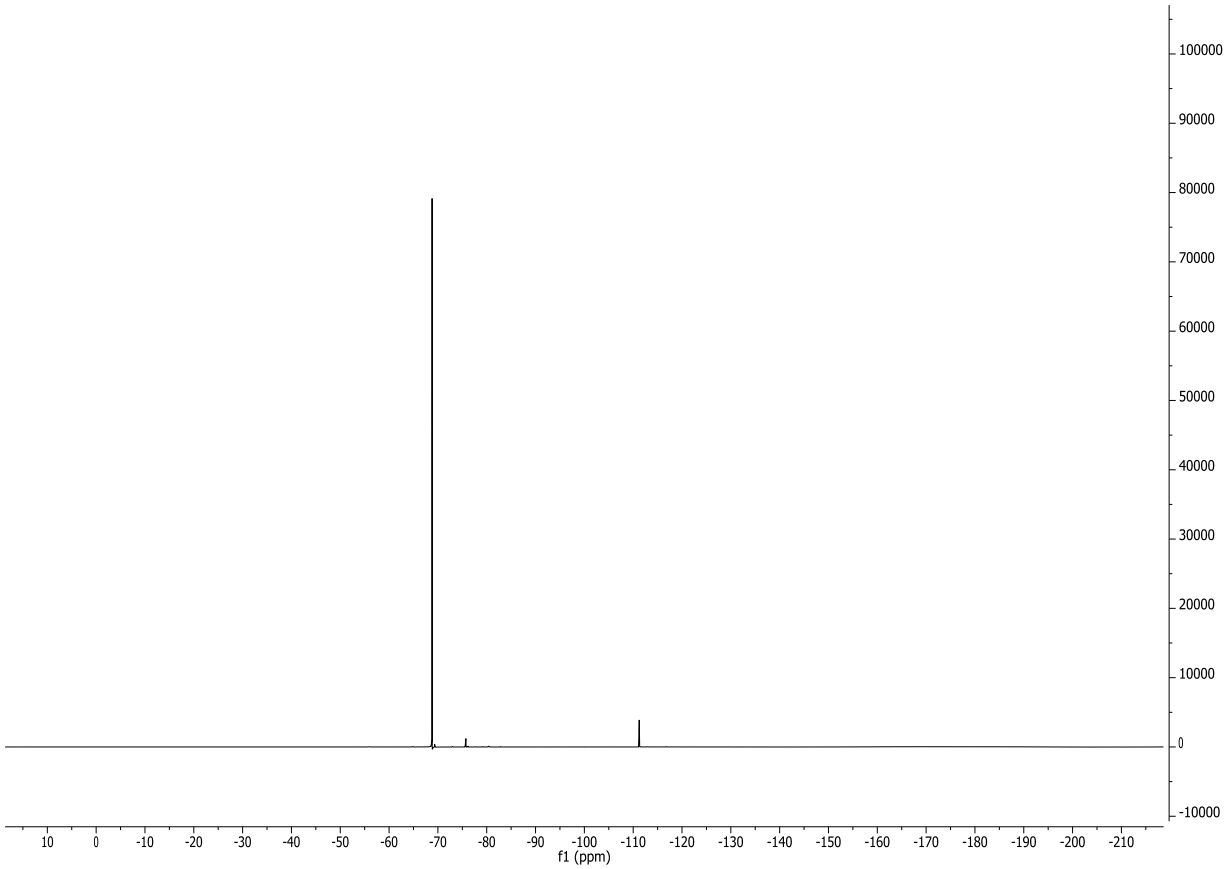
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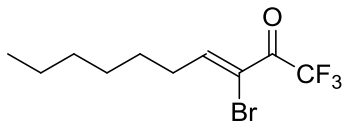
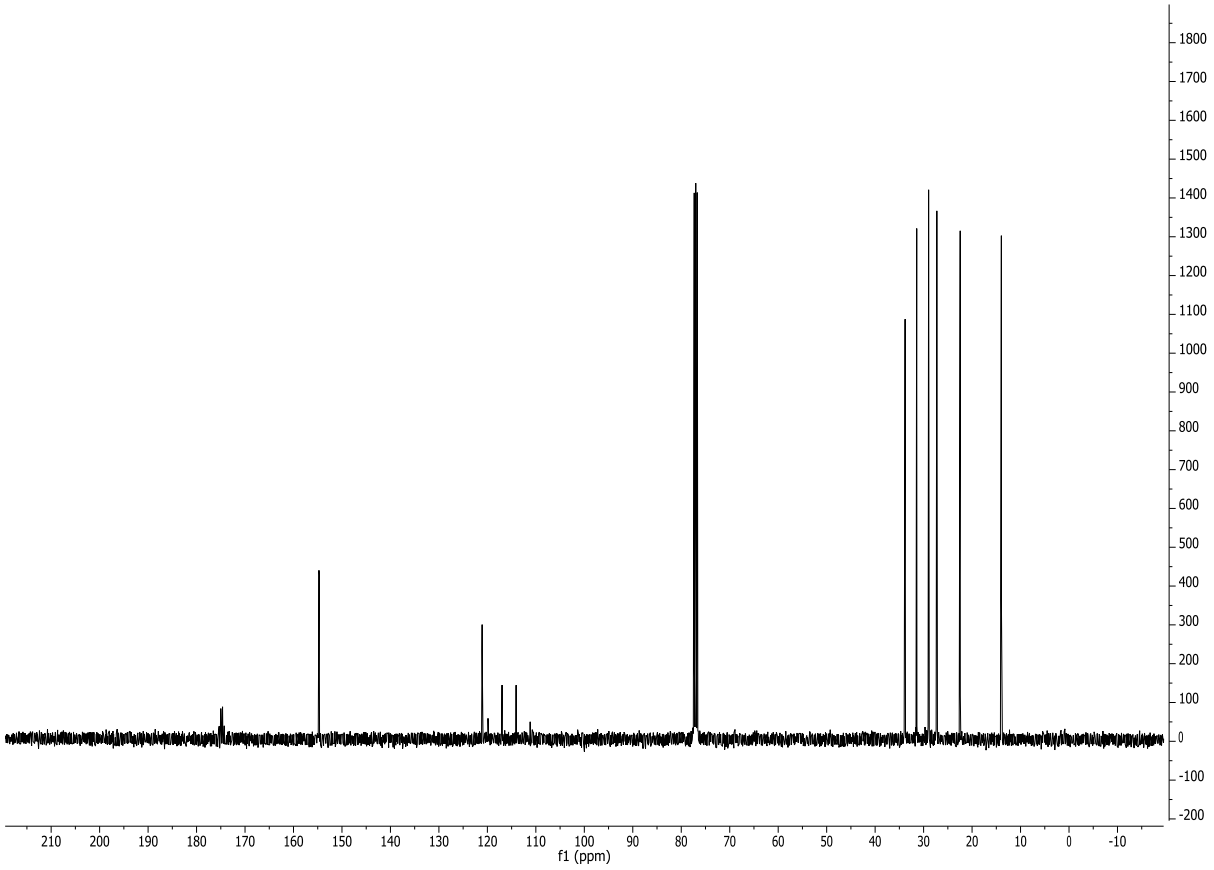
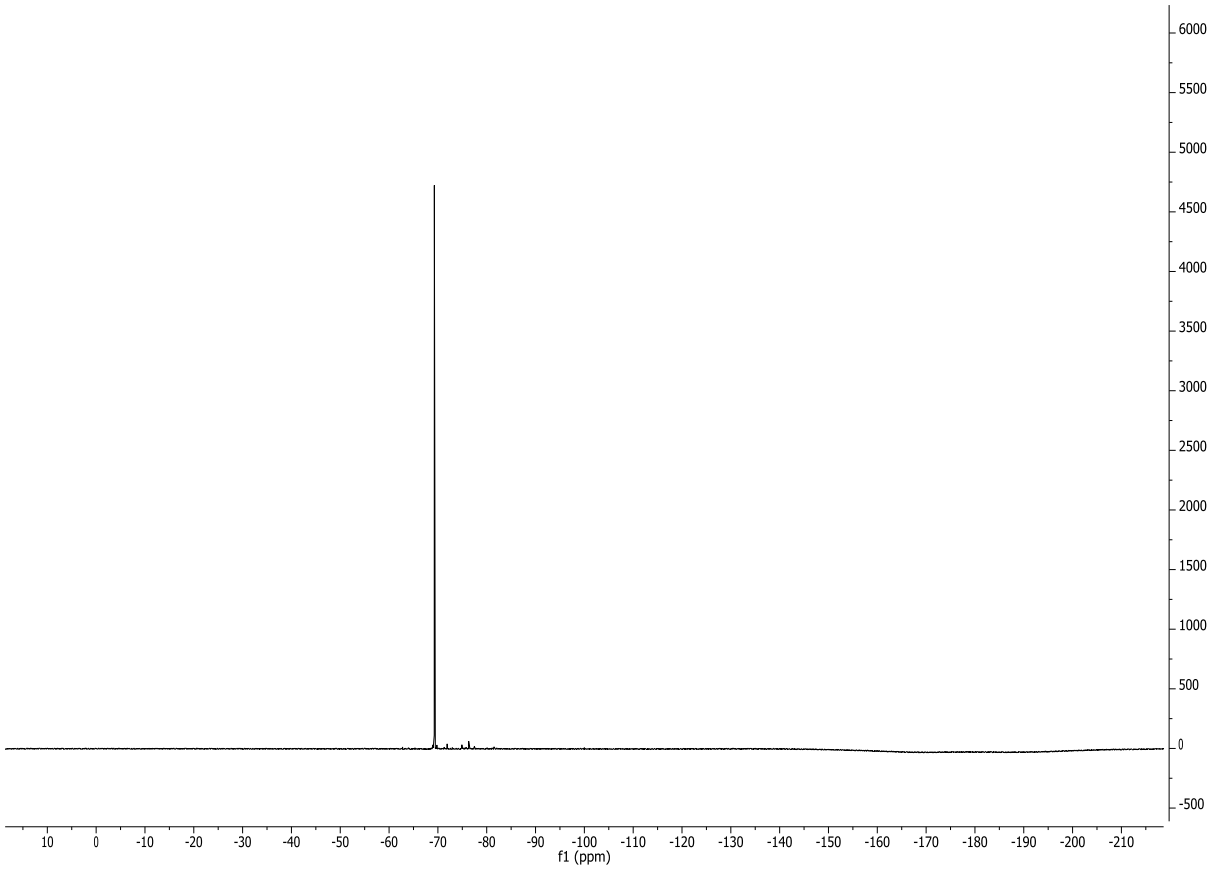
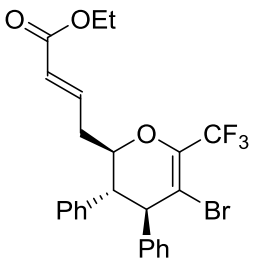
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)



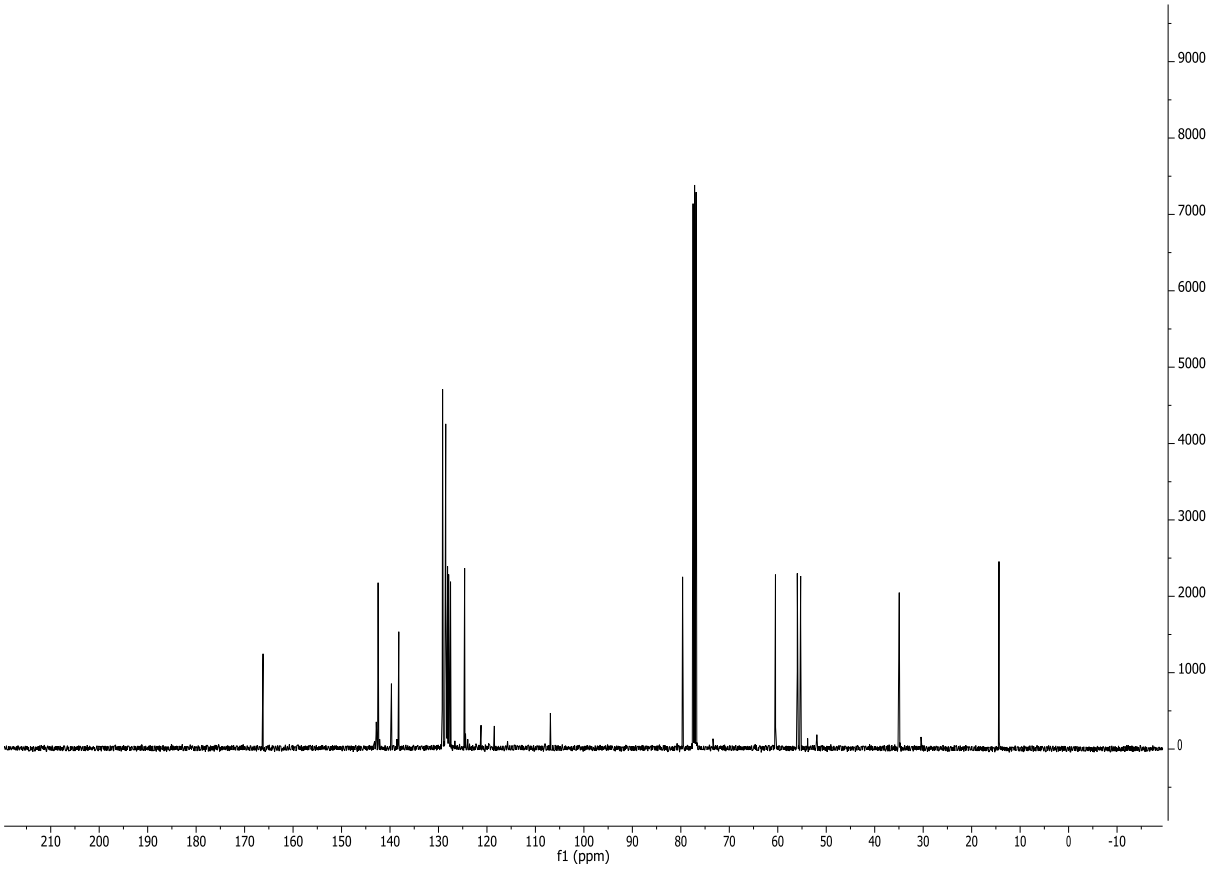
2q

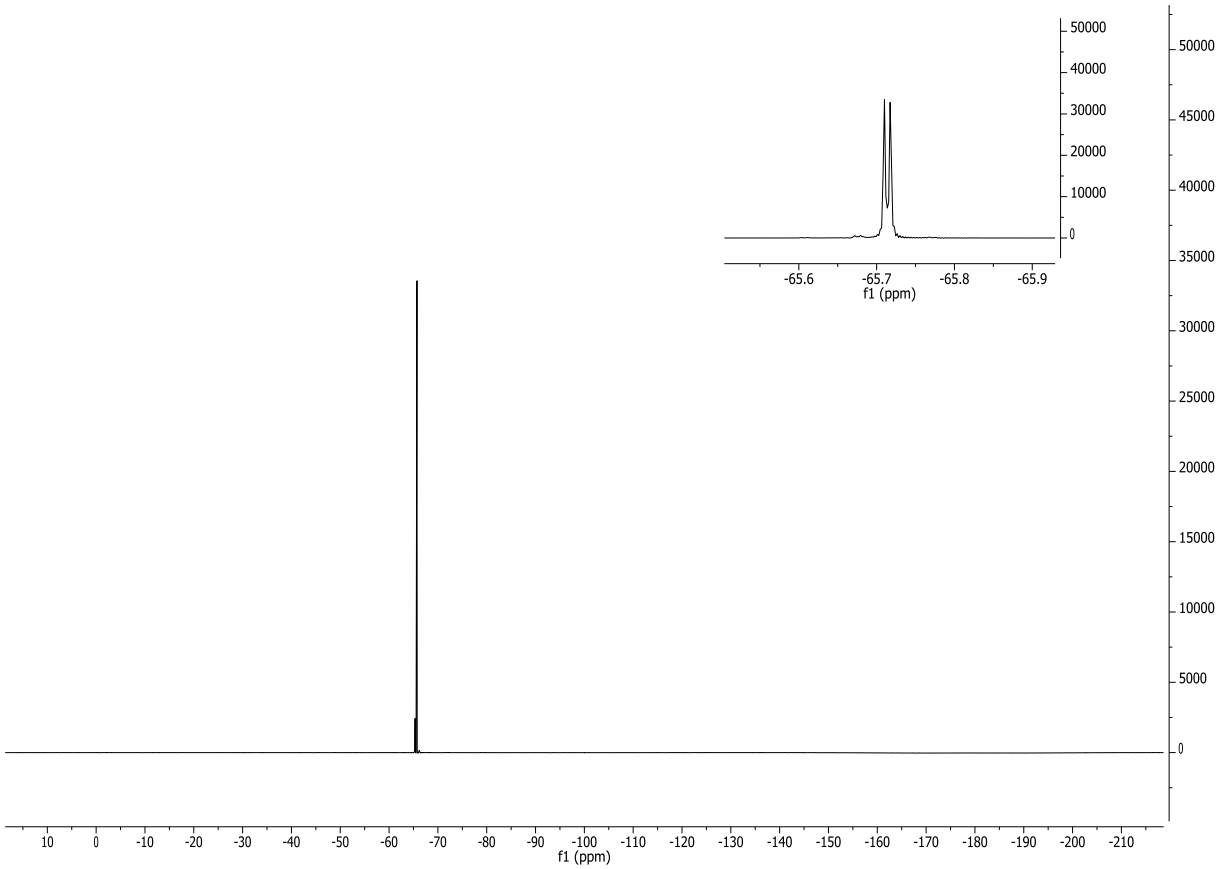


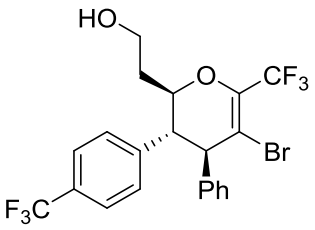

6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)



5a'

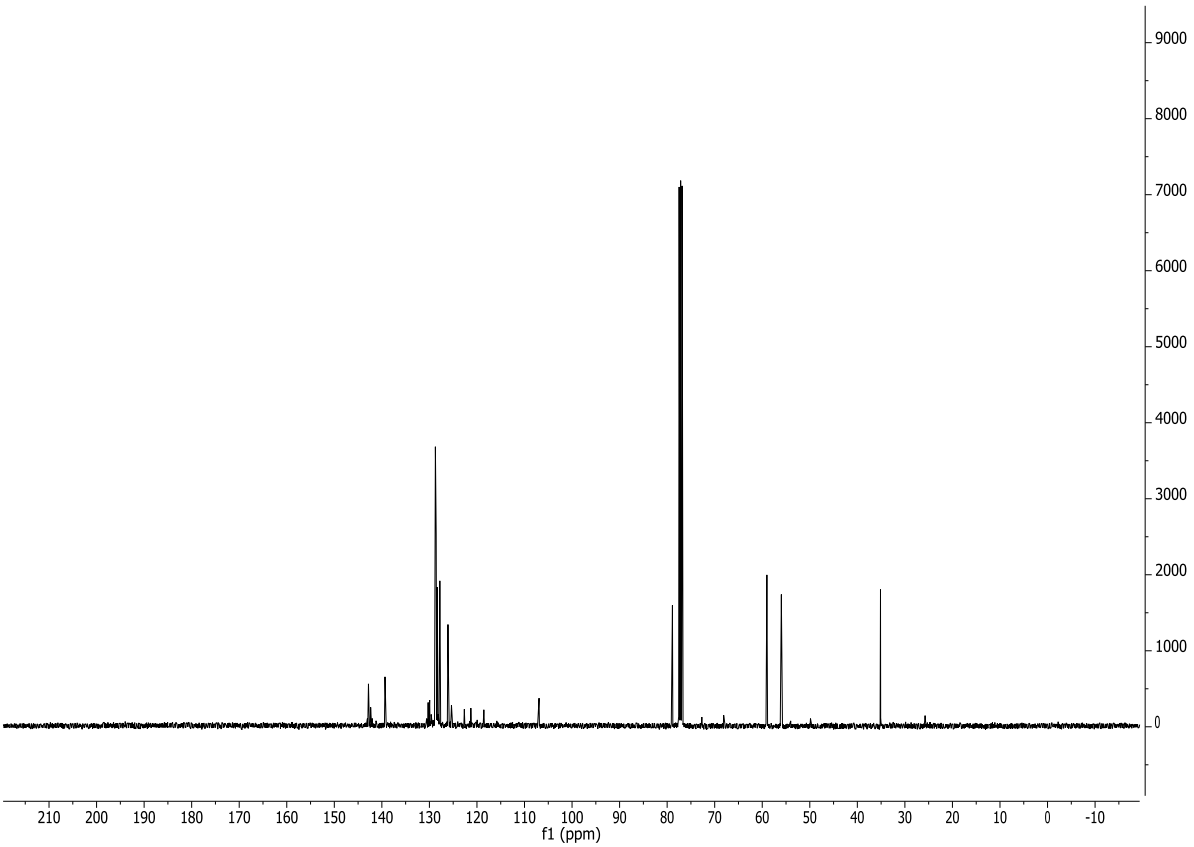


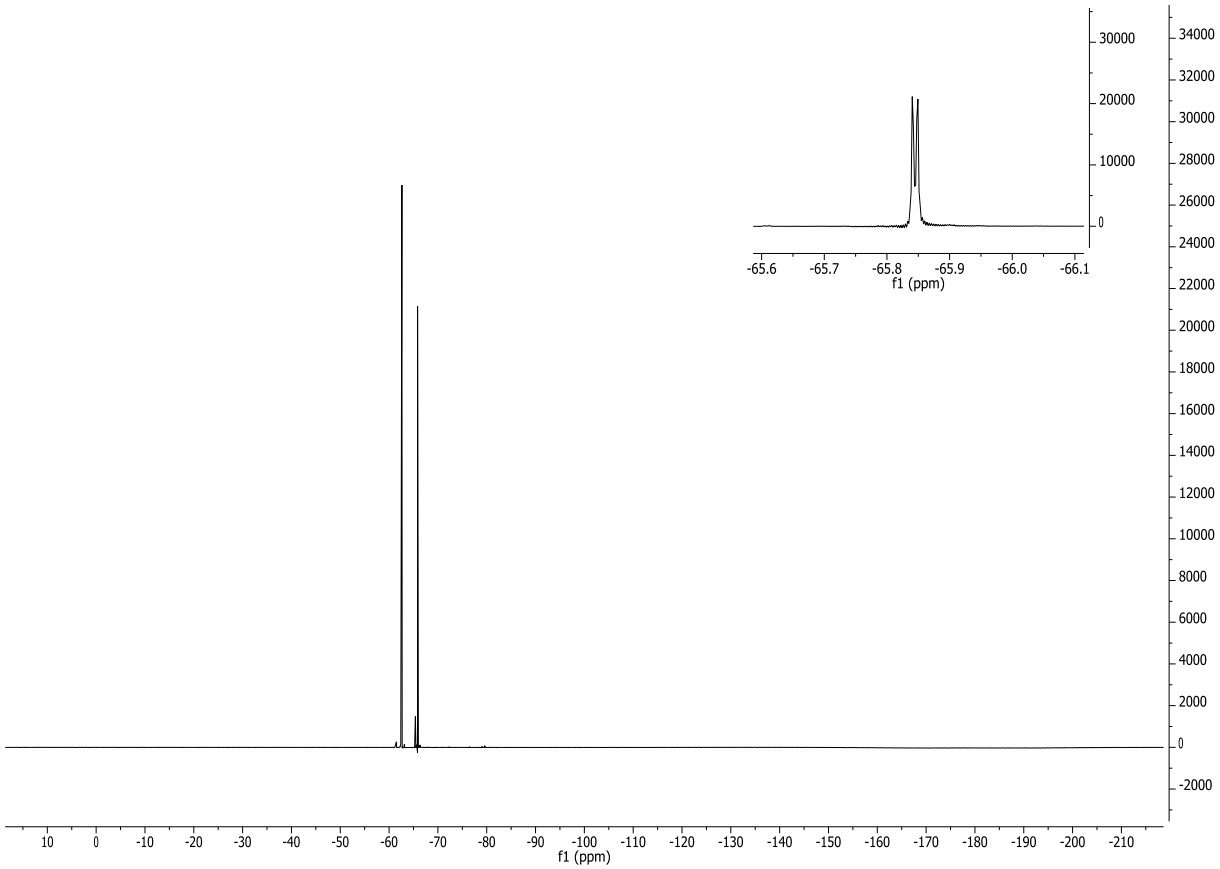

50000
40000
30000
20000
10000
0
-65.6
-65.7
-65.8
-65.9
f1 (ppm)
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

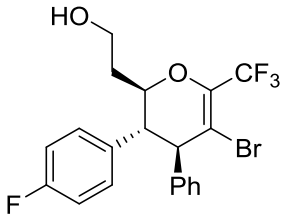

HO
O
CF3
Br
Ph
F3C

5b

7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

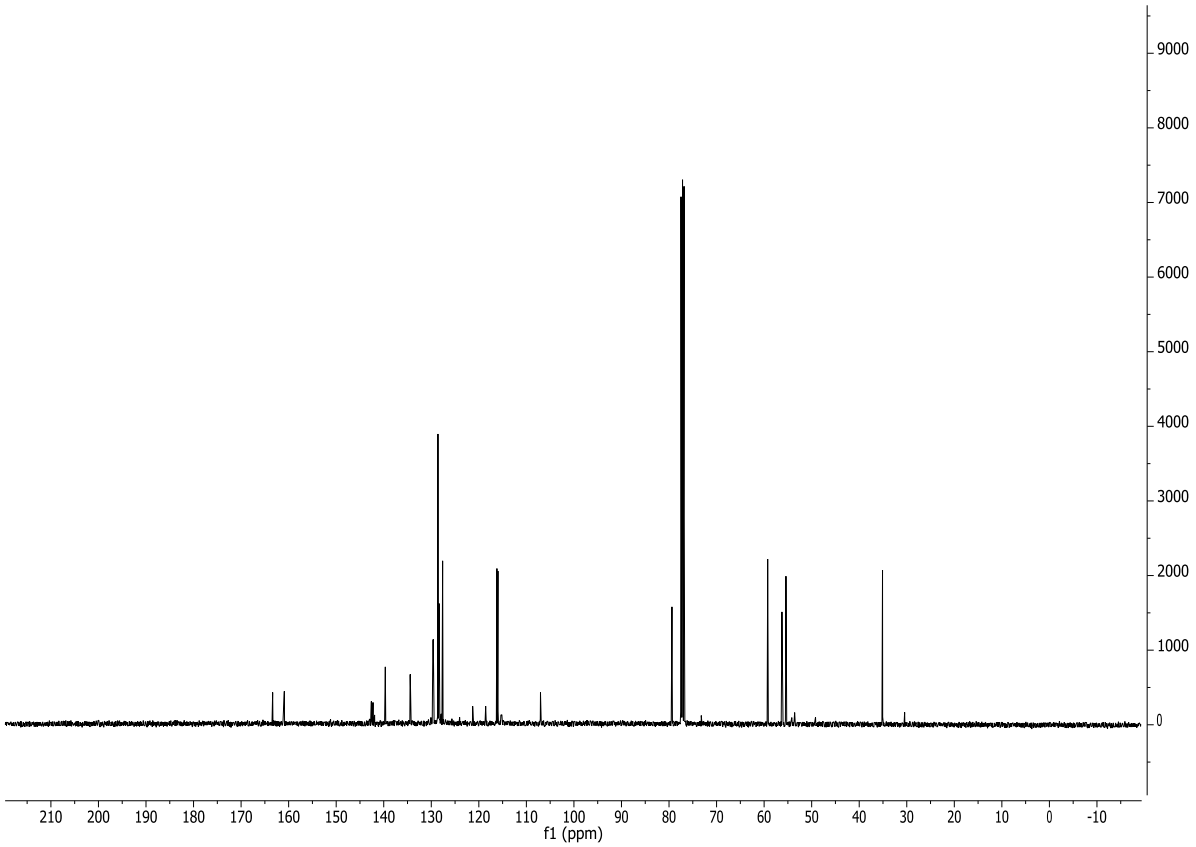

9000
8000
7000
6000
5000
4000
3000
2000
1000
0
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

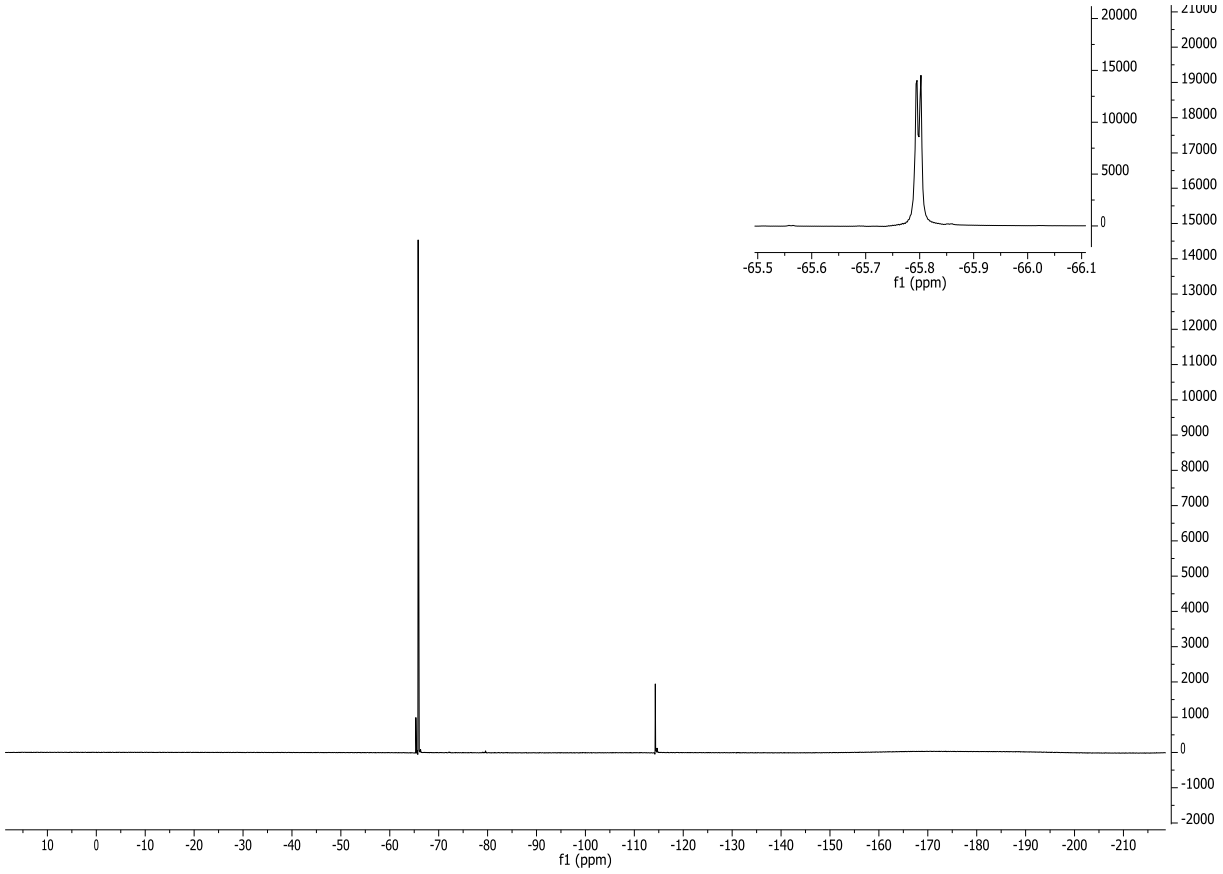

30000
20000
10000
0
-65.6
-65.7
-65.8
-65.9
-66.0
-66.1
f1 (ppm)
34000
32000
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

