Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Enantioselective Construction of Chiral *gem*-Difluorinated C2-quaternary Indoline via dual $MgSO_4$-CPA-Catalyzed Asymmetric Mannich Reactions

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1. General information

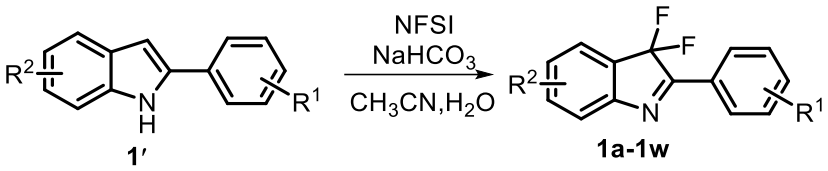
All reactions were performed using oven-dried or flame-dried glassware equipped with a magnetic stir bar before used.

All reagents were purchased from commercial suppliers and used without further purification. All solvents were purified by standard operating method.

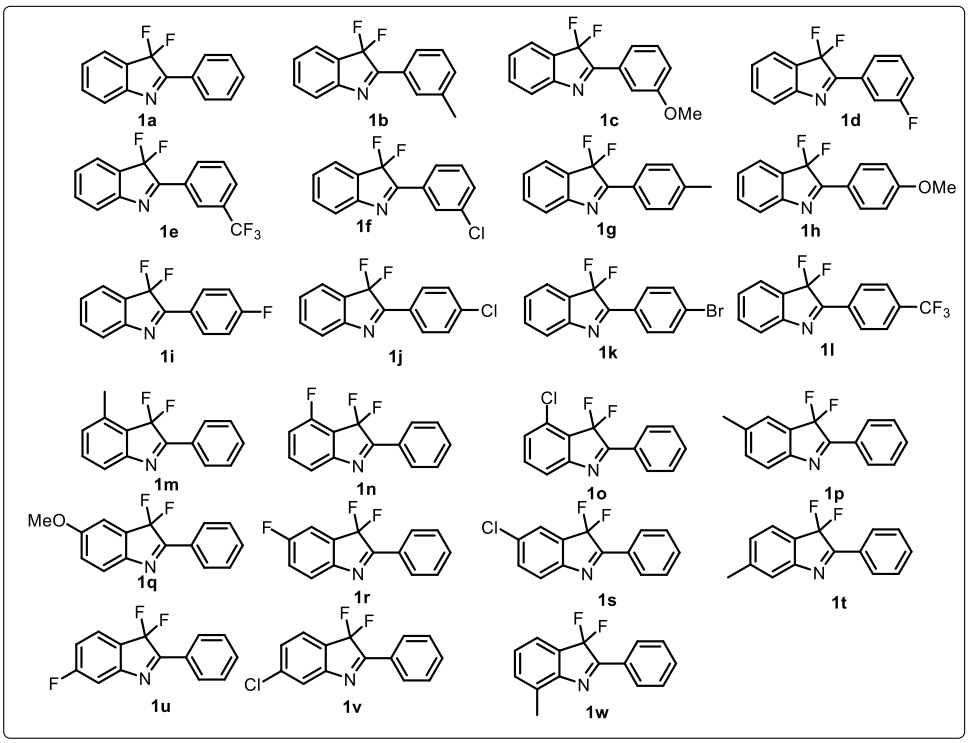
Thin-layer chromatography was performed with EMD silica gel 60 F_{254} plates eluting with solvents indicated, visualized by a 254 nm UV lamp and stained with phosphomolybdic acid (PMA). **^{1}H NMR**, **^{13}C NMR** and **^{19}F NMR** spectra were obtained on Bruker AM-400, Chemical shifts (δ) were quoted in ppm relative to tetramethylsilane or residual protio solvent as internal standard $CDCl_3$: 7.26 ppm for ^{1}H NMR, 77.0 ppm for ^{13}C NMR, multiplicities are as indicated: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. **High-resolution mass spectral analysis (HRMS) data** was measured on a Bruker impact II (Q-TOF) mass spectrum by means of the ESI technique. **Crystallographic data** were obtained from a Bruker D8 Quest diffractometer. **Optical rotations** were detected on RUDOLPH A21202-J APTV/GW. The **enantiomeric excesses** (ee) of the products were determined by high performance liquid chromatography (HPLC) analysis employing Daicel Chiralpak AD-H, OD-H and AS-H columns.

The 3,3-difluoro-3*H*-indoles were prepared according to the reported procedures. [1,5]

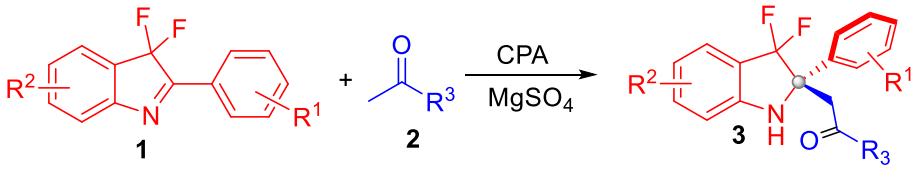
2. General procedure for the synthesis of substrates 1 and 2



General procedure for the preparation of **1**: Unless otherwise noted, reactions were performed: 2-phenylindole **1'** (1 mmol, 1.0 eq.), Selectfluor (2 mmol, 2.0 eq.), $NaHCO_3$ (2 mmol, 2.0 eq.), were added to a 50 mL Schlenk tube at 0 ℃, followed by addition of MeCN (10 mL). The formed mixture was stirred at 0 ℃ under air for 1 h monitored by TLC. The resulting mixture was concentrated under vacuum, the crude product was purified by flash column chromatography using petroleum ether/ EtOAc to give the compound **1**. The compound **1a-1w** are known compound.[1-5]

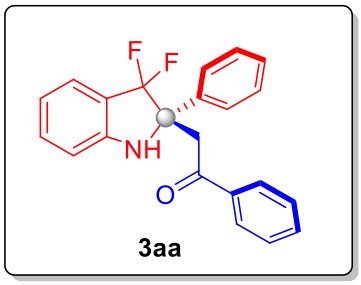


3. General procedure for the synthesis of products



General procedure for the preparation of **3**: Unless otherwise noted, reactions were performed: **1** (0.05 mmol, 1.0 equiv), **2** (0.5 mmol, 10.0 equiv), Cat.**C8** (10 mol%), $MgSO_4$ (10 mg) in DCM (0.5

mL) at 0 ℃ under N_2. The resulting yellow mixture was concentrated under vacuum, the crude product was purified by flash column chromatography using petroleum ether/ EtOAc/ Et_3N to give the title compound **3**.



3aa

(S)-2-(3,3-difluoro-2-phenylindolin-2-yl)-1-phenylethan-1-one (3aa) According to the general procedure, **3aa** was obtained using 3,3-difluoro-2-phenyl-3H-indole **1a** (11.5 mg, 0.05 mmol) and acetophenone **2a** (60.0 mg, 0.5 mmol) in 90% yield (15.7 mg) and 94% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.53 – 7.49 (m, 2H), 7.47 – 7.43 (m, 1H), 7.37 (d, *J* = 7.5 Hz, 1H), 7.32 (t, *J* = 7.8 Hz, 2H), 7.28 – 7.21 (m, 3H), 7.19 – 7.15 (m, 1H), 6.81 – 6.73 (m, 2H), 5.73 (s, 1H), 4.30 (dd, *J* = 17.8, 1.8 Hz, 1H), 3.24 (d, *J* = 17.7 Hz, 1H).

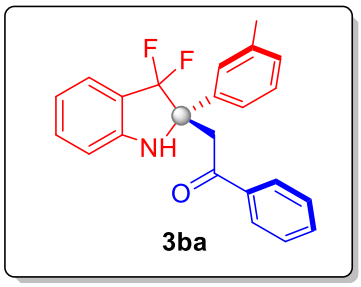
^{13}C NMR (100 MHz, $CDCl_3$) δ 198.3 (d, *J* = 2.0 Hz), 149.6 (dd, *J* = 8.0, 5.0 Hz), 137.4 (d, *J* = 6.0 Hz), 136.8, 133.7, 133.0, 128.6, 128.2, 128.0, 127.7, 126.7 (t, *J* = 250.0 Hz), 126.5, 124.3, 120.1 (dd, *J* = 27.0, 25.0 Hz), 119.2, 111.2, 71.8 (dd, *J* = 28.0, 22.0 Hz), 42.0 (dd, *J* = 10.0, 2.0 Hz).

^{19}F NMR (376 MHz, CDCl3) δ -85.3 (d, *J* = 248.2 Hz), -107.3 (d, *J* = 248.2 Hz).

HRMS (ESI) *m/z* calcd. for $C_{22}H_{17}F_2NO$ $(M+Na)^+$:372.1170, found 372.1165.

Enantiomeric excess is 94% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 11.04 min; minor isomer: tr = 8.47 min.

$[\alpha]^{20}_D$ = +389 (c = 0.35, $CHCl_3$).



(S)-2-(3,3-difluoro-2-(m-tolyl)indolin-2-yl)-1-phenylethan-1-one (3ba) According to the general procedure, **3ba** was obtained using 3,3-difluoro-2-(m-tolyl)-3H-indole **1b** (12.16 mg, 0.05 mmol) and acetophenone 2a (60.0 mg, 0.5 mmol) in 86% yield (15.63 mg) and 92% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 70:1:0.5). R_f = 0.30 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.34 (m, 2H), 7.44 – 7.39 (m, 1H), 7.36 – 7.21 (m, 6H), 7.12 – 7.08 (m, 1H), 6.96 (d, *J* = 7.6 Hz, 1H), 6.77 – 6.72 (m, 2H), 5.76 (s, 1H), 4.27 (dd, *J* = 17.8, 1.9 Hz, 1H), 3.20 (dd, *J* = 17.7, 1.5 Hz, 1H), 2.21 (s, 3H).

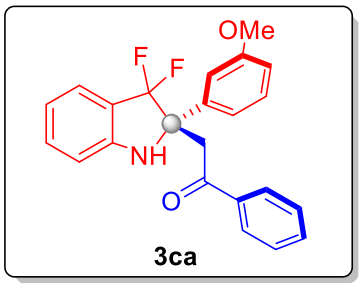
^{13}C NMR (100 MHz, $CDCl_3$) δ 198.3 (d, *J* = 2.0 Hz), 149.6 (dd, *J* = 13.0, 7.0 Hz), 137.7, 137.2 (d, *J* = 5.0 Hz), 136.9, 133.6, 133.0, 128.6, 128.5, 128.1, 128.0, 127.3, 126.7 (t, *J* = 249.0 Hz), 124.3, 123.5, 120.1 (t, *J* = 25.0 Hz), 119.2, 111.2, 71.8 (dd, *J* = 27.0, 21.0 Hz), 42.0 (dd, *J* = 9.0, 2.0 Hz), 21.6.

^{19}F NMR (376 MHz, $CDCl_3$) δ -84.60 – -85.28 (m), -107.39 – -108.08 (m).

HRMS (ESI) *m/z* calcd. for $C_{23}H_{19}F_2NO$ $(M+Na)^+$:386.1327, found 386.1334.

Enantiomeric excess is 92% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 16.40 min; minor isomer: tr = 11.81 min.

$[\alpha]^{20}_D$ = +182 (c = 0.3, $CHCl_3$).



(S)-2-(3,3-difluoro-2-(3-methoxyphenyl)indolin-2-yl)-1-phenylethan-1-one (3ca) According to the general procedure, **3ca** was obtained using 3,3-difluoro-2-(3-methoxyphenyl)-3H-indole **1c**

(13.0 mg, 0.05 mmol) and acetophenone **2a** (60.0 mg, 0.5 mmol) in 76% yield (14.4 mg) and 90% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 60:1:0.5). R_f = 0.30 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.77 (m, 2H), 7.48 – 7.43 (m, 1H), 7.38 – 7.30 (m, 3H), 7.28 – 7.23 (m, 1H), 7.17 – 7.10 (m, 2H), 7.07 – 7.05 (m, 1H), 6.80 – 6.73 (m, 2H), 6.74 – 6.67 (m, 1H), 5.74 (s, 1H), 4.28 (dd, *J* = 17.8, 1.9 Hz, 1H), 3.67 (s, 3H), 3.21 (d, *J* = 17.7 Hz, 1H).

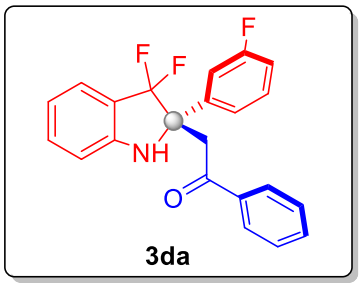
^{13}C NMR (100 MHz, $CDCl_3$) δ 198.3 (d, *J* =2 Hz), 159.5, 149.6 (dd, *J* = 9.0, 6.0 Hz), 139.1 (d, *J* = 6 Hz), 136.9, 133.6, 133.0, 129.2, 128.6, 128.0, 126.7 (t, *J* = 250.0 Hz), 124.3, 120.1 (dd, *J* = 26.0, 25.0 Hz), 119.2, 118.8, 113.0, 112.9, 111.0, 71.8 (dd, *J* = 27.0, 21.0 Hz), 55.1, 42.0 (dd, *J* = 10.0, 3.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -91.1 (d, *J* = 248.2 Hz), -116.2 (d, *J* = 248.2 Hz).

HRMS (ESI) *m/z* calcd. for $C_{23}H_{19}F_2NO_2$ $(M+H)^+$:380.1457, found 380.1450.

Enantiomeric excess is 90% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 13.37 min; minor isomer: tr = 10.58 min.

$[\alpha]^{20}_D$ = +178 (c = 0.2, $CHCl_3$).



3da

(S)-2-(3,3-difluoro-2-(3-fluorophenyl)indolin-2-yl)-1-phenylethan-1-one (3da) According to the general procedure, **3da** was obtained using 3,3-difluoro-2-(3-fluorophenyl)-3H-indole **1d** (16.0 mg, 0.05 mmol) and acetophenone 2a (60.0 mg, 0.5 mmol) in 85% yield (16.0 mg) and 88% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (dd, *J* = 8.5, 1.3 Hz, 2H), 7.59 – 7.55 (m, 1H), 7.50 (d, *J* = 7.4 Hz, 1H), 7.46-7.36 (m, 5H), 7.33 - 7.28 (m, 1H), 7.00 - 6.96 (m, 1.0 Hz, 1H), 6.95 – 6.82 (m, 2H), 5.87 (s, 1H), 4.37 (dd, *J* = 17.9, 1.9 Hz, 1H), 3.43 – 3.31 (m, 1H).

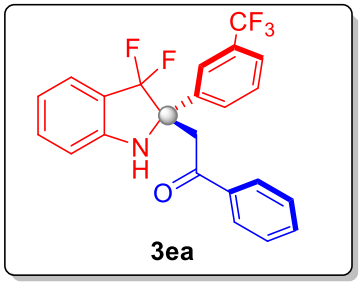
^{13}C NMR (100 MHz, $CDCl_3$) δ 198.0 (d, *J* = 2.0 Hz), 162.8 (d, *J* = 244.0 Hz), 149.4 (dd, *J* = 8.0, 5.0 Hz), 140.3 (dd, *J* =6.0, 5.0 Hz), 136.6, 133.8, 133.1, 129.7 (d, *J* = 5.0 Hz), 129.6, 128.7, 127.9, 126.6 (t, *J* = 250.0 Hz), 124.3, 124.1, 122.1 (d, *J* = 3.0 Hz), 119.8 (dd, *J* =26.0, 25.0 Hz), 114.7 (d, *J* = 21.0 Hz), 114.1 (d, *J* = 21.0 Hz), 111.3, 71.6 (dd, *J* = 28.0, 22.0 Hz), 42.0 (dd, *J* = 10.0, 3.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -84.4(d, *J* = 248.2 Hz), -107.6 (d, *J* = 248.2 Hz), -112.7.

HRMS (ESI) *m/z* calcd. for $C_{22}H_{16}F_3NO$ $(M+Na)^+$:390.1076, found 390.1079.

Enantiomeric excess is 88% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 13.31 min; minor isomer: tr = 10.59 min.

$[\alpha]^{20}_D$ = +280 (c = 0.2, $CHCl_3$).



3ea

(S)-2-(3,3-difluoro-2-(3-(trifluoromethyl)phenyl)indolin-2-yl)-1-phenylethan-1-one (3ea)

According to the general procedure, **3ea** was obtained using 3,3-difluoro-2-(3-(trifluoromethyl)phenyl)-3H-indole **1e** (14.9 mg, 0.05 mmol) and acetophenone 2a (60.0 mg, 0.5 mmol) in 86% yield (17.3 mg) and 86% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.87 (d, *J* = 7.7 Hz, 2H), 7.80 (d, *J* = 7.9 Hz, 1H), 7.59 – 7.53 (m, 2H), 7.51 – 7.36 (m, 5H), 6.95 – 6.85 (m, 2H), 5.87 (s, 1H), 4.38 (d, *J* = 17.9 Hz, 1H), 3.39 (d, *J* = 17.8 Hz, 1H).

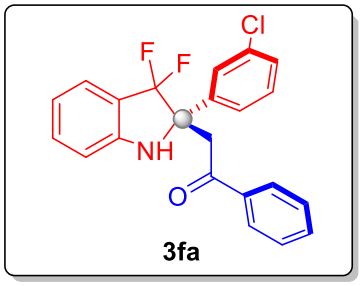
^{13}C NMR (100 MHz, $CDCl_3$) δ 198.0, 149.2 (d, *J* = 8.0, 5.0 Hz), 138.7 (d, *J* = 6.0 Hz), 136.5, 133.9, 133.2, 131.6 (q, *J* = 32.0 Hz), 129.8, 128.71, 128.68, 128.0, 126.6 (t, *J* = 250.0 Hz), 124.7 (q, *J* =4.0 Hz), 124.3, 124.1 (t, *J* = 271.0 Hz), 123.7 (d, *J* = 4.0 Hz), 119.9 - 119.5 (m), 119.7, 111.5, 71.7 (dd, *J* = 28.0, 21.0 Hz), 42.1 (dd, *J* = 9.0, 3.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.4, -82.7 (dd, *J* = 248.2, 7.5 Hz), -108.7 (dd, *J* = 248.2, 7.5 Hz).

HRMS (ESI) *m/z* calcd. for $C_{23}H_{16}F_5NO$ $(M+Na)^+$:418.1225, found 418.1235.

Enantiomeric excess is 86% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 7.70 min; minor isomer: tr = 5.46 min.

$[\alpha]^{20}_{D}$ = +321 (c = 0.2, $CHCl_3$).



3fa

(S)-2-(2-(3-chlorophenyl)-3,3-difluoroindolin-2-yl)-1-phenylethan-1-one (3fa) According to the general procedure, **3fa** was obtained using 2-(3-chlorophenyl)-3,3-difluoro-3H-indole **1f** (13.2 mg, 0.05 mmol) and acetophenone 2a (60.0 mg, 0.5 mmol) in 83% yield (15.9 mg) and 88% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 – 7.81 (m, 2H), 7.64 (s, 1H), 7.57 – 7.52 (m, 1H), 7.48 – 7.38 (m, 4H), 7.34 (t, *J* = 7.6 Hz, 1H), 7.26 – 7.20 (m, 2H), 6.92 – 6.79 (m, 2H), 5.80 (s, 1H), 4.30 (dd, *J* = 17.9, 1.9 Hz, 1H), 3.33 (d, *J* = 17.9 Hz, 1H).

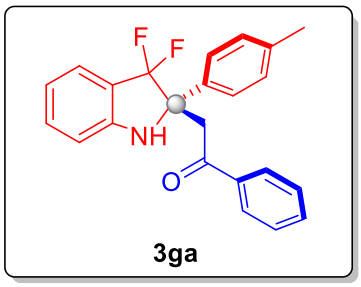
^{13}C NMR (100 MHz, $CDCl_3$) δ 198.0 (d, *J* = 1.0 Hz), 149.3 (dd, *J* = 8.0, 5.0 Hz), 139.7 (d, *J* = 5.0 Hz), 136.6, 134.4, 133.8, 133.2, 129.4, 128.7, 127.98, 127.96, 127.1, 126.6 (t, *J* = 250.0 Hz), 124.6, 124.3, 119.8 (dd, *J* = 26.0, 24.0 Hz), 119.5, 111.4, 71.6 (dd, *J* = 27.0, 21.0 Hz), 42.0 (dd, *J* = 10.0, 3.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -83.3 (d, *J* = 248.2 Hz), -107.9(d, *J* = 248.2 Hz).

HRMS (ESI) *m/z* calcd. for $C_{22}H_{16}ClF_2NO$ $(M+H)^+$:384.0961, found 384.0953.

Enantiomeric excess is 88% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 9.62 min; minor isomer: tr = 7.56 min.

$[\alpha]^{20}_{D}$ = +290 (c = 0.2, $CHCl_3$).



3ga

(S)-2-(3,3-difluoro-2-(p-tolyl)indolin-2-yl)-1-phenylethan-1-one (3ga) According to the general procedure, **3ga** was obtained using 3,3-difluoro-2-(p-tolyl)-3H-indole **1g** (12.2 mg, 0.05 mmol) and acetophenone **2a** (60.0 mg, 0.5 mmol) in 96% yield (17.4 mg) and 90% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 – 7.86 (m, 2H), 7.58 – 7.54 (m, 1H), 7.49 – 7.40 (m, 5H), 7.35 (t, *J* = 7.7 Hz, 1H), 7.14 (d, *J* = 8.0 Hz, 2H), 6.89 – 6.82 (m, 2H), 5.86 (s, 1H), 4.39 (dd, *J* = 17.8, 1.8 Hz, 1H), 3.33 (d, *J* = 17.8 Hz, 1H), 2.31 (s, 3H).

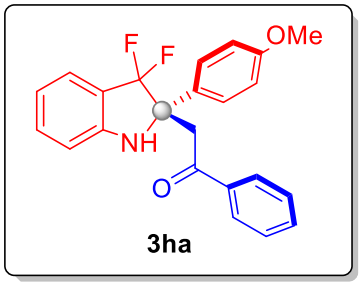
^{13}C NMR (100 MHz, $CDCl_3$) δ 198.3 (d, *J* =2.0 Hz), 149.7 (dd, *J* = 8.0, 5.0 Hz), 137.3, 136.9, 134.4 (d, *J* =26.0 Hz), 133.6, 133.0, 129.0, 128.6, 128.0, 126.7 (t, *J* = 249.0 Hz), 126.4, 124.4, 120.1 (t, *J* = 2.0 Hz), 119.1, 111.1, 71.7 (dd, *J* = 28.0, 22.0 Hz), 41.9 (dd, *J* = 9.0, 2.0 Hz), 21.02.

^{19}F NMR (376 MHz, $CDCl_3$) δ -86.0(d, *J* = 248.2 Hz), -107.2 (d, *J* = 244.4 Hz).

HRMS (ESI) *m/z* calcd. for $C_{23}H_{19}F_2NO$ $(M+Na)^+$: 386.1327, found 386.1329.

Enantiomeric excess is 90% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 8.03 min; minor isomer: tr = 12.67 min.

$[\alpha]^{20}_D$ = +237 (c = 0.2, $CHCl_3$).



3ha

(S)-2-(3,3-difluoro-2-(4-methoxyphenyl)indolin-2-yl)-1-phenylethan-1-one (3ha) According to the general procedure, **3ha** was obtained using 3,3-difluoro-2-(4-methoxyphenyl)-3H-indole **1h** (13.0 mg, 0.05 mmol) and acetophenone 2a (60.0 mg, 0.5 mmol) in 95% yield (18.0 mg) and 92%

ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 60:1:0.5). R_f = 0.20 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 – 7.83 (m, 2H), 7.58 – 7.40 (m, 6H), 7.34 (t, *J* = 7.7 Hz, 1H), 6.96 – 6.77 (m, 4H), 5.87 (s, 1H), 4.36 (dd, *J* = 17.8, 1.8 Hz, 1H), 3.76 (s, 3H), 3.30 (d, *J* = 17.7 Hz, 1H).

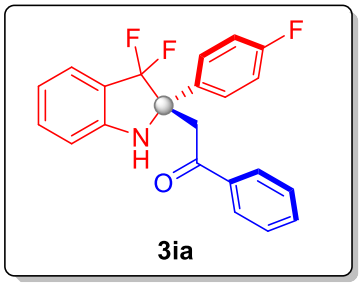
^{13}C NMR (100 MHz, $CDCl_3$) δ 198.4 (d, *J* = 1.0 Hz), 159.0, 149.7 (dd, *J* = 8.0, 6.0 Hz), 136.9, 133.6, 132.9, 129.3 (d, *J* = 6.0 Hz), 128.6, 128.0, 127.7, 126.7 (t, *J* = 249.0 Hz), 124.4, 120.2 (dd, *J* = 25.0, 2.0 Hz), 119.2, 113.7, 111.2, 71.5 (dd, *J* =27.0, 21.0 Hz), 55.1, 41.8 (dd, *J* = 10.0, 3.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -85.9 (d, *J* = 248.2 Hz), -107.6 (d, *J* = 248.2 Hz).

HRMS (ESI) *m/z* calcd. for $C_{23}H_{19}F_2NO_2$ $(M+Na)^+$:402.1276, found 402.1280.

Enantiomeric excess is 92% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 95/5, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 46.28 min; minor isomer: tr = 26.79 min.

$[\alpha]^{20}_D$ = +273 (c = 0.2, $CHCl_3$).



3ia

(S)-2-(3,3-difluoro-2-(4-fluorophenyl)indolin-2-yl)-1-phenylethan-1-one (3ia) According to the general procedure, **3ia** was obtained using 3,3-difluoro-2-(4-fluorophenyl)-3H-indole **1i** (12.4 mg, 0.05 mmol) and acetophenone 2a (60.0 mg, 0.5 mmol) in 91% yield (17.1 mg) and 94% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (dd, *J* = 8.4, 1.4 Hz, 2H), 7.61 – 7.54 (m, 3H), 7.49 – 7.41 (m, 3H), 7.36 (t, *J* = 7.7 Hz, 1H), 7.06 – 6.98 (m, 2H), 6.92 – 6.83 (m, 2H), 5.86 (s, 1H), 4.35 (dd, *J* = 17.9, 1.9 Hz, 1H), 3.33 (d, *J* = 17.8 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 198.2 (d, *J* = 2.0 Hz), 162.3 (d, *J* = 245.0 Hz), 149.4 (dd, *J* = 8.0, 5.0 Hz), 136.7, 133.8, 133.2 (dd, *J* = 6.0, 4.0 Hz), 133.1, 128.7, 128.3 (d, *J* = 8.0 Hz), 128.0, 126.6

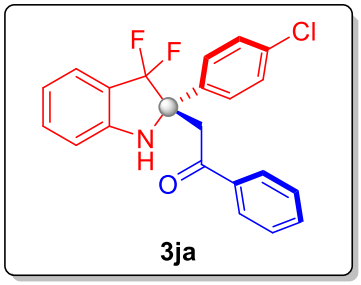
(t, *J* = 249 Hz), 124.4, 120.0 (dd, *J* = 26.0, 25.0 Hz), 119.4, 115.1 (d, *J* = 21.0 Hz), 111.3, 71.5 (dd, *J* = 27.0, 21.0 Hz), 42.0 (dd, *J* = 10.0, 3.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -84.5 (d, *J* = 248.2 Hz), -108.1 (d, *J* = 248.2 Hz), -115.0.

HRMS (ESI) *m/z* calcd. for $C_{22}H_{16}F_3NO$ $(M+H)^+$:368.1257, found 368.1261.

Enantiomeric excess is 94% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 10.88 min; minor isomer: tr = 8.05 min.

$[\alpha]^{20}_D$ = +268 (c = 0.2, $CHCl_3$).



3ja

(S)-2-(2-(4-chlorophenyl)-3,3-difluoroindolin-2-yl)-1-phenylethan-1-one (3ja) According to the general procedure, **3ja** was obtained using 2-(4-chlorophenyl)-3,3-difluoro-3H-indole **1j** (13.2 mg, 0.05 mmol) and acetophenone 2a (60.0 mg, 0.5 mmol) in 84% yield (16.1 mg) and 90% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 – 7.84 (m, 2H), 7.59 – 7.53 (m, 3H), 7.49 – 7.41 (m, 3H), 7.38 – 7.34 (m, 1H), 7.33 – 7.27 (m, 2H), 6.91 – 6.83 (m, 2H), 5.83 (d, *J* = 2.3 Hz, 1H), 4.34 (dd, *J* = 17.9, 1.9 Hz, 1H), 3.34 (d, *J* = 17.9 Hz, 1H).

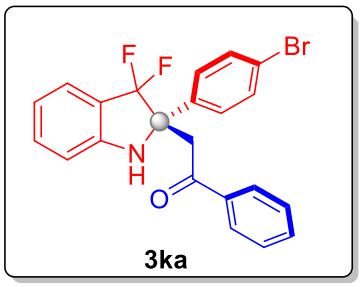
^{13}C NMR (100 MHz, $CDCl_3$) δ 198.1 (d, *J* = 2.0 Hz), 149.4 (dd, *J* = 8.0, 5.0 Hz), 136.7, 136.1 (d, *J* = 6.0 Hz), 133.8, 133.7, 133.1, 128.7, 128.4, 128.02, 127.96, 126.6 (t, *J* = 249.0 Hz), 124.4, 119.9 (dd, *J* = 27.0, 25.0 Hz), 119.5, 111.3, 71.5 (dd, *J* = 27.0, 6.0 Hz), 42.0 (dd, *J* = 10.0, 3.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -84.4 (d, *J* = 248.2 Hz), -107.8 (d, *J* = 248.2 Hz).

HRMS (ESI) *m/z* calcd. for $C_{22}H_{16}ClF_2NO$ $(M+H)^+$:384.0961, found 384.0963.

Enantiomeric excess is 90% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 11.6 min; minor isomer: tr = 8.80 min.

$[\alpha]^{20}_D$ = +169 (c = 0.2, $CHCl_3$).



3ka

(S)-2-(2-(4-bromophenyl)-3,3-difluoroindolin-2-yl)-1-phenylethan-1-one (3ka) According to the general procedure, **3ka** was obtained using 2-(4-bromophenyl)-3,3-difluoro-3H-indole **1k** (15.4 mg, 0.05 mmol) and acetophenone 2a (60.0 mg, 0.5 mmol) in 75% yield (16.1 mg) and 88% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 – 7.83 (m, 2H), 7.59 – 7.55 (m, 1H), 7.46 (m, 7H), 7.36 (t, *J* = 7.8 Hz, 1H), 6.93 – 6.81 (m, 2H), 5.84 (s, 1H), 4.34 (d, *J* = 17.9 Hz, 1H), 3.35 (d, *J* = 17.9 Hz, 1H).

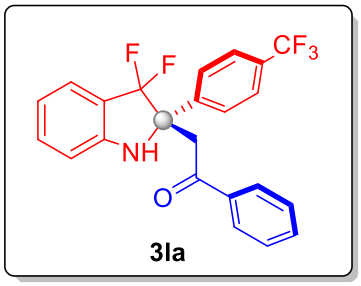
^{13}C NMR (100 MHz, $CDCl_3$) δ 198.0 (d, *J* = 1.0 Hz), 149.4 (dd, *J* = 8.0, 6.0 Hz), 136.7 (d, *J* = 5.0 Hz), 136.6, 133.8, 133.1, 131.3, 128.7, 128.4, 127.9, 126.5 (t, *J* = 249.0 Hz), 124.3, 121.7, 119.8 (t, *J* = 25.0 Hz), 119.5, 111.3, 71.6 (dd, *J* = 28.0, 21.0 Hz), 41.9 (dd, *J* = 9.0, 2.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -84.3 (dd, *J* = 248.2, 11.28 Hz), -107.7 (dd, *J* = 248.2, 15.04 Hz).

HRMS (ESI) *m/z* calcd. for $C_{22}H_{16}BrF_2NO$ $(M+H)^+$:428.0456, found 428.0452.

Enantiomeric excess is 88% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 12.99 min; minor isomer: tr = 9.80 min.

$[\alpha]^{20}_D$ = +277 (c = 0.2, $CHCl_3$).



3la

(S)-2-(3,3-difluoro-2-(4-(trifluoromethyl)phenyl)indolin-2-yl)-1-phenylethan-1-one (3la) According to the general procedure, **3la** was obtained using 3,3-difluoro-2-(4-(trifluoromethyl)phenyl)-3H-indole **1l** (14.9 mg, 0.05 mmol) and acetophenone 2a (60.0 mg, 0.5 mmol) in 86% yield (17.9 mg) and 66% ee as a white solid (silicone alkalized with Et_3N, silica gel

flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 – 7.86 (m, 2H), 7.78 (d, *J* = 8.2 Hz, 2H), 7.64 – 7.55 (m, 3H), 7.50 (d, *J* = 7.6 Hz, 1H), 7.46 – 7.37 (m, 3H), 6.95 – 6.85 (m, 2H), 5.86 (s, 1H), 4.40 (dd, *J* = 18.2, 1.9 Hz, 1H), 3.43 (d, *J* = 18.0 Hz, 1H).

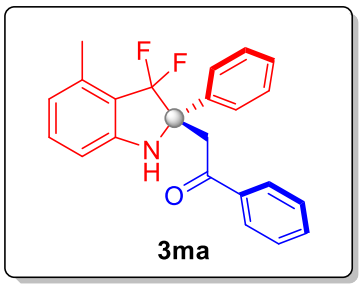
^{13}C NMR (100 MHz, $CDCl_3$) δ 197.9 (d, *J* = 1.0 Hz), 149.3 (dd, *J* = 8.0, 5.0 Hz), 141.7 (d, *J* = 6.0 Hz), 136.4, 134.0, 133.2, 129.8 (q, *J* = 32.0 Hz), 128.7, 127.9, 127.0, 126.6 (t, *J* = 250.0 Hz), 125.2 (q, *J* = 3.2 Hz), 124.4, 124.0 (d, *J* = 270.0 Hz), 119.9 – 119.4 (m), 119.6, 111.4, 71.7 (dd, *J* = 28.0, 21.0 Hz), 42.2 (dd, *J* = 9.0, 2.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.5, -83.7 (d, *J* = 248.2 Hz), -107.7 (d, *J* = 248.2, 7.5 Hz).

HRMS (ESI) *m/z* calcd. for $C_{23}H_{16}F_5NO$ $(M+H)^+$:418.1225, found 418.1219.

Enantiomeric excess is 66% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 7.51 min; minor isomer: tr = 6.83 min.

$[\alpha]^{20}_D$ = +117 (c = 0.2, $CHCl_3$).



3ma

(S)-2-(3,3-difluoro-4-methyl-2-phenylindolin-2-yl)-1-phenylethan-1-one (3ma) According to the general procedure, **3ma** was obtained using 3,3-difluoro-4-methyl-2-phenyl-3H-indole **1m** (12.2 mg, 0.05 mmol) and acetophenone 2a (60.0 mg, 0.5 mmol) in 86% yield (15.6 mg) and 98% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.2 Hz, 2H), 7.51 (d, *J* = 7.6 Hz, 2H), 7.45 (t, *J* = 7.4 Hz, 1H), 7.33 (t, *J* = 7.7 Hz, 2H), 7.24 (t, *J* = 7.4 Hz, 2H), 7.19 – 7.10 (m, 2H), 6.55 (dd, *J* = 11.1, 7.8 Hz, 2H), 5.52 (s, 1H), 4.31 (dd, *J* = 17.8, 1.9 Hz, 1H), 3.27 (d, *J* = 18.0 Hz, 1H), 2.33 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 198.3 (d, *J* = 2.0 Hz), 149.9 (d, *J* = 7.0, 5.0 Hz), 137.6 (d, *J* = 6.0 Hz), 137.2 (d, *J* = 2.0 Hz), 136.8, 133.6, 132.8, 128.6, 128.2, 128.0 (t, *J* = 251.0 Hz), 128.0, 127.6,

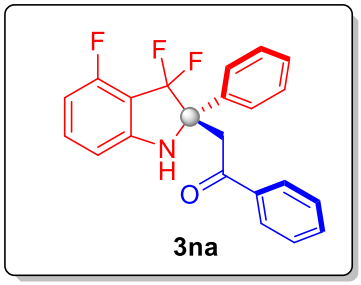
126.5, 121.0, 117.9 (t, J = 24.0 Hz), 108.6, 71.3 (dd, J = 48.0, 21 Hz), 42.2 (dd, J = 10.0, 2.0 Hz), 17.2.

^{19}F NMR (376 MHz, $CDCl_3$) δ-86.5(d, J = 248.2 Hz), -105.2 (d, J = 248.2 Hz).

HRMS (ESI) *m/z* calcd. for $C_{23}H_{19}F_2NO$ $(M+H)^+$:364.1507, found 364.1503.

Enantiomeric excess is 98% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 7.12 min; minor isomer: tr = 8.62 min.

$[\alpha]^{20}_D$ = +178 (c = 0.2, $CHCl_3$).



3na

(S)-1-phenyl-2-(3,3,4-trifluoro-2-phenylindolin-2-yl)ethan-1-one (3na) According to the general procedure, **3na** was obtained using 3,3,4-trifluoro-2-phenyl-3H-indole **1n** (12.4 mg, 0.05 mmol) and acetophenone 2a (60.0 mg, 0.5 mmol) in 85% yield (15.6 mg) and 94% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 6.9 Hz, 2H), 7.63 – 7.55 (m, 3H), 7.44 (t, J = 7.7 Hz, 2H), 7.40 – 7.29 (m, 4H), 6.65 – 6.59 (m, 1H), 6.53 (t, J = 8.7 Hz, 1H), 6.09 (s, 1H), 4.47 (dd, J = 17.9, 1.8 Hz, 1H), 3.40 (d, J = 17.8 Hz, 1H).

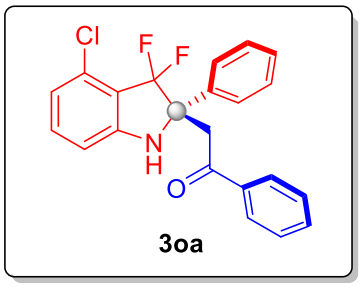
^{13}C NMR (100 MHz, $CDCl_3$) δ 198.1 (d, J = 1.0 Hz), 151.9 (d, J = 252.0 Hz), 151.9 (dd, J = 12.0, 7.0 Hz), 136.8 (d, J = 6.0 Hz), 136.6, 135.0 (d, J = 9.0 Hz), 133.8, 128.7, 128.3, 127.94, 127.87, 126.4, 125.9 (t, J = 250.0 Hz), 107.1 – 106.43 (m) ,106.8 (d, J = 3.0 Hz), 105.9 (d, J = 19.0 Hz), 72.2 (dd, J = 27.0, 22.0 Hz), 41.9 (dd, J = 10.0, 2.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -85.4(d, J = 251.9, 7.5 Hz), -105.0(d, J = 251.9, 7.5 Hz), -117.56 – -117.57 (m).

HRMS (ESI) *m/z* calcd. for $C_{22}H_{16}F_3NO$ $(M+H)^+$:390.1076, found 390.1077.

Enantiomeric excess is 94% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 0.50 mL/min, 254 nm): major isomer: tr = 18.34 min; minor isomer: tr = 17.42 min.

$[\alpha]^{20}_D$ = +178 (c = 0.2, $CHCl_3$).



3oa

(S)-1-phenyl-2-(3,3,4-trifluoro-2-phenylindolin-2-yl)ethan-1-one (3oa) According to the general procedure, **3oa** was obtained using 4-chloro-3,3-difluoro-2-phenyl-3H-indole **1o** (13.2 mg, 0.05 mmol) and acetophenone 2a (60.0 mg, 0.5 mmol) in 88% yield (16.8 mg) and 94% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.0 Hz, 2H), 7.49 – 7.42 (m, 3H), 7.31 (t, *J* = 7.7 Hz, 2H), 7.23 (t, *J* = 7.4 Hz, 2H), 7.19 – 7.11 (m, 2H), 6.69 (d, *J* = 7.9 Hz, 1H), 6.60 (d, *J* = 8.0 Hz, 1H), 5.92 (s, 1H), 4.33 (dd, *J* = 18.0, 1.9 Hz, 1H), 3.25 (d, *J* = 17.5 Hz, 1H).

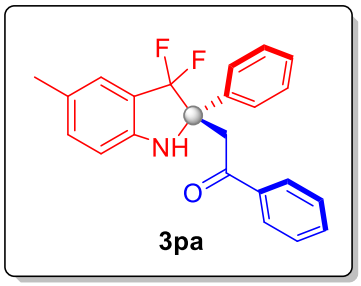
^{13}C NMR (100 MHz, $CDCl_3$) δ 198.1 (d, *J* = 2.0 Hz), 151.4 (dd, *J* = 7.0, 5.0 Hz), 136.8 (d, *J* = 6.0 Hz), 136.6, 134.0, 133.8, 131.8, 128.7, 128.3, 128.0, 127.9, 126.4, 126.2 (t, *J* = 251.0 Hz), 120.0, 116.9 (t, *J* = 24.0 Hz), 109.5, 71.9 (dd, *J* = 27.0, 21.0 Hz), 42.0 (dd, *J* = 10.0, 2.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -87.4(d, *J* = 251.9 Hz), -106.2(d, *J* = 248.2 Hz)

HRMS (ESI) *m/z* calcd. for $C_{22}H_{16}ClF_2NO$ $(M+H)^+$:384.0961, found 384.0966.

Enantiomeric excess is 94% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 0.5 mL/min, 254 nm): major isomer: tr = 19.65 min; minor isomer: tr = 17.13 min.

$[\alpha]^{20}_D$ = +401 (c = 0.2, $CHCl_3$).



3pa

(S)-2-(3,3-difluoro-5-methyl-2-phenylindolin-2-yl)-1-phenylethan-1-one (3pa) According to the

general procedure, **3pa** was obtained using 3,3-difluoro-5-methyl-2-phenyl-3H-indole **1p** (12.2 mg, 0.05 mmol) and acetophenone 2a (60.0 mg, 0.5 mmol) in 89% yield (16.2 mg) and 94% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 – 7.85 (m, 2H), 7.63 (d, *J* = 7.6 Hz, 2H), 7.58 – 7.54 (m, 1H), 7.43 (t, *J* = 7.7 Hz, 2H), 7.35 (t, *J* = 7.4 Hz, 2H), 7.29 (d, *J* = 8.5 Hz, 2H), 7.19 (d, *J* = 8.2 Hz, 1H), 6.79 (d, *J* = 8.1 Hz, 1H), 5.77 (s, 1H), 4.40 (dd, *J* = 17.8, 1.8 Hz, 1H), 3.35 (d, *J* = 17.7 Hz, 1H), 2.34 (s, 3H).

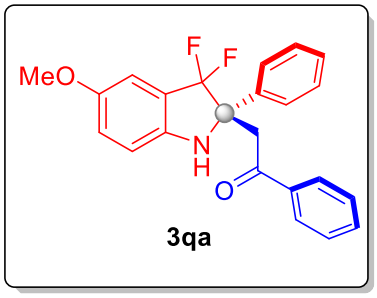
^{13}C NMR (100 MHz, $CDCl_3$) δ 198.3 (d, *J* = 2.0 Hz), 147.4 (dd, *J* = 8.0, 6.0 Hz), 137.6 (d, *J* = 5.0 Hz), 136.9, 133.7, 133.6, 128.8 (t, *J* = 10.0 Hz), 128.6, 128.2, 128.0, 127.6, 126.9 (t, *J* = 249.0 Hz), 126.5, 124.3, 120.2 (t, *J* = 25.0 Hz), 111.2, 72.0 (dd, *J* = 27.0, 21.0 Hz), 42.0 (dd, *J* = 9.0, 2.0 Hz), 20.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ -85.7 (d, *J* = 248.2 Hz), -107.4 (d, *J* = 248.2 Hz).

HRMS (ESI) *m/z* calcd. for $C_{23}H_{19}F_2NO$ $(M+H)^+$:364.1507, found 364.1504.

Enantiomeric excess is 94% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 10.47 min; minor isomer: tr = 8.24 min.

$[\alpha]^{20}_D$ = +206 (c = 0.2, $CHCl_3$).



3qa

(S)-2-(3,3-difluoro-5-methoxy-2-phenylindolin-2-yl)-1-phenylethan-1-one (3qa) According to the general procedure, **3qa** was obtained using 3,3-difluoro-5-methoxy-2-phenyl-3H-indole **1q** (13.0 mg, 0.05 mmol) and acetophenone 2a (60.0 mg, 0.5 mmol) in 85% yield (16.1 mg) and 94% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 60:1:1.2). R_f = 0.20 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 – 7.83 (m, 2H), 7.63 (d, *J* = 7.5 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.35 (t, *J* = 7.5 Hz, 2H), 7.29 (dd, *J* = 6.4, 0.9 Hz, 1H), 7.04 (s, 1H), 7.00 (d, *J* = 8.9 Hz, 1H), 6.83 (d, *J* = 8.6 Hz, 1H), 5.31 (s, 1H), 4.39 (dd, *J* = 17.6, 1.8 Hz, 1H), 3.81 (s, 3H), 3.35 (d, *J* = 17.6 Hz, 1H).

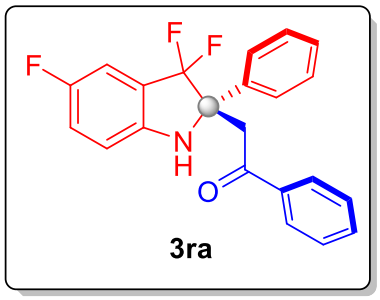
^{13}C NMR (100 MHz, $CDCl_3$) δ 198 (d, *J* = 7.5 Hz), 153.6, 143.7 (dd, *J* = 9.0, 6.0 Hz), 137.5 (d, *J* = 5.0 Hz), 136.9, 133.6, 128.6, 128.2, 128.0, 127.7, 126.9 (d, *J* = 250 Hz), 126.6, 120.7 (dd, *J* = 26.0, 25.0 Hz), 120.5, 112.6, 108.4, 72.4 (dd, *J* = 28.0, 21.0 Hz), 56.0, 42.0 (dd, *J* = 9.0, 2.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -86.3 (d, *J* = 244.4 Hz), -107.6 (d, *J* = 248.2 Hz).

HRMS (ESI) *m/z* calcd. for $C_{23}H_{19}F_2NO_2$ $(M+H)^+$:380.1457, found 382.1453.

Enantiomeric excess is 94% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 12.45 min; minor isomer: tr = 11.26 min.

$[\alpha]^{20}_D$ = +160 (c = 0.2, $CHCl_3$).



(S)-1-phenyl-2-(3,3,5-trifluoro-2-phenylindolin-2-yl)ethan-1-one (3ra) According to the general procedure, **3ra** was obtained using 3,3,5-trifluoro-2-phenyl-3H-indole **1r** (12.4 mg, 0.05 mmol) and acetophenone 2a (60.0 mg, 0.5 mmol) in 87% yield (16.4 mg) and 92% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 – 7.83 (m, 2H), 7.62 (dd, J = 7.4, 1.7 Hz, 2H), 7.58 – 7.54 (m, 1H), 7.43 (t, J = 7.8 Hz, 2H), 7.39 – 7.32 (m, 2H), 7.32 – 7.26 (m, 1H), 7.19 (dd, J = 7.5, 1.4 Hz, 1H), 7.09 (t, J = 8.9 Hz, 1H), 6.85 – 6.73 (m, 1H), 5.81 (s, 1H), 4.40 (d, J = 17.7 Hz, 1H), 3.33 (d, J = 17.7 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 198.2 (d, *J* = 2.0 Hz), 156.5 (d, *J* = 237.0 Hz), 145.8 (t, *J* = 7.0 Hz), 137.0 (d, *J* = 5.0 Hz), 136.7, 133.7, 128.6, 128.3, 127.9, 127.8, 126.5, 126.2 (t, *J* = 250.0 Hz), 121.1

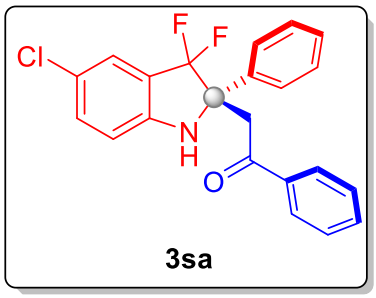
– 120.5 (m), 120.1 (d, *J* = 23.0 Hz), 112.2 (d, *J* = 8.0 Hz), 111.0 (d, *J* = 24.0 Hz), 72.5 (dd, *J* = 27.0, 21.0 Hz), 41.8 (dd, *J* = 9.0, 2.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -86.1(d, *J* = 248.2, 7.5 Hz), -107.5(d, *J* = 248.2, 7.5 Hz), -124.30(d, *J* = 3.8 Hz).

HRMS (ESI) *m/z* calcd. for $C_{22}H_{16}F_3NO$ $(M+H)^+$:368.1257, found 368.1255.

Enantiomeric excess is 92% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 9.85 min; minor isomer: tr = 8.06 min.

$[\alpha]^{20}_D$ = +251 (c = 0.2, $CHCl_3$).



(S)-2-(5-chloro-3,3-difluoro-2-phenylindolin-2-yl)-1-phenylethan-1-one (3sa) According to the general procedure, **3sa** was obtained using 5-chloro-3,3-difluoro-2-phenyl-3H-indole **1s** (13.2 mg, 0.05 mmol) and acetophenone 2a (60.0 mg, 0.5 mmol) in 89% yield (17.1 mg) and 92% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.8 Hz, 2H), 7.58 (dd, *J* = 20.0, 7.5 Hz, 3H), 7.47 – 7.40 (m, 3H), 7.39 – 7.25 (m, 4H), 6.78 (d, *J* = 8.6 Hz, 1H), 5.98 (s, 1H), 4.41 (d, *J* = 17.7 Hz, 1H), 3.34 (d, *J* = 17.7 Hz, 1H).

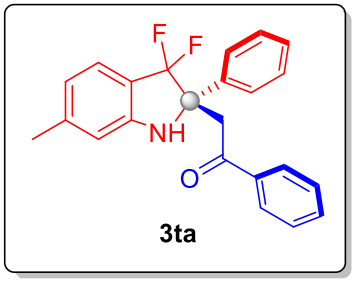
^{13}C NMR (100 MHz, $CDCl_3$) δ 198.1 (d, *J* = 1.0 Hz), 148.1 (dd, *J* = 8.0, 5.0 Hz), 136.9 (d, *J* = 5.0 Hz), 136.7, 133.7, 133.0, 128.6, 128.3, 127.93, 127.85, 126.4, 125.9 (t, *J* = 250.0 Hz), 124.3, 123.7 (t, *J* = 2.0 Hz), 121.5 (t, *J* = 25.0 Hz), 112.3, 72.3 (dd, *J* = 27.0, 21.0 Hz), 41.7 (dd, *J* = 9.0, 2.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -85.9 (d, *J* = 248.2 Hz), -106.9 (d, *J* = 248.2 Hz)

HRMS (ESI) *m/z* calcd. for $C_{22}H_{16}ClF_2NO$ $(M+Na)^+$:406.0781, found 406.0784.

Enantiomeric excess is 92% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 10.595 min; minor isomer: tr = 8.62 min.

$[\alpha]^{20}_D$ = +295 (c = 0.2, $CHCl_3$).



3ta

(S)-2-(3,3-difluoro-6-methyl-2-phenylindolin-2-yl)-1-phenylethan-1-one (3ta) According to the general procedure, **3ta** was obtained using 3,3-difluoro-6-methyl-2-phenyl-3H-indole **1d** (12.2 mg, 0.05 mmol) and acetophenone 2a (60.0 mg, 0.5 mmol) in 82% yield (14.9 mg) and 82% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 – 7.80 (m, 2H), 7.60 – 7.53 (m, 3H), 7.45 – 7.39 (m, 2H), 7.36 – 7.29 (m, 3H), 7.26 (d, *J* = 3.9 Hz, 1H), 6.71 – 6.64 (m, 2H), 5.77 (s, 1H), 4.37 (dd, *J* = 17.8, 1.9 Hz, 1H), 3.33 (dt, *J* = 17.9, 1.3 Hz, 1H), 2.34 (s, 3H).

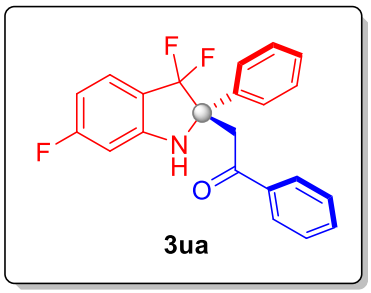
^{13}C NMR (100 MHz, $CDCl_3$) δ 198.4, 149.9 (dd, *J* = 9.0, 7.0 Hz), 143.7, 137.6 (d, *J* = 5.0 Hz), 136.8, 133.6, 128.6, 128.2, 128.0, 127.7, 126.8 (t, *J* = 250.0 Hz), 126.5, 124.1, 120.4, 117.4 (d, *J* = 5.0 Hz), 111.7, 72.9 (dd, *J* = 28.0, 21.0 Hz), 42.2 (dd, *J* = 9.0, 2.0 Hz), 21.9.

^{19}F NMR (376 MHz, $CDCl_3$) δ -84.9 (d, *J* = 244.4 Hz), -106.9 (d, *J* = 244.4 Hz).

HRMS (ESI) *m/z* calcd. for $C_{23}H_{19}F_2NO$ $(M+H)^+$:364.1507, found 364.1517.

Enantiomeric excess is 82% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 11.75 min; minor isomer: tr = 7.90 min.

$[\alpha]^{20}_D$ = +122 (c = 0.2, $CHCl_3$).



3ua

(S)-1-phenyl-2-(3,3,6-trifluoro-2-phenylindolin-2-yl)ethan-1-one (3ua) According to the general procedure, **3ua** was obtained using 3,3,6-trifluoro-2-phenyl-3H-indole **1u** (12.4 mg, 0.05 mmol) and acetophenone 2a (60.0 mg, 0.5 mmol) in 90% yield (16.9 mg) and 90% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 – 7.76 (m, 2H), 7.49 – 7.45 (m, 3H), 7.36 – 7.29 (m, 3H), 7.24 (dd, *J* = 8.3, 6.5 Hz, 2H), 7.20 – 7.16 (m, 1H), 6.48 – 6.42 (m, 2H), 5.92 (s, 1H), 4.31 (dd, *J* = 17.9, 1.8 Hz, 1H), 3.24 (d, *J* = 17.9 Hz, 1H).

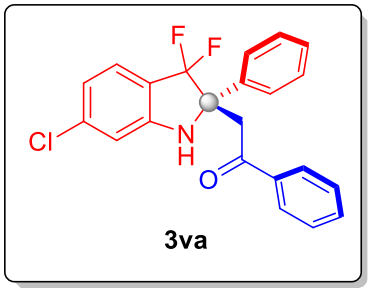
^{13}C NMR (100 MHz, $CDCl_3$) δ 198.2 (d, *J* = 2.0 Hz), 166.5 (d, *J* = 247.0 Hz), 151.4(d, *J* = 7.0 Hz), 137.0 (d, *J* = 5.0 Hz), 136.7, 133.8, 128.7, 128.3, 128.0, 127.9, 126.4, 126.0 (d, *J* = 11.0 Hz), 125.9 (t, *J* = 248.0 Hz), 116.0 (t, *J* = 24.0 Hz), 106.5 (d, *J* = 24.0 Hz), 98.4 (d, *J* = 26.0 Hz), 72.5 (dd, *J* = 27.0, 21.0 Hz), 42.0 (dd, *J* = 9.0, 2.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -84.6 (d, *J* = 248.2, 3.8 Hz), -105.8 (d, *J* = 244.4, 3.8 Hz), -106.91.

HRMS (ESI) *m/z* calcd. for $C_{22}H_{16}F_3NO$ $(M+H)^+$:368.1257, found 368.1251.

Enantiomeric excess is 90% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 10.19 min; minor isomer: tr = 9.00 min.

$[\alpha]^{20}_D$ = 217 (c = 0.2, $CHCl_3$).



3va

(S)-2-(6-chloro-3,3-difluoro-2-phenylindolin-2-yl)-1-phenylethan-1-one (3va) According to the general procedure, **3va** was obtained using 6-chloro-3,3-difluoro-2-phenyl-3H-indole **1v** (13.2 mg, 0.05 mmol) and acetophenone 2a (60.0 mg, 0.5 mmol) in 84% yield (16.1 mg) and 80% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.3 Hz, 2H), 7.68 – 7.65 (m, 3H), 7.43 (t, *J* = 7.8 Hz, 2H), 7.35 (dd, *J* = 13.3, 8.0 Hz, 3H), 7.29 (d, *J* = 7.3 Hz, 1H), 6.83 (dd, *J* = 3.4, 1.7 Hz, 2H), 6.00 (s, 1H), 4.40 (d, *J* = 17.5 Hz, 1H), 3.32 (d, *J* = 17.8 Hz, 1H).

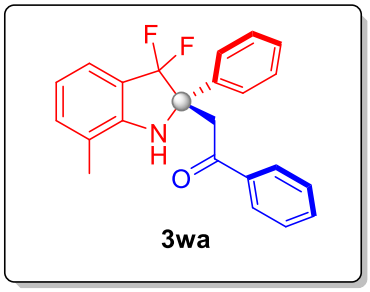
^{13}C NMR (100 MHz, $CDCl_3$) δ 198.1 (d, *J* = 2.0 Hz), 150.6 (dd, *J* = 7.0, 5.0 Hz), 139.0, 136.9 (d, *J* = 6.0 Hz), 136.7, 133.8, 128.7, 128.3, 128.0, 127.9, 126.4, 125.9 (t, *J* = 249.0 Hz), 125.4, 119.4, 118.6 (t, *J* = 26.0 Hz), 111.3, 72.2 (dd, *J* = 27.0, 22.0 Hz), 41.9 (dd, *J* = 10.0, 2.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ-85.6 (d, *J* = 248.2 Hz), -106.4 (d, *J* = 248.2 Hz).

HRMS (ESI) *m/z* calcd. for $C_{22}H_{16}ClF_2NO$ $(M+Na)^+$:406.0781, found 406.0778.

Enantiomeric excess is 80% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 10.38 min; minor isomer: tr = 8.76 min.

$[\alpha]^{20}_D$ = +261 (c = 0.2, $CHCl_3$).



3wa

(S)-2-(3,3-difluoro-7-methyl-2-phenylindolin-2-yl)-1-phenylethan-1-one (3wa) According to the general procedure, **3wa** was obtained using 3,3-difluoro-7-methyl-2-phenyl-3H-indole **1w** (12.2 mg, 0.05 mmol) and acetophenone 2a (60.0 mg, 0.5 mmol) in 87% yield (15.8 mg) and 20% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 80:1:1). R_f = 0.30 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.4 Hz, 2H), 7.53 (d, *J* = 8.2 Hz, 2H), 7.44 (t, *J* = 7.4 Hz, 1H), 7.31 (t, *J* = 7.7 Hz, 2H), 7.24 (t, *J* = 7.6 Hz, 3H), 7.18 – 7.14 (m, 1H), 7.09 (d, *J* = 7.5 Hz, 1H), 6.72 (t, *J* = 7.5 Hz, 1H), 5.67 (s, 1H), 4.29 (d, *J* = 17.7 Hz, 1H), 3.21 (d, *J* = 17.6 Hz, 1H), 2.18 (s, 3H).

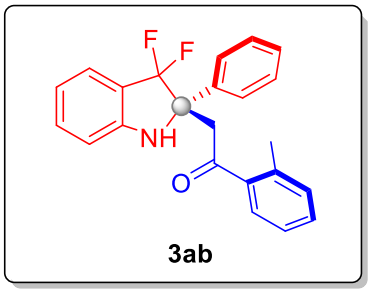
^{13}C NMR (100 MHz, $CDCl_3$) δ 198.5, 148.3 (dd, *J* = 8.0, 6.0 Hz), 137.4 (d, *J* = 6.0 Hz), 136.8, 133.7, 133.5, 128.6, 128.2, 128.0, 127.7, 127.1 (dd, *J* = 250.0 Hz), 126.5, 121.6, 120.6, 119.6 – 119.1 (m), 119.4, 71.8 (dd, *J* = 28.0, 21.0 Hz), 42.1 (dd, *J* = 9.0, 2.0 Hz), 16.2.

^{19}F NMR (376 MHz, $CDCl_3$) δ -85.1 (d, *J* = 244.4 Hz), -106.8 (d, *J* = 248.2 Hz).

HRMS (ESI) *m/z* calcd. for $C_{23}H_{19}F_2NO$ $(M+H)^+$:364.1507, found 364.1514.

Enantiomeric excess is 20% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 9.42 min; minor isomer: tr = 8.58 min.

$[\alpha]^{20}_D$ = +33 (c = 0.2, $CHCl_3$).



3ab

(S)-2-(3,3-difluoro-2-phenylindolin-2-yl)-1-(o-tolyl)ethan-1-one (3ab) According to the general procedure, **3ab** was obtained using 3,3-difluoro-2-phenyl-3H-indole **1a** (11.5 mg, 0.05 mmol) and 1-(o-tolyl)ethan-1-one **2b** (67.1 mg, 0.5 mmol) in 90% yield (16.4 mg) and 86% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 – 7.46 (m, 2H), 7.44 – 7.35 (m, 2H), 7.31 – 7.12 (m, 6H), 7.07 (d, *J* = 7.6 Hz, 1H), 6.86 – 6.75 (m, 2H), 6.07 – 5.75 (m, 1H), 4.16 (dd, *J* = 17.1, 2.0 Hz, 1H), 3.15 (d, *J* = 17.1 Hz, 1H), 2.04 (s, 3H).

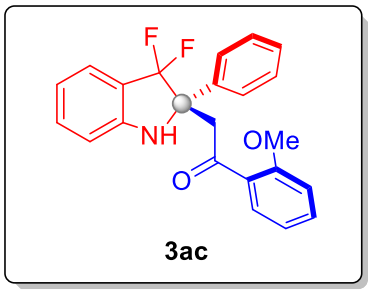
^{13}C NMR (100 MHz, $CDCl_3$) δ 203.1, 149.5 (dd, *J* = 8.0, 5.0 Hz), 138.3, 137.9, 137.3 (d, *J* = 10.0 Hz), 133.0, 131.9, 131.6, 128.2, 128.0, 127.7, 126.7, 126.6 (t, *J* = 249.0 Hz), 125.7, 124.3, 120.2 (dd, *J* = 26.0, 25.0 Hz), 119.3, 111.4, 72.2 (dd, *J* = 27.0, 21.0 Hz), 44.8 (dd, *J* = 9.0. 2.0 Hz), 20.6.

^{19}F NMR (376 MHz, $CDCl_3$) δ -85.6(d, *J* = 248.2 Hz), -107.1 (d, *J* = 248.2 Hz).

HRMS (ESI) *m/z* calcd. for $C_{23}H_{19}F_2NO$ $(M+H)^+$:364.1507, found 365.1549.

Enantiomeric excess is 86% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 6.76 min; minor isomer: tr = 6.29 min.

$[\alpha]^{20}_D$ = +98 (c = 0.2, $CHCl_3$).



3ac

(S)-2-(3,3-difluoro-2-phenylindolin-2-yl)-1-(2-methoxyphenyl)ethan-1-one (3ac) According to the general procedure, **3ac** was obtained using 3,3-difluoro-2-phenyl-3H-indole **1a** (11.5 mg, 0.05 mmol) and 1-(2-methoxyphenyl)ethan-1-one **2c** (76.1 mg, 0.5 mmol) in 84% yield (15.9 mg) and 92% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 70:1:1.5). R_f = 0.30 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 7.9 Hz, 2H), 7.48 – 7.40 (m, 3H), 7.37 – 7.32 (m, 3H), 7.30 – 7.26 (m, 1H), 6.97 – 6.90 (m, 2H), 6.90 – 6.84 (m, 2H), 5.91 (s, 1H), 4.46 (d, *J* = 18.2 Hz, 1H), 3.91 (s, 3H), 3.35 (d, *J* = 18.1 Hz, 1H).

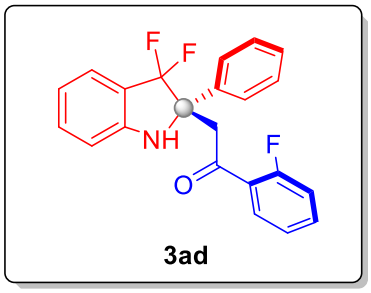
^{13}C NMR (100 MHz, $CDCl_3$) δ 200.7 (d, *J* = 2.0 Hz), 158.6, 149.7 (dd, *J* = 13.0, 5.0 Hz), 137.7 (d, *J* = 5.0 Hz), 134.0, 132.9, 130.0, 128.1, 128.0, 127.5, 126.7,126.7 (t, *J* = 249.0 Hz), 124.3, 120.6, 120.2 (t, *J* = 25.0 Hz), 119.0, 111.5, 111.2, 72.1 (dd, *J* = 27.0, 21.0 Hz), 55.5, 47.2 (d, *J* = 10.0, 2.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -84.9 (d, *J* = 248.2 Hz), -107.4 (d, *J* = 248.2 Hz).

HRMS (ESI) *m/z* calcd. for $C_{23}H_{19}F_2NO_2$ $(M+H)^+$:380.1457, found 380.1456.

Enantiomeric excess is 92% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 0.5 mL/min, 254 nm): major isomer: tr = 21.02 min; minor isomer: tr = 23.67 min.

$[\alpha]^{20}_D$ = +280 (c = 0.2, $CHCl_3$).



3ad

(S)-2-(3,3-difluoro-2-phenylindolin-2-yl)-1-(2-fluorophenyl)ethan-1-one (3ad) According to the

general procedure, **3ad** was obtained using 3,3-difluoro-2-phenyl-3H-indole **1a** (11.5 mg, 0.05 mmol) and 1-(2-fluorophenyl)ethan-1-one **2d** (69.1 mg, 0.5 mmol) in 92% yield (17.3 mg) and 96% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (td, *J* = 7.6, 1.8 Hz, 3H), 7.41 – 7.34 (m, 2H), 7.27 – 7.22 (m, 3H), 7.19 – 7.14 (m, 1H), 7.05 – 6.98 (m, 2H), 6.79 – 6.73 (m, 2H), 5.65 (s, 1H), 4.27 (d, *J* = 18.5 Hz, 1H), 3.31 (dd, *J* = 18.4, 1.4 Hz, 1H).

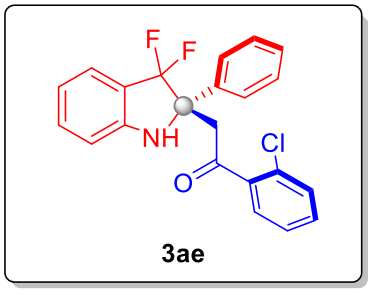
^{13}C NMR (100 MHz, $CDCl_3$) δ 196.8 (dd, *J* = 3.0, 1.0 Hz), 161.8 (d, *J* = 253.0 Hz), 149.6 (dd, *J* = 8.0, 6.0 Hz), 137.5 (d, *J* = 6.0 Hz), 135.1 (d, *J* = 9.0 Hz), 133.0, 130.3 (d, *J* = 3.0 Hz), 128.2, 127.7, 126.5, 126.5 (t, *J* = 249.0 Hz), 125.7 (d, *J* = 12.0 Hz), 124.5 (d, *J* = 3.0 Hz), 124.4, 120.1 (dd, *J* = 51.0, 25.0 Hz), 119.2, 116.7 (d, *J* = 24.0 Hz), 111.1, 71.8 (dd, *J* = 28.0, 21.0 Hz), 47.2 – 47.0 (m).

^{19}F NMR (376 MHz, $CDCl_3$) δ (d, *J* = 248.2, 3.8 Hz), -106.9 (d, *J* = 248.2 Hz), -108.5.

HRMS (ESI) *m/z* calcd. for $C_{22}H_{16}F_3NO$ $(M+H)^+$:368.1257, found 368.1255.

Enantiomeric excess is 96% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 0.5 mL/min, 254 nm): major isomer: tr = 12.84 min; minor isomer: tr = 12.06 min.

$[\alpha]^{20}_D$ = +307 (c = 0.2, $CHCl_3$).



3ae

(S)-1-(2-chlorophenyl)-2-(3,3-difluoro-2-phenylindolin-2-yl)ethan-1-one (3ae) According to the general procedure, **3ae** was obtained using 3,3-difluoro-2-phenyl-3H-indole **1a** (11.5 mg, 0.05 mmol) and 1-(2-chlorophenyl)ethan-1-one **2e** (72.8 mg, 0.5 mmol) in 87% yield (11.4 mg) and 90% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.43 (m, 2H), 7.36 (d, *J* = 7.6 Hz, 1H), 7.31 – 7.16 (m, 6H), 7.09 – 7.06 (m, 1H), 6.93 – 6.75 (m, 3H), 5.87 – 5.70 (m, 1H), 4.18 (dd, *J* = 16.9, 1.9 Hz, 1H), 3.20 (d, *J* = 16.9 Hz, 1H).

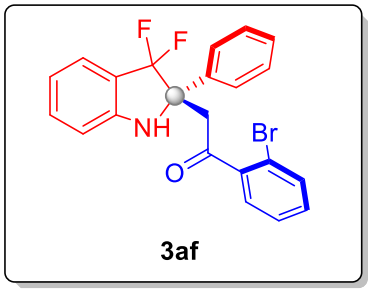
^{13}C NMR (100 MHz, $CDCl_3$) δ 202.3, 149.4 (dd, *J* = 8.0, 6.0 Hz), 139.4, 136.9 (d, *J* = 6.0 Hz), 133.1, 132.0, 130.6, 130.4, 128.6, 128.2, 127.9, 126.8, 126.7, 126.4 (t, *J* = 250.0 Hz), 124.3, 120.2 (dd, *J* = 26.0, 24.0 Hz), 119.5, 111.5, 72.2 (dd, *J* = 28.0, 22.0 Hz), 46.9 (dd, *J* = 10.0, 3.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -85.2 (d, *J* = 248.2 Hz), -107.0 (d, *J* = 248.2 Hz).

HRMS (ESI) *m/z* calcd. for $C_{22}H_{16}ClF_2NO$ $(M+Na)^+$:406.0781, found 406.0773.

Enantiomeric excess is 90% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 7.10 min; minor isomer: tr = 7.51 min.

$[\alpha]^{20}_D$ = +194 (c = 0.2, $CHCl_3$).



(S)-1-(2-bromophenyl)-2-(3,3-difluoro-2-phenylindolin-2-yl)ethan-1-one (3af) According to the general procedure, **3af** was obtained using 3,3-difluoro-2-phenyl-3H-indole **1a** (11.5 mg, 0.05 mmol) and 1-(2-bromophenyl)ethan-1-one **2f** (100 mg, 0.5 mmol) in 84% yield (18.0mg) and 94% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 – 7.61 (m, 2H), 7.51 – 7.44 (m, 4H), 7.37 (d, *J* = 7.9 Hz, 1H), 7.29 – 7.22 (m, 3H), 7.20 – 7.16 (m, 1H), 6.84 – 6.73 (m, 2H), 5.65 (s, 1H), 4.24 (dd, *J* = 17.7, 1.8 Hz, 1H), 3.20 (dt, *J* = 17.7, 1.3 Hz, 1H).

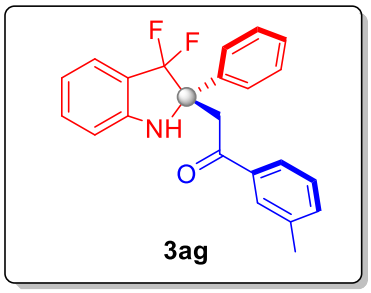
^{13}C NMR (100 MHz, $CDCl_3$) δ 197.3 (d, *J* = 2.0 Hz), 149.5 (dd, *J* = 8.0, 6.0 Hz), 137.2 (d, *J* = 6.0 Hz), 135.5, 133.1, 132.0, 129.5, 129.0, 128.3, 127.8, 126.7 (d, *J* = 249.0 Hz), 126.4, 124.4, 120.0 (dd, *J* = 26.0, 25.0 Hz), 119.4, 111.2, 71.7 (dd, *J* = 28.0, 21.0 Hz), 42.0 (dd, *J* = 10.0, 2.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -85.5 (d, *J* = 248.2 Hz), -106.9 (d, *J* = 248.2 Hz).

HRMS (ESI) *m/z* calcd. for $C_{22}H_{16}BrF_2NO$ $(M+Na)^+$:450.0276, found 450.0270.

Enantiomeric excess is 94% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 7.41 min; minor isomer: tr = 8.01 min.

$[\alpha]^{20}_D$ = +114 (c = 0.2, $CHCl_3$).



(S)-2-(3,3-difluoro-2-phenylindolin-2-yl)-1-(m-tolyl)ethan-1-one (3ag) According to the general procedure, **3ag** was obtained using 3,3-difluoro-2-phenyl-3H-indole **1a** (11.5 mg, 0.05 mmol) and 1-(m-tolyl)ethan-1-one **2g** (67.1 mg, 0.5 mmol) in 95% yield (17.3 mg) and 92% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.2 Hz, 2H), 7.61 (d, *J* = 7.7 Hz, 2H), 7.47 (d, *J* = 7.7 Hz, 1H), 7.34 (m, 5H), 7.28 (dd, *J* = 7.3, 1.3 Hz, 1H), 6.90 – 6.81 (m, 2H), 5.89 (s, 1H), 4.38 (dt, *J* = 17.8, 1.9 Hz, 1H), 3.33 (dt, *J* = 17.9, 1.4 Hz, 1H), 2.38 (s, 3H).

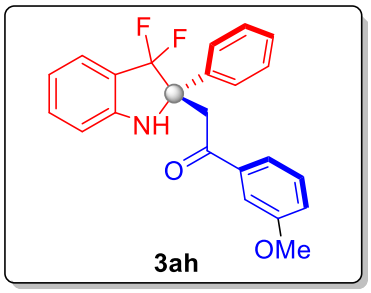
^{13}C NMR (100 MHz, $CDCl_3$) δ 198.5 (d, *J* = 2.0 Hz), 149.7 (dd, *J* = 7.0, 5.0 Hz), 138.5, 137.4 (d, *J* = 5.0 Hz), 136.9, 134.4, 133.0, 128.5, 128.5, 128.2, 127.7, 126.8 (t, *J* = 249.0 Hz), 126.5, 125.2, 124.3, 120.3 (t, *J* = 25.0 Hz), 119.2, 111.2, 71.8 (dd, *J* = 27.0, 21.0 Hz), 42.1 (dd, *J* = 9.0, 2.0 Hz), 21.26.

^{19}F NMR (376 MHz, $CDCl_3$) δ -84.97 – -85.65 (m), -107.02 – -107.70 (m).

HRMS (ESI) *m/z* calcd. for $C_{23}H_{19}F_2NO$ $(M+Na)^+$:386.1327, found 386.1334.

Enantiomeric excess is 92% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 0.5 mL/min, 254 nm): major isomer: tr = 14.39 min; minor isomer: tr = 12.4 min.

$[\alpha]^{20}_D$ = +342 (c = 0.2, $CHCl_3$).



(S)-2-(3,3-difluoro-2-phenylindolin-2-yl)-1-(3-methoxyphenyl)ethan-1-one (3ah) According to the general procedure, **3ah** was obtained using 3,3-difluoro-2-phenyl-3H-indole **1a** (11.5 mg, 0.05 mmol) and 1-(3-methoxyphenyl)ethan-1-one **2h** (76.1 mg, 0.5 mmol) in 90% yield (17.1 mg) and 94% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 70:1:1.5). R_f = 0.30 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.4 Hz, 2H), 7.39 – 7.35 (m, 2H), 7.27 – 7.21 (m, 5H), 7.19 – 7.15 (m, 1H), 7.01 – 6.98 (m, 1H), 6.80 – 6.74 (m, 2H), 5.75 (s, 1H), 4.27 (dd, *J* = 17.9, 1.8 Hz, 1H), 3.70 (s, 3H), 3.27 – 3.20 (m, 1H).

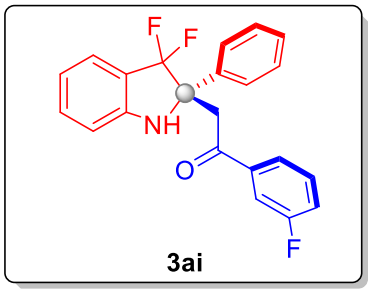
^{13}C NMR (100 MHz, $CDCl_3$) δ 198.1 (d, *J* = 2.0 Hz), 159.8, 149.6 (dd, *J* = 8.0, 5.0 Hz), 138.2, 137.4 (d, *J* = 6.0 Hz), 133.0, 129.6, 128.2, 127.7, 126.7 (t, *J* = 250.0 Hz), 126.5, 124.3, 120.6, 120.2, 120.1 (dd, *J* = 26.0, 25.0 Hz), 119.2, 112.1, 111.2, 71.8 (dd, *J* = 27.0, 21.0 Hz), 55.4, 42.2 (dd, *J* = 9.0, 2.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -85.3(d, *J* = 248.2 Hz), -107.3 (d, *J* = 244.4 Hz).

HRMS (ESI) *m/z* calcd. for $C_{23}H_{19}F_2NO_2$ $(M+Na)^+$:402.1276, found 402.1275.

Enantiomeric excess is 94% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 0.5 mL/min, 254 nm): major isomer: tr = 17.96 min; minor isomer: tr = 14.26 min.

$[\alpha]^{20}_D$ = +326 (c = 0.2, $CHCl_3$).



(S)-2-(3,3-difluoro-2-phenylindolin-2-yl)-1-(3-fluorophenyl)ethan-1-one (3ai) According to the

general procedure, **3ai** was obtained using 3,3-difluoro-2-phenyl-3H-indole **1a** (11.5 mg, 0.05 mmol) and 1-(3-fluorophenyl)ethan-1-one **2i** (69.1 mg, 0.5 mmol) in 93% yield (17.5 mg) and 96% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.8 Hz, 1H), 7.48 (d, *J* = 7.7 Hz, 2H), 7.41 (d, *J* = 9.3 Hz, 1H), 7.36 (d, *J* = 7.7 Hz, 1H), 7.31 – 7.21 (m, 4H), 7.20 – 7.12 (m, 2H), 6.76 (q, *J* = 7.5 Hz, 2H), 5.70 (s, 1H), 4.24 (dd, *J* = 17.8, 1.8 Hz, 1H), 3.22 (d, *J* = 17.8 Hz, 1H).

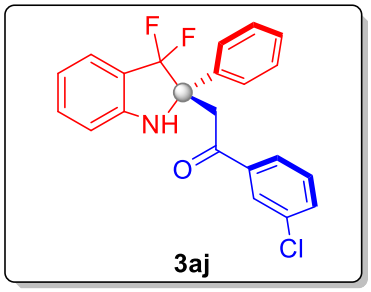
^{13}C NMR (100 MHz, $CDCl_3$) δ 197.1, 163.7 (d, *J* = 247.0 Hz), 149.5 (dd, *J* = 8.0, 6.0 Hz), 138.8 (d, *J* = 6.0 Hz), 137.2 (d, *J* = 6.0 Hz), 133.1, 130.3 (d, *J* = 8.0 Hz), 128.28, 127.8, 126.6 (t, *J* = 250.0 Hz), 126.5, 124.4, 123.8 (d, *J* = 3.0 Hz), 120.7 (d, *J* = 21.0 Hz), 120.0 (t, *J* = 25.0 Hz), 119.3, 114.7 (d, *J* = 23.0 Hz), 111.2, 71.7 (dd, *J* = 28.0, 21.0 Hz), 42.3 (dd, *J* = 10.0, 2.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ-85.6(d, *J* = 248.2 Hz), -106.8 (d, *J* = 248.2 Hz), -111.29.

HRMS (ESI) *m/z* calcd. for $C_{22}H_{16}F_3NO$ $(M+Na)^+$:368.1257, found 368.1264.

Enantiomeric excess is 96% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 0.5 mL/min, 254 nm): major isomer: tr = 14.54 min; minor isomer: tr = 11.70 min.

$[\alpha]^{20}_D$ = +366 (c = 0.2, $CHCl_3$).



3aj

(S)-1-(3-chlorophenyl)-2-(3,3-difluoro-2-phenylindolin-2-yl)ethan-1-one (3aj) According to the general procedure, **3aj** was obtained using 3,3-difluoro-2-phenyl-3H-indole **1a** (11.5 mg, 0.05 mmol) and 1-(3-chlorophenyl)ethan-1-one **2j** (72.8 mg, 0.5 mmol) in 93% yield (17.8 mg) and 96% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (t, *J* = 1.9 Hz, 1H), 7.66 (dt, *J* = 7.9, 1.4 Hz, 1H), 7.52 – 7.47 (m, 2H), 7.45 – 7.43 (m, 1H), 7.38 (d, *J* = 7.5 Hz, 1H), 7.31 – 7.24 (m, 4H), 7.21 – 7.18 (m, 1H),

6.83 – 6.75 (m, 2H), 5.69 (s, 1H), 4.25 (dd, *J* = 17.8, 1.8 Hz, 1H), 3.24 (dt, *J* = 17.9, 1.3 Hz, 1H).

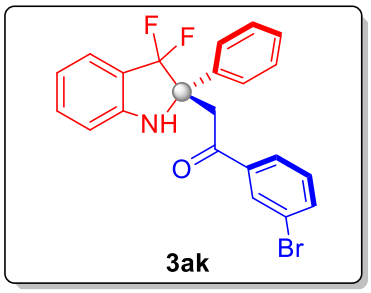
^{13}C NMR (100 MHz, $CDCl_3$) δ 197.1, 149.5 (dd, *J* = 8.0, 6.0 Hz), 138.3, 137.2 (d, *J* = 6.0 Hz), 135.0, 133.6, 133.1, 130.0, 128.3, 128.1, 127.8, 126.6 (t, *J* = 249.0 Hz), 126.5, 126.1, 124.4, 120.0 (t, *J* = 26.0 Hz), 119.4, 111.2, 71.7 (dd, *J* = 28.0, 22.0 Hz), 42.3 (dd, *J* = 10.0, 2.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -85.6 (d, *J* = 244.4 Hz), -106.7 (d, *J* = 248.2 Hz).

HRMS (ESI) *m/z* calcd. for $C_{22}H_{16}ClF_2NO$ $(M+H)^+$:384.0961, found 384.0968.

Enantiomeric excess is 96% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 0.5 mL/min, 254 nm): major isomer: tr = 14.54 min; minor isomer: tr = 12.69 min.

$[\alpha]^{20}_D$ = +226 (c = 0.2, $CHCl_3$).



(S)-1-(3-bromophenyl)-2-(3,3-difluoro-2-phenylindolin-2-yl)ethan-1-one (3ak) According to the general procedure, **3ak** was obtained using 3,3-difluoro-2-phenyl-3H-indole **1a** (11.5 mg, 0.05 mmol) and 1-(3-bromophenyl)ethan-1-one **2k** (100 mg, 0.5 mmol) in 84% yield (18.0 mg) and 94% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (t, *J* = 1.8 Hz, 1H), 7.76 – 7.68 (m, 1H), 7.61 – 7.58 (m, 1H), 7.54 – 7.46 (m, 2H), 7.38 (d, *J* = 7.5 Hz, 1H), 7.30 – 7.18 (m, 5H), 6.79 (td, *J* = 7.7, 6.3 Hz, 2H), 5.68 (s, 1H), 4.24 (dd, *J* = 17.9, 1.8 Hz, 1H), 3.24 (dt, *J* = 17.8, 1.3 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 197.0 (d, *J* = 1.0 Hz), 149.5 – 149.4 (m), 138.5, 137.2 (d, *J* = 6.0 Hz), 136.5, 133.1, 131.0, 130.2, 128.3, 127.8, 126.6 (t, *J* = 250.0 Hz), 126.5, 126.5, 124.4, 123.0, 120.2 (t, *J* = 26.0 Hz), 119.4, 111.2, 71.7 (dd, *J* = 28.0, 21.0 Hz), 42.3 (dd, *J* = 9.0, 2.0 Hz).

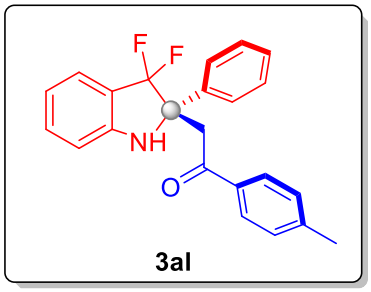
^{19}F NMR (376 MHz, $CDCl_3$) δ -85.3 – -86.0 (m), -106.5 – -107.2 (m).

HRMS (ESI) *m/z* calcd. for $C_{22}H_{16}BrF_2NO$ $(M+H)^+$:428.0456, found 428.0453.

Enantiomeric excess is 94% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20,

flow rate = 0.5mL/min, 254 nm): major isomer: tr = 15.35 min; minor isomer: tr = 13.72 min.

$[\alpha]^{20}_D$ = +342 (c = 0.2, $CHCl_3$).



3al

(S)-2-(3,3-difluoro-2-phenylindolin-2-yl)-1-(p-tolyl)ethan-1-one (3al) According to the general procedure, **3al** was obtained using 3,3-difluoro-2-phenyl-3H-indole **1a** (11.5 mg, 0.05 mmol) and 1-(p-tolyl)ethan-1-one **2l** (67.1 mg, 0.5 mmol) in 91% yield (16.5 mg) and 92% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.65 (m, 2H), 7.53 – 7.49 (m, 2H), 7.37 (d, *J* = 7.1 Hz, 1H), 7.24 (t, *J* = 7.8 Hz, 3H), 7.19 – 7.11 (m, 3H), 6.80 – 6.73 (m, 2H), 5.83 (s, 1H), 4.27 (dd, *J* = 17.7, 1.9 Hz, 1H), 3.20 (d, *J* = 17.7 Hz, 1H), 2.29 (s, 3H).

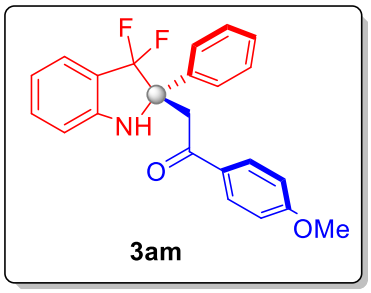
^{13}C NMR (100 MHz, $CDCl_3$) δ 197.9 (d, *J* = 1.0 Hz), 149.7 (dd, *J* = 8.0, 6.0 Hz), 144.6, 137.5 (d, *J* = 5.0 Hz), 134.4, 133.0, 129.3, 128.2, 128.1, 127.7, 126.8 (t, *J* = 250.0 Hz), 126.5, 124.3, 120.1 (dd, *J* = 26.0, 25.0 Hz), 119.2, 111.2, 71.9 (dd, *J* = 27.0, 21.0 Hz), 41.8 (dd, *J* = 9.0, 2.0 Hz), 21.6.

^{19}F NMR (376 MHz, $CDCl_3$) δ -85.1(d, *J* = 248.2 Hz), -107.5 (d, *J* = 244.4 Hz).

HRMS (ESI) *m/z* calcd. for $C_{23}H_{19}F_2NO$ $(M+H)^+$:364.1507, found 364.1510.

Enantiomeric excess is 92% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 12.12 min; minor isomer: tr = 8.56 min.

$[\alpha]^{20}_D$ = +280 (c = 0.2, $CHCl_3$).



3am

(S)-2-(3,3-difluoro-2-phenylindolin-2-yl)-1-(4-methoxyphenyl)ethan-1-one (3am) According to the general procedure, **3am** was obtained using 3,3-difluoro-2-phenyl-3H-indole **1a** (11.5 mg, 0.05 mmol) and 1-(4-methoxyphenyl)ethan-1-one **2m** (76.1mg, 0.5 mmol) in 90% yield (17.1 mg) and 90% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 60:1:1.5). R_f = 0.20 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 – 7.66 (m, 2H), 7.49 (d, *J* = 7.9 Hz, 2H), 7.33 (d, *J* = 7.1 Hz, 1H), 7.22 – 7.15 (m, 3H), 7.13 – 7.07 (m, 1H), 6.72 (dd, *J* = 11.5, 8.0 Hz, 4H), 5.85 (s, 1H), 4.25 – 4.15 (m, 1H), 3.63 (s, 3H), 3.11 (dd, *J* = 17.9, 3.7 Hz, 1H).

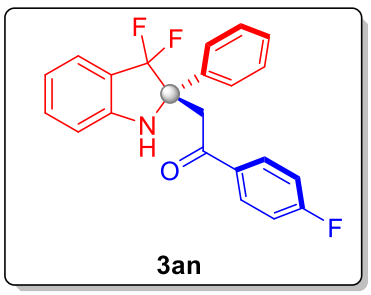
^{13}C NMR (100 MHz, $CDCl_3$) δ 196.6, 163.8, 149.7 – 149.6 (m), 137.5 (d, *J* = 5.0 Hz), 132.9, 130.3, 129.3, 128.1, 127.6, 126.8 (t, *J* = 250.0 Hz), 126.5, 124.2, 120.0 (t, *J* = 25.0 Hz), 119.1, 113.7, 111.2, 71.8 (dd, *J* = 28.0, 21.0 Hz), 55.3, 41.4 – 41.3 (m).

^{19}F NMR (376 MHz, $CDCl_3$) δ 84.6(d, *J* = 248.2 Hz), -107.6 (d, *J* = 248.2 Hz).

HRMS (ESI) *m/z* calcd. for $C_{23}H_{19}F_2NO_2$ $(M+Na)^+$:402.1276, found 402.1280.

Enantiomeric excess is 90% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 23.84 min; minor isomer: tr = 13.08 min.

$[\alpha]^{20}_D$ = +331 (c = 0.2, $CHCl_3$).



3an

(S)-2-(3,3-difluoro-2-phenylindolin-2-yl)-1-(4-fluorophenyl)ethan-1-one (3an) According to the general procedure, **3an** was obtained using 3,3-difluoro-2-phenyl-3H-indole **1a** (11.5 mg, 0.05

mmol) and 1-(47-fluorophenyl)ethan-1-one **2n** (69.1 mg, 0.5 mmol) in 98% yield (18.4 mg) and 94% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 8.7, 5.5 Hz, 2H), 7.59 (dd, *J* = 7.5, 2.3 Hz, 2H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.39 – 7.27 (m, 4H), 7.09 (t, *J* = 8.5 Hz, 2H), 6.91 – 6.84 (m, 2H), 5.85 (s, 1H), 4.35 (d, *J* = 17.8 Hz, 1H), 3.31 (d, *J* = 17.7 Hz, 1H).

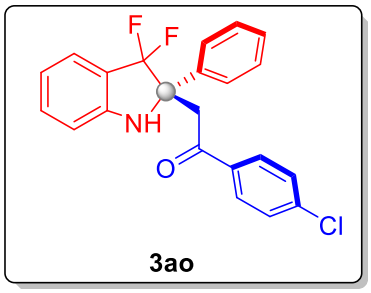
^{13}C NMR (100 MHz, $CDCl_3$) δ 196.7 (d, *J* = 2.0 Hz), 166.0 (d, *J* = 255.0 Hz), 149.6 (d, *J* = 8.0, 6.0 Hz), 137.3 (d, *J* = 5.0 Hz), 133.2 (d, *J* = 3.0 Hz), 133.0, 130.7 (d, *J* = 10.0 Hz), 128.3, 127.8, 126.7 (t, *J* = 249.0 Hz), 126.5, 124.3, 120.0 (t, *J* = 25.0 Hz), 119.3, 115.9, 115.7, 111.2, 71.8 (dd, *J* = 28.0, 21.0 Hz), 42.0 (dd, *J* = 10.0, 3.0 Hz).

^{19}F NMR (376 MHz, CDCl3) δ -85.4 (d, *J* = 248.2 Hz), -103.8, -107.0(d, *J* = 248.2 Hz).

HRMS (ESI) *m/z* calcd. for $C_{22}H_{16}F_3NO$ $(M+H)^+$:368.1257, found368.1248.

Enantiomeric excess is 94% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 13.03 min; minor isomer: tr = 9.18 min.

$[\alpha]^{20}_D$ = +250 (c = 0.2, $CHCl_3$).



3ao

(S)-1-(4-chlorophenyl)-2-(3,3-difluoro-2-phenylindolin-2-yl)ethan-1-one (3ao) According to the general procedure, **3ao** was obtained using 3,3-difluoro-2-phenyl-3H-indole **1a** (11.5 mg, 0.05 mmol) and 1-(4-chlorophenyl)ethan-1-one **2o** (72.8 mg, 0.5 mmol) in 92% yield (17.7 mg) and 94% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 – 7.77 (m, 2H), 7.59 (d, *J* = 7.7 Hz, 2H), 7.54 – 7.43 (m, 2H), 7.40 – 7.37 (m, 2H), 7.34 (t, *J* = 7.9 Hz, 2H), 7.30 – 7.25 (m, 1H), 6.94 – 6.81 (m, 2H), 5.83 (s, 1H), 4.34 (d, *J* = 17.5 Hz, 1H), 3.30 (d, *J* = 17.7 Hz, 1H).

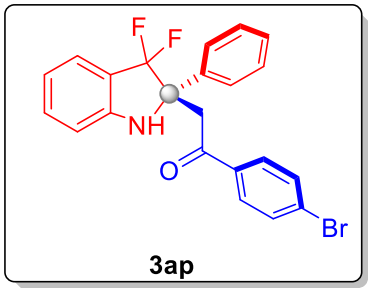
^{13}C NMR (100 MHz, $CDCl_3$) δ 197.1 (d, *J* = 2.0 Hz), 149.5 (dd, *J* = 8.0, 6.0 Hz), 140.2, 137.2 (d, *J* = 6 Hz), 135.1, 133.0, 129.4, 128.9, 128.3, 127.8, 126.7 (t, *J* = 250.0 Hz), 126.4, 124.3, 120.0 (t, *J* = 25.0 Hz), 119.3, 111.2, 71.7 (dd, *J* = 28.0, 22.0 Hz), 42.0 (dd, *J* = 9.0. 2.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -85.5 (d, *J* = 248.2 Hz), -106.9 (d, *J* = 244.4 Hz).

