

Supporting Information to

**A rapid and selective synthesis of α,α -fluorohalo esters via
fluorohalogenative or difluorinative hydration of ynol ethers**

Liang Hu,^{a,b} Chao Che,^a Ze Tan^{b,*} and Gangguo Zhu^{a,*}

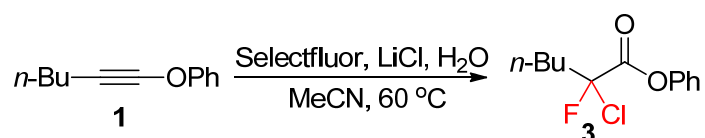
^a*Department of Chemistry, Zhejiang Normal University, 688 Yingbin Road, Jinhua 321004, P. R. China. E-mail: gangguo@zjnu.cn.*

^b*State Key Laboratory of Chemo/Biosensing and Chemometrics, College of Chemistry and Chemical Engineering, Hunan University, Changsha 410082, P. R. China. E-mail: ztanze@gmail.com.*

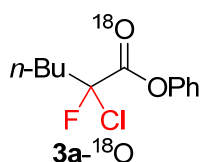
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General: Column chromatography was performed using silica gel (300–400 mesh) with petroleum ethers/EtOAc as the eluent. ^1H NMR, ^{13}C NMR, and ^{19}F NMR spectra are recorded on a 600 MHz or 400 MHz NMR spectrometers. Chemical shifts were reported in ppm downfield from tetramethylsilane with the solvent resonance as the internal standard. All melting points were determined by a micro melting point apparatus and are uncorrected. High-resolution mass spectral (HRMS) analyses were carried out using a TOF MS instrument with an ESI or APCI source.

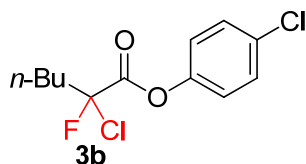
General procedure for the synthesis of α,α -fluorohalo esters via fluorohalogenative hydration of ynol ethers:



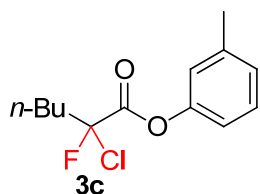
Compound 3a. To a mixture of Selectfluor (177.1 mg, 0.50 mmol), LiCl (12.7 mg, 0.30 mmol), and H₂O (90.1 mg, 5.0 mmol) in 4.0 mL of MeCN was added ynol ether **1a** (43.5 mg, 0.25 mmol). After stirring at 60 °C for 5 h, the reaction mixture was quenched with 5 mL of water, extracted with diethyl ether, washed with brine, dried over anhydrous Na₂SO₄ and concentrated. Column chromatography on silica gel gave **3a** as a colorless oil (53.1 mg, 87% yield); ^1H NMR (600 MHz, CDCl₃): δ 7.44–7.41 (m, 2 H), 7.31–7.28 (m, 1 H), 7.19–7.13 (m, 2 H), 2.54–2.36 (m, 2 H), 1.73–1.65 (m, 1 H), 1.55–1.50 (m, 1 H), 1.48–1.40 (m, 2 H), 0.97 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (151 MHz, CDCl₃): δ 164.2 (d, J = 30.0 Hz), 150.0, 129.7, 126.7, 120.8, 105.5 (d, J = 256.2 Hz), 40.1 (d, J = 21.5 Hz), 25.4 (d, J = 2.0 Hz), 22.1, 13.7; ^{19}F NMR (565 MHz, CDCl₃): δ -116.7; HRMS (ESI) calcd for C₁₂H₁₅O₂³⁵ClF (M+H)⁺ 245.0745, found 245.0749.



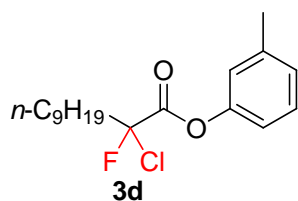
Compound 3a-¹⁸O. It was prepared from **1a** using H₂O¹⁸ in place of H₂O to give 52.3 mg of the title compound (85% yield) as a colorless oil; HRMS (APCI) calcd for C₁₂H₁₅O¹⁸O³⁵ClF (M+H)⁺ 247.0787, found 247.0783.



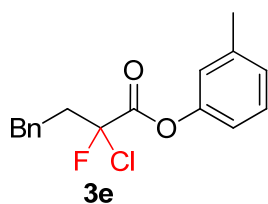
Compound 3b. 57.7 mg, 83% yield, colorless oil; ^1H NMR (600 MHz, CDCl_3): δ 7.39 (d, $J = 8.8$ Hz, 2 H), 7.12 (d, $J = 8.8$ Hz, 2 H), 2.49–2.37 (m, 2 H), 1.72–1.64 (m, 1 H), 1.53–1.40 (m, 3 H), 0.96 (t, $J = 7.3$ Hz, 3 H); ^{13}C NMR (151 MHz, CDCl_3): δ 164.0 (d, $J = 30.2$ Hz), 148.4, 132.2, 129.8, 122.3, 105.4 (d, $J = 256.6$ Hz), 40.0 (d, $J = 21.5$ Hz), 25.3 (d, $J = 2.1$ Hz), 22.1, 13.7; ^{19}F NMR (565 MHz, CDCl_3): δ -116.9; HRMS (APCI) calcd for $\text{C}_{12}\text{H}_{14}\text{O}_2^{35}\text{Cl}_2\text{F}$ ($\text{M}+\text{H}$) $^+$ 279.0355, found 279.0347.



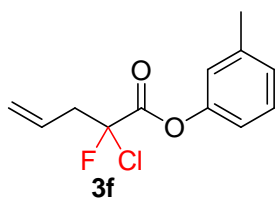
Compound 3c. 56.8 mg, 88% yield, colorless oil; ^1H NMR (600 MHz, CDCl_3): δ 7.31–7.29 (m, 1 H), 7.11–7.10 (m, 1 H), 7.00–6.93 (m, 2 H), 2.51–2.40 (m, 2 H), 2.38 (s, 3 H), 1.72–1.64 (m, 1 H), 1.56–1.49 (m, 1 H), 1.47–1.41 (m, 2 H), 0.97 (t, $J = 7.3$ Hz, 3 H); ^{13}C NMR (151 MHz, CDCl_3): δ 164.3 (d, $J = 30.0$ Hz), 150.0, 140.0, 129.4, 127.5, 121.4, 117.8, 105.5 (d, $J = 256.4$ Hz), 40.1 (d, $J = 21.5$ Hz), 25.4 (d, $J = 2.1$ Hz), 22.1, 21.3, 13.7; ^{19}F NMR (565 MHz, CDCl_3): δ -116.7; HRMS (APCI) calcd for $\text{C}_{13}\text{H}_{17}\text{O}_2^{35}\text{ClF}$ ($\text{M}+\text{H}$) $^+$ 259.0901, found 259.0916.



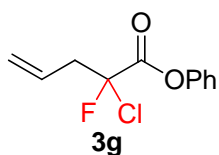
Compound 3d. 61.5 mg, 75% yield, colorless oil; ^1H NMR (600 MHz, CDCl_3): δ 7.30–7.28 (m, 1 H), 7.10–7.09 (m, 1 H), 6.98–6.93 (m, 2 H), 2.51–2.39 (m, 2 H), 2.38 (s, 3 H), 1.74–1.65 (m, 1 H), 1.56–1.50 (m, 1 H), 1.43–1.37 (m, 2 H), 1.35–1.28 (m, 10 H), 0.88 (t, $J = 7.0$ Hz, 3 H); ^{13}C NMR (151 MHz, CDCl_3): δ 164.3 (d, $J = 30.0$ Hz), 150.0, 140.0, 129.4, 127.4, 121.4, 117.8, 105.5 (d, $J = 256.2$ Hz), 40.3 (d, $J = 21.5$ Hz), 31.8, 29.3, 29.2, 28.9, 23.3 (d, $J = 2.0$ Hz), 22.6, 21.2, 14.1; ^{19}F NMR (565 MHz, CDCl_3): δ -116.7; HRMS (APCI) calcd for $\text{C}_{18}\text{H}_{27}\text{O}_2^{35}\text{ClF}$ ($\text{M}+\text{H}$) $^+$ 329.1684, found 329.1672.



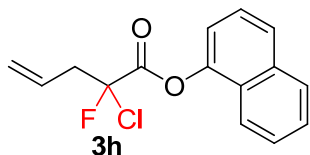
Compound 3e. 61.2 mg, 80% yield, colorless oil; ^1H NMR (600 MHz, CDCl_3): δ 7.33–7.30 (m, 3 H), 7.24–7.23 (m, 3 H), 7.10–7.09 (m, 1 H), 6.92–6.91 (m, 2 H), 3.06–3.01 (m, 1 H), 2.91–2.85 (m, 1 H), 2.83–2.68 (m, 2 H), 2.37 (s, 3 H); ^{13}C NMR (151 MHz, CDCl_3): δ 164.0 (d, $J = 29.7$ Hz), 149.9, 140.0, 139.2, 129.4, 128.7, 128.4, 127.5, 126.6, 121.3, 117.7, 104.8 (d, $J = 256.7$ Hz), 42.0 (d, $J = 21.4$ Hz), 29.6 (d, $J = 2.7$ Hz), 21.3; ^{19}F NMR (565 MHz, CDCl_3): δ -117.3; HRMS (APCI) calcd for $\text{C}_{17}\text{H}_{17}\text{O}_2^{35}\text{ClF}$ ($\text{M}+\text{H}$) $^+$ 307.0901, found 307.0908.



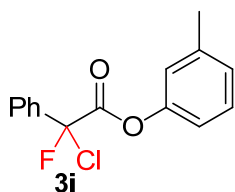
Compound 3f. 50.8 mg, 84% yield, colorless oil; ^1H NMR (600 MHz, CDCl_3): δ 7.30–7.28 (m, 1 H), 7.11–7.09 (m, 1 H), 6.95–6.93 (m, 2 H), 5.95–5.83 (m, 1 H), 5.40–5.33 (m, 2 H), 3.26–3.16 (m, 2 H), 2.38 (s, 3 H); ^{13}C NMR (151 MHz, CDCl_3): δ 163.8 (d, $J = 29.6$ Hz), 149.9, 140.0, 129.4, 128.3 (d, $J = 2.7$ Hz), 127.5, 122.2, 121.4, 117.8, 104.1 (d, $J = 256.6$ Hz), 44.7 (d, $J = 21.4$ Hz), 21.3; ^{19}F NMR (565 MHz, CDCl_3): δ -116.8; HRMS (APCI) calcd for $\text{C}_{12}\text{H}_{13}\text{O}_2^{35}\text{ClF}$ ($\text{M}+\text{H}$) $^+$ 243.0588, found 243.0576.



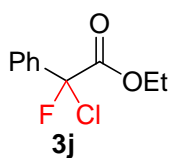
Compound 3g. 45.6 mg, 80% yield, colorless oil; ^1H NMR (400 MHz, CDCl_3): δ 7.43–7.39 (m, 2 H), 7.30–7.24 (m, 1 H), 7.15–7.12 (m, 2 H), 5.93–5.84 (m, 1 H), 5.39–5.35 (m, 2 H), 3.24–3.17 (m, 2 H); ^{13}C NMR (101 MHz, CDCl_3): δ 163.7 (d, $J = 29.8$ Hz), 150.0, 129.7, 128.3 (d, $J = 2.7$ Hz), 126.7, 122.2, 120.8, 104.0 (d, $J = 257.5$ Hz), 44.7 (d, $J = 21.5$ Hz); ^{19}F NMR (565 MHz, CDCl_3): δ -116.8; HRMS (APCI) calcd for $\text{C}_{11}\text{H}_{11}\text{O}_2^{35}\text{ClF}$ ($\text{M}+\text{H}$) $^+$ 229.0432, found 229.0431.



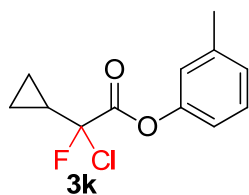
Compound 3h. 50.0 mg, 72% yield, colorless oil; ^1H NMR (600 MHz, CDCl_3): δ 7.97–7.96 (m, 1 H), 7.92–7.88 (m, 1 H), 7.81–7.80 (m, 1 H), 7.59–7.52 (m, 2 H), 7.51–7.46 (m, 1 H), 7.30–7.29 (m, 1 H), 6.03–5.93 (m, 1 H), 5.47–5.39 (m, 2 H), 3.39–3.27 (m, 2 H); ^{13}C NMR (151 MHz, CDCl_3): δ 163.8 (d, $J = 29.5$ Hz), 145.7, 134.7, 128.3, 128.3, 128.0, 126.9 (d, $J = 3.9$ Hz), 126.8, 126.2, 125.2, 122.5, 120.7, 117.5, 104.3 (d, $J = 257.2$ Hz), 44.8 (d, $J = 21.3$ Hz); ^{19}F NMR (565 MHz, CDCl_3): δ -116.4; HRMS (APCI) calcd for $\text{C}_{15}\text{H}_{13}\text{O}_2^{35}\text{ClF}$ ($\text{M}+\text{H}$) $^+$ 279.0588, found 279.0579.



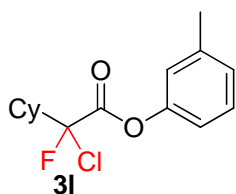
Compound 3i. 57.0 mg, 82% yield, colorless oil; ^1H NMR (600 MHz, CDCl_3): δ 7.82–7.72 (m, 2 H), 7.51–7.45 (m, 3 H), 7.25–7.23 (m, 1 H), 7.07–7.06 (m, 1 H), 6.88–6.87 (m, 2 H), 2.33 (s, 3 H); ^{13}C NMR (151 MHz, CDCl_3): δ 163.8 (d, $J = 31.9$ Hz), 150.1, 140.0, 135.6 (d, $J = 23.1$ Hz), 130.6 (d, $J = 1.3$ Hz), 129.3, 128.6, 127.5, 125.9 (d, $J = 7.0$ Hz), 121.2, 117.6, 104.3 (d, $J = 254.4$ Hz), 21.2; ^{19}F NMR (565 MHz, CDCl_3): δ -111.9; HRMS (APCI) calcd for $\text{C}_{15}\text{H}_{13}\text{O}_2^{35}\text{ClF}$ ($\text{M}+\text{H}$) $^+$ 279.0588, found 279.0581.



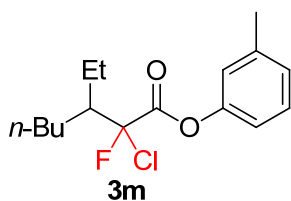
Compound 3j. 41.0 mg, 76% yield, colorless oil; ^1H NMR (600 MHz, CDCl_3): δ 7.73–7.63 (m, 2 H), 7.44–7.43 (m, 3 H), 4.34–4.27 (m, 2 H), 1.30 (t, $J = 7.1$ Hz, 3 H); ^{13}C NMR (151 MHz, CDCl_3): δ 165.3 (d, $J = 30.5$ Hz), 136.1 (d, $J = 23.0$ Hz), 130.3 (d, $J = 1.5$ Hz), 128.5, 125.7 (d, $J = 7.2$ Hz), 104.4 (d, $J = 254.2$ Hz), 63.6, 13.8; ^{19}F NMR (565 MHz, CDCl_3): δ -112.4; HRMS (APCI) calcd for $\text{C}_{10}\text{H}_{11}\text{O}_2^{35}\text{ClF}$ ($\text{M}+\text{H}$) $^+$ 217.0432, found 217.0423.



Compound 3k. 43.6 mg, 72% yield, colorless oil; ^1H NMR (600 MHz, CDCl_3): δ 7.31–7.28 (m, 1 H), 7.10–7.09 (m, 1 H), 7.01–6.95 (m, 2 H), 2.38 (s, 3 H), 2.08–1.86 (m, 1 H), 0.97–0.86 (m, 3 H), 0.83–0.76 (m, 1 H); ^{13}C NMR (151 MHz, CDCl_3): δ 164.1 (d, $J = 31.2$ Hz), 150.0, 140.0, 129.3, 127.4, 121.4, 117.8, 105.1 (d, $J = 254.0$ Hz), 21.2, 19.3 (d, $J = 23.0$ Hz), 3.9 (d, $J = 2.8$ Hz), 2.9 (d, $J = 4.0$ Hz); ^{19}F NMR (565 MHz, CDCl_3): δ -125.2; HRMS (APCI) calcd for $\text{C}_{12}\text{H}_{13}\text{O}_2^{35}\text{ClF}$ ($\text{M}+\text{H}$) $^+$ 243.0588, found 243.0579.

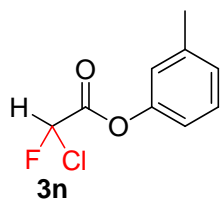


Compound 3l. 47.6 mg, 67% yield, colorless oil; ^1H NMR (600 MHz, CDCl_3): δ 7.31–7.28 (m, 1 H), 7.10–7.09 (m, 1 H), 6.96–6.95 (m, 2 H), 2.38 (s, 3 H), 2.34–2.18 (m, 2 H), 1.93–1.80 (m, 3 H), 1.74–1.72 (m, 1 H), 1.45–1.28 (m, 4 H), 1.21–1.19 (m, 1 H); ^{13}C NMR (151 MHz, CDCl_3): δ 164.4 (d, $J = 30.1$ Hz), 149.9, 140.0, 129.3, 127.4, 121.4, 117.8, 108.3 (d, $J = 258.5$ Hz), 46.5 (d, $J = 20.6$ Hz), 27.2 (d, $J = 2.0$ Hz), 25.7, 25.7, 25.5, 25.3 (d, $J = 2.2$ Hz), 21.3; ^{19}F NMR (565 MHz, CDCl_3): δ -124.5; HRMS (APCI) calcd for $\text{C}_{15}\text{H}_{19}\text{O}_2^{35}\text{ClF}$ ($\text{M}+\text{H}$) $^+$ 285.1058, found 285.1051.

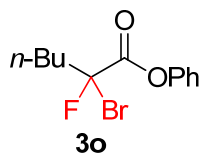


Compound 3m. 23.3 mg, 31% yield, colorless oil; ^1H NMR (600 MHz, CDCl_3): δ 7.31–7.29 (m, 1 H), 7.11–7.10 (m, 1 H), 6.96–6.95 (m, 2 H), 2.39 (s, 3H), 2.33–2.25 (m, 1 H), 1.94–1.86 (m, 1 H), 1.72–1.66 (m, 1 H), 1.59–1.56 (m, 2 H), 1.40–1.36 (m, 4 H), 1.03 (t, $J = 7.5$ Hz, 3 H), 0.95 (t, $J = 7.2$ Hz, 3 H); ^{13}C NMR (151 MHz, CDCl_3): δ 164.6 (d, $J = 29.9$ Hz), 150.0, 140.0, 129.4, 127.4, 121.4, 117.8, 109.6 (d, $J = 260.5$ Hz), 47.9 (d, $J = 19.5$ Hz), 29.7, 27.3, 22.9, 22.9 (d, $J = 1.8$ Hz), 21.3, 13.9, 11.8 (d, $J = 1.1$ Hz); ^{19}F NMR

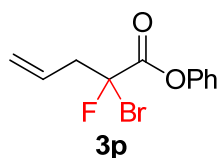
(565 MHz, CDCl₃): δ -121.2; HRMS (APCI) calcd for C₁₆H₂₃O₂³⁵ClF (M+H)⁺ 301.1371, found 301.1388.



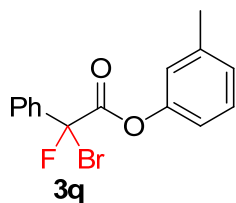
Compound 3n. 35.4 mg, 70% yield, colorless oil; ¹H NMR (600 MHz, CDCl₃): δ 7.32–7.29 (m, 1 H), 7.12–7.11 (m, 1 H), 6.99–6.97 (m, 2 H), 6.50 (d, J = 50.3 Hz, 1 H), 2.38 (s, 3 H); ¹³C NMR (151 MHz, CDCl₃): δ 162.5 (d, J = 27.7 Hz), 149.6, 140.1, 129.4, 127.6, 121.3, 117.7, 91.0 (d, J = 253.5 Hz), 21.3; ¹⁹F NMR (565 MHz, CDCl₃): δ -146.0; HRMS (APCI) calcd for C₉H₉O₂³⁵ClF (M+H)⁺ 203.0275, found 203.0279.



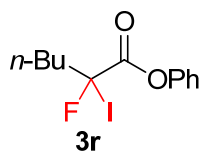
Compound 3o. 54.7 mg, 76% yield, colorless oil; ¹H NMR (600 MHz, CDCl₃): δ 7.45–7.42 (m, 2 H), 7.31–7.29 (m, 1 H), 7.18–7.17 (m, 2 H), 2.60–2.50 (m, 2 H), 1.74–1.68 (m, 1 H), 1.55–1.42 (m, 3 H), 0.97 (t, J = 7.3 Hz, 3 H); ¹³C NMR (151 MHz, CDCl₃): δ 164.7 (d, J = 28.2 Hz), 150.0, 129.7, 126.7, 120.8, 98.1 (d, J = 267.0 Hz), 41.4 (d, J = 20.4 Hz), 26.4 (d, J = 1.8 Hz), 22.1, 13.8; ¹⁹F NMR (565 MHz, CDCl₃): δ -117.2; HRMS (APCI) calcd for C₁₂H₁₅O₂⁷⁹BrF (M+H)⁺ 289.0239, found 289.0247.



Compound 3p. 48.3 mg, 71% yield, colorless oil; ¹H NMR (600 MHz, CDCl₃): δ 7.44–7.41 (m, 2 H), 7.31–7.29 (m, 1 H), 7.16–7.15 (m, 2 H), 5.96–5.85 (m, 1 H), 5.42–5.33 (m, 2 H), 3.35–3.29 (m, 2 H); ¹³C NMR (151 MHz, CDCl₃): δ 164.2 (d, J = 28.2 Hz), 150.0, 129.7, 129.0 (d, J = 2.3 Hz), 126.7, 122.1, 120.8, 96.4 (d, J = 267.2 Hz), 45.9 (d, J = 20.3 Hz); ¹⁹F NMR (565 MHz, CDCl₃): δ -117.8; HRMS (APCI) calcd for C₁₁H₁₁O₂⁷⁹BrF (M+H)⁺ 272.9926, found 272.9917.

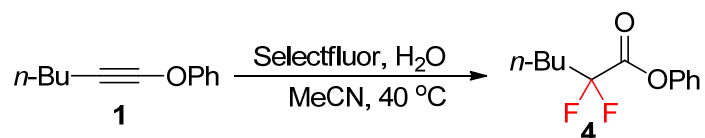


Compound 3q. 48.3 mg, 60% yield, colorless oil; ^1H NMR (600 MHz, CDCl_3): δ 7.83–7.77 (m, 2 H), 7.49–7.36 (m, 3 H), 7.29–7.25 (m, 1 H), 7.10–7.05 (m, 1 H), 6.94–6.90 (m, 2 H), 2.35 (s, 3 H); ^{13}C NMR (151 MHz, CDCl_3): δ 164.1 (d, $J = 30.0$ Hz), 150.1, 140.0, 136.3 (d, $J = 21.6$ Hz), 130.5 (d, $J = 1.2$ Hz), 129.3, 128.6 (d, $J = 1.3$ Hz), 127.5, 127.3, 126.3, 126.2, 121.2, 117.6, 96.4 (d, $J = 264.2$ Hz), 21.2; ^{19}F NMR (565 MHz, CDCl_3): δ -114.1; HRMS (APCI) calcd for $\text{C}_{15}\text{H}_{13}\text{O}_2^{79}\text{BrF}$ ($\text{M}+\text{H}$) $^+$ 323.0083, found 323.0075.



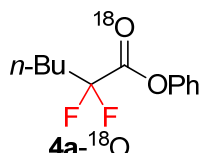
Compound 3r. 48.7 mg, 58% yield, colorless oil; ^1H NMR (600 MHz, CDCl_3): δ 7.45–7.42 (m, 2 H), 7.31–7.29 (m, 1 H), 7.18–7.17 (m, 2 H), 2.71–2.61 (m, 1 H), 2.53–2.43 (m, 1 H), 1.72–1.65 (m, 1 H), 1.52–1.43 (m, 3 H), 0.97 (t, $J = 7.2$ Hz, 3 H); ^{13}C NMR (151 MHz, CDCl_3): δ 166.2 (d, $J = 26.3$ Hz), 150.0, 129.6, 126.6, 120.7, 79.2 (d, $J = 268.2$ Hz), 44.2 (d, $J = 20.0$ Hz), 28.2 (d, $J = 1.6$ Hz), 21.9, 13.8; ^{19}F NMR (565 MHz, CDCl_3): δ -119.6; HRMS (APCI) calcd for $\text{C}_{12}\text{H}_{15}\text{O}_2\text{IF}$ ($\text{M}+\text{H}$) $^+$ 337.0101, found 337.0112.

General procedure for the synthesis of α,α -difluoro esters via difluorinative hydration of ynol ethers:

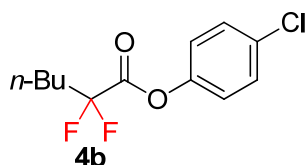


Compound 4a. To a mixture of Selectfluor (265.7 mg, 0.75 mmol) and H_2O (9.0 mg, 0.5 mmol) in 2.0 mL of MeCN was added **1a** (43.5 mg, 0.25 mmol). After stirring at 40 °C for 8 h, the reaction mixture was quenched with 5 mL of water, extracted with diethyl ether, washed with brine, dried over anhydrous Na_2SO_4 and concentrated. Column

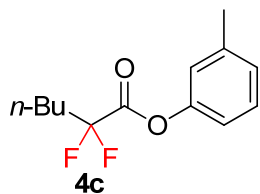
chromatography on silica gel gave **4a** as a colorless oil (51.3 mg, 90% yield); ^1H NMR (600 MHz, CDCl_3): δ 7.46–7.40 (m, 2 H), 7.31–7.29 (m, 1 H), 7.17–7.15 (m, 2 H), 2.27–2.15 (m, 2 H), 1.57–1.54 (m, 2 H), 1.47–1.41 (m, 2 H), 0.96 (t, $J = 7.3$ Hz, 3 H); ^{13}C NMR (151 MHz, CDCl_3): δ 162.8 (t, $J = 34.2$ Hz), 149.8, 129.7, 126.7, 120.9, 116.5 (t, $J = 250.6$ Hz), 34.3 (t, $J = 22.9$ Hz), 23.6 (t, $J = 4.2$ Hz), 22.2, 13.7; ^{19}F NMR (565 MHz, CDCl_3): δ -105.5; HRMS (ESI) calcd for $\text{C}_{12}\text{H}_{15}\text{O}_2\text{F}_2$ ($\text{M}+\text{H}$) $^+$ 229.1040, found 229.1037.



Compound 4a- ^{18}O . It was prepared from **1a** using H_2O^{18} in place of H_2O to give 50.0 mg of the title compound (87% yield) as a colorless oil; HRMS (APCI) calcd for $\text{C}_{12}\text{H}_{15}\text{O}^{18}\text{OF}_2$ ($\text{M}+\text{H}$) $^+$ 231.1083, found 231.1082.

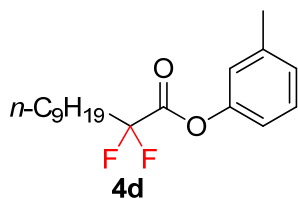


Compound 4b. 55.0 mg, 84% yield, colorless oil; ^1H NMR (600 MHz, CDCl_3): δ 7.41–7.36 (m, 2 H), 7.12–7.11 (m, 2 H), 2.26–2.14 (m, 2 H), 1.57–1.52 (m, 2 H), 1.45–1.41 (m, 2 H), 0.96 (t, $J = 7.3$ Hz, 3 H); ^{13}C NMR (151 MHz, CDCl_3): δ 162.6 (t, $J = 34.5$ Hz), 148.2, 132.2, 129.8, 122.3, 116.4 (t, $J = 250.9$ Hz), 34.2 (t, $J = 22.9$ Hz), 23.5 (t, $J = 4.2$ Hz), 22.2, 13.7; ^{19}F NMR (565 MHz, CDCl_3): δ -105.4; HRMS (APCI) calcd for $\text{C}_{12}\text{H}_{14}\text{O}_2^{35}\text{ClF}_2$ ($\text{M}+\text{H}$) $^+$ 263.0650, found 263.0637.

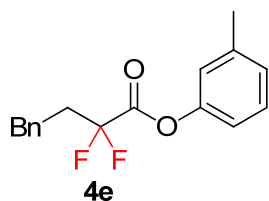


Compound 4c. 54.5 mg, 90% yield, colorless oil; ^1H NMR (600 MHz, CDCl_3): δ 7.30–7.27 (m, 1 H), 7.10–7.09 (m, 1 H), 6.96–6.94 (m, 2 H), 2.37 (s, 3 H), 2.25–2.15 (m, 2 H), 1.57–1.53 (m, 2 H), 1.46–1.41 (m, 2 H), 0.96 (t, $J = 7.3$ Hz, 3 H); ^{13}C NMR (151 MHz, CDCl_3): δ 162.9 (t, $J = 34.1$ Hz), 149.7, 140.0, 129.4, 127.5, 121.4, 117.8, 116.5 (t, $J = 250.7$ Hz), 34.3 (t, $J = 23.0$ Hz), 23.6 (t, $J = 4.2$ Hz), 22.2, 21.2, 13.7; ^{19}F NMR (565

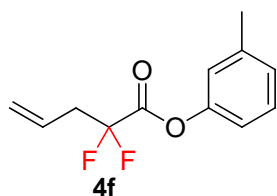
MHz, CDCl₃): δ -105.4; HRMS (APCI) calcd for C₁₃H₁₇O₂F₂ (M+H)⁺ 243.1197, found 243.1203.



Compound 4d. 56.2 mg, 72% yield, colorless oil; ¹H NMR (600 MHz, CDCl₃): δ 7.30–7.27 (m, 1 H), 7.10–7.09 (m, 1 H), 6.96–6.94 (m, 2 H), 2.37 (s, 3H), 2.24–2.14 (m, 2 H), 1.59–1.54 (m, 2 H), 1.43–1.37 (m, 2 H), 1.33–1.25 (m, 10 H), 0.88 (t, J = 7.0 Hz, 3H); ¹³C NMR (151 MHz, CDCl₃): δ 162.9 (t, J = 34.1 Hz), 149.7, 140.0, 129.4, 127.5, 121.4, 117.8, 116.5 (t, J = 250.7 Hz), 34.6 (t, J = 23.0 Hz), 31.8, 29.3, 29.2, 29.0, 22.6, 21.5 (t, J = 4.1 Hz), 21.2, 14.1; ¹⁹F NMR (565 MHz, CDCl₃): δ -105.4; HRMS (APCI) calcd for C₁₈H₂₇O₂F₂ (M+H)⁺ 313.1979, found 313.1983.

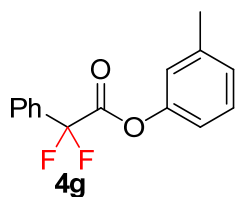


Compound 4e. 58.7 mg, 81% yield, colorless oil; ¹H NMR (600 MHz, CDCl₃): δ 7.33–7.30 (m, 2 H), 7.29–7.22 (m, 4 H), 7.10–7.09 (m, 1 H), 6.90–6.89 (m, 2 H), 2.93–2.90 (m, 2 H), 2.57–2.49 (m, 2 H), 2.36 (s, 3 H); ¹³C NMR (151 MHz, CDCl₃): δ 162.6 (t, J = 33.8 Hz), 149.7, 140.0, 139.3, 129.4, 128.7, 128.4, 127.5, 126.6, 121.4, 117.8, 115.8 (t, J = 251.3 Hz), 36.4 (t, J = 23.1 Hz), 27.8 (t, J = 4.8 Hz), 21.2; ¹⁹F NMR (565 MHz, CDCl₃): δ -105.9; HRMS (APCI) calcd for C₁₇H₁₇O₂F₂ (M+H)⁺ 291.1197, found 291.1189.

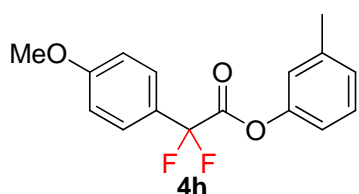


Compound 4f. 40.7 mg, 72% yield, colorless oil; ¹H NMR (600 MHz, CDCl₃): δ 7.30–7.28 (m, 1 H), 7.11–7.10 (m, 1 H), 6.94–6.92 (m, 2 H), 5.88–5.81 (m, 1 H), 5.39–5.33 (m, 2 H), 3.02–2.95 (m, 2 H), 2.38 (s, 3 H); ¹³C NMR (151 MHz, CDCl₃): δ 162.3 (t, J = 33.6 Hz), 149.7, 140.1, 129.4, 127.5, 126.9 (t, J = 5.6 Hz), 122.2, 121.4,

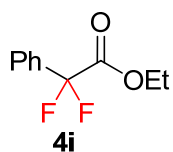
117.8, 115.3 (t, $J = 252.2$ Hz), 39.3 (t, $J = 23.8$ Hz), 21.3; ^{19}F NMR (565 MHz, CDCl_3): δ -105.0; HRMS (APCI) calcd for $\text{C}_{12}\text{H}_{13}\text{O}_2\text{F}_2$ ($\text{M}+\text{H}$) $^+$ 227.0884, found 227.0877.



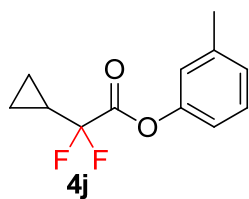
Compound 4g. 46.5 mg, 71% yield, colorless oil; ^1H NMR (600 MHz, CDCl_3): δ 8.22–8.21 (m, 2 H), 7.70–7.64 (m, 1 H), 7.55–7.53 (m, 2 H), 7.27–7.24 (m, 1 H), 7.10–7.05 (m, 3 H), 2.37 (s, 3 H); ^{13}C NMR (151 MHz, CDCl_3): δ 183.2 (t, $J = 34.9$ Hz), 149.5 (t, $J = 2.1$ Hz), 140.0, 134.7, 130.5 (t, $J = 1.9$ Hz), 129.3, 128.7, 126.9, 125.5 (t, $J = 6.1$ Hz), 122.0, 118.3, 115.7 (t, $J = 276.9$ Hz), 21.3; ^{19}F NMR (565 MHz, CDCl_3): δ -73.8; HRMS (APCI) calcd for $\text{C}_{15}\text{H}_{13}\text{O}_2\text{F}_2$ ($\text{M}+\text{H}$) $^+$ 263.0884, found 263.0889.



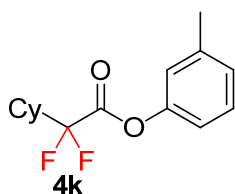
Compound 4h. 59.1 mg, 81% yield, colorless oil; ^1H NMR (600 MHz, CDCl_3): δ 8.20–8.19 (m, 2 H), 7.25–7.23 (m, 1 H), 7.08–7.06 (m, 3 H), 7.01–6.98 (m, 2 H), 3.90 (s, 3 H), 2.37 (s, 3 H); ^{13}C NMR (151 MHz, CDCl_3): δ 181.7 (t, $J = 34.7$ Hz), 164.8, 149.7 (t, $J = 2.0$ Hz), 139.9, 133.0 (t, $J = 2.0$ Hz), 129.3, 126.8, 123.9, 121.9, 118.2, 116.0 (t, $J = 276.9$ Hz), 114.1, 55.6, 21.3; ^{19}F NMR (565 MHz, CDCl_3): δ -73.5; HRMS (APCI) calcd for $\text{C}_{16}\text{H}_{15}\text{O}_3\text{F}_2$ ($\text{M}+\text{H}$) $^+$ 293.0989, found 293.0979.