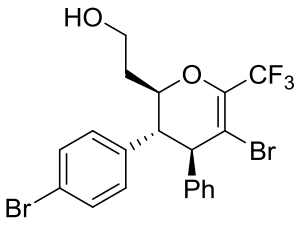

HO
O
CF3
Br
Ph
F

5c

7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

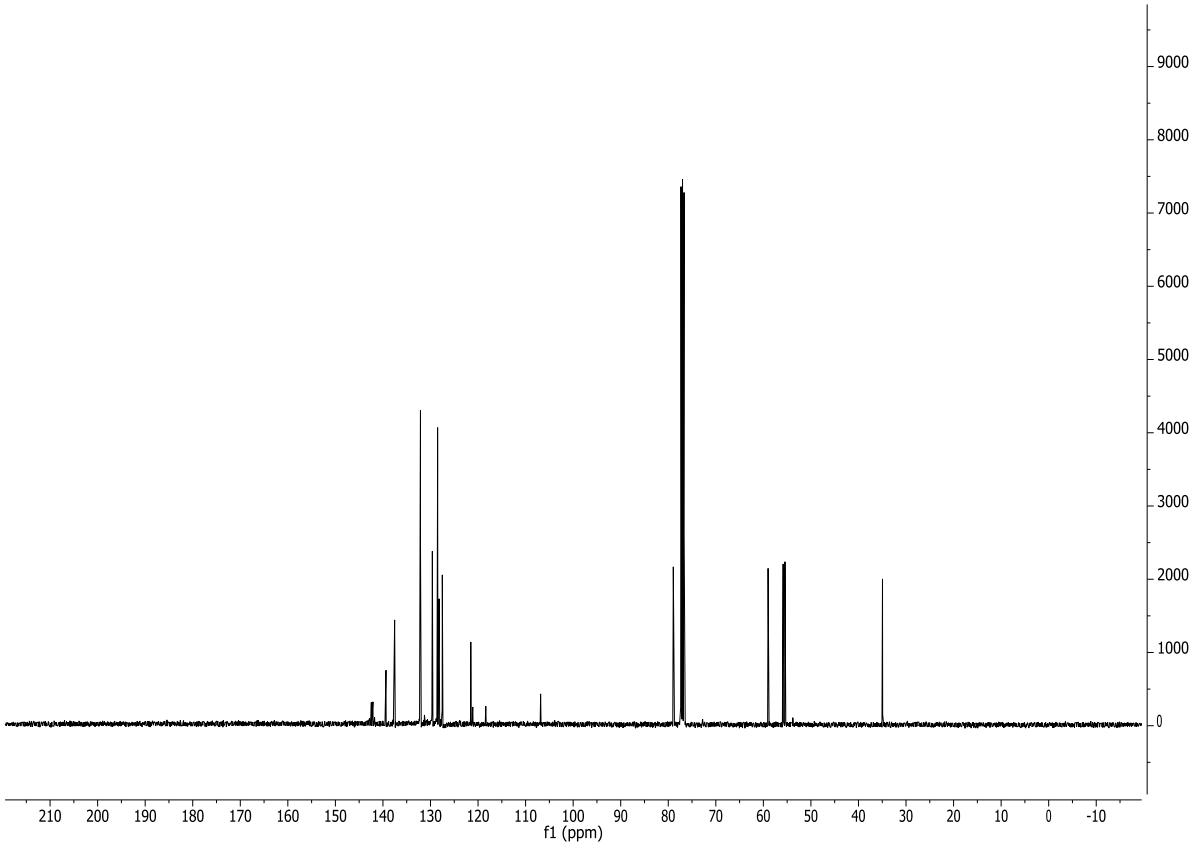

9000
8000
7000
6000
5000
4000
3000
2000
1000
0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

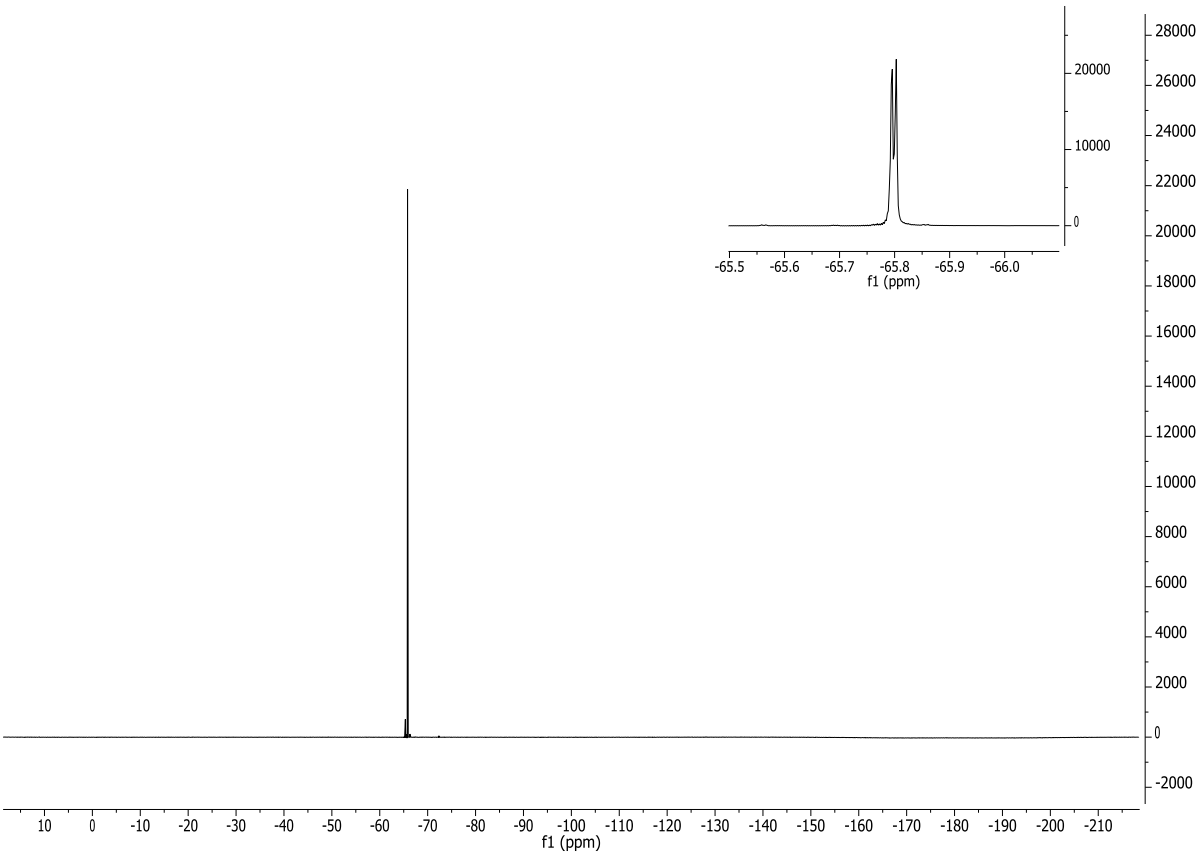

f1 (ppm)
f1 (ppm)

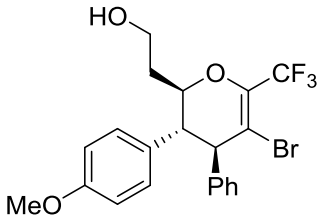

HO
O
CF3
Br
Ph
Br

5d

5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

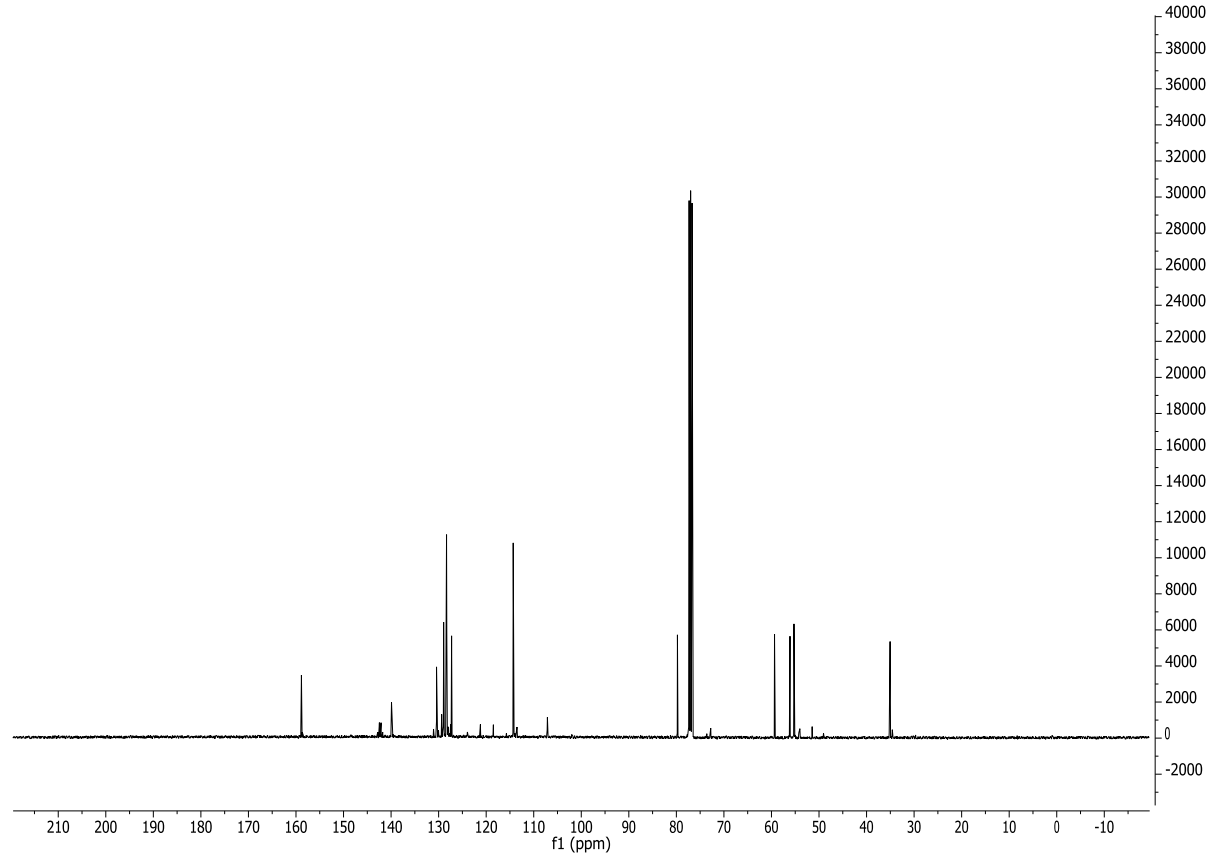

9000
8000
7000
6000
5000
4000
3000
2000
1000
0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

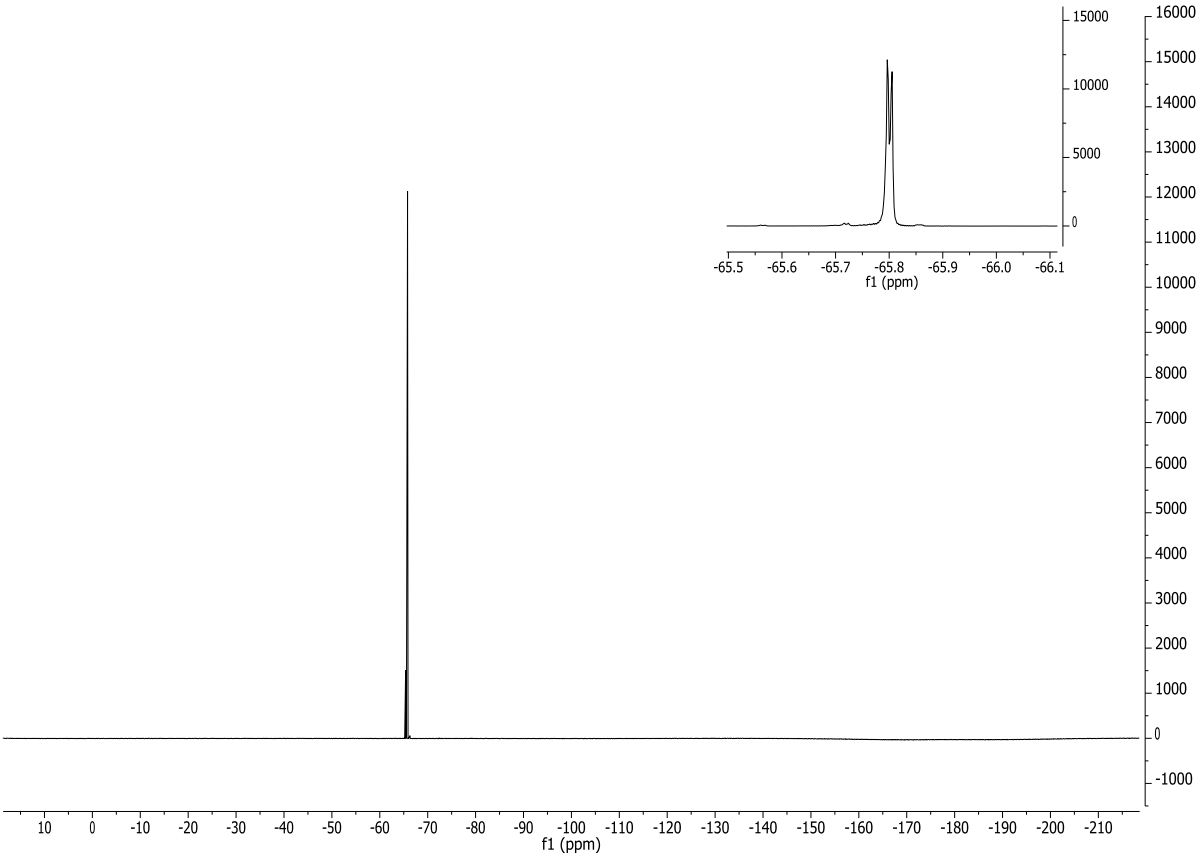

28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)
20000
10000
0
-65.5 -65.6 -65.7 -65.8 -65.9 -66.0
f1 (ppm)

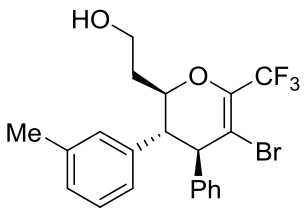

HO
O
CF3
Br
Ph
MeO

5e

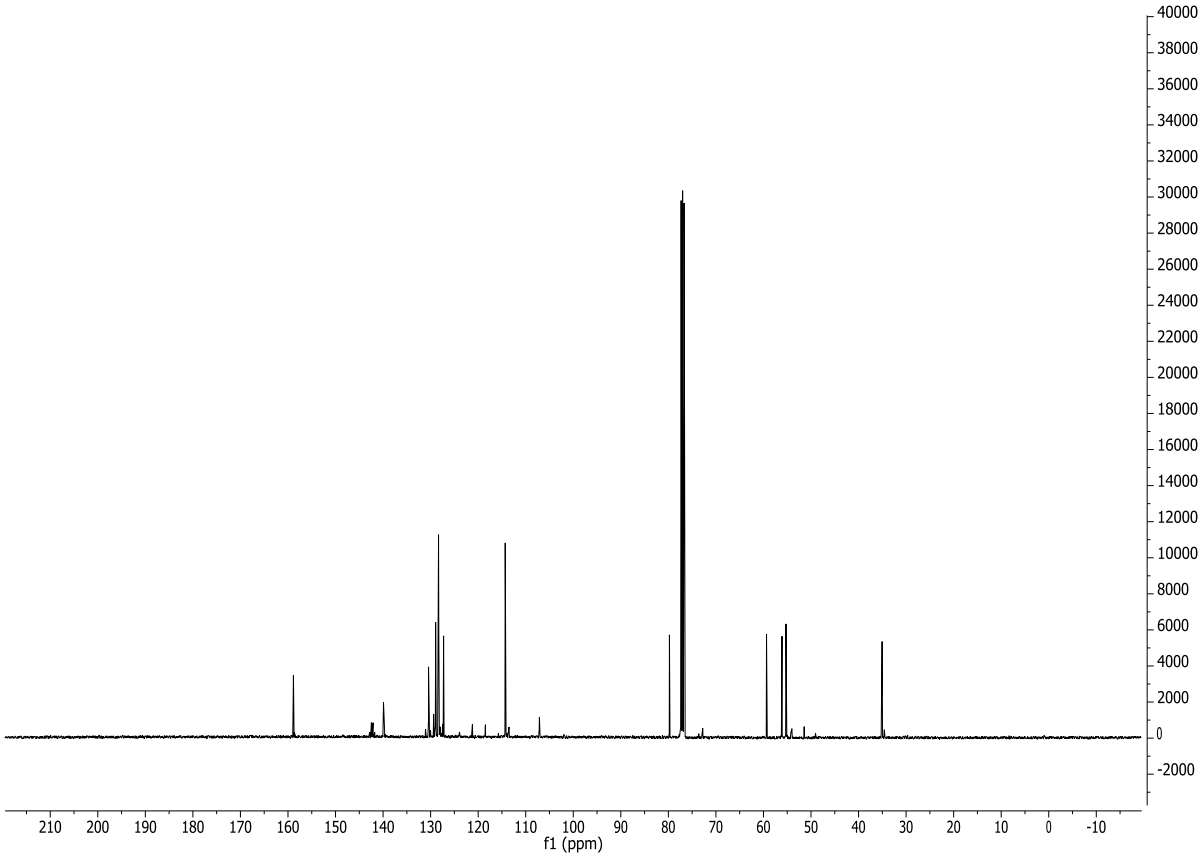
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

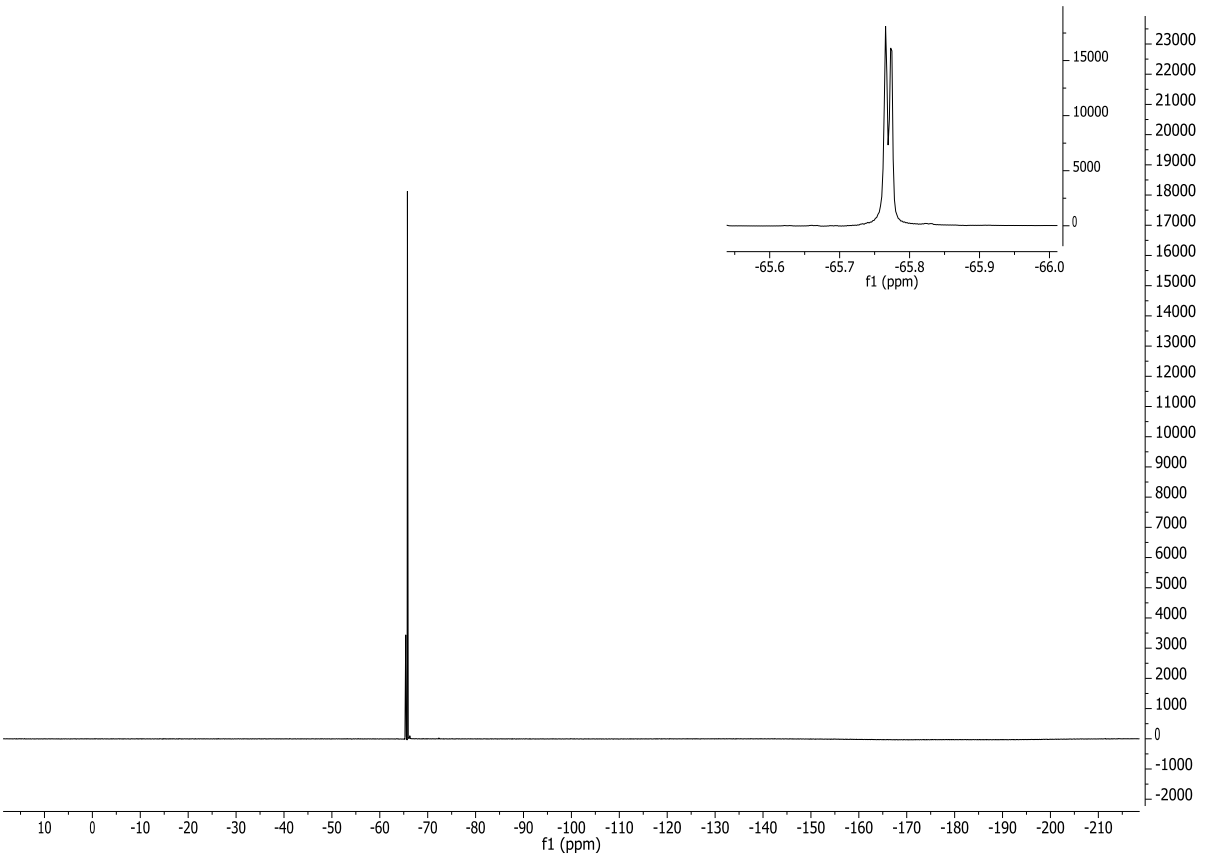

40000
38000
36000
34000
32000
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

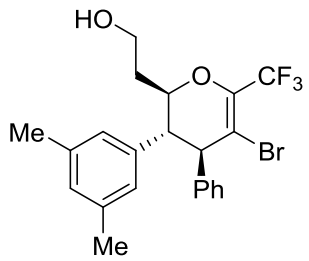

15000
10000
5000
0
-65.5
-65.6
-65.7
-65.8
-65.9
-66.0
-66.1
f1 (ppm)
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)



5f

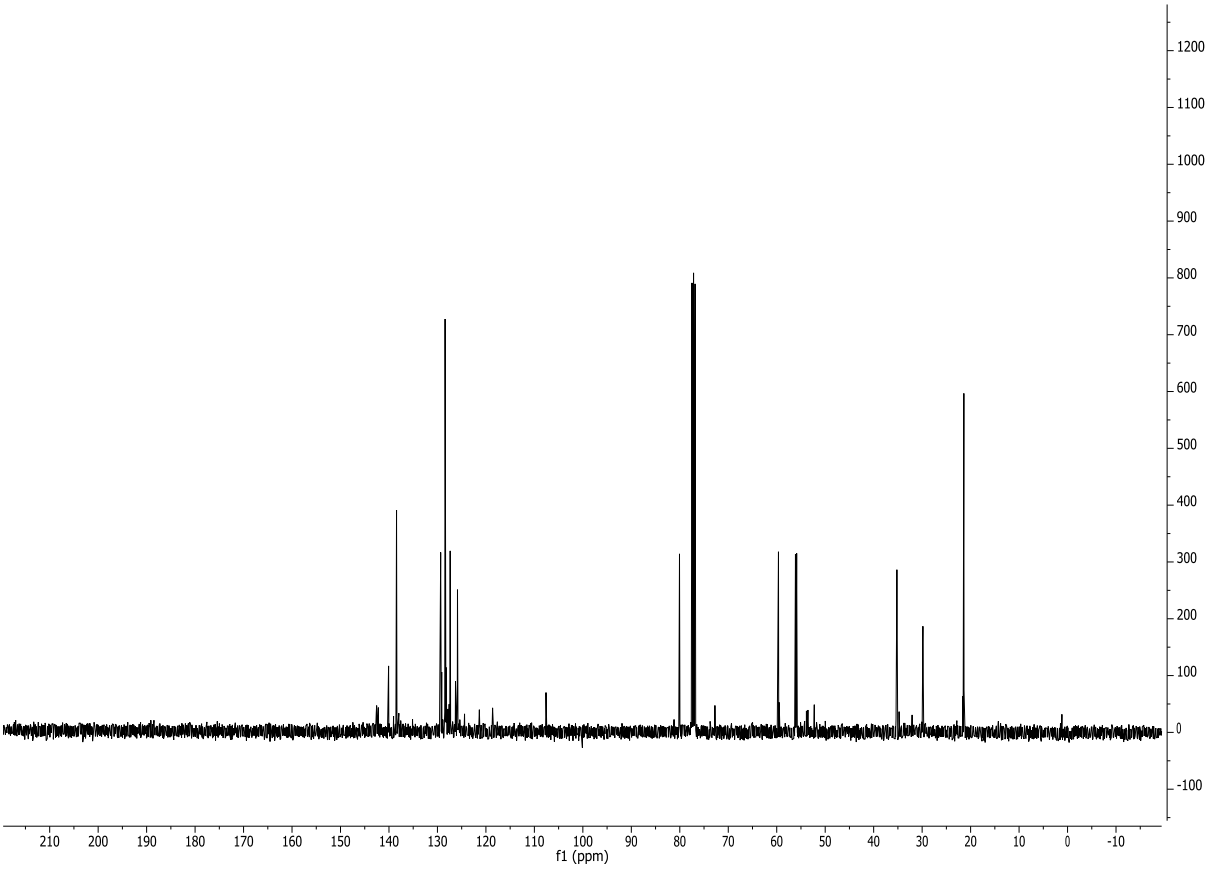


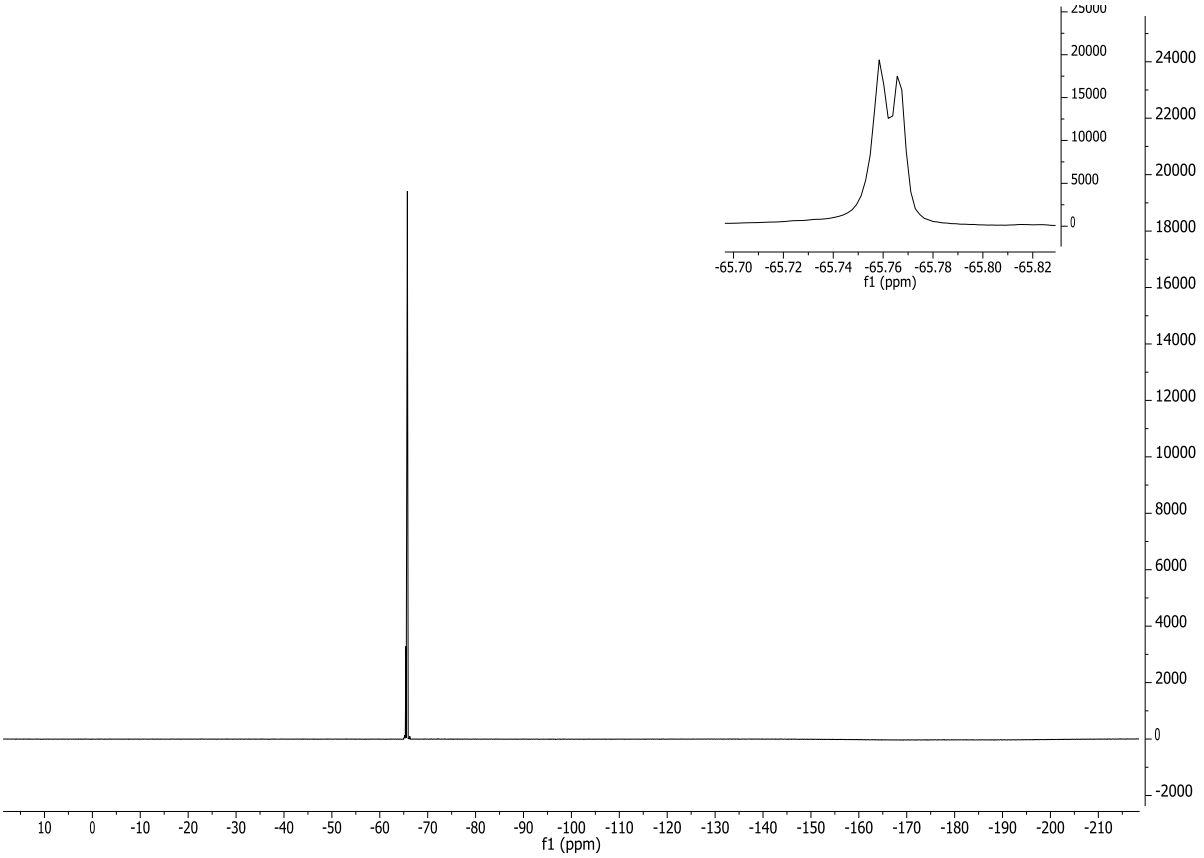

15000
10000
5000
0
-65.6
-65.7
-65.8
-65.9
-66.0
f1 (ppm)
23000
22000
21000
20000
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
-2000
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

