

Supporting Information

Electrochemical Monofluoroalkylation Cyclization of *N*-Arylacrylamides to Construct Monofluorinated 2- Oxindoles

Yanxia Lv,^{a,b} Zhong-Wei Hou,^{*b} Yi Wang,^c Pinhua Li,^a and Lei Wang^{*a,b,c}

^a Advanced Research Institute and School of Pharmaceutical Sciences, Taizhou University, Jiaojiang, Zhejiang 318000, P. R. China

^b Department of Chemistry, Huaibei Normal University, Huaibei, Anhui 235000, P. R. China

^c The Second Hospital of Anhui Medical University, Hefei, Anhui 230601, P. R. China

Table of Contents

1. General Considerations.....	S2
2. General Procedure for the Electrosynthesis	S2
3. Cyclic Voltammetry Studies	S4
4. X-Ray Crystallography	S5
5. Characterization Data for the Electrolysis Products	S7
6. Synthesis and Characterization of Unknown Substrates.....	S20
7. NMR Spectra of the Compounds.....	S22

1. General Considerations

Unless otherwise noted, chemicals and materials were purchased from commercial suppliers and used without further purification. All ^1H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded on a 400 MHz Bruker FT-NMR spectrometer. Data were reported as chemical shifts in ppm relative to TMS (0.00 ppm) for ^1H NMR and CDCl_3 (77.2 ppm) for ^{13}C NMR. The abbreviations used for explaining the multiplicities were as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. The coupling constants, J , are reported in Hertz (Hz). High resolution mass spectroscopy data of the product were collected on a Thermofisher Q Exactive Accurate-Mass Q-Orbitrap LC/MS (HESI). Cyclic voltammograms were obtained on a CHI 660E potentiostat. X-Ray data were collected on a Bruker SMART APEXII instrument with an I μ S Mo microsource ($\lambda = 0.7107 \text{ \AA}$). Products were purified by flash chromatography on 200–300 mesh silica gels, SiO_2 .

2. General Procedure for the Electrosynthesis

General Procedure for the Electrosynthesis of Monofluorinated 2-Oxindoles: A 20 mL three-necked beaker-type cell (Figure S1) was charged with Cp_2Fe (5 mol%), Na_2CO_3 (0.15 mmol), *N*-methyl-*N*-phenylmethacrylamide (**1**, 0.30 mmol), and *n*- Bu_4NBF_4 (0.15 mmol). The cell was equipped with a reticulated vitreous carbon (RVC, 100 PPI, 1.2 cm x 0.8 cm x 0.8 cm) anode and a platinum plate (1 cm x 1 cm x 0.1 mm) cathode (Figure S1B). Dimethyl 2-fluoromalonate (**2**, 0.6 mmol), MeOH (4.0 mL) and THF (2.0 mL) were added. The electrolysis was carried out at 65 °C (oil bath temperature) using a constant current of 10 mA for 3.0 h. The reaction mixture was concentrated under reduced pressure and the residue was chromatographed through silica gel eluting with ethyl acetate/petroleum ether to give the desired product.

General Procedure for the Electrosynthesis of Monofluorinated 2-Azaspiro[4.5]decanes: A 20 mL three-necked beaker-type cell was charged with Cp_2Fe (10 mol%), Na_2CO_3 (0.10 mmol), *N*-(*tert*-butyl)-*N*-(4-

methoxybenzyl)methacrylamide (**1**, 0.20 mmol), and *n*-Bu₄NBF₄ (0.10 mmol). The cell was equipped with a reticulated vitreous carbon (RVC, 100 PPI, 1.2 cm x 0.8 cm x 0.8 cm) anode and a platinum plate (1 cm x 1 cm x 0.1 mm) cathode (Figure S1B). Dimethyl 2-fluoromalonate (**2**, 0.4 mmol), MeOH (5.0 mL) and THF (2.0 mL) were added. The electrolysis was carried out at 65 °C (oil bath temperature) using a constant current of 5.0 mA for 3.0 h. The reaction mixture was concentrated under reduced pressure and the residue was chromatographed through silica gel eluting with ethyl acetate/petroleum ether to give the desired product.

General Procedure for the Gram-Scale Synthesis of 3: The gram-scale electrolysis was conducted in a 100 mL three-necked round-bottomed flask with a piece of RVC (1.2 cm x 2 cm x 2 cm) as the anode, a Pt plate as the cathode (1.5 cm x 1.5 cm x 0.3 mm), and a constant current of 62 mA for 10 h at 65 °C (oil bath temperature). The reaction mixture consisted *N*-methyl-*N*-phenylmethacrylamide (**1**, 0.88 g, 5 mmol), dimethyl 2-fluoromalonate (**2**, 1.5 g, 10 mmol), Cp₂Fe (47 mg, 5 mol %), Na₂CO₃ (210 mg, 2.5 mmol), *n*-Bu₄NBF₄ (823 mg, 2.5 mmol), MeOH (60 mL) and THF (30 mL). When the reaction was complete, the reaction mixture was concentrated under reduced pressure and the residue was chromatographed through silica gel eluting with ethyl acetate/petroleum ether to give the desired product **3** (0.97 g, 60% yield).



Figure S1. The electrolysis setup [The RVC is fixed on a sharpened graphite rod (\varnothing 6 mm)].

3. Cyclic Voltammetry Studies

The cyclic voltammograms were recorded in an electrolyte of $n\text{-Bu}_4\text{NBF}_4$ (0.1 M) in MeOH/THF (4:2, 5 mL) using a glassy carbon disk working electrode (diameter, 3 mm), a Pt wire auxiliary electrode and a Ag/AgCl reference electrode. The scan rate is 100 mV/s.

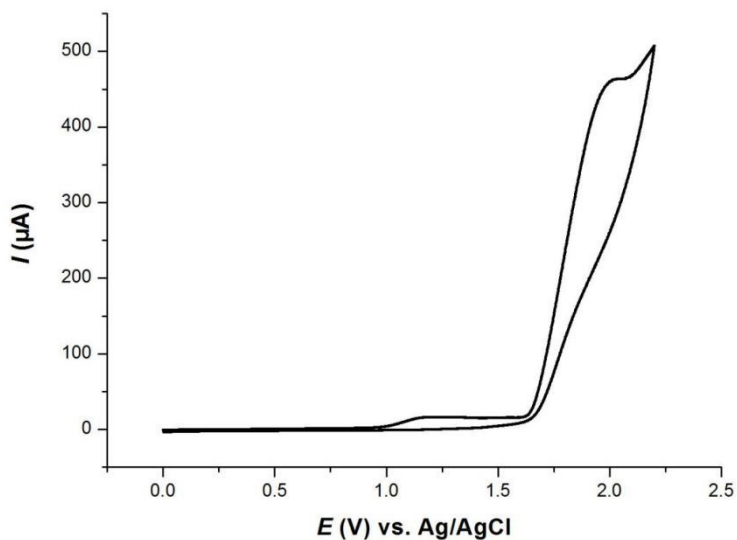


Figure S2. Cyclic voltammogram of **1** in an electrolyte of $n\text{-Bu}_4\text{NBF}_4$ (0.1 M) in MeOH/THF [$E_{p/2} = 1.79$ V].

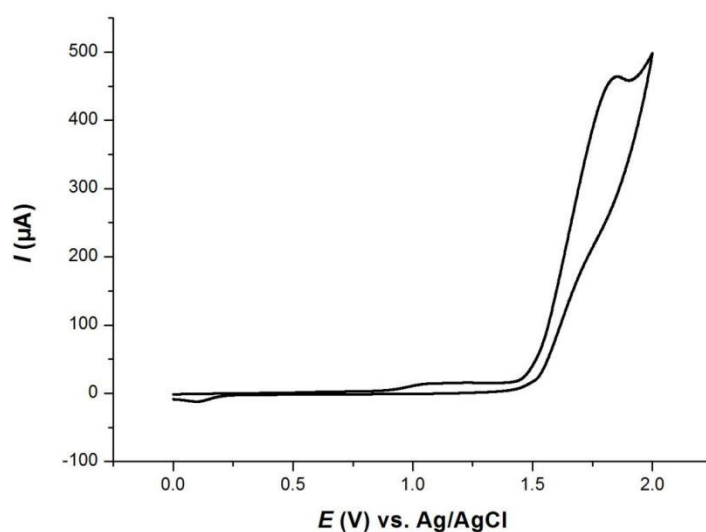
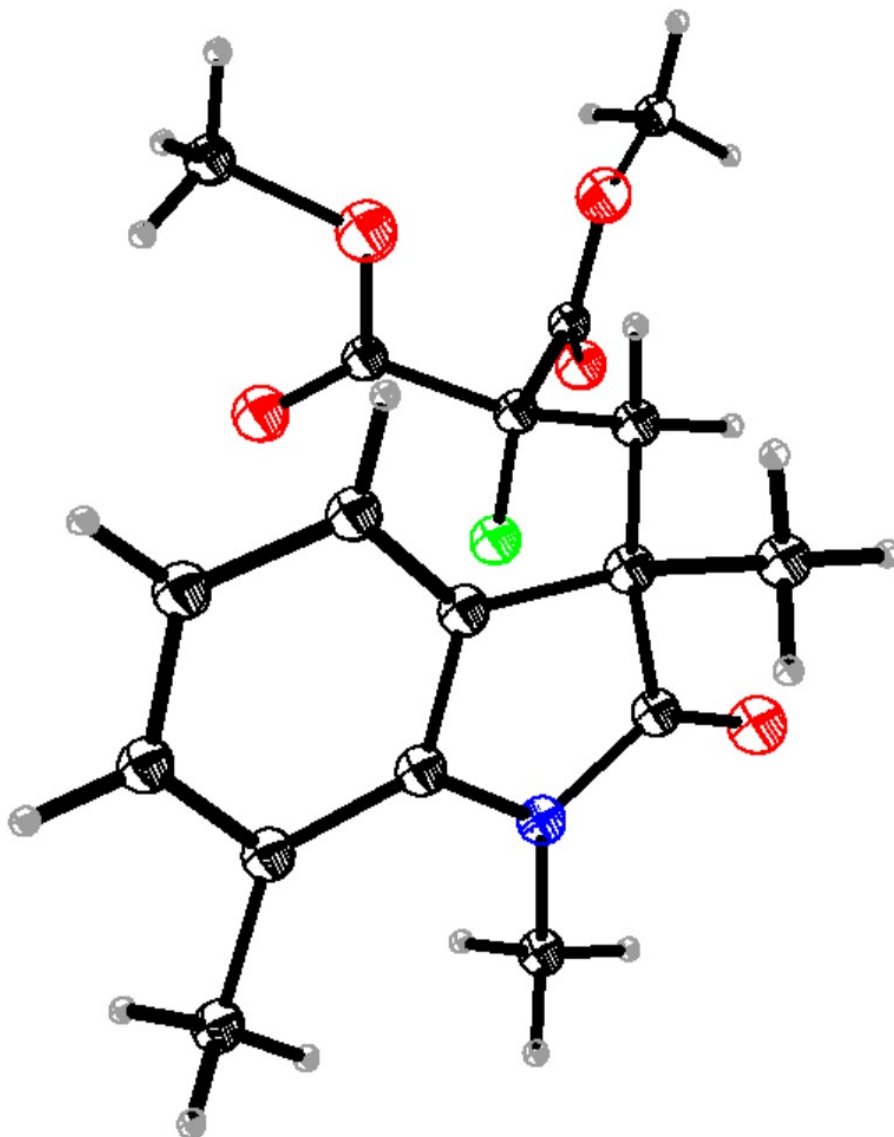


Figure S3. Cyclic voltammograms of **3** in an electrolyte of $n\text{-Bu}_4\text{NBF}_4$ (0.1 M) in MeOH/THF [$E_{p/2} = 1.64$ V].

4. X-Ray Crystallography

X-Ray single crystal diffraction analysis of compound 7 (CCDC: 2177594)

Single crystals suitable for X-ray diffraction were obtained by slow evaporation of a saturated solution of each compound (petroleum ether/ CH_2Cl_2) in a loosely capped vial.



Datablock: a

Bond precision: C-C = 0.0034 A Wavelength=0.71073

Cell: a=15.456(6) b=8.301(3) c=13.506(5)
alpha=90 beta=102.264(7) gamma=90

Temperature: 296 K

	Calculated	Reported
Volume	1693.3(11)	1693.3(12)
Space group	P 21/c	P2(1)/c
Hall group	-P 2ybc	?
Moiety formula	C17 H20 F N O5	?
Sum formula	C17 H20 F N O5	C17 H20 F N O5
Mr	337.34	337.34
Dx, g cm ⁻³	1.323	1.323
Z	4	4
Mu (mm ⁻¹)	0.104	0.104
F000	712.0	712.0
F000'	712.43	
h, k, lmax	18, 9, 16	18, 9, 16
Nref	2972	2963
Tmin, Tmax	0.973, 0.977	0.973, 0.977
Tmin'	0.973	

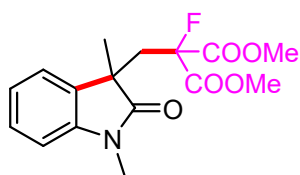
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AbsCorr = MULTI-SCAN

Data completeness= 0.997 Theta(max)= 24.990

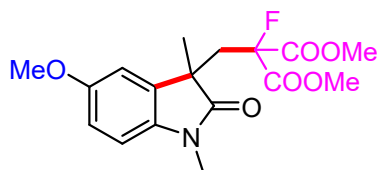
R(reflections)= 0.0474(1928) wR2(reflections)=
0.1245(2963)

S = 1.069 Npar= 217

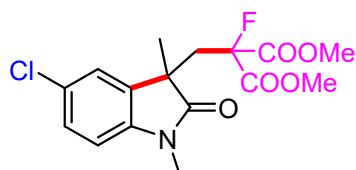
5. Characterization Data for the Electrolysis Products



Dimethyl 2-((1,3-dimethyl-2-oxoindolin-3-yl)methyl)-2-fluoromalonate (3), an known compound, please see: Z.-W. Hou, T. Jiang, T.-X. Wu and L. Wang, *Org. Lett.*, 2021, **23**, 8585–8589). Yellow solid (78 mg, 80% yield); m.p. = 117.6–118.4 °C; ^1H NMR (400 MHz, CDCl_3) δ : 7.31–7.28 (m, 1H), 7.13 (d, $J = 7.4$ Hz, 1H), 7.03 (t, $J = 7.4$ Hz, 1H), 6.87 (d, $J = 7.4$ Hz, 1H), 3.76 (s, 3H), 3.40 (s, 3H), 3.23 (s, 3H), 3.01–2.91 (m, 2H), 1.39 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ : 179.5, 166.3 (d, $J_{\text{C-F}} = 25.1$ Hz), 166.1 (d, $J_{\text{C-F}} = 25.1$ Hz), 144.0, 130.4, 128.7, 124.3, 121.9, 108.5, 93.2 (d, $J_{\text{C-F}} = 204.8$ Hz), 53.7, 53.4, 45.3 (d, $J_{\text{C-F}} = 1.7$ Hz), 41.1 (d, $J_{\text{C-F}} = 19.2$ Hz), 26.5, 25.8; ^{19}F NMR (377 MHz, CDCl_3) δ : –169.2.

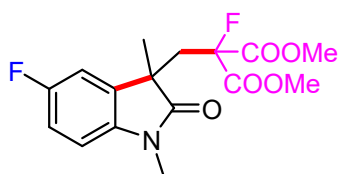


Dimethyl 2-fluoro-2-((5-methoxy-1,3-dimethyl-2-oxoindolin-3-yl)methyl)malonate (4). Yellow oil (62.5 mg, 59% yield); ^1H NMR (400 MHz, CDCl_3) δ : 6.83–6.80 (m, 1H), 6.77–6.75 (m, 2H), 3.80 (s, 3H), 3.76 (s, 3H), 3.46 (s, 3H), 3.20 (s, 3H), 2.98–2.87 (m, 2H), 1.38 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ : 179.1, 166.3 (d, $J_{\text{C-F}} = 25.1$ Hz), 166.0 (d, $J_{\text{C-F}} = 25.1$ Hz), 155.5, 137.4, 131.7, 112.7, 111.9, 108.7, 93.1 (d, $J_{\text{C-F}} = 204.8$ Hz), 55.8, 53.7, 45.7 (d, $J_{\text{C-F}} = 1.8$ Hz), 41.1 (d, $J_{\text{C-F}} = 19.2$ Hz), 26.5, 25.8; ^{19}F NMR (377 MHz, CDCl_3) δ : –169.4; HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. for $\text{C}_{17}\text{H}_{20}\text{FNO}_6^+$: 354.1347, Found: 354.1342.



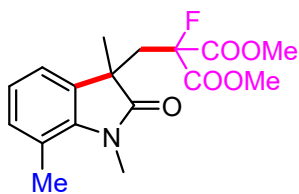
Dimethyl 2-((5-chloro-1,3-dimethyl-2-oxoindolin-3-yl)methyl)-2-fluoromalonate (5).