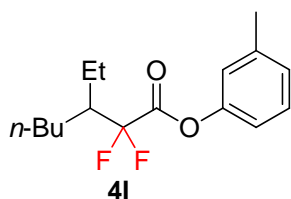
Compound 4i. 36.5 mg, 73% yield, colorless oil; ^1H NMR (600 MHz, CDCl_3): δ 7.62–7.61 (m, 2 H), 7.50–7.44 (m, 3 H), 4.29 (q, $J = 7.1$ Hz, 2 H), 1.29 (t, $J = 7.1$ Hz, 3 H); ^{13}C NMR (151 MHz, CDCl_3): δ 164.2 (t, $J = 35.3$ Hz), 132.8 (t, $J = 25.5$ Hz), 130.9 (t, $J = 1.6$ Hz), 128.6, 125.4 (t, $J = 6.1$ Hz), 113.4 (t, $J = 252.1$ Hz), 63.1, 13.8; ^{19}F NMR (565 MHz, CDCl_3): δ -103.9; HRMS (APCI) calcd for $\text{C}_{10}\text{H}_{11}\text{O}_2\text{F}_2$ ($\text{M}+\text{H}$) $^+$ 201.0727, found 201.0716.



Compound 4j. 37.9 mg, 67% yield, colorless oil; ^1H NMR (600 MHz, CDCl_3): δ 7.32–7.28 (m, 1 H), 7.11–7.10 (m, 1 H), 6.98–6.97 (m, 2 H), 2.38 (s, 3 H), 1.71–1.58 (m, 1 H), 0.90–0.74 (m, 4 H); ^{13}C NMR (151 MHz, CDCl_3): δ 162.8 (t, $J = 36.3$ Hz), 149.8, 140.0, 129.4, 127.5, 121.5, 117.8, 114.8 (t, $J = 249.4$ Hz), 21.3, 14.0 (t, $J = 27.9$ Hz), 1.5 (t, $J = 4.0$ Hz); ^{19}F NMR (565 MHz, CDCl_3): δ -110.1; HRMS (APCI) calcd for $\text{C}_{12}\text{H}_{13}\text{O}_2\text{F}_2$ ($\text{M}+\text{H}$) $^+$ 227.0884, found 227.0887.

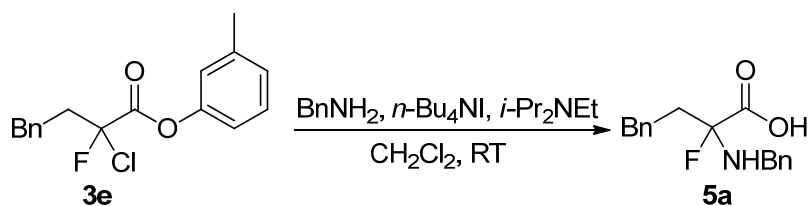


Compound 4k. 43.6 mg, 65% yield, colorless oil; ^1H NMR (600 MHz, CDCl_3): δ 7.30–7.28 (m, 1 H), 7.10–7.09 (m, 1 H), 6.95–6.94 (m, 2 H), 2.38 (s, 3 H), 2.23–2.19 (m, 1 H), 1.91–1.85 (m, 4 H), 1.76–1.71 (m, 1 H), 1.35–1.21 (m, 5 H); ^{13}C NMR (151 MHz, CDCl_3): δ 162.9 (t, $J = 34.2$ Hz), 149.7, 140.0, 129.4, 127.5, 121.5, 117.9, 117.3 (t, $J = 252.7$ Hz), 42.4 (t, $J = 21.9$ Hz), 25.8, 25.3, 24.8 (t, $J = 3.9$ Hz), 21.3; ^{19}F NMR (565 MHz, CDCl_3): δ -113.2; HRMS (APCI) calcd for $\text{C}_{15}\text{H}_{19}\text{O}_2\text{F}_2$ ($\text{M}+\text{H}$) $^+$ 269.1353, found 269.1362.

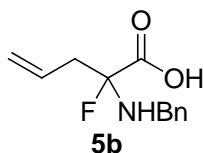


Compound 4l. 31.3 mg, 44% yield, colorless oil; ^1H NMR (600 MHz, CDCl_3): δ 7.31–7.28 (m, 1 H), 7.11–7.09 (m, 1 H), 6.95–6.94 (m, 2 H), 2.38 (s, 3 H), 2.24–2.09 (m, 1 H), 1.74–1.62 (m, 2 H), 1.55–1.41 (m, 3 H), 1.40–1.32 (m, 3 H), 1.03 (t, $J = 7.5$ Hz, 3 H), 0.93 (t, $J = 7.0$ Hz, 3 H); ^{13}C NMR (151 MHz, CDCl_3): δ 163.2 (t, $J = 34.3$ Hz), 149.8, 140.0, 129.4, 127.5, 121.4, 118.4 (t, $J = 253.9$ Hz), 117.8, 43.9 (t, $J = 20.6$ Hz), 29.4, 26.6 (t, $J = 3.6$ Hz), 22.9, 21.3, 20.5 (t, $J = 4.0$ Hz), 13.9, 11.6; ^{19}F NMR (565 MHz, CDCl_3): δ -109.2; HRMS (APCI) calcd for $\text{C}_{16}\text{H}_{23}\text{O}_2\text{F}_2$ ($\text{M}+\text{H}$) $^+$ 285.1666, found 285.1654.

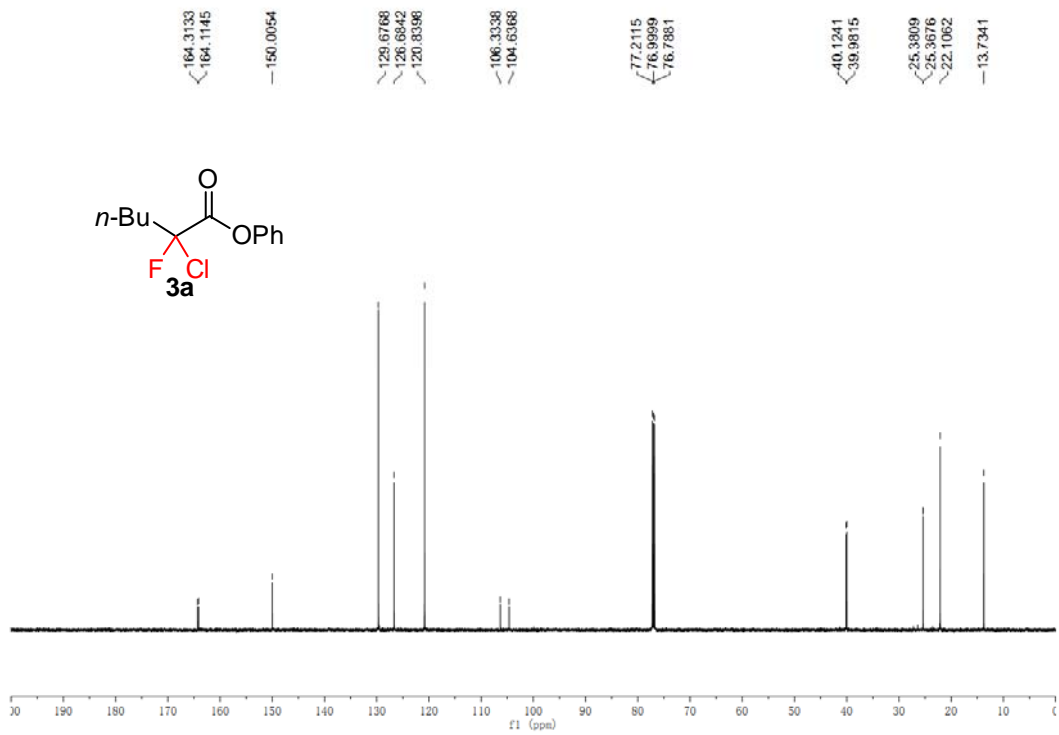
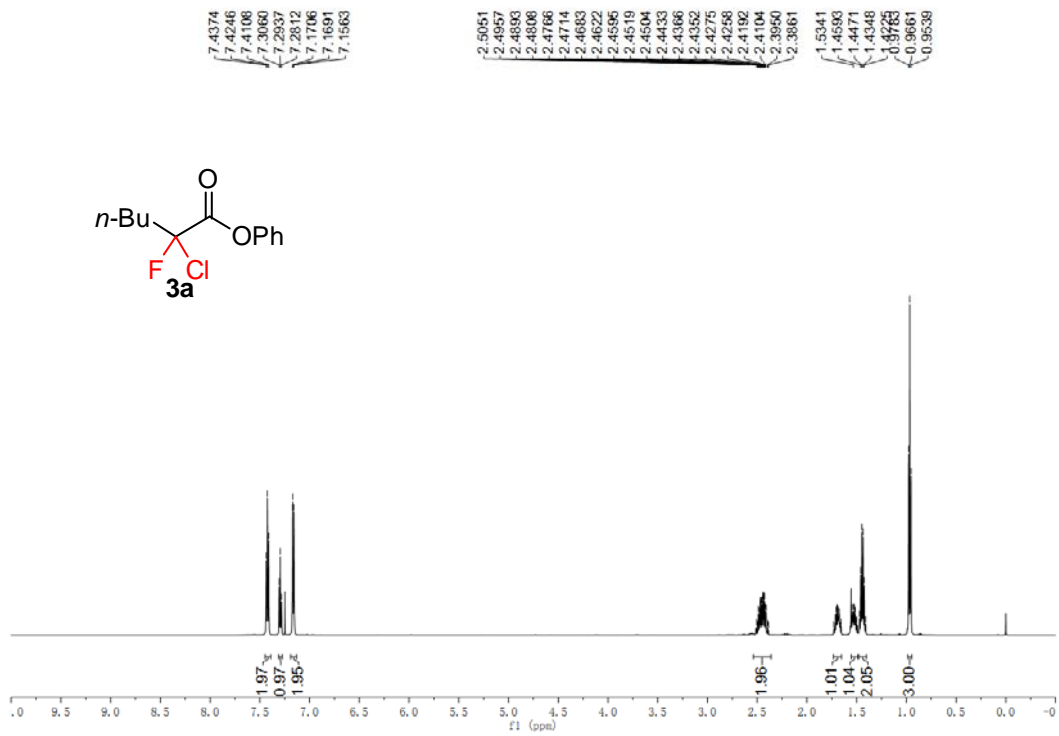
General procedure for the synthesis of α -monofluoro- α -amino acids:

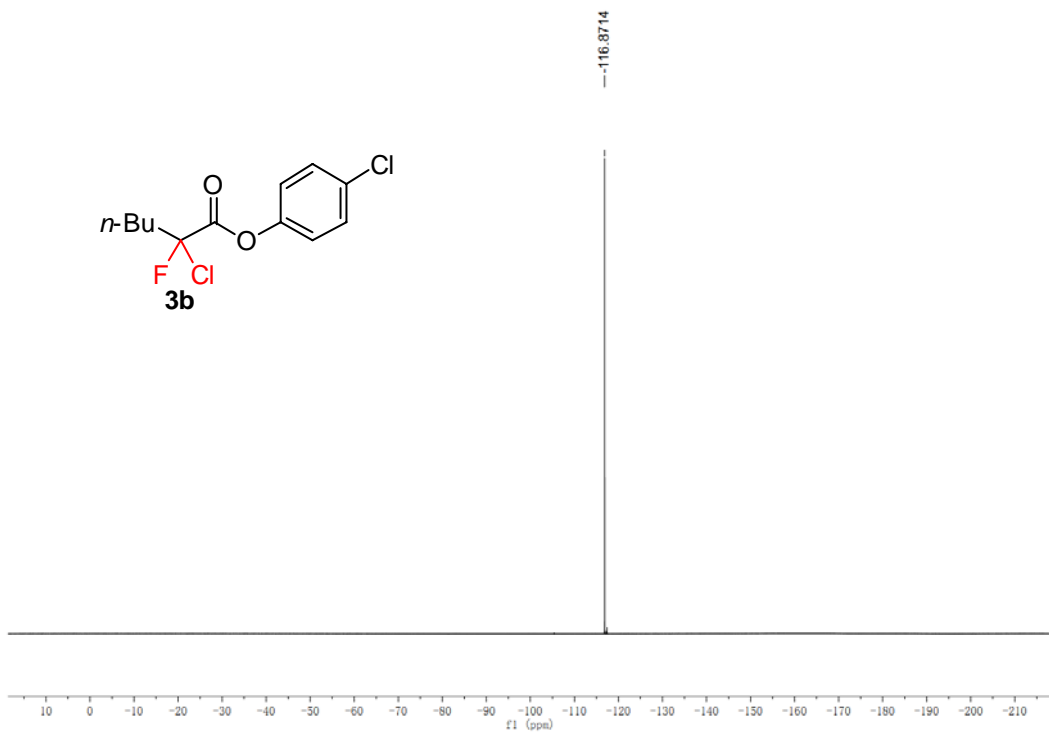
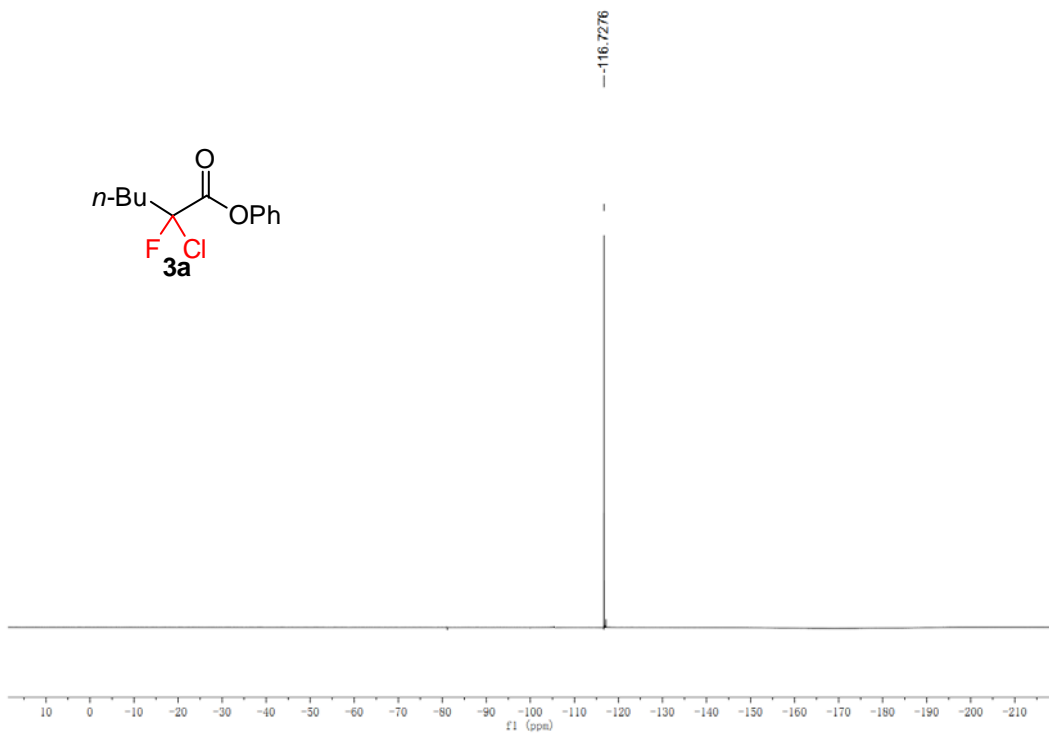


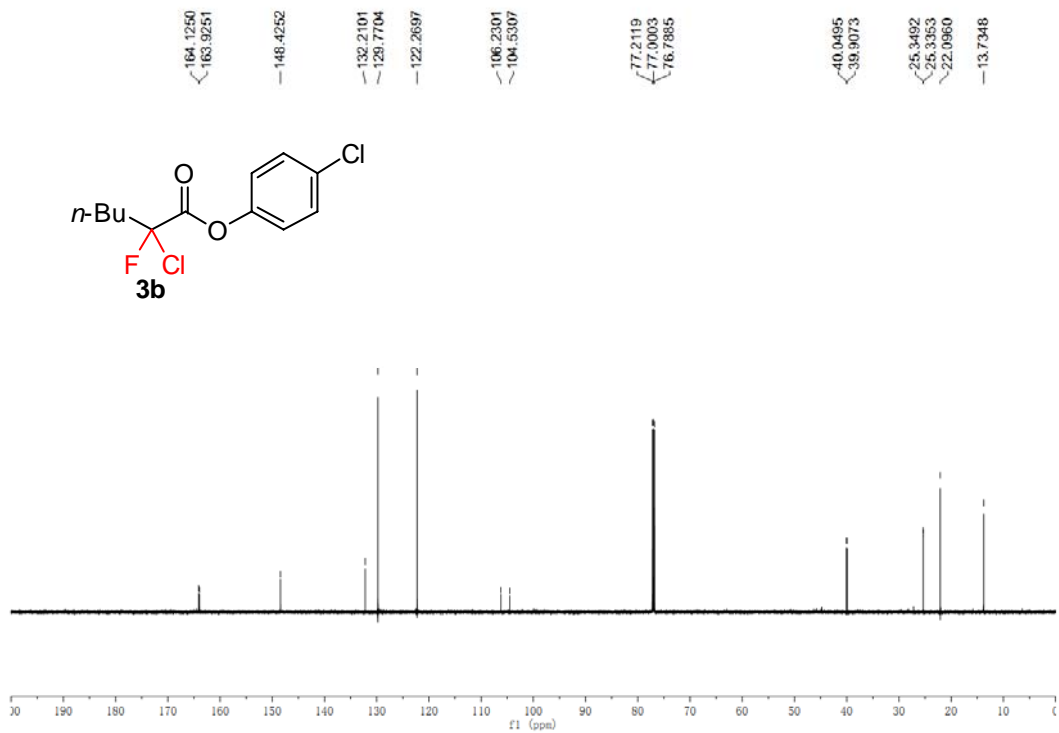
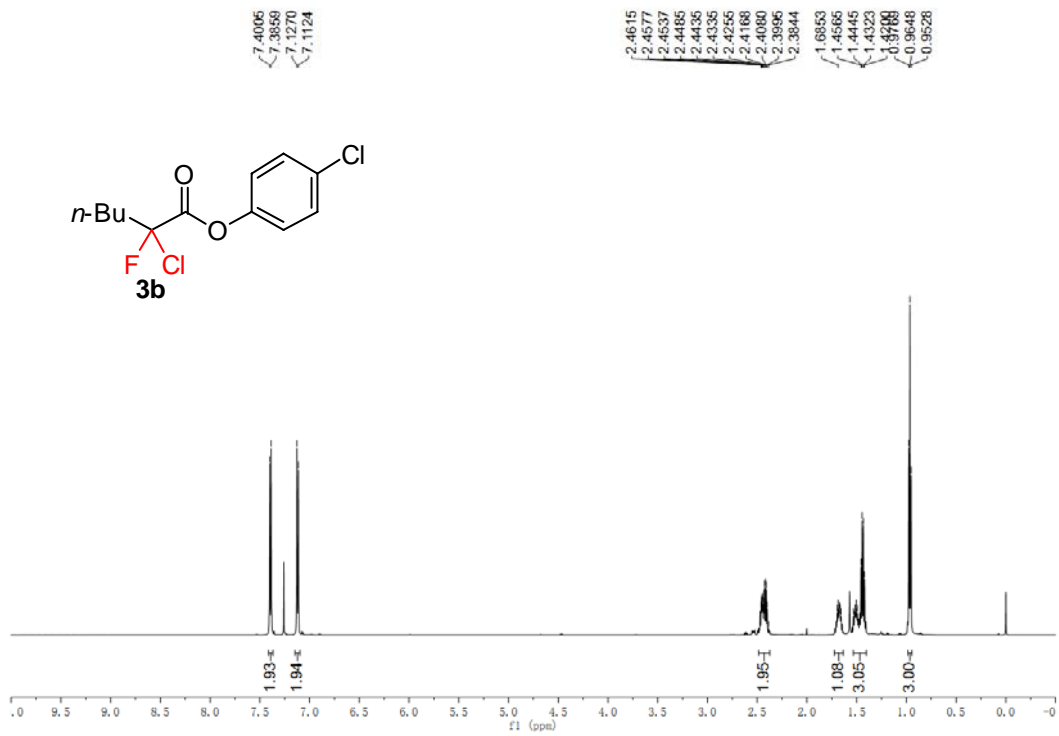
Compound 5a. To a solution of **3e** (76.5 mg, 0.25 mmol) in 2.5 mL of CH_2Cl_2 at room temperature were added $i\text{-Pr}_2\text{NEt}$ (32.3 mg, 0.25 mmol), $n\text{-Bu}_4\text{NI}$ (92.3 mg, 0.25 mmol) and BnNH_2 (32.1 mg, 0.3 mmol). After stirring at room temperature for 10 h, the reaction mixture was quenched with 5 mL of water, extracted with ethyl acetate, washed with brine, dried over anhydrous Na_2SO_4 and concentrated. Column chromatography on silica gel gave **5a** as a white solid (58.1 mg, 81% yield), mp: 88–90 °C; ^1H NMR (600 MHz, CDCl_3): δ 7.37–7.27 (m, 7 H), 7.20 (m, 3 H), 6.75 (br, 1 H), 4.52–4.50 (m, 2 H), 2.92–2.62 (m, 4 H); ^{13}C NMR (151 MHz, CDCl_3): δ 165.6 (d, $J = 27.5$ Hz), 139.5, 136.9, 128.9, 128.6, 128.4, 127.9, 127.7, 126.4, 108.1 (d, $J = 257.2$ Hz), 43.7, 41.5 (d, $J = 21.2$ Hz), 29.6 (d, $J = 2.6$ Hz); ^{19}F NMR (565 MHz, CDCl_3): δ -117.9; HRMS (APCI) calcd for $\text{C}_{17}\text{H}_{18}\text{NO}_2\text{F}$ (M^+) 287.1322, found 287.1342.

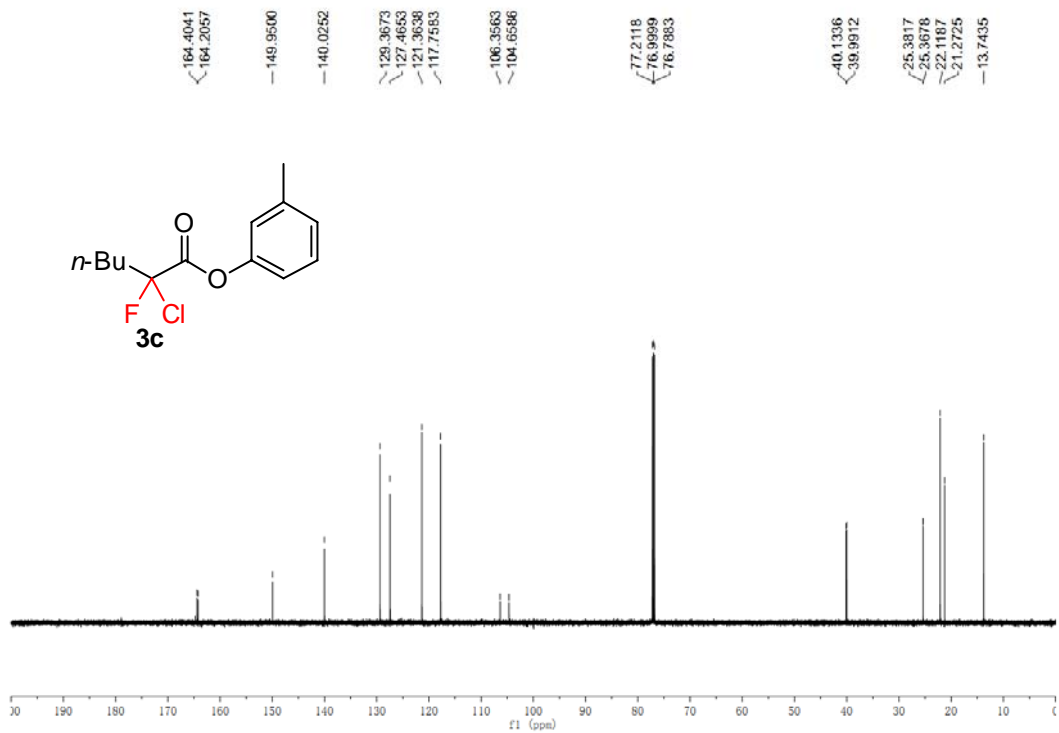
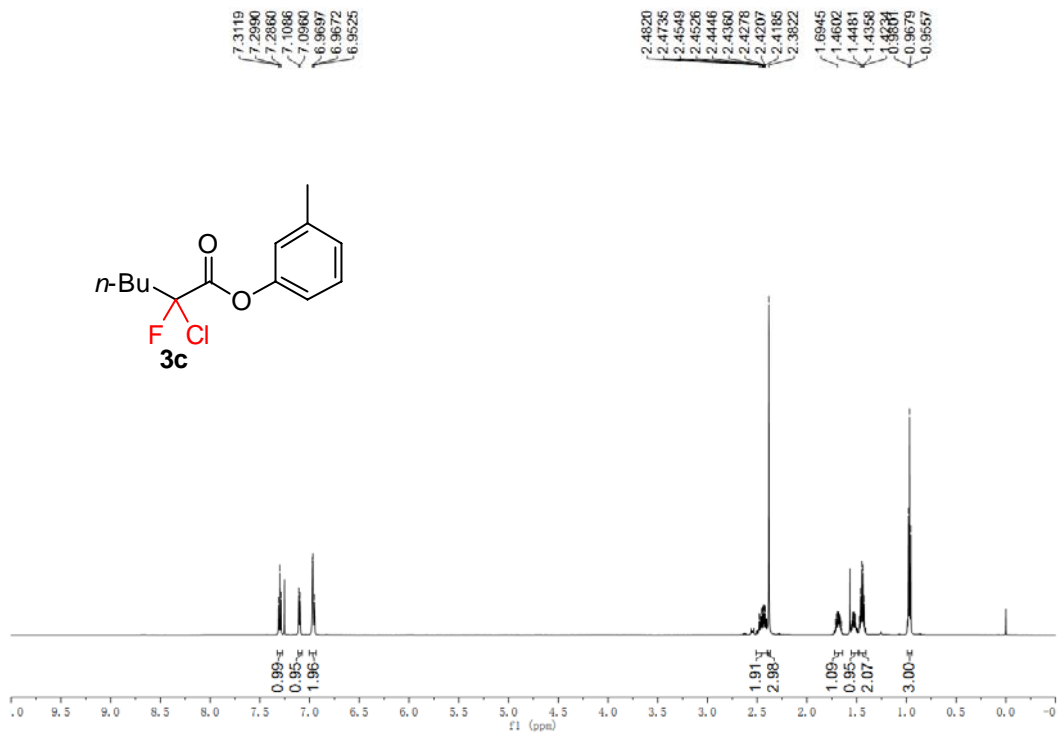


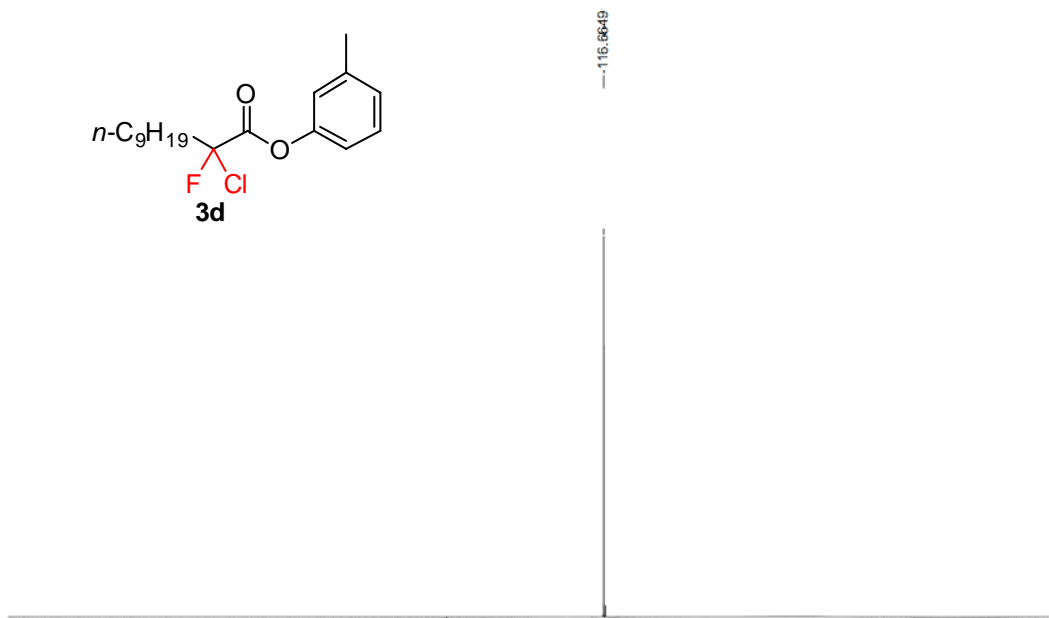
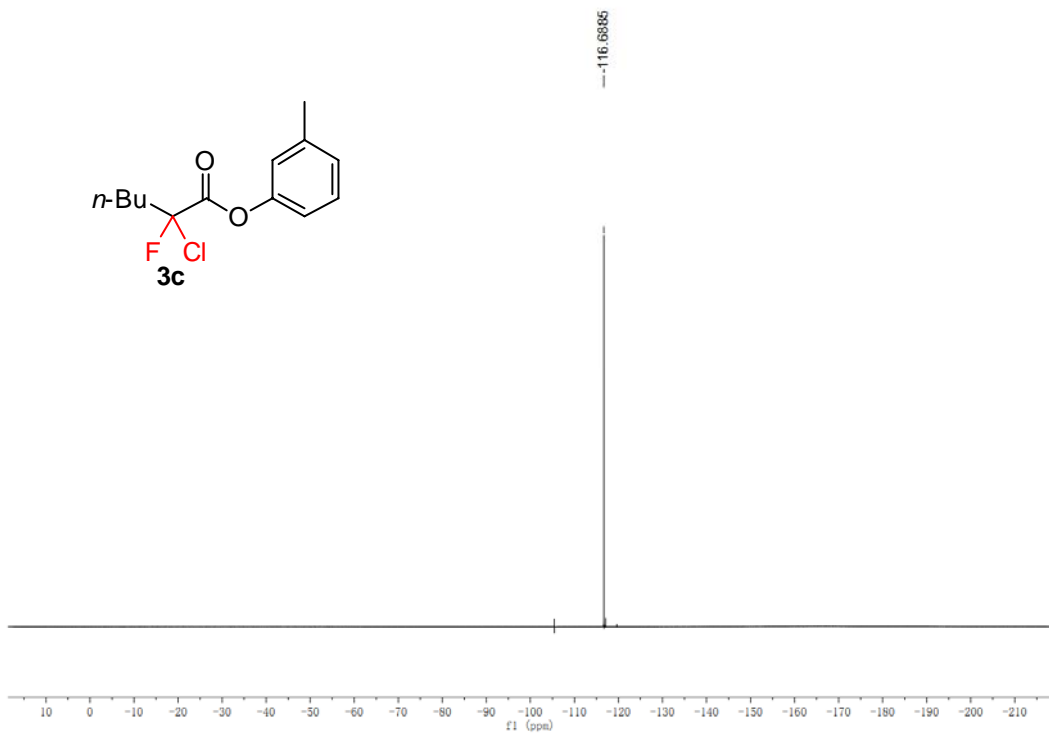
Compound 5b. 41.8 mg, 75% yield, colorless oil; ^1H NMR (600 MHz, CDCl_3): δ 7.37–7.35 (m, 2 H), 7.32–7.26 (m, 3 H), 6.67 (br, 1 H), 5.85–5.73 (m, 1 H), 5.33–5.18 (m, 2 H), 4.51 (d, $J = 5.8$ Hz, 2 H), 3.23–3.03 (m, 2 H); ^{13}C NMR (151 MHz, CDCl_3): δ 165.4 (d, $J = 23.9$ Hz), 136.9, 128.8, 128.6 (d, $J = 2.7$ Hz), 127.9, 127.8, 121.8, 107.3 (d, $J = 257.2$ Hz), 44.0 (d, $J = 21.5$ Hz), 43.7; ^{19}F NMR (565 MHz, CDCl_3): δ -118.0; HRMS (APCI) calcd for $\text{C}_{12}\text{H}_{15}\text{NO}_2\text{F}$ ($\text{M}+\text{H}$) $^+$ 224.1087, found 224.1098.