HRMS (ESI) *m/z* calcd. for $C_{22}H_{16}ClF_2NO$ $(M+H)^+$:384.0961, found 384.0968.

Enantiomeric excess is 94% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 15.17 min; minor isomer: tr = 10.71 min.

$[\alpha]^{20}_D$ = +321 (c = 0.2, $CHCl_3$).



3ap

(S)-1-(4-bromophenyl)-2-(3,3-difluoro-2-phenylindolin-2-yl)ethan-1-one (3ap) According to the general procedure, **3ap** was obtained using 3,3-difluoro-2-phenyl-3H-indole **1a** (11.5 mg, 0.05 mmol) and 1-(4-bromophenyl)ethan-1-one **2p** (100 mg, 0.5 mmol) in 90% yield (15.6 mg) and 92% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.6 Hz, 2H), 7.52 – 7.43 (m, 4H), 7.37 (d, *J* = 7.5 Hz, 1H), 7.29 – 7.16 (m, 4H), 6.84 – 6.68 (m, 2H), 5.72 (s, 1H), 4.24 (dd, *J* = 17.7, 1.8 Hz, 1H), 3.20 (d, *J* = 17.7 Hz, 1H).

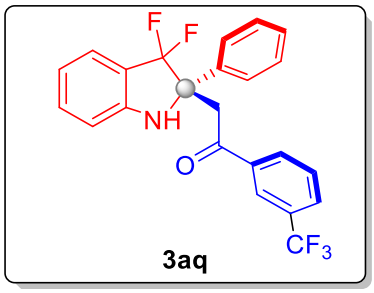
^{13}C NMR (100 MHz, $CDCl_3$) δ 197.3 (d, *J* = 1 Hz), 149.5 (dd, *J* = 8.0, 6.0 Hz), 137.2 (d, *J* = 5 Hz), 135.5, 133.1, 132.0, 129.5, 129.0, 128.3, 127.8, 126.6 (t, *J* = 249.0 Hz), 126.4, 124.4, 120.0 (t, *J* = 25.0 Hz), 119.3, 111.2, 71.7 (dd, *J* = 28.0, 22.0 Hz), 42.0 (dd, *J* = 10.0, 5.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -85.5(d, *J* = 248.2 Hz), -107.0(d, *J* = 244.4 Hz).

HRMS (ESI) *m/z* calcd. for $C_{22}H_{16}BrF_2NO$ $(M+Na)^+$:450.0276, found 450.0284.

Enantiomeric excess is 92% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 0.5 mL/min, 254 nm): major isomer: tr = 23.33 min; minor isomer: tr = 16.98 min.

$[\alpha]^{20}_D$ = +67 (c = 0.2, $CHCl_3$).



(S)-2-(3,3-difluoro-2-phenylindolin-2-yl)-1-(3-(trifluoromethyl)phenyl)ethan-1-one (3aq)

According to the general procedure, **3aq** was obtained using 3,3-difluoro-2-phenyl-3H-indole **1a** (11.5 mg, 0.05 mmol) and 1-(3-(trifluoromethyl)phenyl)ethan-1-one **2q** (94.1 mg, 0.5 mmol) in 90% yield (18.8 mg) and 92% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.96 (d, *J* = 8.1 Hz, 1H), 7.73 (d, *J* = 7.6 Hz, 1H), 7.53 – 7.46 (m, 3H), 7.39 (d, *J* = 7.6 Hz, 1H), 7.31 – 7.23 (m, 3H), 7.21 – 7.18 (m, 1H), 6.86 – 6.75 (m, 2H), 5.66 (s, 1H), 4.29 (dd, *J* = 17.7, 1.8 Hz, 1H), 3.29 (d, *J* = 17.7 Hz, 1H).

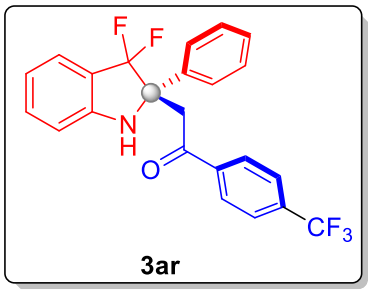
^{13}C NMR (100 MHz, $CDCl_3$) δ 197.1, 149.4 (dd, *J* = 8.0, 6.0 Hz), 137.1 (d, *J* = 6 Hz), 137.1, 133.1, 131.3 (d, *J* = 33 Hz), 131.1, 130.0 (q, *J* = 4.0 Hz), 129.4, 129.1, 128.3, 127.9, 126.6 (t, *J* = 250.0 Hz), 126.4, 124.8 (q, *J* = 4.0 Hz), 124.4, 120.0 (t, *J* = 25.0 Hz), 119.5, 111.2, 71.7 (dd, *J* = 28.0, 21.0 Hz), 42.5 (dd, *J* = 9.0, 2.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.85, -85.6(d, *J* = 248.2 Hz), -106.8(d, *J* = 248.2 Hz).

HRMS (ESI) *m/z* calcd. for $C_{22}H_{16}F_5NO$ $(M+H)^+$:418.1225, found 418.1226.

Enantiomeric excess is 92% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 6.45 min; minor isomer: tr = 5.97 min.

$[\alpha]^{20}_D$ = +291 (c = 0.2, $CHCl_3$).



3ar

(S)-2-(3,3-difluoro-2-phenylindolin-2-yl)-1-(3-(trifluoromethyl)phenyl)ethan-1-one (3ar)

According to the general procedure, **3ar** was obtained using 3,3-difluoro-2-phenyl-3H-indole **1a** (11.5 mg, 0.05 mmol) and 1-(4-(trifluoromethyl)phenyl)ethan-1-one **2r** (94.1 mg, 0.5 mmol) in 90% yield (18.8 mg) and 96% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.1 Hz, 2H), 7.59 (d, *J* = 8.2 Hz, 2H), 7.48 (d, *J* = 7.6 Hz, 2H), 7.38 (d, *J* = 7.6 Hz, 1H), 7.26 (dt, *J* = 11.7, 7.8 Hz, 3H), 7.20 – 7.16 (m, 1H), 6.84 – 6.74 (m, 2H), 5.69 (s, 1H), 4.29 (dd, *J* = 17.9, 1.7 Hz, 1H), 3.28 (d, *J* = 17.8 Hz, 1H).

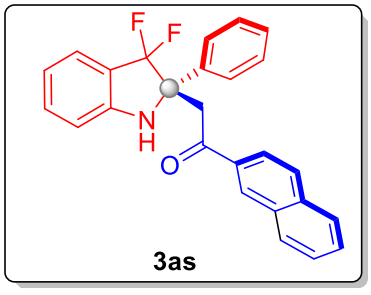
^{13}C NMR (100 MHz, $CDCl_3$) δ 197.5, 149.5 (dd, *J* = 8.0, 6.0 Hz), 139.4, 137.1 (d, *J* = 5.0 Hz), 134.8 (d, *J* = 33.0 Hz), 133.1, 128.3, 128.3, 127.9, 126.6 (t, *J* = 250.0 Hz), 126.4, 125.7 (q, *J* = 4.0 Hz), 124.4,123.4 (d, *J* = 272.0 Hz), 120.0 (t, *J* = 25.0 Hz), 119.4, 111.2, 71.7 (dd, *J* = 27.0, 21.0 Hz), 42.6 (dd, *J* = 9.0, 2.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.18, -85.8 (d, *J* = 248.2 Hz), -106.5 (d, *J* = 248.2 Hz).

HRMS (ESI) *m/z* calcd. for $C_{23}H_{16}F_5NO$ $(M+H)^+$:418.1225, found 418.1224.

Enantiomeric excess is 96% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 12.76 min; minor isomer: tr = 10.25 min.

$[\alpha]^{20}_D$ = +231 (c = 0.2, $CHCl_3$).



3as

(S)-2-(3,3-difluoro-2-phenylindolin-2-yl)-1-(naphthalen-2-yl)ethan-1-one (3as) According to the general procedure, **3as** was obtained using 3,3-difluoro-2-phenyl-3H-indole **1a** (11.5 mg, 0.05 mmol) and 1-(naphthalen-2-yl)ethan-1-one **2s** (85.1 mg, 0.5 mmol) in 87% yield (17.4 mg) and 90% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (s, 1H), 7.96 (d, *J* = 7.9 Hz, 1H), 7.92 – 7.90 (m, 1.8 Hz, 1H), 7.89 – 7.83 (m, 2H), 7.66 (d, *J* = 7.3 Hz, 2H), 7.63 – 7.55 (m, 2H), 7.52 (d, *J* = 7.5 Hz, 1H), 7.41 – 7.34 (m, 3H), 7.29 (d, *J* = 7.4 Hz, 1H), 6.91 (t, *J* = 7.6 Hz, 2H), 5.96 (s, 1H), 4.57 (d, *J* = 17.4 Hz, 1H), 3.48 (d, *J* = 17.7 Hz, 1H).

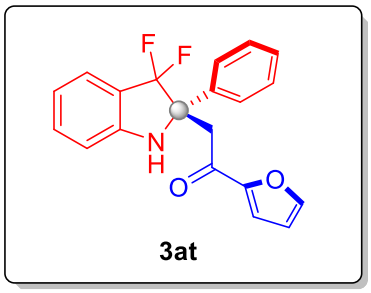
^{13}C NMR (100 MHz, $CDCl_3$) δ 198.2, 149.7 (dd, *J* = 7.0, 5.0 Hz), 137.4 (d, *J* = 5.0 Hz), 135.7, 134.2, 133.0, 132.3, 130.0, 129.6, 128.8, 128.7 – 127.8 (m), 128.5, 128.3 (t, *J* = 50.0 Hz), 128.3, 127.7, 126.8 (t, *J* = 199.0 Hz), 126.5, 124.4, 123.3, 120.1 (t, *J* = 26.0 Hz), 119.3, 111.3, 71.9 (dd, *J* = 27.0, 21.0 Hz), 42.0 (dd, *J* = 9.0, 2.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -85.2(d, *J* = 244.4 Hz), -107.2 (d, *J* = 248.2 Hz).

HRMS (ESI) *m/z* calcd. for $C_{26}H_{19}F_2NO$ $(M+Na)^+$:422.1327, found 422.1322.

Enantiomeric excess is 90% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 0.5 mL/min, 254 nm): major isomer: tr = 31.00 min; minor isomer: tr = 19.67 min.

$[\alpha]^{20}_D$ = +335 (c = 0.2, $CHCl_3$).



3at

(S)-2-(3,3-difluoro-2-phenylindolin-2-yl)-1-(furan-2-yl)ethan-1-one (3at) According to the general procedure, **3at** was obtained using 3,3-difluoro-2-phenyl-3H-indole **1a** (11.5 mg, 0.05 mmol) and 1-(furan-2-yl)ethan-1-one **2t** (55.1 mg, 0.5 mmol) in 90% yield (15.3 mg) and 70% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.0 Hz, 2H), 7.55 – 7.51 (m, 1H), 7.48 (d, *J* = 7.6 Hz, 1H), 7.39 – 7.32 (m, 3H), 7.29 – 7.24 (m, 1H), 7.13 (d, *J* = 3.6 Hz, 1H), 6.90 – 6.87 (m, 2H), 6.46 (dd, *J* = 3.6, 1.7 Hz, 1H), 5.95 (s, 1H), 4.26 (dd, *J* = 17.1, 2.0 Hz, 1H), 3.10 (d, *J* = 17.0 Hz, 1H).

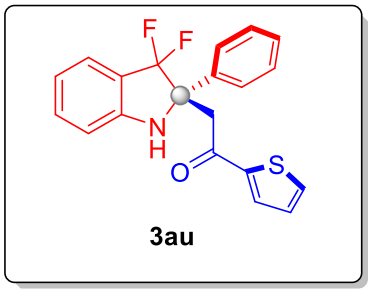
^{13}C NMR (100 MHz, $CDCl_3$) δ 187.1 (d, *J* = 2.0 Hz), 152.5, 149.5 (dd, *J* = 8.0, 5.0 Hz), 149.4, 146.9, 136.9 (d, *J* = 5.0 Hz), 133.0, 128.2, 127.8, 126.6, 126.6 (t, *J* = 250.0 Hz), 126.6, 124.2, 120.1 (dd, *J* = 26.0, 24.0 Hz), 119.3, 118.1, 112.5, 111.5, 71.9 (dd, *J* = 28.0, 21.0 Hz), 41.7 (dd, *J* = 9.0, 2.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -84.7 (dd, *J* = 248.2, 7.5 Hz), -107.9 (d, *J* = 244.4, 3.8 Hz).

HRMS (ESI) *m/z* calcd. for $C_{20}H_{15}F_2NO_2$ $(M+H)^+$:340.1144, found 340.1136.

Enantiomeric excess is 70% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 0.5 mL/min, 254 nm): major isomer: tr = 22.69 min; minor isomer: tr = 16.97 min.

$[\alpha]^{20}_D$ = +234 (c = 0.2, $CHCl_3$).



3au

(S)-2-(3,3-difluoro-2-phenylindolin-2-yl)-1-(thiophen-2-yl)ethan-1-one (3au) According to the general procedure, **3au** was obtained using 3,3-difluoro-2-phenyl-3H-indole **1a** (11.5 mg, 0.05 mmol) and 1-(thiophen-2-yl)ethan-1-one **2u** (63.1 mg, 0.5 mmol) in 89% yield (15.8 mg) and 86% ee as a white solid (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1). R_f = 0.40 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 3.9, 1.1 Hz, 1H), 7.65 – 7.59 (m, 3H), 7.47 (d, *J* = 7.3 Hz, 1H), 7.39 – 7.32 (m, 3H), 7.30 – 7.25 (m, 1H), 7.08 (dd, *J* = 4.9, 3.8 Hz, 1H), 6.91 – 6.86 (m, 2H), 5.96 (s, 1H), 4.26 (dd, *J* = 17.1, 1.9 Hz, 1H), 3.24 (d, *J* = 17.2, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 191.0 (d, *J* = 2.0 Hz), 149.5 (dd, *J* = 8.0, 6.0 Hz), 144.1, 137.0 (d, *J* = 6.0 Hz), 134.7, 133.0 (d, *J* = 1.0 Hz), 132.6, 128.23, 128.22, 127.8, 126.6 (t, *J* = 250.0 Hz),

126.5, 124.3, 120.1 (dd, *J* = 26.0, 25.0 Hz), 119.8, 119.3, 111.5, 72.9 (dd, *J* = 28.0, 22.0 Hz), 42.7 (dd, *J* = 10.0, 2.0 Hz).

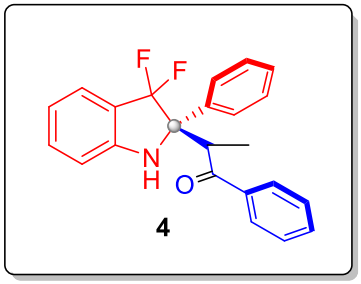
^{19}F NMR (376 MHz, $CDCl_3$) δ -84.6 (d, *J* = 244.4 Hz), -107.8 (d, *J* = 248.2 Hz).

HRMS (ESI) *m/z* calcd. for $C_{20}H_{15}F_2NOS$ $(M+H)^+$:356.0915, found 356.0916.

Enantiomeric excess is 86% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 13.65 min; minor isomer: tr = 9.19 min.

$[\alpha]^{20}_D$ = +228 (c = 0.2, $CHCl_3$).

4. Synthesis applications of 3aa



4

(S)-2-((S)-3,3-difluoro-2-phenylindolin-2-yl)-1-phenylpropan-1-one (4). Dissolve **(3aa)** (17.5 mg, 0.05 mmol) and NaH (1.9 mg, 0.08 mmol) in DMF at 0 ° C, stir for 30 minutes, and then react overnight with MeI (42.6 mg, 0.08 mmol) at room temperature. Then the reaction was quenched with water, followed by extraction using ethyl acetate (10 mL × 3), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1) to afford **4** (15.26 mg, 84%, 94% ee) as white solid. R_f = 0.50 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.73 (m, 2H), 7.59 (d, *J* = 7.5 Hz, 2H), 7.52 – 7.48 (m, 1H), 7.43 (d, *J* = 7.5 Hz, 1H), 7.39 – 7.33 (m, 3H), 7.22 (t, *J* = 7.6 Hz, 2H), 7.15 – 7.10 (m, 1H), 6.90 (d, *J* = 8.1 Hz, 1H), 6.84 (t, *J* = 7.4 Hz, 1H), 6.06 (s, 1H), 4.75 (q, *J* = 6.9 Hz, 1H), 1.15 (d, *J* = 6.9 Hz, 3H).

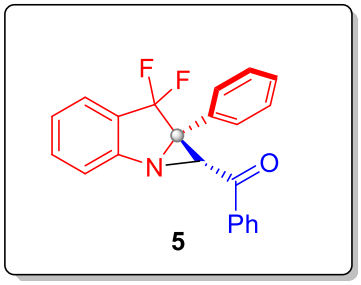
^{13}C NMR (100 MHz, $CDCl_3$) δ 204.3 (d, *J* = 2.0 Hz), 151.0 (dd, *J* = 8.0, 5.0 Hz), 138.4 (d, *J* = 7.0 Hz), 136.09, 133.4, 133.2 (d, *J* = 2.0 Hz), 128.6, 128.04, 127.95, 127.5, 126.8 (t, *J* = 249.0 Hz), 126.5, 123.5, 121.2 (t, *J* = 25.0 Hz), 118.8, 110.1, 74.1 (dd, *J* = 27.0, 21.0 Hz), 46.1 (dd, *J* = 7.0, 2.0 Hz), 14.7 (d, *J* = 3.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -71.6 (d, *J* = 251.9 Hz), -107.6 (d, *J* = 255.7 Hz).

HRMS (ESI) *m/z* calcd. for $C_{23}H_{19}F_2NO$ $(M+H)^+$:364.1507, found 364.1499.

Enantiomeric excess is 94% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 7.35 min; minor isomer: tr = 5.10 min.

$[\alpha]^{20}_D$ = +272 (c = 0.2, $CHCl_3$).



5

((1R,7aR)-7,7-difluoro-7a-phenyl-7,7a-dihydro-1H-azirino[1,2-a]indol-1-yl)(phenyl)methanone (5) A mixture of **3aa** (34.9 mg, 0.1 mmol), I_2 (50.8 mg, 0.2 mmol), and DBU (30.4 mg, 0.2 mmol) was stirred in 2.0 mL of THF at 40 °C for react overnight until the disappearance of **3aa** as determined by TLC. The reaction mixture was quenched with aqueous $Na_2S_2O_3$ and extracted with CH_2Cl_2 (15 mL × 3). The organic extracts were dried over Na_2SO_4, filtered, and concentrated to give a residue, which was purified by column chromatography on silica gel (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1) to afford the product **5** (30.2 mg, 87%, 94% ee). R_f = 0.30 (petroleum ether/EtOAc = 10:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 – 7.76 (m, 2H), 7.47 (t, *J* = 8.8 Hz, 2H), 7.43 – 7.33 (m, 4H), 7.30 – 7.24 (m, 2H), 7.19 (t, *J* = 7.5 Hz, 1H), 7.12 (dd, *J* = 5.1, 2.0 Hz, 3H), 3.75 (d, *J* = 1.4 Hz, 1H).

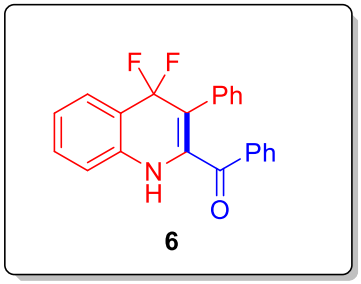
^{13}C NMR (100 MHz, $CDCl_3$) δ 188.6, 155.8 (t, *J* = 8.0 Hz), 135.3, 133.7, 132.7, 129.3 (dd, *J* = 29.0, 25.0 Hz), 128.6, 128.6, 128.3, 128.0, 127.8 (d, *J* = 2.0 Hz), 126.6, 126.4 (t, *J* = 247.0 Hz), 125.0, 120.8, 65.4, 59.5 (dd, *J* = 33.0, 26.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -84.1 (d, *J* = 259.4 Hz), -88.2 (d, *J* = 259.4 Hz).

HRMS (ESI) *m/z* calcd. for $C_{22}H_{15}F_2NO$ $(M+H)^+$:348.1194, found 348.1184.

Enantiomeric excess is 94% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 9.89 min; minor isomer: tr = 7.22 min.

$[\alpha]^{20}_D$ = +214 (c = 0.2, $CHCl_3$).



6

(4,4-difluoro-3-phenyl-1,4-dihydroquinolin-2-yl)(phenyl)methanone (6) A mixture of **5** (17.4 mg, 0.05 mmol), K_2CO_3 (1.4 mg, 20 mmol%), was stirred in DMSO of 0.5 mL at 120 °C for react overnight until the disappearance of **5** as determined by TLC. Then the reaction was quenched with water, followed by extraction using ethyl acetate (10 mL × 3), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silicone alkalized with Et_3N, silica gel flash chromatography: petroleum ether/ EtOAc/ Et_3N = 90:1:1) to afford **6** (14.9 mg, 86%) as white solid. R_f = 0.50 (petroleum ether/EtOAc = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 – 8.09 (m, 2H), 7.78 – 7.72 (m, 3H), 7.64 – 7.59 (m, 1H), 7.47 – 7.42 (m, 1H), 7.36 – 7.19 (m, 8H).

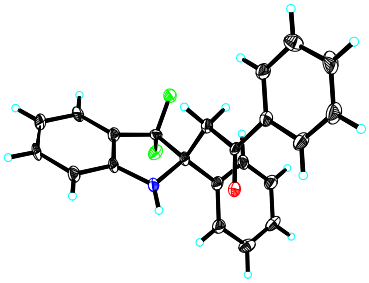
^{13}C NMR (100 MHz, $CDCl_3$) δ 193.8 (d, *J* = 4.0 Hz), 163.25, 160.58, 158.1 (d, *J* = 3.0 Hz), 148.0 (d, *J* = 6 Hz), 135.78, 133.66, 131.01, 130.64, 130.30, 130.0 (d, *J* = 1 Hz), 129.5 (d, *J* = 3.0 Hz), 128.39, 128.36, 128.2 (d, *J* = 2.0 Hz), 120.7 (d, *J* = 6.0 Hz), 119.3 (d, *J* = 2.0 Hz), 119.1 (d, *J* = 5.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -115.46.

HRMS (ESI) *m/z* calcd. for $C_{22}H_{15}F_2NO$ $(M+Na)^+$:370.1014, found 370.1015.

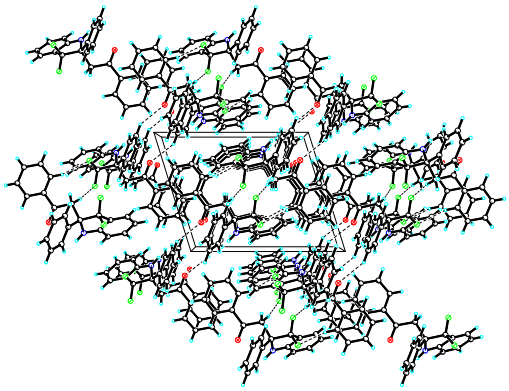
5. Crystal of 3aa

Crystal data for **3aa**: $C_{22}H_{17}F_2NO$, M = 349.36, a = 9.5585(4) Å, b = 7.8842(3) Å, c = 11.8135(5) Å, α = 90°, β = 107.2350(10)°, γ = 90°, V = 850.30(6) Å^3, T = 150.(2) K, space group $P1211$, Z = 2, μ(Cu Kα) = 0.814 mm^{-1}, 17617 reflections measured, 3037 independent reflections (R_{int} = 0.0493). The final R_1 values were 0.0347 ($I > 2\sigma(I)$). The final $wR(F^2)$ values were 0.0933 ($I > 2\sigma(I)$). The final R_1 values were 0.0358 (all data). The final $wR(F^2)$ values were 0.0958 (all data). The goodness of fit on F^2 was 1.080. Flack parameter = 0.00(7).



View of a molecule of **3aa**.

Displacement ellipsoids are drawn at the 30% probability level.



View of the pack drawing of **3aa**.

Hydrogen-bonds are shown as dashed lines.

Table 1. Crystal data and structure refinement for **3aa**.		
Identification code	global	
Empirical formula	C22 H17 F2 N O	
Formula weight	349.36	
Temperature	150(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	a = 9.5585(4) Å	α= 90°.
	b = 7.8842(3) Å	β= 107.2350(10)°.

	c = 11.8135(5) Å γ = 90°.
Volume	850.30(6) $Å^3$
Z	2
Density (calculated)	1.365 Mg/m^3
Absorption coefficient	0.814 mm^{-1}
F(000)	364
Crystal size	0.300 x 0.200 x 0.100 mm^3
Theta range for data collection	3.92 to 68.48°.
Index ranges	-11<=h<=11, -8<=k<=9, -14<=l<=14
Reflections collected	17617
Independent reflections	3037 [R(int) = 0.0493]
Completeness to theta = 68.48°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.92 and 0.78
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3037 / 1 / 235
Goodness-of-fit on F^2	1.080
Final R indices [I>2sigma(I)]	R1 = 0.0347, wR2 = 0.0933
R indices (all data)	R1 = 0.0358, wR2 = 0.0958
Absolute structure parameter	0.00(7)
Largest diff. peak and hole 0.403 and -0.284 $e.Å^{-3}$	

6. References

1, R. Lin, S. Ding, Z. Shi, N. Jiao, *Org. Lett.,* **2011**, *13*, 4498-4501

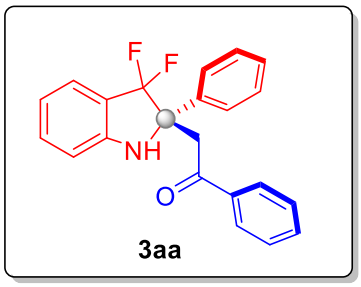
2, Y.-L. Liu, X.-Y. Mao, X.-T. Lin, G.-S. Chen, *Org. Chem. Front.,* **2018**, *5*, 2303-2307

3, L. Yang, Y. Ma, F. Song, J. You, *Chem. Commun.,* **2014**, *50*, 3024-3026.

4, A. Arcadi, E. Pietropaolo, A. Alvino, V. Michelet, *Org. Lett.,* **2013**, *15*, 2766-2769.

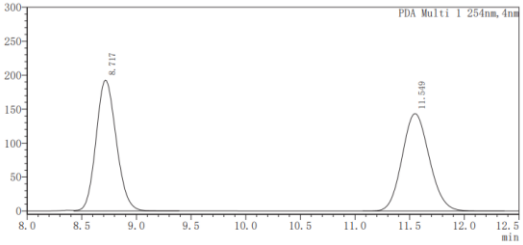
5, T. Ma, X.-P. Wei, X.-C. Wang, X.-X. Qiao, G. Li, Y. He, X.-J. Zhao, *Org. Lett.*, **2023**, 25, 8666-8671.

7. Copies of HPLC



Enantiomeric excess is 94% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 11.04 min; minor isomer: tr = 8.47 min.

$[\alpha]^{20}_{D}$ = +389 (c = 0.35, $CHCl_3$).



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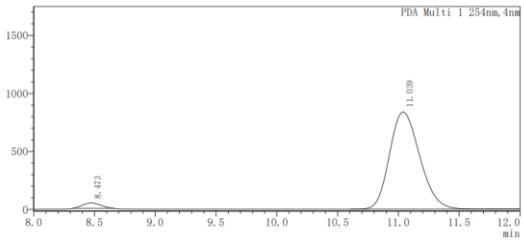
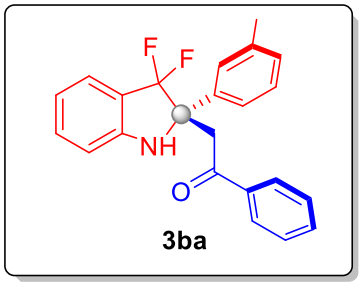
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	8.717	2482236	192728	49.951
2	11.549	2487096	143552	50.049
Totals		4969332	336280	100.000



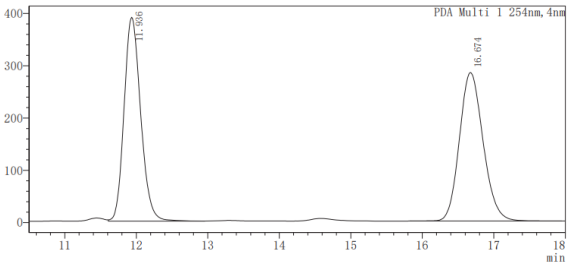
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	8.473	487609	46067	3.263
2	11.039	14456424	837254	96.737
Totals		14944033	883321	100.000



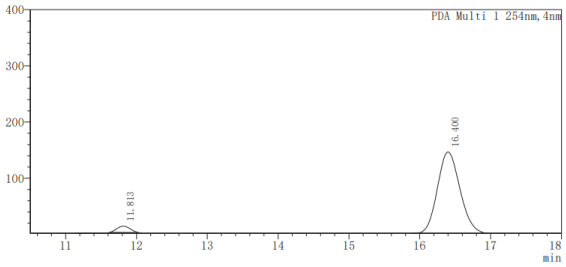
Enantiomeric excess is 92% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 16.40 min; minor isomer: tr = 11.81 min.

$[\alpha]^{20}_{D}$ = +182 (c = 0.3, $CHCl_3$).



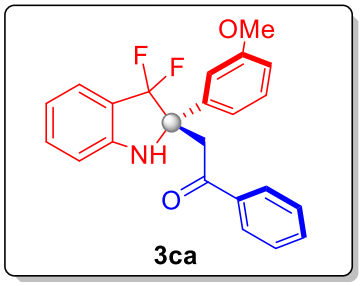
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	11.936	6290762	389735	49.039
2	16.674	6537246	284042	50.961
Totals		12828008	673778	100.000



<Signal>
PDA Ch1 254nm

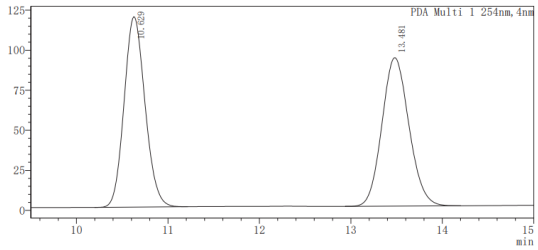
Peak	RetTime	Area	Height	Area%
1	11.813	141553	11125	4.051
2	16.400	3352895	146574	95.949
Totals		3494448	157699	100.000



3ca

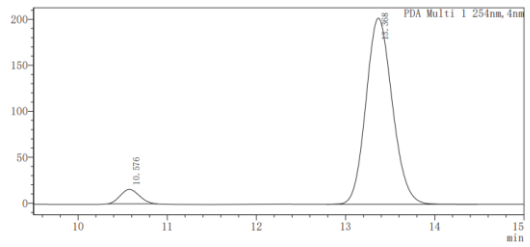
Enantiomeric excess is 90% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 13.37 min; minor isomer: tr = 10.58 min.

$[\alpha]^{20}_{D}$ = +178 (c = 0.2, $CHCl_3$).



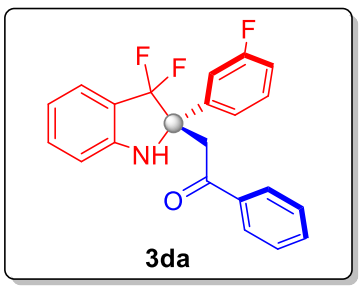
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	10.629	1891841	118726	49.857
2	13.481	1902728	92675	50.143
Totals		3794569	211402	100.000



<Signal>
PDA Ch1 254nm

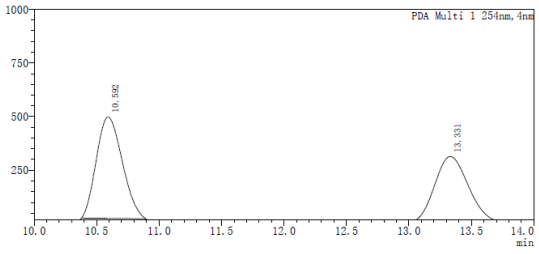
Peak	RetTime	Area	Height	Area%
1	10.576	231176	15622	5.255
2	13.368	4167584	202538	94.745
Totals		4398760	218160	100.000



3da

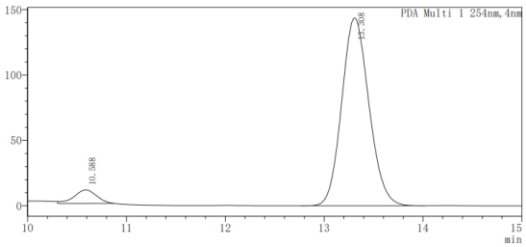
Enantiomeric excess is 88% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 13.31 min; minor isomer: tr = 10.59 min.

$[\alpha]^{20}_{D}$ = +280 (c = 0.2, $CHCl_3$).



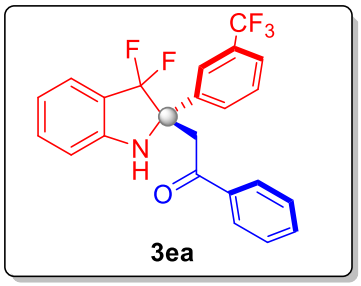
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	10.592	6776913	472189	52.785
2	13.331	6061814	313531	47.215
Totals		12838727	785719	100.000



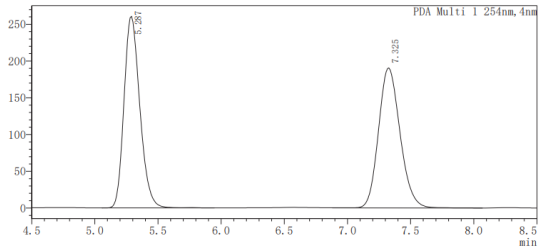
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	10.588	163736	10361	5.620
2	13.308	2749677	143640	94.380
Totals		2913414	154001	100.000



Enantiomeric excess is 86% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 7.70 min; minor isomer: tr = 5.46 min.

$[\alpha]^{20}_{D}$ = +321 (c = 0.2, $CHCl_3$).



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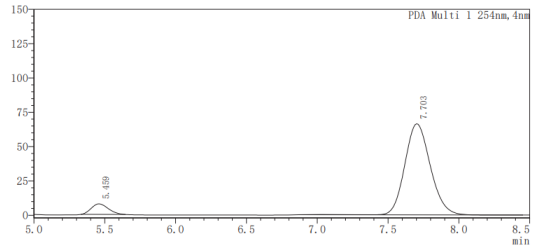
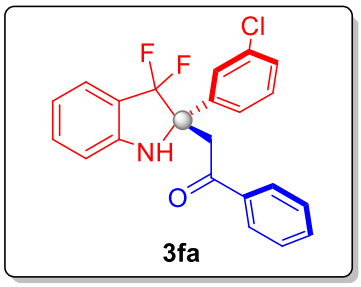
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	5.287	2267028	260388	50.105
2	7.325	2257522	190486	49.895
Totals		4524550	450874	100.000



<Signal>
PDA Ch1 254nm

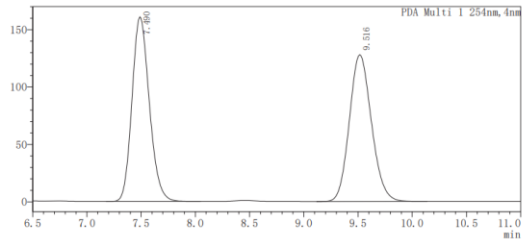
Peak	RetTime	Area	Height	Area%
1	5.459	63787	7695	7.112
2	7.703	833056	66435	92.888
Totals		896843	74130	100.000



3fa

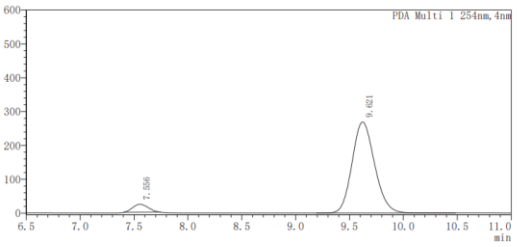
Enantiomeric excess is 88% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 9.62 min; minor isomer: tr = 7.56 min.

$[\alpha]^{20}_{D}$ = +290 (c = 0.2, $CHCl_3$).



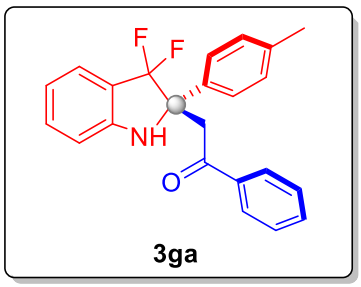
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	7.490	1788417	160717	49.724
2	9.516	1808274	127750	50.276
Totals		3596691	288466	100.000



<Signal>
PDA Ch1 254nm

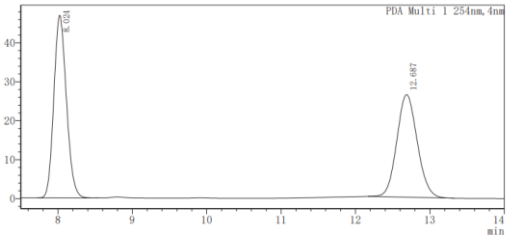
Peak	RetTime	Area	Height	Area%
1	7.556	236988	23650	5.718
2	9.621	3907858	268865	94.282
Totals		4144846	292515	100.000



3ga

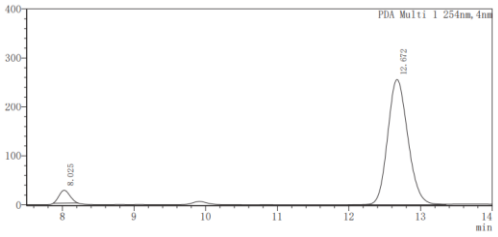
Enantiomeric excess is 90% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 8.03 min; minor isomer: tr = 12.67 min.

$[\alpha]^{20}_{D}$ = +237 (c = 0.2, $CHCl_3$).



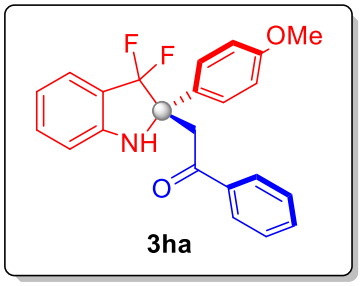
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	8.024	551729	46927	52.277
2	12.687	503668	26338	47.723
Totals		1055397	73265	100.000



<Signal>
PDA Ch1 254nm

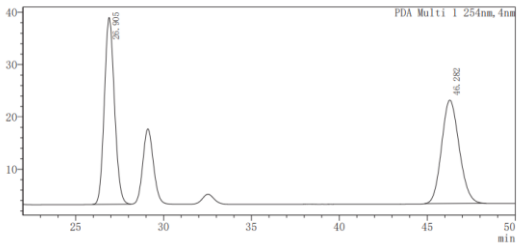
Peak	RetTime	Area	Height	Area%
1	8.025	271155	26232	5.137
2	12.672	5007612	255854	94.863
Totals		5278768	282086	100.000



3ha

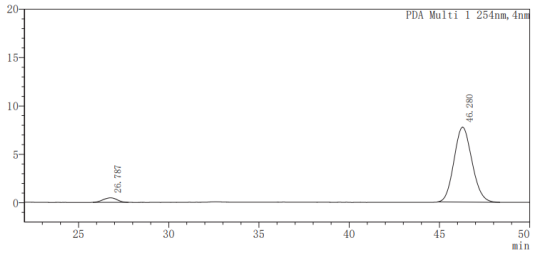
Enantiomeric excess is 92% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 95/5, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 46.28 min; minor isomer: tr = 26.79 min.

$[\alpha]^{20}_{D}$ = +273 (c = 0.2, $CHCl_3$).



<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	26.905	1432040	35717	50.980
2	46.282	1376974	19777	49.020
Totals		2809014	55494	100.000



<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
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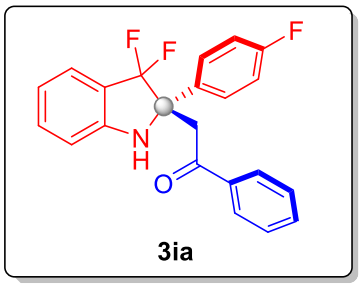
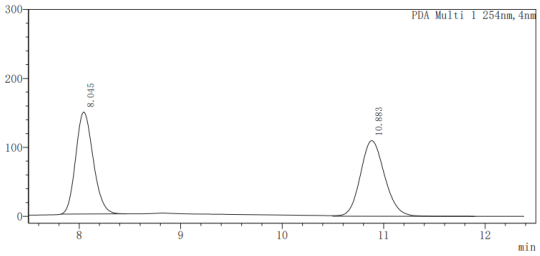
2	46.280	537836	7746	95.587
Totals		562668	8213	100.000



3ia

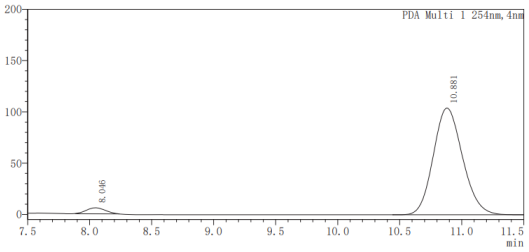
Enantiomeric excess is 94% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 10.88 min; minor isomer: tr = 8.05 min.

$[\alpha]^{20}_{D}$ = +268 (c = 0.2, $CHCl_3$).



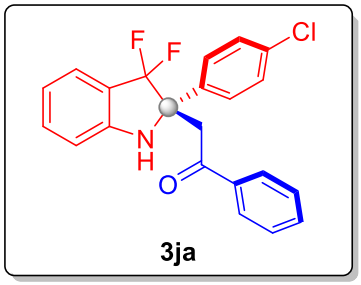
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	8.045	1773984	147905	49.357
2	10.883	1820220	109596	50.643
Totals		3594204	257501	100.000



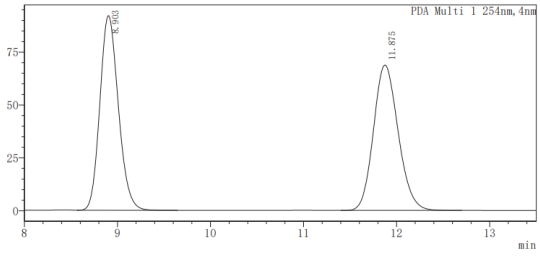
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	8.046	61920	5827	3.495
2	10.881	1709961	104117	96.505
Totals		1771882	109944	100.000



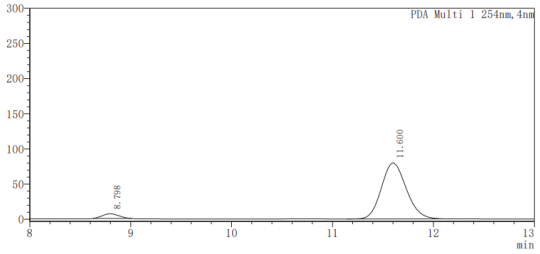
Enantiomeric excess is 90% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 11.6 min; minor isomer: tr = 8.80 min.

$[\alpha]^{20}_{D}$ = +169 (c = 0.2, $CHCl_3$).



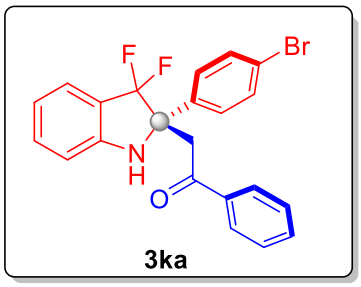
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	8.903	1267724	91910	49.932
2	11.875	1271175	68704	50.068
Totals		2538899	160613	100.000



<Signal>
PDA Ch1 254nm

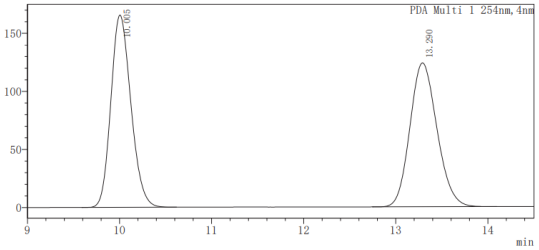
Peak	RetTime	Area	Height	Area%
1	8.798	74227	6580	5.147
2	11.600	1367786	79395	94.853
Totals		1442013	85975	100.000



3ka

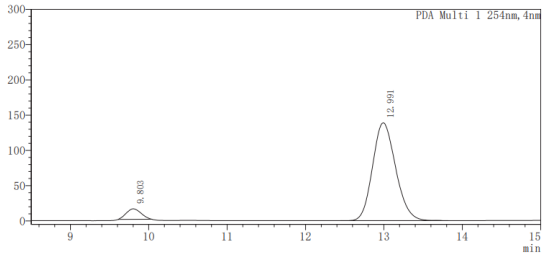
Enantiomeric excess is 88% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 12.99 min; minor isomer: tr = 9.80 min.

$[\alpha]^{20}_{D}$ = +277 (c = 0.2, $CHCl_3$).



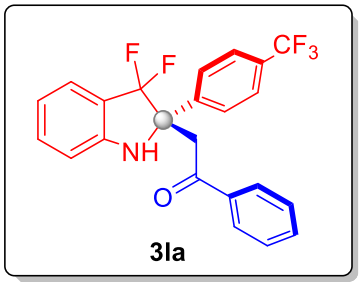
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	10.005	2511328	165606	49.825
2	13.290	2528967	123953	50.175
Totals		5040295	289559	100.000



<Signal>
PDA Ch1 254nm

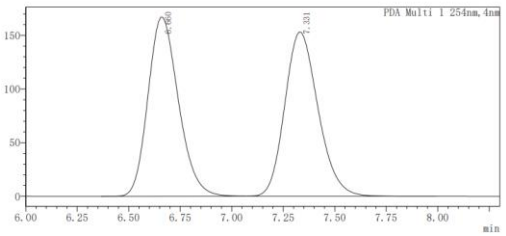
Peak	RetTime	Area	Height	Area%
1	9.803	194244	14832	6.399
2	12.991	2841422	138835	93.601
Totals		3035666	153667	100.000



3la

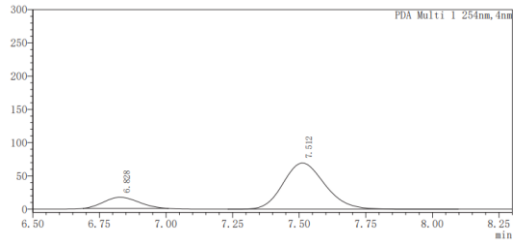
Enantiomeric excess is 66% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 7.51 min; minor isomer: tr = 6.83 min.

$[\alpha]^{20}_{D}$ = +117 (c = 0.2, $CHCl_3$).



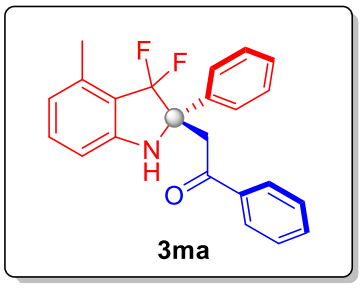
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	6.660	1723917	167174	49.941
2	7.331	1727964	153301	50.059
Totals		3451881	320474	100.000



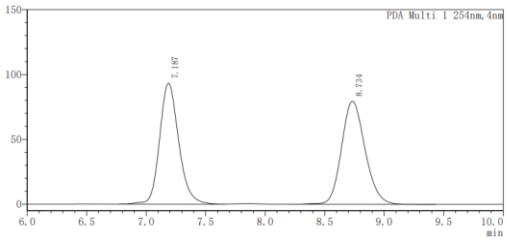
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	6.828	152206	16760	16.701
2	7.512	759123	69500	83.299
Totals		911329	86259	100.000



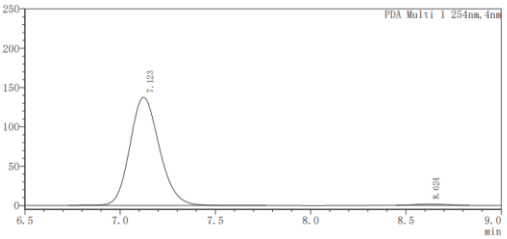
Enantiomeric excess is 98% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 7.12 min; minor isomer: tr = 8.62 min.

$[\alpha]^{20}_{D}$ = +178 (c = 0.2, $CHCl_3$).



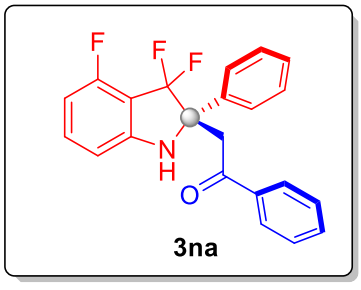
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	7.187	1043132	93352	48.725
2	8.734	1097737	79604	51.275
Totals		2140869	172956	100.000

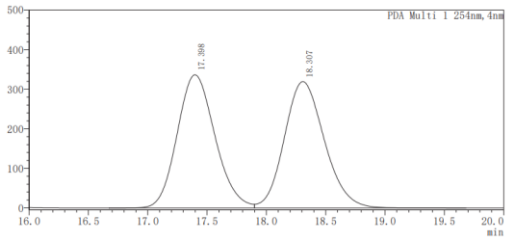


<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	7.123	1483813	137552	98.778
2	8.624	18357	1603	1.222
Totals		1502170	139155	100.000

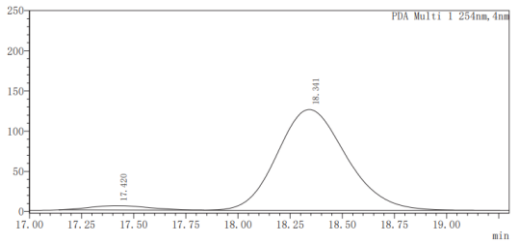


Enantiomeric excess is 94% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 0.50 mL/min, 254 nm): major isomer: tr = 18.34 min; minor isomer: tr = 17.42 min. $[\alpha]^{20}_{D}$ = +178 (c = 0.2, $CHCl_3$).



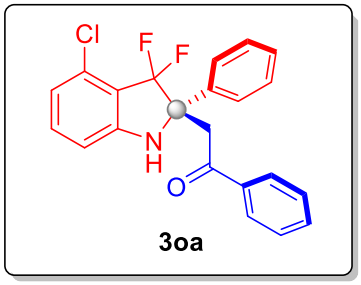
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	17.398	7472229	336690	49.895
2	18.307	7503764	319370	50.105
Totals		14975993	656060	100.000



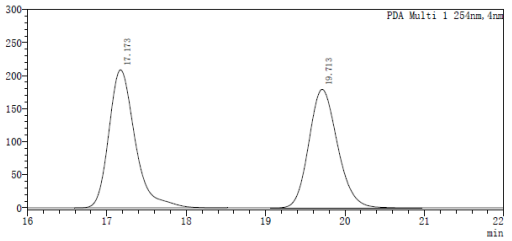
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	17.420	104018	5358	3.465
2	18.341	2897739	125395	96.535
Totals		3001757	130753	100.000



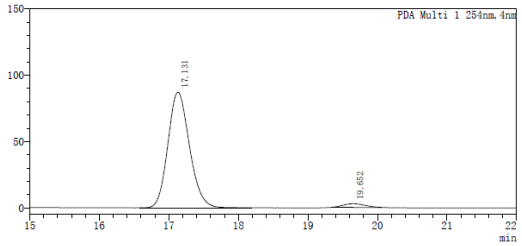
3oa

Enantiomeric excess is 94% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 0.5 mL/min, 254 nm): major isomer: tr = 19.65 min; minor isomer: tr = 17.13 min. $[\alpha]^{20}_{D}$ = +401 (c = 0.2, $CHCl_3$).



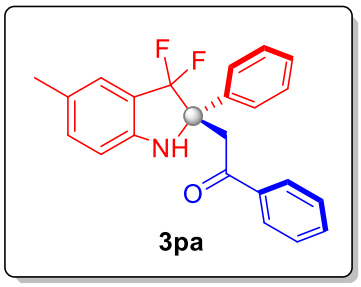
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	17.173	4791309	208969	51.601
2	19.713	4493906	179451	48.399
Totals		9285215	388421	100.000



<Signal>
PDA Ch1 254nm

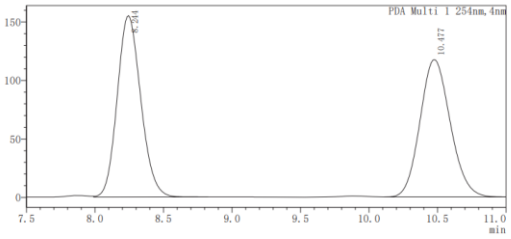
Peak	RetTime	Area	Height	Area%
1	17.131	1876433	87166	96.901
2	19.652	60011	2794	3.099
Totals		1936444	89960	100.000



3pa

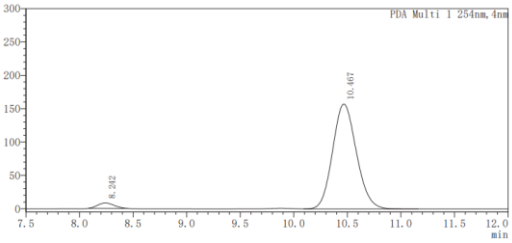
Enantiomeric excess is 94% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 10.47 min; minor isomer: tr = 8.24 min.

$[\alpha]^{20}_{D}$ = +206 (c = 0.2, $CHCl_3$).



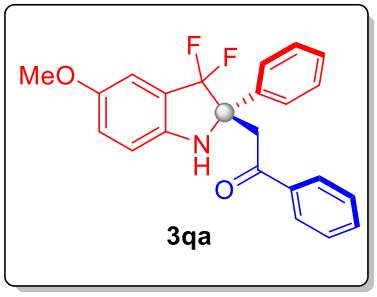
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	8.244	1855764	155130	50.609
2	10.477	1811071	117618	49.391
Totals		3666835	272749	100.000



<Signal>
PDA Ch1 254nm

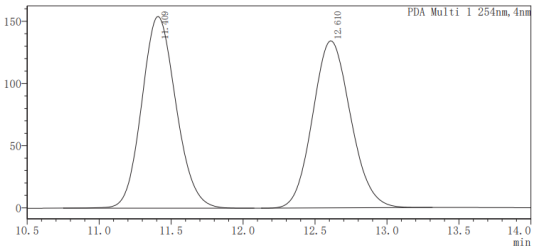
Peak	RetTime	Area	Height	Area%
1	8.242	87273	8153	3.466
2	10.467	2430798	157336	96.534
Totals		2518072	165489	100.000



3qa

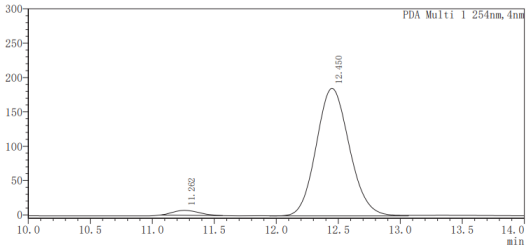
Enantiomeric excess is 94% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 12.45 min; minor isomer: tr = 11.26 min.

$[\alpha]^{20}_{D}$ = +160 (c = 0.2, $CHCl_3$).



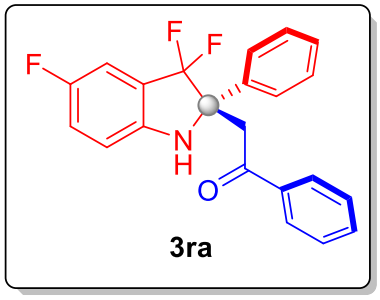
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	11.409	2551398	154003	50.768
2	12.610	2474244	134337	49.232
Totals		5025643	288340	100.000



<Signal>
PDA Ch1 254nm

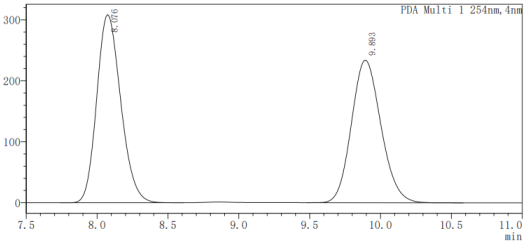
Peak	RetTime	Area	Height	Area%
1	11.262	105005	7226	2.945
2	12.450	3460796	185754	97.055
Totals		3565800	192979	100.000



3ra

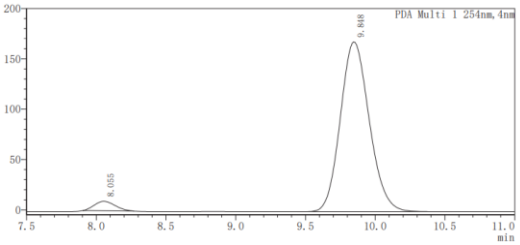
Enantiomeric excess is 92% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 9.85 min; minor isomer: tr = 8.06 min.

$[\alpha]^{20}_{D}$ = +251 (c = 0.2, $CHCl_3$).



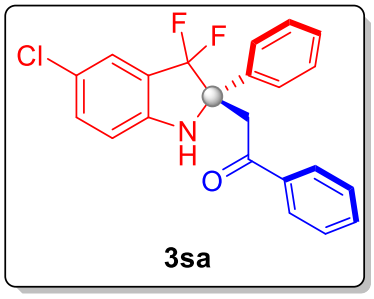
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	8.076	3646617	308636	51.777
2	9.893	3396361	233831	48.223
Totals		7042978	542467	100.000



<Signal>
PDA Ch1 254nm

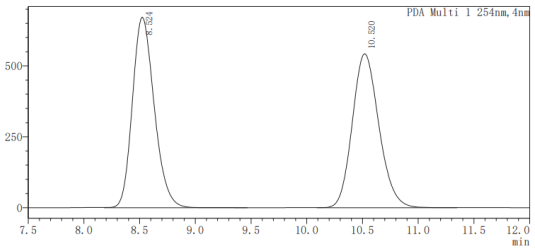
Peak	RetTime	Area	Height	Area%
1	8.055	97939	9389	3.870
2	9.848	2432512	168829	96.130
Totals		2530451	178218	100.000



3sa

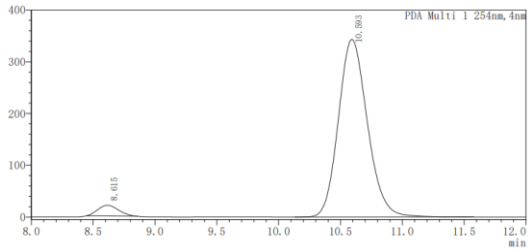
Enantiomeric excess is 92% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 10.595 min; minor isomer: tr = 8.62 min.

$[\alpha]^{20}_{D}$ = +295 (c = 0.2, $CHCl_3$).



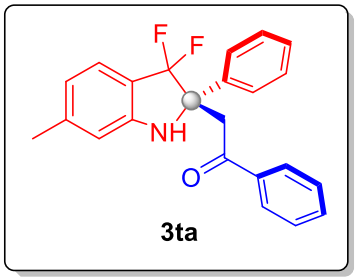
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	8.524	9152992	671955	50.376
2	10.520	9016229	543100	49.624
Totals		18169221	1215055	100.000



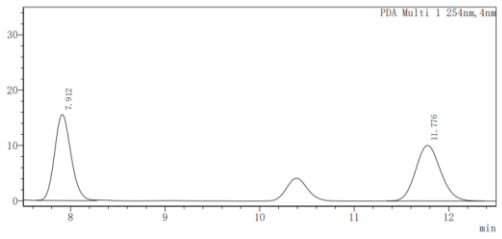
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	8.615	240969	20649	4.129
2	10.593	5595598	343423	95.871
Totals		5836567	364072	100.000



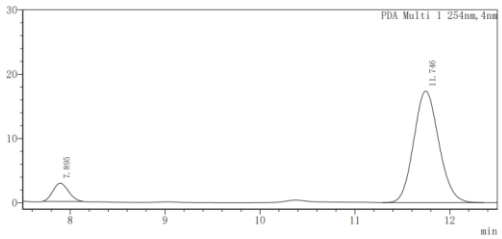
Enantiomeric excess is 82% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 11.75 min; minor isomer: tr = 7.90 min.

$[\alpha]^{20}_{D}$ = +122 (c = 0.2, $CHCl_3$).



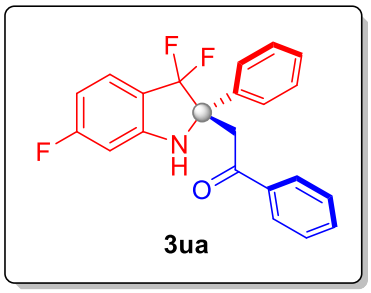
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	7.912	187644	15543	50.355
2	11.776	185001	10063	49.645
Totals		372646	25606	100.000



<Signal>
PDA Ch1 254nm

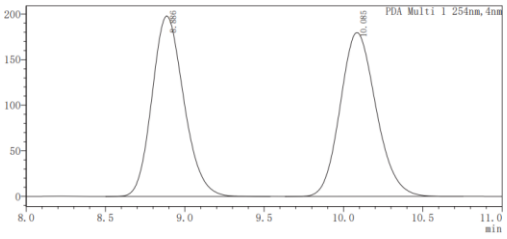
Peak	RetTime	Area	Height	Area%
1	7.895	32061	2829	9.135
2	11.746	318913	17337	90.865
Totals		350974	20166	100.000



3ua

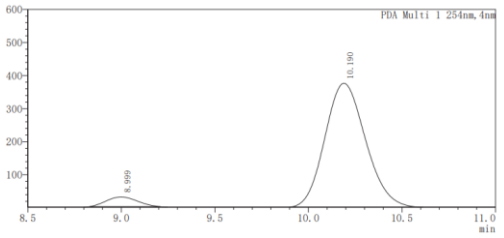
Enantiomeric excess is 90% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 10.19 min; minor isomer: tr = 9.00 min.

$[\alpha]^{20}_{D}$ = +217 (c = 0.2, $CHCl_3$).



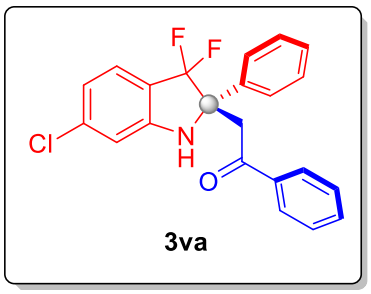
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	8.886	2765821	198129	49.375
2	10.085	2835877	179719	50.625
Totals		5601698	377848	100.000



<Signal>
PDA Ch1 254nm

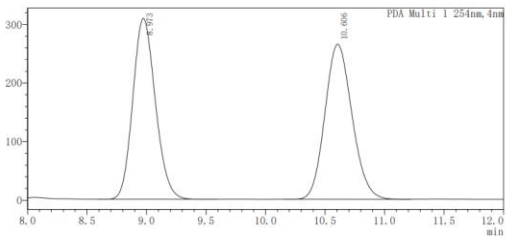
Peak	RetTime	Area	Height	Area%
1	8.999	333205	29187	5.472
2	10.190	5755641	376730	94.528
Totals		6088846	405917	100.000



3va

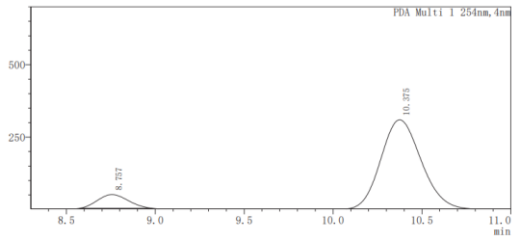
Enantiomeric excess is 80% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 10.38 min; minor isomer: tr = 8.76 min.

$[\alpha]^{20}_{D}$ = +261 (c = 0.2, $CHCl_3$).



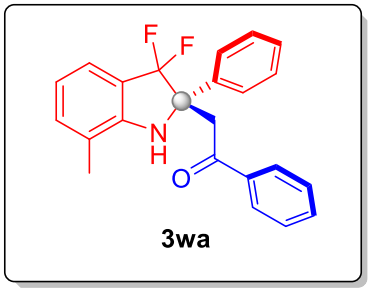
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	8.973	4081903	308855	49.300
2	10.606	4197835	264679	50.700
Totals		8279738	573534	100.000



<Signal>
PDA Ch1 254nm

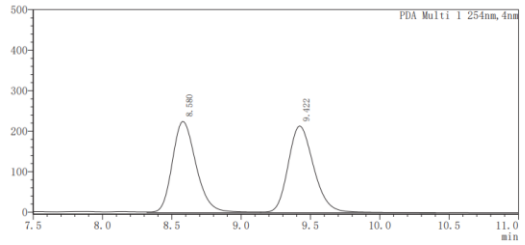
Peak	RetTime	Area	Height	Area%
1	8.757	562001	47429	10.253
2	10.375	4919235	309765	89.747
Totals		5481236	357195	100.000



3wa

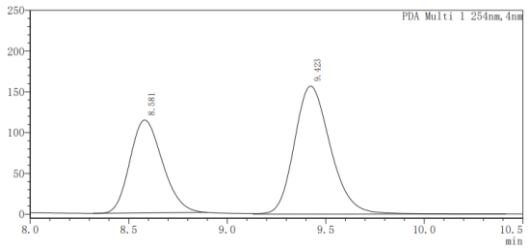
Enantiomeric excess is 20% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 9.42 min; minor isomer: tr = 8.58 min.

$[\alpha]^{20}_{D}$ = +33 (c = 0.2, $CHCl_3$).



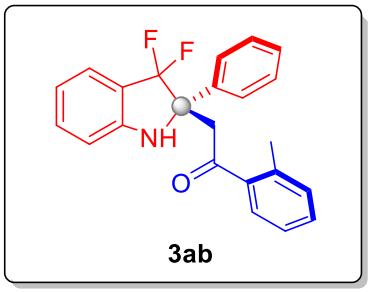
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	8.580	2683545	224756	49.517
2	9.422	2735939	213474	50.483
Totals		5419484	438230	100.000



<Signal>
PDA Ch1 254nm

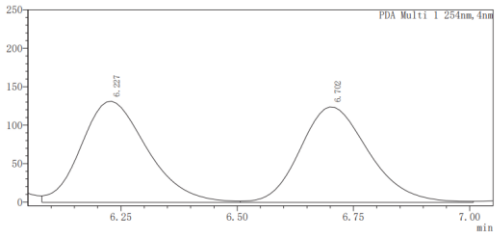
Peak	RetTime	Area	Height	Area%
1	8.581	1313366	113888	39.603
2	9.423	2002936	156774	60.397
Totals		3316302	270662	100.000



3ab

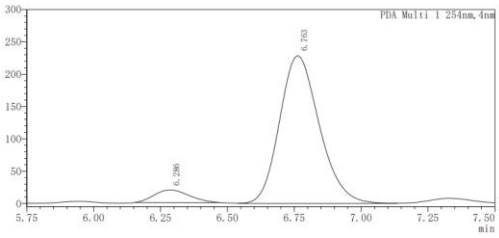
Enantiomeric excess is 86% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 6.76 min; minor isomer: tr = 6.29 min.

$[\alpha]^{20}_D$ = +98 (c = 0.2, $CHCl_3$).



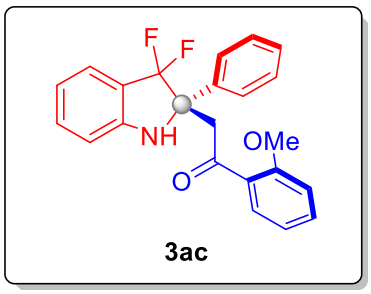
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	6.227	1298352	131555	50.465
2	6.702	1274446	124101	49.535
Totals		2572799	255656	100.000



<Signal>
PDA Ch1 254nm

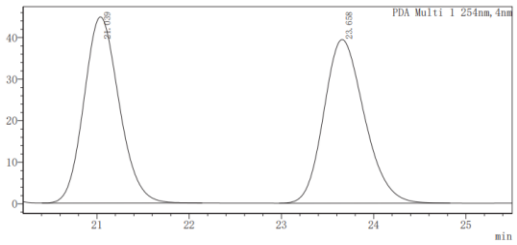
Peak	RetTime	Area	Height	Area%
1	6.286	175974	19529	6.911
2	6.763	2370333	228912	93.089
Totals		2546307	248441	100.000



3ac

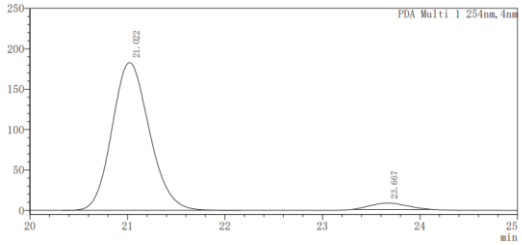
Enantiomeric excess is 92% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 0.5 mL/min, 254 nm): major isomer: tr = 21.02 min; minor isomer: tr = 23.67 min.

$[\alpha]^{20}_D$ = +280 (c = 0.2, $CHCl_3$).



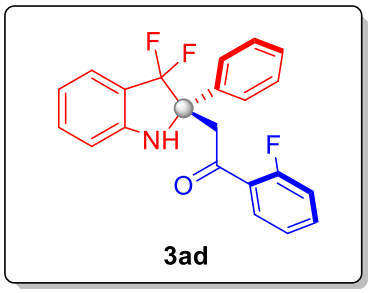
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	21.039	1188529	44765	49.703
2	23.658	1202751	39363	50.297
Totals		2391280	84128	100.000



<Signal>
PDA Ch1 254nm

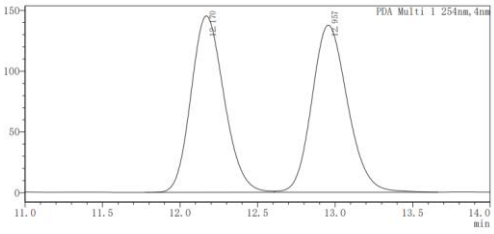
Peak	RetTime	Area	Height	Area%
1	21.022	4873649	182922	95.929
2	23.667	206809	7924	4.071
Totals		5080458	190846	100.000



3ad

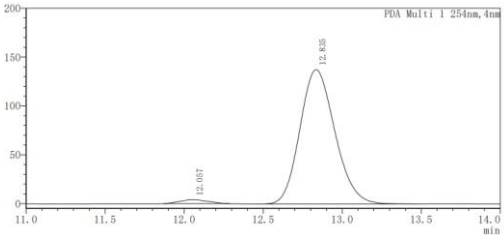
Enantiomeric excess is 96% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 0.5 mL/min, 254 nm): major isomer: tr = 12.84 min; minor isomer: tr = 12.06 min.

$[\alpha]^{20}_{D}$ = +307 (c = 0.2, $CHCl_3$).



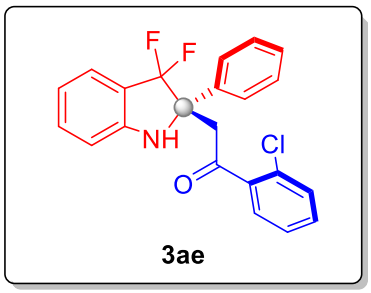
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	12.170	2152565	145200	49.423
2	12.957	2202868	137495	50.577
Totals		4355433	282694	100.000



<Signal>
PDA Ch1 254nm

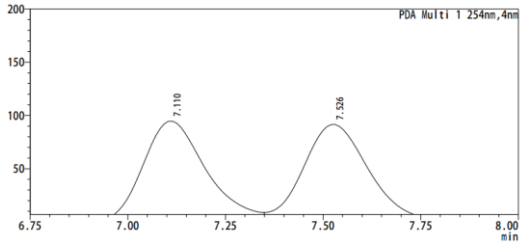
Peak	RetTime	Area	Height	Area%
1	12.057	49523	3910	2.281
2	12.835	2121398	137580	97.719
Totals		2170922	141490	100.000



3ae

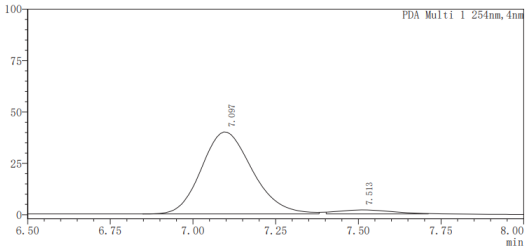
Enantiomeric excess is 90% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 7.10 min; minor isomer: tr = 7.51 min.

$[\alpha]^{20}_{D}$ = +194 (c = 0.2, $CHCl_3$).



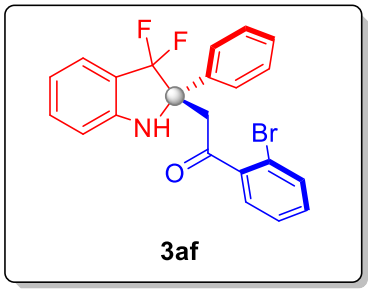
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	7.110	1076555	94622	50.039
2	7.526	1074868	91528	49.961
Totals		2151422	186150	100.000



<Signal>
PDA Ch1 254nm

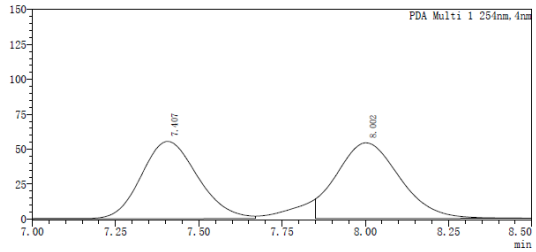
Peak	RetTime	Area	Height	Area%
1	7.097	428342	39890	95.059
2	7.513	22266	1968	4.941
Totals		450608	41859	100.000



3af

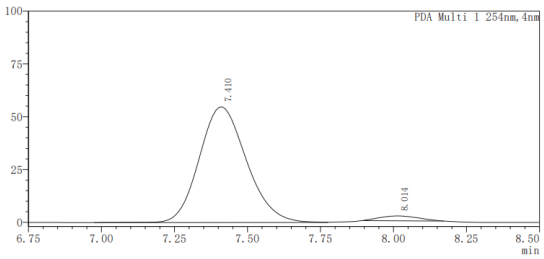
Enantiomeric excess is 94% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 7.41 min; minor isomer: tr = 8.01 min.

$[\alpha]^{20}_{D}$ = +114 (c = 0.2, $CHCl_3$).



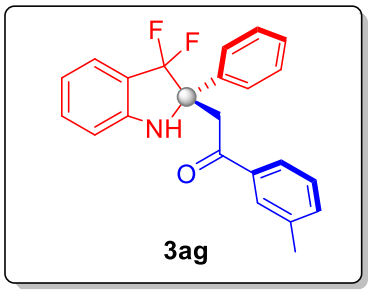
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	7.407	652161	55270	47.962
2	8.002	707573	54174	52.038
Totals		1359733	109444	100.000



<Signal>
PDA Ch1 254nm

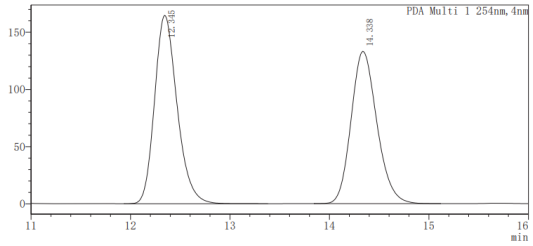
Peak	RetTime	Area	Height	Area%
1	7.410	617016	54782	96.682
2	8.014	21172	2286	3.318
Totals		638188	57068	100.000



3ag

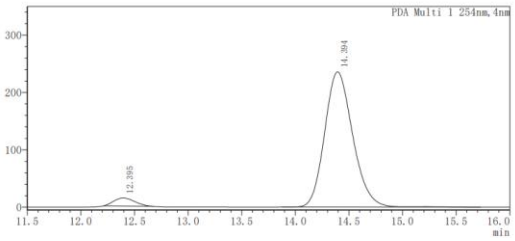
Enantiomeric excess is 92% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 0.5 mL/min, 254 nm): major isomer: tr = 14.39 min; minor isomer: tr = 12.4 min.

$[\alpha]^{20}_D$ = +342 (c = 0.2, $CHCl_3$).



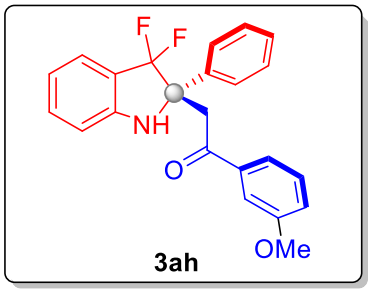
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	12.345	2595073	164523	51.916
2	14.338	2403502	133085	48.084
Totals		4998574	297608	100.000



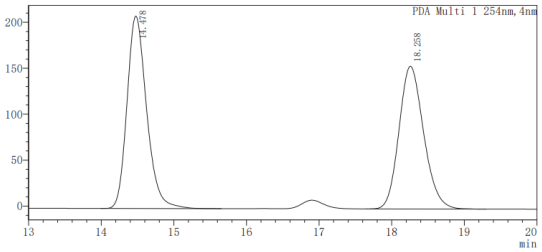
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	12.395	190413	14125	4.244
2	14.394	4296753	235773	95.756
Totals		4487166	249897	100.000



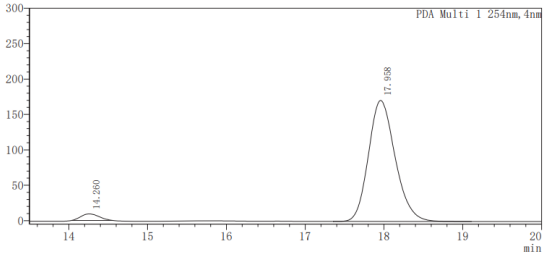
Enantiomeric excess is 94% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 0.5 mL/min, 254 nm): major isomer: tr = 17.96 min; minor isomer: tr = 14.26 min.

$[\alpha]^{20}_D$ = +326 (c = 0.2, $CHCl_3$).



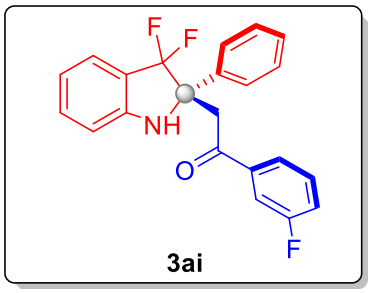
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	14.478	3941833	209201	51.819
2	18.258	3665035	155099	48.181
Totals		7606869	364300	100.000



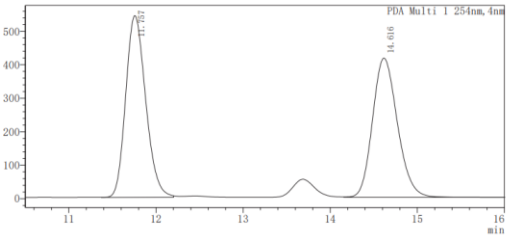
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	14.260	144781	9232	3.466
2	17.958	4031905	170957	96.534
Totals		4176685	180189	100.000



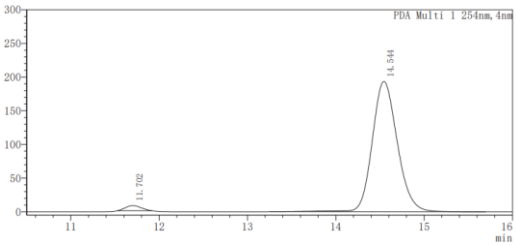
Enantiomeric excess is 96% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 0.5 mL/min, 254 nm): major isomer: tr = 14.54 min; minor isomer: tr = 11.70 min.

$[\alpha]^{20}_{D}$ = +366 (c = 0.2, $CHCl_3$).



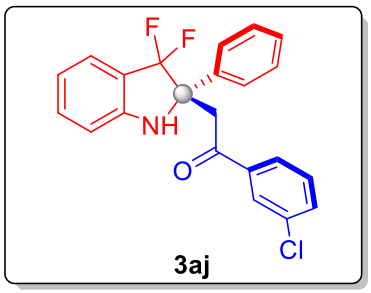
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	11.757	8658900	542666	51.127
2	14.616	8277257	415553	48.873
Totals		16936157	958219	100.000



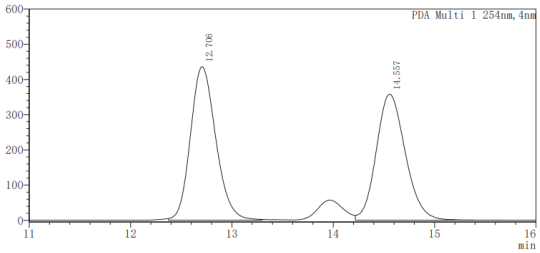
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	11.702	94049	7575	2.396
2	14.544	3831390	193574	97.604
Totals		3925440	201149	100.000



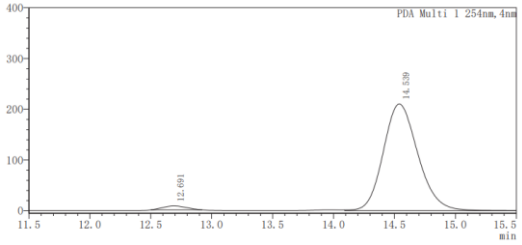
Enantiomeric excess is 96% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 0.5 mL/min, 254 nm): major isomer: tr = 14.54 min; minor isomer: tr = 12.69 min.

$[\alpha]^{20}_{D}$ = +226 (c = 0.2, $CHCl_3$).



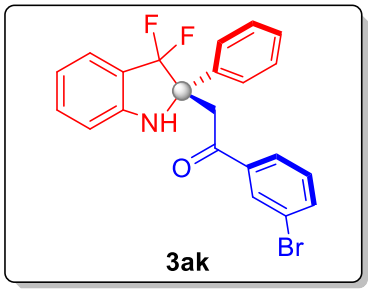
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	12.706	7578545	436295	51.542
2	14.557	7124984	357893	48.458
Totals		14703529	794189	100.000



<Signal>
PDA Ch1 254nm

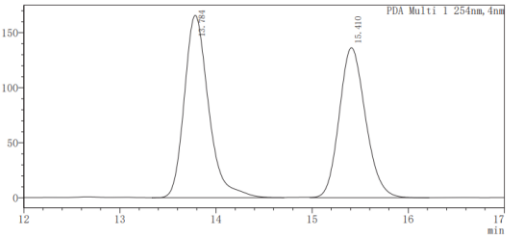
Peak	RetTime	Area	Height	Area%
1	12.691	104592	7738	2.447
2	14.539	4169731	210375	97.553
Totals		4274324	218112	100.000



3ak

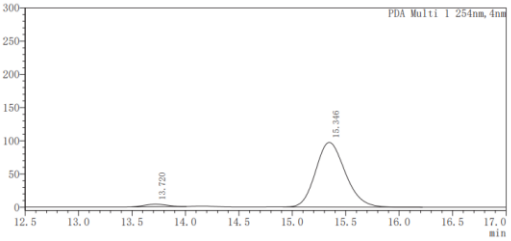
Enantiomeric excess is 94% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 0.5mL/min, 254 nm): major isomer: tr = 15.35 min; minor isomer: tr = 13.72 min.

$[\alpha]^{20}_{D}$ = +342 (c = 0.2, $CHCl_3$).



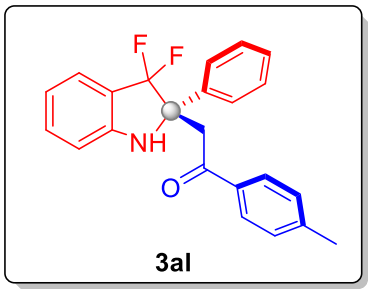
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	13.784	2914609	165605	52.901
2	15.410	2594991	136160	47.099
Totals		5509600	301765	100.000



<Signal>
PDA Ch1 254nm

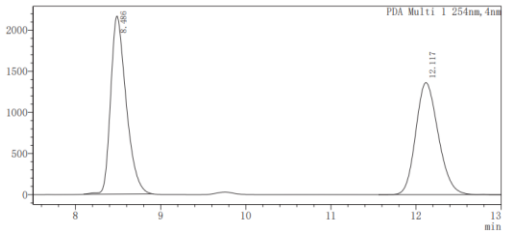
Peak	RetTime	Area	Height	Area%
1	13.720	54640	3783	2.811
2	15.346	1889040	97500	97.189
Totals		1943679	101283	100.000



3al

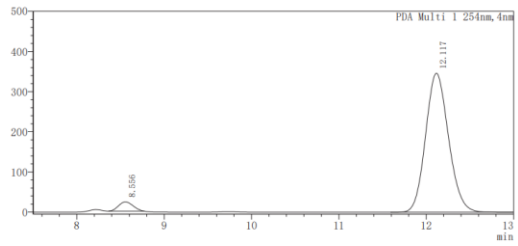
Enantiomeric excess is 92% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 12.12 min; minor isomer: tr = 8.56 min.

$[\alpha]^{20}_{D}$ = +280 (c = 0.2, $CHCl_3$).



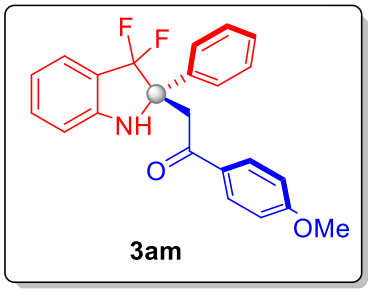
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	8.486	27318575	2162258	52.196
2	12.117	25019766	1361136	47.804
Totals		52338341	3523394	100.000

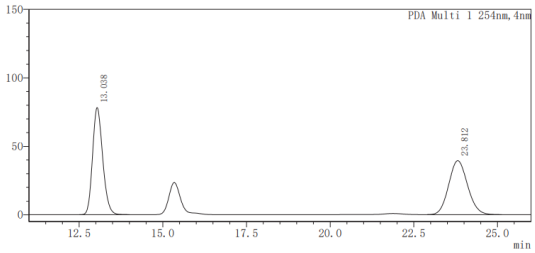


<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	8.556	266297	23151	4.052
2	12.117	6306055	346142	95.948
Totals		6572352	369293	100.000

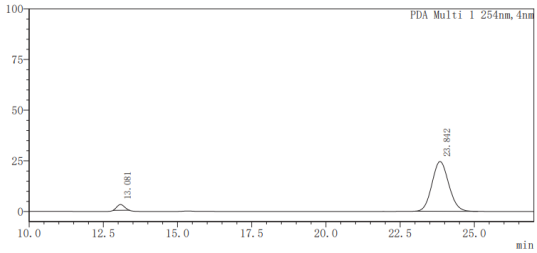


Enantiomeric excess is 90% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 23.84 min; minor isomer: tr = 13.08 min. $[\alpha]^{20}_{D}$ = +331 (c = 0.2, $CHCl_3$).



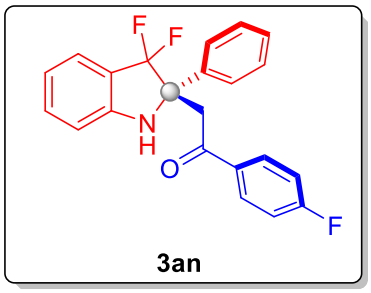
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	13.038	1648062	78199	51.587
2	23.812	1546674	39434	48.413
Totals		3194736	117633	100.000



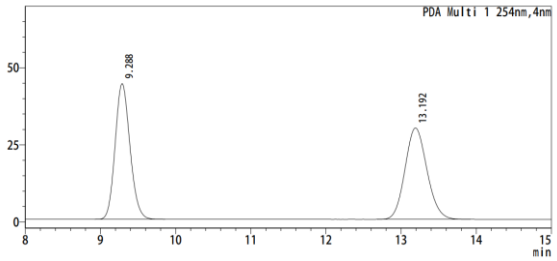
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	13.081	50017	2854	4.914
2	23.842	967781	24590	95.086
Totals		1017798	27444	100.000



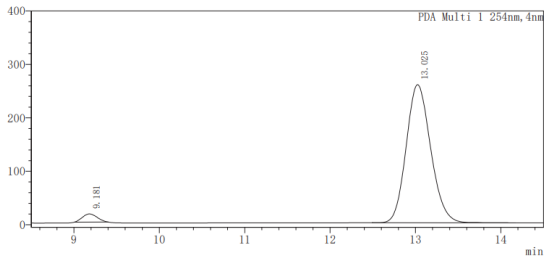
3an

Enantiomeric excess is 94% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 13.03 min; minor isomer: tr = 9.18 min. $[\alpha]^{20}_{D}$ = +250 (c = 0.2, $CHCl_3$).



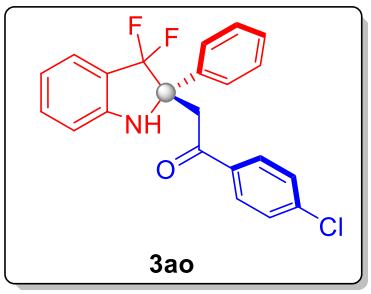
〈Signal〉
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	9.288	602968	44021	50.059
2	13.192	601537	29654	49.941
Totals		1204506	73675	100.000



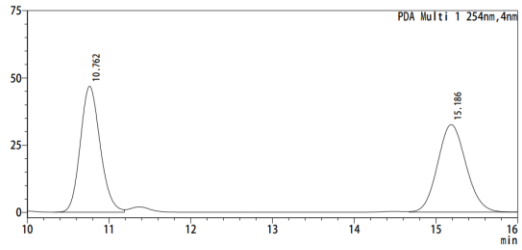
〈Signal〉
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	9.181	183874	15360	3.439
2	13.025	5162368	258629	96.561
Totals		5346243	273988	100.000



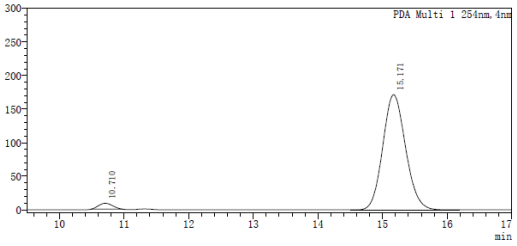
3ao

Enantiomeric excess is 94% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 15.17 min; minor isomer: tr = 10.71 min.$[\alpha]^{20}_{D}$ = +321 (c = 0.2, $CHCl_3$).



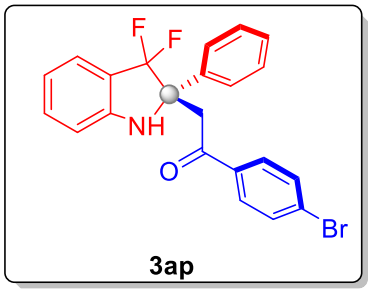
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	10.762	790101	46796	50.123
2	15.186	786212	32531	49.877
Totals		1576313	79327	100.000



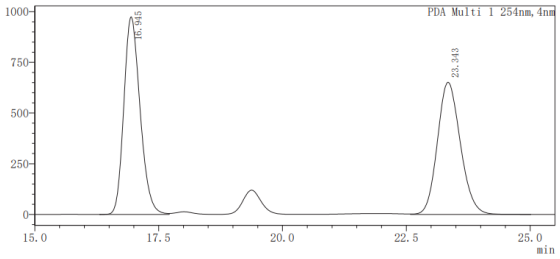
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	10.710	128444	8703	2.959
2	15.171	4212776	171550	97.041
Totals		4341220	180253	100.000



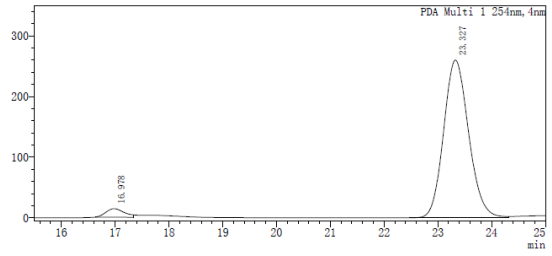
Enantiomeric excess is 92% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 0.5 mL/min, 254 nm): major isomer: tr = 23.33 min; minor isomer: tr = 16.98 min.

$[\alpha]^{20}_{D}$ = +67 (c = 0.2, $CHCl_3$).



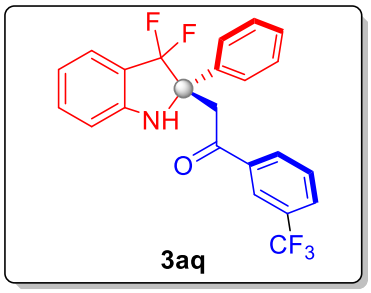
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	16.945	22271063	973945	51.478
2	23.343	20991818	651756	48.522
Totals		43262880	1625700	100.000



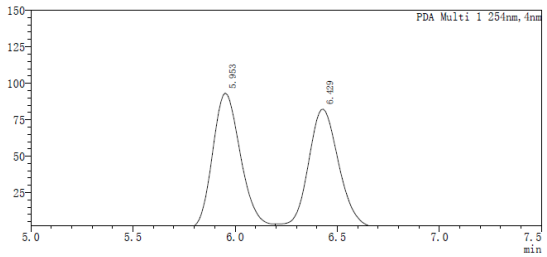
<Siganl>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	16.978	334124	13998	3.823
2	23.327	8405363	259888	96.177
Totals		8739488	273886	100.000



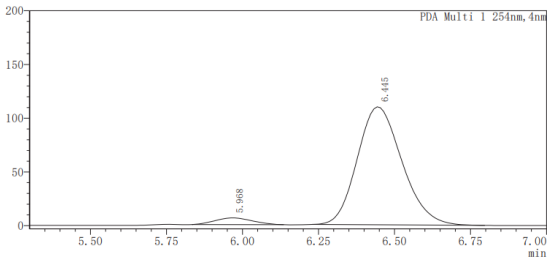
Enantiomeric excess is 92% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 6.45 min; minor isomer: tr = 5.97 min.

$[\alpha]^{20}_{D}$ = +291 (c = 0.2, $CHCl_3$).



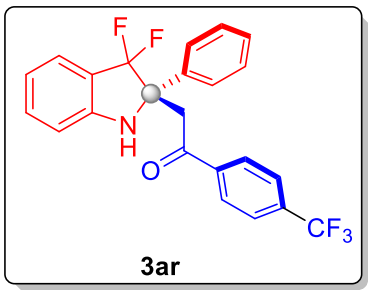
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	5.953	901469	93181	50.899
2	6.429	869628	82165	49.101
Totals		1771096	175347	100.000



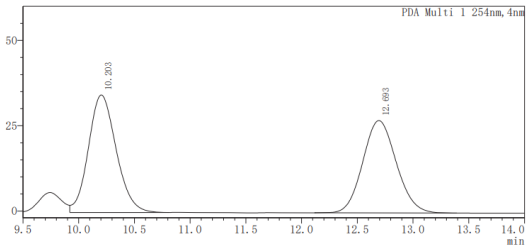
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	5.968	52559	6164	4.469
2	6.445	1123409	109773	95.531
Totals		1175968	115937	100.000



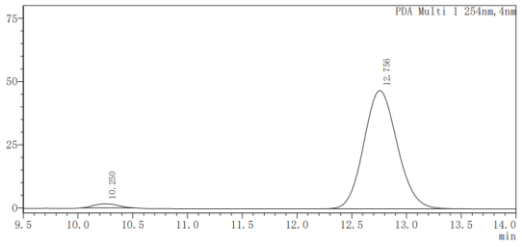
Enantiomeric excess is 96% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 12.76 min; minor isomer: tr = 10.25 min.

