

Supporting Information

Table of Contents

Part 1. General Information (S2)

Part 2. General procedure for the synthesis of products (S3)

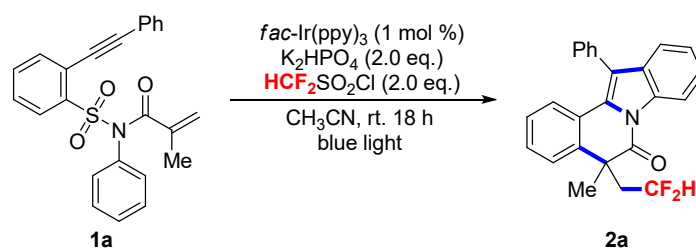
Part 3. Characterizations of products (S4 – S18)

Part 4. ^1H NMR, ^{13}C NMR and ^{19}F NMR Spectra (S19 – S53)

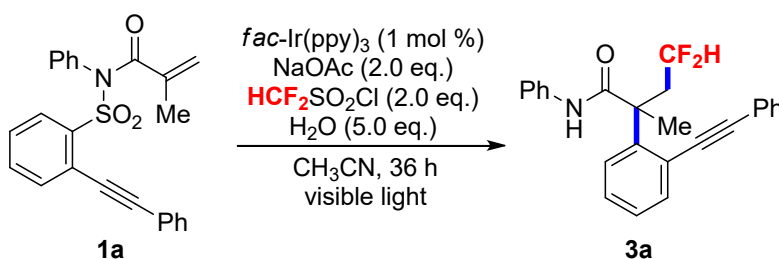
Part 1. General Information

Unless otherwise noted, materials obtained from commercial suppliers were used directly without further purification. Proton nuclear magnetic resonance (^1H NMR) spectra were recorded on Bruker 600 MHz spectrometer and Bruker 400 MHz spectrometer. Chemical shifts were recorded in parts per million (ppm, δ) relative to tetramethylsilane ($\delta = 0.00$) or chloroform ($\delta = 7.26$, singlet). ^1H NMR splitting patterns are designated as singlet (s), doublet (d), triplet (t), quartet (q), dd (doublet of doublets), m (multiplets), and etc. All first-order splitting patterns were assigned on the basis of the appearance of the multiplet. Splitting patterns that could not be easily interpreted are designated as multiplet (m) or broad (br). Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Bruker 600 MHz (150 MHz) spectrometer and Bruker 400 MHz (100 MHz) spectrometer. High-resolution mass spectrometry (HRMS) analysis was carried out using a MS instrument with ESI source.

Part 2. General procedure for the synthesis of products



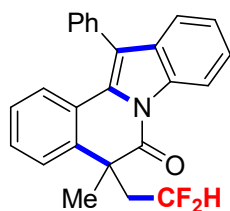
To an oven-dried Schlenk tube equipped with a magnetic stirrer, were added **1a** (80.3 mg, 0.2 mmol), *fac*-Ir(ppy)₃ (2.4 mg, 0.004 mmol, 0.002 eq) and K₂HPO₄ (68 mg, 0.4 mmol, 2.0 equiv). To this mixture were added 2 mL CH₃CN, 8 mg deionized CF₂HSO₂Cl (60 mg, 0.4 mmol, 2 equiv) under a blanket of nitrogen. The vial was sealed, and stirred under blue light at room temperature for 18 hr. After this time, the CH₃CN was removed in vacuo, and the residue purified by column chromatography on silica gel. This gave product **2a** as light yellow solid (66.0 mg, 85% yield).



To an oven-dried Schlenk tube equipped with a magnetic stirrer, were added **1a** (80.3 mg, 0.2 mmol), *fac*-Ir(ppy)₃ (2.4 mg, 0.004 mmol, 0.002 eq) and NaOAc (33 mg, 0.4 mmol, 2.0 equiv). To this mixture were added 2 mL CH₃CN, CF₂HSO₂Cl (60 mg, 0.4 mmol, 2 equiv) and H₂O (18 mg, 1.0 mmol, 5 equiv) under a blanket of nitrogen. The vial was sealed, and stirred under visible light at room temperature for 36 hr. After this time, the CH₃CN was removed in vacuo, and the residue purified by column chromatography on silica gel. This gave product **3a** as light yellow solid (53.1 mg, 68% yield).

Part 3. Characterizations of products

5-(2,2-difluoroethyl)-5-methyl-12-phenylindolo[2,1-a]isoquinolin-6(5H)-one (2a)



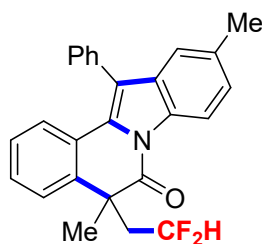
Prepared according to general method and isolated in 85% yield after chromatography as light yellow solid (66.0 mg)

^1H NMR (400 MHz, CDCl_3) δ 8.66 (d, $J = 8.2$ Hz, 1H), 7.62 – 7.49 (m, 5H), 7.49 – 7.38 (m, 3H), 7.35 – 7.28 (m, 3H), 7.11 – 7.01 (m, 1H), 5.59 (tdd, $J = 56.1, 6.4, 3.5$ Hz, 1H), 3.10 (tdd, $J = 15.0, 12.1, 6.5$ Hz, 1H), 2.58 (dddd, $J = 24.9, 14.4, 10.6, 3.5$ Hz, 1H), 1.79 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 171.74, 136.67, 134.28, 133.92, 132.33, 130.18, 129.33, 129.00, 128.57, 128.23, 127.27, 126.18, 126.16, 125.68, 125.09, 124.77, 120.87, 119.59, 116.72, 115.47 (t, $J = 240.2$ Hz), 44.98 – 44.92 (m), 44.69 (t, $J = 21.6$ Hz), 29.91.

^{19}F NMR (565 MHz, CDCl_3) δ -114.21 – -115.73 (m).

HRMS (ESI): calculated for $[\text{C}_{25}\text{H}_{20}\text{F}_2\text{NO}]^+$: $m/z = 388.1507$, found: $m/z = 388.1511$.

5-(2,2-difluoroethyl)-5,10-dimethyl-12-phenylindolo[2,1-a]isoquinolin-6(5H)-one (2b)



Prepared according to general method and isolated in 66% yield after chromatography as light yellow solid (53.0 mg)

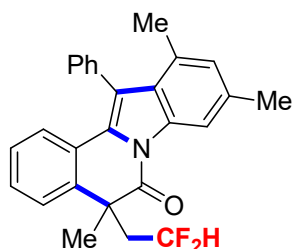
^1H NMR (400 MHz, CDCl_3) δ 8.51 (d, $J = 8.4$ Hz, 1H), 7.59 – 7.50 (m, 5H), 7.42 (t, $J = 8.2$ Hz, 2H), 7.30 (t, $J = 7.6$ Hz, 1H), 7.25 (d, $J = 9.0$ Hz, 1H), 7.10 – 6.98 (m, 2H), 5.57 (tdd, $J = 56.1, 6.3, 3.5$ Hz, 1H), 3.08 (tdd, $J = 14.9, 12.3, 6.4$ Hz, 1H), 2.55 (dddd,

$J = 24.9, 14.4, 10.7, 3.5$ Hz, 1H), 2.41 (s, 3H), 1.77 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 171.49, 136.68, 134.55, 134.07, 132.52, 132.44, 130.19, 129.31, 129.05, 128.43, 128.16, 127.43, 127.21, 126.16, 125.58, 125.18, 120.68, 119.42, 116.36, 115.46 (t, $J = 240.1$ Hz), 44.87 – 44.80 (m), 44.73 (t, $J = 21.4$ Hz), 29.86, 21.46.

^{19}F NMR (565 MHz, CDCl_3) δ -114.24 – -115.75 (m).

HRMS (ESI): calculated for $[\text{C}_{26}\text{H}_{22}\text{F}_2\text{NO}]^+$: $m/z = 402.1664$, found: $m/z = 402.1667$.

5-(2,2-difluoroethyl)-5,9,11-trimethyl-12-phenylindolo[2,1-a]isoquinolin-6(5H)-one (2c)



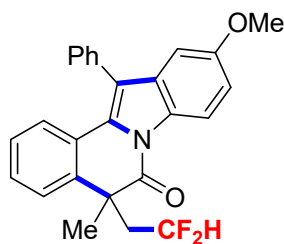
Prepared according to general method and isolated in 80% yield after chromatography as light yellow solid (66.7 mg)

^1H NMR (400 MHz, CDCl_3) δ 8.48 (s, 1H), 7.62 – 7.42 (m, 5H), 7.39 (d, $J = 7.9$ Hz, 1H), 7.30 – 7.20 (m, 2H), 7.10 (d, $J = 8.1$ Hz, 1H), 6.98 (t, $J = 7.7$ Hz, 1H), 6.89 (s, 1H), 5.57 (tdd, $J = 56.2, 6.6, 3.3$ Hz, 1H), 3.11 (tdd, $J = 14.8, 11.9, 6.6$ Hz, 1H), 2.64 – 2.50 (m, 1H), 2.50 (s, 3H), 1.92 (s, 3H), 1.77 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 171.80, 136.53, 136.28, 136.22, 134.88, 131.12, 130.54, 130.31, 129.20, 128.42, 128.21, 128.04, 127.42, 127.22, 126.11, 125.44, 125.27, 121.76, 115.54 (t, $J = 240.1$ Hz), 114.90, 44.89 – 44.83 (m), 44.75 (t, $J = 21.6$ Hz), 30.18, 21.82, 19.76.

^{19}F NMR (565 MHz, CDCl_3) δ -114.25 – -115.95 (m).

HRMS (ESI): calculated for $[\text{C}_{27}\text{H}_{24}\text{F}_2\text{NO}]^+$: $m/z = 416.1820$, found: $m/z = 416.1820$.

5-(2,2-difluoroethyl)-10-methoxy-5-methyl-12-phenylindolo[2,1-a]isoquinolin-6(5H)-one (2d)



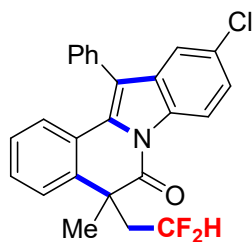
Prepared according to general method and isolated in 10% yield after chromatography as light yellow solid (8.4 mg)

^1H NMR (400 MHz, CDCl_3) δ 8.53 (d, $J = 9.0$ Hz, 1H), 7.55 - 7.49 (m, 5H), 7.40 (d, $J = 8.3$ Hz, 2H), 7.30 (t, $J = 7.6$ Hz, 1H), 7.10 - 6.97 (m, 2H), 6.72 (d, $J = 2.5$ Hz, 1H), 5.56 (tdd, $J = 56.2, 6.4, 3.5$ Hz, 1H), 3.79 (s, 3H), 3.08 (tdd, $J = 15.0, 12.1, 6.5$ Hz, 1H), 2.55 (dddd, $J = 24.8, 14.3, 10.6, 3.5$ Hz, 1H), 1.77 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 171.28, 157.45, 136.79, 133.93, 133.42, 130.14, 129.66, 129.39, 128.88, 128.48, 128.22, 127.21, 126.18, 125.56, 125.06, 120.66, 117.58, 115.45 (t, $J = 240.2$ Hz), 114.30, 102.34, 55.73, 44.75 - 44.69 (m), 44.73 (t, $J = 21.5$ Hz), 29.93.

^{19}F NMR (565 MHz, CDCl_3) δ -114.28 - -115.83 (m).

HRMS (ESI): calculated for $[\text{C}_{26}\text{H}_{22}\text{F}_2\text{NO}_2]^+$: $m/z = 418.1613$, found: $m/z = 418.1618$.

10-chloro-5-(2,2-difluoroethyl)-5-methyl-12-phenylindolo[2,1-a]isoquinolin-6(5H)-one (2e)



Prepared according to general method and isolated in 55% yield after chromatography as light yellow solid (46.5 mg)

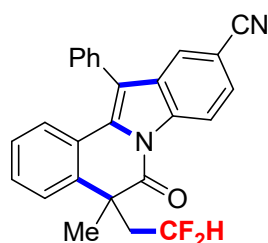
^1H NMR (600 MHz, CDCl_3) δ 8.57 (d, $J = 8.7$ Hz, 1H), 7.58 (t, $J = 7.3$ Hz, 2H), 7.53 (t, $J = 7.4$ Hz, 1H), 7.49 (d, $J = 7.1$ Hz, 2H), 7.46 (d, $J = 8.1$ Hz, 1H), 7.42 (d, $J = 7.9$ Hz, 1H), 7.37 (dd, $J = 8.7, 2.0$ Hz, 1H), 7.35 - 7.31 (m, 1H), 7.25 (d, $J = 2.0$ Hz, 1H), 7.08 - 7.06 (m, 1H), 5.55 (tdd, $J = 56.1, 6.6, 3.3$ Hz, 1H), 3.09 (tdd, $J = 14.9, 11.8, 6.6$ Hz, 1H), 2.57 (dddd, $J = 26.7, 14.5, 9.0, 3.3$ Hz, 1H), 1.78 (s, 3H). ^{13}C NMR (151 MHz,

CDCl₃) δ 171.70, 136.80, 133.70, 133.24, 132.57, 130.51, 130.25, 130.09, 129.49, 128.99, 128.50, 127.40, 126.22, 126.14, 125.81, 124.67, 119.92, 119.18, 117.78, 115.36 (t, $J = 240.2$ Hz), 44.91 – 44.84 (m), 44.77 (t, $J = 19.7$ Hz), 29.93.

¹⁹F NMR (565 MHz, CDCl₃) δ -114.34 – -116.04 (m).

HRMS (ESI): calculated for [C₂₅H₁₉ClF₂NO]⁺ : $m/z = 422.1118$, found: $m/z = 422.1120$.

5-(2,2-difluoroethyl)-5-methyl-6-oxo-12-phenyl-5,6-dihydroindolo[2,1-a]isoquinoline-10-carbonitrile (2f)



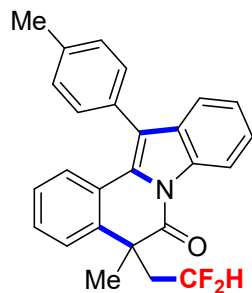
Prepared according to general method and isolated in 58% yield after chromatography as yellow solid (48.2 mg)

¹H NMR (400 MHz, CDCl₃) δ 8.73 (d, $J = 8.5$ Hz, 1H), 7.66 (dd, $J = 8.5, 1.6$ Hz, 1H), 7.63 – 7.52 (m, 4H), 7.51 – 7.41 (m, 4H), 7.37 (td, $J = 7.7, 1.2$ Hz, 1H), 7.14 – 7.05 (m, 1H), 5.54 (tdd, $J = 56.1, 6.7, 3.2$ Hz, 1H), 3.09 (tdd, $J = 14.7, 12.0, 6.7$ Hz, 1H), 2.66–2.52 (m 1H), 1.80 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 172.09, 136.73, 136.04, 132.56, 132.53, 131.10, 130.00, 129.65, 129.48, 129.07, 128.82, 127.60, 126.26, 126.04, 124.23, 119.85, 119.36, 117.48, 115.23 (t, $J = 240.3$ Hz), 108.20, 45.10 – 45.04 (m), 44.83 (t, $J = 21.7$ Hz), 29.89.

¹⁹F NMR (565 MHz, CDCl₃) δ -114.49 – -116.24 (m).

HRMS (ESI): calculated for [C₂₆H₁₉F₂N₂O]⁺ : $m/z = 413.1460$, found: $m/z = 413.1461$.

5-(2,2-difluoroethyl)-5-methyl-12-(p-tolyl)indolo[2,1-a]isoquinolin-6(5H)-one (2g)



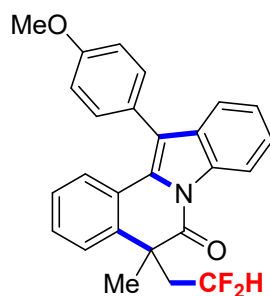
Prepared according to general method and isolated in 84% yield after chromatography as light yellow solid (67.5 mg)

^1H NMR (400 MHz, CDCl_3) δ 8.66 (d, $J = 8.2$ Hz, 1H), 7.53 (d, $J = 8.1$ Hz, 1H), 7.48 – 7.35 (m, 6H), 7.35 – 7.27 (m, 3H), 7.08 (t, $J = 7.6$ Hz, 1H), 5.59 (tdd, $J = 56.1, 6.2, 3.5$ Hz, 1H), 3.19 – 3.01 (m, 1H), 2.66 – 2.53 (m, 1H), 2.51 (s, 3H), 1.78 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 171.71, 137.97, 136.61, 134.29, 132.47, 130.74, 130.06, 129.99, 128.90, 128.49, 127.24, 126.13, 126.10, 125.69, 125.22, 124.71, 120.93, 119.64, 116.70, 115.48 (t, $J = 240.1$ Hz), 44.98 – 44.91 (m), 44.67 (t, $J = 21.6$ Hz), 29.89, 21.49.

^{19}F NMR (565 MHz, CDCl_3) δ -114.20, -115.75 (m).

HRMS (ESI): calculated for $[\text{C}_{26}\text{H}_{22}\text{F}_2\text{NO}]^+$: $m/z = 402.1664$, found: $m/z = 402.1670$.

5-(2,2-difluoroethyl)-12-(4-methoxyphenyl)-5-methylindolo[2,1-a]isoquinolin-6(5H)-one (2h)



Prepared according to general method and isolated in 76% yield after chromatography as yellow solid (63.5 mg)

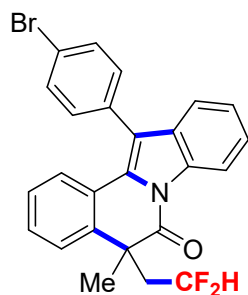
^1H NMR (600 MHz, CDCl_3) δ 8.65 (d, $J = 8.2$ Hz, 1H), 7.54 (dd, $J = 8.1, 0.8$ Hz, 1H), 7.47 – 7.40 (m, 4H), 7.35 – 7.29 (m, 3H), 7.13 – 7.06 (m, 3H), 5.59 (tdd, $J = 56.1, 6.4, 3.5$ Hz, 1H), 3.94 (s, 3H), 3.10 (tdd, $J = 15.2, 11.8, 6.5$ Hz, 1H), 2.65 – 2.51 (m, 1H),

1.78 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 171.72, 159.54, 136.62, 134.28, 132.59, 131.33, 128.98, 128.50, 127.28, 126.17, 126.11, 125.83, 125.62, 125.26, 124.74, 120.63, 119.61, 116.72, 115.50 (t, $J = 240.1$ Hz), 114.80, 55.39, 44.97 – 44.90 (m), 44.68 (t, $J = 21.7$ Hz), 29.87.

^{19}F NMR (565 MHz, CDCl_3) δ -114.18, -115.71 (m).

HRMS (ESI): calculated for $[\text{C}_{26}\text{H}_{22}\text{F}_2\text{NO}_2]^+$: $m/z = 418.1613$, found: $m/z = 418.1618$.

12-(4-bromophenyl)-5-(2,2-difluoroethyl)-5-methylindolo[2,1-a]isoquinolin-6(5H)-one (2i)



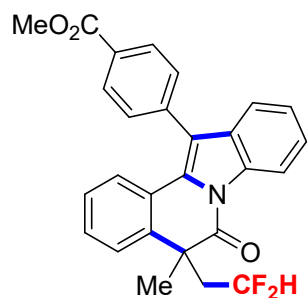
Prepared according to general method and isolated in 70% yield after chromatography as yellow solid (65.3 mg)

^1H NMR (400 MHz, CDCl_3) δ 8.66 (d, $J = 8.2$ Hz, 1H), 7.71 (d, $J = 8.4$ Hz, 2H), 7.50 – 7.38 (m, 5H), 7.38 – 7.26 (m, 3H), 7.14-7.10 (m, 1H), 5.58 (tdd, $J = 56.1, 6.3, 3.5$ Hz, 1H), 3.10 (tdd, $J = 15.0, 12.3, 6.4$ Hz, 1H), 2.64-2.51 (m, 1H), 1.78 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 171.70, 136.83, 134.29, 132.97, 132.63, 131.96, 131.92, 129.22, 128.82, 127.40, 126.33, 125.57, 124.90, 124.83, 122.43, 119.40, 119.28, 116.80, 115.41 (t, $J = 240.2$ Hz), 45.01 – 44.94 (m), 44.68 (t, $J = 21.8$ Hz), 29.89.

^{19}F NMR (565 MHz, CDCl_3) δ -114.28 – -115.83 (m).

HRMS (ESI): calculated for $[\text{C}_{25}\text{H}_{19}\text{BrF}_2\text{NO}]^+$: $m/z = 466.0613$, found: $m/z = 466.0617$.

Methyl 4-(5-(2,2-difluoroethyl)-5-methyl-6-oxo-5,6-dihydroindolo[2,1-a]-isoquinolin-12-yl)-benzoate (2j)

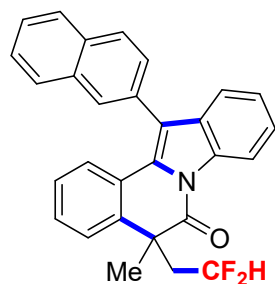


Prepared according to general method and isolated in 64% yield after chromatography as yellow solid (57.2 mg)

^1H NMR (600 MHz, CDCl_3) δ 8.66 (d, $J = 8.2$ Hz, 1H), 8.25 (d, $J = 8.2$ Hz, 2H), 7.62 (d, $J = 7.9$ Hz, 2H), 7.45 – 7.43 (m, 2H), 7.40 (d, $J = 8.1$ Hz, 1H), 7.36 – 7.25 (m, 3H), 7.06 (t, $J = 7.6$ Hz, 1H), 5.58 (tdd, $J = 56.1, 6.4, 3.5$ Hz, 1H), 4.01 (s, 3H), 3.10 (tdd, $J = 15.1, 11.9, 6.5$ Hz, 1H), 2.65 – 2.50 (m, 1H), 1.78 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 171.72, 166.88, 139.08, 136.87, 134.33, 131.73, 130.58, 130.40, 129.98, 129.35, 128.89, 127.38, 126.37, 126.32, 125.65, 124.94, 124.71, 119.63, 119.26, 116.82, 115.40 (t, $J = 240.2$ Hz), 52.36, 45.03 – 44.96 (m), 44.65 (t, $J = 21.4$ Hz), 29.91. ^{19}F NMR (565 MHz, CDCl_3) δ -114.27 – -115.81 (m).

HRMS (ESI): calculated for $[\text{C}_{27}\text{H}_{22}\text{F}_2\text{NO}_3]^+$: $m/z = 446.1562$, found: $m/z = 446.1570$.

5-(2,2-difluoroethyl)-5-methyl-12-(naphthalen-2-yl)indolo[2,1-a]isoquinolin-6(5H)-one (2k)



Prepared according to general method and isolated in 66% yield after chromatography as yellow solid (57.8 mg)

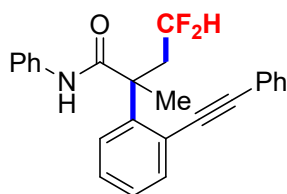
^1H NMR (400 MHz, CDCl_3) δ 8.67 (d, $J = 8.2$ Hz, 1H), 8.03 (d, $J = 7.8$ Hz, 2H), 8.01 – 7.95 (m, 1H), 7.94 – 7.88 (m, 1H), 7.63 – 7.54 (m, 3H), 7.44 (ddd, $J = 11.9, 9.9, 6.5$ Hz, 3H), 7.35 – 7.26 (m, 3H), 6.97 (dd, $J = 11.3, 4.1$ Hz, 1H), 5.60 (tdd, $J = 56.1, 6.4,$

3.5 Hz, 1H), 3.10 (qd, $J = 15.0, 6.6$ Hz, 1H), 2.58 (dddd, $J = 24.9, 14.4, 10.9, 3.4$ Hz, 1H), 1.80 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 171.77, 136.70, 134.34, 133.87, 133.04, 132.41, 131.39, 129.23, 129.21, 129.10, 128.63, 128.15, 128.08, 127.93, 127.35, 126.53, 126.51, 126.23, 126.18, 125.77, 125.06, 124.83, 120.69, 119.60, 116.77, 115.47 (t, $J = 240.1$ Hz), 45.02 – 44.95 (m), 44.64 (t, $J = 21.4$ Hz), 30.15.