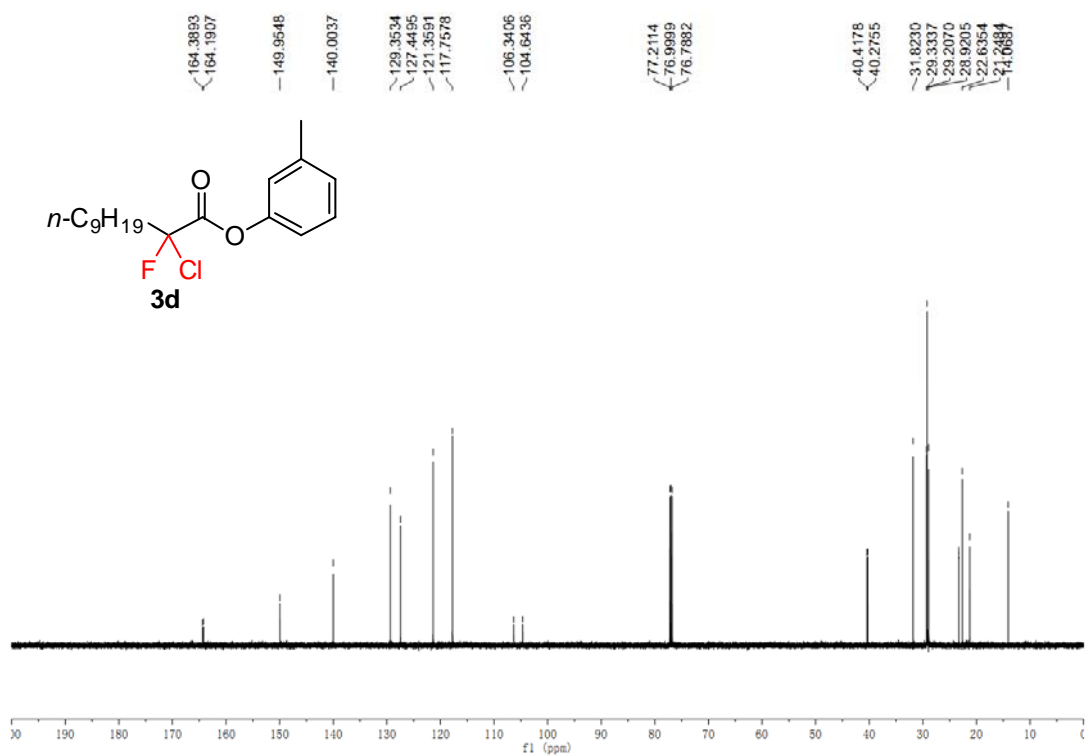
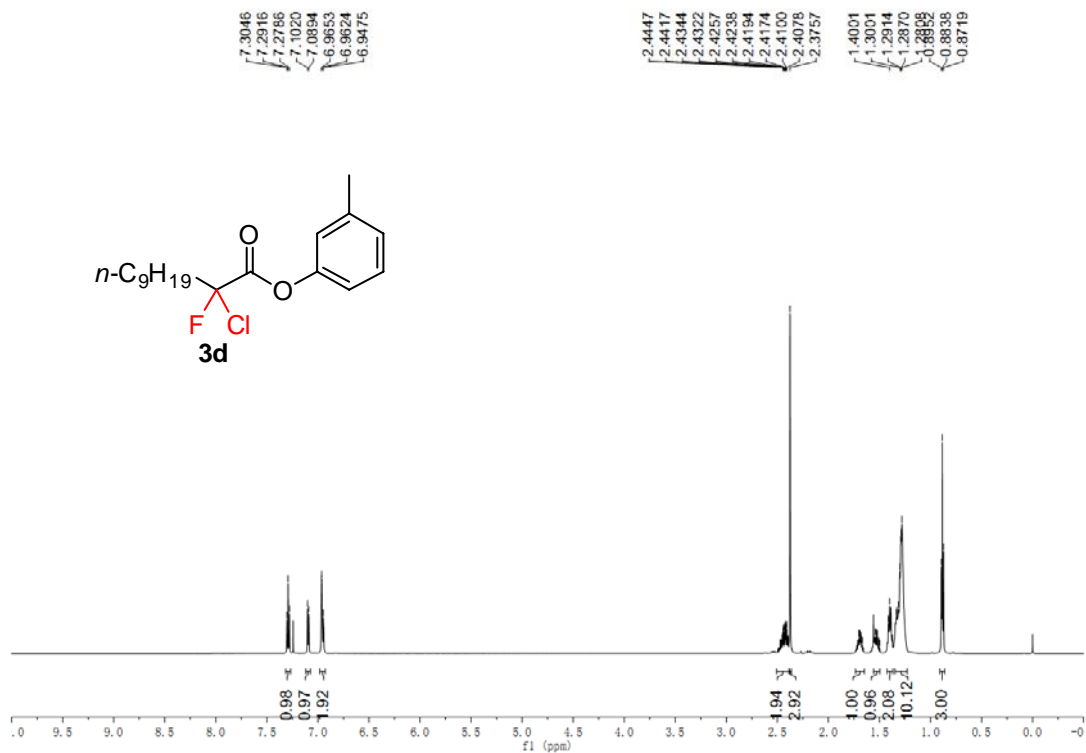


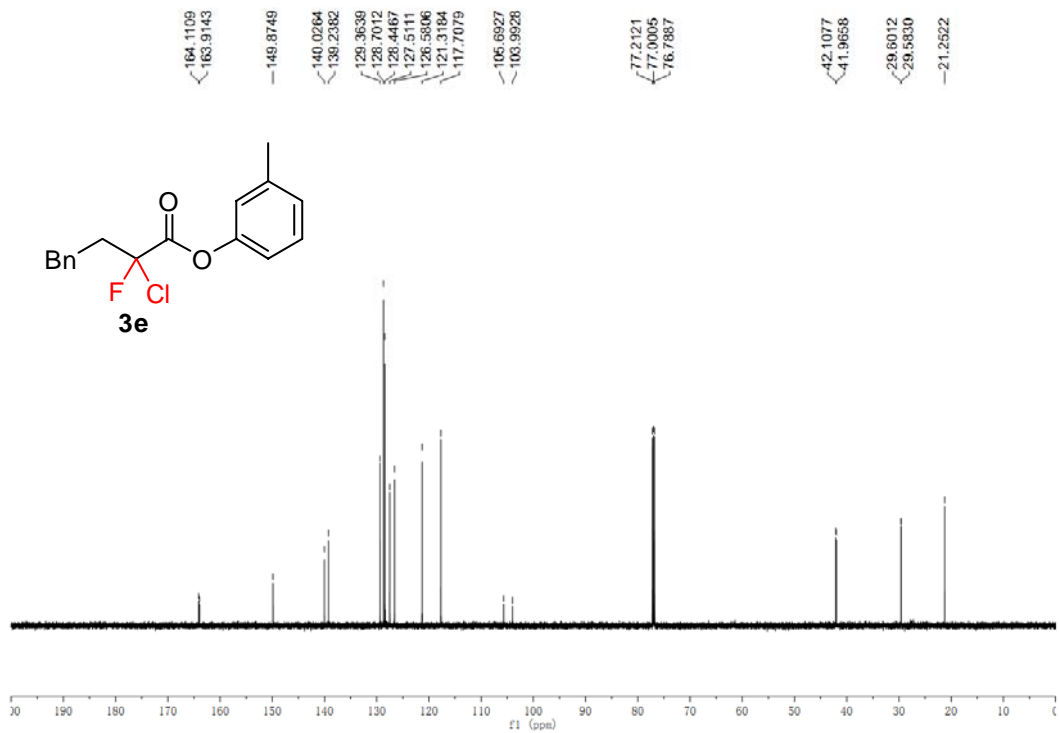
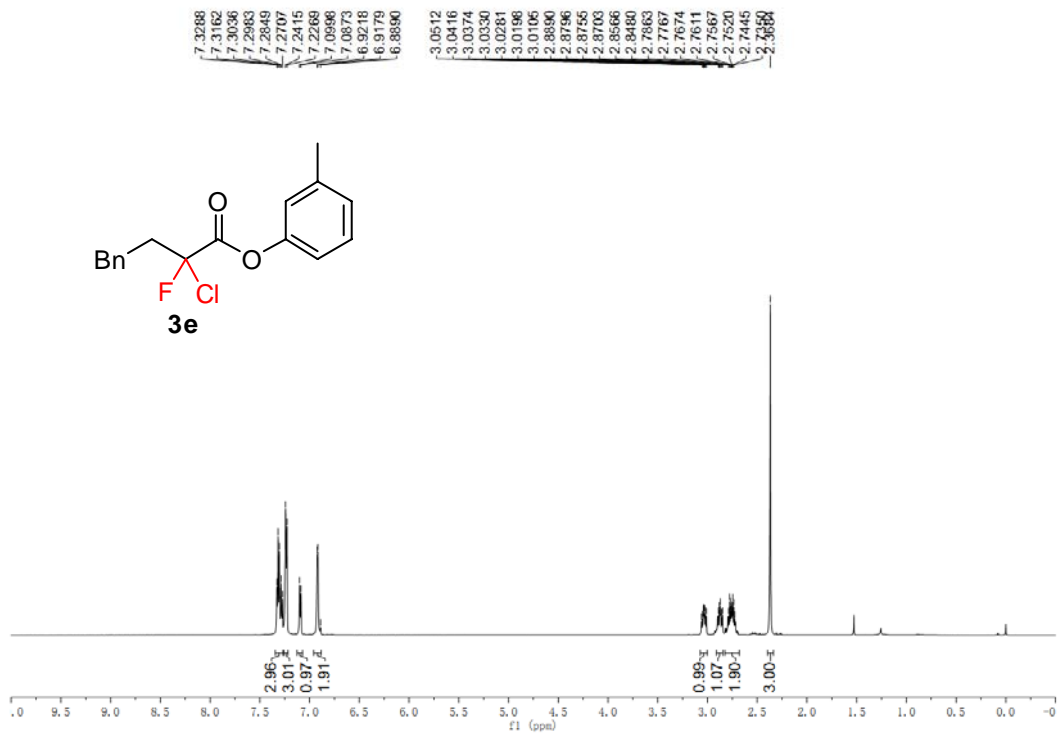


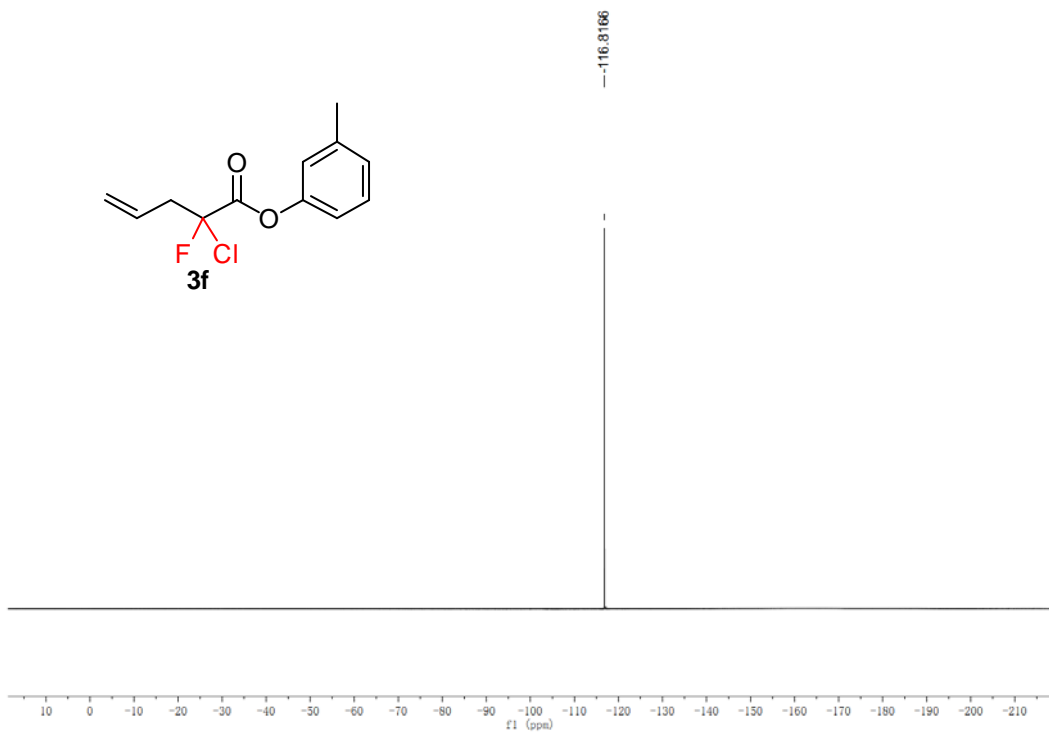
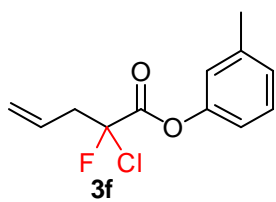
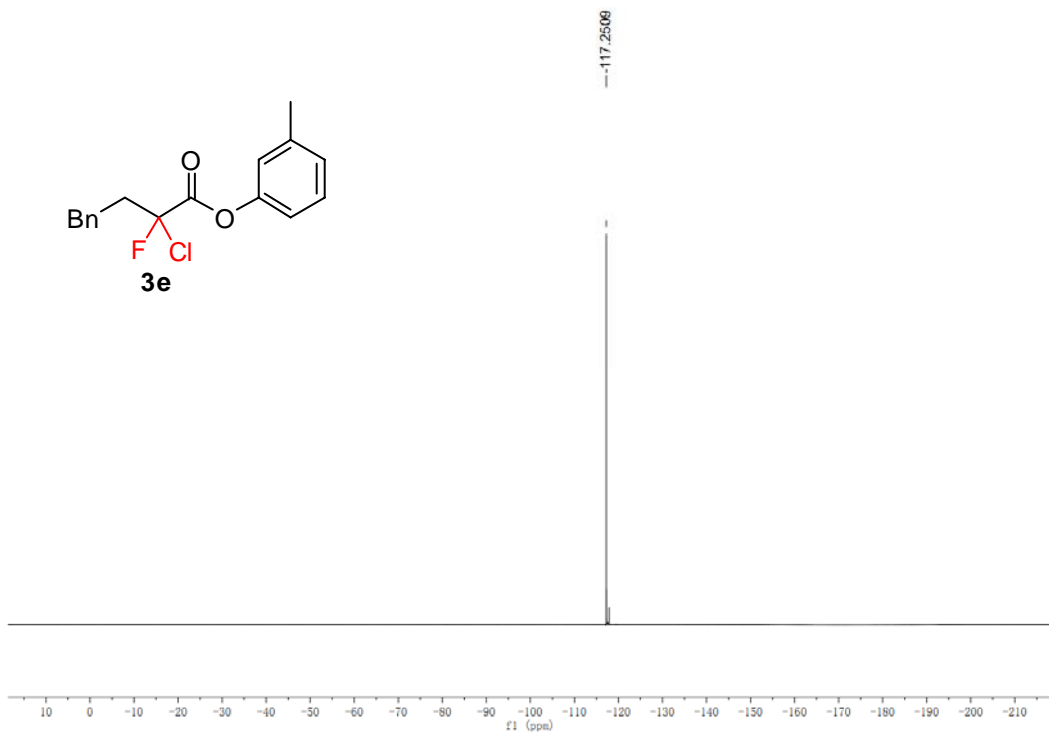
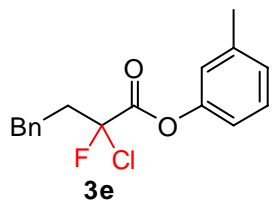


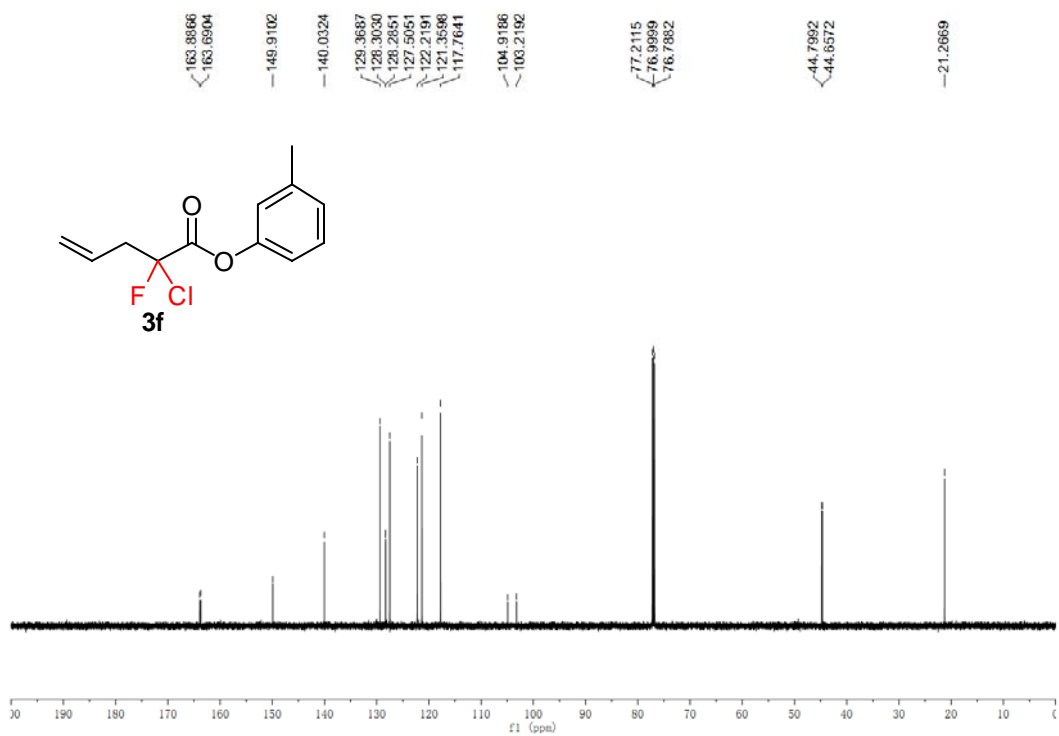
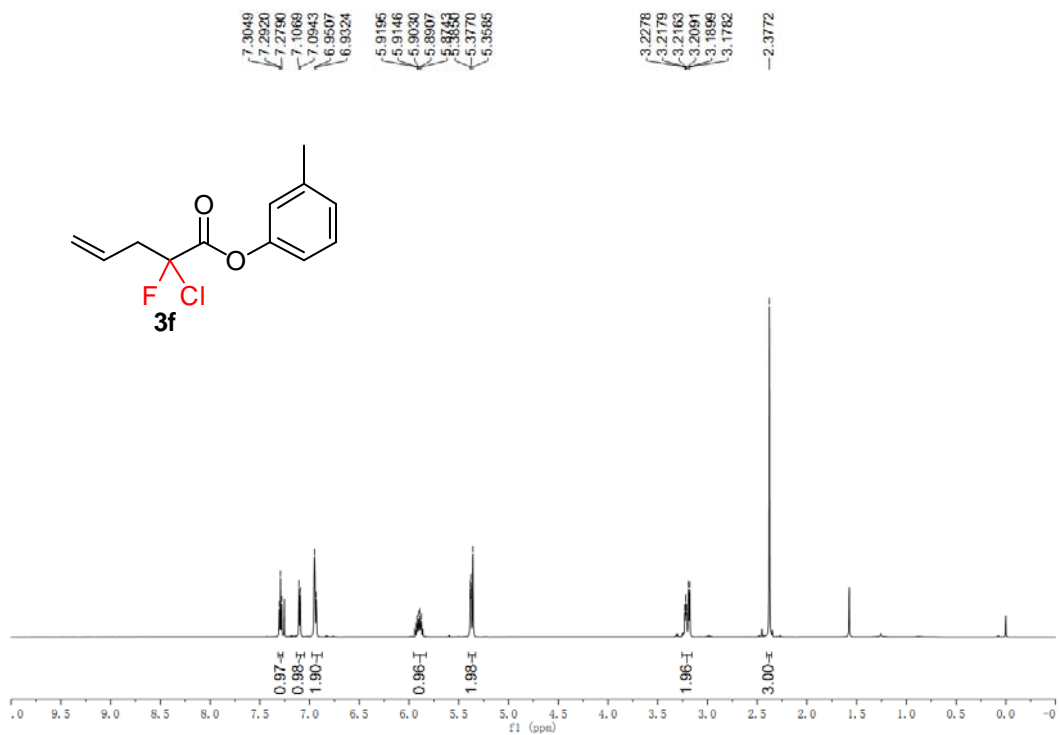


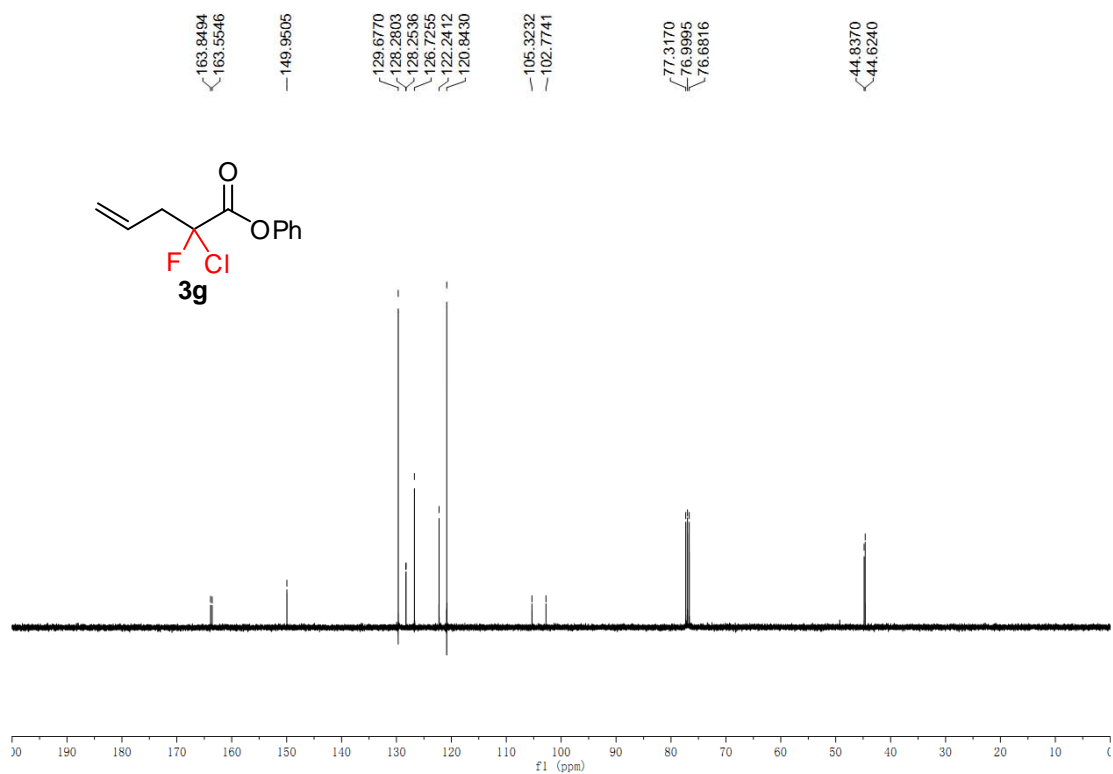
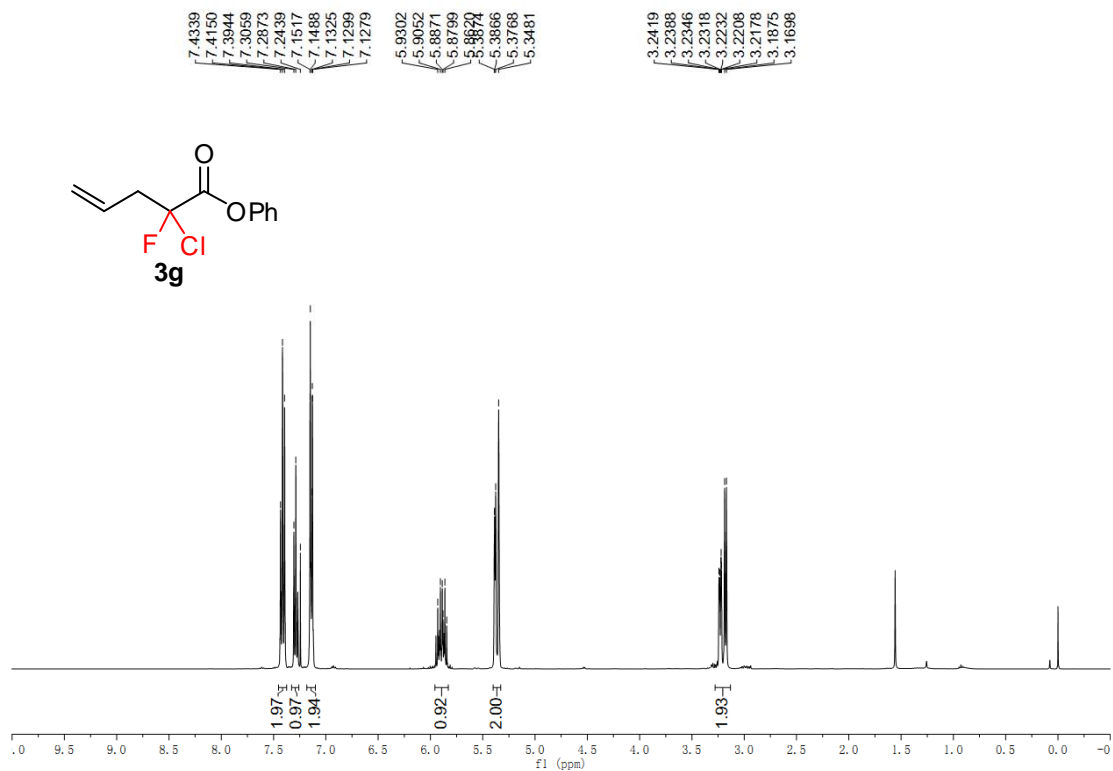


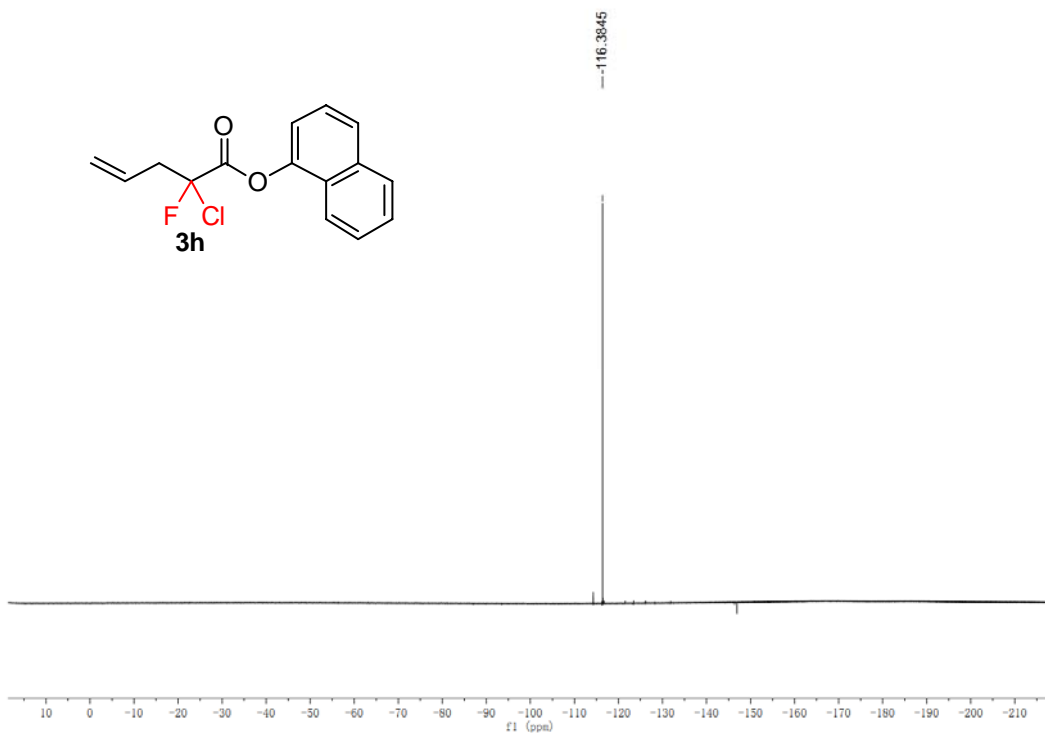
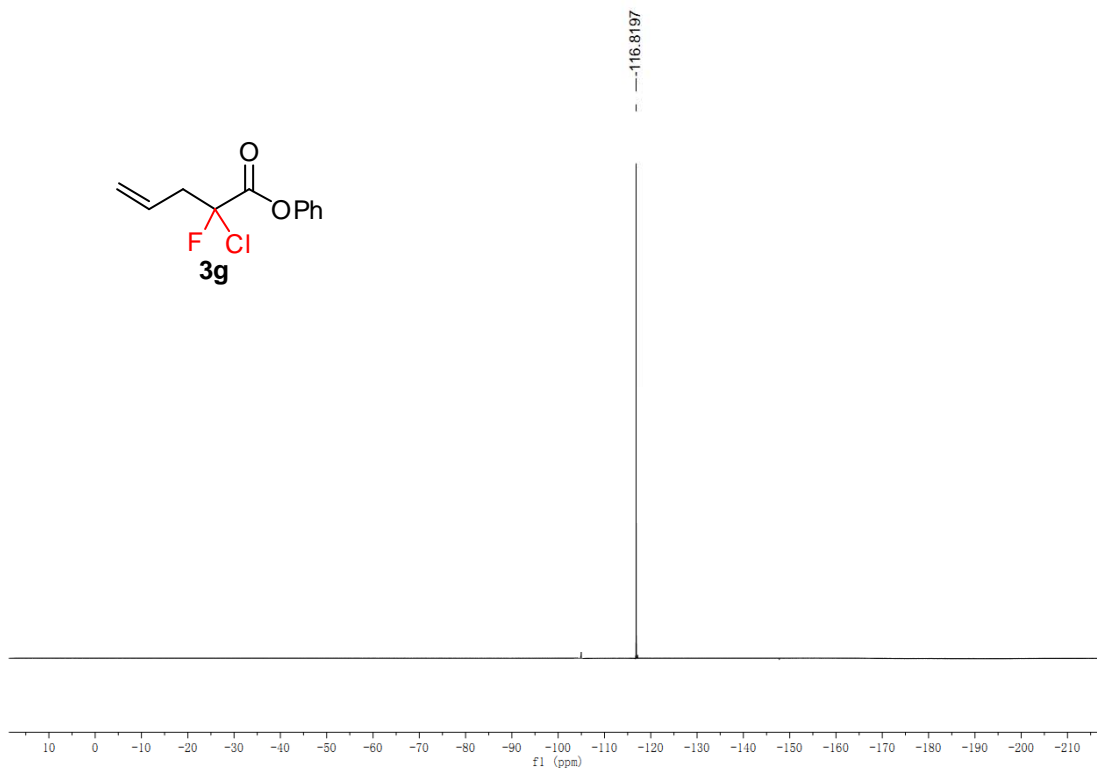


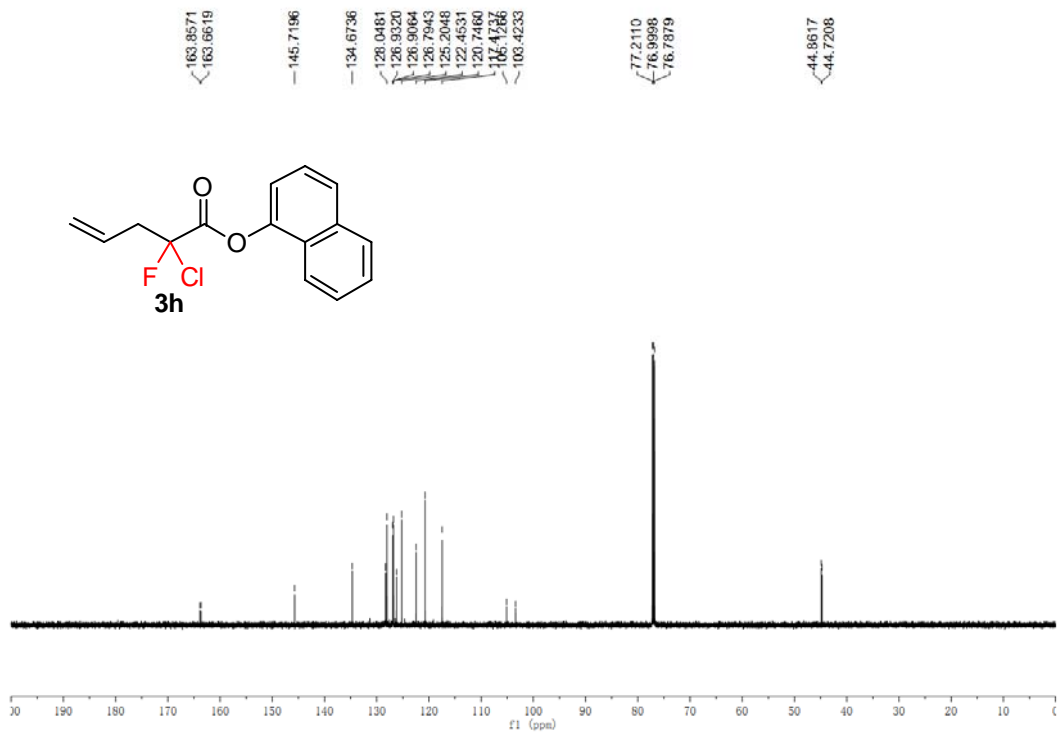
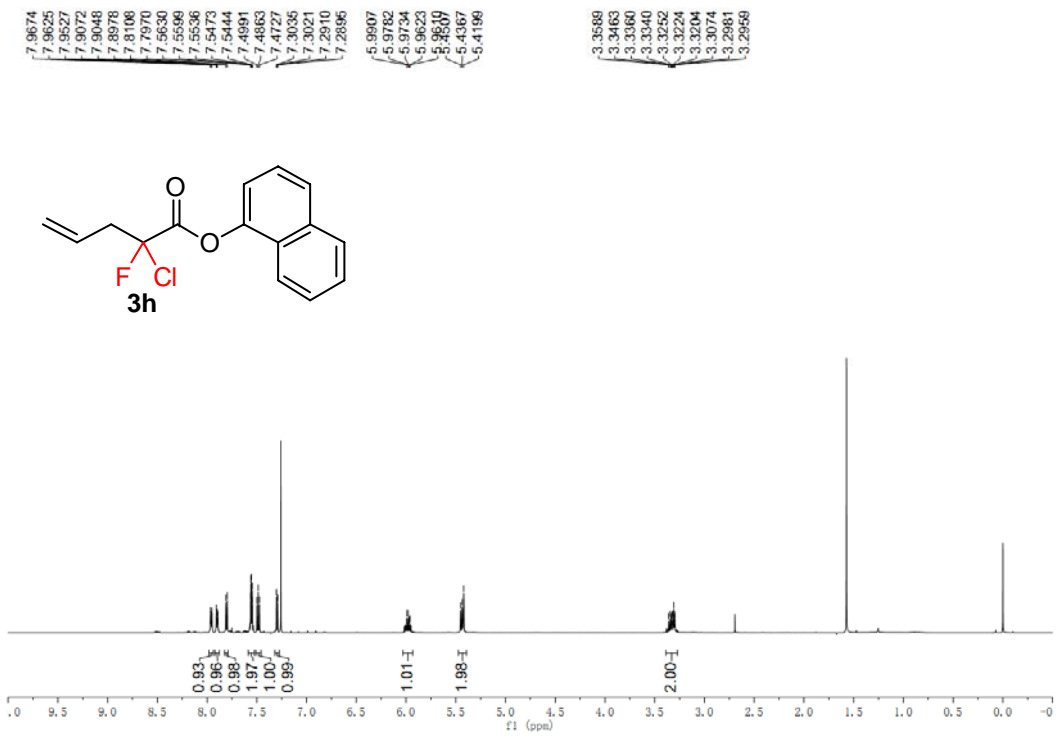


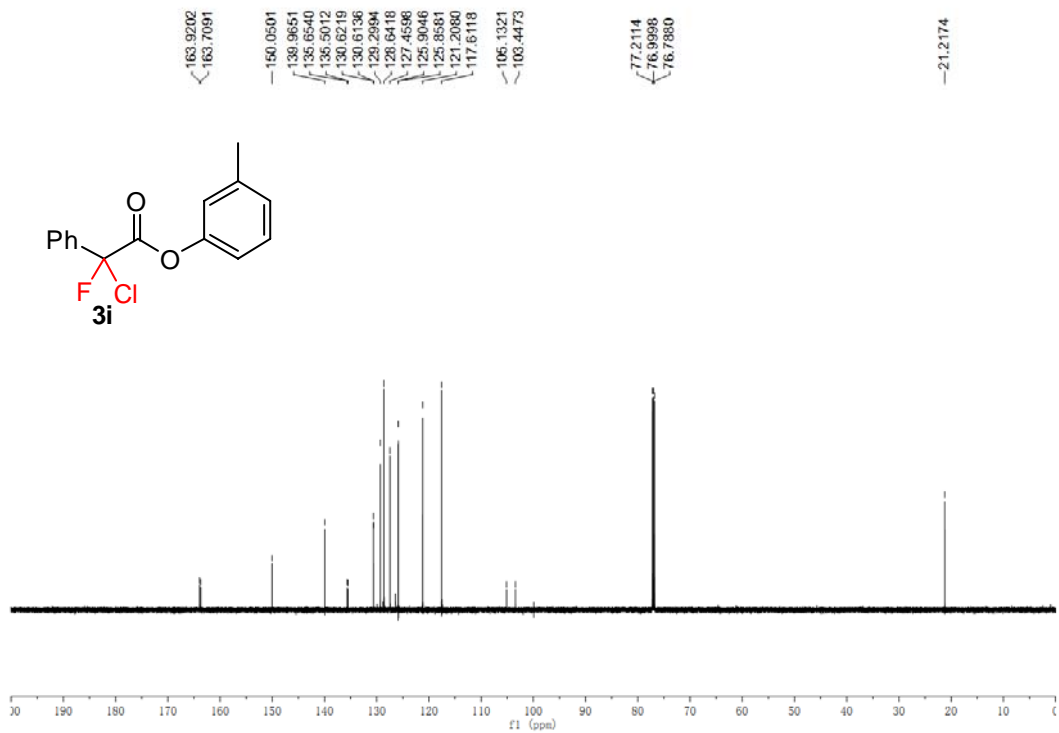
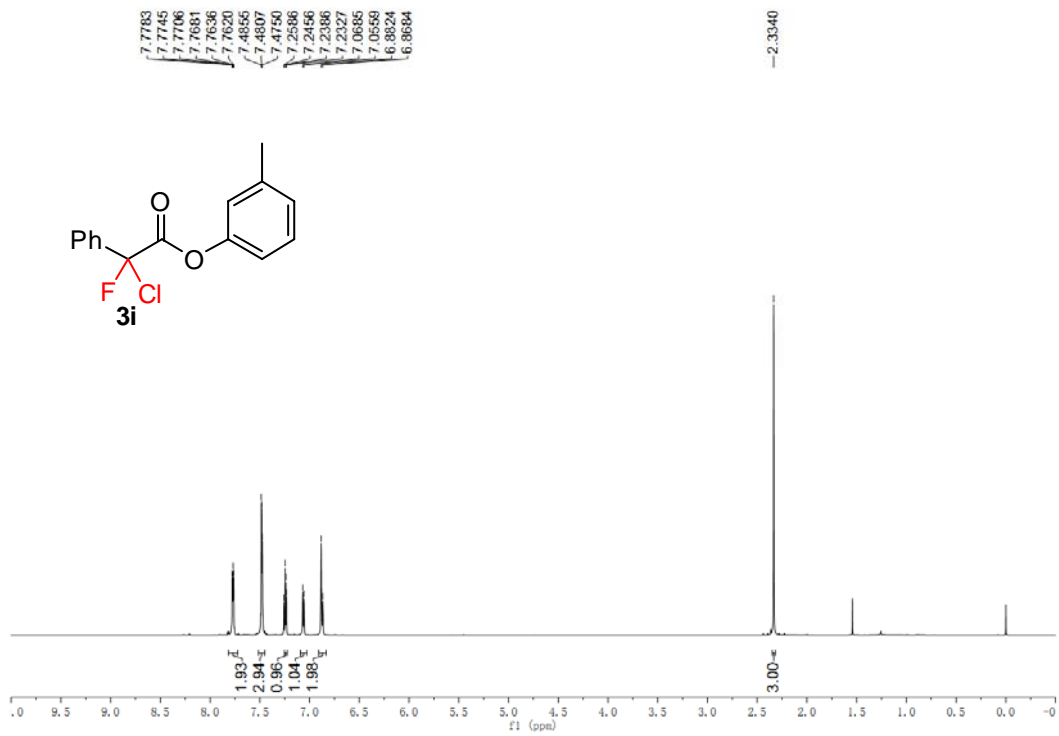