White solid (86 mg, 80% yield); m.p. = 107.8–109.6 °C; ¹H NMR (400 MHz, CDCl₃) δ: 7.28–7.26 (m, 1H), 7.09 (d, *J* = 2.0 Hz, 1H), 6.79 (d, *J* = 8.3 Hz, 1H), 3.77 (s, 3H), 3.54 (s, 3H), 3.21 (s, 3H), 3.01–2.87 (m, 2H), 1.39 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ: 179.0, 166.1 (d, *J*_{C-F} = 25.1 Hz), 165.9 (d, *J*_{C-F} = 25.1 Hz), 142.6, 132.3, 128.7, 127.3, 124.7, 109.5, 93.0 (d, *J*_{C-F} = 204.1 Hz), 53.9, 53.5, 45.5 (d, *J*_{C-F} = 2.1 Hz), 41.0 (d, *J*_{C-F} = 19.2 Hz), 26.7, 25.7; ¹⁹F NMR (377 MHz, CDCl₃) δ: –168.9; HRMS (ESI) ([M+H]⁺) Calcd. for C₁₆H₁₈ClFNO₅⁺: 358.0852, Found: 358.0849.



Dimethyl 2-fluoro-2-((5-fluoro-1,3-dimethyl-2-oxoindolin-3-yl)methyl)malonate (6).

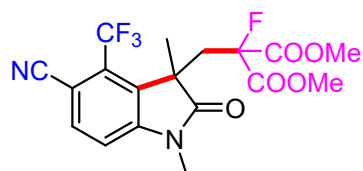
Yellow oil (56 mg, 55% yield); ¹H NMR (400 MHz, CDCl₃) δ: 7.00 (td, *J* = 8.7, 2.6 Hz, 1H), 6.89 (dd, *J* = 8.0, 2.6 Hz, 1H), 6.79 (dd, *J* = 8.7, 4.1 Hz, 1H), 3.77 (s, 3H), 3.52 (s, 3H), 3.21 (s, 3H), 3.03–2.87 (m, 2H), 1.39 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ: 179.1, 166.1 (d, *J*_{C-F} = 26.4 Hz), 165.9 (d, *J*_{C-F} = 26.4 Hz), 159.9 (d, *J*_{C-F} = 239.9 Hz), 139.9 (d, *J*_{C-F} = 2.0 Hz), 132.2 (d, *J*_{C-F} = 7.9 Hz), 114.9 (d, *J*_{C-F} = 23.3 Hz), 112.2 (d, *J*_{C-F} = 24.8 Hz), 109.0 (d, *J*_{C-F} = 8.3 Hz), 93.0 (d, *J*_{C-F} = 204.2 Hz), 53.8, 53.3, 45.7 (d, *J*_{C-F} = 3.4 Hz), 40.8 (d, *J*_{C-F} = 19.1 Hz), 26.6, 25.7; ¹⁹F NMR (377 MHz, CDCl₃) δ: –121.6, –168.9; HRMS (ESI) ([M+H]⁺) Calcd. for C₁₆H₁₈F₂NO₅⁺: 342.1148, Found: 342.1144.



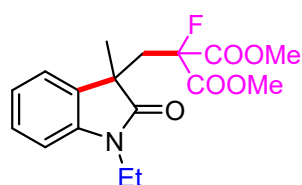
Dimethyl 2-fluoro-2-((1,3,7-trimethyl-2-oxoindolin-3-yl)methyl)malonate (7).

White solid (40.5 mg, 40% yield); m.p. = 99.9–102.2 °C; ¹H NMR (400 MHz, CDCl₃) δ: 7.00 (d, *J* = 8.3 Hz, 1H), 6.95–6.88 (m, 2H), 3.76 (s, 3H), 3.50 (s, 3H), 3.41 (s, 3H), 2.99–2.86 (m, 2H), 2.58 (s, 3H), 1.37 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ: 180.3, 166.3 (d, *J*_{C-F} = 30.3 Hz), 166.2 (d, *J*_{C-F} = 30.3 Hz), 141.8, 132.4, 131.0, 122.1, 121.8, 120.2, 93.2, (d, *J*_{C-F} = 202.0 Hz), 53.8,

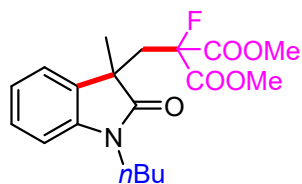
53.4, 44.6 (d, $J_{C-F} = 2.1$ Hz), 41.3 (d, $J_{C-F} = 20.2$ Hz), 29.9, 26.2, 19.3; ^{19}F NMR (377 MHz, CDCl_3) δ : -169.1; HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. for $\text{C}_{17}\text{H}_{21}\text{FNO}_5^+$: 338.1398, Found: 338.1394.



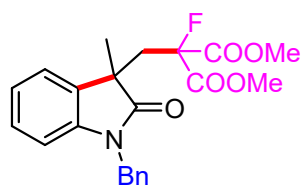
Dimethyl 2-((5-cyano-1,3-dimethyl-2-oxo-4-(trifluoromethyl)indolin-3-yl)methyl)-2-fluoromalonate (8). Yellow solid (51 mg, 41% yield); m.p. = 104.5–105.7 °C; ^1H NMR (400 MHz, CDCl_3) δ : 7.85 (d, $J = 8.0$ Hz, 1H), 7.12 (d, $J = 8.2$ Hz, 1H), 3.76 (s, 3H), 3.61 (s, 3H), 3.28 (s, 3H), 3.17–3.02 (m, 2H), 1.53 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ : 178.4, 165.7 (d, $J_{C-F} = 26.0$ Hz), 165.5 (d, $J_{C-F} = 26.0$ Hz), 148.9, 137.0, 130.5, 129.9 (q, $J_{C-F} = 33.9$ Hz), 122.7 (q, $J_{C-F} = 275.2$ Hz), 116.5, 111.4, 104.0 (q, $J_{C-F} = 2.8$ Hz), 92.6 (d, $J_{C-F} = 199.8$ Hz), 53.8, 53.7, 47.2, 40.3 (dq, $J_{C-F} = 18.5, 4.5$ Hz), 27.1, 24.5 (q, $J_{C-F} = 3.6$ Hz); ^{19}F NMR (377 MHz, CDCl_3) δ : -55.8, -165.4; HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. for $\text{C}_{18}\text{H}_{17}\text{F}_4\text{N}_2\text{O}_5^+$: 417.1068, Found: 417.1068.



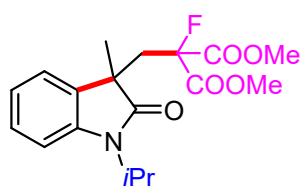
Dimethyl 2-((1-ethyl-3-methyl-2-oxoindolin-3-yl)methyl)-2-fluoromalonate (9). Yellow oil (70 mg, 69% yield); ^1H NMR (400 MHz, CDCl_3) δ : 7.29–7.25 (m, 1H), 7.12 (d, $J = 7.5$ Hz, 1H), 7.01 (t, $J = 7.5$ Hz, 1H), 6.87 (d, $J = 7.5$ Hz, 1H), 3.91–3.86 (m, 1H), 3.76 (s, 3H), 3.70–3.61 (m, 1H), 3.37 (s, 3H), 3.00–2.89 (m, 2H), 1.38 (s, 3H), 1.27 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ : 179, 166.3 (d, $J_{C-F} = 25.0$ Hz), 166.1 (d, $J_{C-F} = 25.0$ Hz), 143.2, 130.6, 128.6, 124.6, 121.6, 108.6, 93.3 (d, $J_{C-F} = 205.6$ Hz), 53.7, 53.3, 45.2 (d, $J_{C-F} = 1.0$ Hz), 40.1 (d, $J_{C-F} = 19.6$ Hz), 34.8, 25.9, 12.2; ^{19}F NMR (377 MHz, CDCl_3) δ : -168.3; HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. for $\text{C}_{17}\text{H}_{21}\text{FNO}_5^+$: 338.1398, Found: 338.1396.



Dimethyl 2-((1-butyl-3-methyl-2-oxoindolin-3-yl)methyl)-2-fluoromalonate (10). Yellow oil (67 mg, 60% yield); ^1H NMR (400 MHz, CDCl_3) δ : 7.28–7.24 (m, 1H), 7.12 (d, $J = 7.3$ Hz, 1H), 7.00 (t, $J = 7.5$ Hz, 1H), 6.87 (d, $J = 7.8$ Hz, 1H), 3.81–3.75 (m, 4H), 3.66–3.58 (m, 1H), 3.37 (s, 3H), 3.00–2.89 (m, 2H), 1.71–1.64 (m, 2H), 1.49–1.40 (m, 2H), 1.38 (s, 3H), 0.97 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ : 179.3, 166.3 (d, $J_{\text{C-F}} = 25.0$ Hz), 166.1 (d, $J_{\text{C-F}} = 25.0$ Hz), 143.6, 130.5, 128.6, 124.5, 121.6, 108.7, 93.2 (d, $J_{\text{C-F}} = 205.7$ Hz), 53.7, 53.3, 45.2, 40.9 (d, $J_{\text{C-F}} = 19.6$ Hz), 40.0, 29.2, 26.2, 20.3, 13.9; ^{19}F NMR (377 MHz, CDCl_3) δ : –168.5; HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. for $\text{C}_{19}\text{H}_{25}\text{F}_2\text{NO}_5^+$: 361.1711, Found: 361.1707.

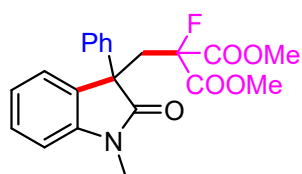


Dimethyl 2-((1-benzyl-3-methyl-2-oxoindolin-3-yl)methyl)-2-fluoromalonate (11). White solid (66 mg, 55% yield); m.p. = 82.4–85.3 °C; ^1H NMR (400 MHz, CDCl_3) δ : 7.33 (d, $J = 4.4$ Hz, 5H), 7.16–7.11 (m, 2H), 6.99 (t, $J = 7.5$ Hz, 1H), 6.68 (t, $J = 7.5$ Hz, 1H), 4.94 (s, 2H), 3.78 (s, 3H), 3.32 (s, 3H), 3.06–2.96 (m, 2H), 1.45 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ : 179.6, 166.4 (d, $J_{\text{C-F}} = 24.9$ Hz), 166.2 (d, $J_{\text{C-F}} = 24.9$ Hz), 143.1, 136.0, 130.4, 128.9, 128.6, 127.6, 127.3 (d, $J_{\text{C-F}} = 1.1$ Hz), 124.4, 122.0, 109.7, 93.3 (d, $J_{\text{C-F}} = 205.7$ Hz), 53.8, 53.3, 45.3, 44.1, 40.8 (d, $J_{\text{C-F}} = 19.5$ Hz), 26.7; ^{19}F NMR (377 MHz, CDCl_3) δ : –167.9; HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. for $\text{C}_{22}\text{H}_{23}\text{FNO}_5^+$: 400.1555, Found: 400.1555.



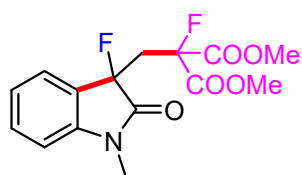
Dimethyl 2-fluoro-2-((1-isopropyl-3-methyl-2-oxoindolin-3-yl)methyl)malonate (12). Yellow oil (79 mg, 75% yield); ^1H NMR (400 MHz, CDCl_3) δ : 7.24 (t, $J = 7.7$ Hz, 1H), 7.12

(d, $J = 7.3$, 1H), 7.03–6.97 (m, 2H), 4.67–4.60 (m, 1H), 3.76 (s, 3H), 3.35 (s, 3H), 2.9 8–2.87 (m, 2H), 1.49 (t, $J = 6.9$ Hz, 6H), 1.37 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ : 179.0, 166.2 (d, $J_{\text{C-F}} = 24.8$ Hz), 166.1 (d, $J_{\text{C-F}} = 24.8$ Hz), 142.7, 130.8, 128.4, 124.6, 121.3, 110.2, 93.2 (d, $J_{\text{C-F}} = 205.7$ Hz), 54.2, 53.7, 53.3, 44.9, 43.9, 41.1 (d, $J_{\text{C-F}} = 19.1$ Hz), 26.1, 19.4, 18.9; ^{19}F NMR (377 MHz, CDCl_3) δ : -168.5; HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. for $\text{C}_{18}\text{H}_{23}\text{FNO}_5^+$: 352.1555, Found: 352.1552.



Dimethyl 2-fluoro-2-((1-methyl-2-oxo-3-phenylindolin-3-yl)methyl)malonate (13).

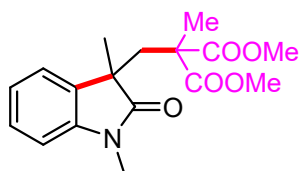
Yellow oil (71 mg, 61% yield); ^1H NMR (400 MHz, CDCl_3) δ : 7.37–7.33 (m, 3H), 7.31–7.24 (m, 3H), 7.20 (d, $J = 7.9$ Hz, 1H), 7.08 (t, $J = 7.5$ Hz, 1H), 6.92 (d, $J = 7.9$ Hz, 1H), 3.79 (s, 3H), 3.54 (dd, $J = 15.0, 6.8$ Hz, 1H), 3.46–3.35 (m, 4H), 3.23 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ : 177.7, 166.4 (d, $J_{\text{C-F}} = 25.4$ Hz), 166.1 (d, $J_{\text{C-F}} = 25.4$ Hz), 144.9, 139.7, 129.2, 128.8, 128.7, 127.8, 126.9, 126.7, 121.9, 108.9, 93.3 (d, $J_{\text{C-F}} = 206.2$ Hz), 53.9, 53.5, 53.1 (d, $J_{\text{C-F}} = 1.7$ Hz), 40.9 (d, $J_{\text{C-F}} = 18.4$ Hz), 26.8; ^{19}F NMR (377 MHz, CDCl_3) δ : -169.1 (dd, $J = 31.4, 6.8$ Hz); HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. for $\text{C}_{21}\text{H}_{21}\text{FNO}_5^+$: 386.1398, Found: 386.1398.



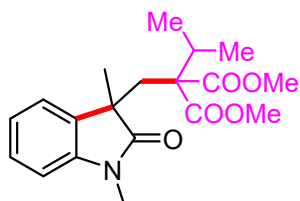
Dimethyl 2-fluoro-2-((3-fluoro-1-methyl-2-oxoindolin-3-yl)methyl)malonate (14).

White solid (40.5 mg, 40% yield); m.p. = 86.8–87.9 °C; ^1H NMR (400 MHz, CDCl_3) δ : 7.50–7.45 (m, 1H), 7.44–7.38 (m, 1H), 7.13–7.07 (m, 1H), 6.86 (d, $J = 7.9$ Hz, 1H), 3.80 (s, 3H), 3.60 (s, 3H), 3.36 (ddd, $J = 32.6, 15.0, 10.0$ Hz, 1H), 3.20 (s, 3H), 3.10 (td, $J = 15.0, 10.0$ Hz, 1H); ^{13}C NMR (101 MHz, CDCl_3) δ : 171.8 (d, $J_{\text{C-F}} = 20.2$ Hz), 165.8 (d, $J_{\text{C-F}} = 25.0$ Hz), 165.4 (d, $J_{\text{C-F}} = 25.1$ Hz), 144.9 (d, $J_{\text{C-F}} = 5.5$ Hz), 132.1 (d, $J_{\text{C-F}} = 3.2$ Hz), 126.7 (dd, $J_{\text{C-F}} = 4.1, 1.4$ Hz), 123.5 (d, $J_{\text{C-F}} = 18.1$ Hz), 123.0 (d, $J_{\text{C-F}} = 2.9$ Hz), 109.1 (d, $J_{\text{C-F}} = 1.4$ Hz), 91.9 (dd, $J_{\text{C-F}}$

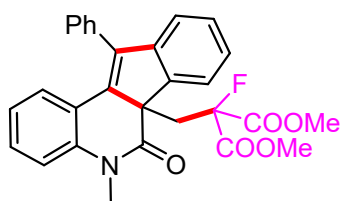
= 202.7, 9.0 Hz), 90.6 (d, J_{C-F} = 186.1 Hz), 54.0, 53.7, 38.5 (dd, J_{C-F} = 32.0, 19.3 Hz), 26.5;
 ^{19}F NMR (377 MHz, CDCl_3) δ : -152.2 (dd, J = 15.0, 10.0 Hz), -165.7 (dd, J = 32.6, 10.0 Hz);
HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. for $\text{C}_{15}\text{H}_{16}\text{F}_2\text{NO}_5^+$: 328.0991, Found: 328.0990.



Dimethyl 2-((1,3-dimethyl-2-oxoindolin-3-yl)methyl)-2-methylmalonate (15). Yellow oil (46 mg, 48% yield); ^1H NMR (400 MHz, CDCl_3) δ : 7.26 (dd, J = 7.7, 1.4 Hz, 1H), 7.10 (dd, J = 7.5, 1.4 Hz, 1H), 7.03 (td, J = 7.4, 1.1 Hz, 1H), 6.86 (d, J = 7.7 Hz, 1H), 3.67 (s, 3H), 3.39 (s, 3H), 3.22 (s, 3H), 2.81–2.72 (m, 2H), 1.36 (s, 3H), 1.03 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ : 180.0, 172.6, 171.8, 143.3, 131.8, 128.3, 124.1, 122.2, 108.4, 53.0, 52.9, 52.4, 46.3, 41.3, 28.0, 26.4, 19.1; HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. for $\text{C}_{17}\text{H}_{22}\text{FNO}_5^+$: 320.1492, Found: 320.1491.