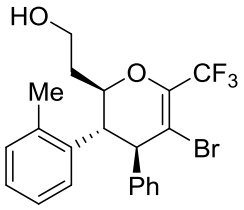

HO
O
CF3
Me
Br
Ph
Me

5g

11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

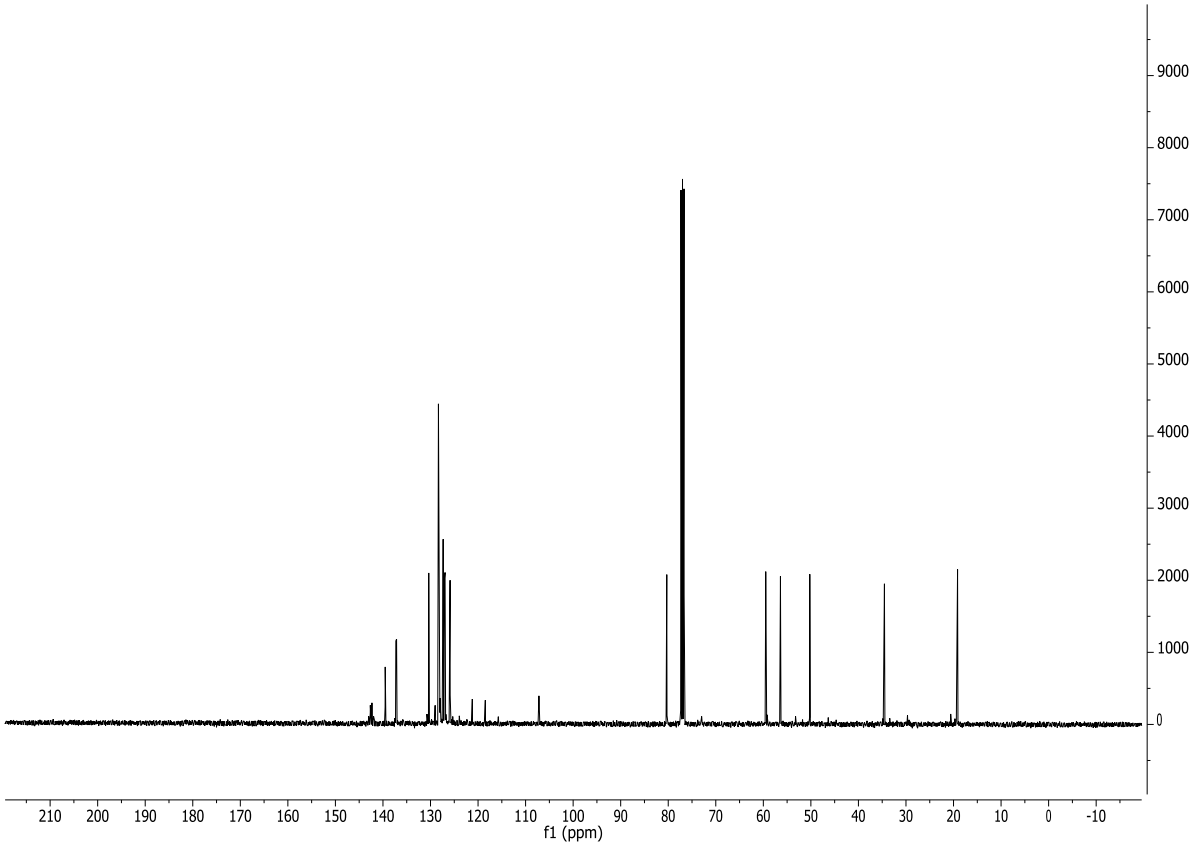

1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

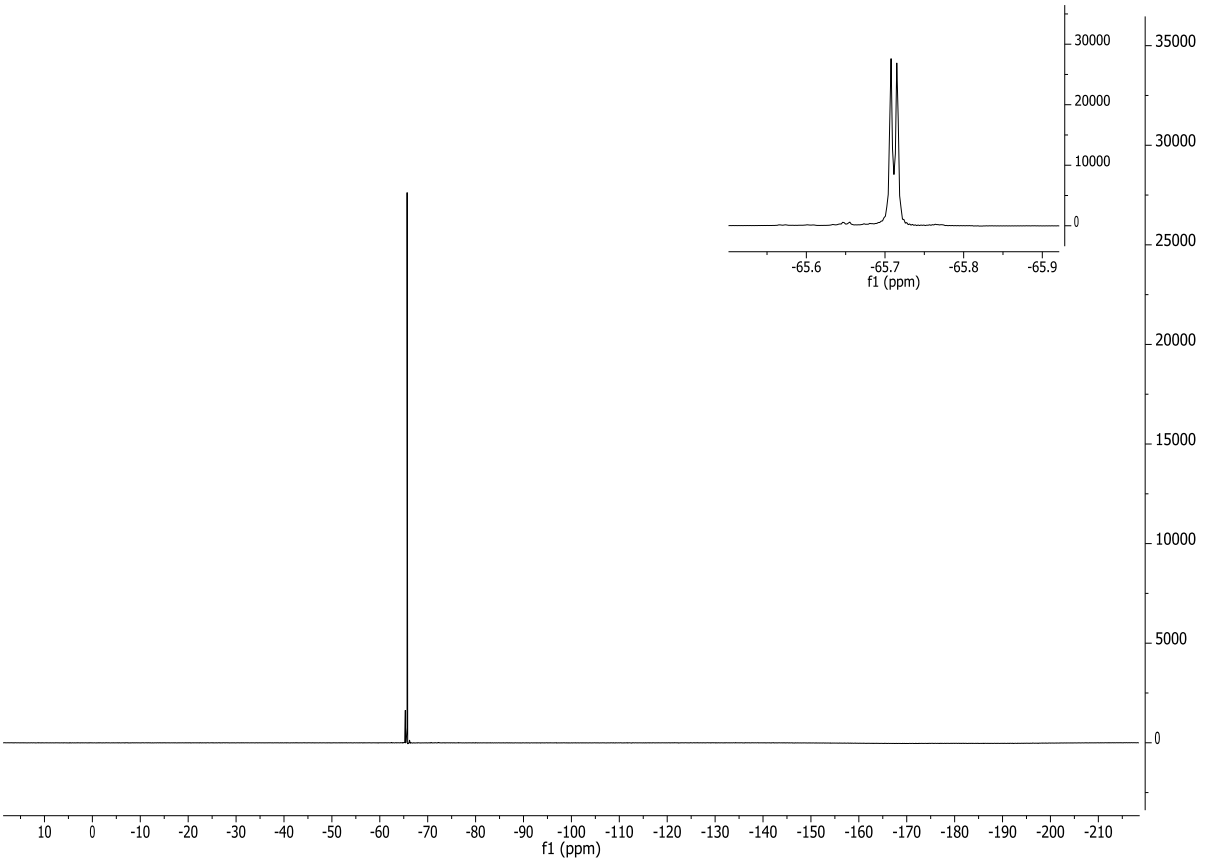

25000
20000
15000
10000
5000
0
-65.70 -65.72 -65.74 -65.76 -65.78 -65.80 -65.82
f1 (ppm)
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

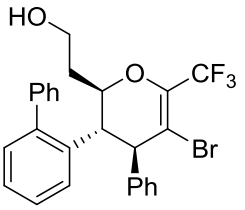

HO
O
CF3
Me
Br
Ph

5h

8000
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

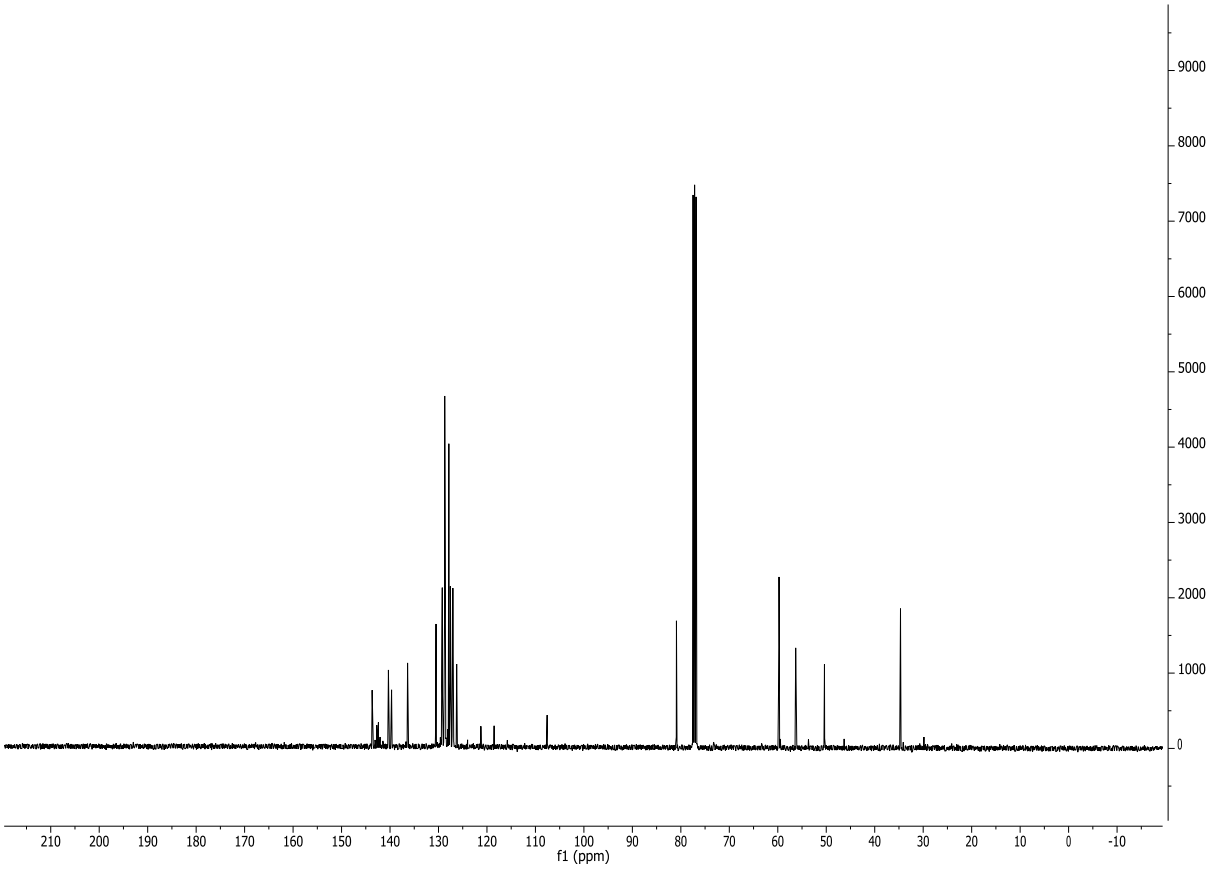

9000
8000
7000
6000
5000
4000
3000
2000
1000
0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

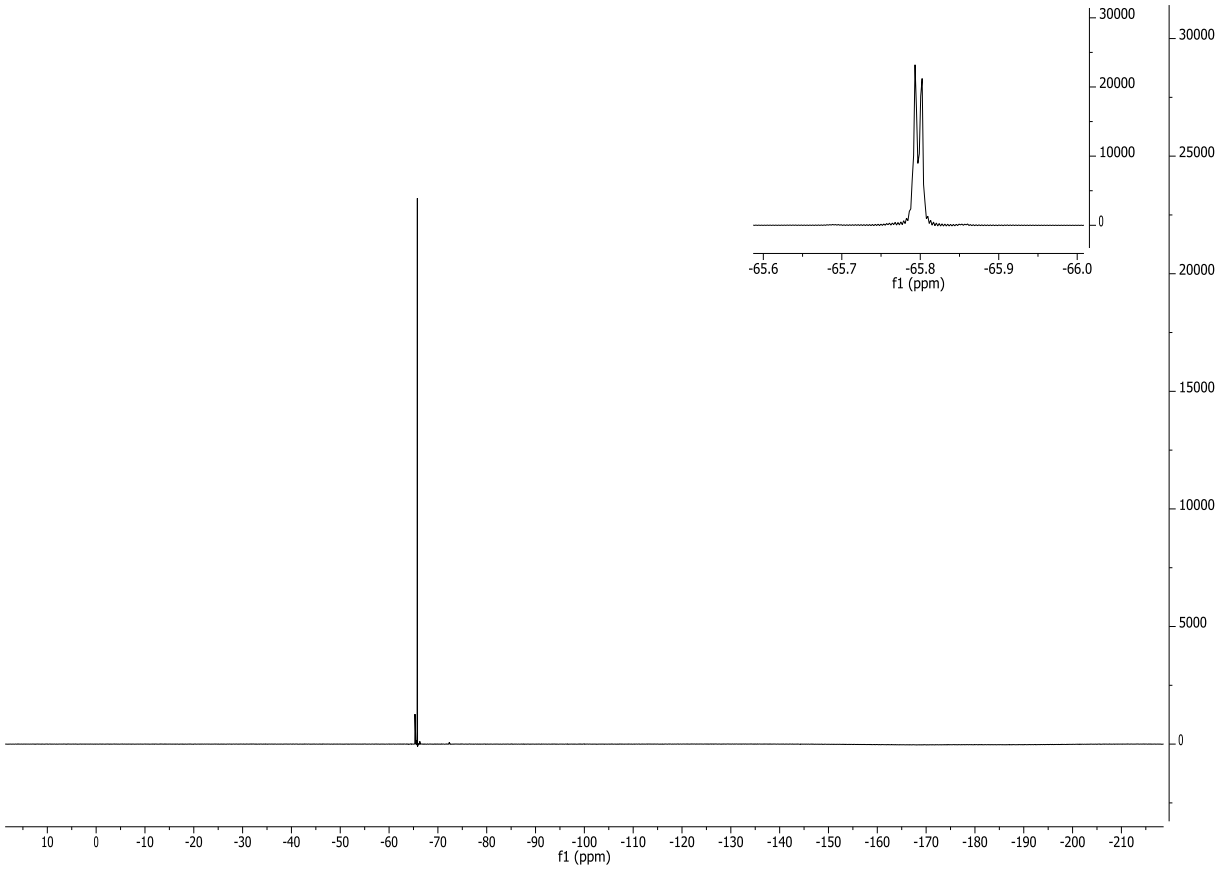

30000
20000
10000
0
-65.6
-65.7
-65.8
-65.9
f1 (ppm)
35000
30000
25000
20000
15000
10000
5000
0
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

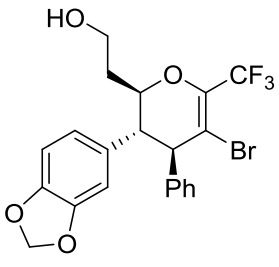

HO
O
CF3
Ph
Br
Ph

5i

4000
3500
3000
2500
2000
1500
1000
500
0
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

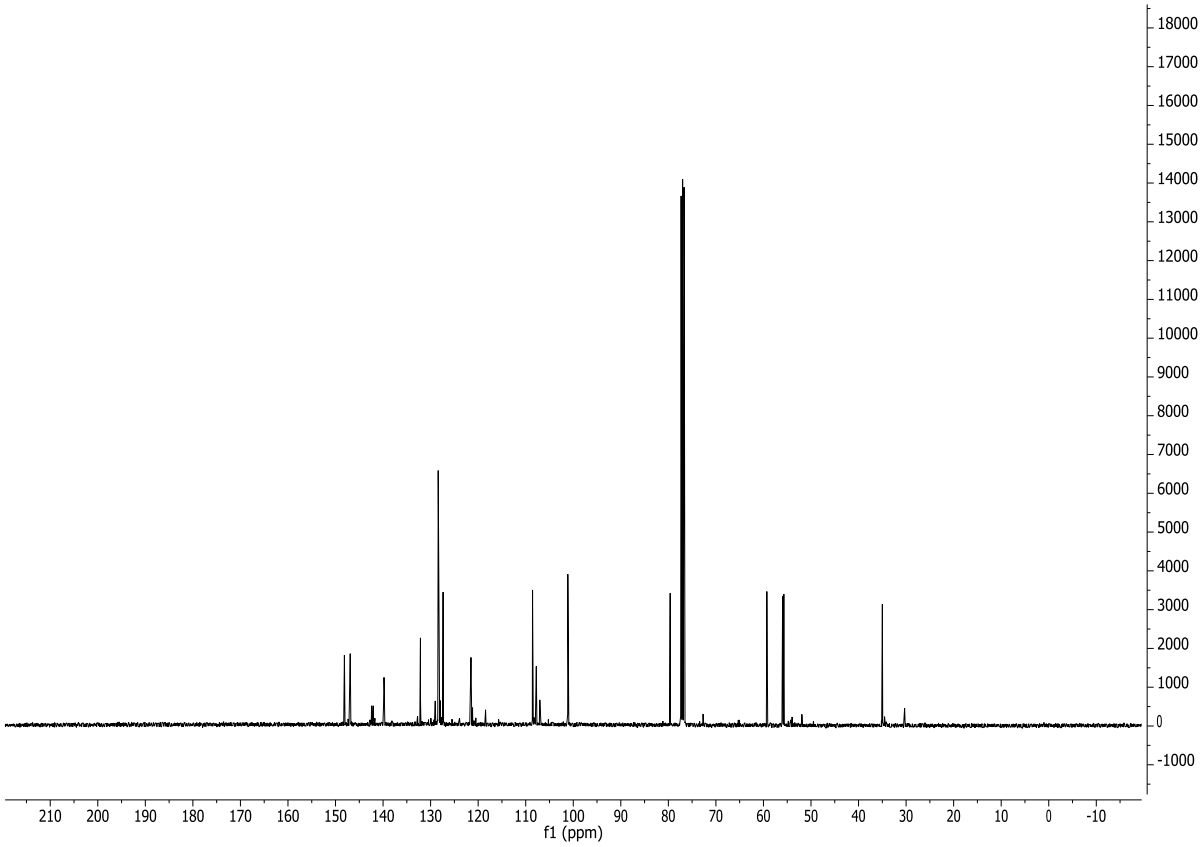

9000
8000
7000
6000
5000
4000
3000
2000
1000
0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

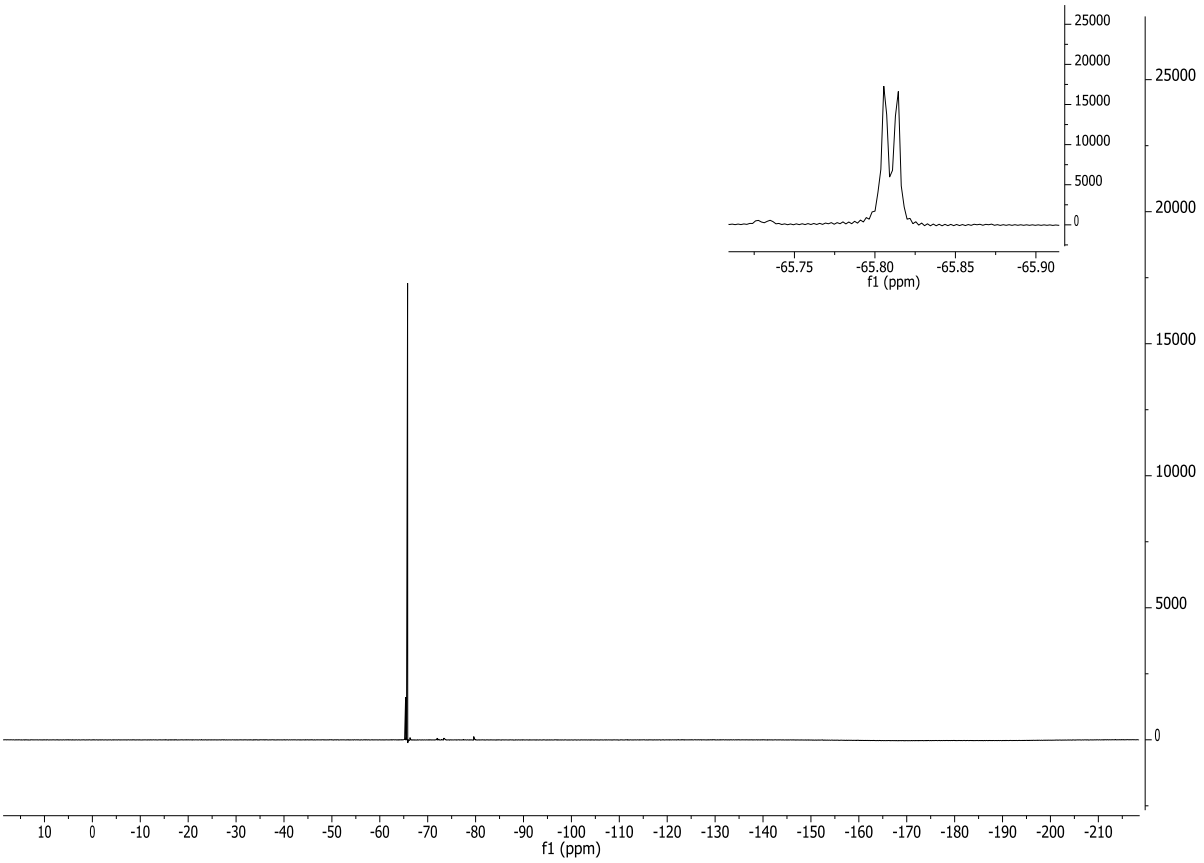

30000
20000
10000
0
-65.6
-65.7
-65.8
-65.9
-66.0
f1 (ppm)
30000
25000
20000
15000
10000
5000
0
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

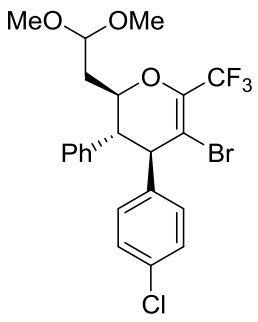

HO
O
CF3
Br
Ph
O
O

5j

5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

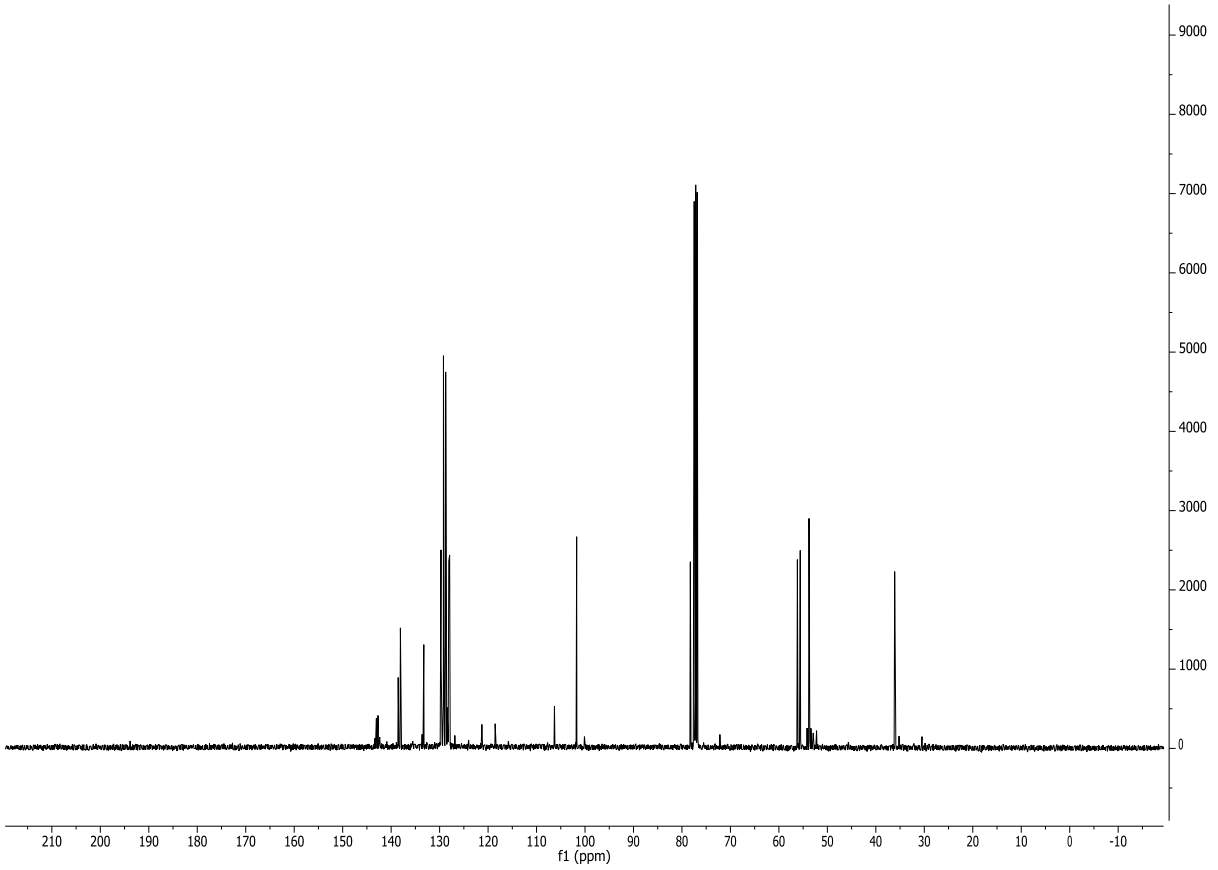

18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

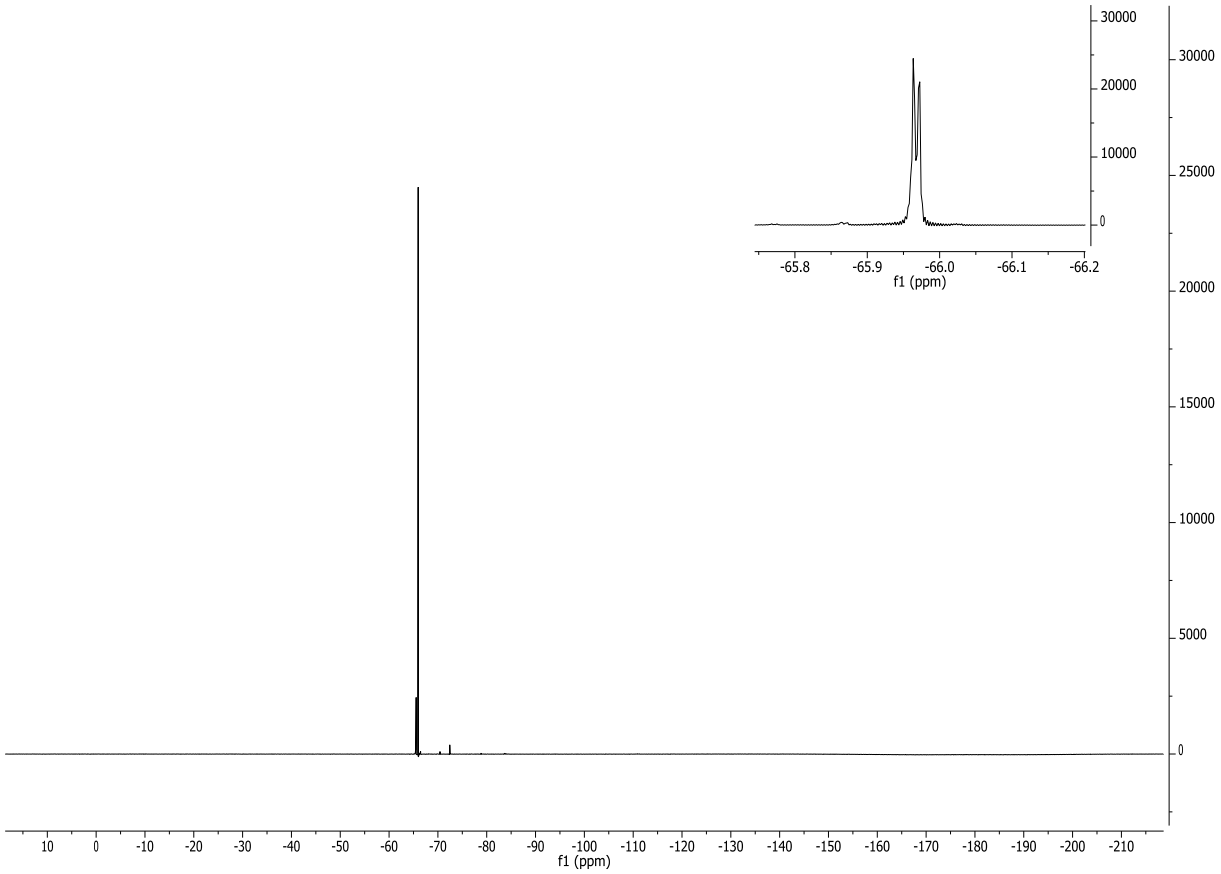

25000
20000
15000
10000
5000
0
-65.75
-65.80
-65.85
-65.90
f1 (ppm)
25000
20000
15000
10000
5000
0
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

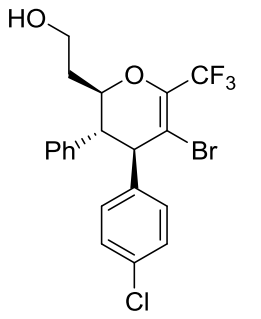

MeO
OMe
O
CF3
Ph
Br
Cl

5k''

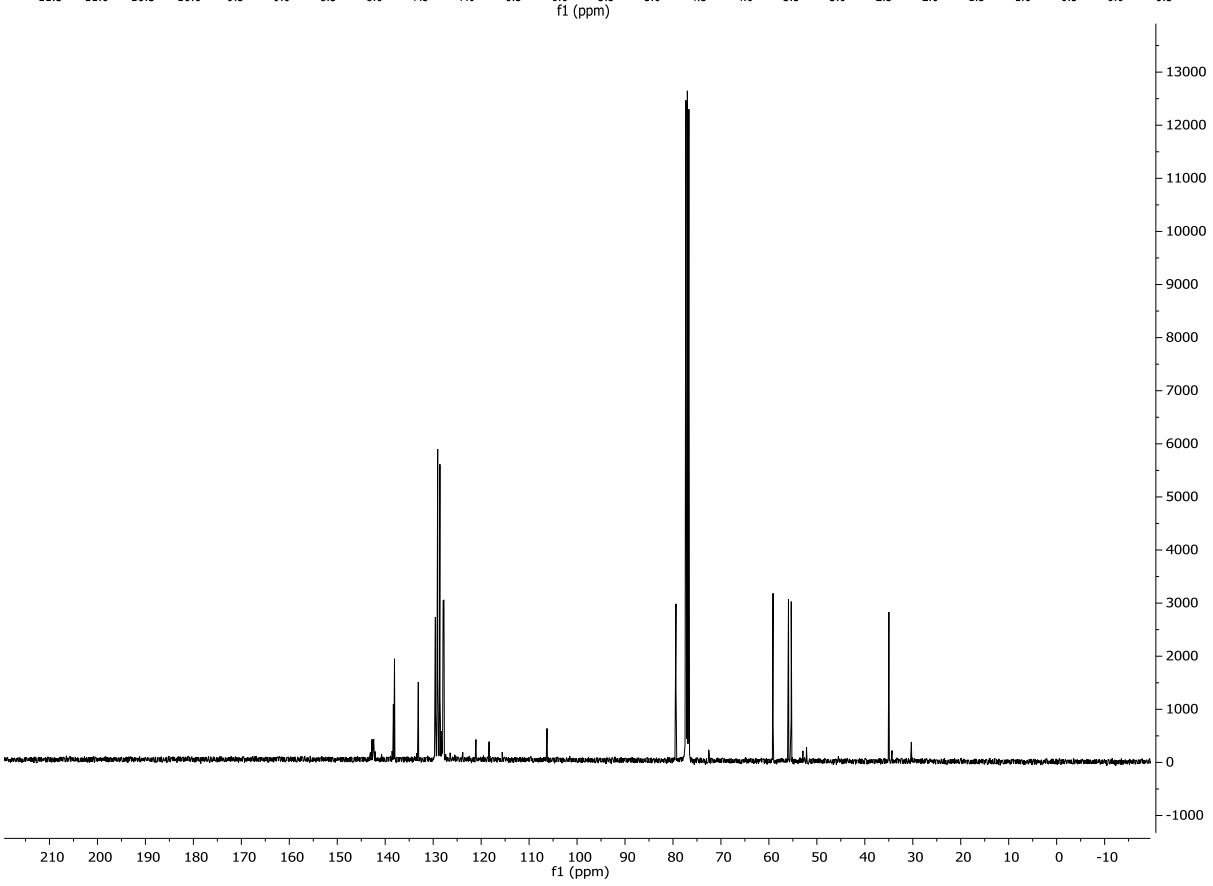
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