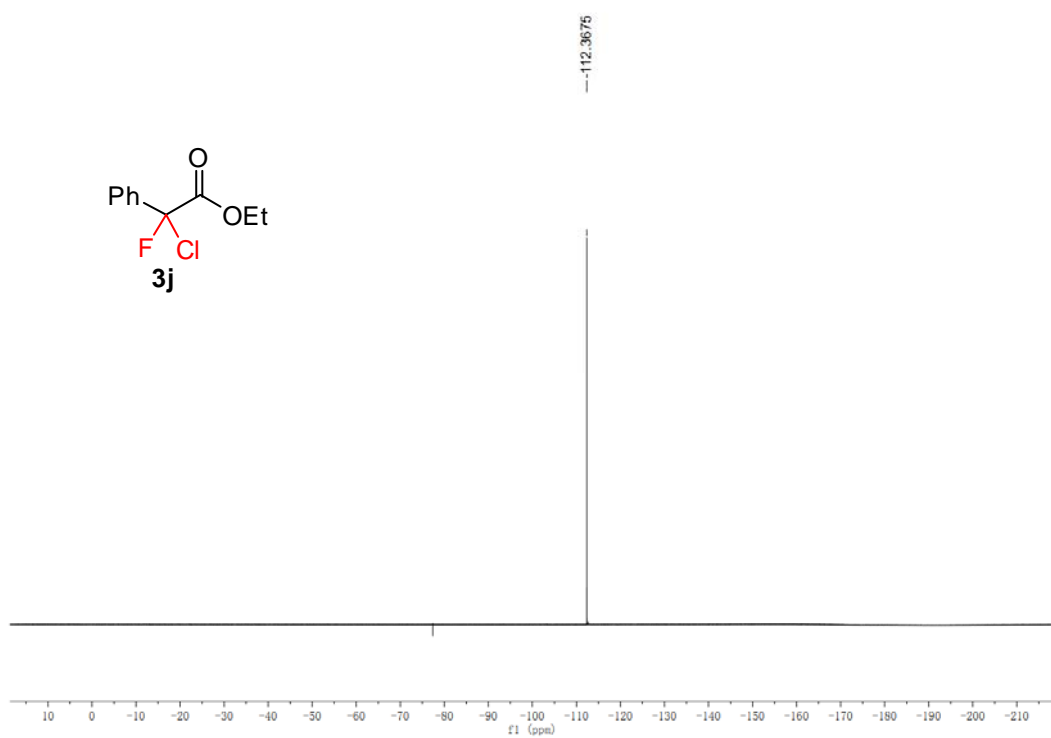
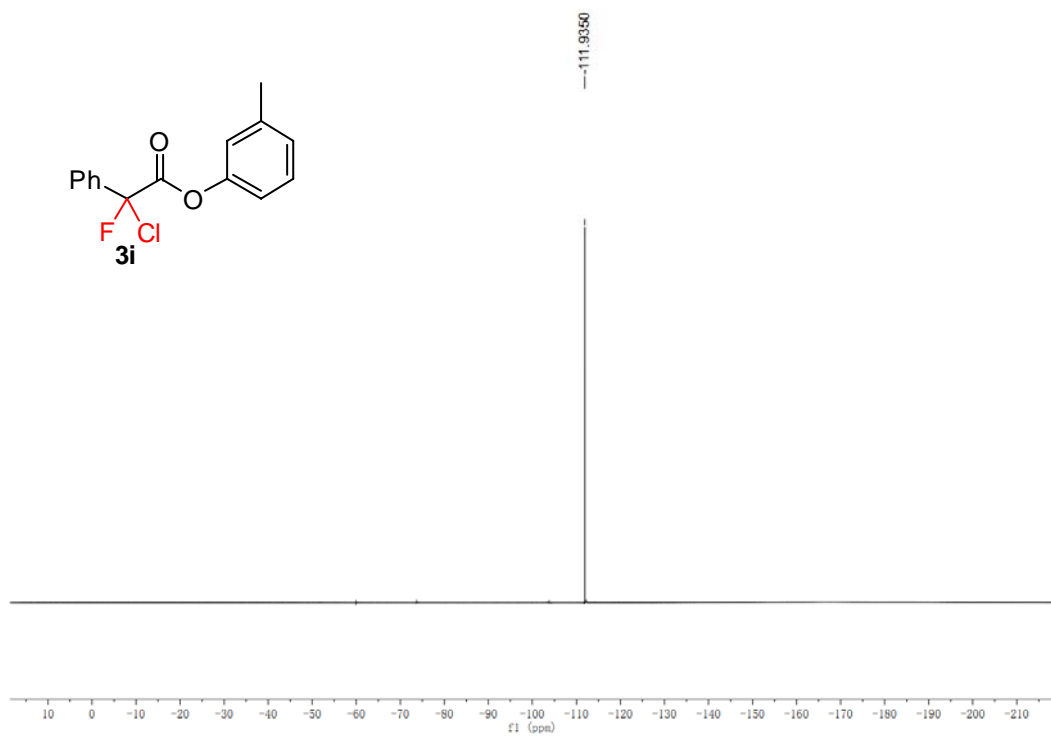


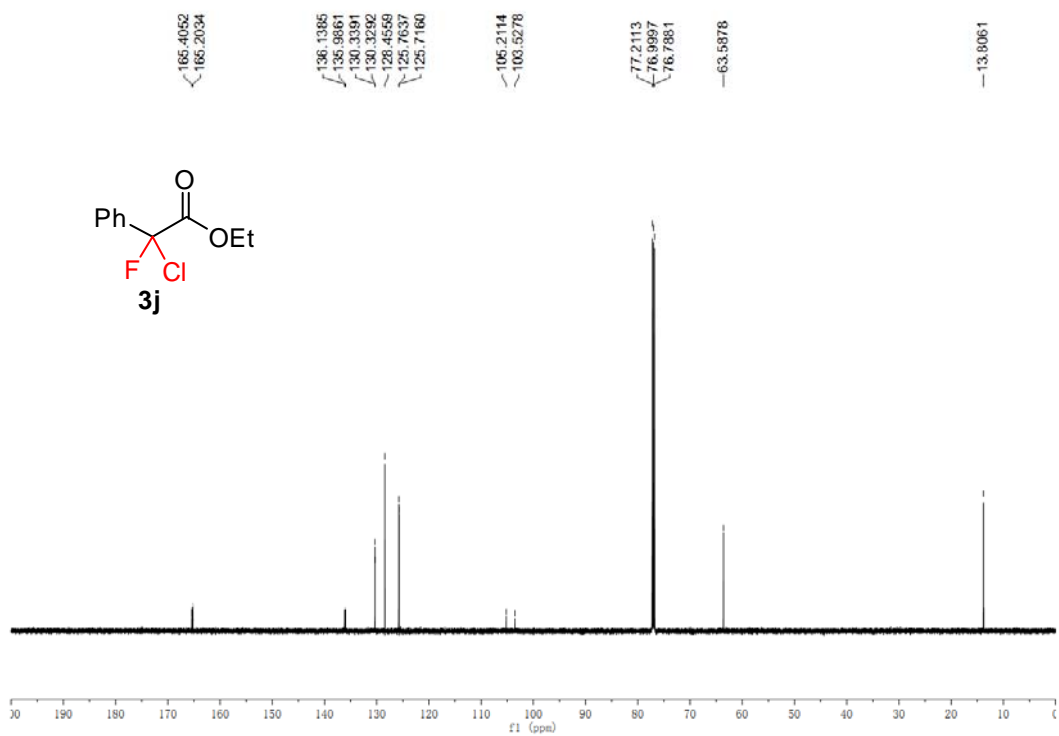
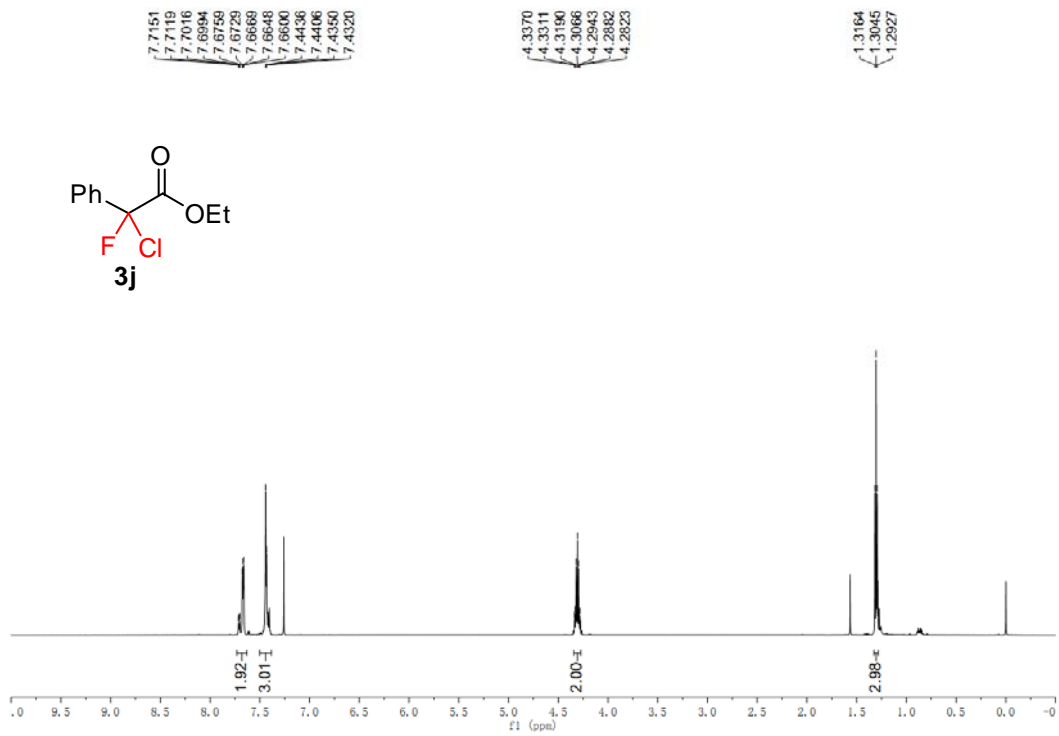


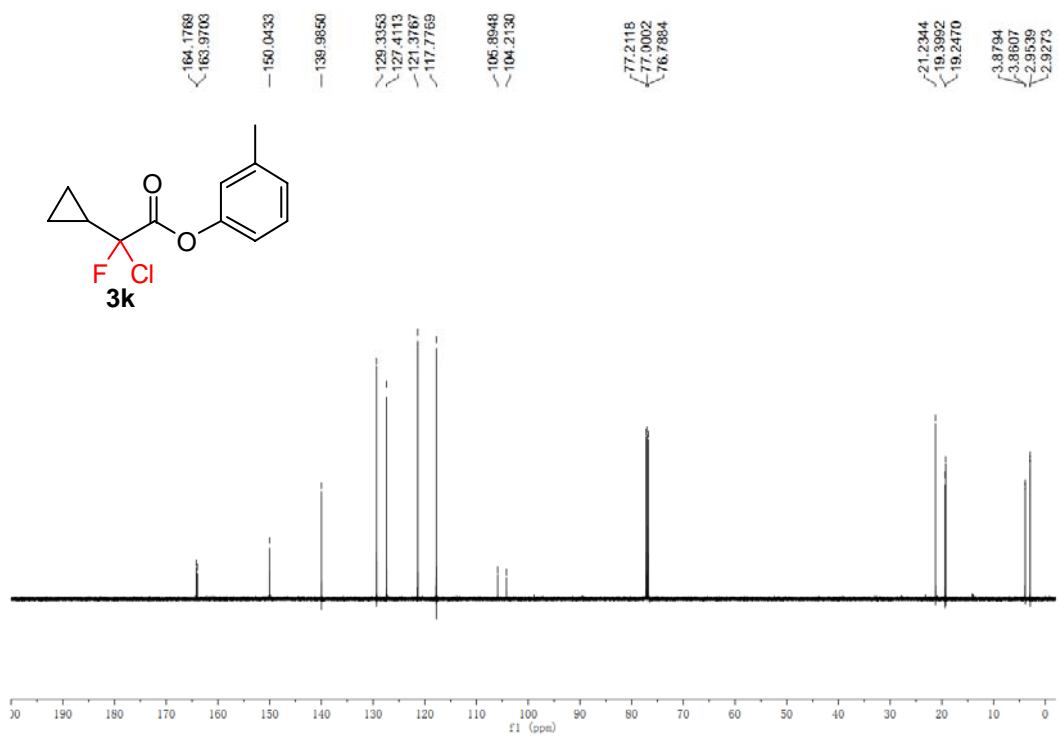
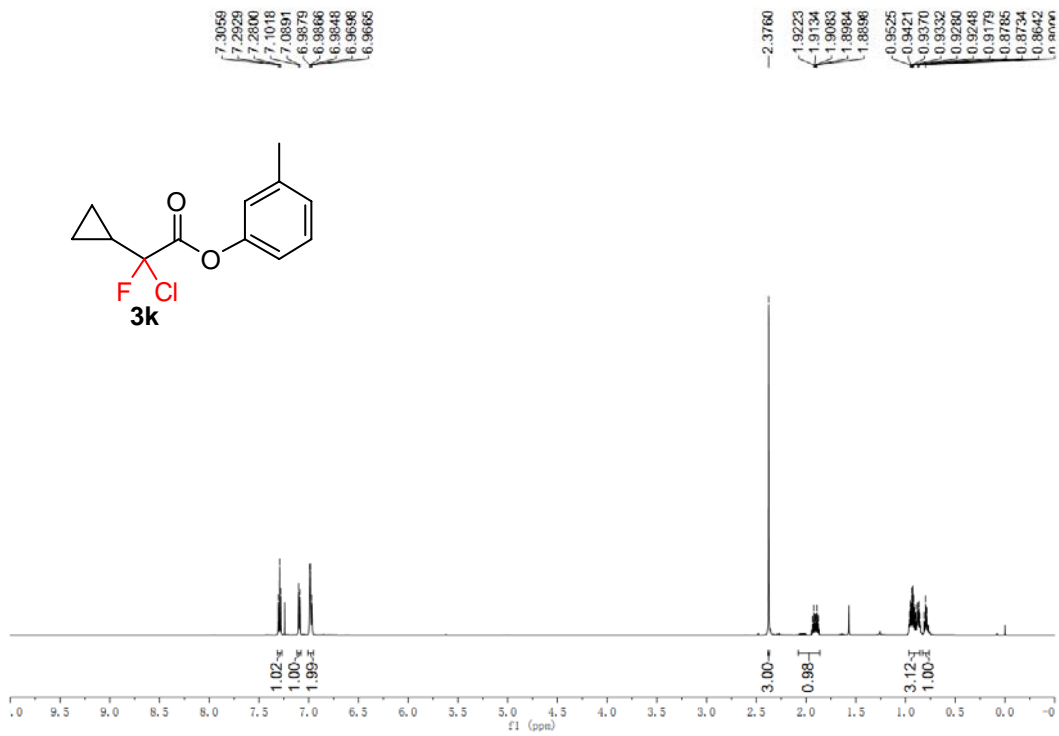


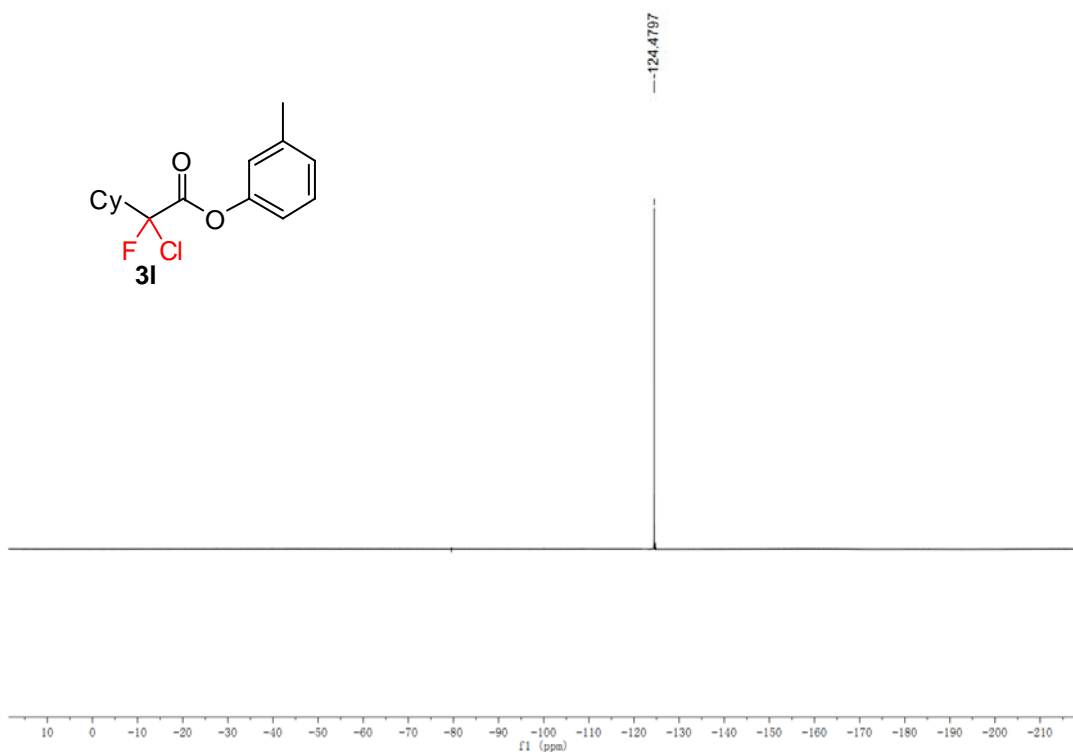
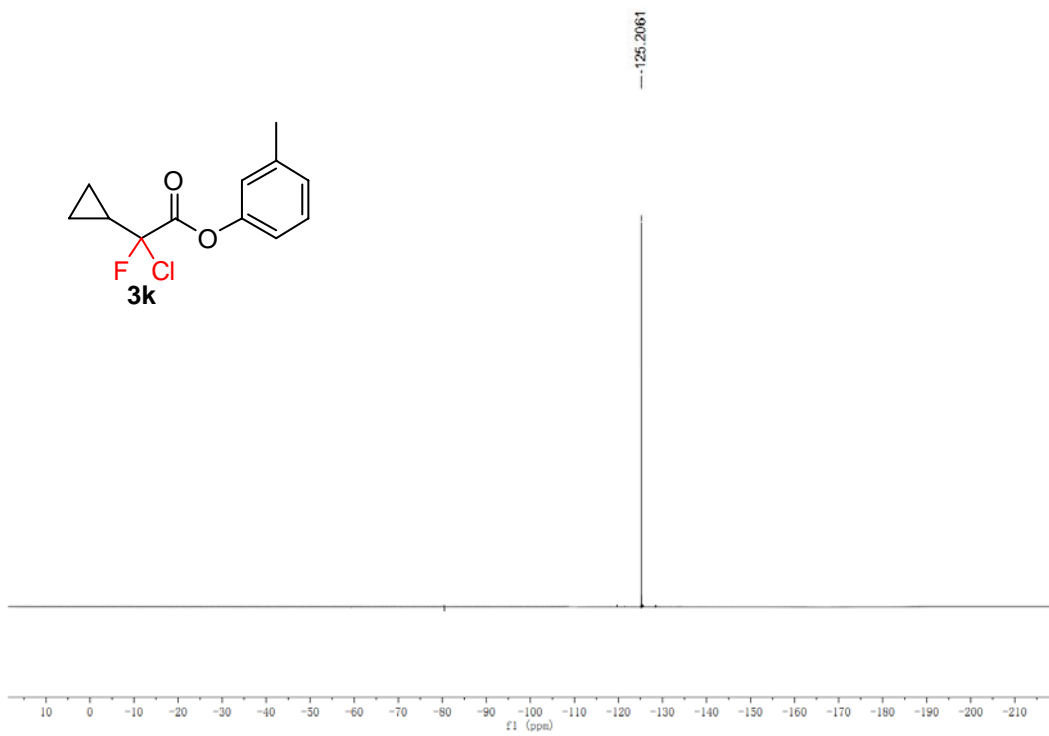


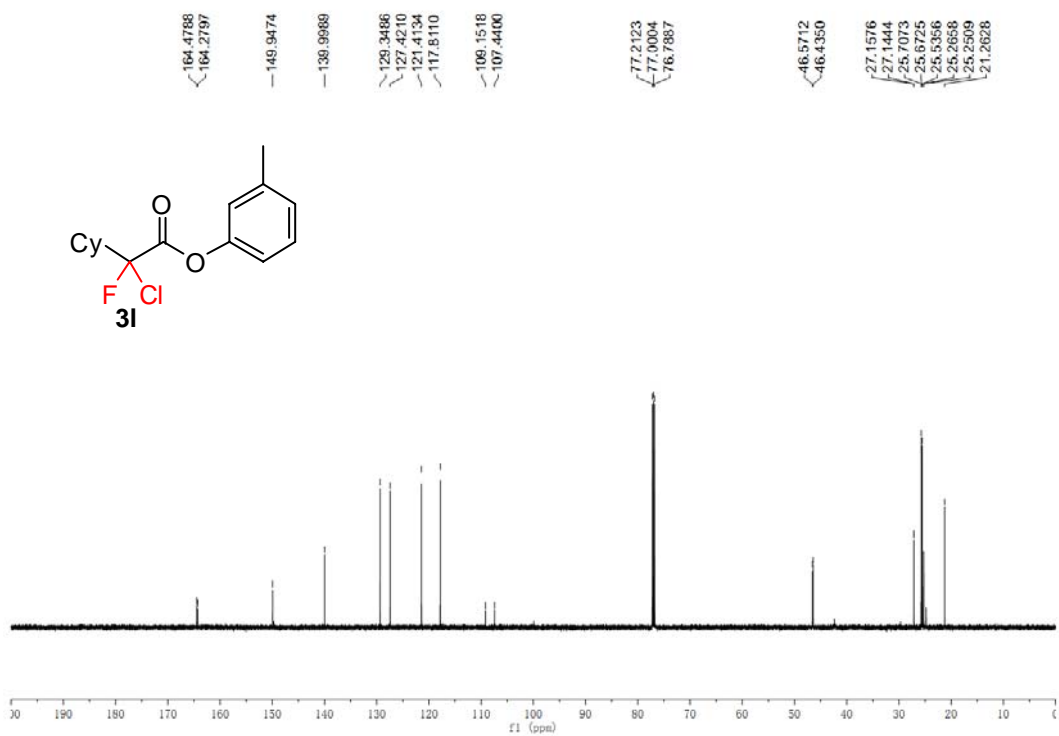
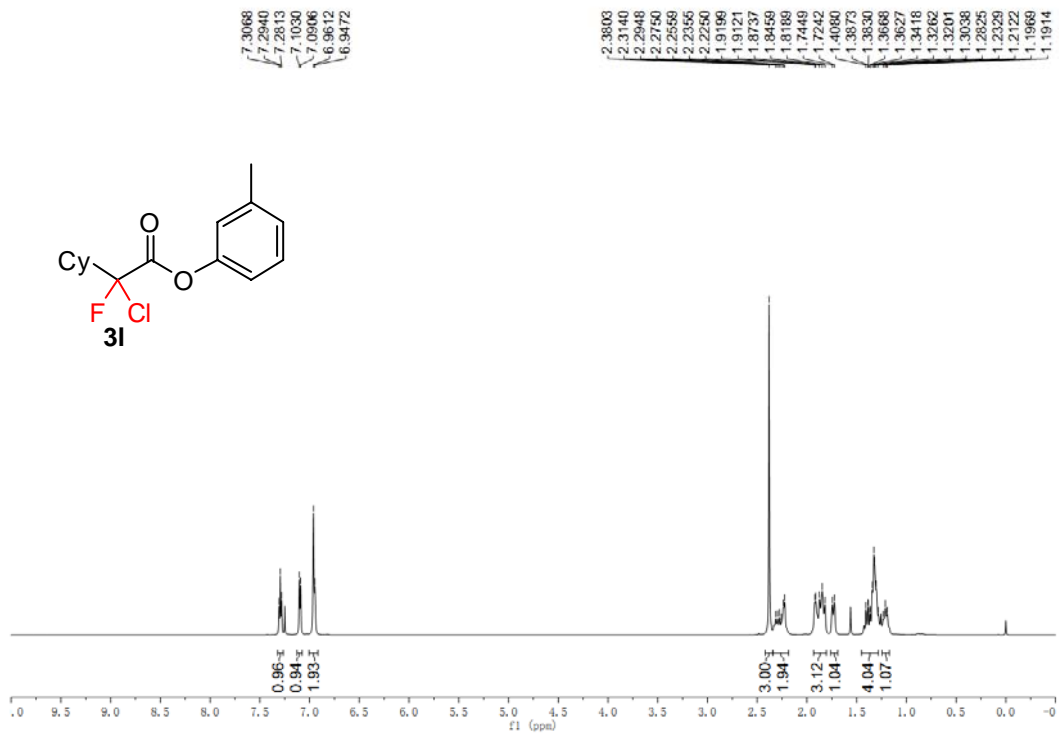


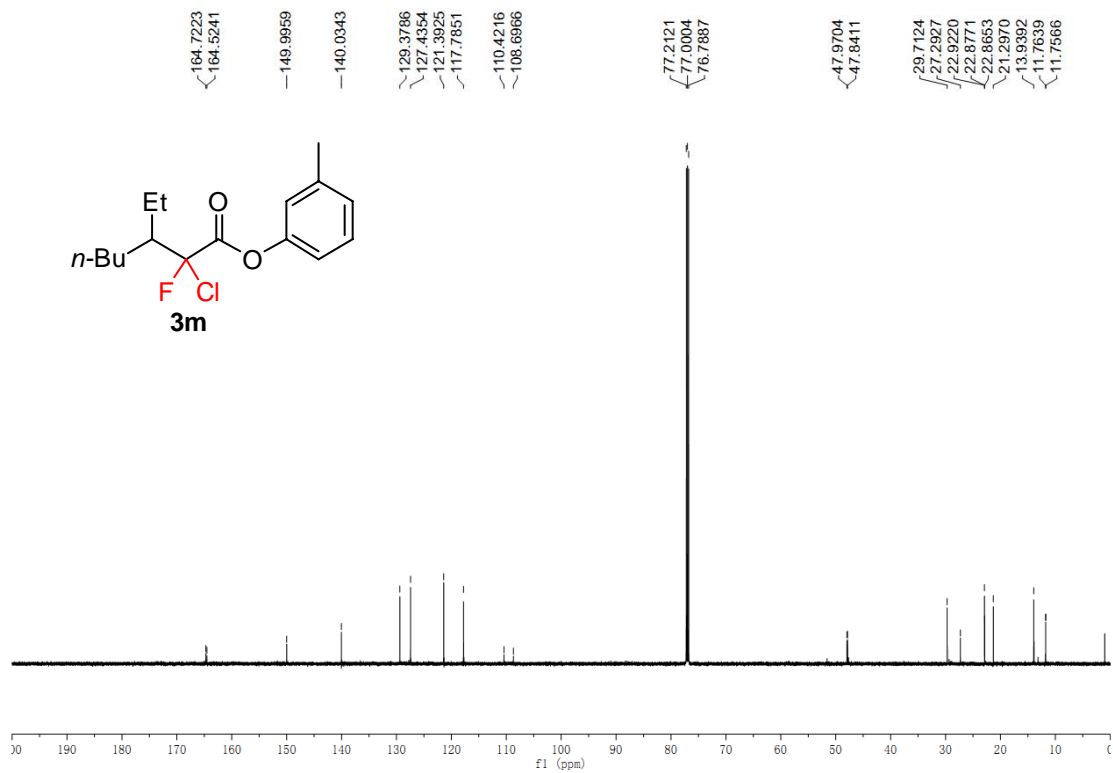
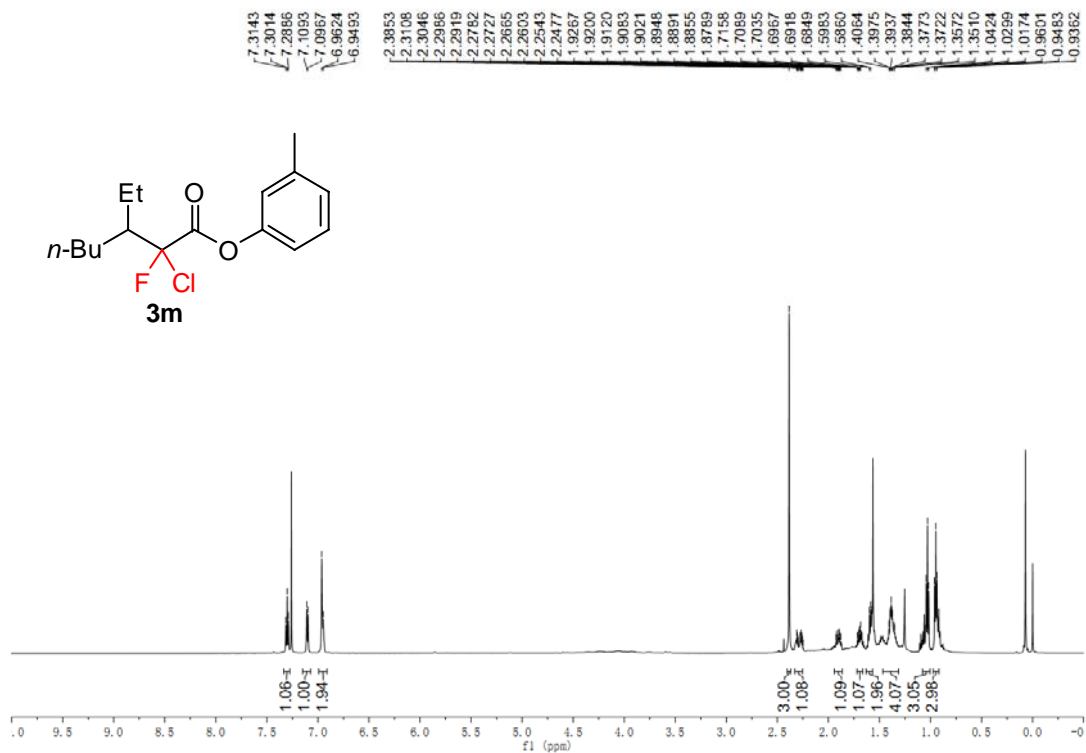


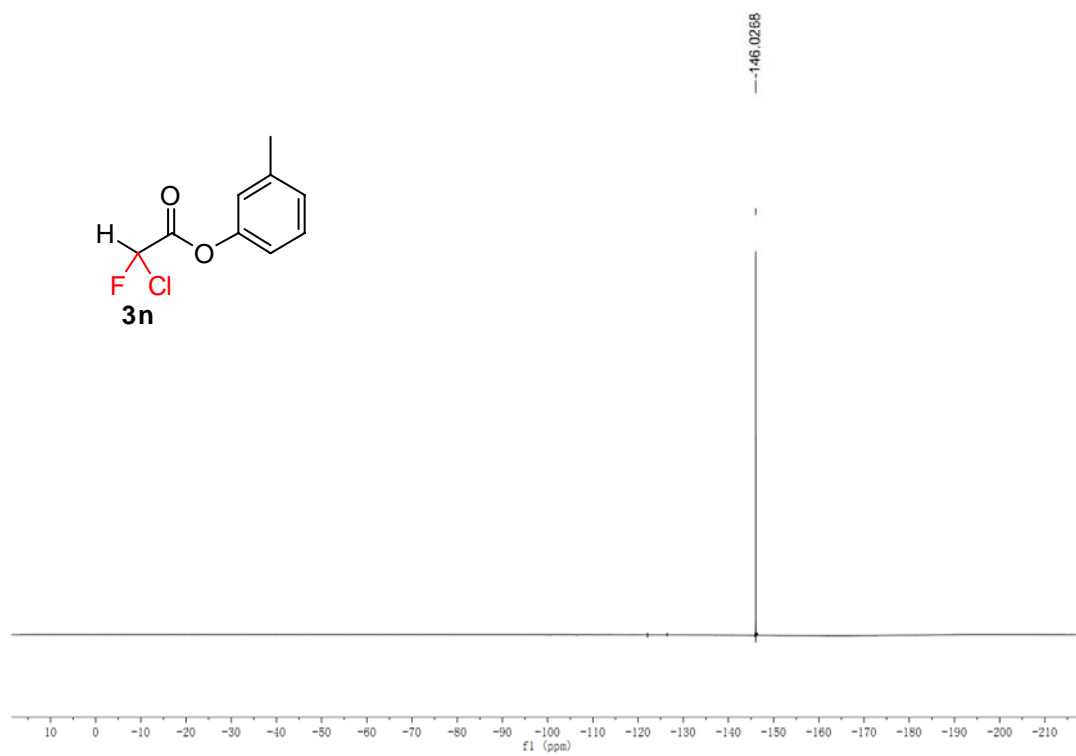
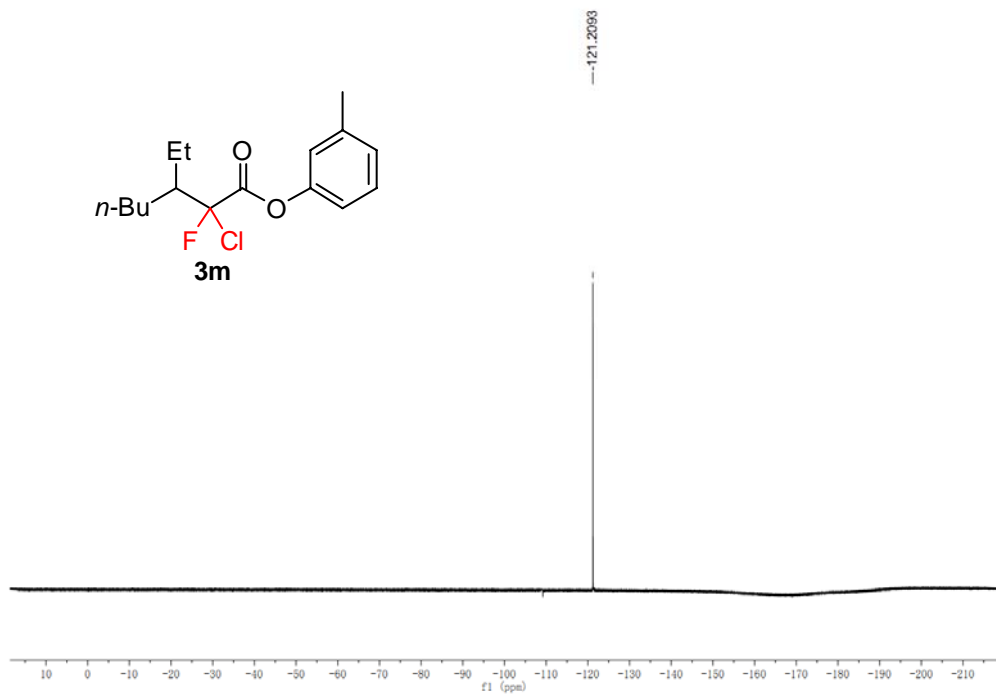