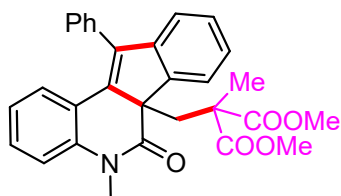


Dimethyl 2-((1,3-dimethyl-2-oxoindolin-3-yl)methyl)-2-isopropylmalonate (16). Yellow solid (26 mg, 25% yield); m.p. = 101.6–103.2 °C; ^1H NMR (400 MHz, CDCl_3) δ : 7.24 (td, J = 7.8, 1.2 Hz, 1H), 7.16 (dd, J = 7.8, 1.2 Hz, 1H), 7.00 (td, J = 7.8, 1.2 Hz, 1H), 6.82 (d, J = 7.8 Hz, 1H), 3.56 (s, 3H), 3.35 (s, 3H), 3.20 (s, 3H), 2.68 (s, 2H), 2.17–2.09 (m, 1H), 1.35 (s, 3H), 0.90 (d, J = 6.8 Hz, 3H), 0.84 (d, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ : 179.8, 171.0, 170.2, 143.6, 132.3, 128.0, 124.0, 121.9, 108.1, 60.3, 52.0, 51.7, 46.8, 40.0, 33.3, 29.0, 26.4, 19.2, 18.5; HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. for $\text{C}_{19}\text{H}_{26}\text{NO}_5^+$: 348.1805 Found: 348.1805.

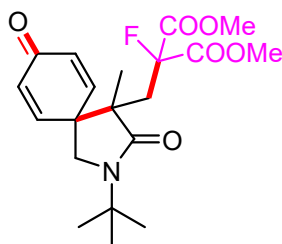


Dimethyl

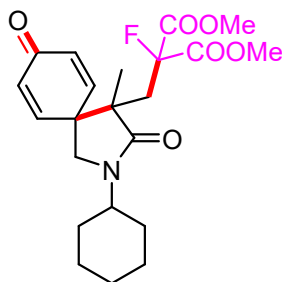
2-fluoro-2-((5-methyl-6-oxo-11-phenyl-5,6-dihydro-6aH-indeno[1,2-c]quinolin-6a-yl)methyl)malonate (17). White solid (64 mg, 66% yield); m.p. = 152.4–153.2 °C; ¹H NMR (400 MHz, CDCl₃) δ: 7.99–7.94 (m, 1H), 7.46–7.37 (m, 5H), 7.34–7.26 (m, 3H), 7.18–7.09 (m, 3H), 6.94–6.89 (m, 1H), 3.63 (s, 3H), 3.44 (s, 3H), 3.35–3.22 (m, 4H), 2.68 (dd, *J* = 15.2, 11.4 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃) δ: 168.6, 165.9 (d, *J*_{C-F} = 25.6 Hz), 165.2 (d, *J*_{C-F} = 25.6 Hz), 146.3, 140.7, 139.4, 135.6, 134.0, 129.3, 128.8, 128.7, 128.5, 128.1, 127.6, 127.4, 125.5, 123.2, 121.9, 121.8, 120.8, 115.3, 92.9 (d, *J*_{C-F} = 205.4 Hz), 57.5, 53.7, 53.2, 39.4 (d, *J*_{C-F} = 19.2 Hz), 30.9; ¹⁹F NMR (377 MHz, CDCl₃) δ: -162.9 (dd, *J* = 32.7, 11.4 Hz); HRMS (ESI) ([M+H]⁺) Calcd. for C₂₉H₂₅FNO₅⁺: 486.1711, Found: 486.1708.



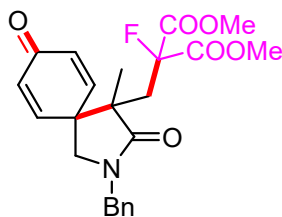
Dimethyl 2-methyl-2-((5-methyl-6-oxo-11-phenyl-5,6-dihydro-6aH-indeno[1,2-c]quinolin-6a-yl)methyl)malonate (18). White solid (56.7 mg, 59% yield); m.p. = 208.3–209.1 °C; ¹H NMR (400 MHz, CDCl₃) δ: 7.94–7.89 (m, 1H), 7.47–7.37 (m, 5H), 7.32–7.25 (m, 3H), 7.19–7.14 (m, 1H), 7.12–7.07 (m, 2H), 6.92–6.87 (m, 1H), 3.44 (s, 3H), 3.43 (s, 3H), 3.33 (s, 3H), 3.13 (d, *J* = 14.6 Hz, 1H), 2.57 (d, *J* = 14.6 Hz, 1H), 1.05 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ: 172.3, 171.2, 169.5, 145.6, 141.8, 141.1, 139.8, 136.0, 134.0, 129.0, 128.9, 128.7, 128.3, 128.1, 127.4 (2C), 125.5, 122.9, 121.9, 120.9, 115.5, 59.2, 53.2, 52.7, 52.3, 39.8, 31.0, 19.9; HRMS (ESI) ([M+H]⁺) Calcd. for C₃₀H₂₈FNO₅⁺: 482.1962, Found: 482.1962.



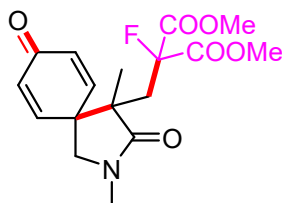
Dimethyl 2-((2-(*tert*-butyl)-4-methyl-8-oxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)methyl)-2-fluoromalonate (19). Yellow oil (53 mg, 70% yield); ^1H NMR (400 MHz, CDCl_3) δ : 6.96 (dd, $J = 10.1, 3.1$ Hz, 1H), 6.86 (dd, $J = 10.1, 3.1$ Hz, 1H), 6.45–6.38 (m, 2H), 3.84 (s, 3H), 3.78 (s, 3H), 3.49 (d, $J = 10.4$ Hz, 1H), 3.25 (d, $J = 10.4$ Hz, 1H), 2.15 (dd, $J = 15.7, 8.1$ Hz, 1H), 1.40 (s, 9H), 1.25 (s, 3H); ^{13}C NMR (151 MHz, CDCl_3) δ : 185.1, 175.0, 167.0(d, $J_{\text{C-F}} = 26.1$ Hz), 166.6 (d, $J_{\text{C-F}} = 25.1$ Hz), 148.8, 147.5, 131.8, 130.6, 93.59 (d, $J_{\text{C-F}} = 205.1$ Hz), 54.8, 53.8, 53.6, 52.6, 50.2, 48.0, 36.8 (d, $J_{\text{C-F}} = 19.5$ Hz), 27.6, 17.8 (d, $J_{\text{C-F}} = 3.4$ Hz); ^{19}F NMR (377 MHz, CDCl_3) δ : -163.9; HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. for $\text{C}_{22}\text{H}_{27}\text{FNO}_6^+$: 396.1817, Found: 396.1817.



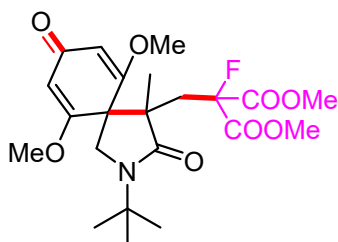
Dimethyl 2-((2-(cyclohexyl)-4-methyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)methyl)-2-fluoromalonate (20). Yellow oil (52 mg, 64% yield); ^1H NMR (400 MHz, CDCl_3) δ : 6.95–6.83 (m, 2H), 6.50–6.35 (m, 2H), 3.85 (s, 3H), 3.79 (s, 3H), 3.40 (d, $J = 10.4$ Hz, 1H), 3.22 (d, $J = 10.4$ Hz, 1H), 2.85 (dd, $J = 35.5, 15.6$ Hz, 1H), 2.13 (dd, $J = 15.6, 8.9$ Hz, 1H), 1.90–1.64 (m, 6H), 1.44–1.29 (m, 5H), 1.27 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ : 185.0, 174.1, 166.8 (d, $J_{\text{C-F}} = 25.3$ Hz), 166.5 (d, $J_{\text{C-F}} = 25.0$ Hz), 148.2, 147.6, 131.7, 130.9, 93.6 (d, $J_{\text{C-F}} = 206.2$ Hz), 53.9, 53.6, 52.0, 51.1, 48.9, 48.0, 36.6 (d, $J_{\text{C-F}} = 19.7$ Hz), 30.0, 25.4, 25.3, 18.2 (d, $J_{\text{C-F}} = 4.6$ Hz); ^{19}F NMR (376 MHz, CDCl_3) δ : -164.2; HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. for $\text{C}_{22}\text{H}_{29}\text{FNO}_6^+$: 422.1973, Found: 422.1975.



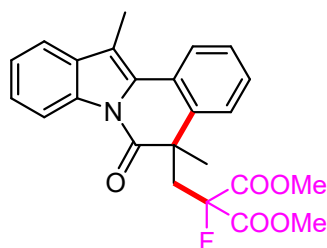
Dimethyl 2-((2-benzyl-4-methyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)methyl)-2-fluoromalonate (21). Yellow oil (26 mg, 30% yield); ^1H NMR (400 MHz, CDCl_3) δ : 7.38–7.32 (m, 3H), 7.24 (d, $J = 7.8$ Hz, 2H), 6.87 (dd, $J = 10.4, 3.1$ Hz, 1H), 6.77 (dd, $J = 10.4, 3.1$ Hz, 1H), 6.38–6.34 (m, 2H), 4.67 (d, $J = 14.5$ Hz, 1H), 4.29 (d, $J = 14.5$ Hz, 1H), 3.88 (s, 3H), 3.81 (s, 3H), 3.27 (d, $J = 10.5$ Hz, 1H), 3.11 (d, $J = 10.5$ Hz, 1H), 2.89 (dd, $J = 34.9, 15.6$ Hz, 1H), 2.17 (dd, $J = 15.6, 9.1$ Hz, 1H), 1.29 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ : 184.9, 174.8, 166.9 (d, $J_{\text{C-F}} = 25.5$ Hz), 166.6 (d, $J_{\text{C-F}} = 25.1$ Hz), 148.0, 147.2, 135.5, 131.7, 130.9, 129.2, 128.6, 128.3, 93.7 (d, $J_{\text{C-F}} = 206.3$ Hz), 54.0, 53.7, 51.8, 51.8, 51.0, 48.8, 47.2, 36.9 (d, $J_{\text{C-F}} = 19.8$ Hz), 18.5 (d, $J_{\text{C-F}} = 4.5$ Hz); ^{19}F NMR (376 MHz, CDCl_3) δ : -164.3; HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. for $\text{C}_{23}\text{H}_{25}\text{FNO}_6^+$: 430.16601711, Found: 430.1664.



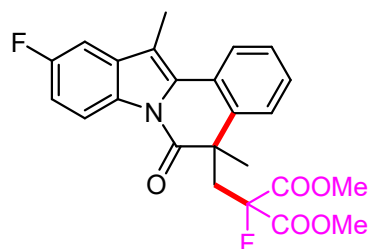
Dimethyl 2-((2,4-dimethyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)methyl)-2-fluoromalonate (22). Yellow oil (35 mg, 50% yield); ^{13}C NMR (101 MHz, CDCl_3) δ : 185.0, 174.8, 166.9, 166.8 (d, $J_{\text{C-F}} = 25.7$ Hz), 166.5 (d, $J_{\text{C-F}} = 25.7$ Hz), 147.8, 147.7, 131.4, 93.7 (d, $J_{\text{C-F}} = 207.0$ Hz), 54.0, 53.8, 53.7, 51.7 (d, $J_{\text{C-F}} = 2.1$ Hz), 49.1, 37.0 (d, $J_{\text{C-F}} = 19.4$ Hz), 30.3, 18.7 (d, $J_{\text{C-F}} = 5.0$ Hz); ^{19}F NMR (376 MHz, CDCl_3) δ : -165.0; HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. for $\text{C}_{17}\text{H}_{21}\text{FNO}_6^+$: 354.1347, Found: 354.1346.



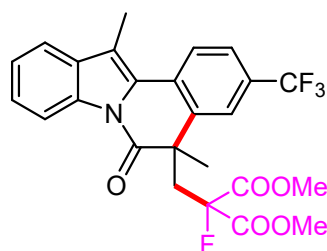
Dimethyl 2-((2-(tert-butyl)-6,10-dimethoxy-4-methyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)methyl)-2-fluoromalonate (23). Yellow oil (40 mg, 45% yield); ^1H NMR (400 MHz, DMSO- d_6) δ : 5.50 (d, $J = 10.3$ Hz, 2H), 3.74 (s, 6H), 3.70 (d, $J = 17.7$ Hz, 2H), 3.65 (d, $J = 4.4$ Hz, 6H), 2.07 (dd, $J = 15.9, 6.3$ Hz, 1H), 1.32 (s, 9H), 0.99 (s, 3H); ^{13}C NMR (101 MHz, DMSO- d_6) δ : 186.6, 174.2, 171.6, 170.8, 167.0 (d, $J_{\text{C-F}} = 25.3$ Hz), 166.7 (d, $J_{\text{C-F}} = 25.3$ Hz), 166.6, 103.4, 102.8, 93.7 (d, $J_{\text{C-F}} = 205.3$ Hz), 56.4, 56.3, 54.4, 54.3, 54.0, 53.6, 52.5, 47.8, 37.2 (d, $J_{\text{C-F}} = 19.4$ Hz), 27.4, 19.4 (d, $J_{\text{C-F}} = 4.4$ Hz); ^{19}F NMR (376 MHz, DMSO- d_6) δ : -164.0; HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. for $\text{C}_{22}\text{H}_{31}\text{FNO}_8^+$: 456.2028, Found: 456.2027.



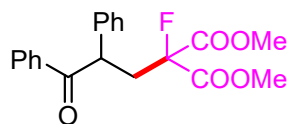
Dimethyl 2-((5,12-dimethyl-6-oxo-5,6-dihydroindolo[2,1-*a*]isoquinolin-5-yl)methyl)-2-fluoromalonate (24). Yellow solid (101.5 mg, 80% yield); m.p. = 143.2–144.1 °C; ^1H NMR (400 MHz, CDCl_3) δ : 8.60 (dd, $J = 7.4, 2.2$ Hz, 1H), 8.04 (d, $J = 7.5$ Hz, 1H), 7.58 (dd, $J = 6.3, 1.7$ Hz, 1H), 7.42–7.32 (m, 5H), 3.68 (s, 3H), 3.53 (dd, $J = 15.2, 7.8$ Hz, 1H), 3.34 (s, 3H), 3.11 (dd, $J = 29.1, 15.2$ Hz, 1H), 2.66 (s, 3H), 1.74 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ : 171.8, 166.2 (d, $J_{\text{C-F}} = 25.1$ Hz), 166.1 (d, $J_{\text{C-F}} = 25.1$ Hz), 135.5, 134.5, 132.6, 129.6, 127.8, 127.7, 127.2, 127.0, 125.9, 125.2, 124.4, 118.6, 117.0, 114.9, 93.0 (d, $J_{\text{C-F}} = 204.9$ Hz), 53.7, 53.3, 45.3 (d, $J_{\text{C-F}} = 2.6$ Hz), 44.4 (d, $J_{\text{C-F}} = 18.9$ Hz), 31.4, 11.8; ^{19}F NMR (377 MHz, CDCl_3) δ : -167.0 (dd, $J = 29.1, 8.2$ Hz); HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. for $\text{C}_{24}\text{H}_{23}\text{FNO}_5^+$: 424.1555, Found: 424.1555.



Dimethyl 2-fluoro-2-((10-fluoro-5,12-dimethyl-6-oxo-5,6-dihydroindolo[2,1-*a*]-isoquinolin-5-yl)methyl)malonate (25). White solid (35.7 mg, 27% yield); m.p. = 166.7–177.7 °C; ¹H NMR (400 MHz, CDCl₃) δ: 8.34 (dd, *J* = 10.1, 2.4 Hz, 1H), 8.00 (t, *J* = 7.8 Hz, 1H), 7.49 (dd, *J* = 8.6, 5.5 Hz, 1H), 7.42–7.38 (m, 2H), 7.32 (t, *J* = 7.5 Hz, 1H), 7.09 (td, *J* = 8.6, 2.4 Hz, 1H), 3.71 (s, 3H), 3.51 (dd, *J* = 15.2, 7.1 Hz, 1H), 3.34 (s, 3H), 3.12 (dd, *J* = 29.8, 15.2 Hz, 1H), 2.64 (s, 3H), 1.74 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ: 171.9, 166.1 (d, *J*_{C-F} = 25.1 Hz), 166.0 (d, *J*_{C-F} = 25.1 Hz), 161.8 (d, *J*_{C-F} = 241.5 Hz), 135.2, 134.5 (d, *J*_{C-F} = 13.1 Hz), 129.9 (d, *J*_{C-F} = 4.3 Hz), 128.9, 127.8 (d, *J*_{C-F} = 2.9 Hz), 127.2, 126.9, 124.9, 119.2 (d, *J*_{C-F} = 9.7 Hz), 114.5, 112.4 (d, *J*_{C-F} = 24.2 Hz), 104.5 (d, *J*_{C-F} = 28.6 Hz), 93.0 (d, *J*_{C-F} = 204.2 Hz), 53.8, 53.3, 45.2 (d, *J*_{C-F} = 2.8 Hz), 44.5 (d, *J*_{C-F} = 18.9 Hz), 31.3, 11.8; ¹⁹F NMR (377 MHz, CDCl₃) δ: -115.8, -166.9; HRMS (ESI) ([M+H]⁺) Calcd. for C₂₄H₂₂F₂NO₅⁺: 442.1461, Found: 442.1461.