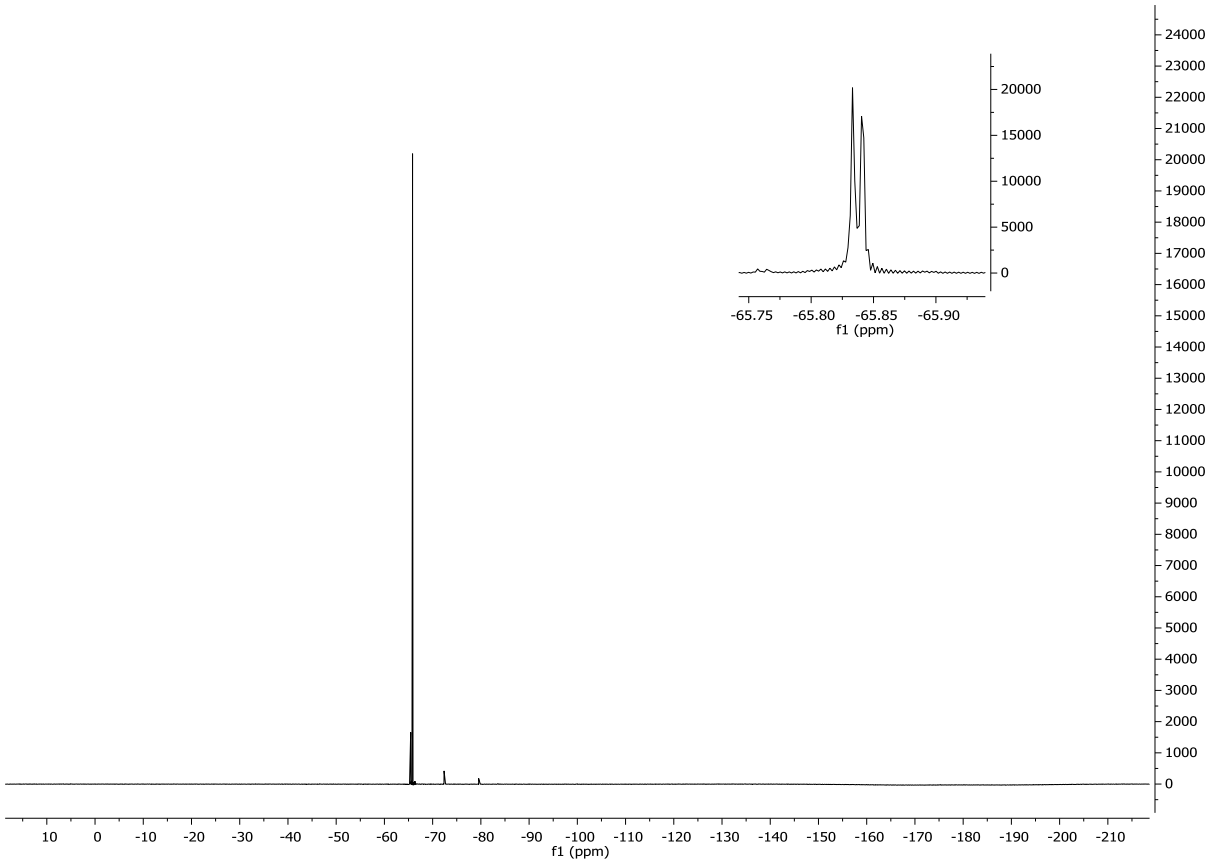

9000
8000
7000
6000
5000
4000
3000
2000
1000
0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

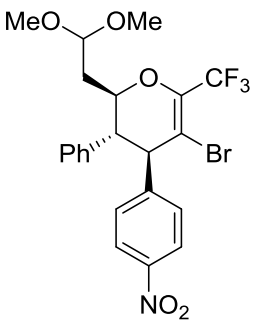

30000
20000
10000
0
-65.8
-65.9
-66.0
-66.1
-66.2
f1 (ppm)
30000
25000
20000
15000
10000
5000
0
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)



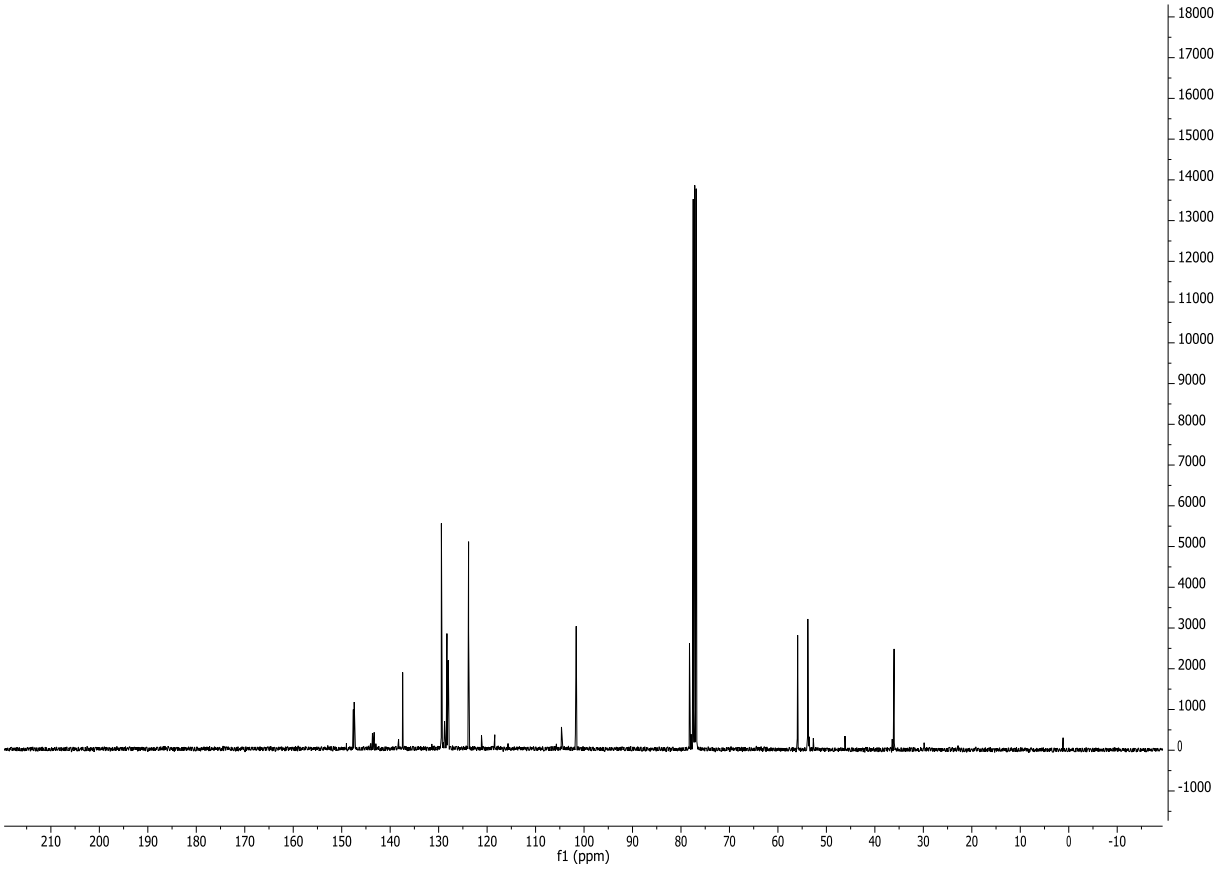
5k

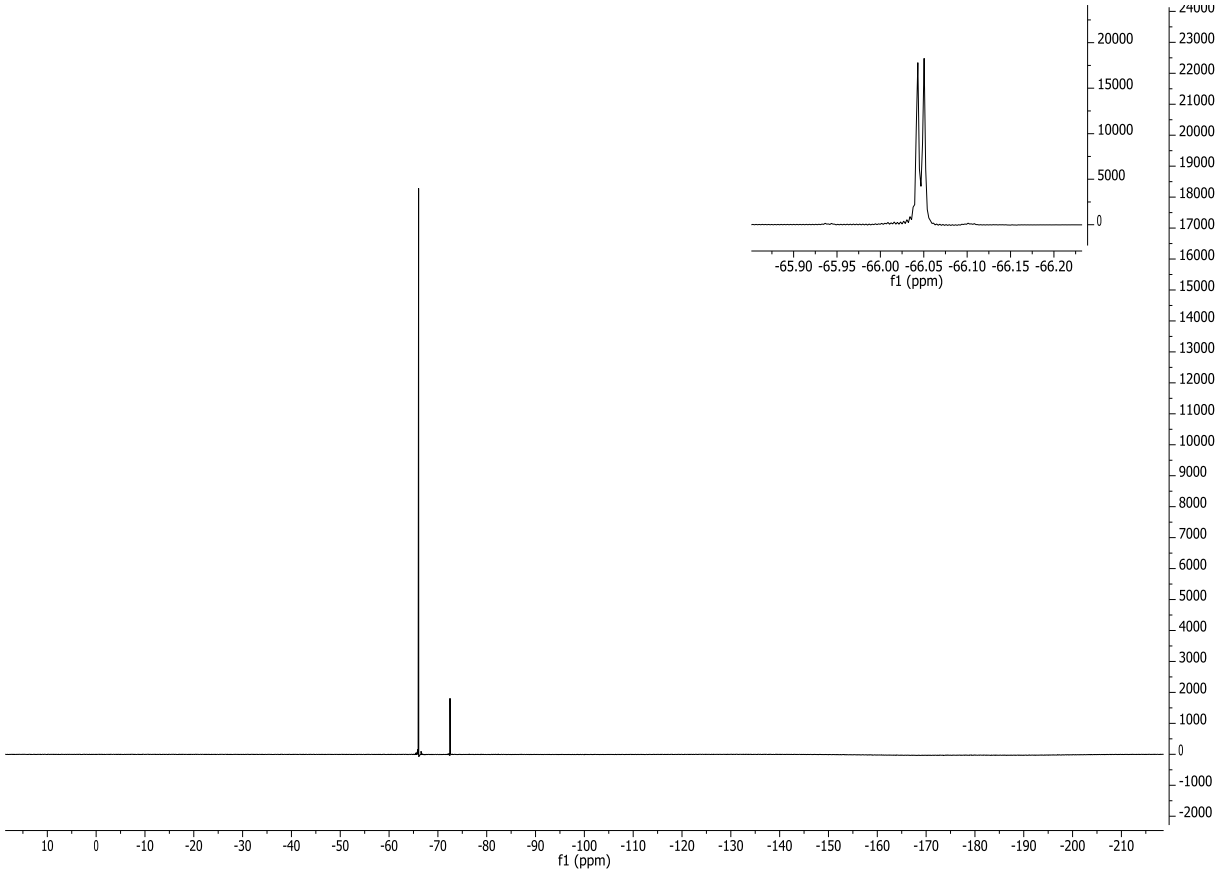


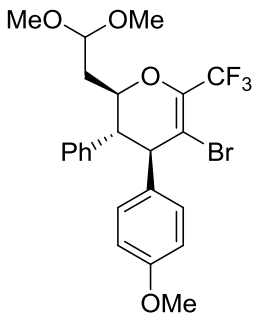

24000
23000
22000
21000
20000
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)
20000
15000
10000
5000
0
-65.75 -65.80 -65.85 -65.90
f1 (ppm)



5l''

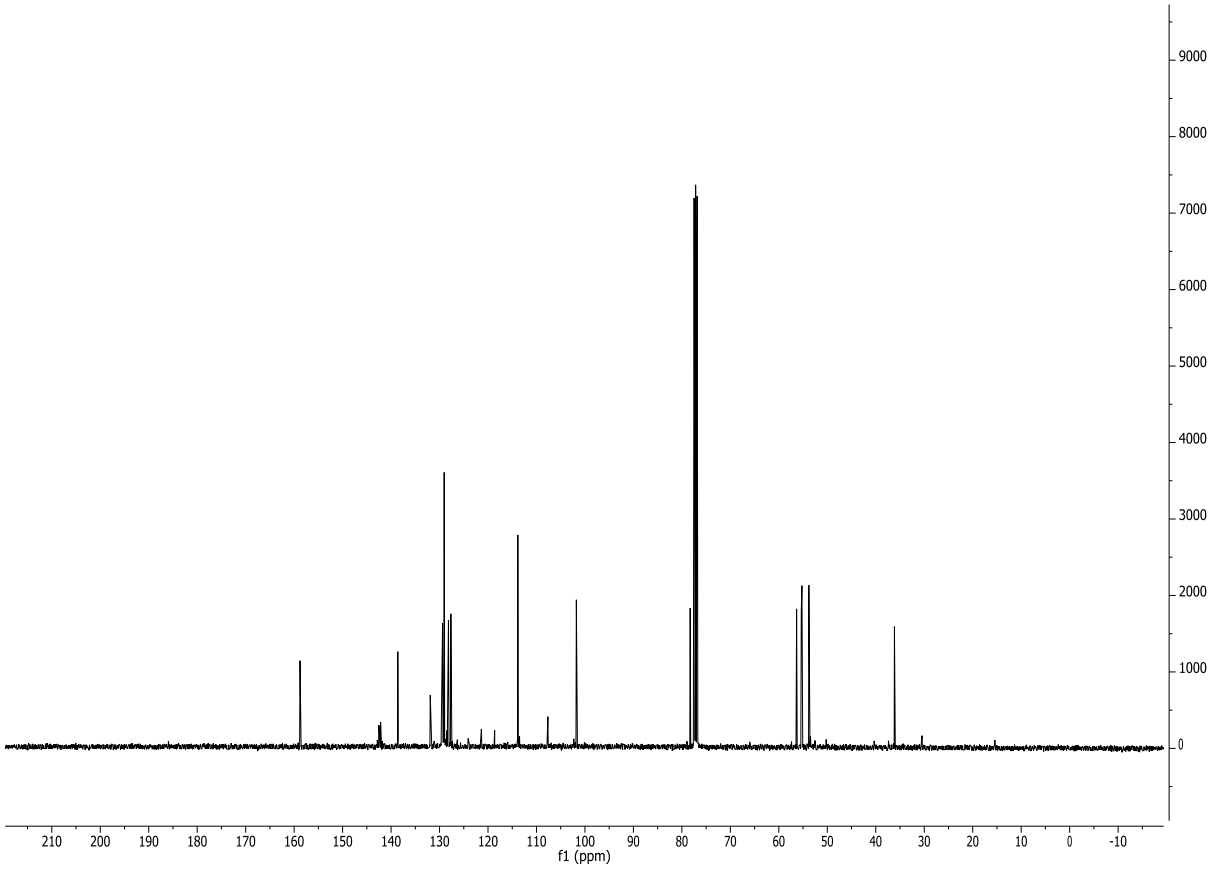


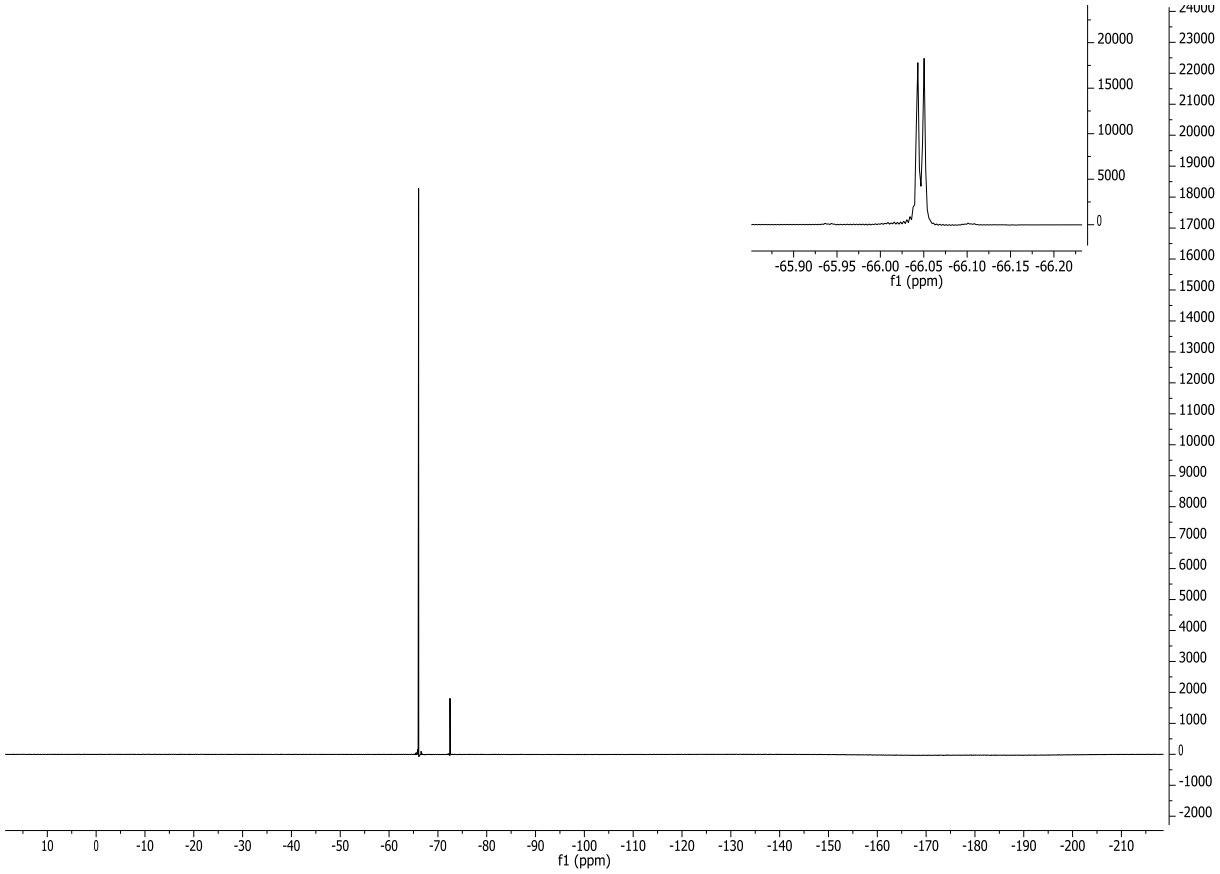

f1 (ppm)
-65.90 -65.95 -66.00 -66.05 -66.10 -66.15 -66.20
f1 (ppm)

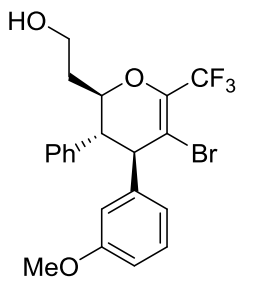

MeO
OMe
O
CF3
Ph
Br
OMe

5m''

9000
8000
7000
6000
5000
4000
3000
2000
1000
0
2.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

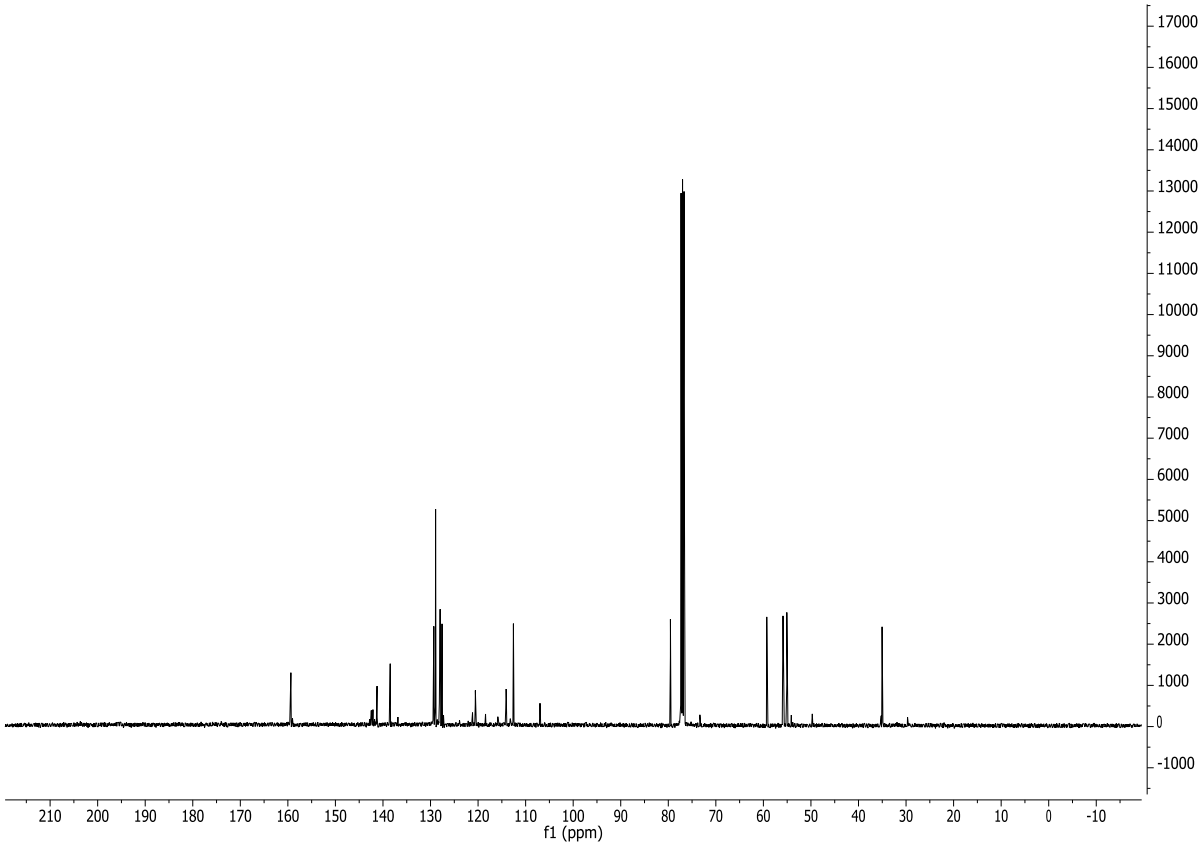

9000
8000
7000
6000
5000
4000
3000
2000
1000
0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

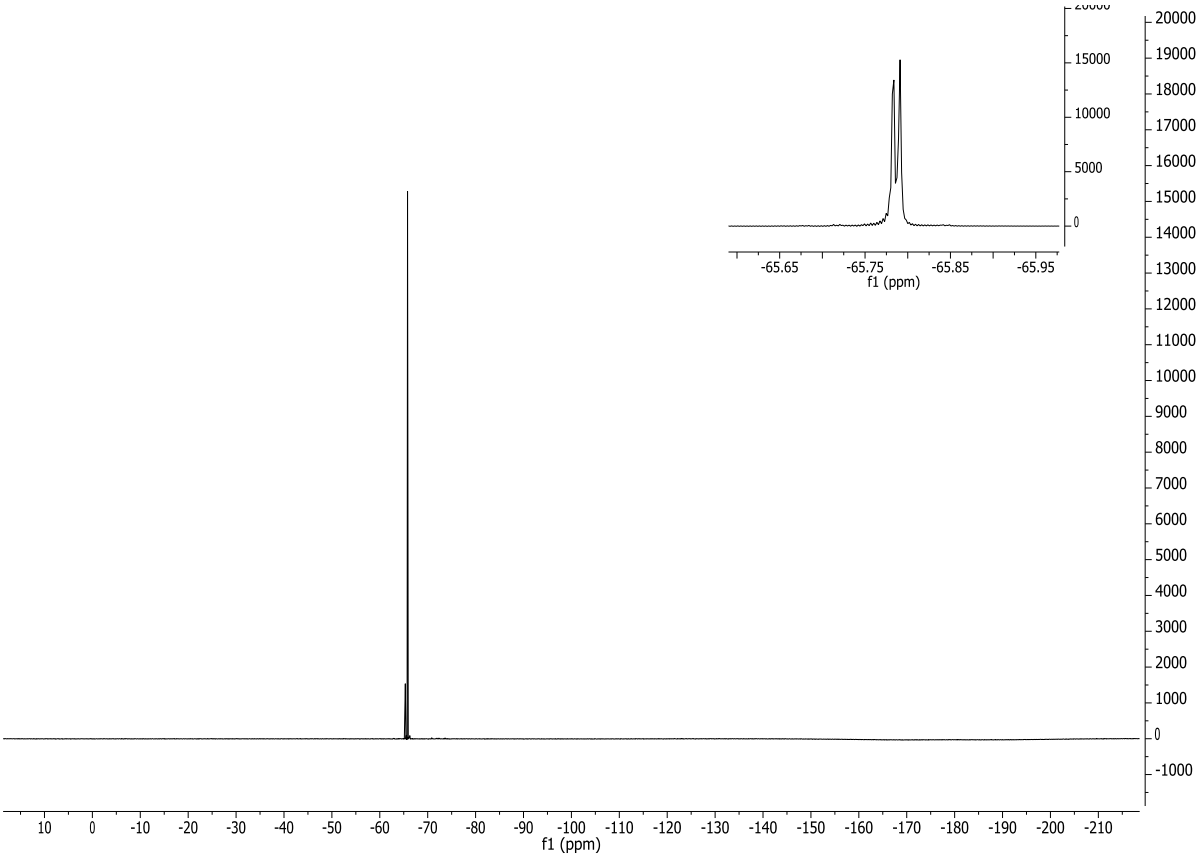

f1 (ppm)
-65.90 -65.95 -66.00 -66.05 -66.10 -66.15 -66.20
f1 (ppm)

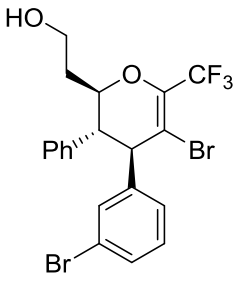

HO
O
CF3
Ph
Br
MeO

5n

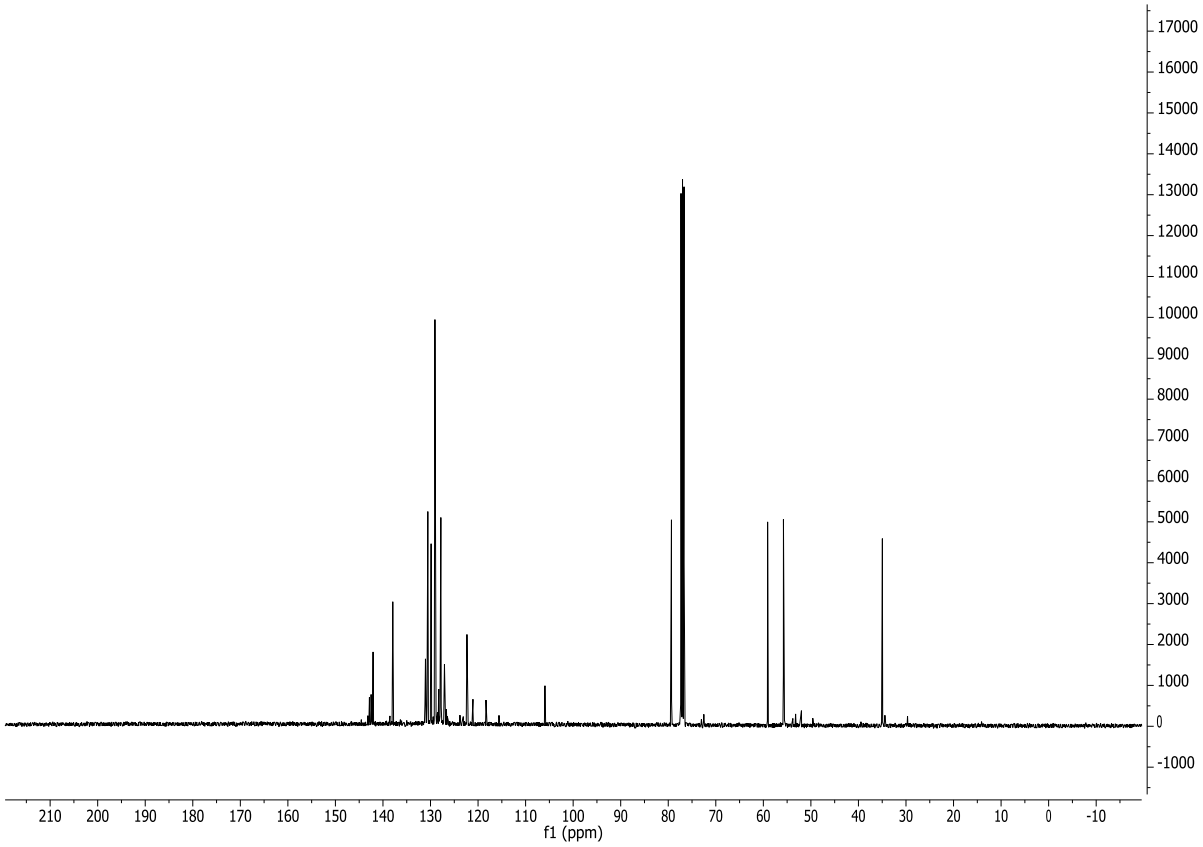
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

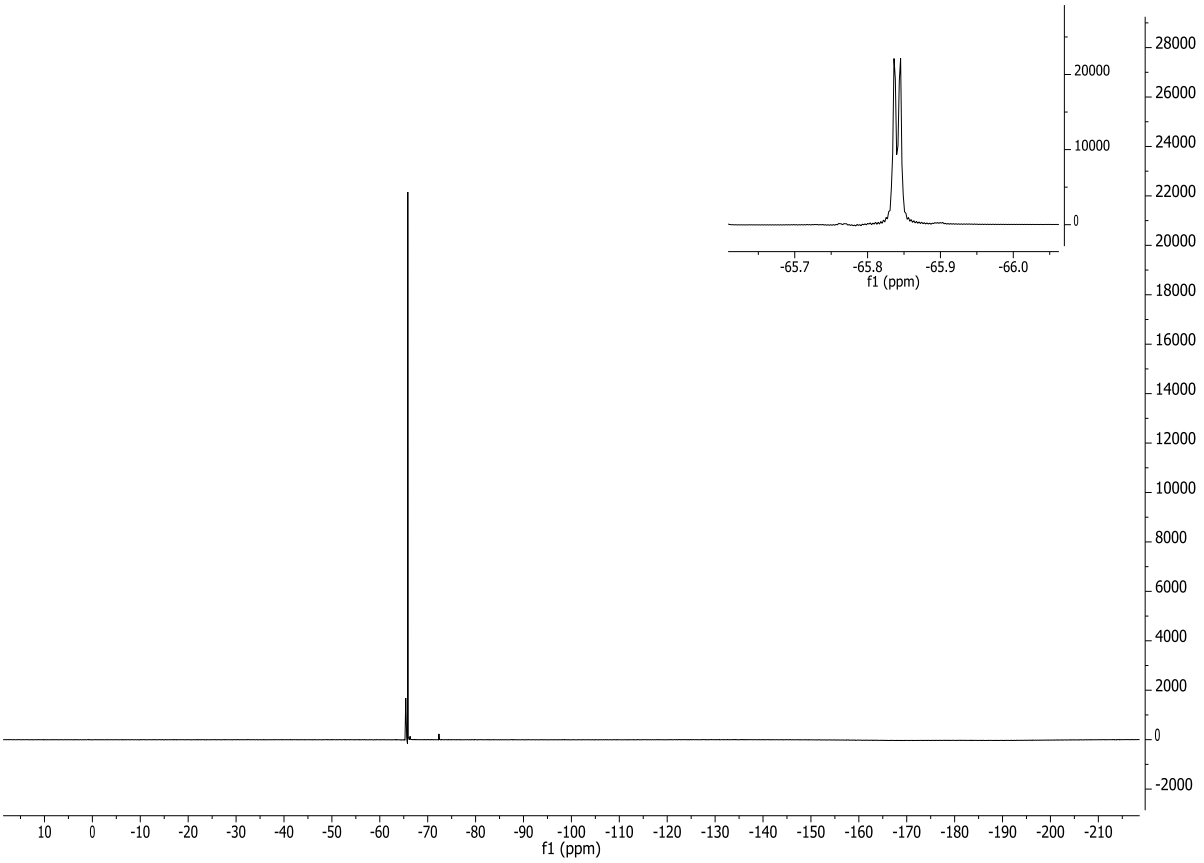

17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

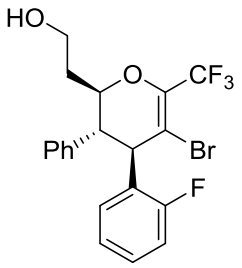

20000
15000
10000
5000
0
-65.65
-65.75
-65.85
-65.95
f1 (ppm)
20000
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)