$[\alpha]^{20}_{D}$ = +231 (c = 0.2, $CHCl_3$).



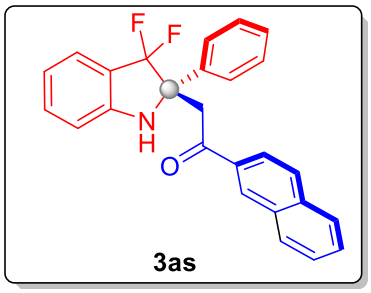
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	10.203	596859	34422	51.281
2	12.693	567044	27094	48.719
Totals		1163903	61516	100.000

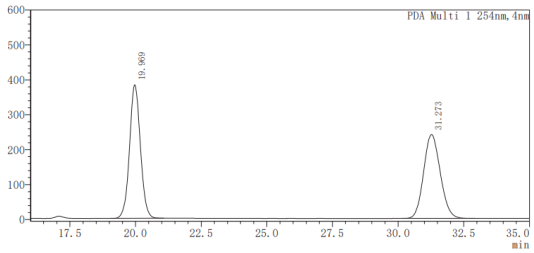


<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	10.250	24978	1688	2.456
2	12.756	992108	46677	97.544
Totals		1017086	48364	100.000

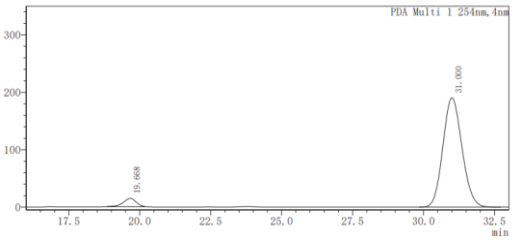


Enantiomeric excess is 90% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 0.5 mL/min, 254 nm): major isomer: tr = 31.00 min; minor isomer: tr = 19.67 min. $[\alpha]^{20}_{D}$ = +335 (c = 0.2, $CHCl_3$).



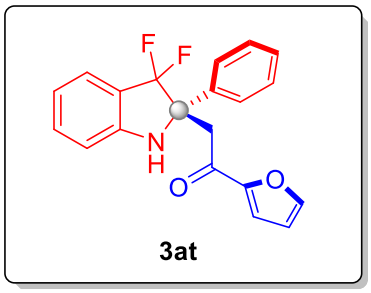
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	19.969	10992209	382119	50.998
2	31.273	10561931	240137	49.002
Totals		21554140	622256	100.000



<Signal>
PDA Ch1 254nm

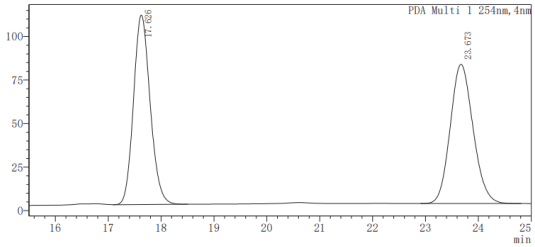
Peak	RetTime	Area	Height	Area%
1	19.668	467982	14835	4.990
2	31.000	8909478	190384	95.010
Totals		9377460	205218	100.000



3at

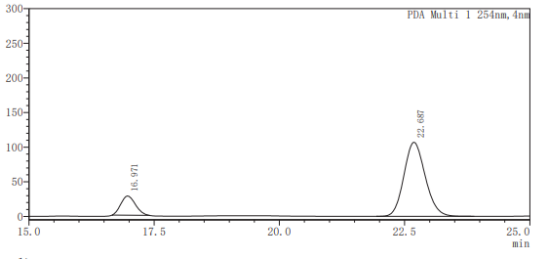
Enantiomeric excess is 70% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 0.5 mL/min, 254 nm): major isomer: tr = 22.69 min; minor isomer: tr = 16.97 min.

$[\alpha]^{20}_{D}$ = +234 (c = 0.2, $CHCl_3$).



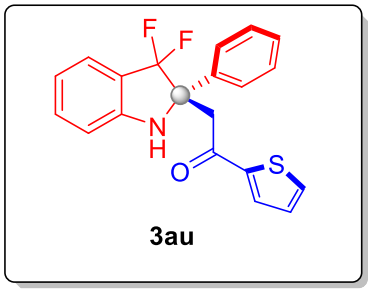
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	17.626	2388934	108728	49.854
2	23.673	2402968	79880	50.146
Totals		4791902	188608	100.000



<Signal>
PDA Ch1 254nm

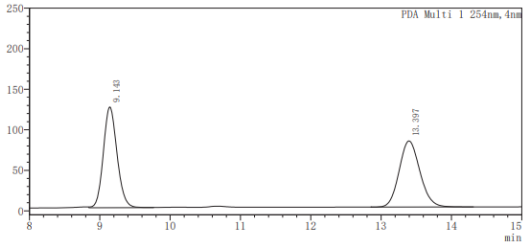
Peak	RetTime	Area	Height	Area%
1	16.971	559674	27738	15.024
2	22.687	3165537	106838	84.976
Totals		3725211	134575	100.000



3au

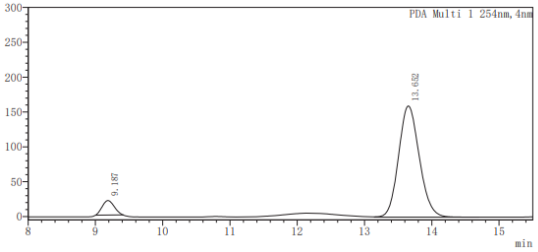
Enantiomeric excess is 86% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 13.65 min; minor isomer: tr = 9.19 min.

$[\alpha]^{20}_{D}$ = +228 (c = 0.2, $CHCl_3$).



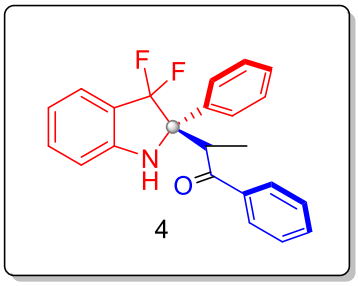
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	9.143	1682180	124282	50.165
2	13.397	1671124	81548	49.835
Totals		3353304	205830	100.000



<Signal>
PDA Ch1 254nm

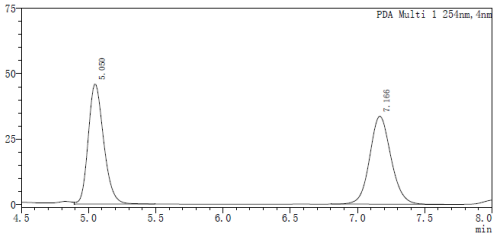
Peak	RetTime	Area	Height	Area%
1	9.187	257658	20807	7.014
2	13.652	3416058	159518	92.986
Totals		3673716	180324	100.000



4

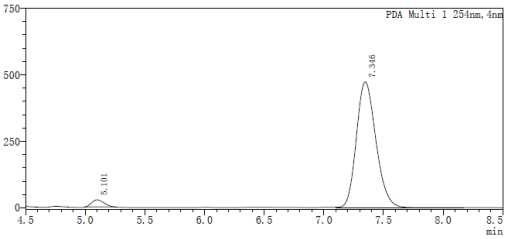
Enantiomeric excess is 94% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 7.35 min; minor isomer: tr = 5.10 min.

$[\alpha]^{20}_{D}$ = +272 (c = 0.2, $CHCl_3$).



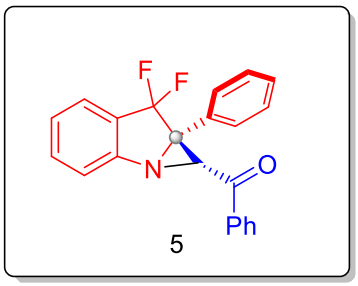
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	5.050	365904	45809	49.644
2	7.166	371150	33595	50.356
Totals		737054	79404	100.000



<Signal>
PDA Ch1 254nm

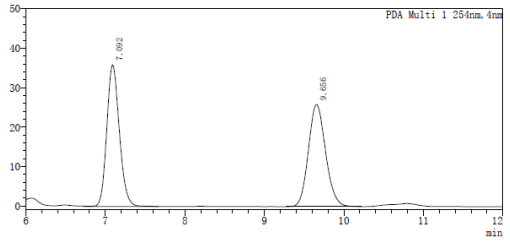
Peak	RetTime	Area	Height	Area%
1	5.101	190599	26516	3.404
2	7.346	5409358	473723	96.596
Totals		5599957	500239	100.000



5

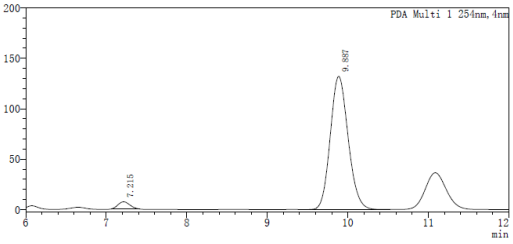
Enantiomeric excess is 94% determined by HPLC (Chiralpak AD-H, Hexane/Isopropanol 80/20, flow rate = 1.0 mL/min, 254 nm): major isomer: tr = 9.89 min; minor isomer: tr = 7.22 min.

$[\alpha]^{20}_{D}$ = +214 (c = 0.2, $CHCl_3$).



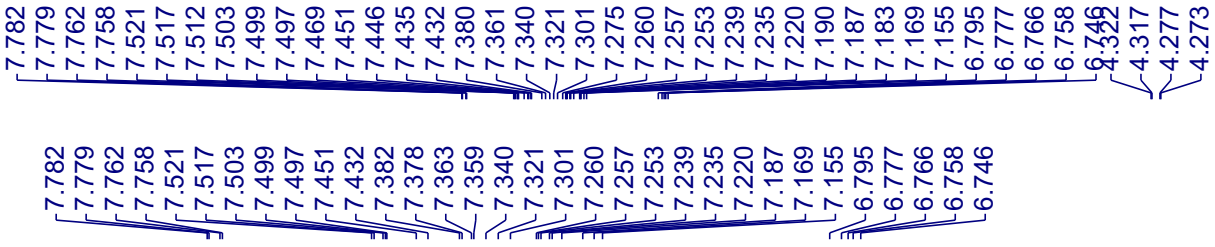
<Signal>
PDA Ch1 254nm

Peak	RetTime	Area	Height	Area%
1	7.092	393475	35869	50.306
2	9.656	388691	25880	49.694
Totals		782166	61750	100.000



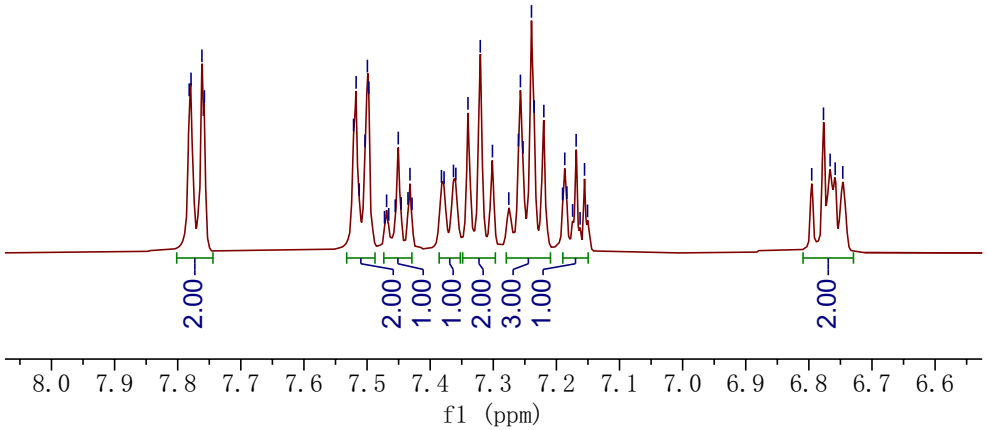
<Signal>
PDA Ch1 254nm

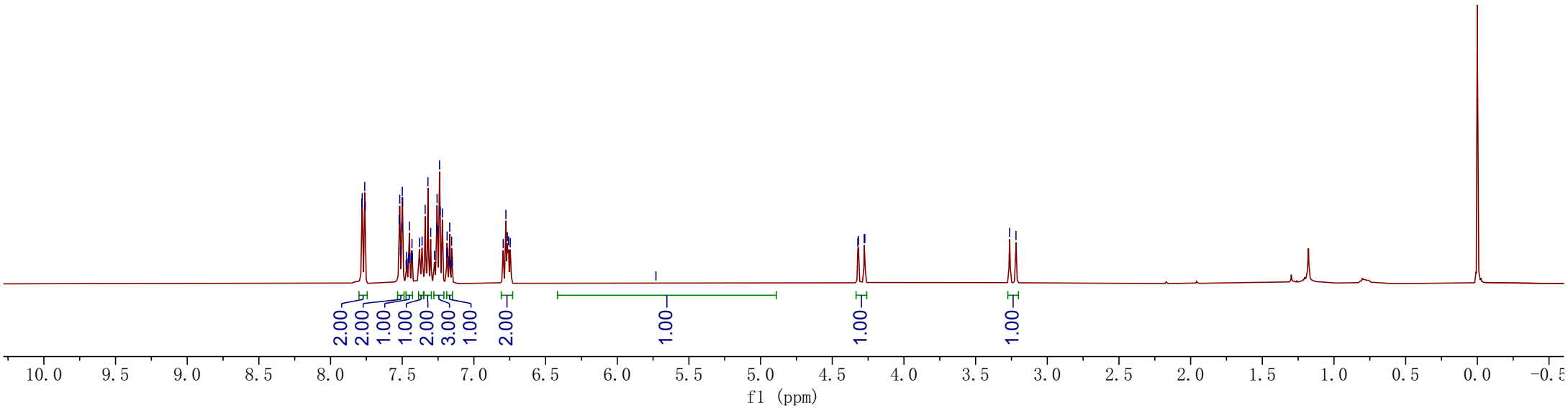
Peak	RetTime	Area	Height	Area%
1	7.215	72212	7133	3.413
2	9.887	2043423	132138	96.587
Totals		2115636	139271	100.000

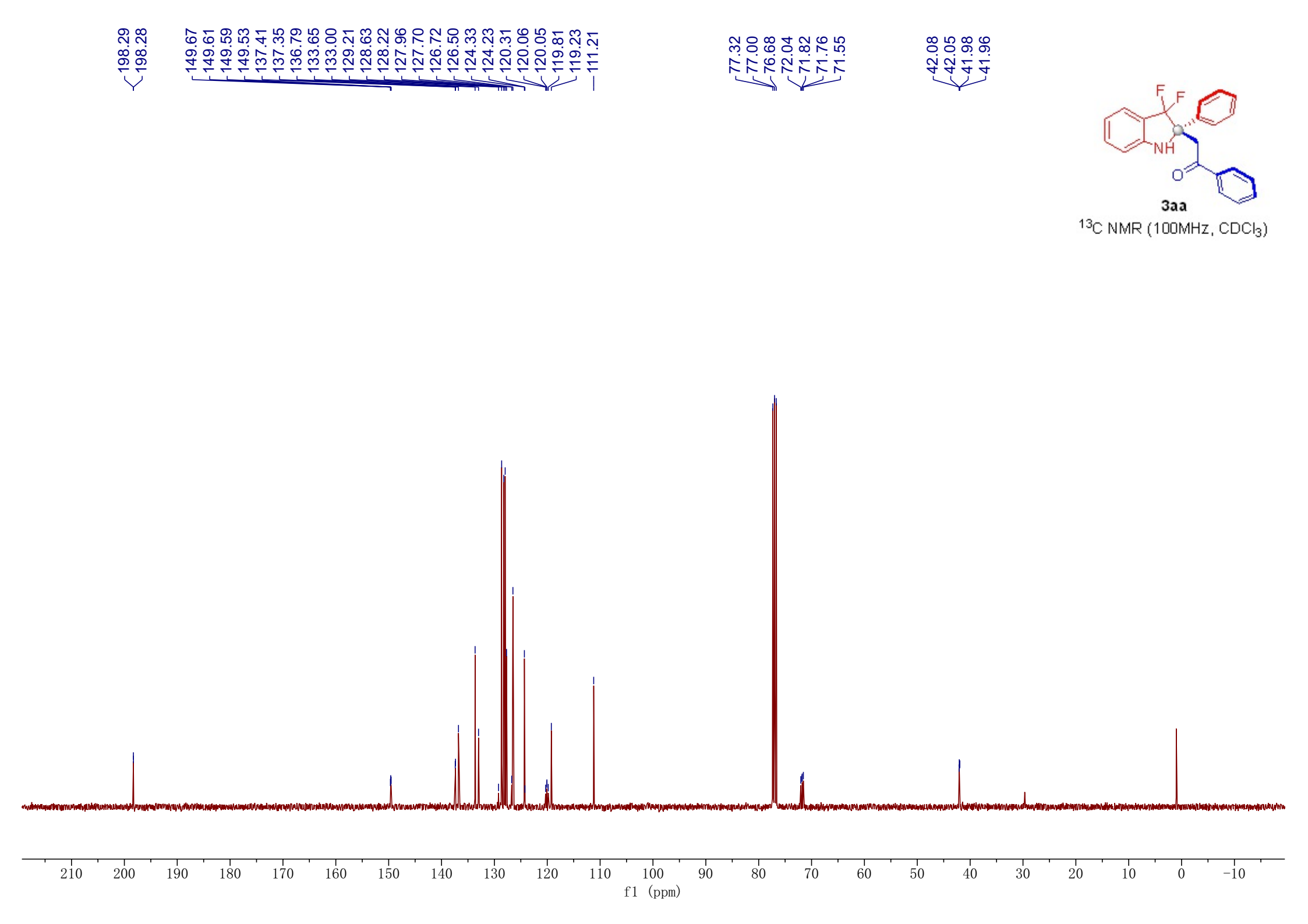


3aa

^{1}H NMR (400MHz, $CDCl_3$)






198.29
198.28
149.67
149.61
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149.53
137.41
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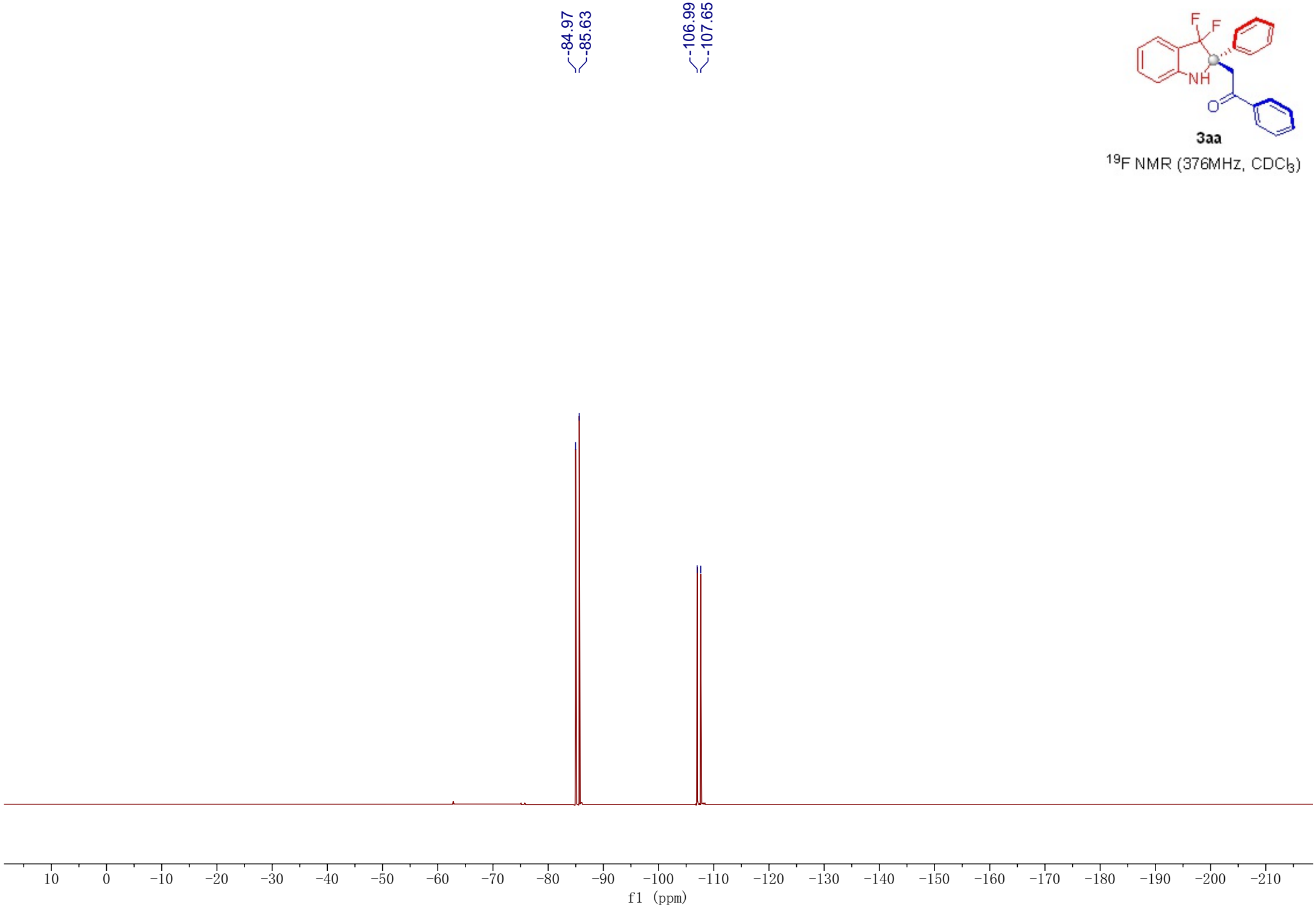
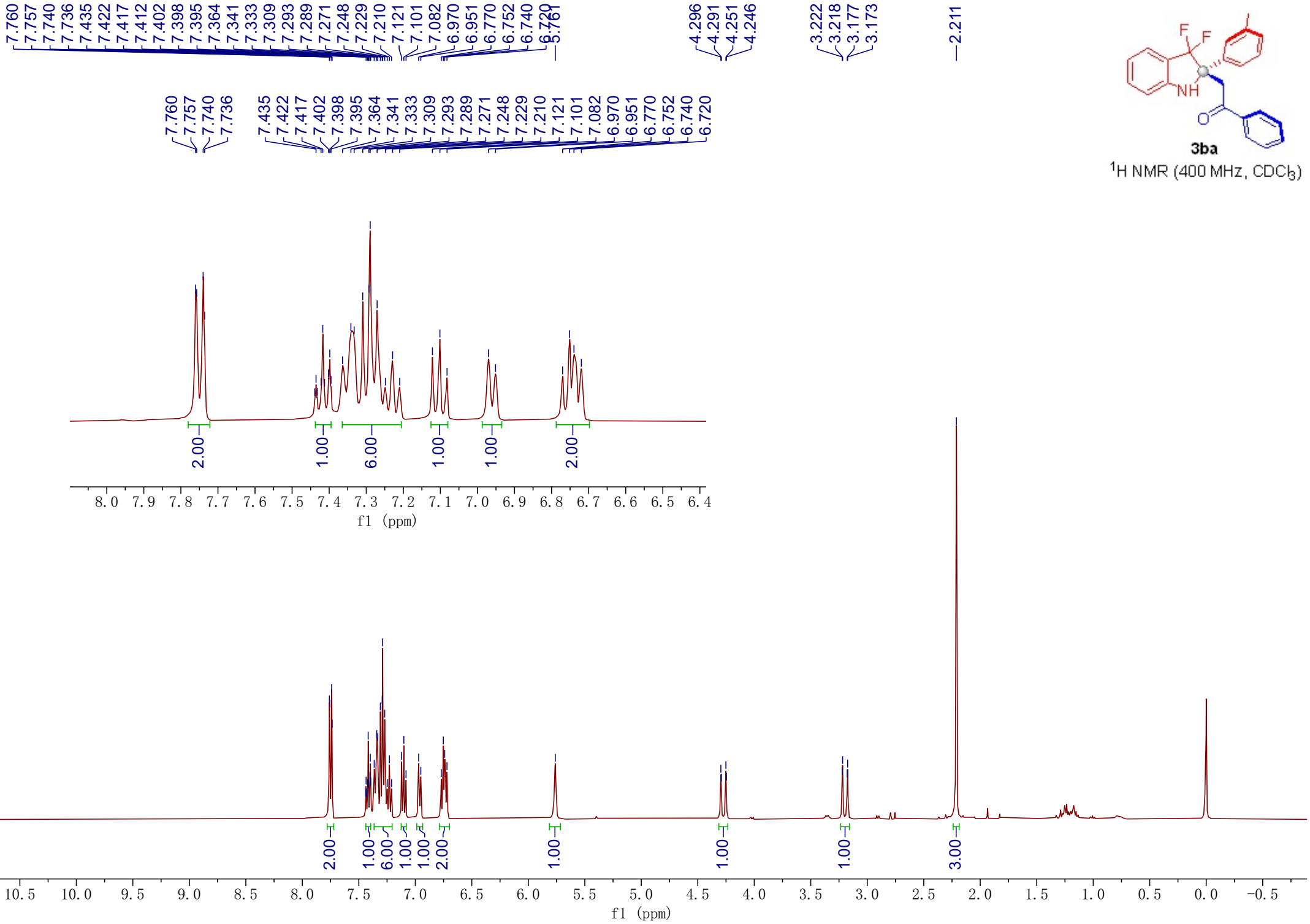
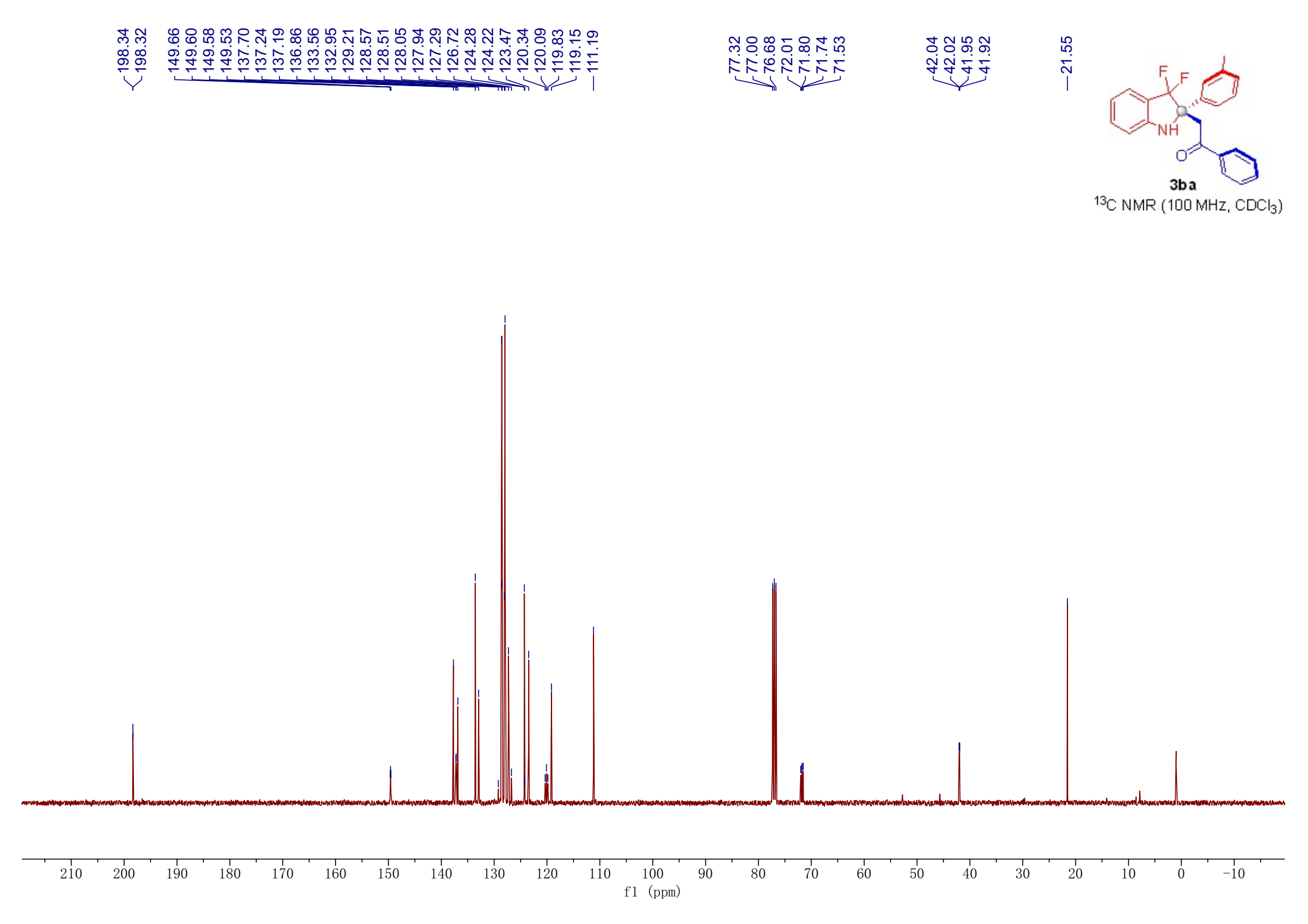
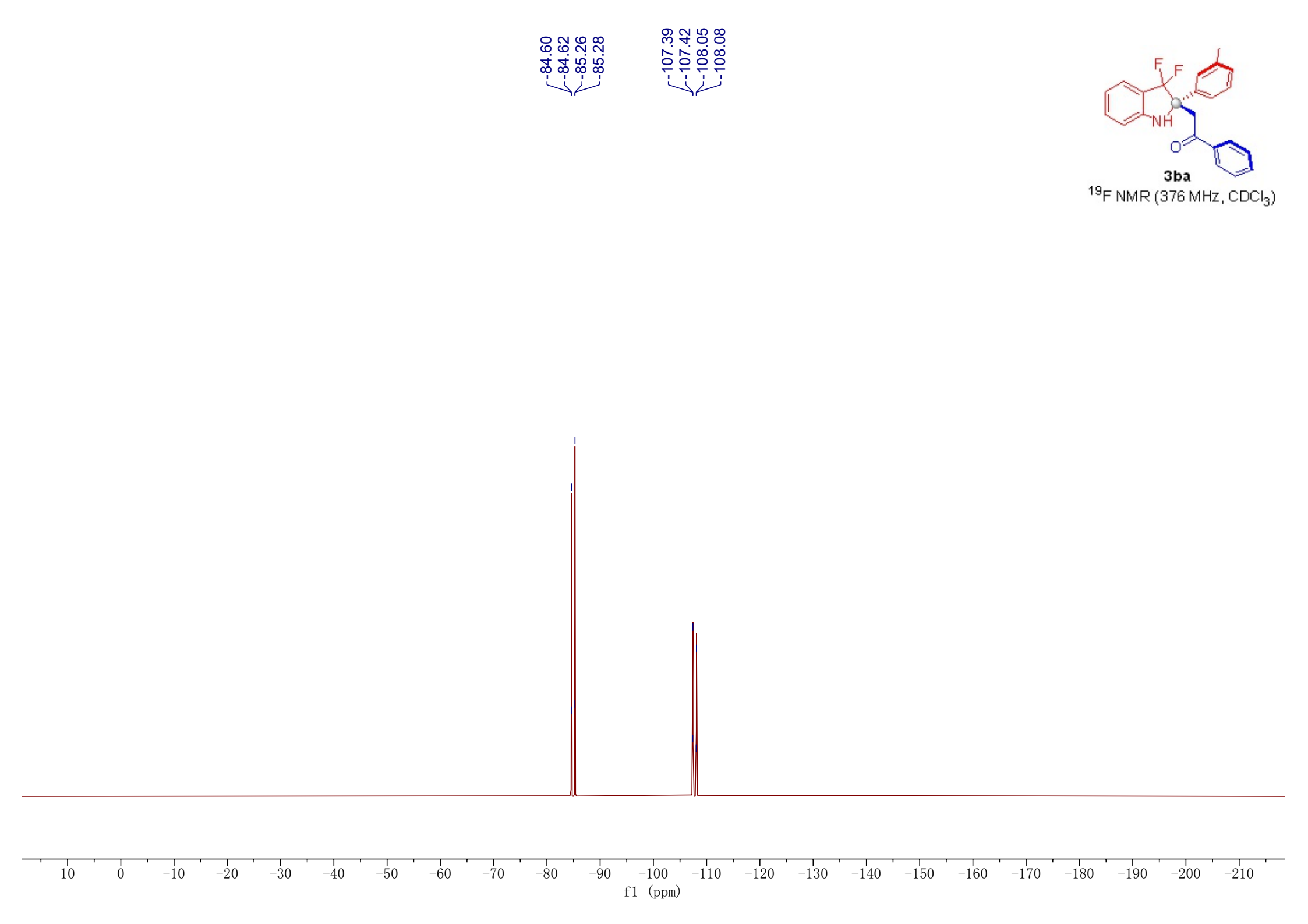
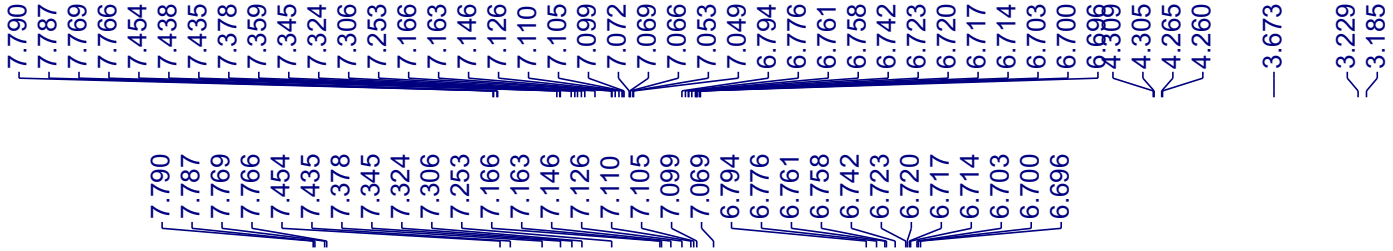
133.00
129.21
128.63
128.22
127.96
127.70
126.72
126.50
124.33
124.23
120.31
120.06
120.05
119.81
119.23
111.21
77.32
77.00
76.68
72.04
71.82
71.76
71.55
42.08
42.05
41.98
41.96
F
F
NH
O
3aa
13C NMR (100MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

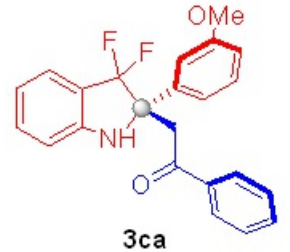

-84.97
-85.63
-106.99
-107.65
F
F
NH
O
3aa
^{19}F NMR (376MHz, $CDCl_3$)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)


7.760
7.757
7.740
7.736
7.435
7.422
7.417
7.412
7.402
7.398
7.395
7.364
7.341
7.333
7.309
7.293
7.289
7.271
7.248
7.229
7.210
7.121
7.101
7.082
6.970
6.951
6.770
6.752
6.740
6.720
4.296
4.291
4.251
4.246
3.222
3.218
3.177
3.173
2.211
F
F
NH
O
3ba
1H NMR (400 MHz, CDCl3)
2.00
1.00
6.00
1.00
1.00
2.00
f1 (ppm)
3.00


198.34
198.32
149.66
149.60
149.58
149.53
137.70
137.24
137.19
136.86
133.56
132.95
129.21
128.57
128.51
128.05
127.94
127.29
126.72
124.28
124.22
123.47
120.34
120.09
119.83
119.15
111.19
77.32
77.00
76.68
72.01
71.80
71.74
71.53
42.04
42.02
41.95
41.92
21.55
F
F
NH
O
3ba
13C NMR (100 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

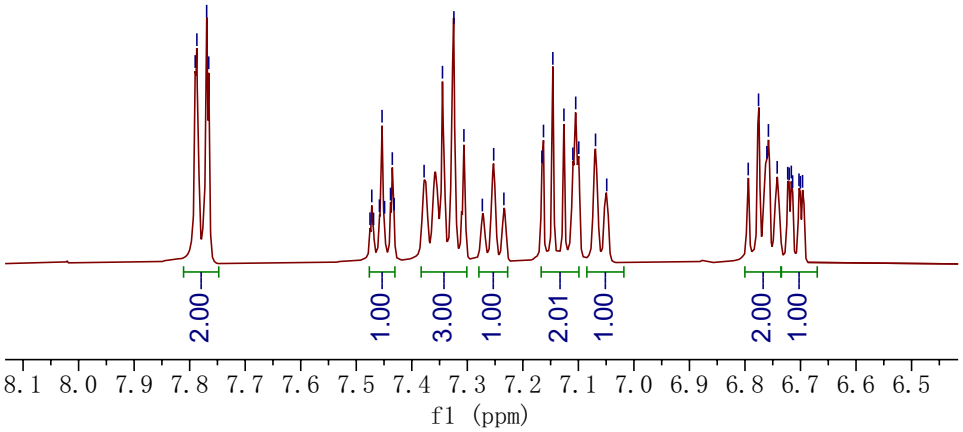

-84.60
-84.62
-85.26
-85.28
-107.39
-107.42
-108.05
-108.08
F
F
NH
O
3ba
^{19}F NMR (376 MHz, $CDCl_3$)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)





3ca

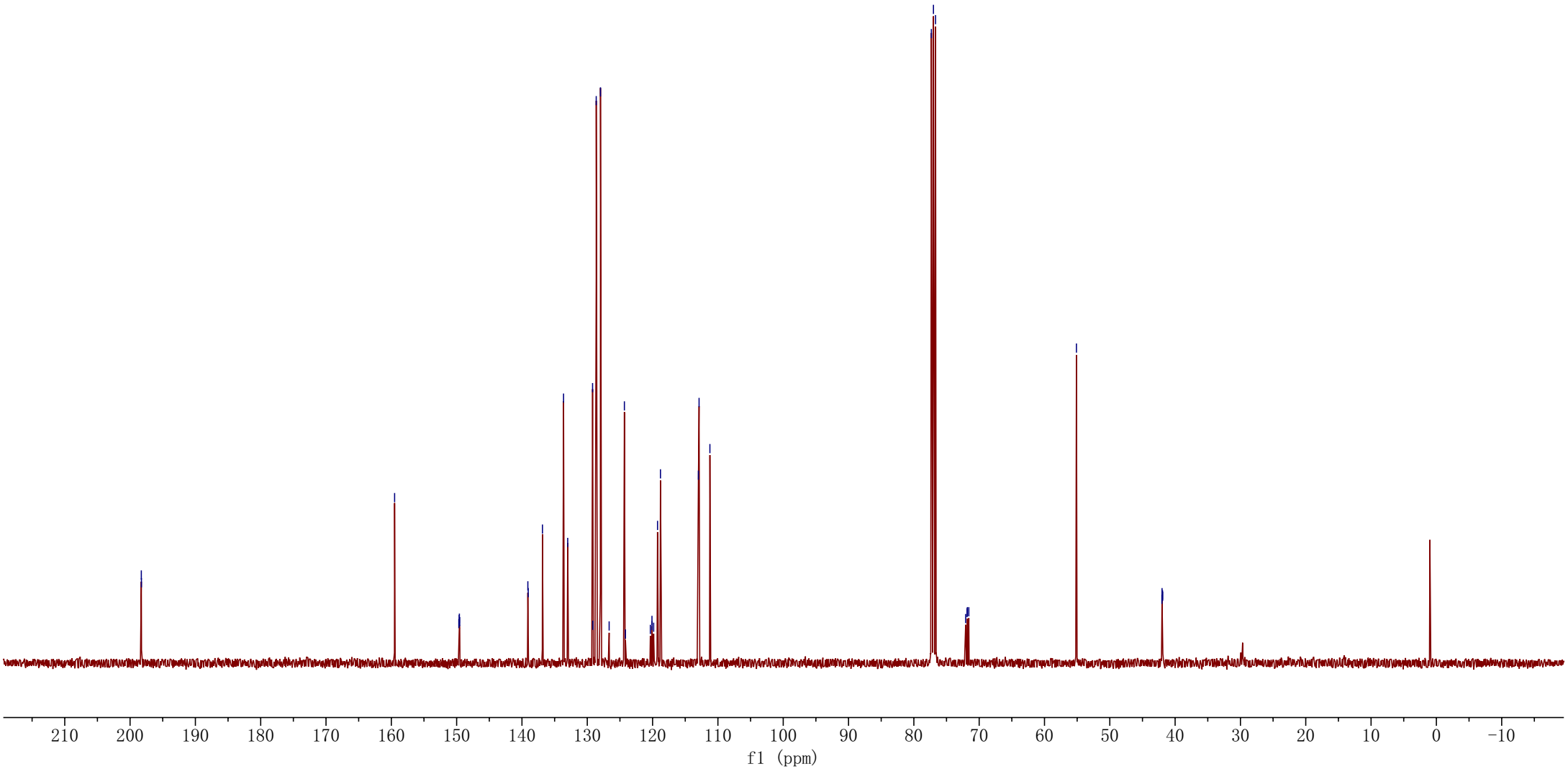
^{1}H NMR (400 MHz, $CDCl_3$)

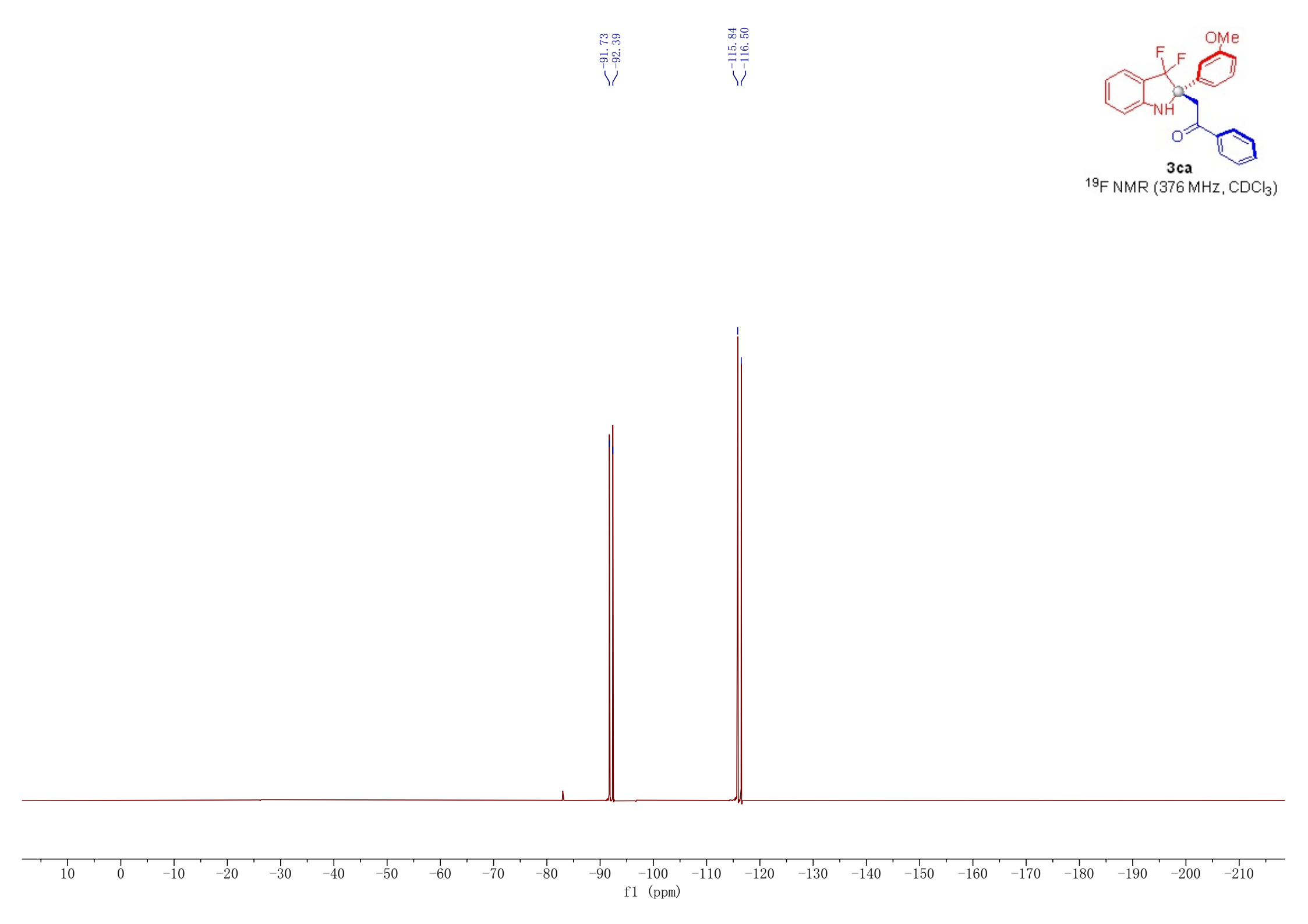


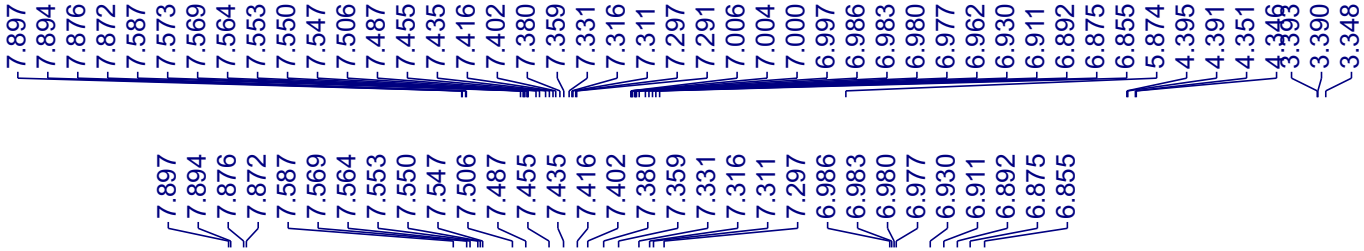
198.28
198.26
159.50
149.67
149.61
149.58
149.53
139.10
139.04
136.86
133.63
133.00
129.19
129.15
128.63
127.98
126.65
124.32
124.15
120.34
120.09
120.08
119.84
119.24
118.79
112.99
112.88
111.23
77.32
77.00
76.68
72.07
71.86
71.80
71.59
55.11
42.02
42.00
41.93
41.90

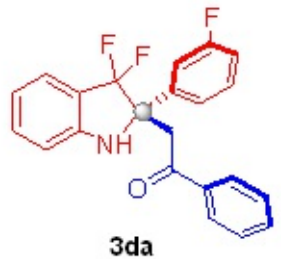
3ca

^{13}C NMR (100 MHz, $CDCl_3$)



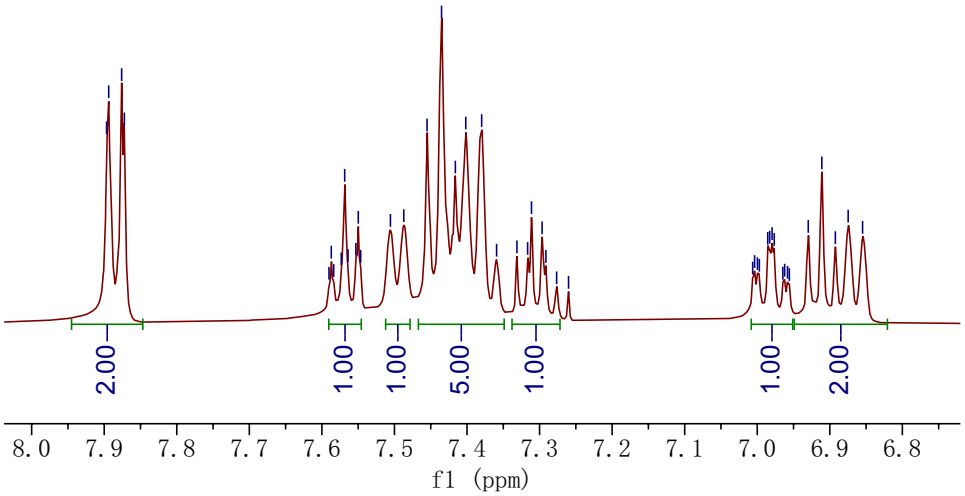

-91.73
-92.39
-115.84
-116.50
OMe
F
F
NH
O
3ca
19F NMR (376 MHz, CDCl3)
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

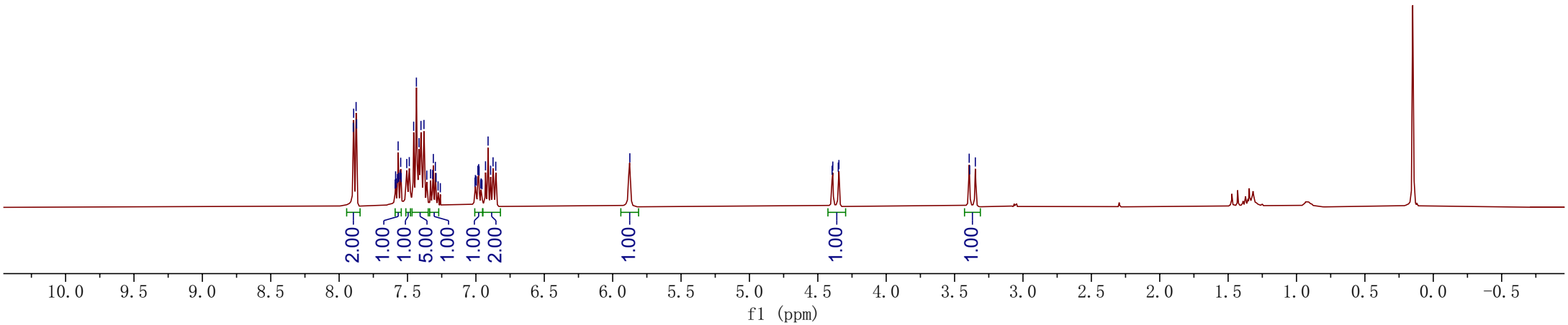




3da

^{1}H NMR (400 MHz, $CDCl_3$)

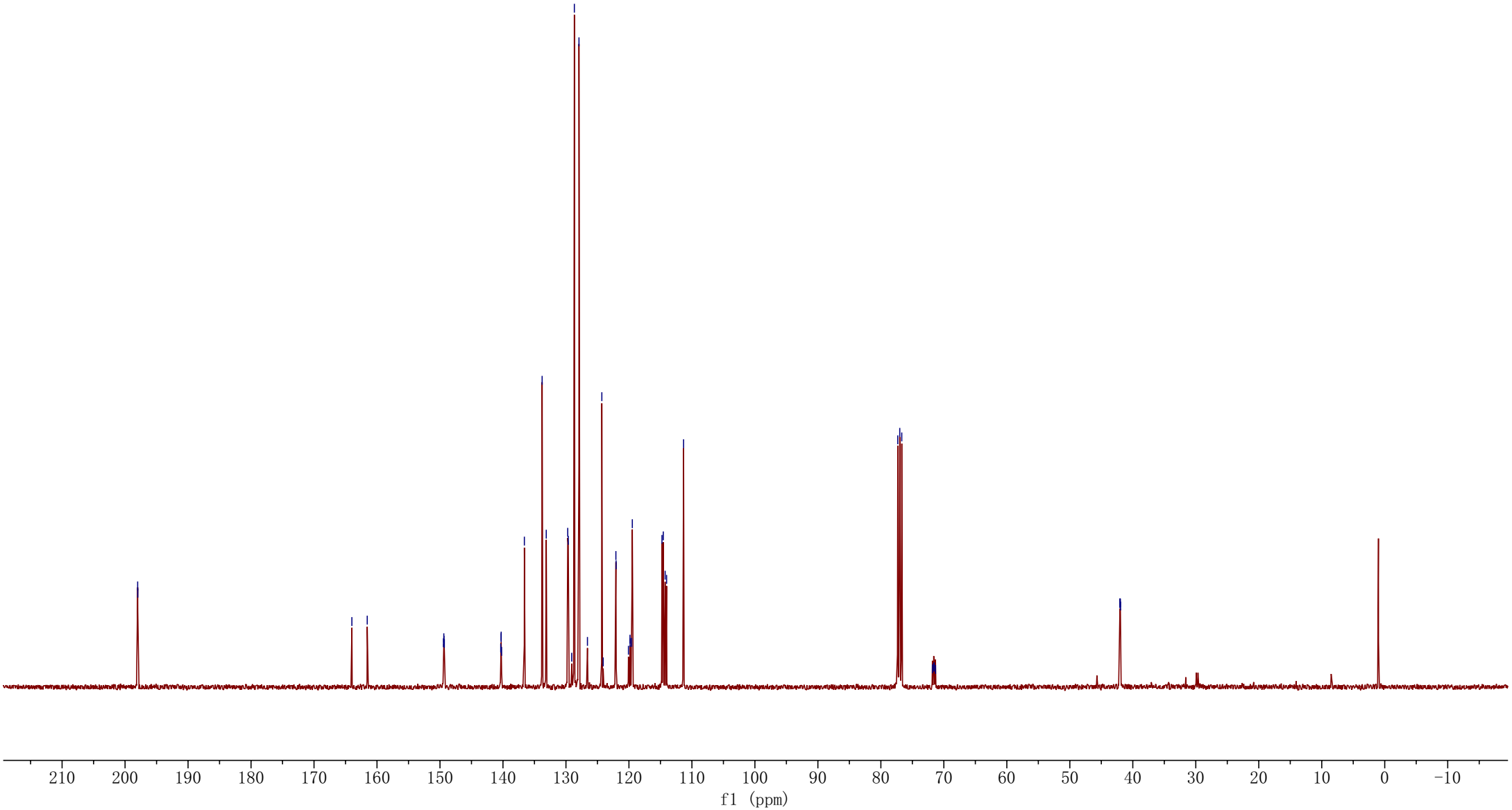


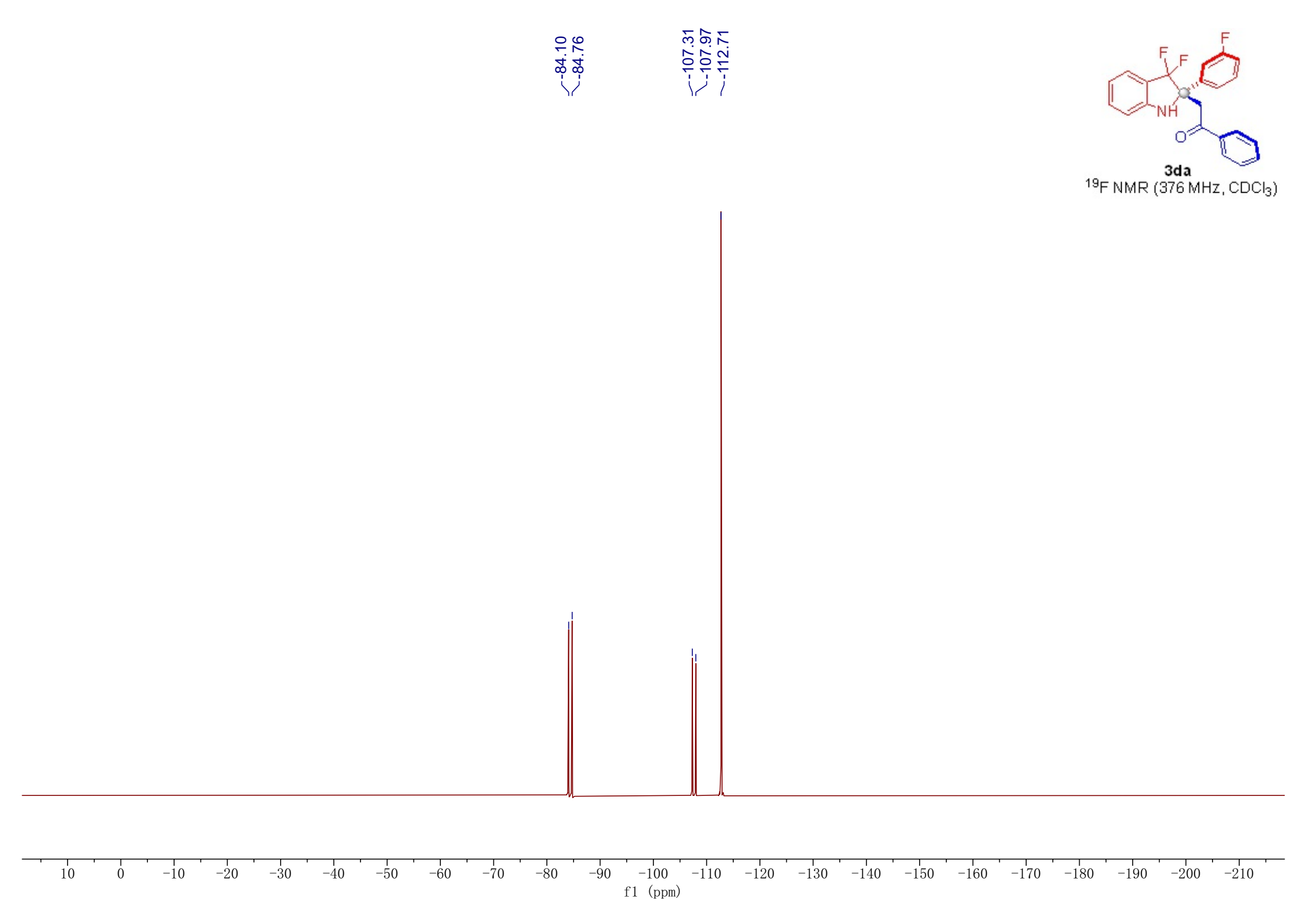


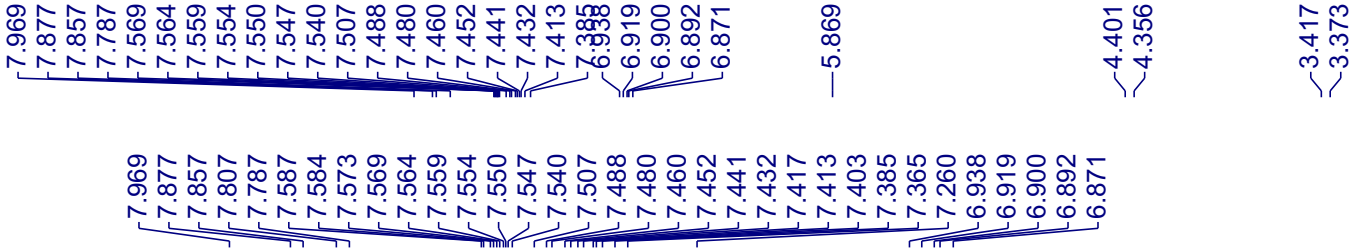
198.00
197.98
163.99
161.55
149.45
149.39
149.37
149.31
140.35
140.30
140.29
140.23
136.60
133.78
133.13
129.72
129.63
129.09
128.67
127.93
126.59
124.30
124.09
122.07
122.04
120.08
119.83
119.82
119.57
119.46
114.76
114.55
114.25
114.02
111.32
77.32
77.00
76.68
71.81
71.59
71.53
71.32
42.07
42.04
41.97
41.95

3da

^{13}C NMR (100 MHz, $CDCl_3$)

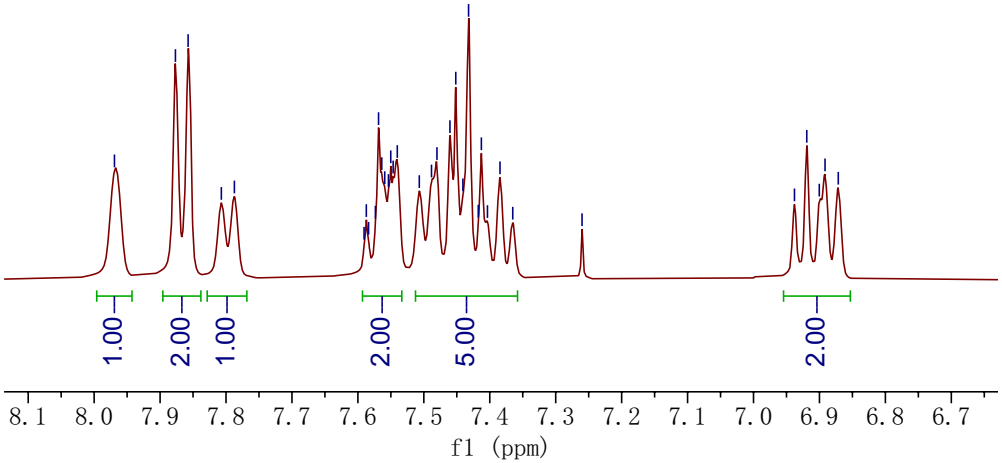


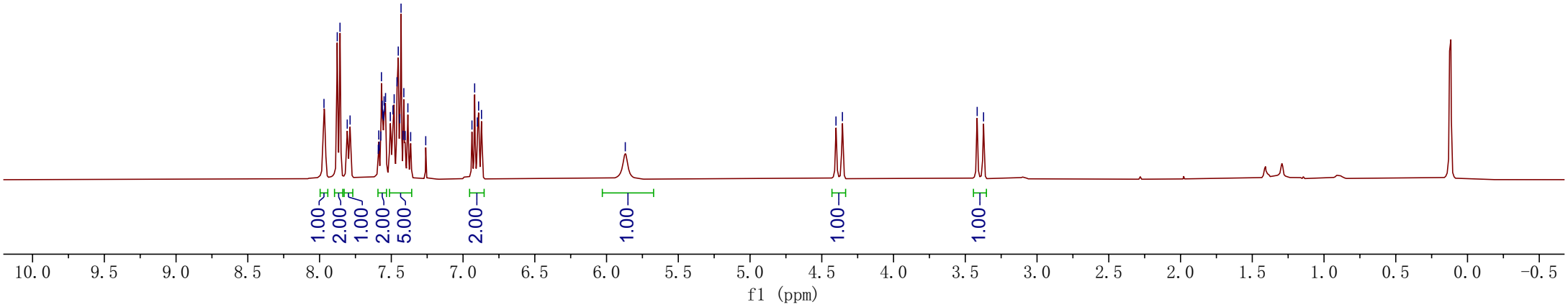

-84.10
-84.76
-107.31
-107.97
-112.71
F
F
F
NH
O
3da
19F NMR (376 MHz, CDCl3)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

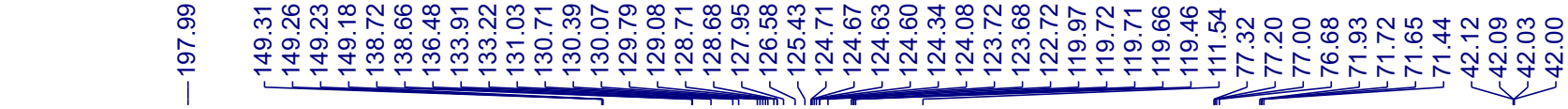


3ea

^{1}H NMR (400 MHz, $CDCl_3$)

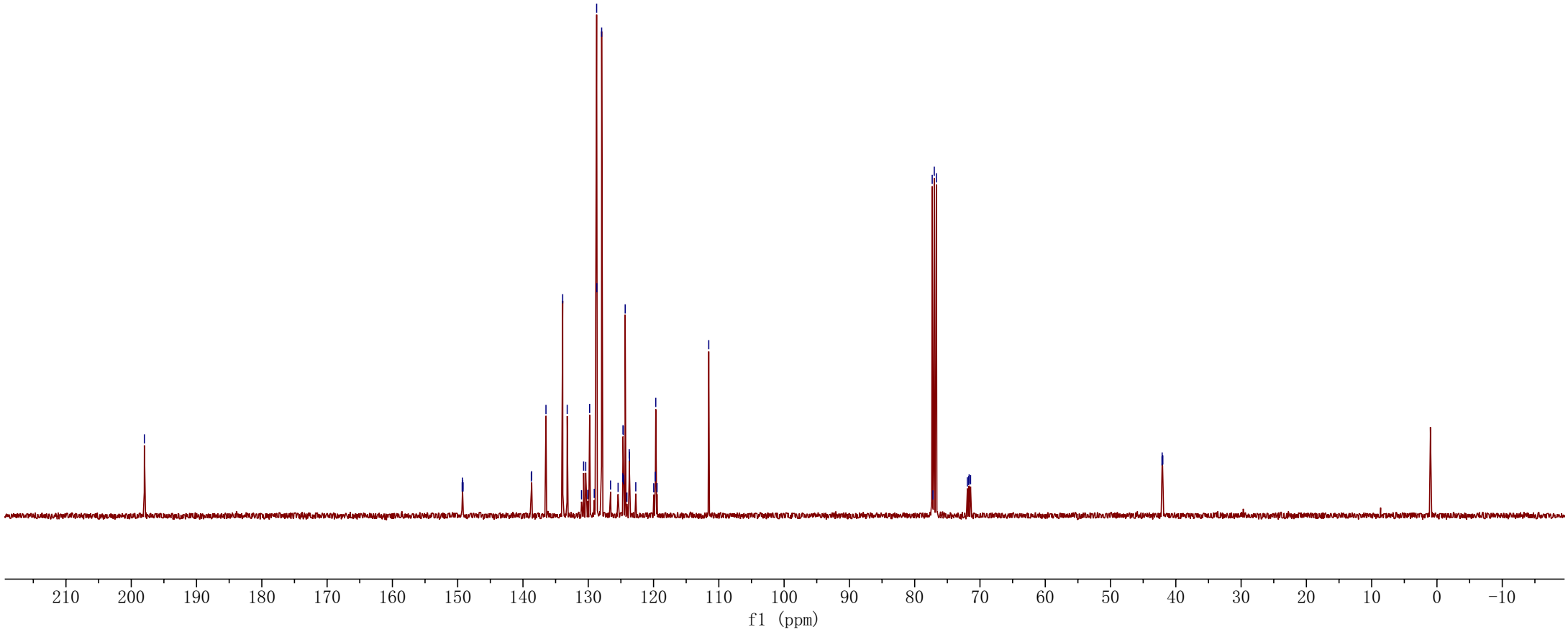


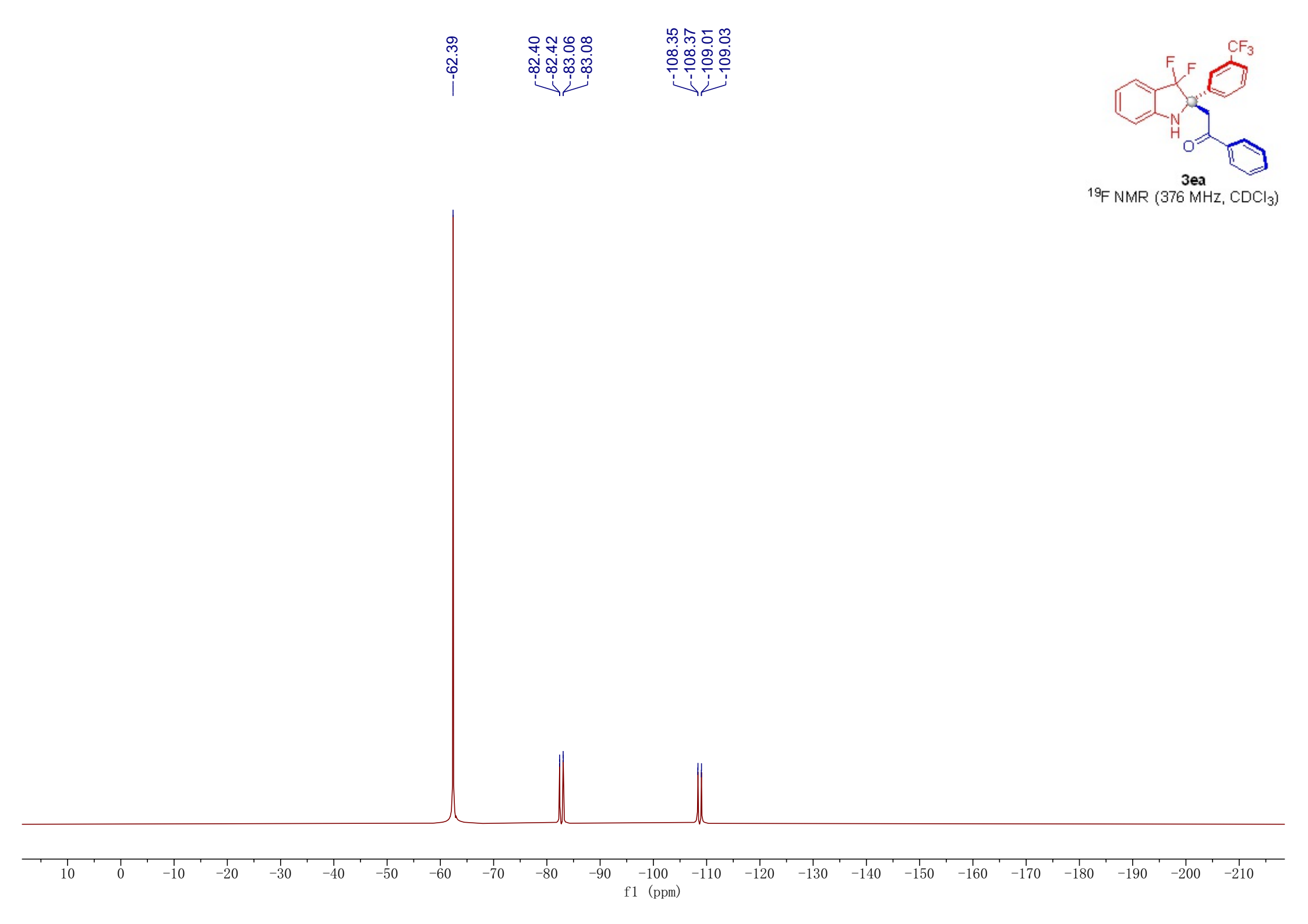


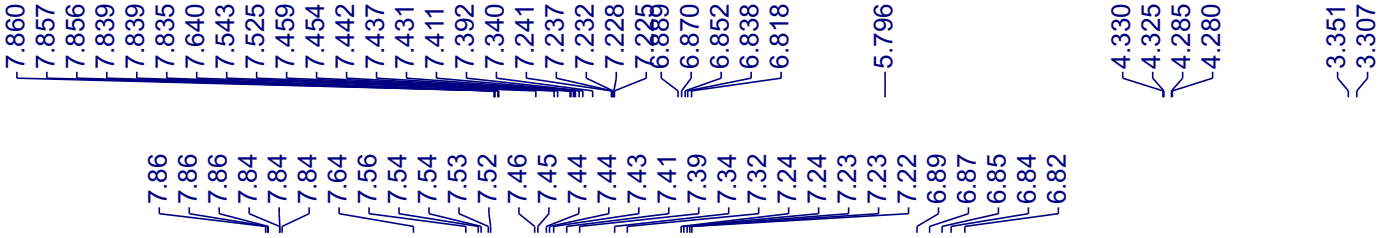


3ea

^{13}C NMR (100 MHz, $CDCl_3$)

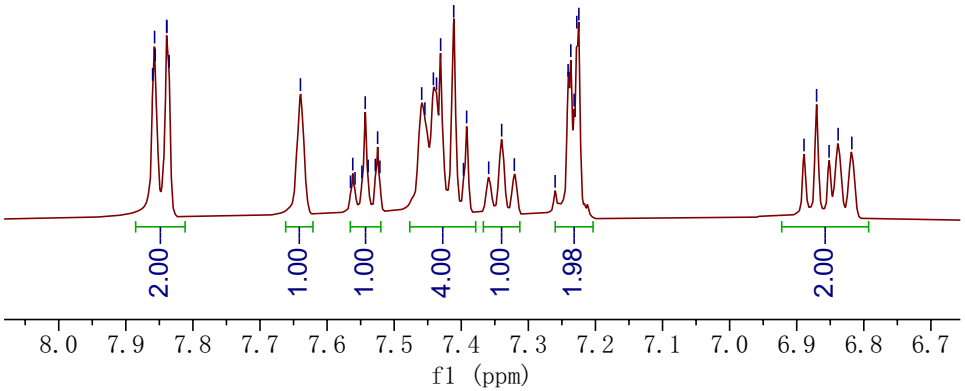


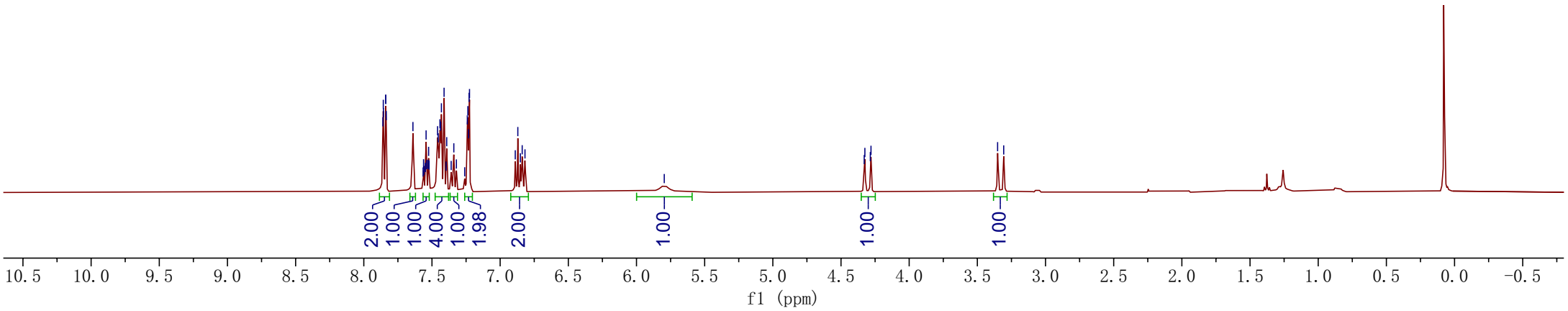

-62.39
-82.40
-82.42
-83.06
-83.08
-108.35
-108.37
-109.01
-109.03
CF3
F
F
N
H
O
3ea
19F NMR (376 MHz, CDCl3)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

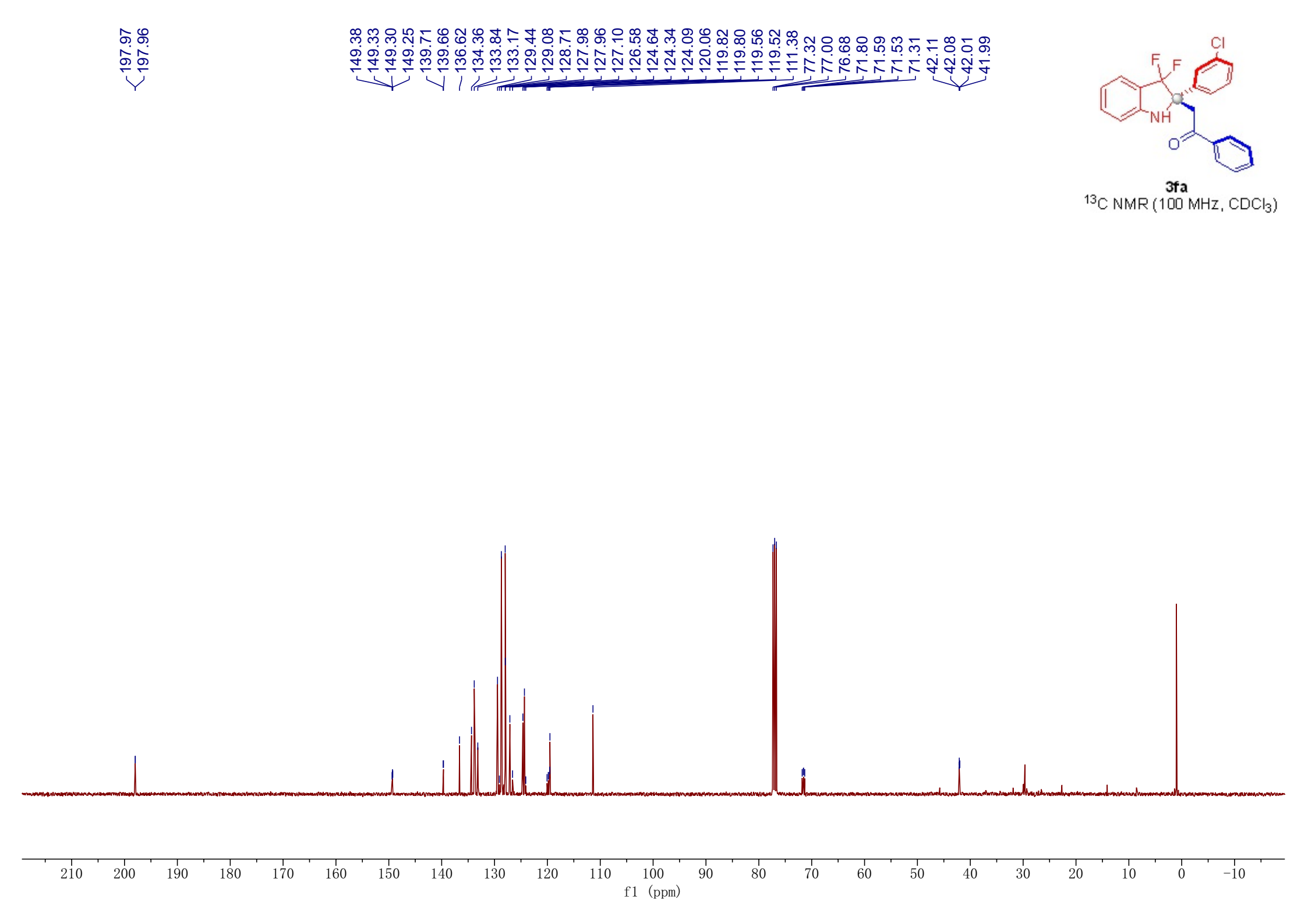


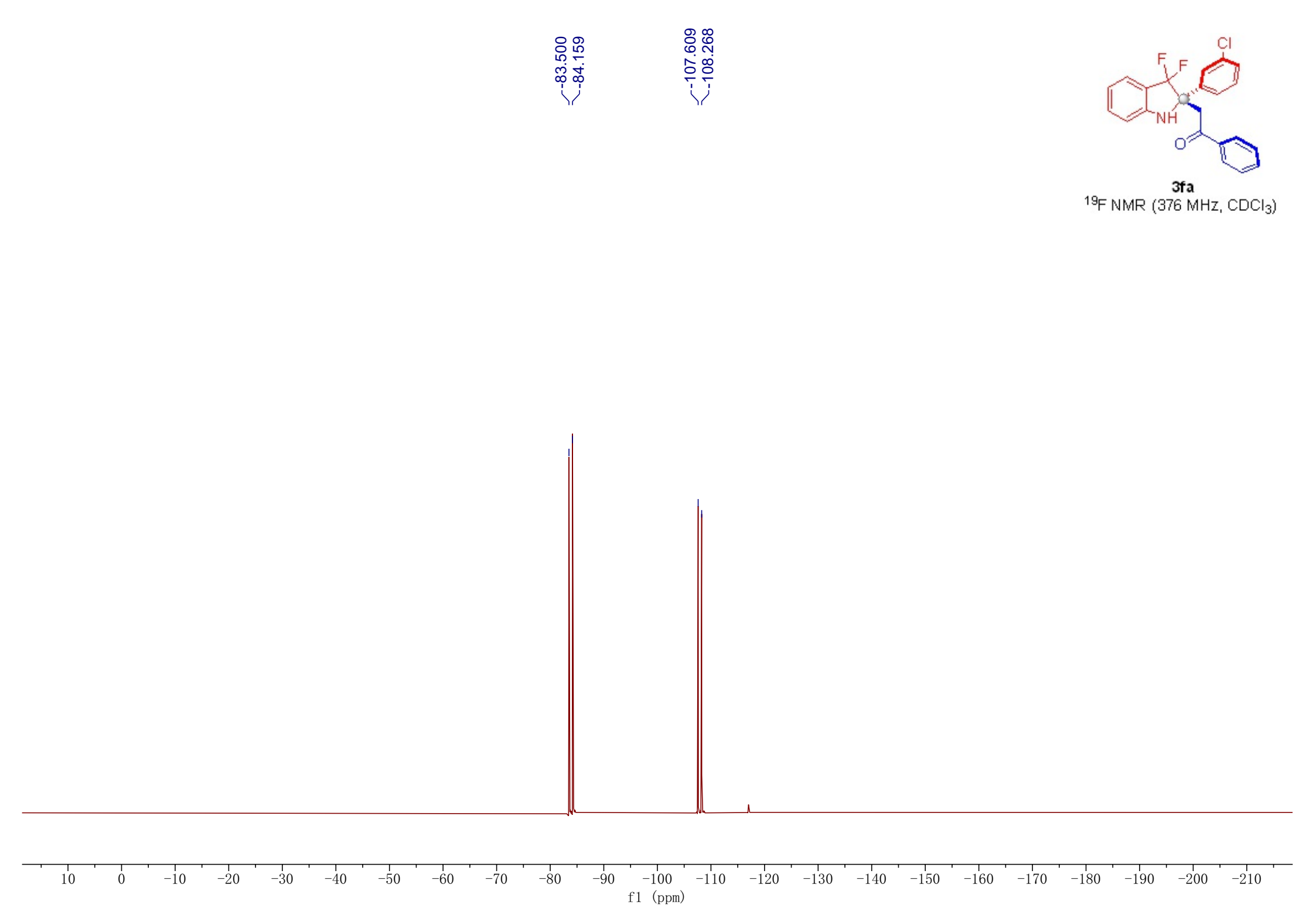
3fa

^{1}H NMR (400 MHz, $CDCl_3$)



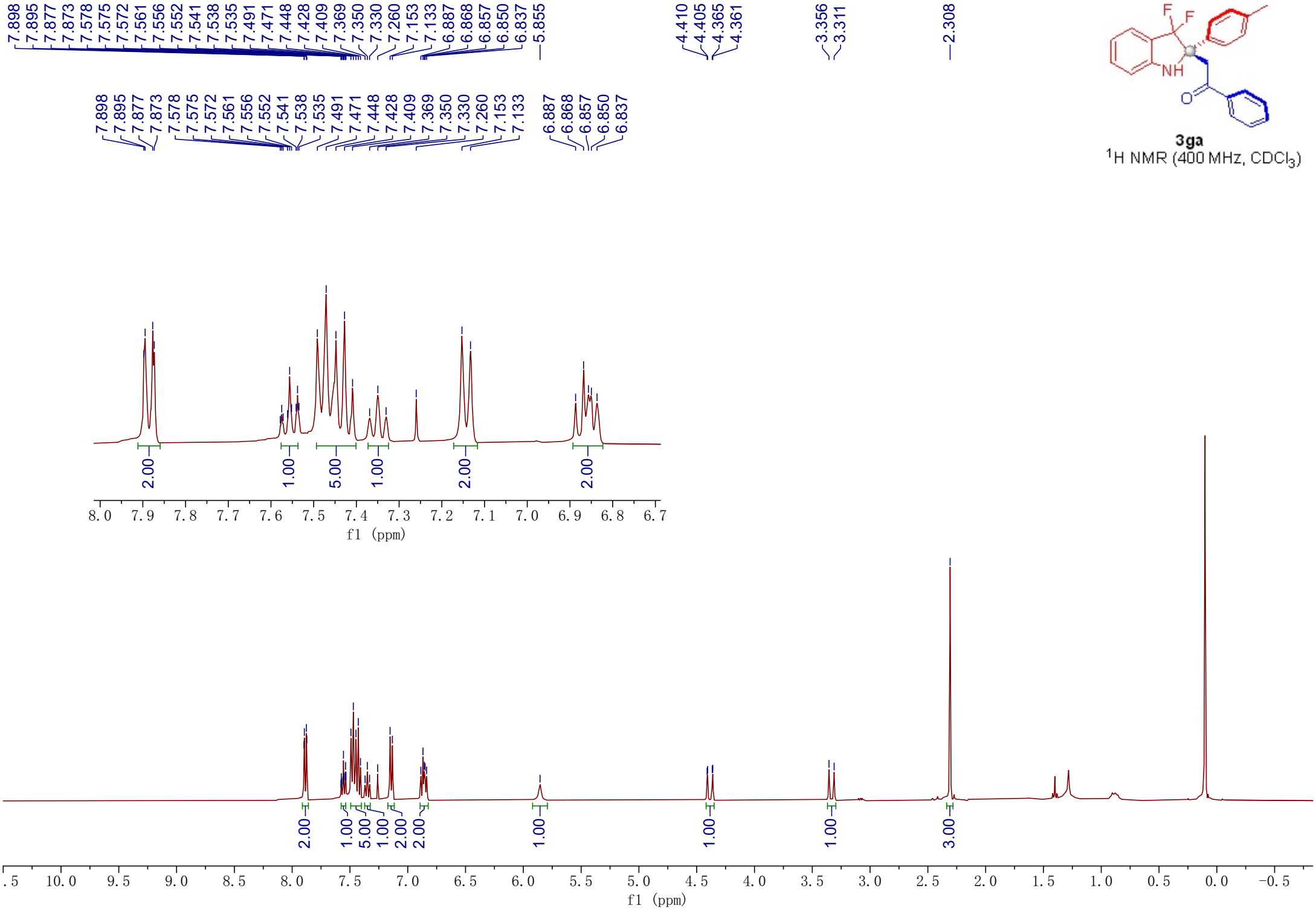


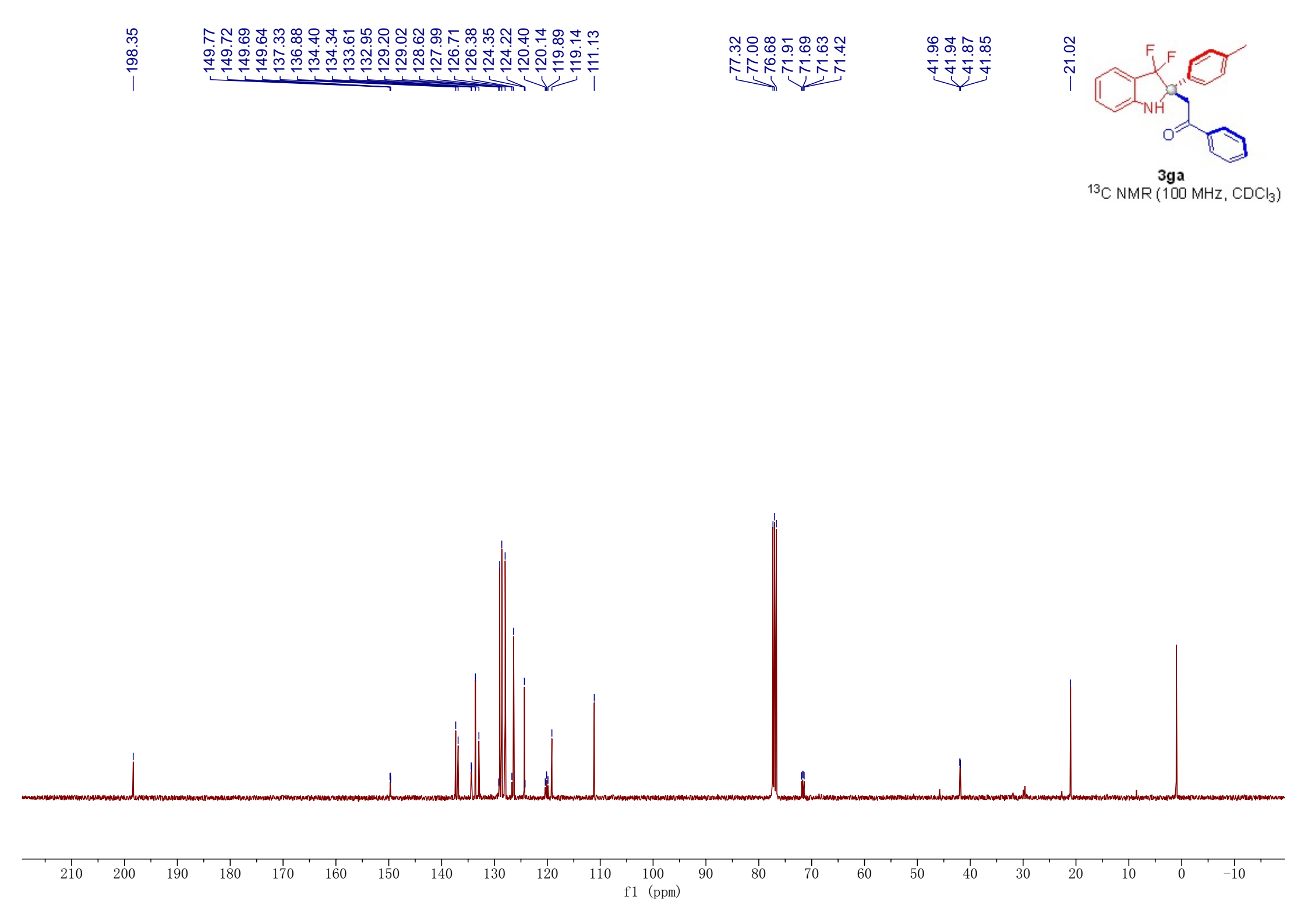

197.97
197.96
149.38
149.33
149.30
149.25
139.71
139.66
136.62
134.36
133.84
133.17
129.44
129.08
128.71
127.98
127.96
127.10
126.58
124.64
124.34
124.09
120.06
119.82
119.80
119.56
119.52
111.38
77.32
77.00
76.68
71.80
71.59
71.53
71.31
42.11
42.08
42.01
41.99
Cl
F
F
NH
O
3fa
13C NMR (100 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

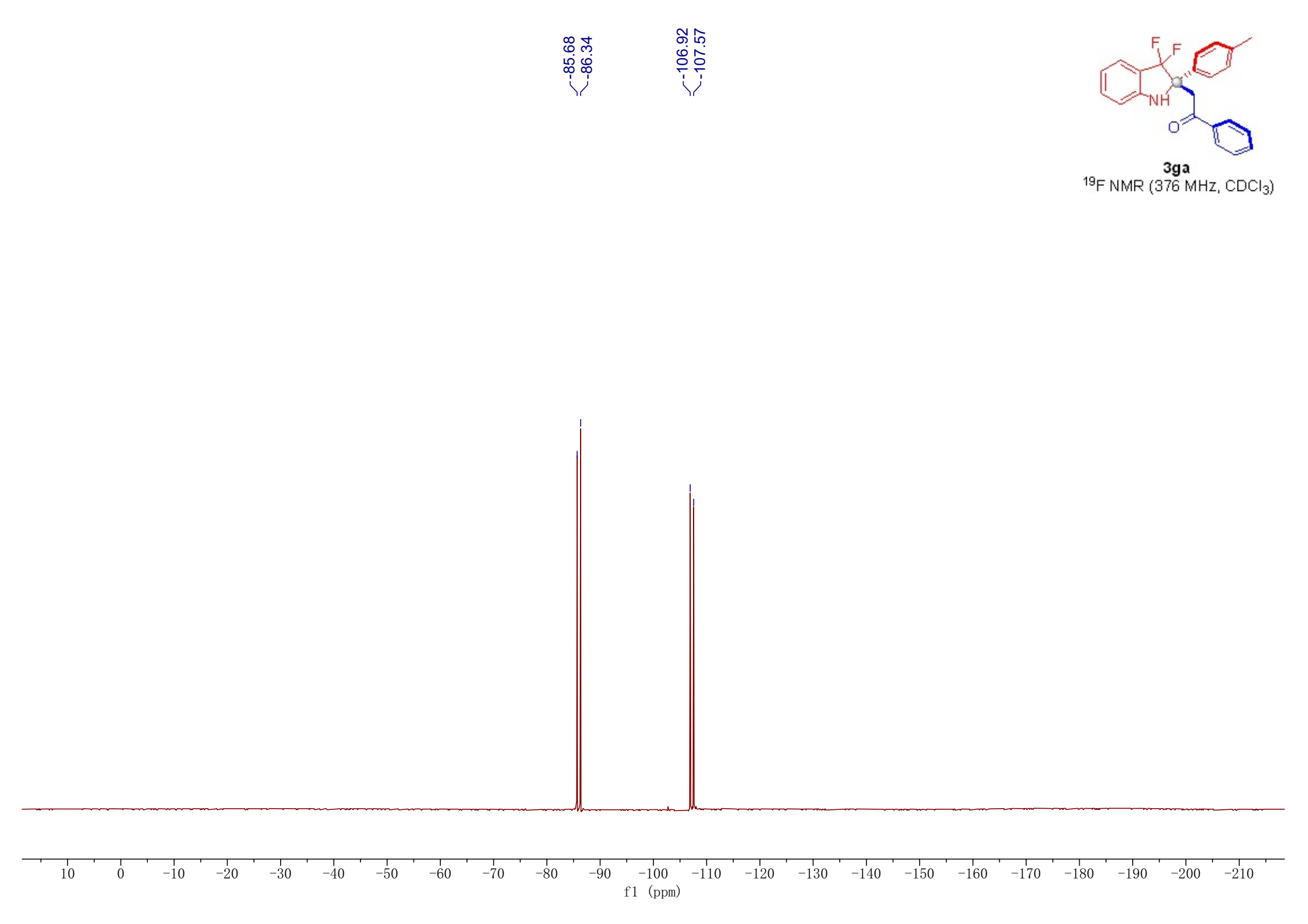


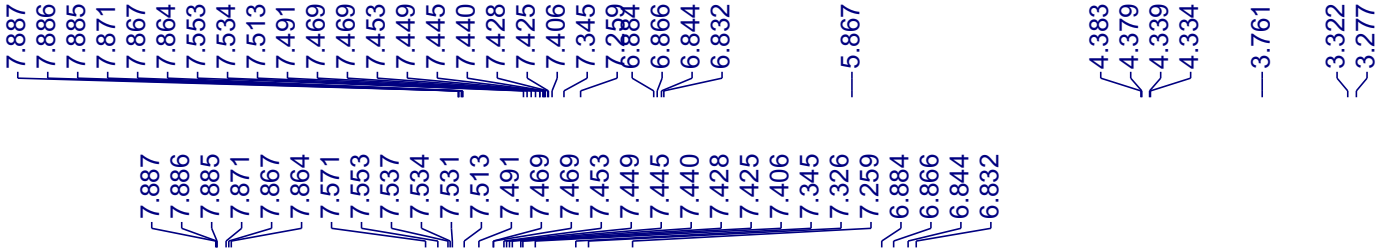
3fa

^{19}F NMR (376 MHz, $CDCl_3$)


