

One-pot Fluorination and Organocatalytic Robinson Annulation for Asymmetric Synthesis of Mono- and Difluorinated Cyclohexenones

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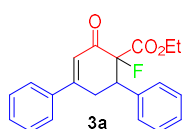
1. General Information

Chemicals and solvents were purchased from commercial suppliers and used as received. ^1H and ^{13}C NMR spectra were recorded on a 400 MHz Agilent NMR spectrometer. Chemical shifts were reported in parts per million (ppm), and the residual solvent peak was used as an internal reference: proton (chloroform δ 7.26), carbon (chloroform δ 77.0). Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet), br s (broad singlet). Coupling constants were reported in Hertz (Hz). LC-MS were performed on an Agilent 2100 system. A C_{18} column (5.0 μm , 6.0 x 50 mm) was used for the separation. The mobile phases were methanol and water both containing 0.05% trifluoro acetic acid. A linear gradient was used to increase from 25:75 v/v methanol/water to 100% methanol over 7.0 min at a flow rate of 0.7 mL/min. UV detections were conducted at 210 nm, 254 nm and 365 nm. Low resolution mass spectra were recorded in APCI (atmospheric pressure chemical ionization). The high resolution mass spectra were obtained on a Waters Micromass GCT Premier. Sorbent silica gel XHL TLC plates (130815) were used for the thin-layer chromatography (TLC). Flash chromatography separations were performed on YAMAZEN AI-580 flash column system with Agela silica gel columns (230-400 μm mesh) and Angela Flash/Cheeta System with Venusil PrepG C_{18} column (10 μm , 120 \AA , 21.2 mm x 250 mm). The enantiomeric excesses of products were determined by chiral phase HPLC analysis on a SHIMADZU LC-20AD system with Venusil Chiral CA, CD-H, and Regis (R,R)-Whelk-O1 column.

1.1 General procedure for Asymmetric Synthesis of Fluorinated Cyclohexanones:

To a solution of β -ketoesters **8** (0.1 mmol) in CH_3CN (0.5 mL) was added SelectfluorTM (0.15 mmol). After being stirred and heated at 120 $^\circ\text{C}$ in microwave reaction station for 20 min, the reaction mixture was allowed to cool to room temperature and then **cat-1** (7 mg, 0.02 mmol), $\text{CF}_3\text{C}_6\text{H}_4\text{COOH}$ (4 mg, 0.02 mmol) and α,β -unsaturated ketones **6** (0.15 mmol) were added. The reaction mixture was stirred for 30 min before the addition of Na_2CO_3 (16 mg, 1.5 equiv.) After being stirred for 48 h, the resulting fluorinated cyclohexenones **3-4** were purified by YAMAZEN AI-580 flash column system with Agela silica gel columns (hexanes/ethyl acetate as eluent).

2. Analytical Data of Products



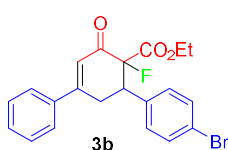
The enantiomeric excess was determined by HPLC analysis (Venusil Chiral CD column, 90:10 hexane/*i*-PrOH, 1.0 mL/min, $\lambda = 254$ nm): $t_{\text{minor}} = 12.15$ min, $t_{\text{major}} = 9.38$ min, 99% ee.

$^1\text{H NMR}$ (400 MHz, cdCl_3) δ 7.72 – 7.54 (m, 2H), 7.50 – 7.42 (m, 3H), 7.41 – 7.31 (m, 5H), 6.63 (dd, $J = 2.9, 2.2$ Hz, 1H), 4.15 (q, $J = 7.1$ Hz, 2H), 3.90 – 3.74 (m, 2H), 3.23 – 3.10 (m, 1H), 1.13 (t, $J = 7.1$ Hz, 3H).

$^{19}\text{F NMR}$ (376 MHz, cdCl_3) δ -165.47.

$^{13}\text{C NMR}$ (101 MHz, cdCl_3) δ 189.86 (d, $J = 17.7$ Hz), 165.61 (d, $J = 26.3$ Hz), 161.33, 137.42, 136.12, 130.94, 128.99, 128.69, 128.50, 128.36, 126.35, 122.61, 95.05 (d, $J = 204.0$ Hz), 62.3, 48.81 (d, $J = 21.2$ Hz), 32.64 (d, $J = 4.0$ Hz), 13.87.

HRMS (EI, m/z): calcd. for $\text{C}_{21}\text{H}_{19}\text{FO}_3$ $[\text{M}]^+$: 338.1318, Found: 338.1321.



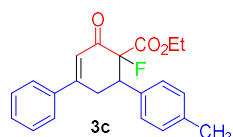
The enantiomeric excess was determined by HPLC analysis (Venusil Chiral CD column, 95:5 hexane/*i*-PrOH, 1.0 mL/min, $\lambda = 254$ nm): $t_{\text{minor}} = 14.58$ min, $t_{\text{major}} = 11.55$ min, 99% ee.

$^1\text{H NMR}$ (400 MHz, cdCl_3) δ 7.65 – 7.56 (m, 2H), 7.54 – 7.40 (m, 5H), 7.22 (d, $J = 8.3$ Hz, 2H), 6.62 (dd, $J = 2.9, 2.1$ Hz, 1H), 4.15 (q, $J = 7.1$ Hz, 2H), 3.88 – 3.71 (m, 2H), 3.20 – 3.06 (m, 1H), 1.16 (t, $J = 7.1$ Hz, 3H).

$^{19}\text{F NMR}$ (376 MHz, cdCl_3) δ -165.24.

$^{13}\text{C NMR}$ (101 MHz, cdCl_3) δ 189.42 (d, $J = 17.2$ Hz), 165.41 (d, $J = 27.3$ Hz), 161.01, 137.28, 135.08, 131.82, 131.02, 130.18, 129.01, 128.36, 126.32, 122.59, 94.72 (d, $J = 204.0$ Hz), 62.50, 48.21 (d, $J = 21.2$ Hz), 32.41 (d, $J = 8.1$ Hz), 13.90.

HRMS (EI, m/z): calcd. for $\text{C}_{21}\text{H}_{18}\text{BrFO}_3$ $[\text{M}]^+$: 416.0423, Found: 416.0426.



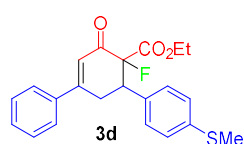
The enantiomeric excess was determined by HPLC analysis (Venusil Chiral CD column, 95:5 hexane/*i*-PrOH, 1.0 mL/min, $\lambda = 254$ nm): $t_{\text{minor}} = 15.34$ min, $t_{\text{major}} = 16.24$ min, 96% ee.

$^1\text{H NMR}$ (400 MHz, cdCl_3) δ 7.62 – 7.56 (m, 2H), 7.44 (qdd, $J = 5.6, 3.6, 1.6$ Hz, 3H), 7.30 (dd, $J = 8.1, 1.2$ Hz, 2H), 7.15 (dd, $J = 8.3, 0.6$ Hz, 2H), 6.61 (d, $J = 2.0$ Hz, 1H), 4.16 (q, $J = 7.1$, 2H), 4.00 – 3.80 (m, 1H), 3.35 (ddd, $J = 18.3, 10.9, 2.4$ Hz, 1H), 3.04 (dd, $J = 18.3, 4.7$ Hz, 1H), 2.34 (s, 3H), 1.13 (t, $J = 7.1$ Hz, 3H).

$^{19}\text{F NMR}$ (376 MHz, cdCl_3) δ -175.16.

$^{13}\text{C NMR}$ (101 MHz, cdCl_3) δ 188.58 (d, $J = 17.2$ Hz), 166.56 (d, $J = 26.2$ Hz), 161.24, 137.94, 137.43, 133.84, 130.92, 129.40, 128.97, 128.55 (d, $J = 2.5$ Hz), 126.30, 121.99, 94.59 (d, $J = 197.2$ Hz), 61.90, 47.24 (d, $J = 22.0$ Hz), 32.00 (d, $J = 5.6$ Hz), 21.09, 13.96.

HRMS (EI, m/z): calcd. for $\text{C}_{22}\text{H}_{21}\text{FO}_3$ $[\text{M}]^+$: 352.1475, Found: 352.1477.



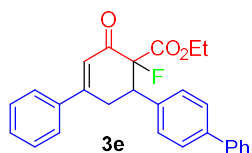
The enantiomeric excess was determined by HPLC analysis (Venusil Chiral CD column, 95:5 hexane/*i*-PrOH, 1.0 mL/min, $\lambda = 254$ nm): $t_{\text{minor}} = 9.05$ min, $t_{\text{major}} = 7.11$ min, 97% ee.

$^1\text{H NMR}$ (400 MHz, cdCl_3) δ 7.65 – 7.58 (m, 2H), 7.50 – 7.40 (m, 3H), 7.25 (s, 4H), 6.62 (dd, $J = 2.9, 2.1$ Hz, 1H), 4.16 (q, $J = 7.2$ Hz, 2H), 3.93 – 3.65 (m, 2H), 3.14 (ddt, $J = 16.7, 13.8, 7.1$ Hz, 1H), 2.49 (s, 3H), 1.15 (t, $J = 7.1$ Hz, 3H).

$^{19}\text{F NMR}$ (376 MHz, cdCl_3) δ -165.53.

^{13}C NMR (101 MHz, cdCl_3) δ 188.76 (d, $J = 18.2$ Hz), 166.54 (d, $J = 26.3$ Hz), 161.24, 138.87, 137.40, 132.76, 130.94, 128.98, 128.90, 126.58, 126.27, 122.60, 95.01 (d, $J = 204.0$ Hz), 62.39, 48.32 (d, $J = 22.2$ Hz), 32.63 (d, $J = 8.1$ Hz), 15.65, 13.91.

HRMS (EI, m/z): calcd. for $\text{C}_{22}\text{H}_{21}\text{FO}_3\text{S}$ $[\text{M}]^+$: 384.1195, Found: 384.1196.



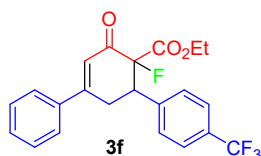
The enantiomeric excess was determined by HPLC analysis (Venusil Chiral CA column, 90:10 hexane/*i*-PrOH, 1.0 mL/min, $\lambda = 254$ nm): $t_{\text{minor}} = 15.57$ min, $t_{\text{major}} = 10.60$ min, 93% ee.

^1H NMR (400 MHz, cdCl_3) δ 7.67 – 7.55 (m, 6H), 7.52 – 7.40 (m, 7H), 7.36 (dt, $J = 9.4, 4.3$ Hz, 1H), 6.64 (d, $J = 2.1$ Hz, 1H), 4.18 (q, $J = 7.1$, 2H), 4.00 (ddd, $J = 35.8, 10.9, 4.7$ Hz, 1H), 3.41 (ddd, $J = 18.3, 11.0, 2.4$ Hz, 1H), 3.10 (dd, $J = 18.3, 4.7$ Hz, 1H), 1.13 (t, $J = 7.1$ Hz, 3H).

^{19}F NMR (376 MHz, cdCl_3) δ -175.02.

^{13}C NMR (101 MHz, cdCl_3) δ 188.42 (d, $J = 20.2$ Hz), 166.7, 161.13, 140.45, 137.37, 130.98, 129.14, 129.12, 129.00, 128.80, 127.47, 127.41, 127.06, 127.03, 126.32, 122.02, 94.49 (d, $J = 197.0$ Hz), 62.02, 47.30 (d, $J = 22.2$ Hz), 31.92 (d, $J = 6.1$ Hz), 13.91.

HRMS (EI, m/z): calcd. for $\text{C}_{27}\text{H}_{23}\text{FO}_3$ $[\text{M}]^+$: 414.1631, Found: 414.1633.



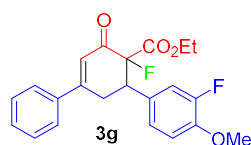
The enantiomeric excess was determined by HPLC analysis (Venusil Chiral CA column, 90:10 hexane/*i*-PrOH, 1.0 mL/min, $\lambda = 254$ nm): $t_{\text{minor}} = 19.43$ min, $t_{\text{major}} = 13.77$ min, 99% ee.

^1H NMR (400 MHz, cdCl_3) δ 7.67 – 7.52 (m, 6H), 7.53 – 7.39 (m, 3H), 6.63 (d, $J = 2.1$ Hz, 1H), 4.17 (q, $J = 7.1$, 2H), 4.11 – 3.96 (m, 1H), 3.37 (ddd, $J = 18.2, 11.0, 2.4$ Hz, 1H), 3.07 (dd, $J = 18.2, 4.8$ Hz, 1H), 1.11 (t, $J = 7.1$ Hz, 3H).

^{19}F NMR (376 MHz, cdCl_3) δ -62.76, -174.96.

^{13}C NMR (101 MHz, cdCl_3) δ 187.82 (d, $J = 20.2$ Hz), 166.29 (d, $J = 26.3$ Hz), 160.67, 140.85, 137.12, 131.13, 130.36, 129.15 (d, $J = 3.0$ Hz), 129.06, 126.29, 125.71 (q, $J = 3.7$ Hz), 122.54, 94.00 (d, $J = 198.0$ Hz), 62.19, 47.31 (d, $J = 22.2$ Hz), 31.66 (d, $J = 6.1$ Hz), 13.91.

HRMS (EI, m/z): calcd. for $\text{C}_{22}\text{H}_{18}\text{F}_4\text{O}_3$ $[\text{M}]^+$: 406.1192, Found: 406.1192.



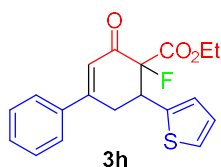
The enantiomeric excess was determined by HPLC analysis (Venusil Chiral CD column, 95:5 hexane/*i*-PrOH, 1.0 mL/min, $\lambda = 254$ nm): $t_{\text{minor}} = 3.25$ min, $t_{\text{major}} = 3.73$ min, 93% ee.

^1H NMR (400 MHz, cdCl_3) δ 7.63 – 7.55 (m, 2H), 7.51 – 7.39 (m, 3H), 7.10 – 6.99 (m, 2H), 6.95 – 6.90 (m, 1H), 6.61 (d, $J = 2.0$ Hz, 1H), 4.18 (q, $J = 7.2$ Hz, 2H), 4.02 – 3.81 (m, 4H), 3.32 (ddd, $J = 18.2, 11.0, 2.4$ Hz, 1H), 3.06 (dd, $J = 18.2, 4.7$ Hz, 1H), 1.14 (t, $J = 7.1$ Hz, 3H).

^{19}F NMR (376 MHz, cdCl_3) δ -135.60, -175.19.

^{13}C NMR (101 MHz, cdCl_3) δ 188.20 (d, $J = 20.2$ Hz), 166.47 (d, $J = 27.3$ Hz), 160.93 (s), 152.2 (d, $J = 248.5$ Hz), 147.63 (d, $J = 10.8$ Hz), 137.24, 133.30 (d, $J = 3.6$ Hz), 132.82, 131.05, 129.02, 128.55 (d, $J = 16.6$ Hz), 126.31, 121.98, 121.22 (d, $J = 7.0$ Hz), 116.13 (d, $J = 18.4$ Hz), 113.86, 94.40 (d, $J = 198.0$ Hz), 62.05, 56.30, 47.19, 3(d, $J = 22.2$ Hz), 2.09 (d, $J = 5.4$ Hz), 14.01.

HRMS (EI, m/z): calcd. for $\text{C}_{22}\text{H}_{20}\text{F}_2\text{O}_3$ $[\text{M}]^+$: 386.1330, Found: 386.1342.



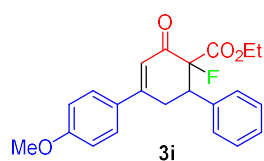
The enantiomeric excess was determined by HPLC analysis (Venusil Chiral CD column, 95:5 hexane/*i*-PrOH, 1.0 mL/min, $\lambda = 254$ nm): $t_{\text{minor}} = 18.64$ min, $t_{\text{major}} = 14.40$ min, 96% ee.

$^1\text{H NMR}$ (400 MHz, cdCl_3) δ 7.68 – 7.56 (m, 2H), 7.52 – 7.41 (m, 3H), 7.28 (dd, $J = 5.1, 1.2$ Hz, 1H), 7.10 (ddd, $J = 3.5, 2.0, 0.9$ Hz, 1H), 7.03 (dd, $J = 5.1, 3.6$ Hz, 1H), 6.66 – 6.58 (m, 1H), 4.25 – 4.06 (m, 3H), 3.75 (ddd, $J = 18.0, 11.7, 2.5$ Hz, 1H), 3.32 (ddd, $J = 18.0, 5.2, 2.4$ Hz, 1H), 1.15 (t, $J = 7.1$ Hz, 3H).

$^{19}\text{F NMR}$ (376 MHz, cdCl_3) δ -163.76.

$^{13}\text{C NMR}$ (101 MHz, cdCl_3) δ 189.28 (d, $J = 17.7$ Hz), 165.24, 160.58, 138.63, 137.23, 131.01, 129.02, 127.01, 126.76, 126.34, 125.10, 122.67, 94.63 (d, $J = 203.0$ Hz), 62.50, 44.10 (d, $J = 22.2$ Hz), 34.02 (d, $J = 7.7$ Hz), 13.83.

HRMS (EI, m/z): calcd. for $\text{C}_{19}\text{H}_{17}\text{FO}_3\text{S}$ $[\text{M}]^+$: 344.0882, Found: 344.0990.



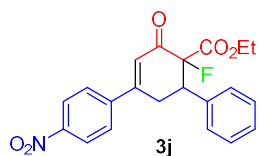
The enantiomeric excess was determined by HPLC analysis (Venusil Chiral CD column, 95:5 hexane/*i*-PrOH, 1.0 mL/min, $\lambda = 254$ nm): $t_{\text{minor}} = 24.75$ min, $t_{\text{major}} = 12.14$ min, 89% ee.