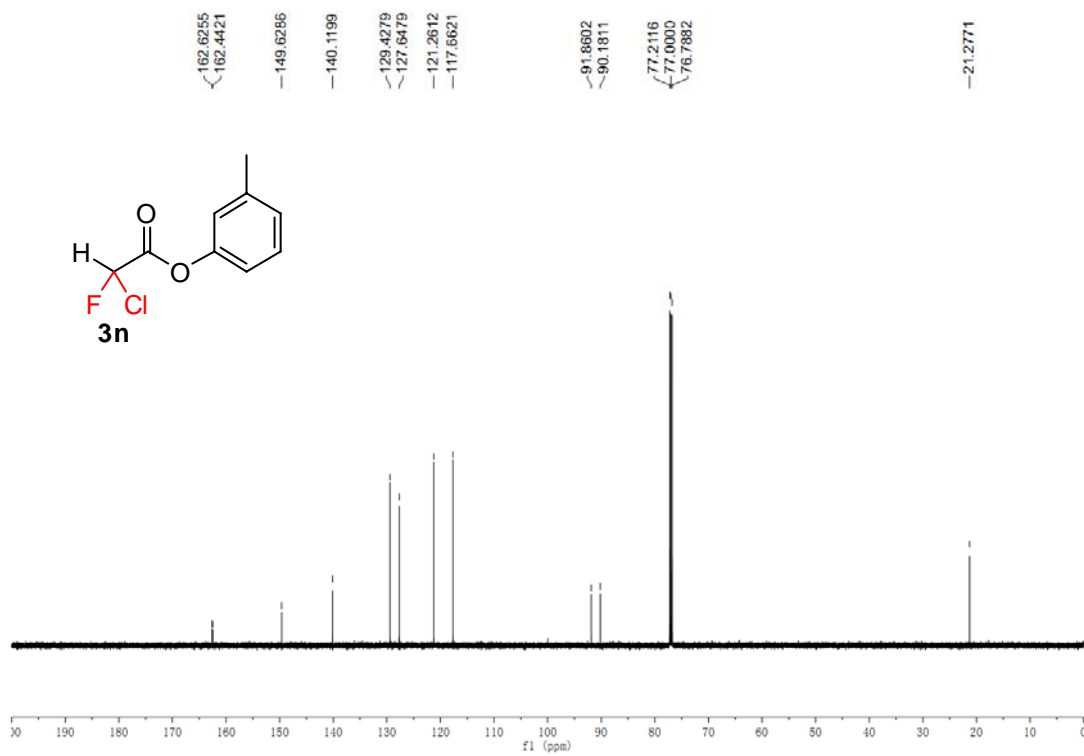
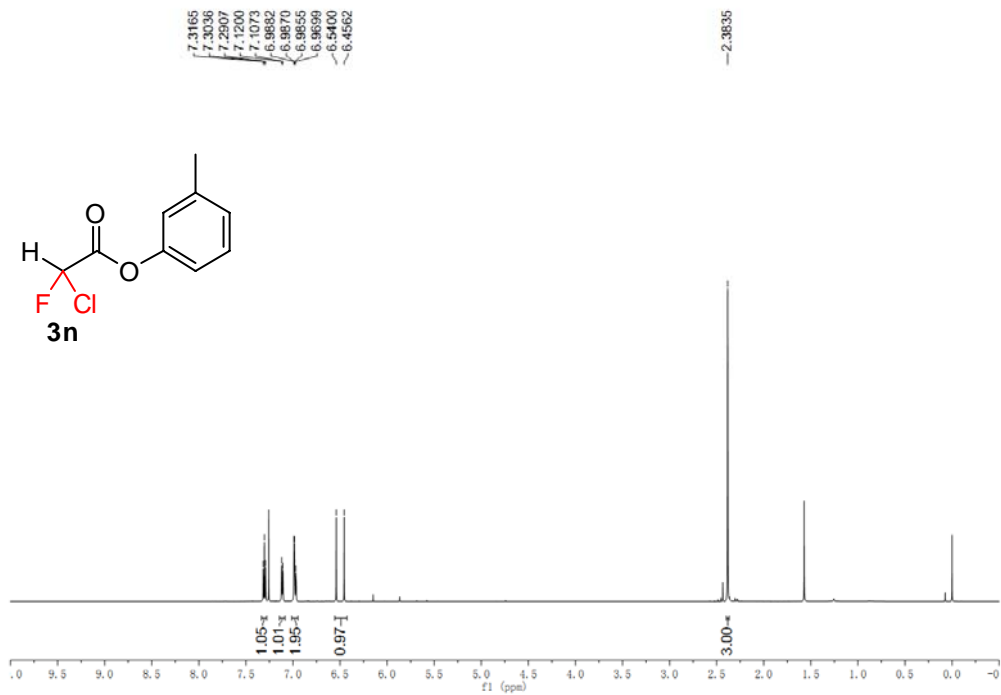


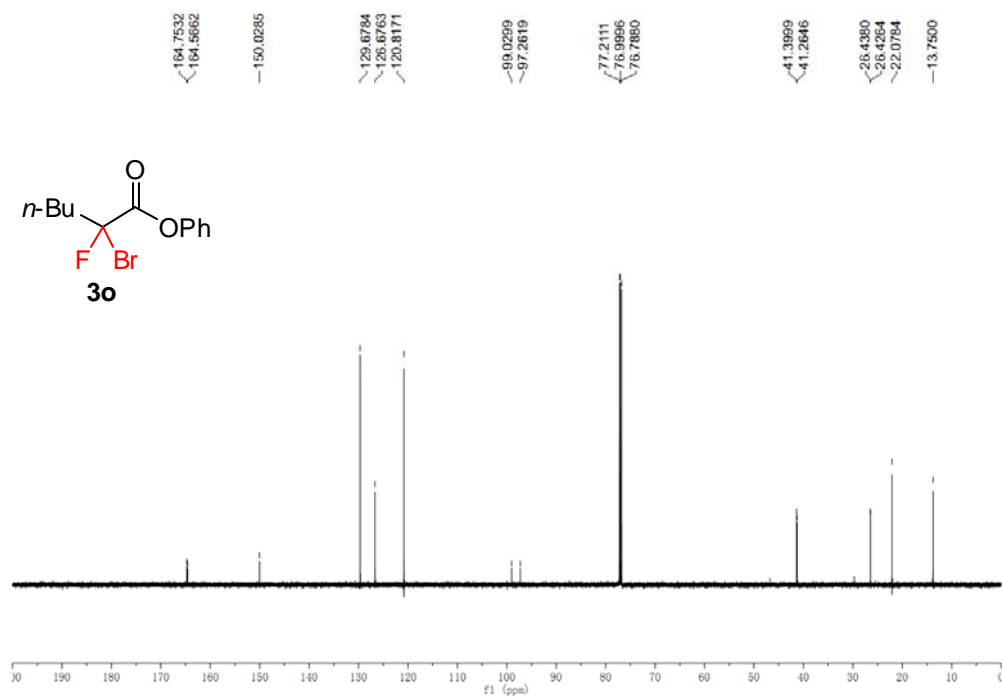
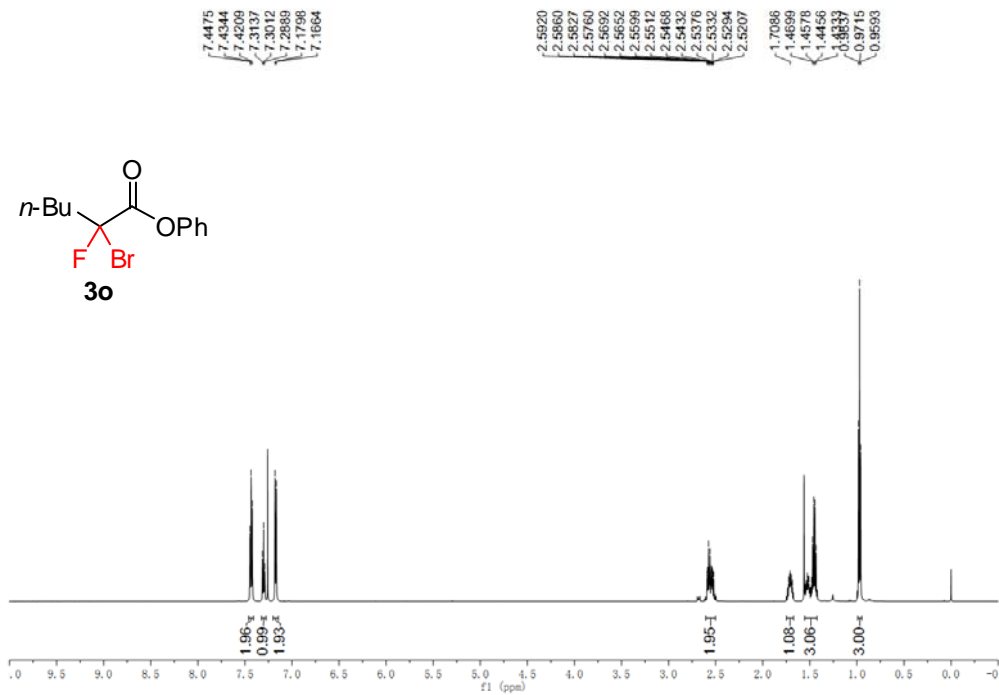


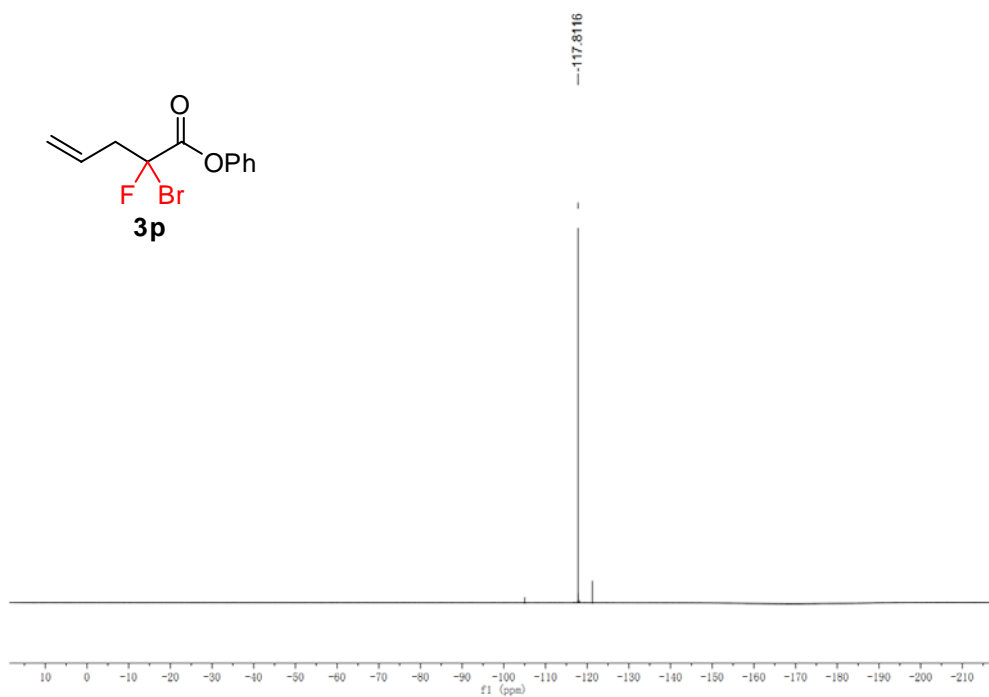
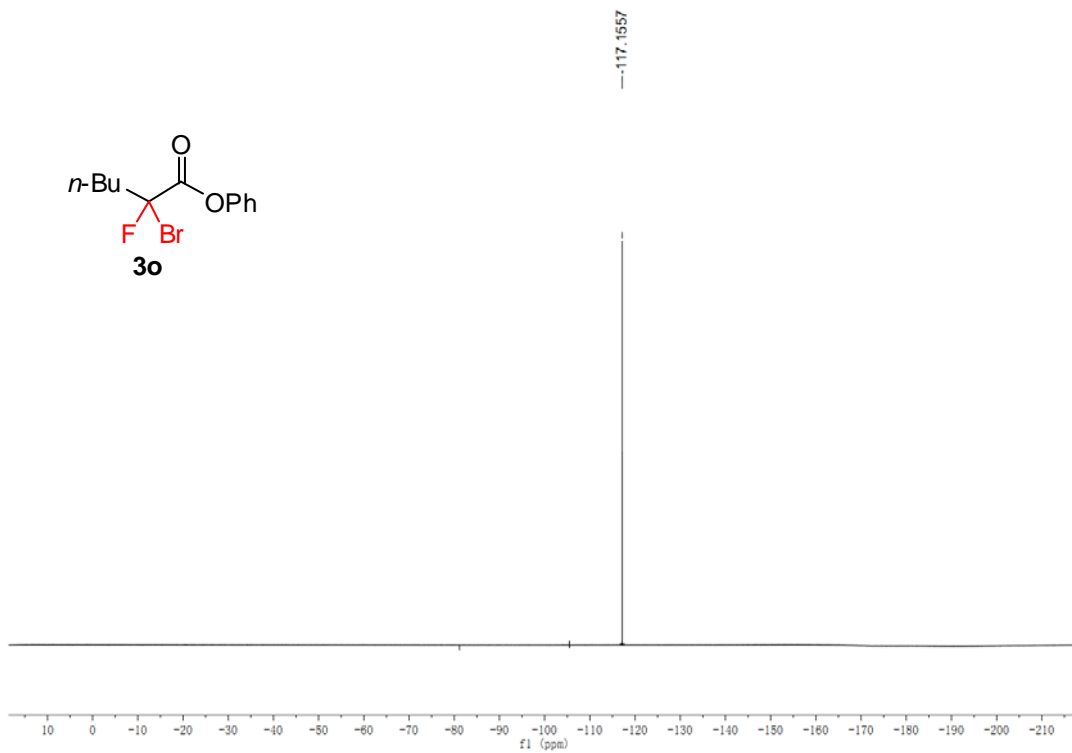


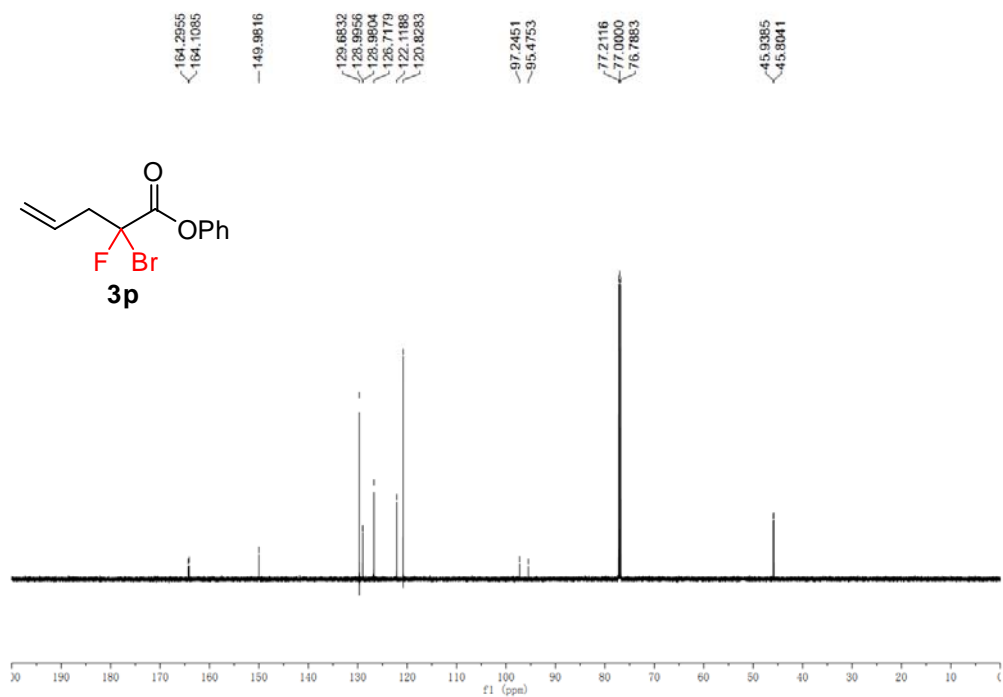
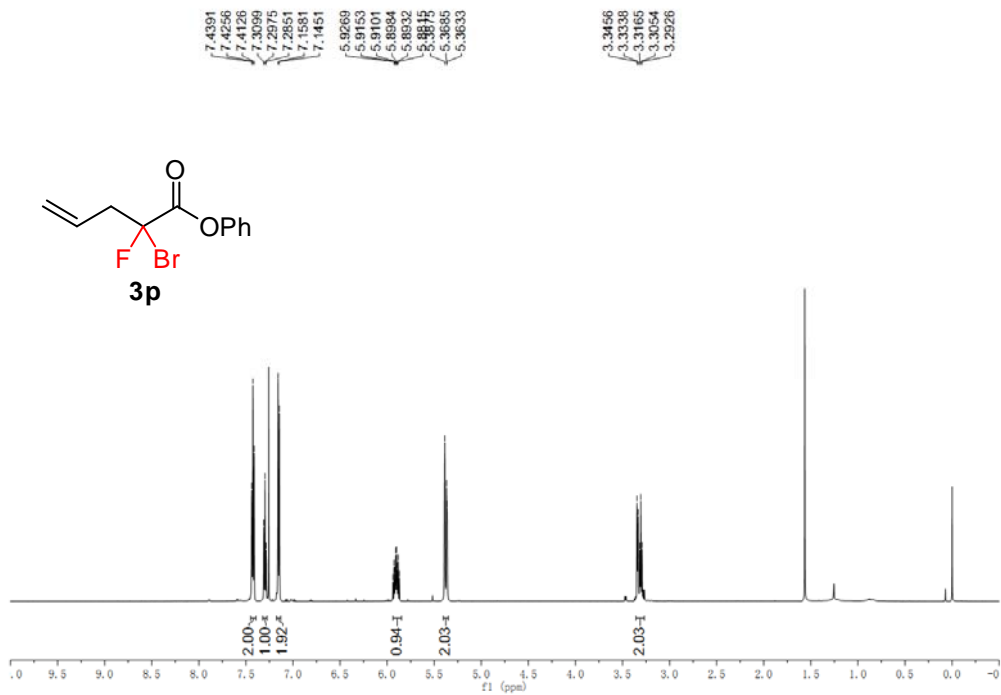


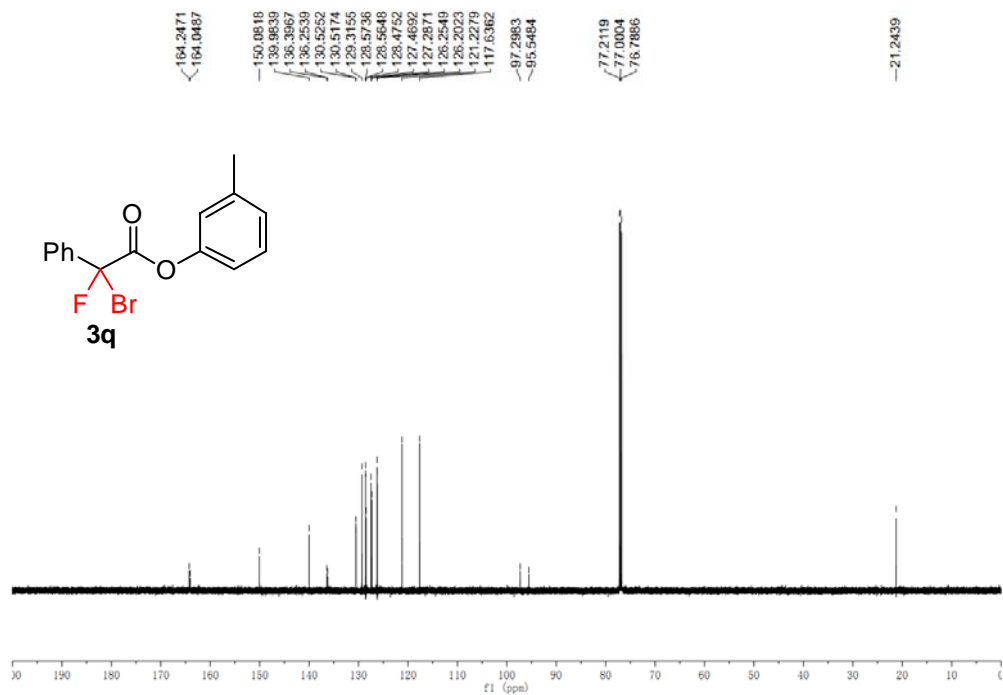
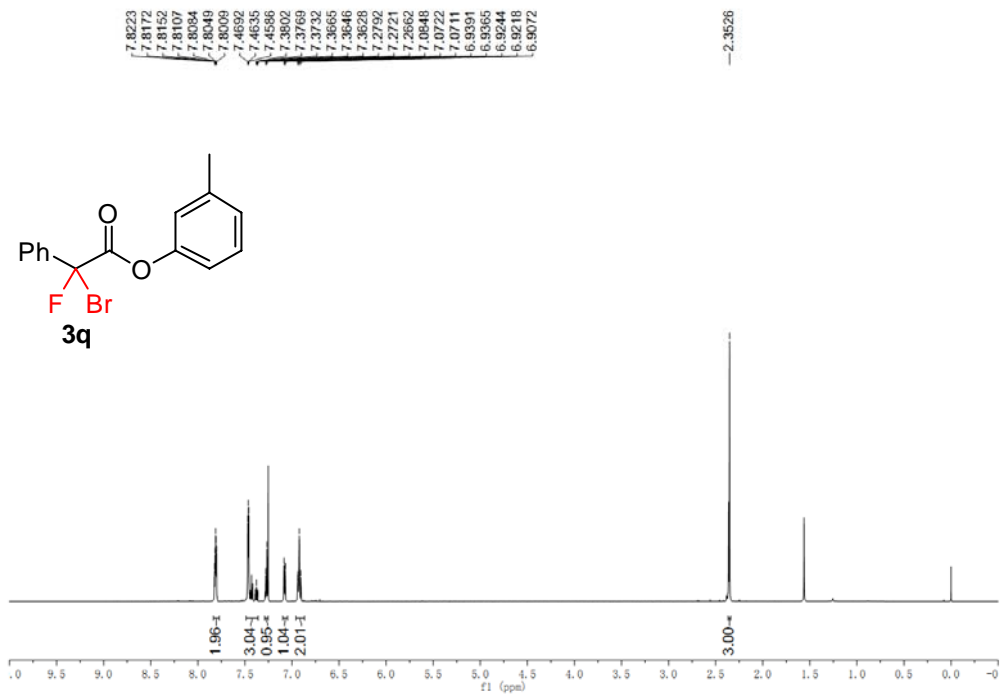


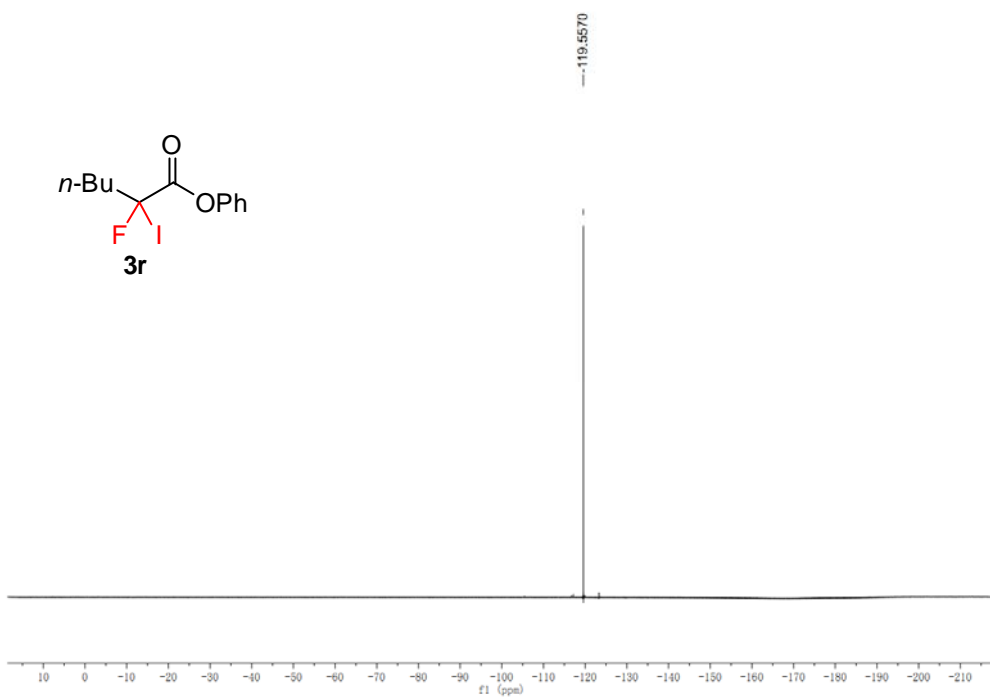
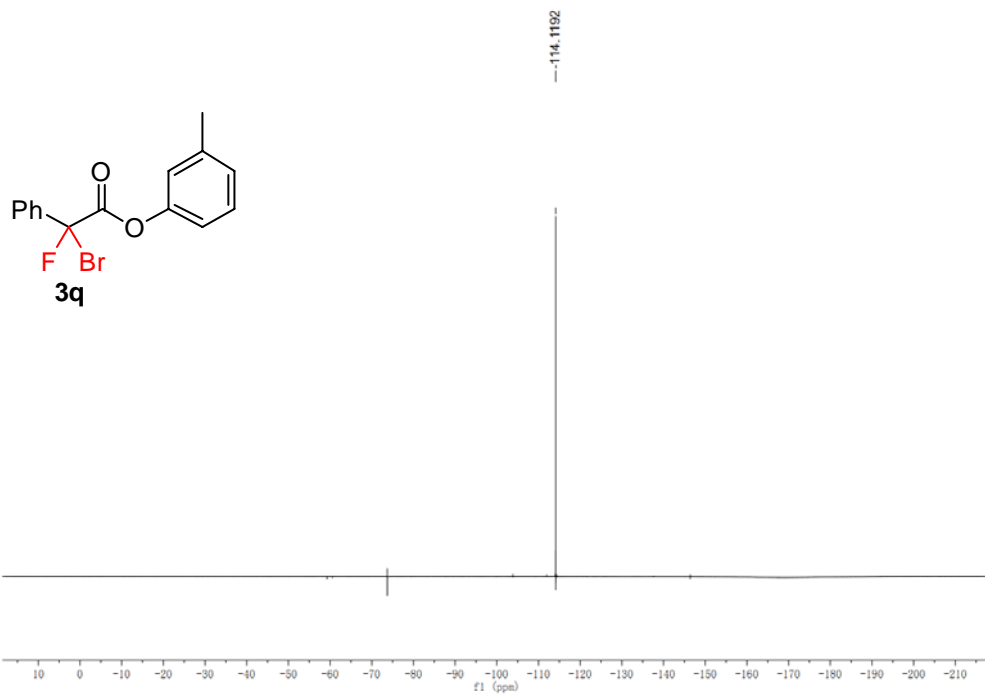


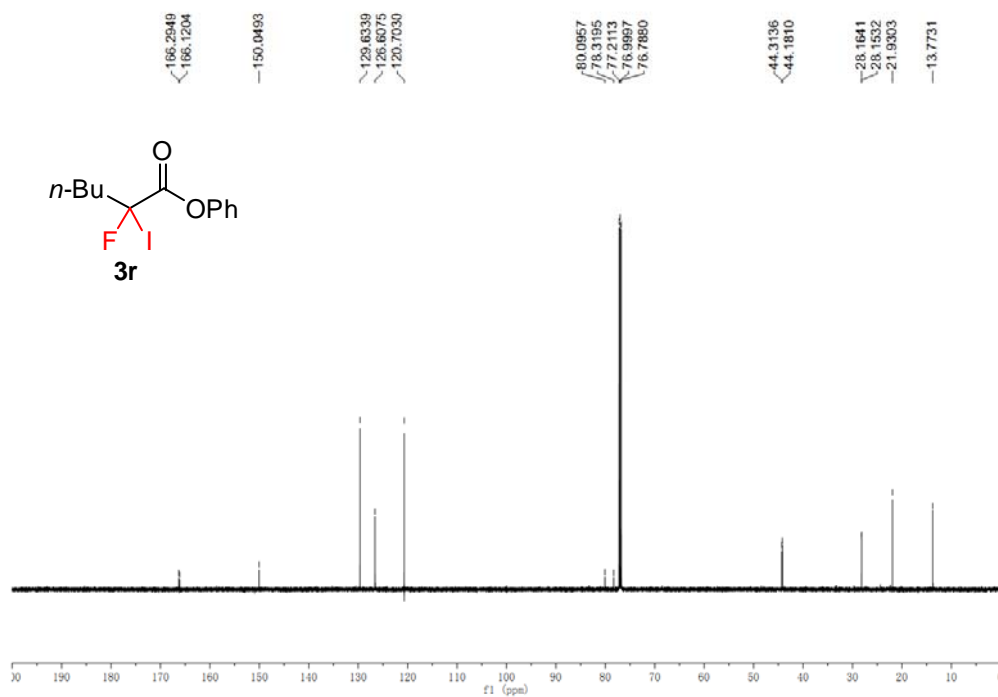
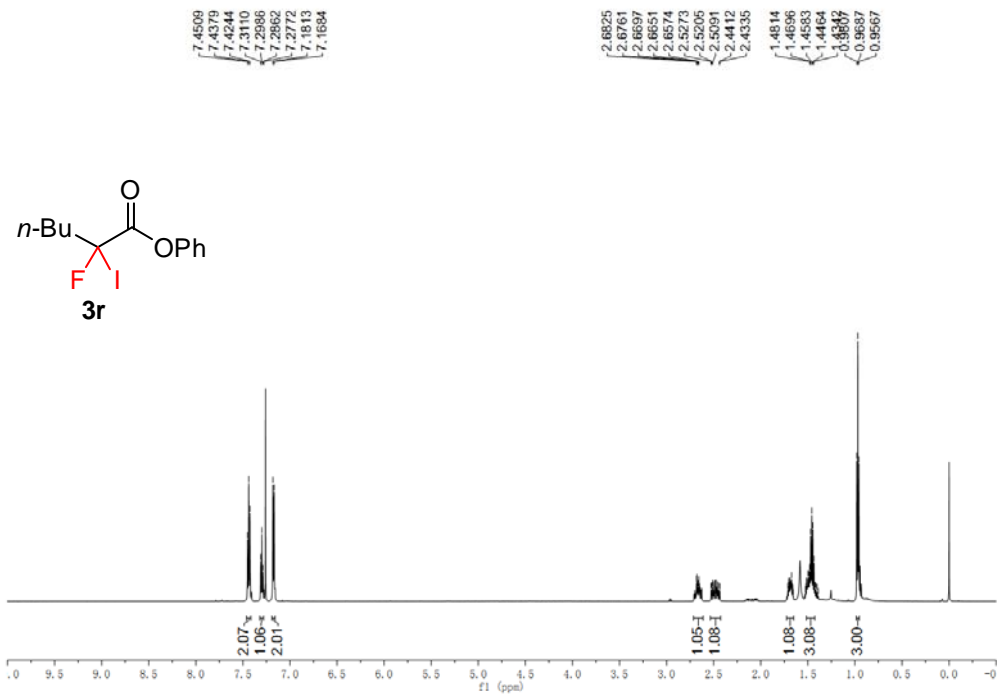


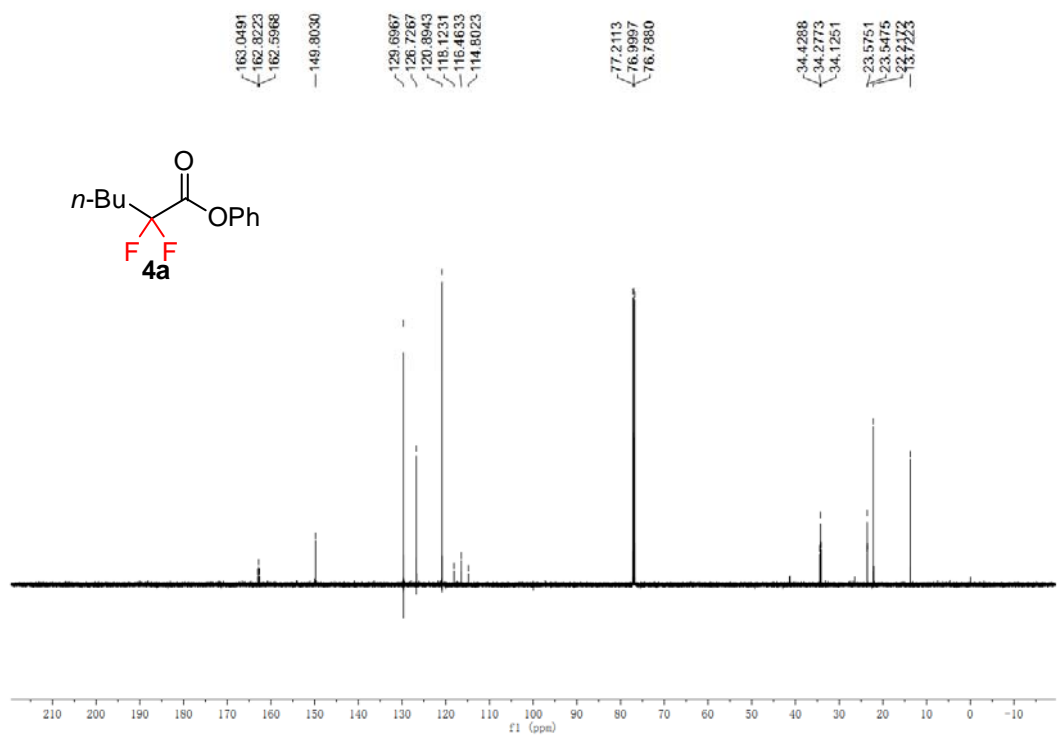
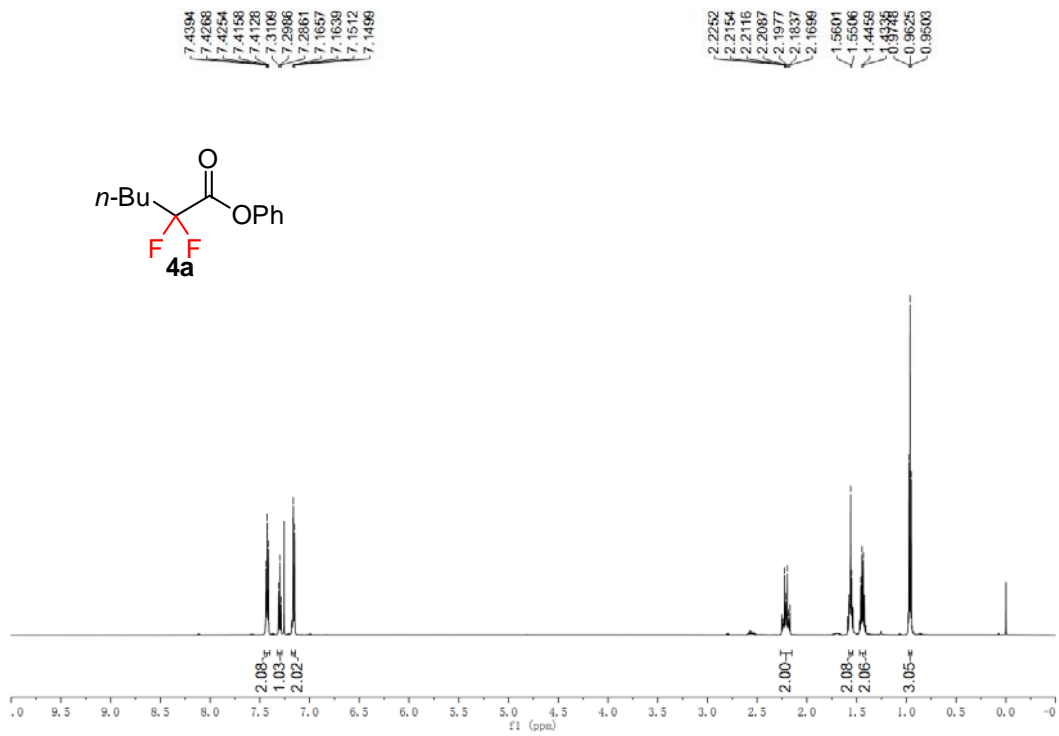