^{19}F NMR (377 MHz, CDCl_3) δ -114.00 – -115.90 (m).

HRMS (ESI): calculated for $[\text{C}_{29}\text{H}_{22}\text{F}_2\text{NO}]^+$: $m/z = 438.1664$, found: $m/z = 438.1665$.

4,4-difluoro-2-methyl-N-phenyl-2-(2-(phenylethynyl)phenyl)butanamide (3a)



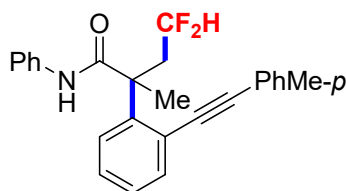
Prepared according to general method and isolated in 68% yield after chromatography as light yellow solid (53.1 mg)

^1H NMR (400 MHz, CDCl_3) δ 7.66 (dd, $J = 7.5, 1.4$ Hz, 1H), 7.57 (d, $J = 7.8$ Hz, 1H), 7.52 – 7.44 (m, 3H), 7.41 (td, $J = 7.5, 1.2$ Hz, 1H), 7.35 – 7.27 (m, 5H), 7.21 (t, $J = 7.9$ Hz, 2H), 7.03 (t, $J = 7.4$ Hz, 1H), 6.77 (s, 1H), 5.60 (tdd, $J = 56.5, 6.0, 3.7$ Hz, 1H), 3.24 – 3.03 (m, 1H), 2.86 (qd, $J = 15.4, 6.0$ Hz, 1H), 1.88 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 174.07, 141.71, 137.80, 134.59, 131.57, 129.08, 128.82, 128.71, 128.36, 128.32, 127.29, 124.43, 123.46, 122.51, 120.54, 116.88 (t, $J = 238.5$ Hz), 96.79, 86.99, 49.24 – 49.17 (m), 40.57 (t, $J = 21.7$ Hz), 24.93.

^{19}F NMR (565 MHz, CDCl_3) δ -110.66 – -111.76 (m).

HRMS (ESI): calculated for $[\text{C}_{25}\text{H}_{22}\text{F}_2\text{NO}]^+$: $m/z = 390.1664$, found: $m/z = 390.1659$.

4,4-difluoro-2-methyl-N-phenyl-2-(2-(p-tolyethynyl)phenyl)butanamide (3b)



Prepared according to general method and isolated in 52% yield after chromatography

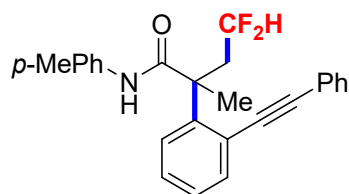
as light yellow solid (42.2 mg).

^1H NMR (400 MHz, CDCl_3) δ 7.64 (dd, $J = 7.5, 1.5$ Hz, 1H), 7.56 (dd, $J = 7.8, 0.8$ Hz, 1H), 7.45 (td, $J = 7.6, 1.6$ Hz, 1H), 7.42 – 7.35 (m, 3H), 7.34 – 7.29 (m, 2H), 7.21 (t, $J = 7.9$ Hz, 2H), 7.11 (d, $J = 7.9$ Hz, 2H), 7.03 (t, $J = 7.4$ Hz, 1H), 6.77 (s, 1H), 5.59 (tdd, $J = 56.5, 6.0, 3.7$ Hz, 1H), 3.24 – 3.03 (m, 1H), 2.85 (qd, $J = 15.4, 6.1$ Hz, 1H), 2.35 (s, 3H), 1.87 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 174.09, 141.56, 138.93, 137.82, 134.46, 131.46, 129.10, 128.86, 128.81, 128.33, 127.27, 124.39, 123.68, 120.56, 119.45, 116.91 (t, $J = 238.5$ Hz), 97.09, 86.42, 49.22 – 49.16 (m), 40.48 (t, $J = 22.0$ Hz), 24.95, 21.59.

^{19}F NMR (565 MHz, CDCl_3) δ -110.69 – -111.79 (m).

HRMS (ESI): calculated for $[\text{C}_{26}\text{H}_{24}\text{F}_2\text{NO}]^+$: $m/z = 404.1820$, found: $m/z = 404.1825$.

4,4-difluoro-2-methyl-2-(2-(phenylethynyl)phenyl)-N-(p-tolyl)butanamide (3c)



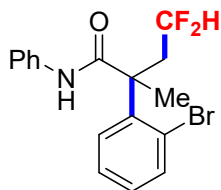
Prepared according to general method and isolated in 59% yield after chromatography as solid (47.7 mg).

^1H NMR (400 MHz, CDCl_3) δ 7.65 (dd, $J = 7.5, 1.5$ Hz, 1H), 7.56 (d, $J = 7.8$ Hz, 1H), 7.50 – 7.44 (m, 3H), 7.40 (td, $J = 7.5, 1.2$ Hz, 1H), 7.32 – 7.30 (m, 3H), 7.19 (d, $J = 8.4$ Hz, 2H), 7.00 (d, $J = 8.3$ Hz, 2H), 6.69 (s, 1H), 5.60 (tdd, $J = 56.5, 5.9, 3.7$ Hz, 1H), 3.24 – 3.00 (m, 1H), 2.85 (qd, $J = 15.4, 6.0$ Hz, 1H), 2.24 (s, 3H), 1.86 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 173.97, 141.86, 135.21, 134.55, 134.06, 131.59, 129.29, 129.00, 128.65, 128.29, 128.27, 127.26, 123.48, 122.56, 120.67, 116.90 (t, $J = 238.4$ Hz), 96.76, 87.03, 49.15 – 49.09 (m), 40.58 (t, $J = 21.7$ Hz), 24.93, 20.80.

^{19}F NMR (565 MHz, CDCl_3) δ -110.68 – -111.79 (m).

HRMS (ESI): calculated for $[\text{C}_{26}\text{H}_{24}\text{F}_2\text{NO}]^+$: $m/z = 404.1820$, found: $m/z = 404.1821$.

2-(2-bromophenyl)-4,4-difluoro-2-methyl-N-phenylbutanamide (3d)



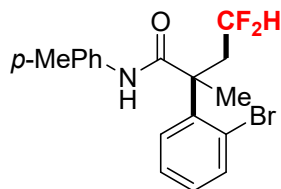
Prepared according to general method and isolated in 90% yield after chromatography as solid (66.2 mg).

^1H NMR (400 MHz, CDCl_3) δ 7.69 (dd, $J = 7.9, 1.3$ Hz, 1H), 7.59 (dd, $J = 7.9, 1.5$ Hz, 1H), 7.47 (td, $J = 7.7, 1.3$ Hz, 1H), 7.37 – 7.26 (m, 5H), 7.15 – 7.06 (m, 1H), 6.70 (s, 1H), 5.56 (tdd, $J = 56.3, 5.9, 3.8$ Hz, 1H), 3.08 (dtd, $J = 22.2, 15.6, 3.8$ Hz, 1H), 2.74 (qd, $J = 15.3, 5.9$ Hz, 1H), 1.87 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 173.45, 139.30, 137.51, 135.58, 130.14, 129.57, 128.97, 128.36, 124.74, 124.48, 120.58, 116.58 (t, $J = 238.7$ Hz), 49.96 – 49.89 (m), 39.50 (t, $J = 22.1$ Hz), 25.81.

^{19}F NMR (565 MHz, CDCl_3) δ -111.17 – -112.34 (m).

HRMS (ESI): calculated for $[\text{C}_{17}\text{H}_{16}\text{BrF}_2\text{NNaO}]^+$: $m/z = 390.0276$, found: $m/z = 390.0272$.

2-(2-bromophenyl)-4,4-difluoro-2-methyl-N-(p-tolyl)butanamide (3e)



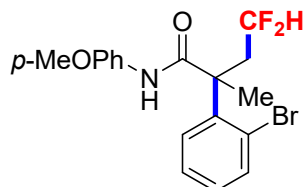
Prepared according to general method and isolated in 80% yield after chromatography as solid (60.8 mg).

^1H NMR (500 MHz, cdCl_3) δ 7.68 (d, $J = 8.0$ Hz, 1H), 7.57 (d, $J = 8.0$ Hz, 1H), 7.45 (t, $J = 7.6$ Hz, 1H), 7.30 – 7.24 (m, 1H), 7.21 (d, $J = 8.3$ Hz, 2H), 7.09 (d, $J = 8.2$ Hz, 2H), 6.67 (s, 1H), 5.56 (tdd, $J = 56.2, 5.6, 3.8$ Hz, 1H), 3.13 – 2.98 (m, 1H), 2.73 (qd, $J = 15.2, 5.8$ Hz, 1H), 2.29 (s, 3H), 1.86 (s, 3H). ^{13}C NMR (126 MHz, cdCl_3) δ 173.40, 139.44, 135.55, 134.94, 134.44, 130.07, 129.56, 129.45, 128.33, 124.48, 120.74, 116.62 (t, $J = 238.7$ Hz), 49.88 – 49.80 (m), 39.57 (t, $J = 22.1$ Hz), 25.79, 20.88.

^{19}F NMR (565 MHz, CDCl_3) δ -111.15 – -112.32 (m).

HRMS (ESI): calculated for $[C_{18}H_{19}BrF_2NO]^+$: $m/z = 382.0613$, found: $m/z = 382.0612$.

2-(2-bromophenyl)-4,4-difluoro-N-(4-methoxyphenyl)-2-methylbutanamide (3f)



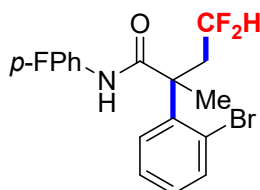
Prepared according to general method and isolated in 77% yield after chromatography as solid (61.3 mg).

1H NMR (600 MHz, $CDCl_3$) δ 7.69 (d, $J = 7.9$ Hz, 1H), 7.58 (d, $J = 7.8$ Hz, 1H), 7.46 (t, $J = 7.6$ Hz, 1H), 7.28 (t, $J = 7.6$ Hz, 1H), 7.24 (d, $J = 8.9$ Hz, 2H), 6.83 (d, $J = 8.9$ Hz, 2H), 6.61 (s, 1H), 5.73 – 5.42 (m, 1H), 3.77 (s, 3H), 3.08-3.03 (m, 1H), 2.73 (qd, $J = 15.5, 5.8$ Hz, 1H), 1.86 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 173.54, 156.83, 139.47, 135.52, 130.42, 130.07, 129.58, 128.33, 124.43, 122.83, 116.63 (t, $J = 238.6$ Hz), 114.10, 55.49, 49.70 – 49.63 (m), 39.58 (t, $J = 21.9$ Hz), 25.81.

^{19}F NMR (565 MHz, $CDCl_3$) δ -111.06 – -112.20 (m).

HRMS (ESI): calculated for $[C_{18}H_{19}BrF_2NO_2]^+$: $m/z = 398.0562$, found: $m/z = 398.0563$.

2-(2-bromophenyl)-4,4-difluoro-N-(4-fluorophenyl)-2-methylbutanamide (3g)



Prepared according to general method and isolated in 85% yield after chromatography as solid (65.6 mg).

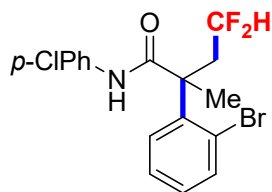
1H NMR (400 MHz, $CDCl_3$) δ 7.69 (dd, $J = 7.9, 1.3$ Hz, 1H), 7.58 (dd, $J = 7.9, 1.5$ Hz, 1H), 7.47 (td, $J = 7.7, 1.3$ Hz, 1H), 7.33 – 7.22 (m, 3H), 6.98 (t, $J = 8.7$ Hz, 2H), 6.72 (s, 1H), 5.55 (tdd, $J = 56.3, 5.9, 3.8$ Hz, 1H), 3.17 – 2.96 (m, 1H), 2.72 (qd, $J = 15.3, 5.9$ Hz, 1H), 1.86 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 173.64, 159.73 (d, $J = 244.1$

Hz), 139.21, 135.57, 133.38 (d, $J = 2.5$ Hz), 130.20, 129.61, 128.42, 124.38, 122.81 (d, $J = 8.0$ Hz), 116.52 (t, $J = 238.7$ Hz), 115.62 (d, $J = 22.6$ Hz), 49.81 – 49.74 (m), 39.53 (t, $J = 21.9$ Hz), 25.77.

^{19}F NMR (565 MHz, CDCl_3) δ -111.13 – -112.27 (m), -117.39 (s).

HRMS (ESI): calculated for $[\text{C}_{17}\text{H}_{16}\text{BrF}_3\text{NO}]^+$: $m/z = 386.0362$, found: $m/z = 386.0364$.

2-(2-bromophenyl)-N-(4-chlorophenyl)-4,4-difluoro-2-methylbutanamide (3h)



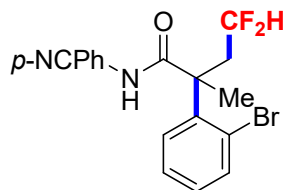
Prepared according to general method and isolated in 88% yield after chromatography as solid (70.6 mg).

^1H NMR (600 MHz, CDCl_3) δ 7.70 (dd, $J = 7.9, 1.2$ Hz, 1H), 7.59 (dd, $J = 7.9, 1.3$ Hz, 1H), 7.54 (d, $J = 8.6$ Hz, 2H), 7.51 – 7.47 (m, 3H), 7.31 (td, $J = 7.7, 1.5$ Hz, 1H), 6.84 (s, 1H), 5.54 (tdd, $J = 56.3, 5.9, 3.8$ Hz, 1H), 3.12 – 3.02 (m, 1H), 2.73 (qd, $J = 15.4, 6.0$ Hz, 1H), 1.88 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 173.53, 139.11, 136.09, 135.60, 130.24, 129.81, 129.59, 128.98, 128.43, 124.40, 121.85, 116.46 (t, $J = 238.8$ Hz), 49.97 – 49.90 (m), 39.49 (t, $J = 22.2$ Hz), 25.75.

^{19}F NMR (565 MHz, CDCl_3) δ -111.21 – -112.37 (m).

HRMS (ESI): calculated for $[\text{C}_{17}\text{H}_{16}\text{BrClF}_2\text{NO}]^+$: $m/z = 402.0066$, found: $m/z = 402.0062$.

2-(2-bromophenyl)-N-(4-cyanophenyl)-4,4-difluoro-2-methylbutanamide (3i)



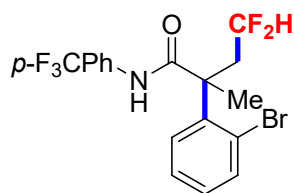
Prepared according to general method and isolated in 76% yield after chromatography as solid (59.7 mg).

^1H NMR (400 MHz, CDCl_3) δ 7.69 (dd, $J = 7.9, 1.2$ Hz, 1H), 7.60 – 7.53 (m, 3H), 7.52 – 7.45 (m, 3H), 7.30 (td, $J = 7.7, 1.6$ Hz, 1H), 6.93 (s, 1H), 5.53 (tdd, $J = 56.1, 6.0, 3.7$ Hz, 1H), 3.15 – 2.96 (m, 1H), 2.71 (qd, $J = 15.4, 6.0$ Hz, 1H), 1.86 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 173.78, 141.72, 138.62, 135.64, 133.18, 130.46, 129.65, 128.57, 124.30, 120.10, 118.69, 116.29 (t, $J = 238.8$ Hz), 107.50, 50.25 – 50.18 (m), 39.46 (t, $J = 22.1$ Hz), 25.60.

^{19}F NMR (565 MHz, CDCl_3) δ -111.27 – -112.41 (m).

HRMS (ESI): calculated for $[\text{C}_{18}\text{H}_{16}\text{BrF}_2\text{N}_2\text{O}]^+$: $m/z = 393.0409$, found: $m/z = 393.0406$.

2-(2-bromophenyl)-4,4-difluoro-2-methyl-N-(4-(trifluoromethyl)phenyl)butanamide (3j)



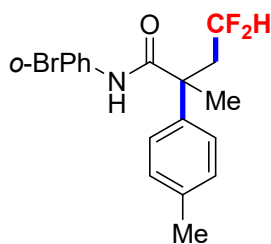
Prepared according to general method and isolated in 74% yield after chromatography as solid (64.6 mg).

^1H NMR (600 MHz, CDCl_3) δ 7.70 (dd, $J = 7.9, 1.2$ Hz, 1H), 7.59 (dd, $J = 7.9, 1.3$ Hz, 1H), 7.54 (d, $J = 8.6$ Hz, 2H), 7.49 (m, 3H), 7.31 (td, $J = 7.7, 1.5$ Hz, 1H), 6.84 (s, 1H), 5.54 (tdd, $J = 56.3, 5.9, 3.8$ Hz, 1H), 3.07 (m, 1H), 2.73 (qd, $J = 15.4, 6.0$ Hz, 1H), 1.88 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 173.69, 140.67, 138.86, 135.64, 130.37, 129.61, 128.52, 126.42 (q, $J = 32.6$ Hz), 126.22 (q, $J = 3.8$ Hz), 123.99 (q, $J = 271.6$ Hz), 124.37, 119.94, 116.38 (t, $J = 238.8$ Hz), 50.15 – 50.08 (m), 39.46 (t, $J = 21.7$ Hz), 25.69.

^{19}F NMR (565 MHz, CDCl_3) δ -62.18 (s), -111.26 – -112.42 (m).

HRMS (ESI): calculated for $[\text{C}_{18}\text{H}_{16}\text{BrF}_5\text{NO}]^+$: $m/z = 436.0330$, found: $m/z = 436.0325$.

N-(2-bromophenyl)-4,4-difluoro-2-methyl-2-(p-tolyl)butanamide (3k)



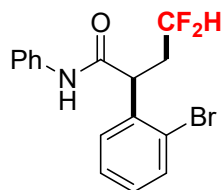
Prepared according to general method and isolated in 75% yield after chromatography as solid (57.4 mg).

^1H NMR (600 MHz, CDCl_3) δ 8.26 (dd, $J = 8.2, 1.0$ Hz, 1H), 7.47 – 7.41 (m, 2H), 7.34 – 7.23 (m, 5H), 6.93 (td, $J = 7.9, 1.3$ Hz, 1H), 5.69 (tdd, $J = 56.3, 5.4, 3.8$ Hz, 1H), 2.73 (qd, $J = 15.2, 5.6$ Hz, 1H), 2.63 – 2.47 (m, 1H), 2.37 (s, 3H), 1.81 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 174.39, 138.06, 135.48, 132.18, 130.13, 128.31, 126.70, 125.23, 121.57, 116.63 (t, $J = 238.6$ Hz), 113.60, 48.83- 48.76 (m), 43.05 (t, $J = 21.7$ Hz), 23.46, 21.03.

^{19}F NMR (377 MHz, CDCl_3) δ -110.01, – -110.05 (m).

HRMS (ESI): calculated for $[\text{C}_{18}\text{H}_{19}\text{BrF}_2\text{NO}]^+$: $m/z = 382.0613$, found: $m/z = 382.0612$.

2-(2-bromophenyl)-4,4-difluoro-N-phenylbutanamide (3I)



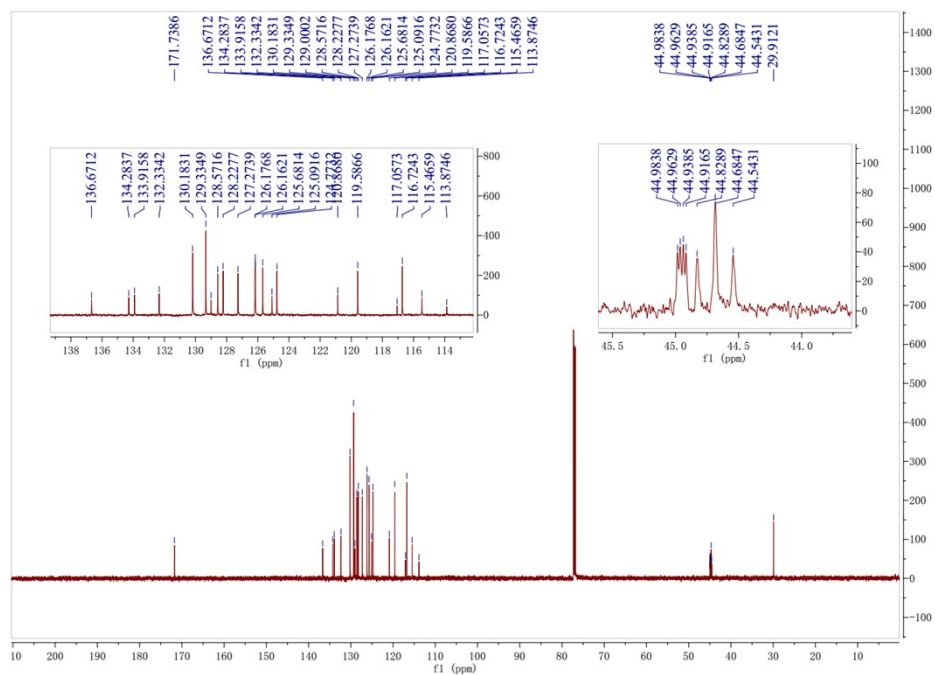
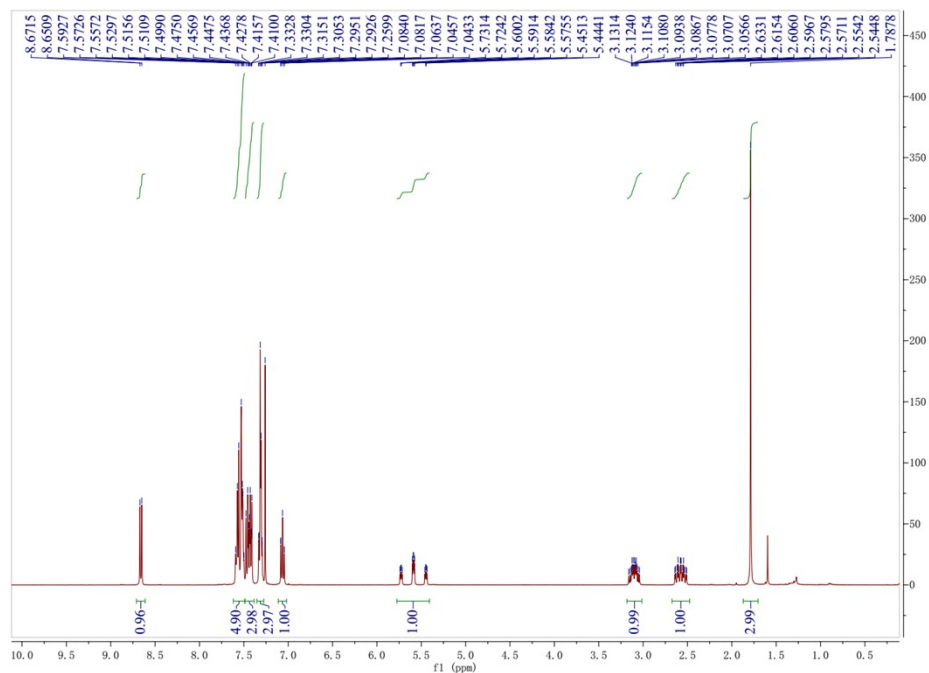
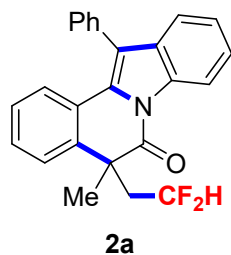
Prepared according to general method and isolated in 84% yield after chromatography as liquid (59.5 mg).