$^1\text{H NMR}$ (400 MHz, cdCl_3) δ 7.63 – 7.53 (m, 2H), 7.41 (dt, $J = 8.0, 1.4$ Hz, 2H), 7.39 – 7.28 (m, 3H), 7.01 – 6.89 (m, 2H), 6.58 (d, $J = 2.0$ Hz, 1H), 4.14 (dq, $J = 7.1, 3.5$ Hz, 2H), 4.02 – 3.79 (m, 4H), 3.32 (ddd, $J = 18.1, 11.0, 2.3$ Hz, 1H), 3.06 (dd, $J = 18.1, 4.8$ Hz, 1H), 1.09 (t, $J = 7.1$ Hz, 3H).

$^{19}\text{F NMR}$ (376 MHz, cdCl_3) δ -174.75.

$^{13}\text{C NMR}$ (101 MHz, cdCl_3) δ 188.38 (d, $J = 20.2$ Hz), 166.72 (d, $J = 25.4$ Hz), 162.06, 160.42, 137.02, 129.33, 128.75, 128.72, 128.17, 128.03, 120.00, 114.39, 94.51 (d, $J = 196.0$ Hz), 61.87, 55.45, 47.54 (d, $J = 22.2$ Hz), 31.57 (d, $J = 5.4$ Hz), 13.93.

HRMS (EI, m/z): calcd. for $\text{C}_{22}\text{H}_{21}\text{FO}_4$ $[\text{M}]^+$: 368.1424, Found: 368.1421.



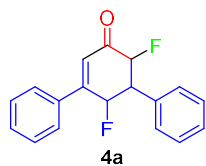
The enantiomeric excess was determined by HPLC analysis (Venusil Chiral CD column, 95:5 hexane/*i*-PrOH, 1.0 mL/min, $\lambda = 254$ nm): $t_{\text{minor}} = 15.74$ min, $t_{\text{major}} = 14.36$ min, 85% ee.

$^1\text{H NMR}$ (400 MHz, cdCl_3) δ 8.28 – 8.16 (m, 2H), 7.67 – 7.55 (m, 4H), 7.53 – 7.39 (m, 3H), 6.64 (d, $J = 2.0$ Hz, 1H), 4.23 – 4.02 (m, 3H), 3.37 (ddd, $J = 18.1, 11.0, 2.4$ Hz, 1H), 3.08 (dd, $J = 18.1, 4.8$ Hz, 1H), 1.14 (t, $J = 7.1$ Hz, 3H).

$^{19}\text{F NMR}$ (376 MHz, cdCl_3) δ -174.84.

$^{13}\text{C NMR}$ (101 MHz, cdCl_3) δ 187.43 (d, $J = 20.2$ Hz), 166.12 (d, $J = 25.3$ Hz), 160.40, 147.79, 144.06, 136.96, 131.25, 129.77 (d, $J = 2.9$ Hz), 129.11, 126.29, 123.95, 122.02, 93.73 (d, $J = 197.0$ Hz), 62.36, 47.19 (d, $J = 21.2$ Hz), 31.49 (d, $J = 5.2$ Hz), 14.00.

HRMS (EI, m/z): calcd. for $\text{C}_{21}\text{H}_{18}\text{FNO}_5$ $[\text{M}]^+$: 383.1169, Found: 383.1167.



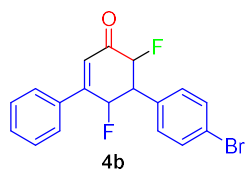
The enantiomeric excess was determined by HPLC analysis (Venusil Chiral CD column, 90:10 hexane/*i*-PrOH, 1.0 mL/min, $\lambda = 254$ nm): $t_{\text{minor}} = 16.54$ min, $t_{\text{major}} = 14.48$ min, 93% ee.

$^1\text{H NMR}$ (400 MHz, cdCl_3) δ 7.63 – 7.55 (m, 2H), 7.52 (ddd, $J = 4.0, 3.4, 1.6$ Hz, 2H), 7.49 – 7.41 (m, 2H), 7.34 – 7.28 (m, 2H), 7.27 – 7.24 (m, 2H), 6.48 (d, $J = 4.3$ Hz, 1H), 5.92 (ddd, $J = 11.4, 9.4, 1.5$ Hz, 1H), 5.22 (ddd, $J = 47.6, 12.8, 0.8$ Hz, 1H), 3.94 – 3.70 (m, 1H).

^{19}F NMR (376 MHz, cdCl_3) δ -177.97, -196.93.

^{13}C NMR (101 MHz, cdCl_3) δ 202.07, 191.22, 156.95, 133.80, 132.66, 132.26, 130.98, 129.79, 128.93, 127.37, 127.35, 124.44, 122.51, 90.70, 89.99, 79.02, 77.30, 77.18, 76.98, 76.66, 63.70, 53.41.

HRMS (ESI, m/z): calcd. for $\text{C}_{18}\text{H}_{14}\text{F}_2\text{ONa}$ $[\text{M}+\text{Na}]^+$: 307.0910, Found: 307.0910.



The enantiomeric excess was determined by HPLC analysis (Venusil Chiral CD column, 90:10 hexane/*i*-PrOH, 1.0 mL/min, λ = 254 nm): t_{minor} = 12.53 min, t_{major} = 9.39 min, 89% ee.

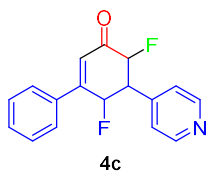
^1H NMR (400 MHz, cdCl_3) δ 7.58 – 7.49 (m, 2H), 7.50 – 7.32 (m, 7H), 6.48 (d, J = 4.3 Hz, 1H), 5.97 (ddd, J = 46.8, 9.3, 1.6 Hz, 1H), 5.26 (ddd, J = 47.6, 12.8,

0.8 Hz, 1H), 3.98 – 3.68 (m, 1H).

^{19}F NMR (376 MHz, cdCl_3) δ -177.60, -196.92.

^{13}C NMR (101 MHz, cdCl_3) δ 191.92 (d, J = 15.7 Hz), 157.37 (d, J = 21.2 Hz), 134.83, 133.93, 130.87, 129.08, 128.89, 128.70, 128.44, 128.11, 127.38 (d, J = 1.9 Hz), 124.47 (d, J = 4.6 Hz), 90.64 (d, J = 11.4 Hz), 90.30 (dd, J = 34.3, 10.3 Hz), 88.60 (dd, J = 20.4, 10.9 Hz), 54.14 (m), 25.35.

HRMS (EI, m/z): calcd. for $\text{C}_{18}\text{H}_{13}\text{BrF}_2\text{O}$ $[\text{M}]^+$: 362.0118, Found: 362.0127.



The enantiomeric excess was determined by HPLC analysis (Venusil Chiral CD column, 90:10 hexane/*i*-PrOH, 1.0 mL/min, λ = 254 nm): t_{minor} = 28.12 min, t_{major} = 20.48 min, 93% ee.

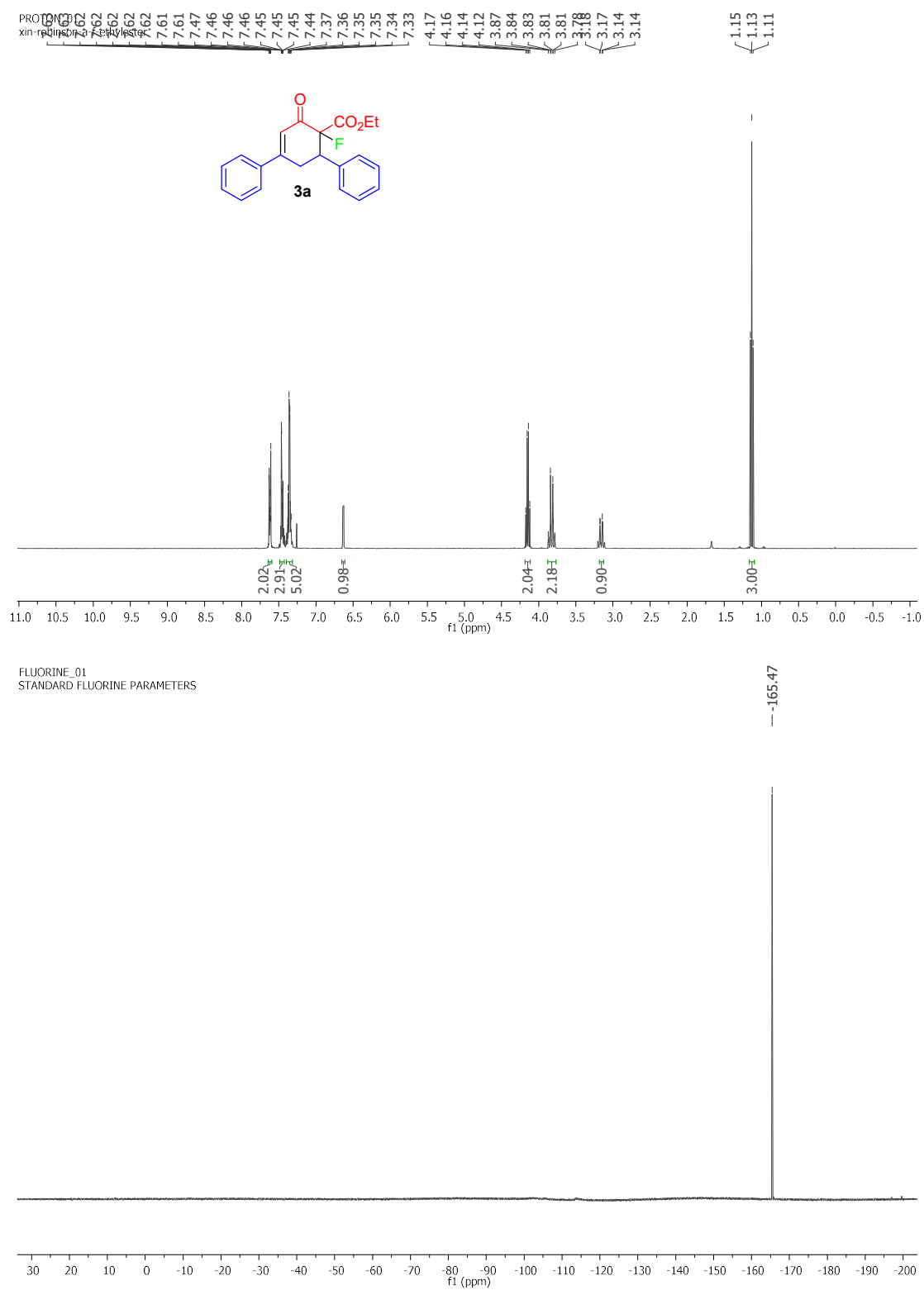
^1H NMR (400 MHz, cdCl_3) δ 8.71 (d, J = 5.8 Hz, 2H), 7.52 (ddt, J = 6.1, 4.3, 2.0 Hz, 2H), 7.50 – 7.42 (m, 2H), 7.37 (d, J = 6.0 Hz, 2H), 7.27 – 7.25 (m, 1H), 6.50 (d, J = 4.4 Hz, 1H), 5.97 (ddd, J = 47.0, 9.4, 1.6 Hz, 1H), 5.26 (ddd, J = 47.7, 12.9, 0.8 Hz, 1H), 3.99 – 3.67 (m, 1H).

^{19}F NMR (376 MHz, cdCl_3) δ -177.98, -196.91.

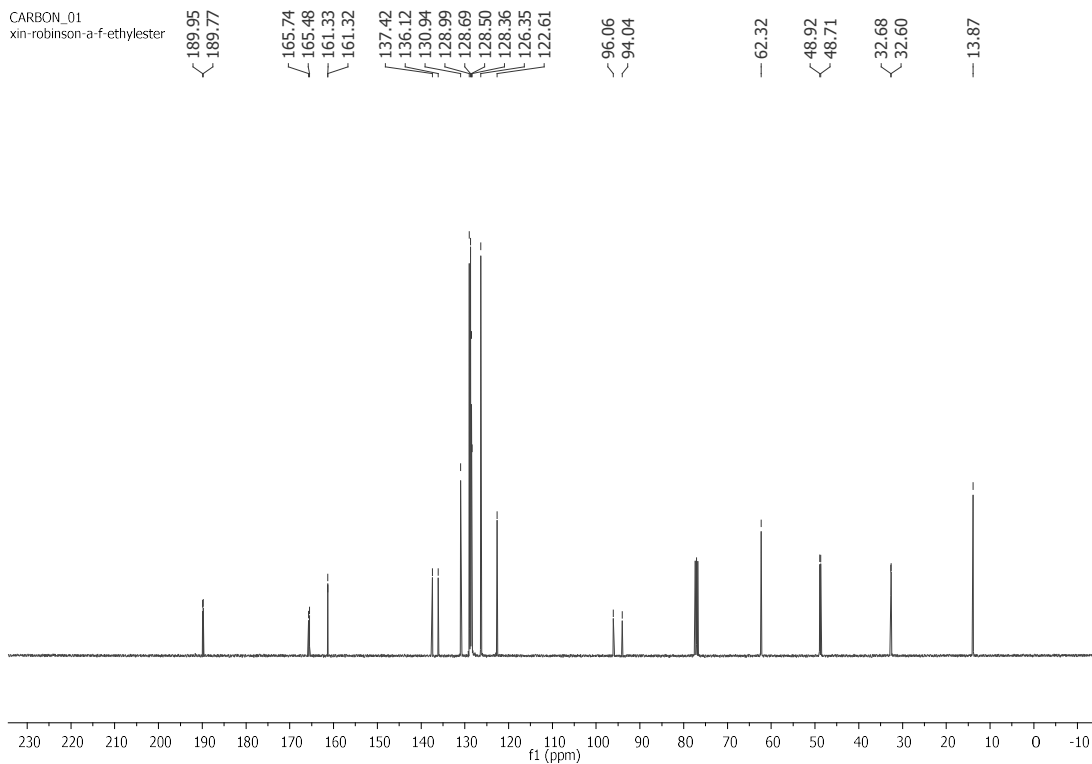
^{13}C NMR (101 MHz, cdCl_3) δ 176.46, 150.50, 143.73, 131.11, 128.99, 127.36, 127.34, 124.45, 123.35, 89.49, 87.70, 77.30, 76.98, 76.66, 53.19, 39.15, 38.29.

HRMS (EI, m/z): calcd. for $\text{C}_{17}\text{H}_{13}\text{F}_2\text{NO}$ $[\text{M}]^+$: 285.0965, Found: 285.0963.

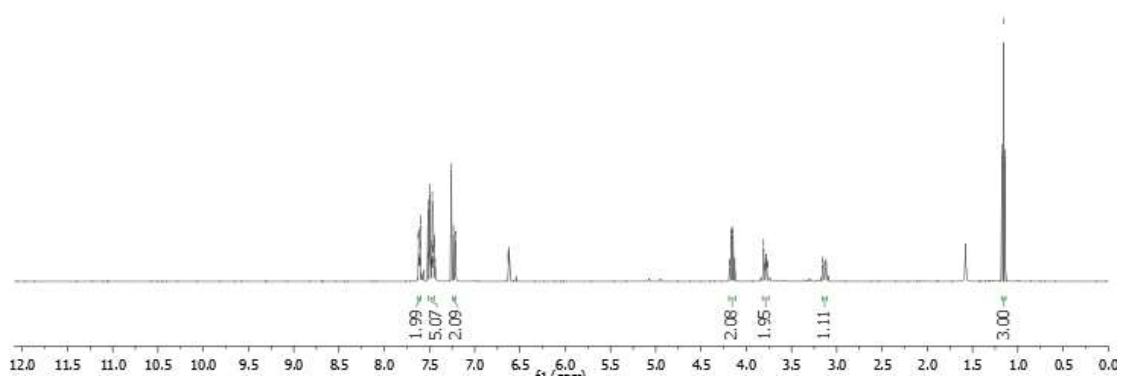
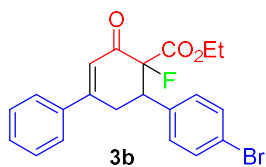
3. NMR Spectra of Products



CARBON_01
xin-robinson-a-f-ethylester

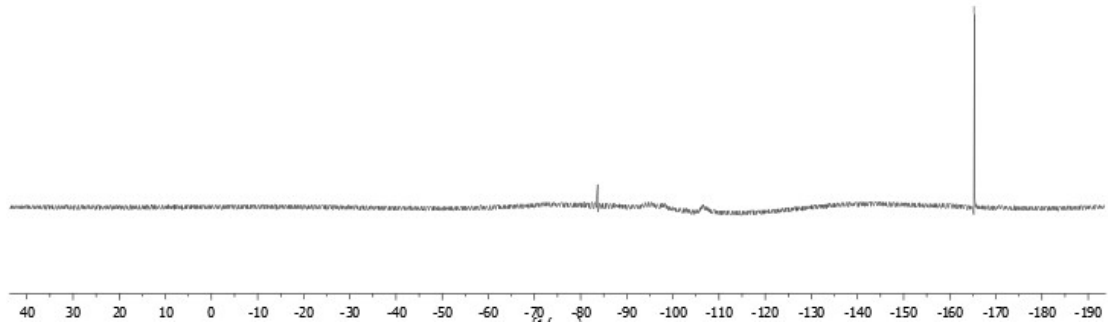


7.66, 7.64, 7.61, 7.61, 7.60, 7.60, 7.60, 7.51, 7.51, 7.50, 7.49, 7.49, 7.48, 7.48, 7.47, 7.47, 7.47, 7.46, 7.46, 7.46, 7.45, 7.45, 7.45, 7.44, 7.26, 7.23, 7.21, 6.63, 6.63, 6.62, 6.62, 4.18, 4.18, 4.16, 4.16, 4.15, 4.14, 4.13, 4.13, 3.81, 3.78, 3.78, 3.77, 3.77, 3.77, 3.15, 3.15, 3.12, 1.17, 1.16, 1.14