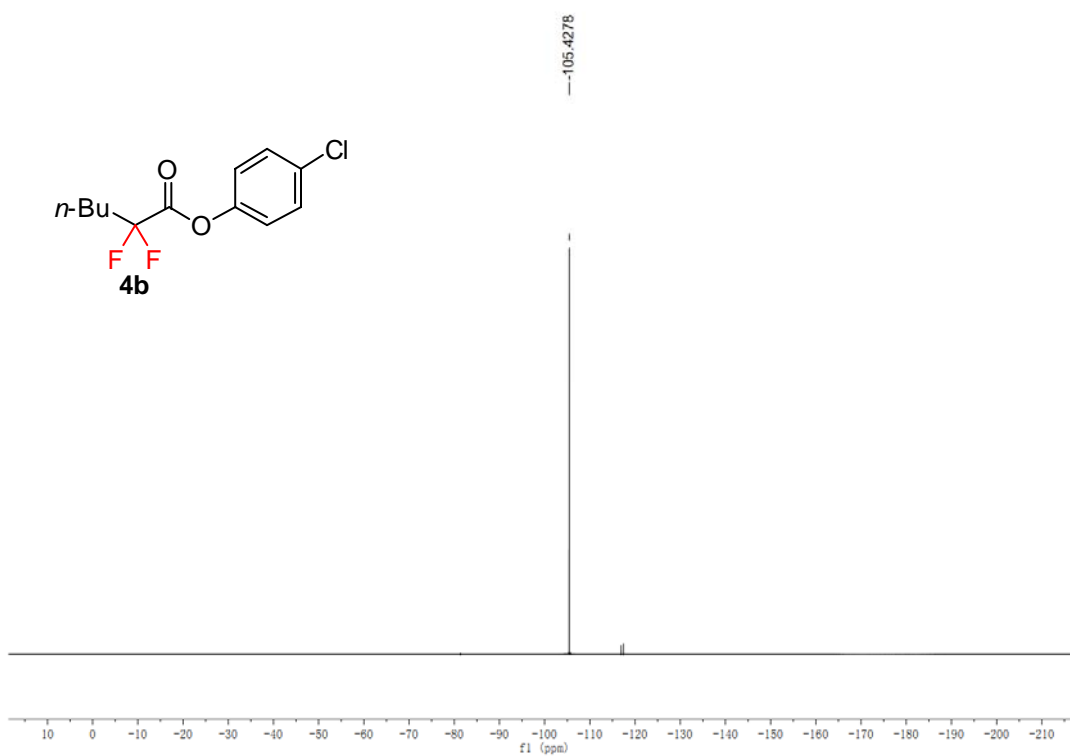
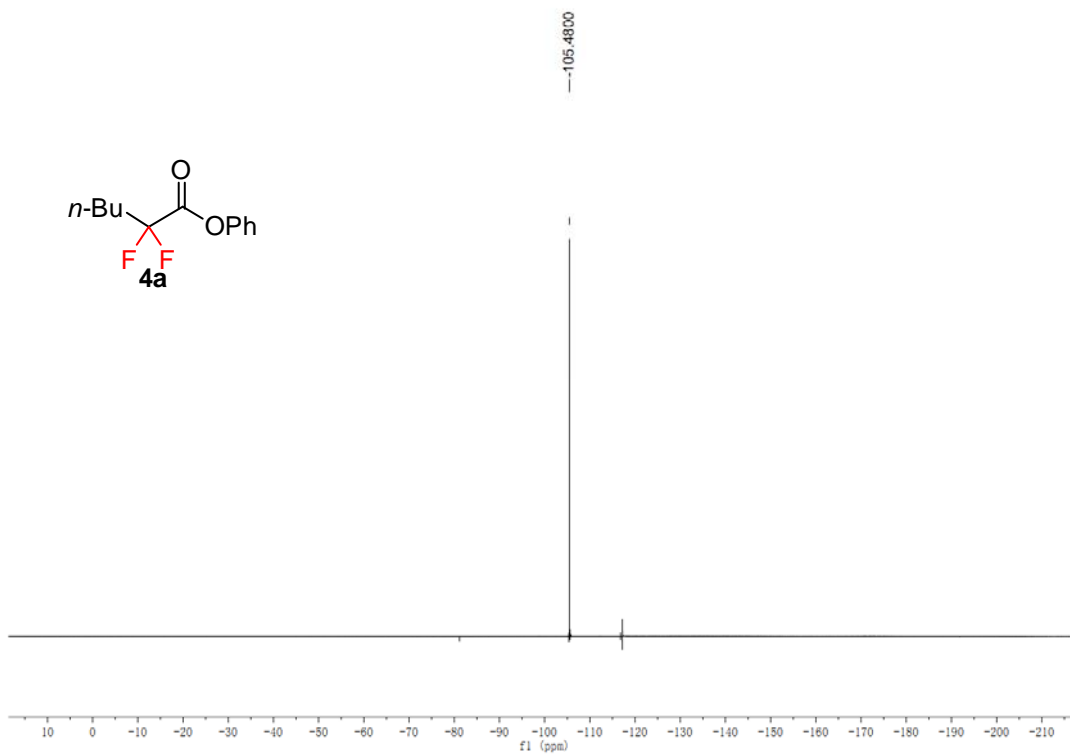


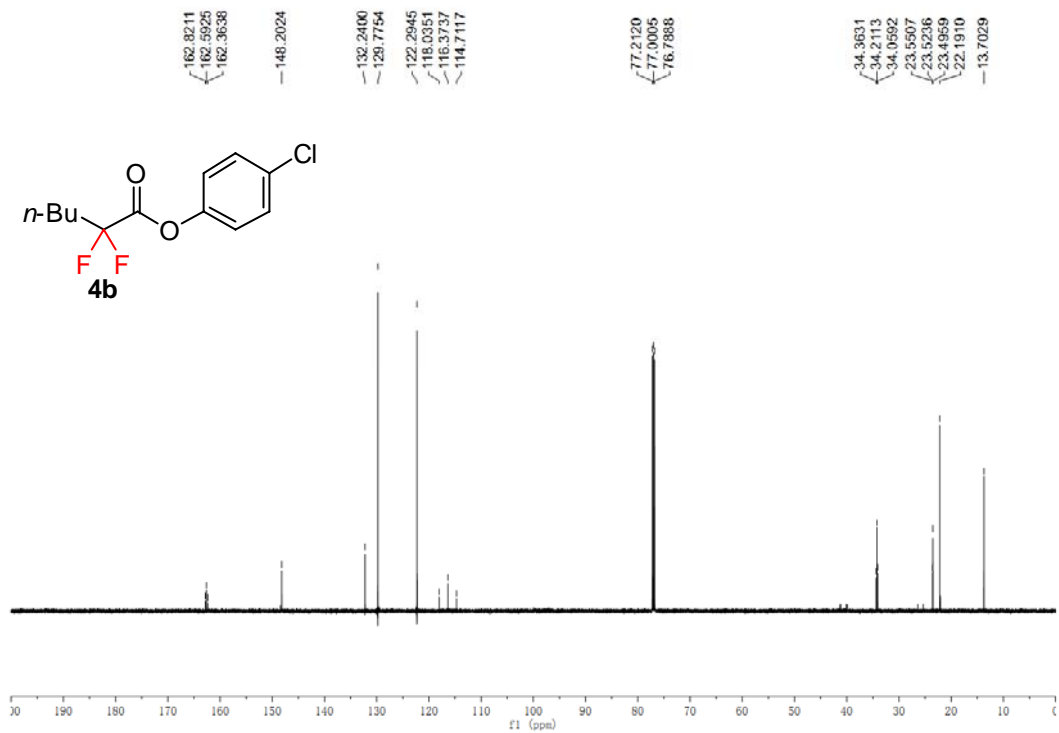
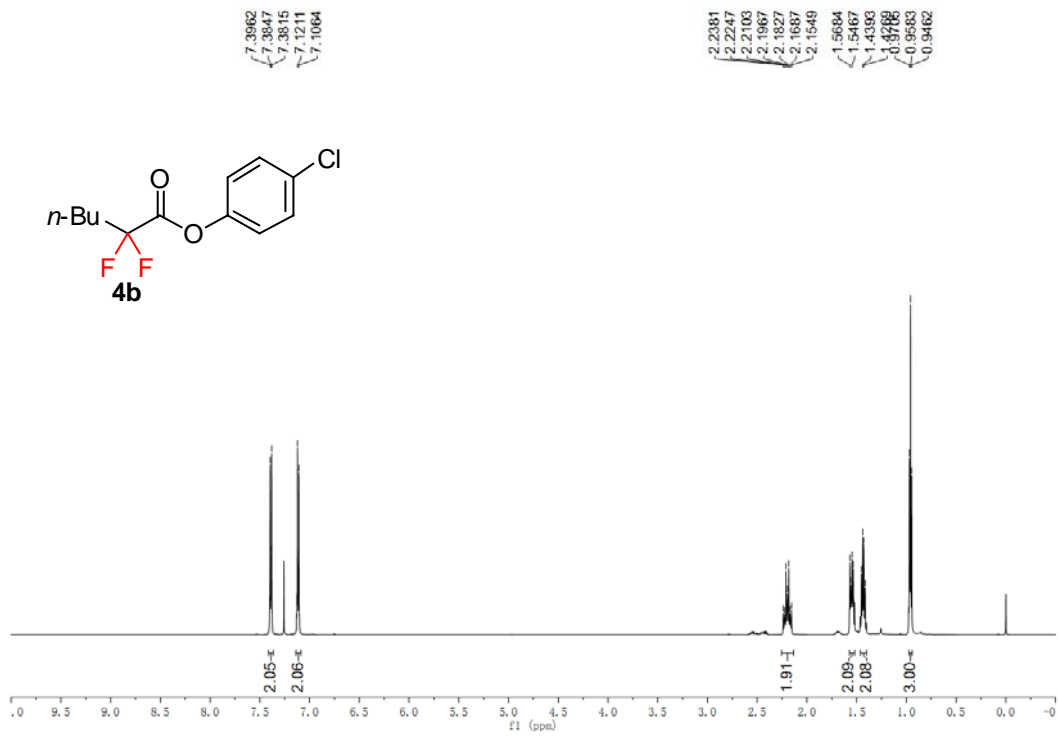


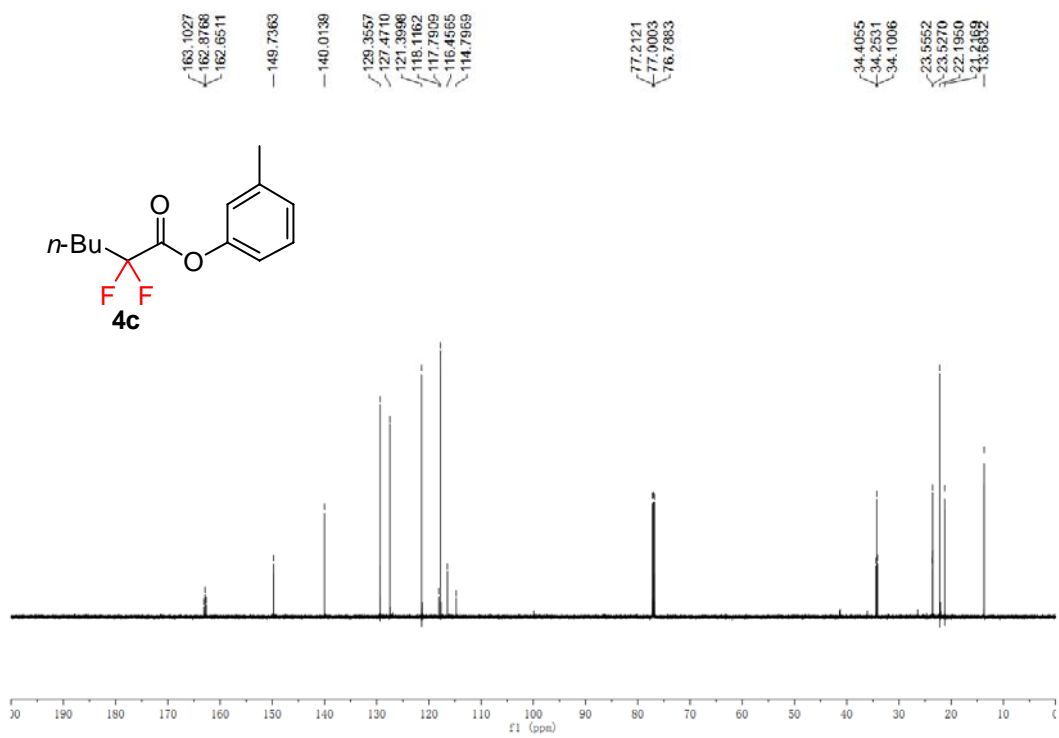
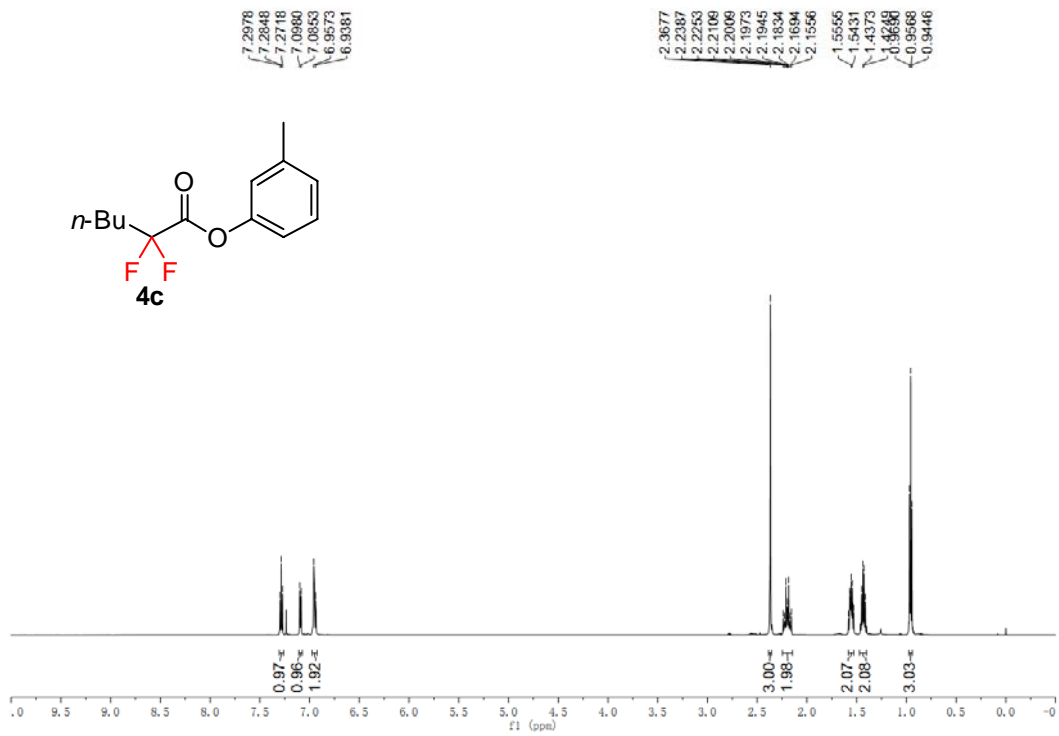


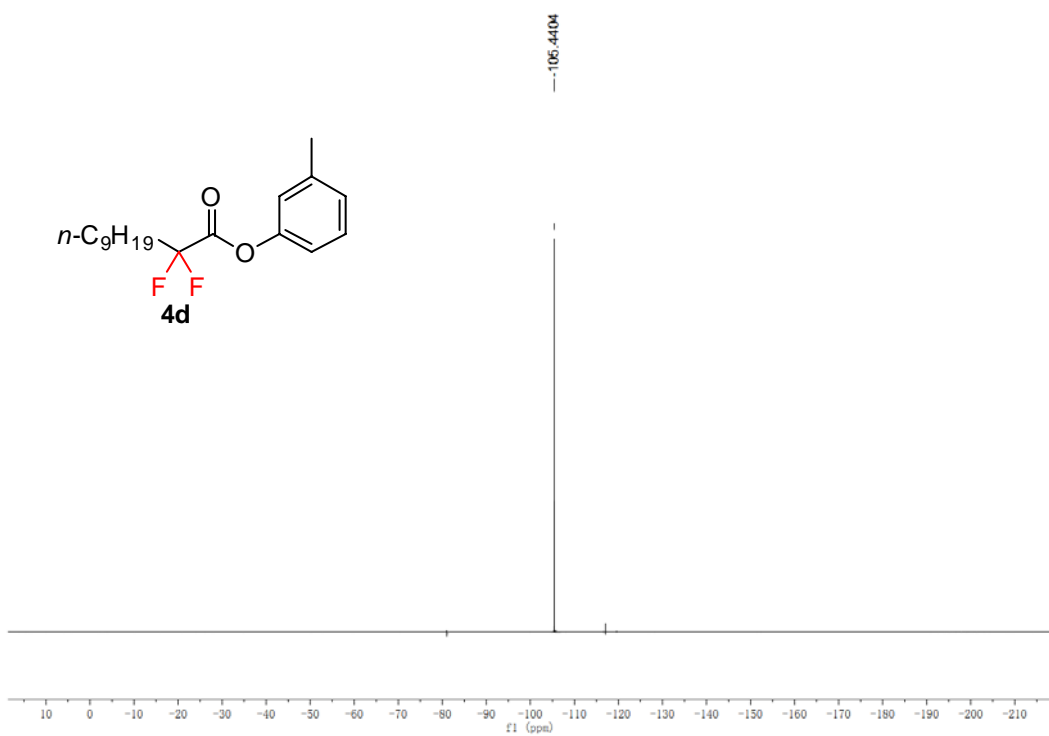
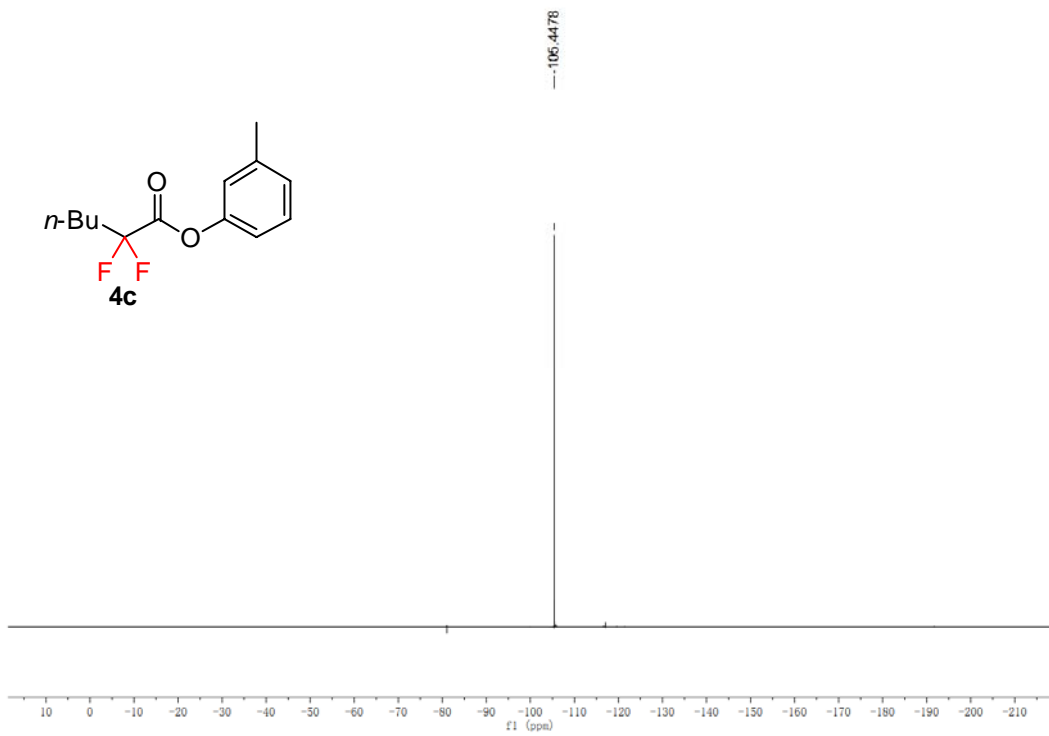


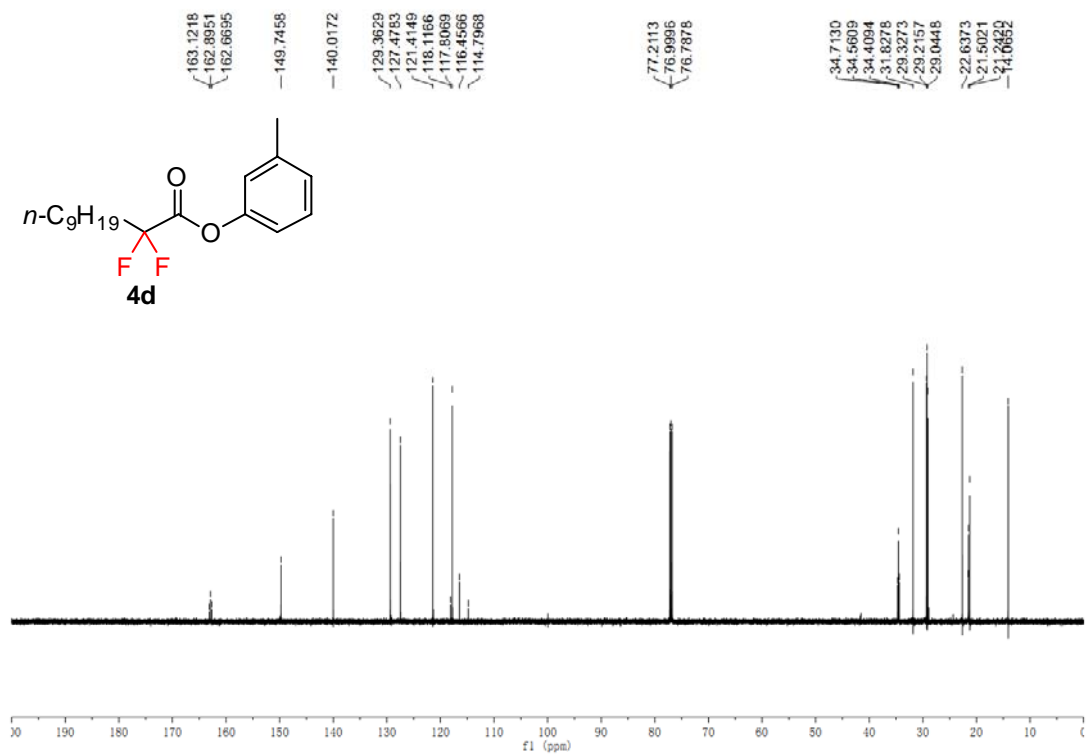
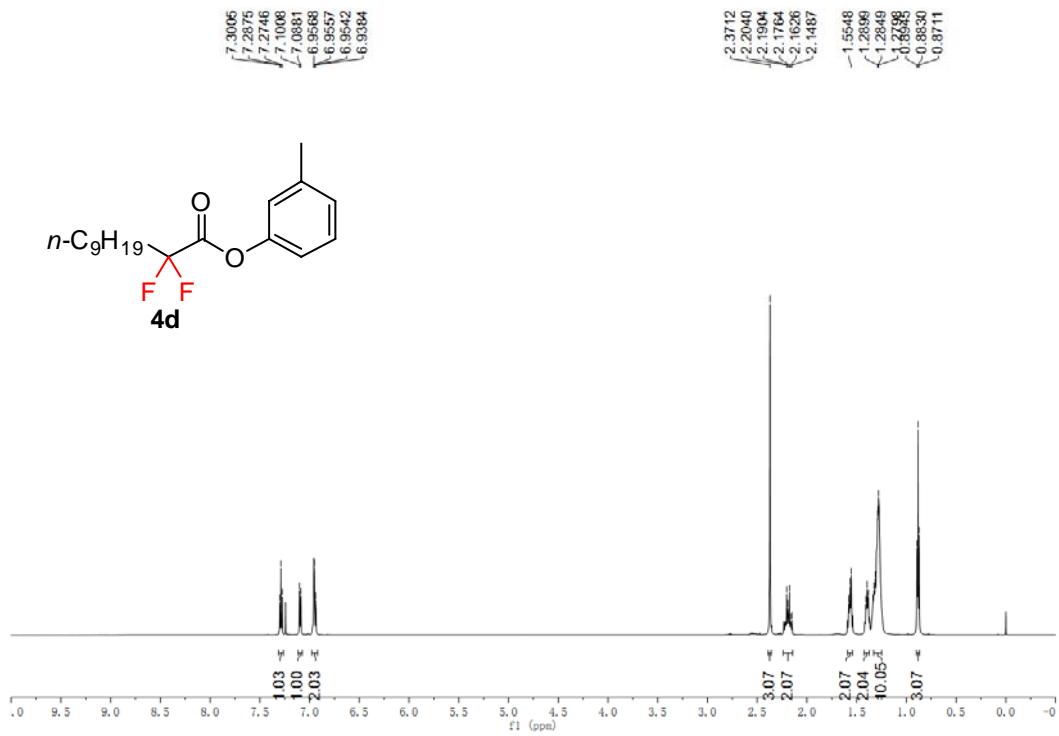


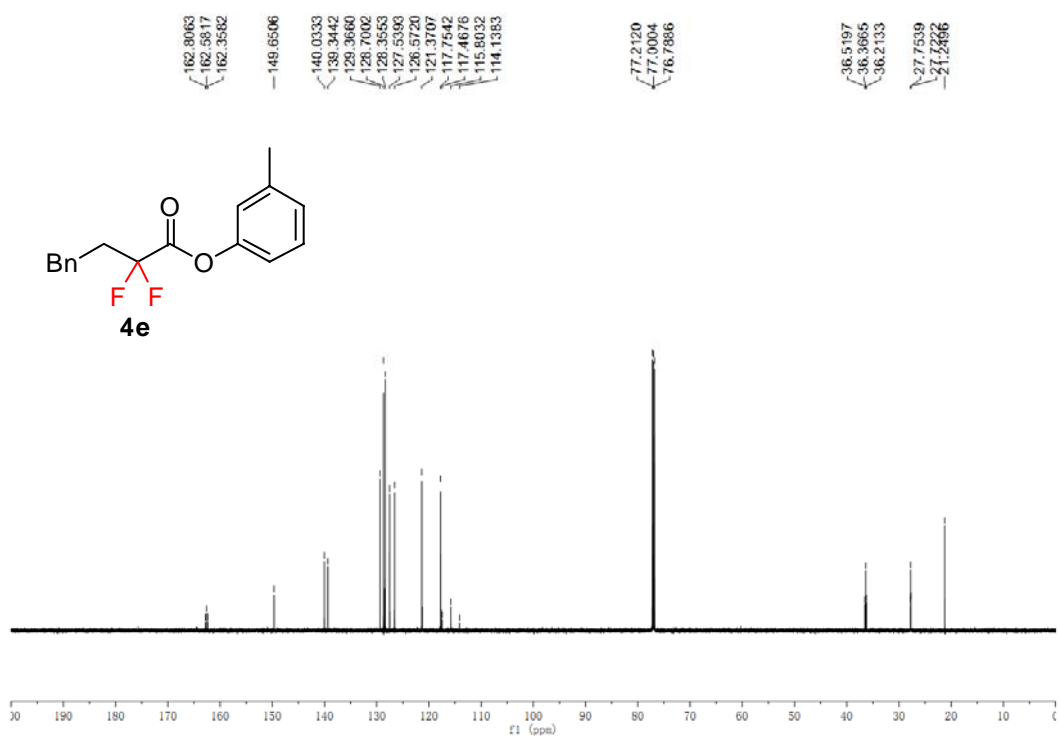
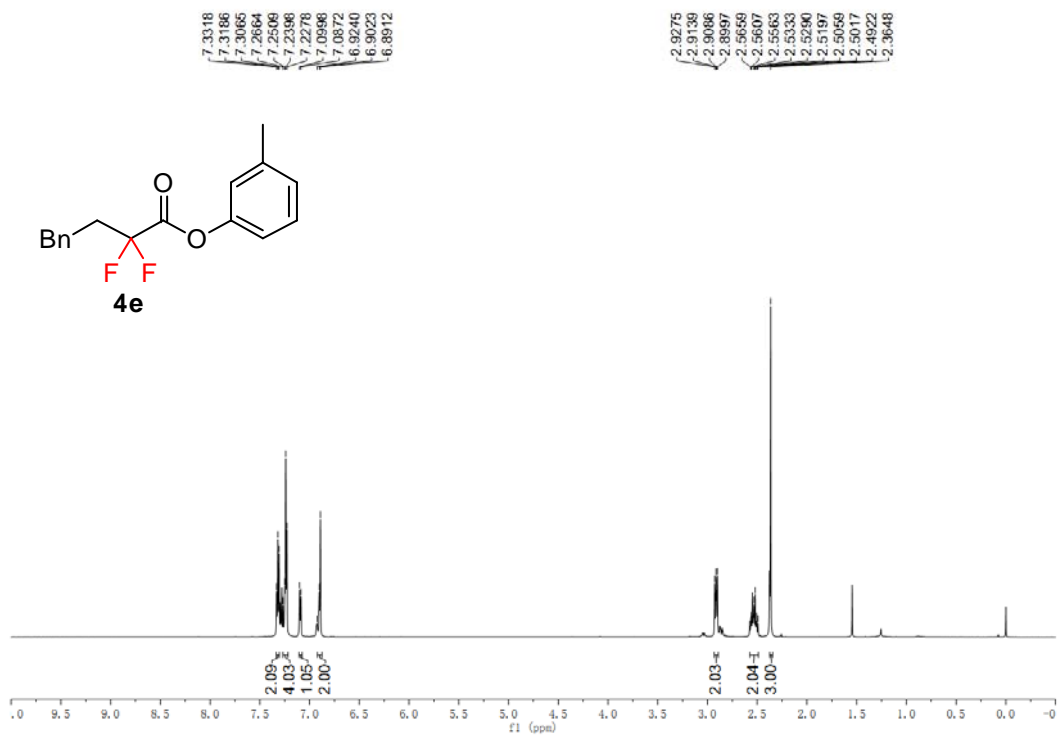


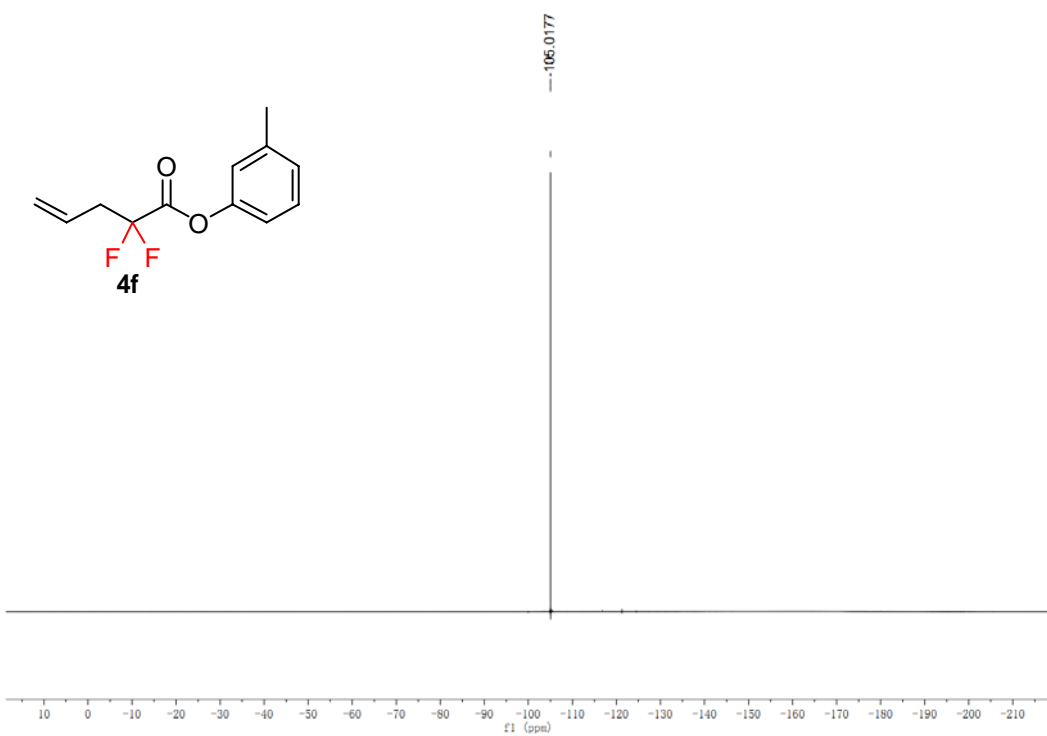
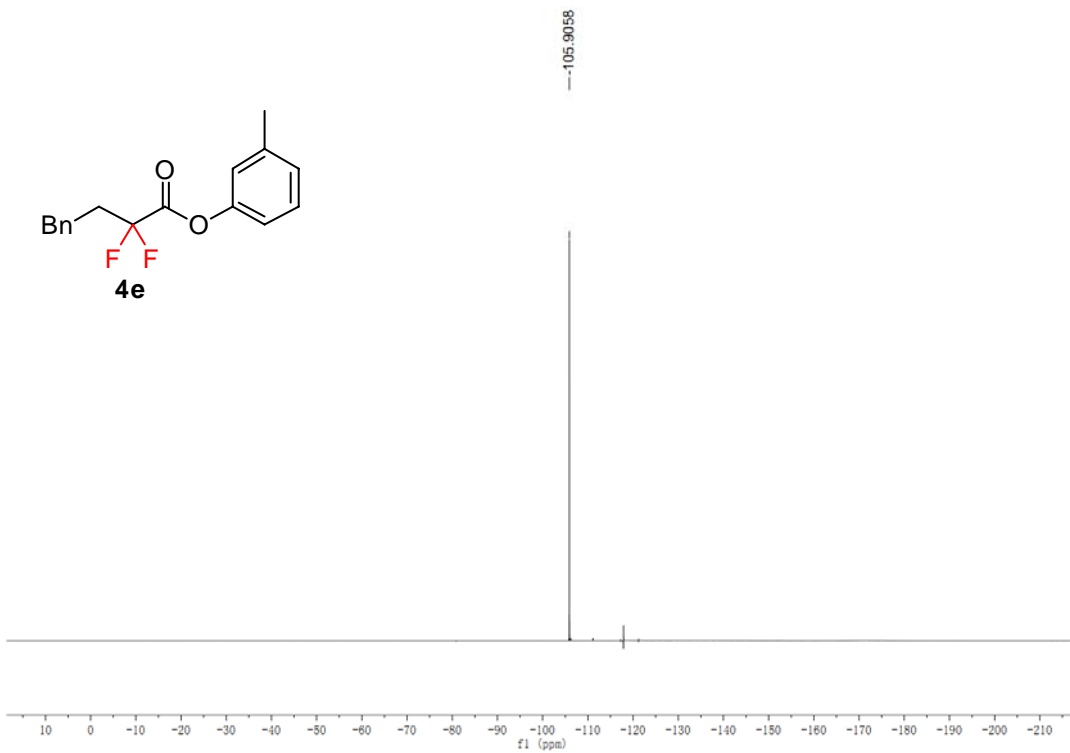