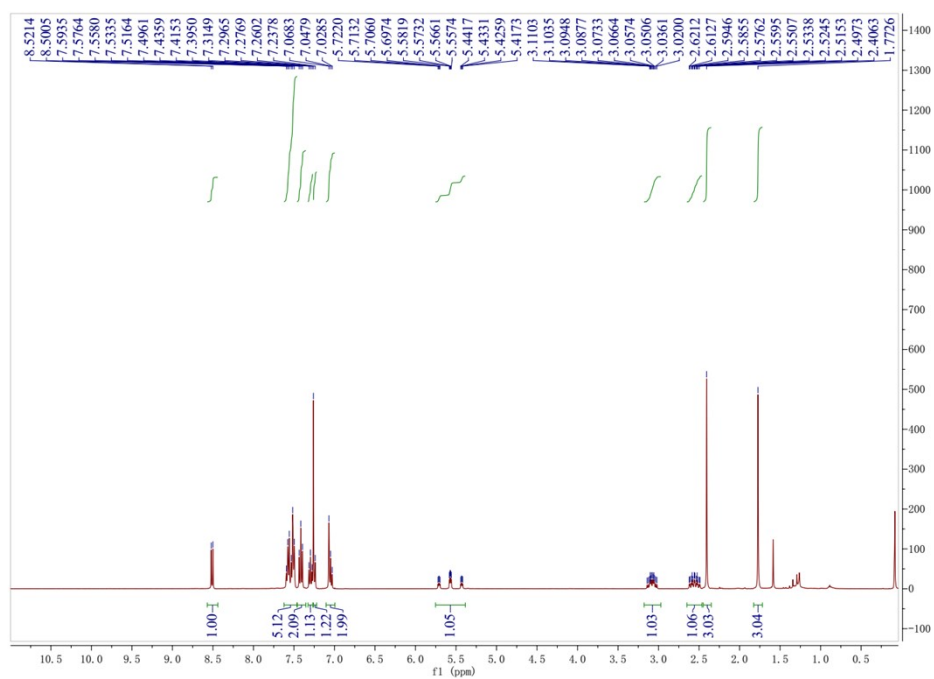
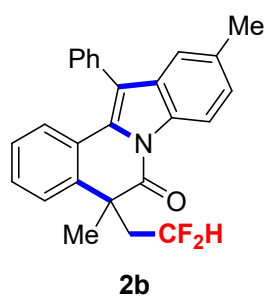
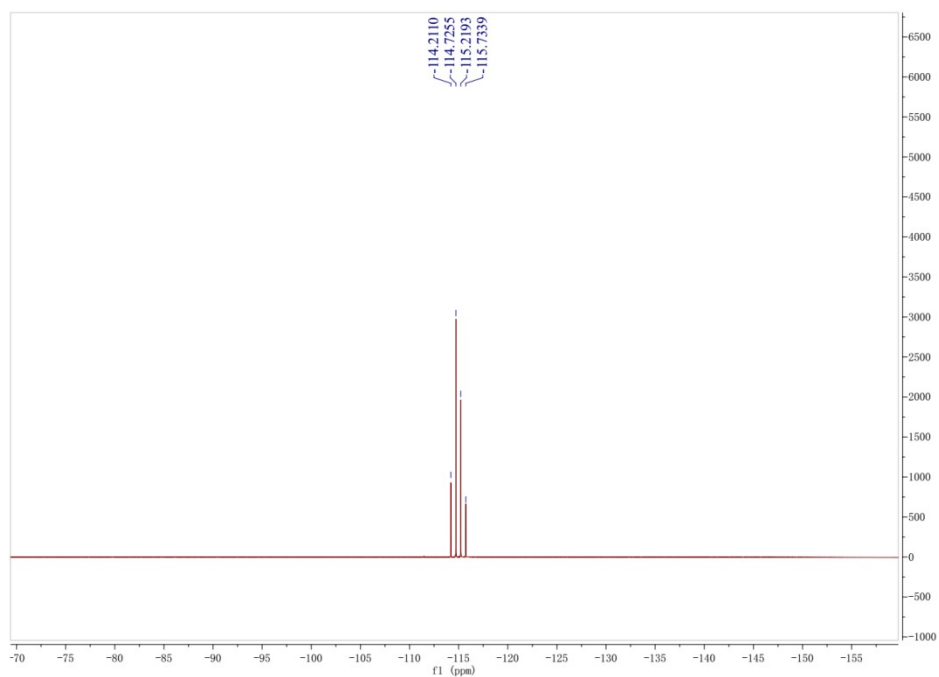
^1H NMR (400 MHz, CDCl_3) δ 7.63 (dd, $J = 8.0, 1.1$ Hz, 1H), 7.49 – 7.39 (m, 3H), 7.39 – 7.26 (m, 4H), 7.19 (td, $J = 7.9, 1.6$ Hz, 1H), 7.10 (t, $J = 7.4$ Hz, 1H), 6.10 – 5.73 (m, 1H), 4.37 (dd, $J = 8.7, 5.8$ Hz, 1H), 3.00 – 2.78 (m, 1H), 2.37 – 2.18 (m, 1H); ^{13}C NMR (101 MHz, CDCl_3) δ 168.93, 137.42, 133.47, 129.65, 129.05, 128.87, 128.70, 124.73, 124.16, 119.98, 115.88 (t, $J = 239.5$ Hz), 46.28 – 45.37 (m), 36.58 (t, $J = 22.2$ Hz).

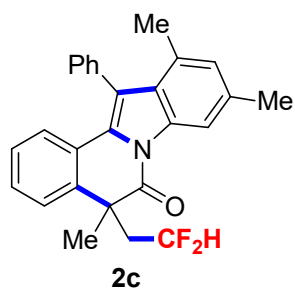
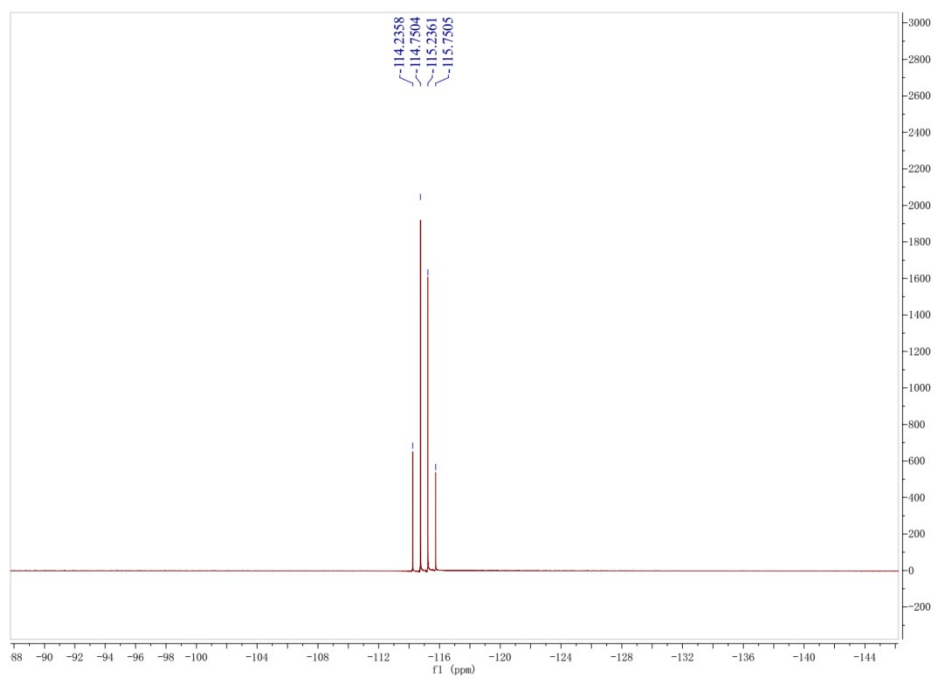
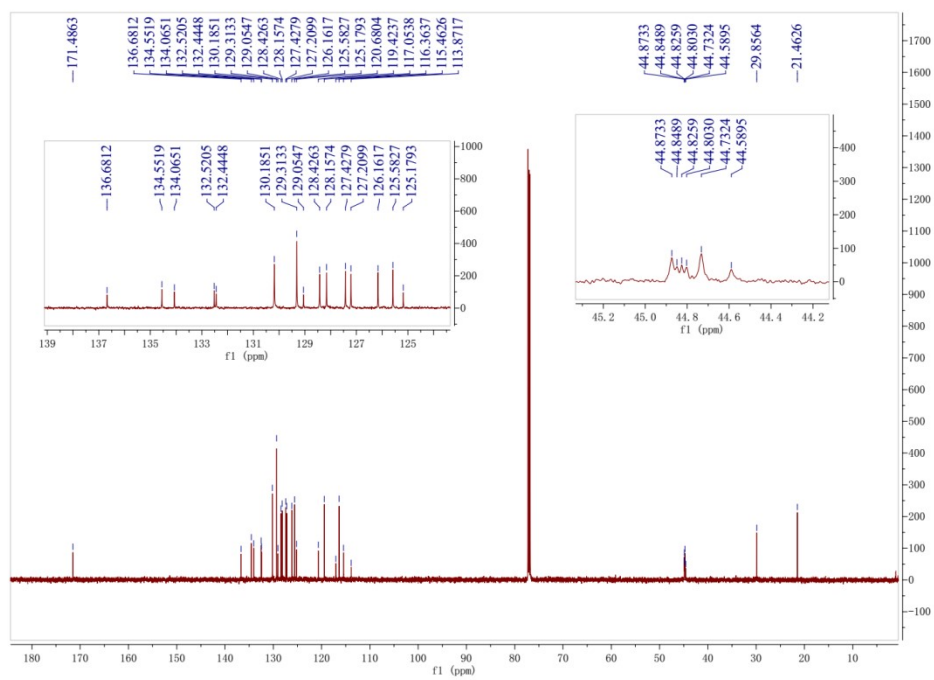
^{19}F NMR (377 MHz, CDCl_3) δ -114.68, – -118.34.

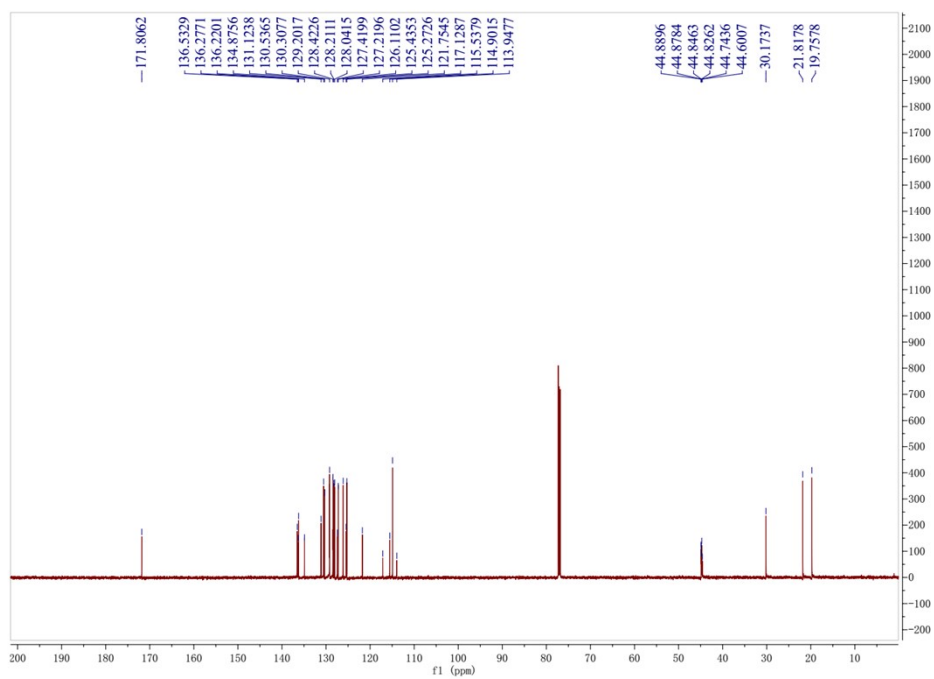
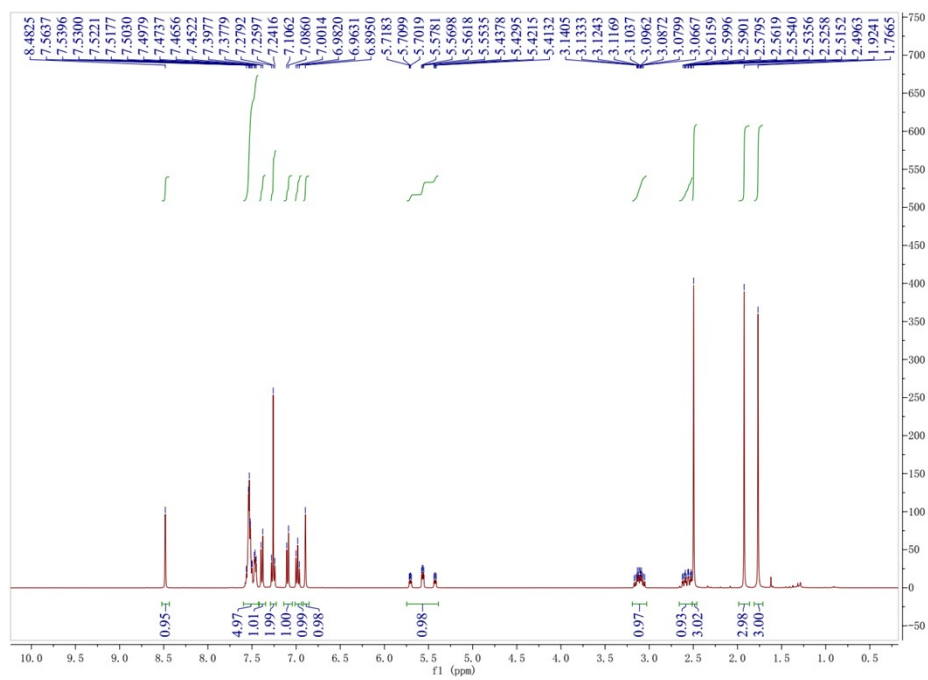
HRMS (ESI): calculated for $[\text{C}_{16}\text{H}_{14}\text{B}_r\text{F}_2\text{NNaO}]^+$: $m/z = 376.0119$, found: $m/z = 376.0107$.

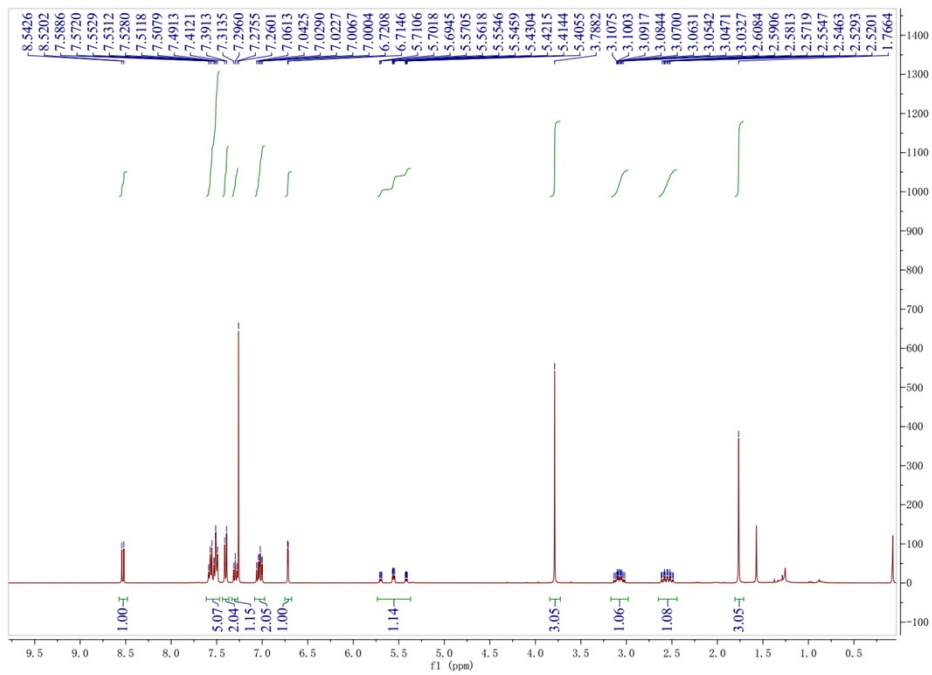
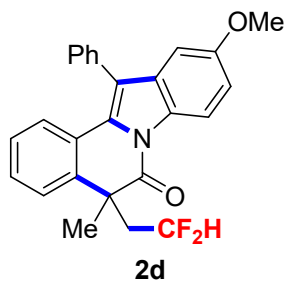
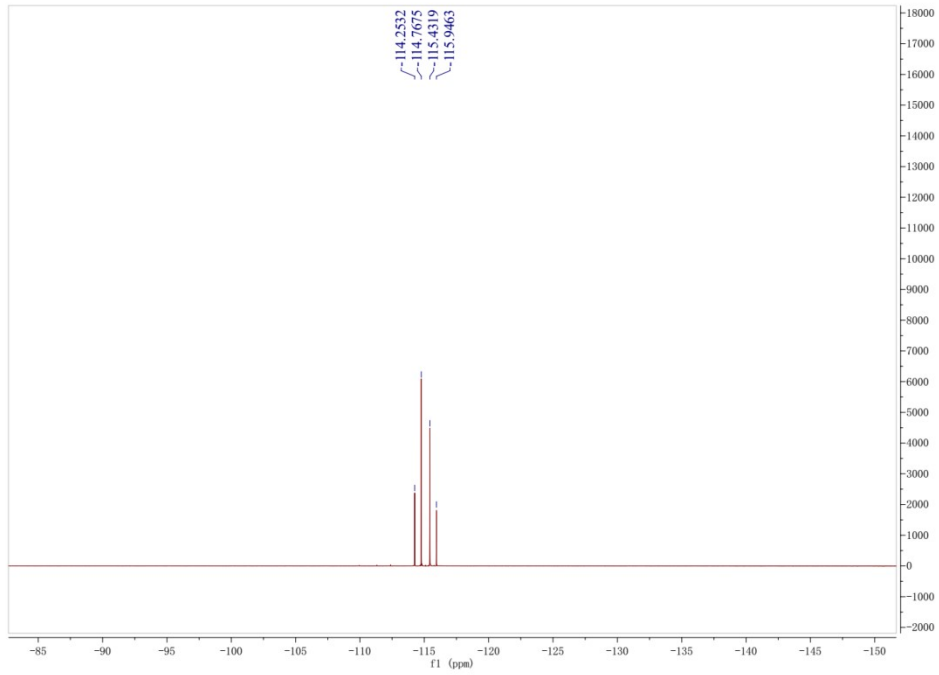
Part 4. ^1H NMR, ^{13}C NMR and ^{19}F NMR Spectra

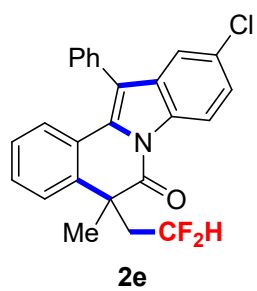
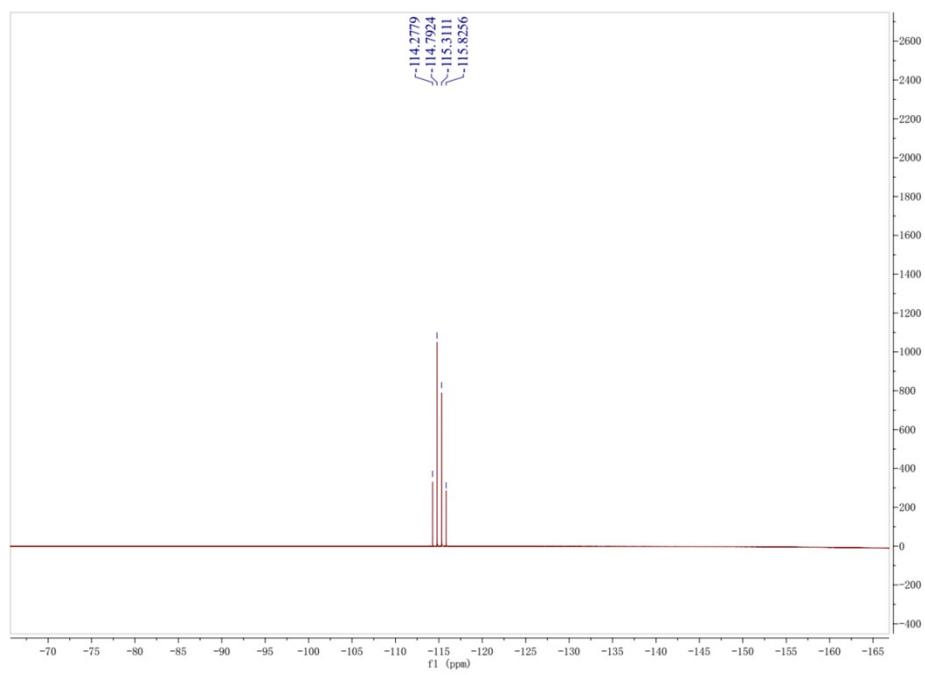
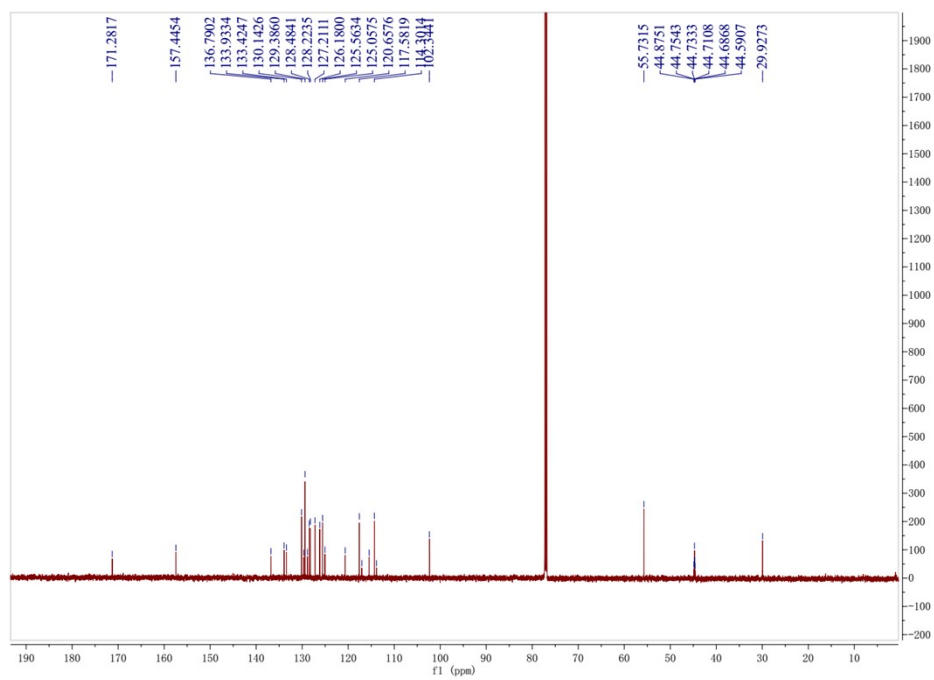