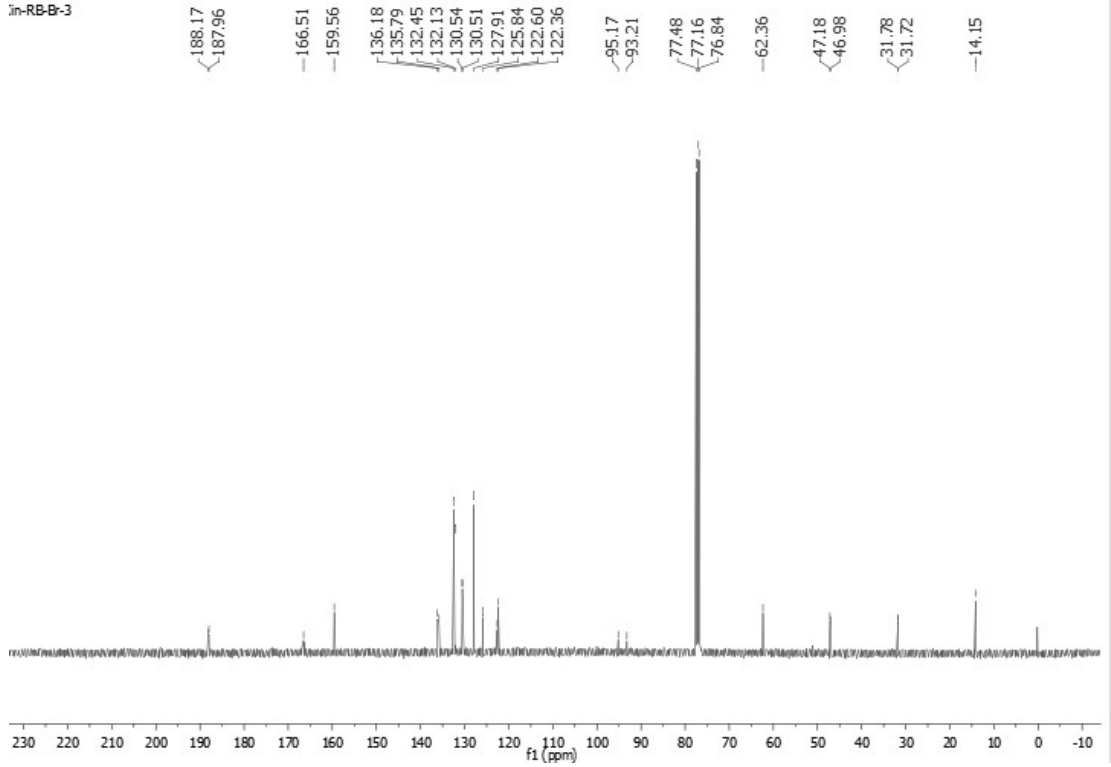


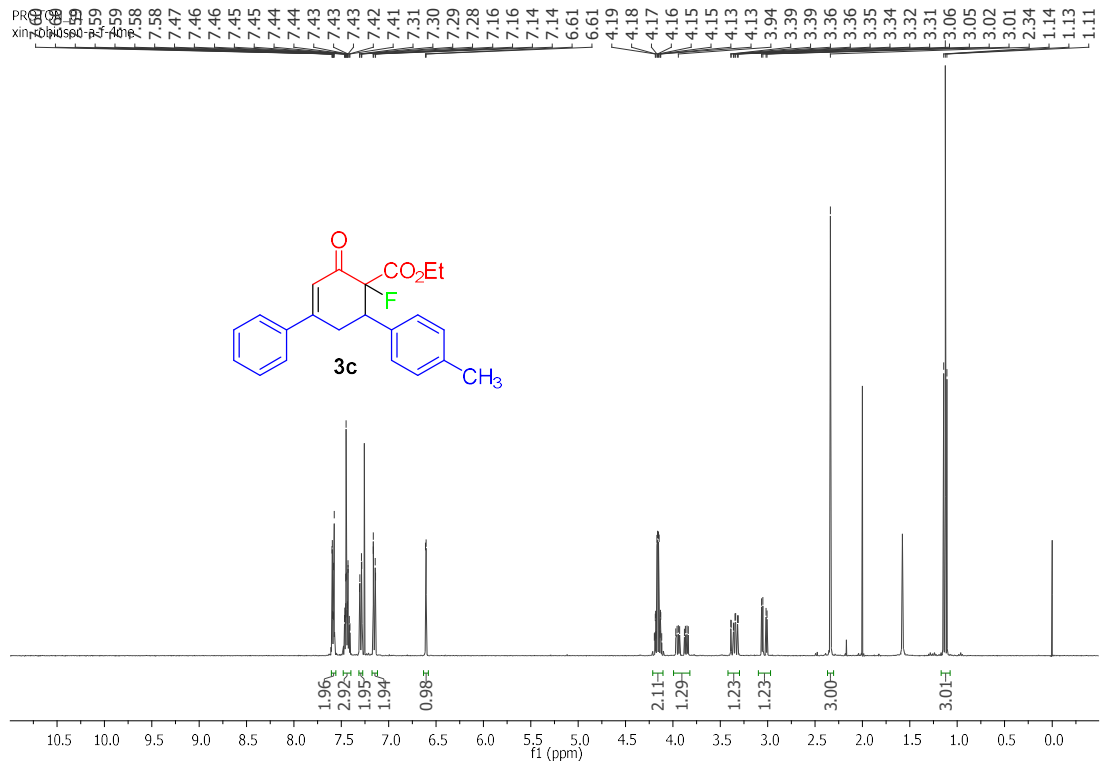
Xin-RB-B-3

---165.24



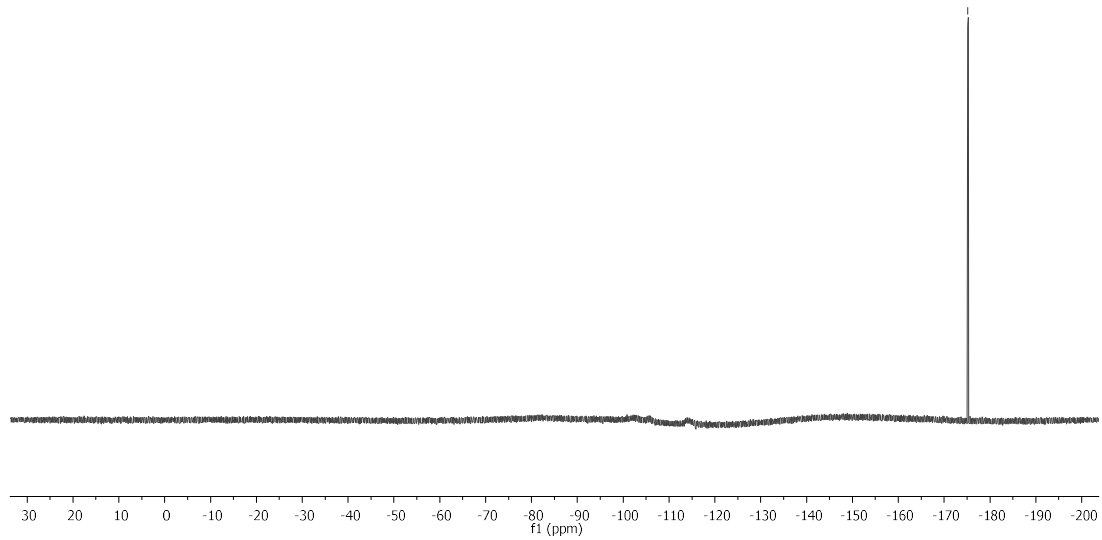
in-RB-B-3



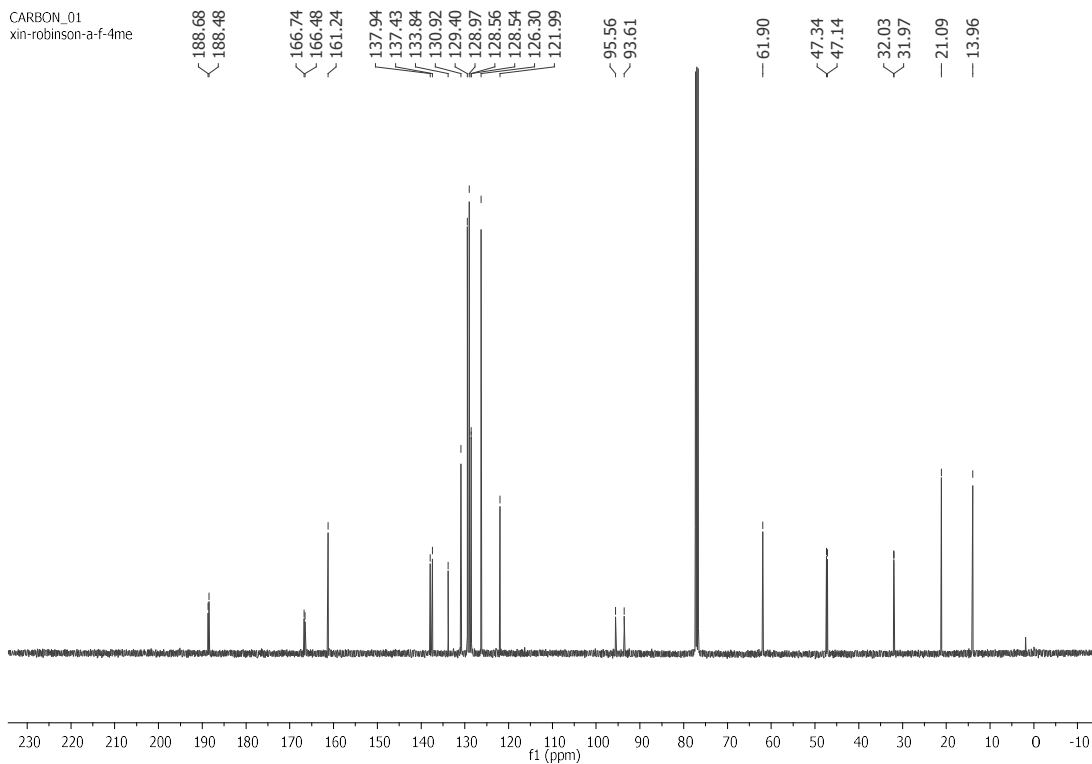


FLUORINE_01
STANDARD FLUORINE PARAMETERS

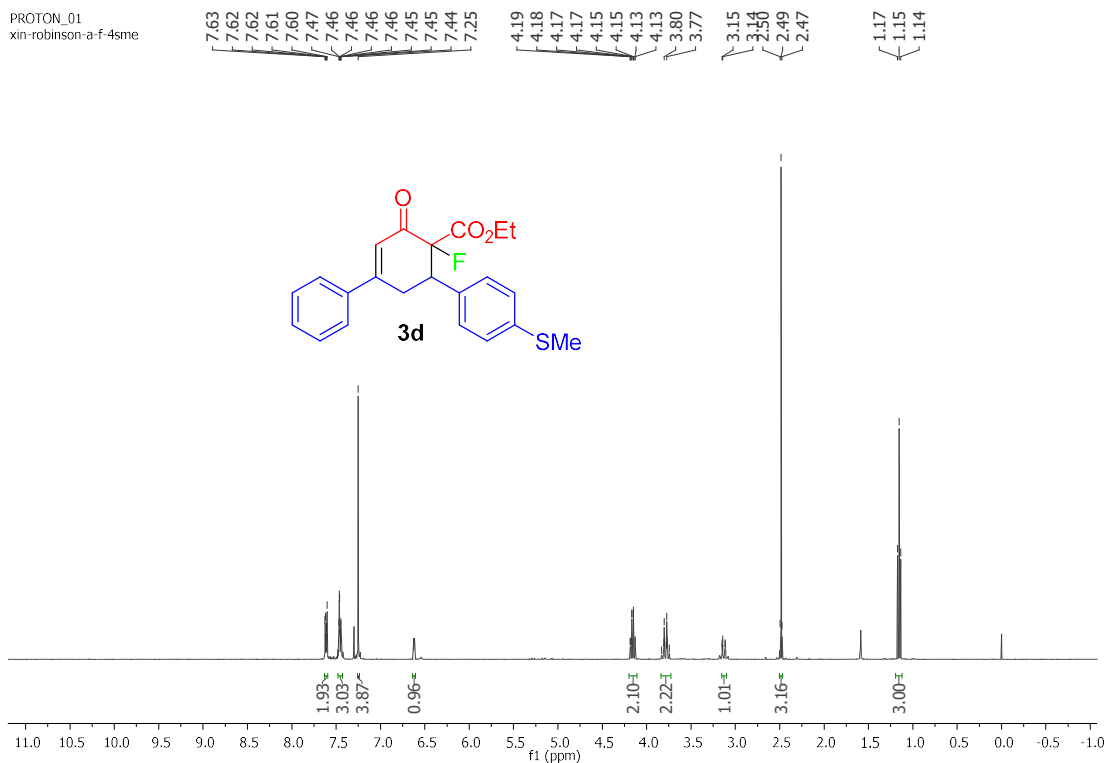
--175.16



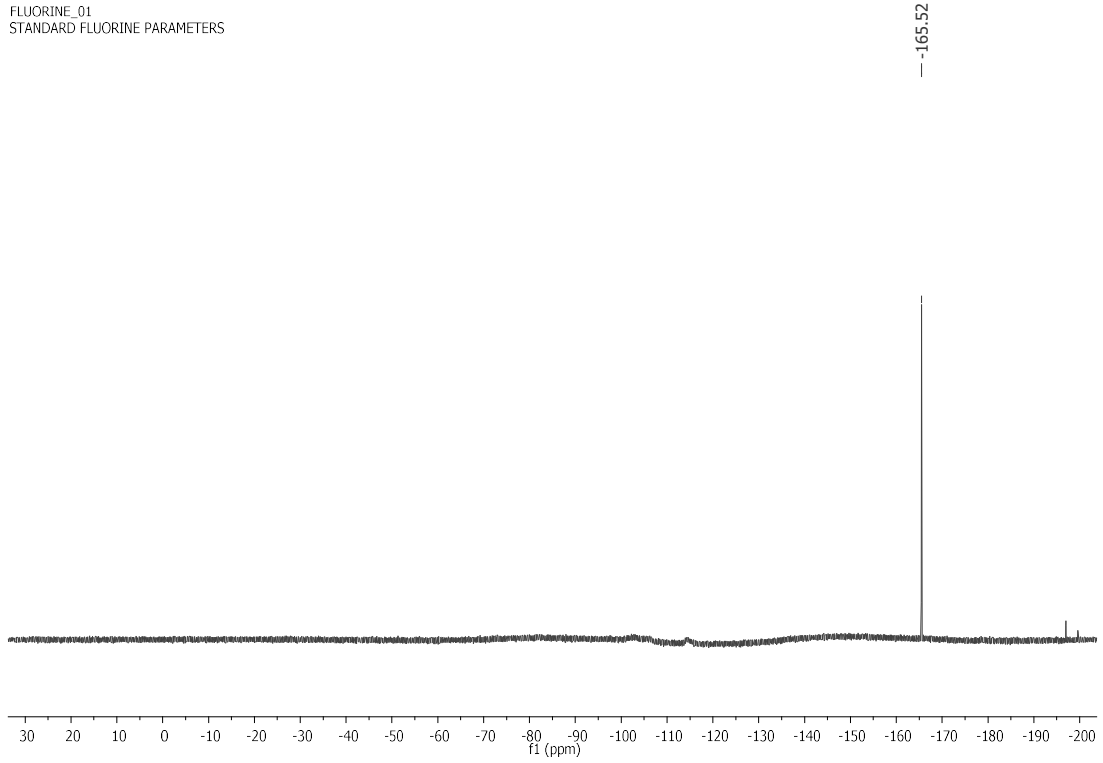
CARBON_01
xin-robinson-a-f-4me



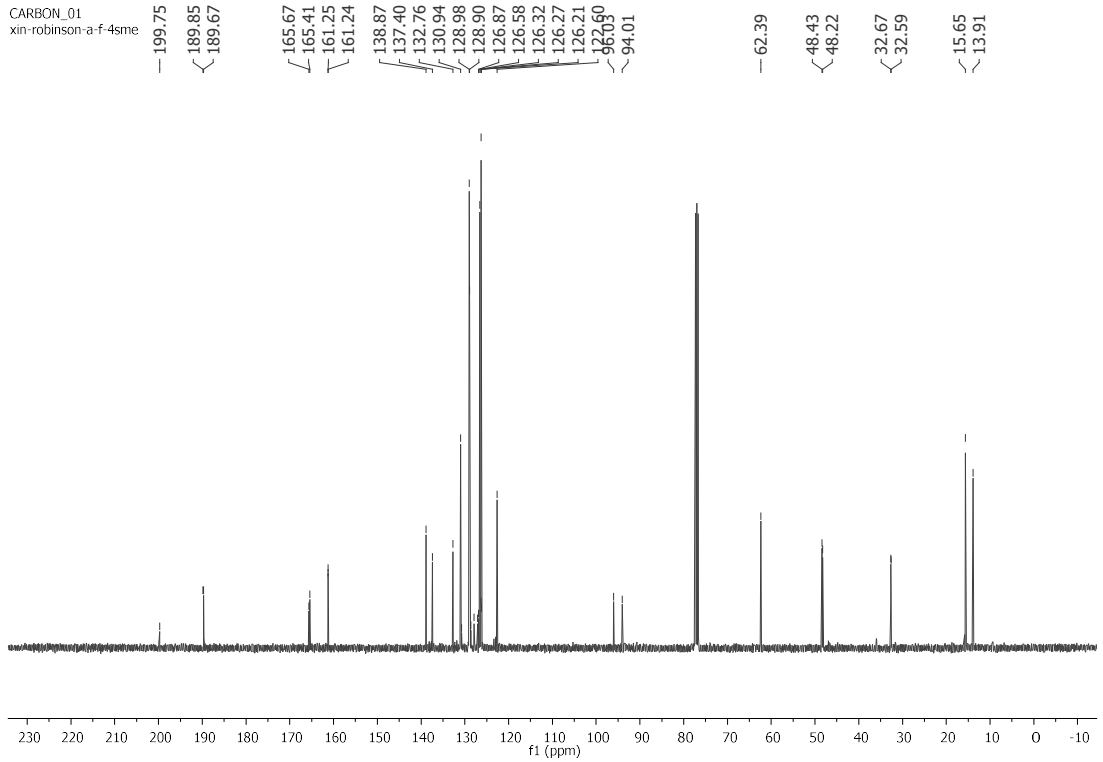
PROTON_01
xin-robinson-a-f-4me

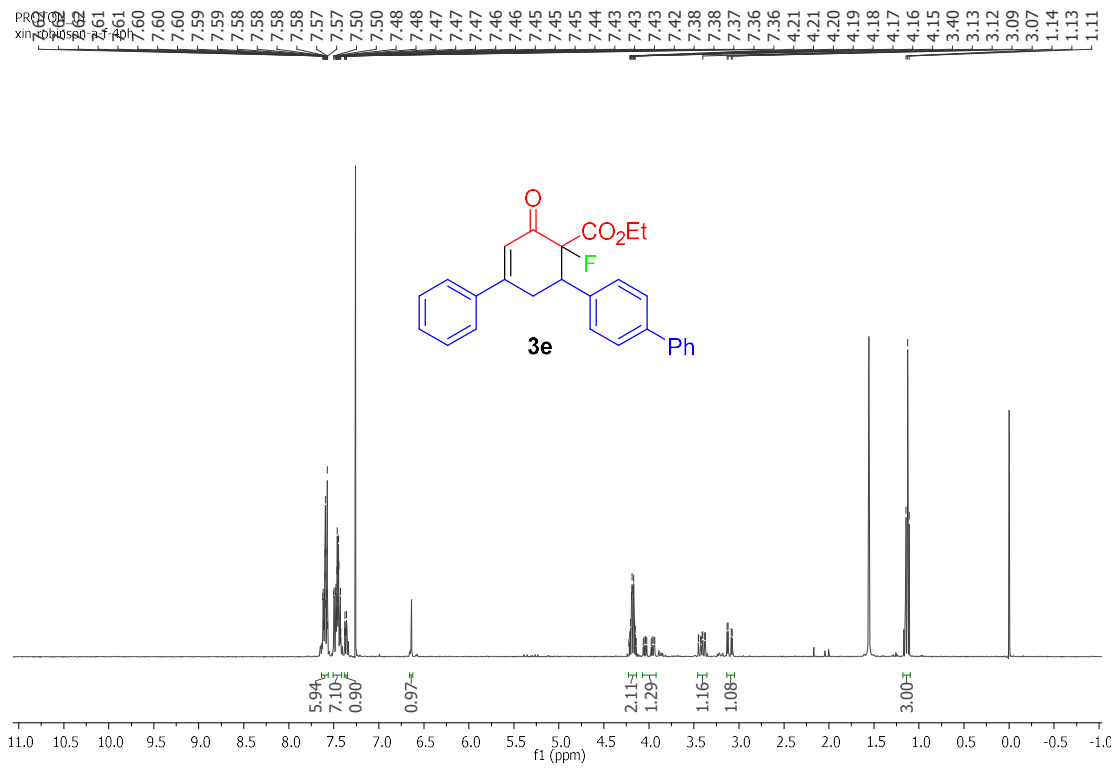