5o

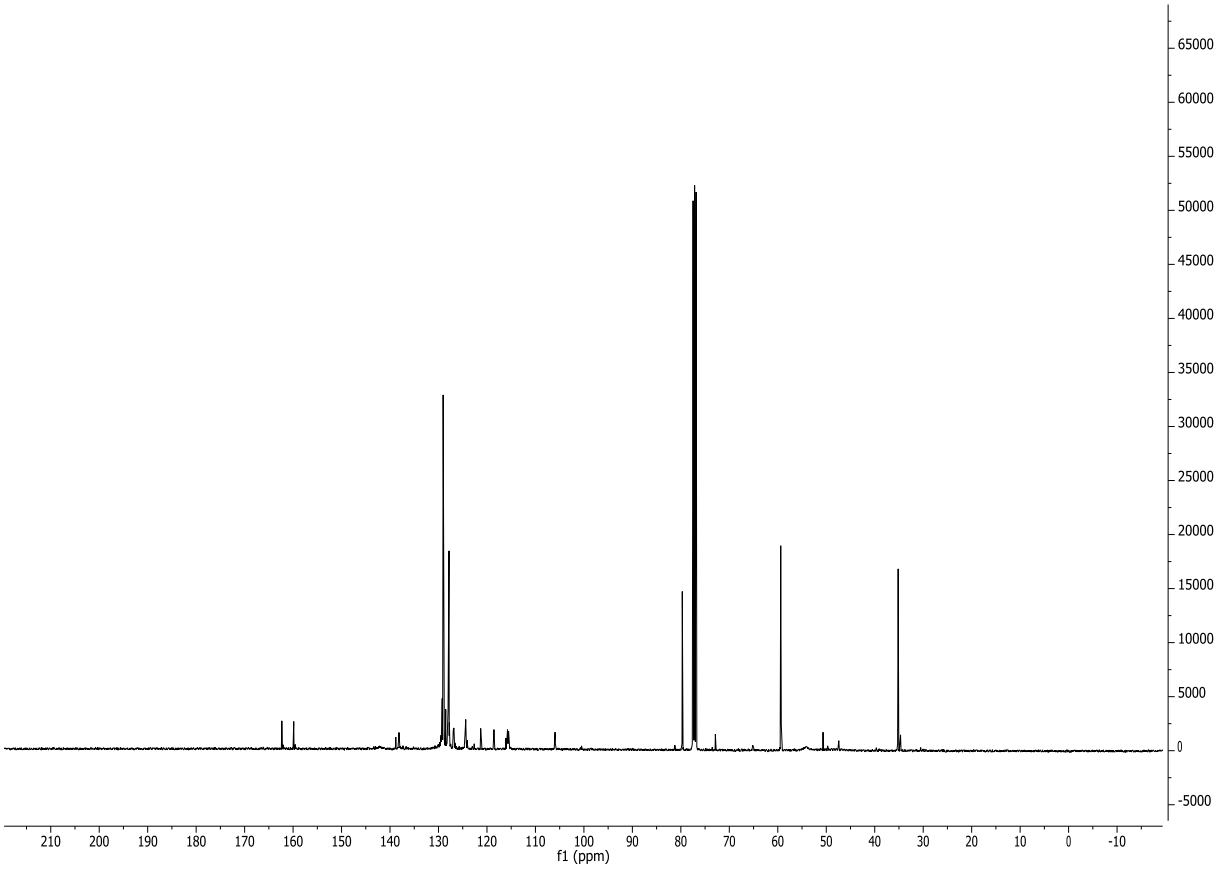


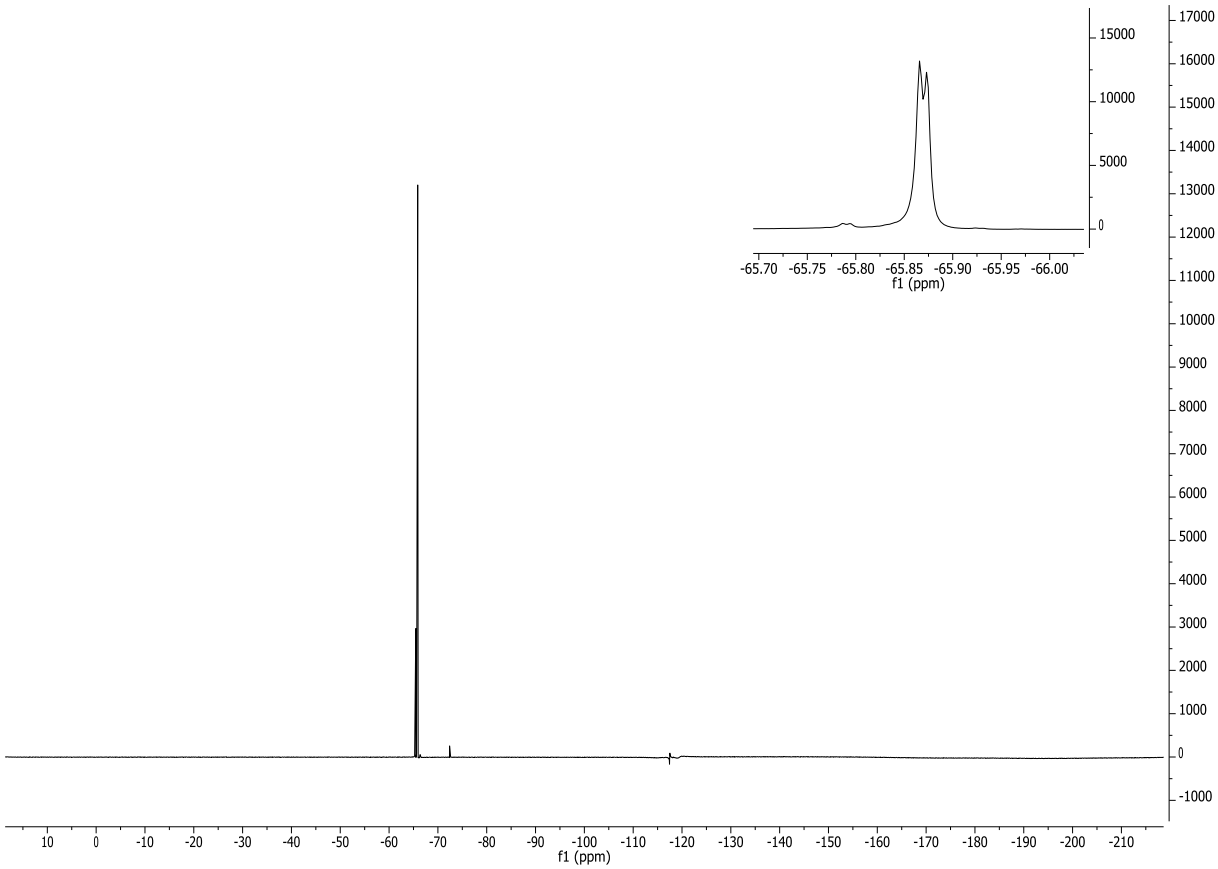

20000
10000
0
-65.7
-65.8
-65.9
-66.0
f1 (ppm)
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

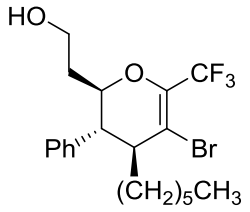

HO
O
CF3
Ph
Br
F

5p

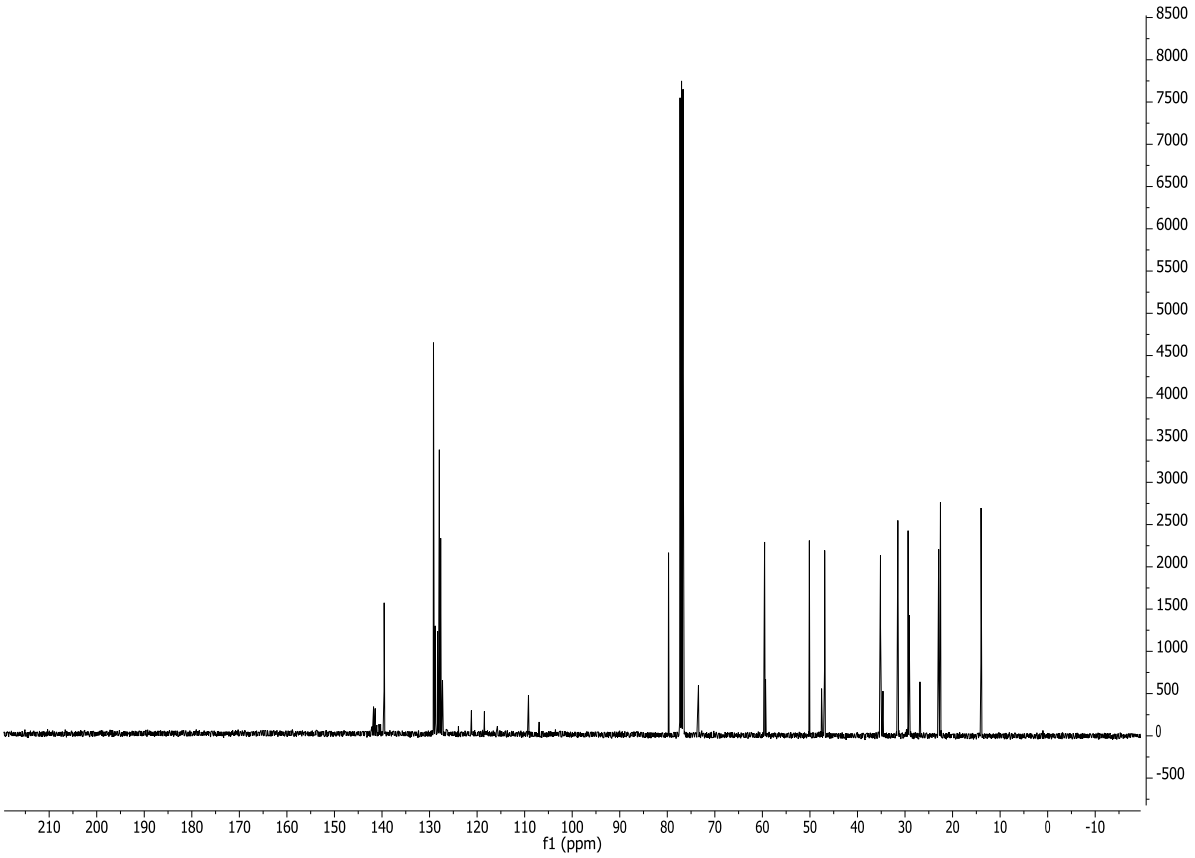
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

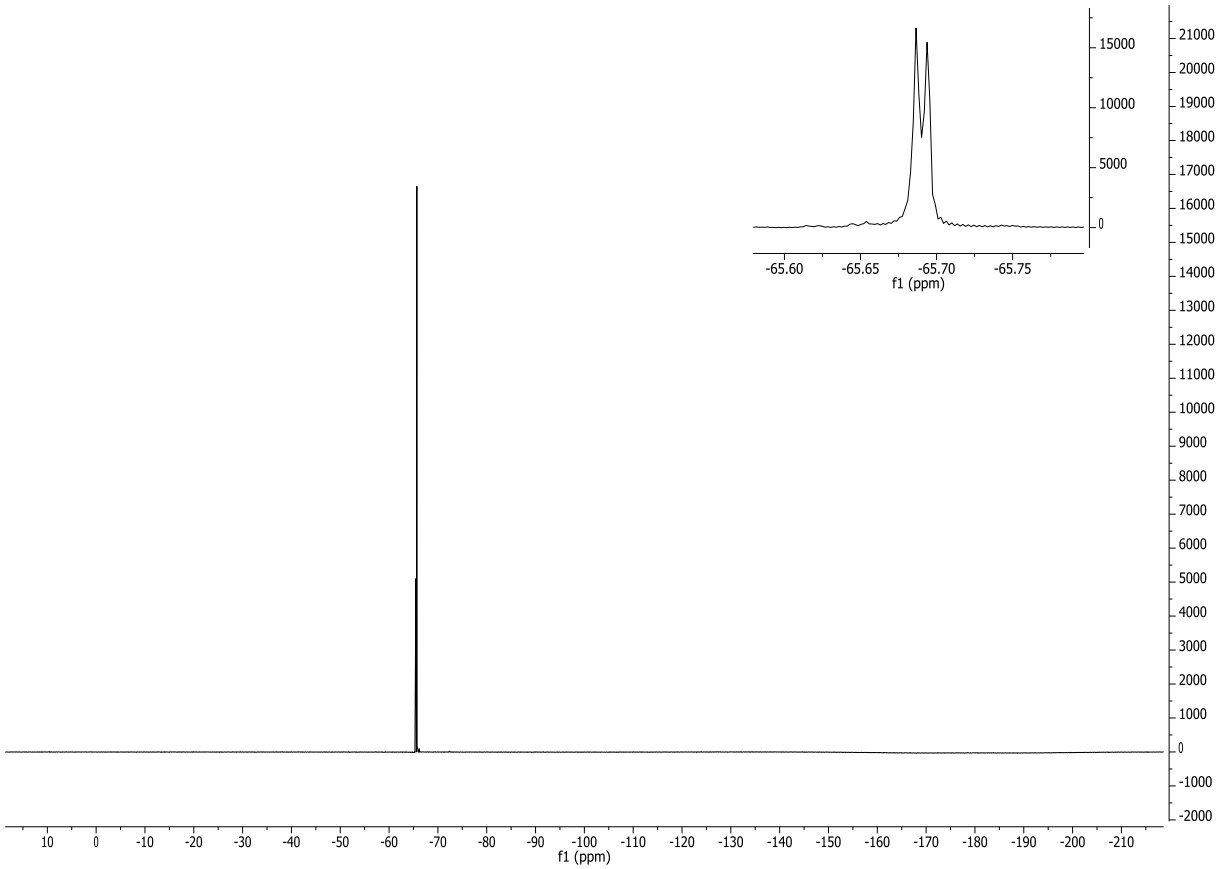

65000
60000
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

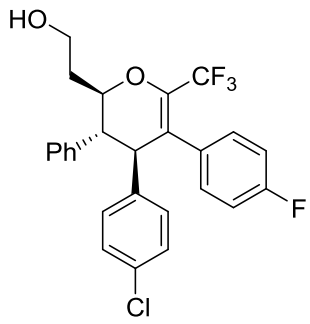

17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)
15000
10000
5000
0
-65.70 -65.75 -65.80 -65.85 -65.90 -65.95 -66.00
f1 (ppm)



5q

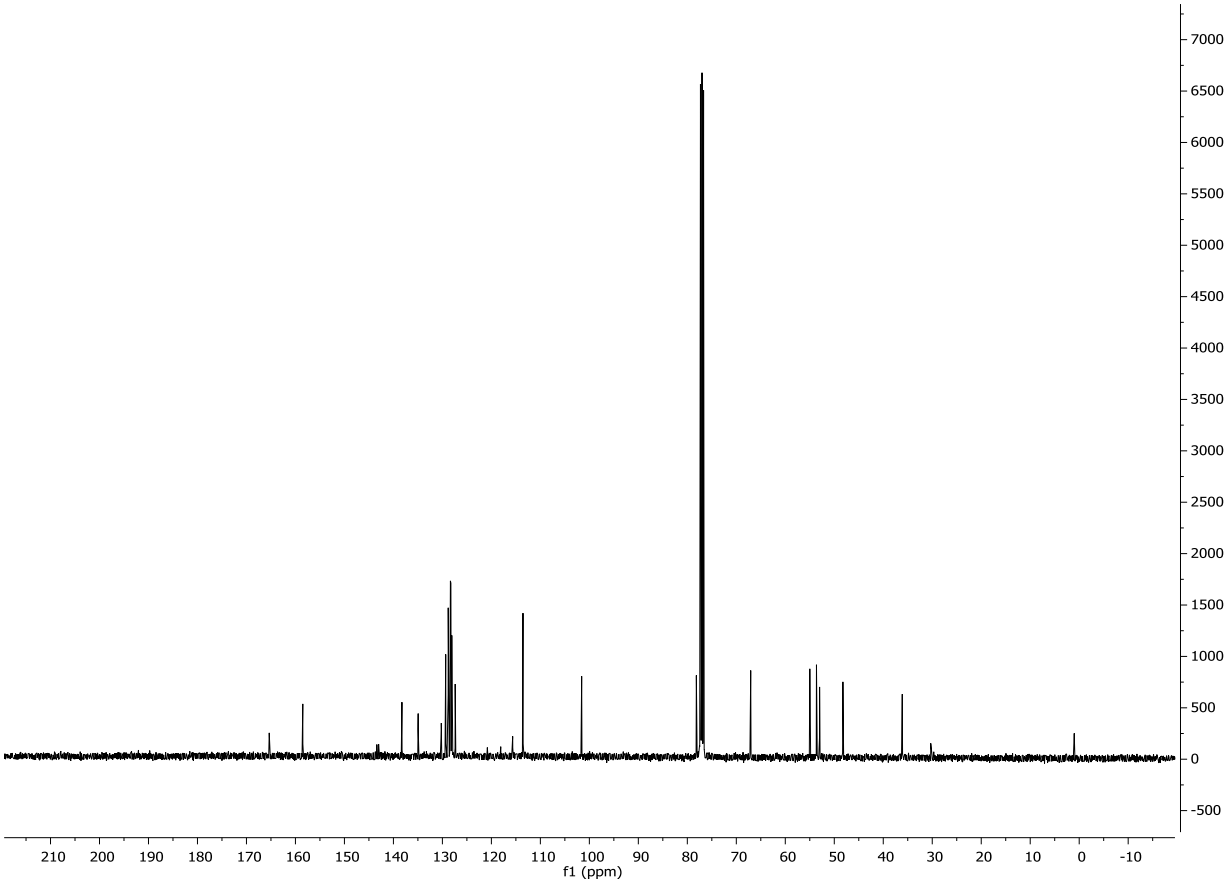


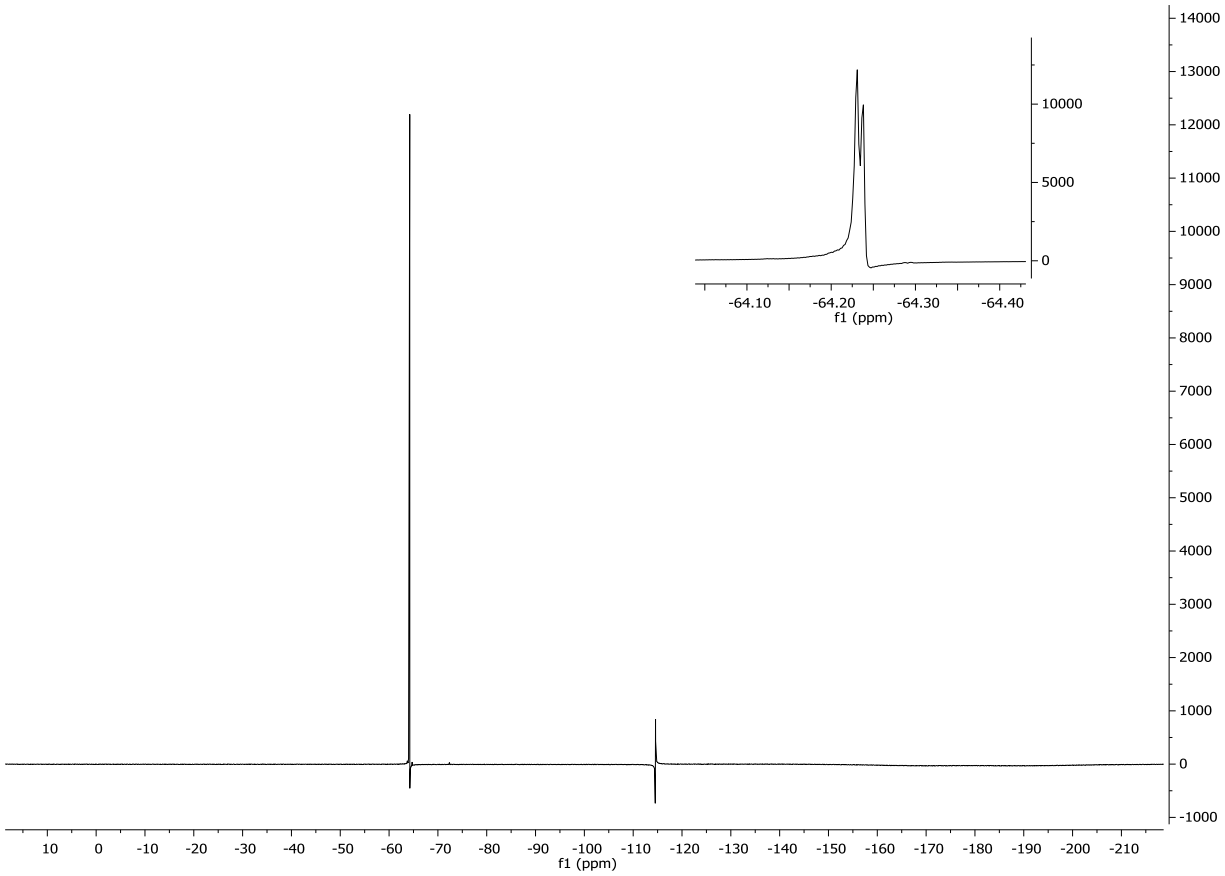

15000
10000
5000
0
-65.60
-65.65
-65.70
-65.75
f1 (ppm)
21000
20000
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
-2000
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

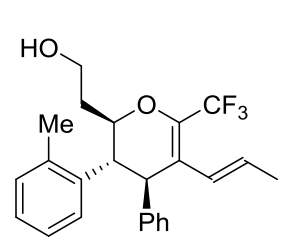

HO
O
CF3
Ph
F
Cl

9

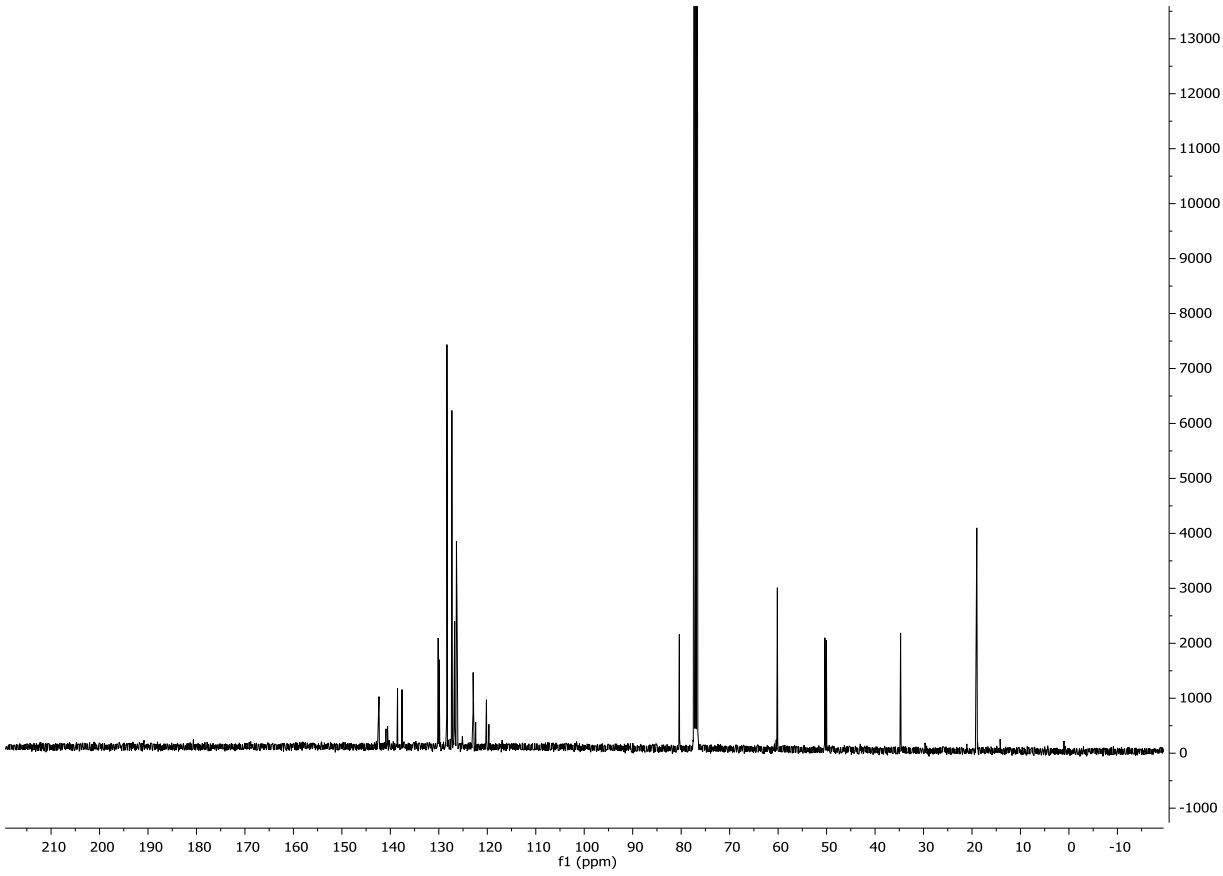
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

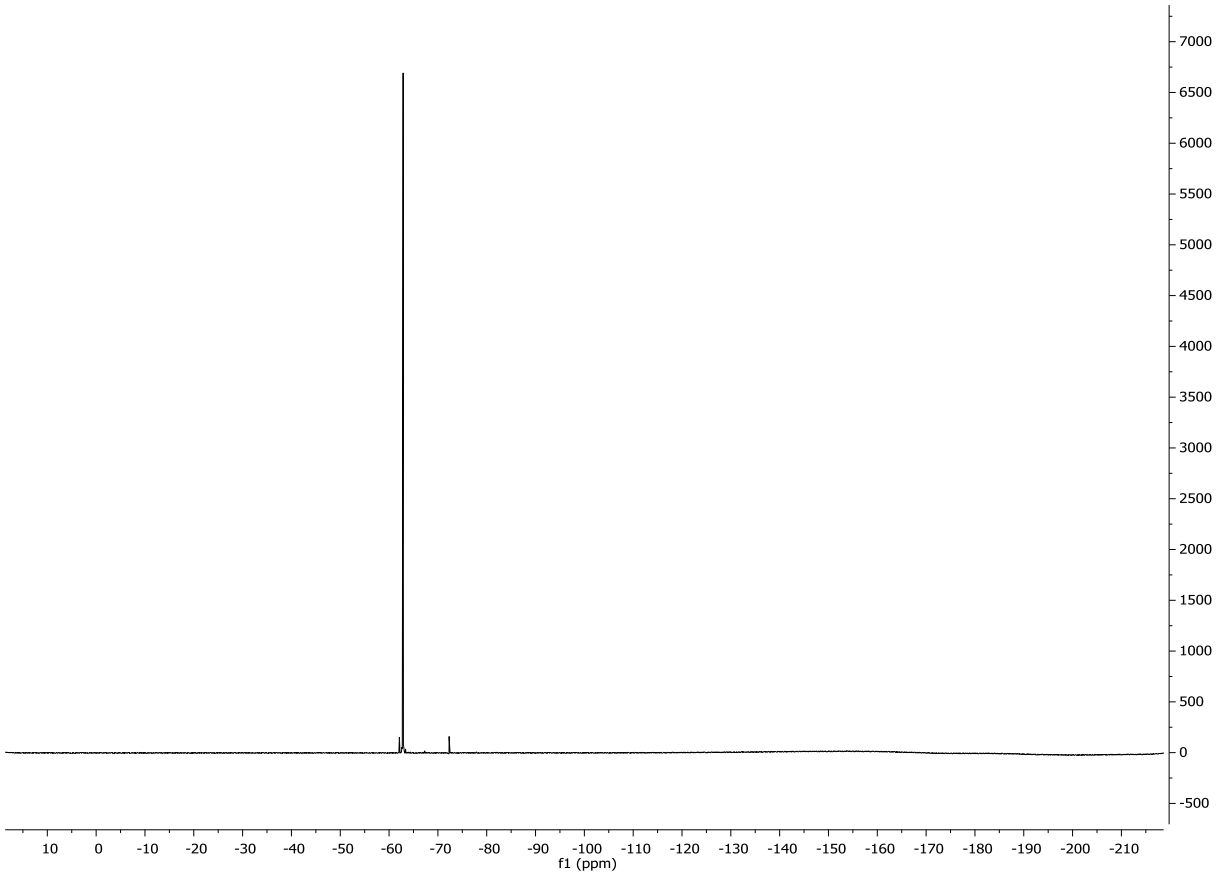

7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

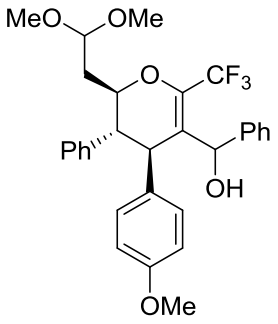

14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)
10000
5000
0
-64.10 -64.20 -64.30 -64.40
f1 (ppm)