7.898
7.895
7.877
7.873
7.578
7.575
7.572
7.561
7.556
7.552
7.541
7.538
7.535
7.491
7.471
7.448
7.428
7.409
7.369
7.350
7.330
7.260
7.153
7.133
6.887
6.868
6.857
6.850
6.837
5.855
4.410
4.405
4.365
4.361
3.356
3.311
2.308
F
F
NH
O
3ga
1H NMR (400 MHz, CDCl3)
2.00
1.00
5.00
1.00
2.00
2.00
f1 (ppm)
2.00
1.00
5.00
1.00
2.00
2.00
1.00
1.00
1.00
3.00
f1 (ppm)

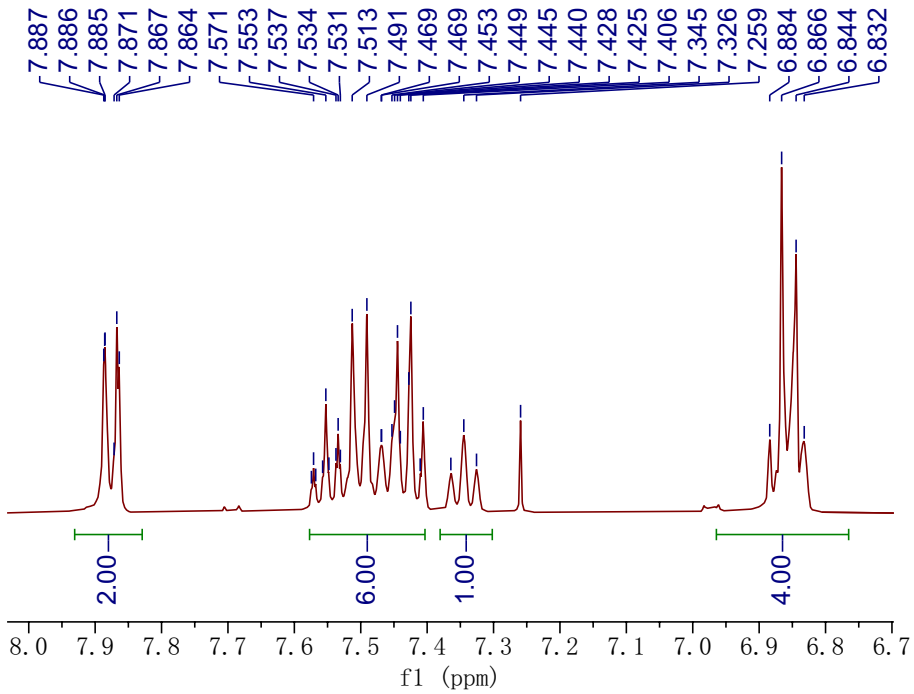

198.35
149.77
149.72
149.69
149.64
137.33
136.88
134.40
134.34
133.61
132.95
129.20
129.02
128.62
127.99
126.71
126.38
124.35
124.22
120.40
120.14
119.89
119.14
111.13
77.32
77.00
76.68
71.91
71.69
71.63
71.42
41.96
41.94
41.87
41.85
21.02
F
F
NH
O
3ga
13C NMR (100 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

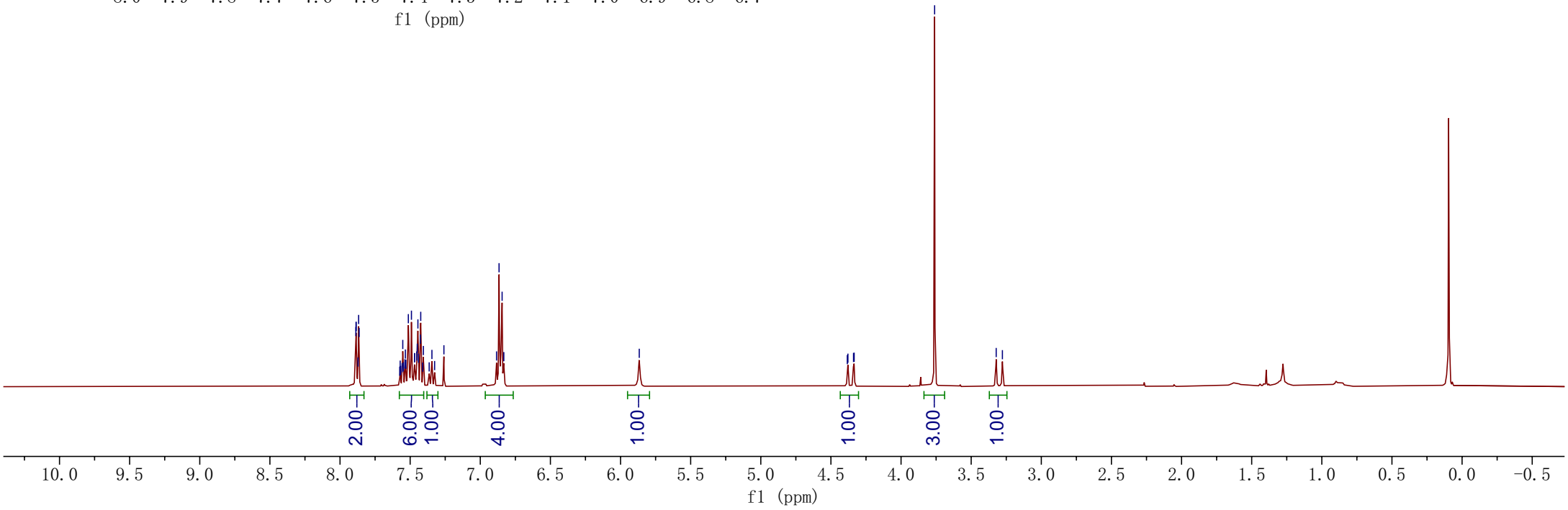

-85.68
-86.34
-106.92
-107.57
F
F
NH
O
3ga
19F NMR (376 MHz, CDCl3)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

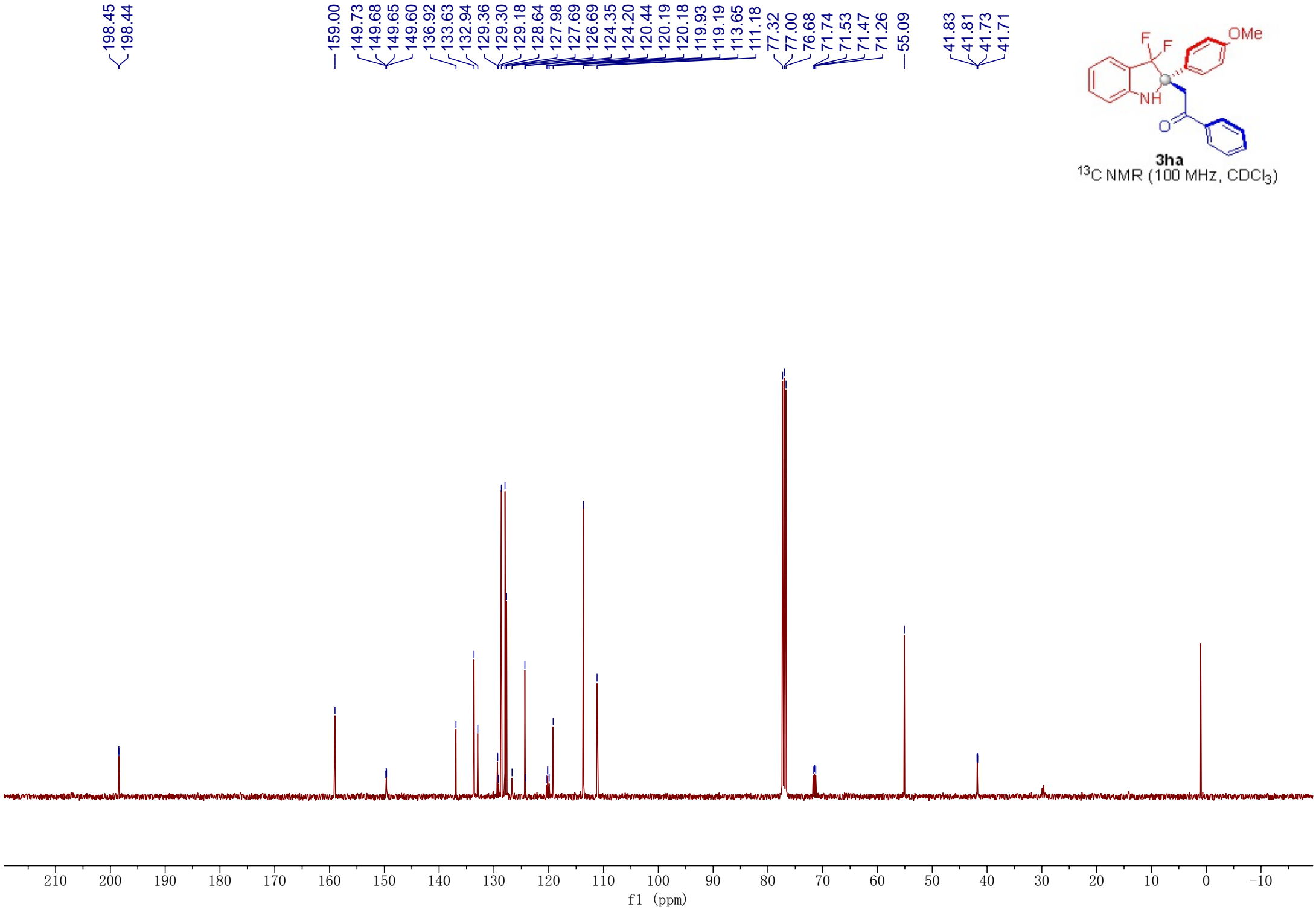


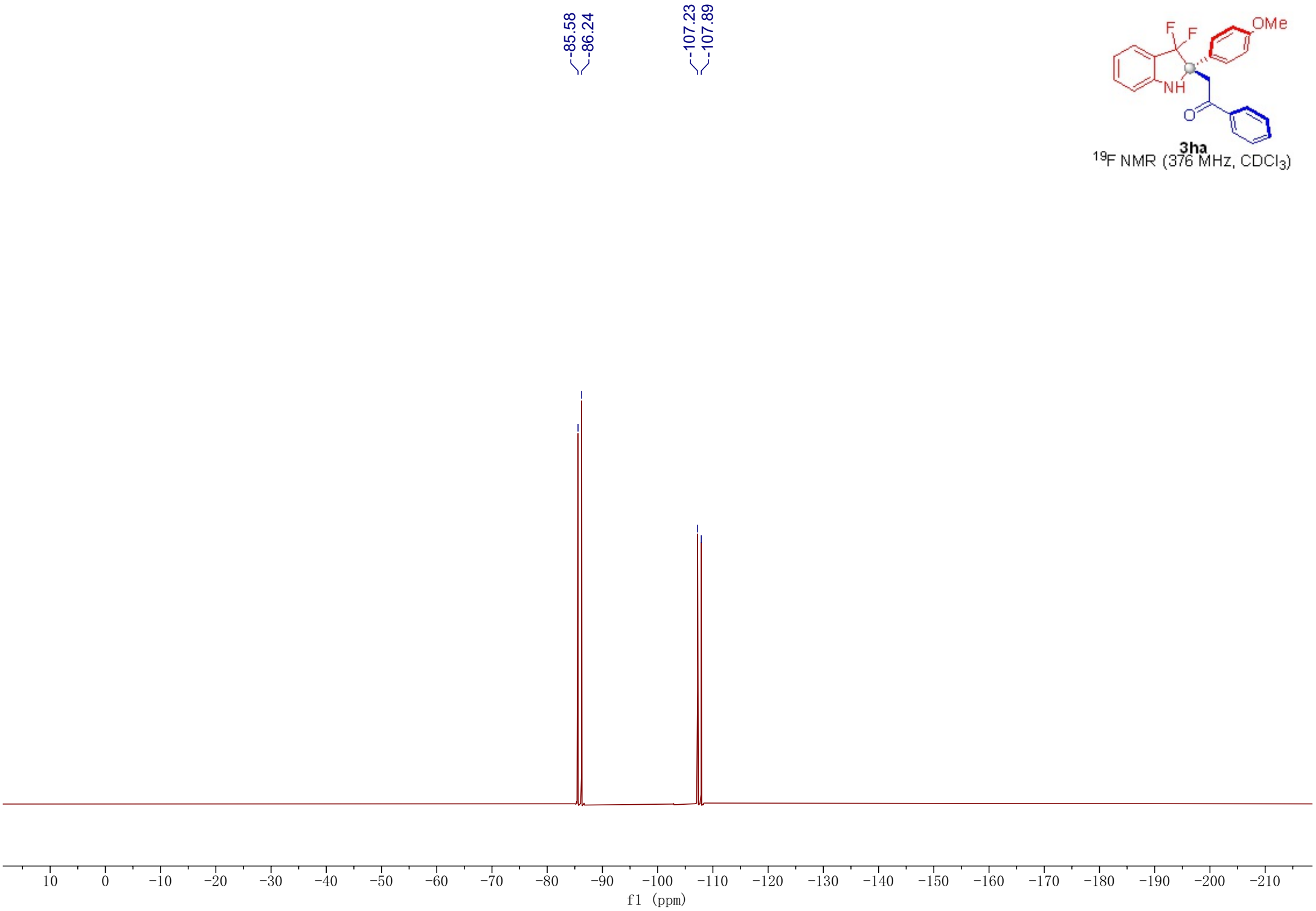
3ha

^{1}H NMR (400 MHz, $CDCl_3$)



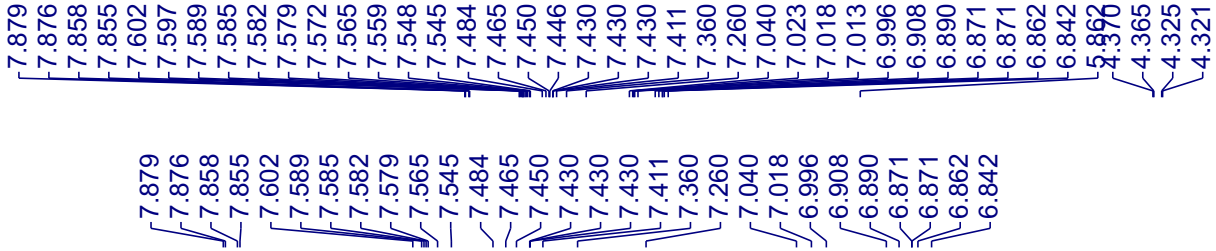



198.45
198.44
159.00
149.73
149.68
149.65
149.60
136.92
133.63
132.94
129.36
129.30
129.18
128.64
127.98
127.69
126.69
124.35
124.20
120.44
120.19
120.18
119.93
119.19
113.65
111.18
77.32
77.00
76.68
71.74
71.53
71.47
71.26
55.09
41.83
41.81
41.73
41.71
F
F
OMe
NH
O
3ha
13C NMR (100 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



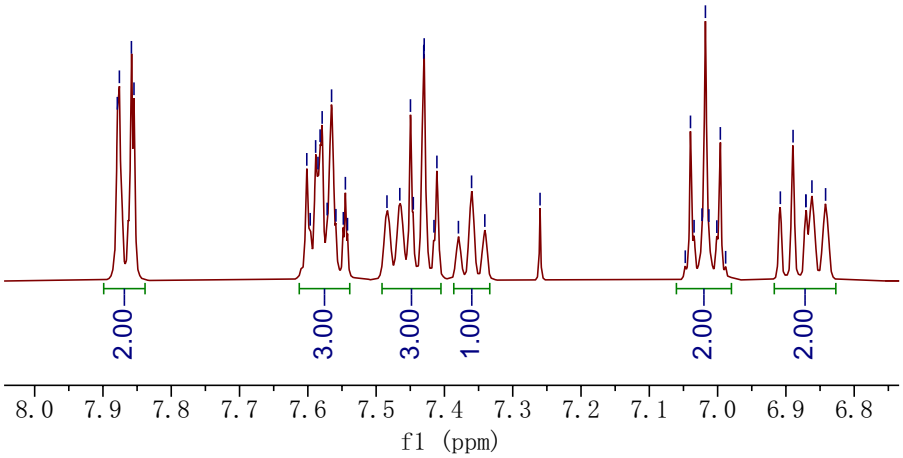
3ha

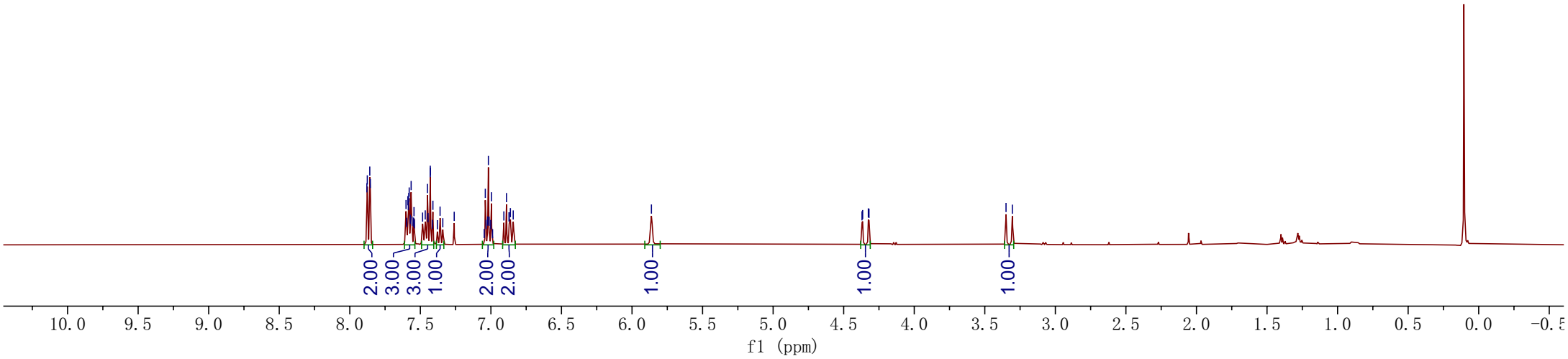
^{19}F NMR (376 MHz, $CDCl_3$)



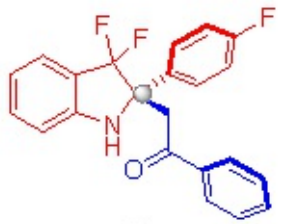
3ia

^{1}H NMR (400 MHz, $CDCl_3$)



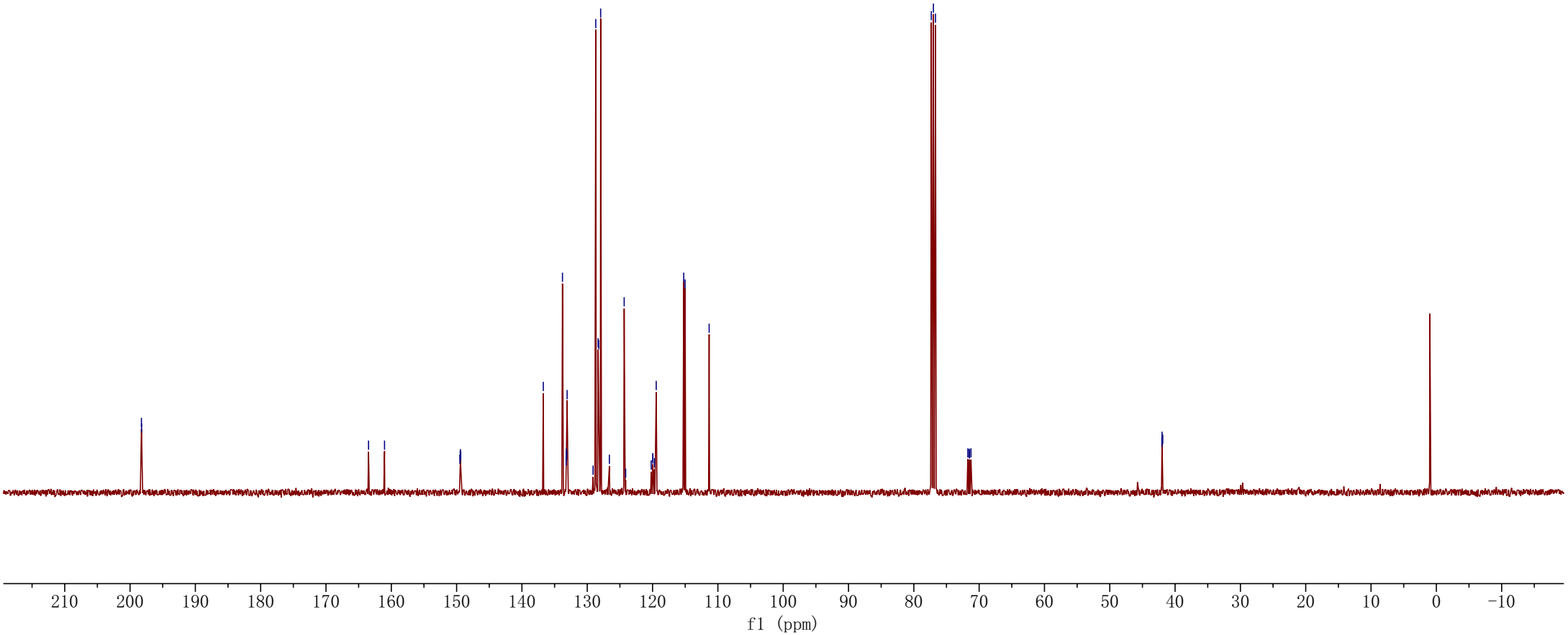


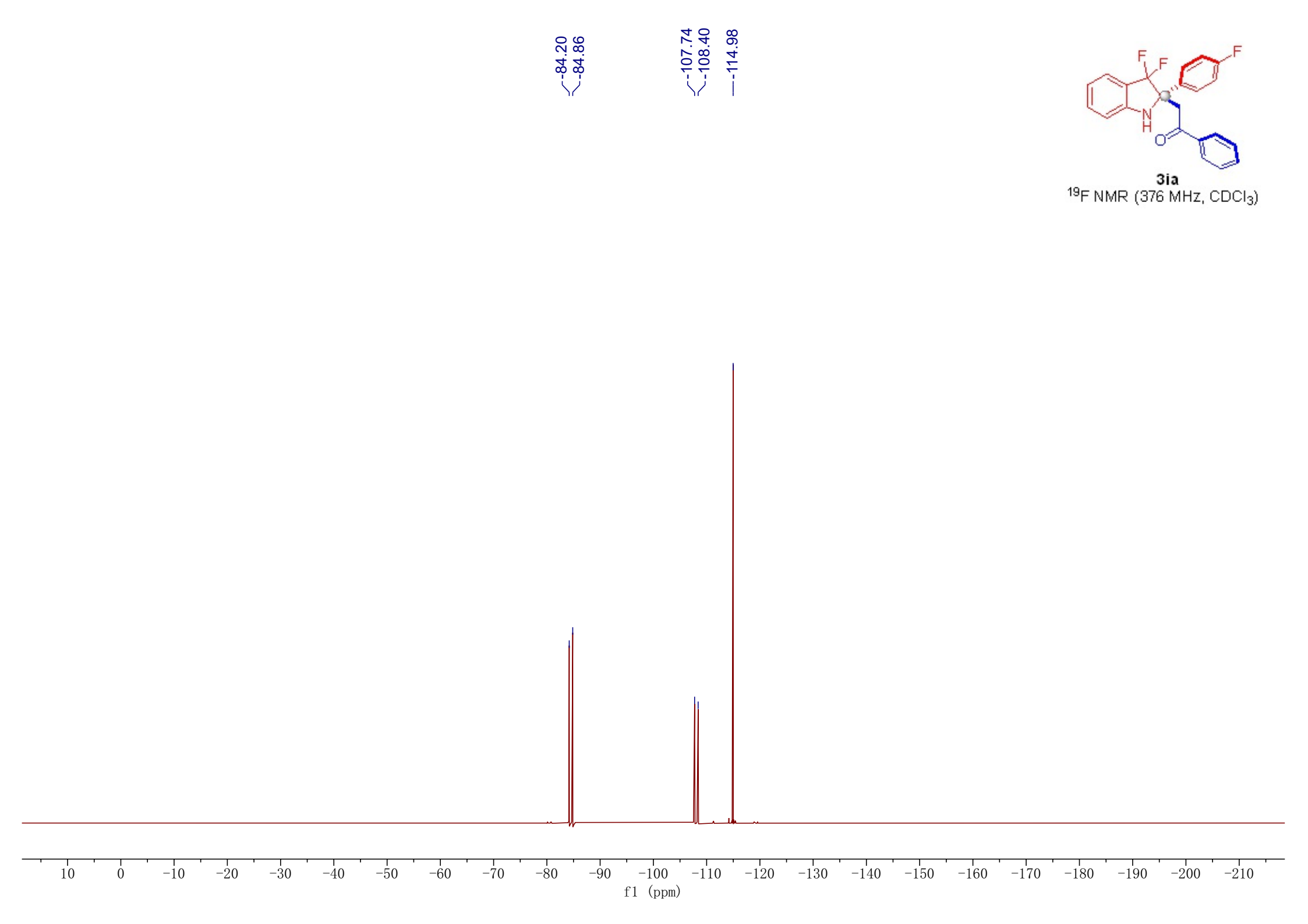
198.25
198.24
163.49
161.04
149.50
149.45
149.42
149.37
136.73
133.79
133.23
133.20
133.17
133.14
133.08
129.11
128.69
128.34
128.26
127.95
126.61
124.35
124.12
120.21
119.96
119.95
119.70
119.44
115.23
115.02
111.34
77.32
77.00
76.69
71.74
71.52
71.46
71.25
42.02
42.00
41.93
41.90

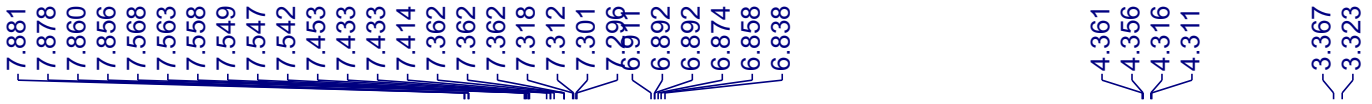


3ia

^{13}C NMR (100 MHz, $CDCl_3$)

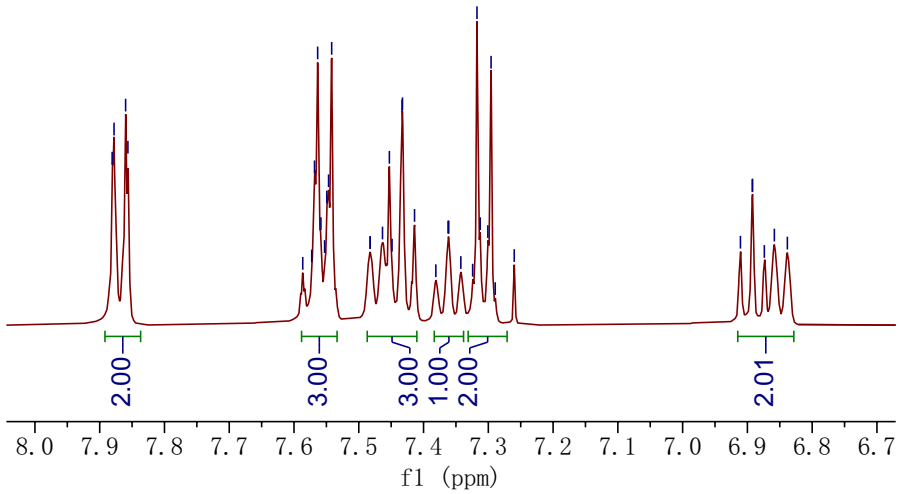


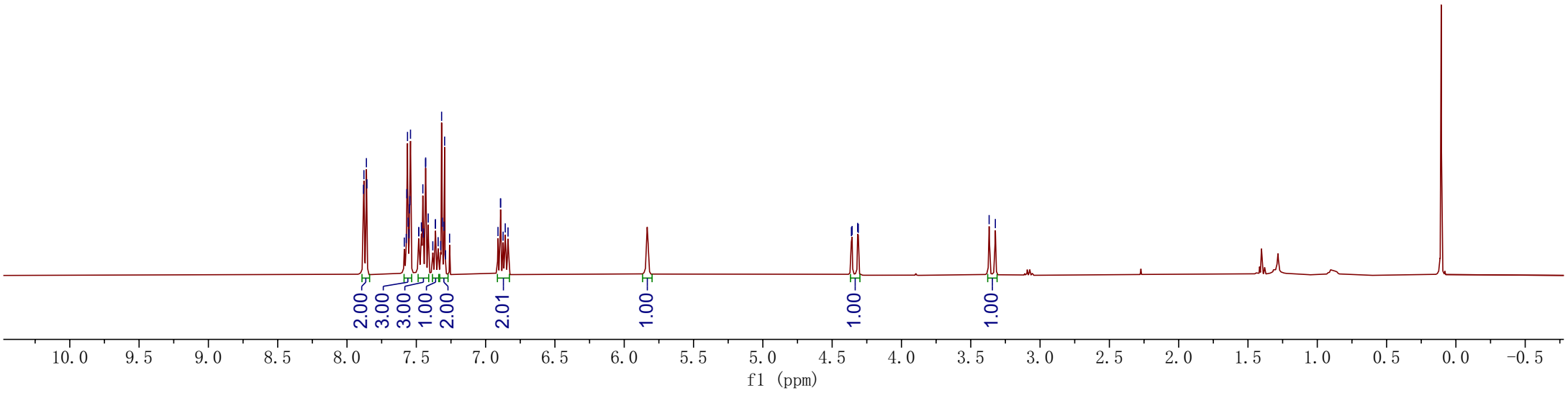

-84.20
-84.86
-107.74
-108.40
-114.98
F
F
F
N
H
O
3ia
19F NMR (376 MHz, CDCl3)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

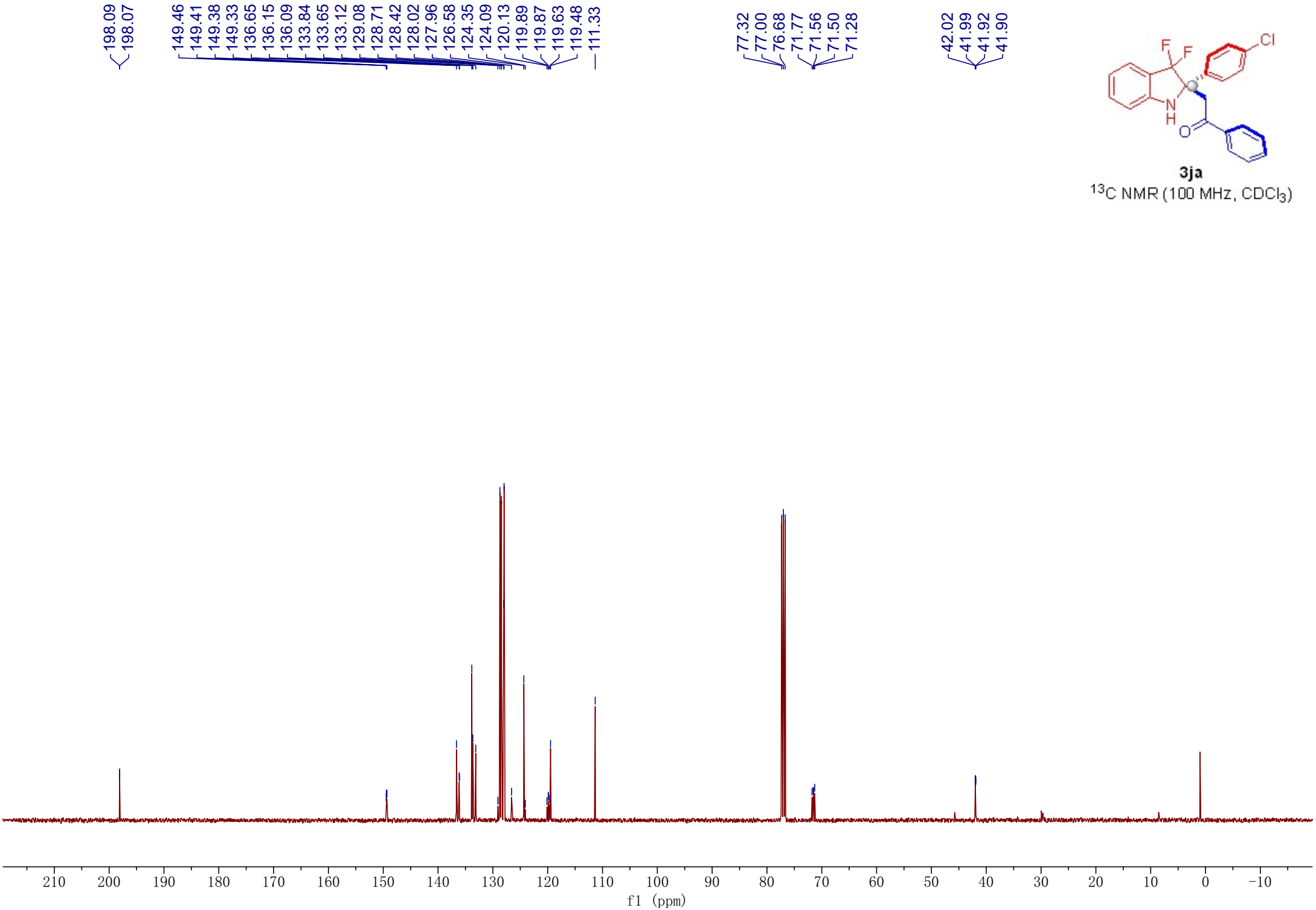


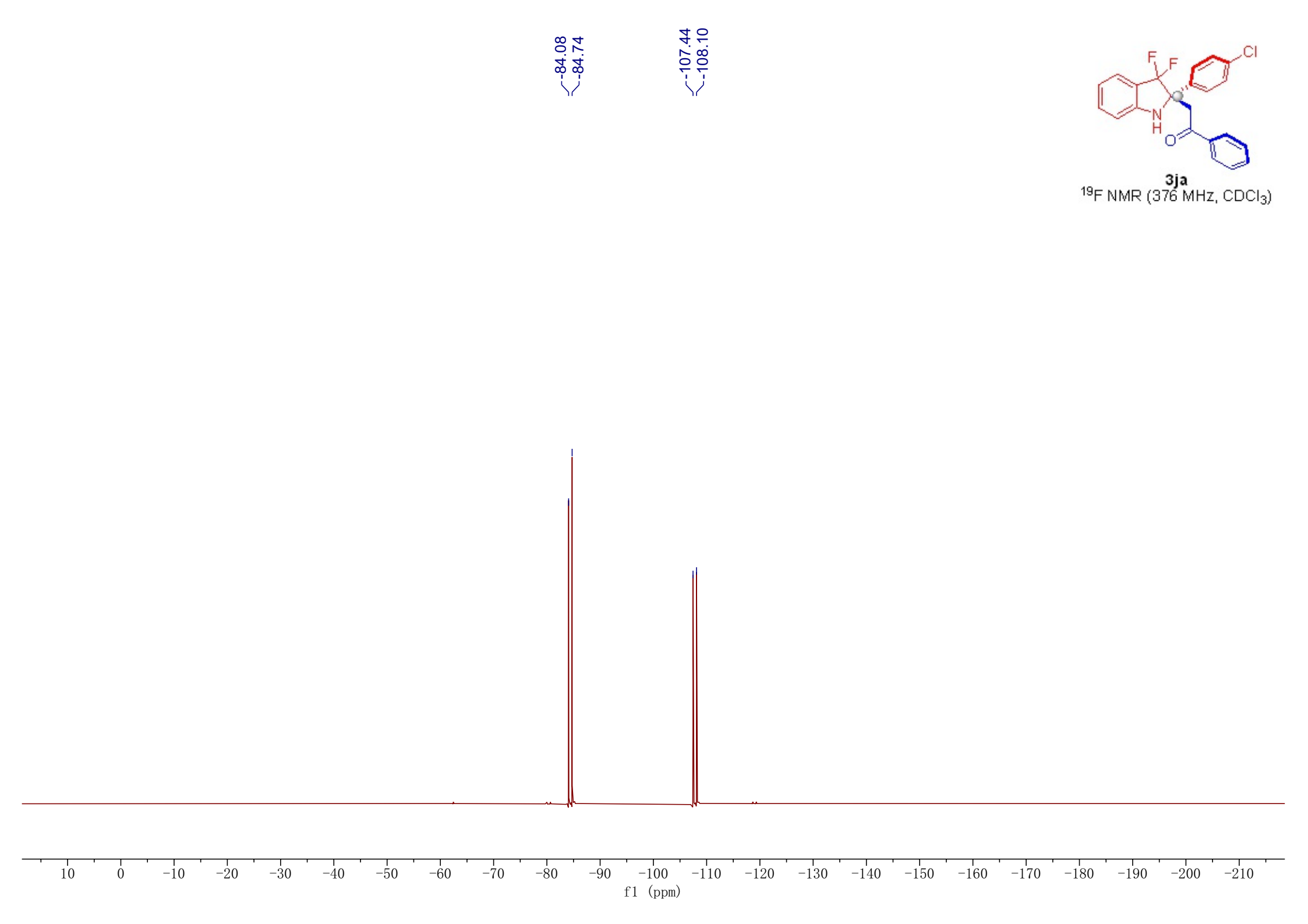
3ja

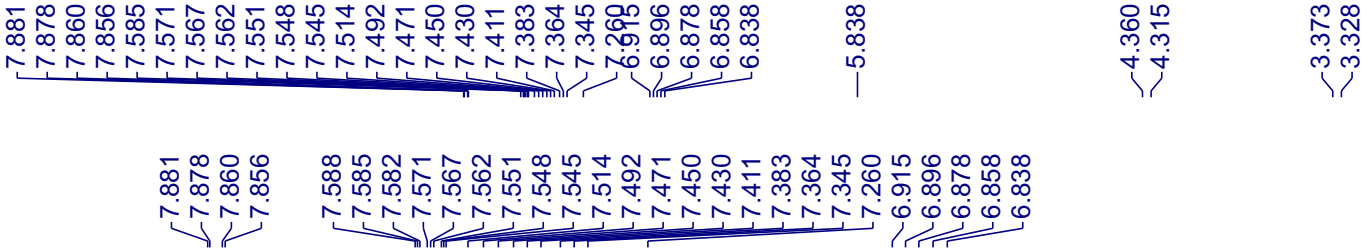
^{1}H NMR (400 MHz, $CDCl_3$)





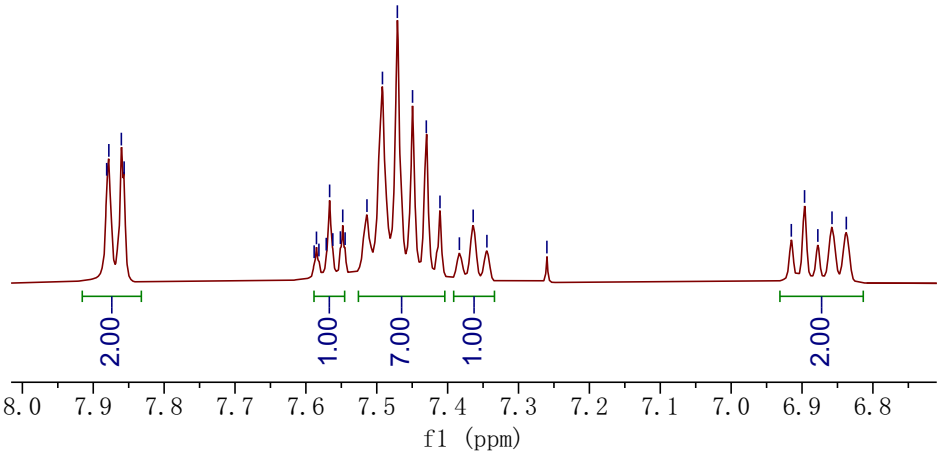

198.09
198.07
149.46
149.41
149.38
149.33
136.65
136.15
136.09
133.84
133.65
133.12
129.08
128.71
128.42
128.02
127.96
126.58
124.35
124.09
120.13
119.89
119.87
119.63
119.48
111.33
77.32
77.00
76.68
71.77
71.56
71.50
71.28
42.02
41.99
41.92
41.90
F
F
Cl
N
H
O
3ja
13C NMR (100 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

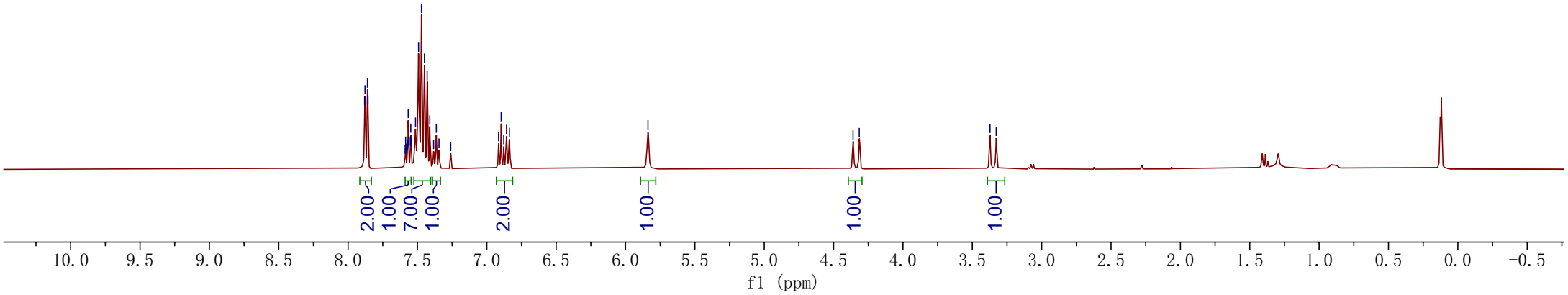

-84.08
-84.74
-107.44
-108.10
F
F
Cl
N
H
O
3ja
19F NMR (376 MHz, CDCl3)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

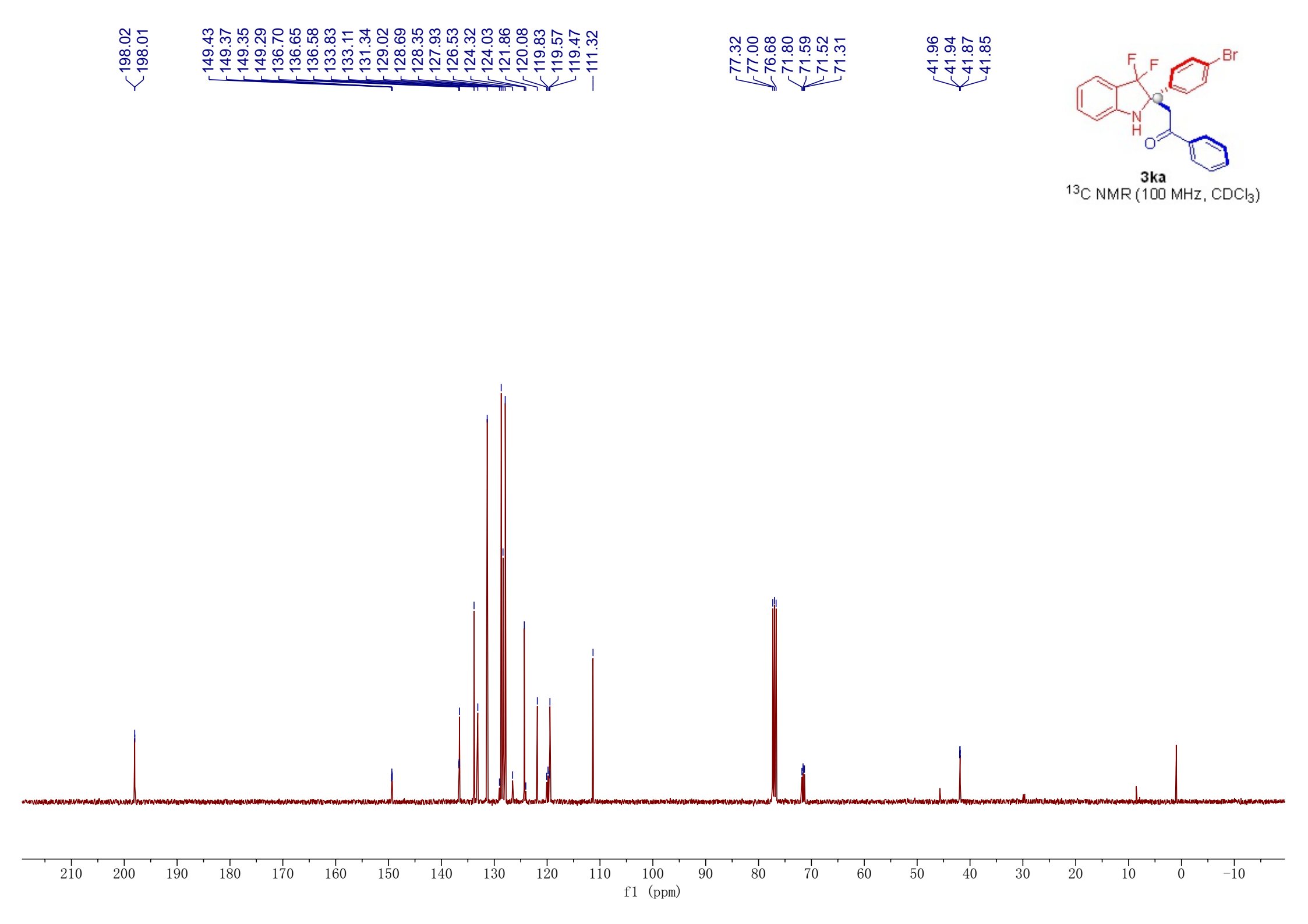


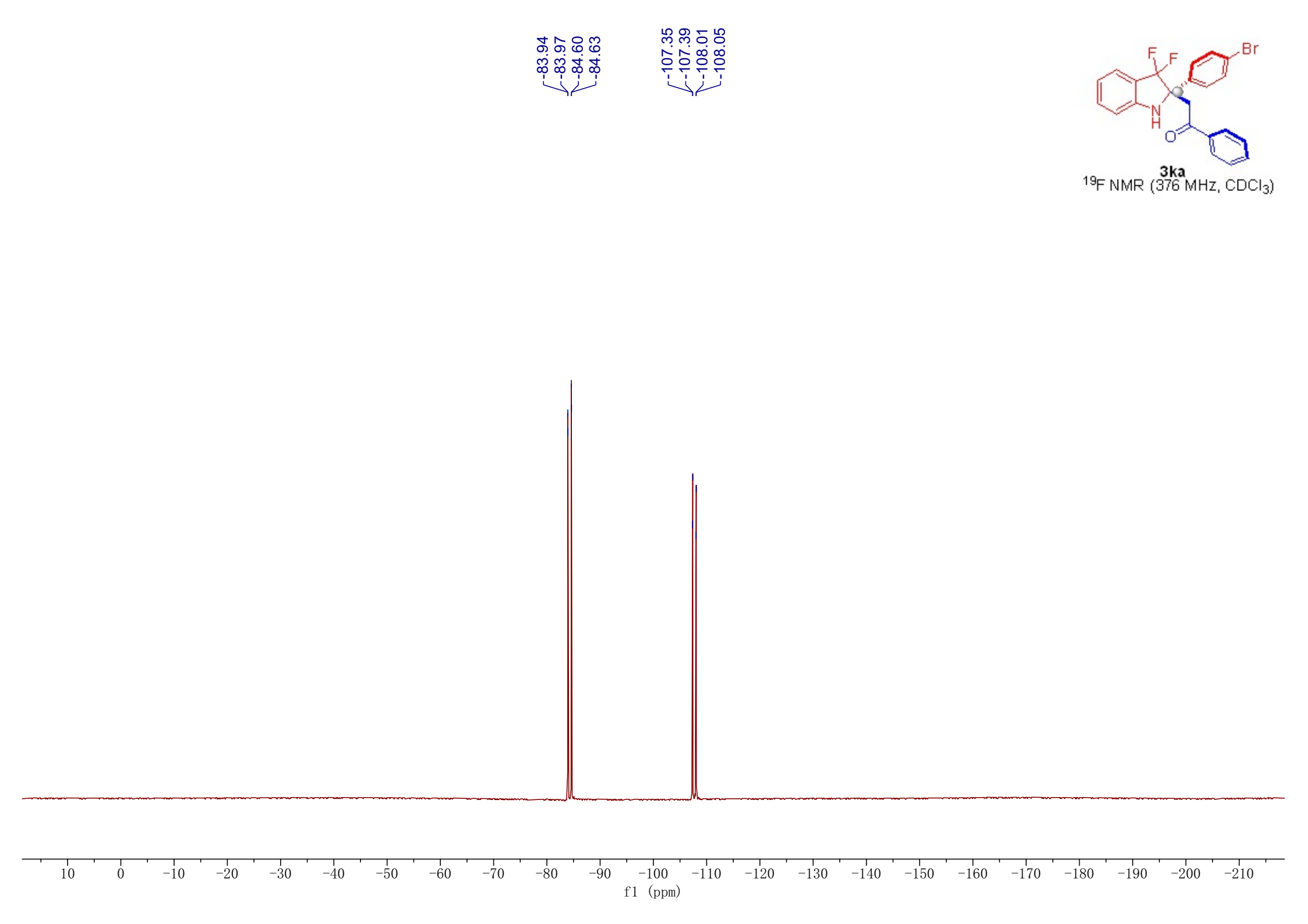
3ka

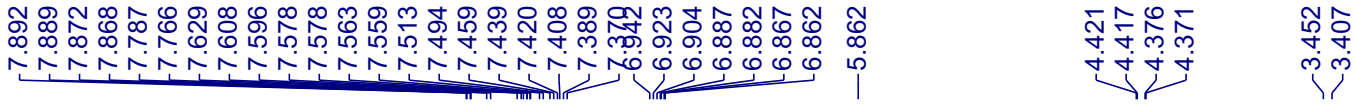
^{1}H NMR (400 MHz, $CDCl_3$)





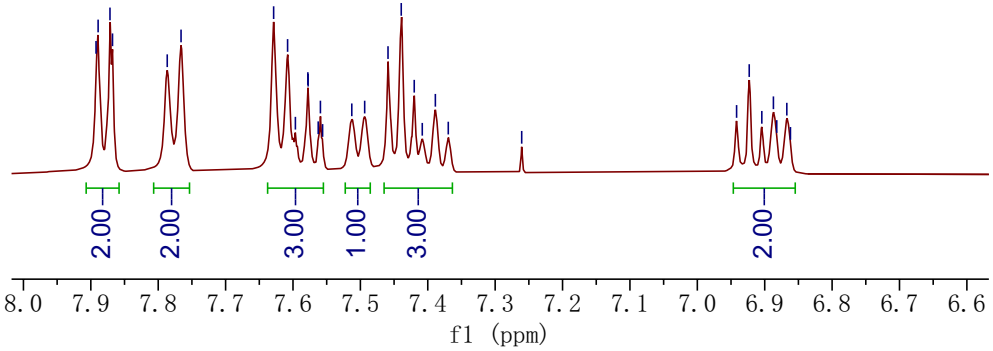

198.02
198.01
149.43
149.37
149.35
149.29
136.70
136.65
136.58
133.83
133.11
131.34
129.02
128.69
128.35
127.93
126.53
124.32
124.03
121.86
120.08
119.83
119.57
119.47
111.32
77.32
77.00
76.68
71.80
71.59
71.52
71.31
41.96
41.94
41.87
41.85
F
F
Br
N
H
O
3ka
13C NMR (100 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

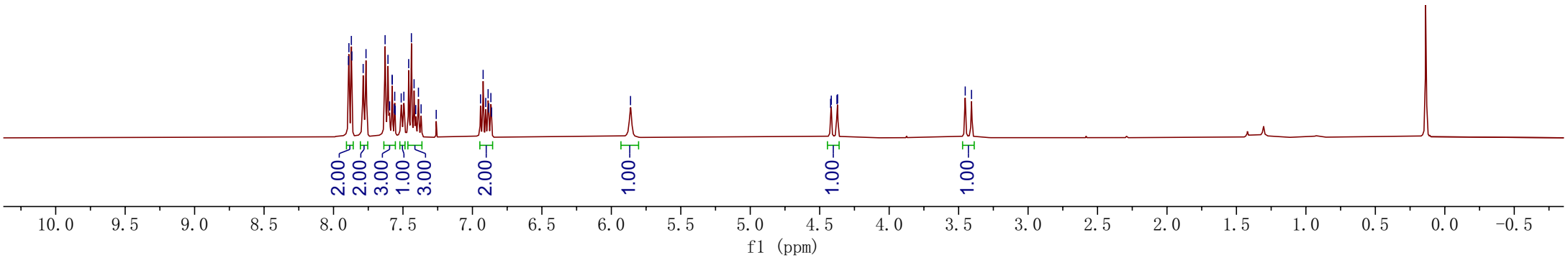

-83.94
-83.97
-84.60
-84.63
-107.35
-107.39
-108.01
-108.05
F
F
Br
N
H
O
3ka
19F NMR (376 MHz, CDCl3)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

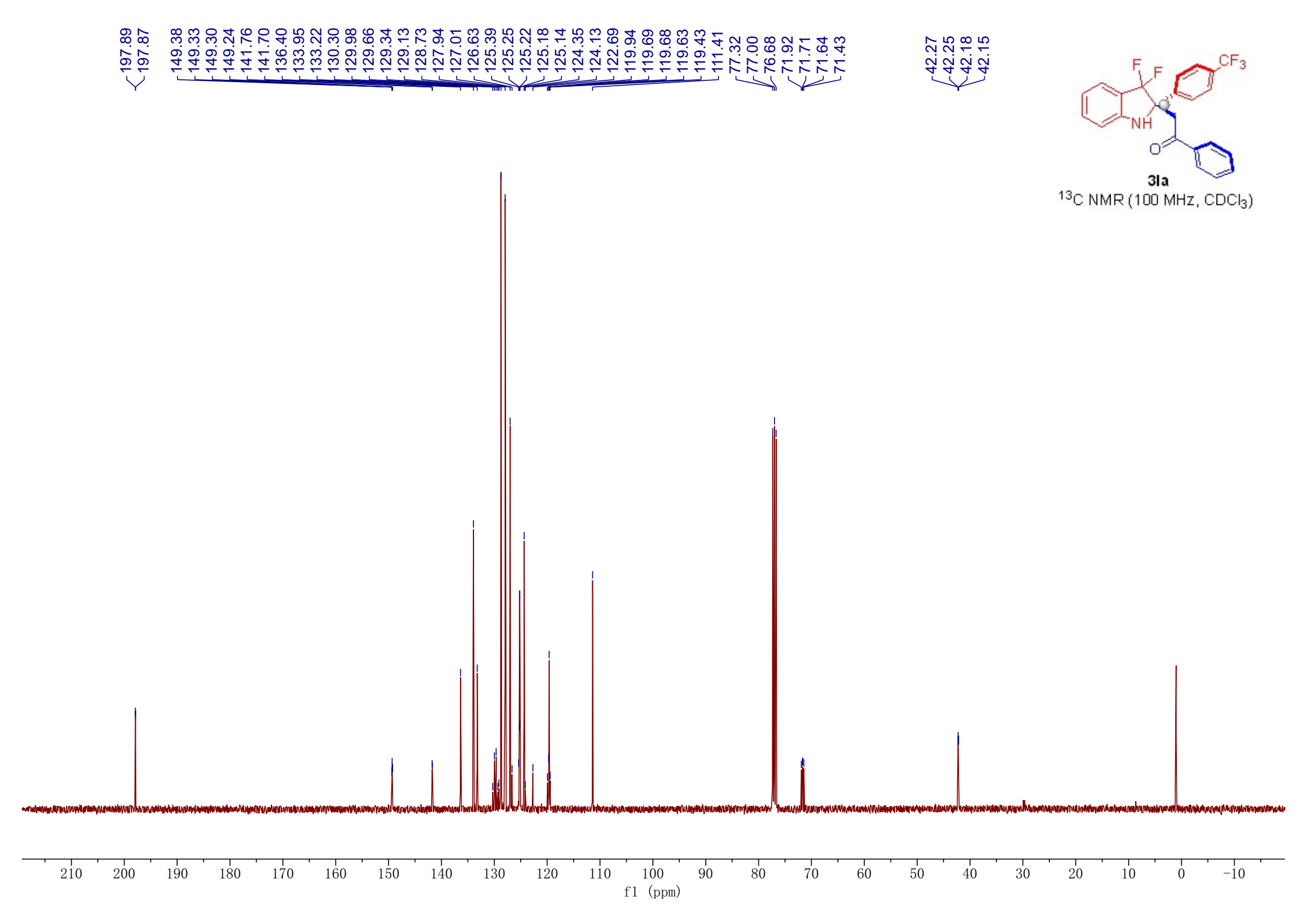


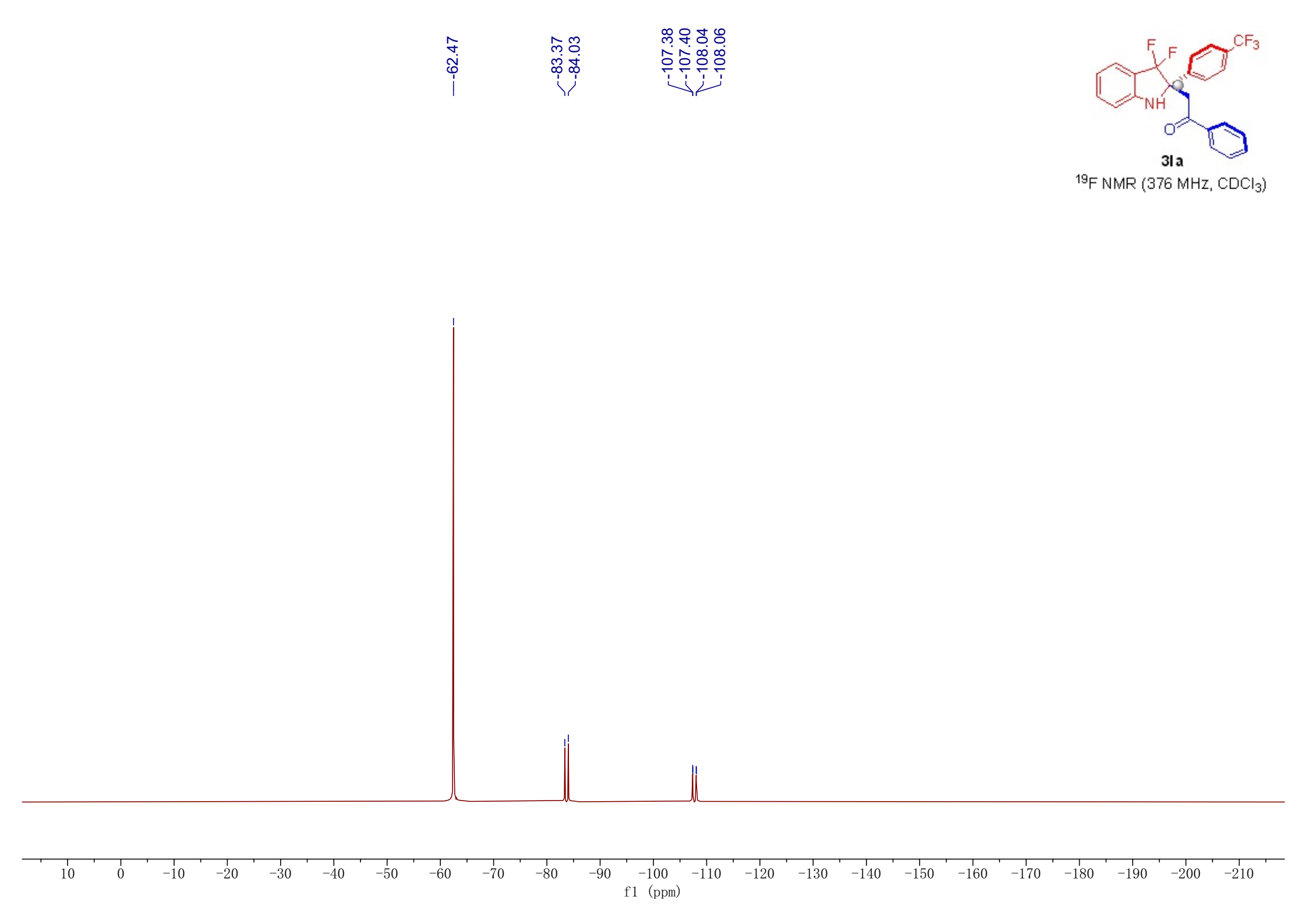
3la

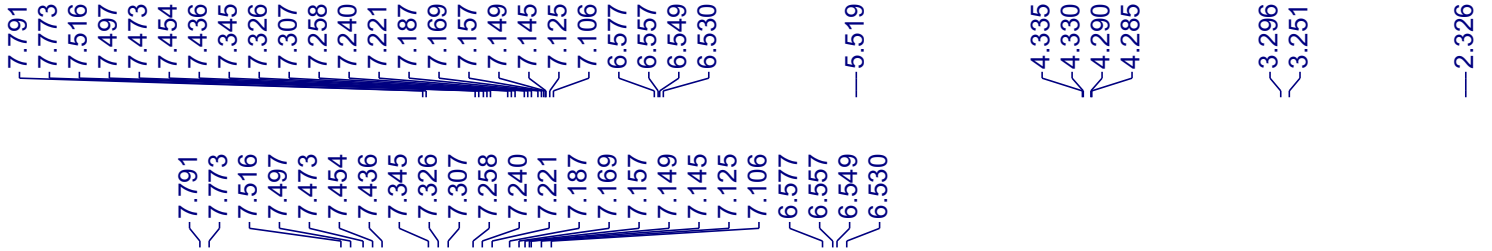
^{1}H NMR (400 MHz, $CDCl_3$)





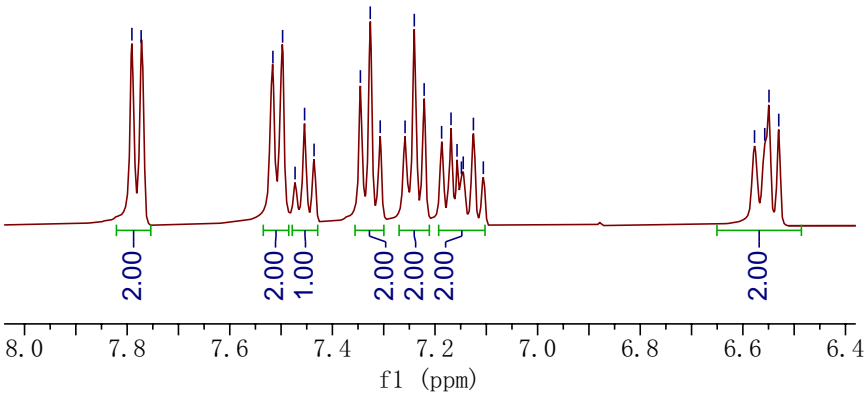

197.89
197.87
149.38
149.33
149.30
149.24
141.76
141.70
136.40
133.95
133.22
130.30
129.98
129.66
129.34
129.13
128.73
127.94
127.01
126.63
125.39
125.25
125.22
125.18
125.14
124.35
124.13
122.69
119.94
119.69
119.68
119.63
119.43
111.41
77.32
77.00
76.68
71.92
71.71
71.64
71.43
42.27
42.25
42.18
42.15
F
F
CF3
NH
O
3la
13C NMR (100 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

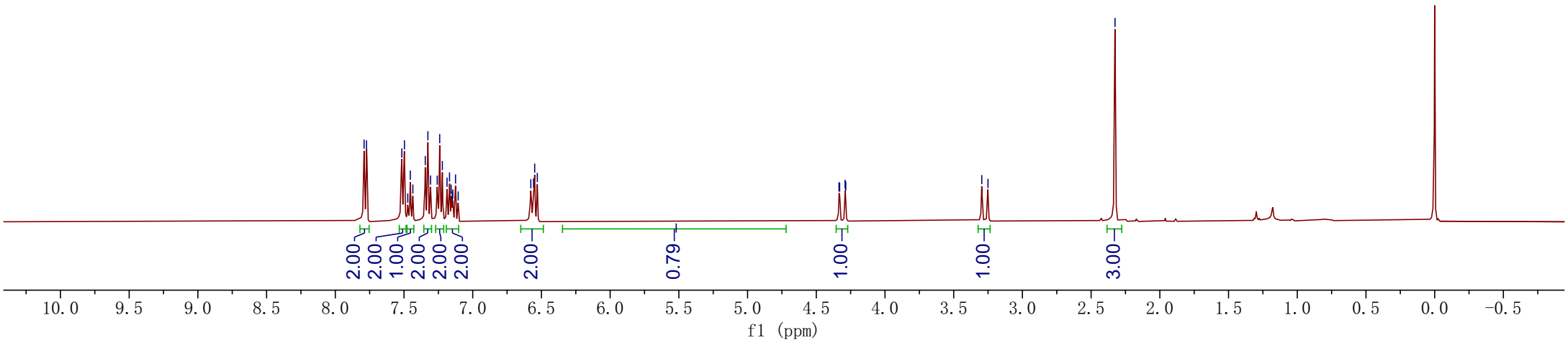

-62.47
-83.37
-84.03
-107.38
-107.40
-108.04
-108.06
F
F
CF3
NH
O
3la
19F NMR (376 MHz, CDCl3)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

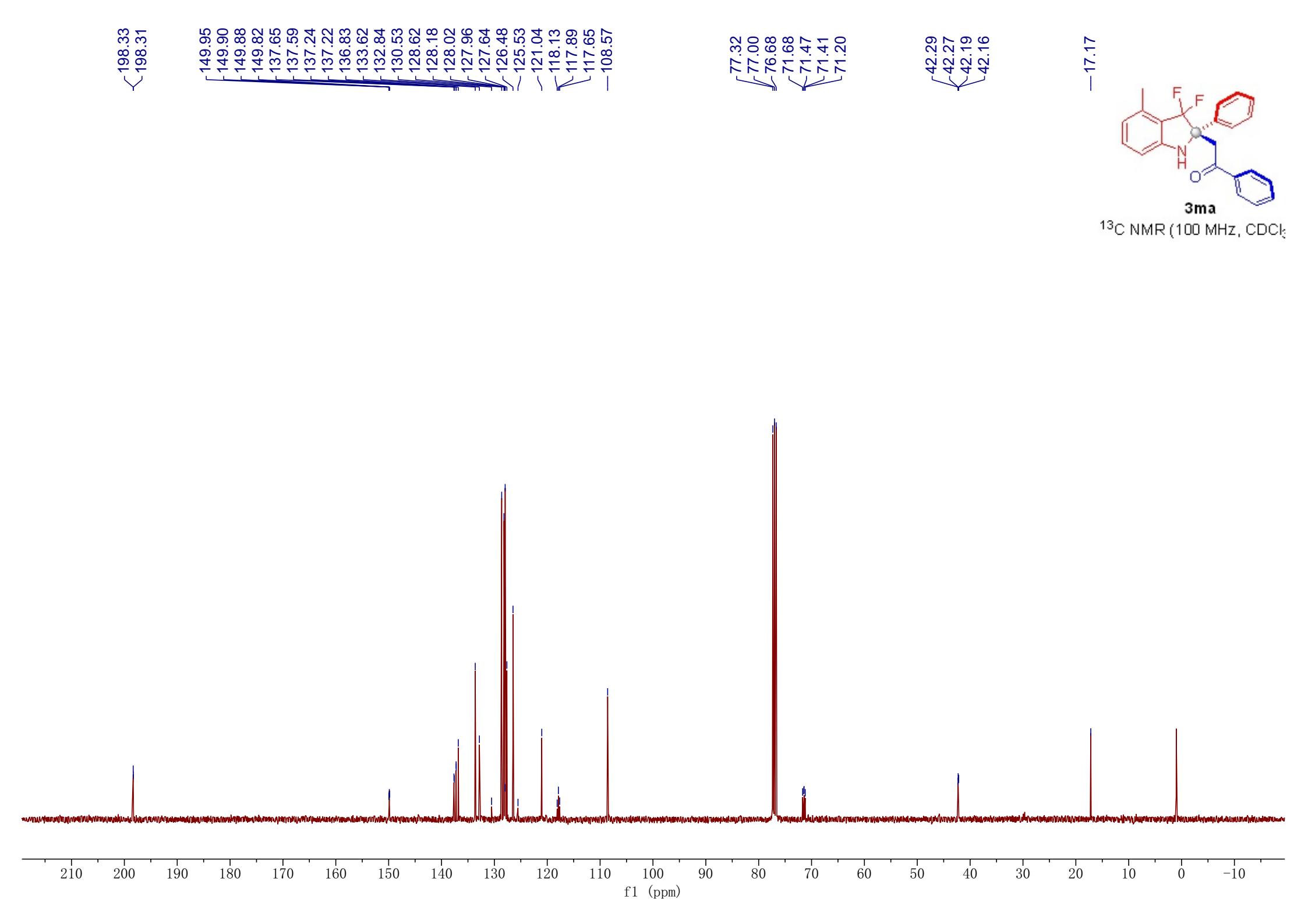


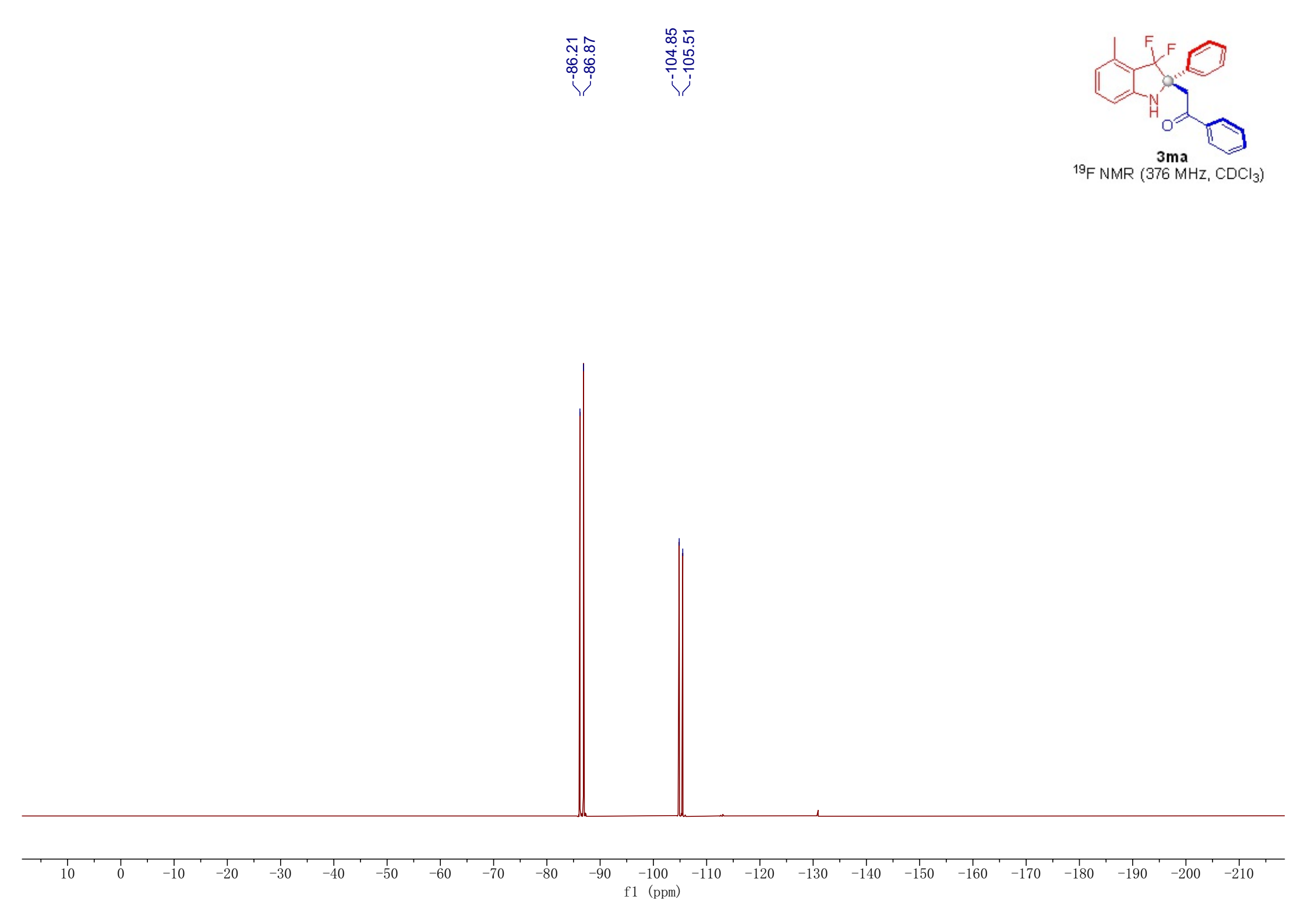
3ma

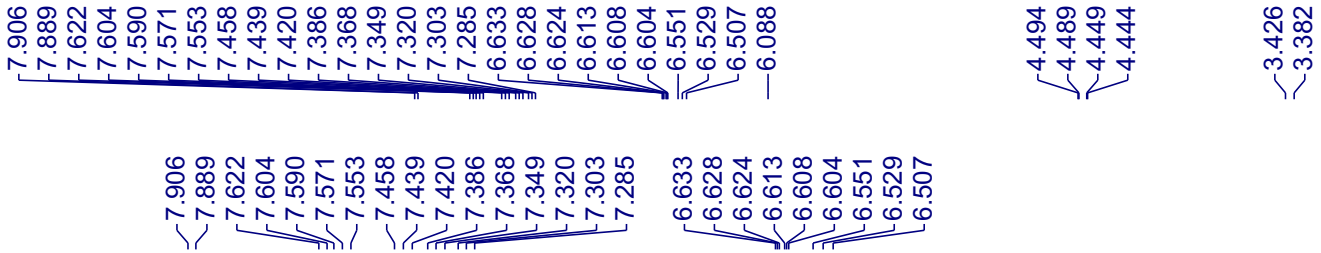
^{1}H NMR (400 MHz, $CDCl_3$)





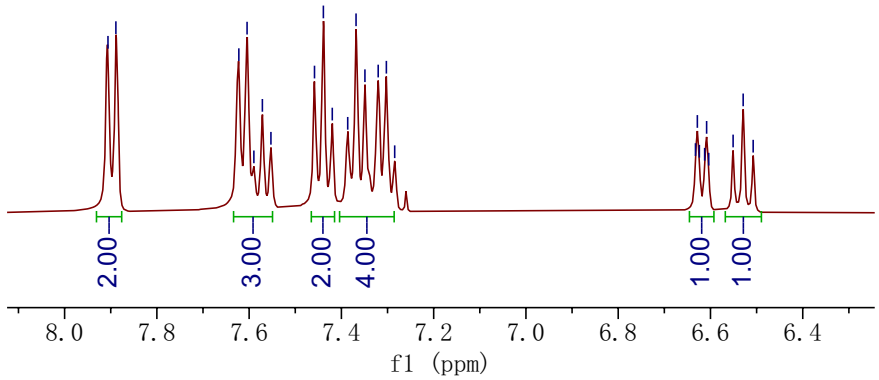

198.33
198.31
149.95
149.90
149.88
149.82
137.65
137.59
137.24
137.22
136.83
133.62
132.84
130.53
128.62
128.18
128.02
127.96
127.64
126.48
125.53
121.04
118.13
117.89
117.65
108.57
77.32
77.00
76.68
71.68
71.47
71.41
71.20
42.29
42.27
42.19
42.16
17.17
F
F
N
H
O
3ma
13C NMR (100 MHz, CDCl
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

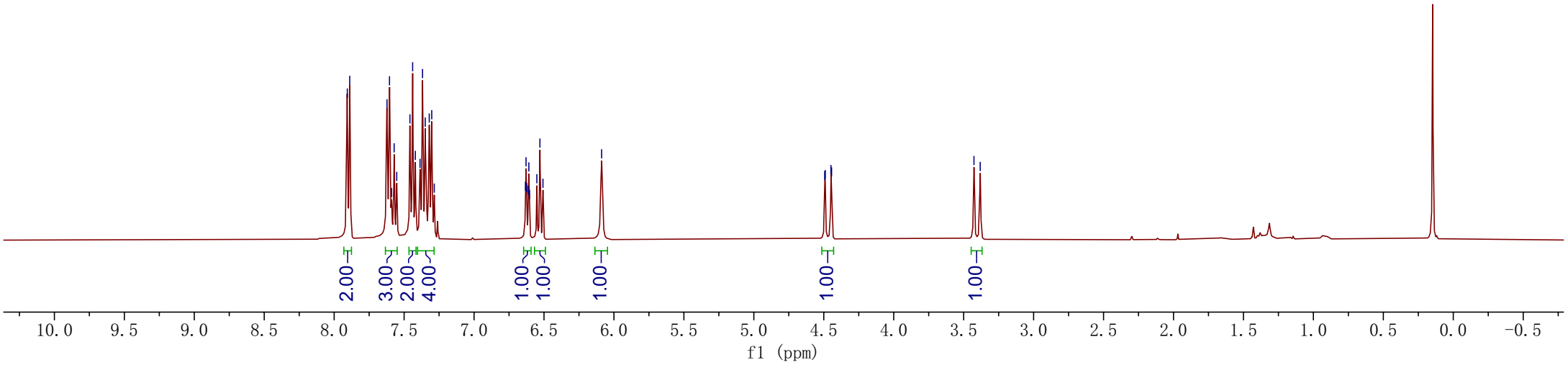

-86.21
-86.87
-104.85
-105.51
F
F
N
H
O
3ma
^{19}F NMR (376 MHz, $CDCl_3$)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

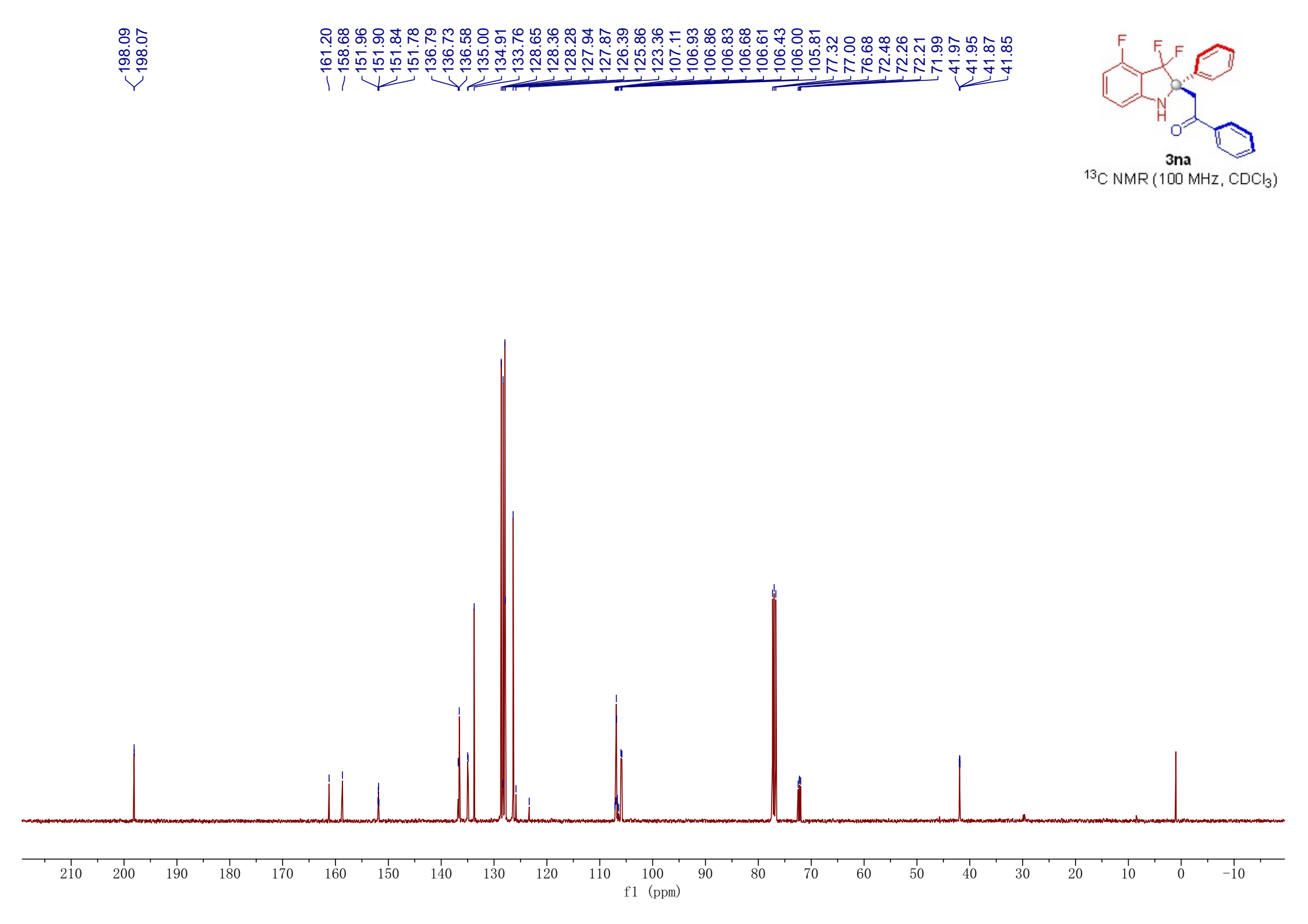


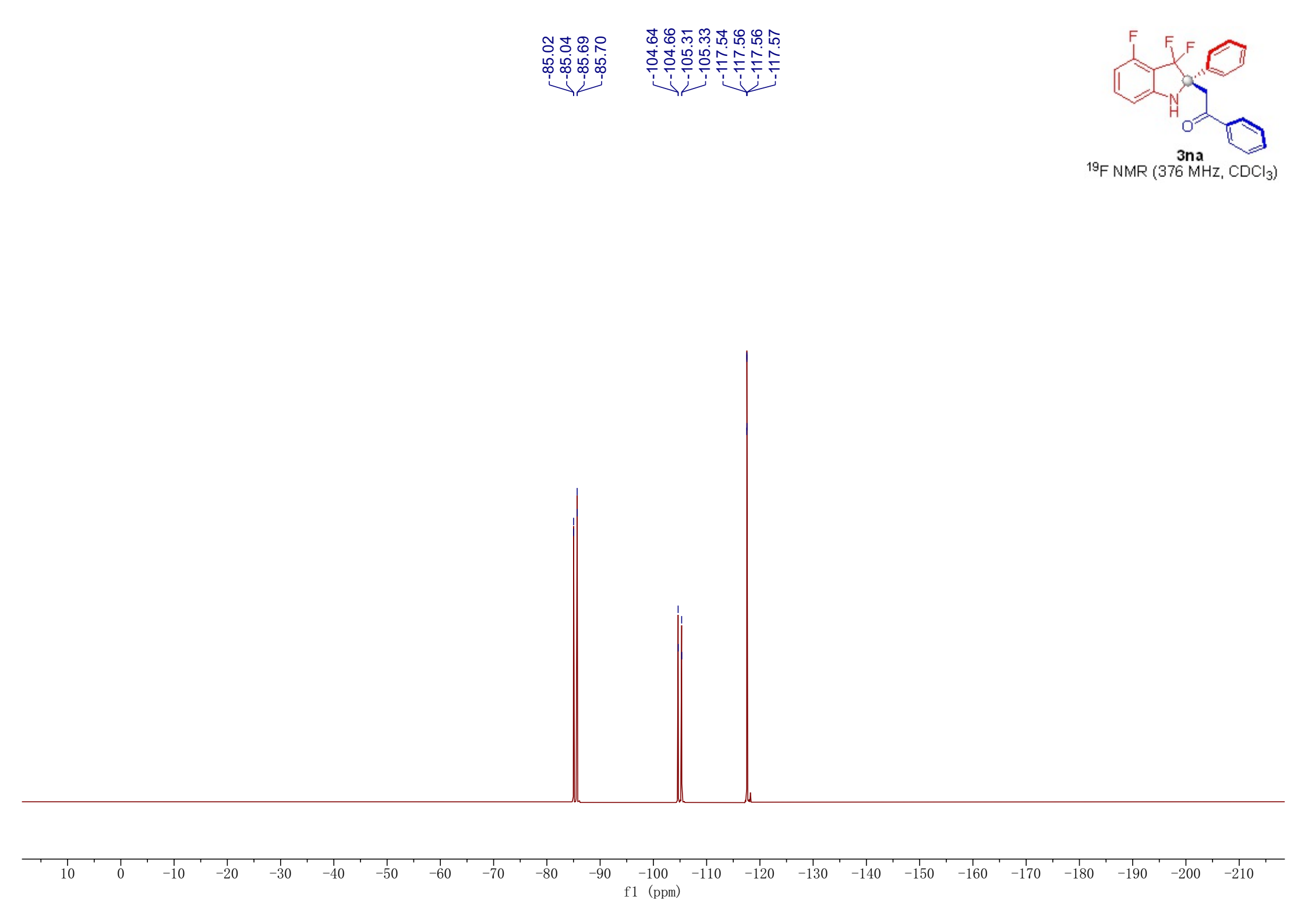
3na

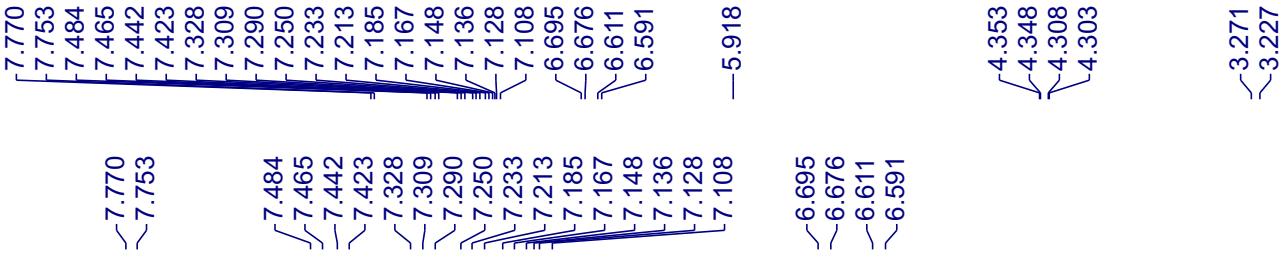
^{1}H NMR (400 MHz, $CDCl_3$)





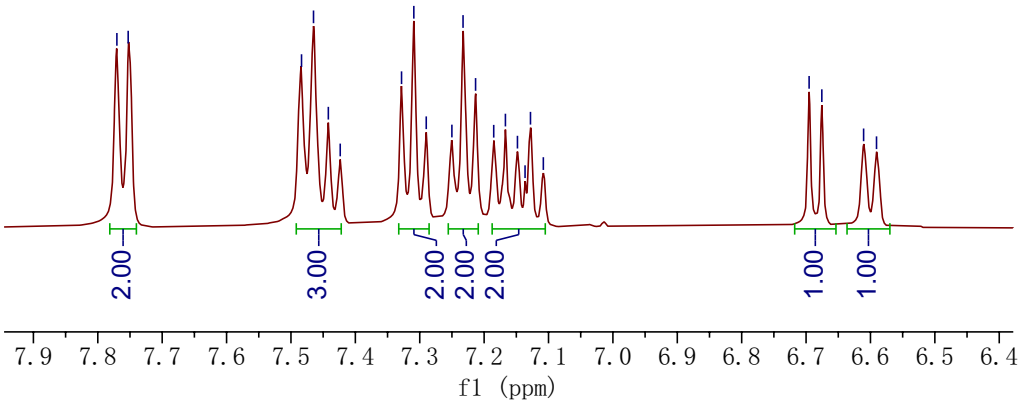

198.09
198.07
161.20
158.68
151.96
151.90
151.84
151.78
136.79
136.73
136.58
135.00
134.91
133.76
128.65
128.36
128.28
127.94
127.87
126.39
125.86
123.36
107.11
106.93
106.86
106.83
106.68
106.61
106.43
106.00
105.81
77.32
77.00
76.68
72.48
72.26
72.21
71.99
41.97
41.95
41.87
41.85
F
F
F
N
H
O
3na
13C NMR (100 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

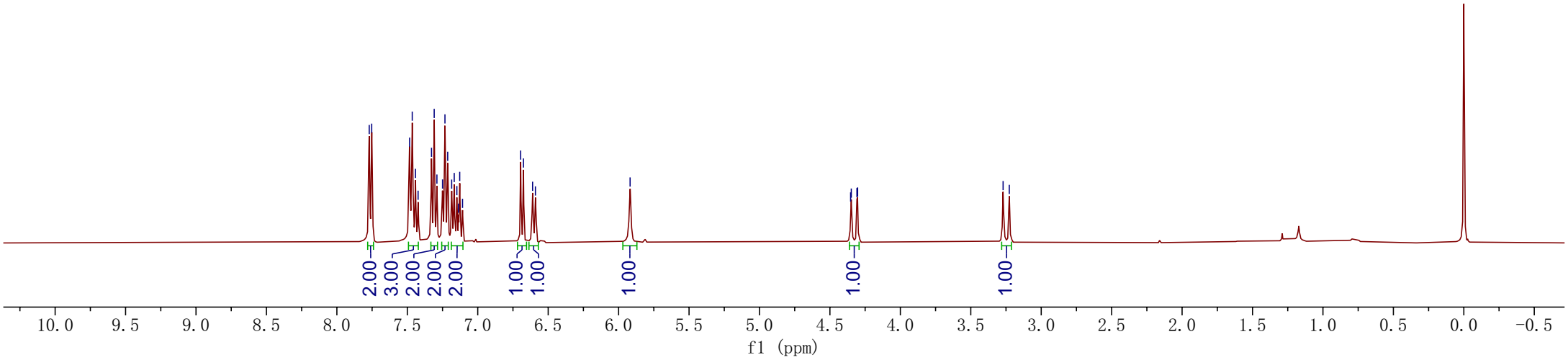

-85.02
-85.04
-85.69
-85.70
-104.64
-104.66
-105.31
-105.33
-117.54
-117.56
-117.56
-117.57
F
F
F
N
H
O
3na
19F NMR (376 MHz, CDCl3)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