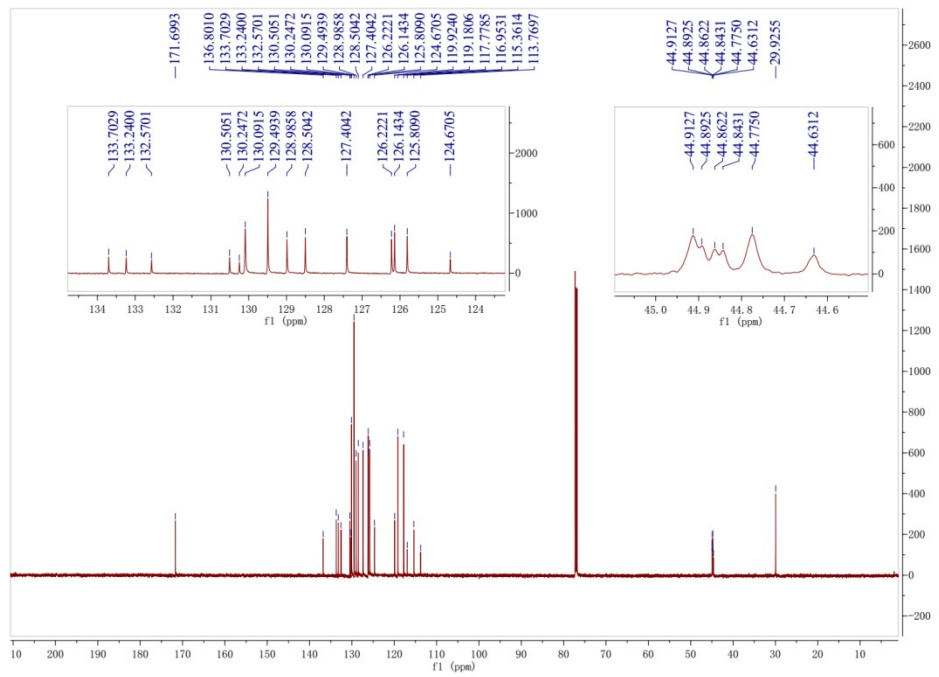
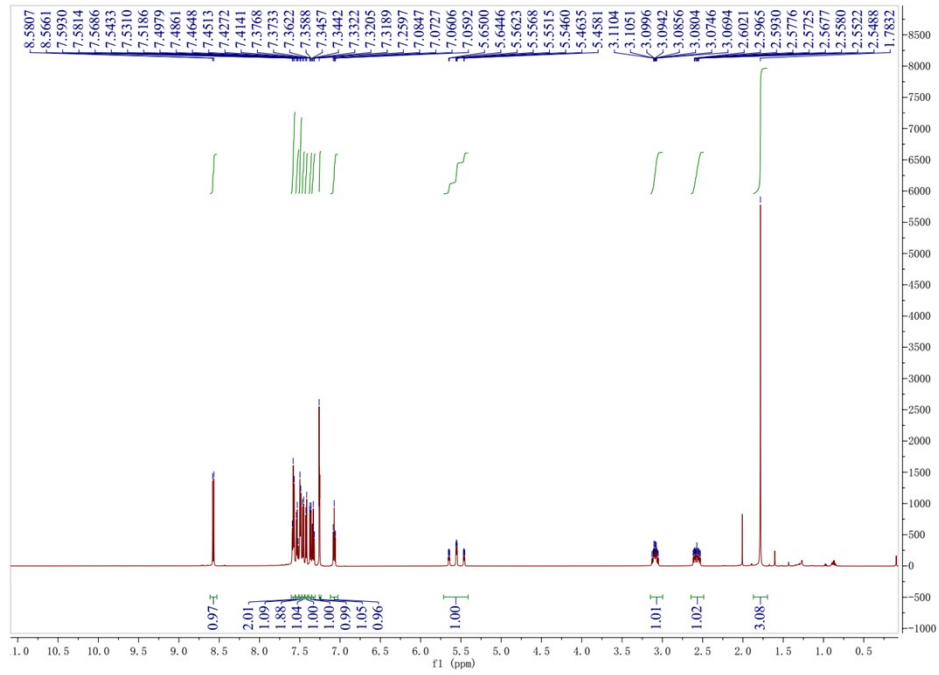


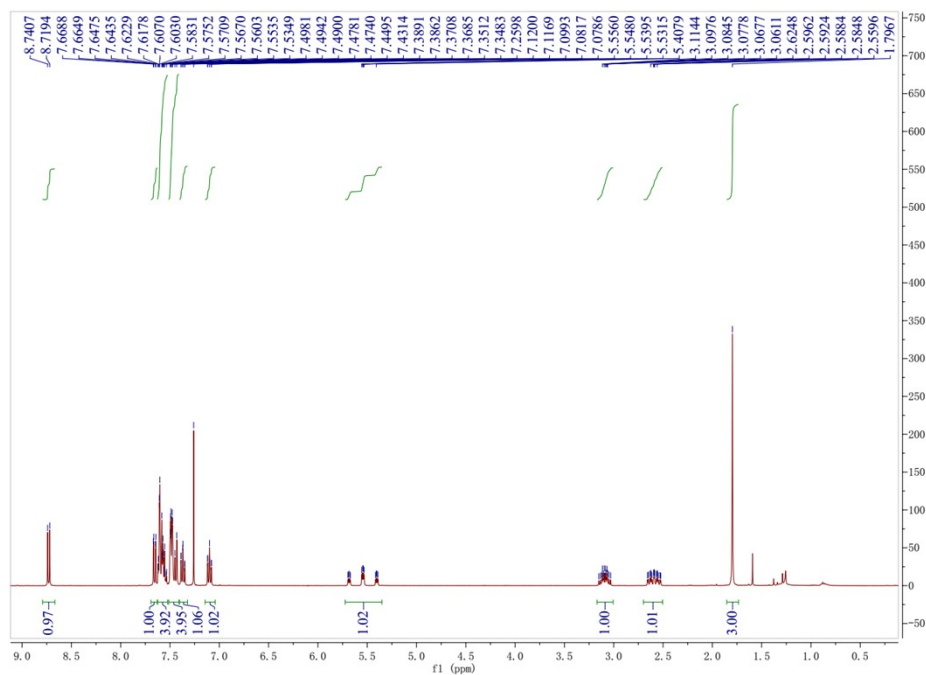
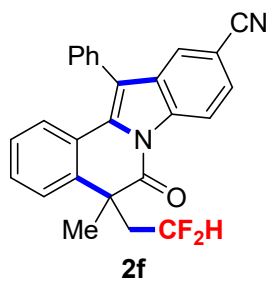
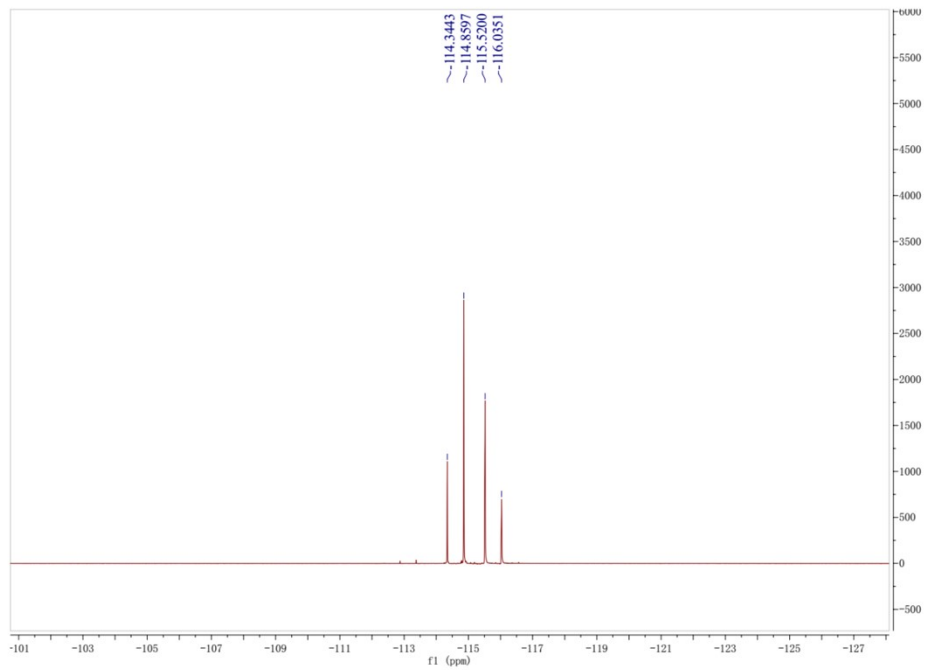


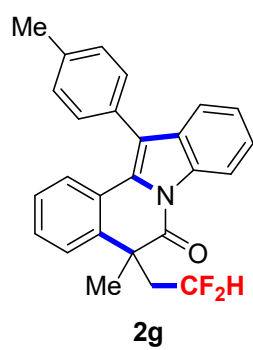
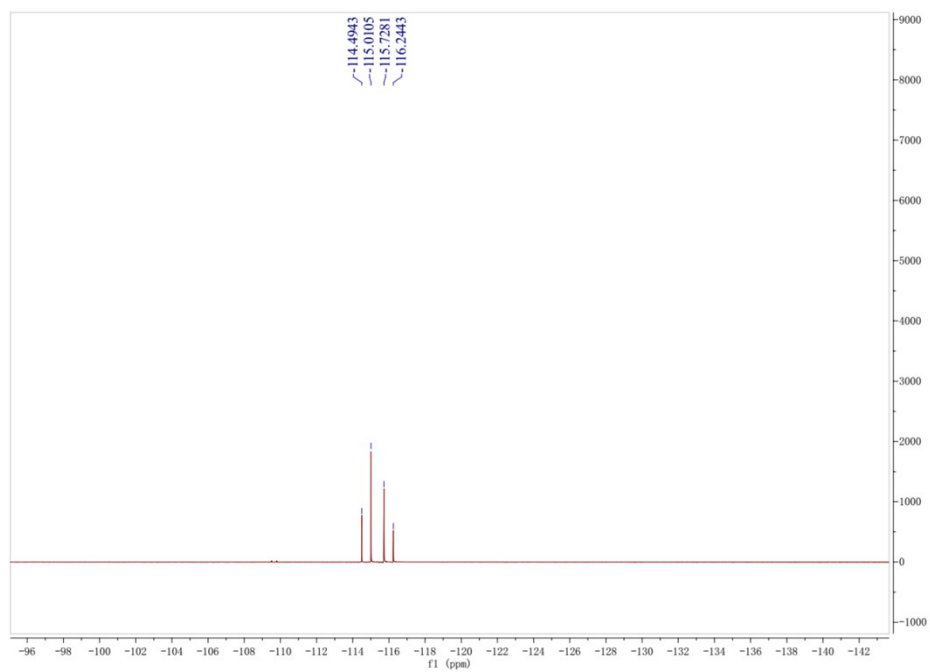
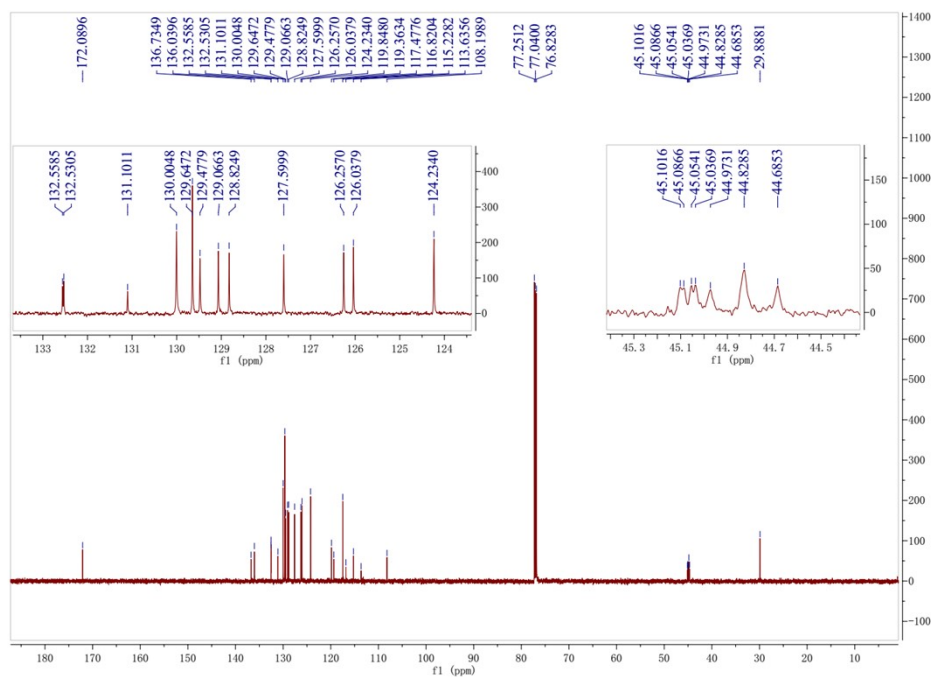


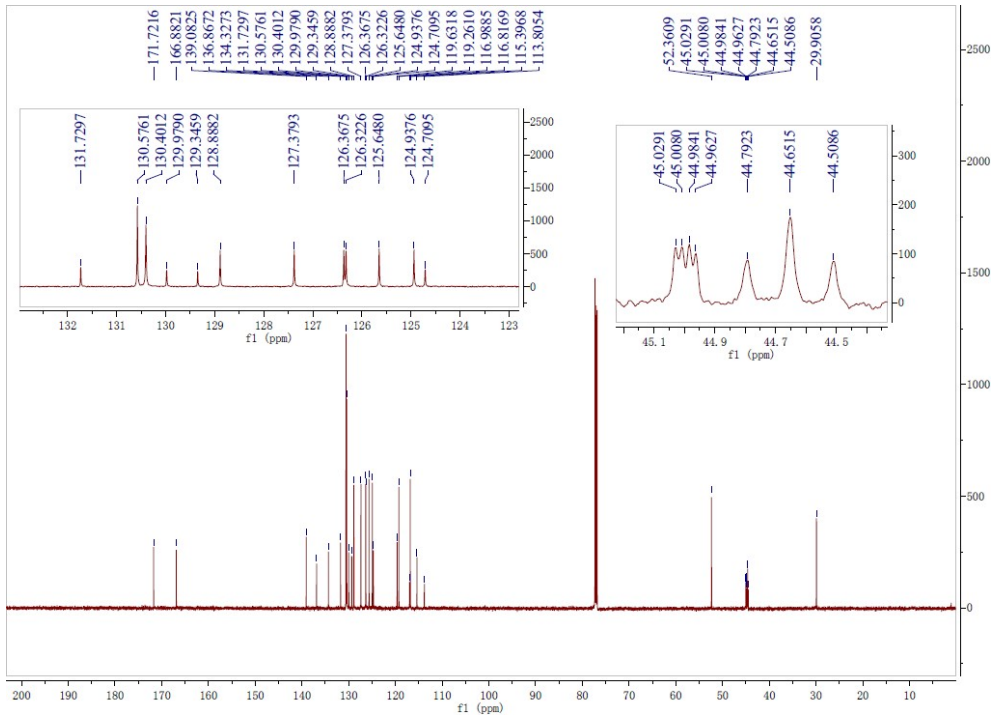
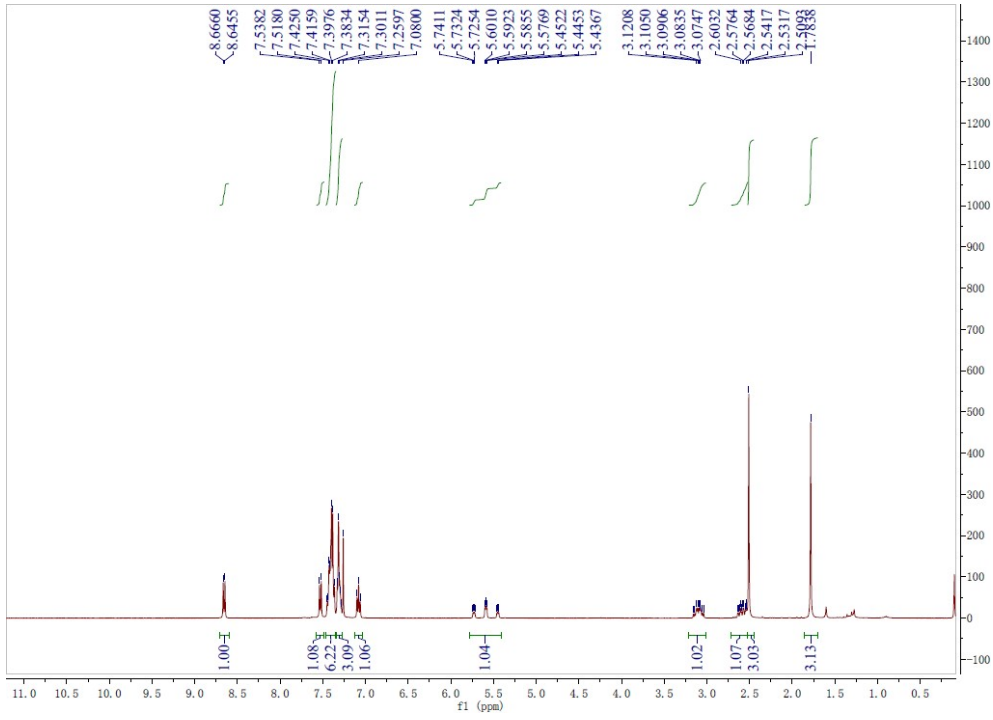


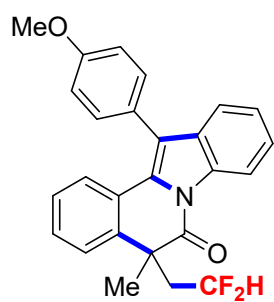
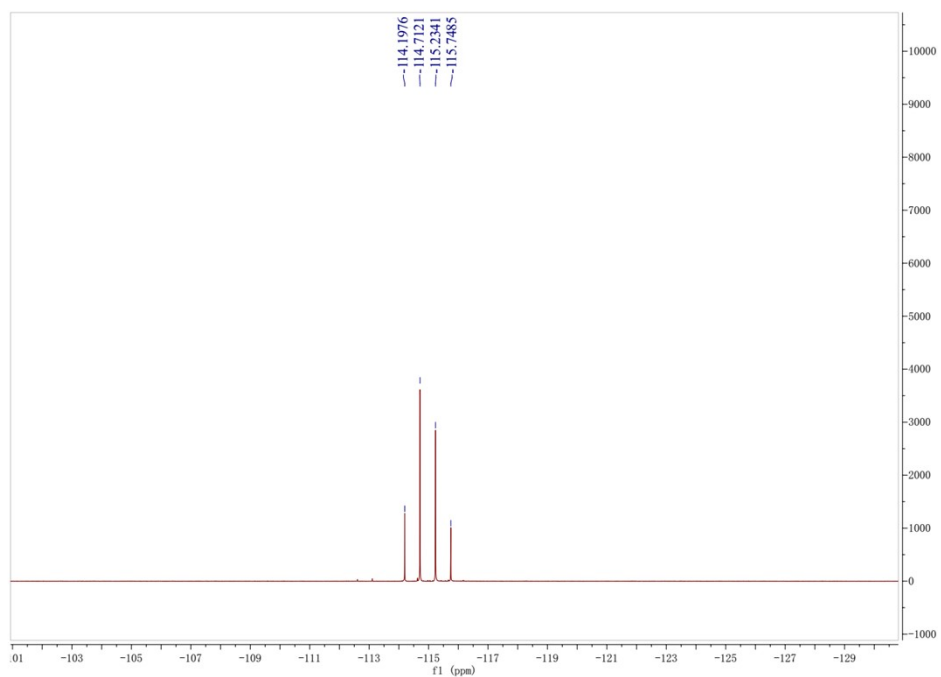




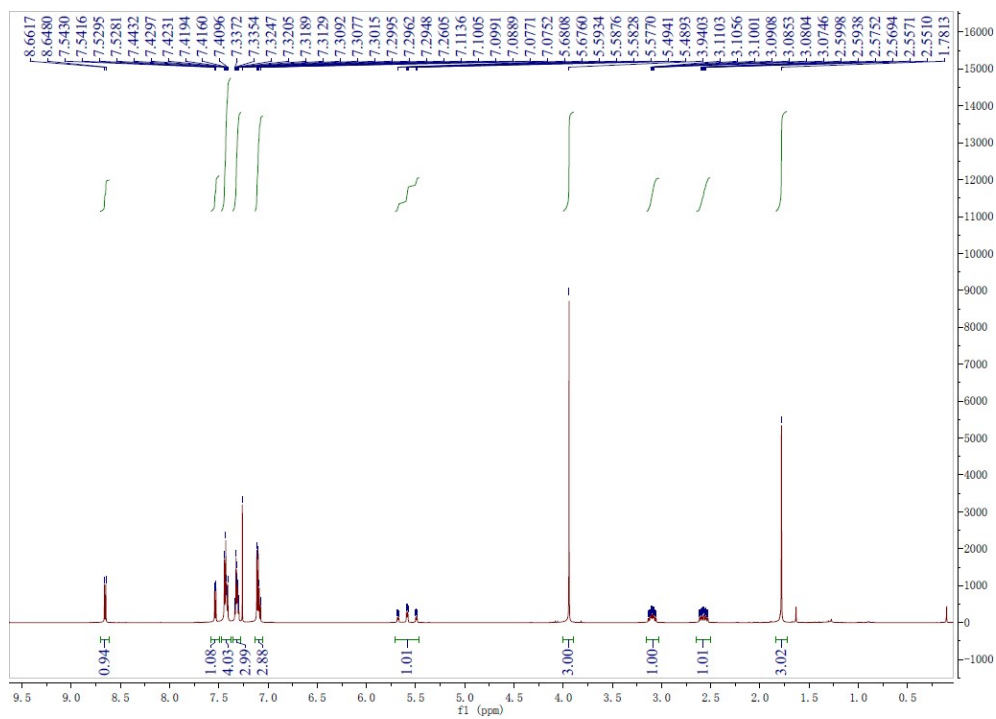


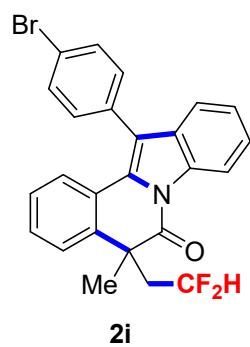
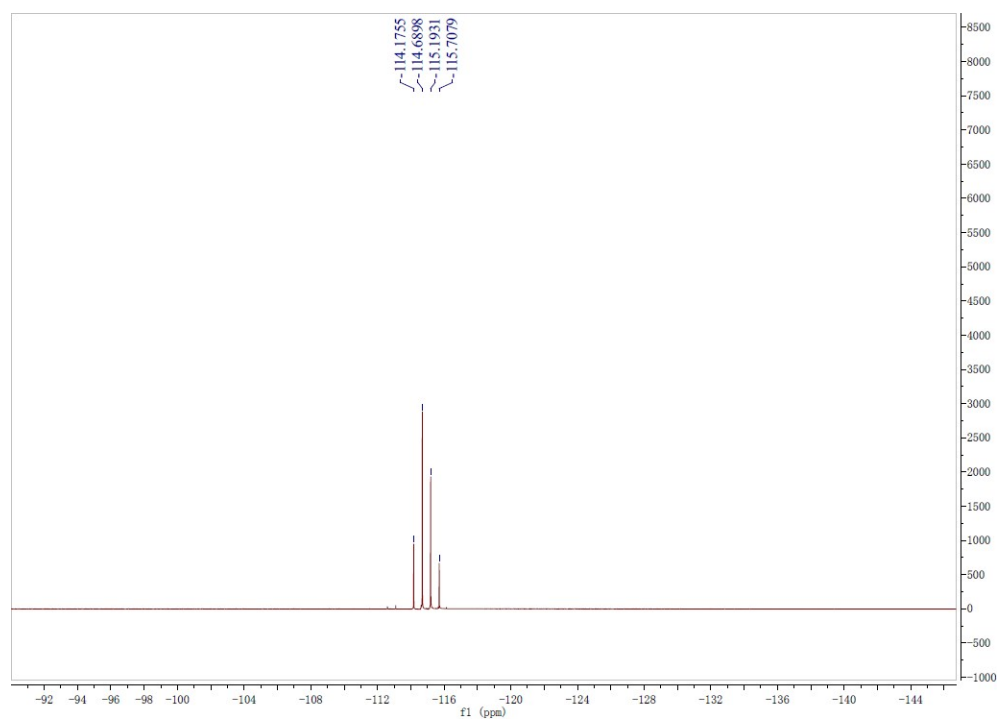
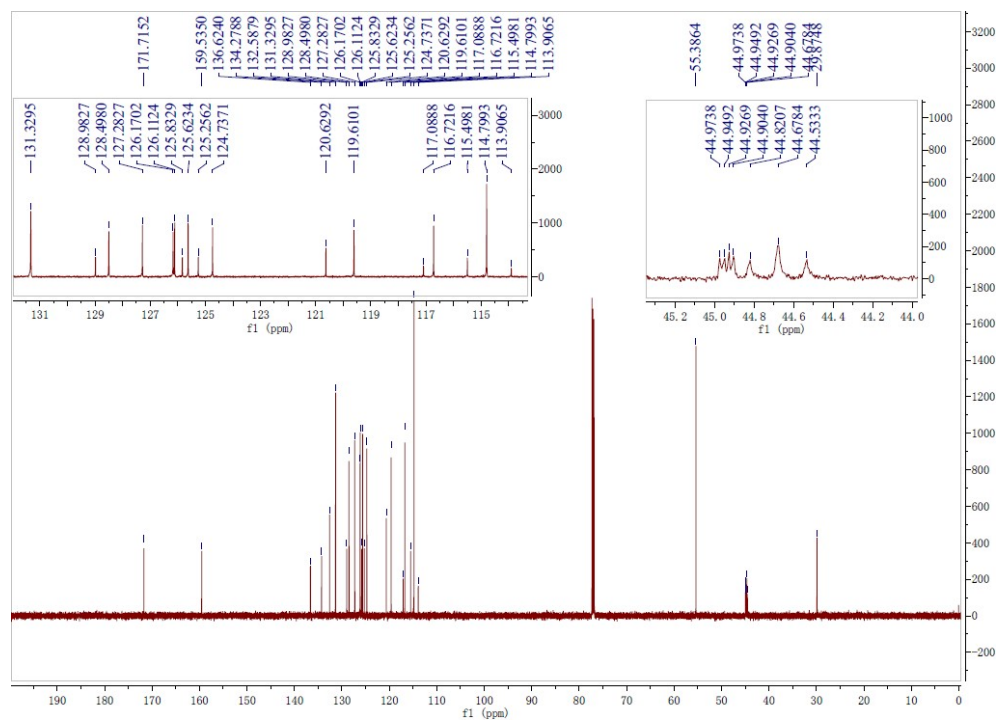