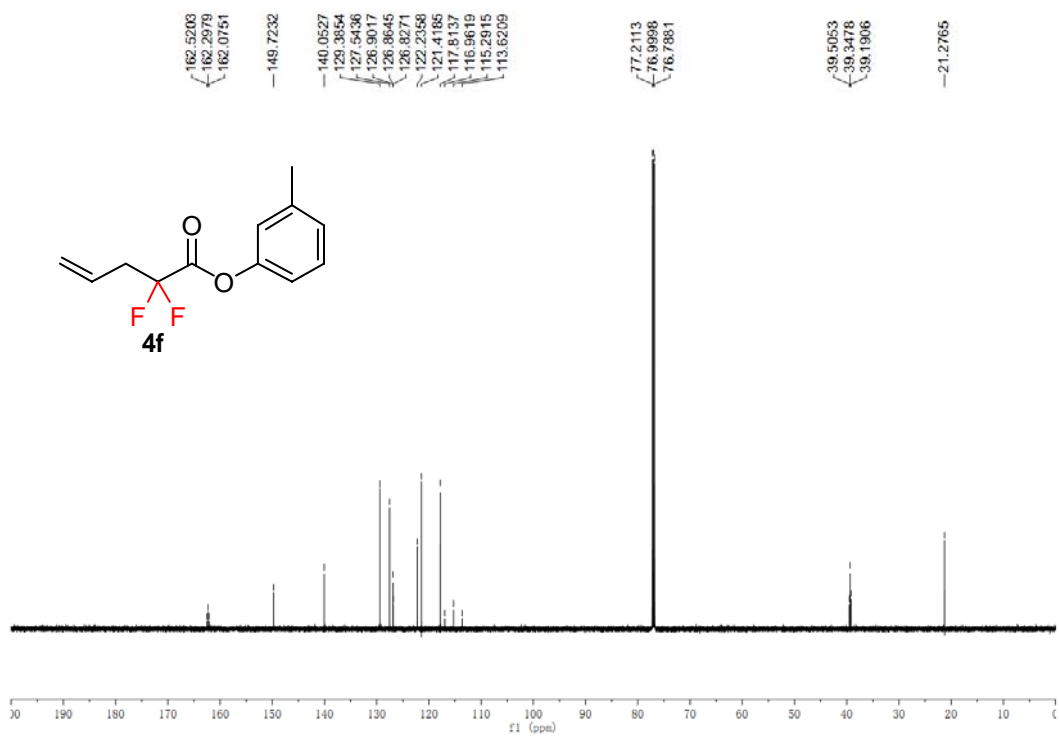
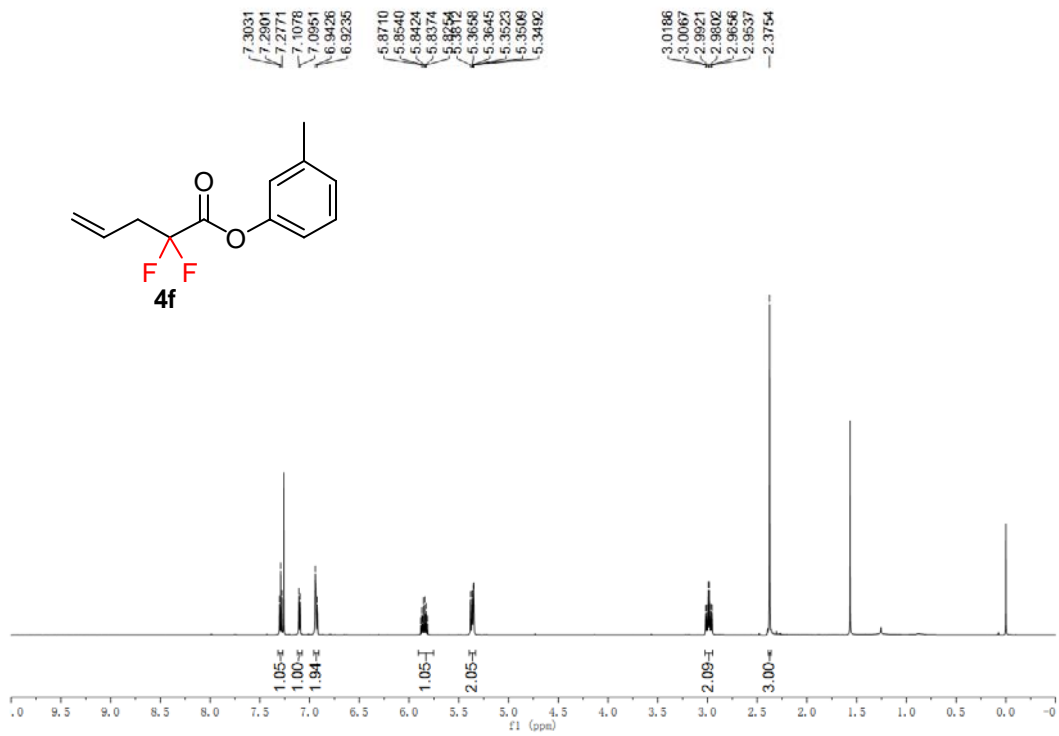


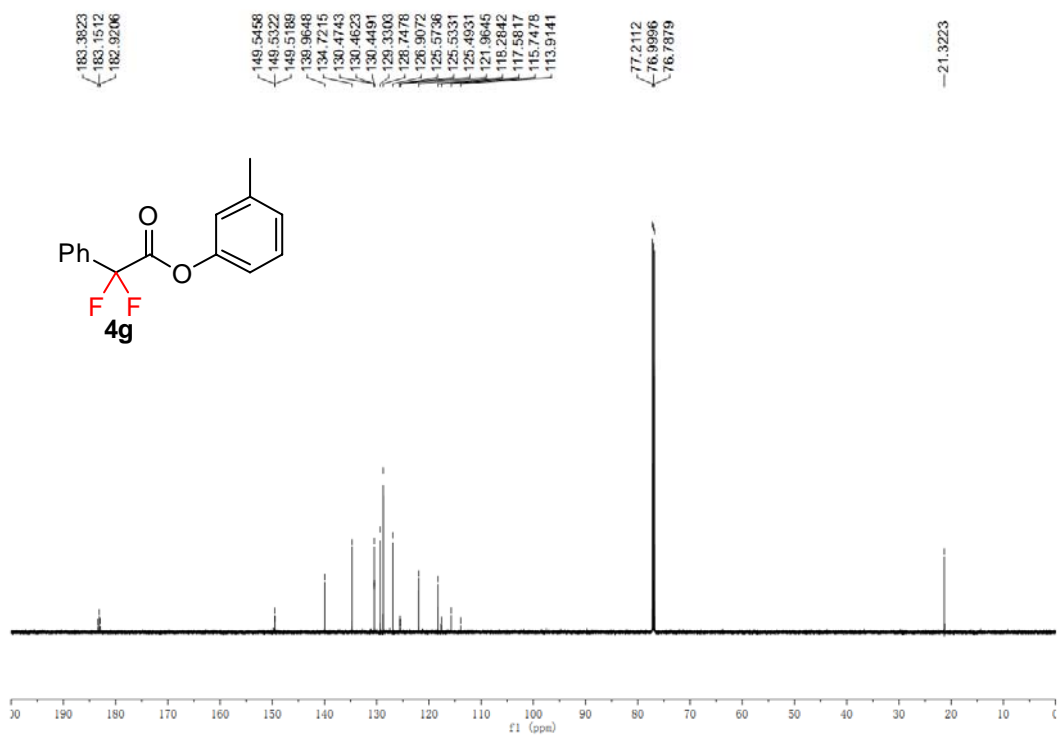
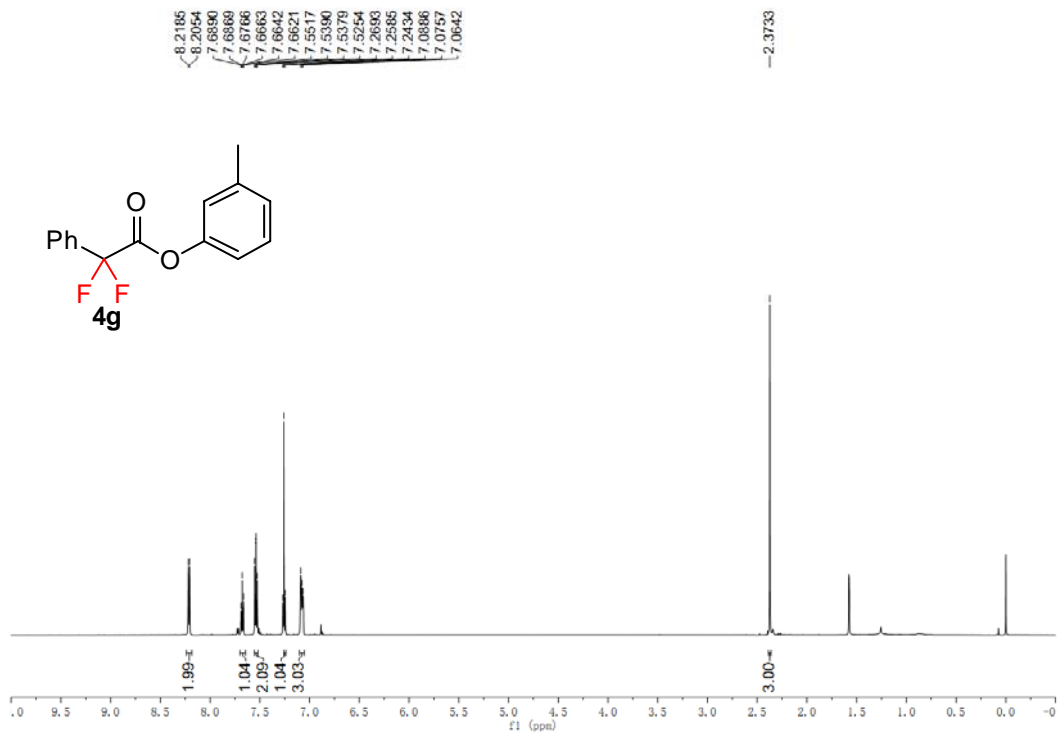


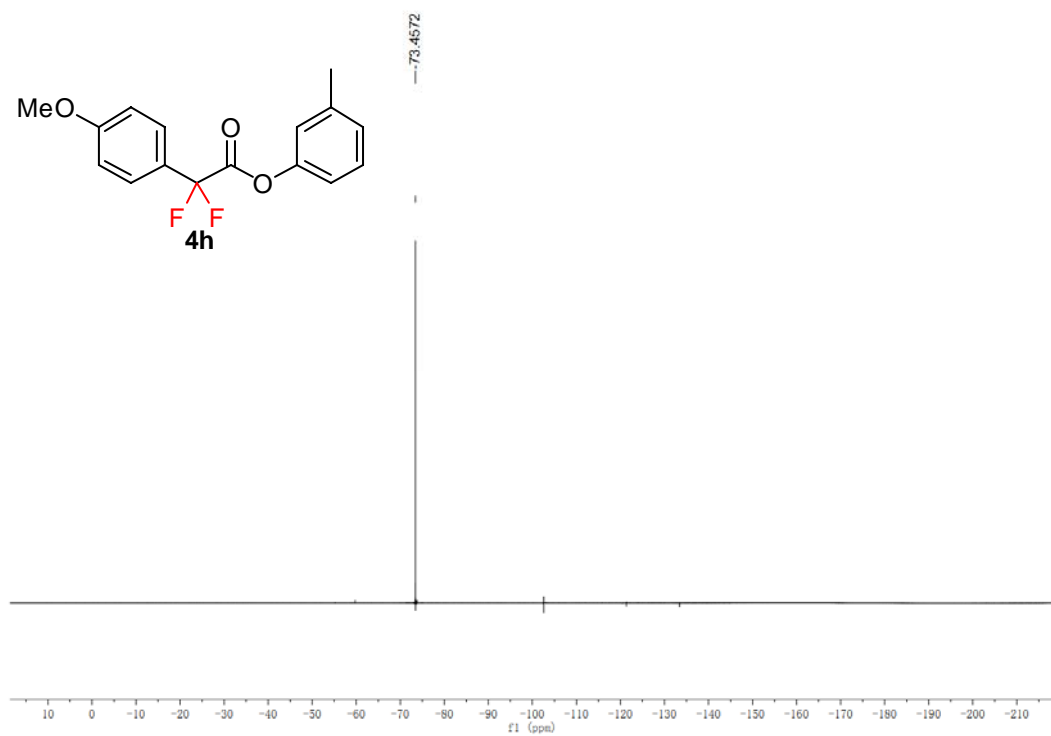
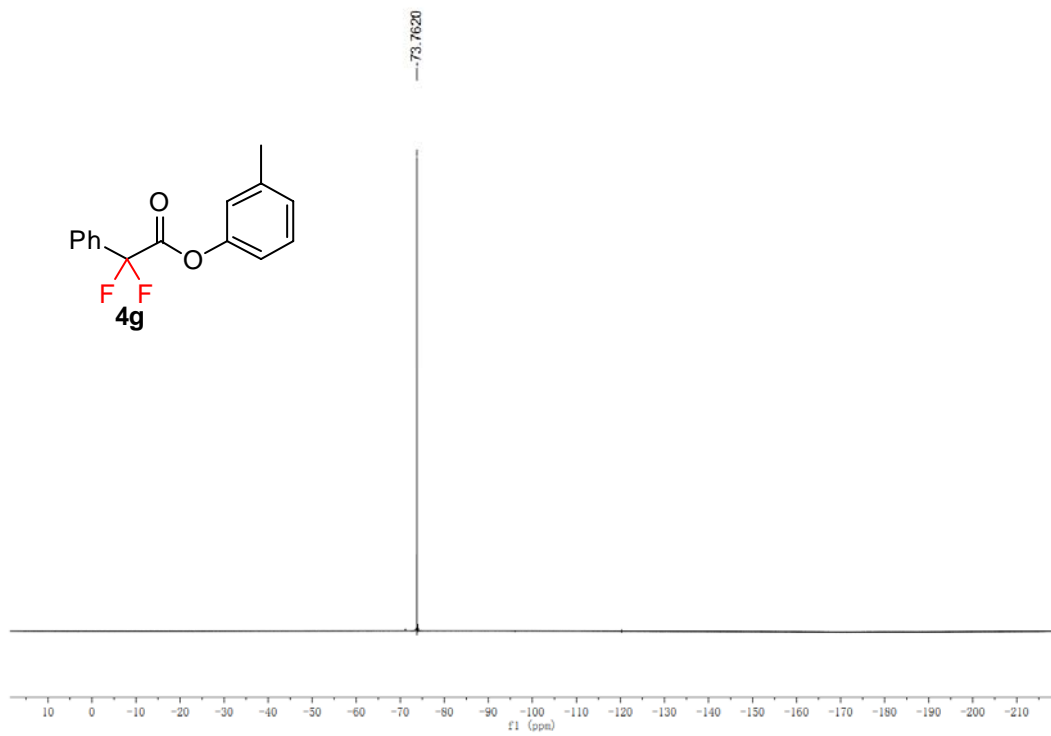


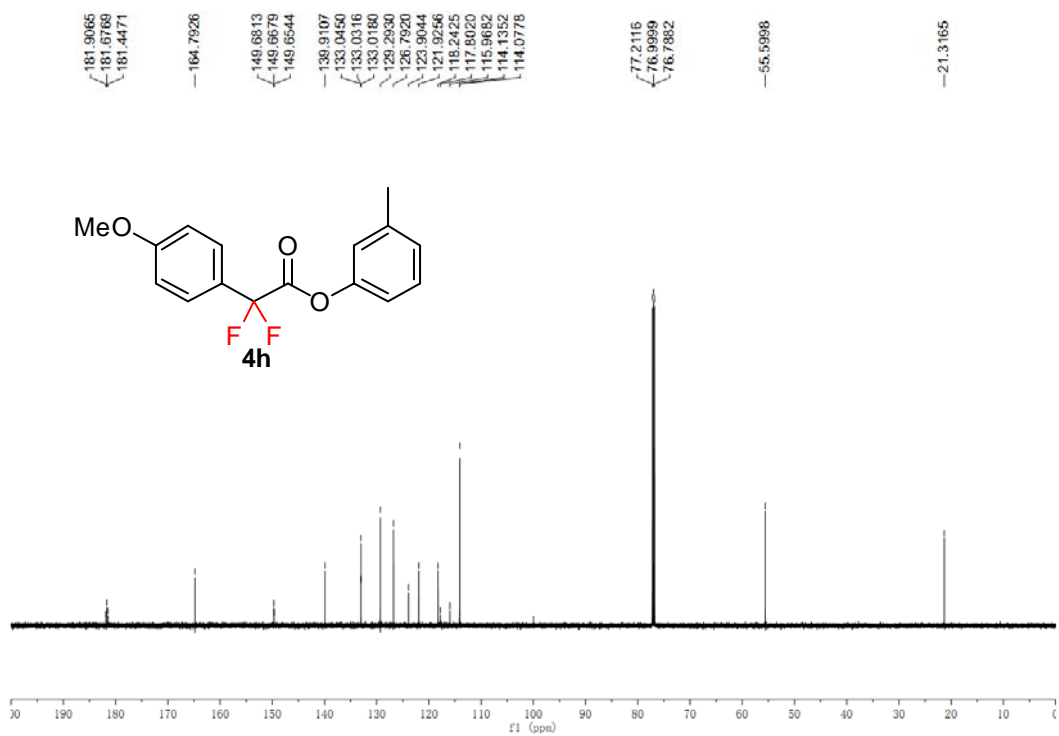
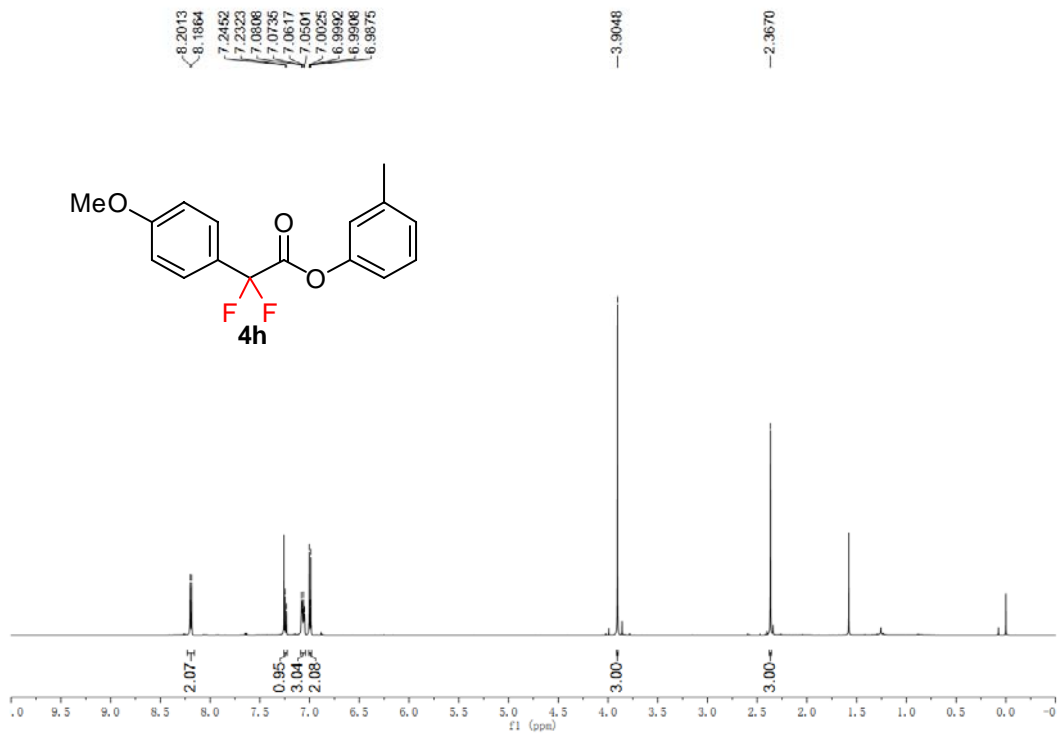


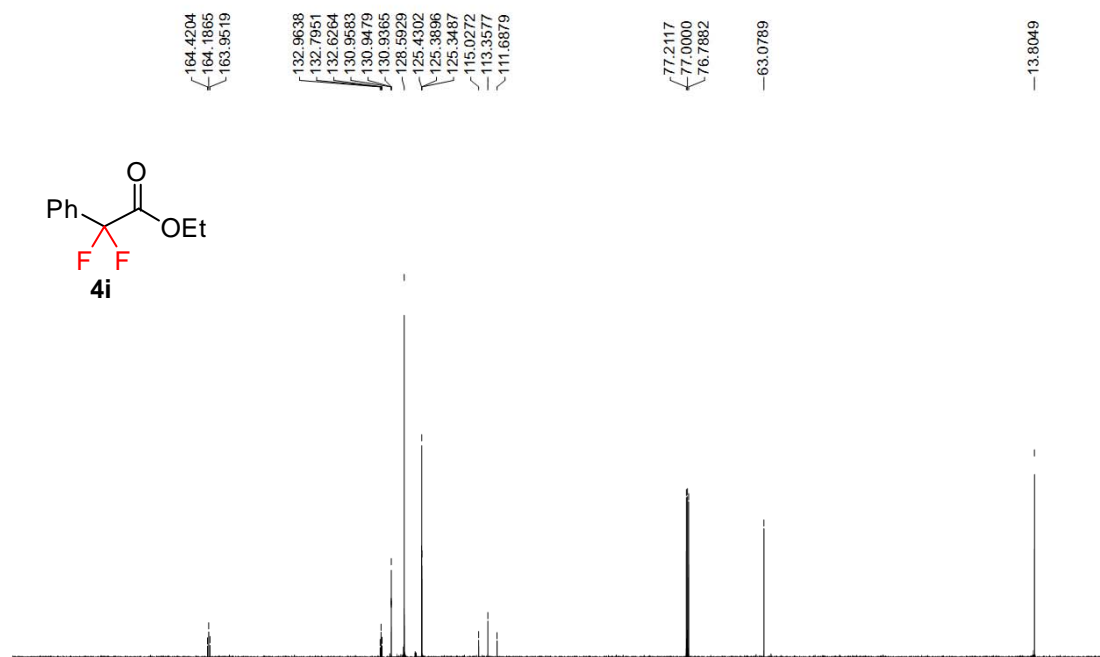
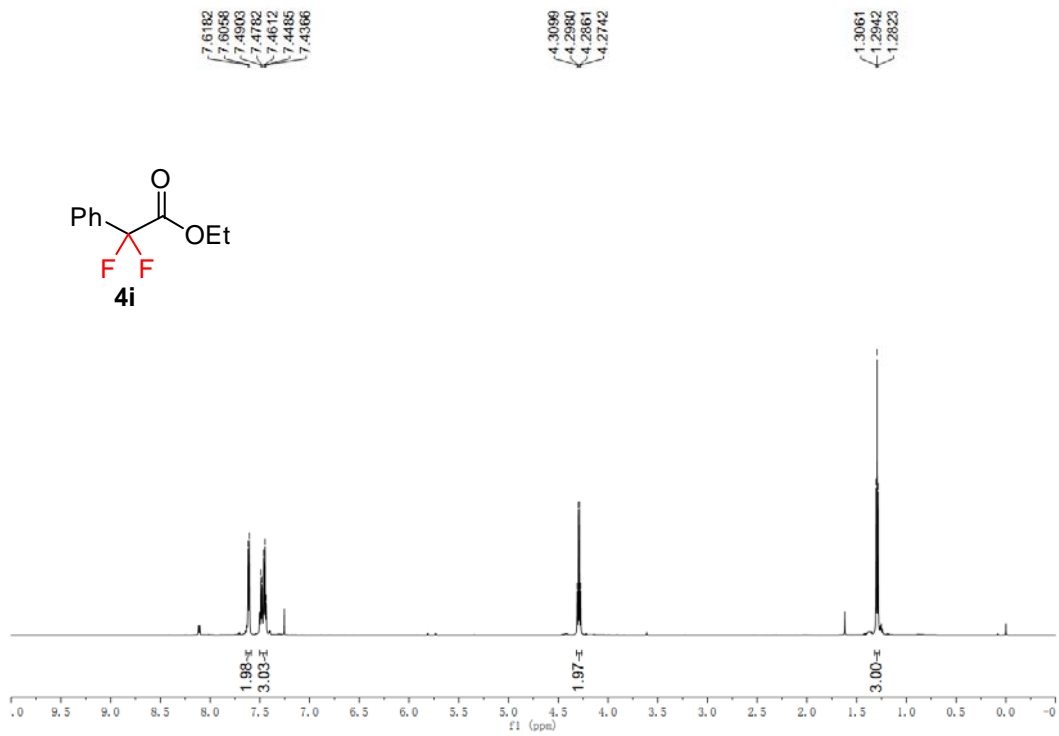


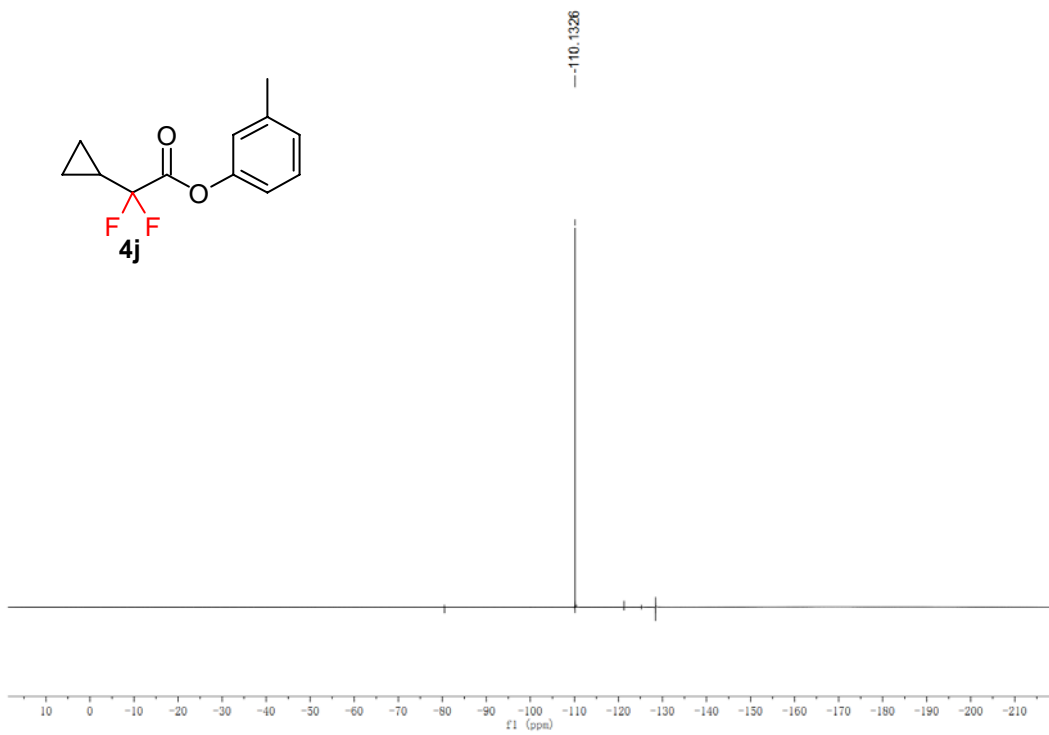
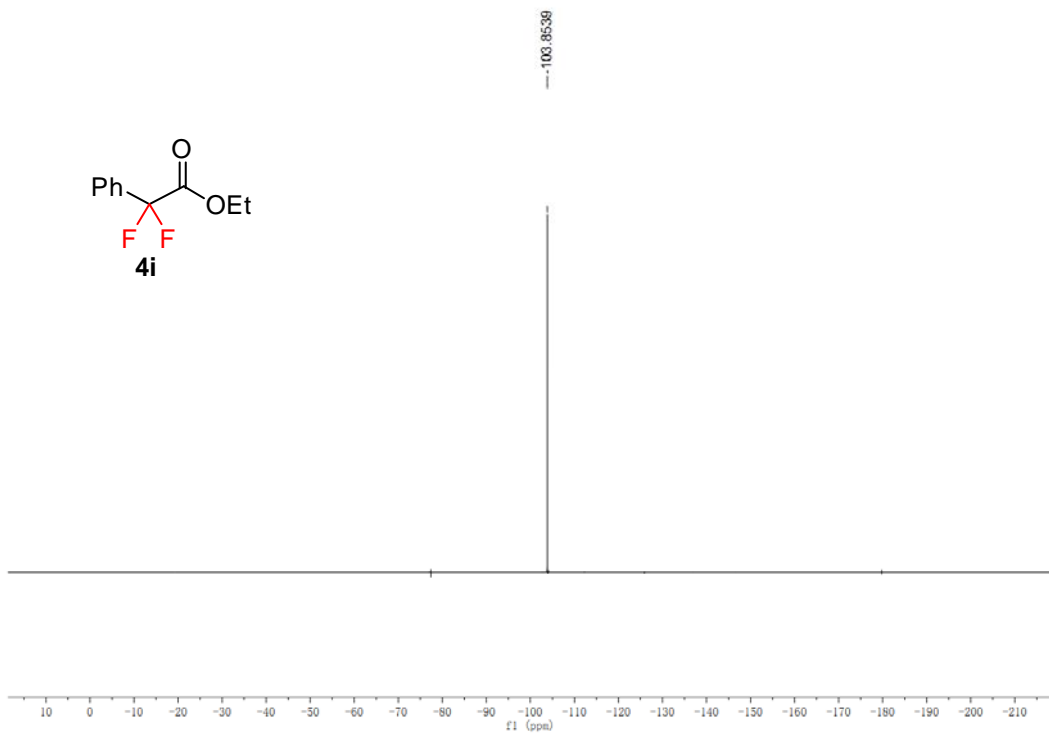


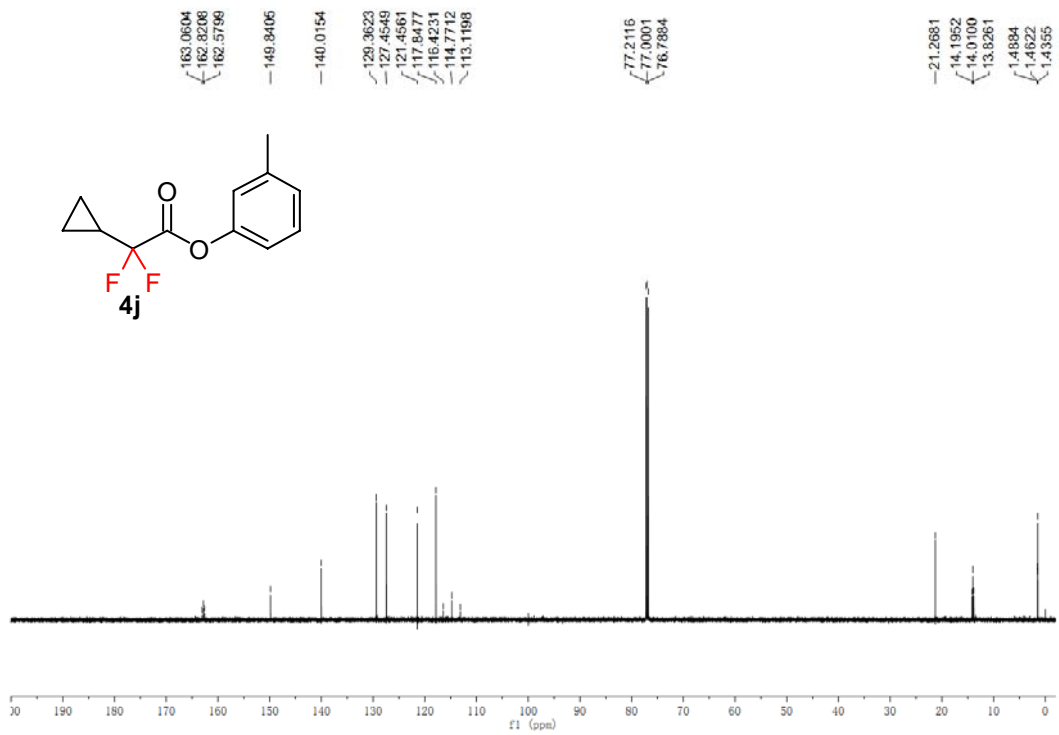
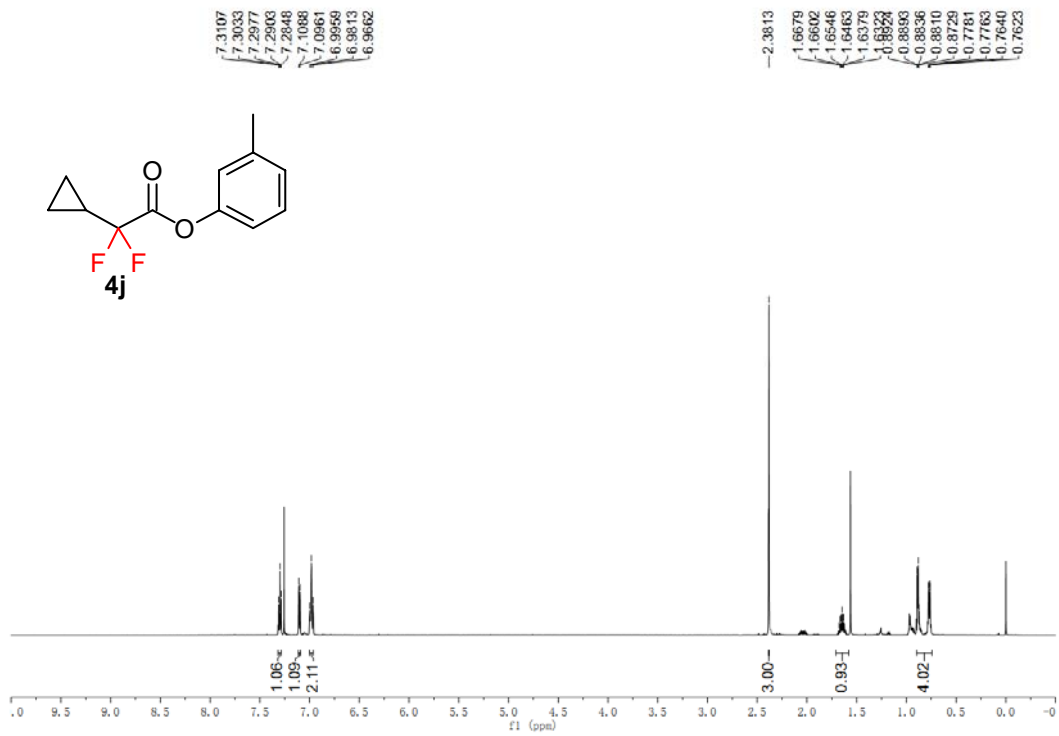