FLUORINE_01
STANDARD FLUORINE PARAMETERS



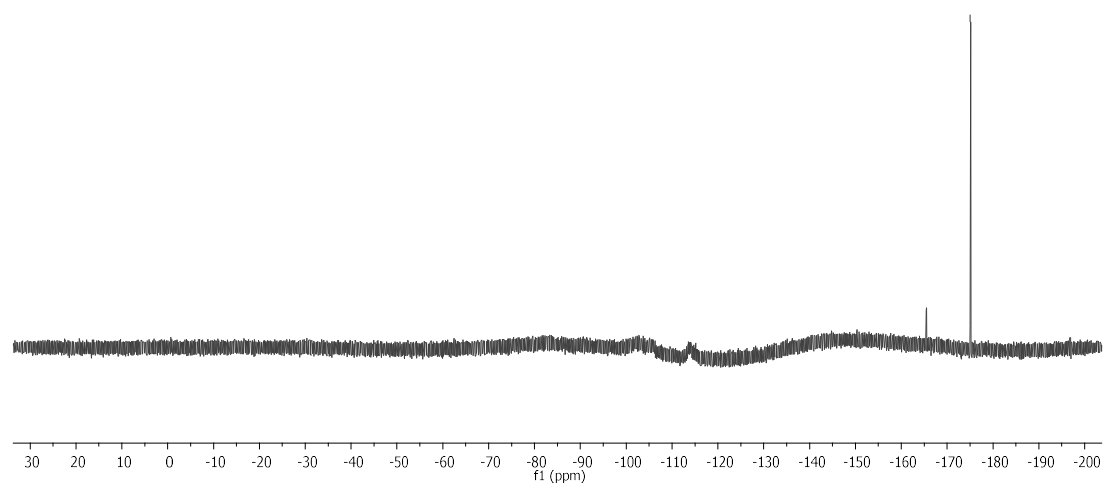
CARBON_01
xin-robinson-a-f-4sme



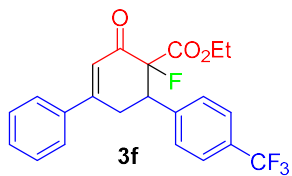
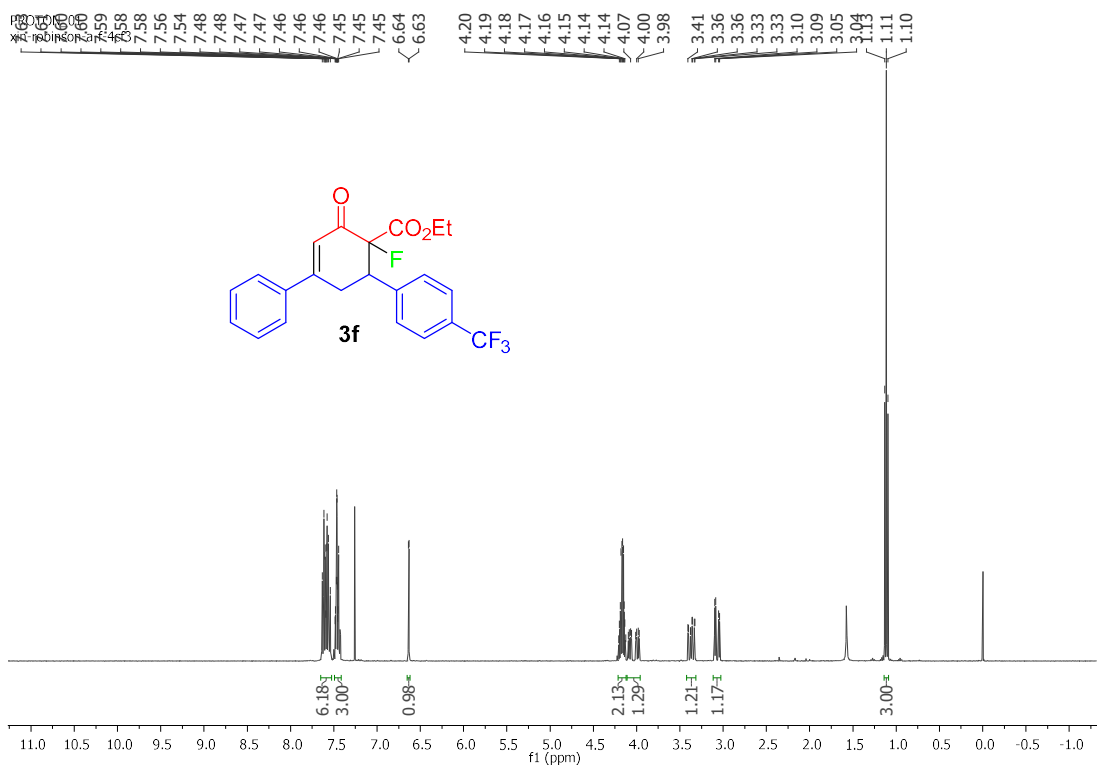
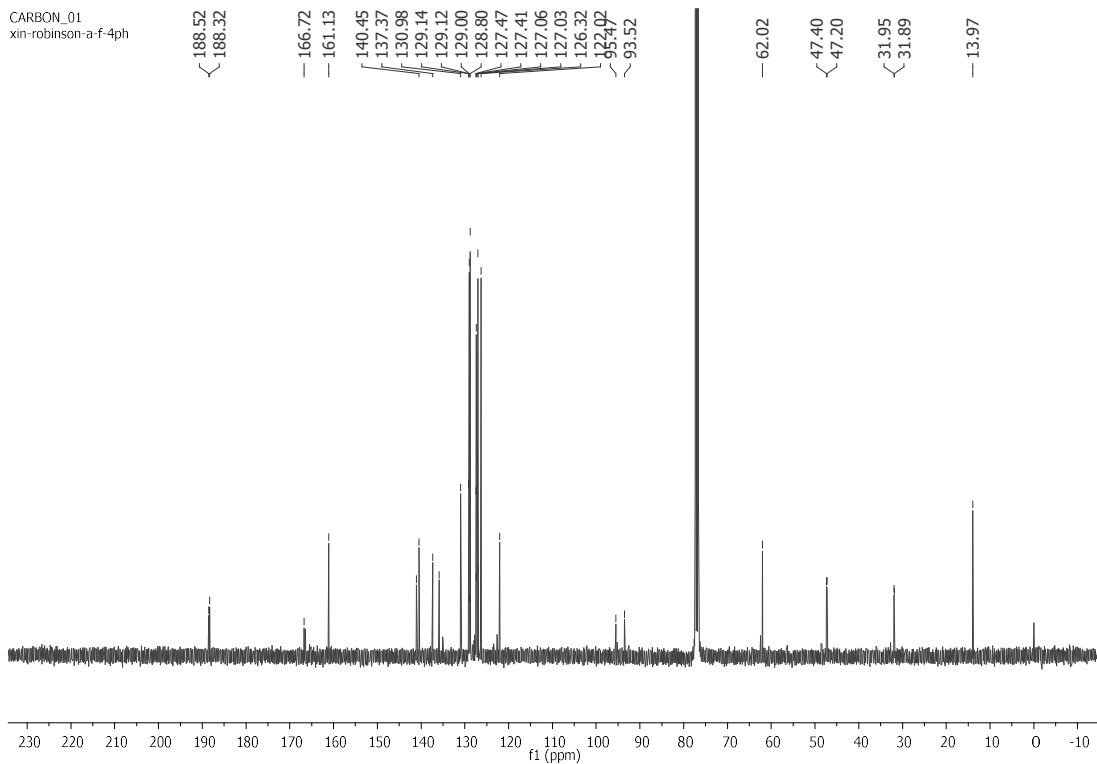


FLUORINE_01
xin-robinson-a-f-4ph

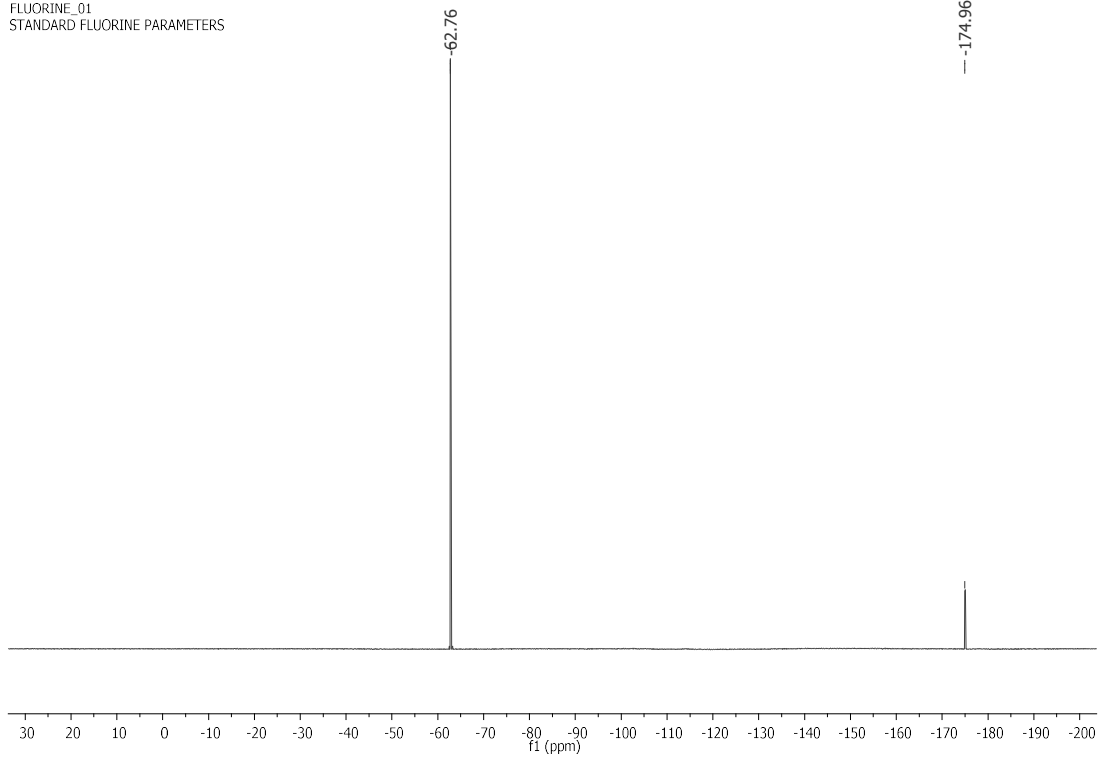
-- -175.02



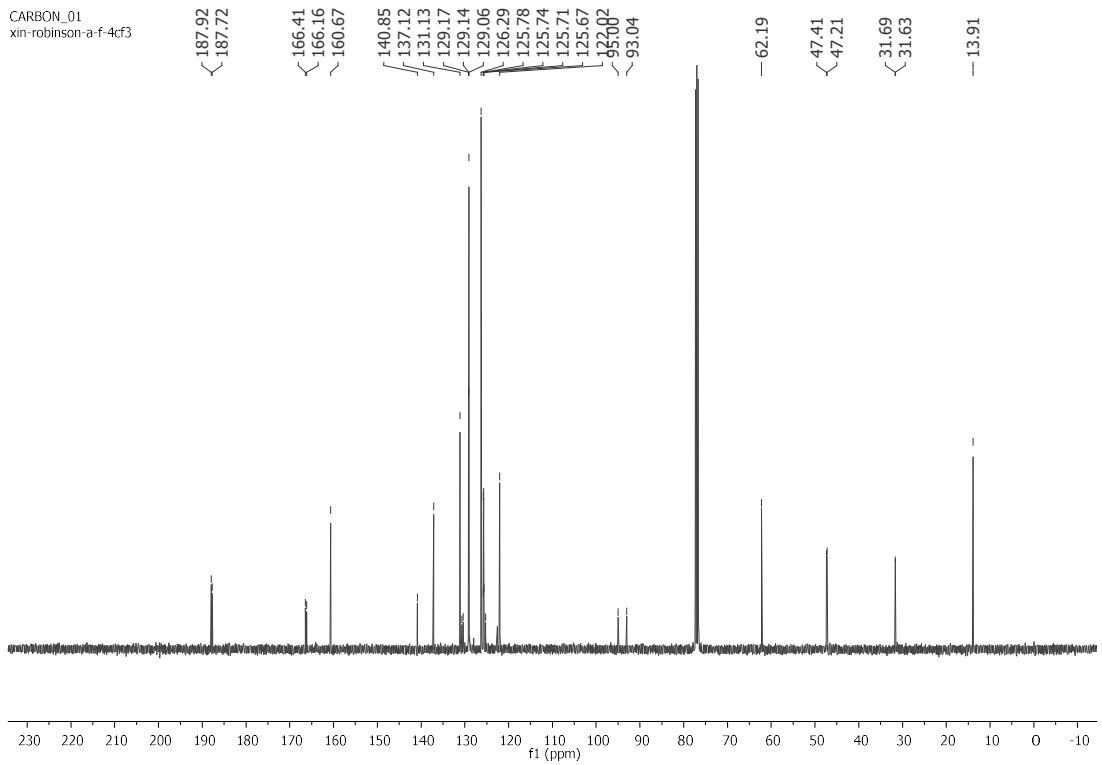
CARBON_01
xin-robinson-a-f-4ph

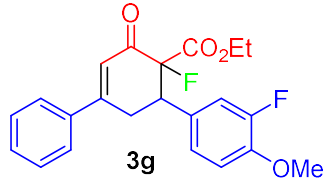
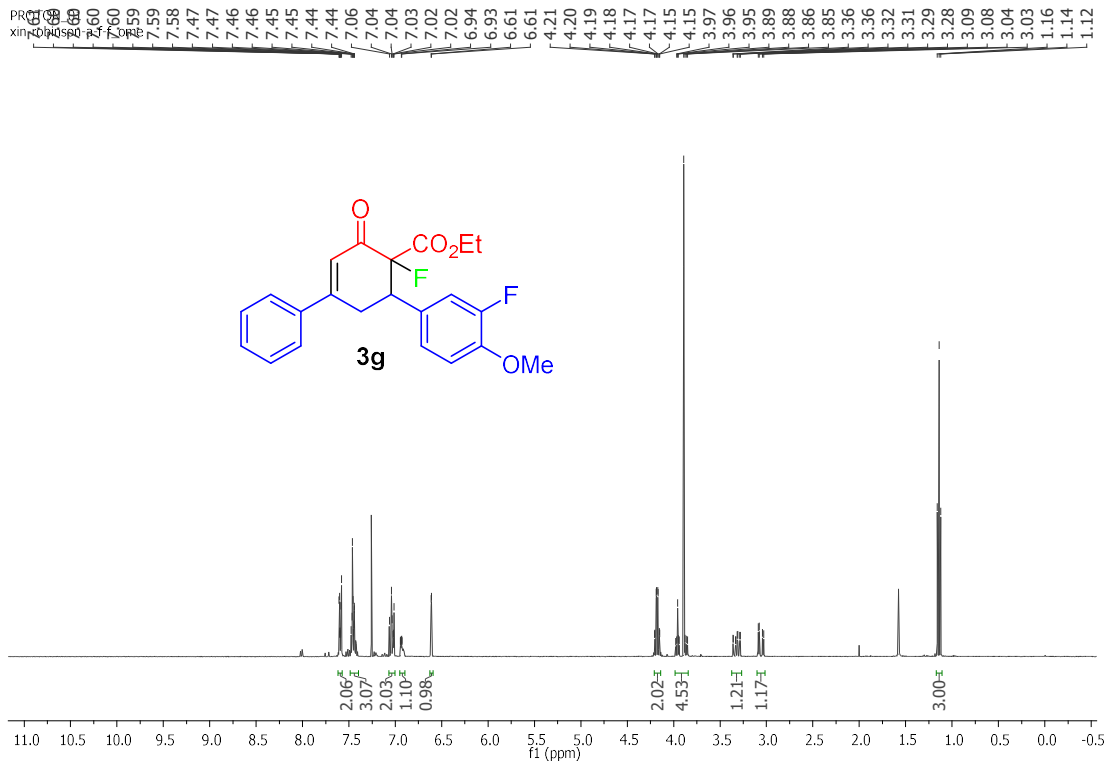