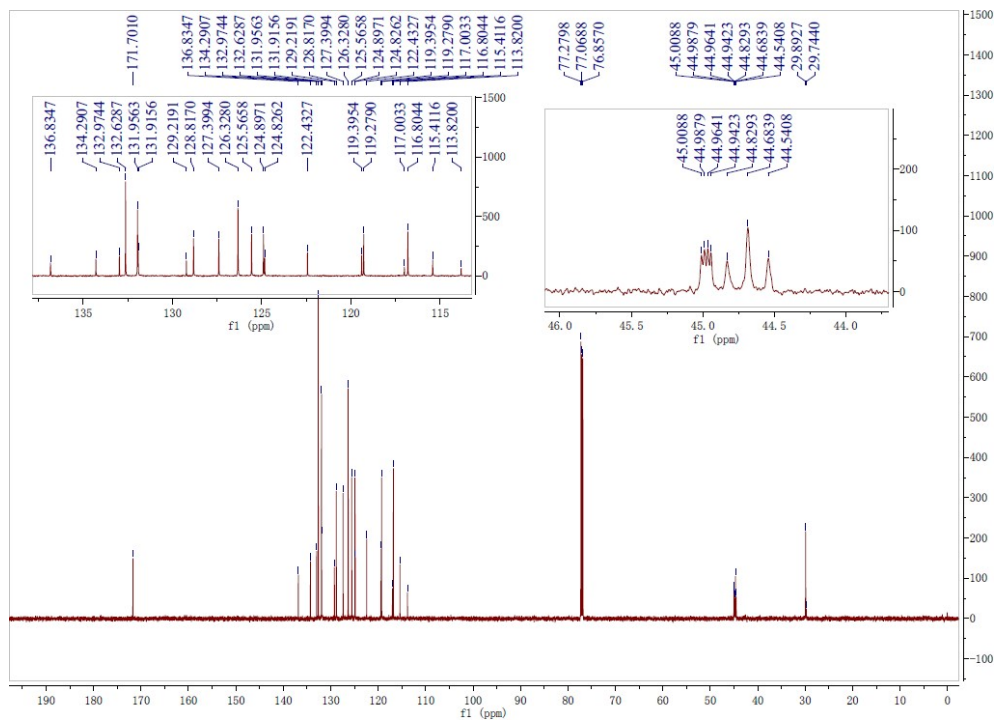
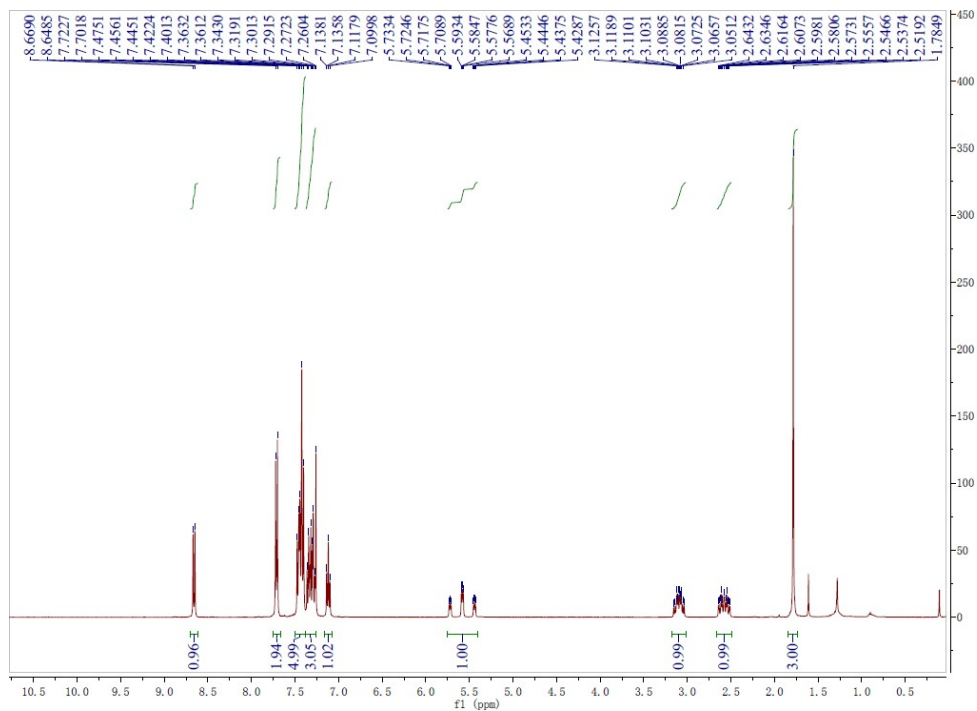


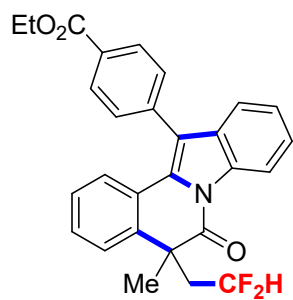
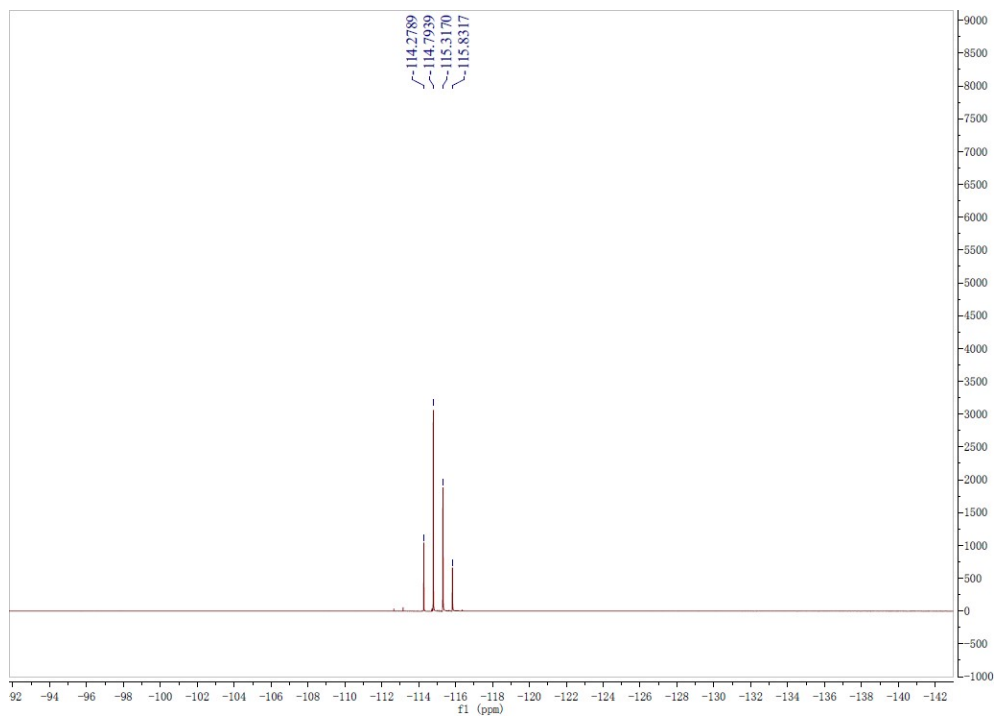


2h

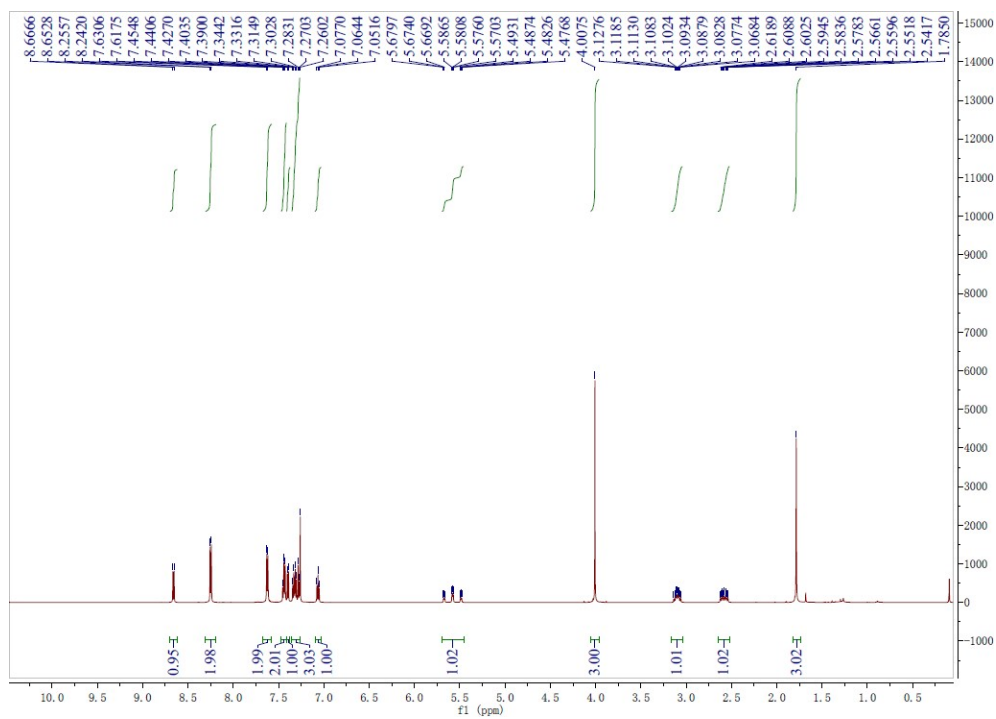


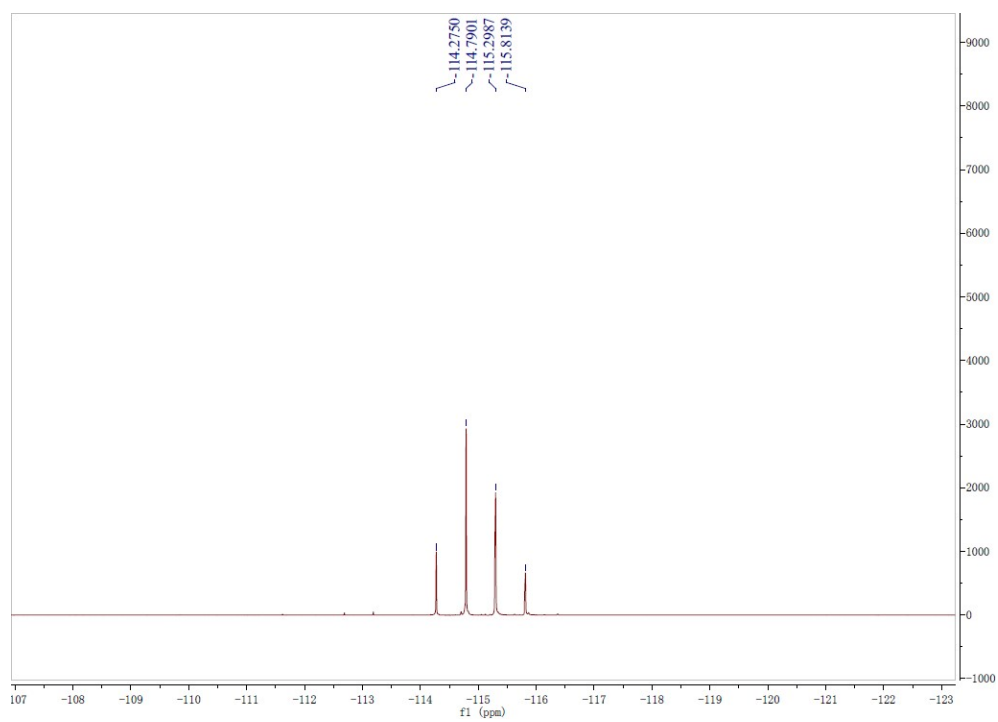
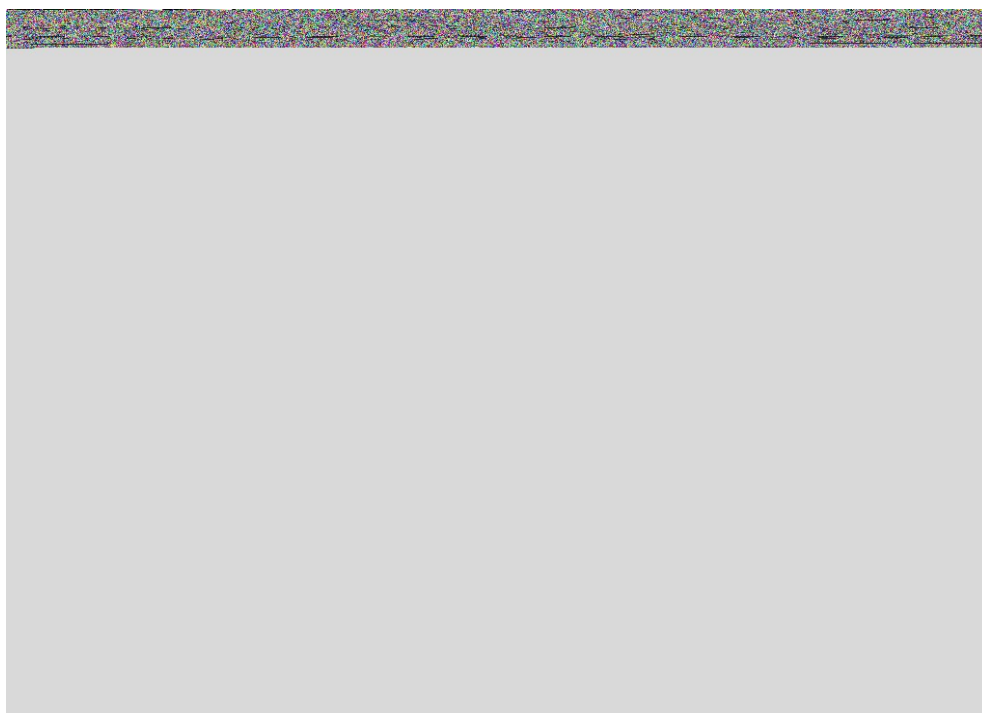


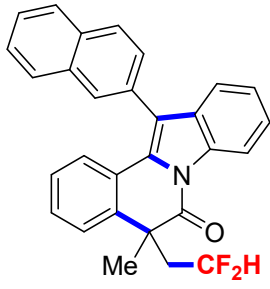




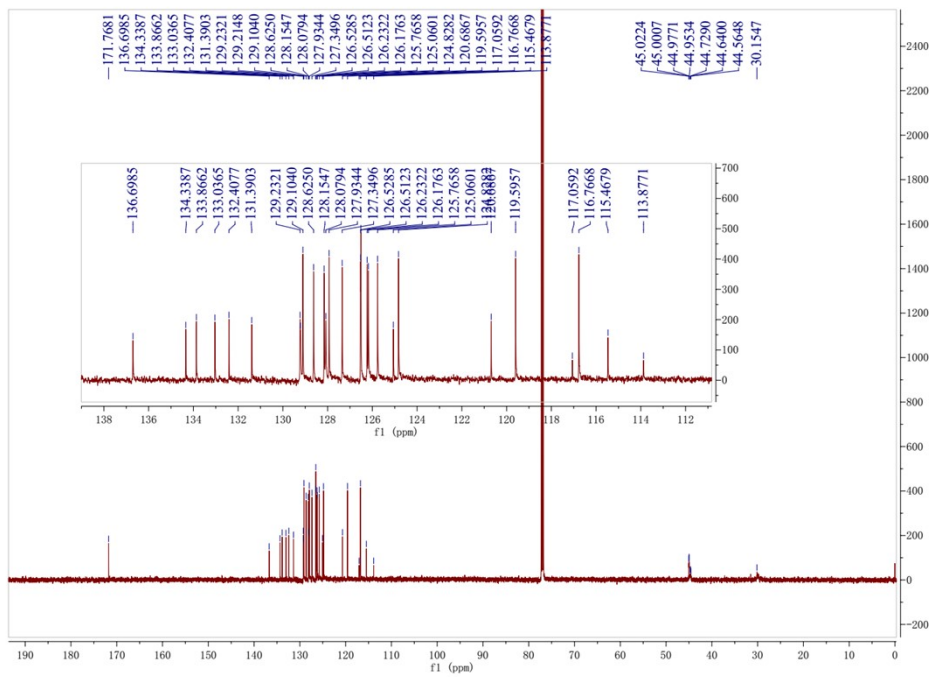
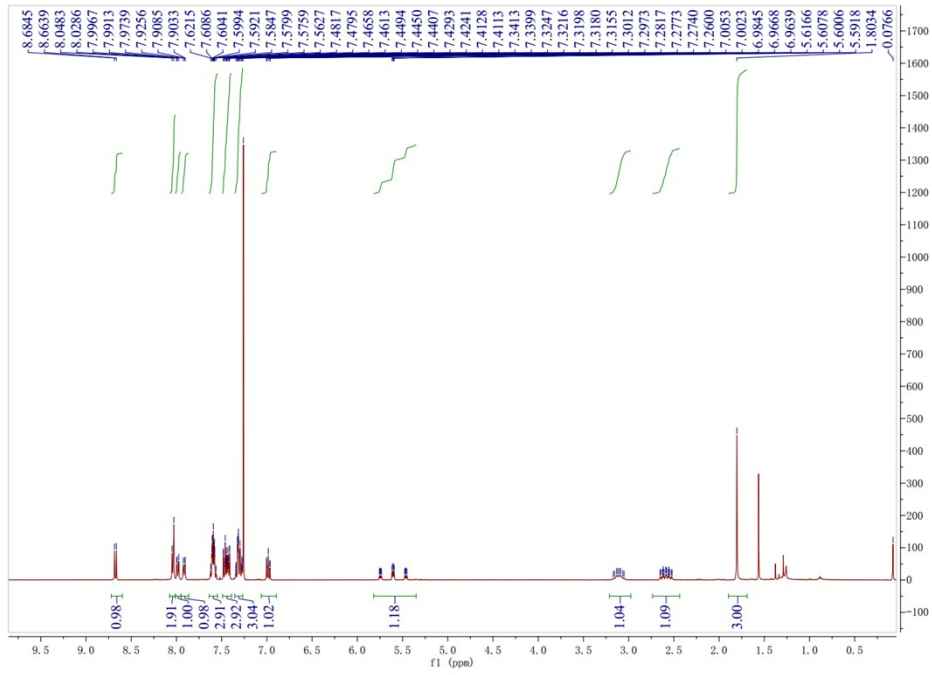
2j

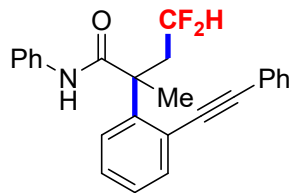
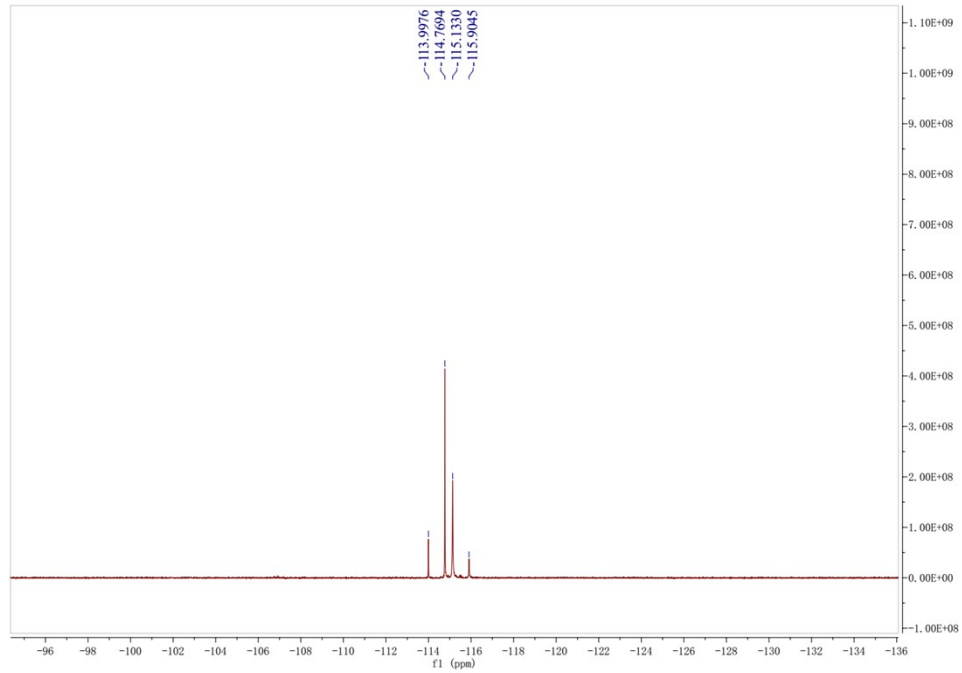