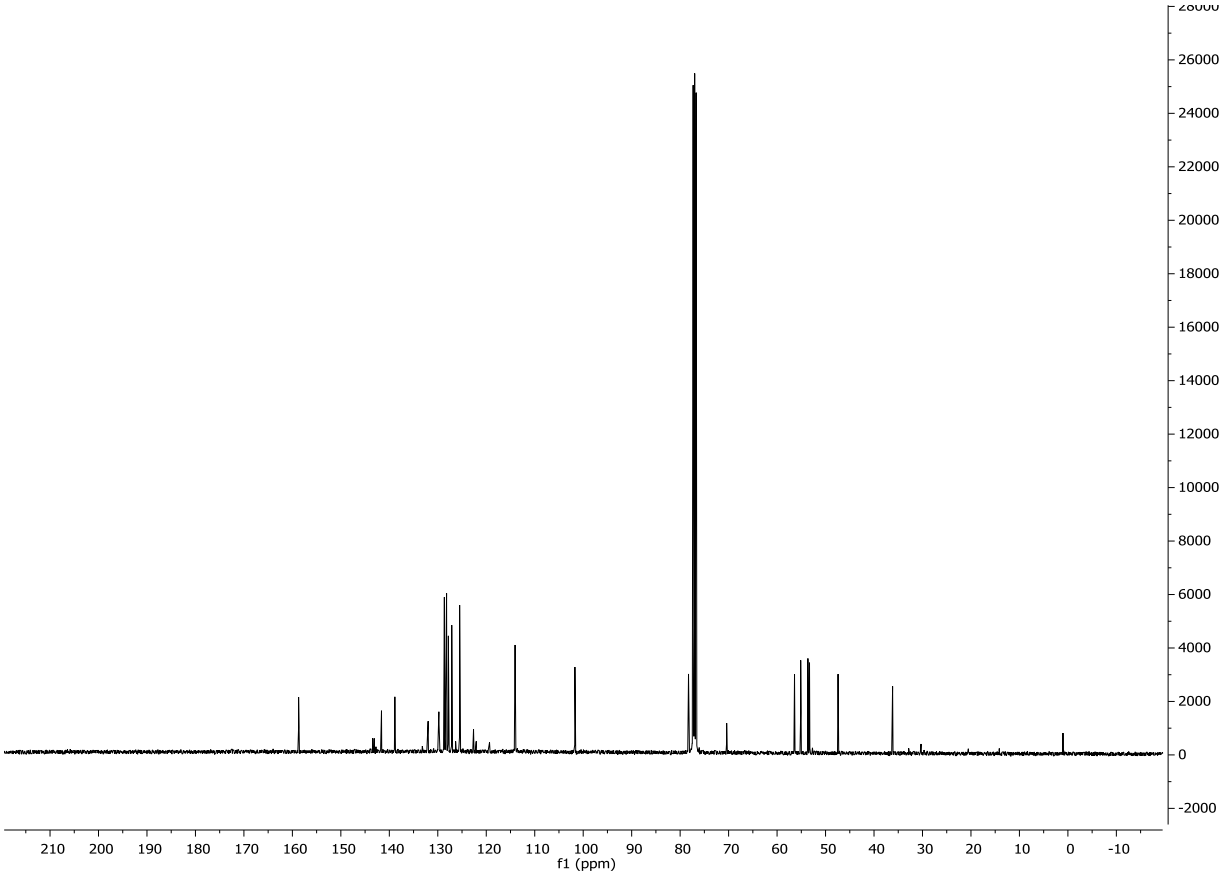
10

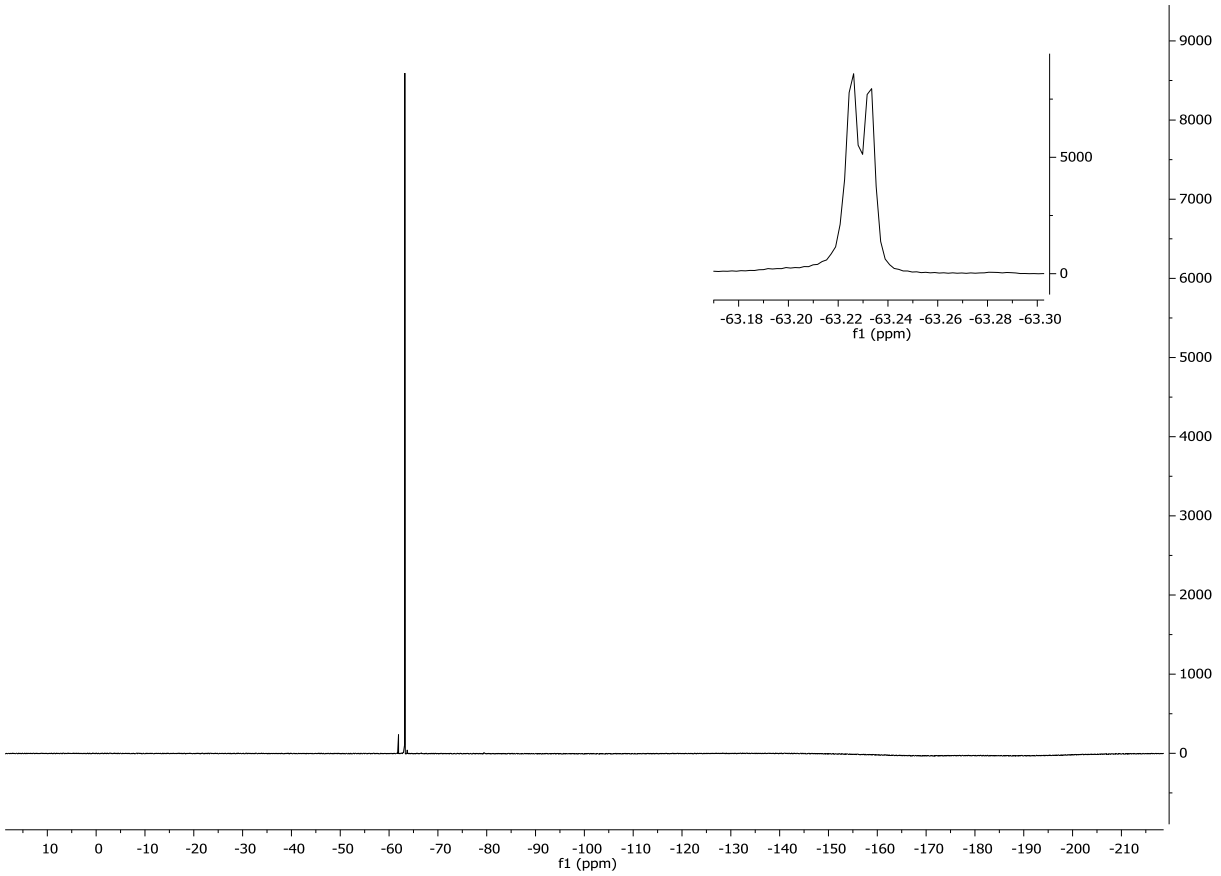


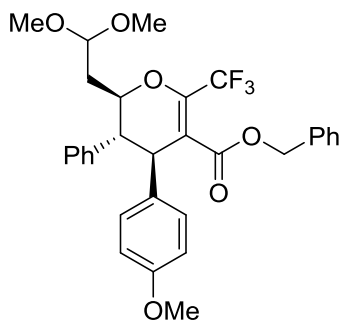

7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)



11

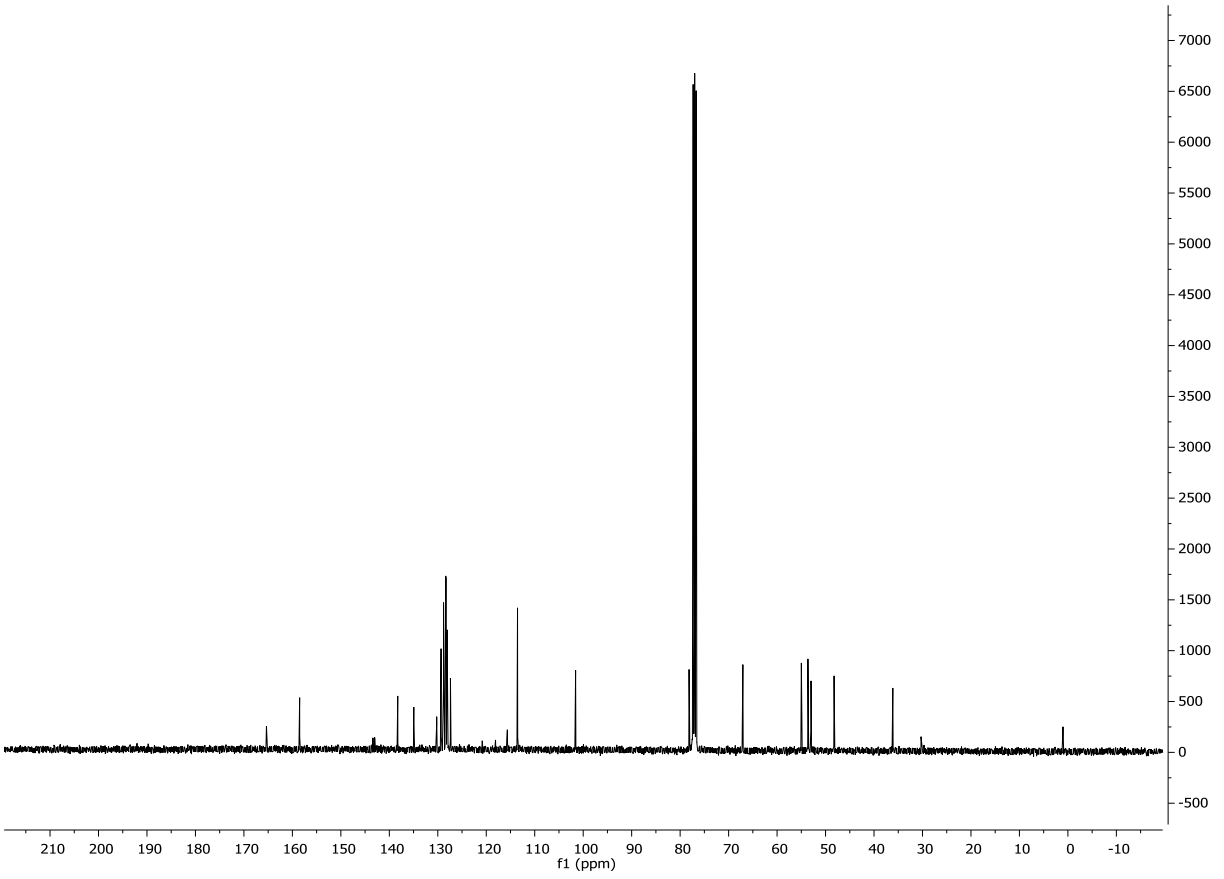


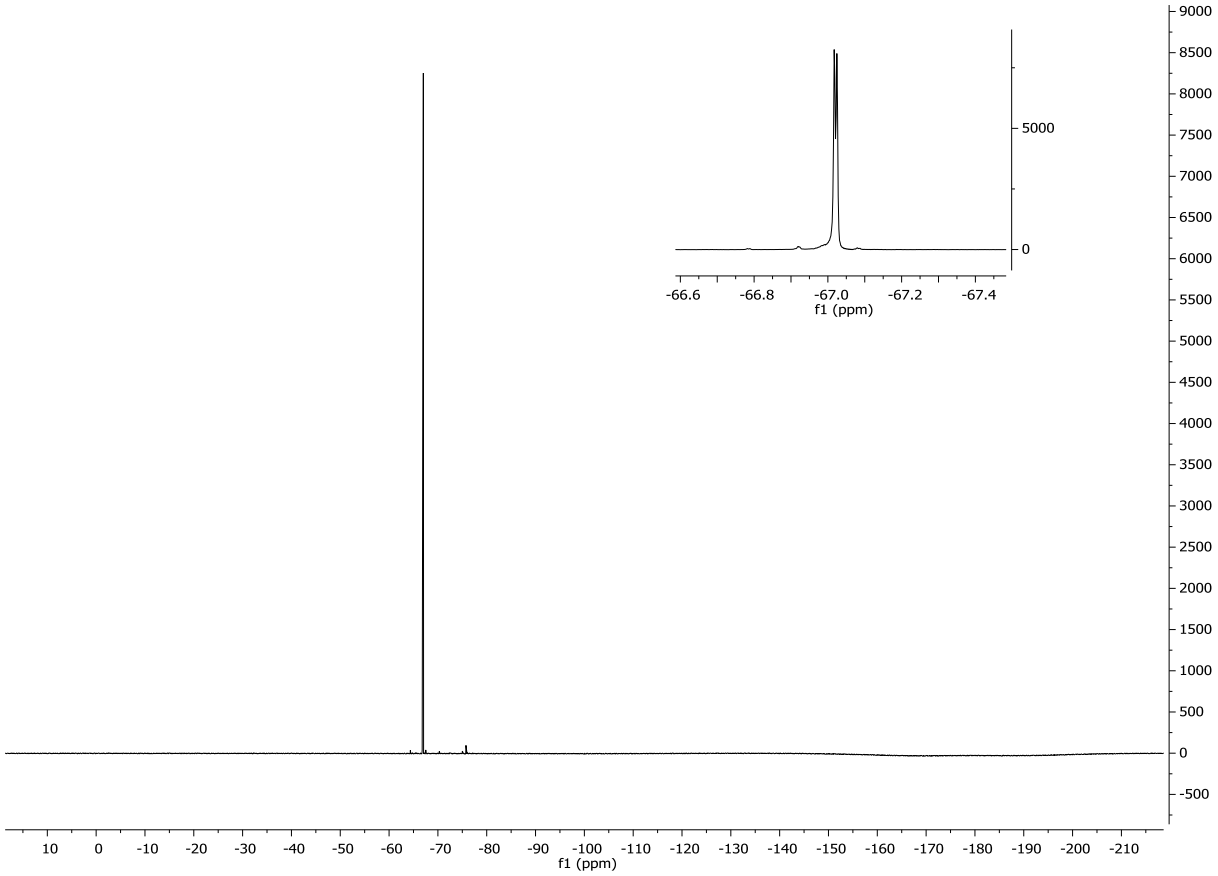

9000
8000
7000
6000
5000
4000
3000
2000
1000
0
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)
5000
0
-63.18 -63.20 -63.22 -63.24 -63.26 -63.28 -63.30
f1 (ppm)

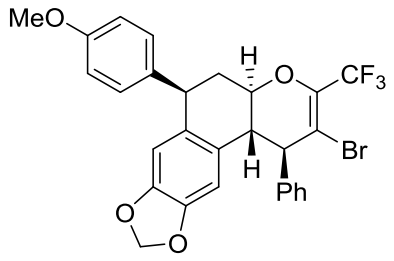

MeO
OMe
O
CF3
Ph
O
O
Ph
OMe

12

12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

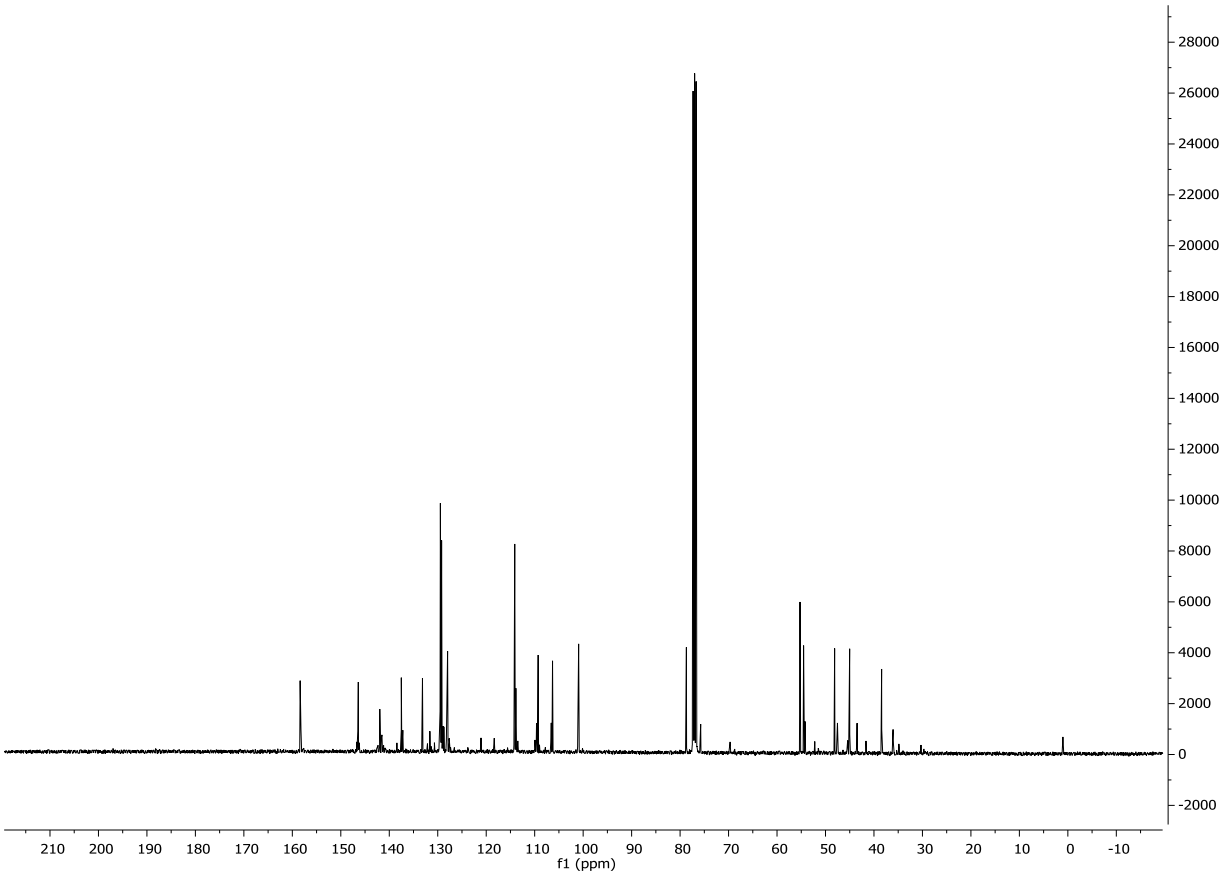

7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

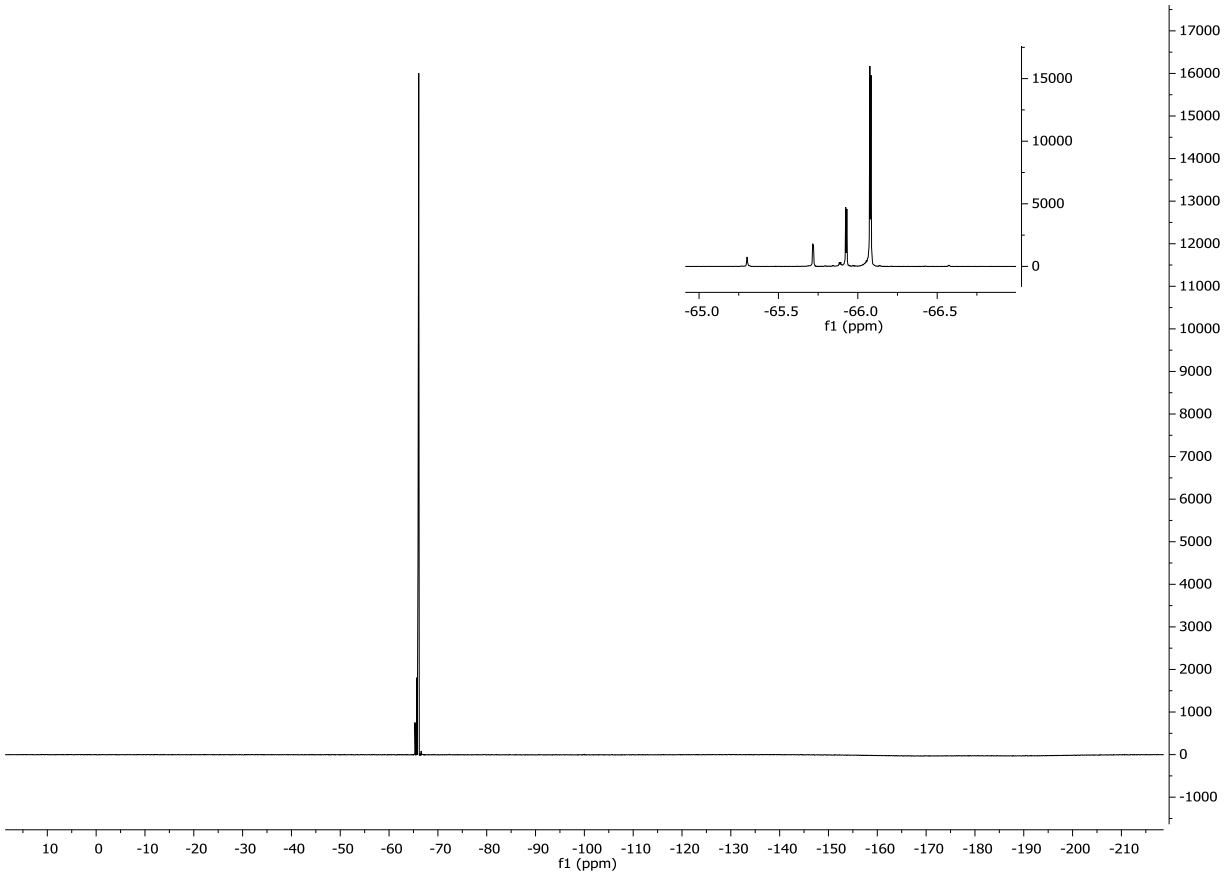

9000
8500
8000
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)
5000
0
-66.6 -66.8 -67.0 -67.2 -67.4
f1 (ppm)


MeO
H
O
CF3
Br
H
Ph
O
O

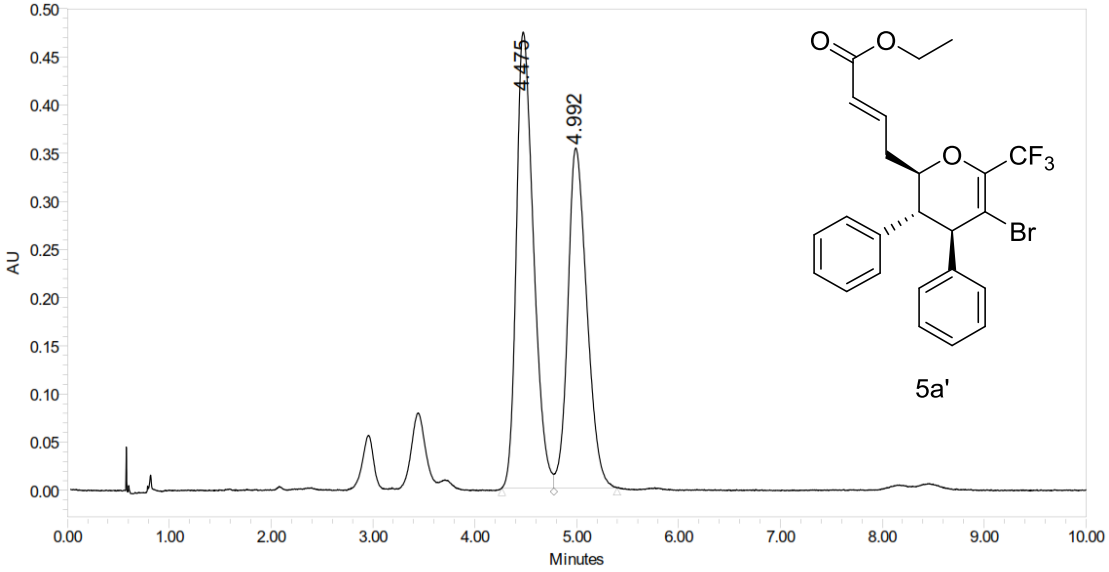
13

6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
2.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

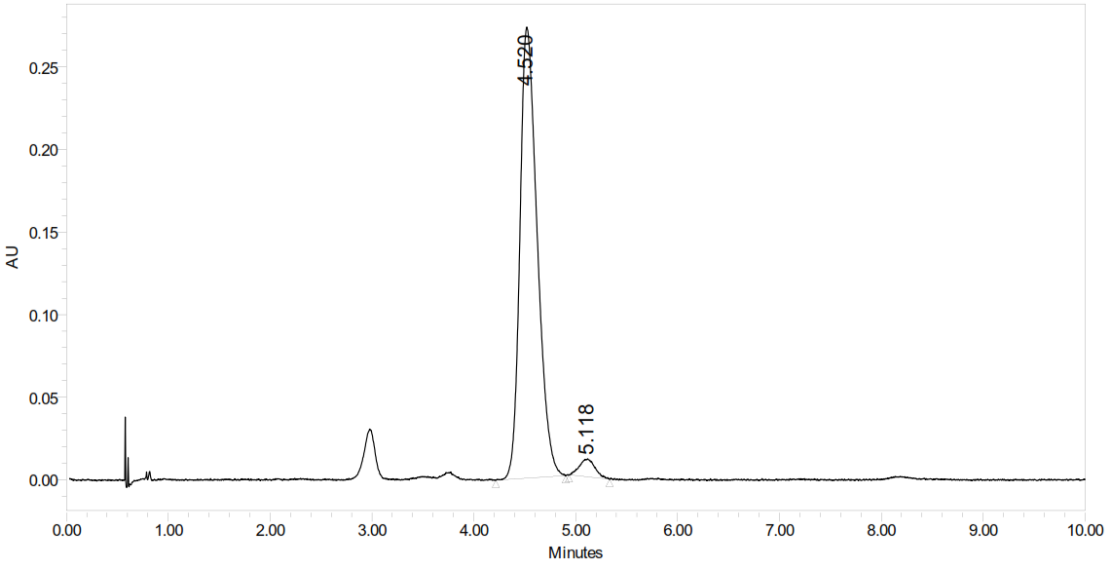

28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)
15000
10000
5000
0
-65.0 -65.5 -66.0 -66.5
f1 (ppm)

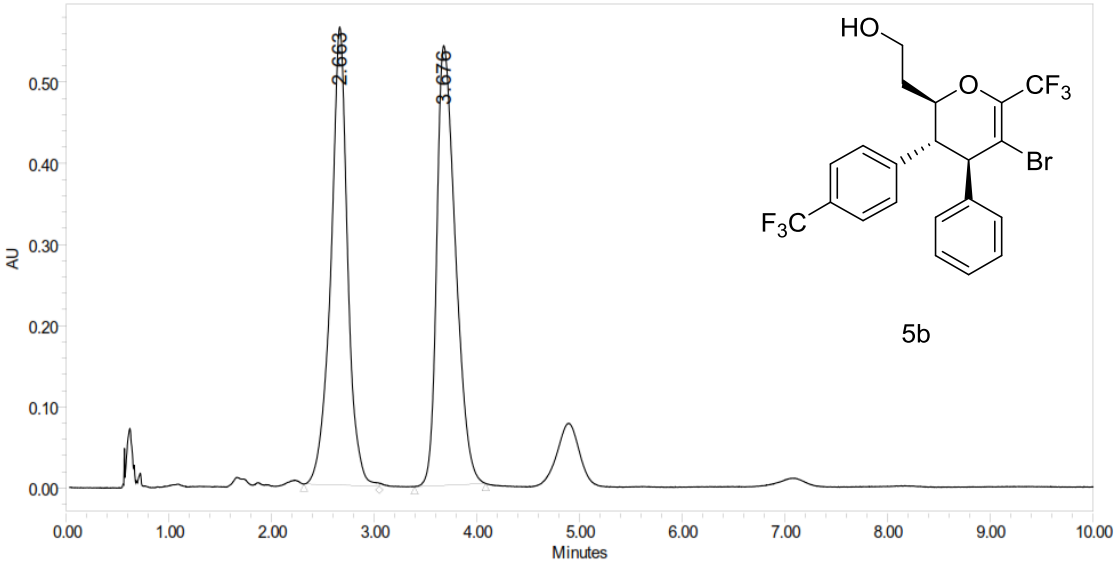
UPC^2 - traces



	Retention Time (min)	% Area
1	4.475	54.67
2	4.992	45.33

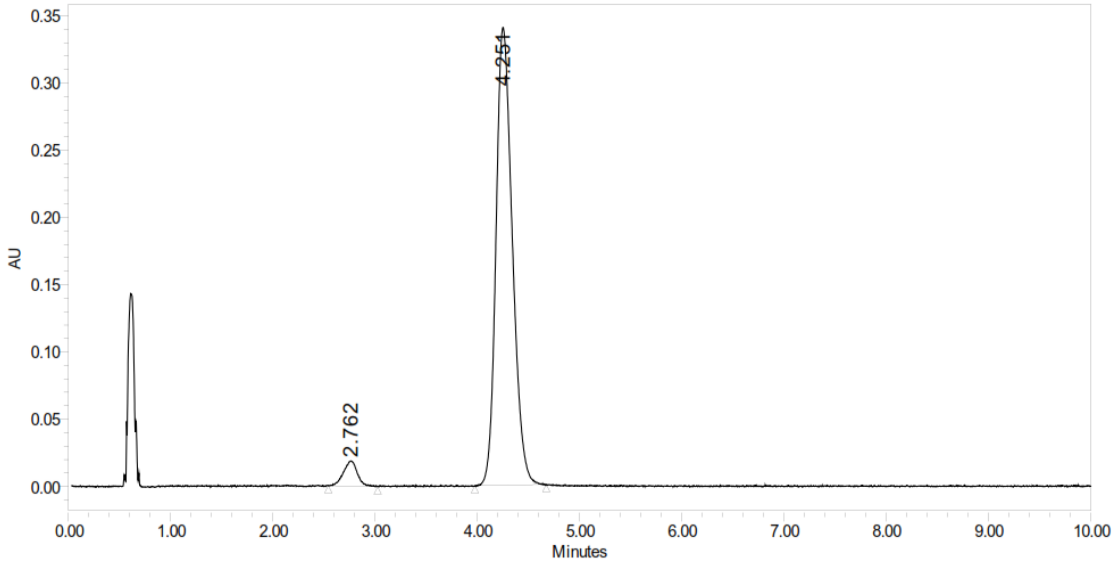


	Retention Time (min)	% Area
1	4.520	96.55
2	5.118	3.45

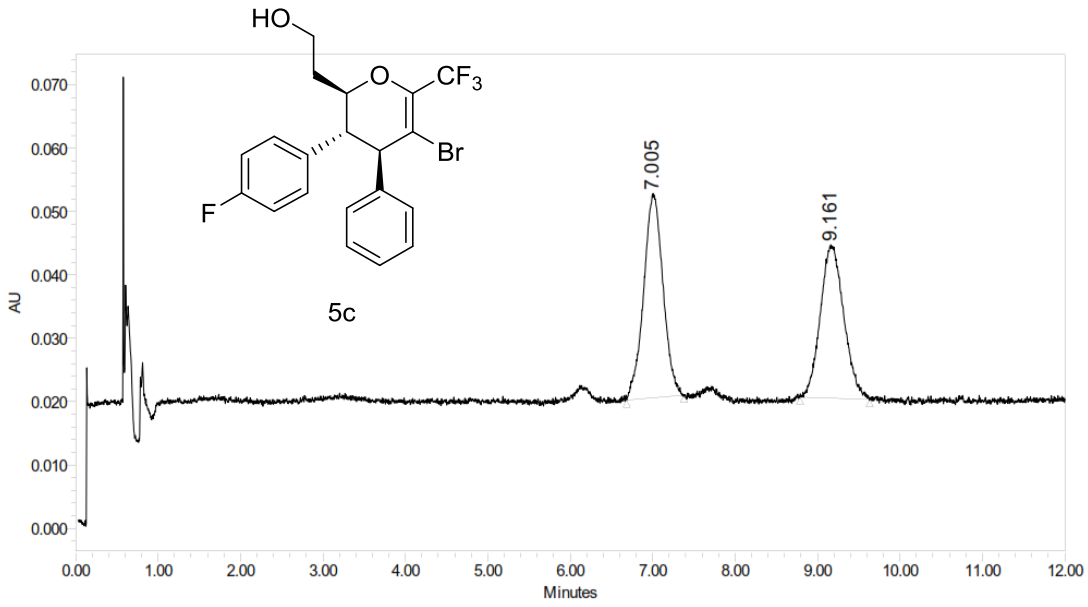


5b

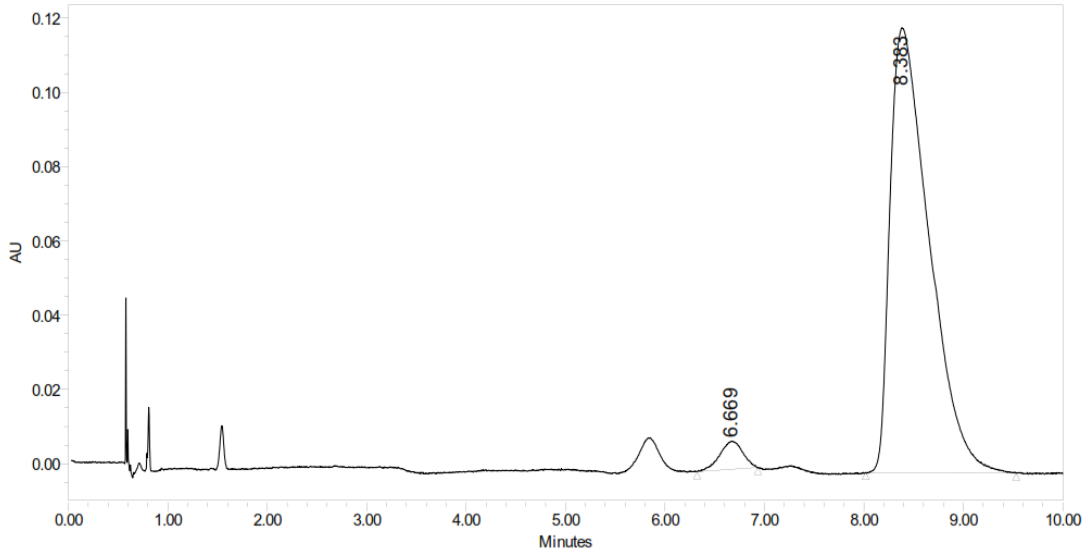
	Retention Time (min)	% Area
1	2.663	48.22
2	3.676	51.78