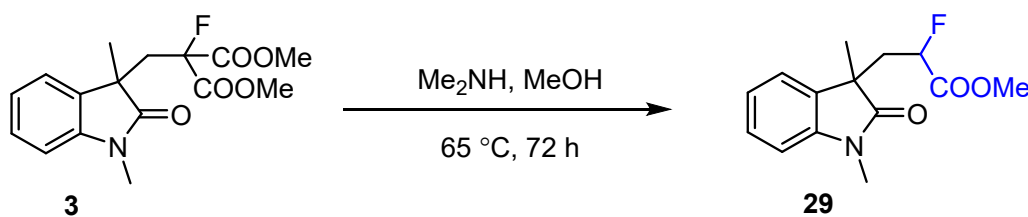


Dimethyl 2-((5,12-dimethyl-6-oxo-3-(trifluoromethyl)-5,6-dihydroindolo[2,1-*a*]-isoquinolin-5-yl)methyl)-2-fluoromalonate (26). White solid (82.5 mg, 56% yield); m.p. = 144.6–145.8 °C; ¹H NMR (400 MHz, CDCl₃) δ: 8.60 (d, *J* = 7.5 Hz, 1H), 8.15 (d, *J* = 8.4 Hz, 1H), 7.68–7.59 (m, 3H), 7.44–7.36 (m, 2H), 3.69 (s, 3H), 3.58 (dd, *J* = 15.4, 7.8 Hz, 1H), 3.38 (s, 3H), 3.12 (ddd, *J* = 28.2, 15.4, 1.1 Hz, 1H), 2.69 (s, 3H), 1.77 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 170.9, 165.9 (d, *J*_{C-F} = 24.6 Hz), 165.8 (d, *J*_{C-F} = 26.2 Hz), 136.2, 134.7, 132.2, 130.3, 128.8 (d, *J*_{C-F} = 32.7 Hz), 128.3, 126.7, 125.5, 124.7, 124.6 (q, *J*_{C-F} = 3.9 Hz), 124.5, 124.0 (d, *J*_{C-F} = 271.9 Hz), 119.0, 117.3, 117.1, 92.7 (d, *J*_{C-F} = 203.3 Hz), 53.8, 53.3, 45.4 (d, *J*_{C-F} = 2.9 Hz), 44.2 (d, *J*_{C-F} = 18.8 Hz), 31.3, 11.9; ¹⁹F NMR (377 MHz, CDCl₃) δ: -62.4, -166.5 (dd, *J* = 28.2, 7.8 Hz); HRMS (ESI) ([M+H]⁺) Calcd. for C₂₅H₂₂F₄NO₅⁺: 492.1429, Found: 492.1426.



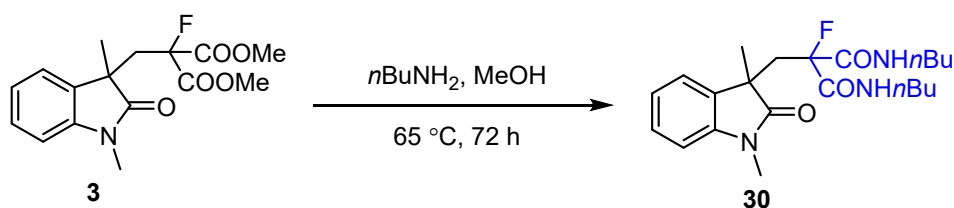
Dimethyl 2-fluoro-2-(3-oxo-2,3-diphenylpropyl)malonate (28). Yellow oil (46 mg, 43% yield); ^1H NMR (400 MHz, CDCl_3) δ : 7.96–7.91 (m, 2H), 7.50–7.45 (m, 1H), 7.40–7.35 (m, 2H), 7.32–7.25 (m, 4H), 7.22–7.17 (m, 1H), 4.93 (dd, $J = 7.2, 5.8$ Hz, 1H), 3.76 (s, 3H), 3.54 (s, 3H), 3.27 (ddd, $J = 18.8, 15.2, 7.2$ Hz, 1H), 2.74 (ddd, $J = 24.0, 15.2, 5.8$ Hz, 1H); ^{13}C NMR (101 MHz, CDCl_3) δ : 198.0, 166.5 (d, $J_{\text{C-F}} = 25.8$ Hz), 166.3 (d, $J_{\text{C-F}} = 25.8$ Hz), 137.9, 136.0, 133.3, 129.2, 128.9, 128.8, 128.7, 127.7, 93.4 (d, $J_{\text{C-F}} = 198.0$ Hz), 53.6, 53.3, 47.7 (d, $J_{\text{C-F}} = 3.3$ Hz), 37.6 (d, $J_{\text{C-F}} = 20.6$ Hz); ^{19}F NMR (377 MHz, CDCl_3) δ : -165.1 (dd, $J = 24.0, 18.8$ Hz); HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. for $\text{C}_{20}\text{H}_{20}\text{FNO}_5^+$: 359.1289, Found: 359.1287.

Methyl 3-(1,3-dimethyl-2-oxoindolin-3-yl)-2-fluoropropanoate (29)



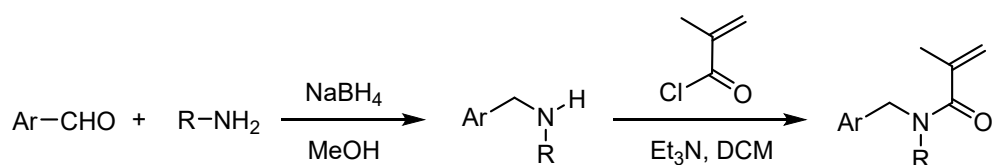
Methyl 3-(1,3-dimethyl-2-oxoindolin-3-yl)-2-fluoropropanoate (29). To a solution of **3** (0.20 mmol) in MeOH (2 mL) was added dimethylamine (2 mmol). The reaction mixture was stirred at 65 °C for 72 h. The solvent was evaporated under reduced pressure and the residue was chromatographed through silica gel eluting with ethyl acetate/petroleum ether to give the desired product as a yellow oil (**29**, 26 mg, 50% yield). ^1H NMR (400 MHz, CDCl_3) δ : 7.31–7.27 (m, 1H), 7.20 (dd, $J = 7.5, 1.4$ Hz, 1H), 7.08 (dd, $J = 7.5, 1.0$ Hz, 1H), 6.87 (d, $J = 7.8$ Hz, 1H), 4.88–4.73 (m, 1H), 3.60 (s, 3H), 3.24 (s, 3H), 2.63–2.53 (m, 1H), 2.53–2.42 (m, 1H), 1.41 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ : 179.6, 169.7 (d, $J_{\text{C-F}} = 23.5$ Hz), 143.4, 132.1, 128.5, 123.6, 122.6, 108.5, 86.9 (d, $J_{\text{C-F}} = 187.1$ Hz), 52.6, 46.2, 39.5 (d, $J_{\text{C-F}} = 19.8$ Hz), 26.5, 25.1; ^{19}F NMR (377 MHz, CDCl_3) δ : -190.8; HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd. for $\text{C}_{14}\text{H}_{17}\text{FNO}_3^+$: 266.1187, Found: 266.1187.

*N*¹,*N*³-Dibutyl-2-((1,3-dimethyl-2-oxoindolin-3-yl)methyl)-2-fluoromalonamide (**30**)



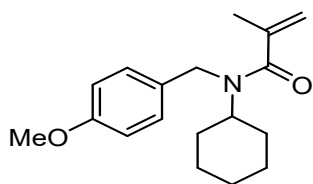
*N*¹,*N*³-Dibutyl-2-((1,3-dimethyl-2-oxoindolin-3-yl)methyl)-2-fluoromalonamide (**30**). To a solution of **3** (0.20 mmol) in MeOH (2 mL) was added butan-1-amine (2 mmol). The reaction mixture was stirred at 50 °C for 42 h. The solvent was evaporated under reduced pressure and the residue was chromatographed through silica gel eluting with ethyl acetate/petroleum ether to give the desired product as a yellow oil (**30**, 66 mg, 34% yield). ¹H NMR (400 MHz, CDCl₃) δ: 7.28–7.21 (m, 2H), 7.02 (tt, *J* = 7.5, 0.9 Hz, 1H), 6.83 (d, *J* = 7.7 Hz, 1H), 6.56 (t, *J* = 6.0 Hz, 1H), 6.02 (q, *J* = 5.0 Hz, 1H), 3.26–3.18 (m, 4H), 3.16–3.08 (m, 1H), 3.04–2.91 (m, 2H), 2.80 (ddd, *J* = 14.9, 8.5, 0.9 Hz, 1H), 2.66–2.58 (m, 1H), 2.24–2.11 (m, 1H), 1.47–1.39 (m, 2H), 1.34 (s, 3H), 1.28 (dt, *J* = 7.7, 6.1 Hz, 2H), 1.22–1.16 (m, 3H), 0.93–0.83 (m, 6H); ¹³C NMR (101 MHz, CDCl₃) δ: 179.7, 166.8 (d, *J*_{C-F} = 22.2 Hz), 166.2 (d, *J*_{C-F} = 22.7 Hz), 143.6, 130.7, 128.3, 125.0, 122.0, 107.9, 95.6 (d, *J*_{C-F} = 200.8 Hz), 45.8 (d, *J*_{C-F} = 2.0 Hz), 42.2 (d, *J*_{C-F} = 20.3 Hz), 39.5, 39.4, 31.2, 30.9, 26.5, 26.2, 20.0 (2C), 13.8 (2C); ¹⁹F NMR (377 MHz, CDCl₃) δ: -171.4. HRMS (ESI) ([*M*+*H*]⁺) Calcd. for C₂₂H₃₃FN₃O₃⁺: 406.2500, Found: 406.2501.

6. Synthesis and Characterization of Unknown Substrates

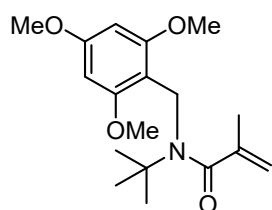


Step 1: To a solution of ArCHO (3.0 mmol) and RNH₂ (3.0 mmol) in MeOH (15 mL) was added NaBH₄ (3.6 mmol). The reaction mixture was stirred at rt for 6 h. The solvent was evaporated under reduced pressure and extracted with EtOAc. The organic layer was dried over Na₂SO₄, and concentrated to afford the crude product. The crude product was directly used in the next step without purification.

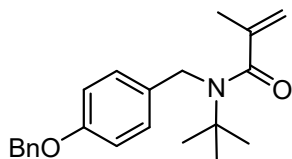
Step 2: To a solution of above crude product and Et₃N (6.0 mmol) in DCM (15 mL) was added methacryloyl chloride (3.6 mmol). The reaction mixture was stirred at rt for 12 h. The solvent was evaporated under reduced pressure and the residue was chromatographed through silica gel eluting with ethyl acetate/petroleum ether to give the desired product.



***N*-Cyclohexyl-*N*-(4-methoxybenzyl)methacrylamide (S1).** Yellow oil (54% yield); ¹H NMR (400 MHz, CDCl₃) δ: 7.16 (d, *J* = 8.2 Hz, 2H), 6.83 (d, *J* = 8.2 Hz, 2H), 5.29 (s, 1H), 5.09 (d, *J* = 27.2 Hz, 2H), 4.51 (s, 2H), 3.78 (s, 3H), 2.13–1.87 (m, 3H), 1.76–1.61 (m, 5H), 1.47–1.37 (m, 2H), 1.31–1.18 (m, 2H), 1.08–0.96 (m, 1H); ¹³C NMR (101 MHz, CDCl₃) δ: 173.3, 158.4, 141.8, 131.6, 128.2, 114.0, 113.8, 58.9, 55.3, 53.5, 43.4, 32.3, 26.0, 25.3, 20.9; HRMS (ESI) ([M+H]⁺) Calcd. for C₁₈H₂₆NO₂⁺: 288.1958, Found:288.1955.



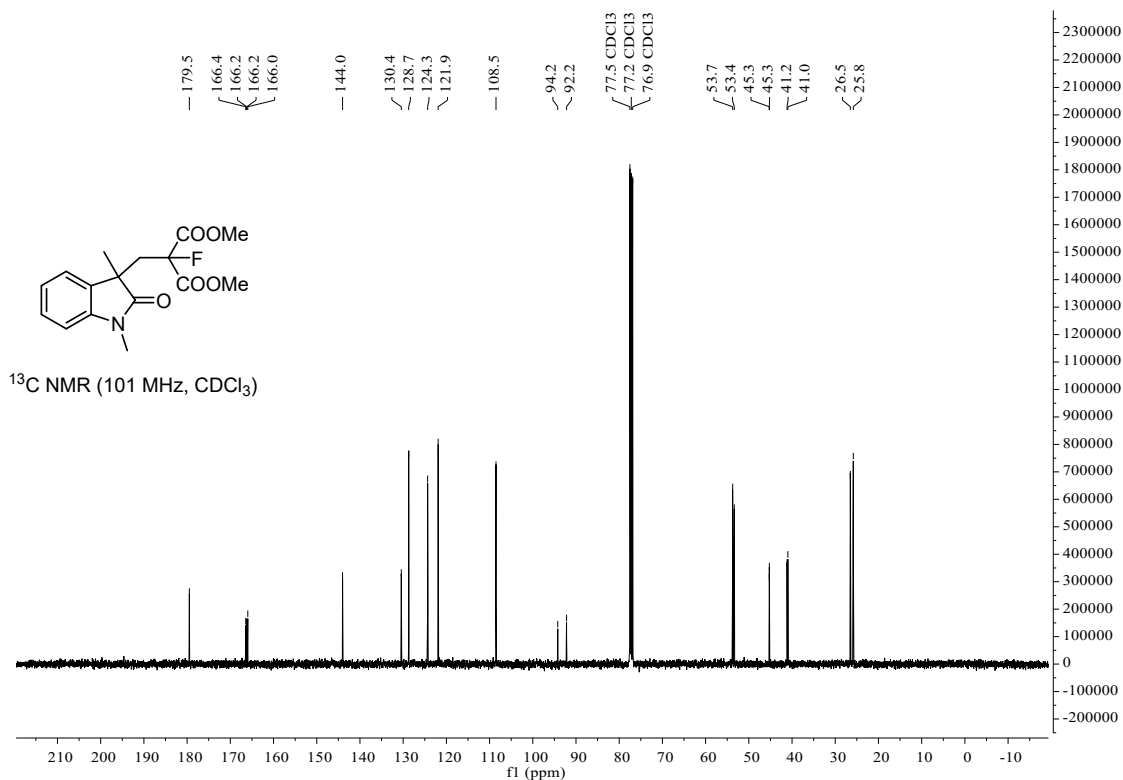
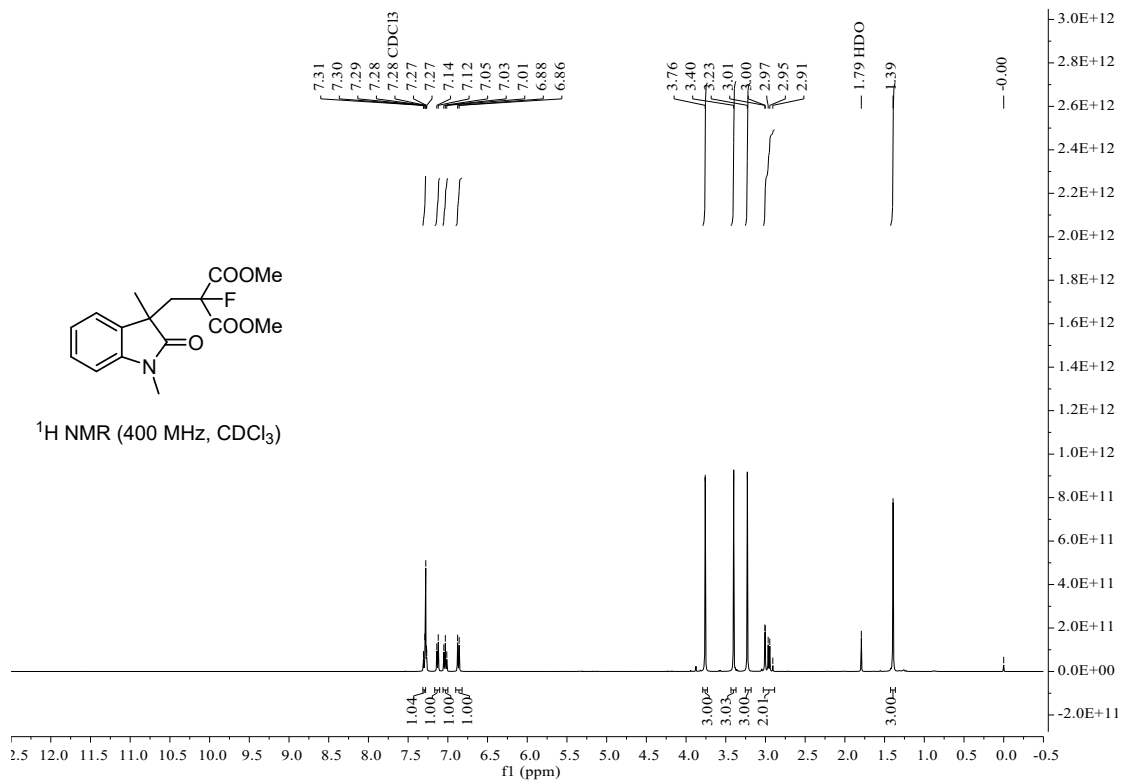
***N*-(*tert*-Butyl)-*N*-(2,4,6-trimethoxybenzyl)methacrylamide (S2).** White solid (70% yield); m.p. = 126.9–127.6 °C; ¹H NMR (400 MHz, CDCl₃) δ: 6.09 (s, 2H), 5.14–5.06 (m, 3H), 4.71 (s, 2H), 3.81 (s, 4H), 3.78 (s, 7H), 1.99 (t, *J* = 1.3 Hz, 3H), 1.27 (s, 10H); ¹³C NMR (101 MHz, CDCl₃) δ: 176.2, 160.7, 159.4, 144.6, 115.2, 107.7, 90.6, 56.4, 55.5, 55.4, 41.9, 28.4, 19.9; HRMS (ESI) ([*M*+*H*]⁺) Calcd. for C₁₈H₂₈NO₄⁺: 322.2013, Found: 322.2007.