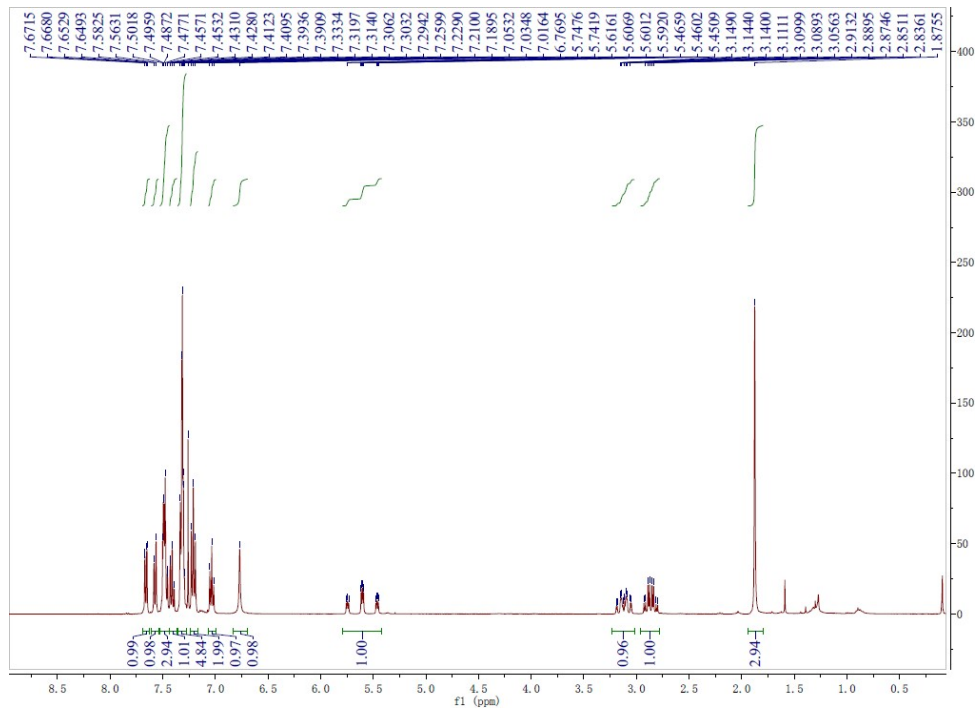


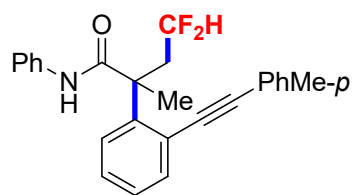
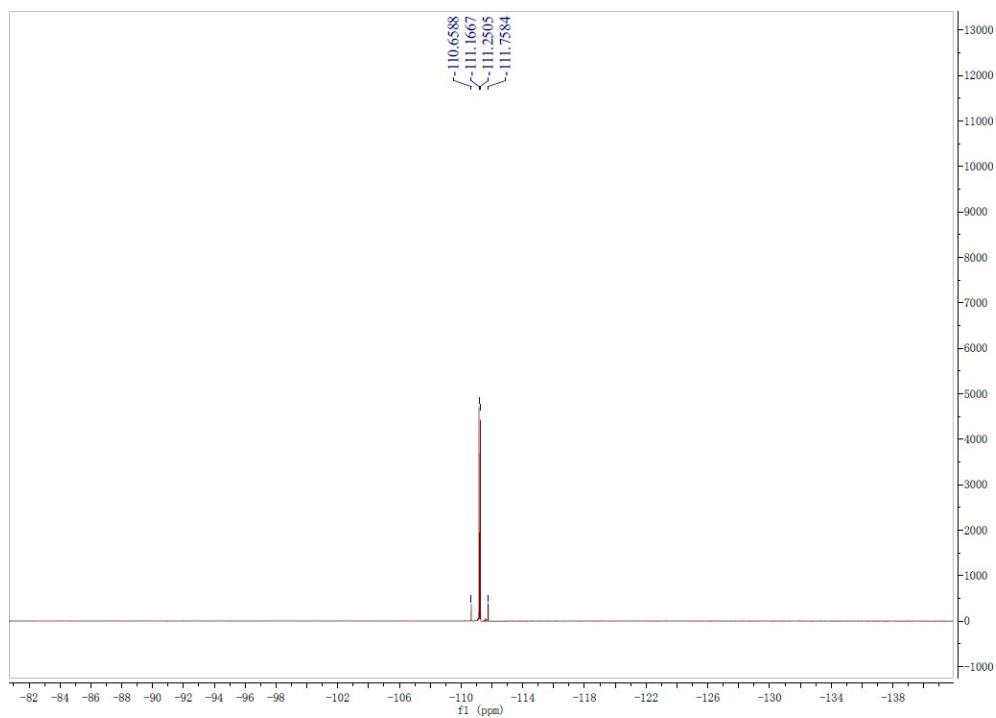
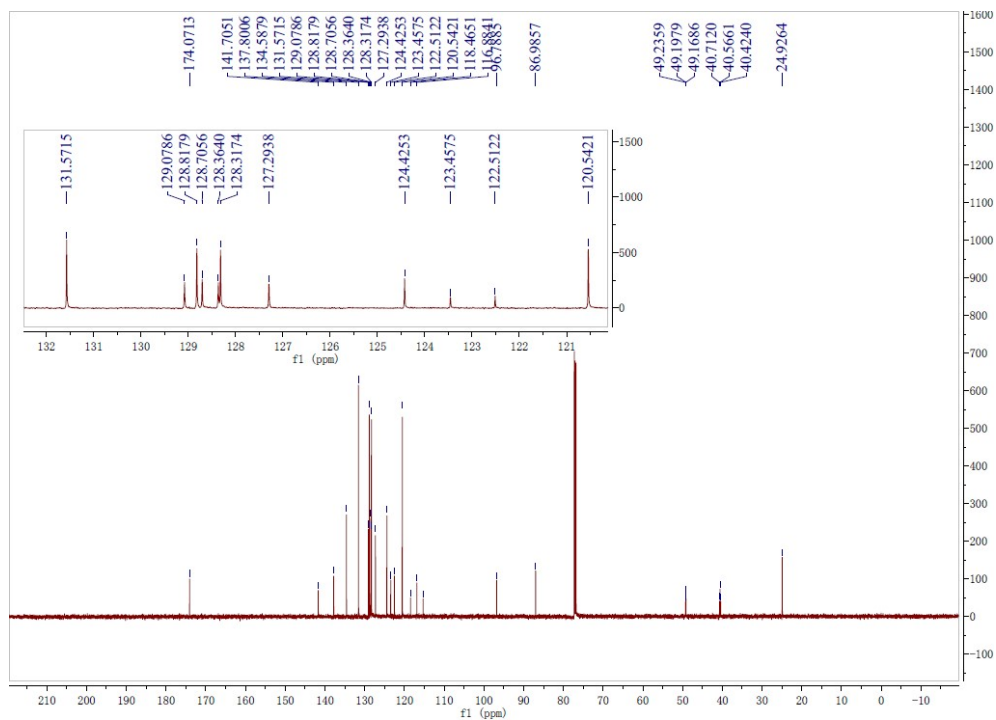
2k



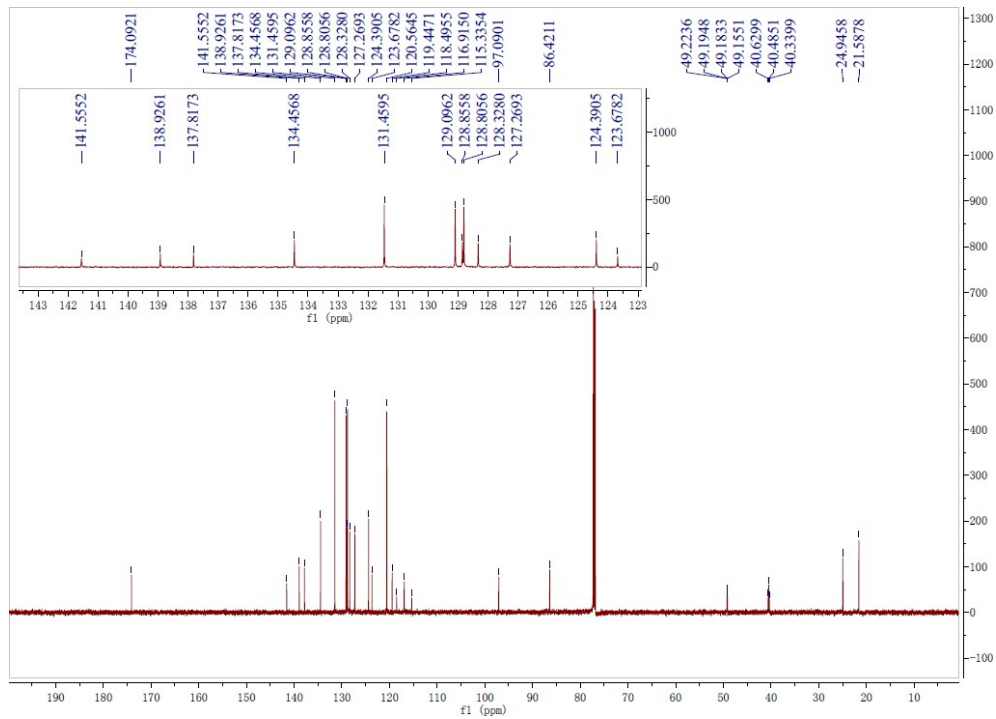
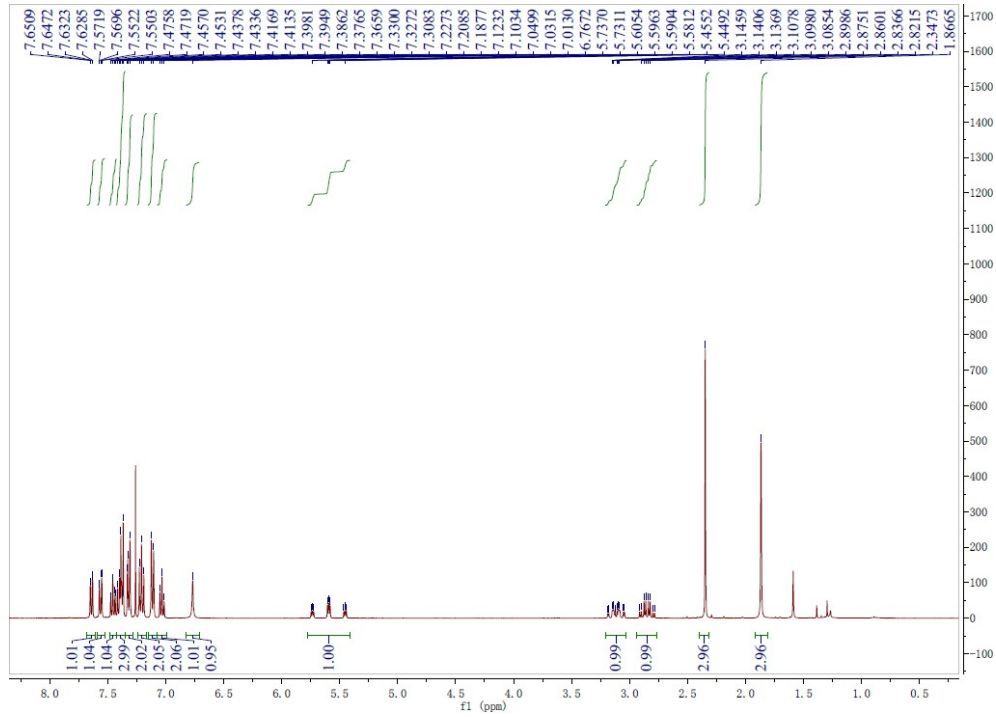


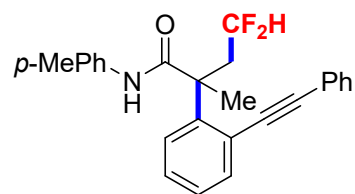
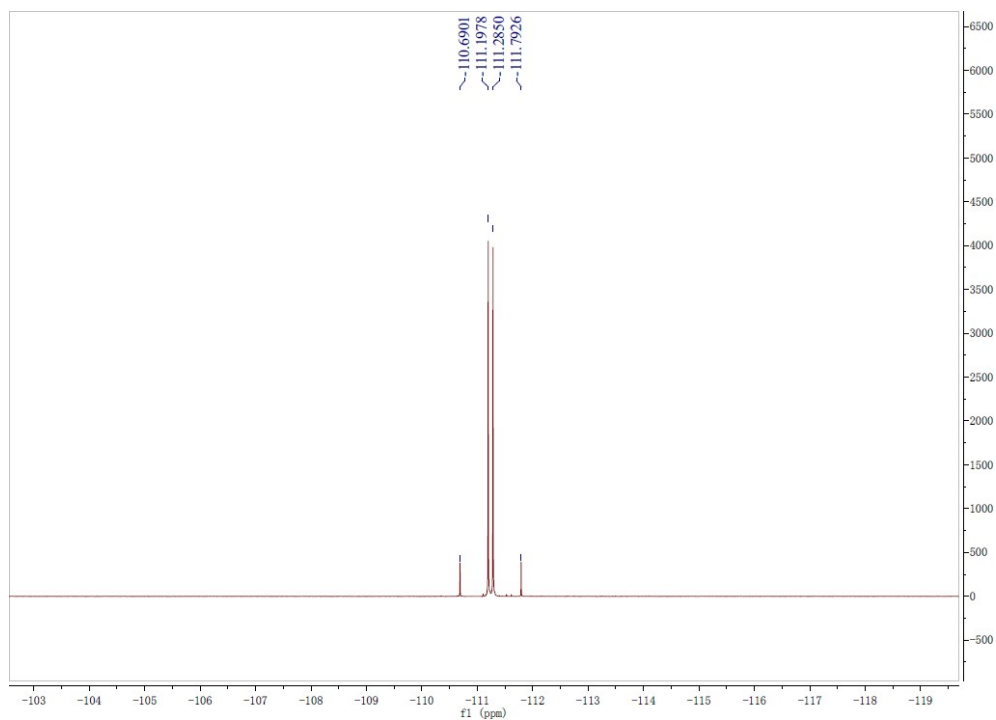
3a



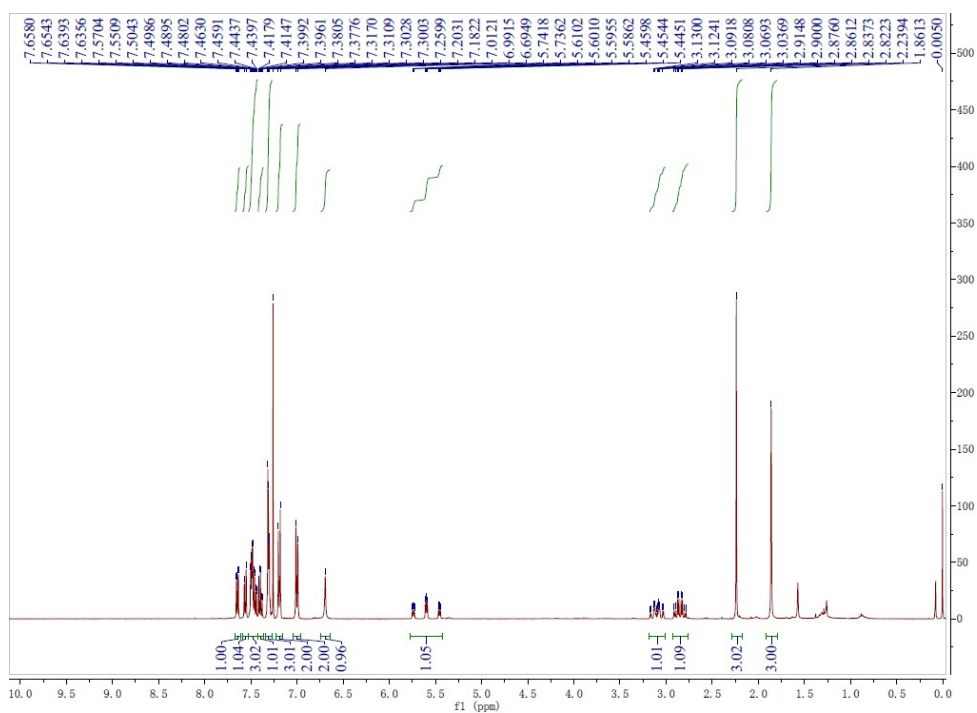


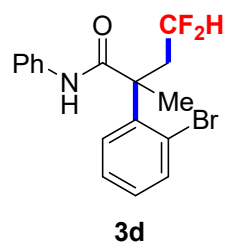
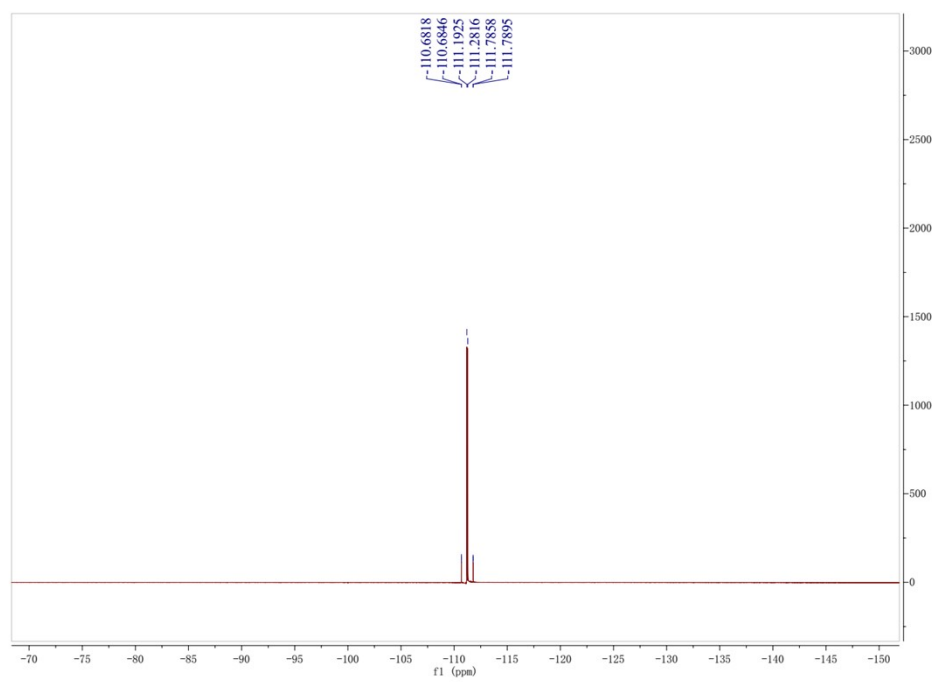
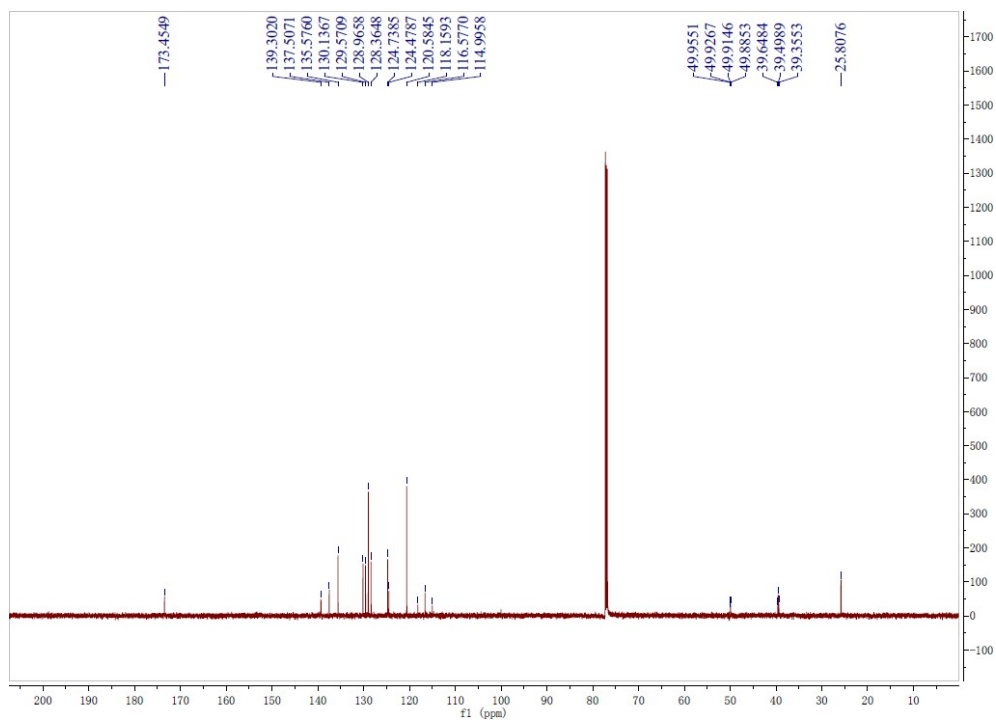
3b

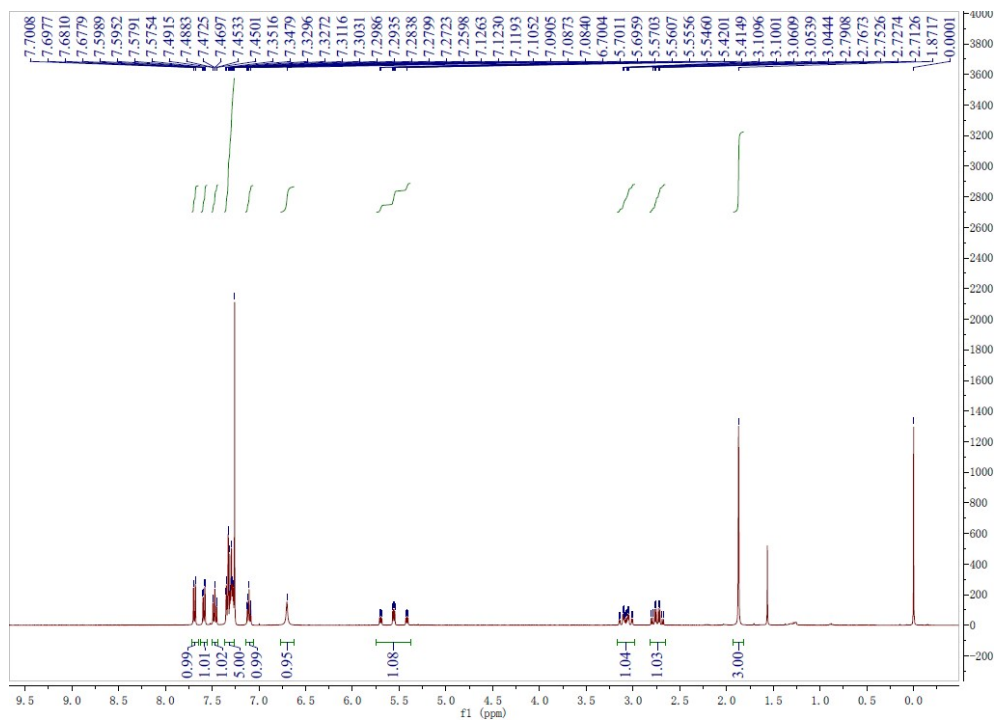


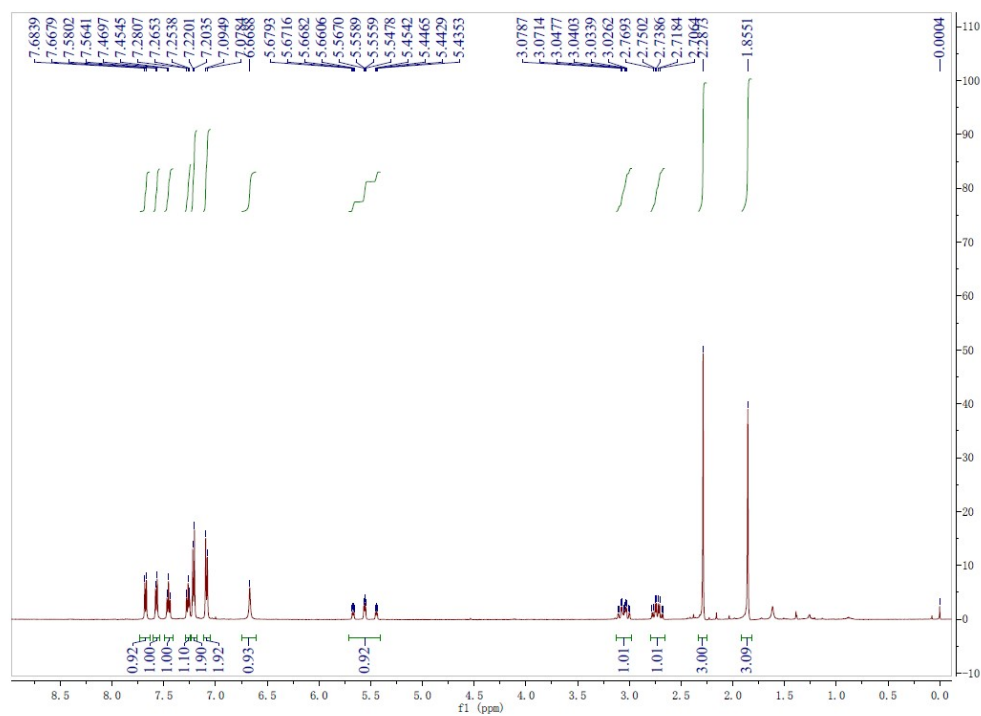
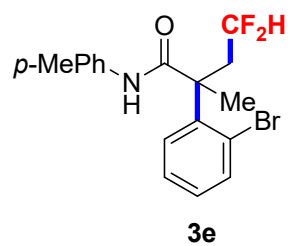
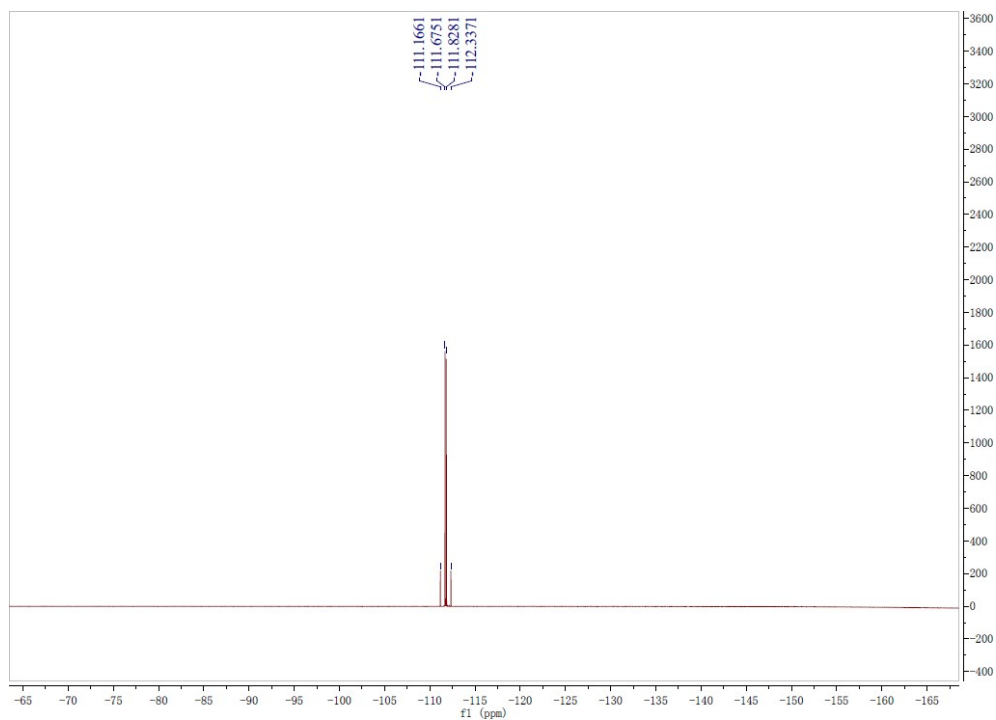