FLUORINE_01
STANDARD FLUORINE PARAMETERS



CARBON_01
xin-robinson-a-f-4cf3

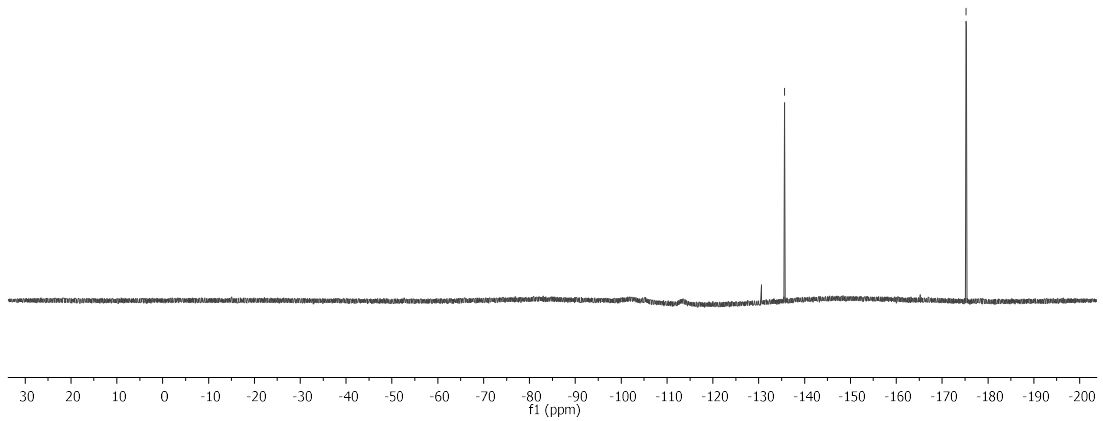




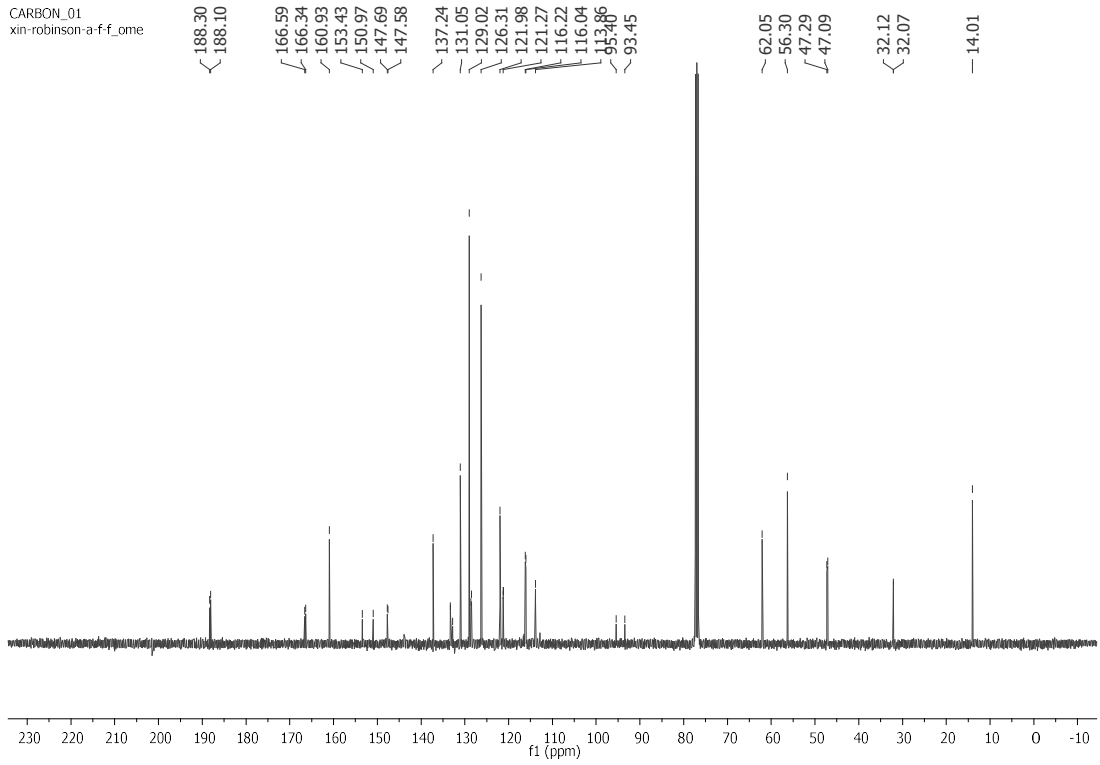
FLUORINE_01
xin-robinson-a-f-f_ome

-135.60

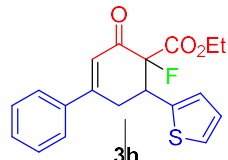
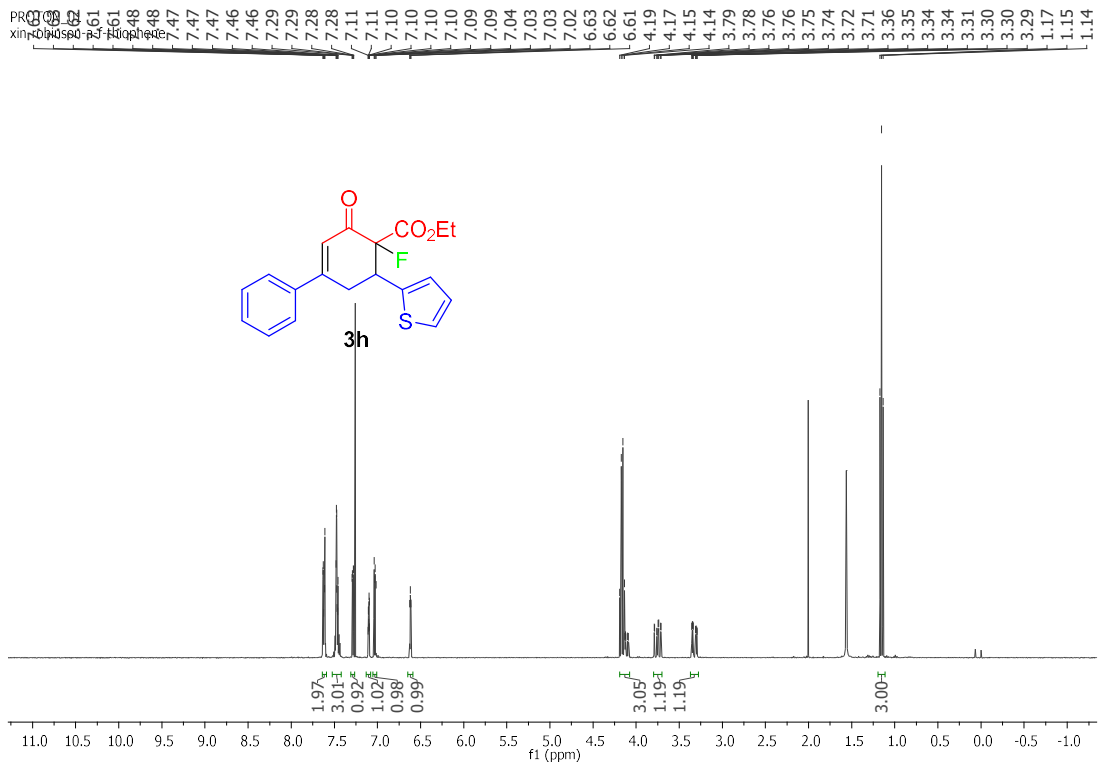
-175.19