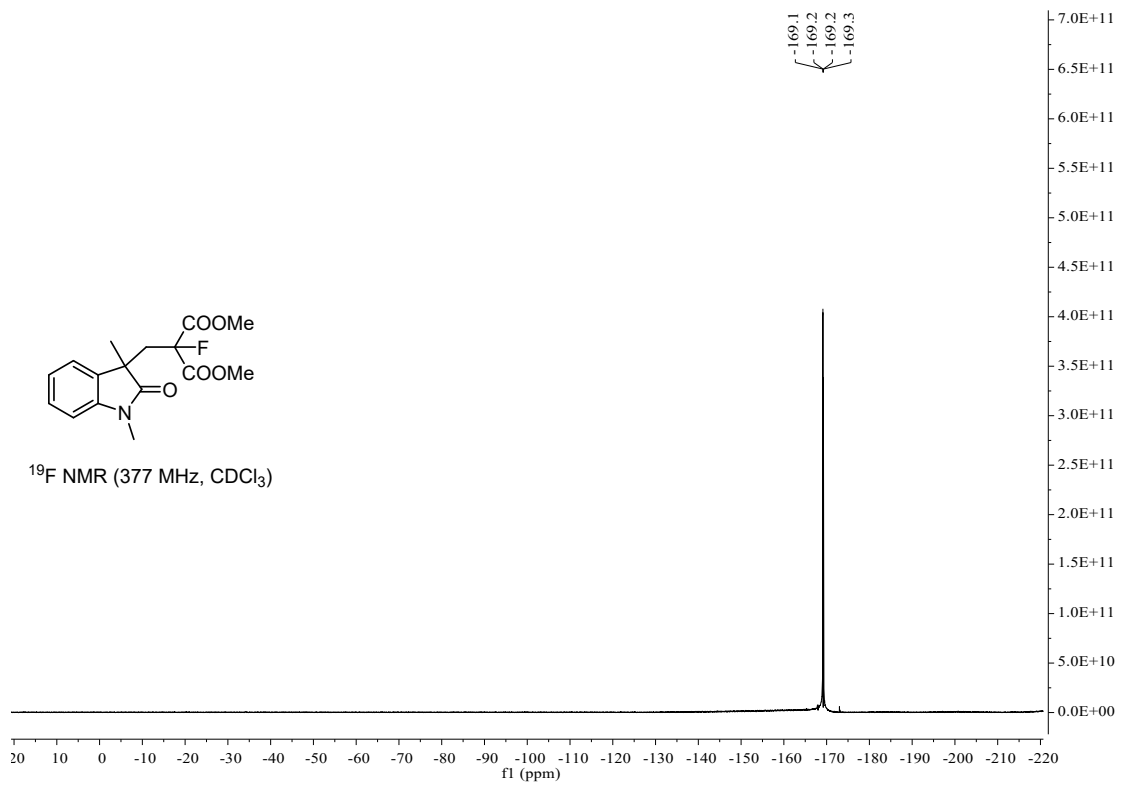


***N*-(4-(Benzyloxy)benzyl)-*N*-(*tert*-butyl)methacrylamide (S3).** White solid (85% yield); m.p. = 77.4–78.2 °C; ¹H NMR (400 MHz, CDCl₃) δ: 7.45–7.32 (m, 5H), 7.13 (d, *J* = 8.5 Hz, 2H), 6.97–6.93 (m, 2H), 5.05 (s, 2H), 5.02 (s, 1H), 4.94–4.93 (m, *J* = 1.5 Hz, 1H), 4.61 (s, 2H), 1.93 (s, 2H), 1.42 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ: 174.8, 158.0, 143.3, 137.1, 132.5, 128.8, 128.2, 127.7, 127.4, 115.0, 113.5, 70.3, 57.7, 50.4, 28.8, 21.0; HRMS (ESI) ([*M*+*H*]⁺) Calcd. for C₁₈H₂₆NO₂⁺: 338.2115, Found: 338.2113.

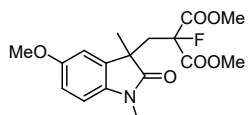
7. NMR Spectra for Products

Compound 3

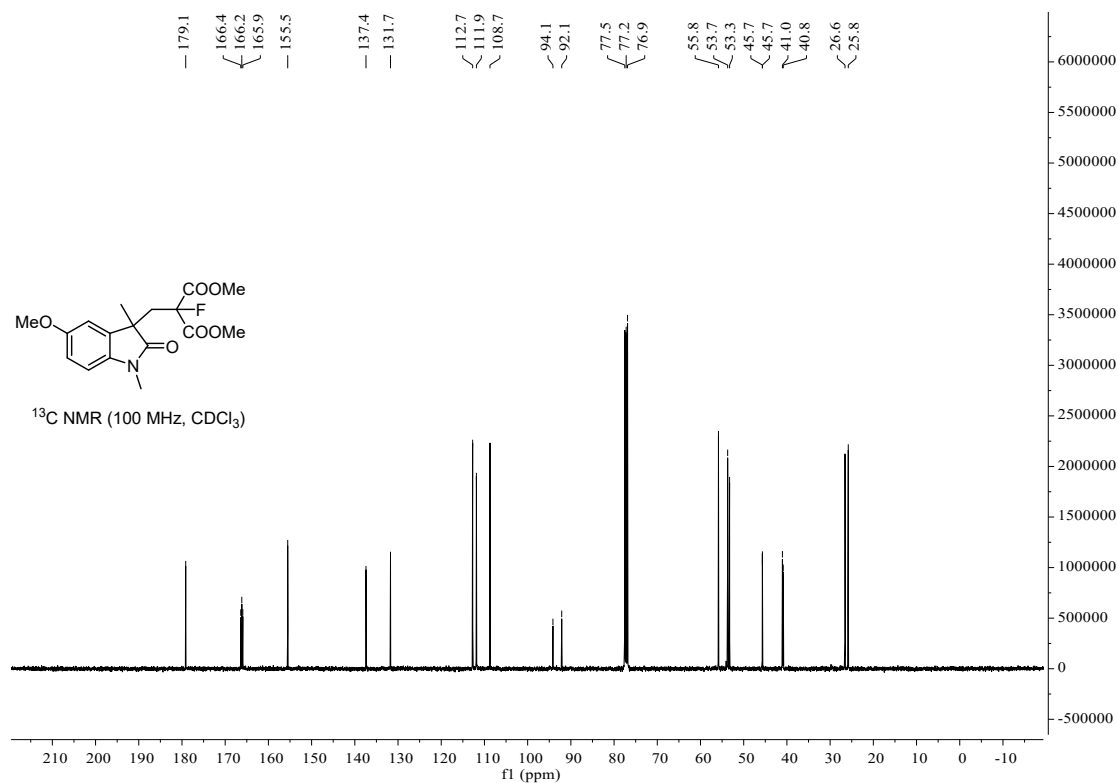
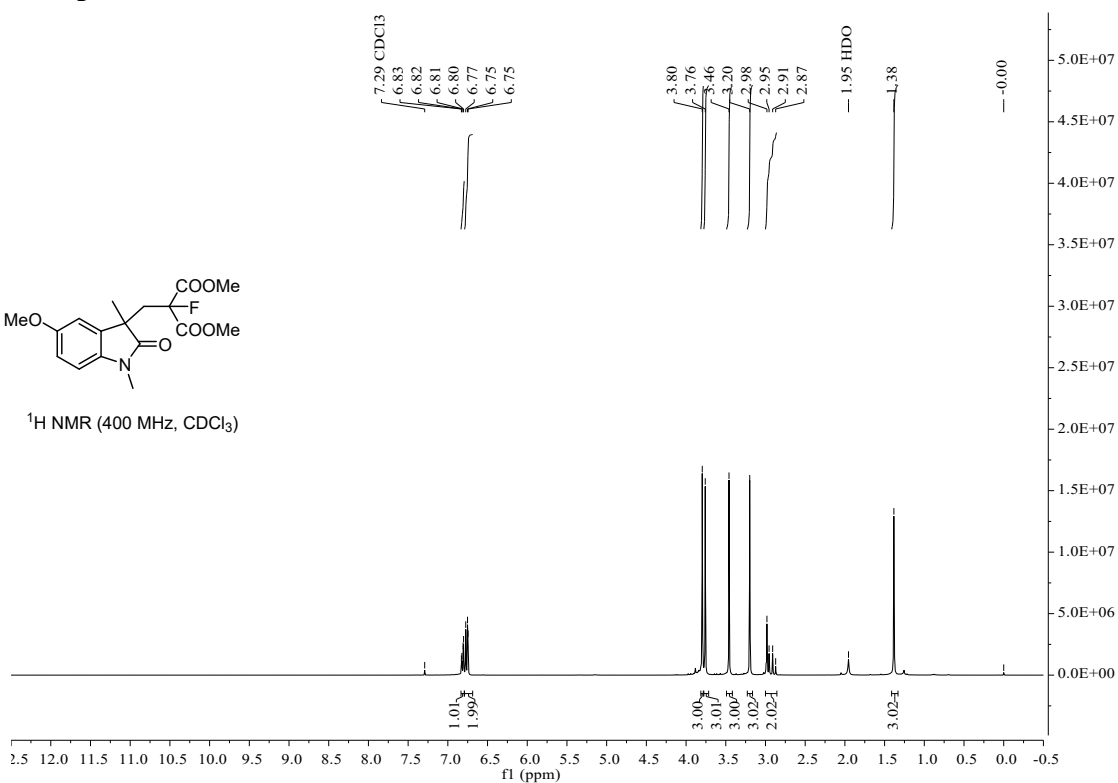


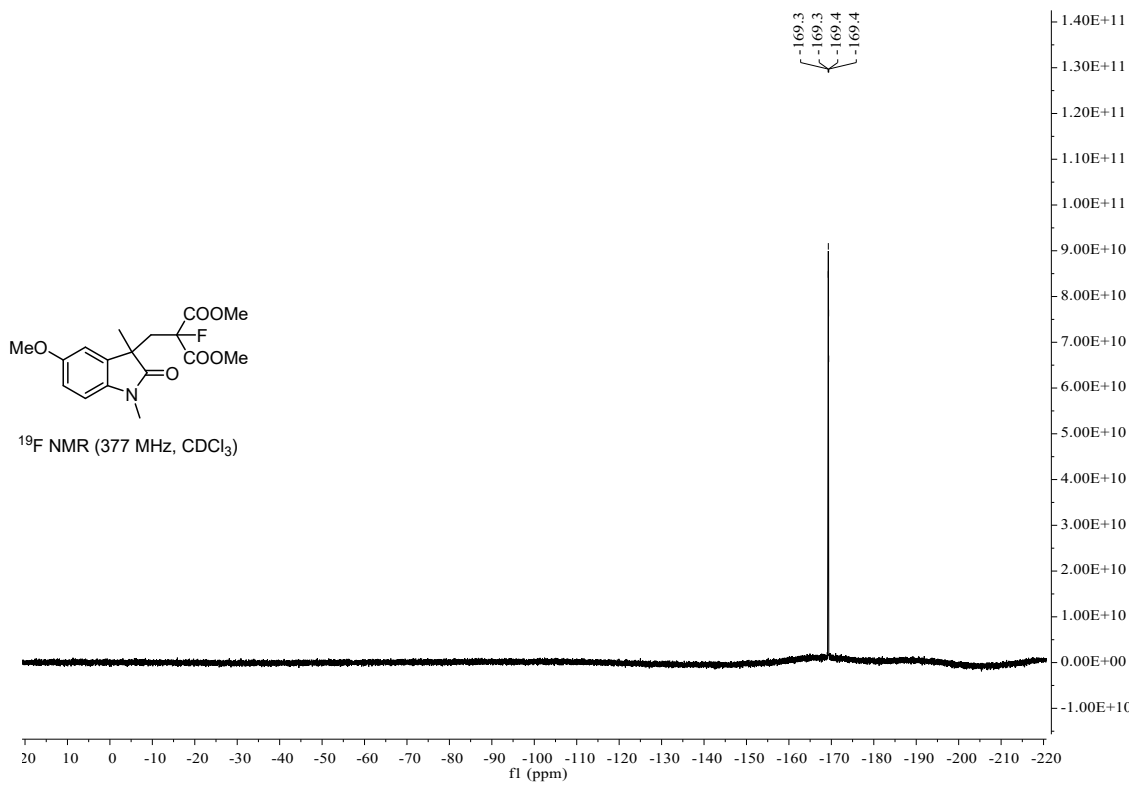


Compound 4

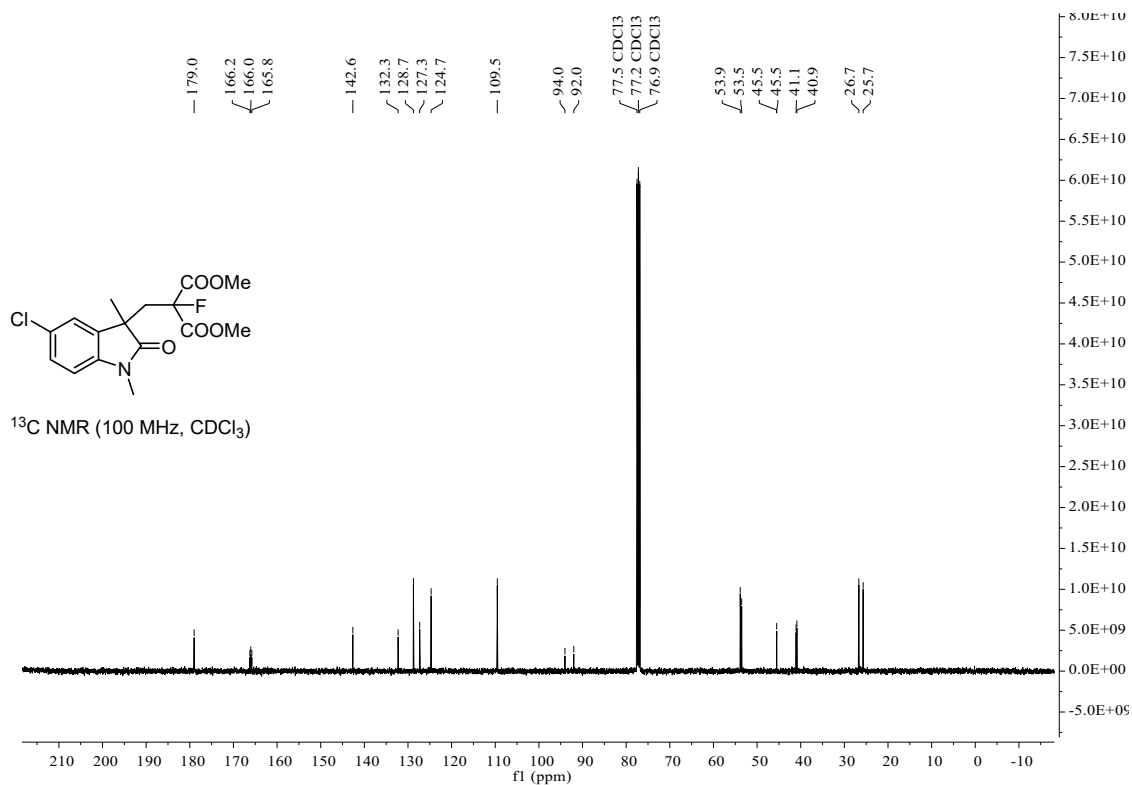
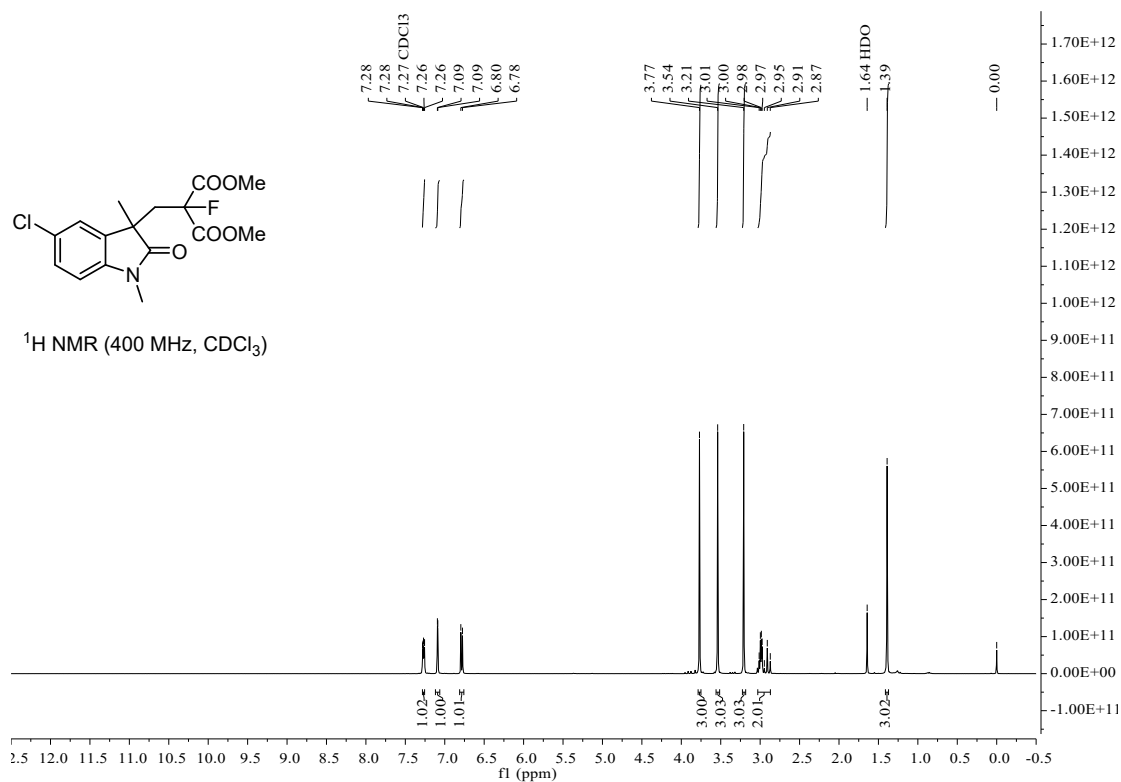