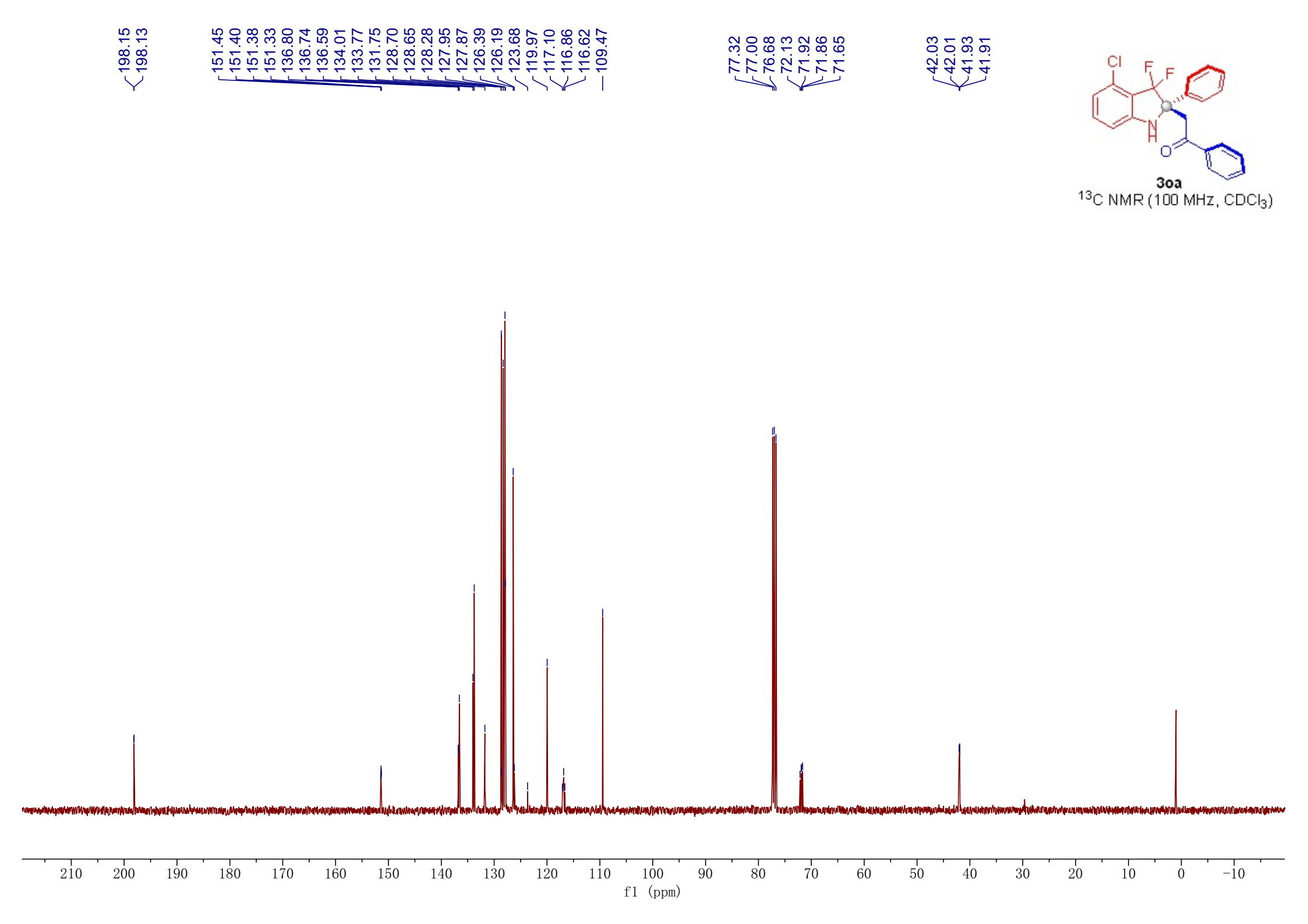


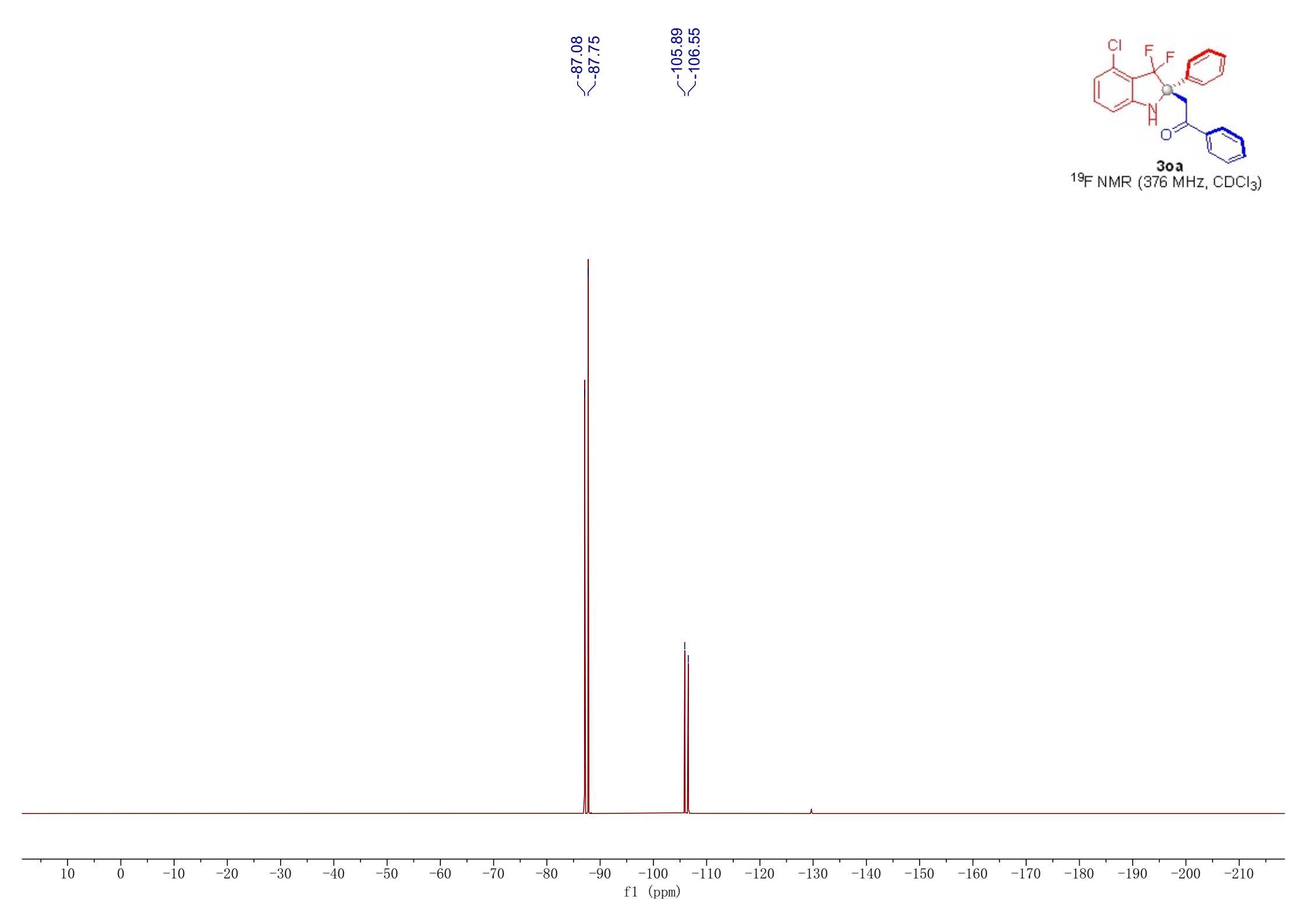
3oa

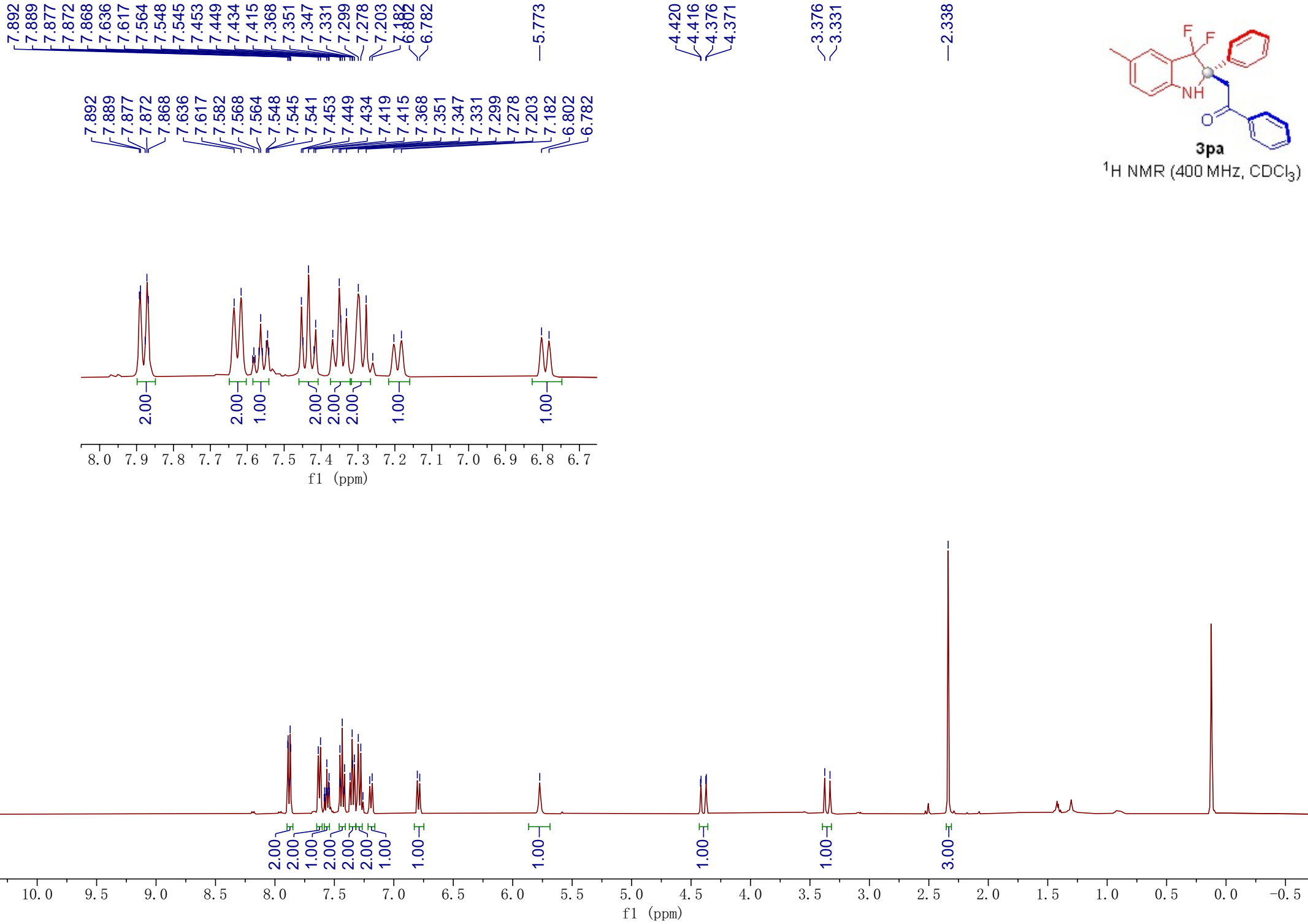
^{1}H NMR (400 MHz, $CDCl_3$)

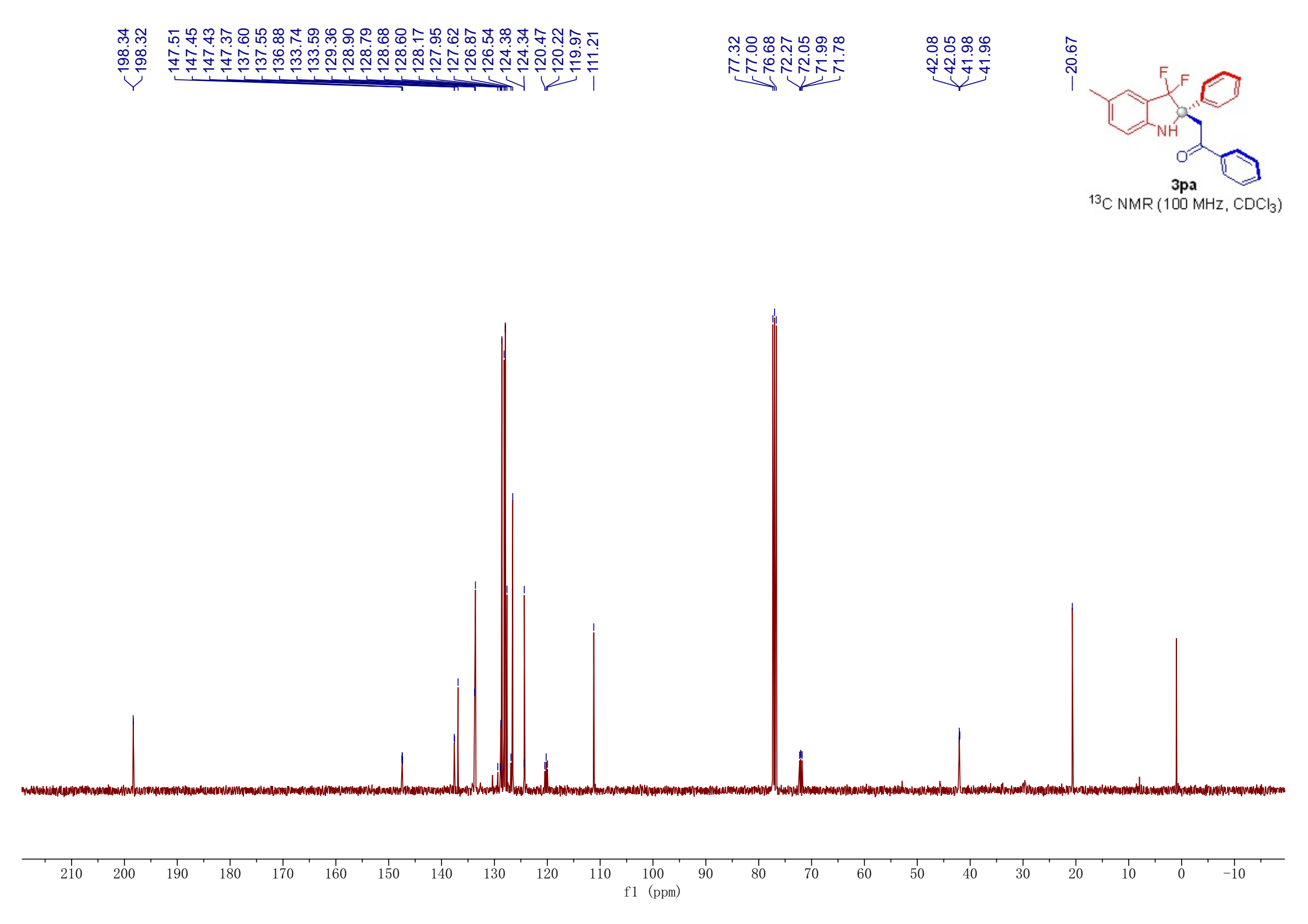


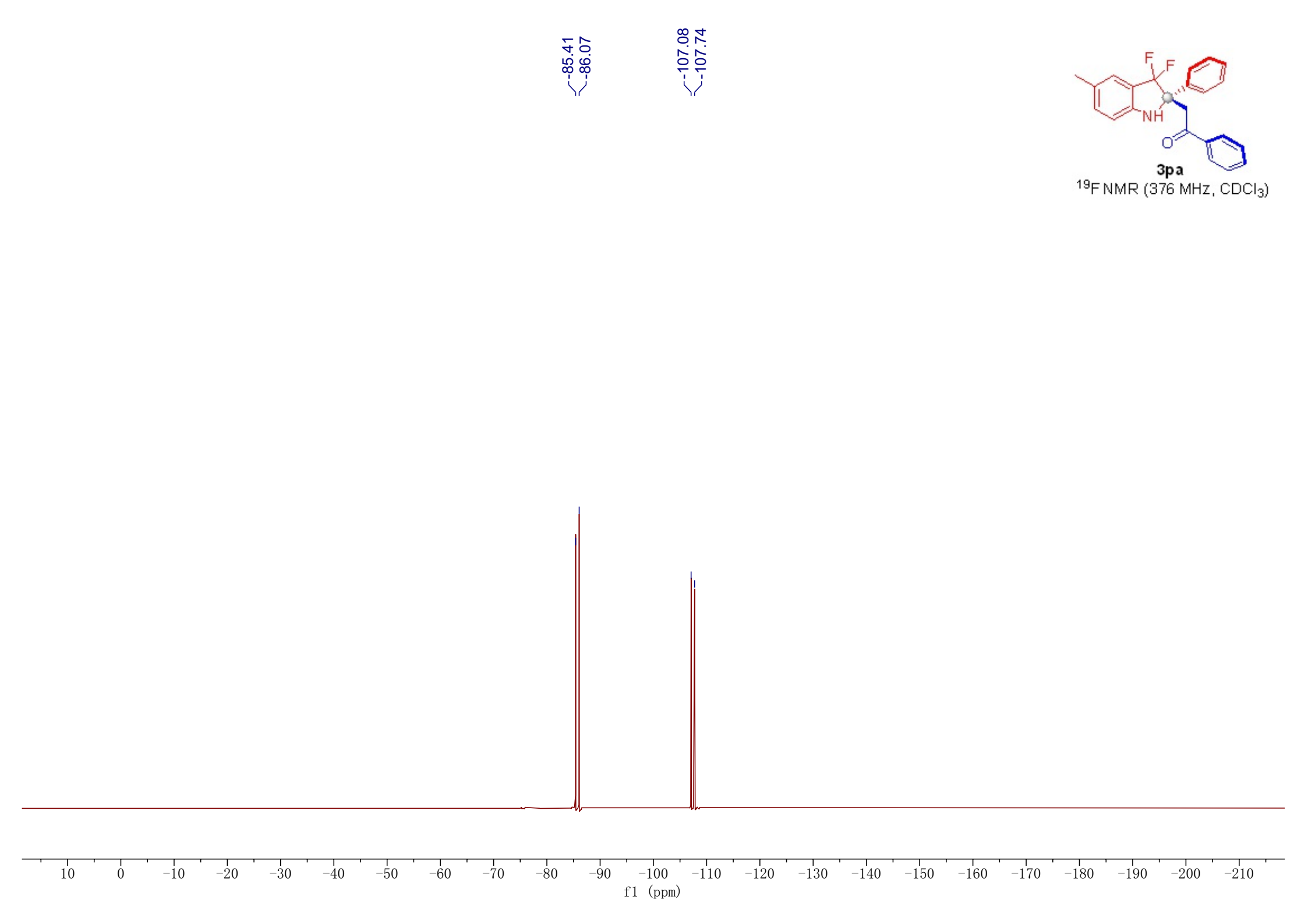


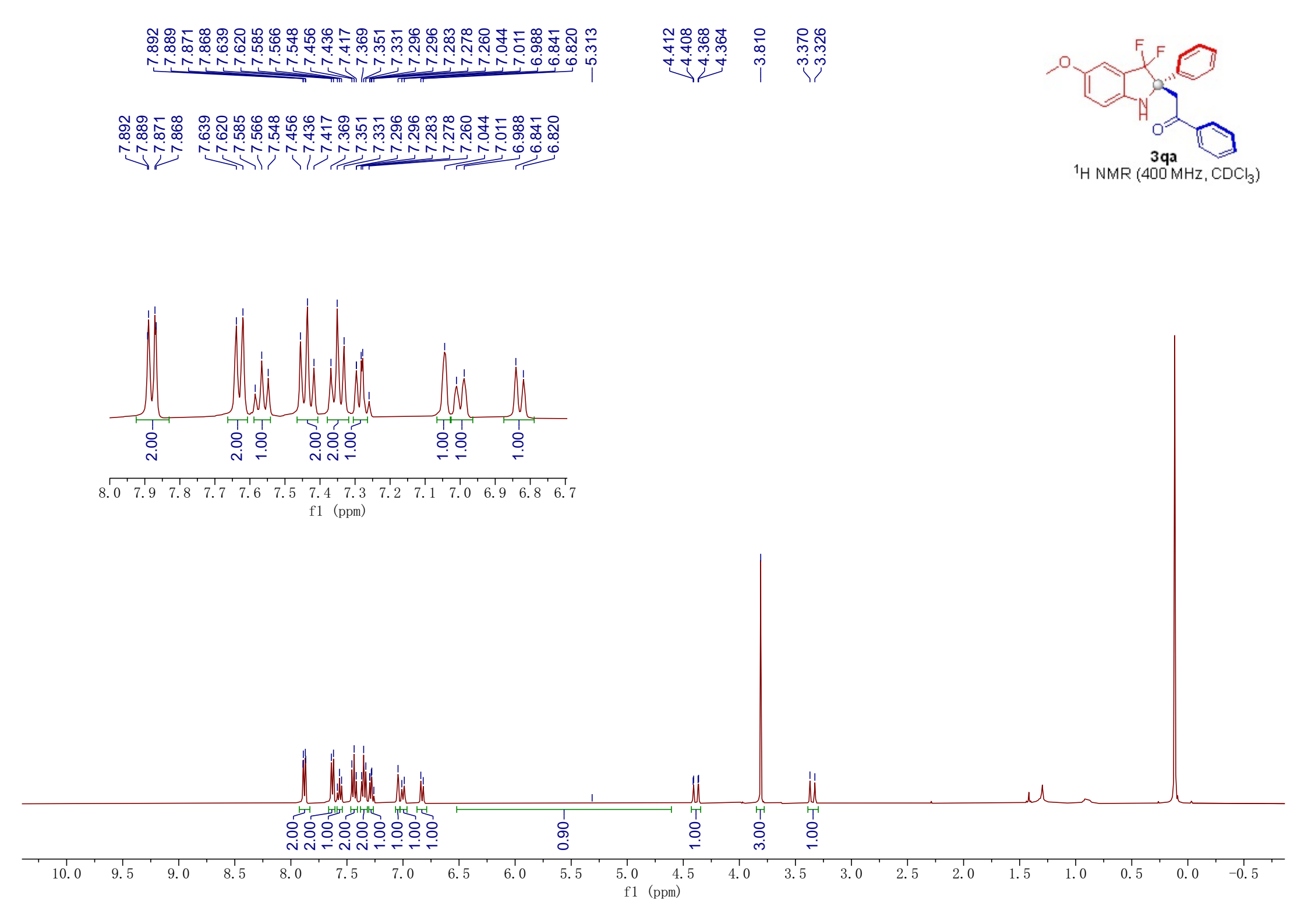

198.15
198.13
151.45
151.40
151.38
151.33
136.80
136.74
136.59
134.01
133.77
131.75
128.70
128.65
128.28
127.95
127.87
126.39
126.19
123.68
119.97
117.10
116.86
116.62
109.47
77.32
77.00
76.68
72.13
71.92
71.86
71.65
42.03
42.01
41.93
41.91
Cl
F
F
N
H
O
3oa
13C NMR (100 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


-87.08
-87.75
-105.89
-106.55
Cl
F
F
N
H
O
3oa
19F NMR (376 MHz, CDCl3)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)


7.892
7.889
7.877
7.872
7.868
7.636
7.617
7.564
7.548
7.545
7.453
7.449
7.434
7.415
7.368
7.351
7.347
7.331
7.299
7.278
7.203
7.182
6.802
6.782
5.773
4.420
4.416
4.376
4.371
3.376
3.331
2.338
F
F
NH
O
3pa
1H NMR (400 MHz, CDCl3)
2.00
2.00
1.00
2.00
2.00
2.00
1.00
1.00
8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7
f1 (ppm)
2.00
2.00
1.00
2.00
2.00
2.00
1.00
1.00
1.00
1.00
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


198.34
198.32
147.51
147.45
147.43
147.37
137.60
137.55
136.88
133.74
133.59
129.36
128.90
128.79
128.68
128.60
128.17
127.95
127.62
126.87
126.54
124.38
124.34
120.47
120.22
119.97
111.21
77.32
77.00
76.68
72.27
72.05
71.99
71.78
42.08
42.05
41.98
41.96
20.67
F
F
NH
O
3pa
13C NMR (100 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

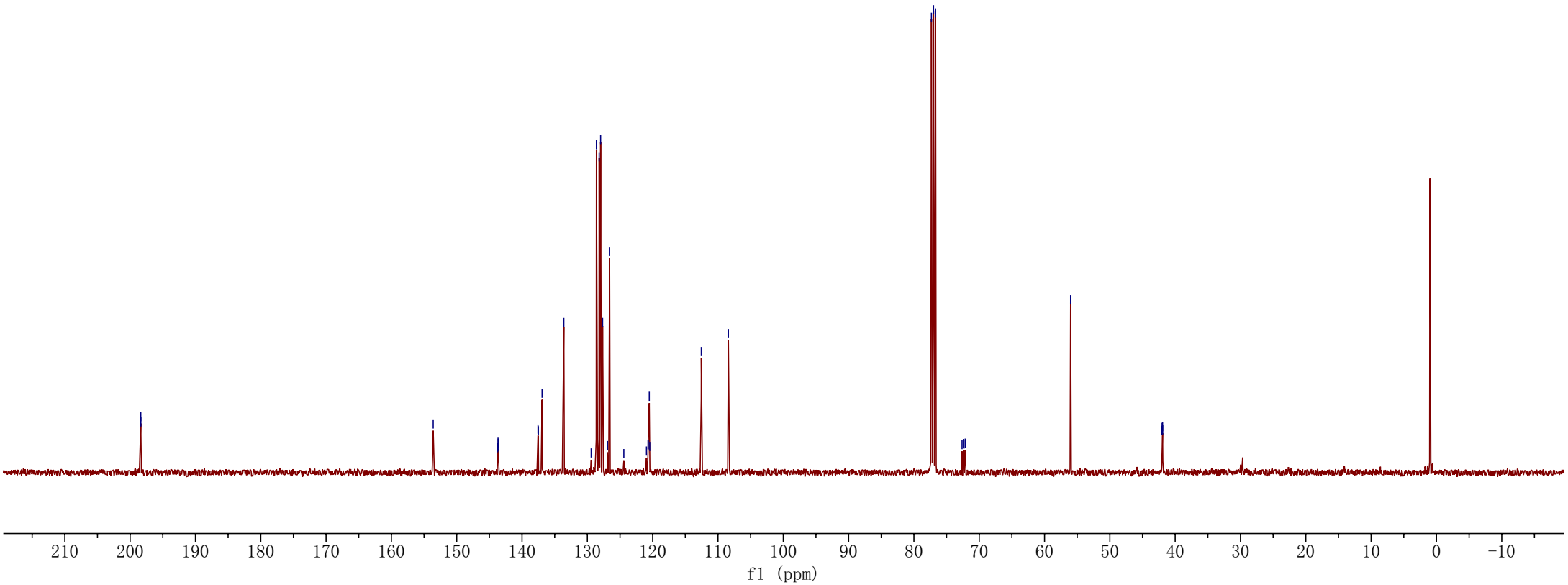

-85.41
-86.07
-107.08
-107.74
F
F
NH
O
3pa
^{19}F NMR (376 MHz, $CDCl_3$)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

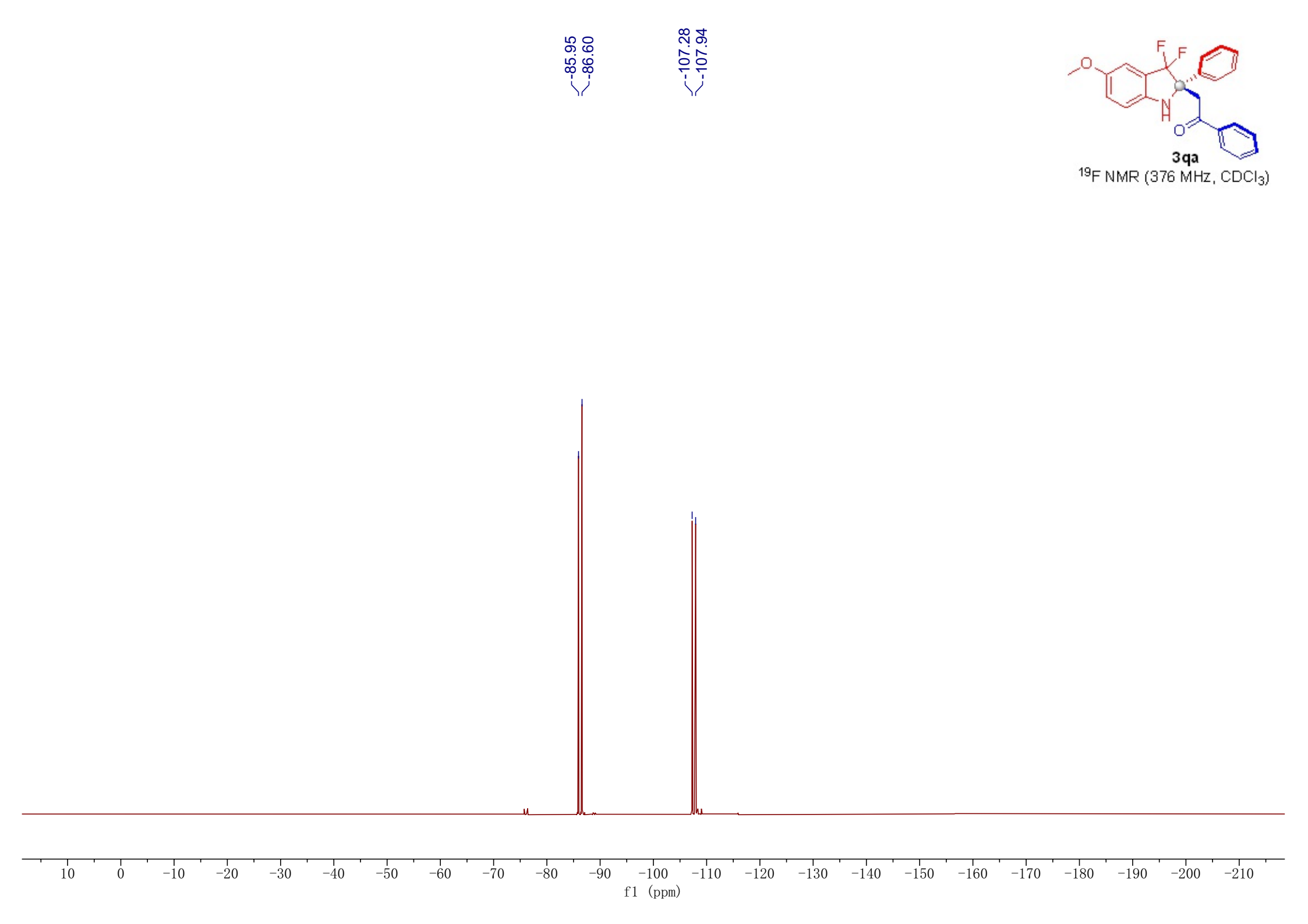

7.892
7.889
7.871
7.868
7.639
7.620
7.585
7.566
7.548
7.456
7.436
7.417
7.369
7.351
7.331
7.296
7.296
7.283
7.278
7.260
7.044
7.011
6.988
6.841
6.820
5.313
4.412
4.408
4.368
4.364
3.810
3.370
3.326
F
F
O
N
H
O
3qa
1H NMR (400 MHz, CDCl3)
2.00
2.00
1.00
2.00
2.00
1.00
1.00
1.00
1.00
8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7
f1 (ppm)
2.00
2.00
1.00
2.00
2.00
1.00
1.00
1.00
1.00
0.90
1.00
3.00
1.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

198.37
198.35
153.60
143.74
143.68
143.65
143.59
137.55
137.50
136.93
133.60
129.41
128.61
128.19
127.97
127.67
126.91
126.59
124.42
120.95
120.70
120.69
120.52
120.45
112.55
108.41
77.32
77.00
76.68
72.63
72.42
72.35
72.15
56.01
42.02
42.00
41.93
41.91

3qa

^{13}C NMR (100 MHz, $CDCl_3$)



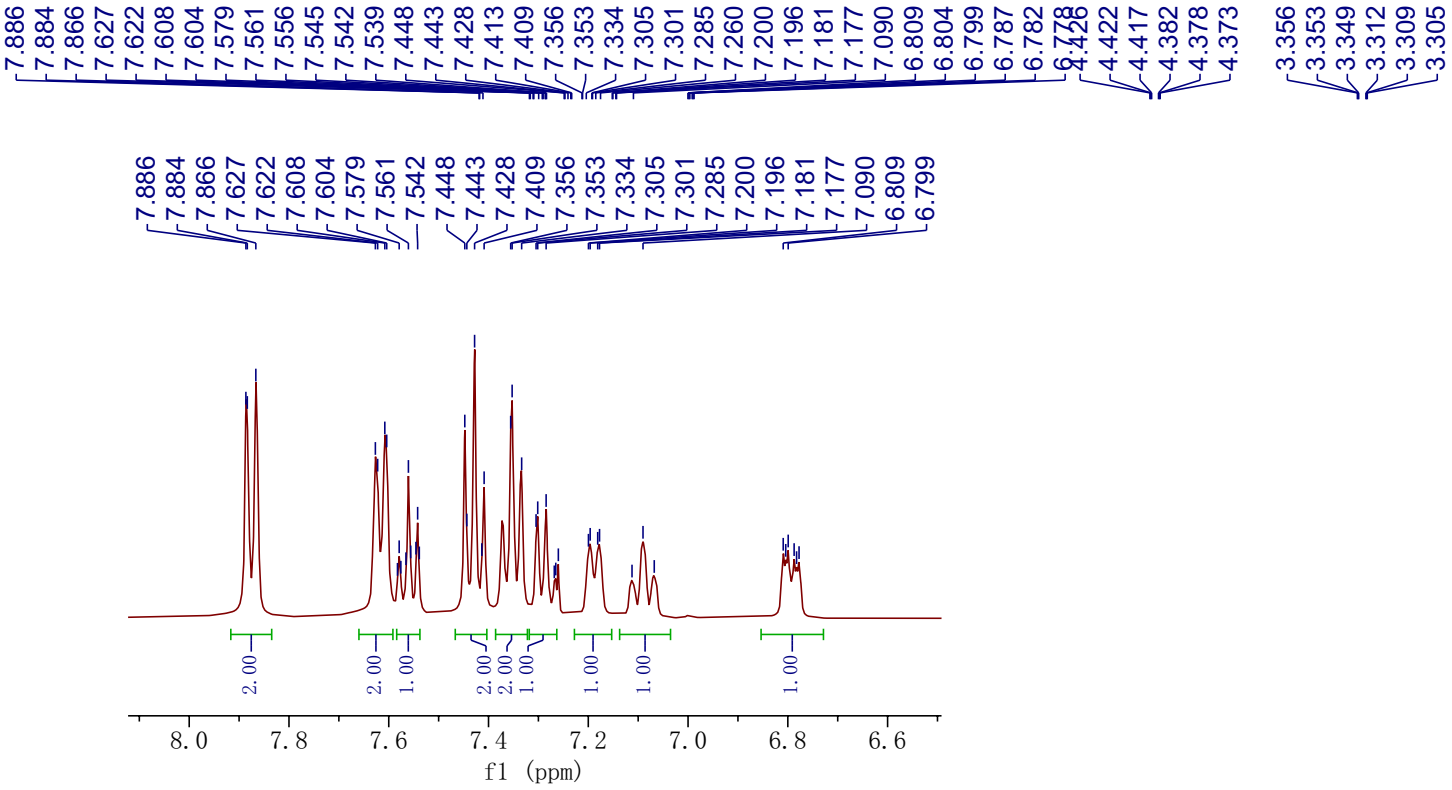


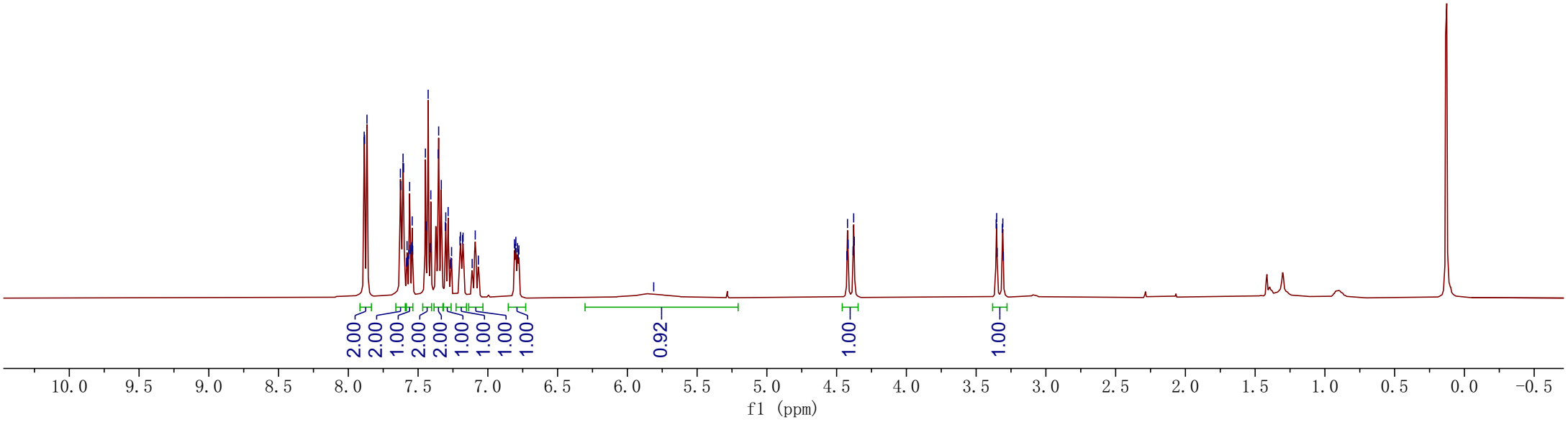
3qa

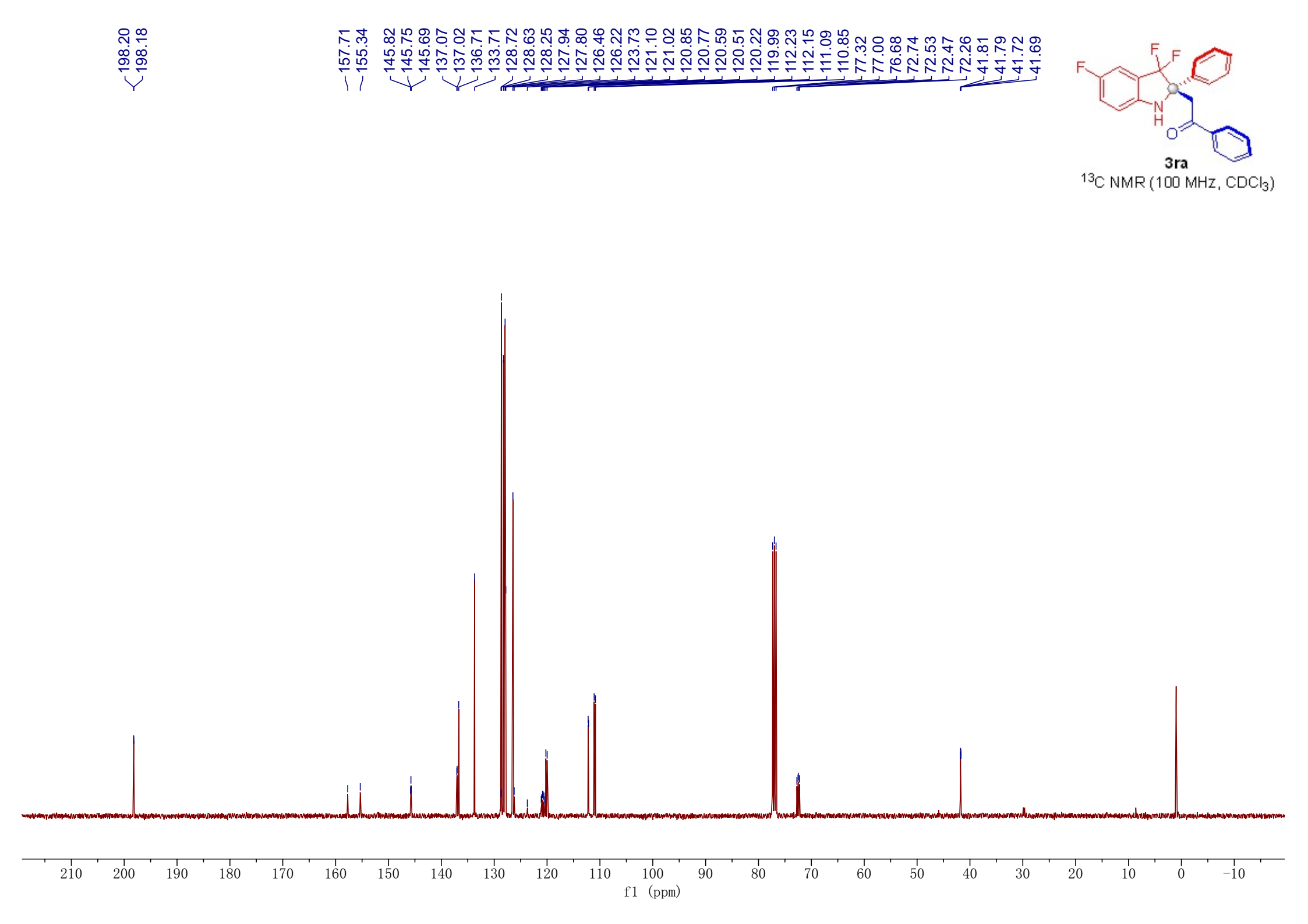
^{19}F NMR (376 MHz, $CDCl_3$)

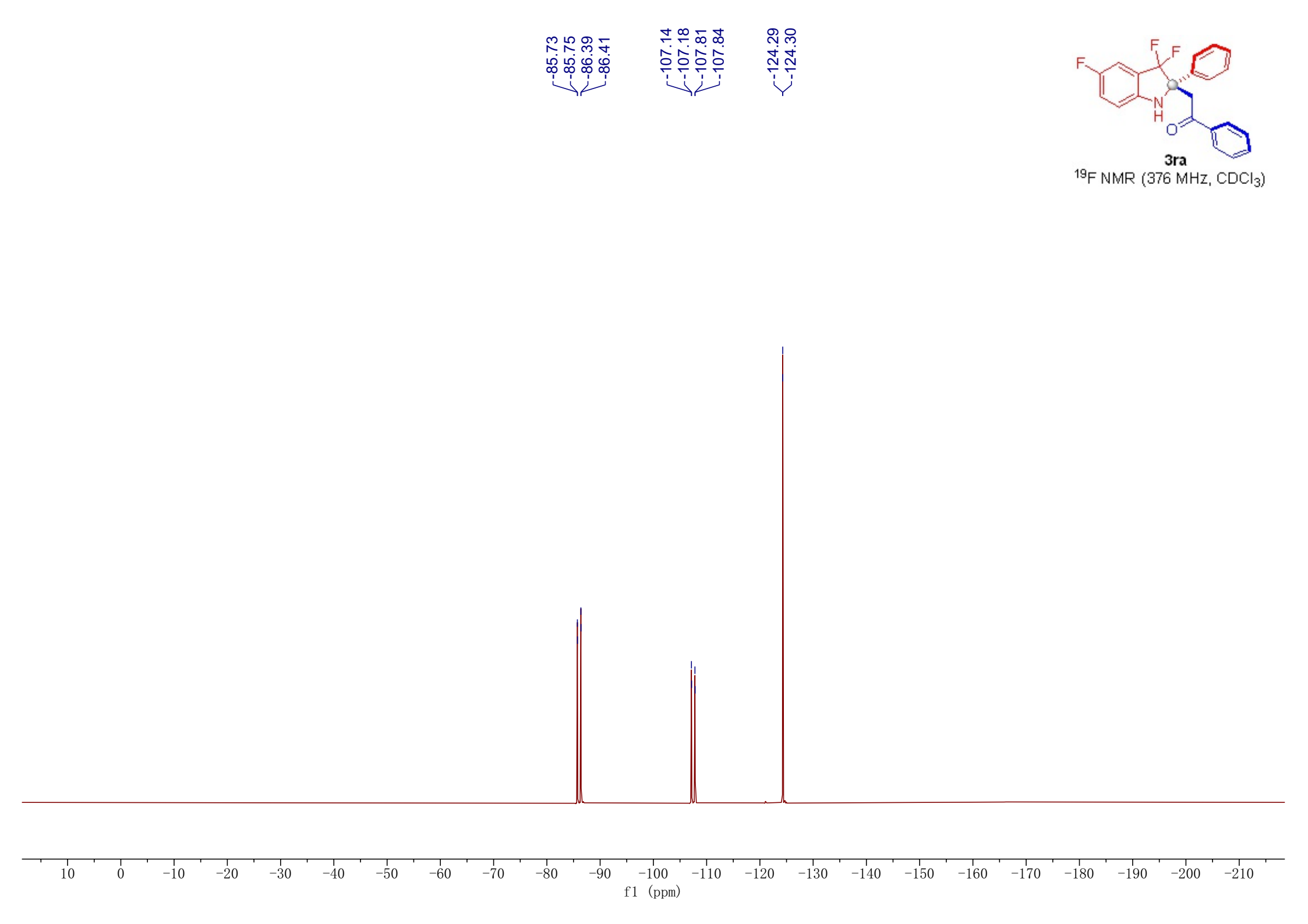
3ra

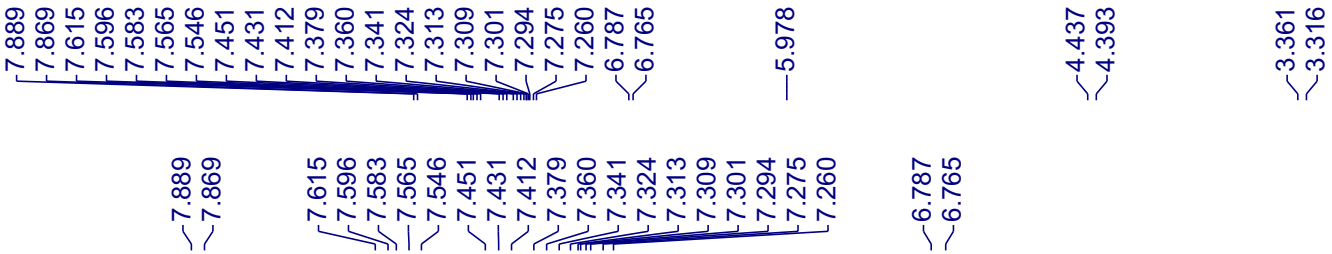
^{1}H NMR (400 MHz, $CDCl_3$)





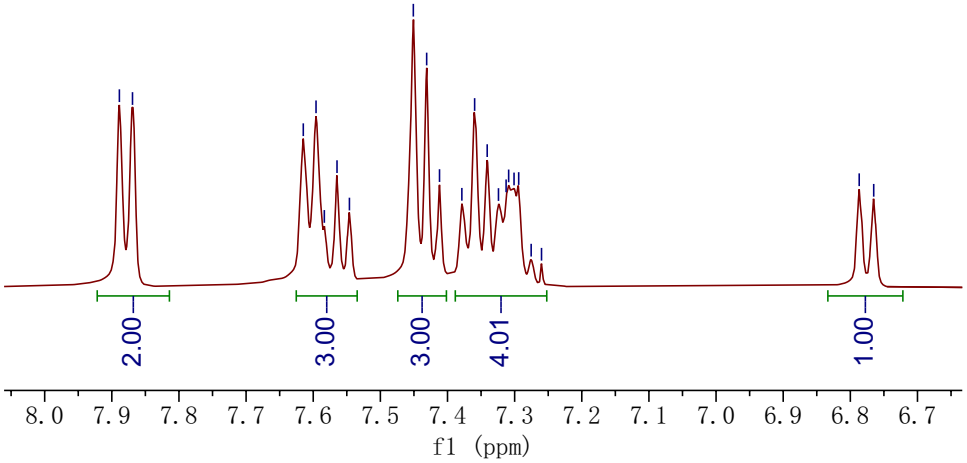

198.20
198.18
157.71
155.34
145.82
145.75
145.69
137.07
137.02
136.71
133.71
128.72
128.63
128.25
127.94
127.80
126.46
126.22
123.73
121.10
121.02
120.85
120.77
120.59
120.51
120.22
119.99
112.23
112.15
111.09
110.85
77.32
77.00
76.68
72.74
72.53
72.47
72.26
41.81
41.79
41.72
41.69
F
F
F
N
H
O
3ra
13C NMR (100 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

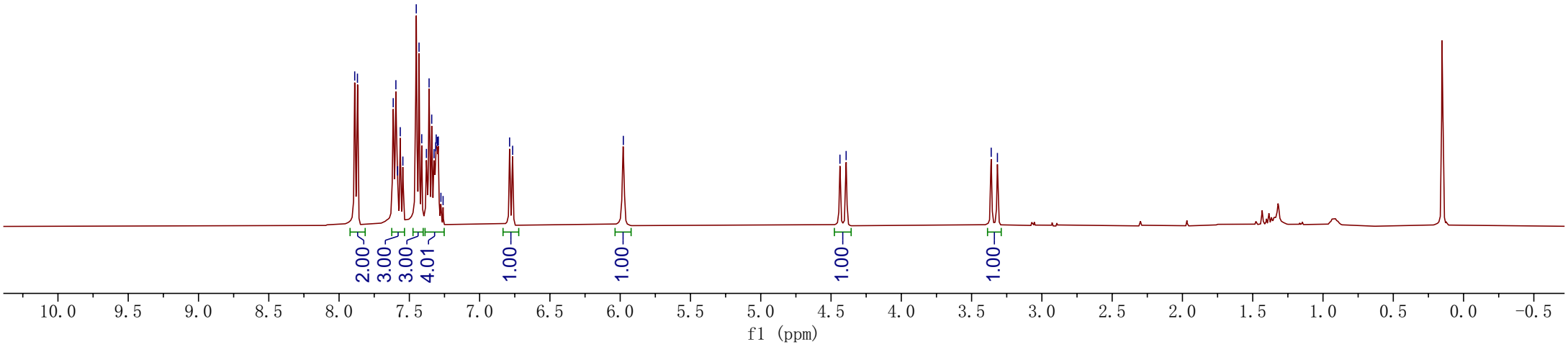

-85.73
-85.75
-86.39
-86.41
-107.14
-107.18
-107.81
-107.84
-124.29
-124.30
F
F
F
N
H
O
3ra
19F NMR (376 MHz, CDCl3)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

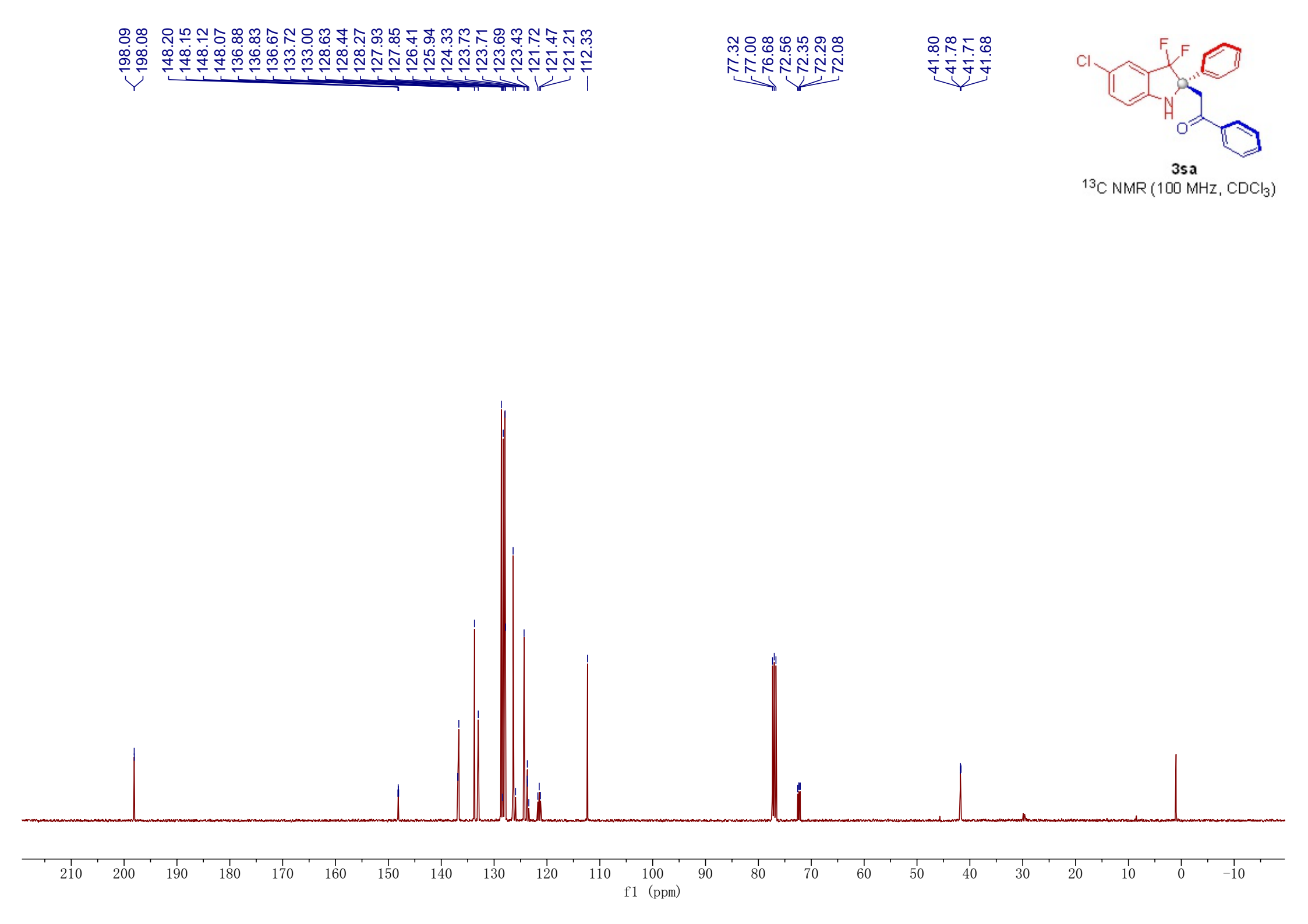


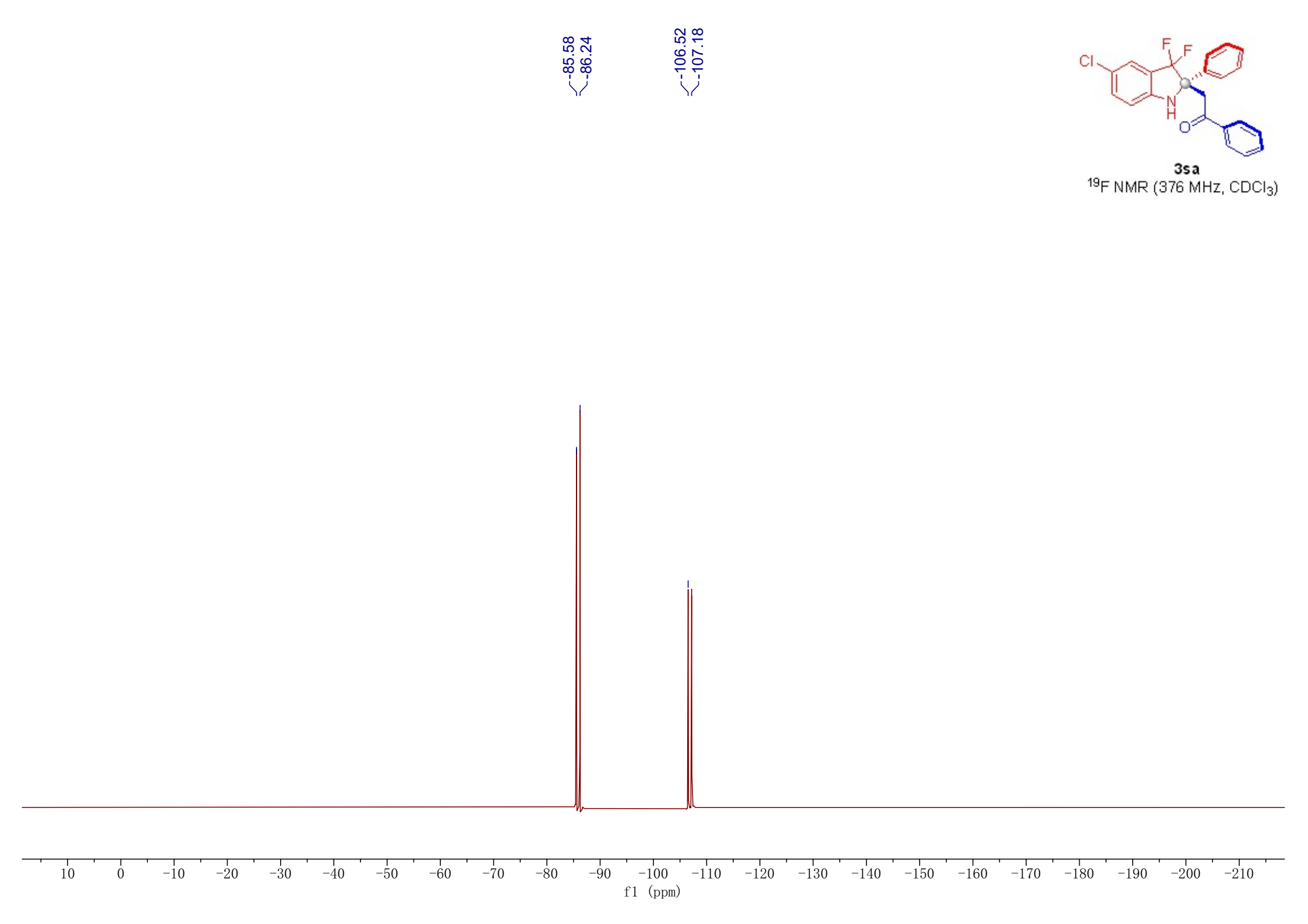
3sa

^{1}H NMR (400 MHz, $CDCl_3$)



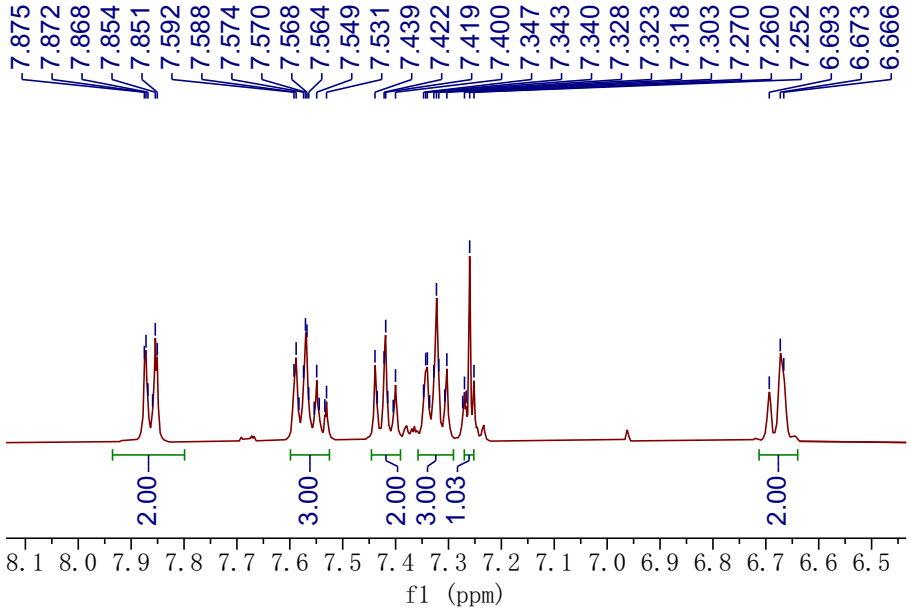


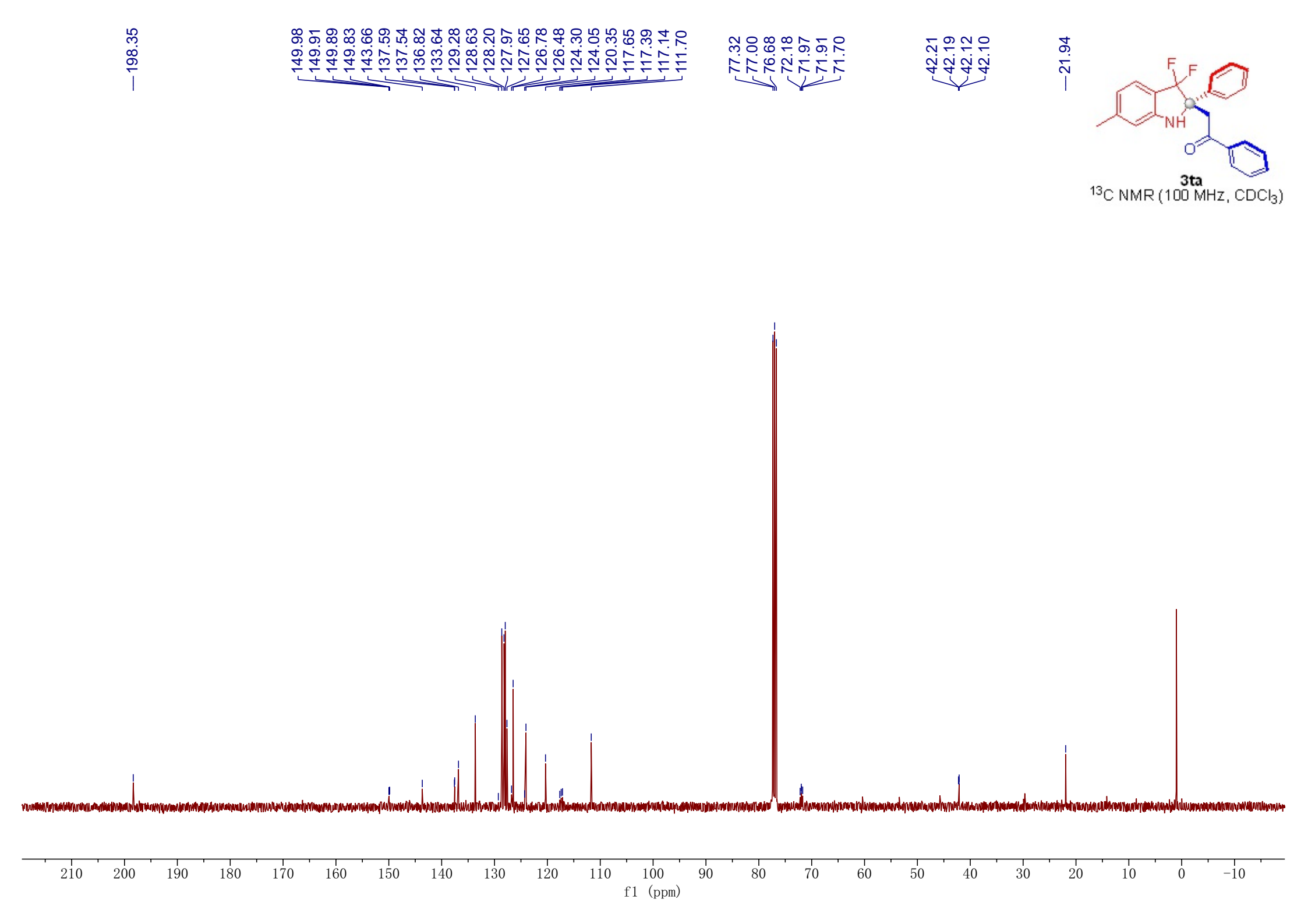

198.09
198.08
148.20
148.15
148.12
148.07
136.88
136.83
136.67
133.72
133.00
128.63
128.44
128.27
127.93
127.85
126.41
125.94
124.33
123.73
123.71
123.69
123.43
121.72
121.47
121.21
112.33
77.32
77.00
76.68
72.56
72.35
72.29
72.08
41.80
41.78
41.71
41.68
Cl
F
F
N
H
O
3sa
13C NMR (100 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

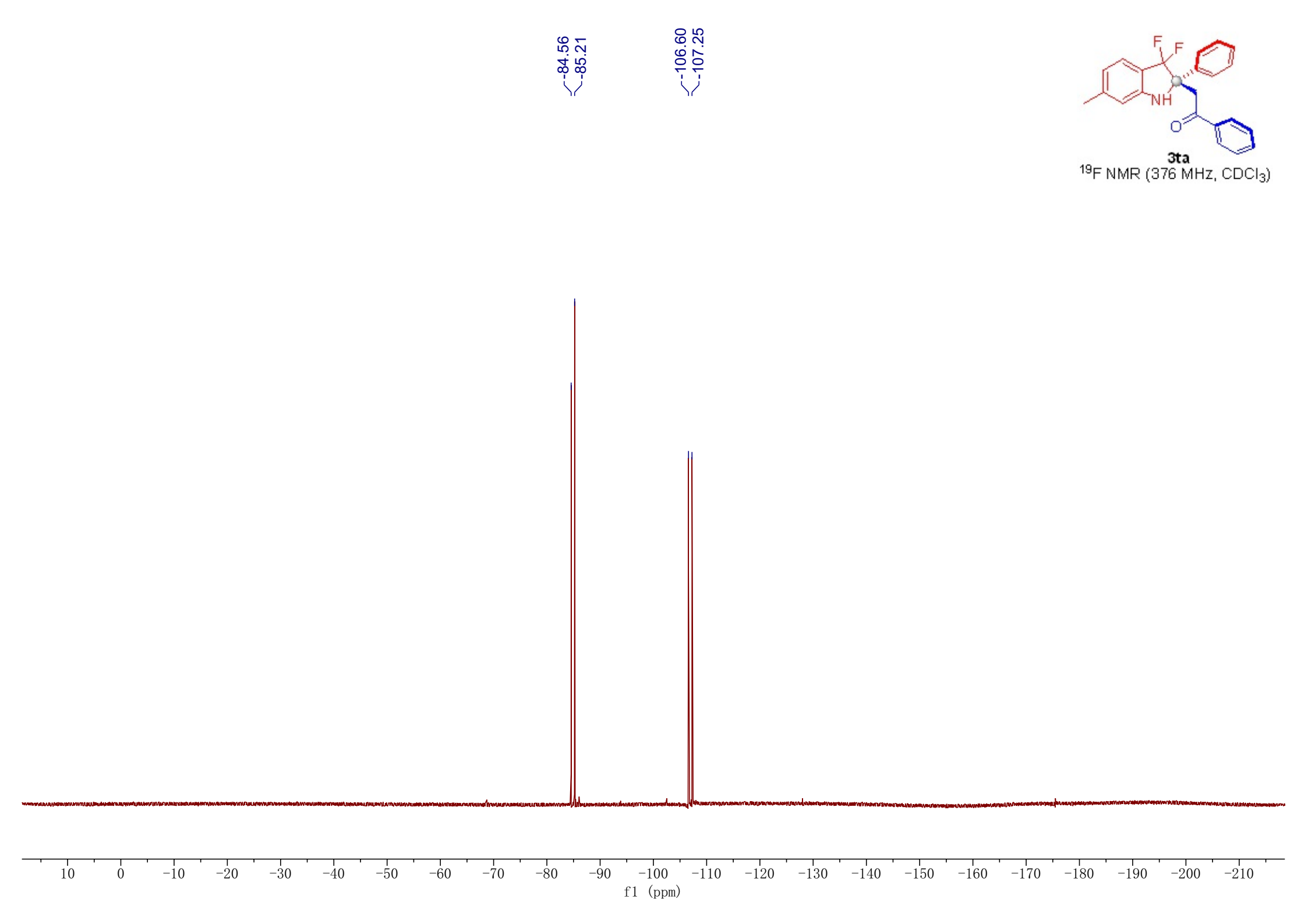

-85.58
-86.24
-106.52
-107.18
F
F
Cl
N
H
O
3sa
19F NMR (376 MHz, CDCl3)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

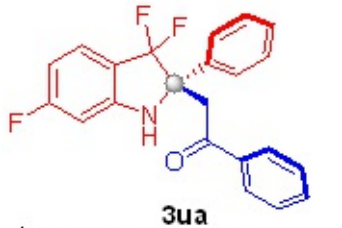
3ta

^{1}H NMR (400 MHz, $CDCl_3$)



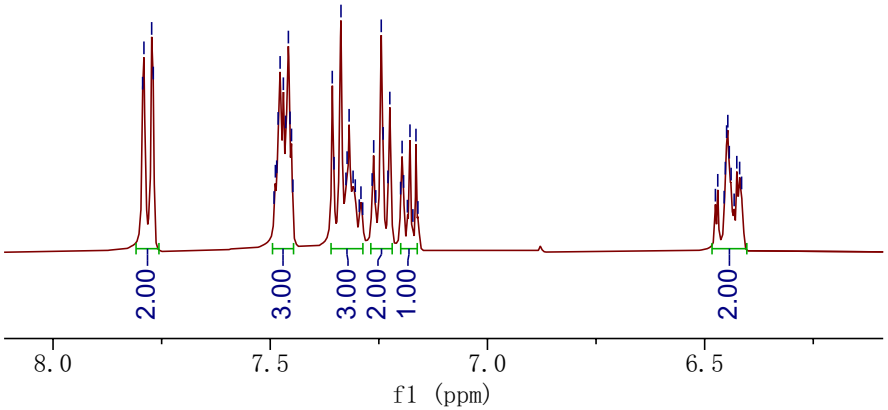

198.35
149.98
149.91
149.89
149.83
143.66
137.59
137.54
136.82
133.64
129.28
128.63
128.20
127.97
127.65
126.78
126.48
124.30
124.05
120.35
117.65
117.39
117.14
111.70
77.32
77.00
76.68
72.18
71.97
71.91
71.70
42.21
42.19
42.12
42.10
21.94
F
F
NH
O
3ta
13C NMR (100 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

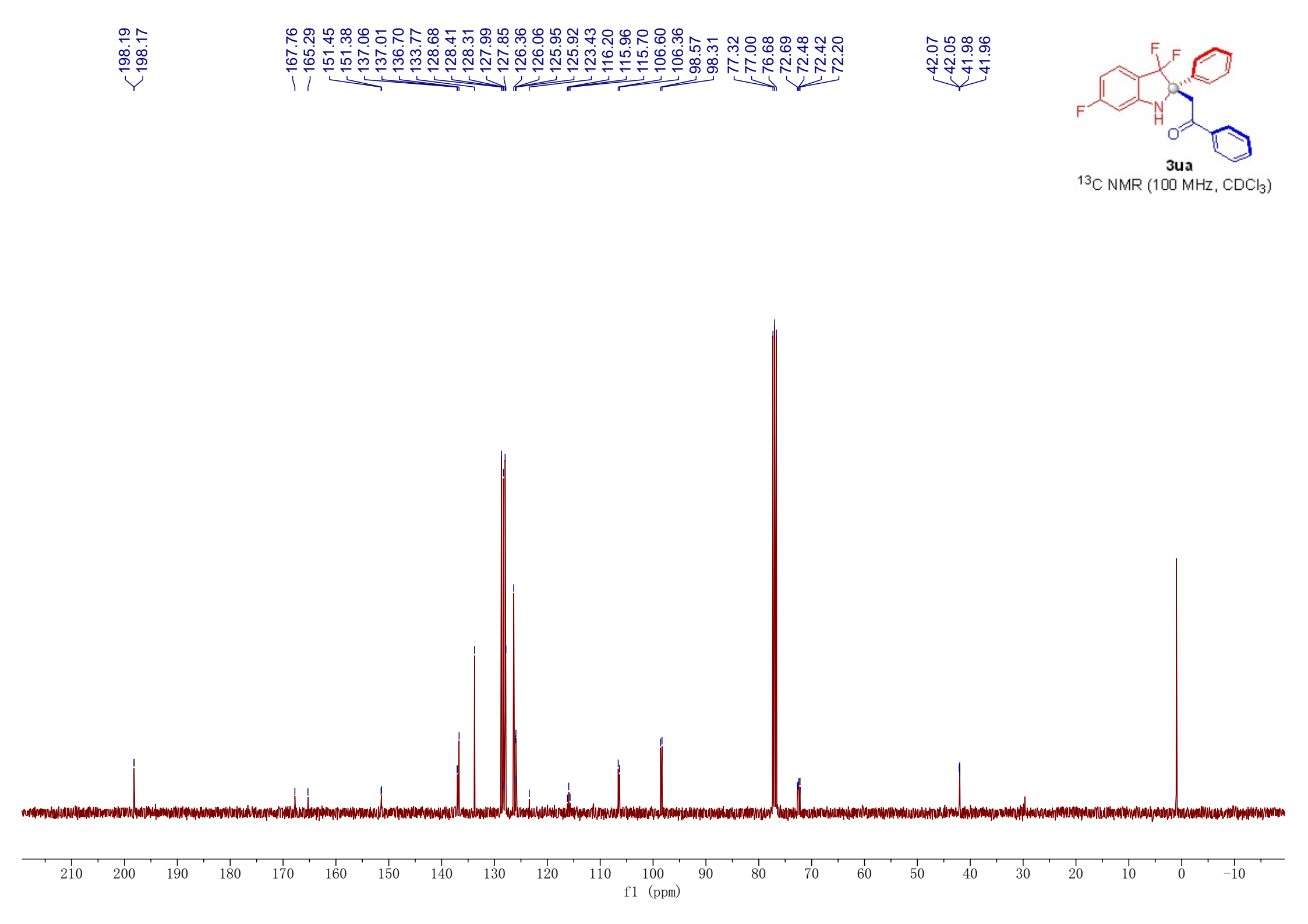

-84.56
-85.21
-106.60
-107.25
F
F
NH
O
3ta
19F NMR (376 MHz, CDCl3)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

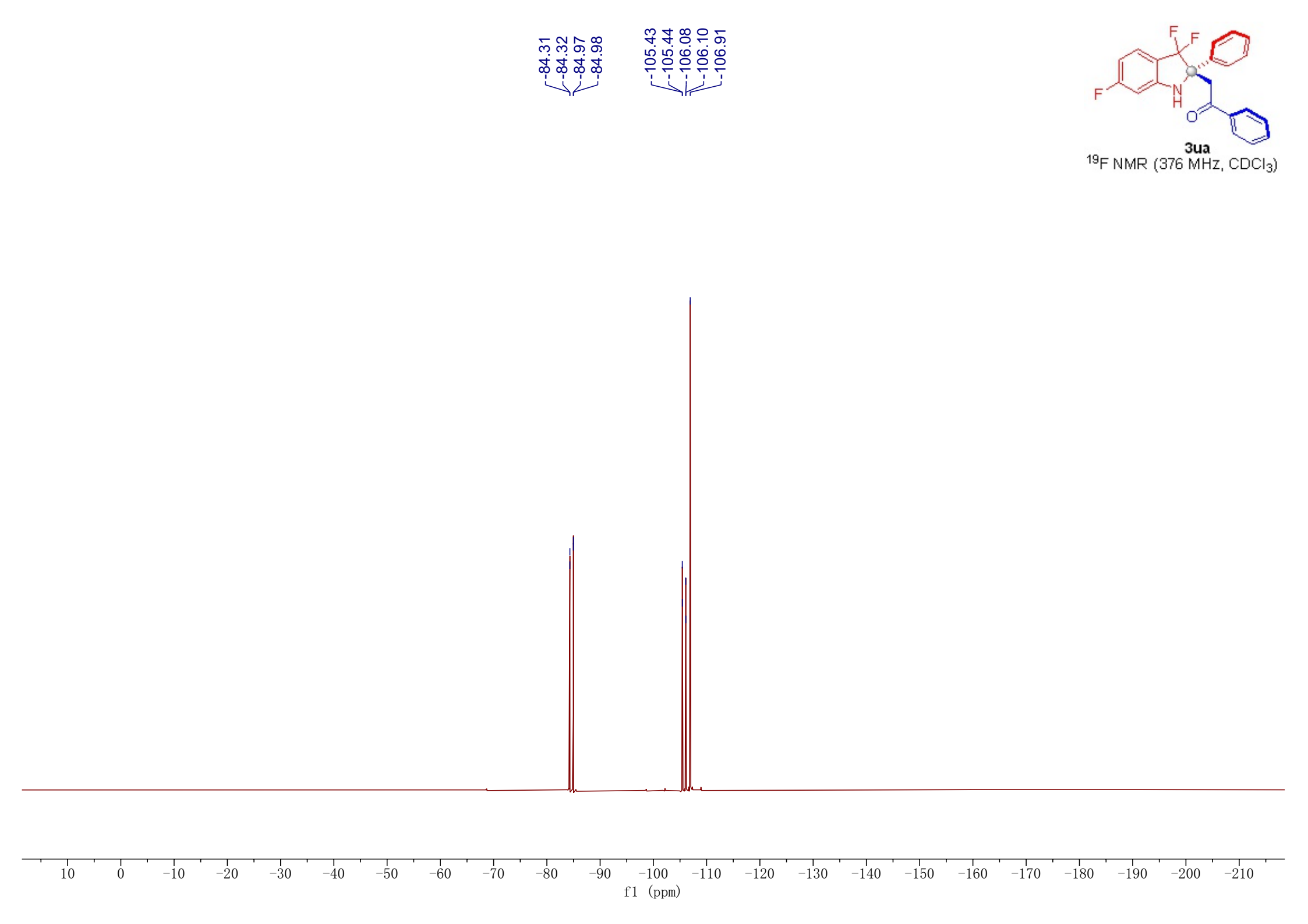


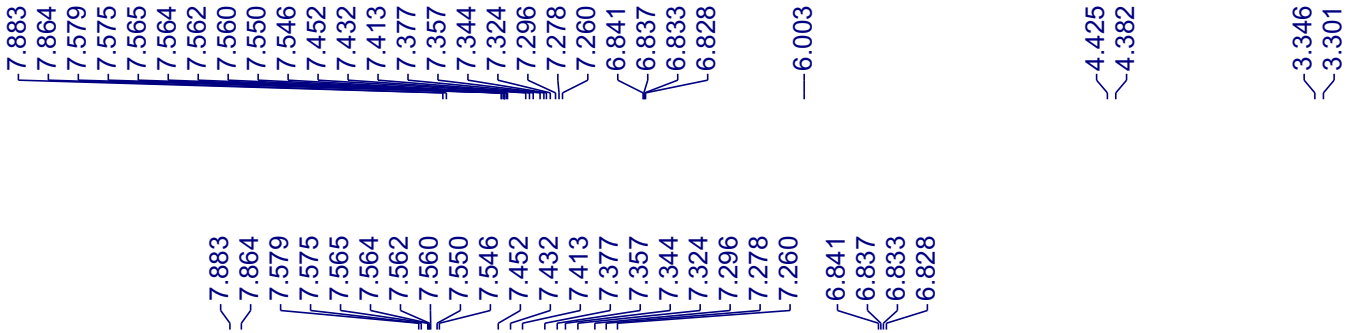
3ua

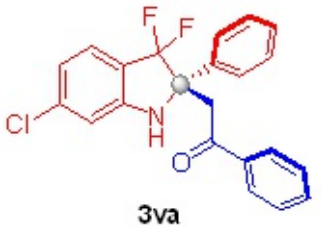
^{1}H NMR (400 MHz, $CDCl_3$)




198.19
198.17
167.76
165.29
151.45
151.38
137.06
137.01
136.70
133.77
128.68
128.41
128.31
127.99
127.85
126.36
126.06
125.95
125.92
123.43
116.20
115.96
115.70
106.60
106.36
98.57
98.31
77.32
77.00
76.68
72.69
72.48
72.42
72.20
42.07
42.05
41.98
41.96
F
F
F
N
H
O
3ua
13C NMR (100 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

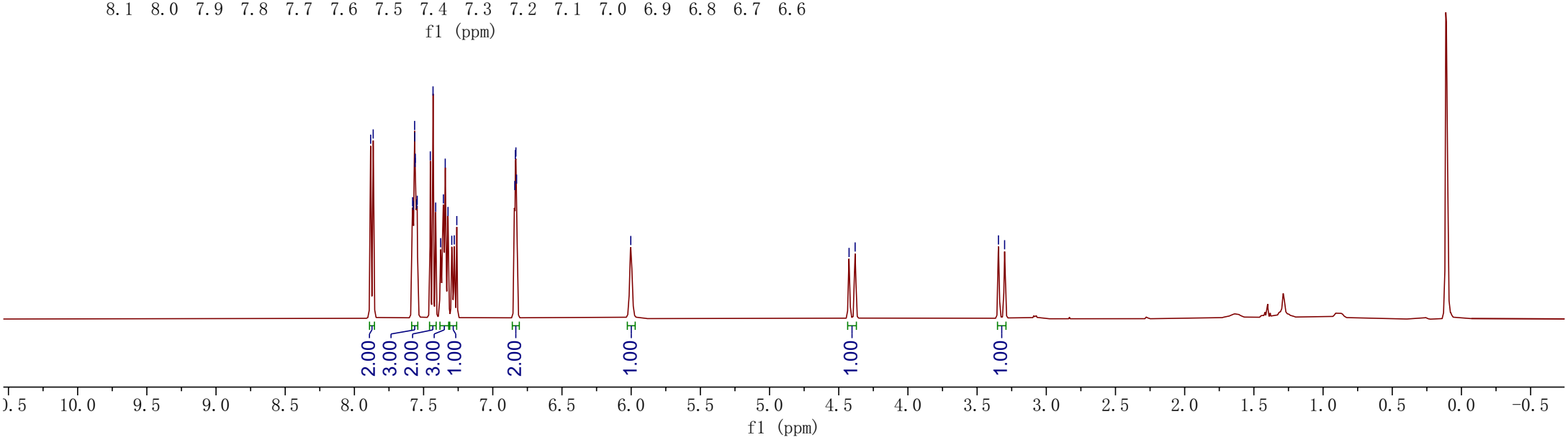

-84.31
-84.32
-84.97
-84.98
-105.43
-105.44
-106.08
-106.10
-106.91
F
F
F
N
H
O
3ua
19F NMR (376 MHz, CDCl3)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

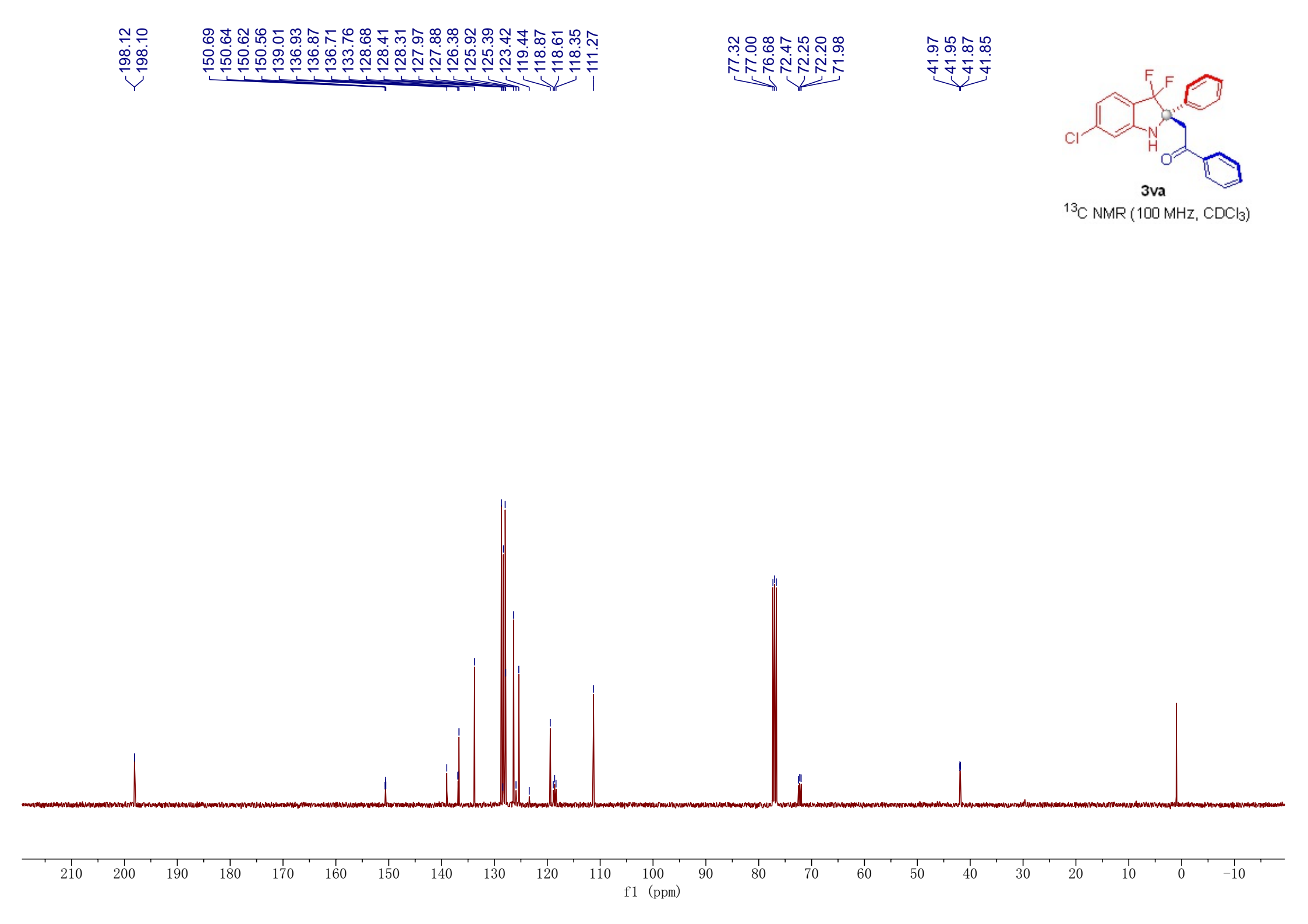


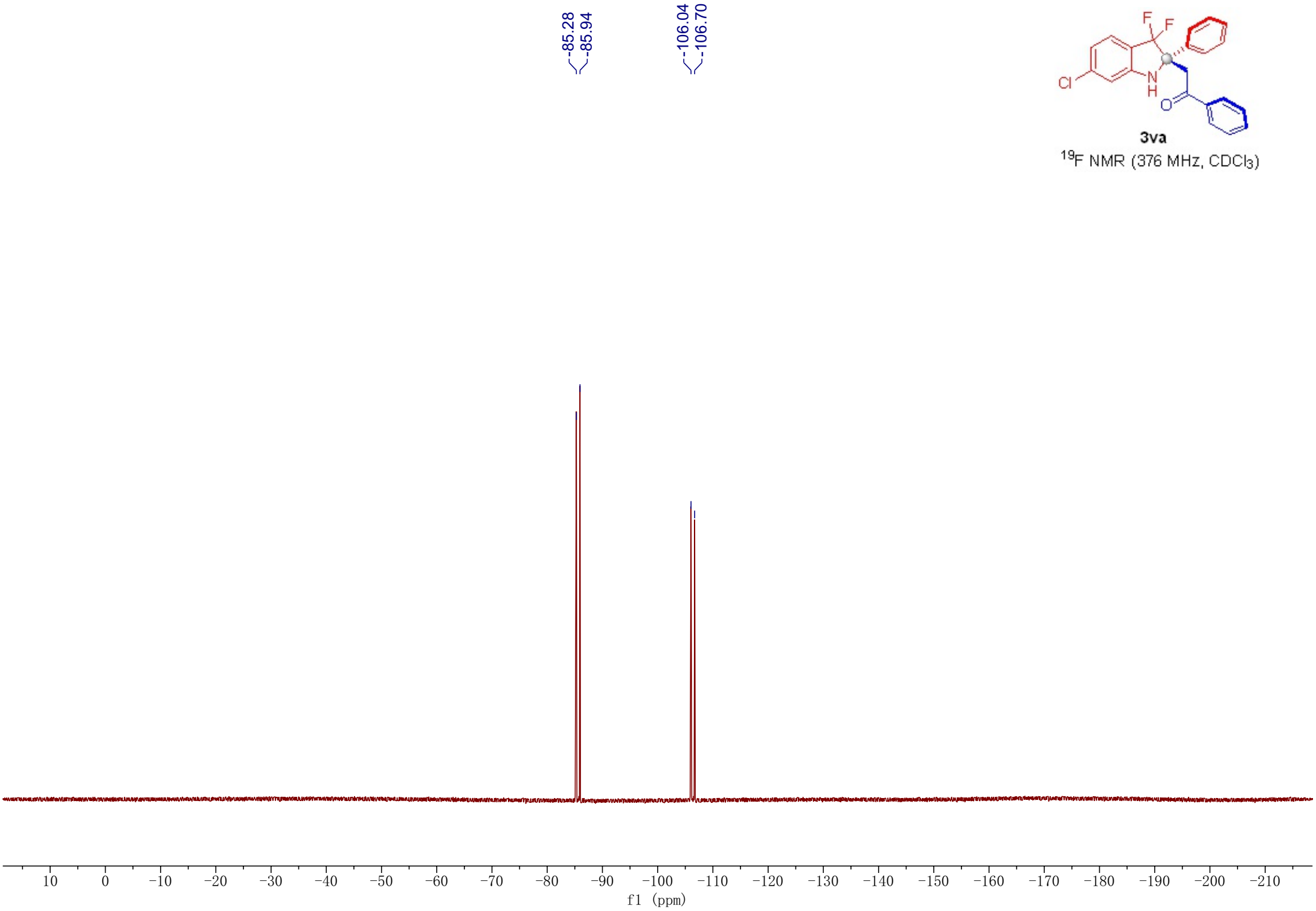


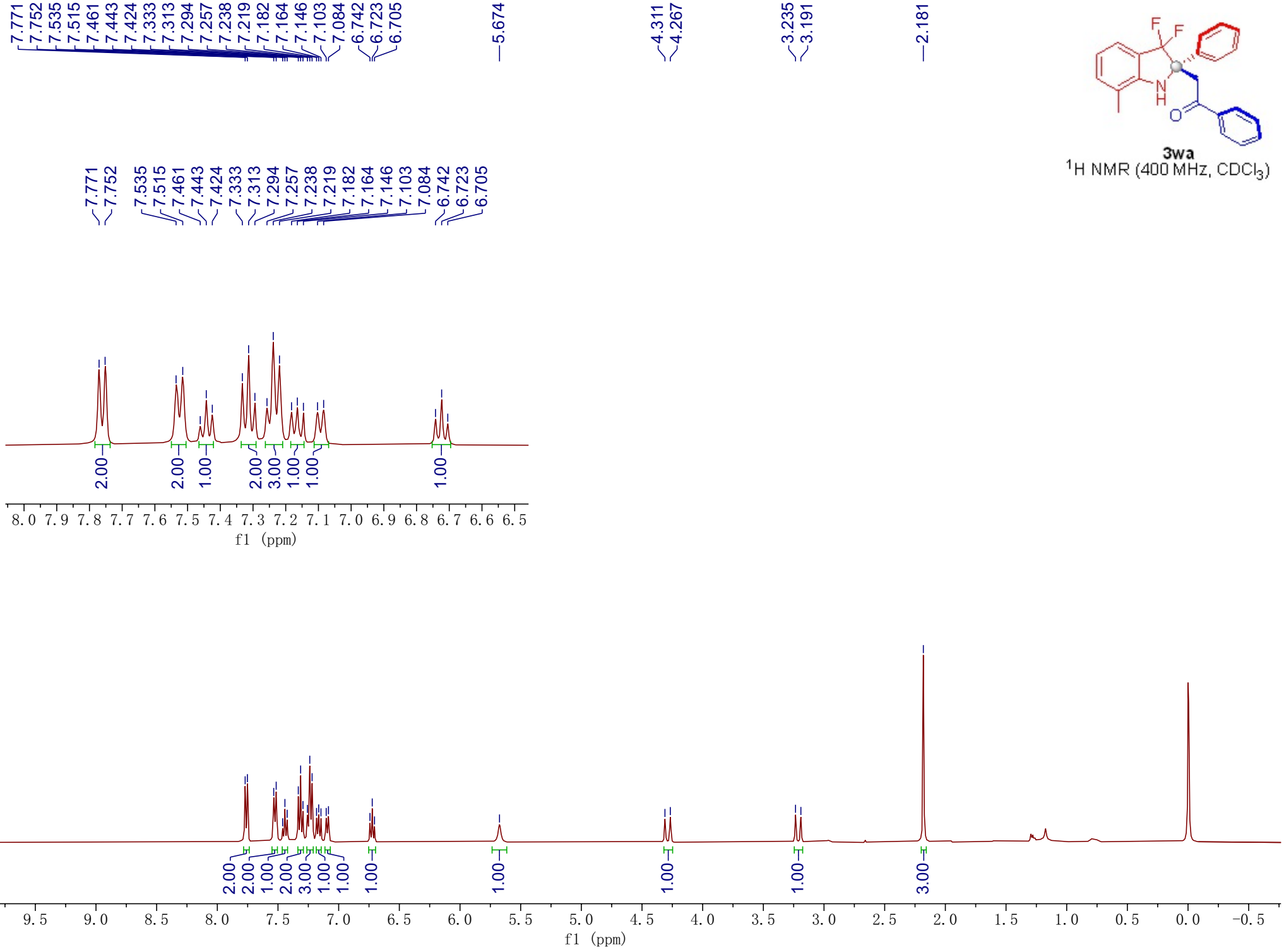
3va

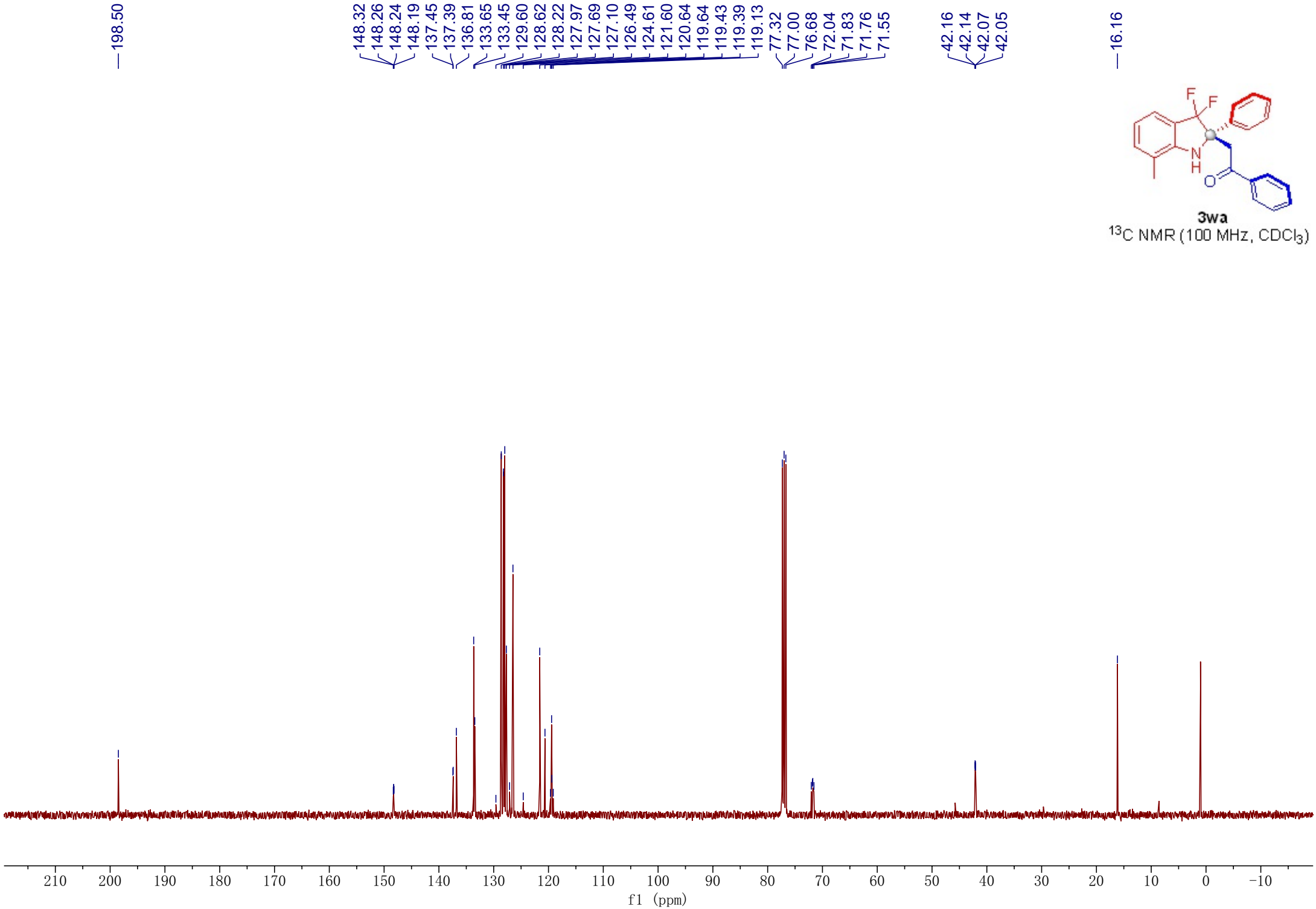
^{1}H NMR (400 MHz, $CDCl_3$)