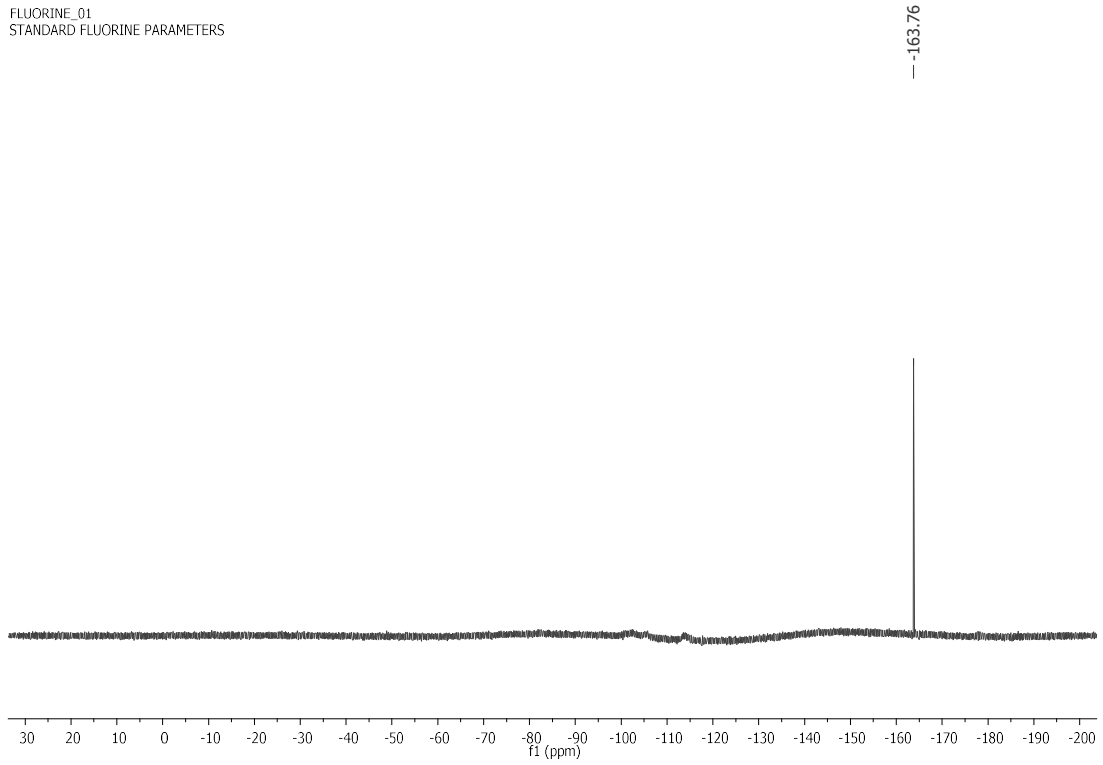
CARBON_01
xin-robinson-a-f-f_ome



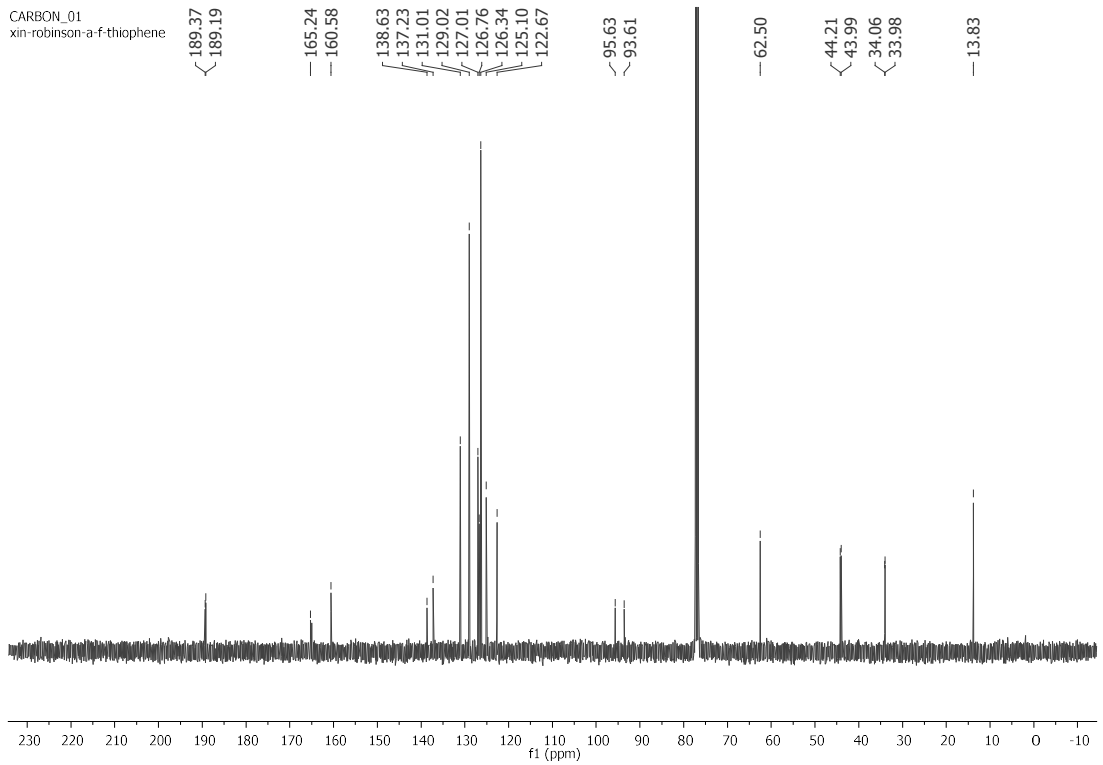
PROB 125
xin-robinson-a-f-f_ome

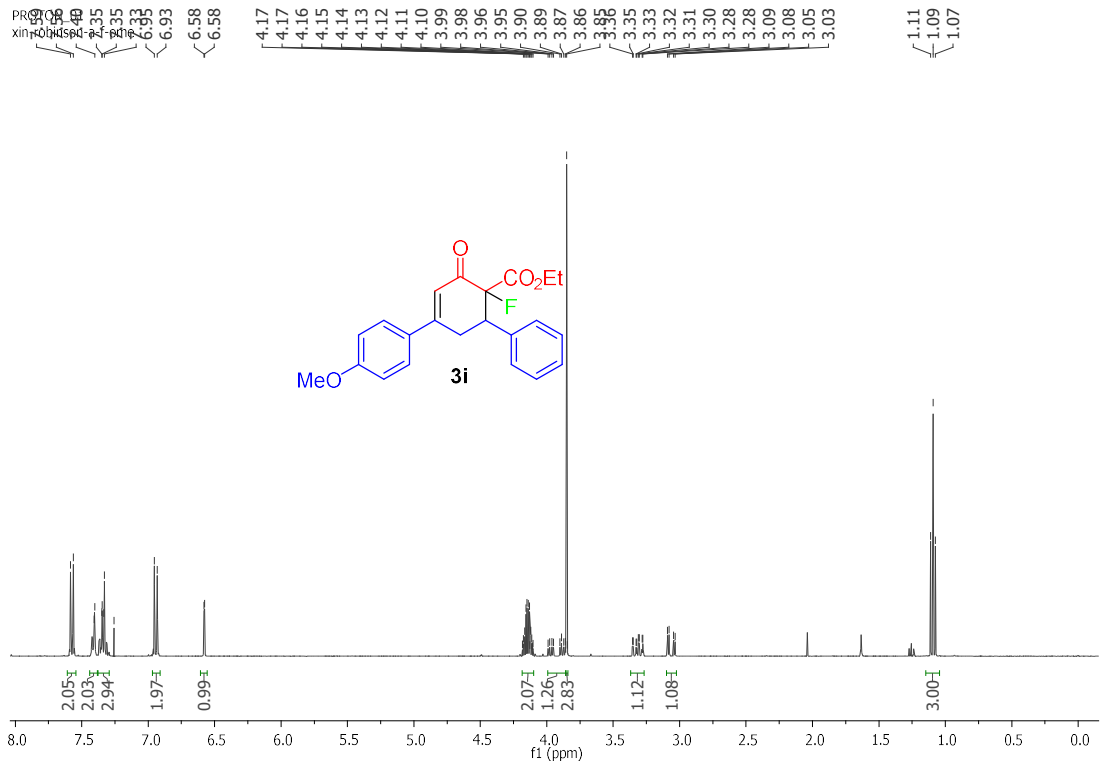


FLUORINE_01
STANDARD FLUORINE PARAMETERS



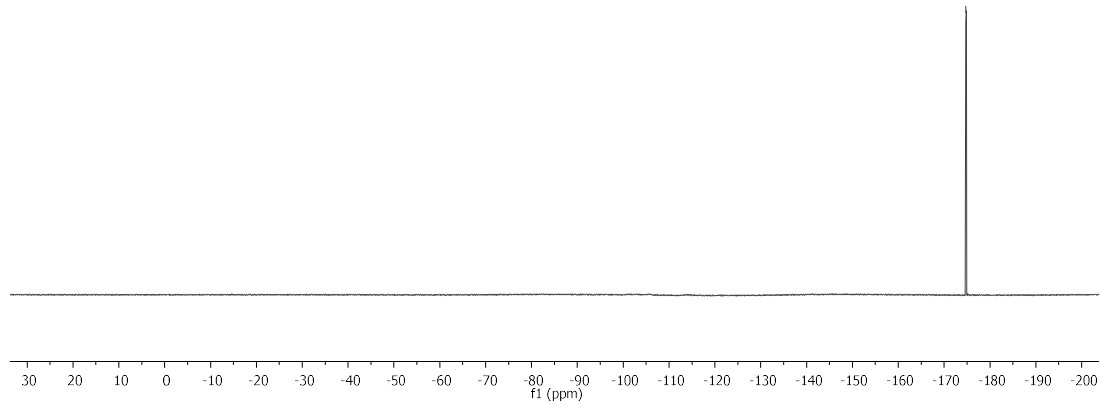
CARBON_01
xin-robinson-a-f-thiophene





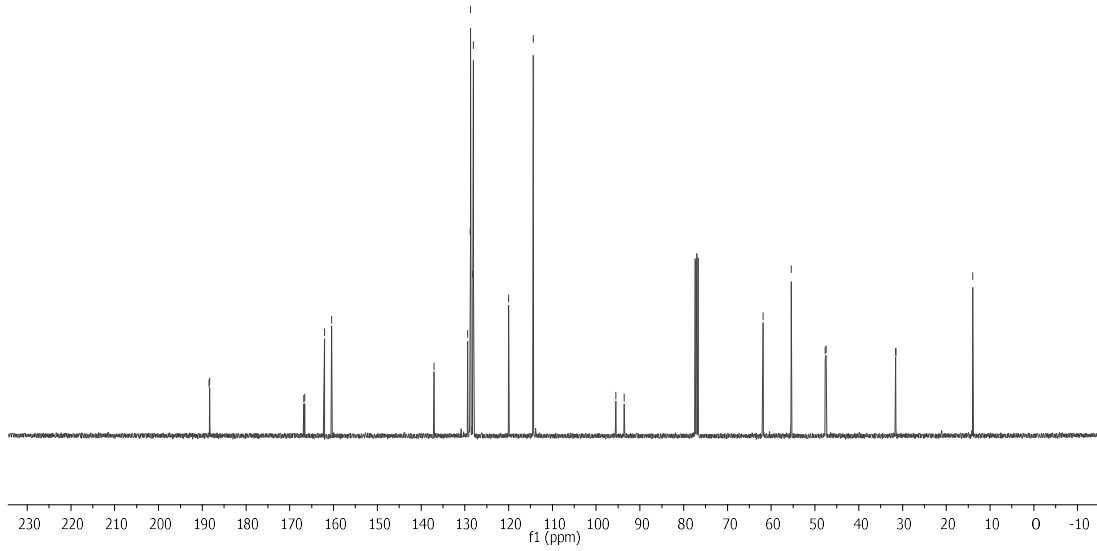
FLUORINE_01
 STANDARD FLUORINE PARAMETERS

--174.75



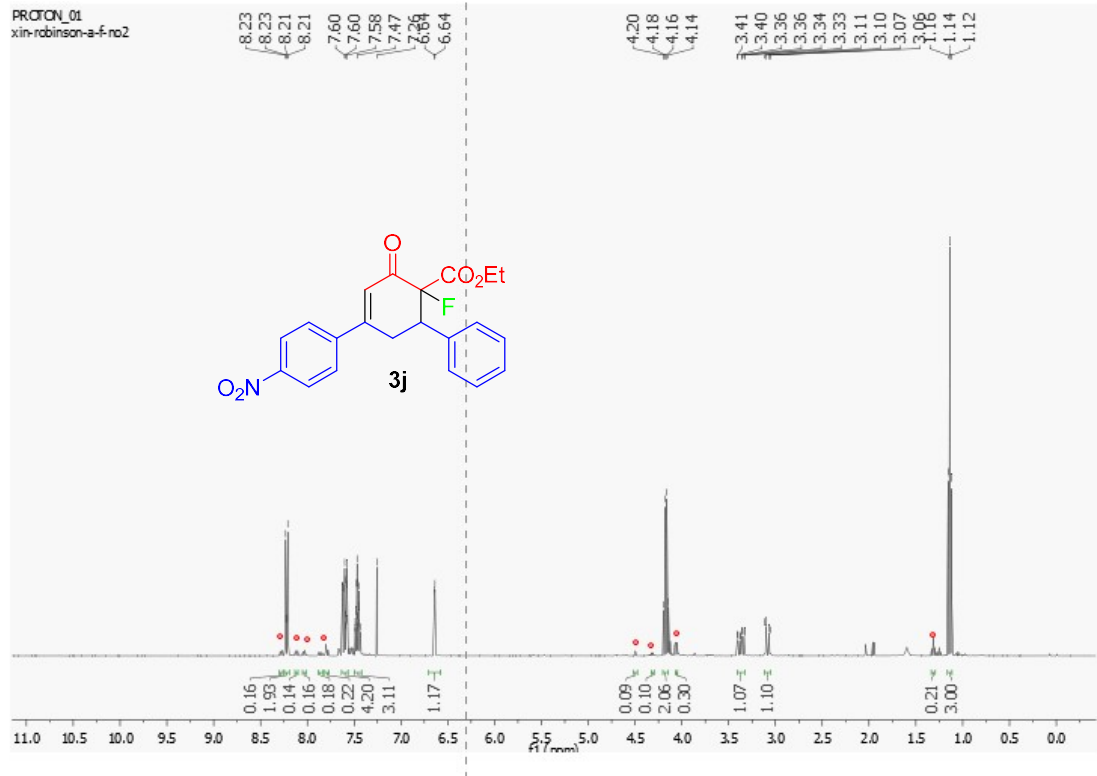
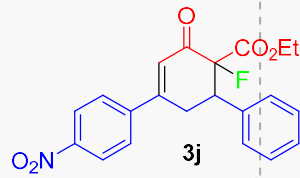
CARBON_01
xin-robinson-a-f-ome

188.48
188.28
166.84
166.59
162.06
160.42
137.02
129.33
128.75
128.72
128.17
128.03
120.00
114.39
95.51
93.56
61.87
55.45
47.64
47.44
31.59
31.54
13.93



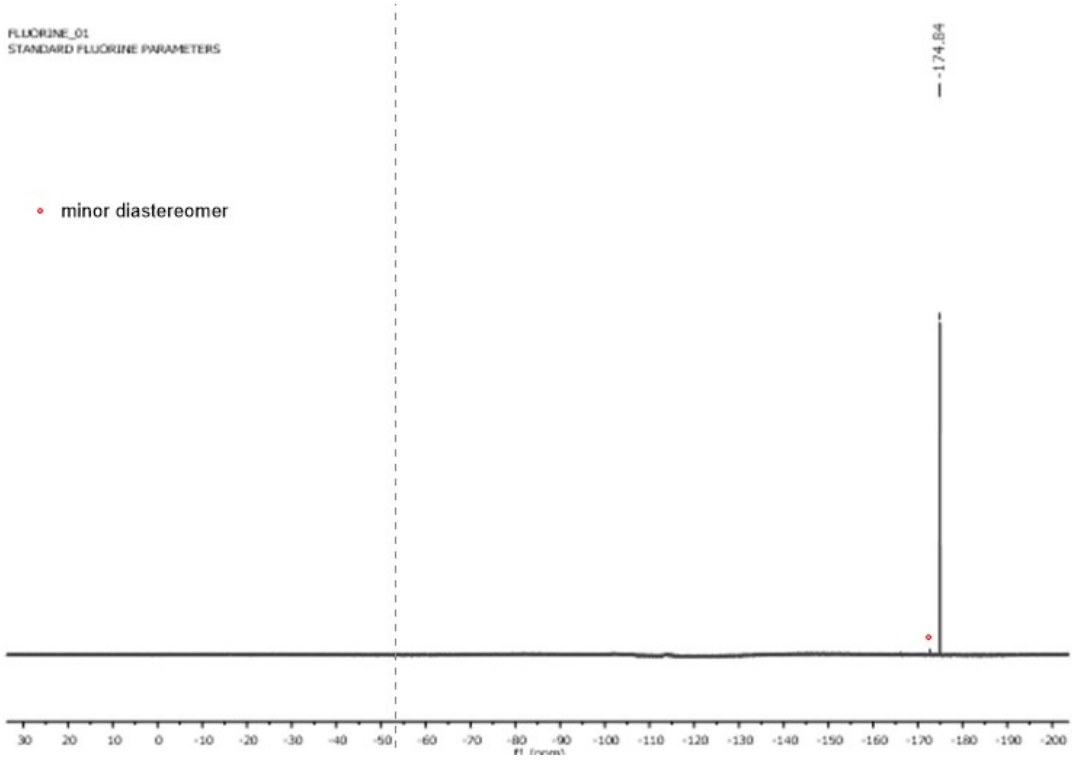
PROTON_01
xin-robinson-a-f-no2

8.23
8.23
8.21
8.21
7.60
7.60
7.58
7.47
7.36
7.36
6.64
4.20
4.18
4.16
4.14
3.41
3.40
3.36
3.36
3.34
3.33
3.11
3.10
3.07
3.06
1.14
1.12



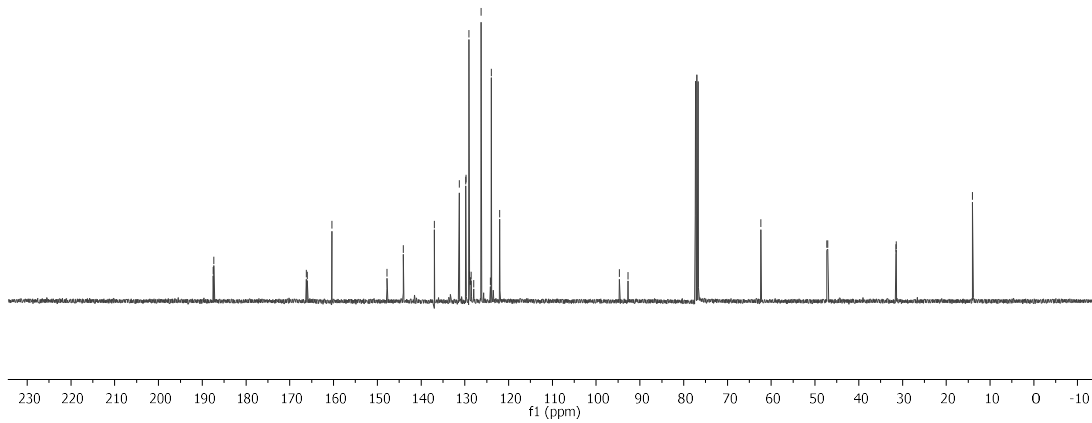
FLUORINE_01
STANDARD FLUORINE PARAMETERS

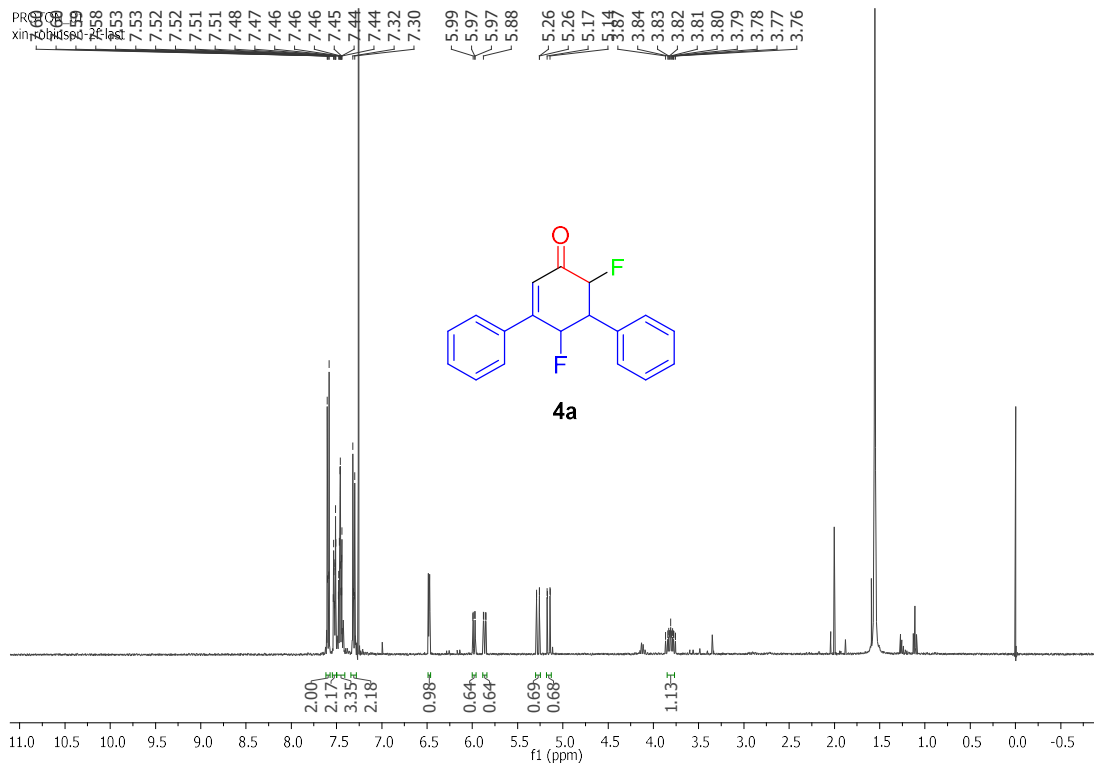
• minor diastereomer



CARBON_01
xin-robinson-a-f-no2

187.53
187.33
166.24
165.99
160.40
147.79
144.06
136.96
131.25
129.79
129.76
129.11
128.92
128.57
126.29
123.95
87.02
82.73
92.73
62.36
47.30
47.09
31.52
31.46
14.00