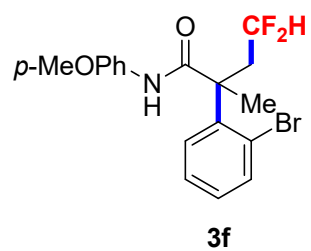
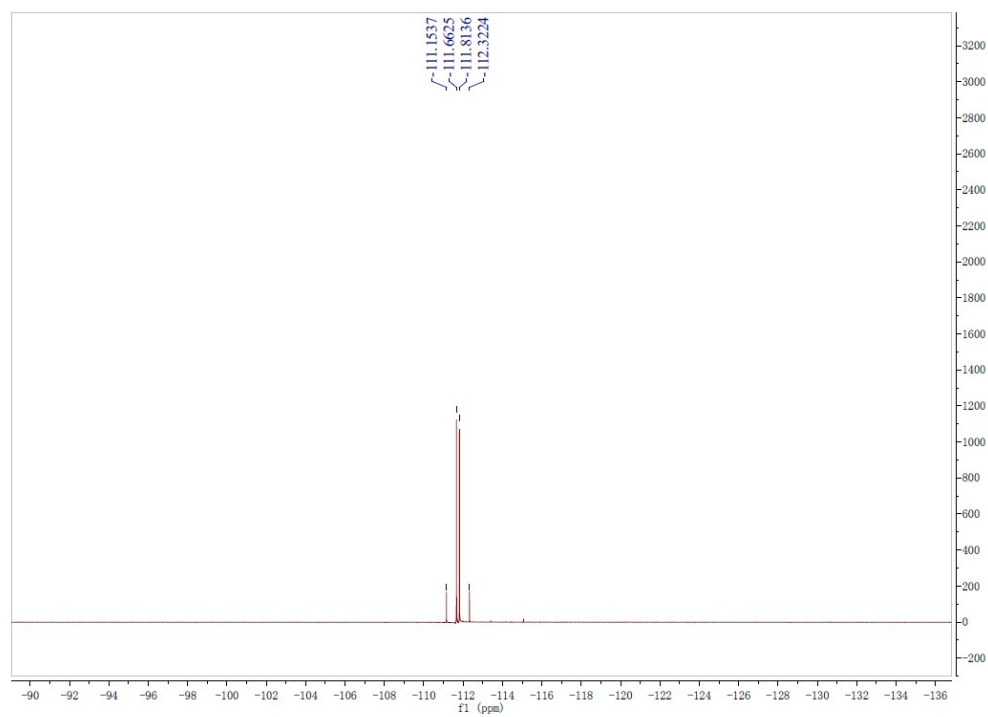
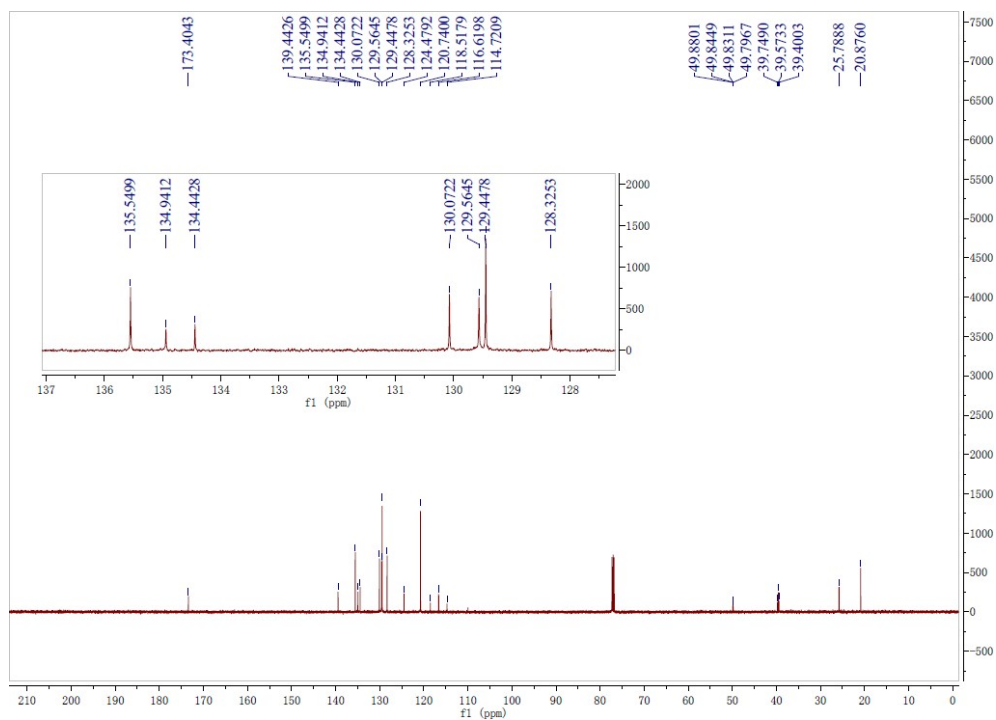
3c

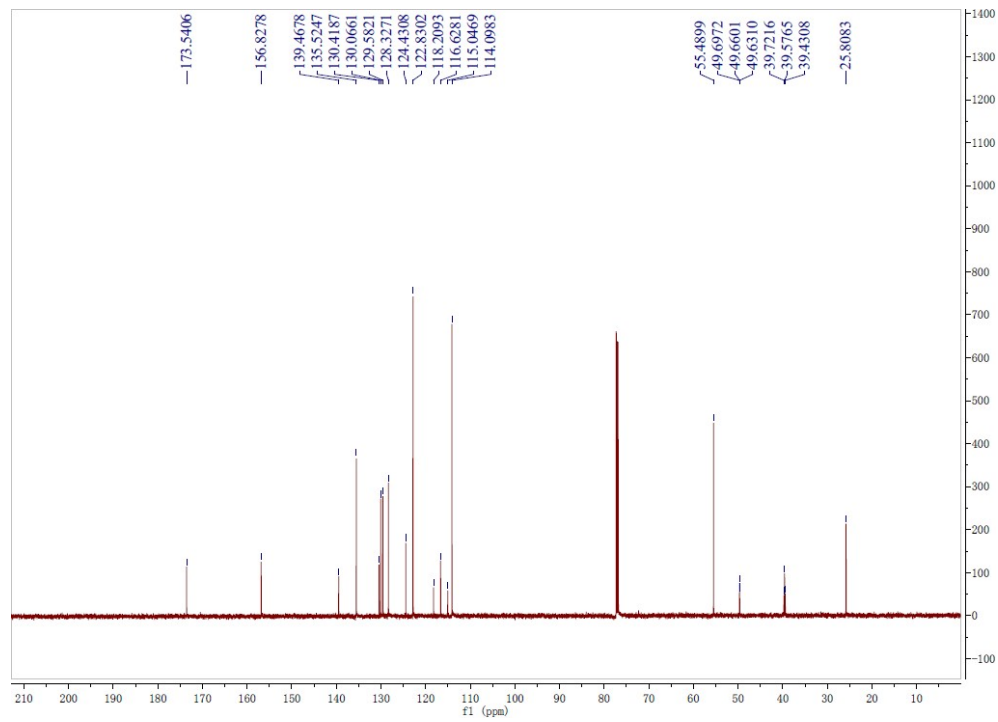
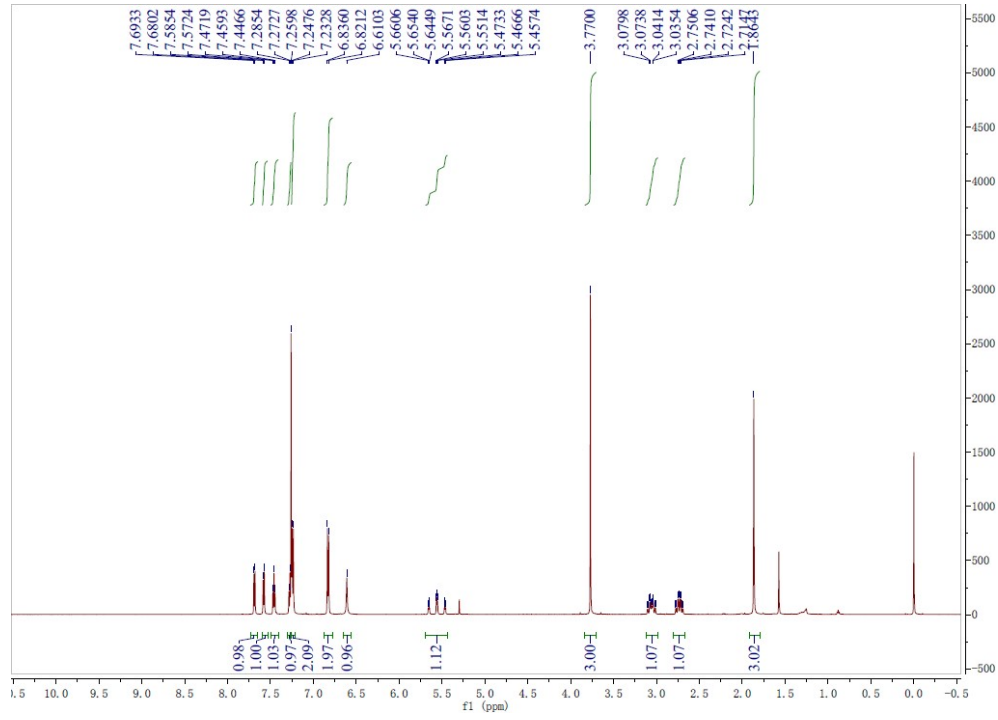


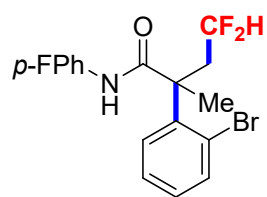
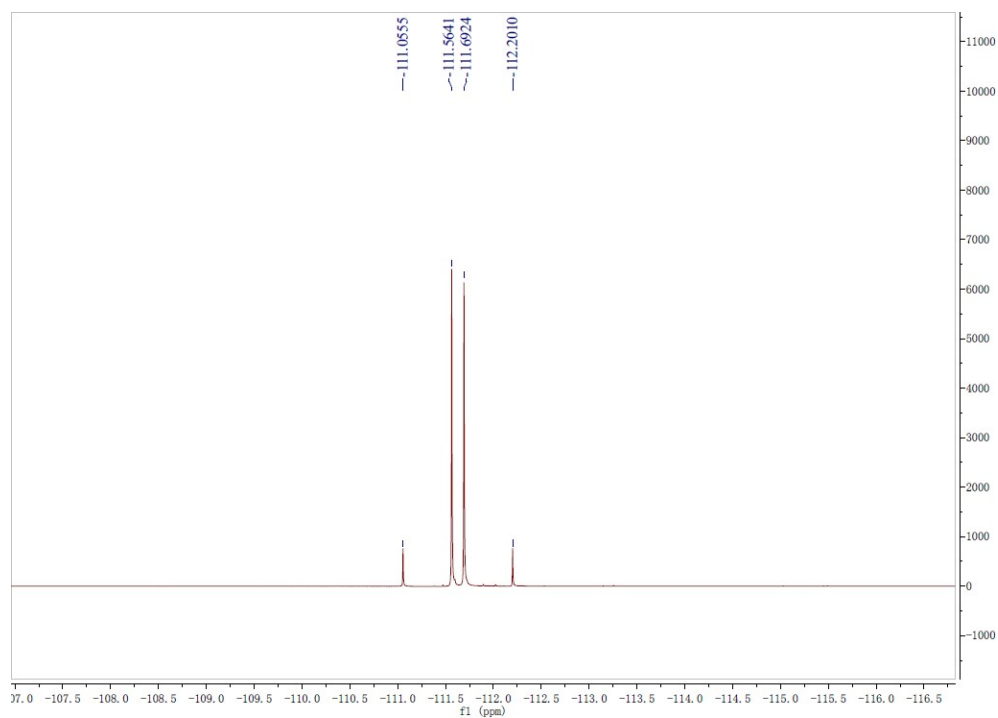




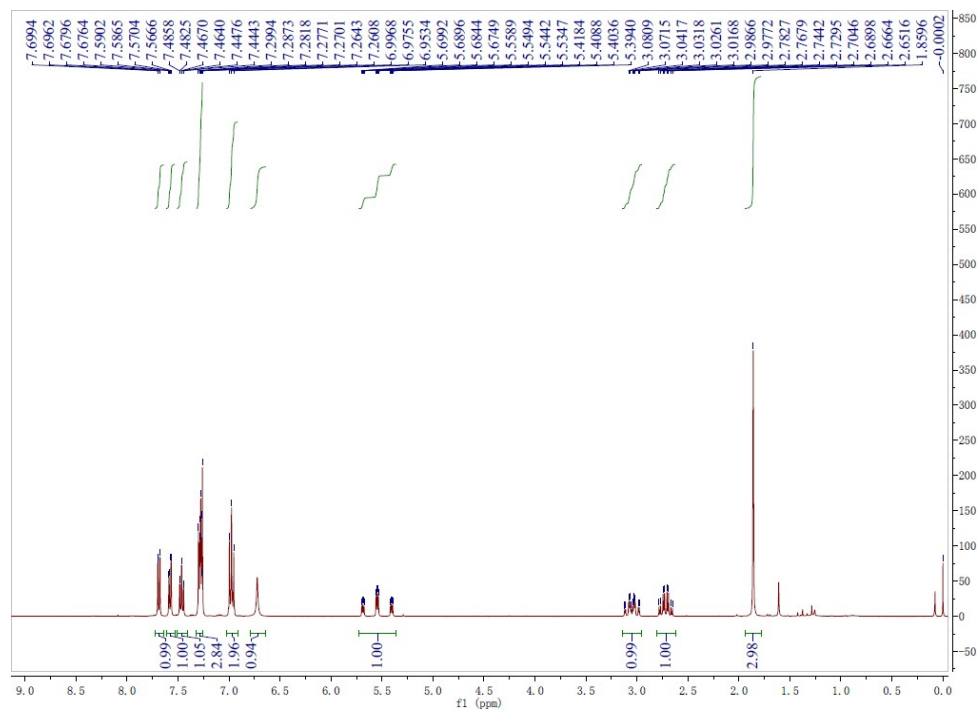


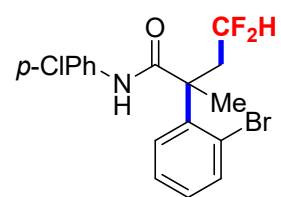
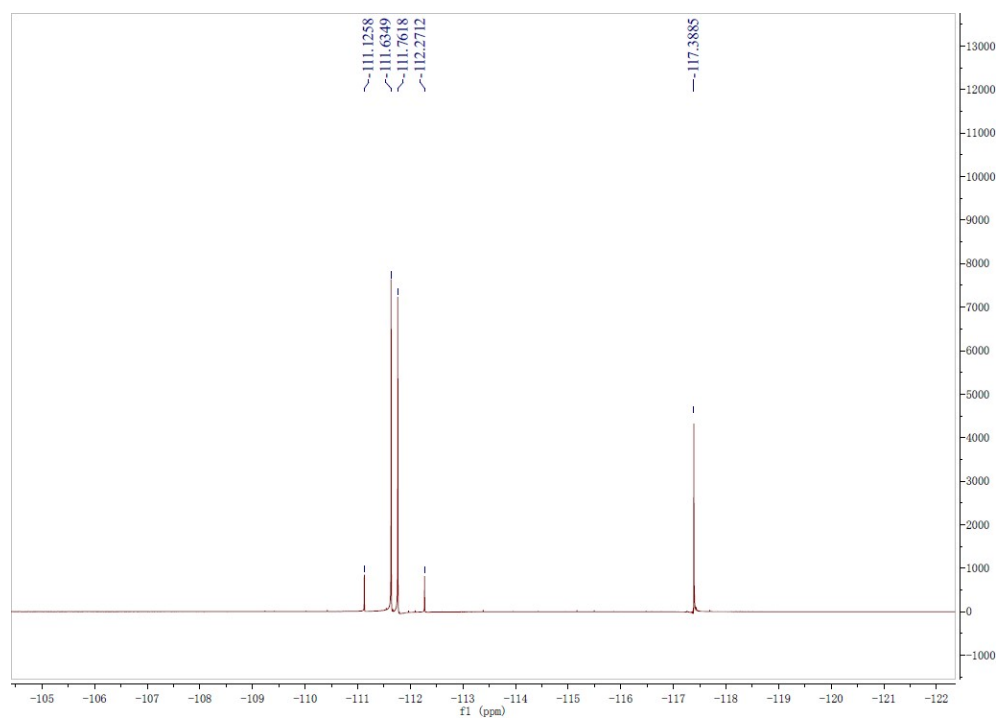
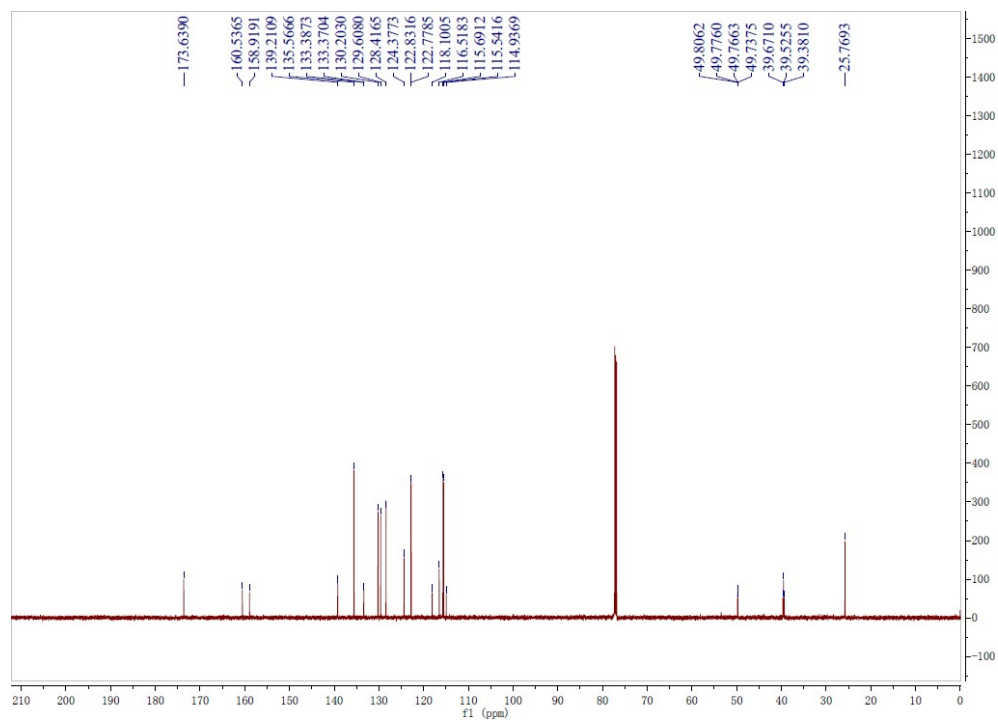




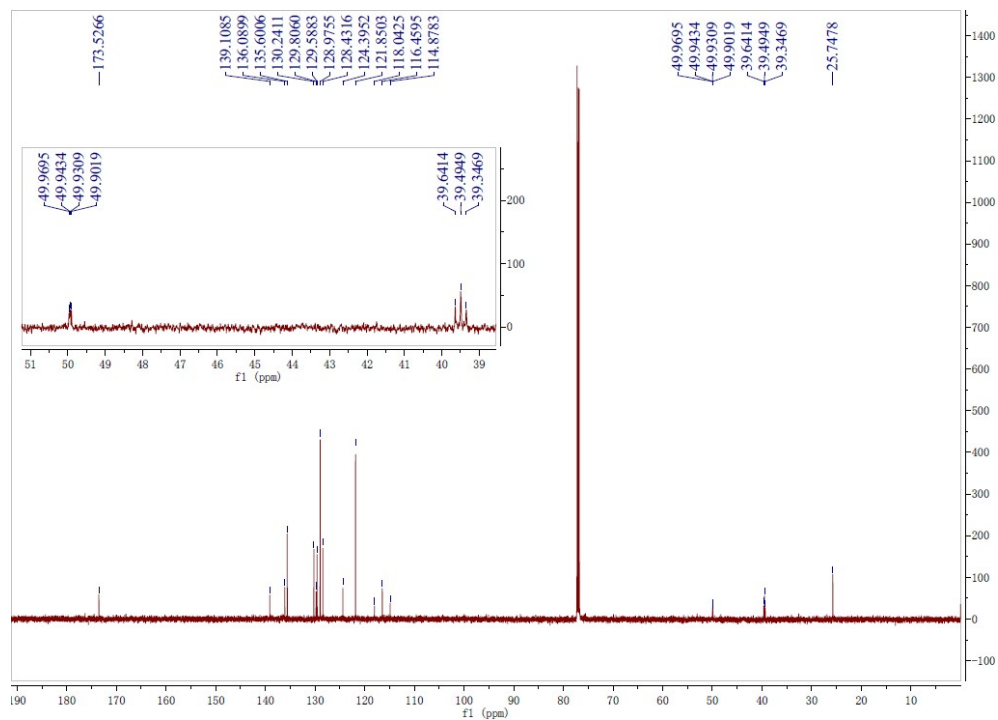
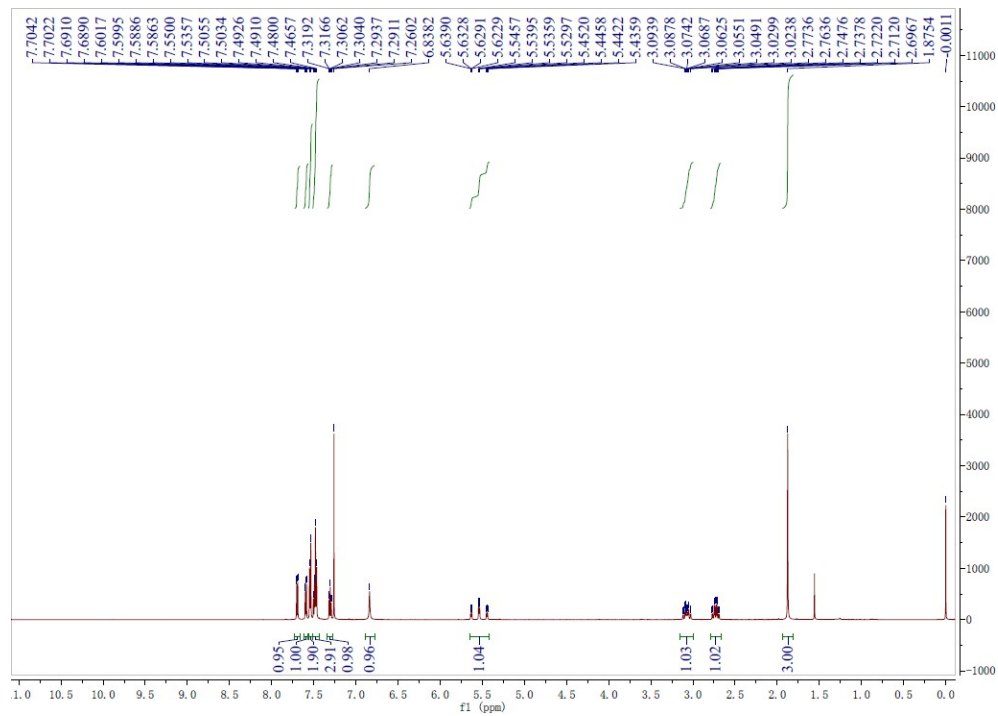