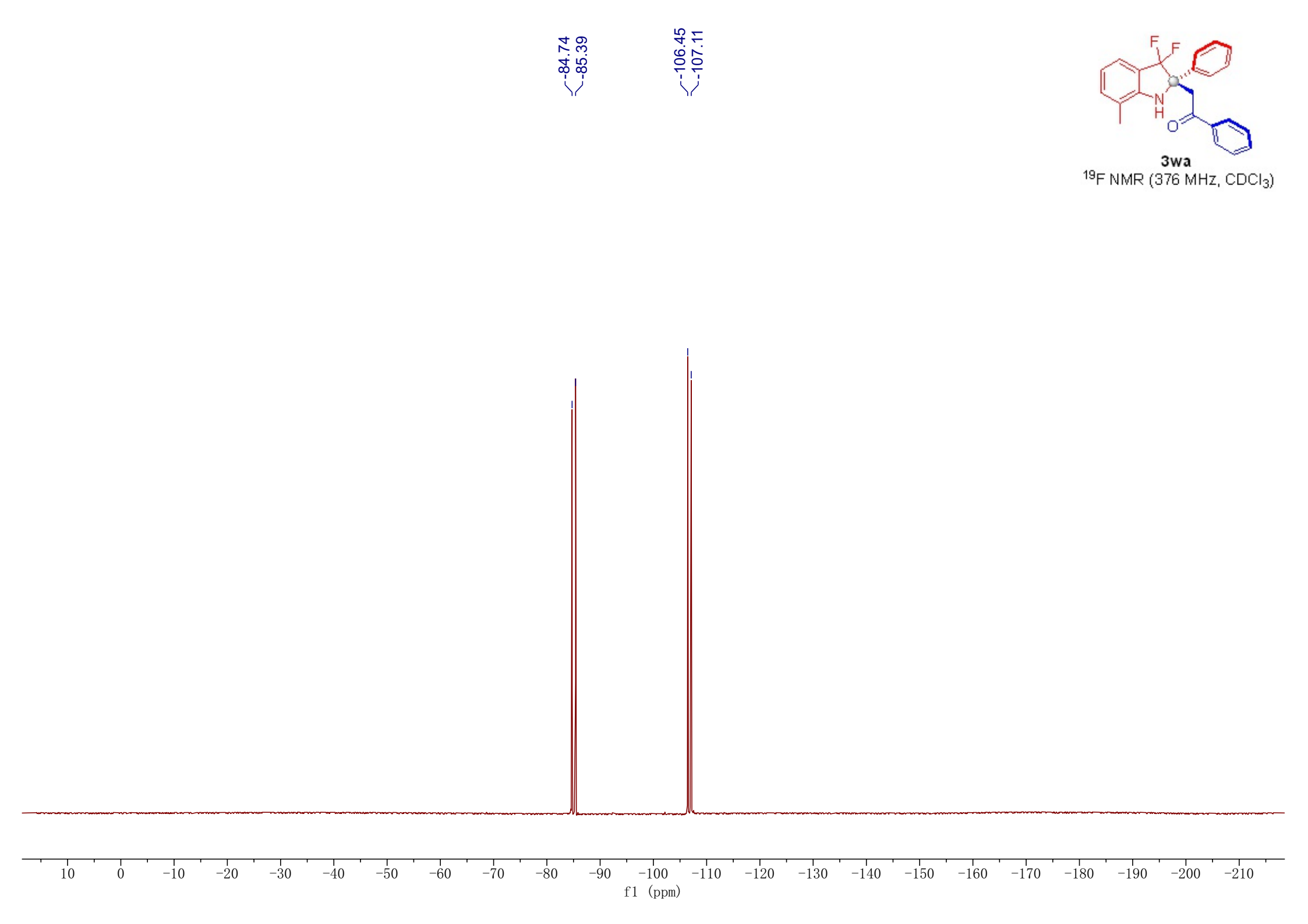


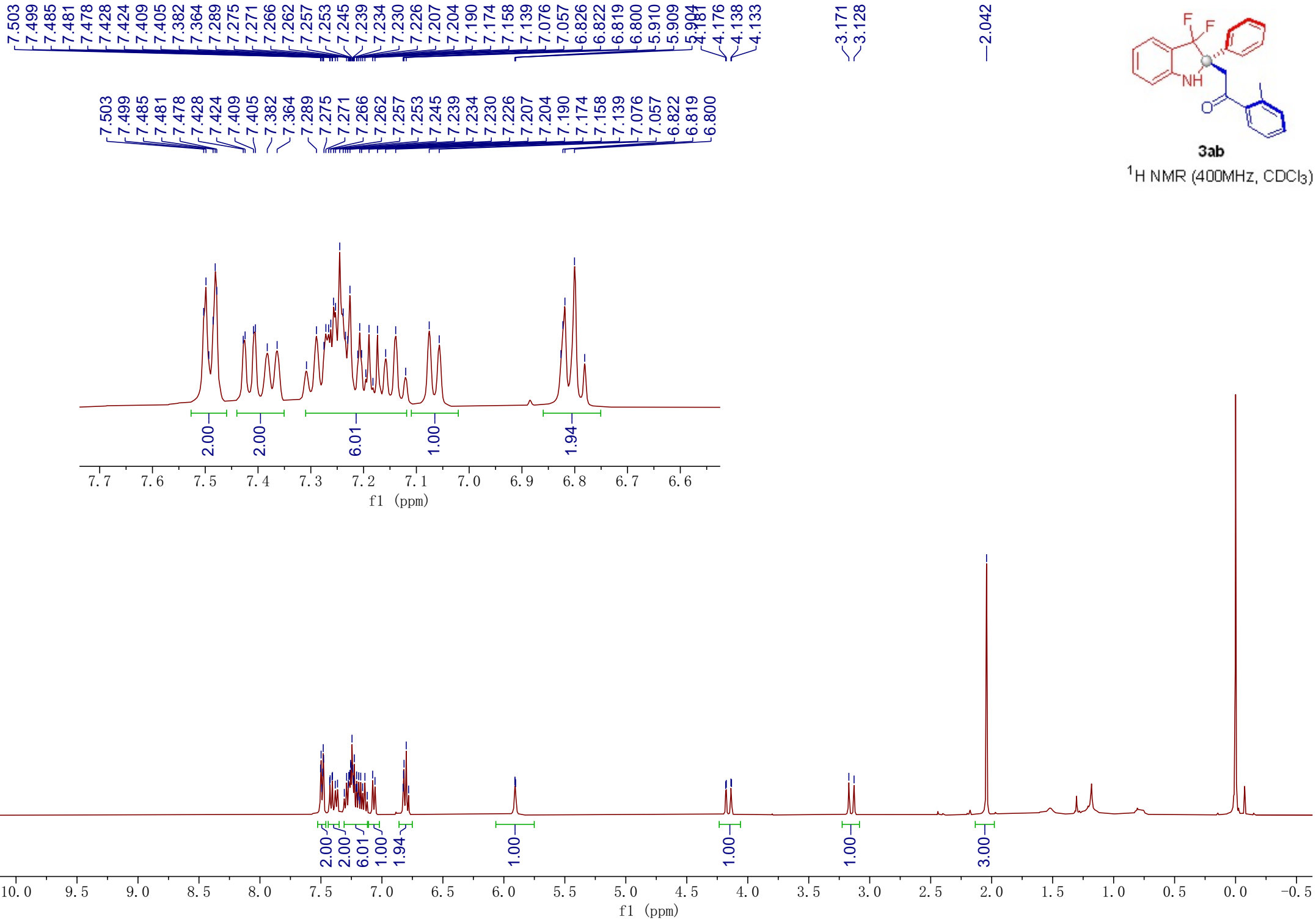

198.12
198.10
150.69
150.64
150.62
150.56
139.01
136.93
136.87
136.71
133.76
128.68
128.41
128.31
127.97
127.88
126.38
125.92
125.39
123.42
119.44
118.87
118.61
118.35
111.27
77.32
77.00
76.68
72.47
72.25
72.20
71.98
41.97
41.95
41.87
41.85
F
F
Cl
N
H
O
3va
13C NMR (100 MHz, CDCl3)
f1 (ppm)

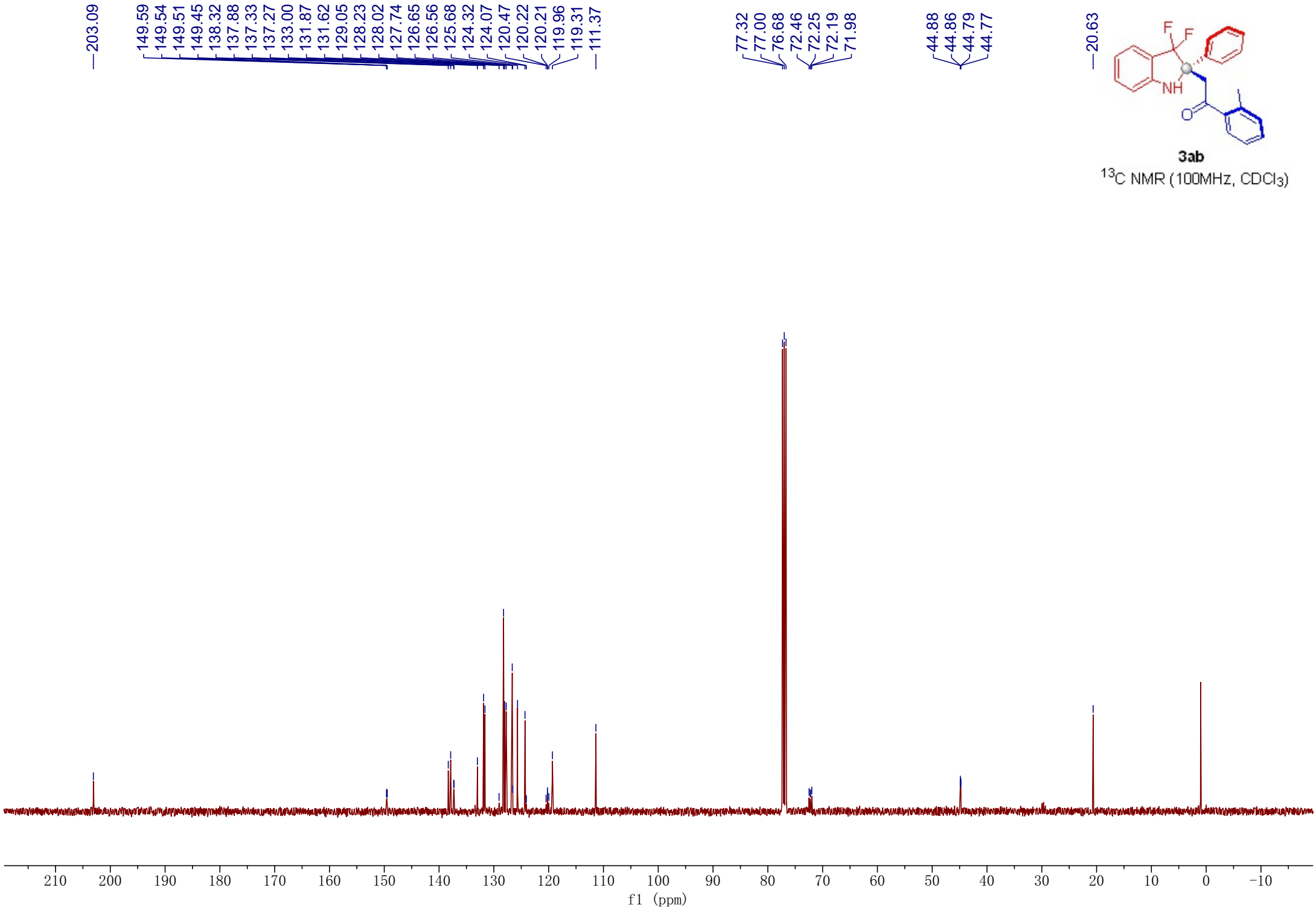

-85.28
-85.94
-106.04
-106.70
F
F
Cl
N
H
O
3va
^{19}F NMR (376 MHz, $CDCl_3$)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

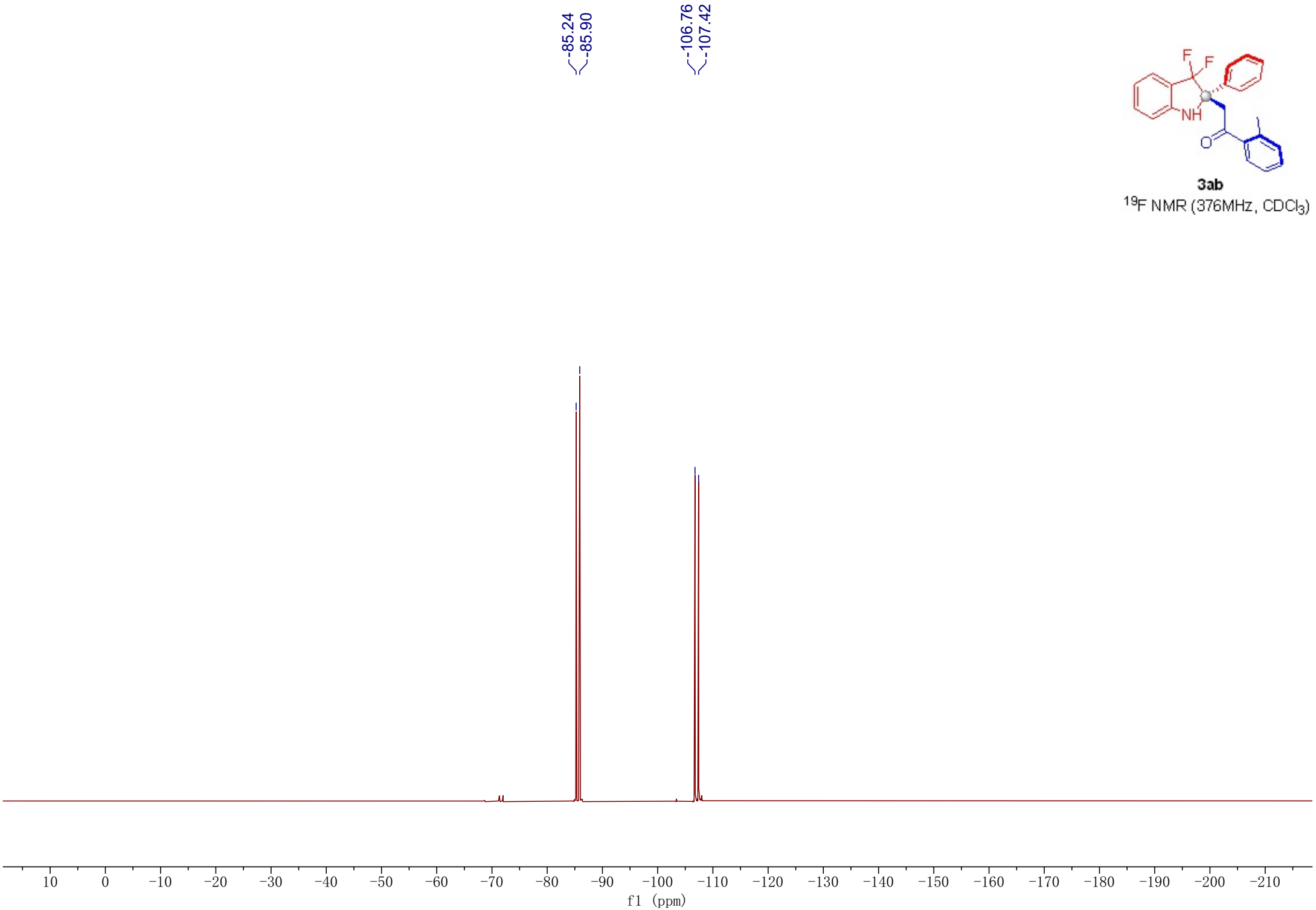

7.771
7.752
7.535
7.515
7.461
7.443
7.424
7.333
7.313
7.294
7.257
7.238
7.219
7.182
7.164
7.146
7.103
7.084
6.742
6.723
6.705
5.674
4.311
4.267
3.235
3.191
2.181
F
F
N
H
O
3wa
1H NMR (400 MHz, CDCl3)
2.00
2.00
1.00
2.00
3.00
1.00
1.00
1.00
8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7 6.6 6.5
f1 (ppm)
2.00
2.00
1.00
2.00
3.00
1.00
1.00
1.00
1.00
1.00
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5
f1 (ppm)


198.50
148.32
148.26
148.24
148.19
137.45
137.39
136.81
133.65
133.45
129.60
128.62
128.22
127.97
127.69
127.10
126.49
124.61
121.60
120.64
119.64
119.43
119.39
119.13
77.32
77.00
76.68
72.04
71.83
71.76
71.55
42.16
42.14
42.07
42.05
16.16
F
F
N
H
O
3wa
13C NMR (100 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


-84.74
-85.39
-106.45
-107.11
F
F
N
H
O
3wa
19F NMR (376 MHz, CDCl3)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

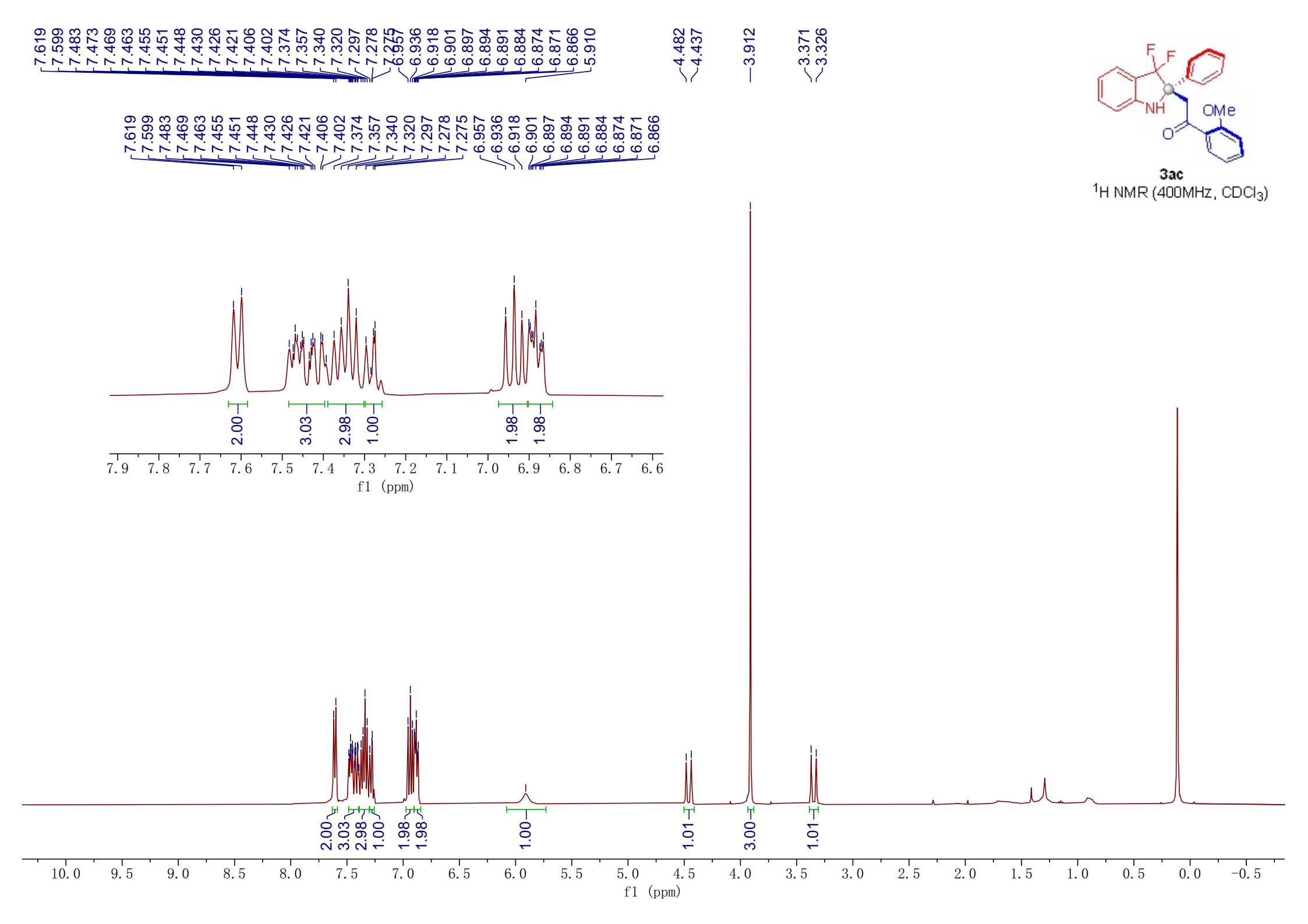

7.503 7.499 7.485 7.481 7.478 7.428 7.424 7.409 7.405 7.382 7.364 7.289 7.275 7.271 7.266 7.262 7.257 7.253 7.245 7.239 7.234 7.230 7.226 7.207 7.204 7.190 7.174 7.158 7.139 7.076 7.057 6.826 6.822 6.819 6.800 5.910 5.909 5.904 4.181 4.176 4.138 4.133
3.171 3.128
2.042
F F NH O
3ab
1H NMR (400MHz, CDCl3)
2.00 2.00 6.01 1.00 1.94
7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7 6.6
f1 (ppm)
2.00 2.00 6.01 1.00 1.94 1.00 1.00 1.00 3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

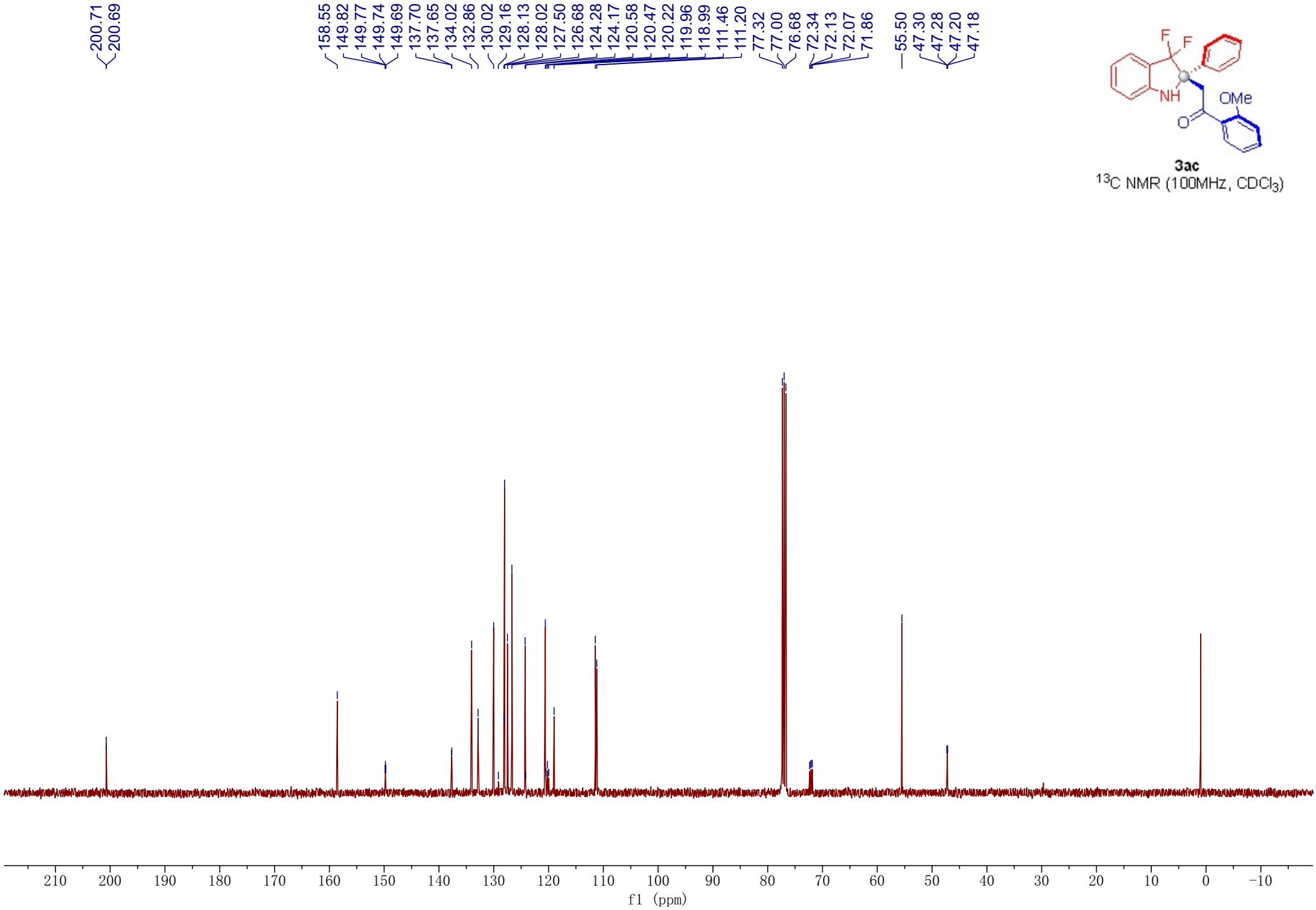

203.09
149.59
149.54
149.51
149.45
138.32
137.88
137.33
137.27
133.00
131.87
131.62
129.05
128.23
128.02
127.74
126.65
126.56
125.68
124.32
124.07
120.47
120.22
120.21
119.96
119.31
111.37
77.32
77.00
76.68
72.46
72.25
72.19
71.98
44.88
44.86
44.79
44.77
20.63
F
F
NH
O
3ab
13C NMR (100MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

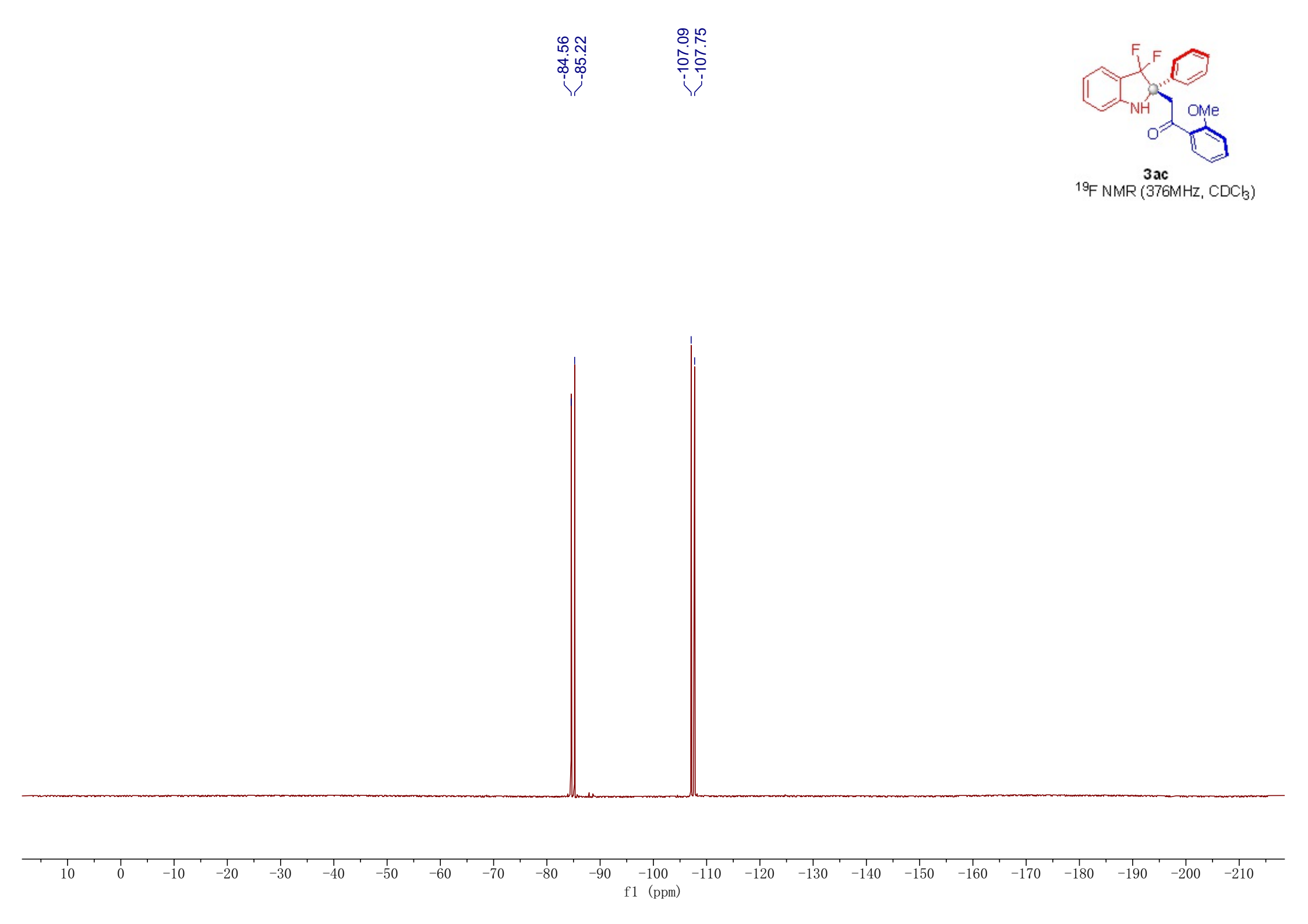


3ab

^{19}F NMR (376MHz, $CDCl_3$)

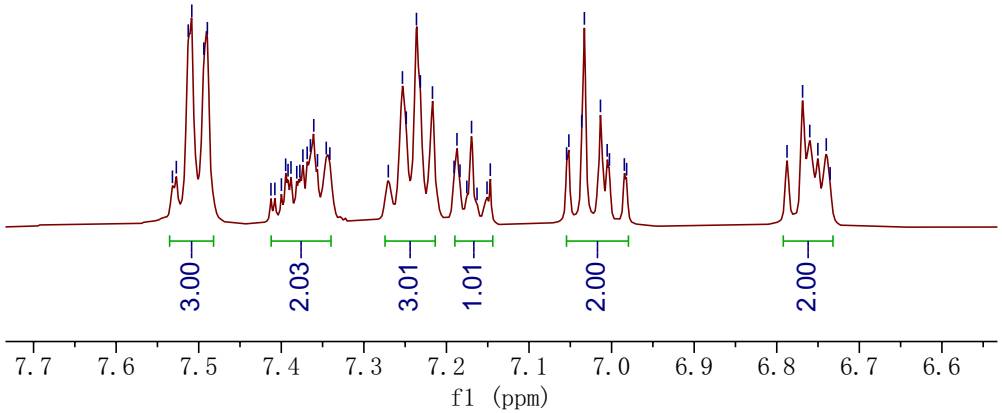

7.619
7.599
7.483
7.473
7.469
7.463
7.455
7.451
7.448
7.430
7.426
7.421
7.406
7.402
7.374
7.357
7.340
7.320
7.297
7.278
7.275
6.957
6.936
6.918
6.901
6.897
6.894
6.891
6.884
6.874
6.871
6.866
5.910
4.482
4.437
3.912
3.371
3.326
F
F
NH
OMe
O
3ac
1H NMR (400MHz, CDCl3)
2.00
3.03
2.98
1.00
1.98
1.98
f1 (ppm)
1.01
3.00
1.01

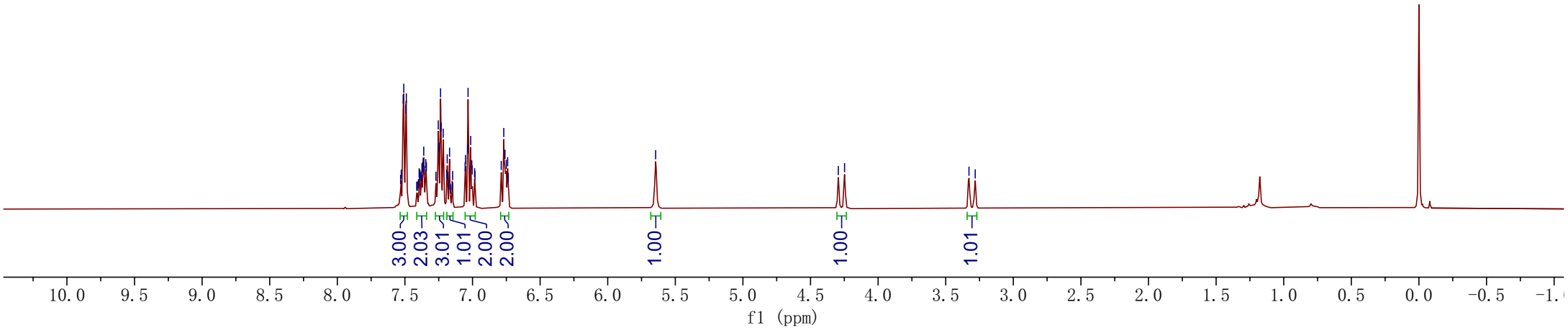

200.71
200.69
158.55
149.82
149.77
149.74
149.69
137.70
137.65
134.02
132.86
130.02
129.16
128.13
128.02
127.50
126.68
124.28
124.17
120.58
120.47
120.22
119.96
118.99
111.46
111.20
77.32
77.00
76.68
72.34
72.13
72.07
71.86
55.50
47.30
47.28
47.20
47.18
F
F
NH
OMe
O
3ac
13C NMR (100MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


-84.56
-85.22
-107.09
-107.75
F
F
NH
OMe
O
3ac
19F NMR (376MHz, CDCl3)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

3ad

^{1}H NMR (400MHz, $CDCl_3$)

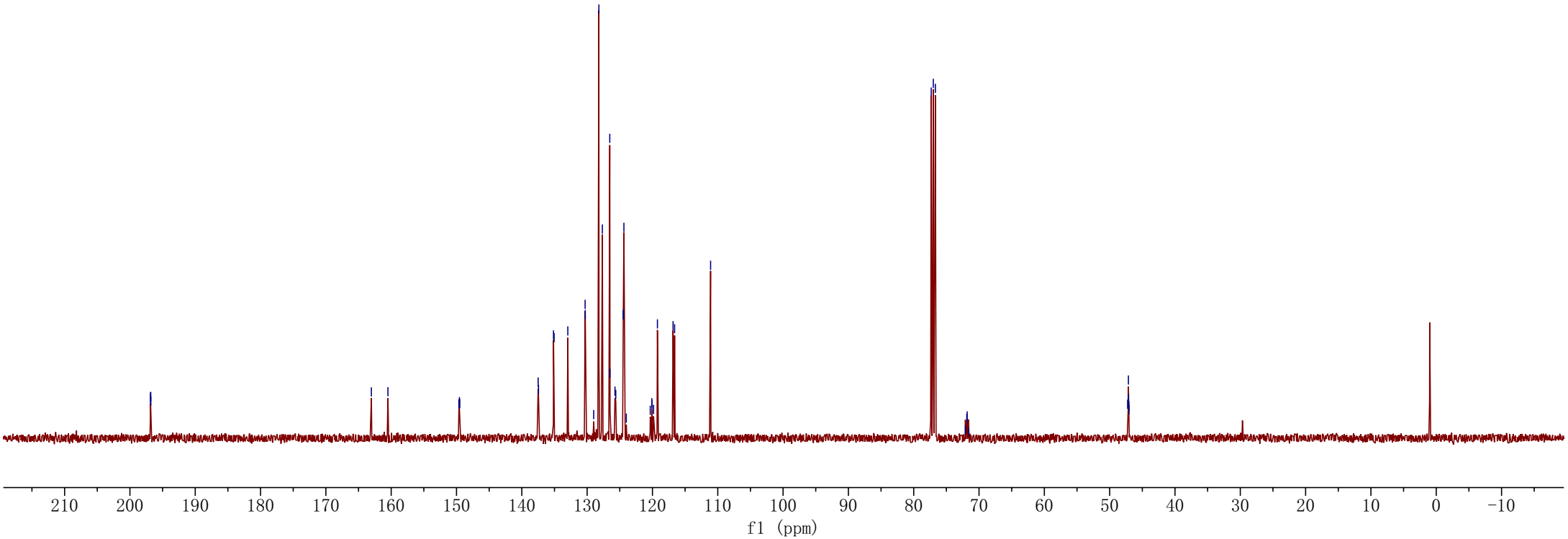


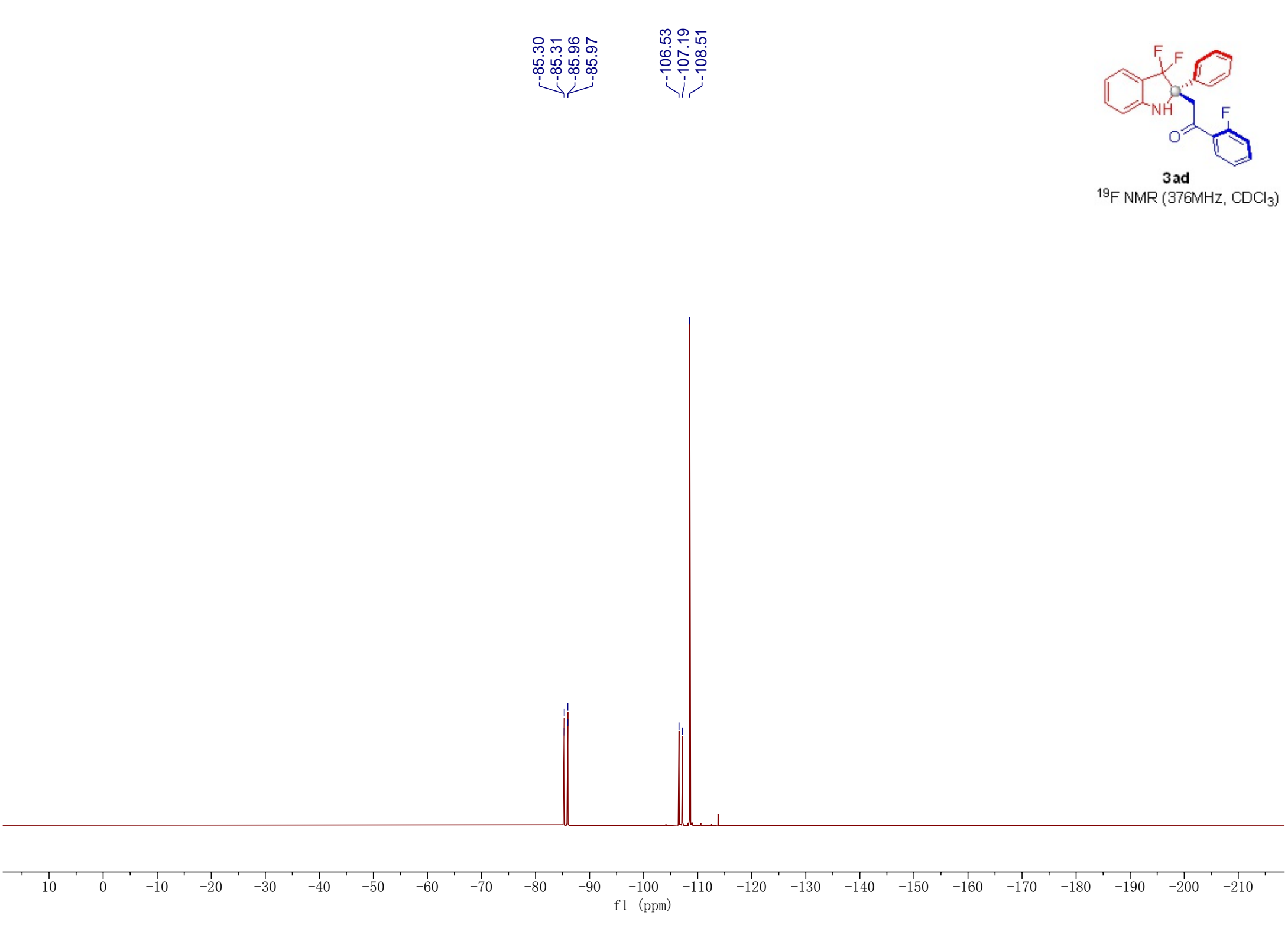


196.85
196.84
196.82
196.80
163.03
160.50
149.64
149.58
149.56
149.50
137.50
137.44
135.15
135.06
132.96
130.31
130.28
128.99
128.20
127.67
126.53
126.51
125.74
125.62
124.47
124.44
124.37
124.00
120.34
120.09
120.08
119.83
119.24
116.84
116.61
111.10
77.32
77.00
76.68
72.09
71.88
71.81
71.60
47.23
47.21
47.15
47.13
47.11
47.05
47.03

3ad

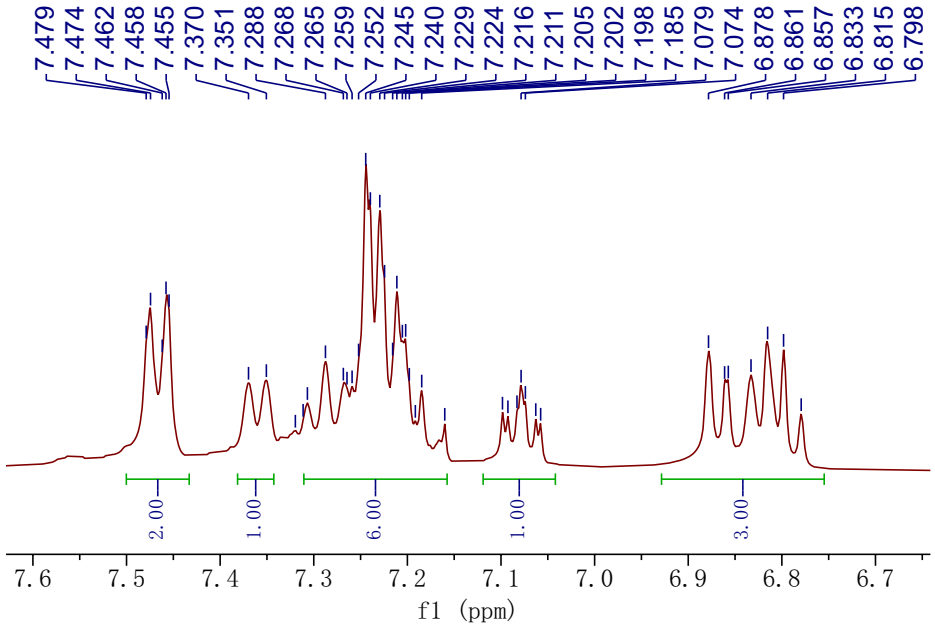
^{13}C NMR (100MHz, $CDCl_3$)

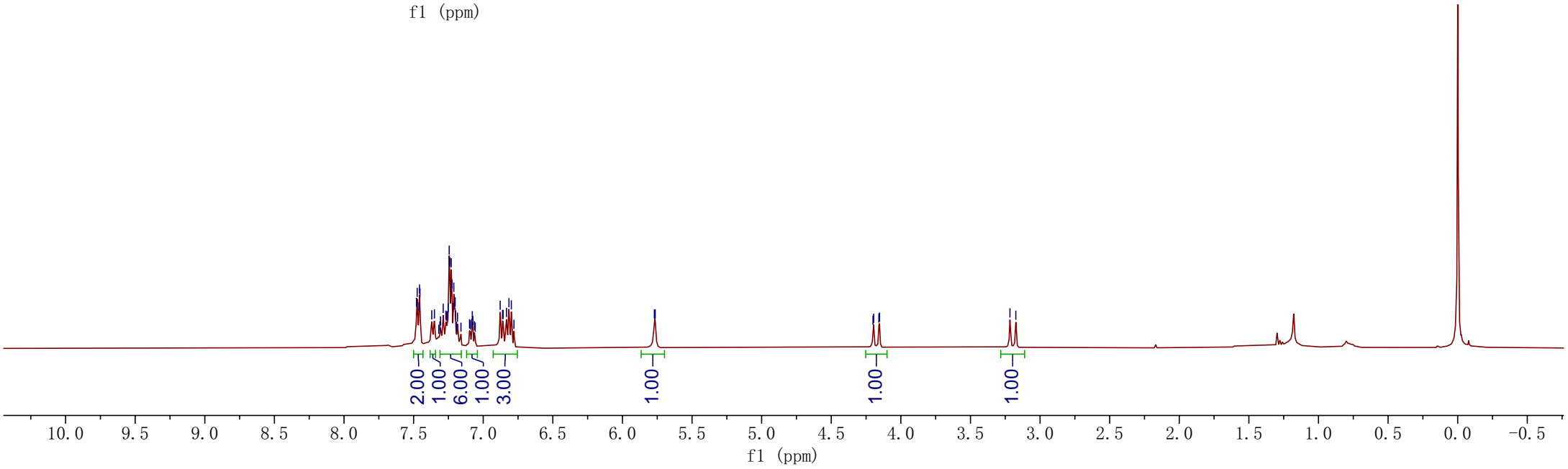


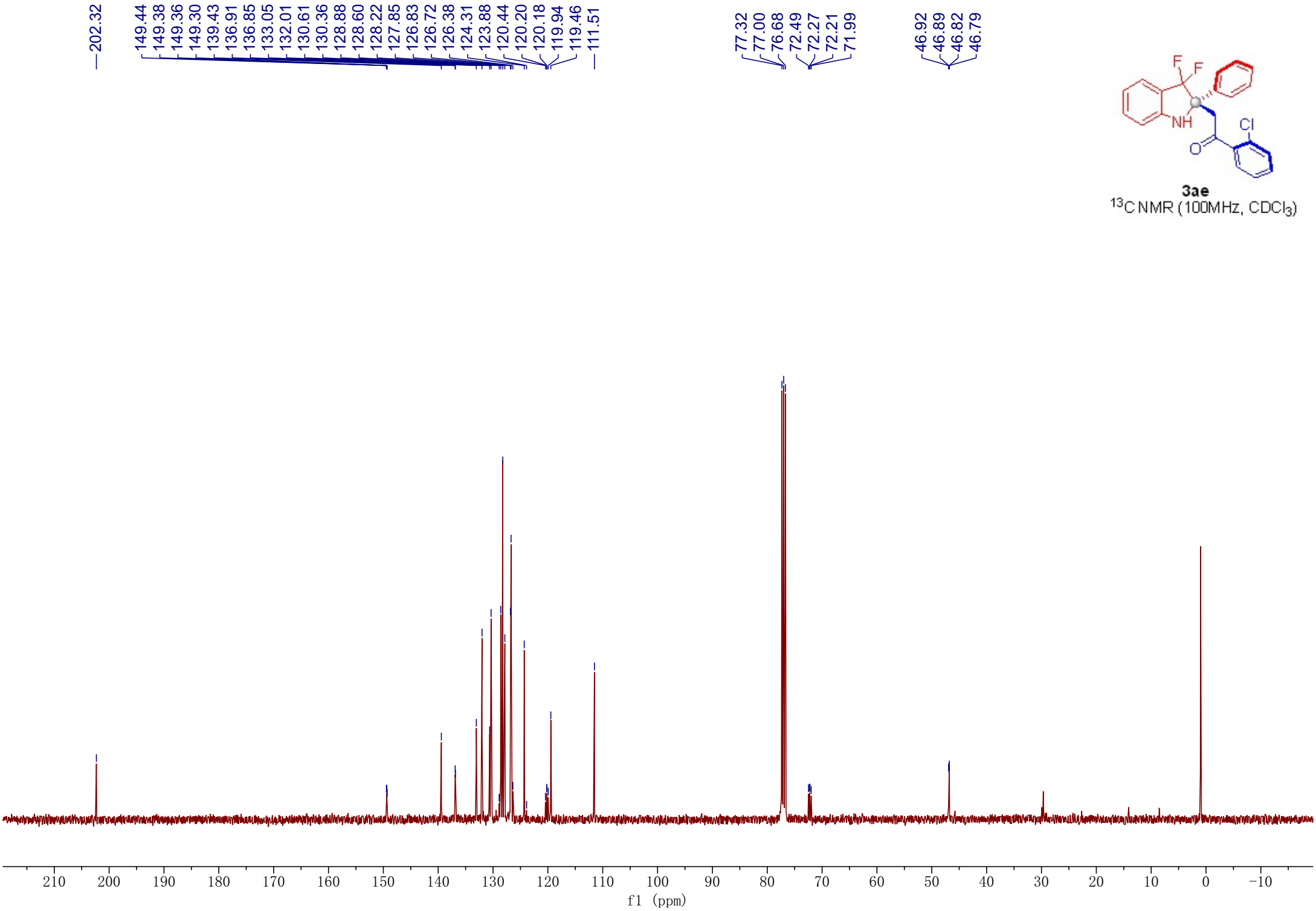

-85.30
-85.31
-85.96
-85.97
-106.53
-107.19
-108.51
F
F
NH
O
F
3ad
19F NMR (376MHz, CDCl3)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

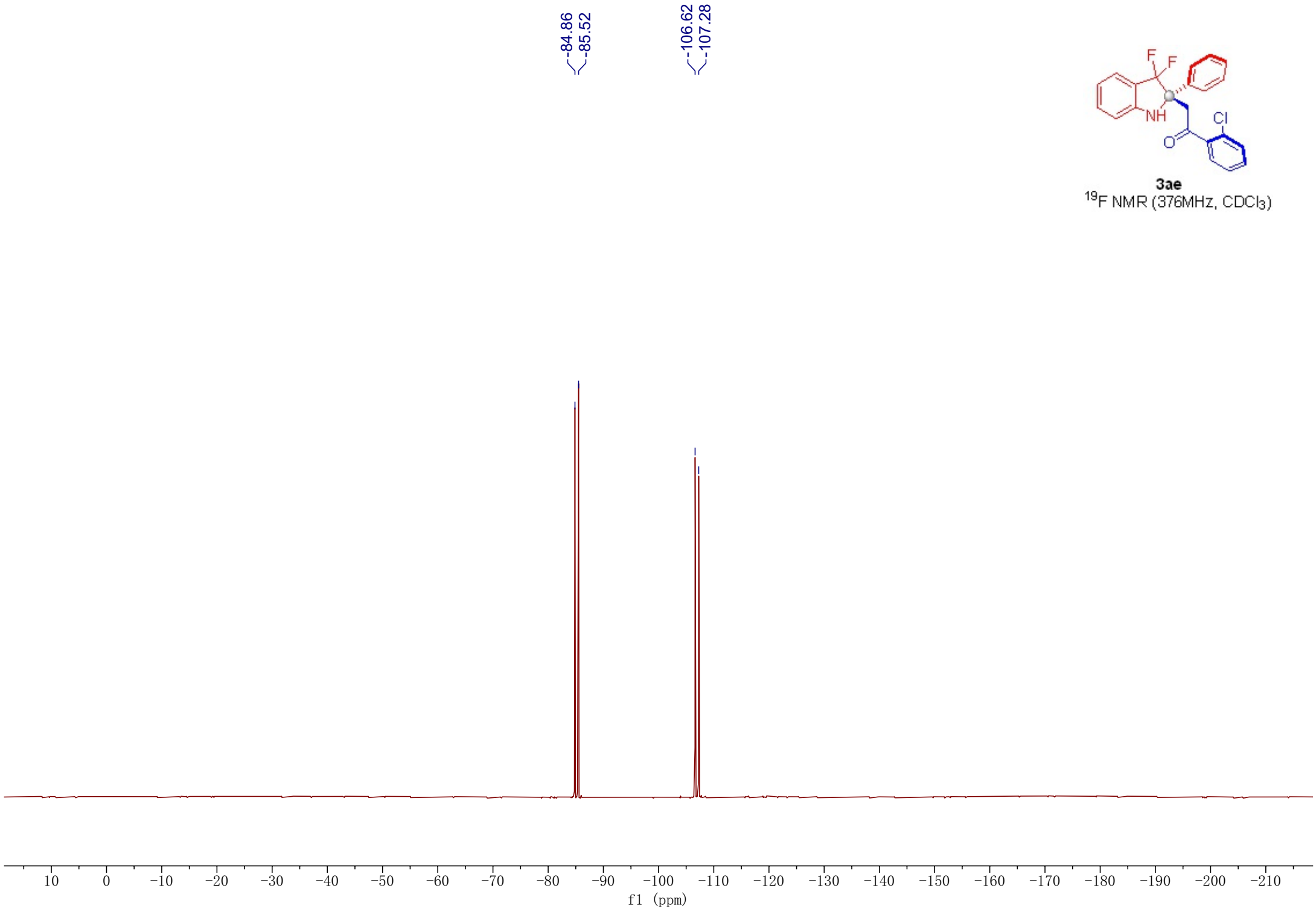
3ae

^{1}H NMR (400MHz, $CDCl_3$)



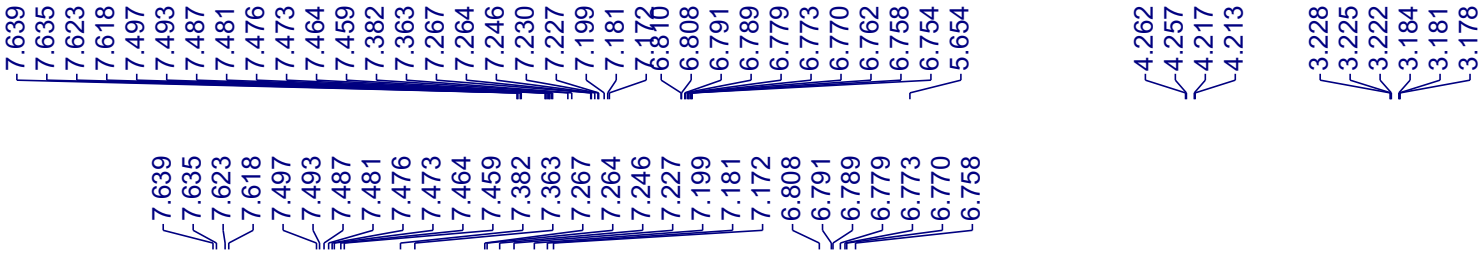



202.32
149.44
149.38
149.36
149.30
149.43
136.91
136.85
133.05
132.01
130.61
130.36
128.88
128.60
128.22
127.85
126.83
126.72
126.38
124.31
123.88
120.44
120.20
120.18
119.94
119.46
111.51
77.32
77.00
76.68
72.49
72.27
72.21
71.99
46.92
46.89
46.82
46.79
F
F
NH
Cl
O
3ae
13C NMR (100MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



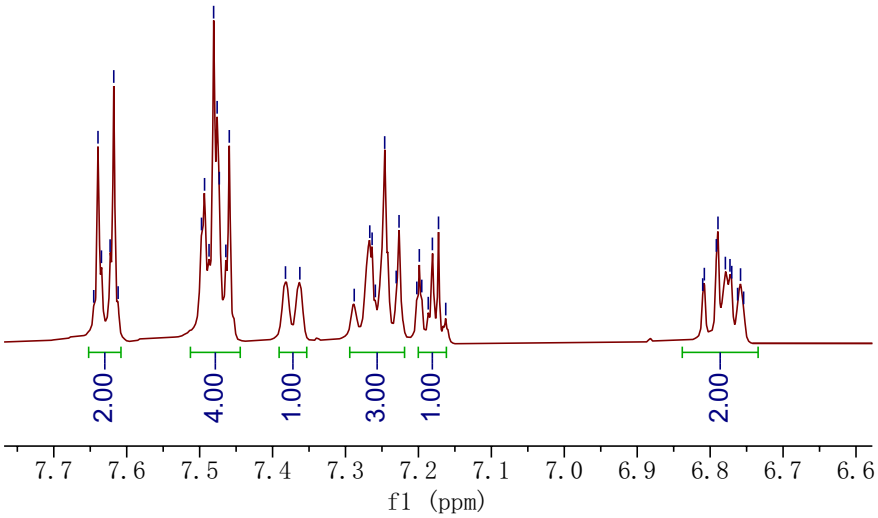
3ae

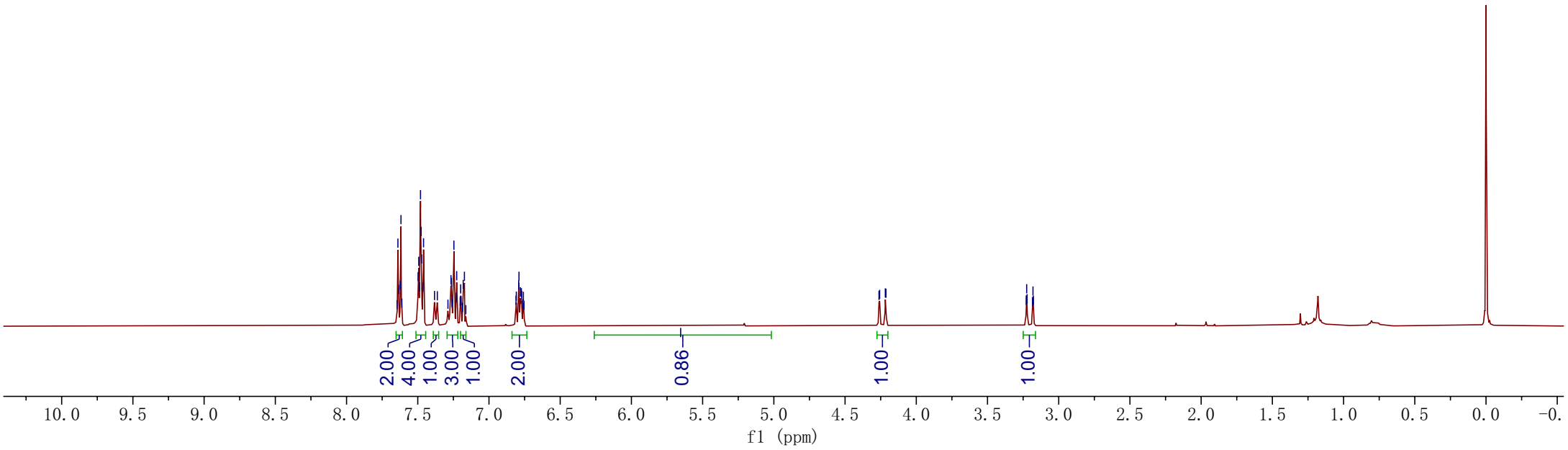
^{19}F NMR (376MHz, $CDCl_3$)

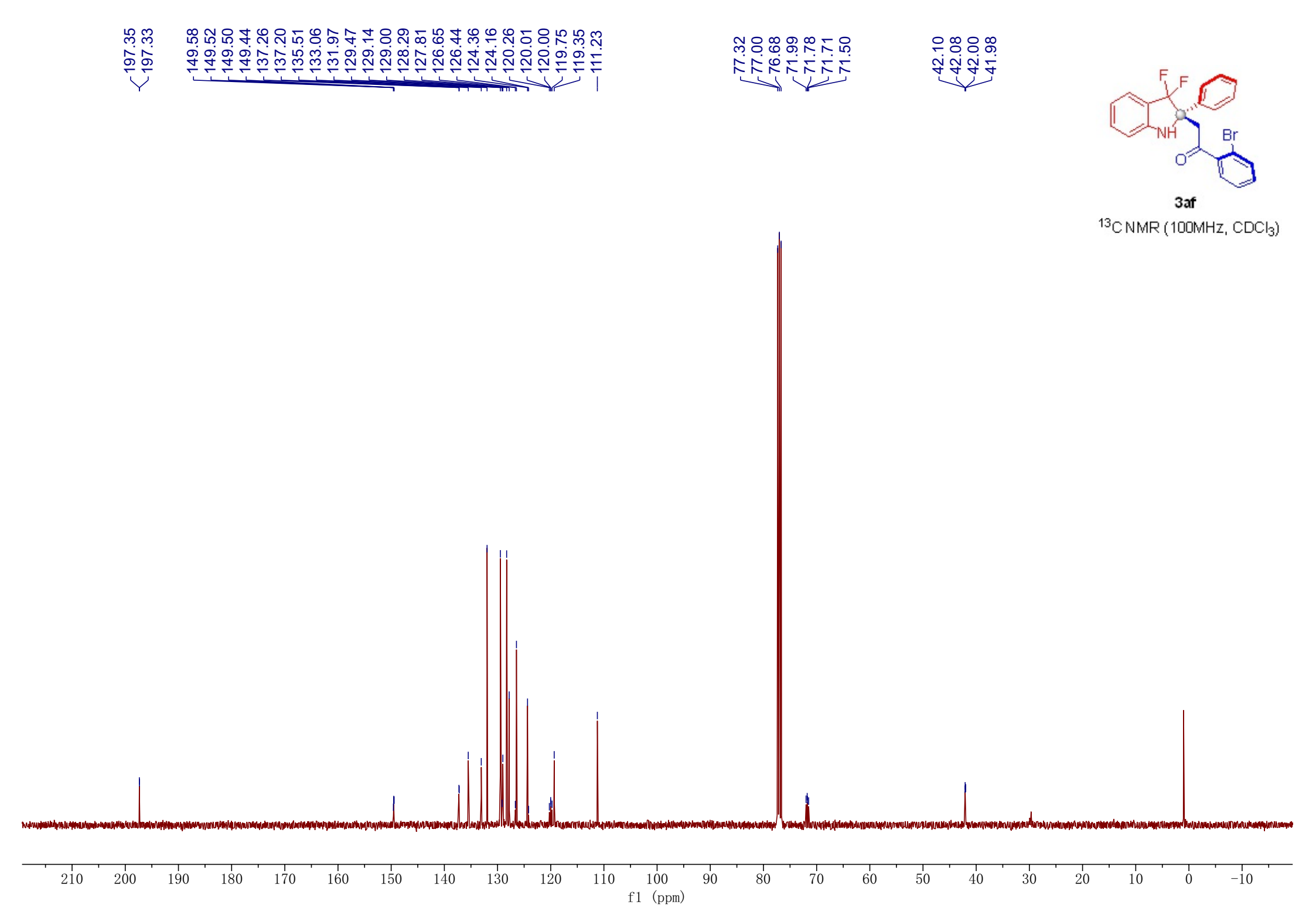


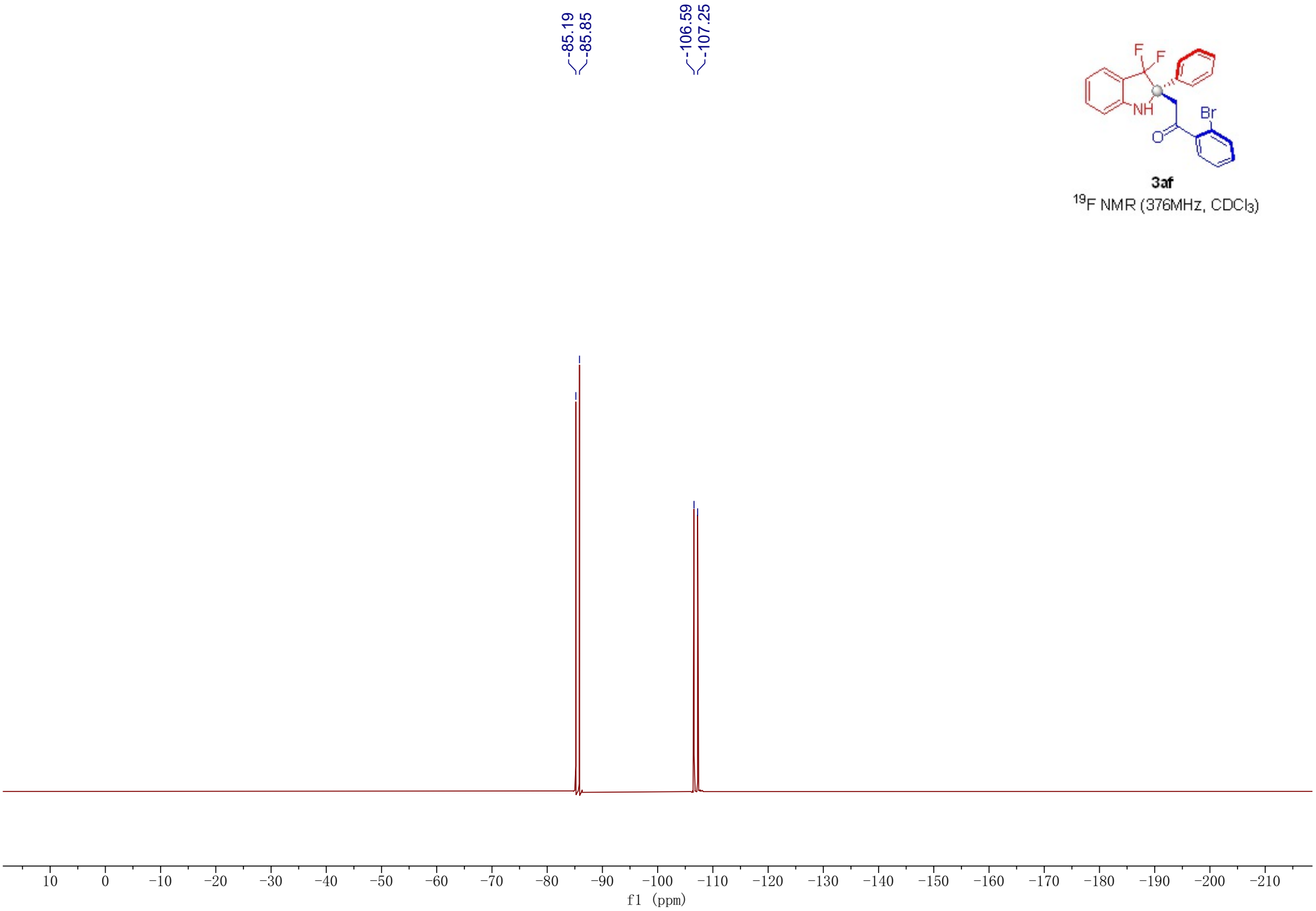
3af

^{1}H NMR (400MHz, $CDCl_3$)






197.35
197.33
149.58
149.52
149.50
149.44
137.26
137.20
135.51
133.06
131.97
129.47
129.14
129.00
128.29
127.81
126.65
126.44
124.36
124.16
120.26
120.01
120.00
119.75
119.35
111.23
77.32
77.00
76.68
71.99
71.78
71.71
71.50
42.10
42.08
42.00
41.98
F
F
NH
Br
O
3af
13C NMR (100MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

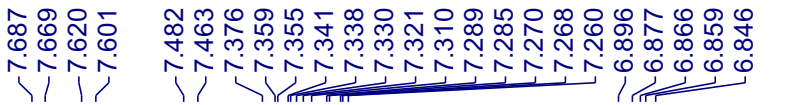


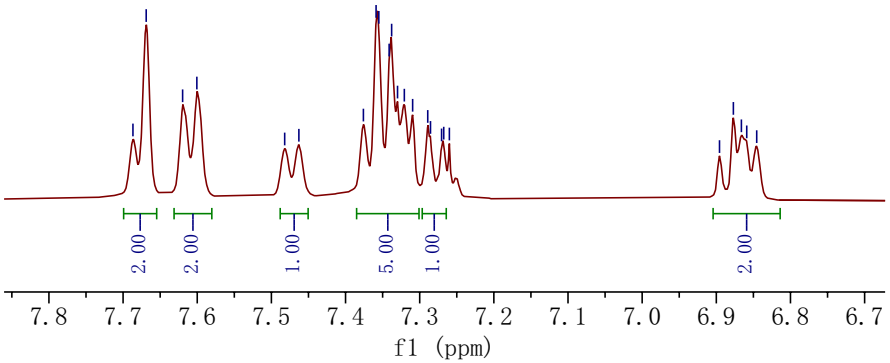
3af

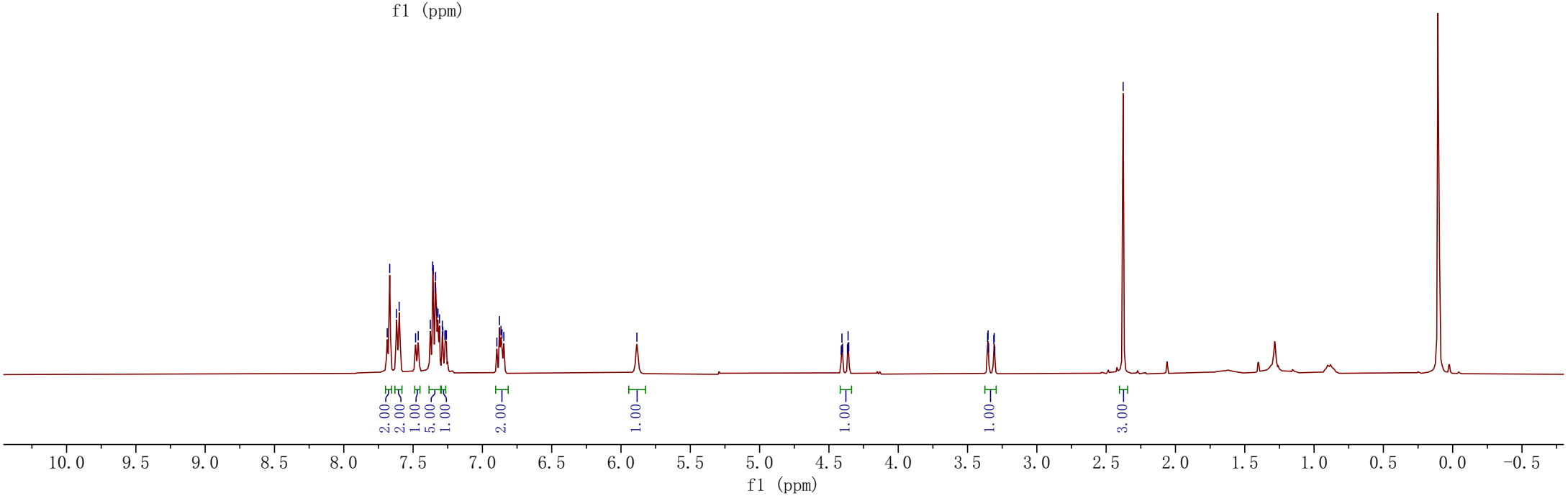
^{19}F NMR (376MHz, $CDCl_3$)

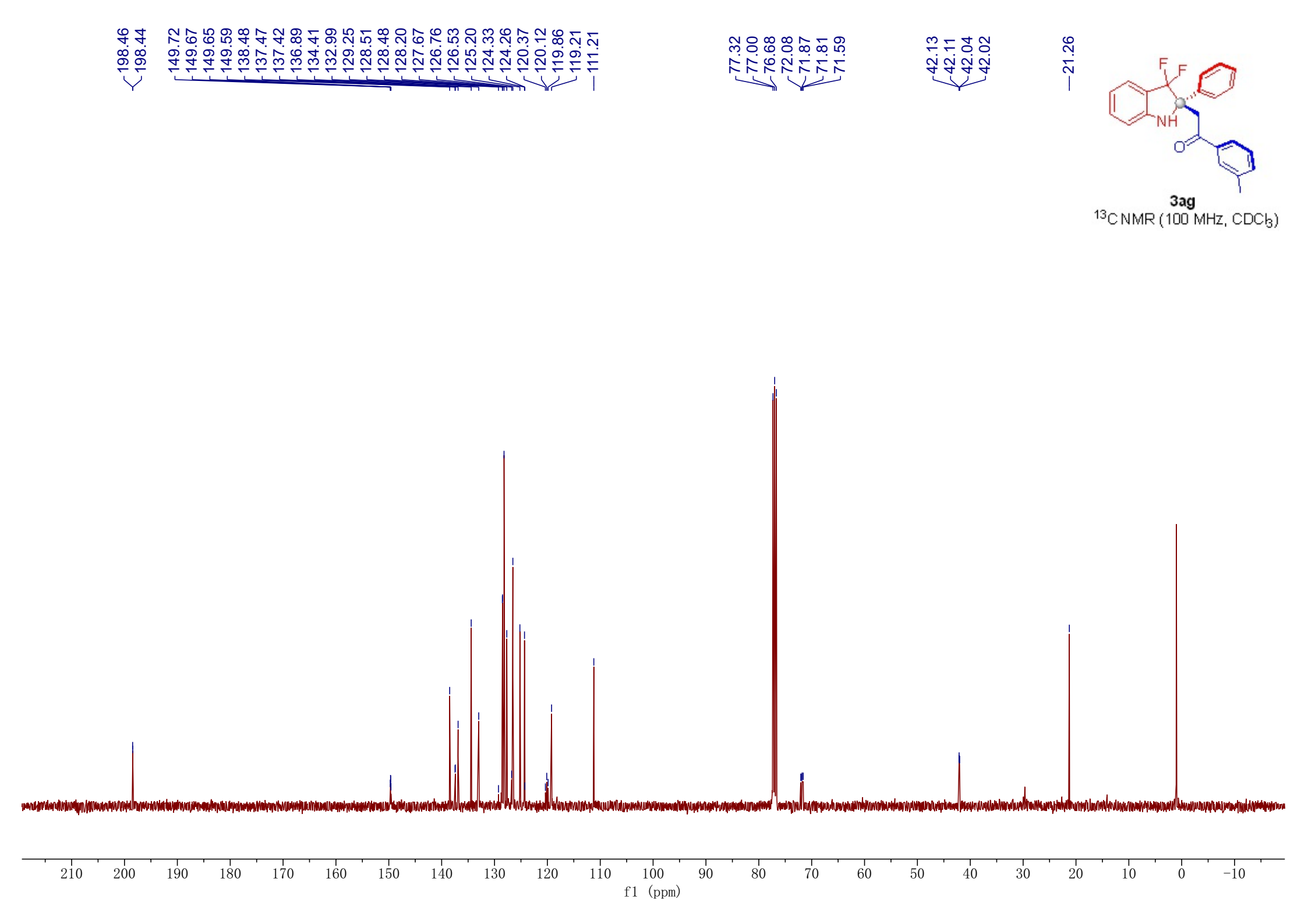
3ag

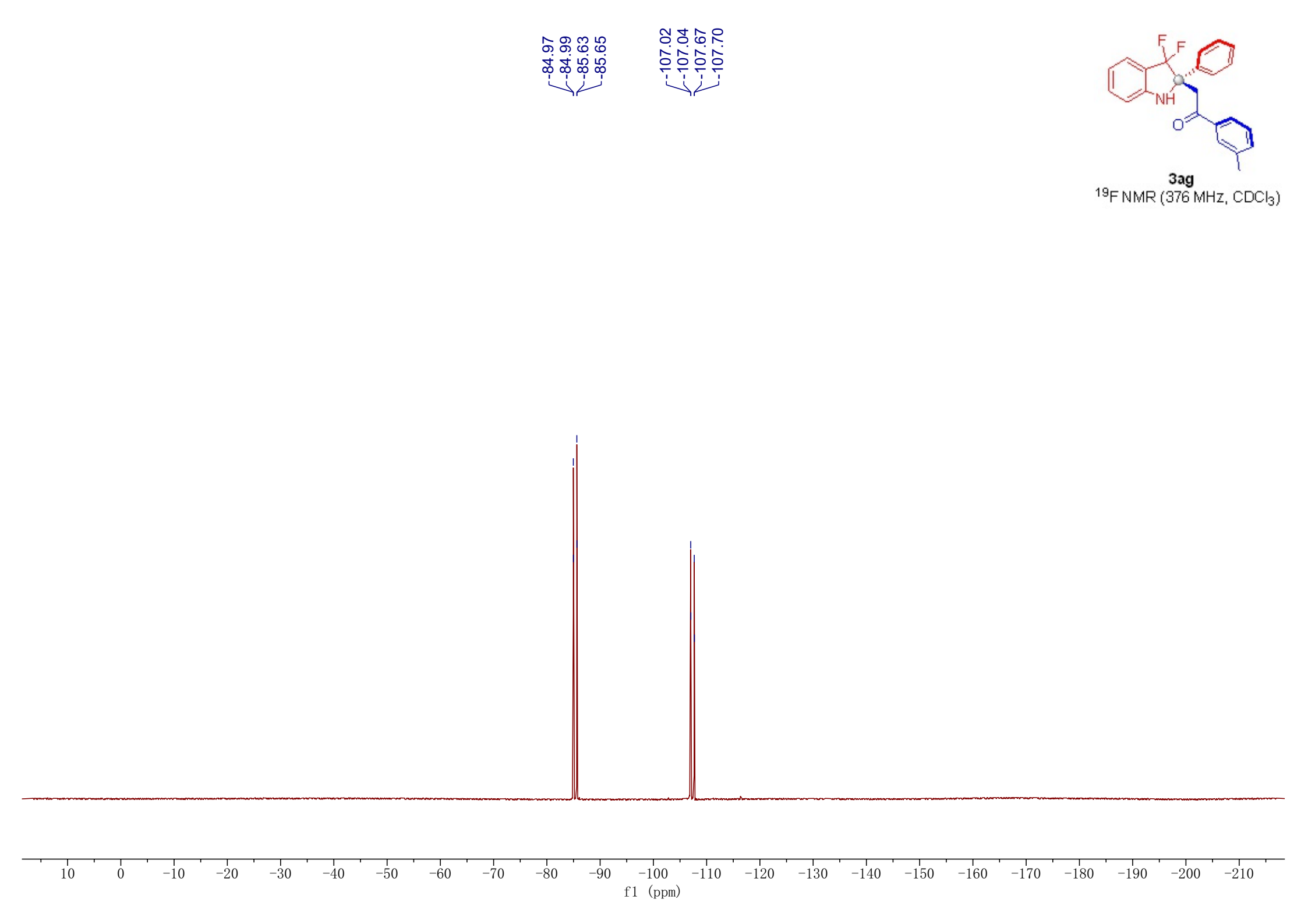
^{1}H NMR (400 MHz, $CDCl_3$)

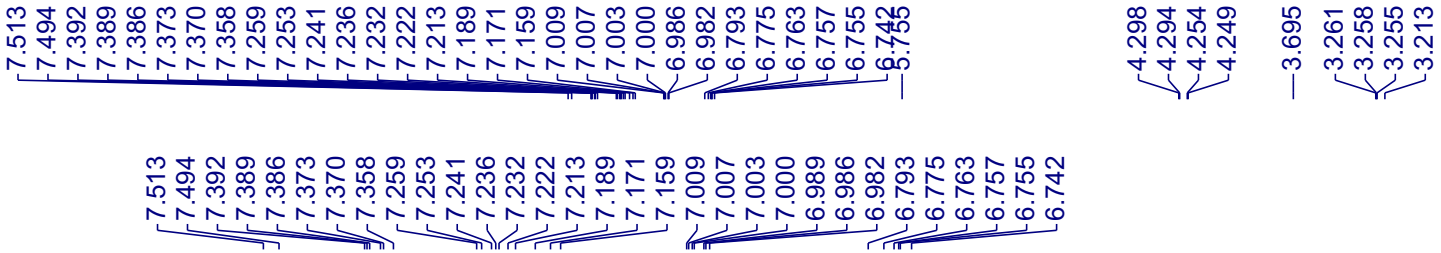


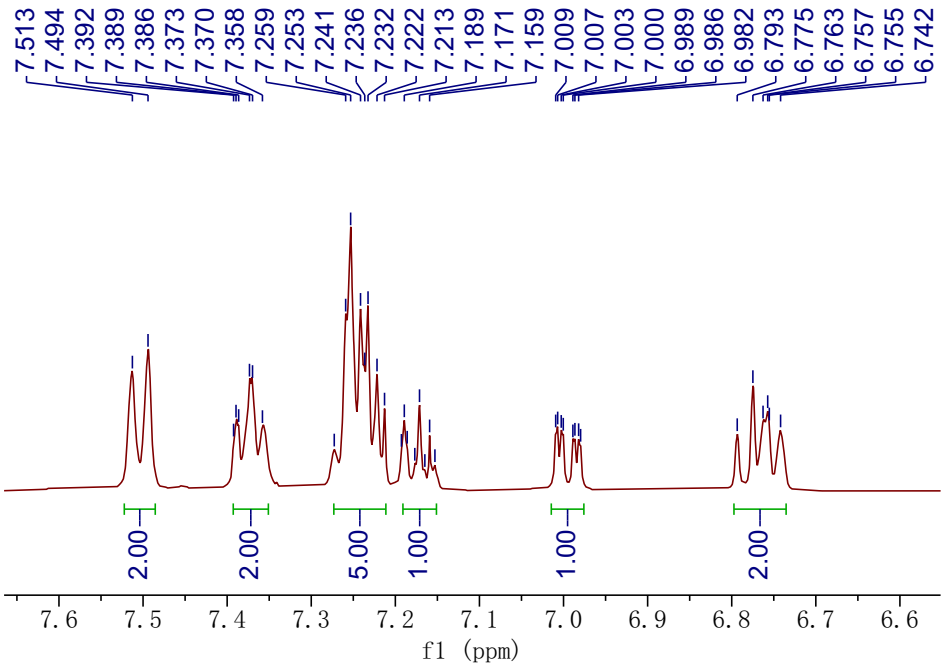





198.46
198.44
149.72
149.67
149.65
149.59
138.48
137.47
137.42
136.89
134.41
132.99
129.25
128.51
128.48
128.20
127.67
126.76
126.53
125.20
124.33
124.26
120.37
120.12
119.86
119.21
111.21
77.32
77.00
76.68
72.08
71.87
71.81
71.59
42.13
42.11
42.04
42.02
21.26
F
F
NH
O
3ag
13C NMR (100 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

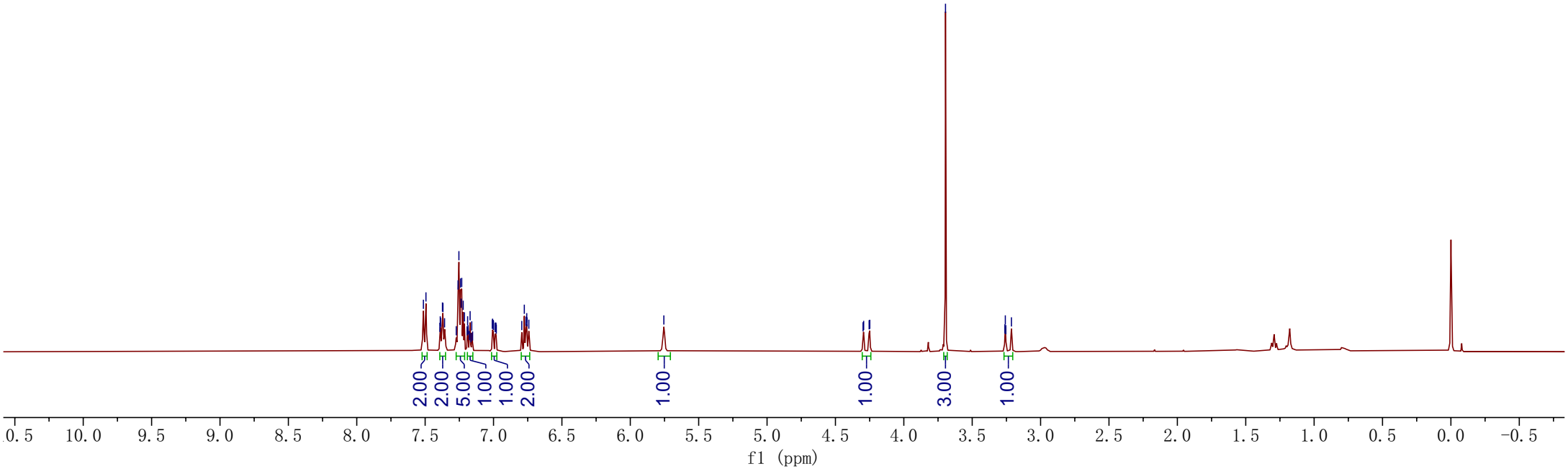

-84.97
-84.99
-85.63
-85.65
-107.02
-107.04
-107.67
-107.70
F
F
NH
O
3ag
19F NMR (376 MHz, CDCl3)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

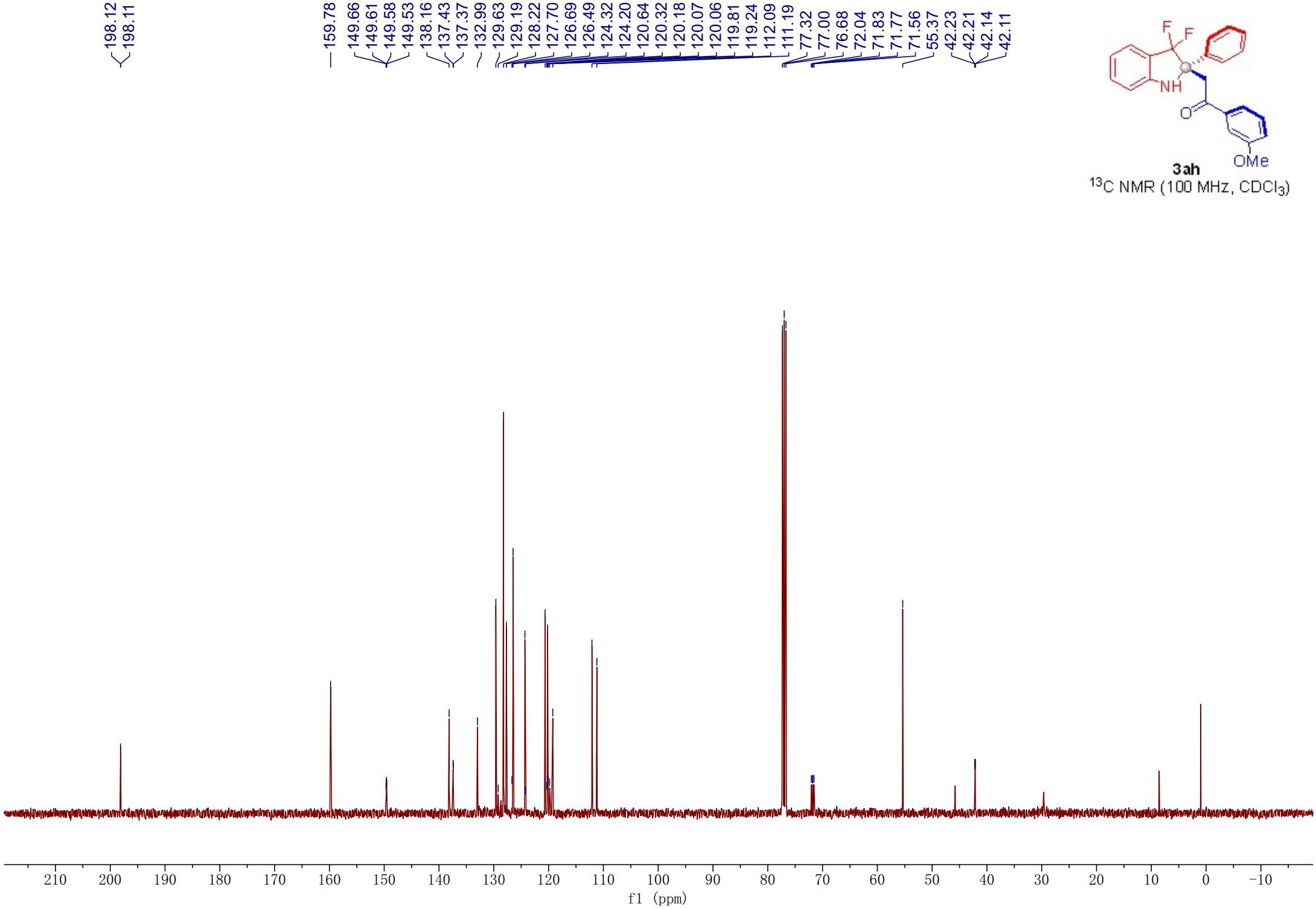


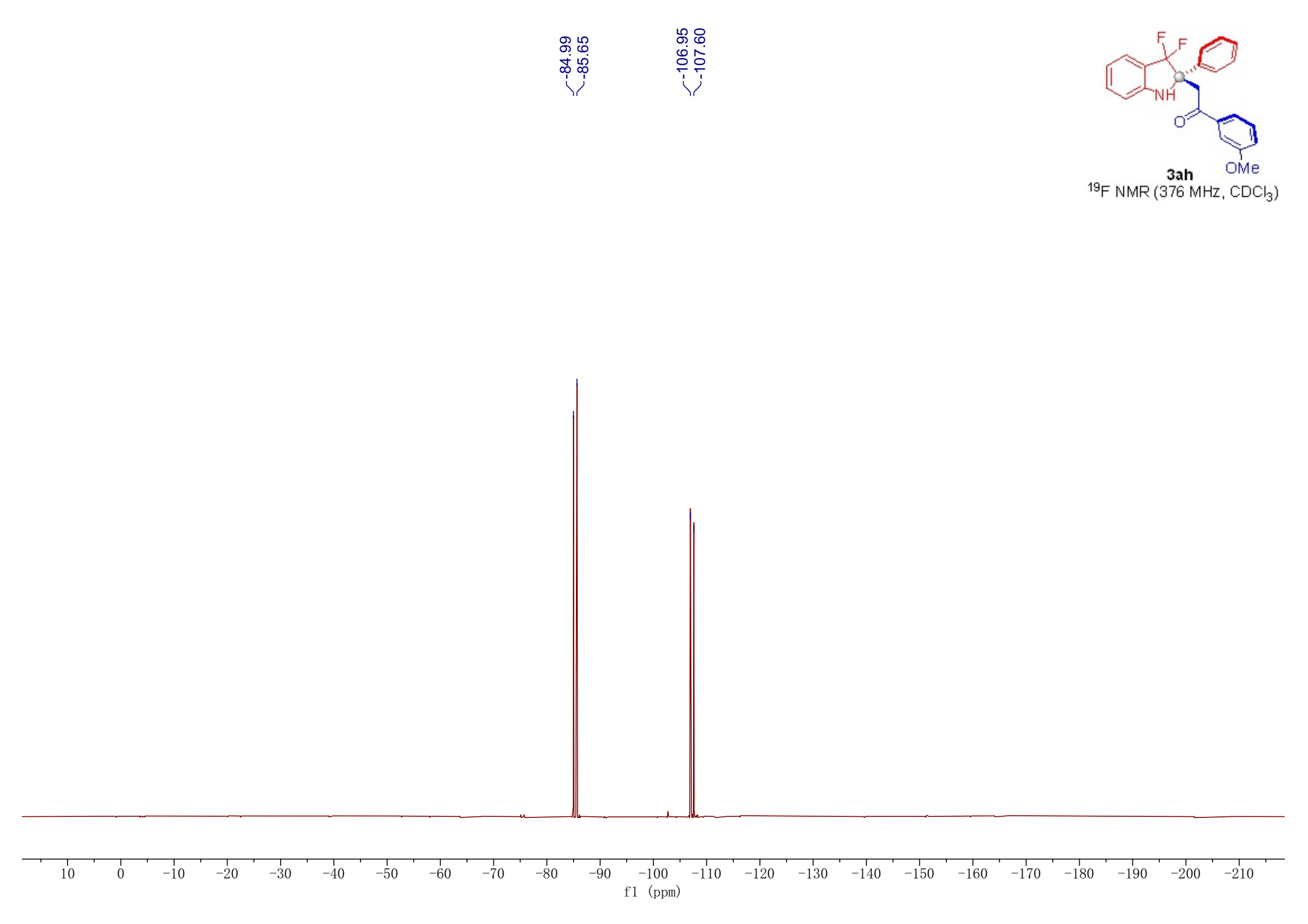


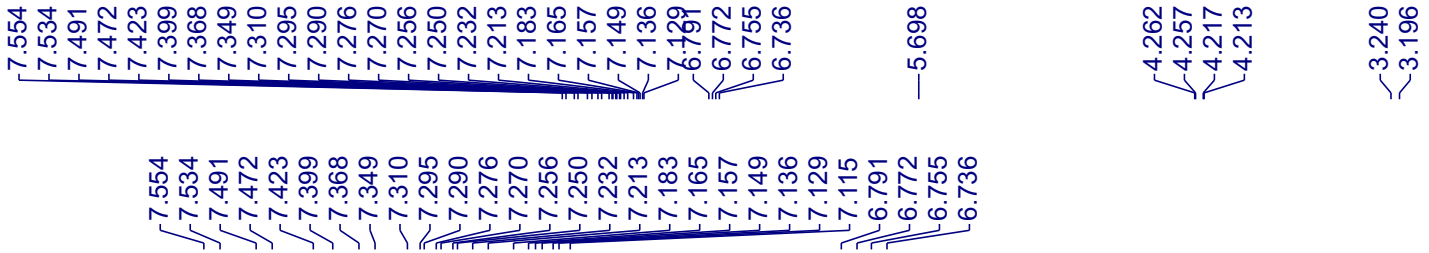
3ah

^{1}H NMR (400 MHz, $CDCl_3$)



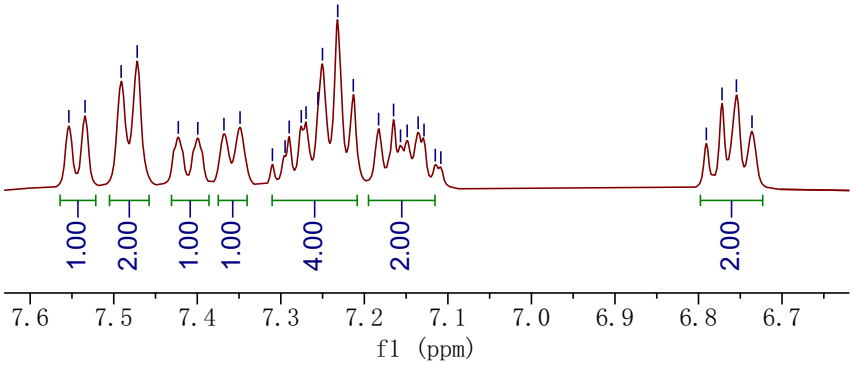

198.12
198.11
159.78
149.66
149.61
149.58
149.53
138.16
137.43
137.37
132.99
129.63
129.19
128.22
127.70
126.69
126.49
124.32
124.20
120.64
120.32
120.18
120.07
120.06
119.81
119.24
112.09
111.19
77.32
77.00
76.68
72.04
71.83
71.77
71.56
55.37
42.23
42.21
42.14
42.11
F
F
NH
O
OMe
3ah
13C NMR (100 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