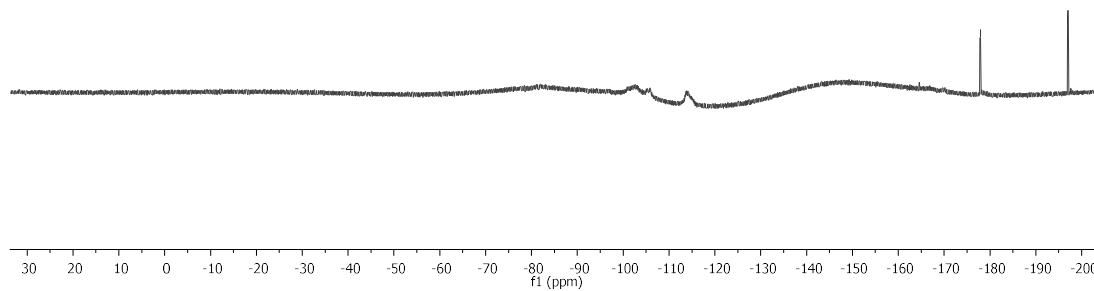


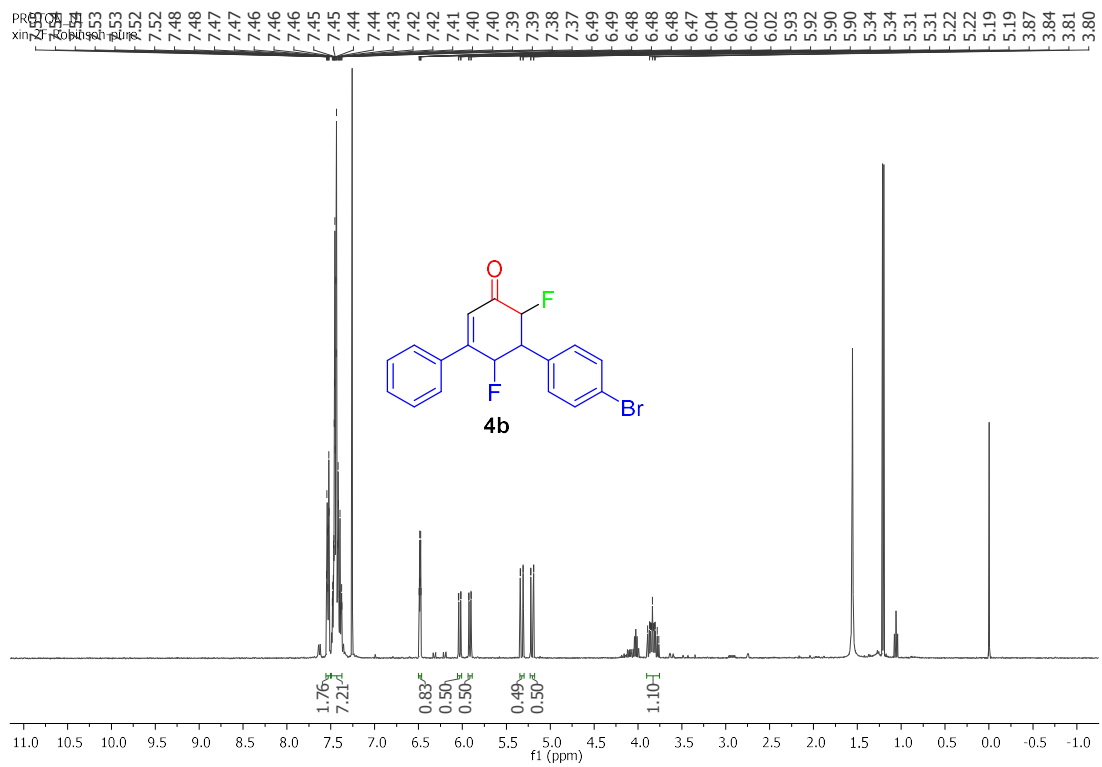
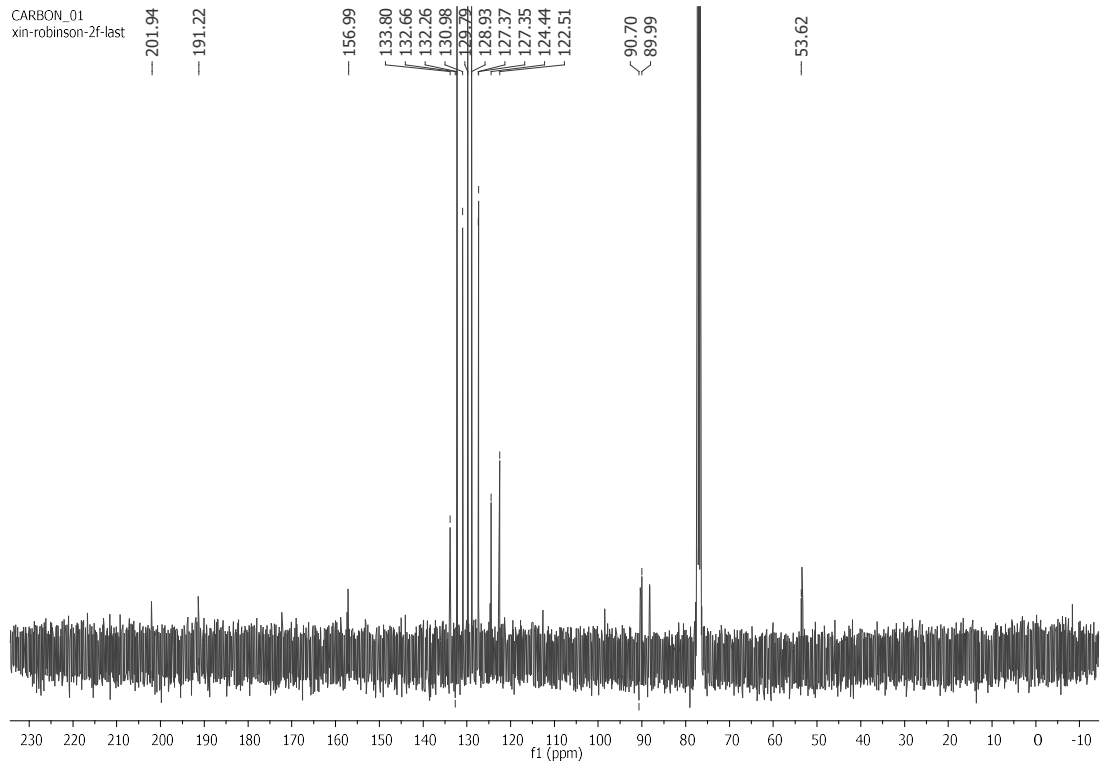


FLUORINE_02
STANDARD FLUORINE PARAMETERS

-177.97

-196.93

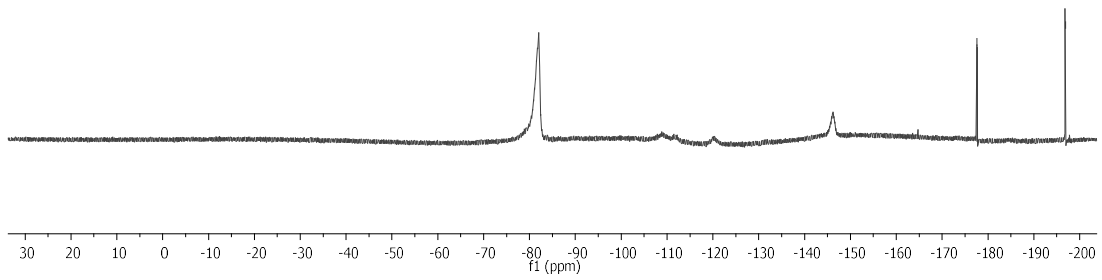




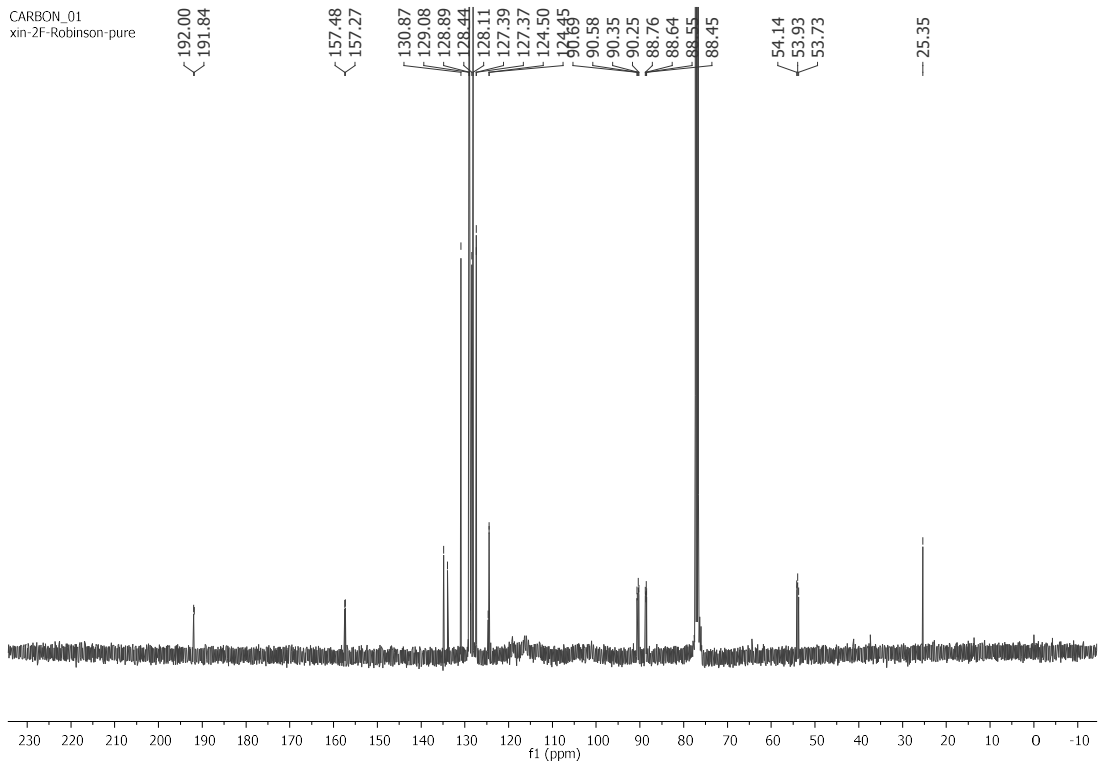
FLUORINE_01
STANDARD FLUORINE PARAMETERS

--177.60

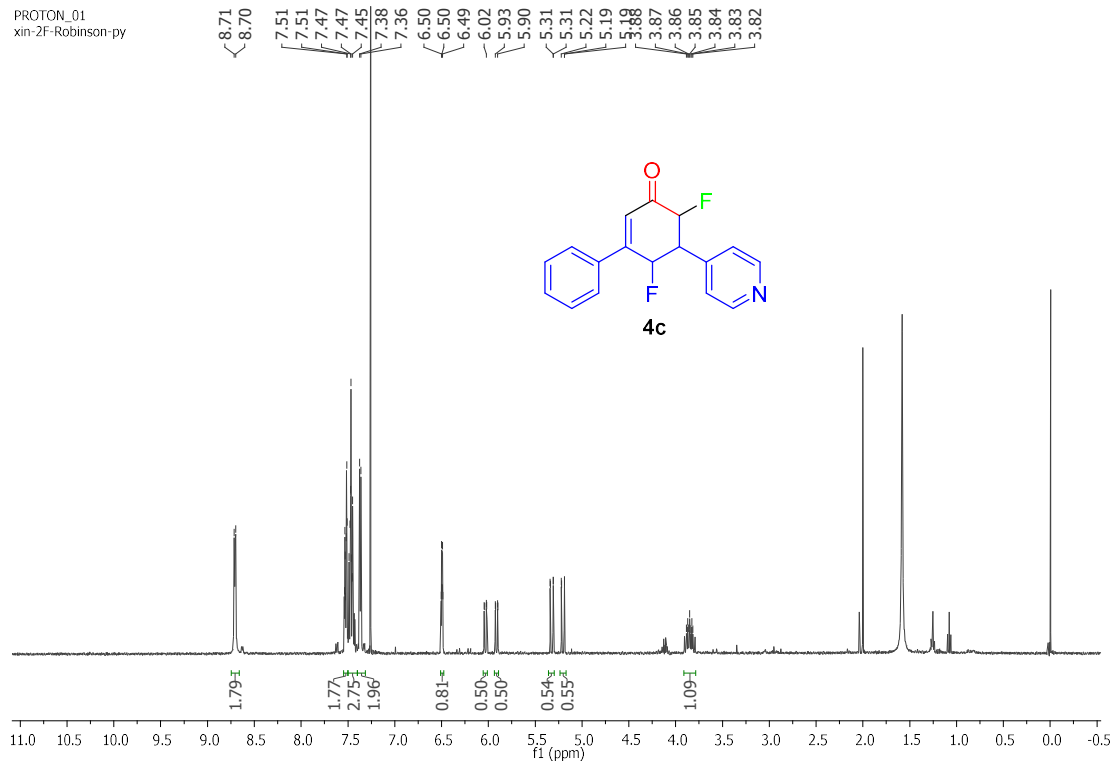
--196.92



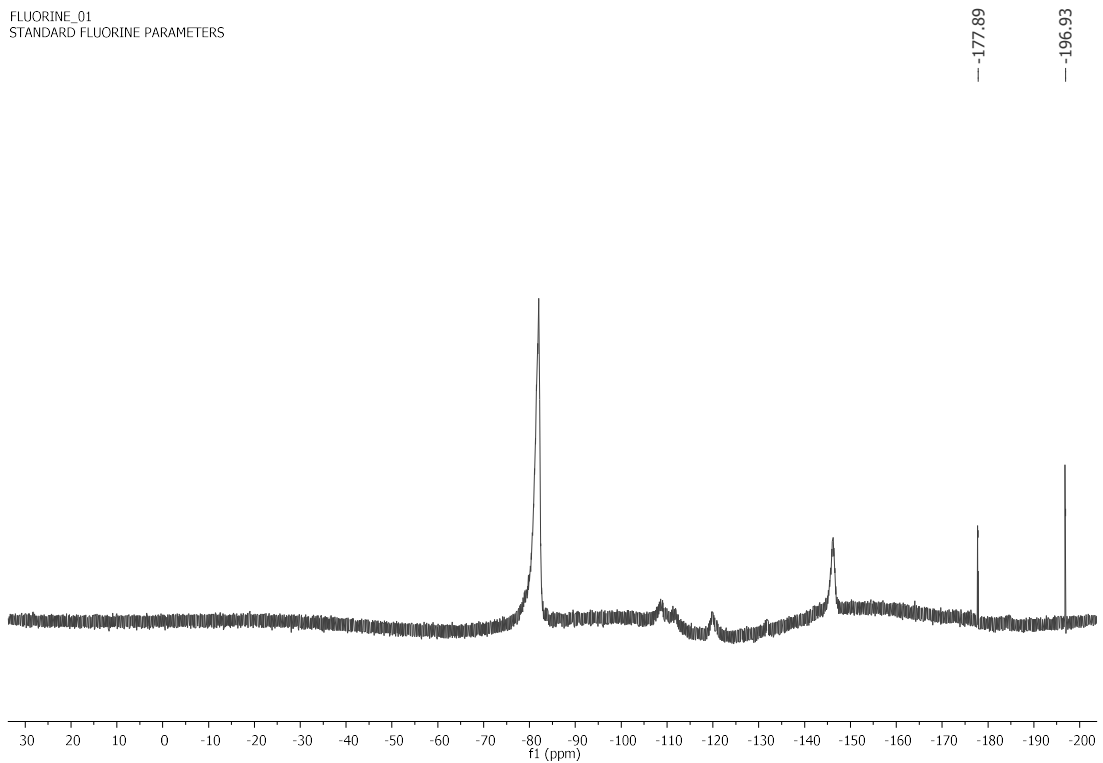
CARBON_01
xin-2F-Robinson-pure



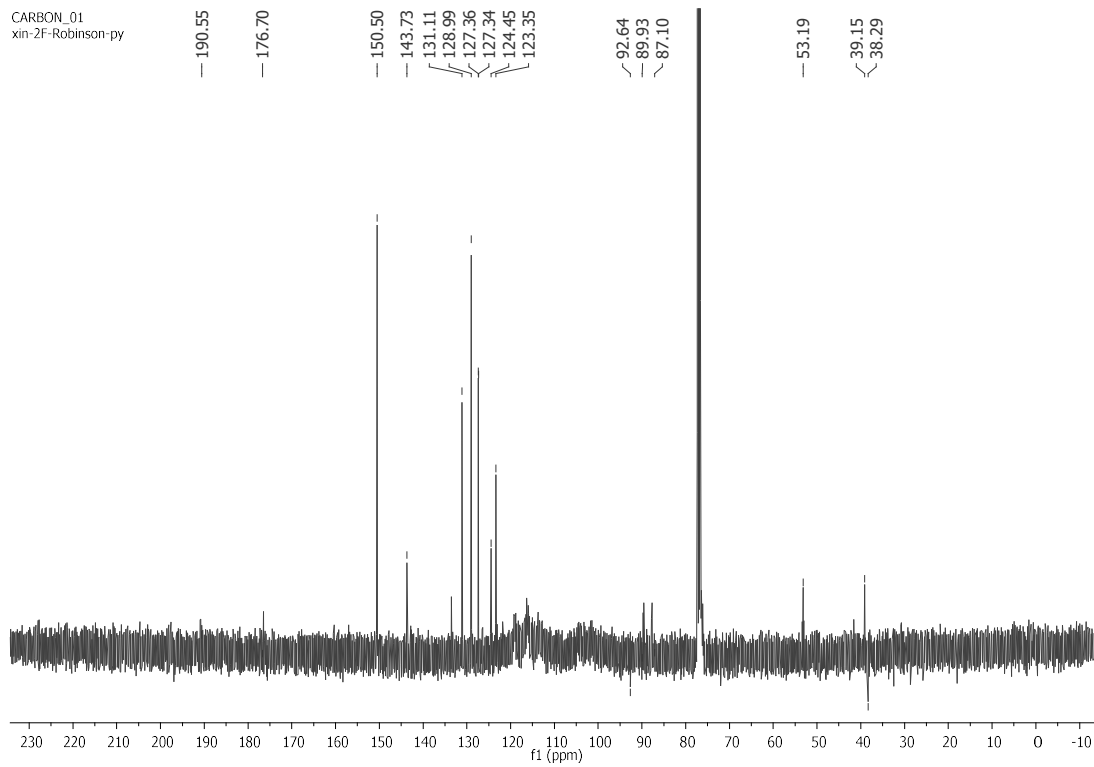
PROTON_01
xin-2F-Robinson-py



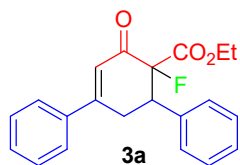
FLUORINE_01
STANDARD FLUORINE PARAMETERS



CARBON_01
xin-2F-Robinson.py

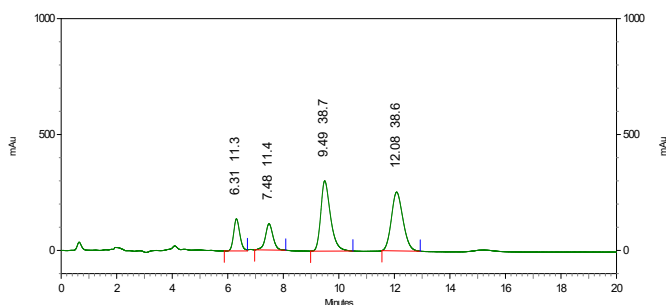


4. Chiral LC of Products



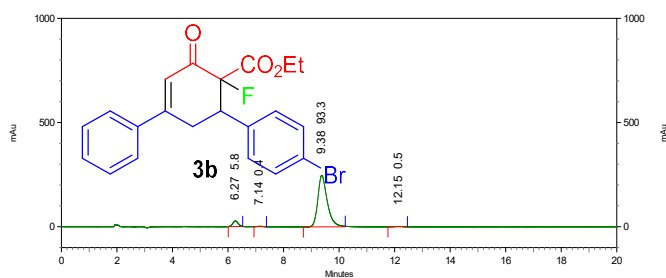
Racemic sample

Retention	Area %	Height %
6.312	11.35	17.12
7.484	11.37	14.00
9.492	38.68	37.50
12.084	38.61	31.38
Totals	100.00	100.00



Enantioenriched sample

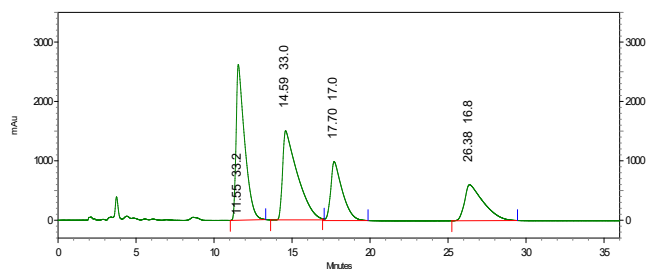
Retention	Area %	Height %
6.268	5.80	9.54
7.136	0.38	0.57
9.376	93.28	89.35
12.152	0.55	0.54
Totals	100.00	100.00