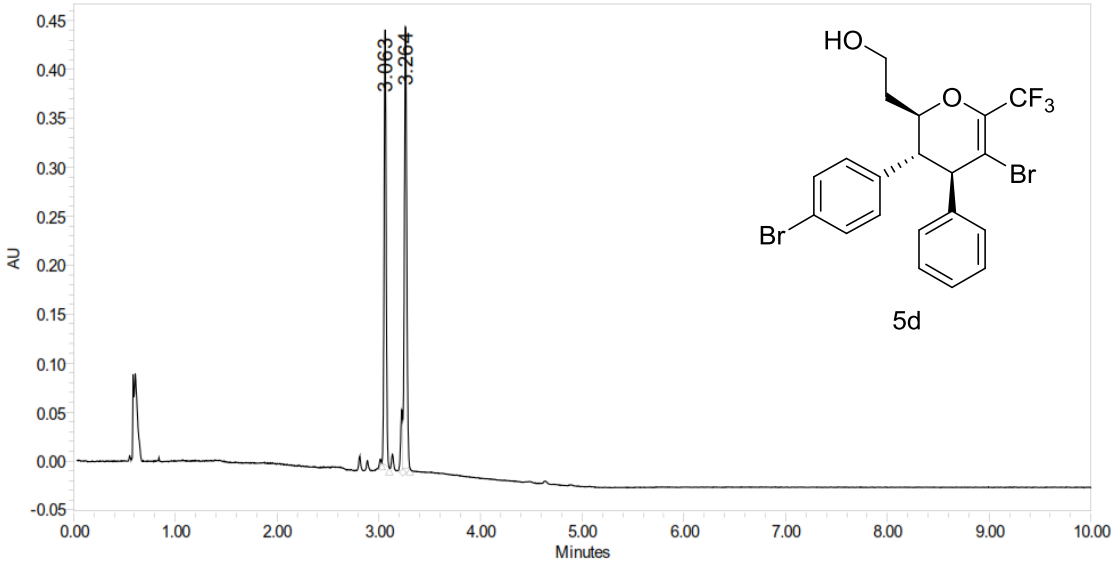
	Retention Time (min)	% Area
1	2.762	4.47
2	4.251	95.53



	Retention Time (min)	% Area
1	7.005	52.36
2	9.161	47.64

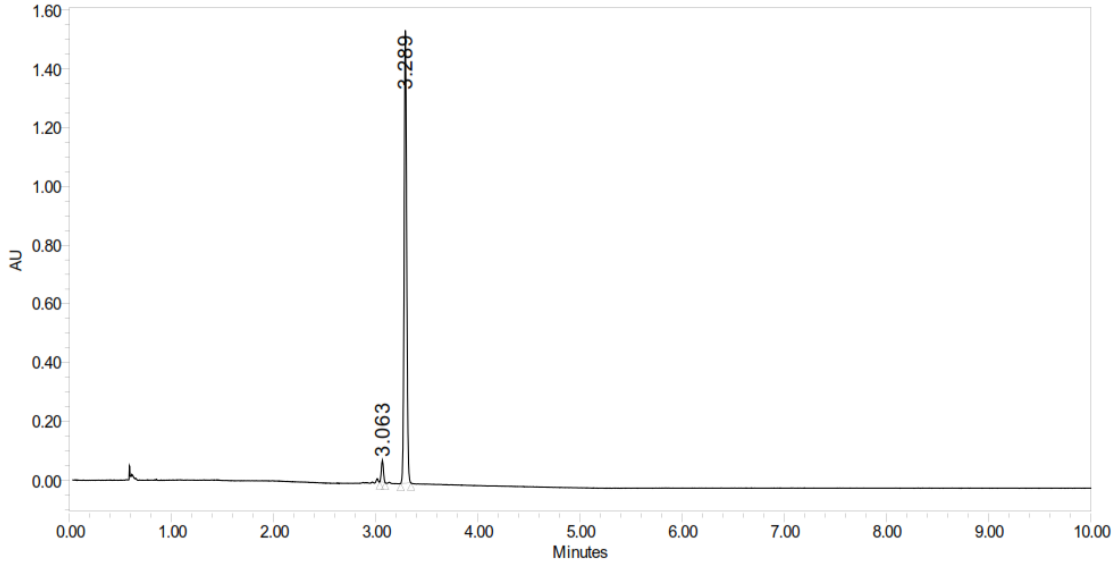


	Retention Time (min)	% Area
1	6.669	3.59
2	8.383	96.41

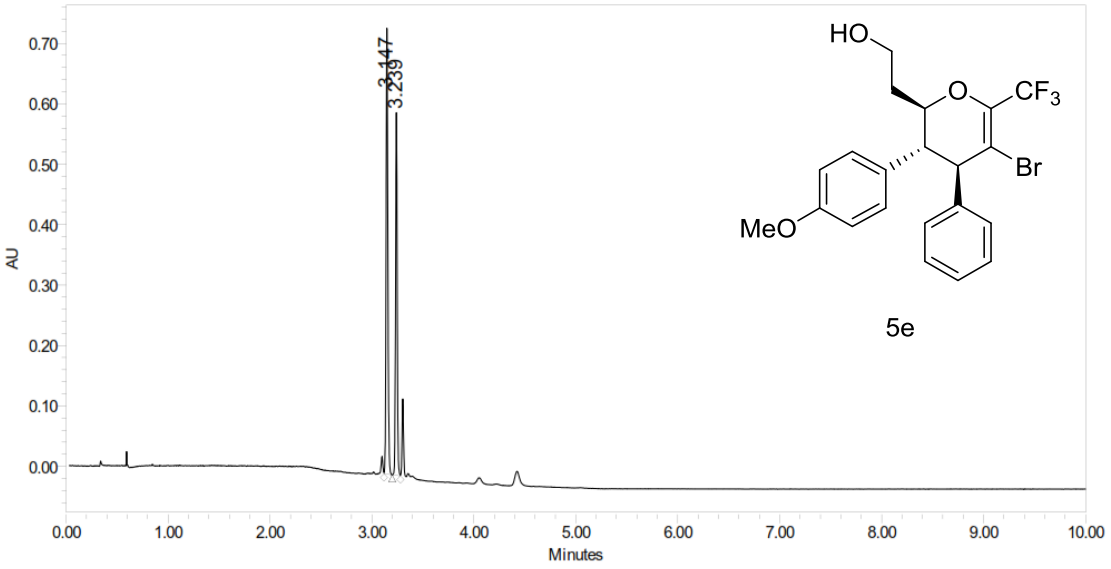


5d

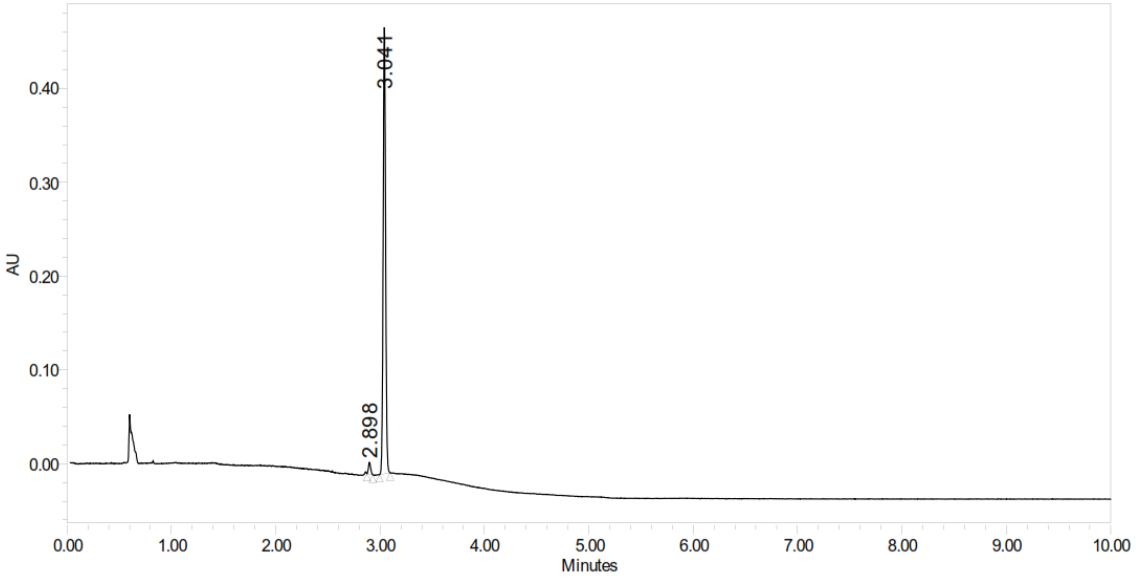
	Retention Time (min)	% Area
1	3.063	45.50
2	3.264	54.50



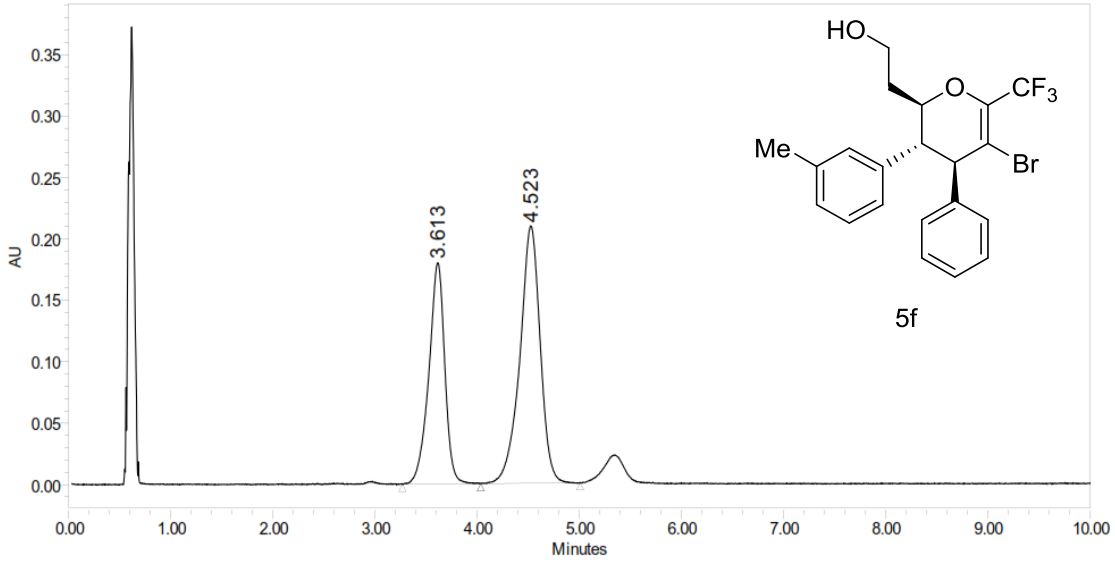
	Retention Time (min)	% Area
1	3.063	3.79
2	3.289	96.21



	Retention Time (min)	% Area
1	3.147	56.83
2	3.239	43.17

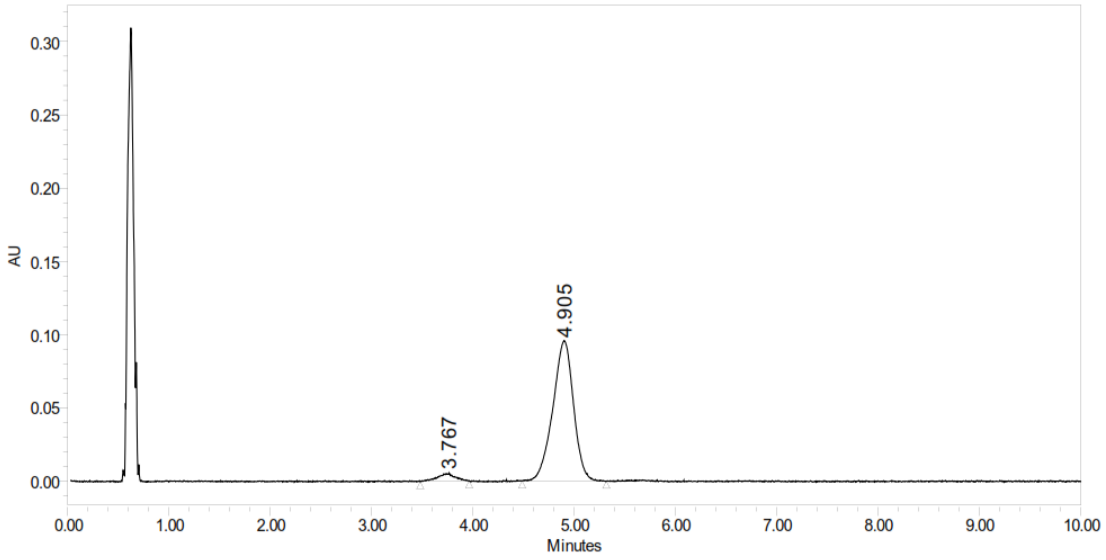


	Retention Time (min)	% Area
1	2.898	2.33
2	3.041	97.67

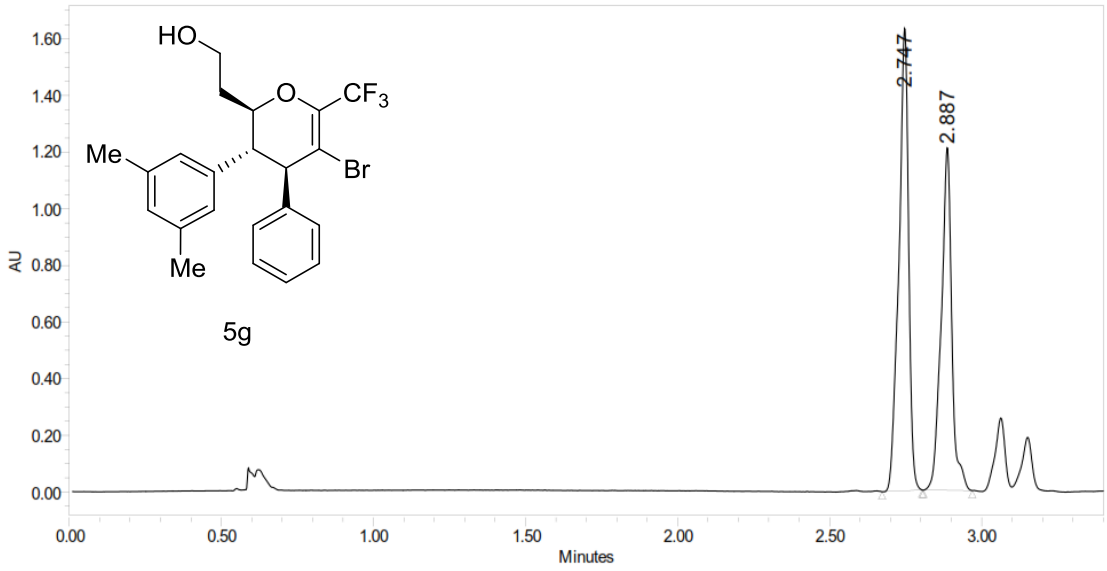


5f

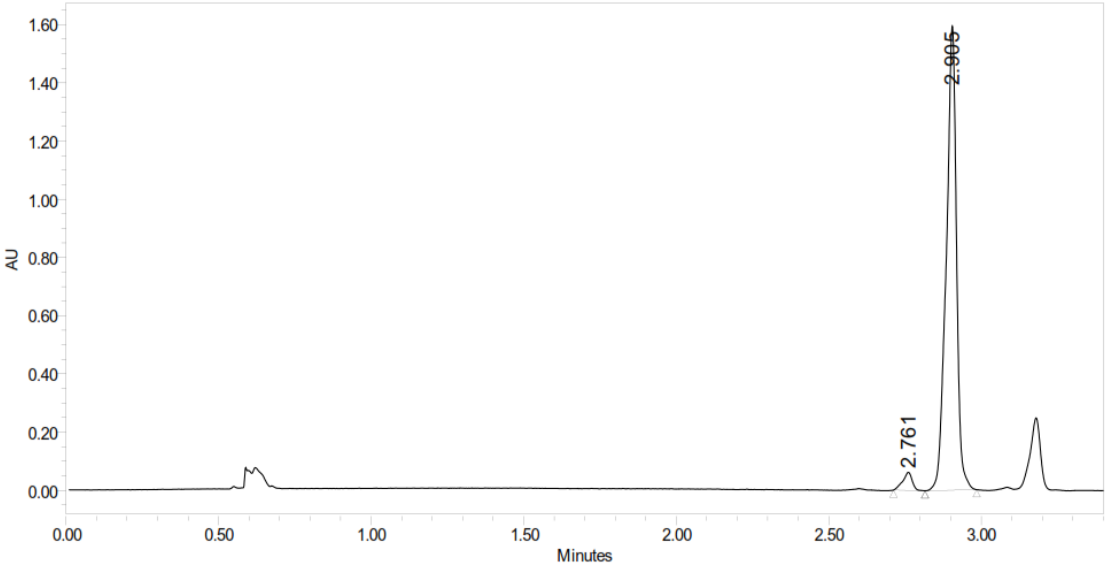
	Retention Time (min)	% Area
1	3.613	40.30
2	4.523	59.70



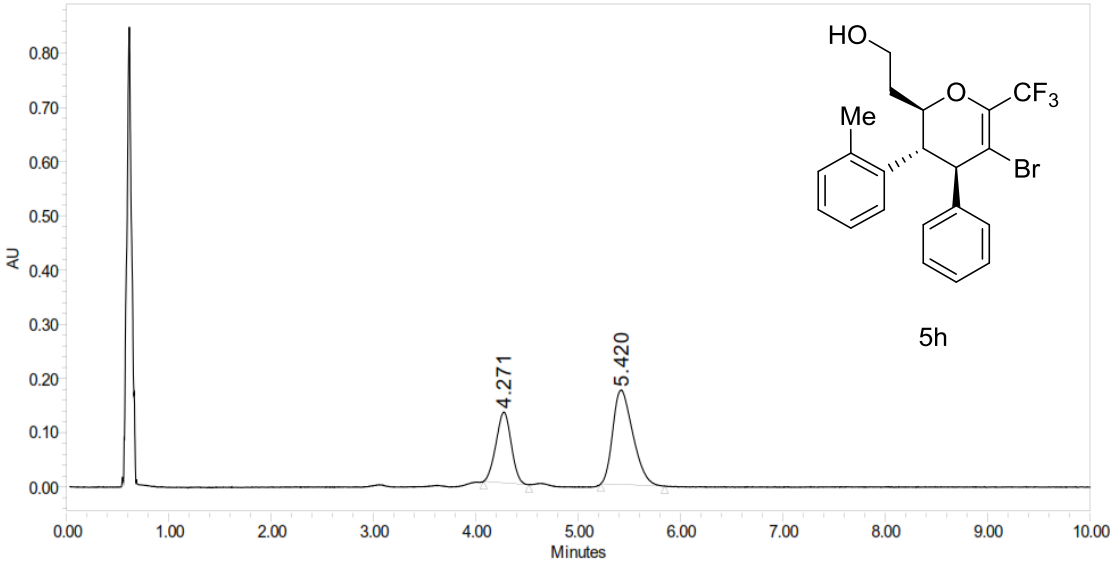
	Retention Time (min)	% Area
1	3.767	4.51
2	4.905	95.49



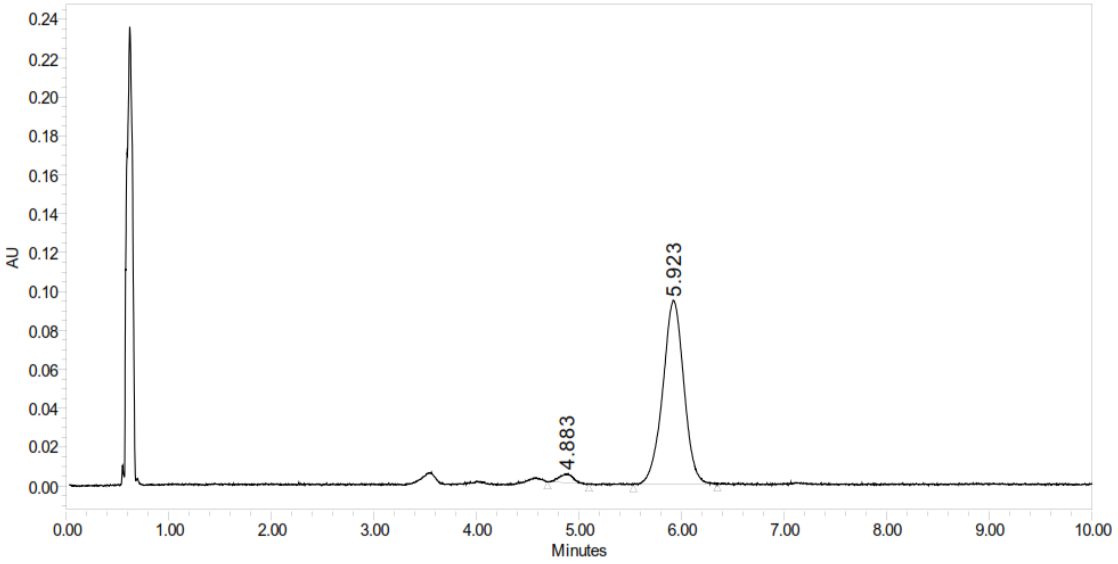
	Retention Time (min)	% Area
1	2.747	55.46
2	2.887	44.54



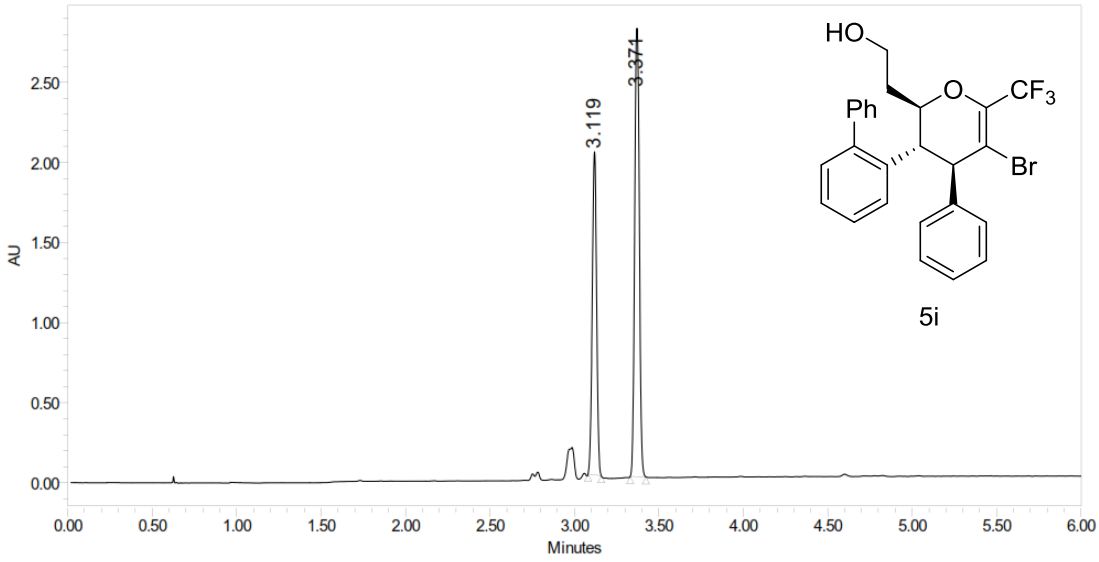
	Retention Time (min)	% Area
1	2.761	3.44
2	2.905	96.56



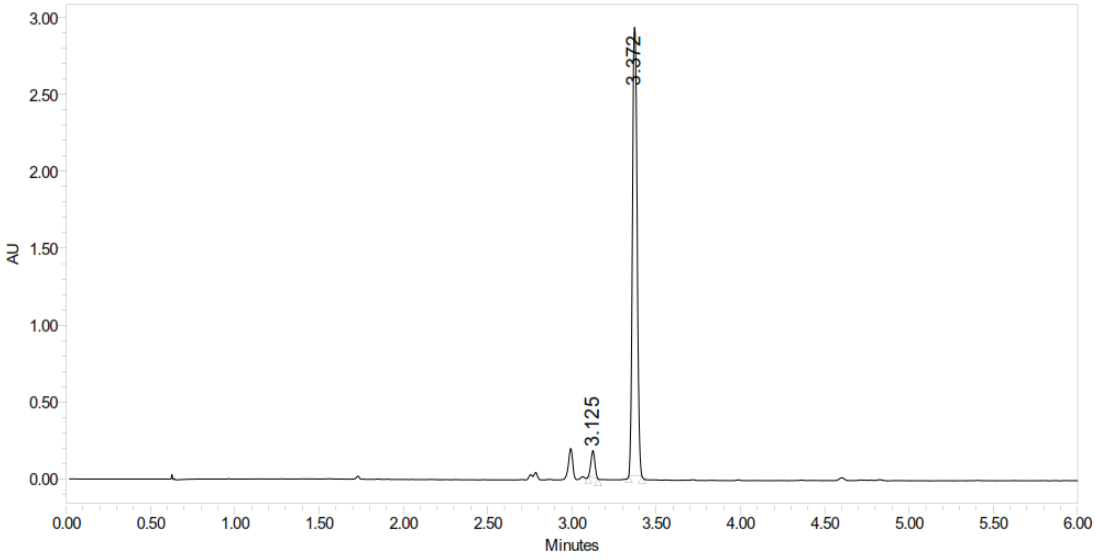
	Retention Time (min)	% Area
1	4.271	36.23
2	5.420	63.77



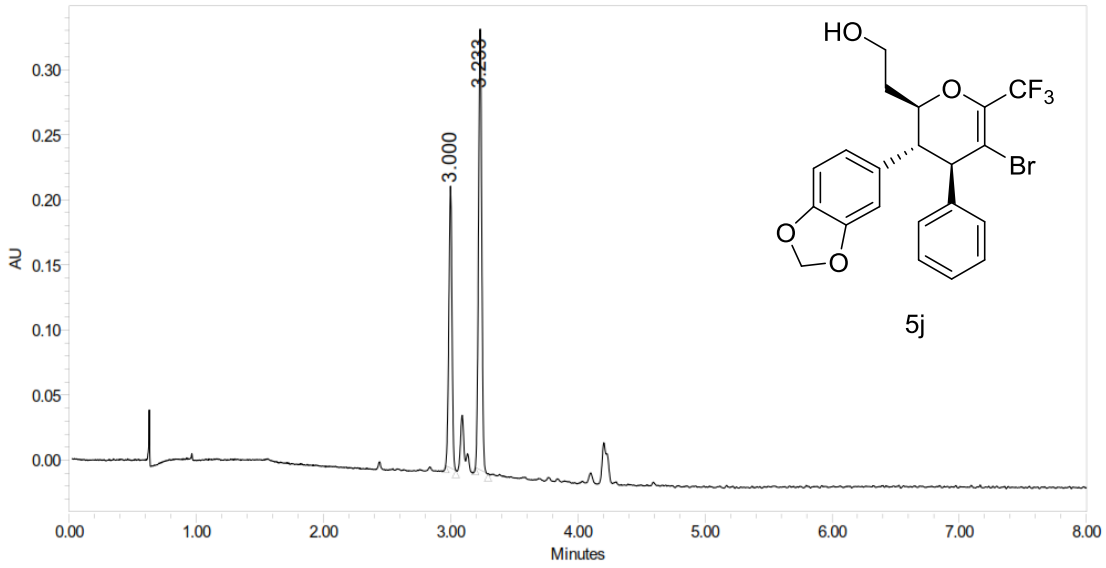
	Retention Time (min)	% Area
1	4.883	3.10
2	5.923	96.90