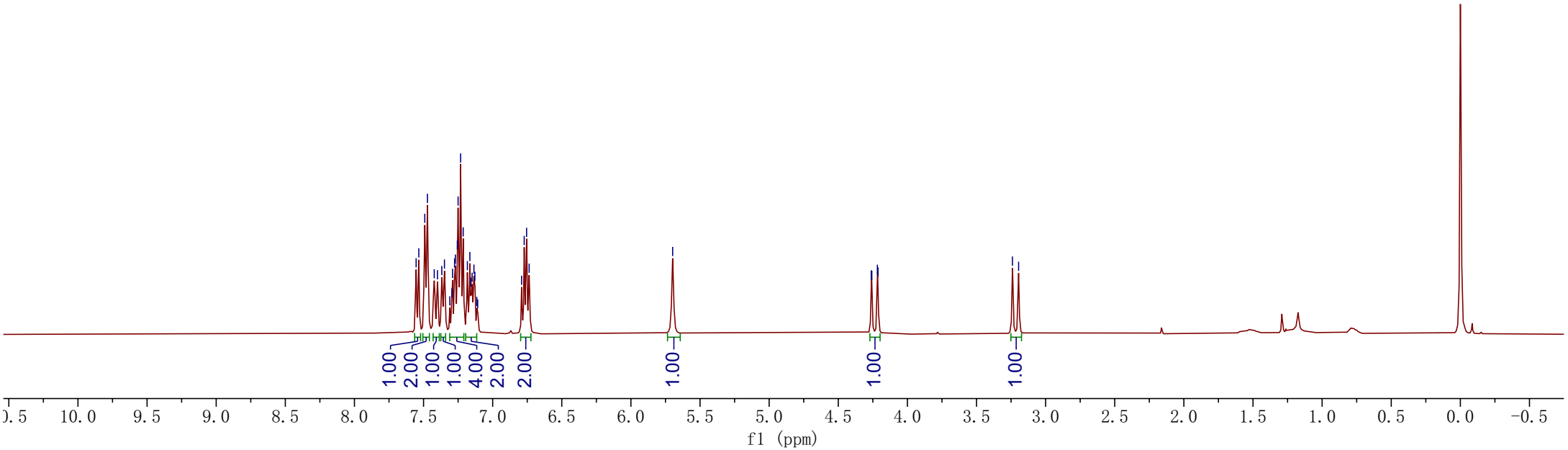

-84.99
-85.65
-106.95
-107.60
F
F
NH
O
OMe
3ah
19F NMR (376 MHz, CDCl3)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

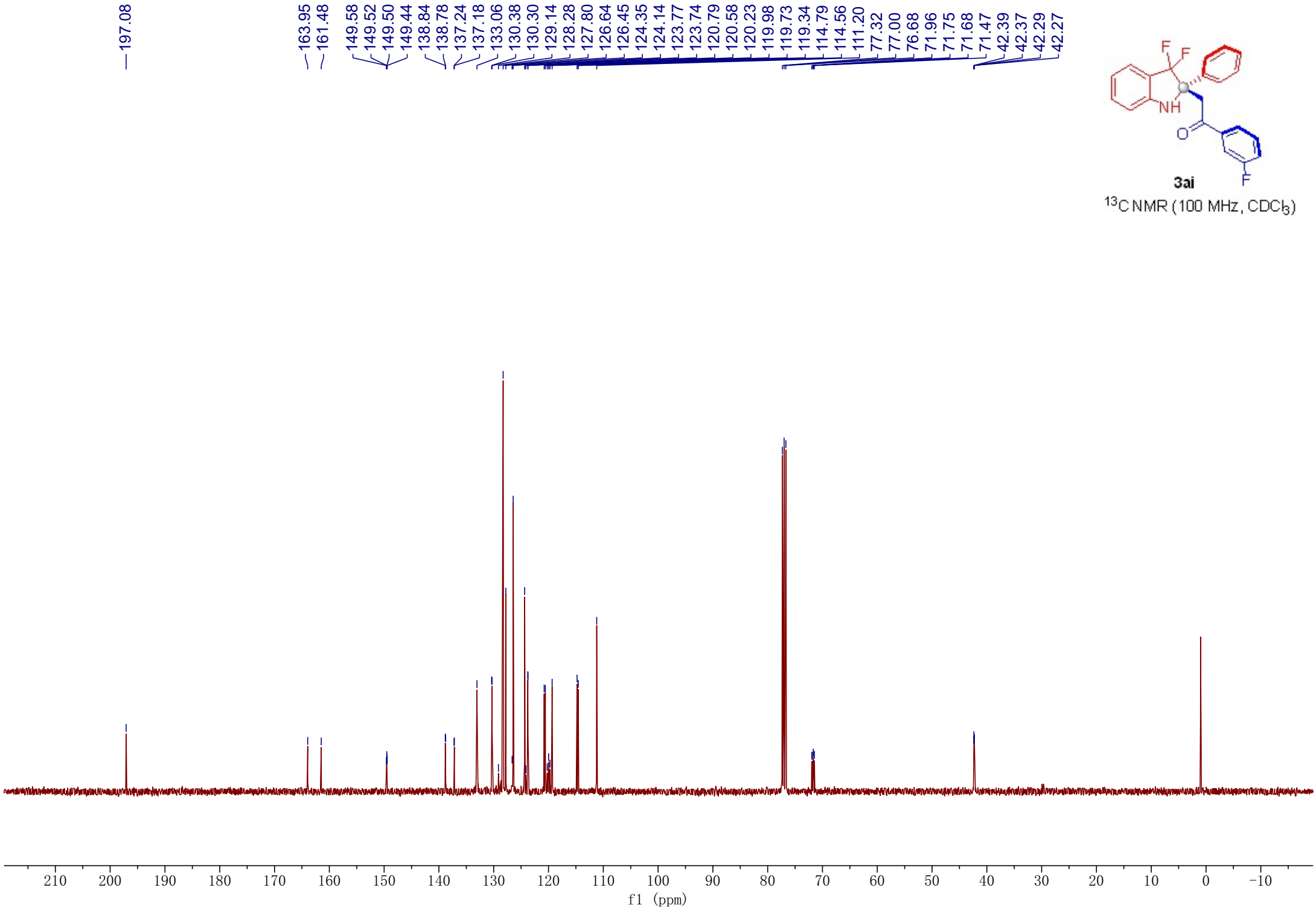


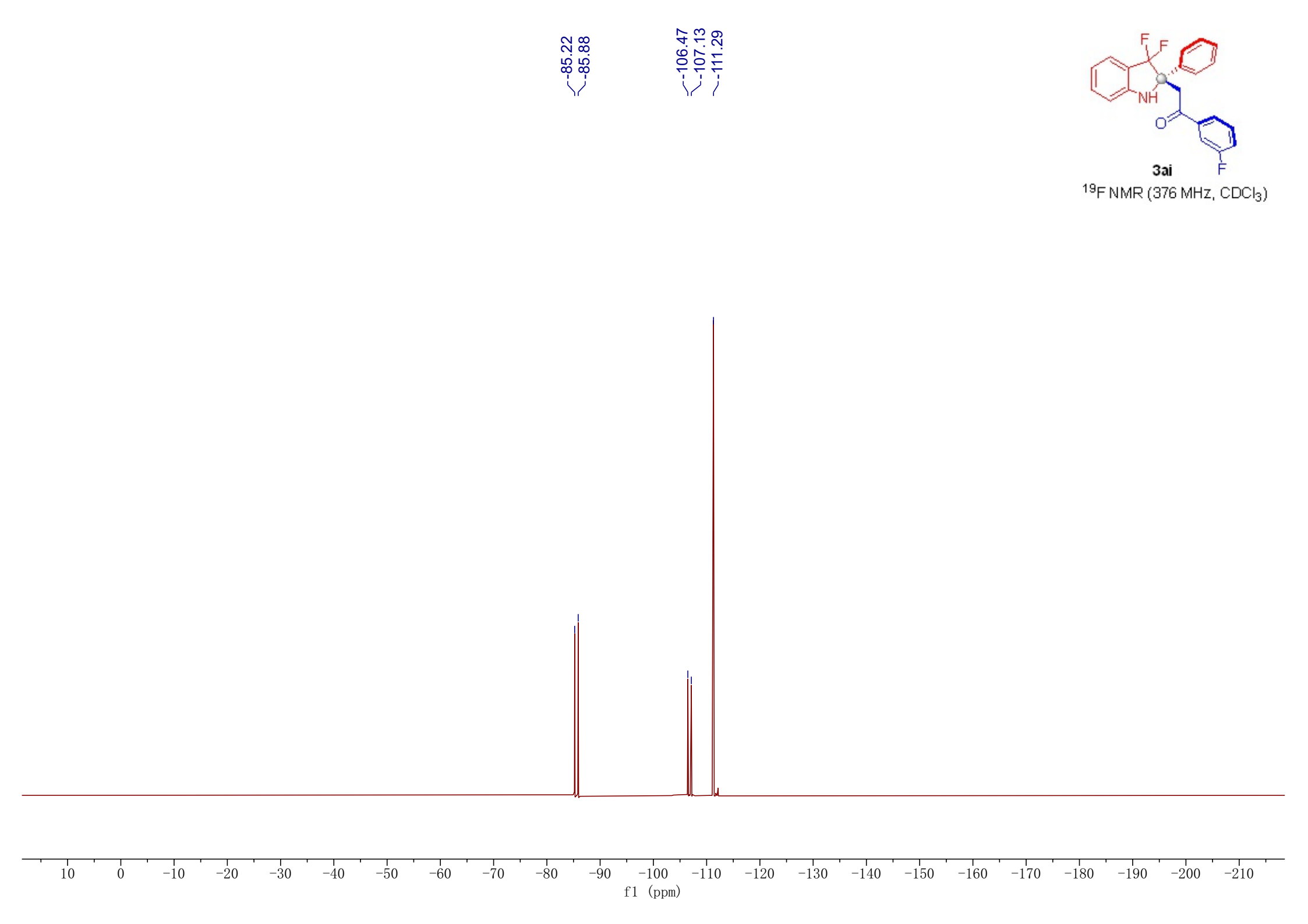
3ai

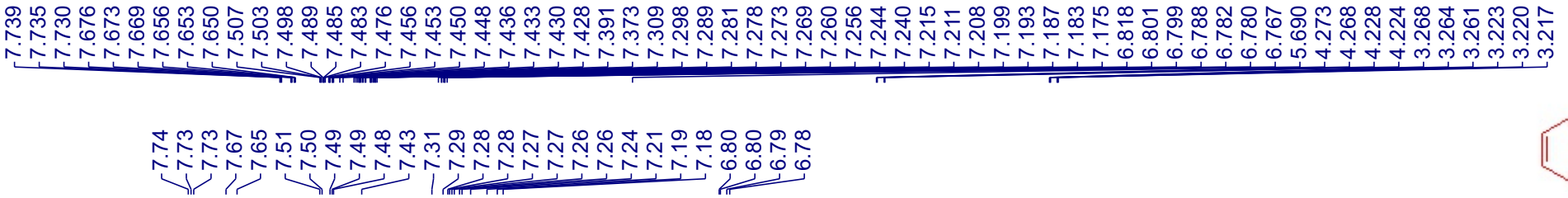
^{1}H NMR (400 MHz, $CDCl_3$)





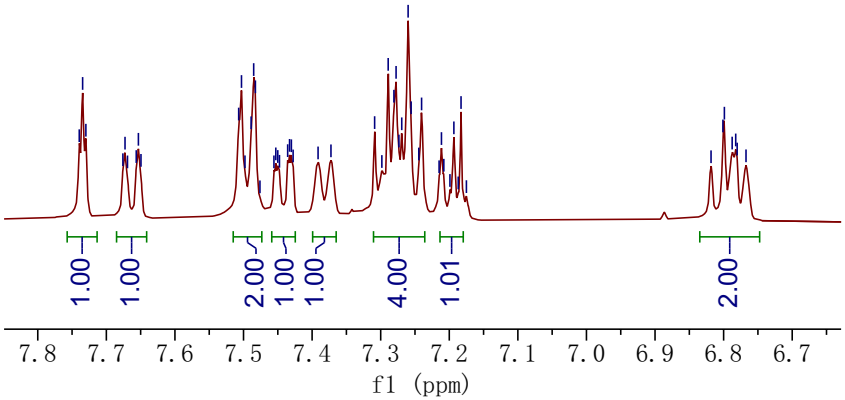

197.08
163.95
161.48
149.58
149.52
149.50
149.44
138.84
138.78
137.24
137.18
133.06
130.38
130.30
129.14
128.28
127.80
126.64
126.45
124.35
124.14
123.77
123.74
120.79
120.58
120.23
119.98
119.73
119.34
114.79
114.56
111.20
77.32
77.00
76.68
71.96
71.75
71.68
71.47
42.39
42.37
42.29
42.27
F
F
NH
O
F
3ai
13C NMR (100 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

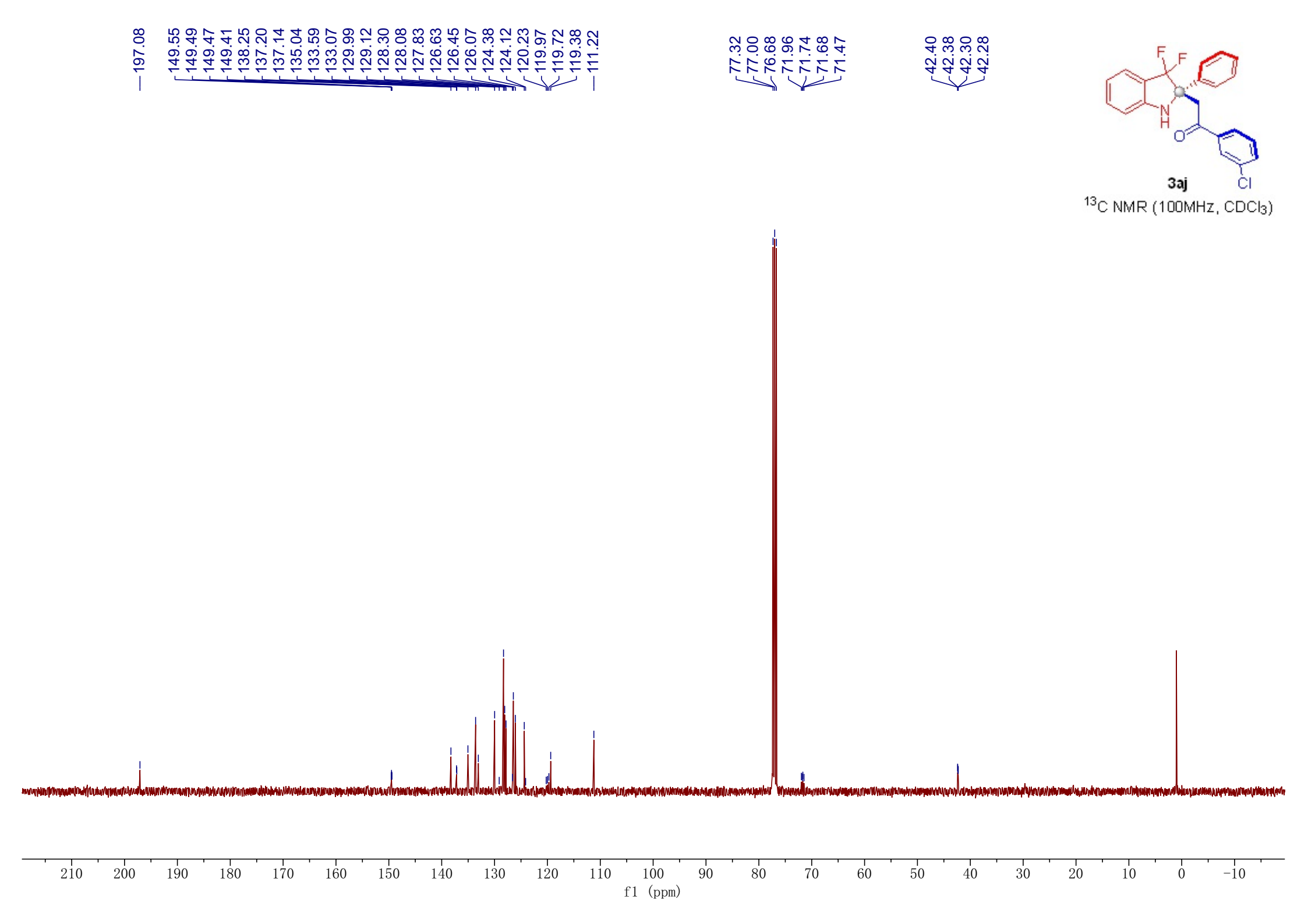

-85.22
-85.88
-106.47
-107.13
-111.29
F
F
NH
O
F
3ai
19F NMR (376 MHz, CDCl3)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

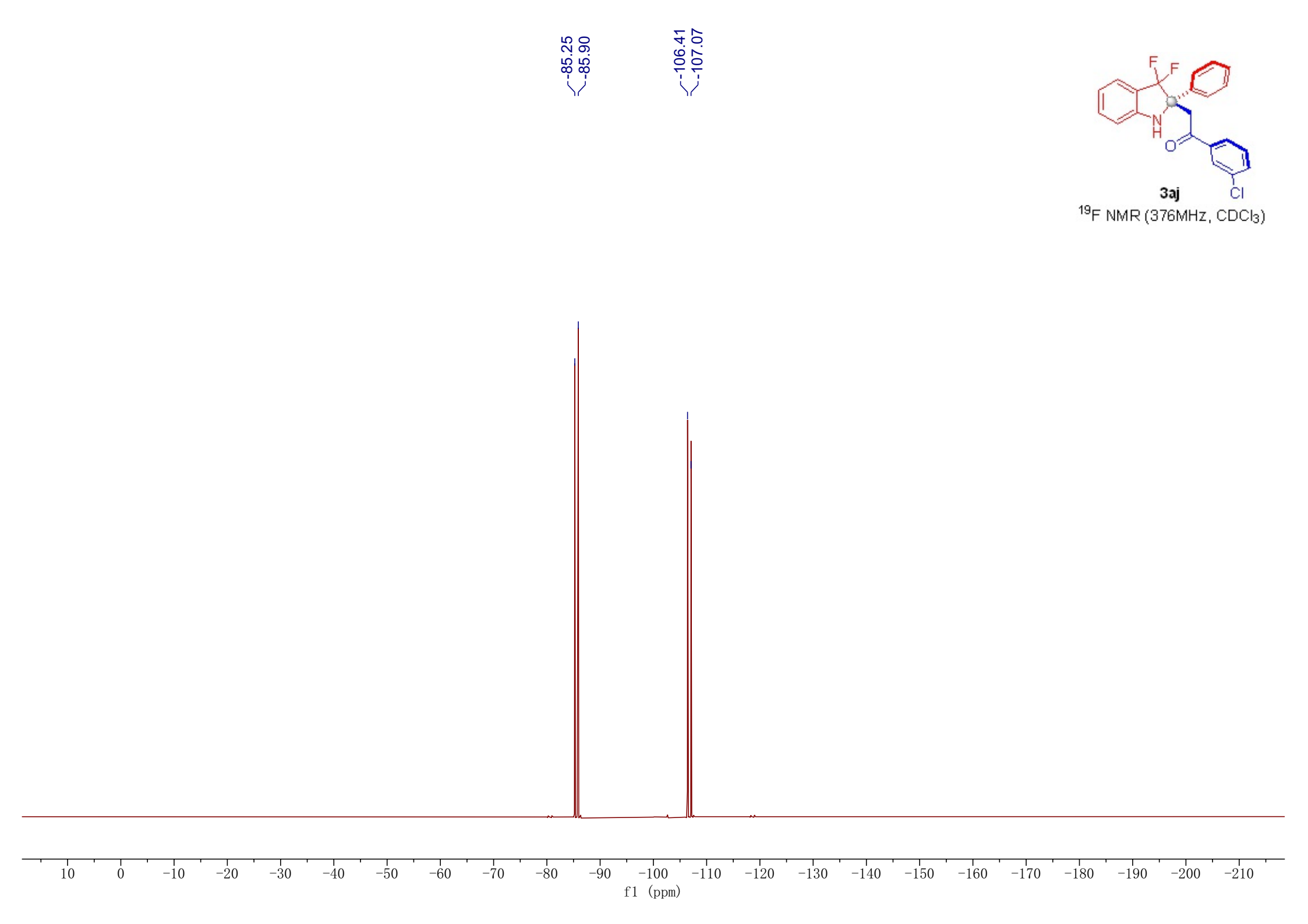


3aj

^{1}H NMR (400MHz, $CDCl_3$)

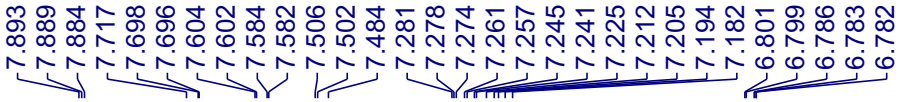


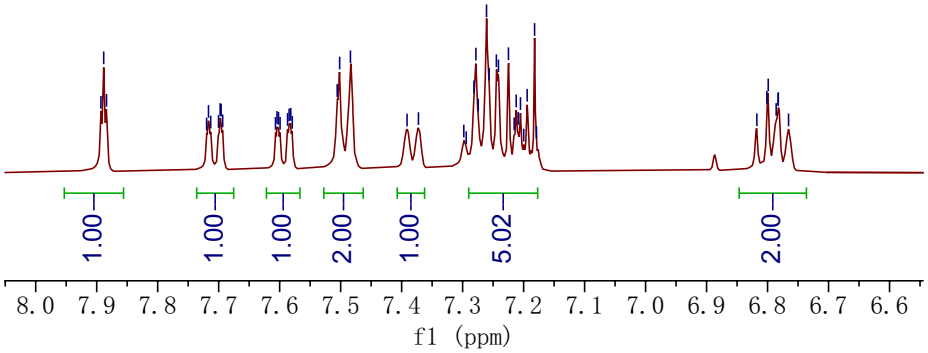

197.08
149.55
149.49
149.47
149.41
138.25
137.20
137.14
135.04
133.59
133.07
129.99
129.12
128.30
128.08
127.83
126.63
126.45
126.07
124.38
124.12
120.23
119.97
119.72
119.38
111.22
77.32
77.00
76.68
71.96
71.74
71.68
71.47
42.40
42.38
42.30
42.28
F
F
N
H
O
Cl
3aj
13C NMR (100MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

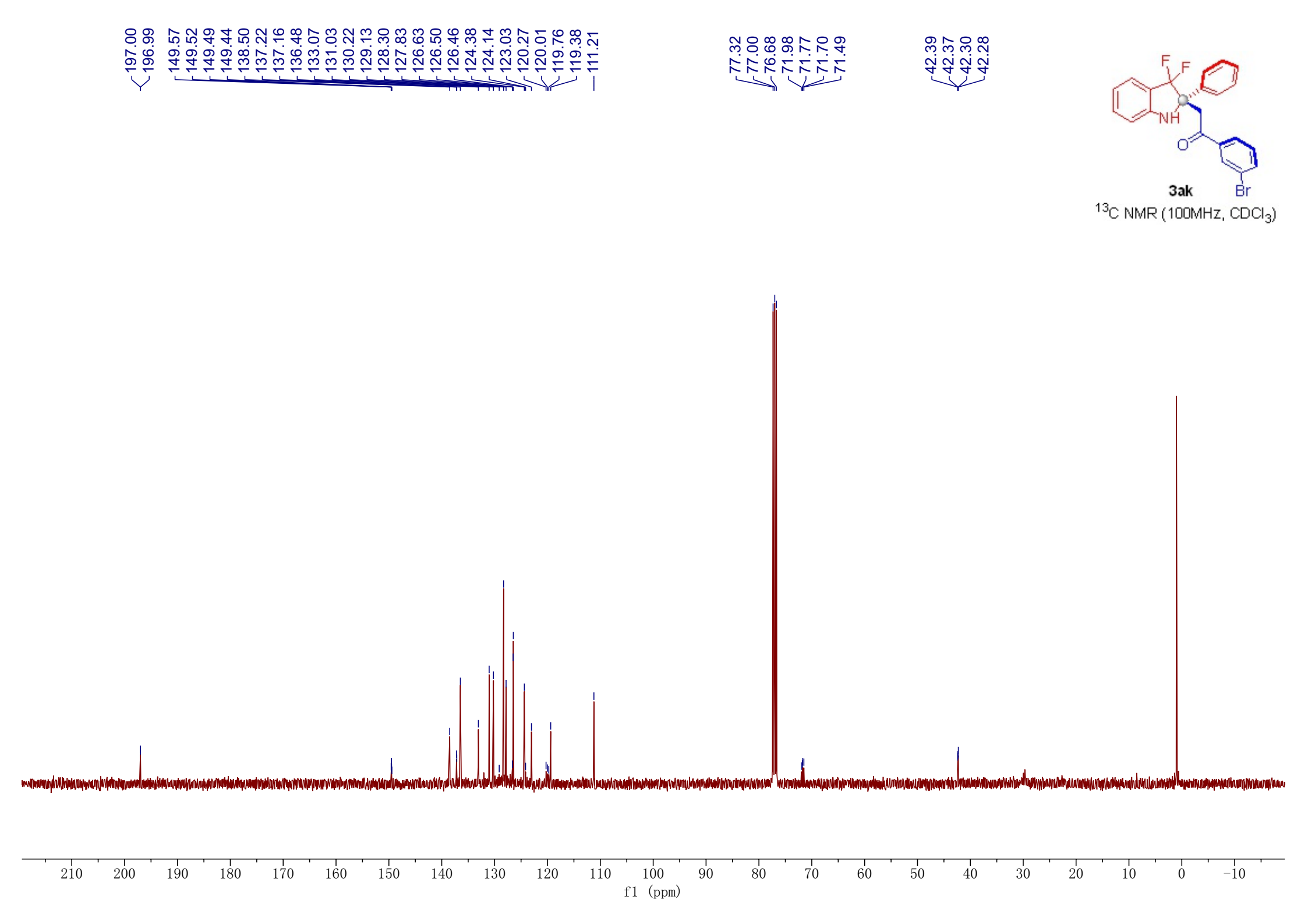

-85.25
-85.90
-106.41
-107.07
F
F
N
H
O
Cl
3aj
^{19}F NMR (376MHz, $CDCl_3$)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

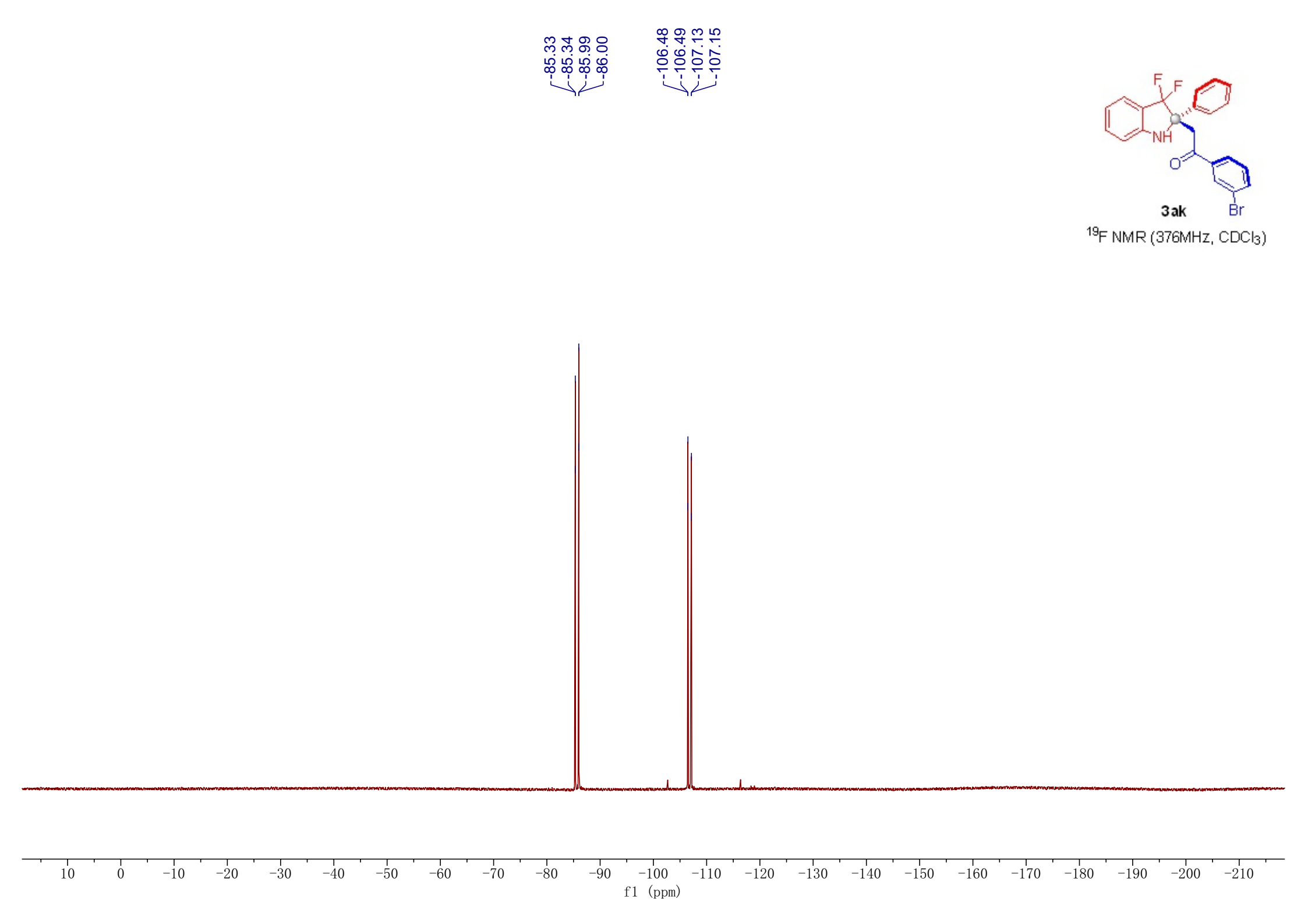
3ak

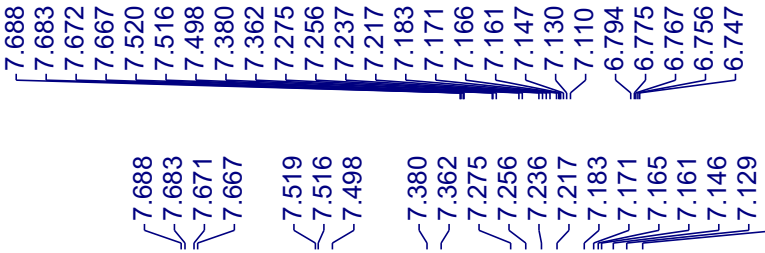
^{1}H NMR (400MHz, $CDCl_3$)

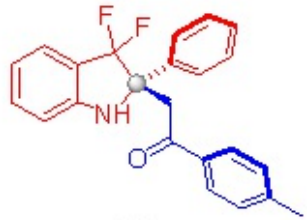





197.00
196.99
149.57
149.52
149.49
149.44
138.50
137.22
137.16
136.48
133.07
131.03
130.22
129.13
128.30
127.83
126.63
126.50
126.46
124.38
124.14
123.03
120.27
120.01
119.76
119.38
111.21
77.32
77.00
76.68
71.98
71.77
71.70
71.49
42.39
42.37
42.30
42.28
F
F
NH
O
Br
3ak
13C NMR (100MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

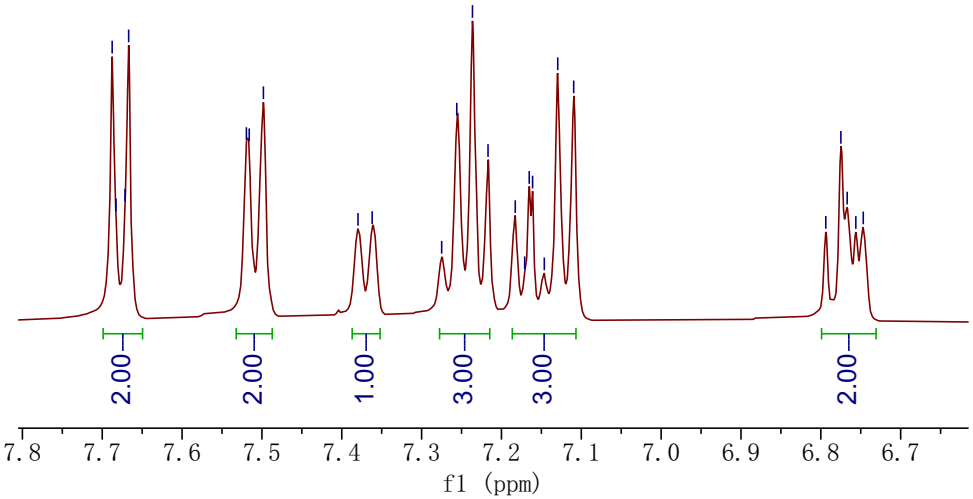

-85.33
-85.34
-85.99
-86.00
-106.48
-106.49
-107.13
-107.15
F
F
NH
O
Br
3ak
19F NMR (376MHz, CDCl3)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

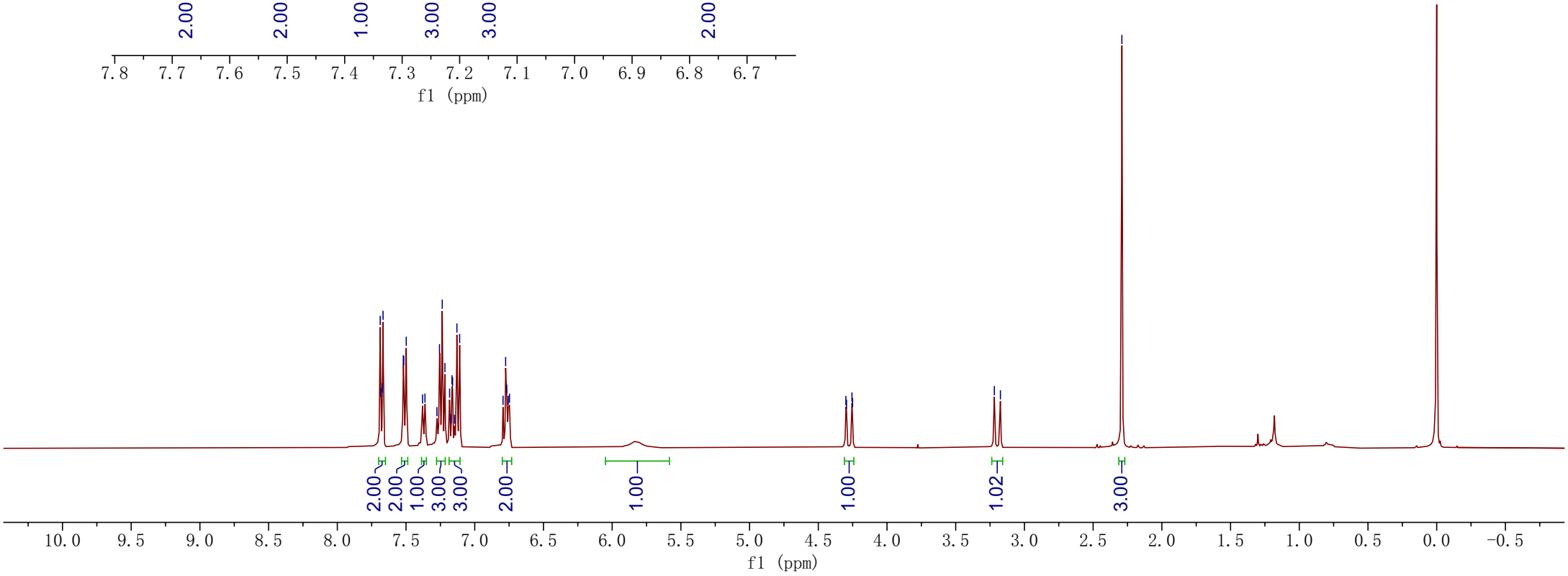


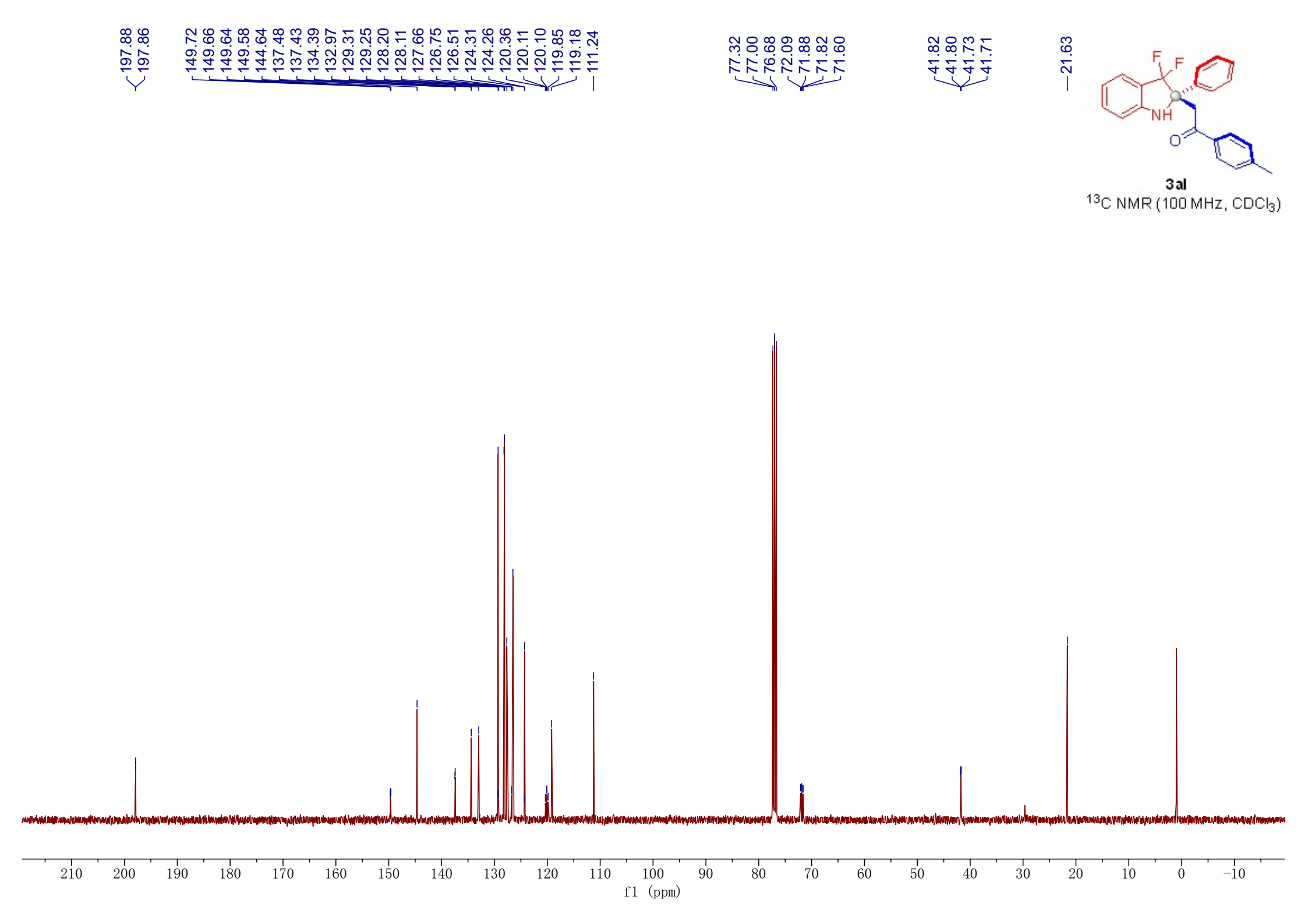


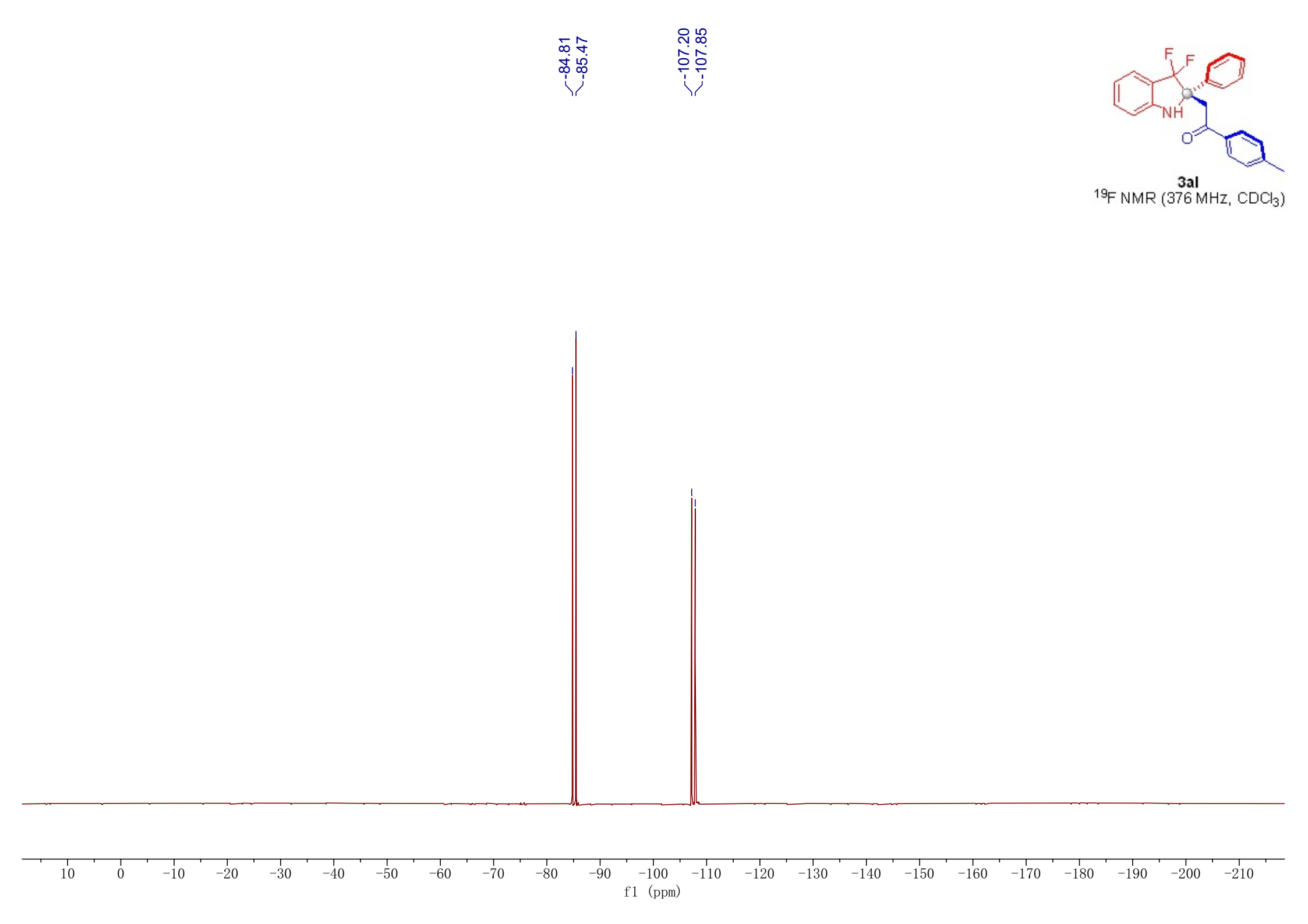
3al

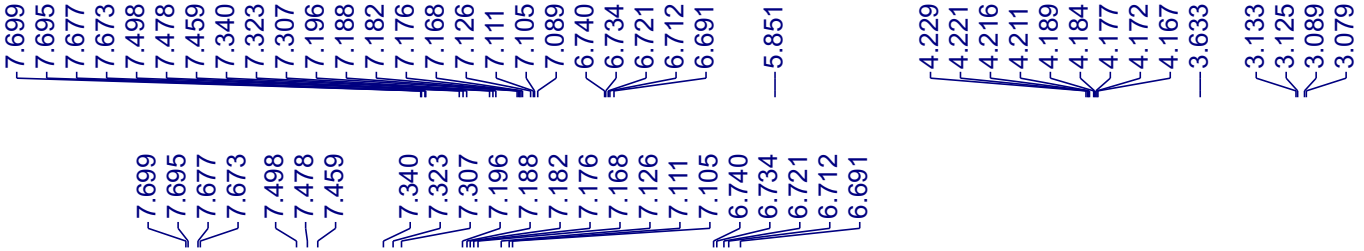
^{1}H NMR (400 MHz, $CDCl_3$)

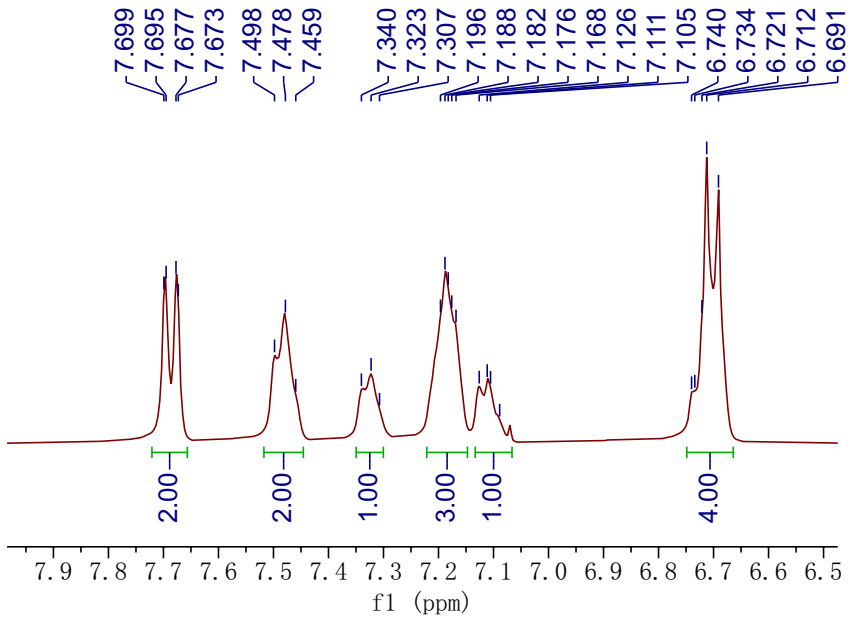





197.88
197.86
149.72
149.66
149.64
149.58
144.64
137.48
137.43
134.39
132.97
129.31
129.25
128.20
128.11
127.66
126.75
126.51
124.31
124.26
120.36
120.11
120.10
119.85
119.18
111.24
77.32
77.00
76.68
72.09
71.88
71.82
71.60
41.82
41.80
41.73
41.71
21.63
F
F
NH
O
3al
13C NMR (100 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

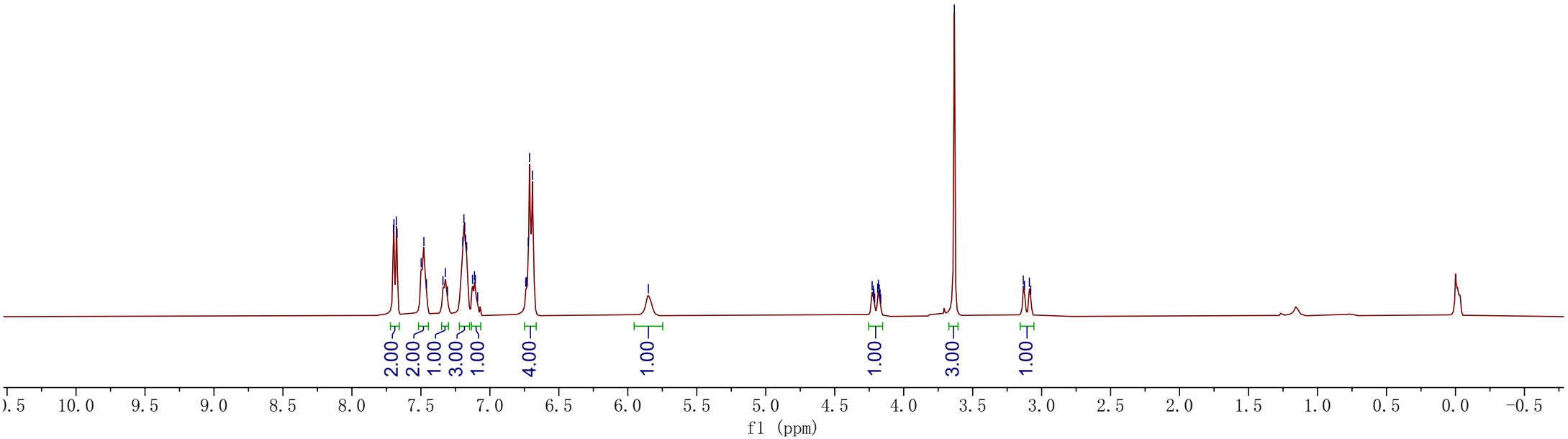

-84.81
-85.47
-107.20
-107.85
F
F
NH
O
3al
19F NMR (376 MHz, CDCl3)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

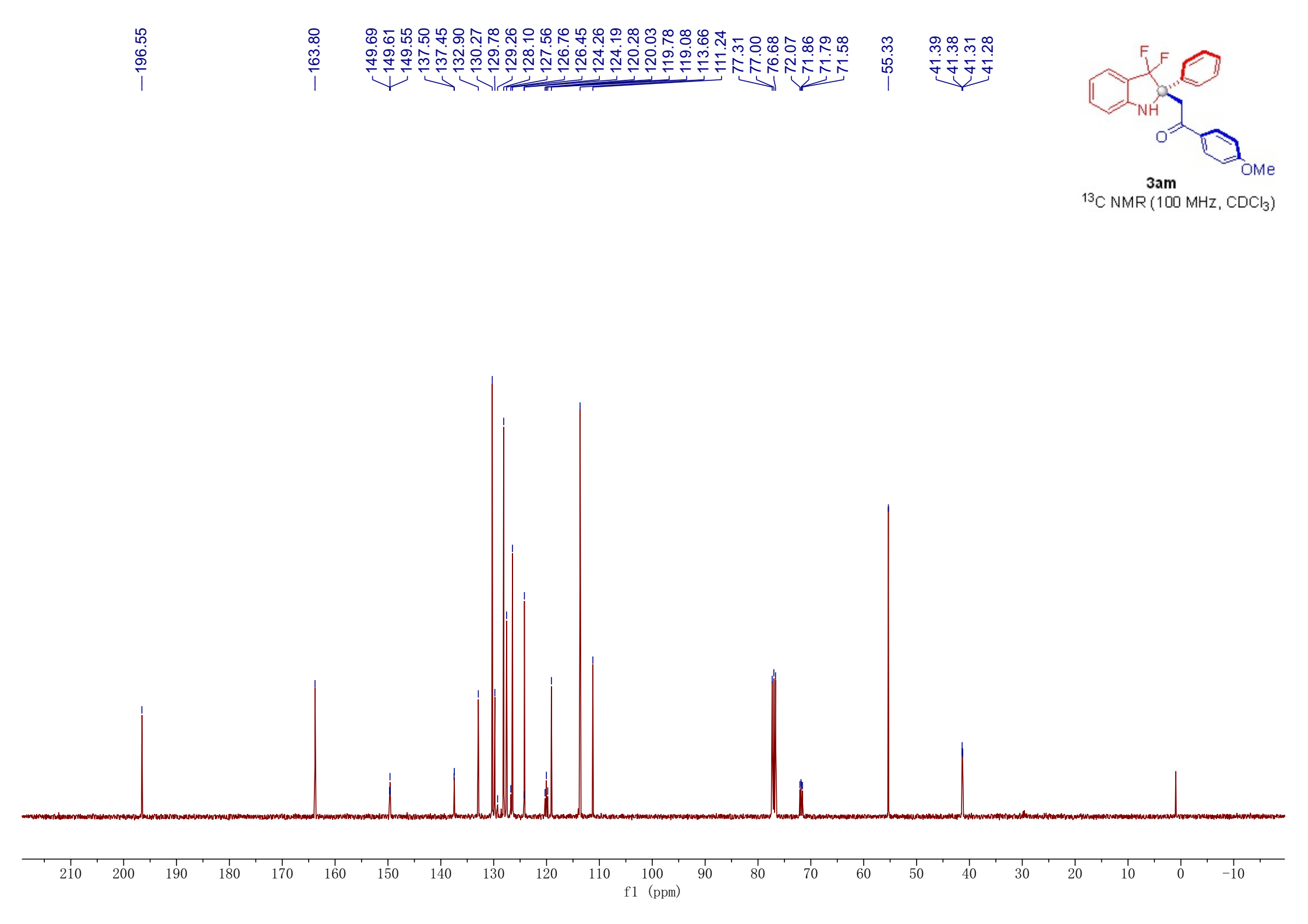


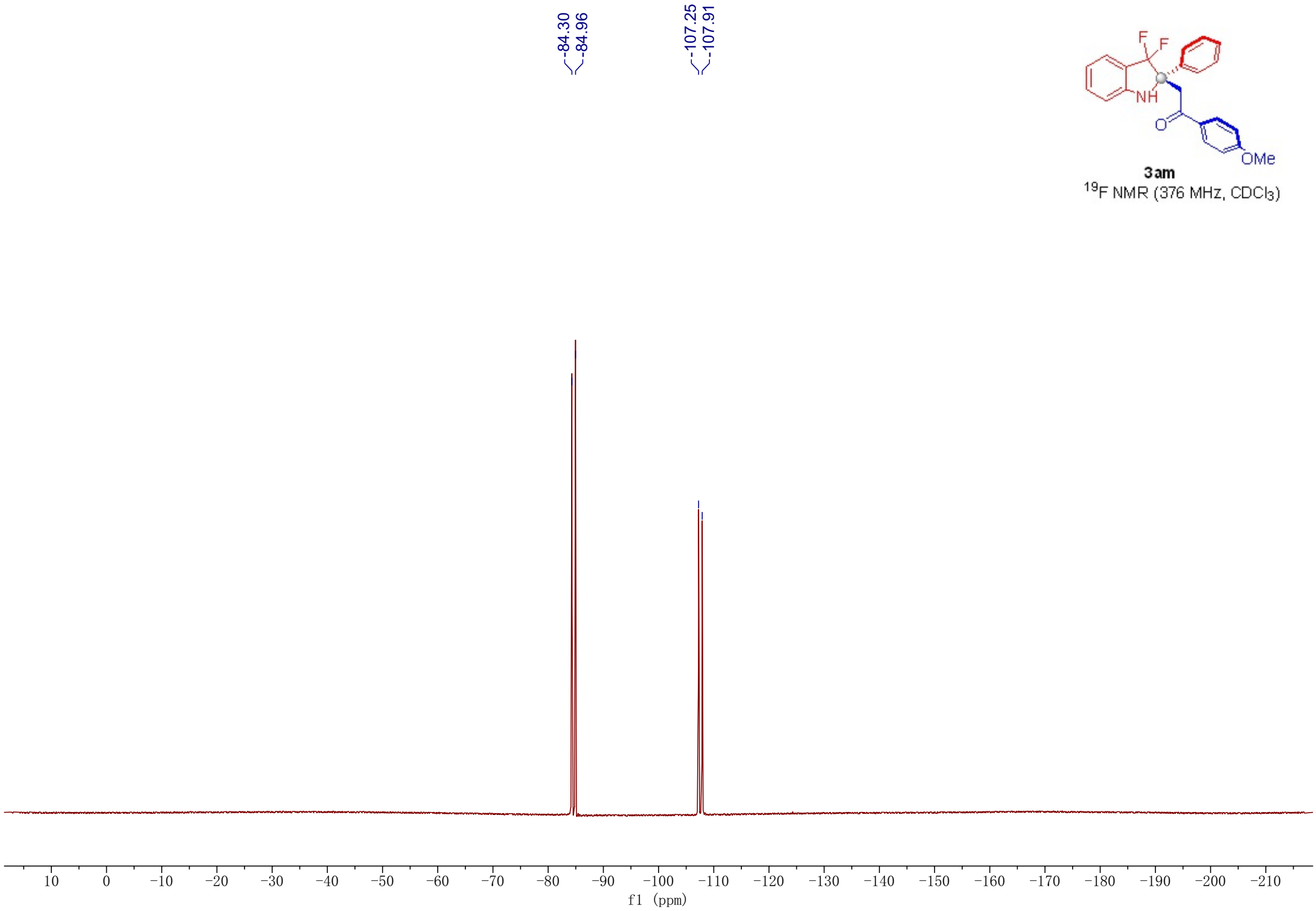


3am

^{1}H NMR (400 MHz, $CDCl_3$)

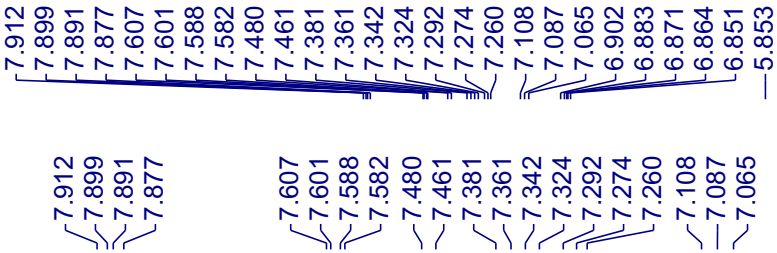



196.55
163.80
149.69
149.61
149.55
137.50
137.45
132.90
130.27
129.78
129.26
128.10
127.56
126.76
126.45
124.26
124.19
120.28
120.03
119.78
119.08
113.66
111.24
77.31
77.00
76.68
72.07
71.86
71.79
71.58
55.33
41.39
41.38
41.31
41.28
F
F
NH
O
OMe
3am
13C NMR (100 MHz, CDCl3)
f1 (ppm)



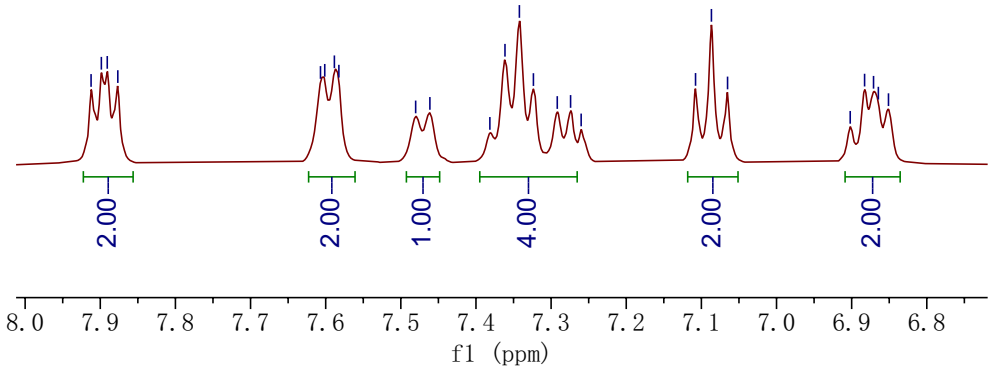
3am

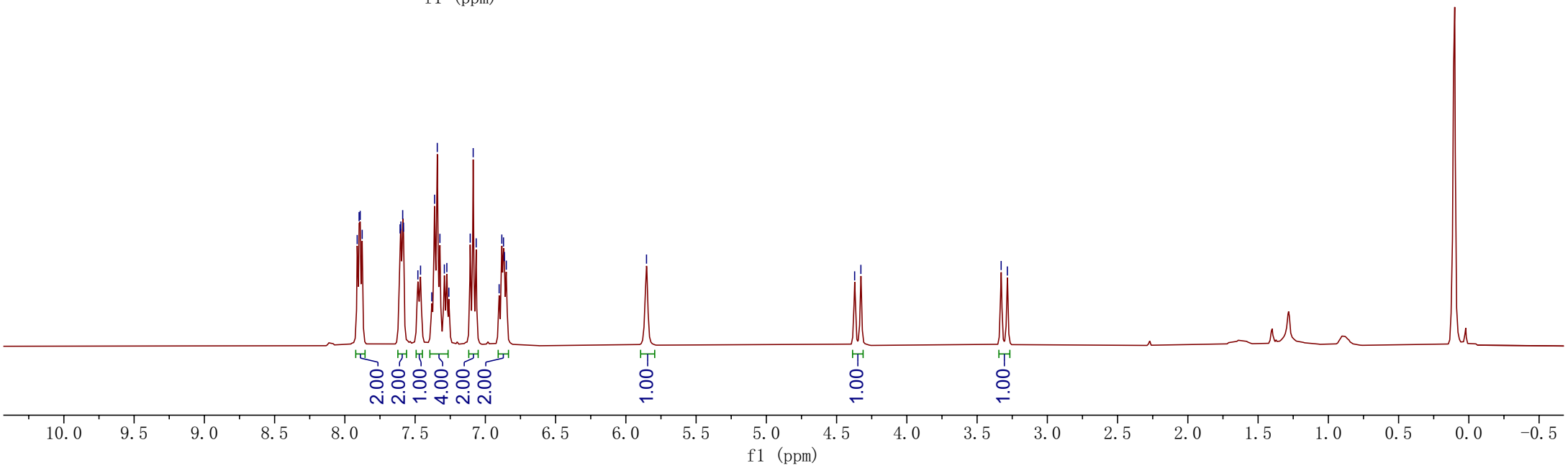
^{19}F NMR (376 MHz, $CDCl_3$)

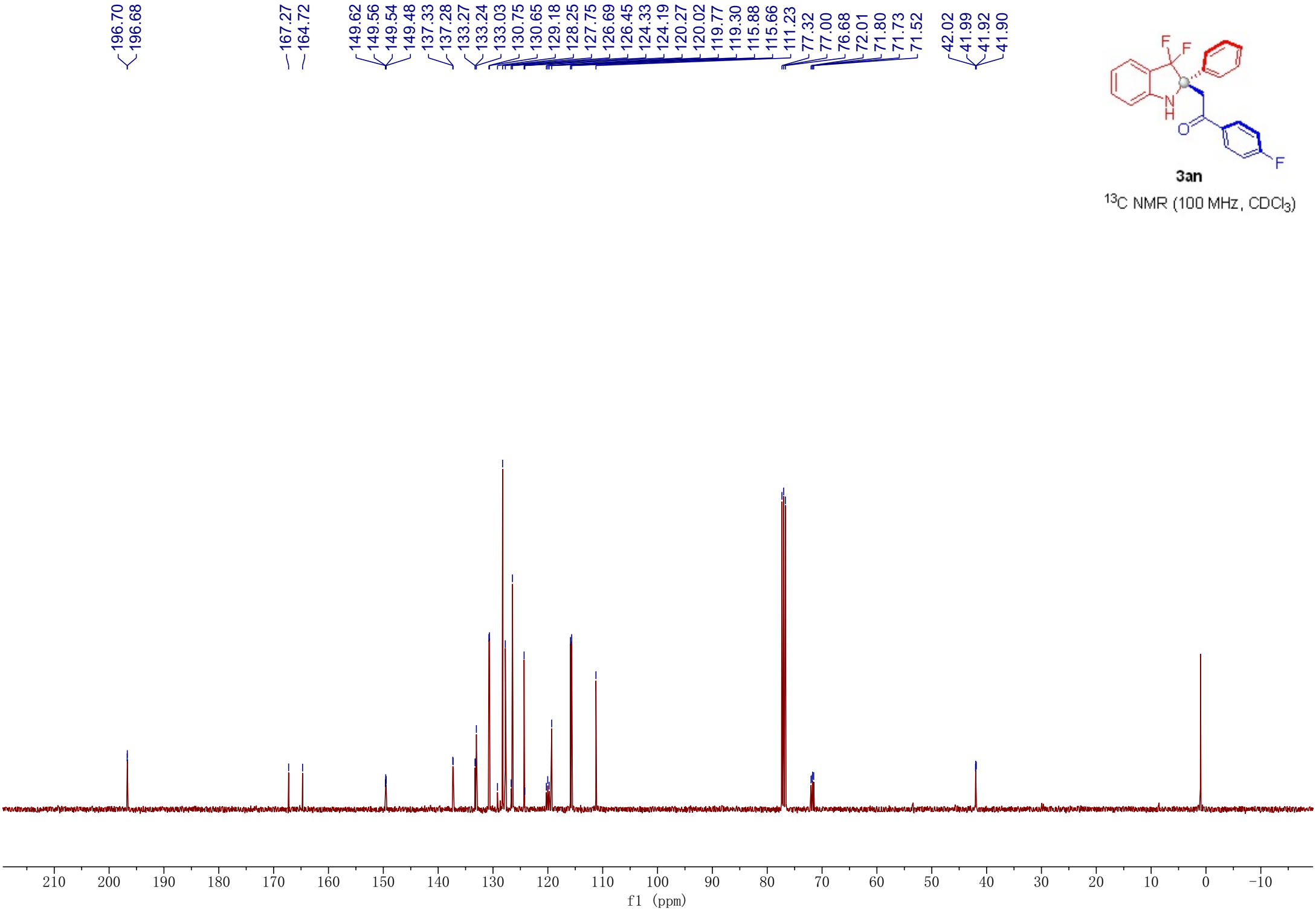


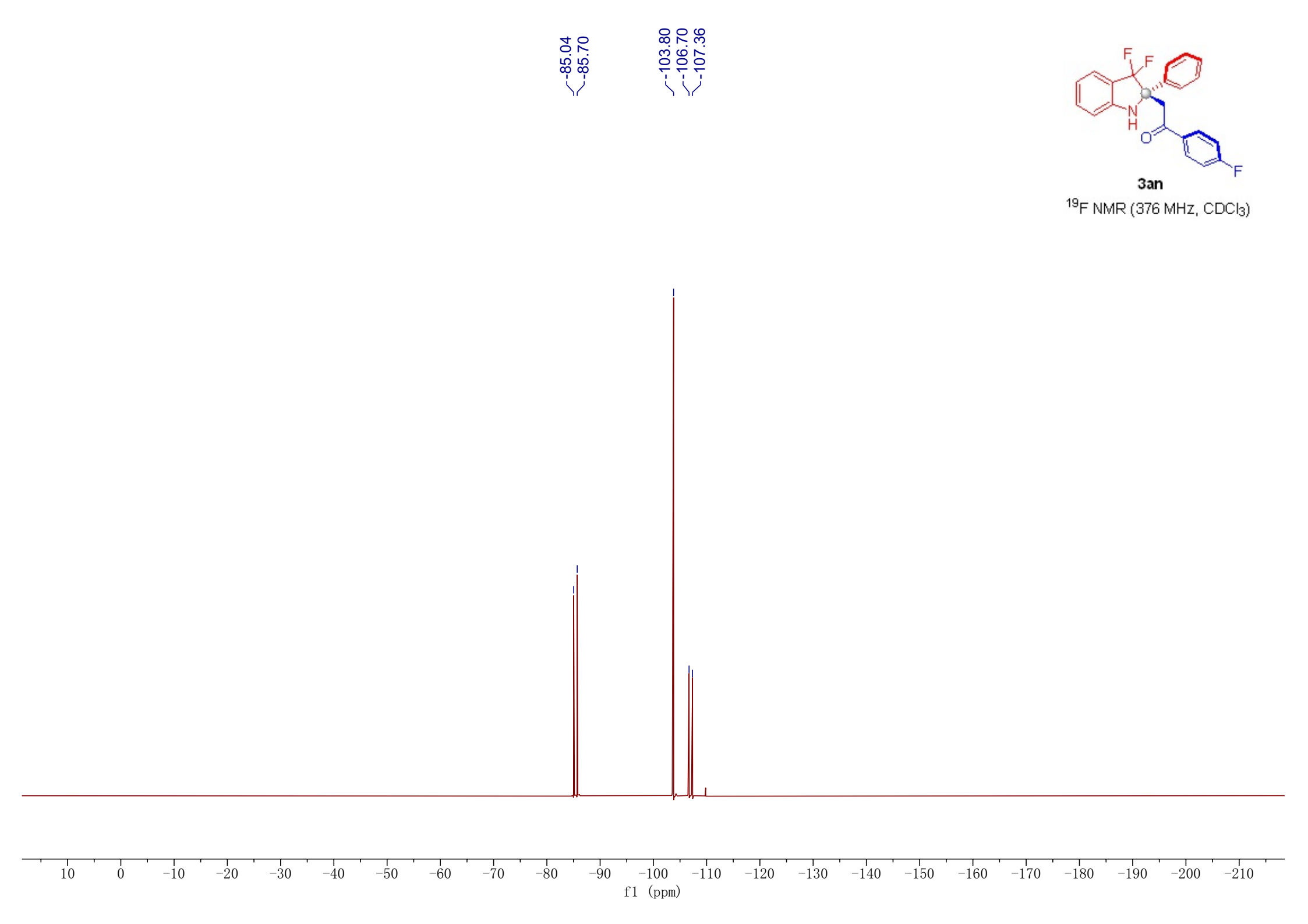
3an

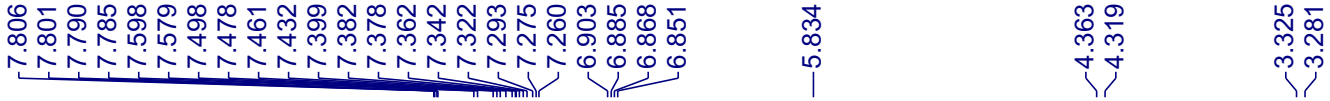
^{1}H NMR (400 MHz, $CDCl_3$)





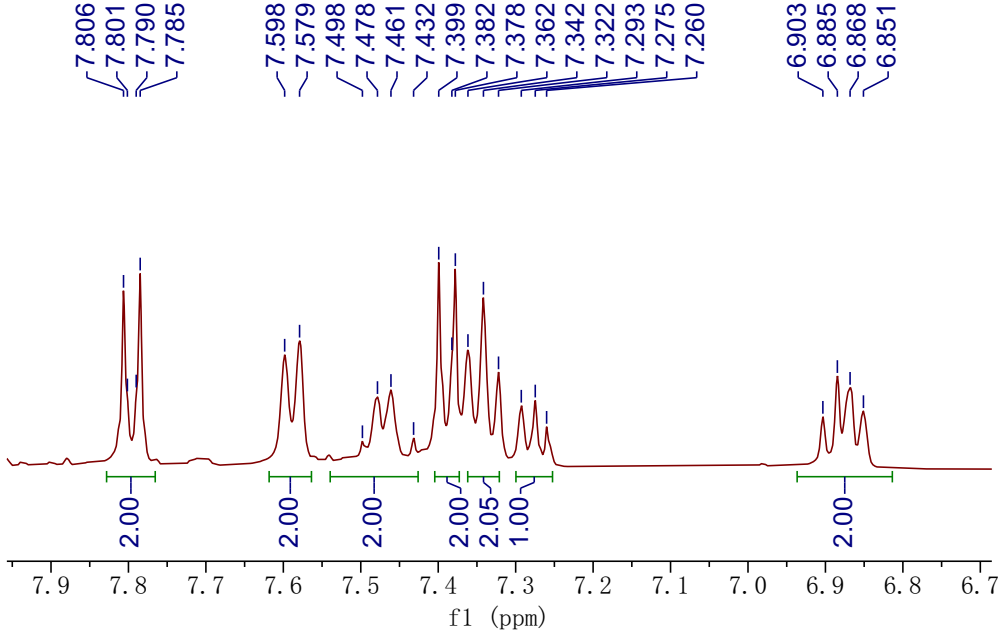

196.70
196.68
167.27
164.72
149.62
149.56
149.54
149.48
137.33
137.28
133.27
133.24
133.03
130.75
130.65
129.18
128.25
127.75
126.69
126.45
124.33
124.19
120.27
120.02
119.77
119.30
115.88
115.66
111.23
77.32
77.00
76.68
72.01
71.80
71.73
71.52
42.02
41.99
41.92
41.90
F
F
N
H
O
F
3an
13C NMR (100 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

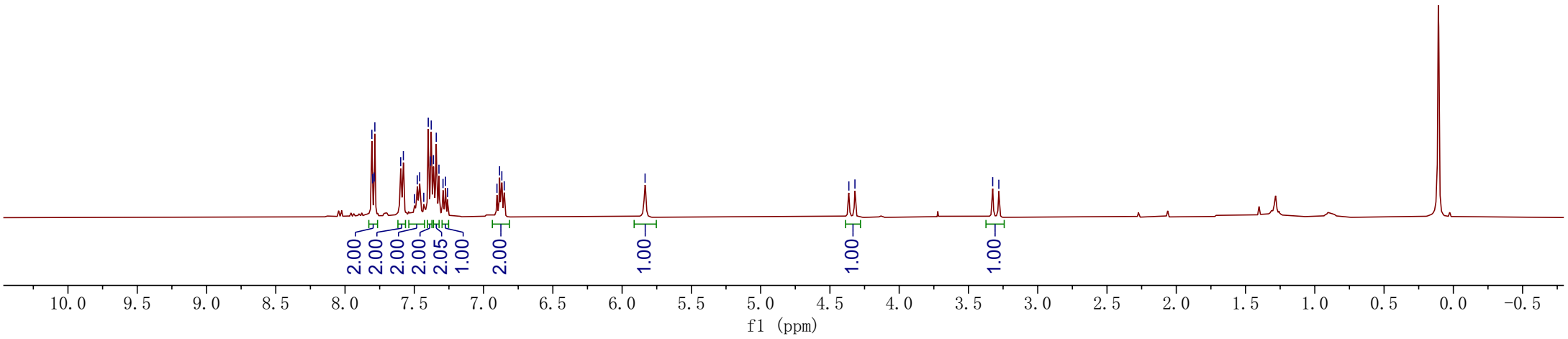

-85.04
-85.70
-103.80
-106.70
-107.36
F
F
N
H
O
F
3an
^{19}F NMR (376 MHz, $CDCl_3$)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

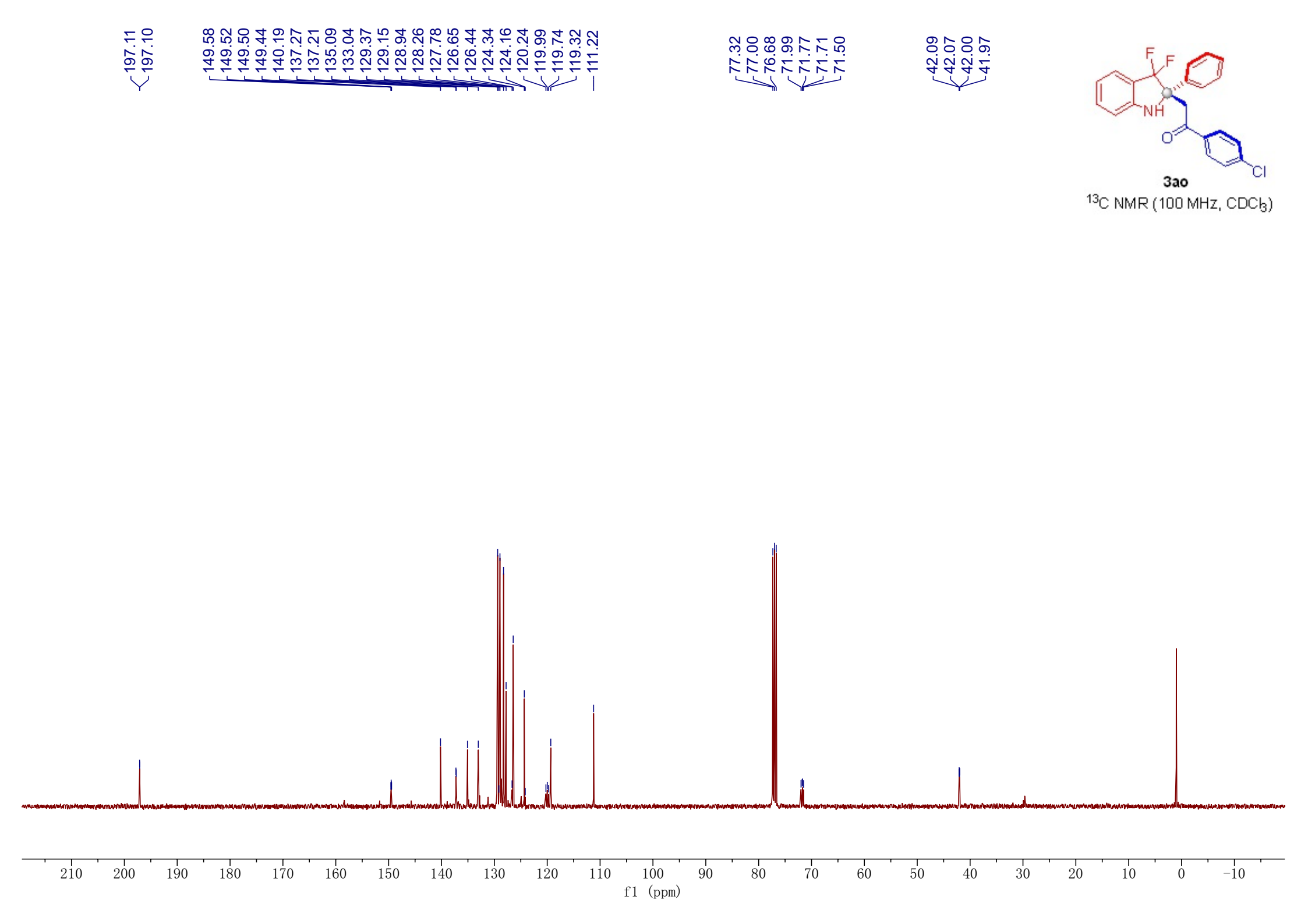


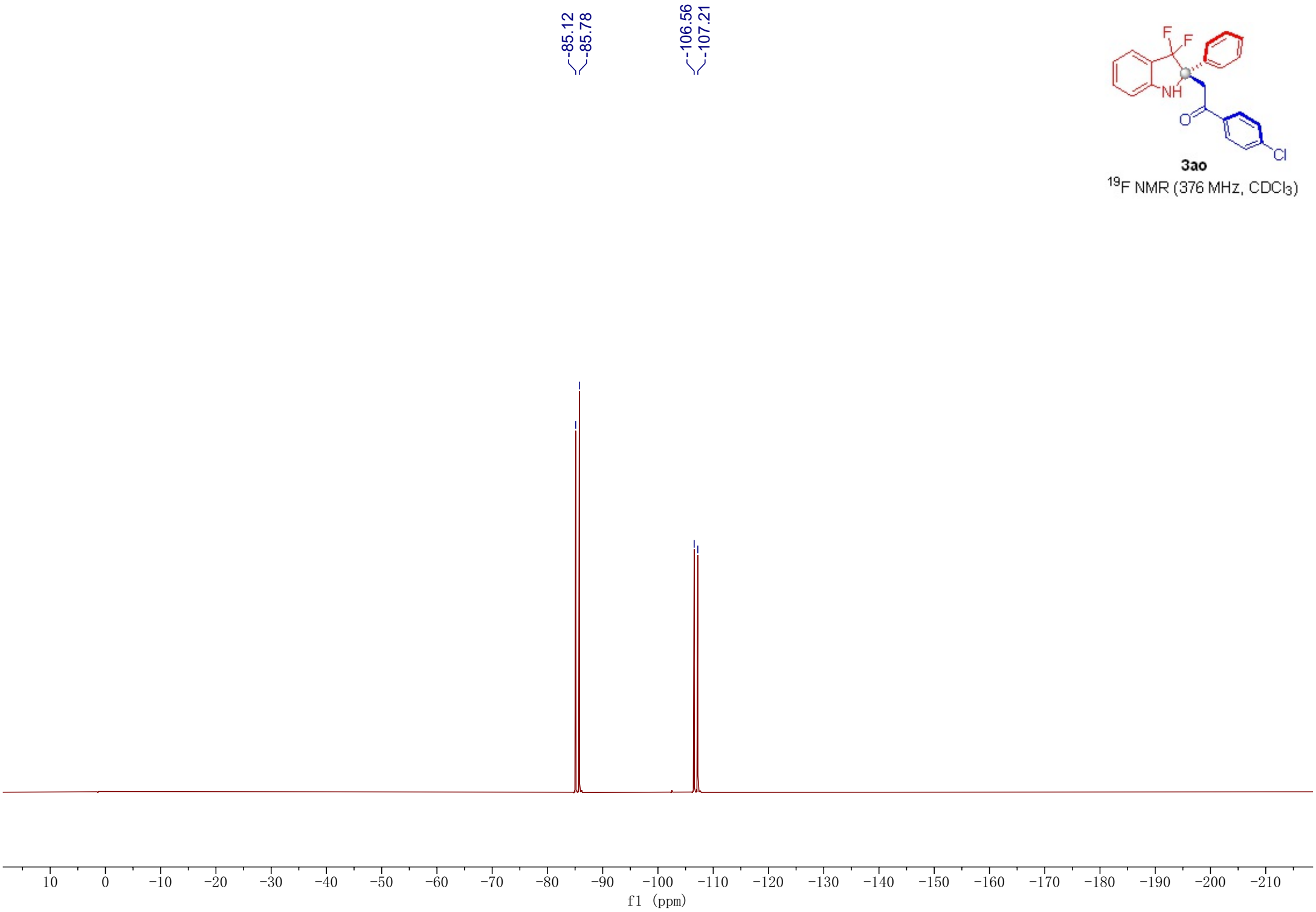
3ao

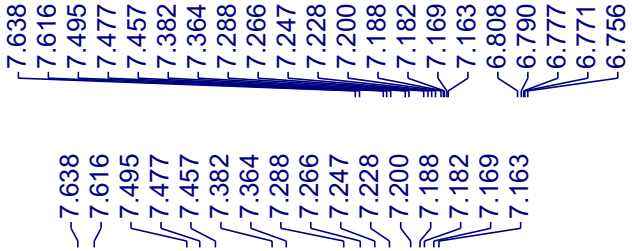
^{1}H NMR (400 MHz, $CDCl_3$)





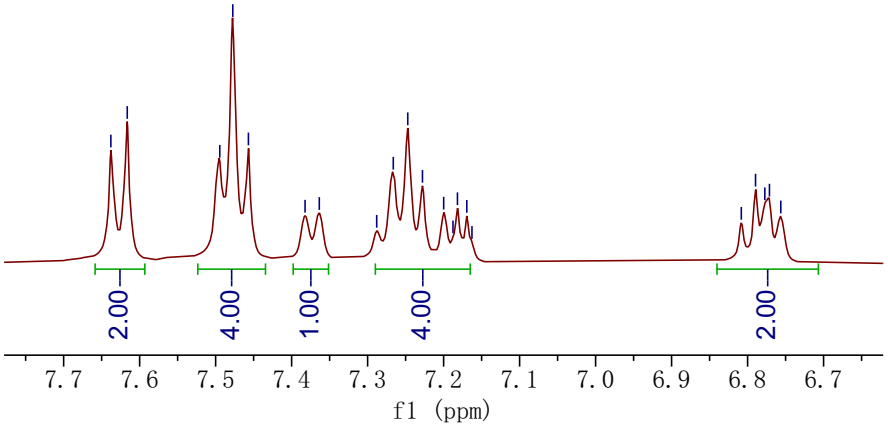

197.11
197.10
149.58
149.52
149.50
149.44
140.19
137.27
137.21
135.09
133.04
129.37
129.15
128.94
128.26
127.78
126.65
126.44
124.34
124.16
120.24
119.99
119.74
119.32
111.22
77.32
77.00
76.68
71.99
71.77
71.71
71.50
42.09
42.07
42.00
41.97
F
F
NH
O
Cl
3ao
13C NMR (100 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

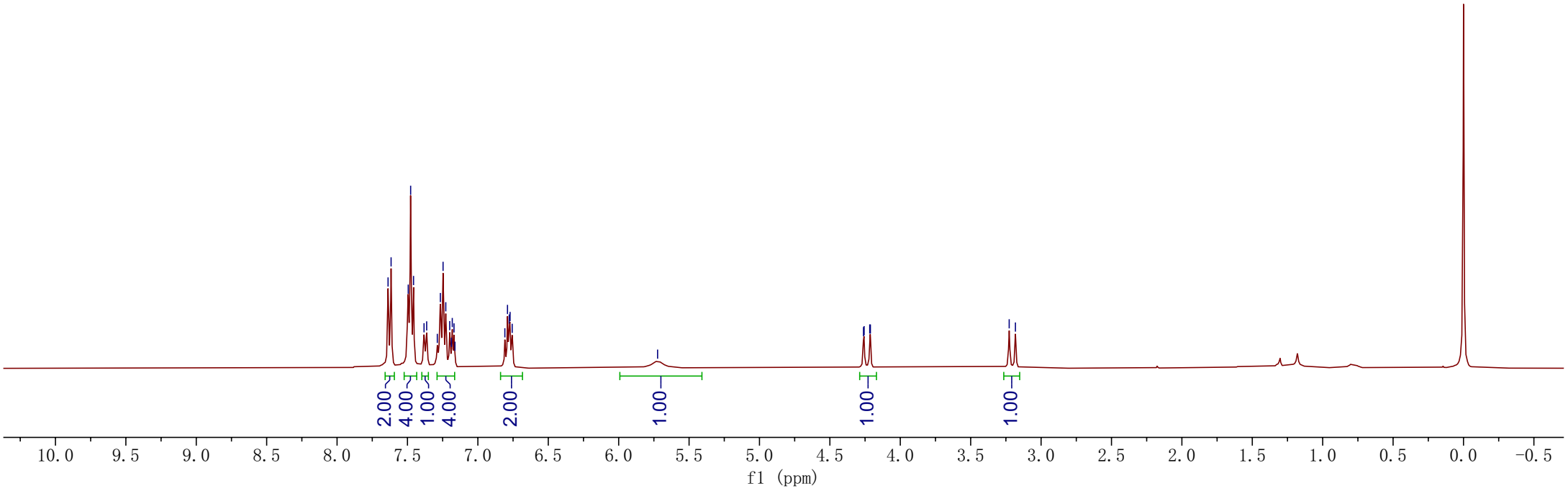

-85.12
-85.78
-106.56
-107.21
F
F
NH
O
Cl
3ao
19F NMR (376 MHz, CDCl3)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

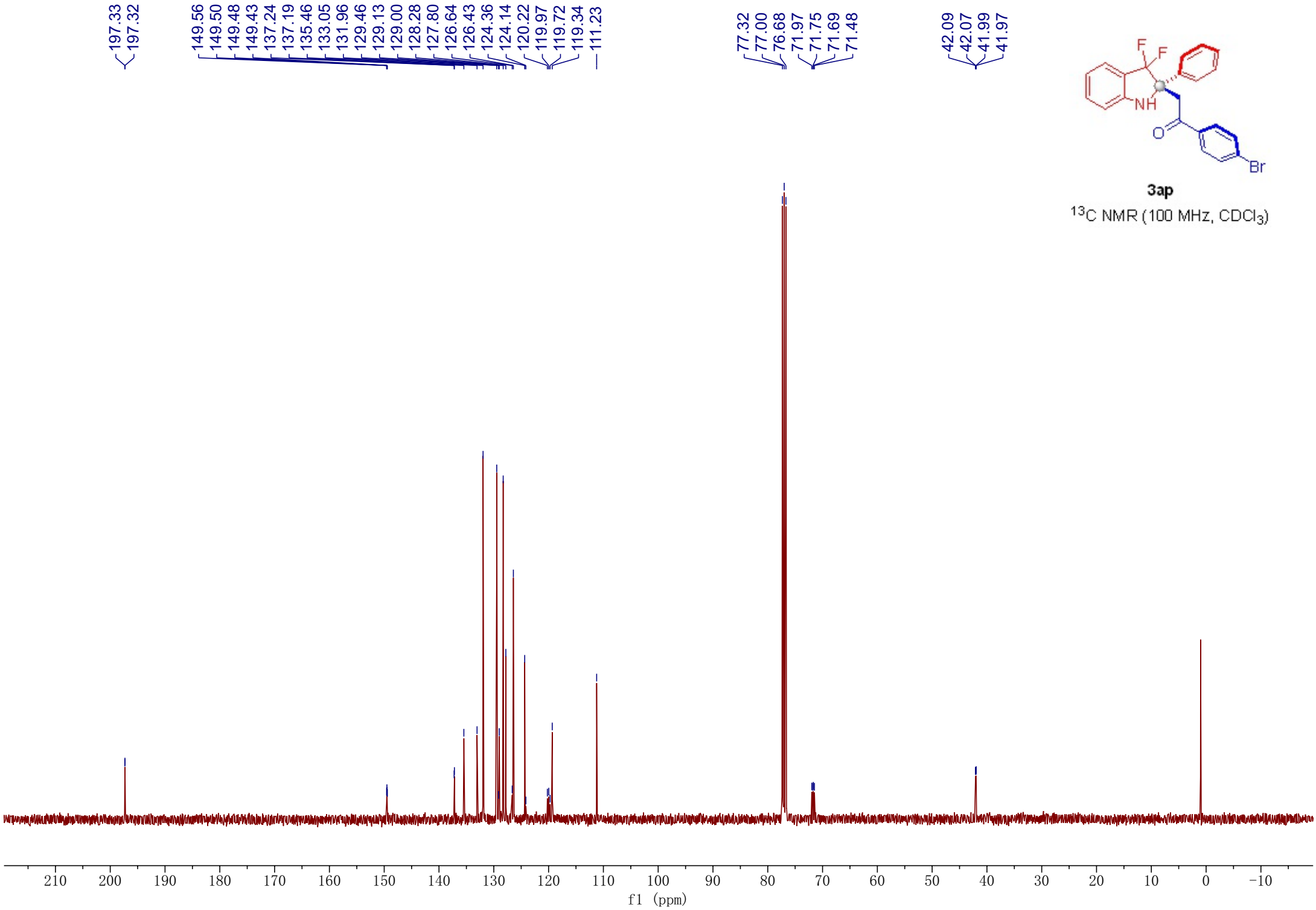


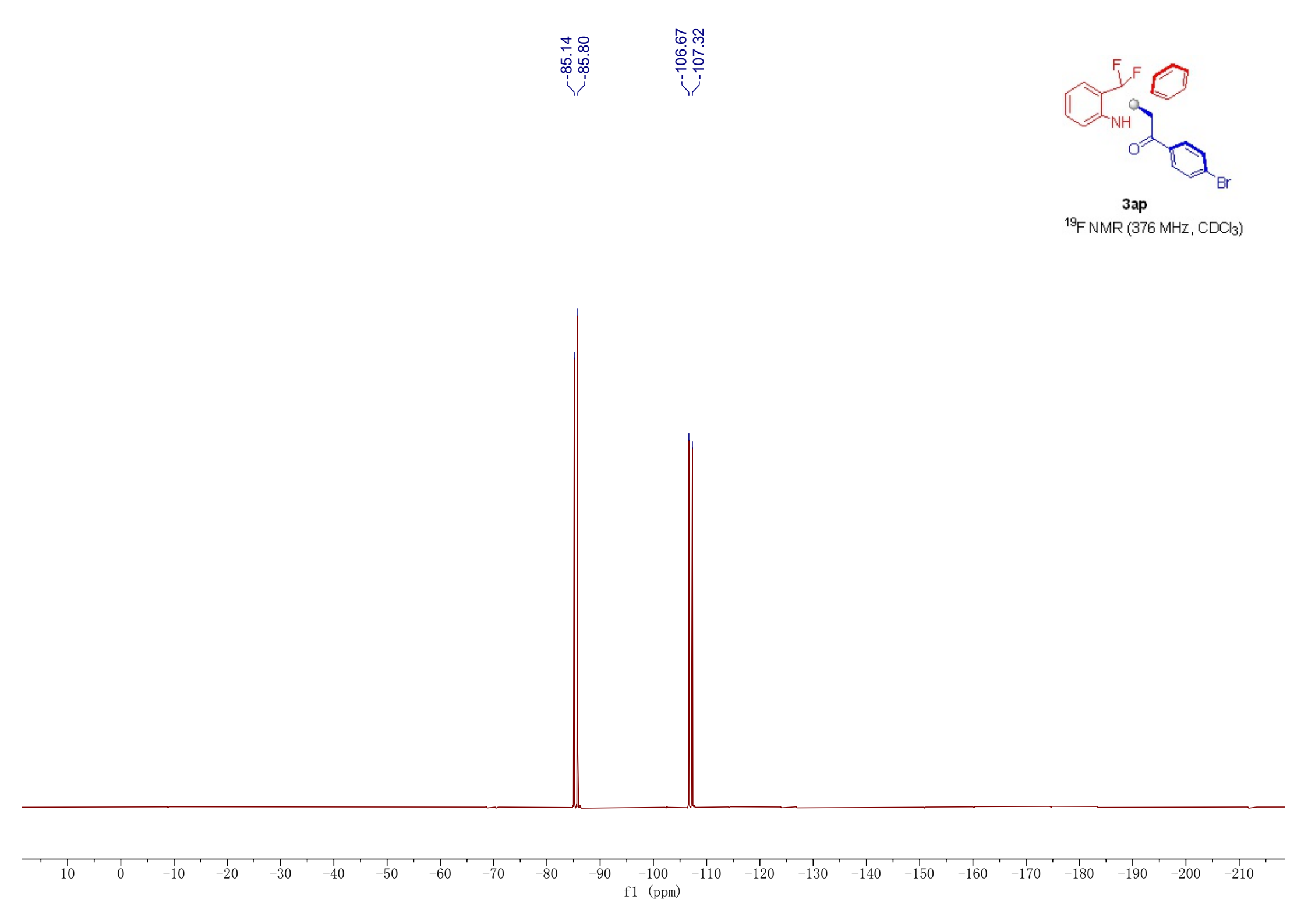
3ap

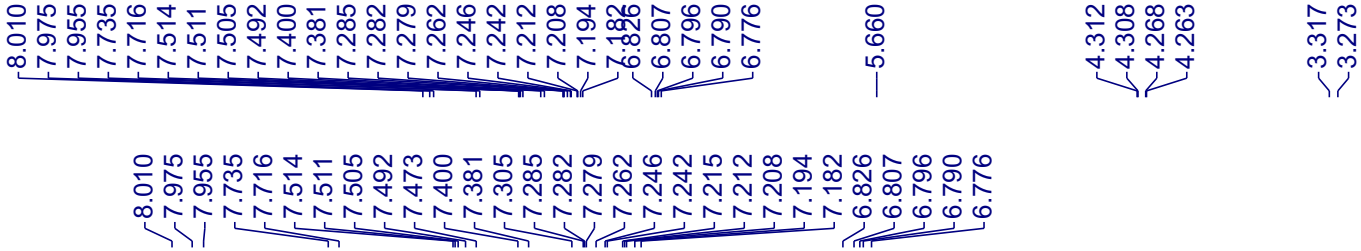
^{1}H NMR (400 MHz, $CDCl_3$)