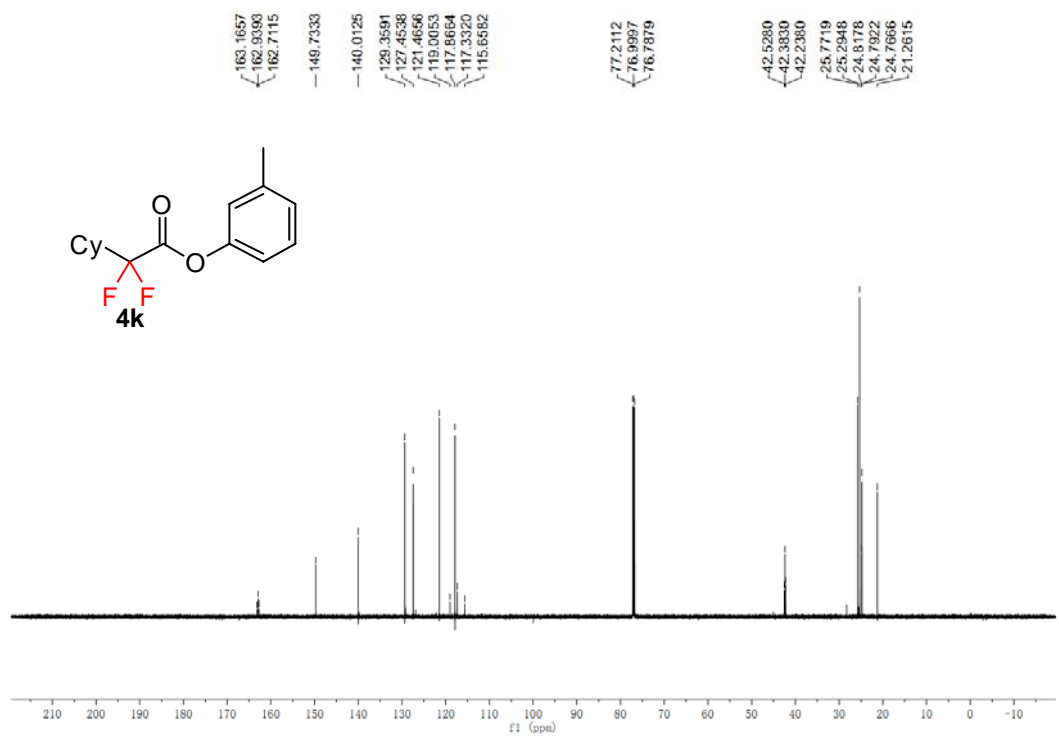
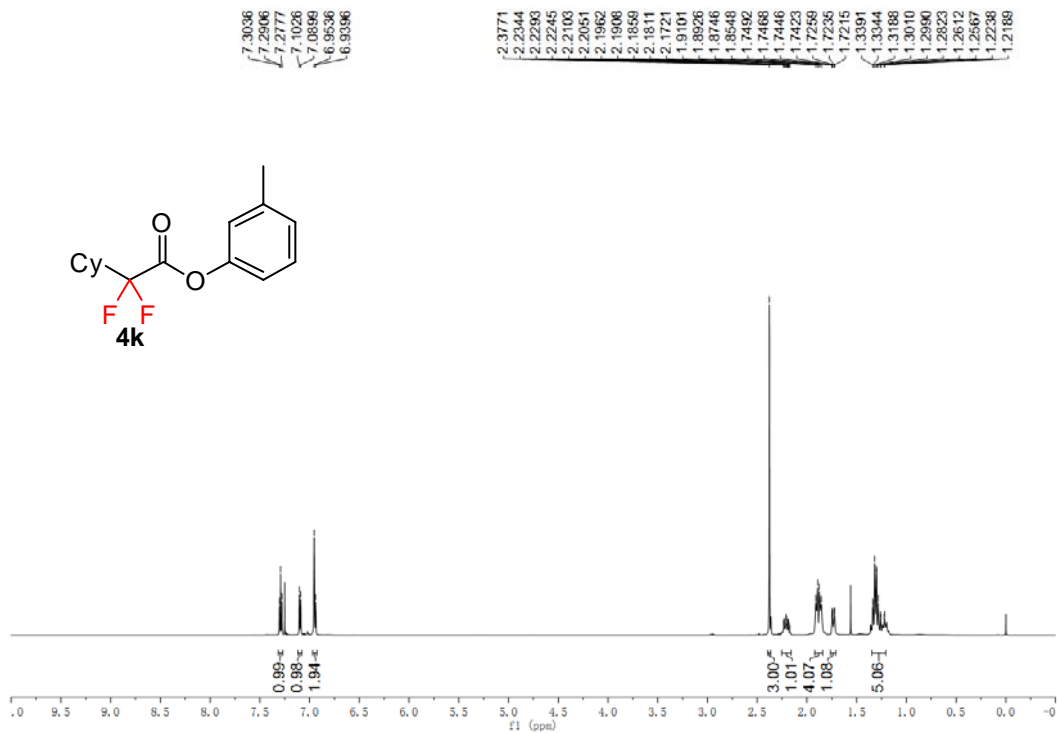


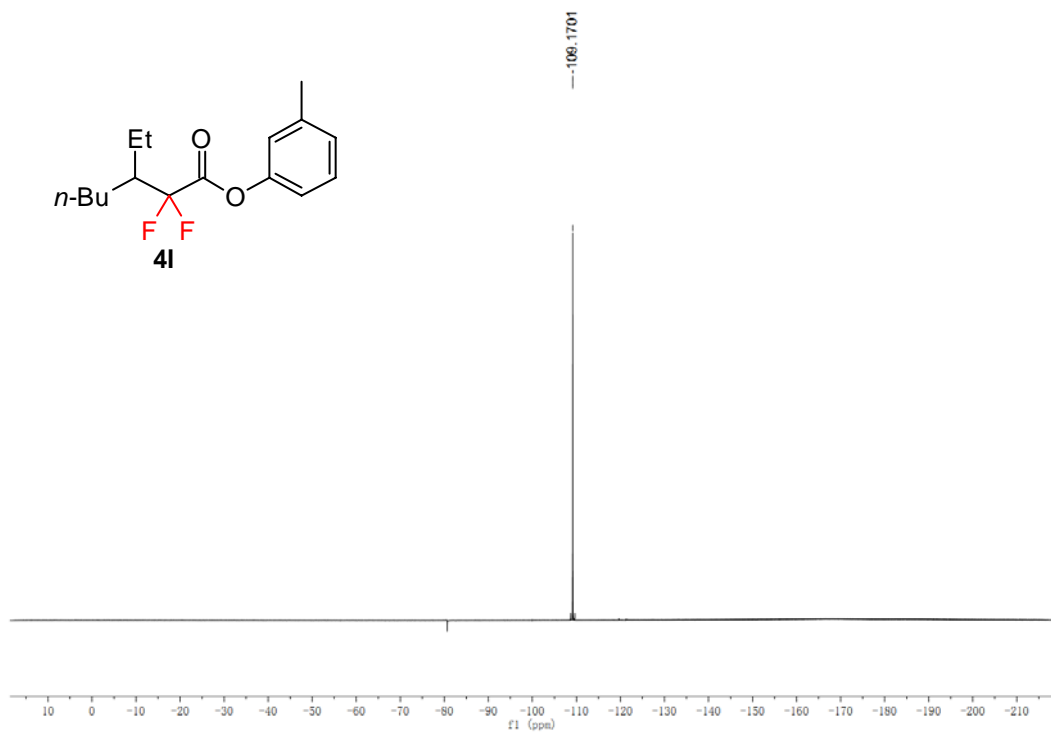
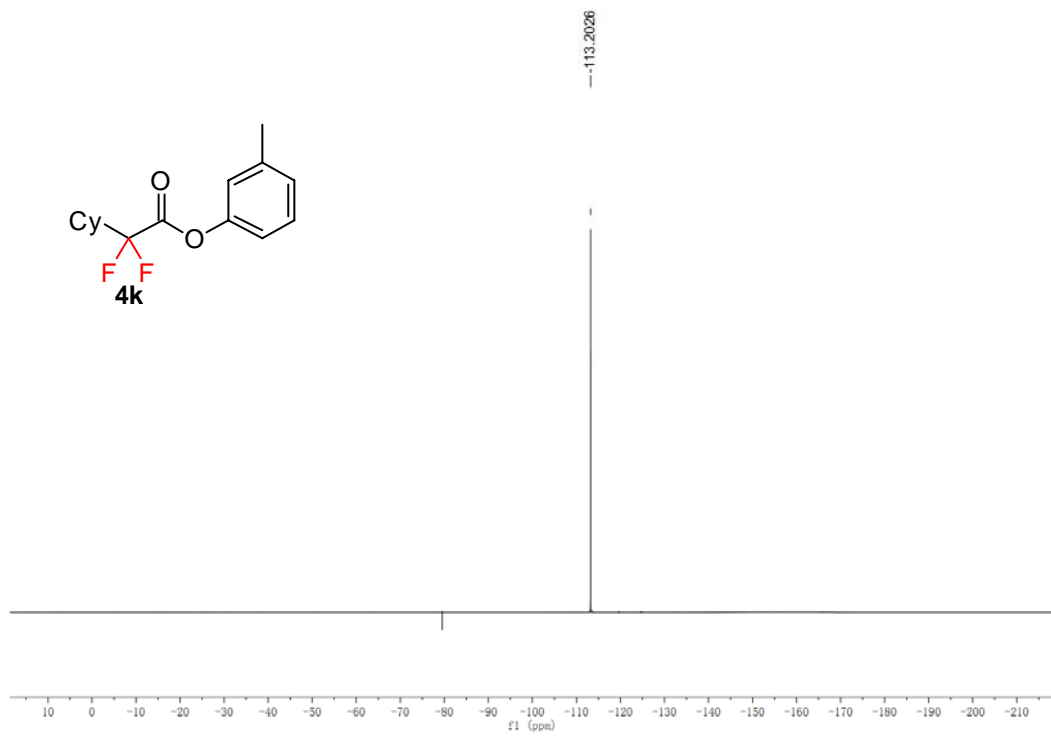


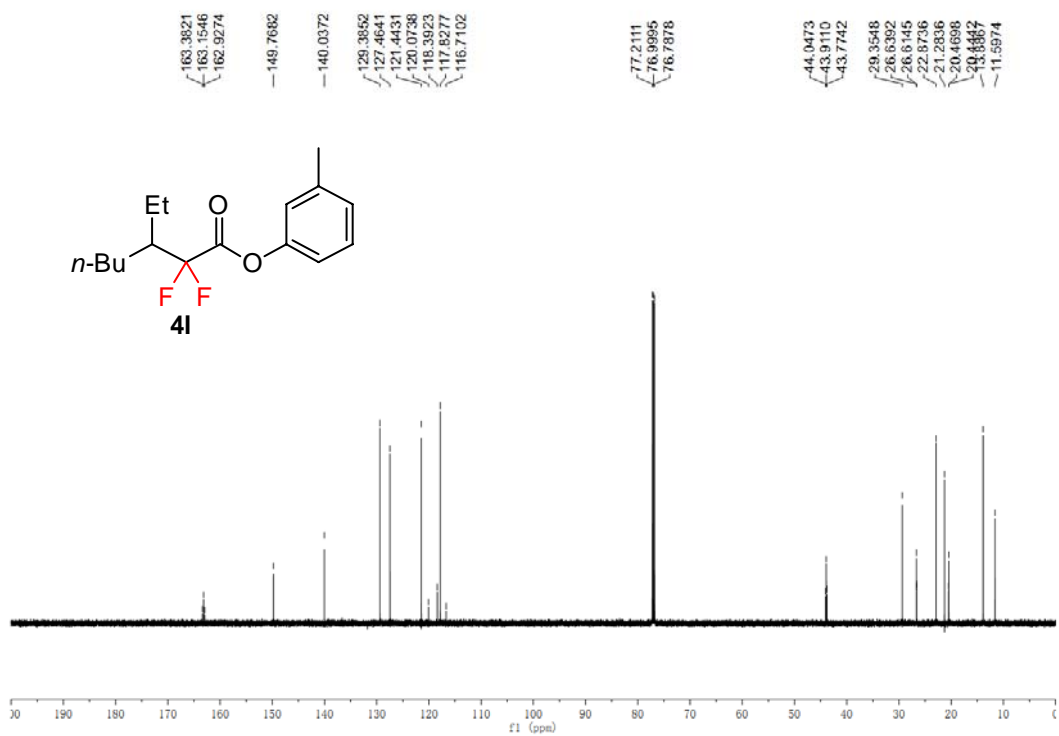
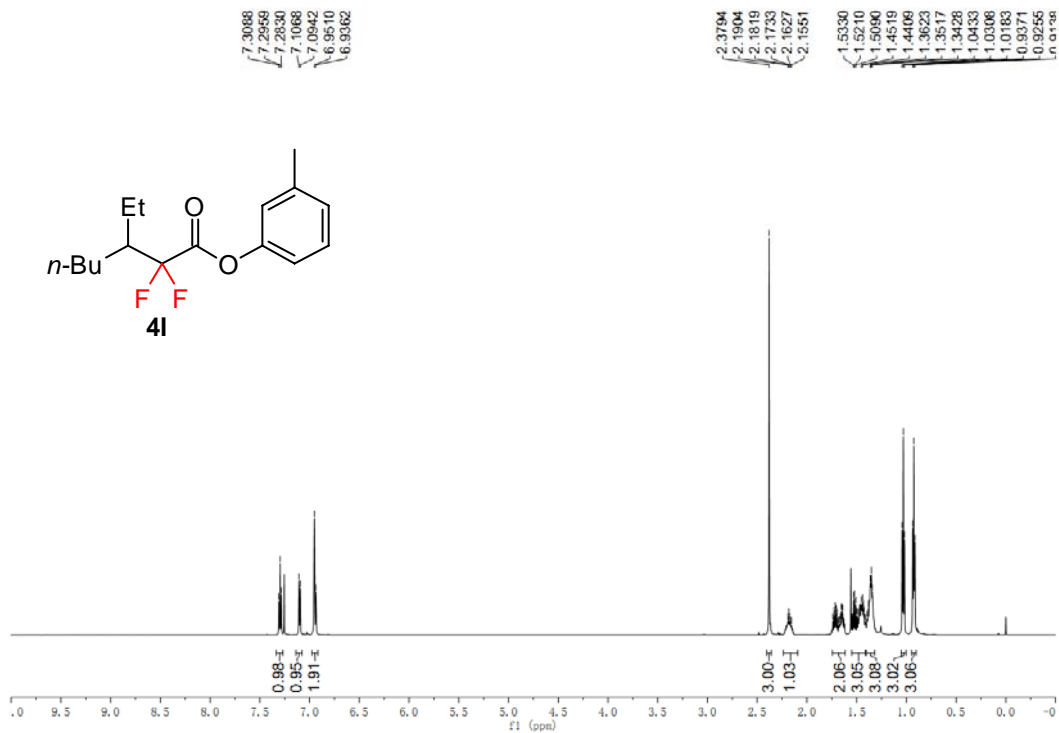


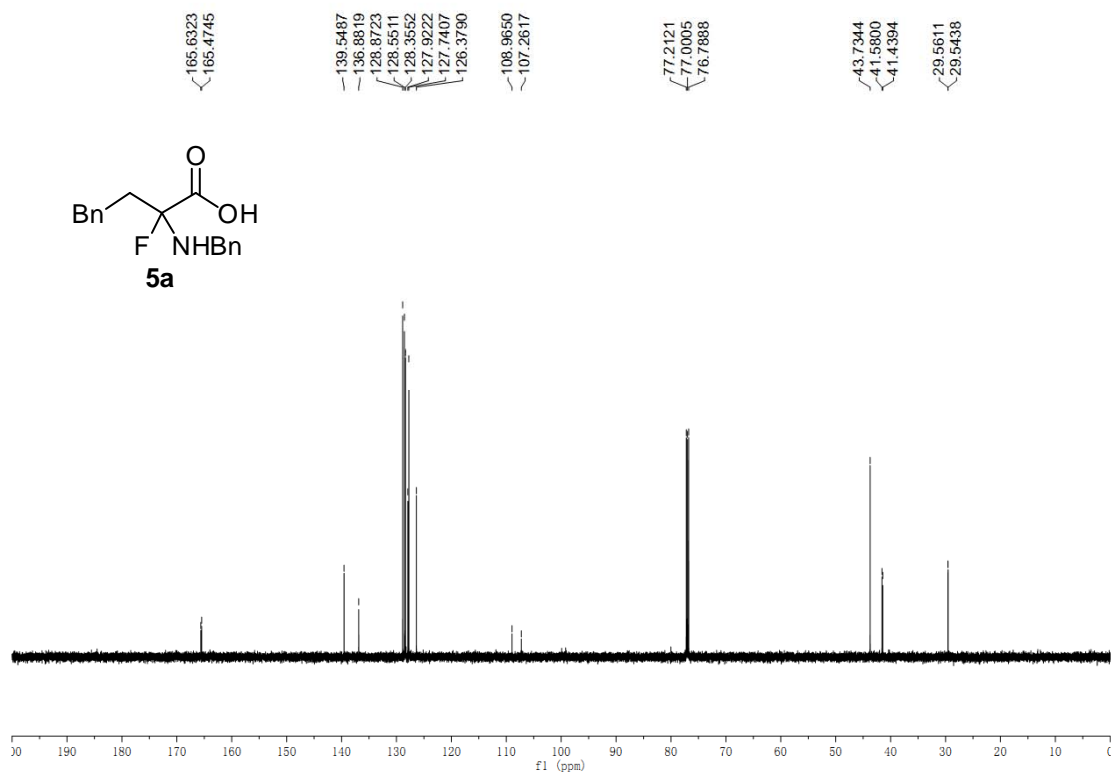
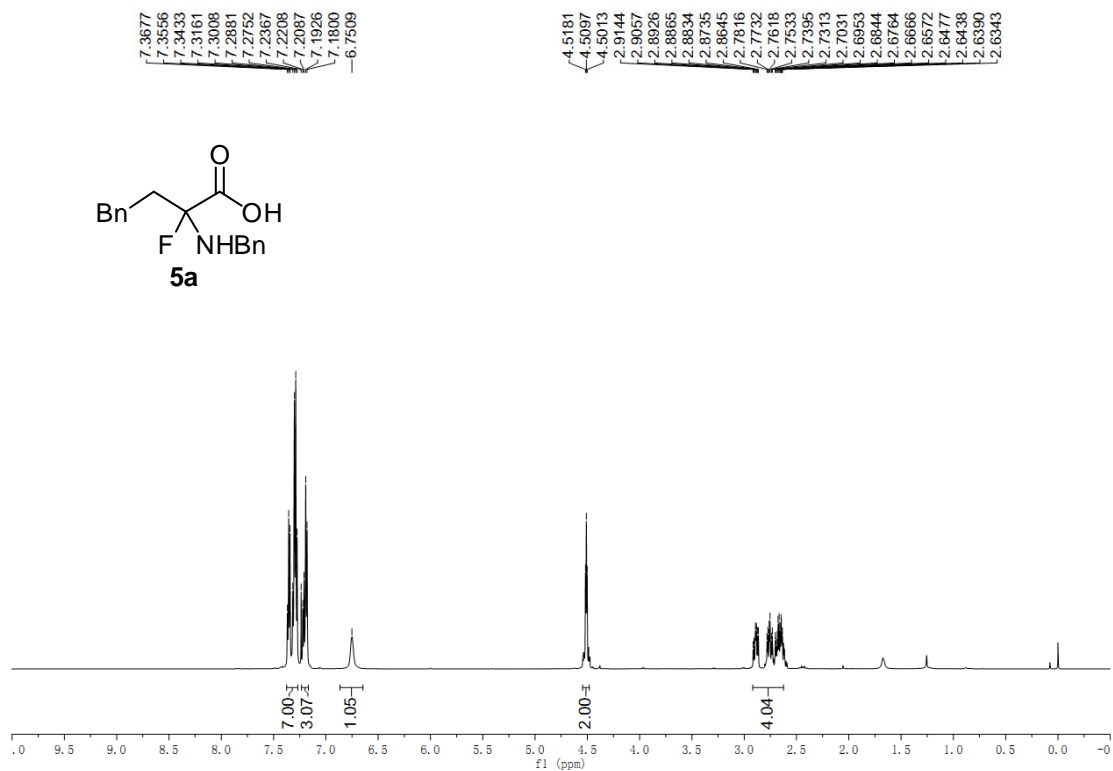


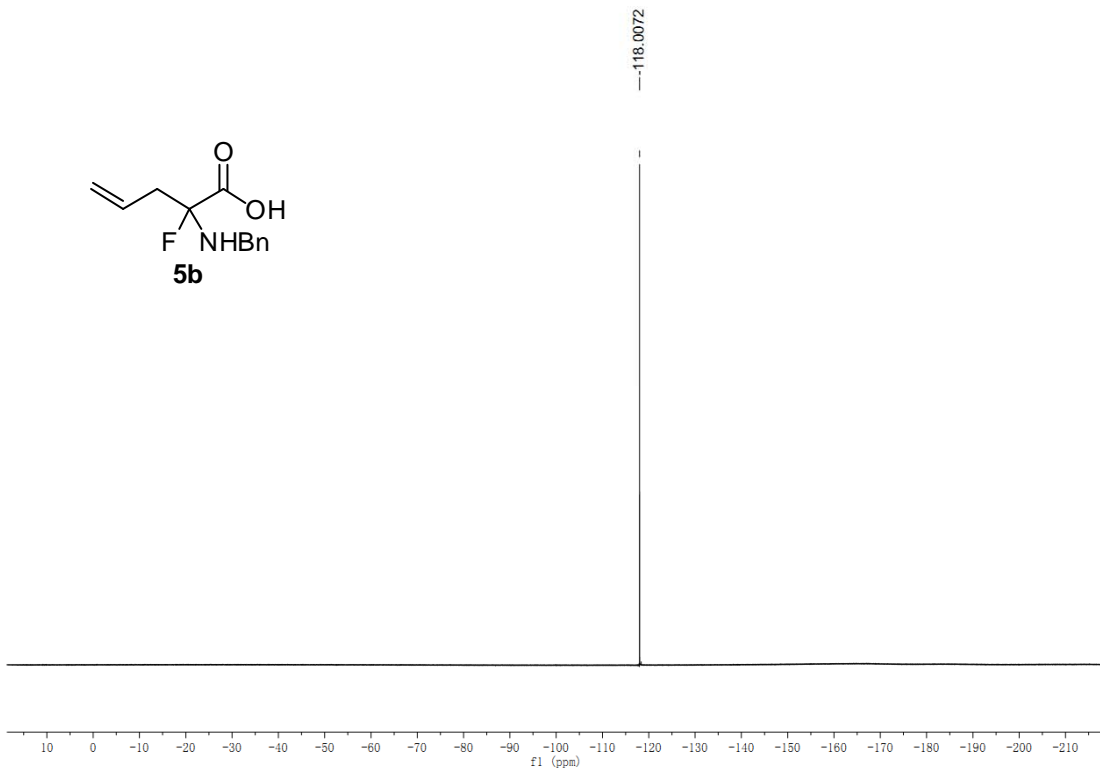
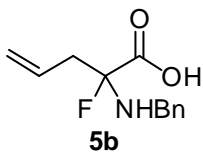
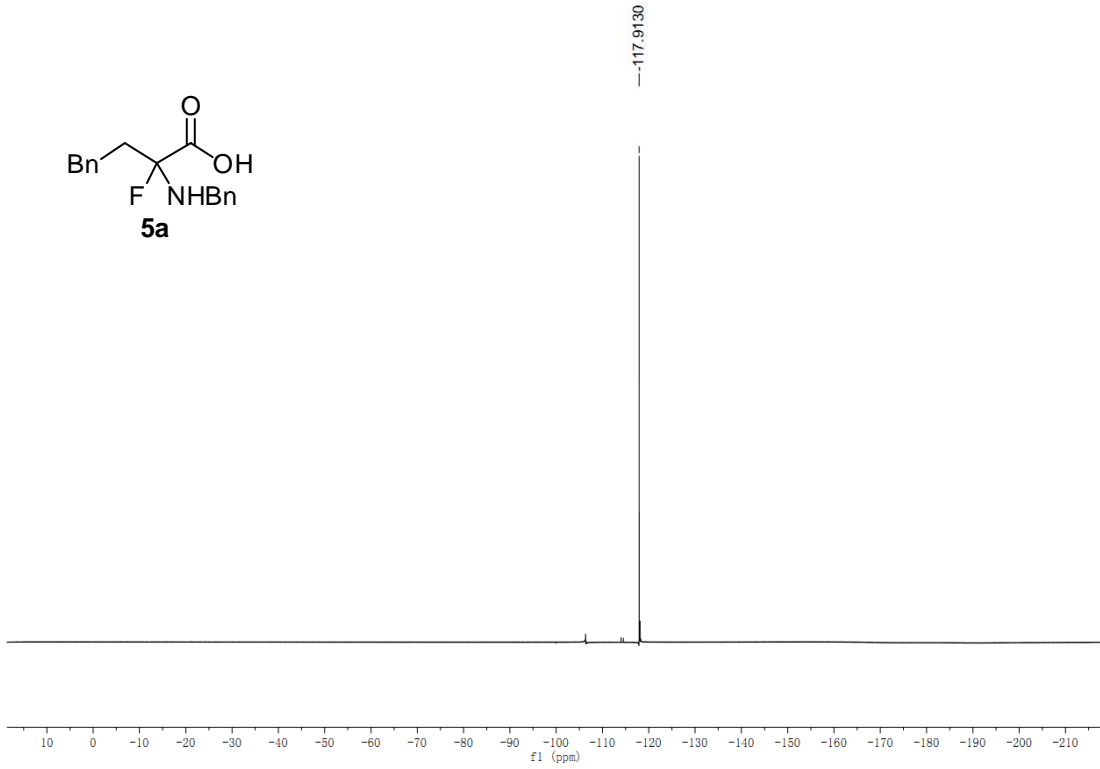
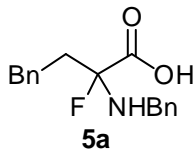


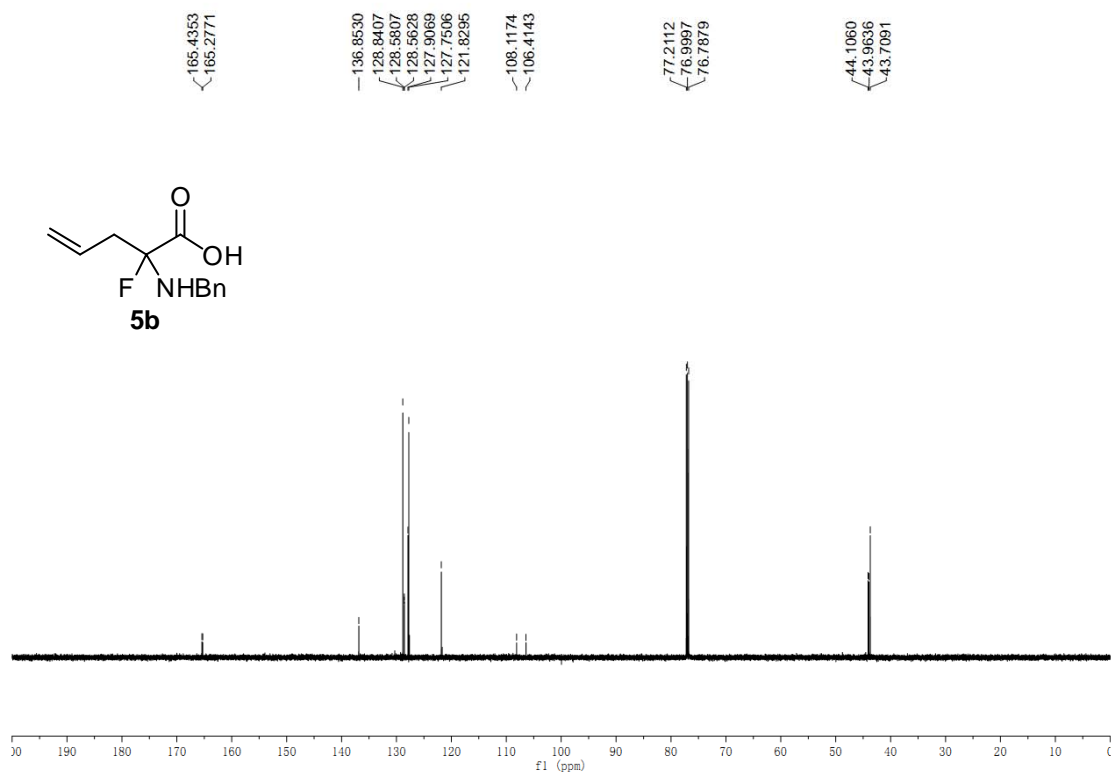
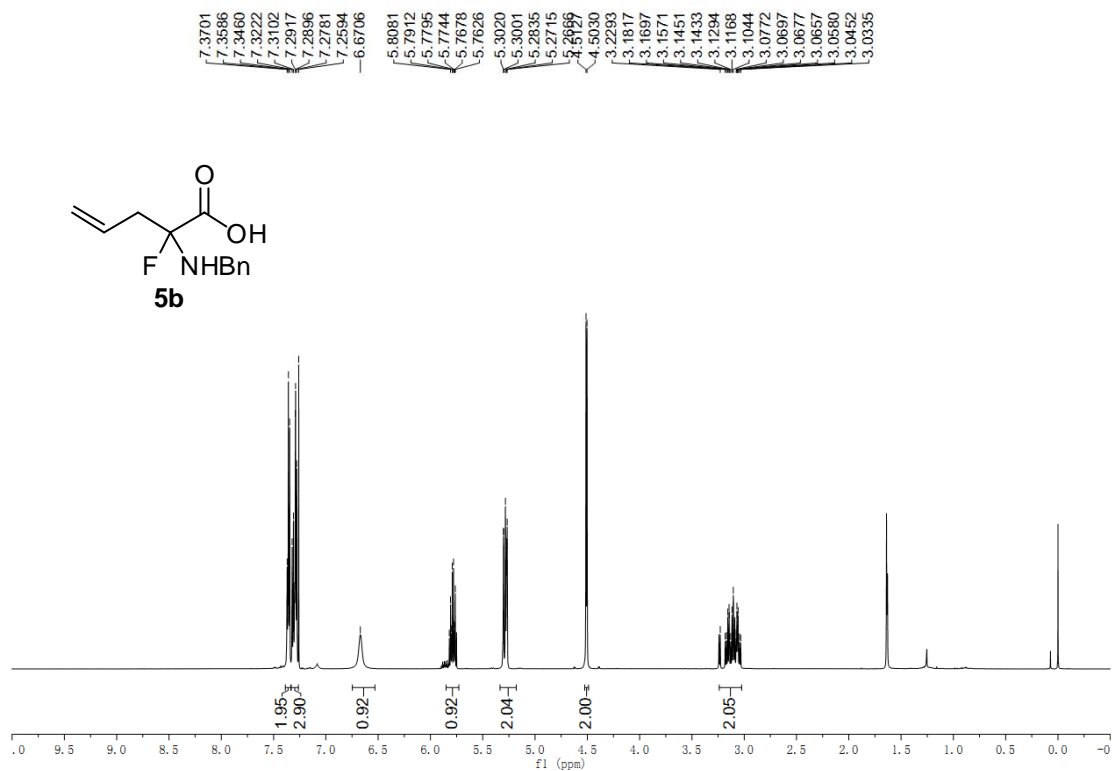




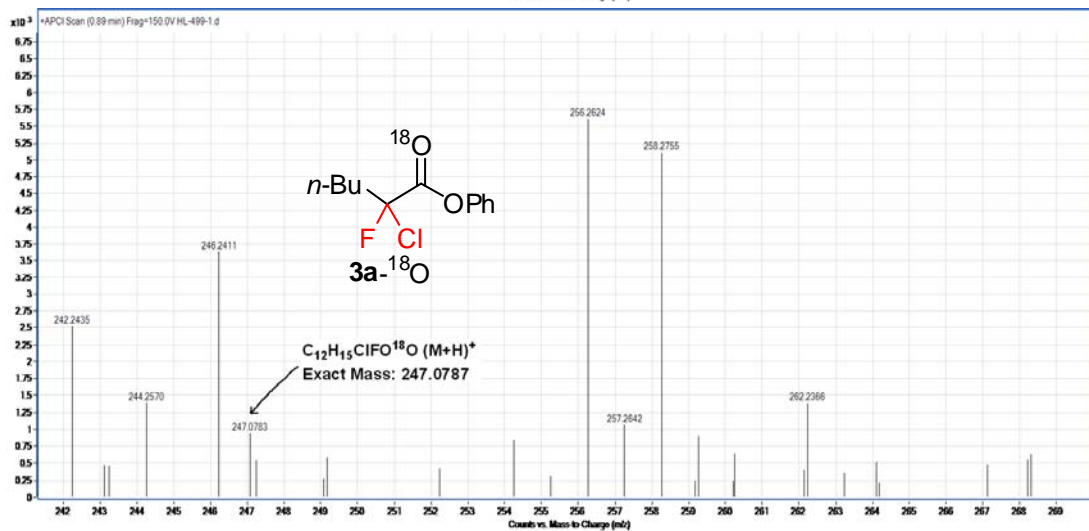
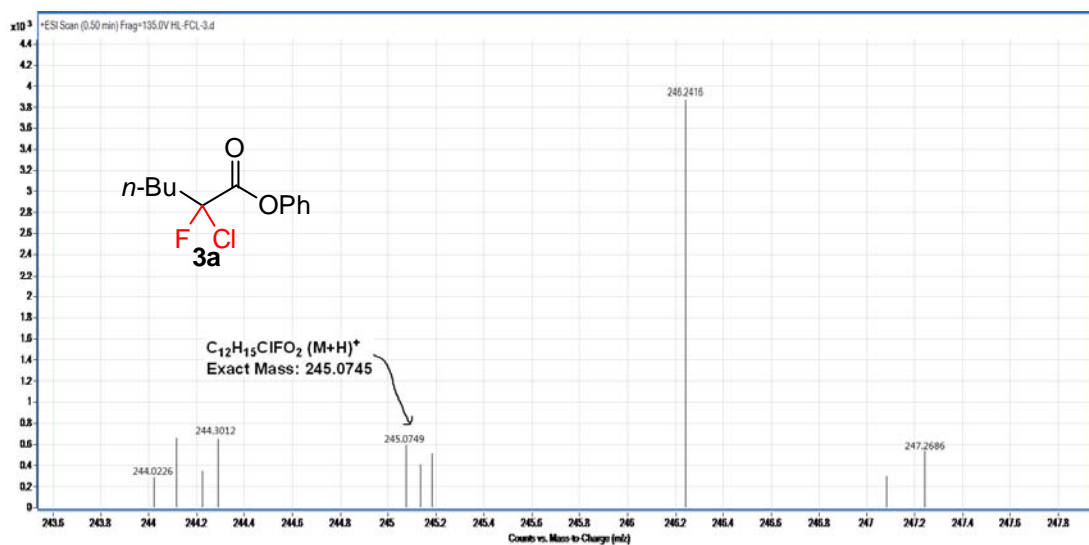








HRMS Spectra of 3a and 3a-¹⁸O :



HRMS Spectra of 4a and 4a-¹⁸O :