	Retention Time (min)	% Area
1	3.371	60.05
2	3.119	39.95

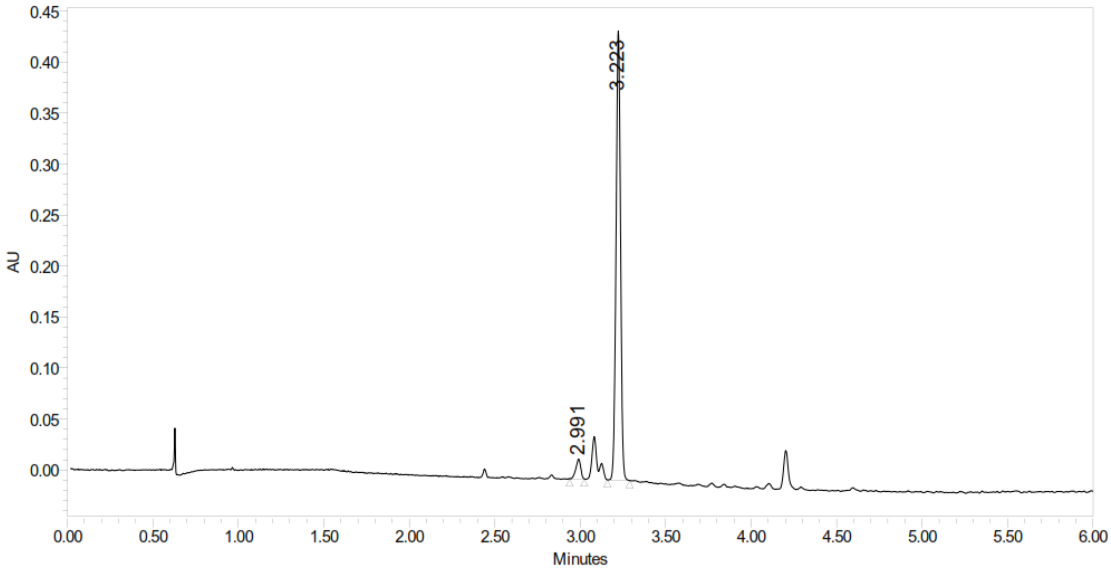


	Retention Time (min)	% Area
1	3.372	95.24
2	3.125	4.76

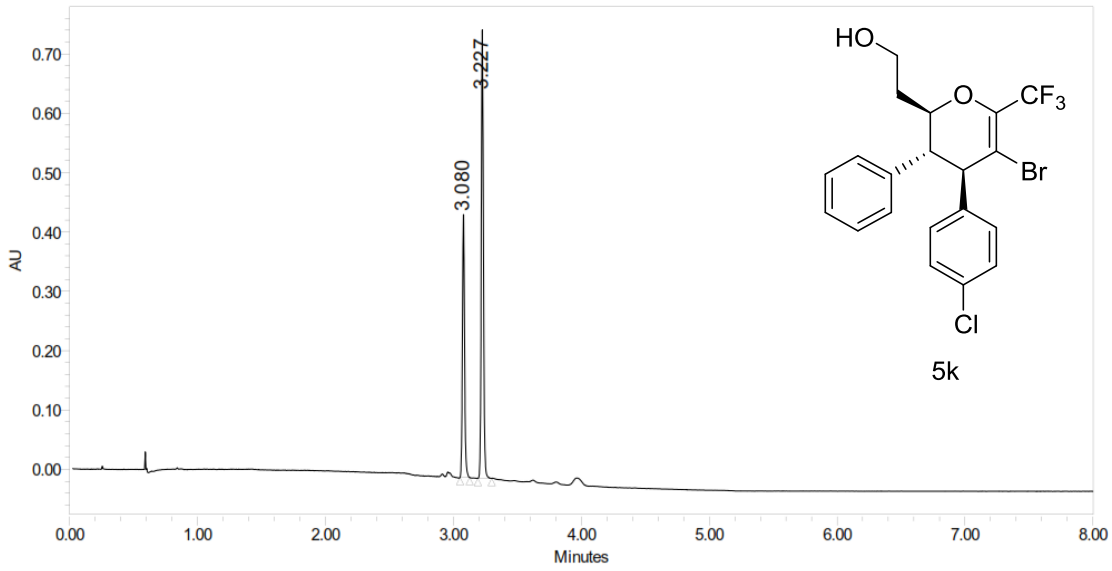


5j

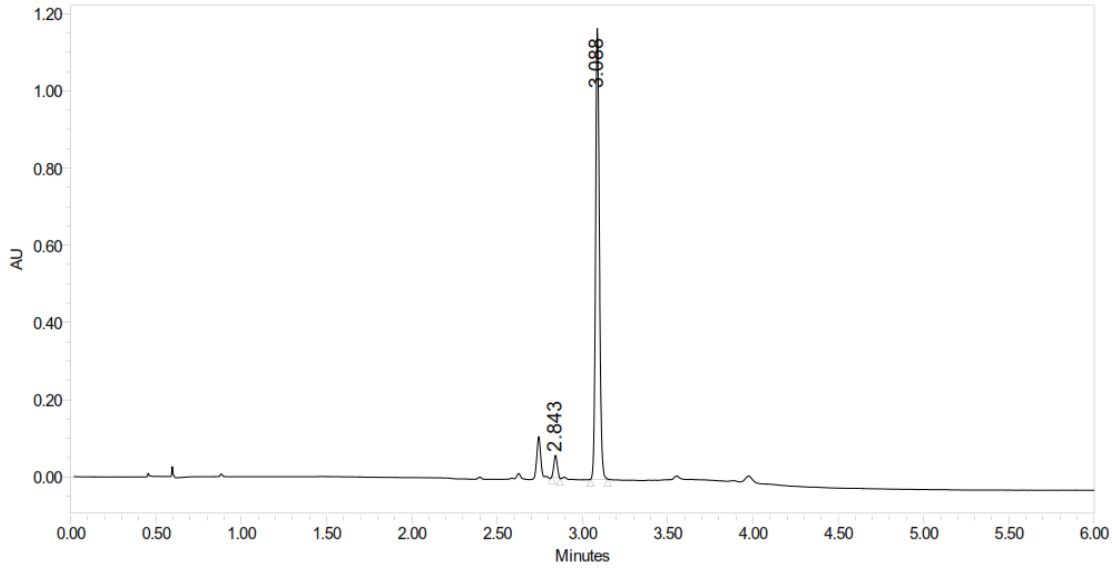
	Retention Time (min)	% Area
1	3.000	38.20
2	3.233	61.80



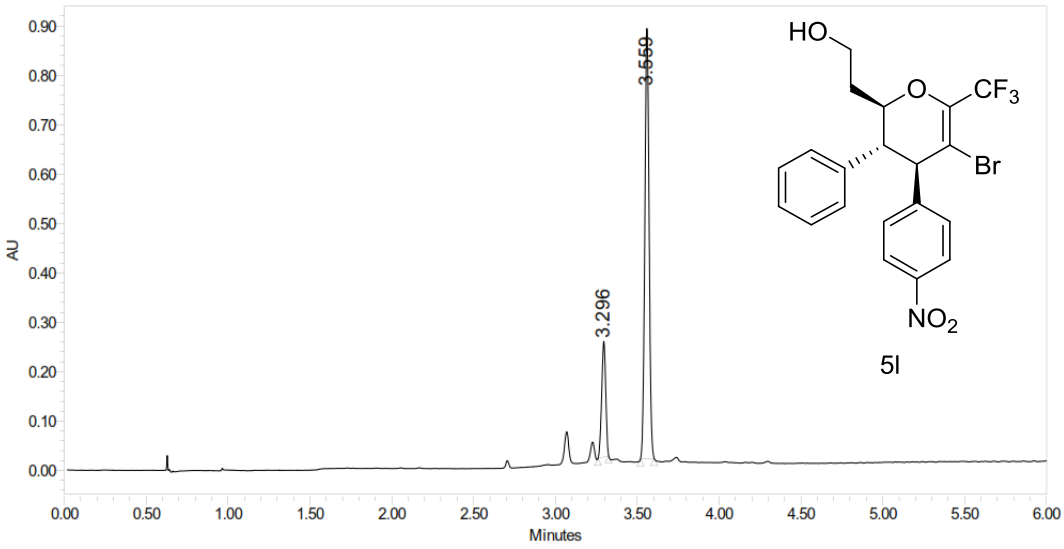
	Retention Time (min)	% Area
1	2.991	4.55
2	3.223	95.45



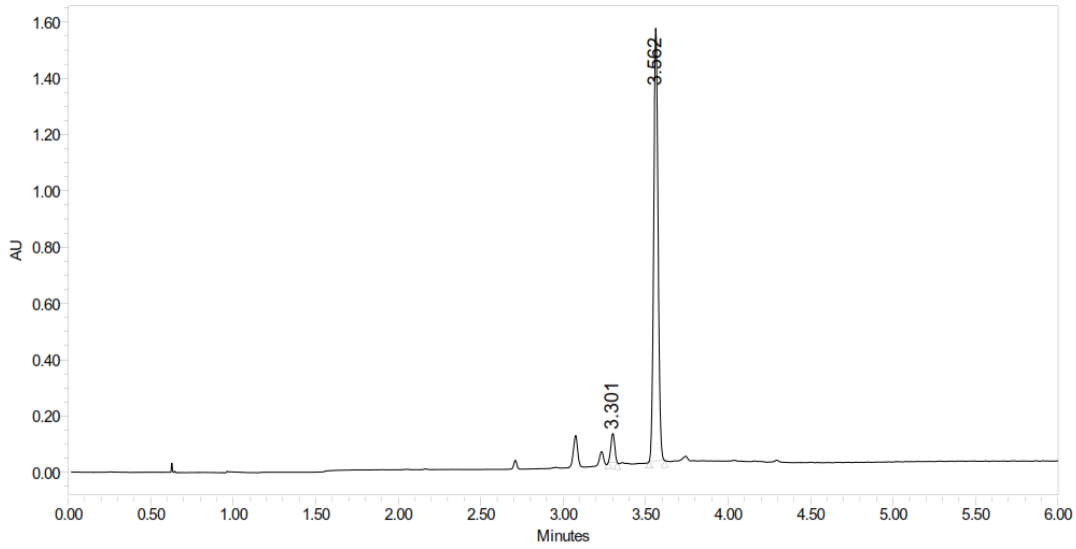
	Retention Time (min)	% Area
1	3.080	36.92
2	3.227	63.08



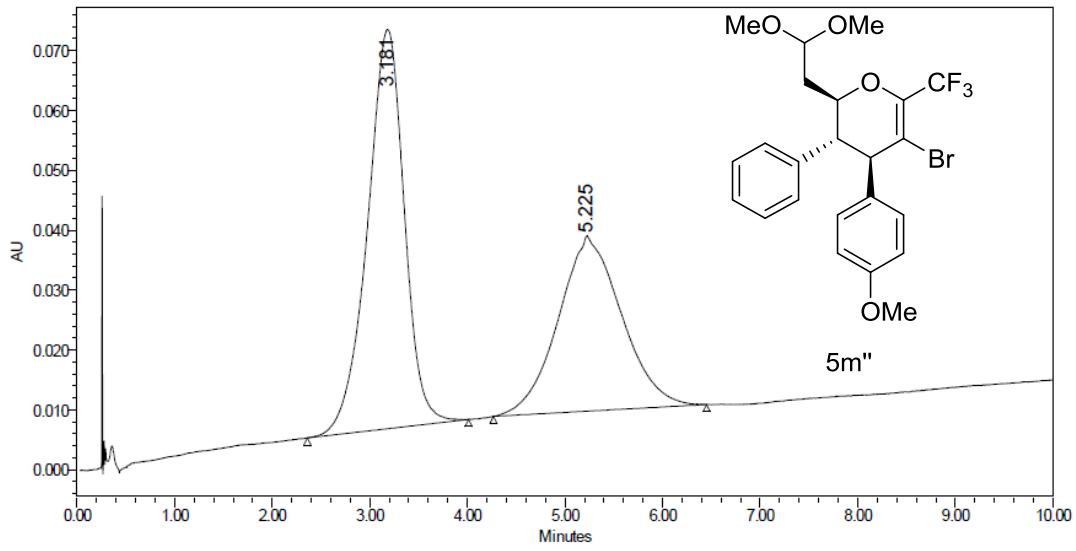
	Retention Time (min)	% Area
1	2.843	4.05
2	3.088	95.95



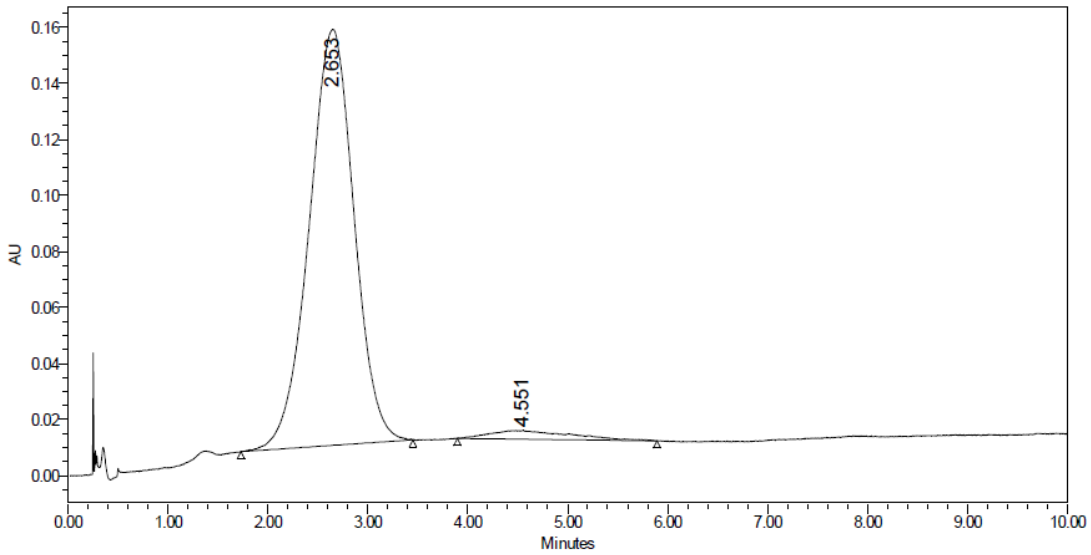
	Retention Time (min)	% Area
1	3.559	79.66
2	3.296	20.34



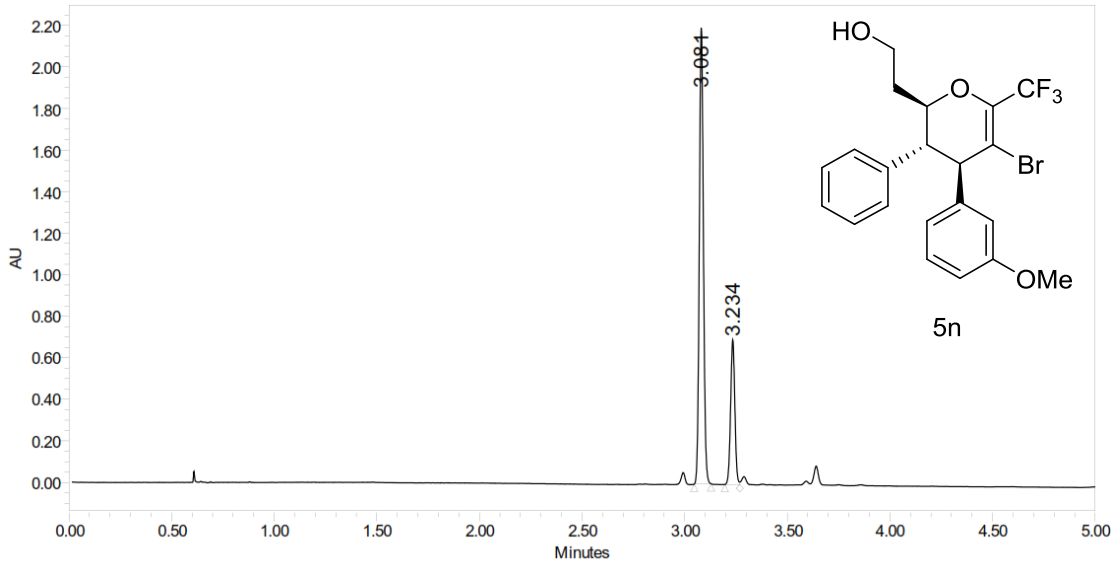
	Retention Time (min)	% Area
1	3.562	94.61
2	3.301	5.39



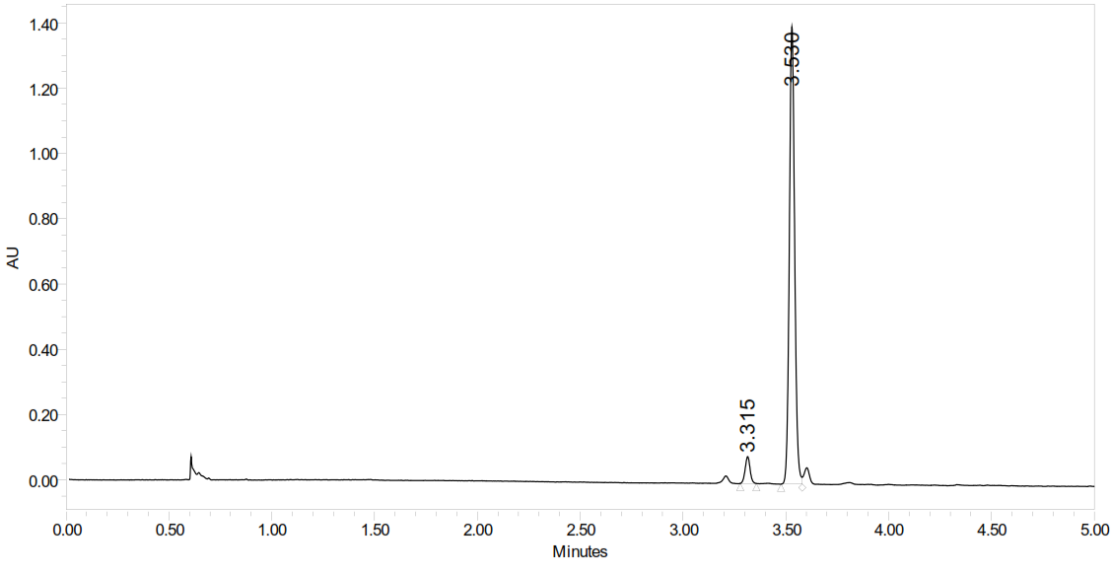
	Retention Time (min)	% Area
1	3.181	57.18
2	5.225	42.82



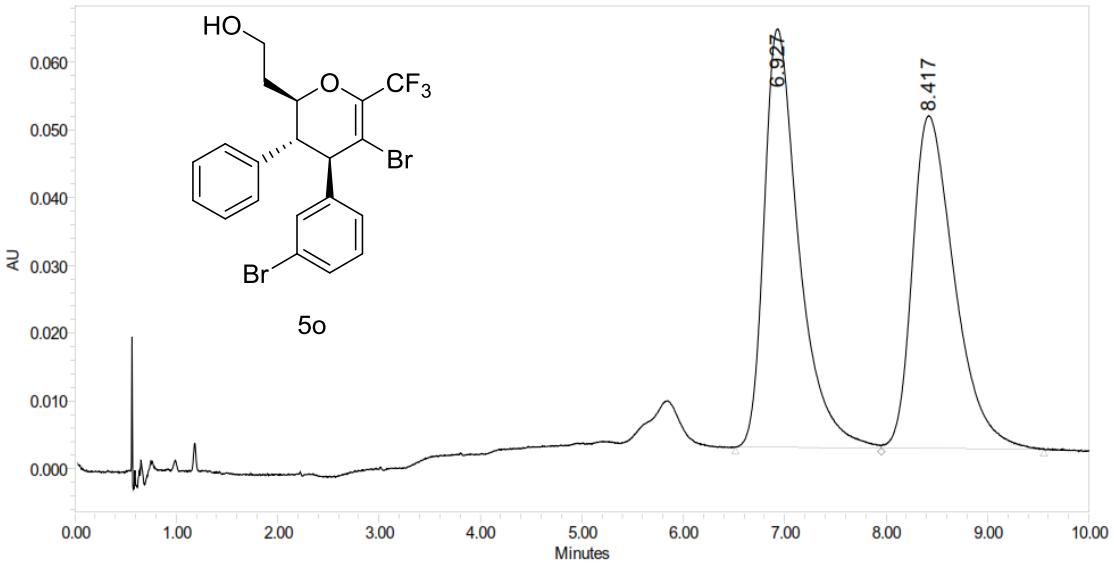
	Retention Time (min)	% Area
1	2.653	96.34
2	4.551	3.66



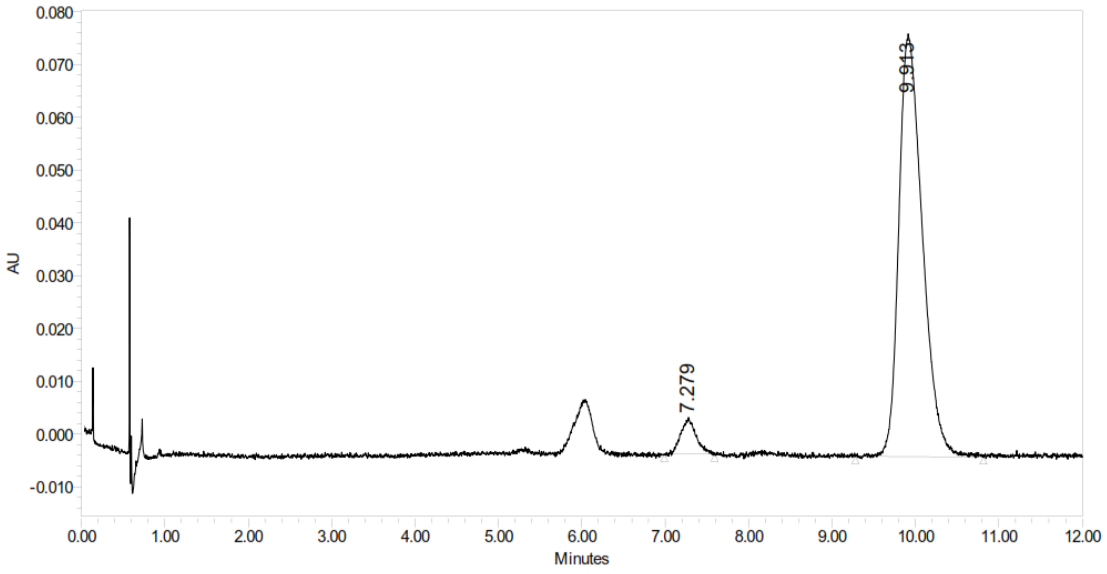
	Retention Time (min)	% Area
1	3.081	75.25
2	3.234	24.75



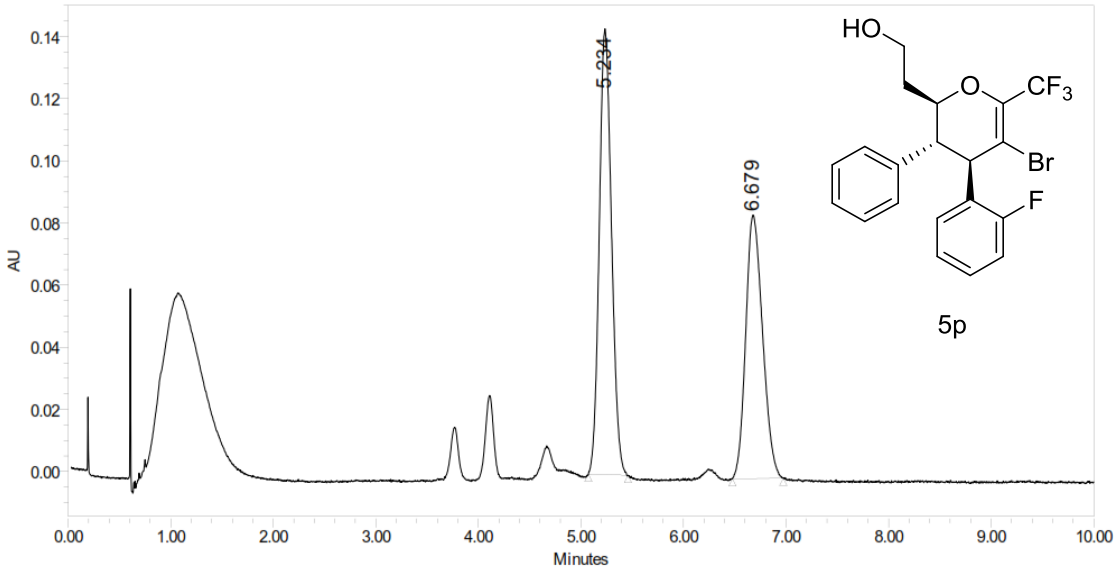
	Retention Time (min)	% Area
1	3.315	5.09
2	3.530	94.91



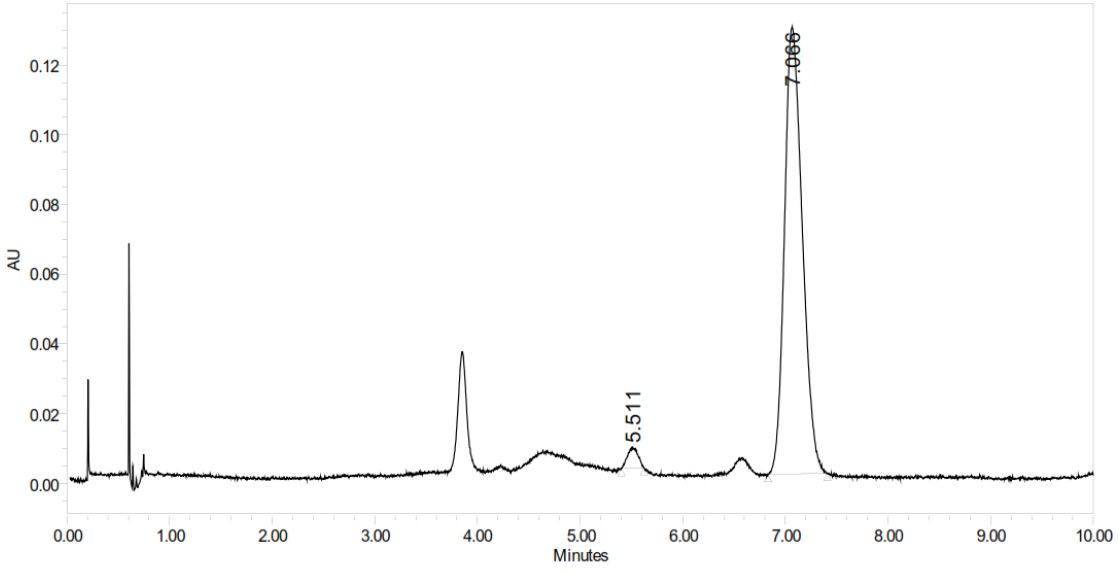
	Retention Time (min)	% Area
1	6.927	51.02
2	8.417	48.98



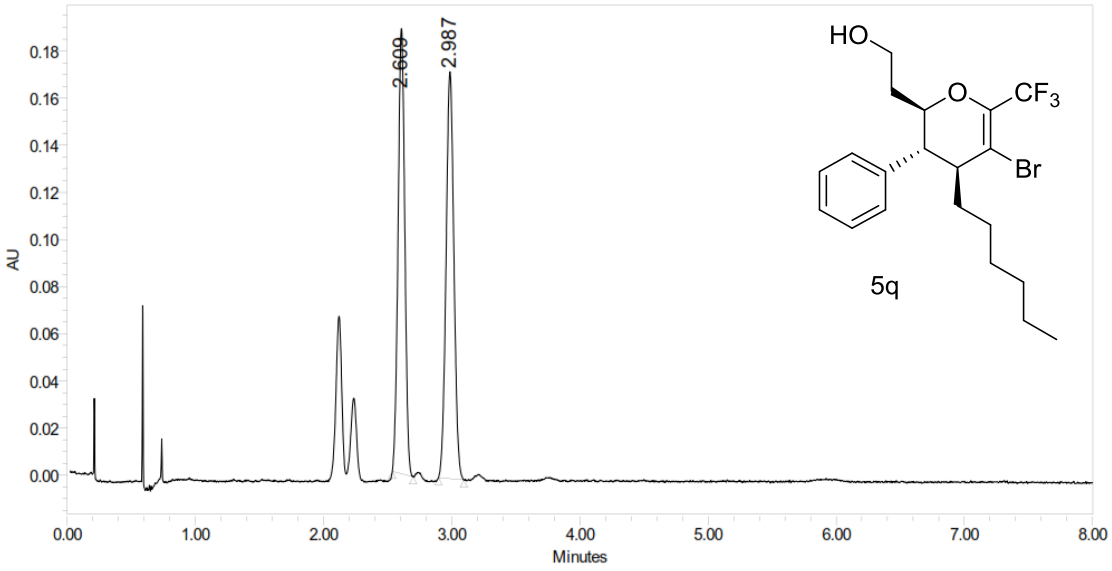
	Retention Time (min)	% Area
1	7.279	5.18
2	9.913	94.82



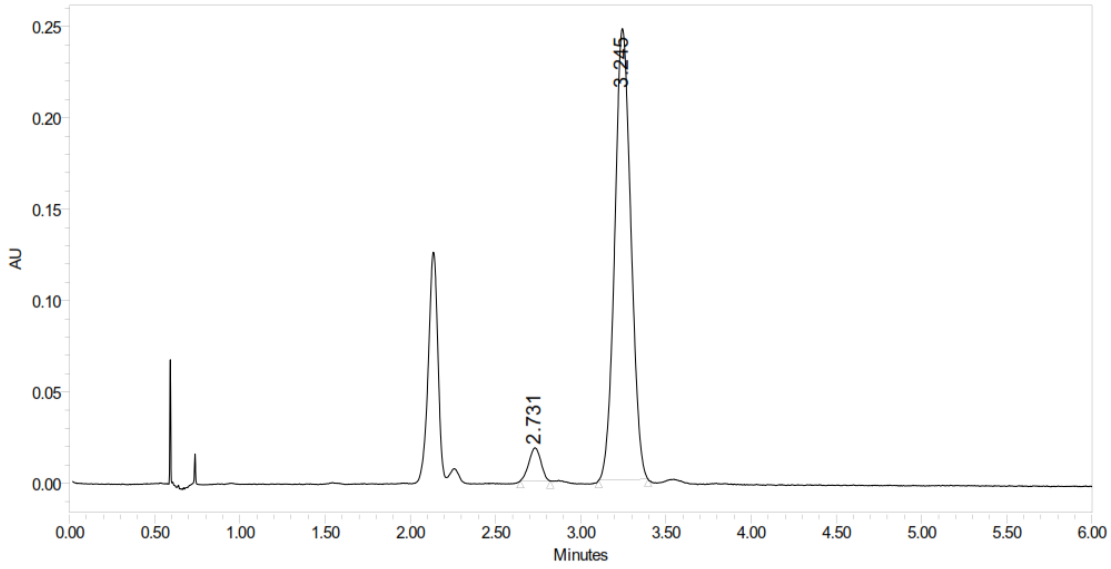
	Retention Time (min)	% Area
1	5.234	55.12
2	6.679	44.88



	Retention Time (min)	% Area
1	5.511	2.64
2	7.066	97.36



	Retention Time (min)	% Area
1	2.609	48.28
2	2.987	51.72



	Retention Time (min)	% Area
1	2.731	5.09
2	3.245	94.91