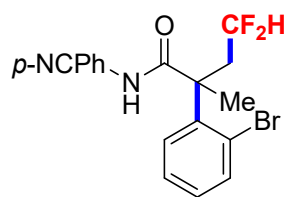
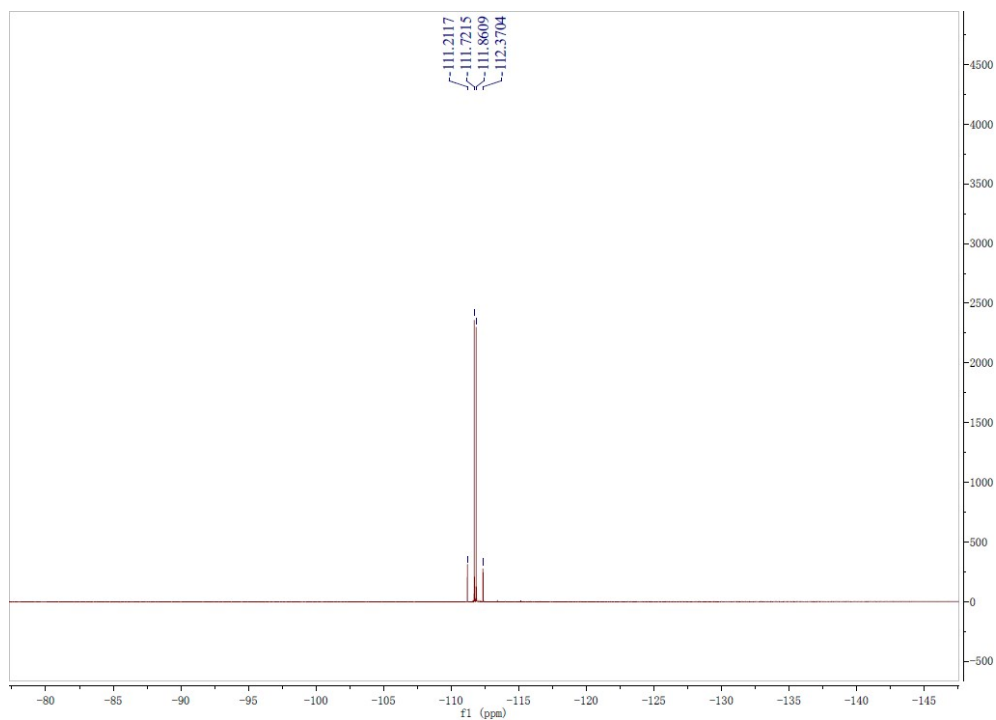
3g



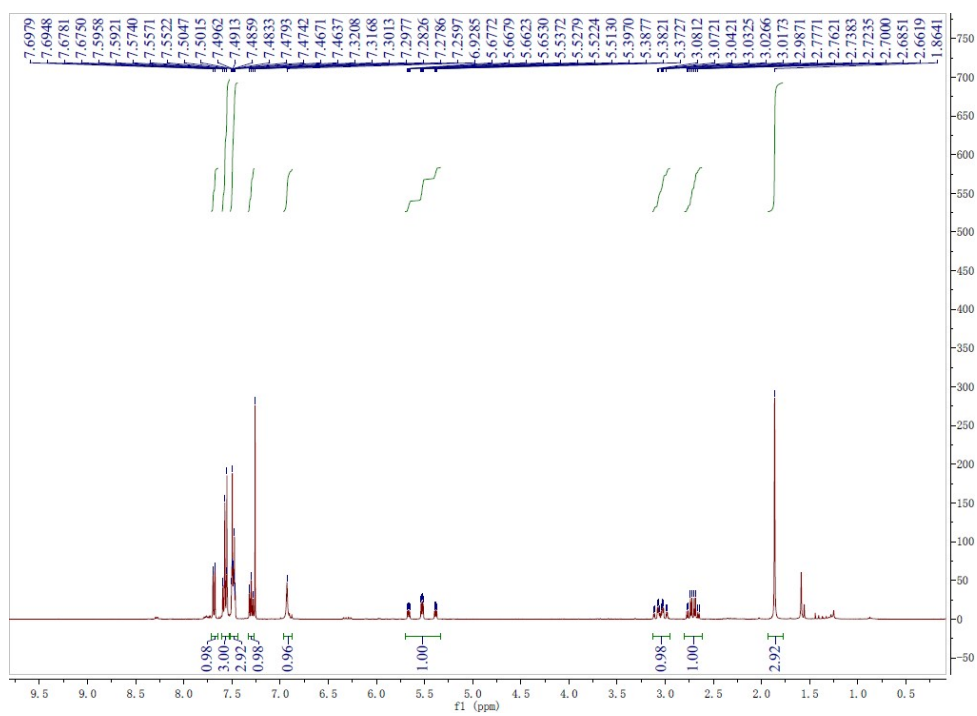


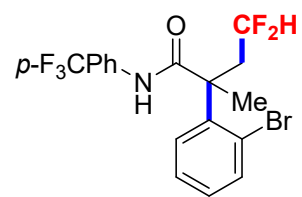
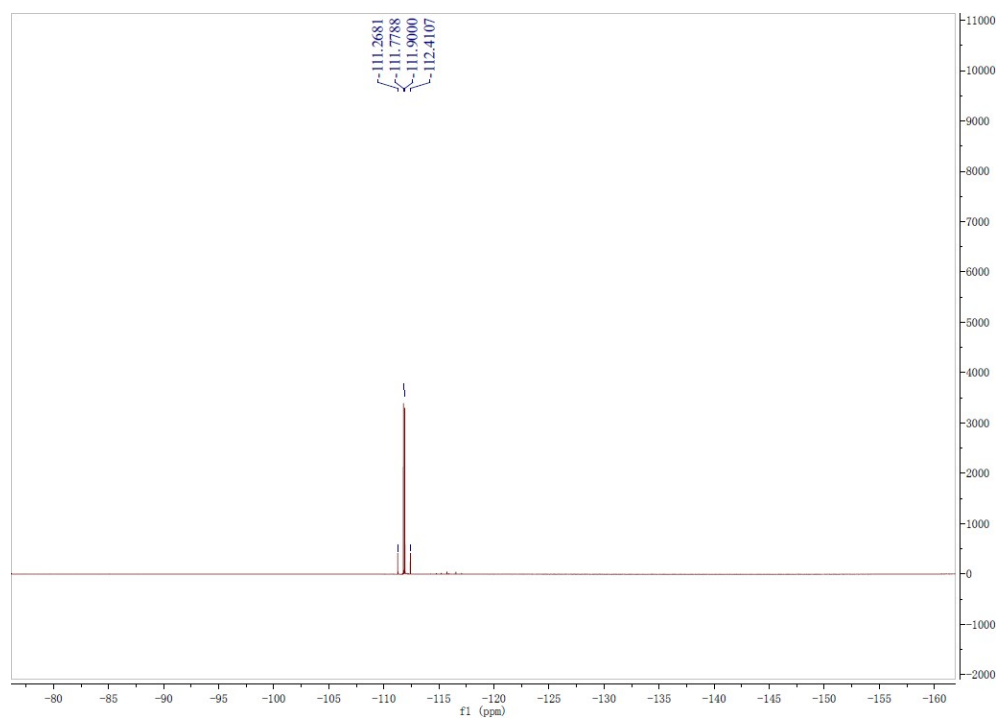
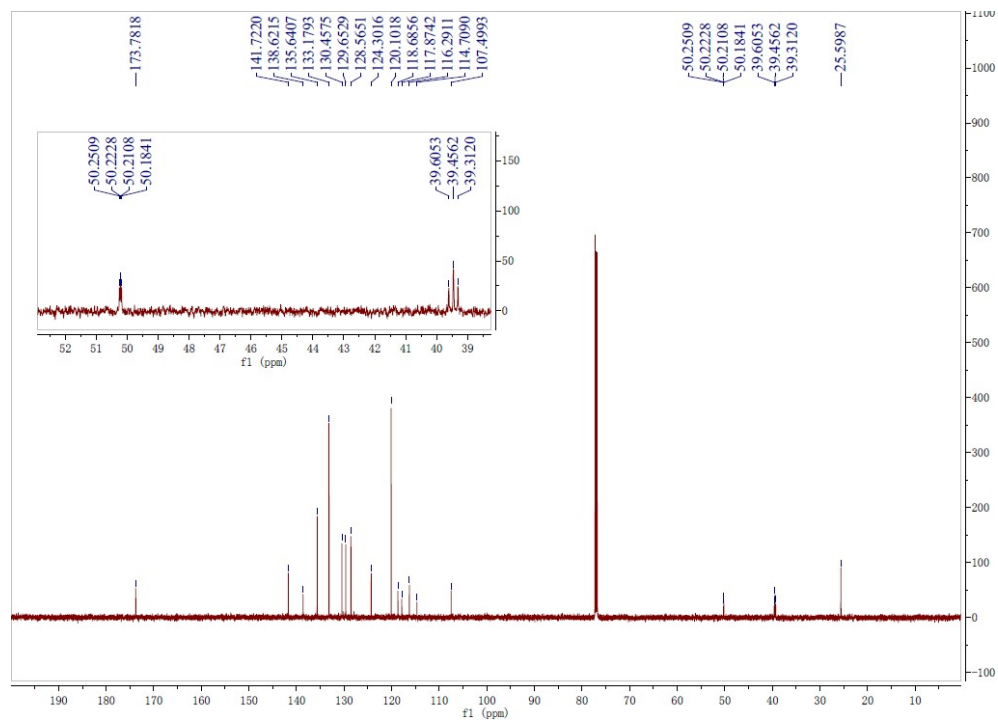
3h



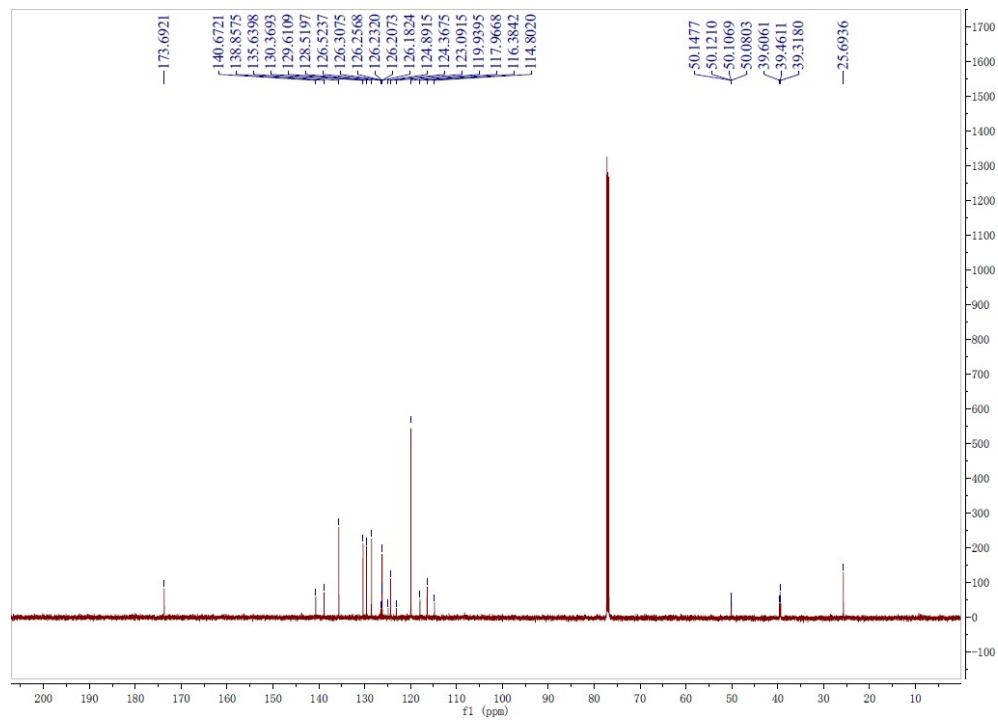
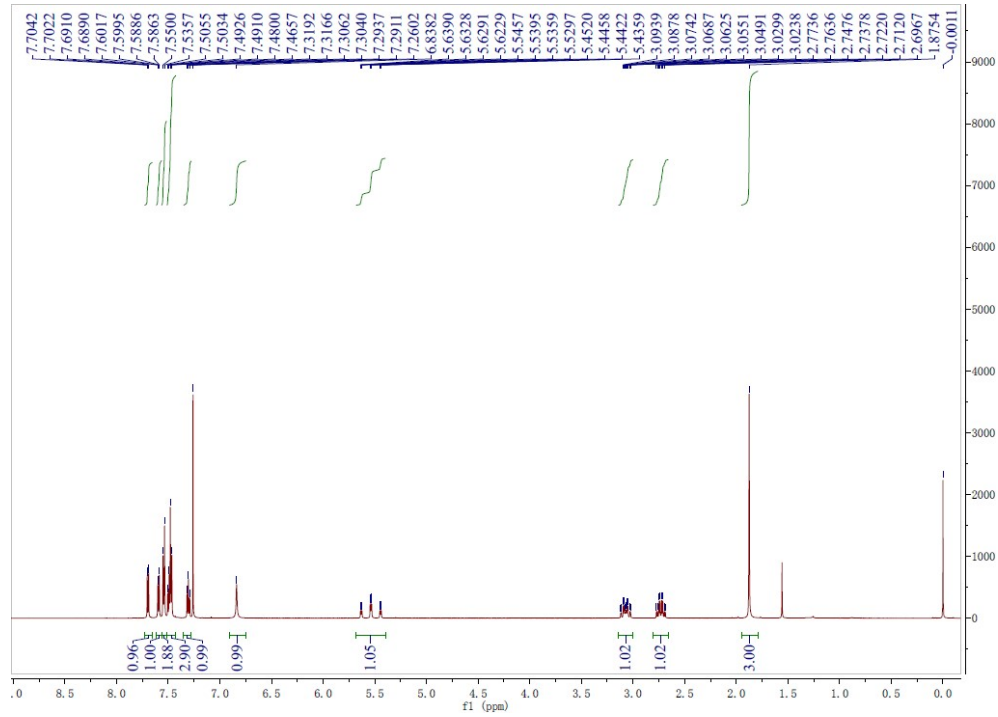


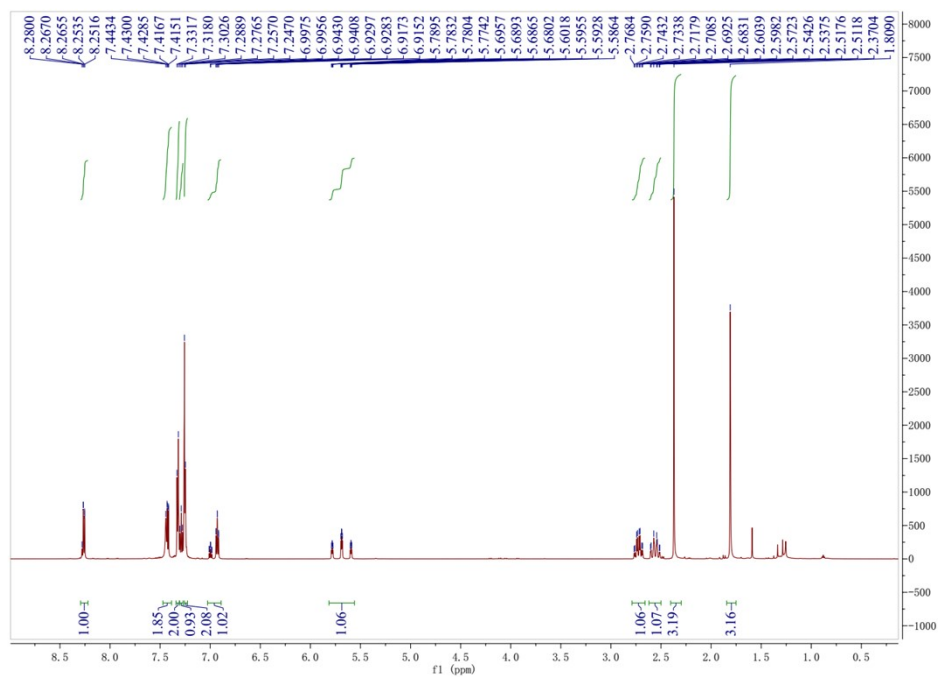
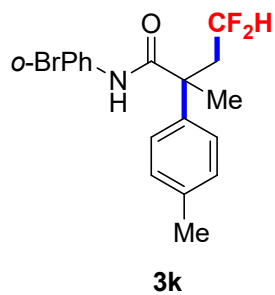
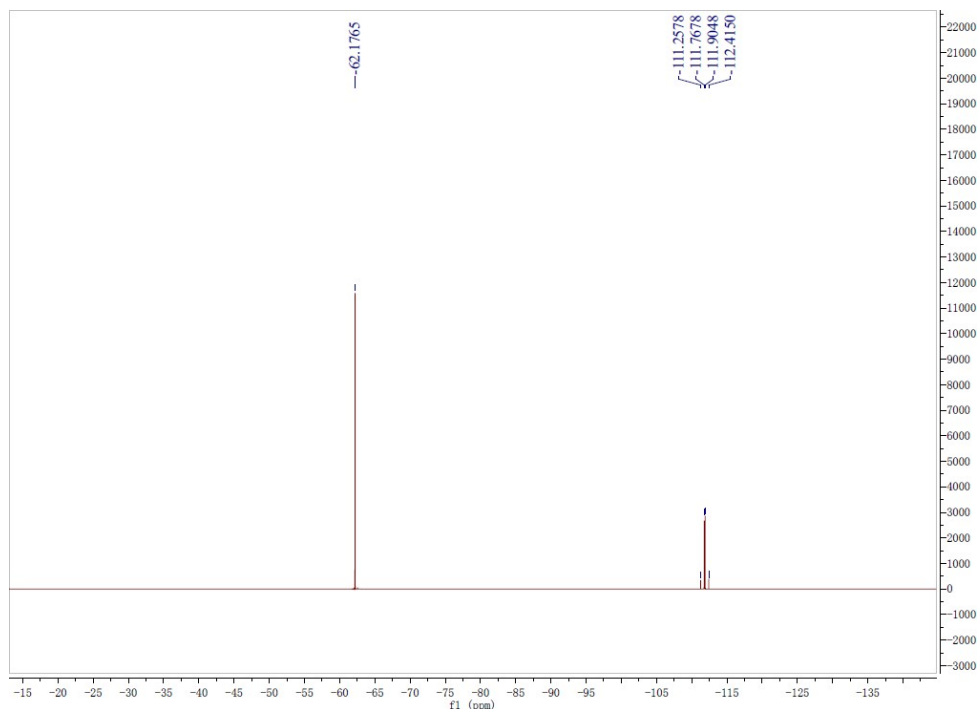
3i

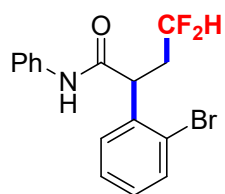
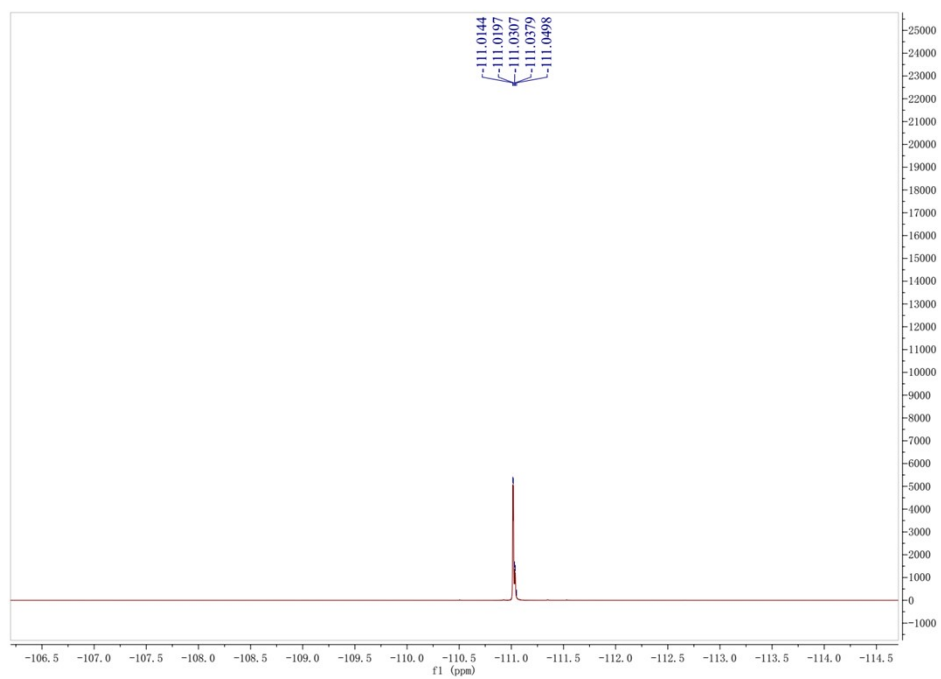
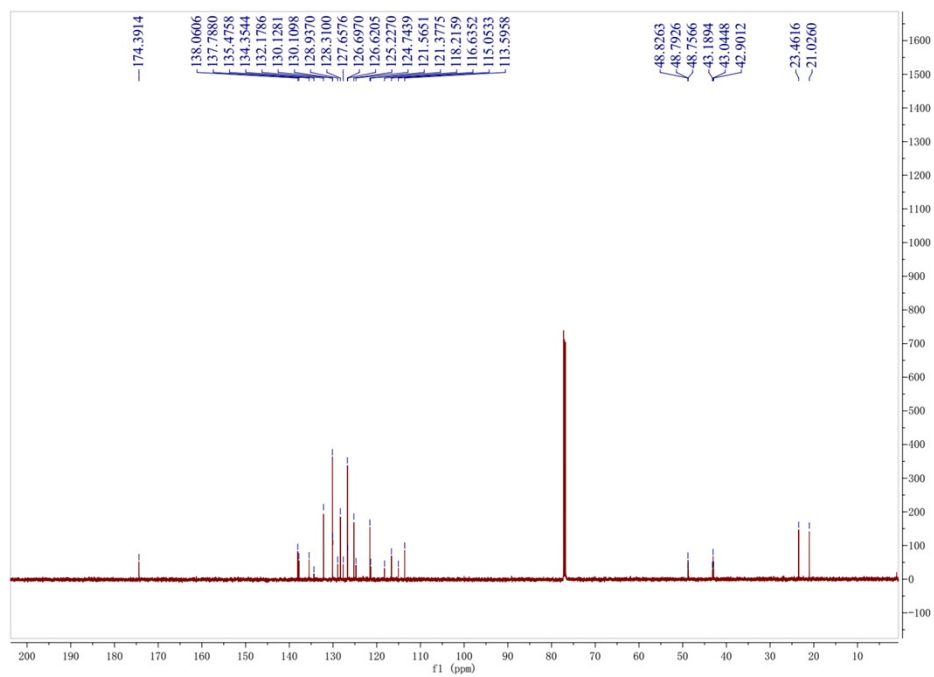




3j







31