Racemic sample

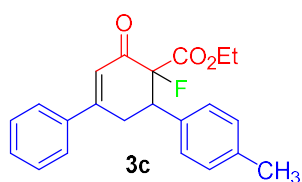
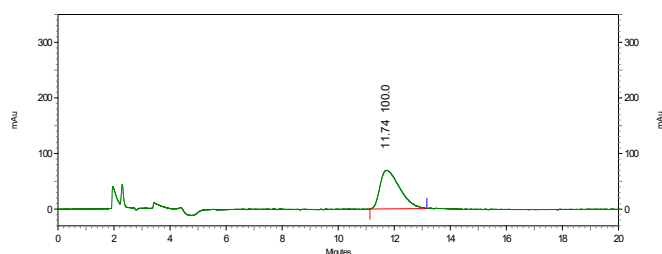
Retention	Area %	Height %
11.552	33.19	45.82
14.588	33.00	26.23
17.700	16.99	17.34

26.384	16.81	10.61
Totals	100.00	100.00



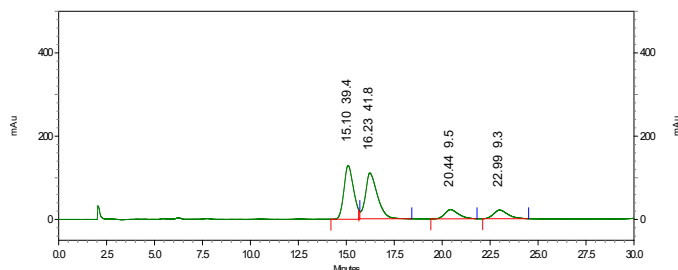
Enantioenriched sample

Retention	Area %	Height %
11.743	100.00	10.00
Totals	100.00	100.00



Racemic sample

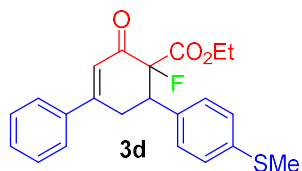
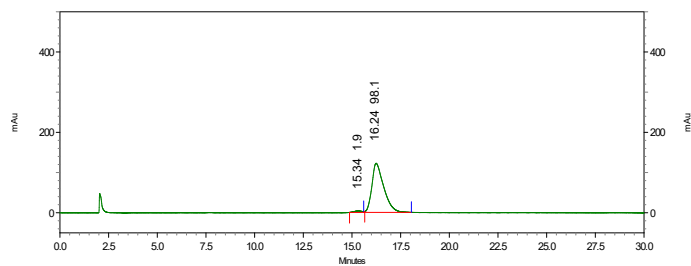
Retention	Area %	Height %
15.096	39.39	45.80
16.228	41.84	38.98
20.436	9.48	7.86
22.988	9.29	7.36
Totals	100.00	100.00



Enantioenriched sample

Retention	Area %	Height %
15.340	1.92	2.96

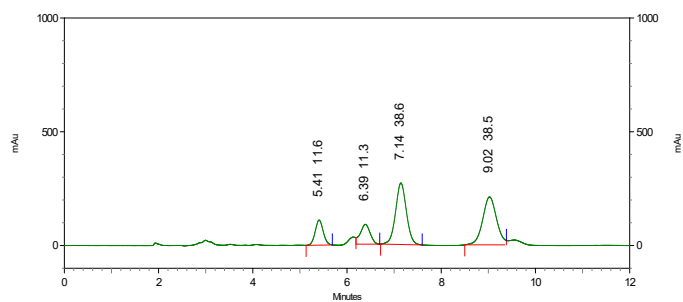
16.240	98.08	97.04
Totals	100.00	100.00



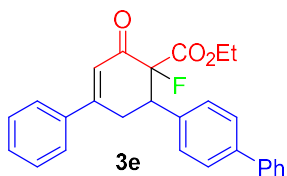
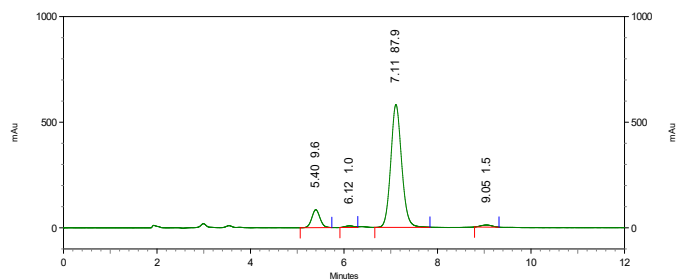
Racemic sample

Retention	Area %	Height %
5.408	11.61	16.22
6.388	11.27	12.83
7.144	38.65	39.87
9.024	38.48	31.07
Totals	100.00	100.00

Retention	Area %	Height %
5.396	9.60	12.41
6.120	0.97	1.12
7.112	87.91	85.04
9.052	1.51	1.43
Totals	100.00	100.00

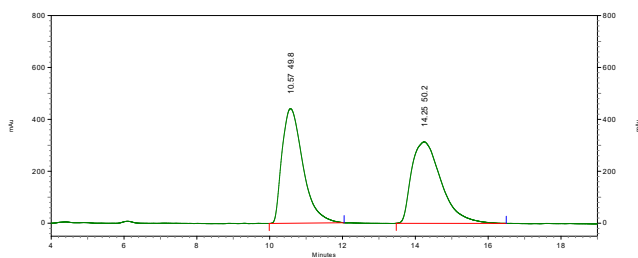


Enantioenriched sample



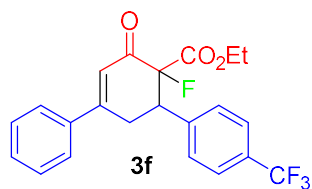
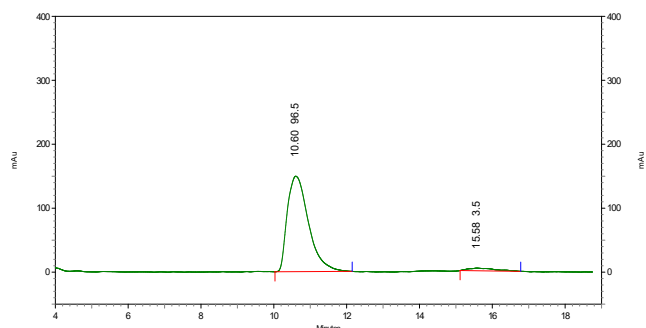
Racemic sample

Retention	Area %	Height %
10.568	49.84	58.43
14.248	50.16	41.57
Totals	100.00	100.00



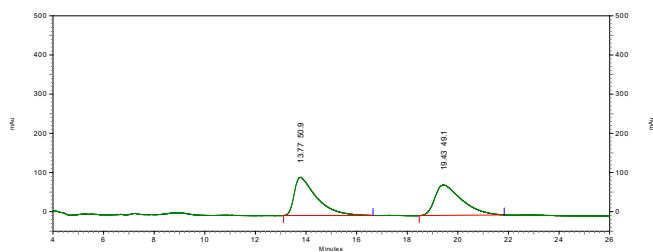
Enantioenriched sample

Retention	Area %	Height %
10.604	96.52	97.31
15.576	3.48	2.69
Totals	100.00	100.00



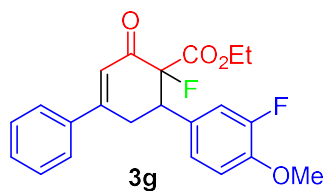
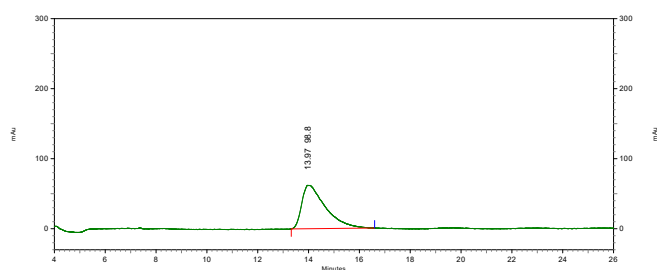
Racemic sample

Retention	Area %	Height %
13.772	50.91	55.65
19.428	49.09	44.35
Totals	100.00	100.00



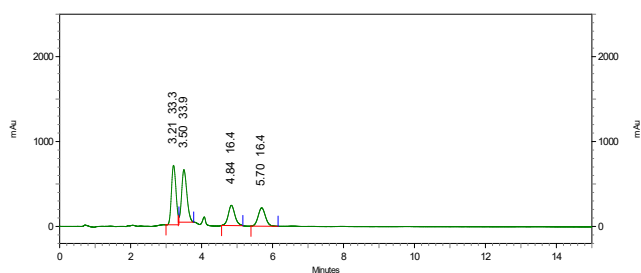
Enantioenriched sample

Retention	Area %	Height %
13.968	100.00	100.00
Totals	100.00	100.00



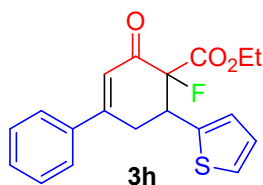
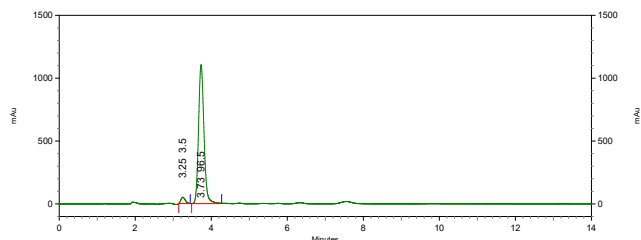
Racemic sample

Retention	Area %	Height %
3.212	33.35	39.53
3.504	33.89	34.83
4.840	16.40	13.45
5.696	16.35	12.19
Totals	100.00	100.00



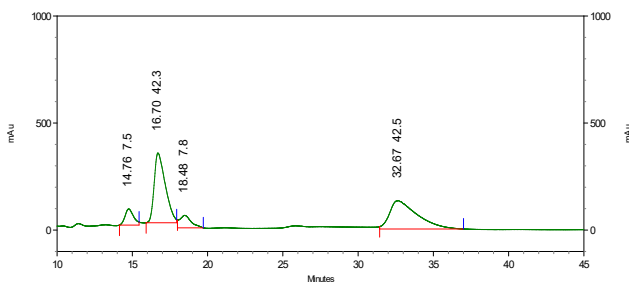
Enantioenriched sample

Retention	Area %	Height %
3.252	3.46	4.30
3.732	96.54	95.70
Totals	100.00	100.00



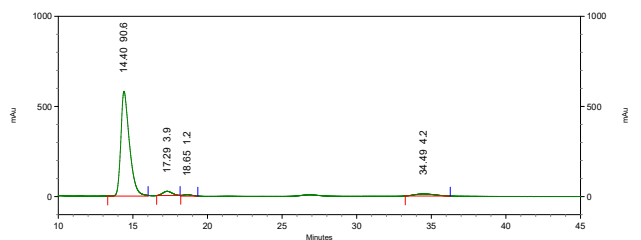
Racemic sample

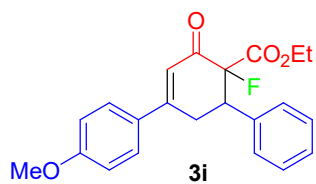
Retention	Area %	Height %
14.764	7.48	12.71
16.696	42.26	55.03
18.480	7.77	9.85
32.668	42.48	22.41
Totals	100.00	100.00



Enantioenriched sample

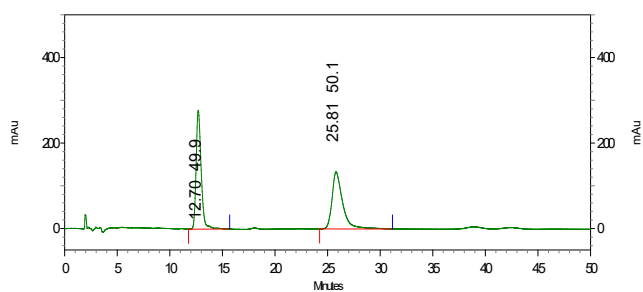
Retention	Area %	Height %
14.402 (major)	90.62	93.22
17.293 (minor)	3.88	3.83
18.649 (major)	1.21	1.12
34.490 (minor)	4.19	1.83
Totals	100.00	100.00





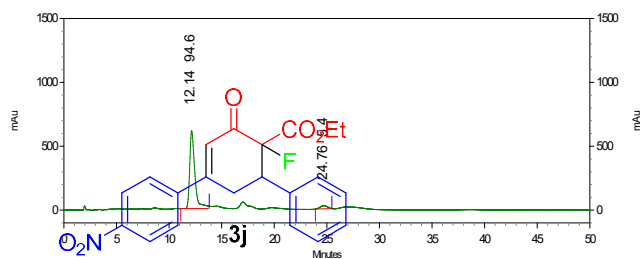
Racemic sample

Retention	Area %	Height %
12.704	49.88	67.54
25.808	50.12	32.46
Totals	100.00	100.00



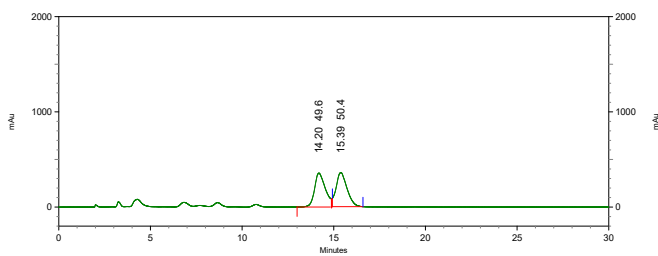
Enantioenriched sample

Retention	Area %	Height %
12.144	94.62	96.17
24.756	5.38	3.83
Totals	100.00	100.00



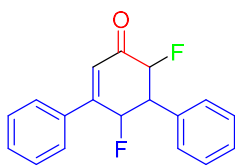
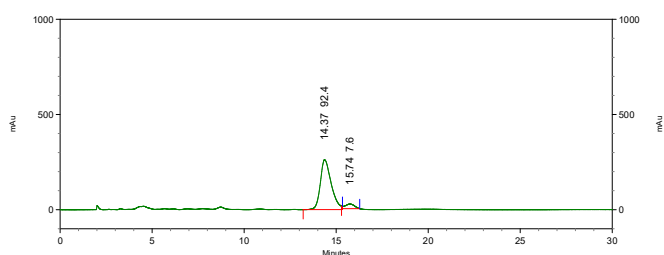
Racemic sample

Retention	Area %	Height %
14.196	49.56	49.90
15.392	50.44	50.10
Totals	100.00	100.00



Enantioenriched sample

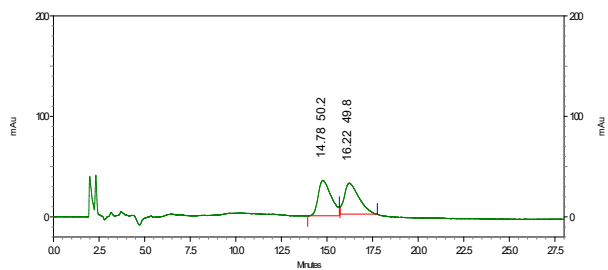
Retention	Area %	Height %
14.368	92.42	91.57
15.740	7.58	8.43
Totals	100.00	100.00



4a

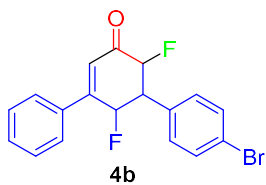
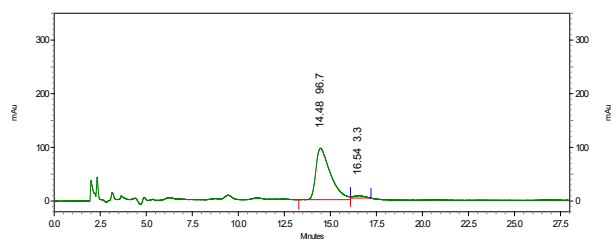
Racemic sample

Retention	Area %	Height %
14.780	50.16	53.33
16.220	49.84	46.67
Totals	100.00	100.00



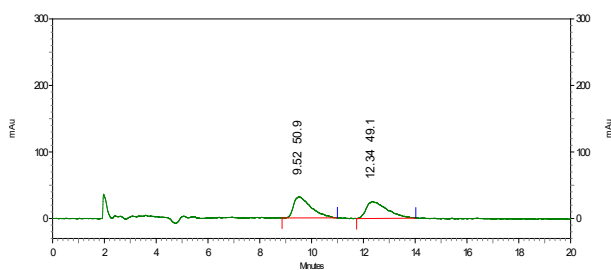
Enantioenriched sample

Retention	Area %	Height %
14.484	96.69	95.59
16.540	3.31	4.41
Totals	100.00	100.00



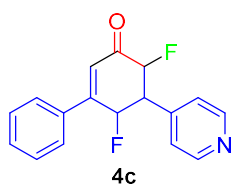
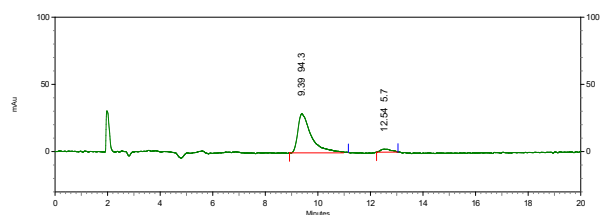
Racemic sample

Retention	Area %	Height %
9.520	50.87	55.40
12.340	49.13	44.60
Totals	100.00	100.00



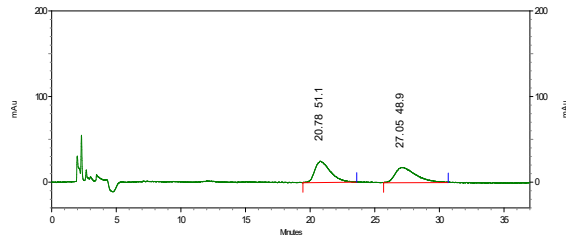
Enantioenriched sample

Retention	Area %	Height %
9.392	94.28	93.10
12.536	5.72	6.90
Totals	100.00	100.00



Racemic sample

Retention	Area %	Height %
20.776	51.06	58.25
27.052	48.94	41.75
Totals	100.00	100.00



Enantioenriched sample

Retention	Area %	Height %
20.488	96.57	96.19
28.120	3.43	3.81
Totals	100.00	100.00