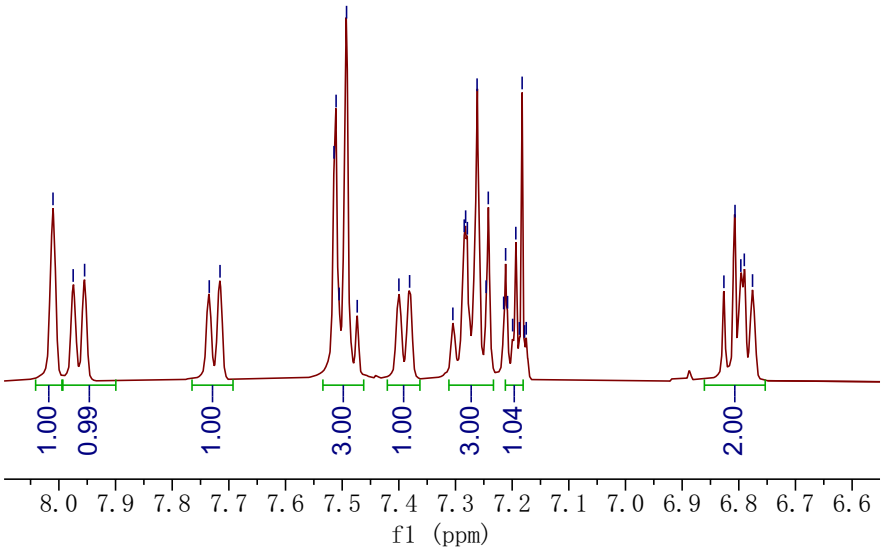

197.33
197.32
149.56
149.50
149.48
149.43
137.24
137.19
135.46
133.05
131.96
129.46
129.13
129.00
128.28
127.80
126.64
126.43
124.36
124.14
120.22
119.97
119.72
119.34
111.23
77.32
77.00
76.68
71.97
71.75
71.69
71.48
42.09
42.07
41.99
41.97
F
F
NH
O
Br
3ap
13C NMR (100 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

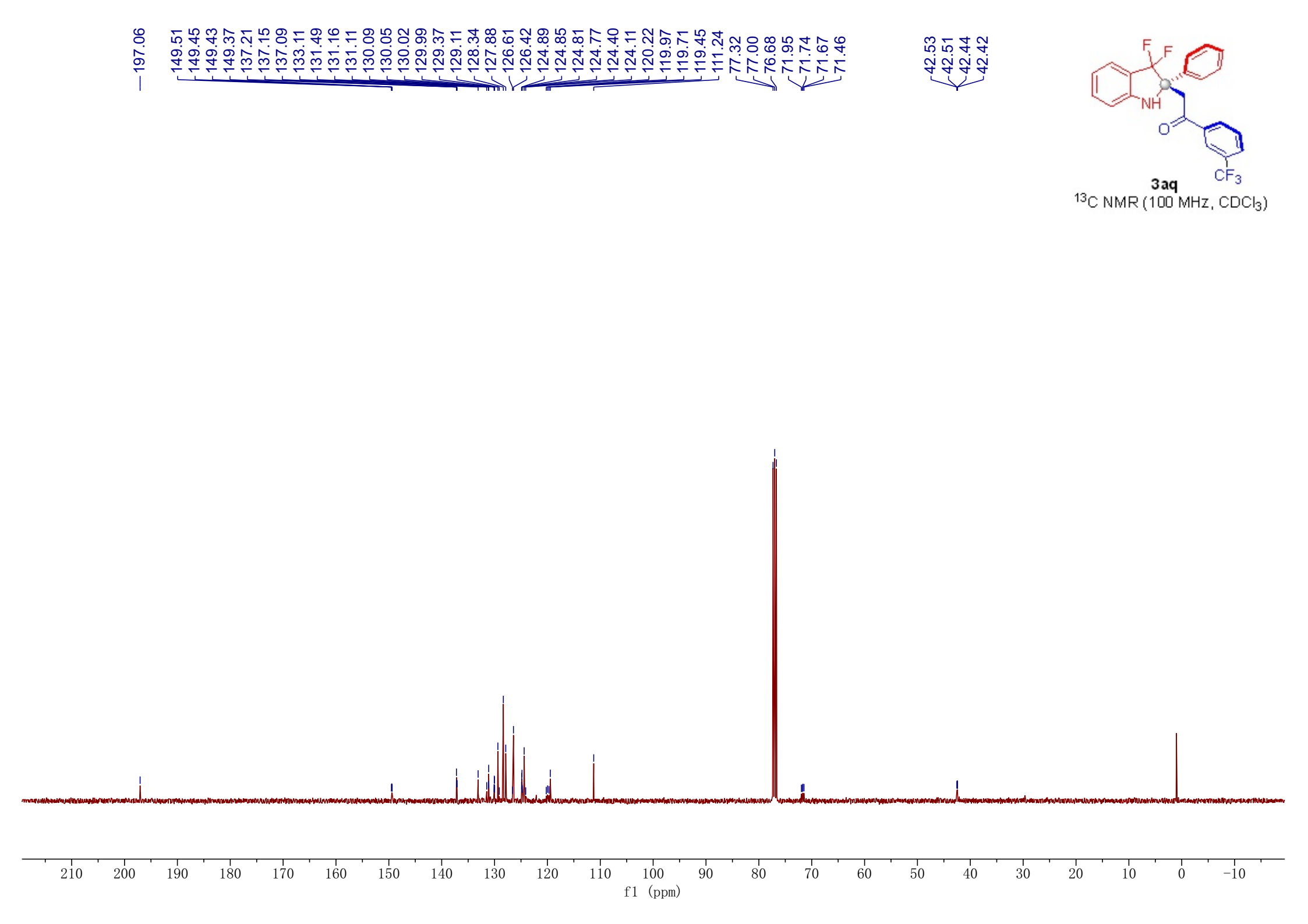

-85.14
-85.80
-106.67
-107.32
F
F
NH
O
Br
3ap
19F NMR (376 MHz, CDCl3)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

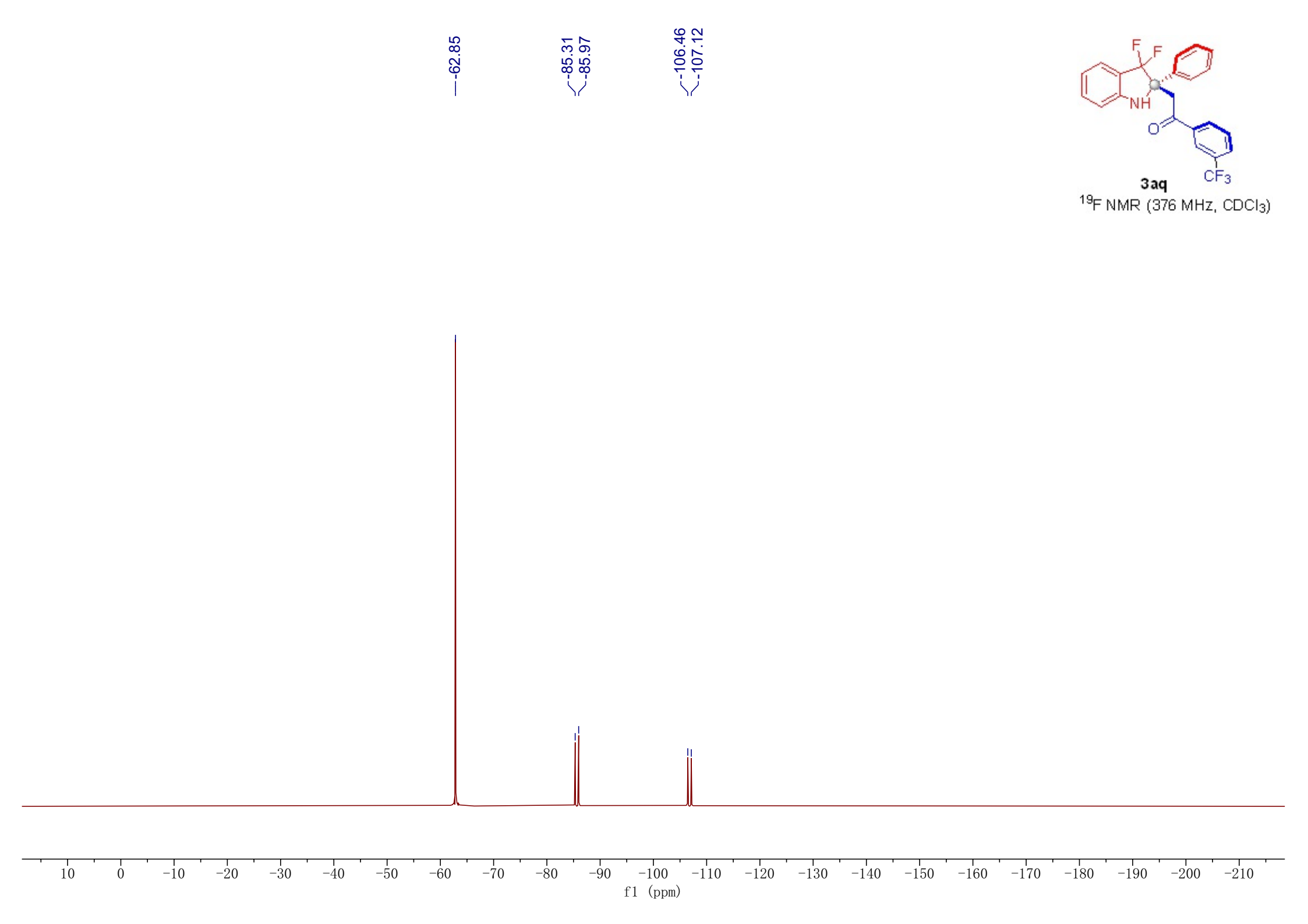


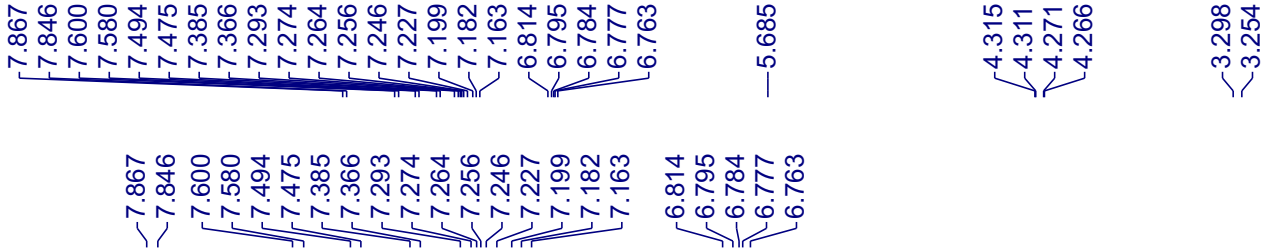
3aq

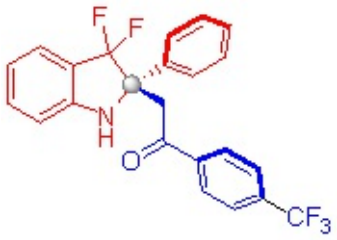
^{1}H NMR (400 MHz, $CDCl_3$)




197.06
149.51
149.45
149.43
149.37
137.21
137.15
137.09
133.11
131.49
131.16
131.11
130.09
130.05
130.02
129.99
129.37
129.11
128.34
127.88
126.61
126.42
124.89
124.85
124.81
124.77
124.40
124.11
120.22
119.97
119.71
119.45
111.24
77.32
77.00
76.68
71.95
71.74
71.67
71.46
42.53
42.51
42.44
42.42
F
F
NH
O
CF3
3aq
13C NMR (100 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

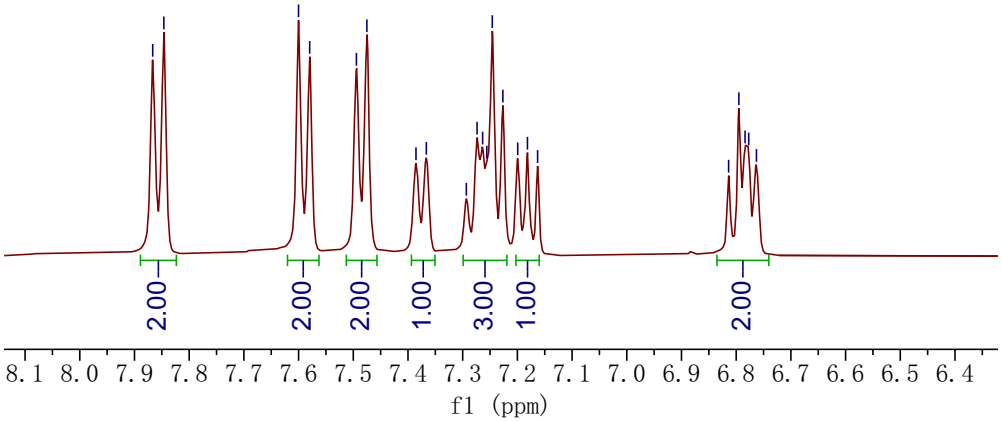

-62.85
-85.31
-85.97
-106.46
-107.12
F
F
NH
O
CF3
3aq
19F NMR (376 MHz, CDCl3)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

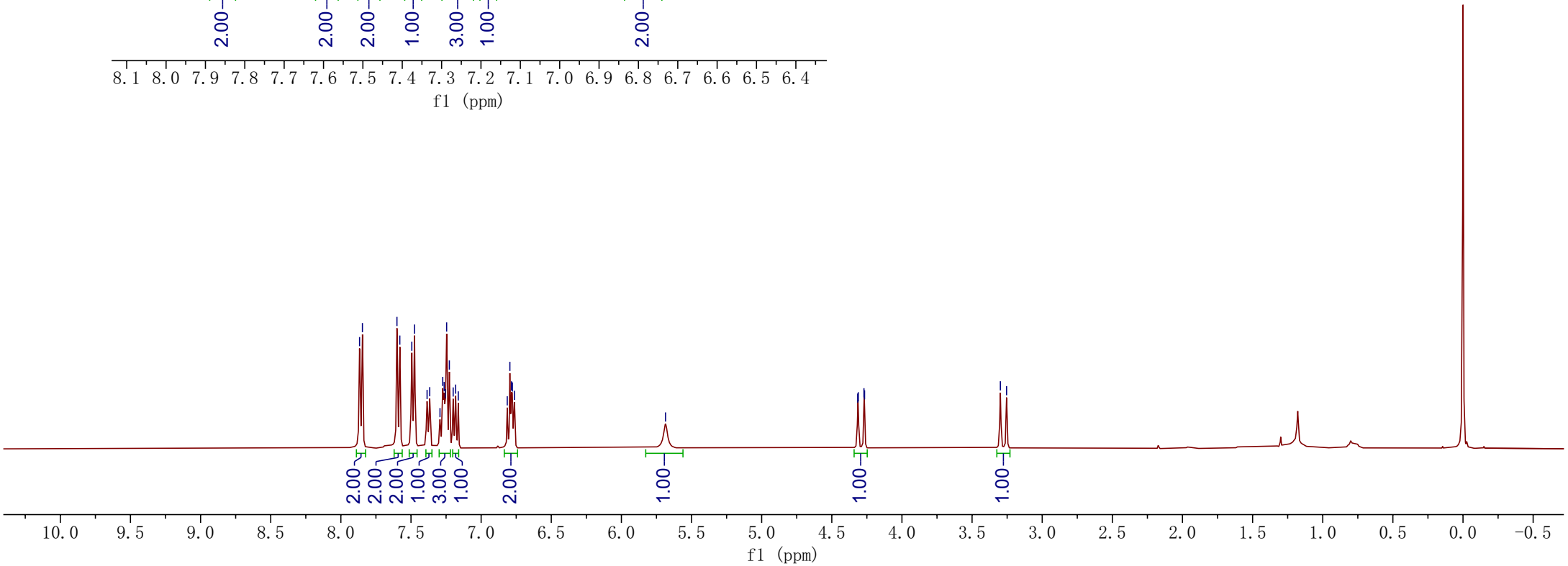


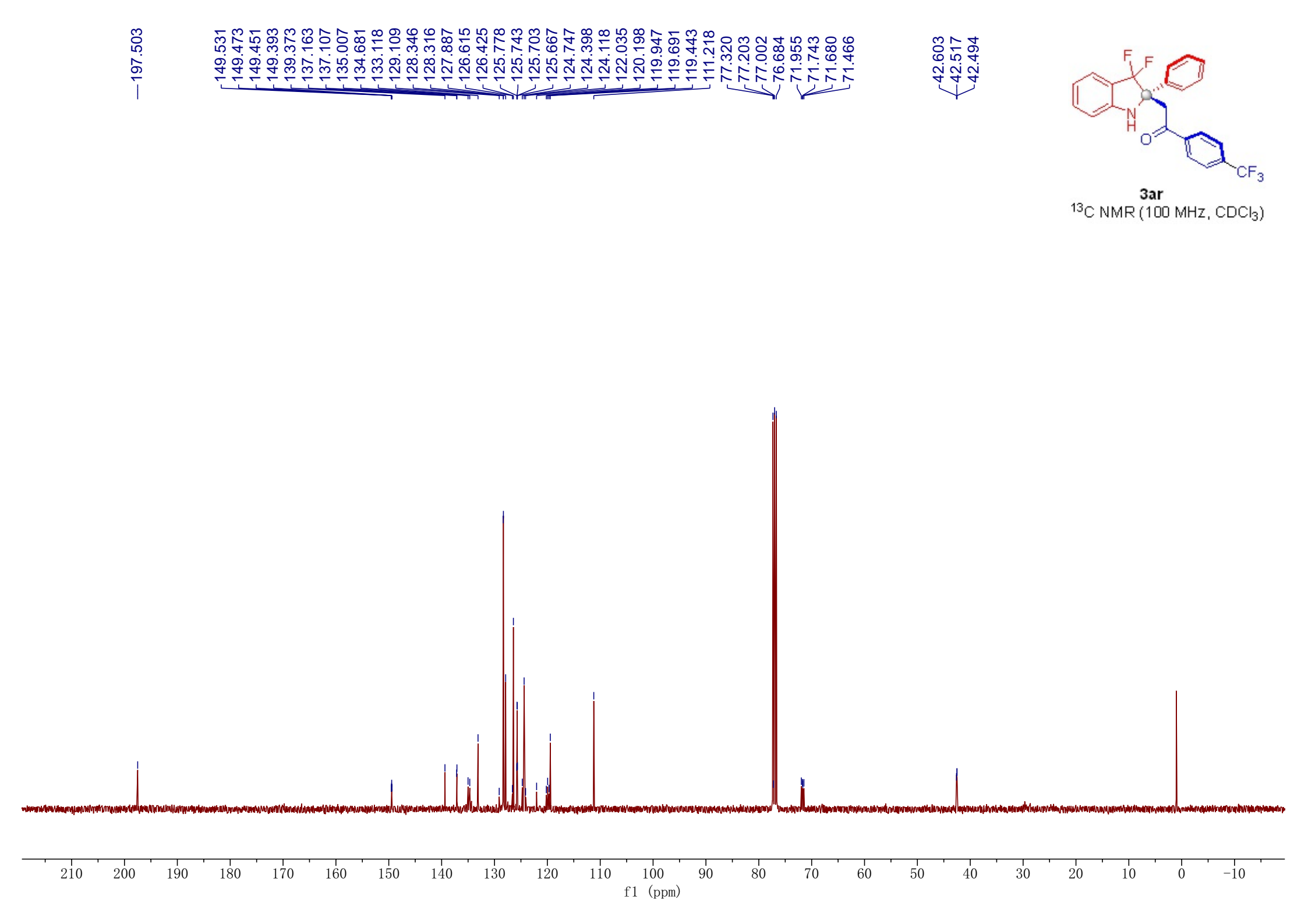


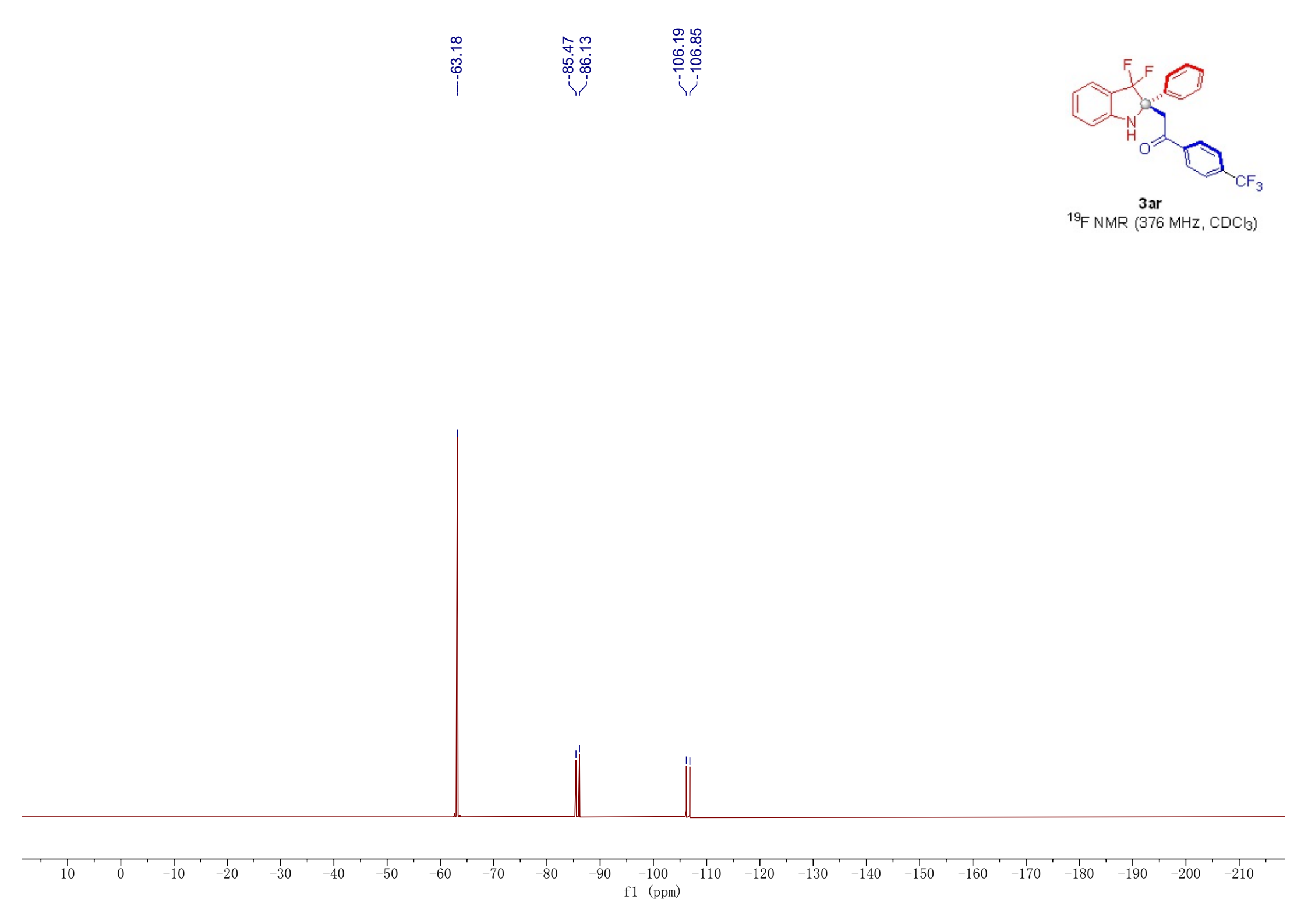
3ar

^{1}H NMR (400 MHz, $CDCl_3$)



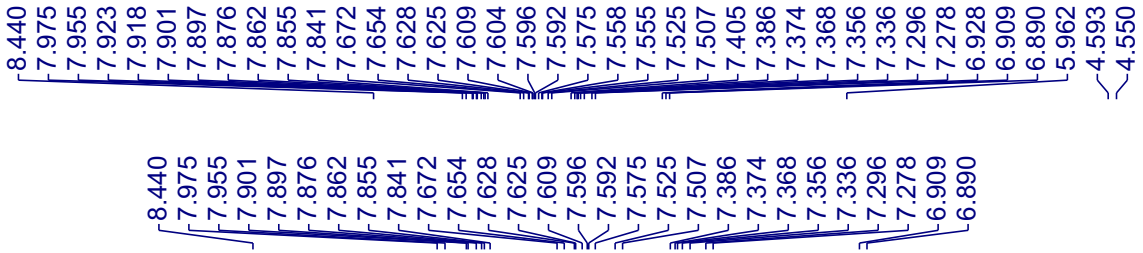



197.503
149.531
149.473
149.451
149.393
139.373
137.163
137.107
135.007
134.681
133.118
129.109
128.346
128.316
127.887
126.615
126.425
125.778
125.743
125.703
125.667
124.747
124.398
124.118
122.035
120.198
119.947
119.691
119.443
111.218
77.320
77.203
77.002
76.684
71.955
71.743
71.680
71.466
42.603
42.517
42.494
F
F
N
H
O
CF3
3ar
13C NMR (100 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



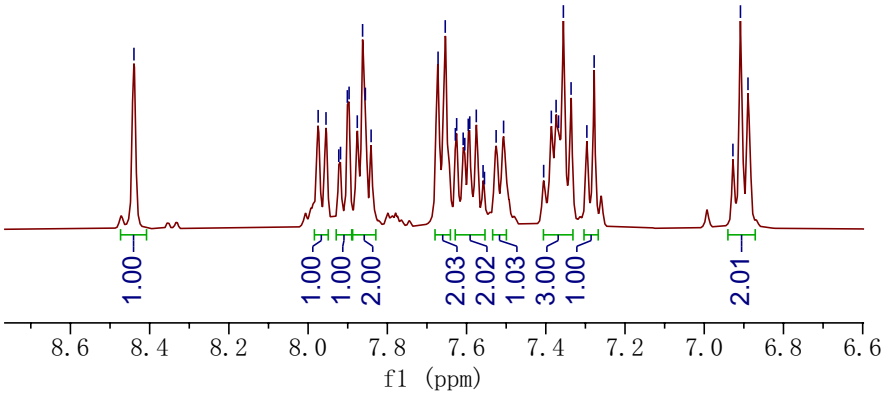
3ar

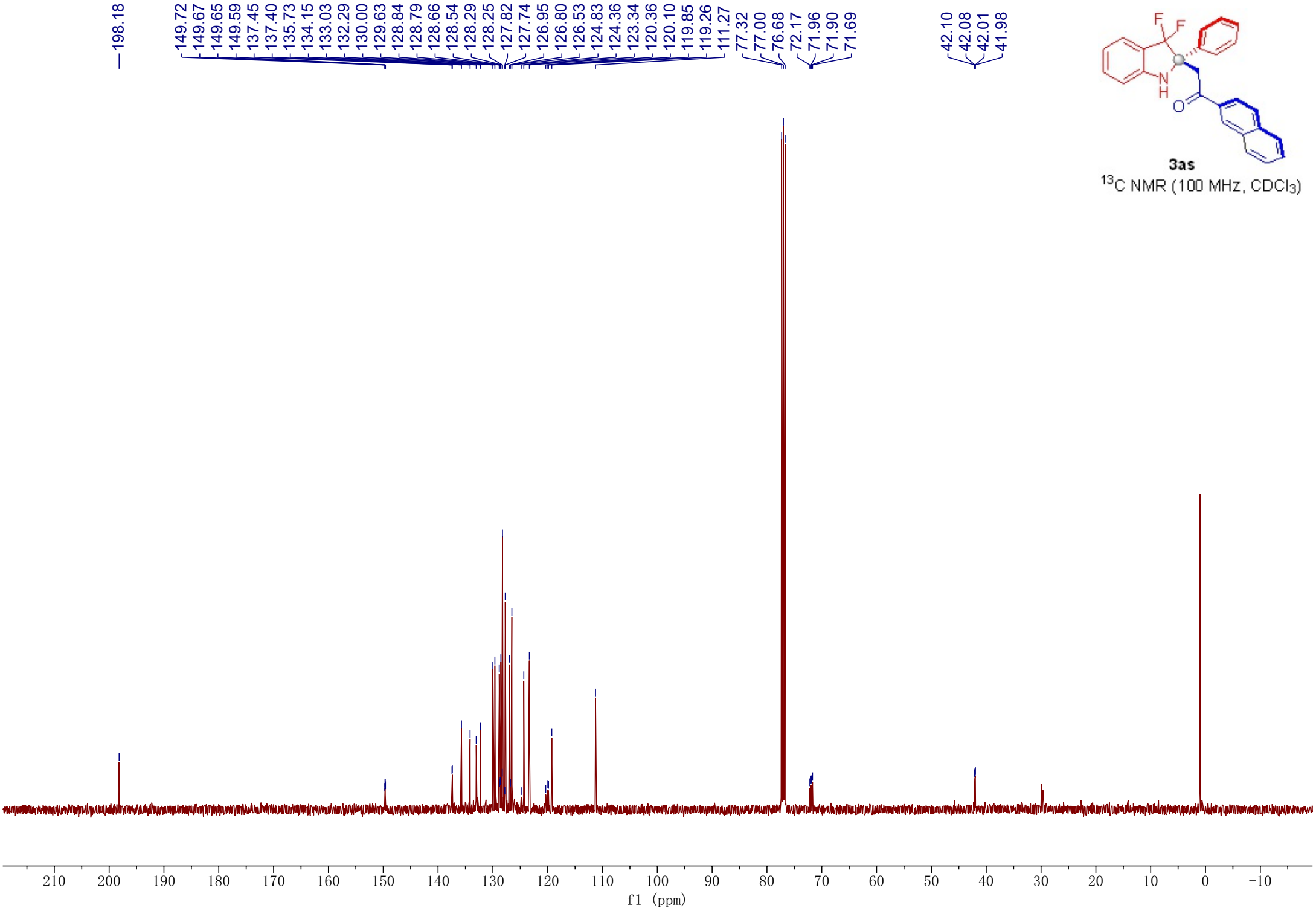
^{19}F NMR (376 MHz, $CDCl_3$)

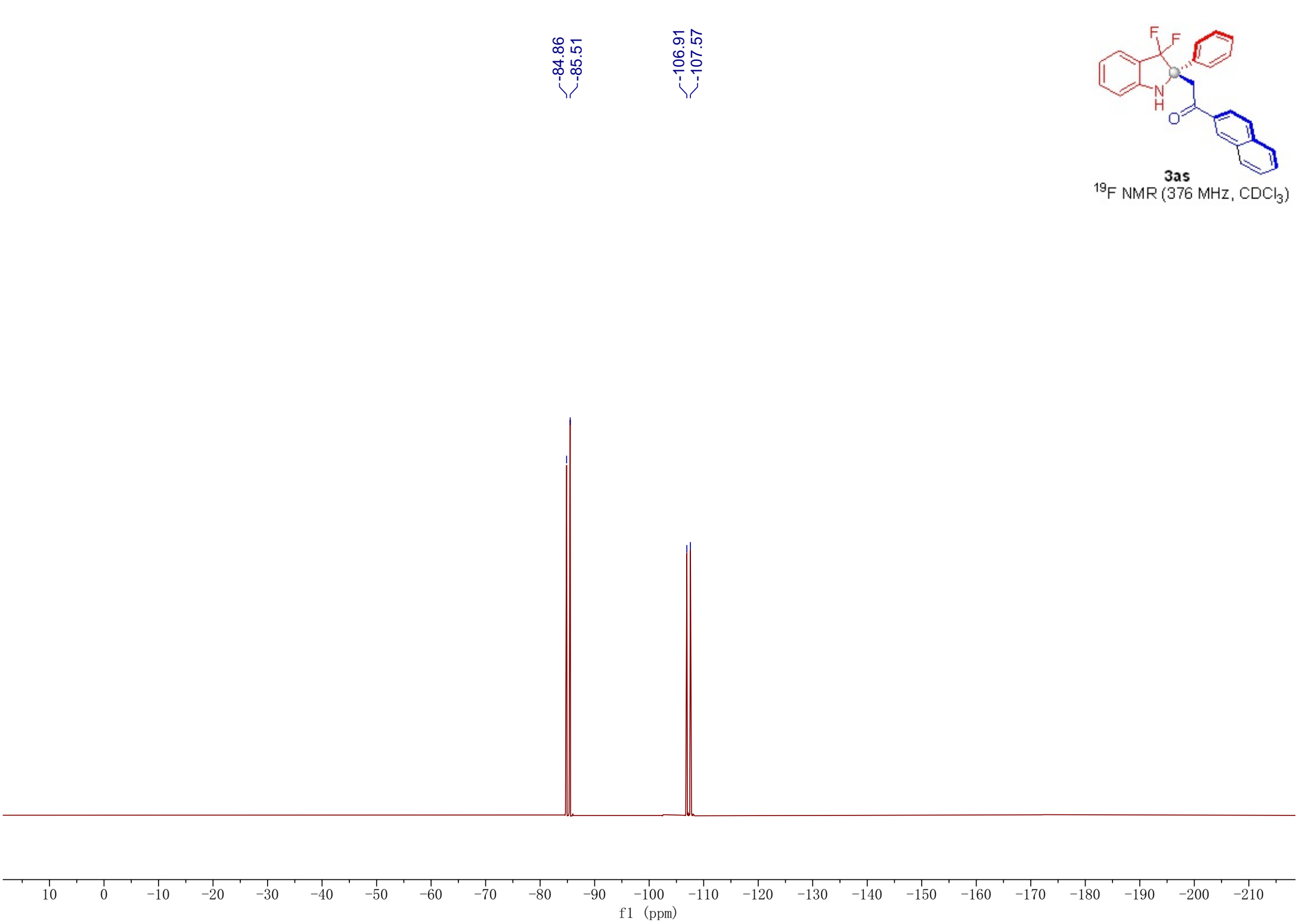


3as

^{1}H NMR (400 MHz, $CDCl_3$)

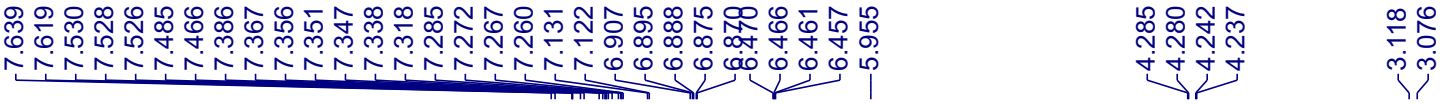



198.18
149.72
149.67
149.65
149.59
137.45
137.40
135.73
134.15
133.03
132.29
130.00
129.63
128.84
128.79
128.66
128.54
128.29
128.25
127.82
127.74
126.95
126.80
126.53
124.83
124.36
123.34
120.36
120.10
119.85
119.26
111.27
77.32
77.00
76.68
72.17
71.96
71.90
71.69
42.10
42.08
42.01
41.98
F
F
N
H
O
3as
13C NMR (100 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



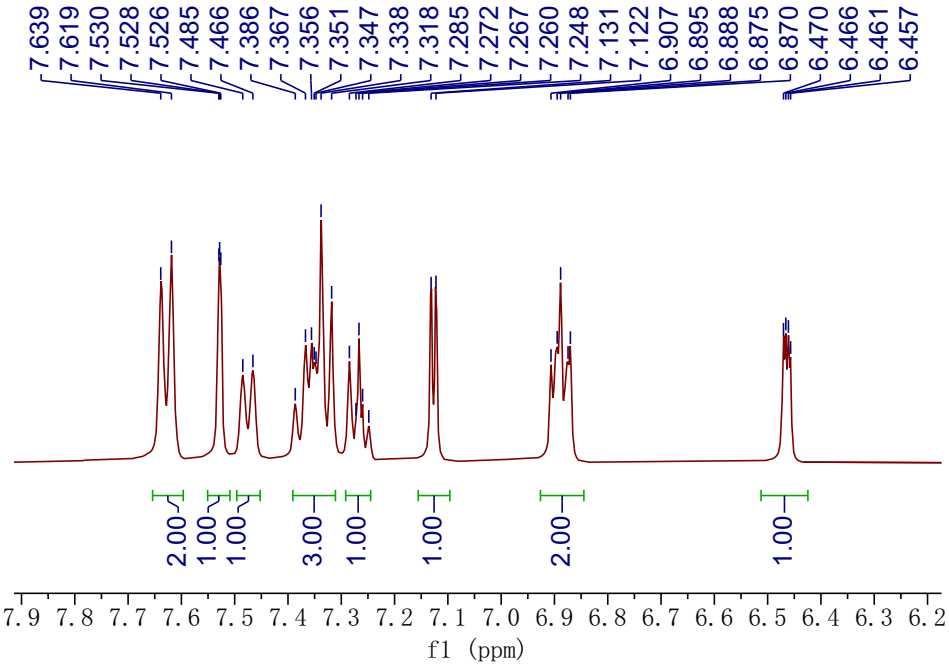
3as

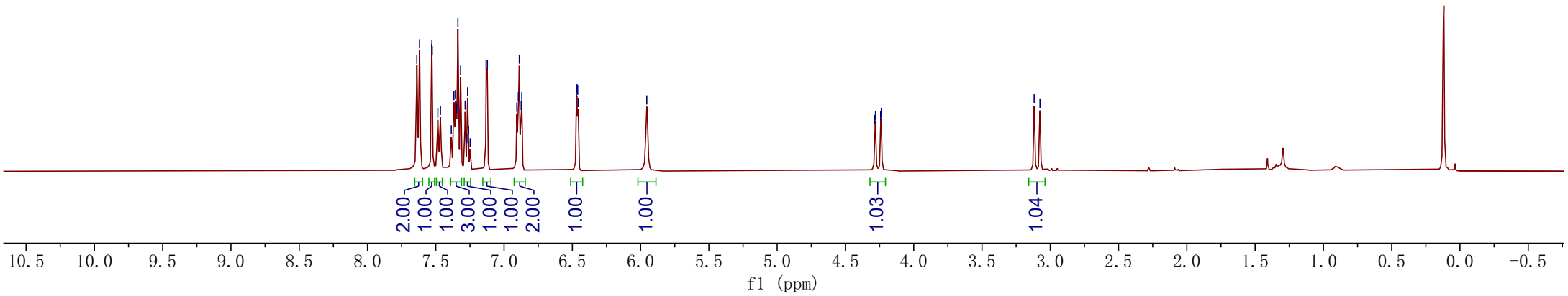
^{19}F NMR (376 MHz, $CDCl_3$)

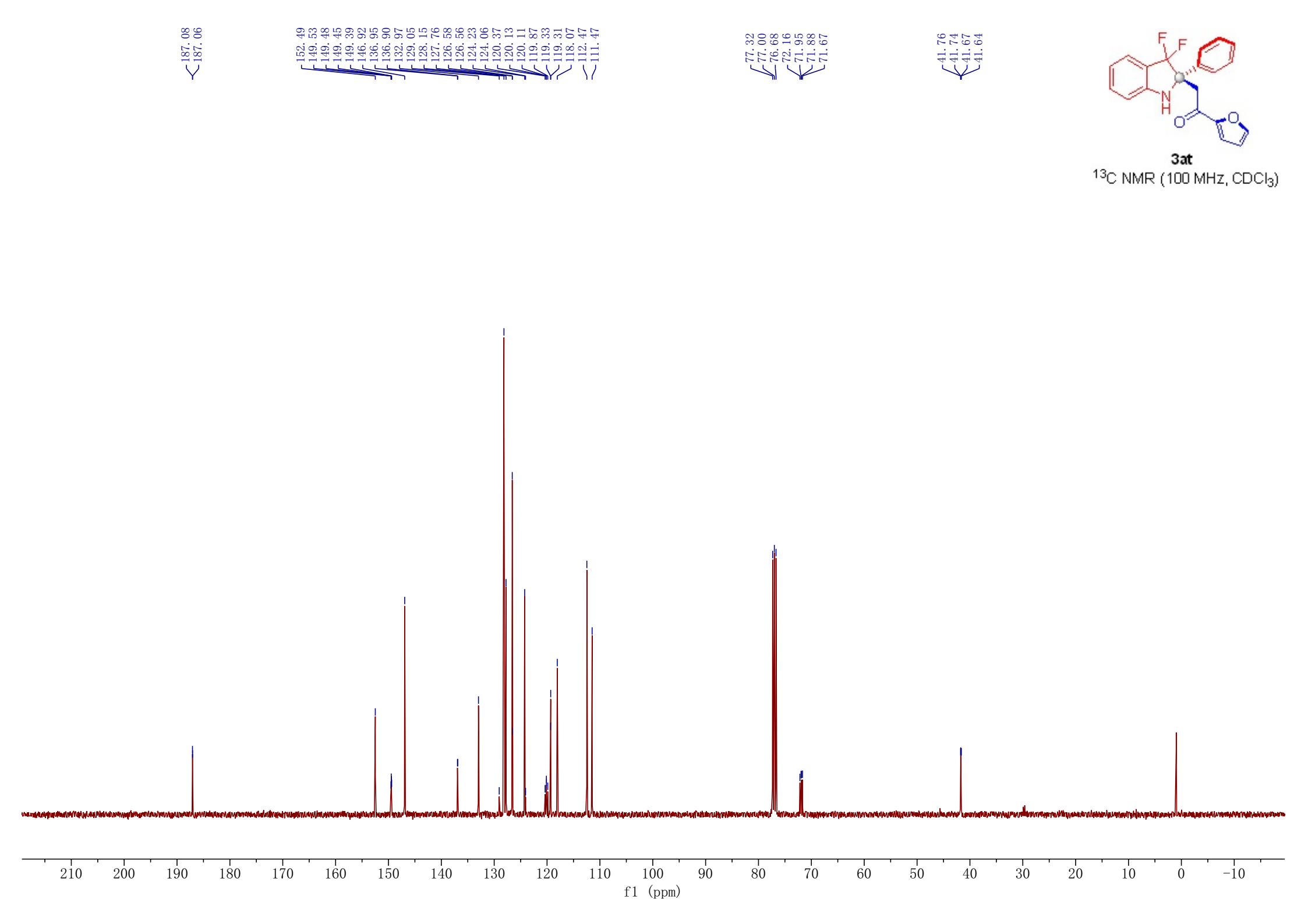


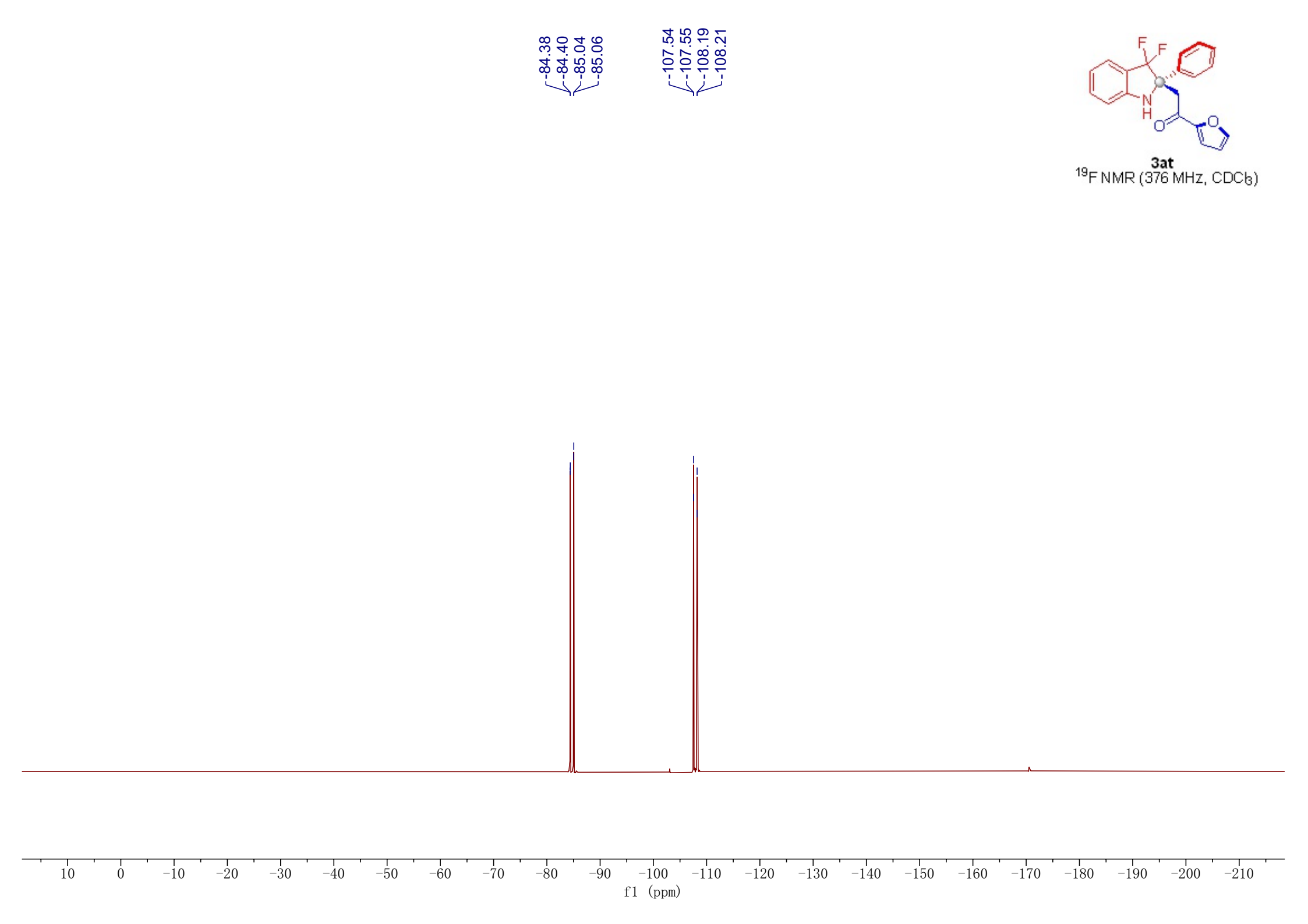
3at

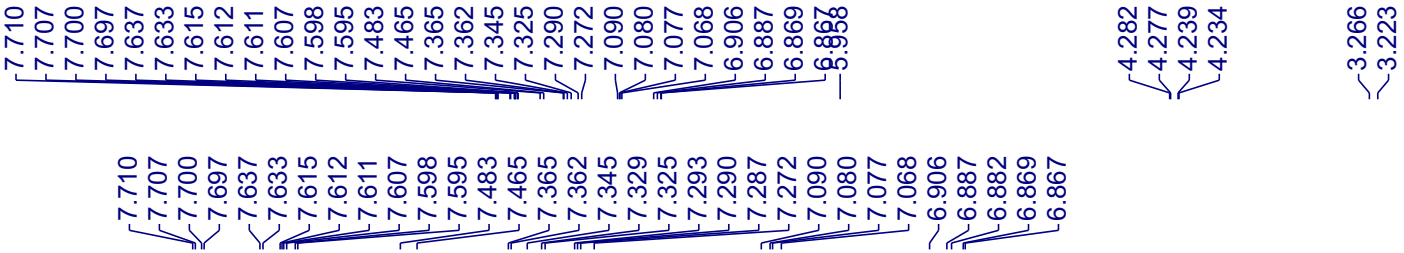
^{1}H NMR (400 MHz, $CDCl_3$)





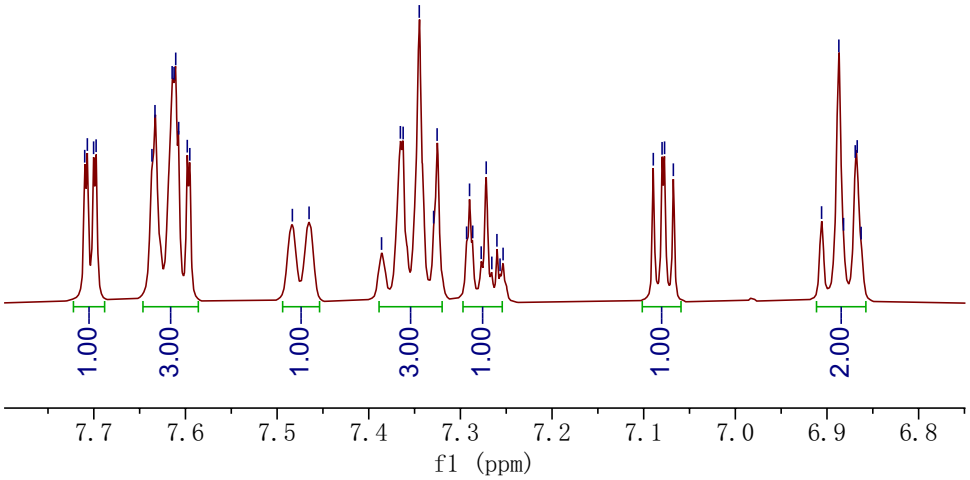

187.08
187.06
152.49
149.53
149.48
149.45
149.39
146.92
136.95
136.90
132.97
129.05
128.15
127.76
126.58
126.56
124.23
124.06
120.37
120.13
120.11
119.87
119.33
119.31
118.07
112.47
111.47
77.32
77.00
76.68
72.16
71.95
71.88
71.67
41.76
41.74
41.67
41.64
F
F
N
H
O
O
3at
13C NMR (100 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

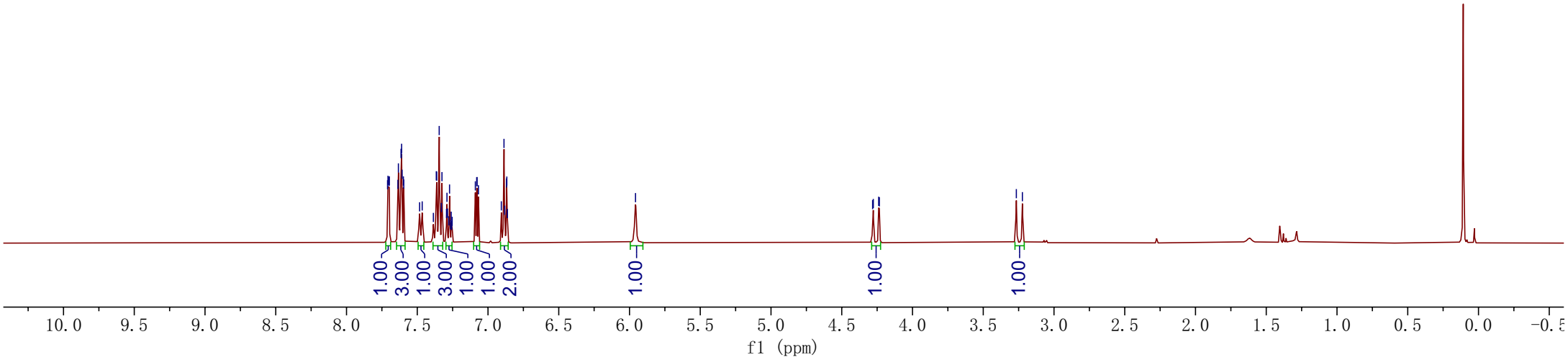

-84.38
-84.40
-85.04
-85.06
-107.54
-107.55
-108.19
-108.21
F
F
N
H
O
O
3at
19F NMR (376 MHz, CDCl3)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

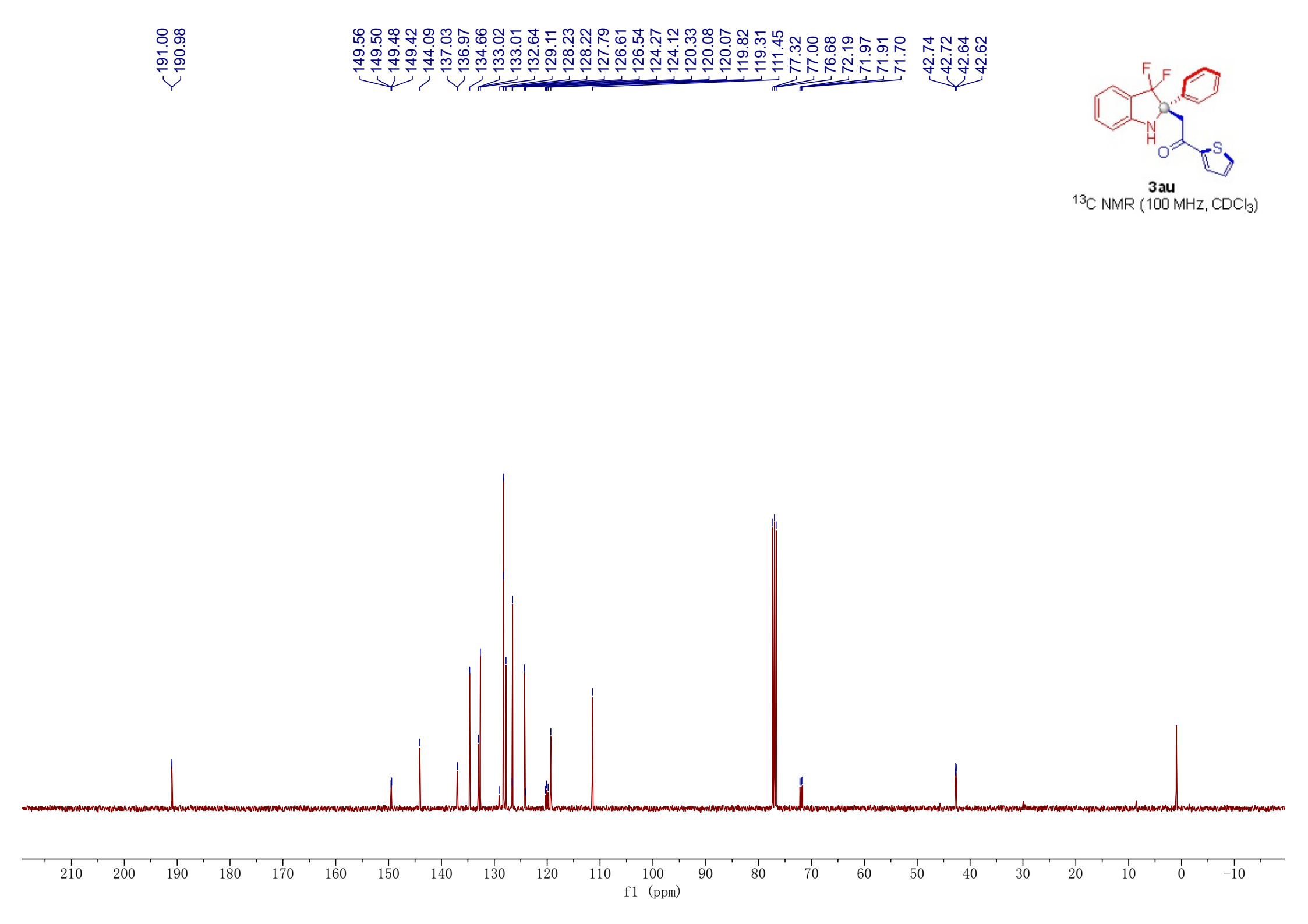


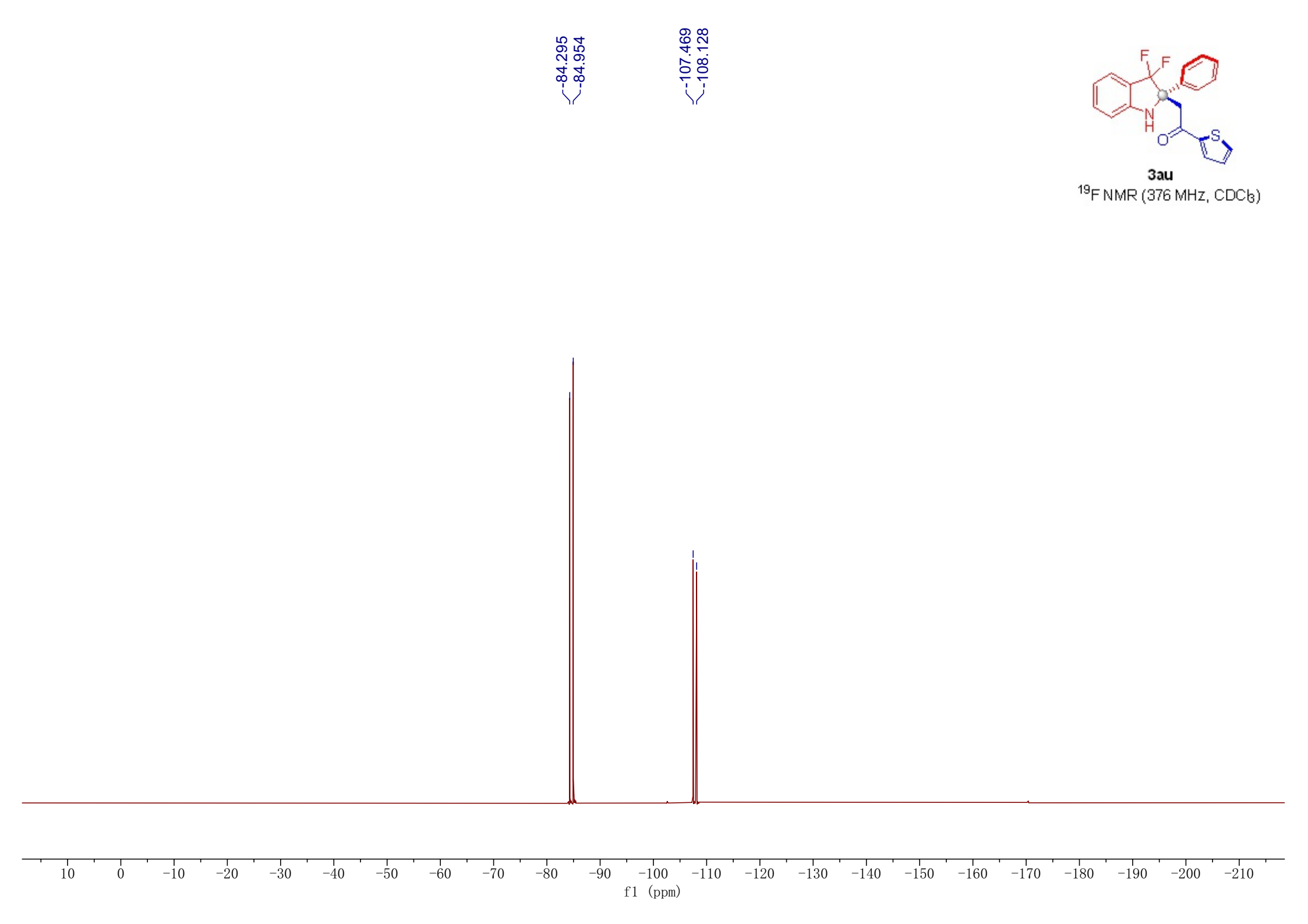
3au

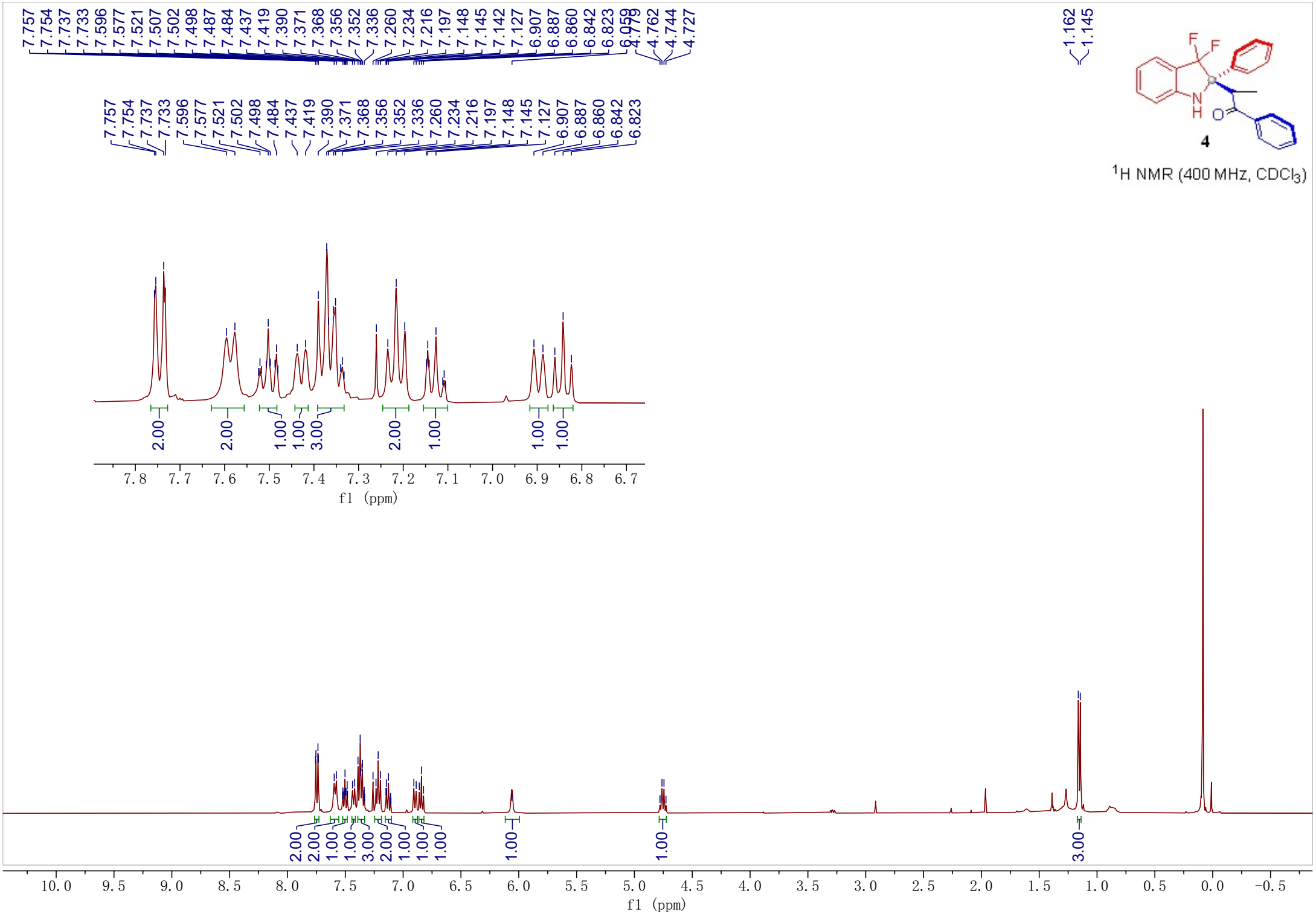
^{1}H NMR (400 MHz, $CDCl_3$)



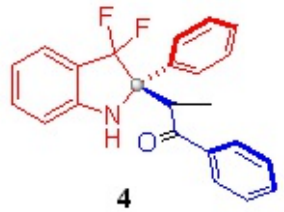



191.00
190.98
149.56
149.50
149.48
149.42
144.09
137.03
136.97
134.66
133.02
133.01
132.64
129.11
128.23
128.22
127.79
126.61
126.54
124.27
124.12
120.33
120.08
120.07
119.82
119.31
111.45
77.32
77.00
76.68
72.19
71.97
71.91
71.70
42.74
42.72
42.64
42.62
F
F
N
H
O
S
3au
13C NMR (100 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


-84.295
-84.954
-107.469
-108.128
F
F
N
H
O
S
3au
^{19}F NMR (376 MHz, $CDCl_3$)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

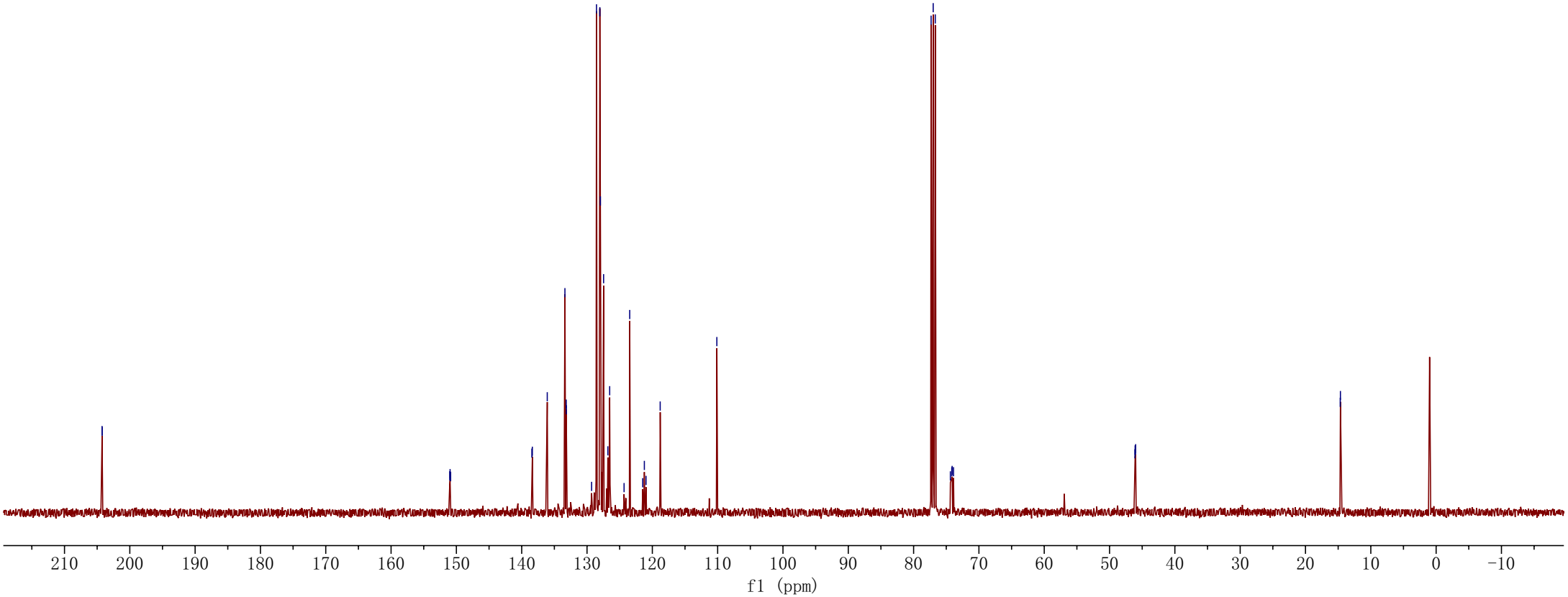

7.757
7.754
7.737
7.733
7.596
7.577
7.521
7.507
7.502
7.498
7.487
7.484
7.437
7.419
7.390
7.371
7.368
7.356
7.352
7.336
7.260
7.234
7.216
7.197
7.148
7.145
7.142
7.127
6.907
6.887
6.860
6.842
6.823
6.959
4.779
4.762
4.744
4.727
1.162
1.145
F
F
N
H
O
4
1H NMR (400 MHz, CDCl3)
2.00
2.00
1.00
1.00
3.00
2.00
1.00
1.00
1.00
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
6.9
6.8
6.7
f1 (ppm)
2.00
2.00
1.00
1.00
3.00
2.00
1.00
1.00
1.00
1.00
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

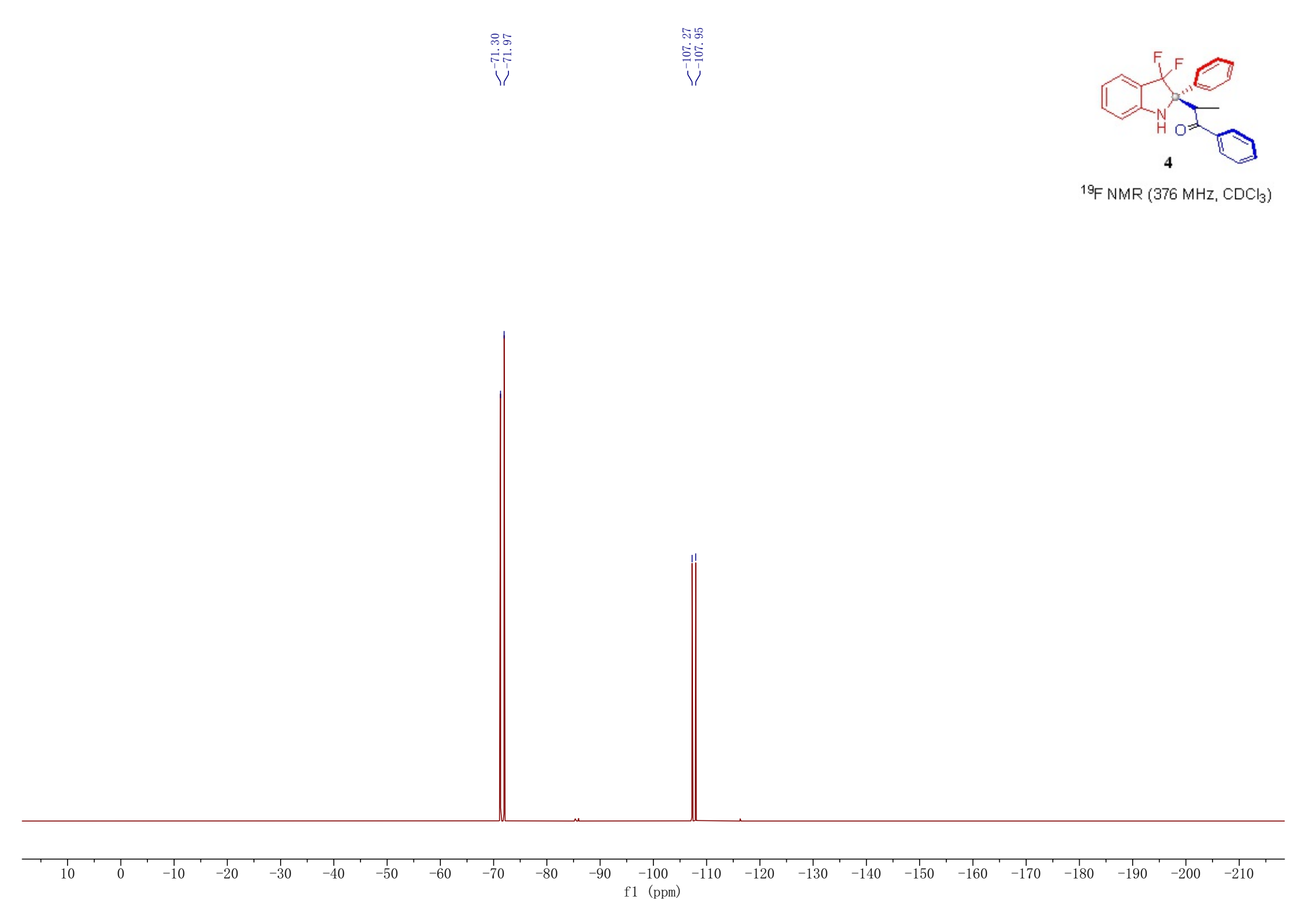
204.25
204.24
151.02
150.97
150.94
150.88
138.44
138.37
136.09
133.38
133.18
133.16
129.30
128.55
128.04
127.95
127.46
126.81
126.53
124.33
123.46
121.47
121.22
120.97
118.80
110.12
77.32
77.00
76.68
74.37
74.16
74.10
73.89
46.11
46.09
46.04
46.00
14.68
14.65

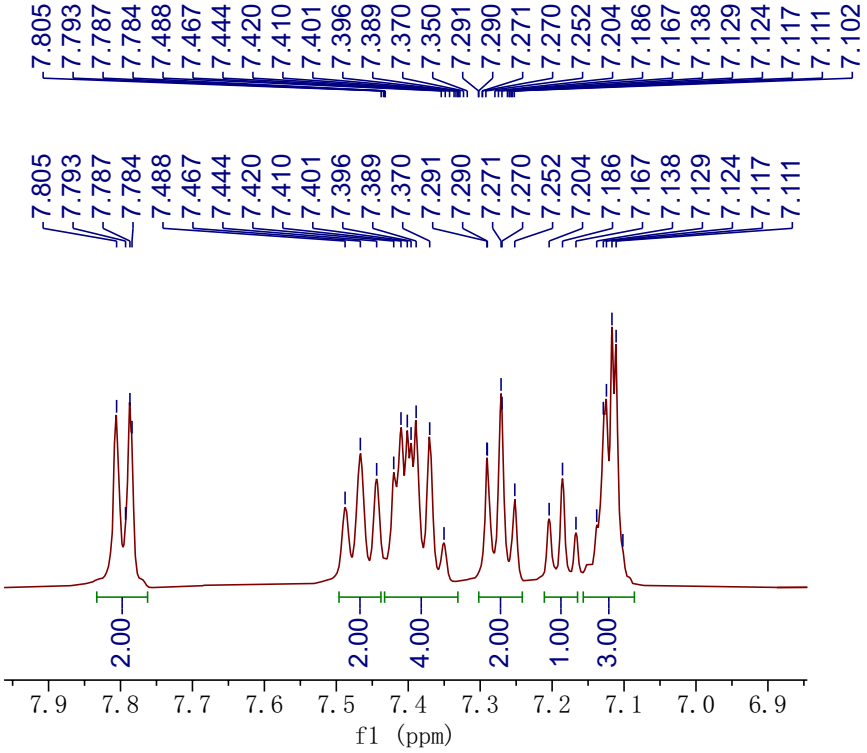


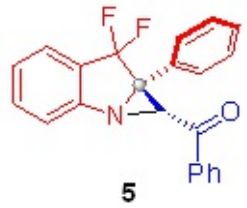
4

^{13}C NMR (100 MHz, $CDCl_3$)



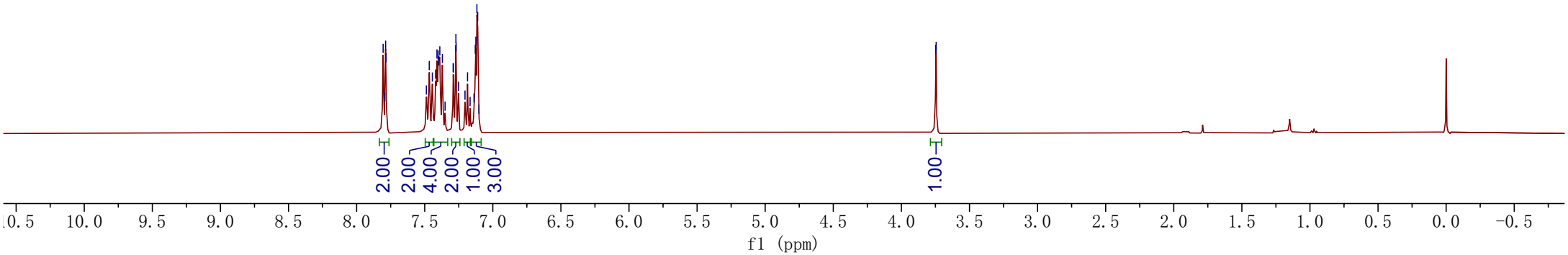

-71.30
-71.97
-107.27
-107.95
F
F
N
H
O
4
19F NMR (376 MHz, CDCl3)
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

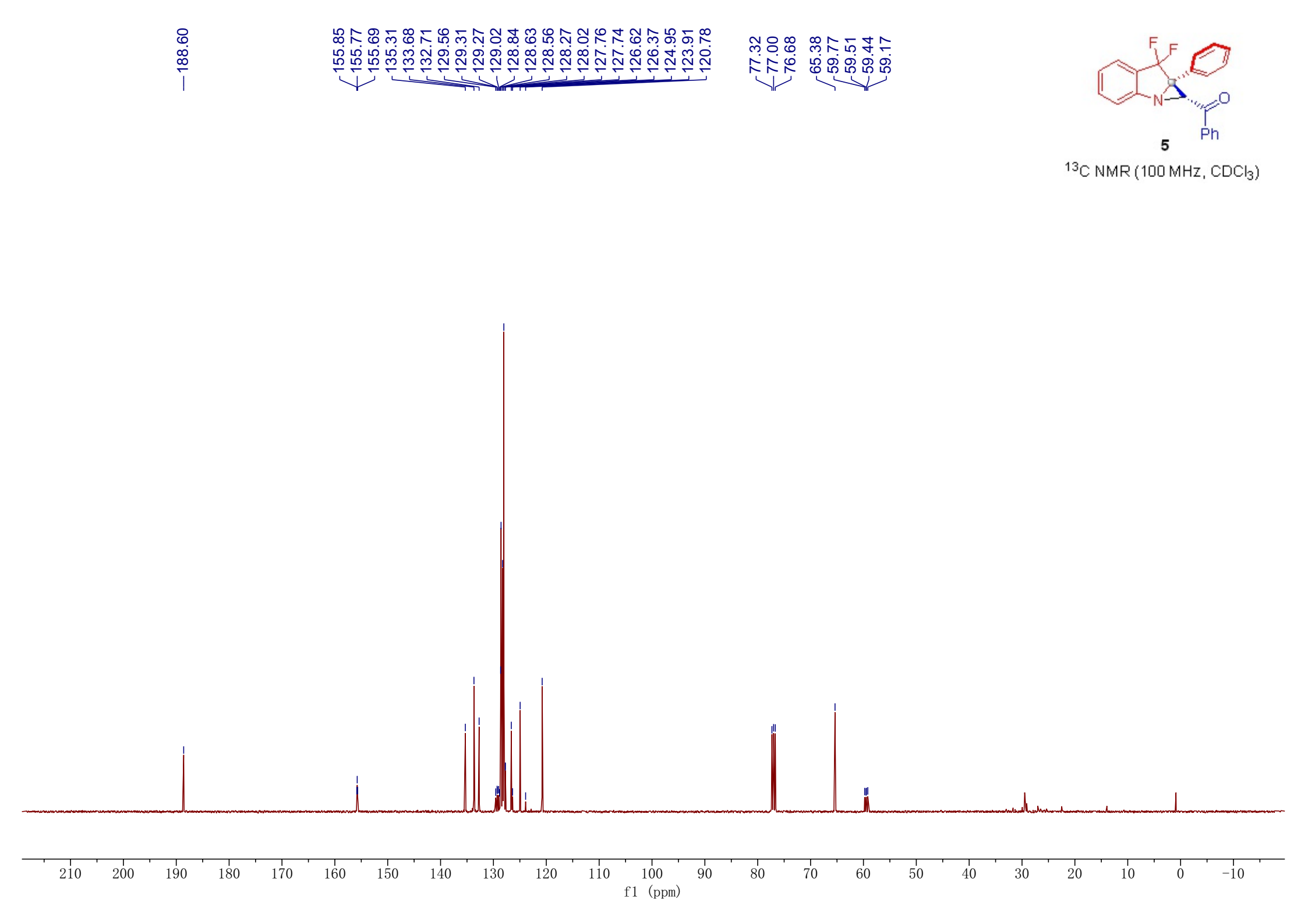


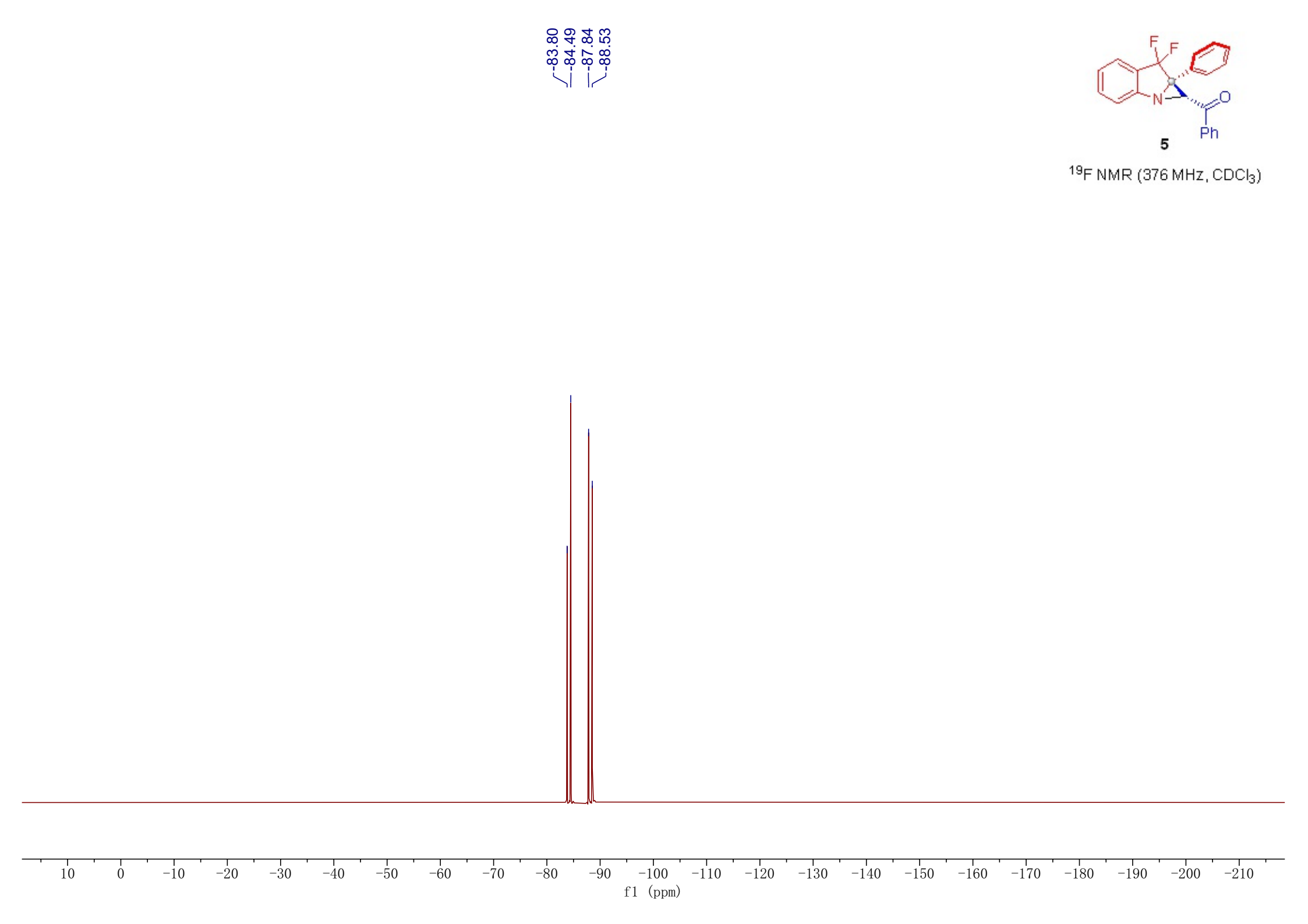


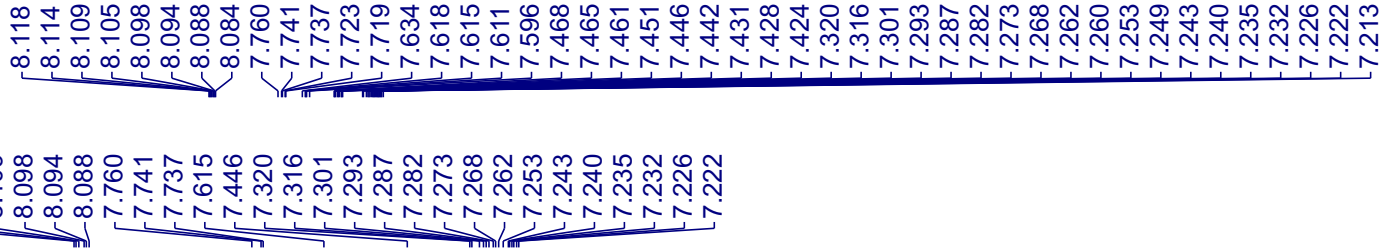
5

^{1}H NMR (400 MHz, $CDCl_3$)



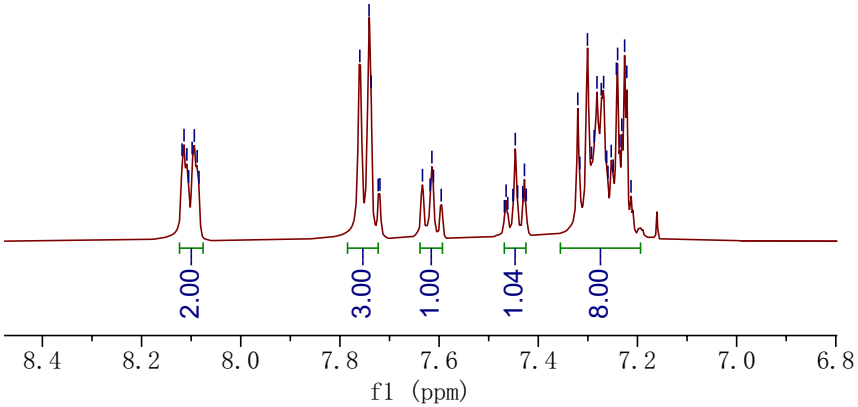

188.60
155.85
155.77
155.69
135.31
133.68
132.71
129.56
129.31
129.27
129.02
128.84
128.63
128.56
128.27
128.02
127.76
127.74
126.62
126.37
124.95
123.91
120.78
77.32
77.00
76.68
65.38
59.77
59.51
59.44
59.17
F
F
N
O
Ph
5
13C NMR (100 MHz, CDCl3)
f1 (ppm)

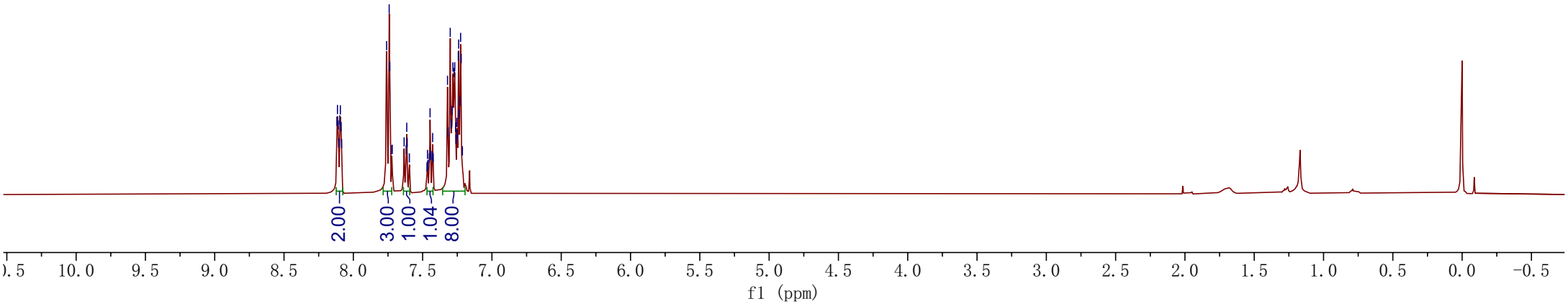

-83.80
-84.49
-87.84
-88.53
F
F
N
O
Ph
5
^{19}F NMR (376 MHz, $CDCl_3$)
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

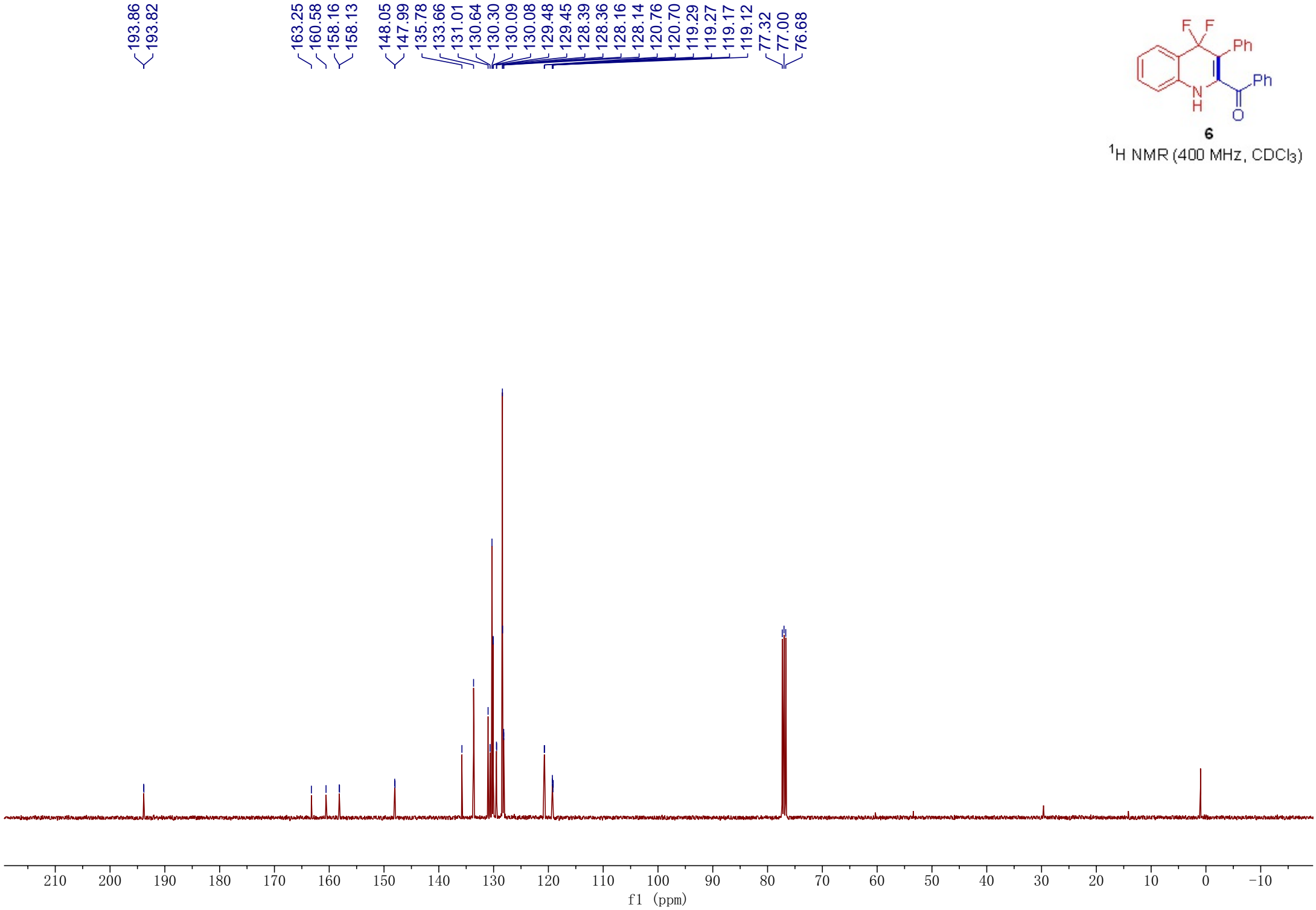


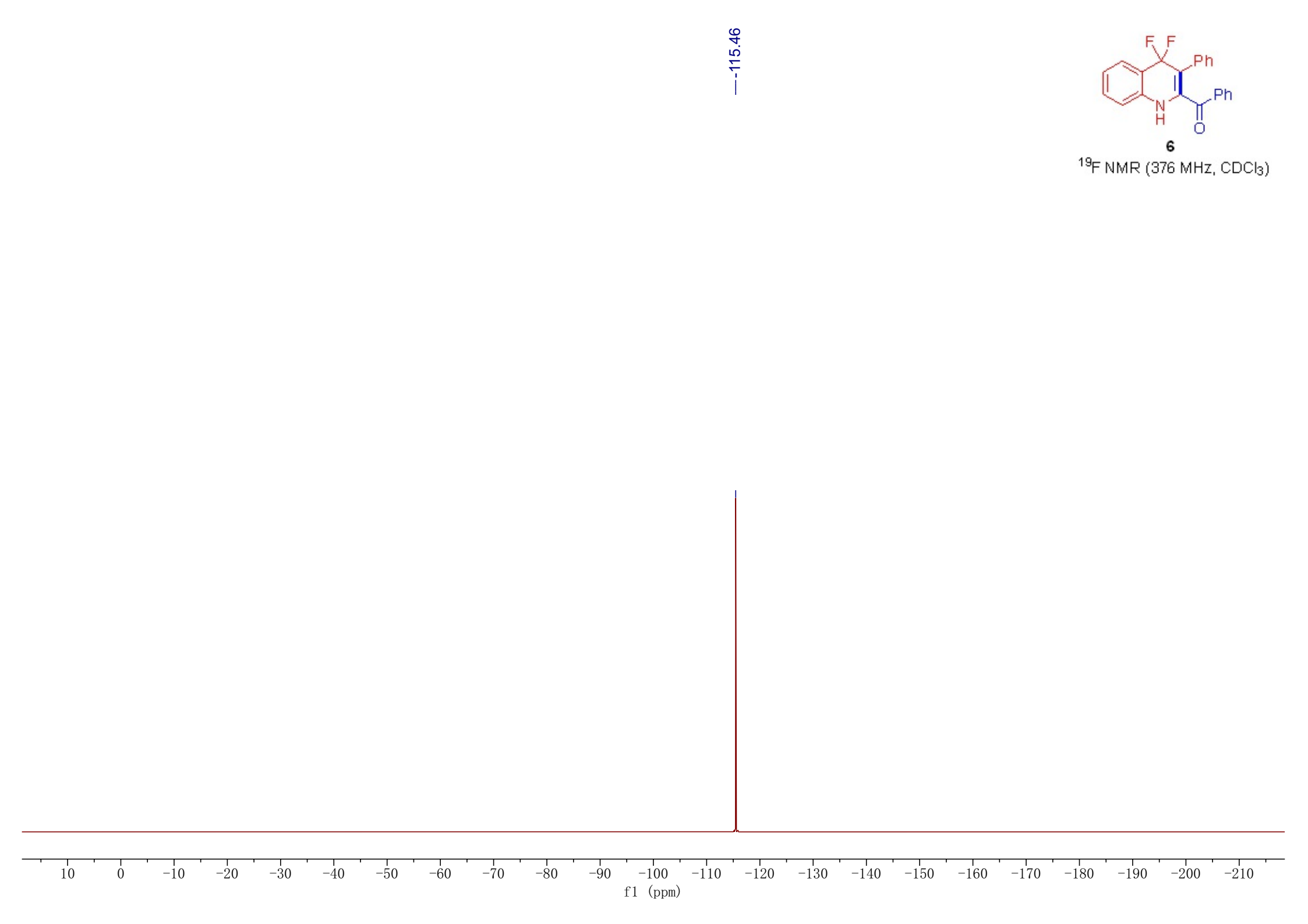
6

^{1}H NMR (400 MHz, $CDCl_3$)






193.86
193.82
163.25
160.58
158.16
158.13
148.05
147.99
135.78
133.66
131.01
130.64
130.30
130.09
130.08
129.48
129.45
128.39
128.36
128.16
128.14
120.76
120.70
119.29
119.27
119.17
119.12
77.32
77.00
76.68
F
F
Ph
Ph
N
H
O
6
1H NMR (400 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


-115.46
F
F
Ph
Ph
N
H
O
6
19F NMR (376 MHz, CDCl3)
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)