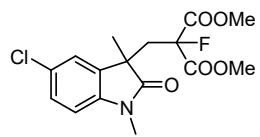
¹H NMR (400 MHz, CDCl₃)



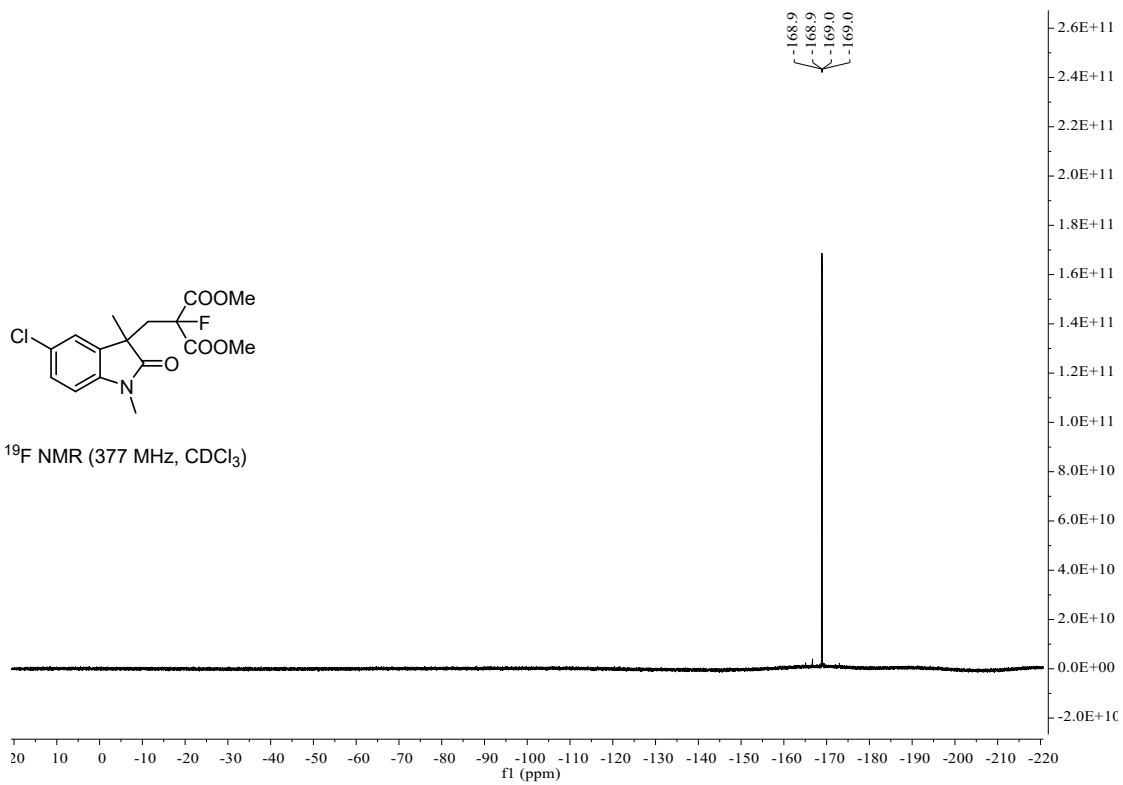


Compound 5

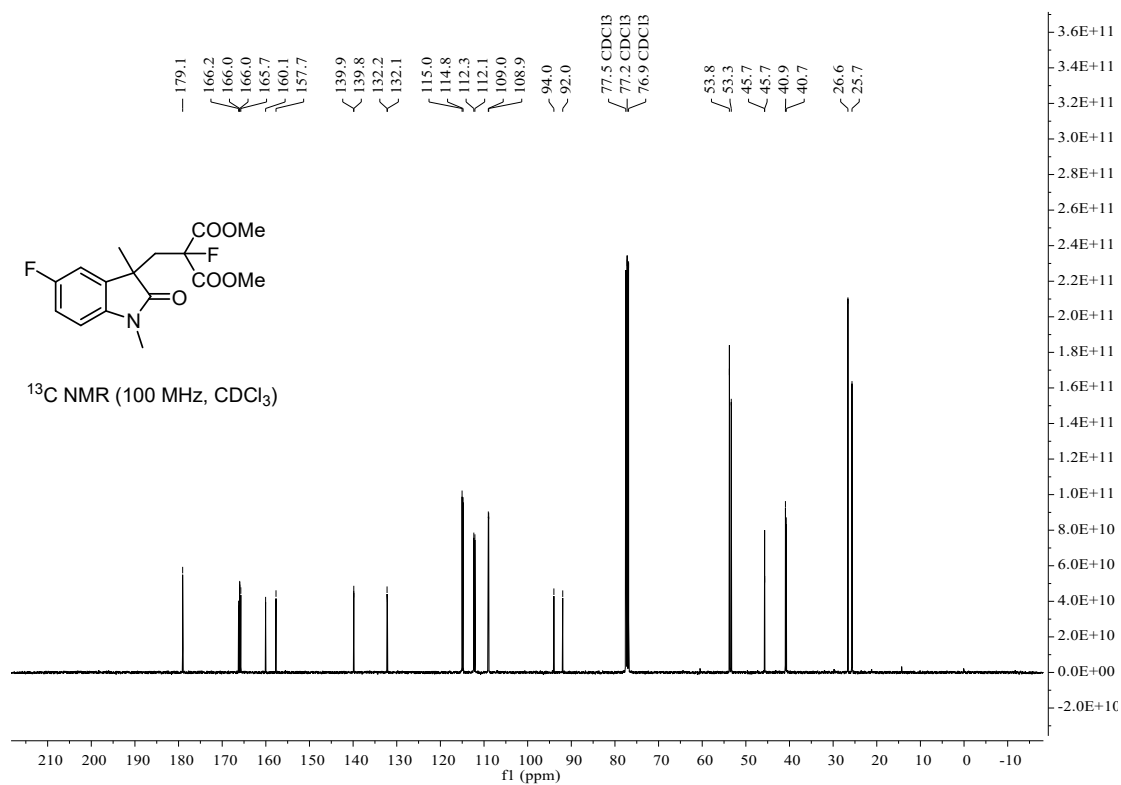
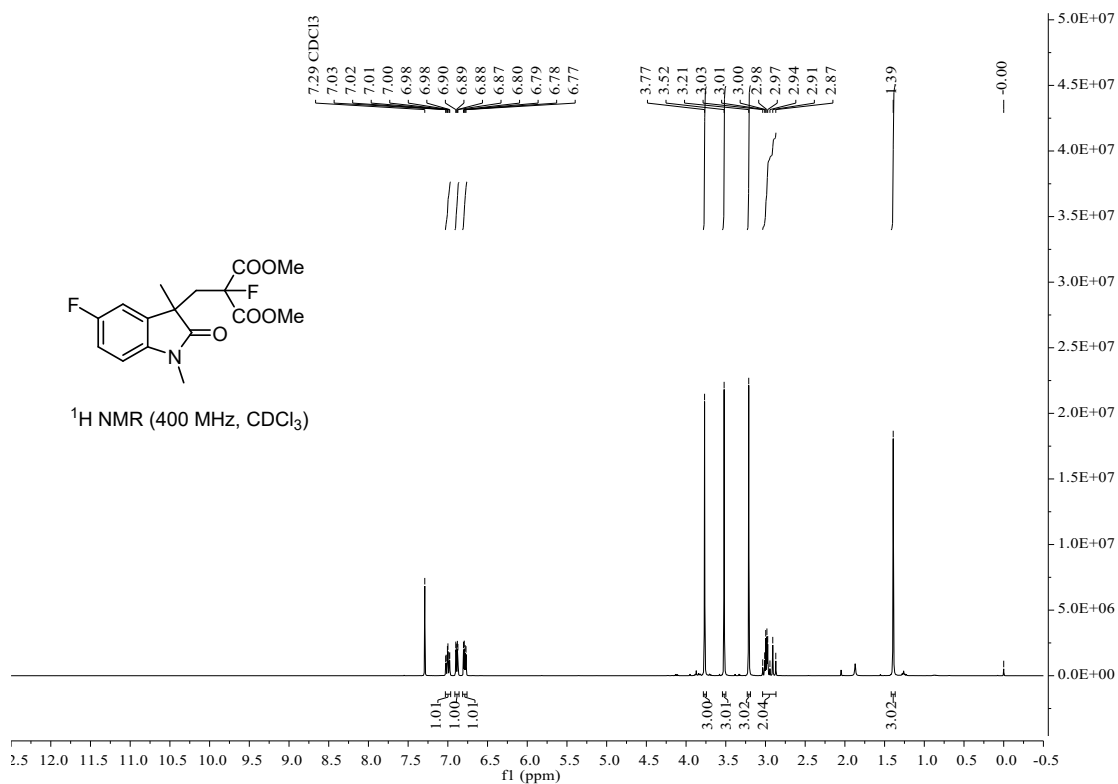


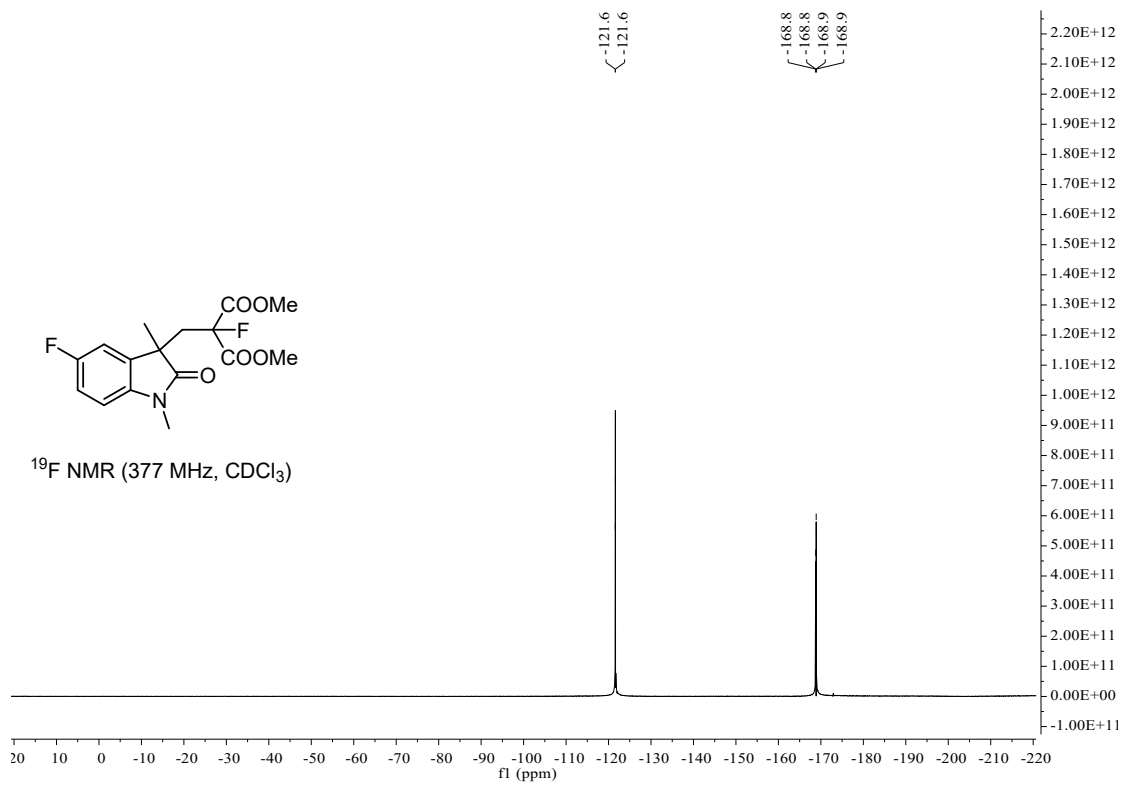


^{19}F NMR (377 MHz, CDCl_3)

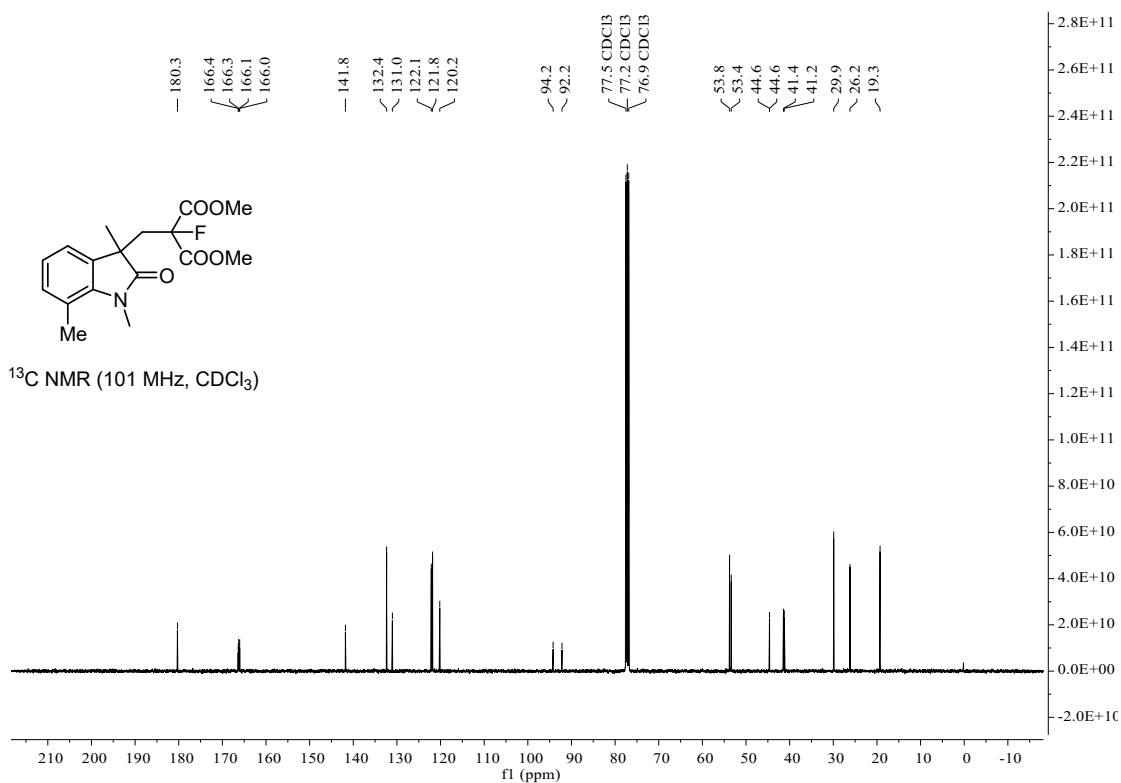
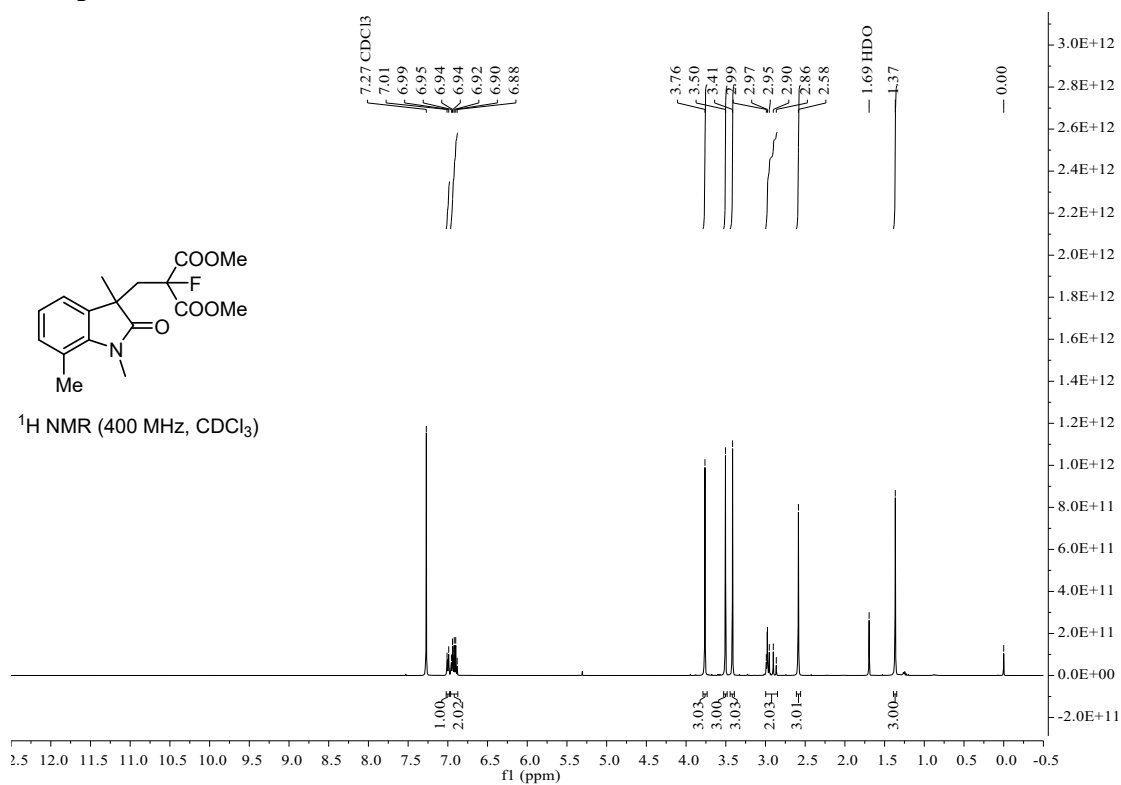


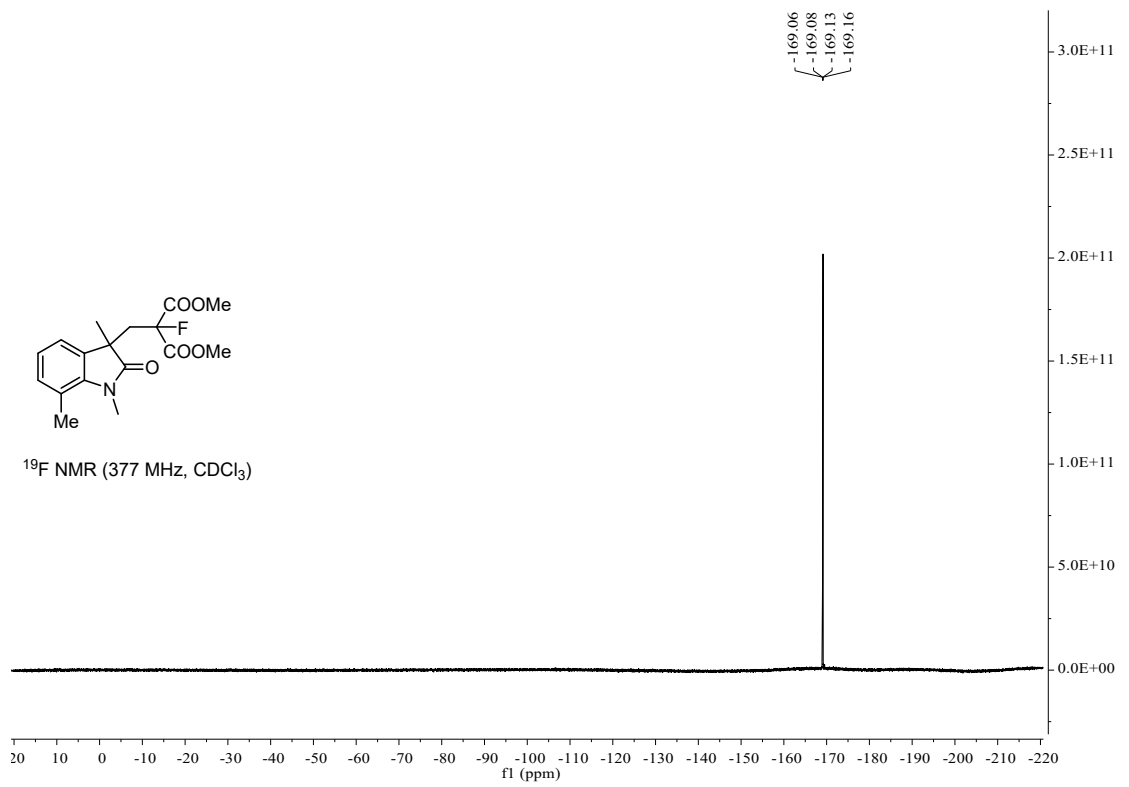
Compound 6



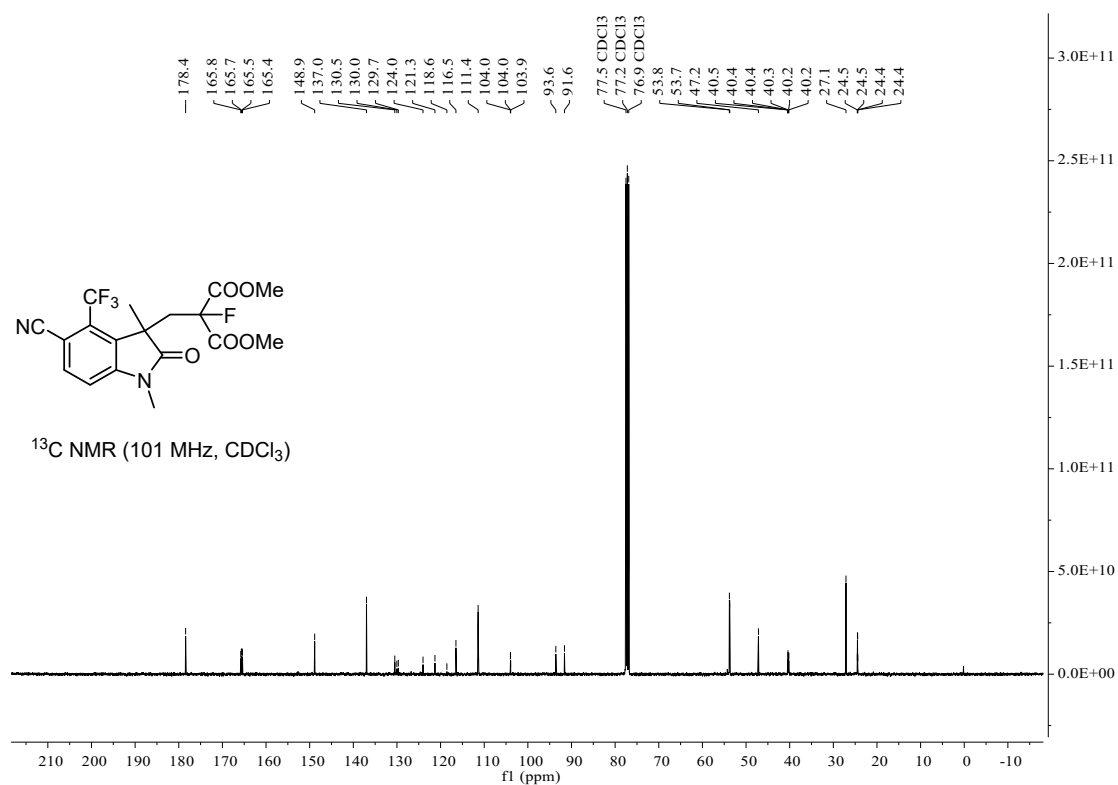
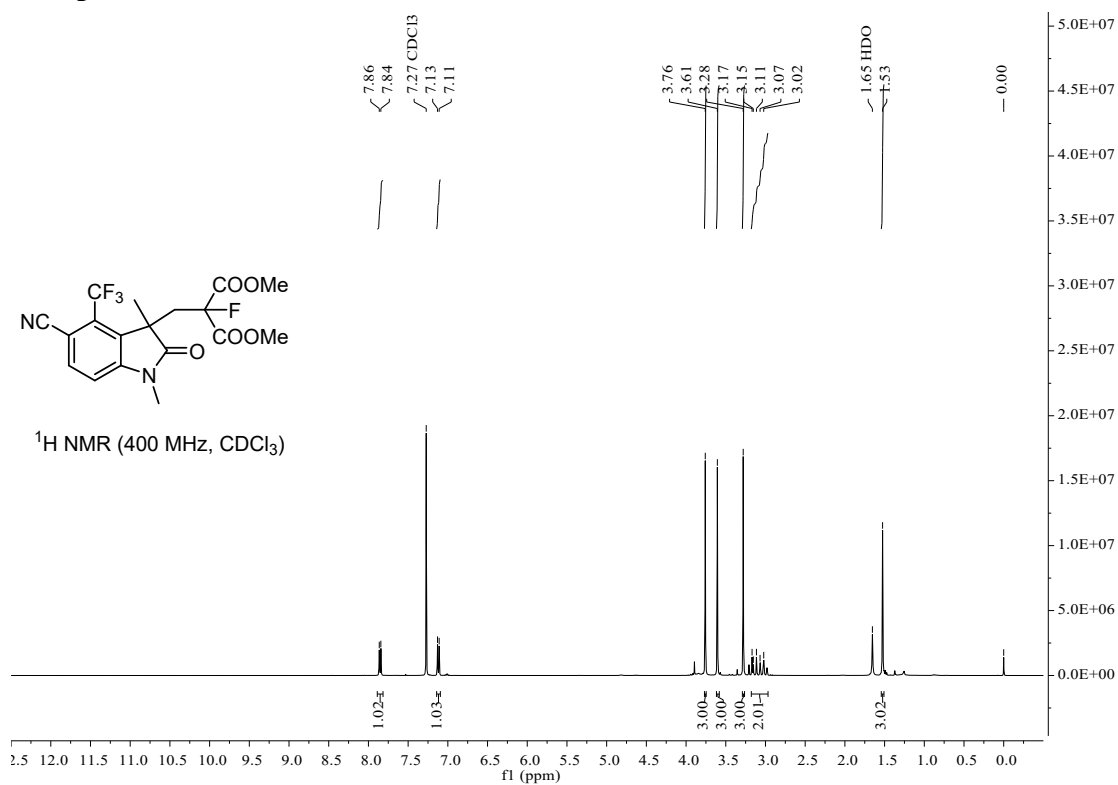


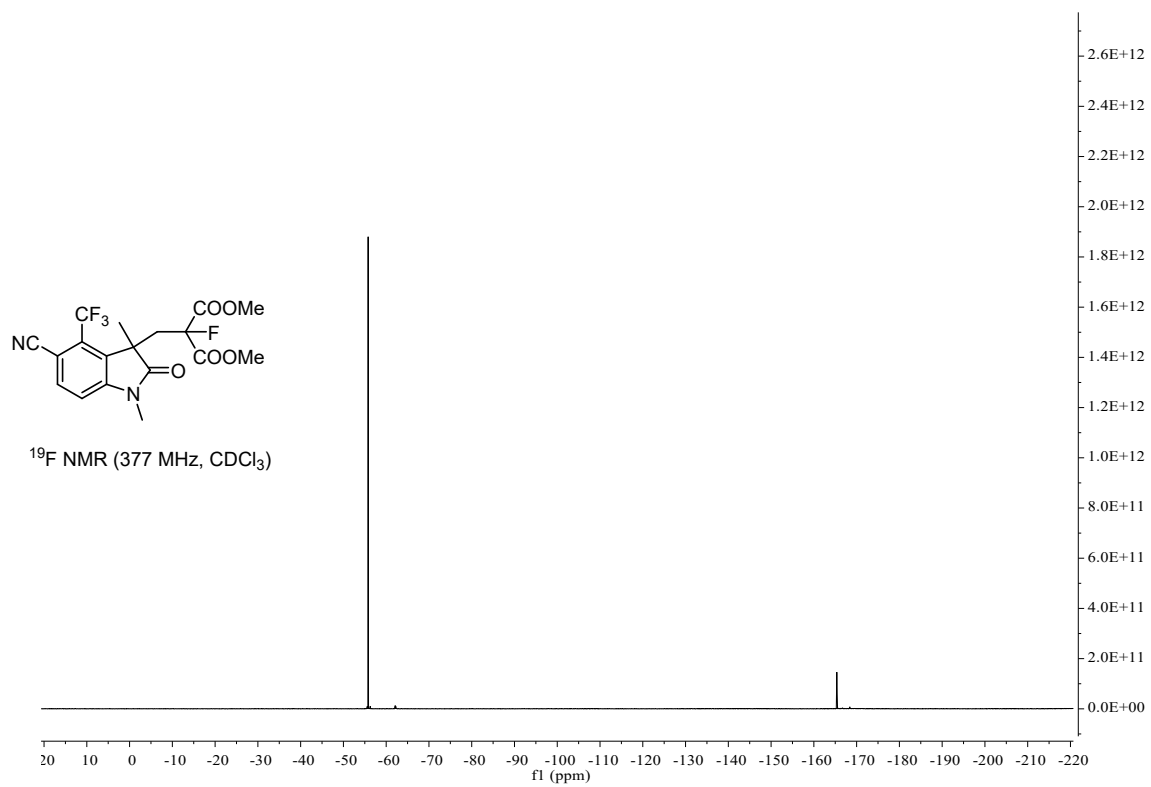
Compound 7



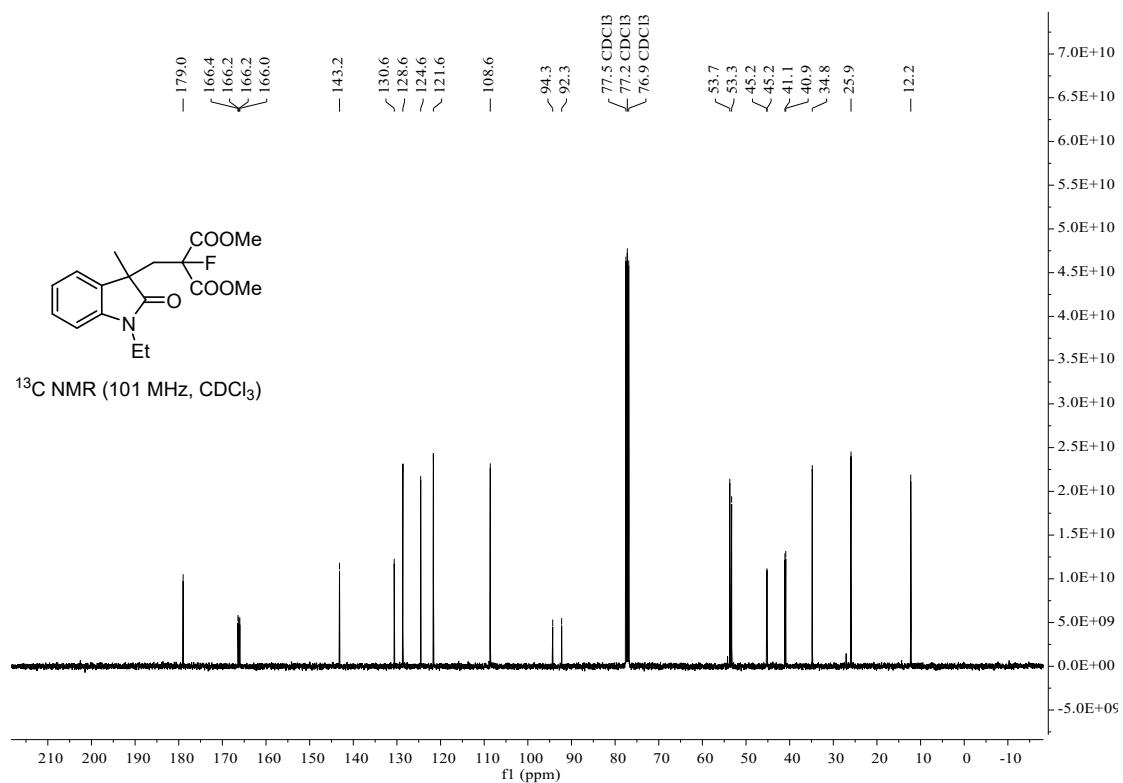
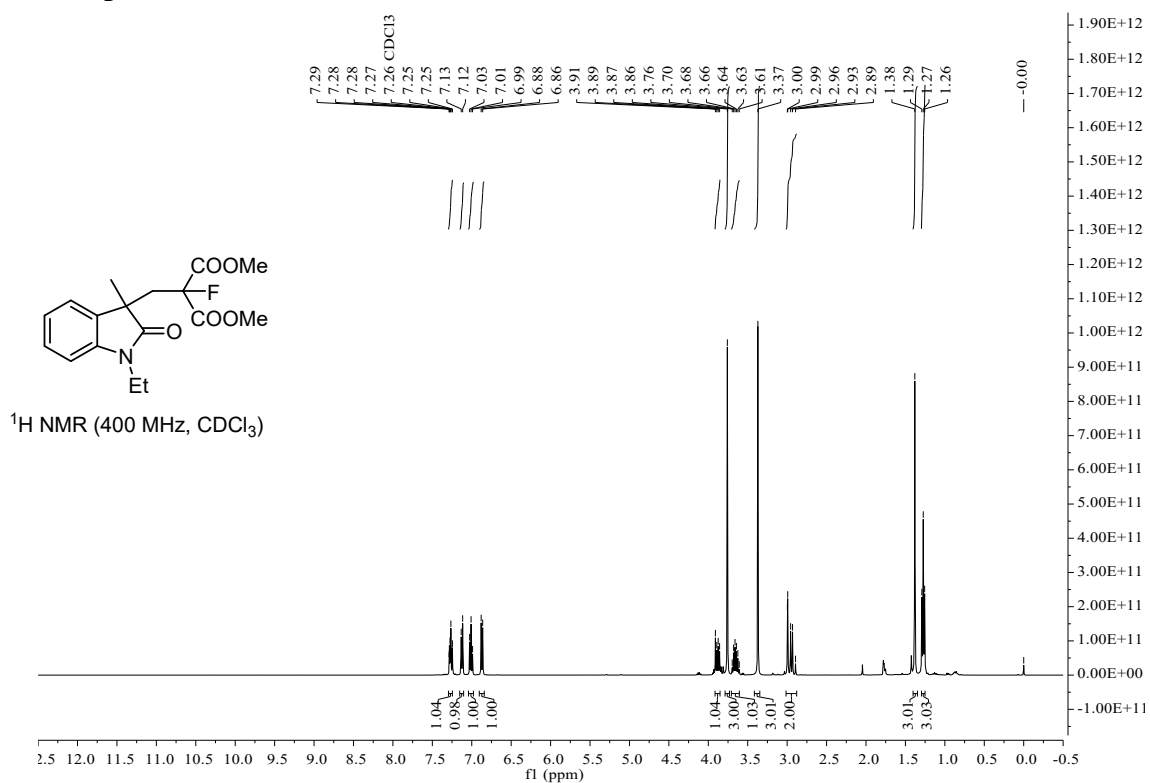


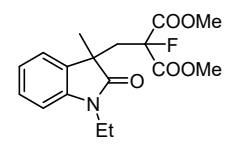
Compound 8



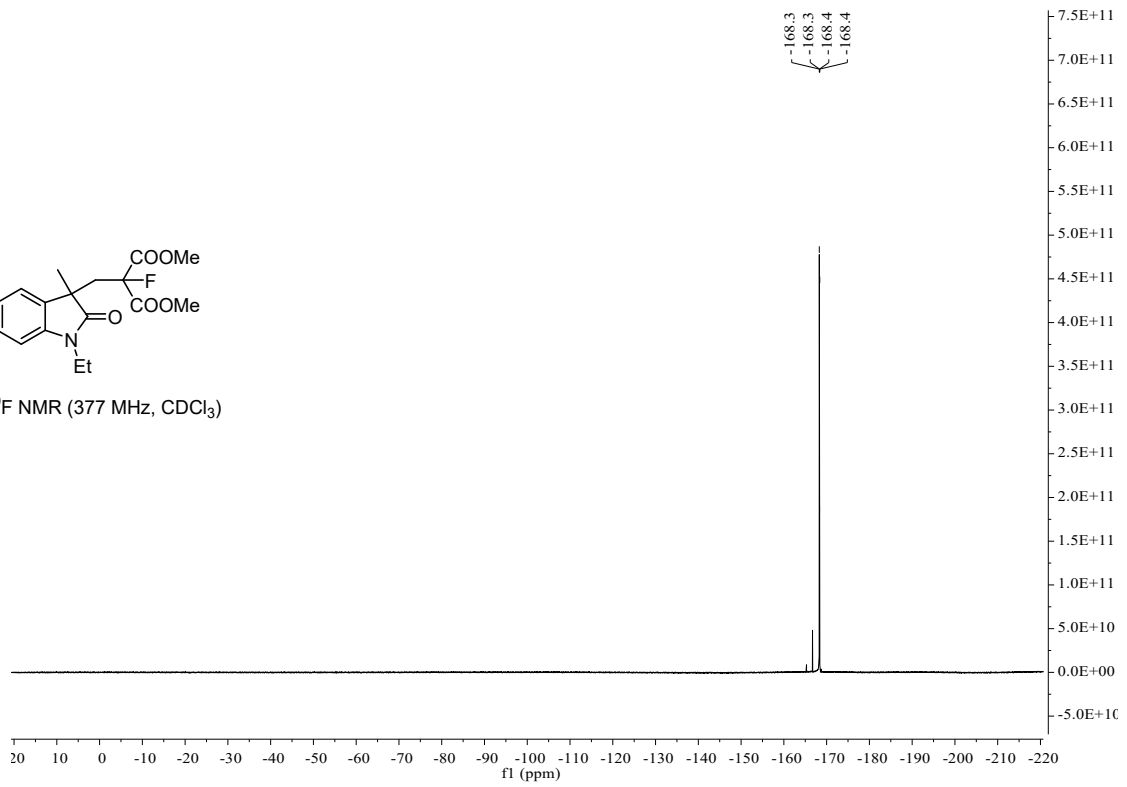


Compound 9

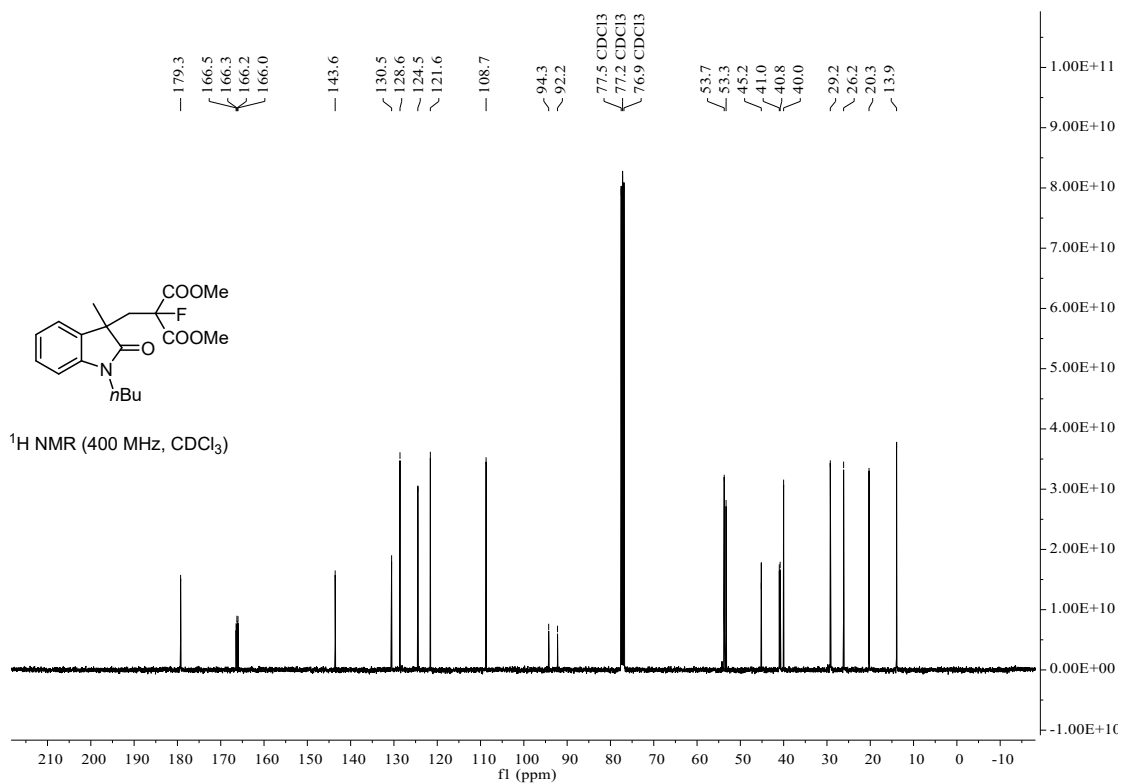
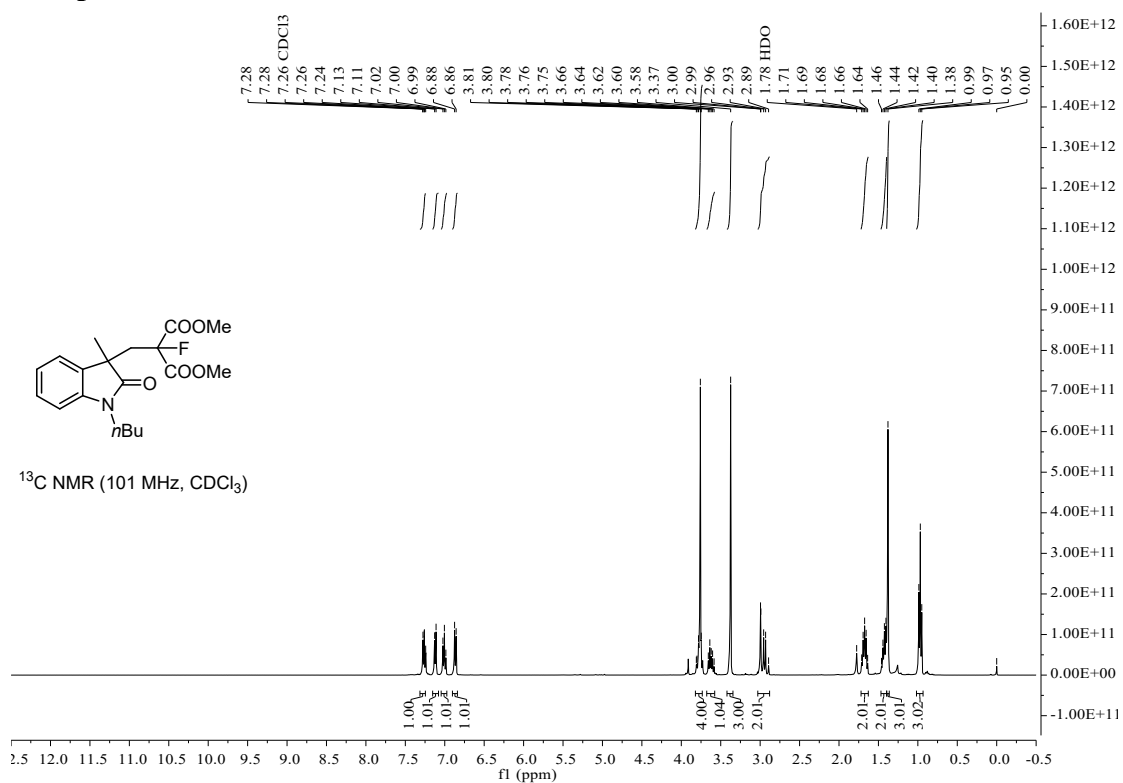


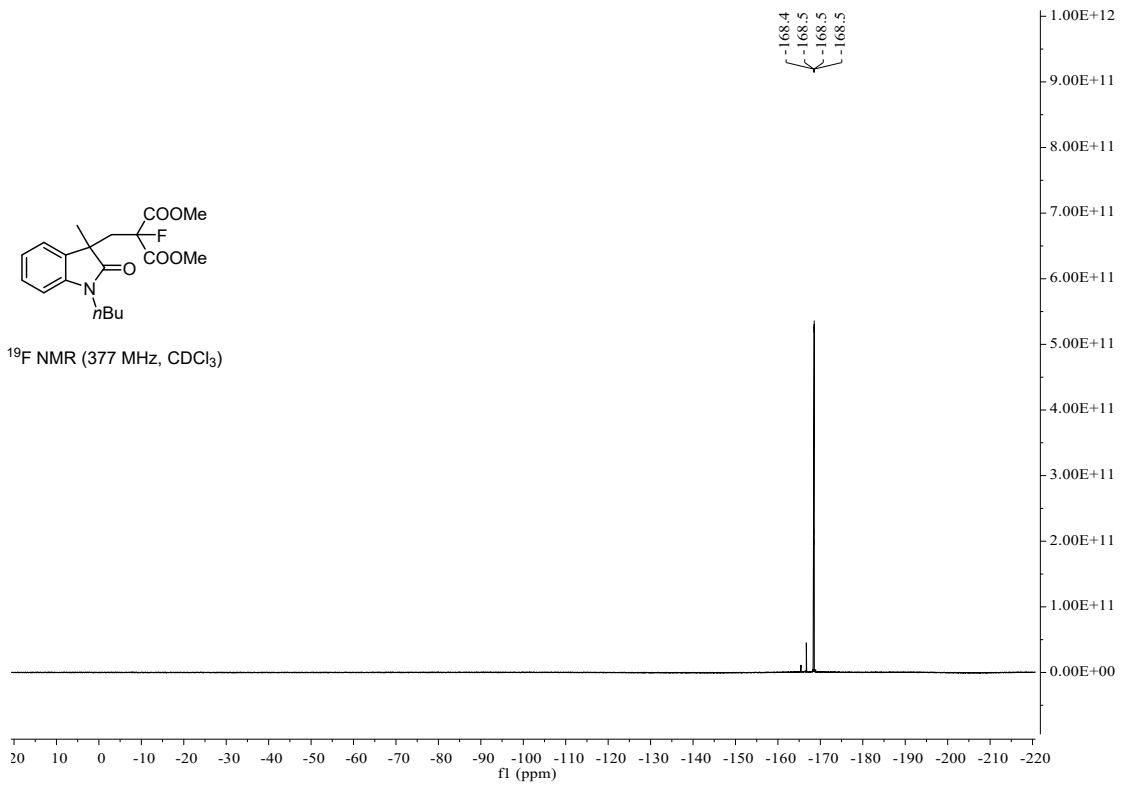


^{19}F NMR (377 MHz, CDCl_3)

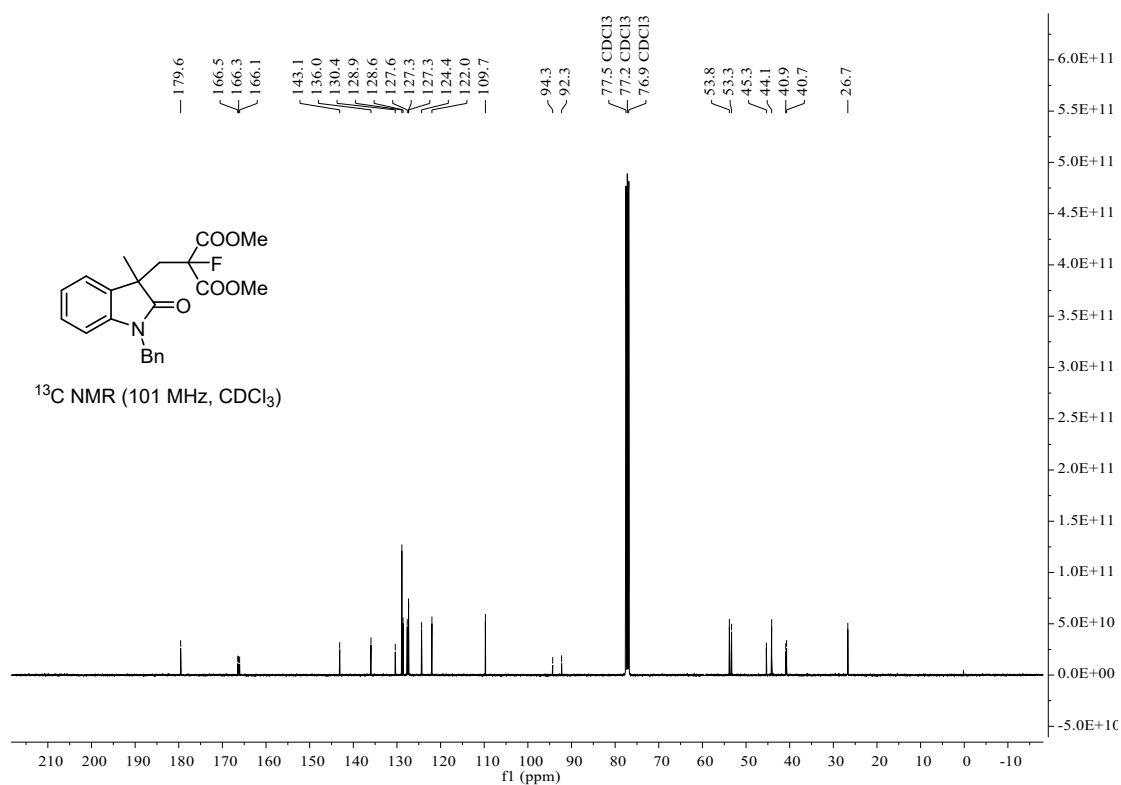
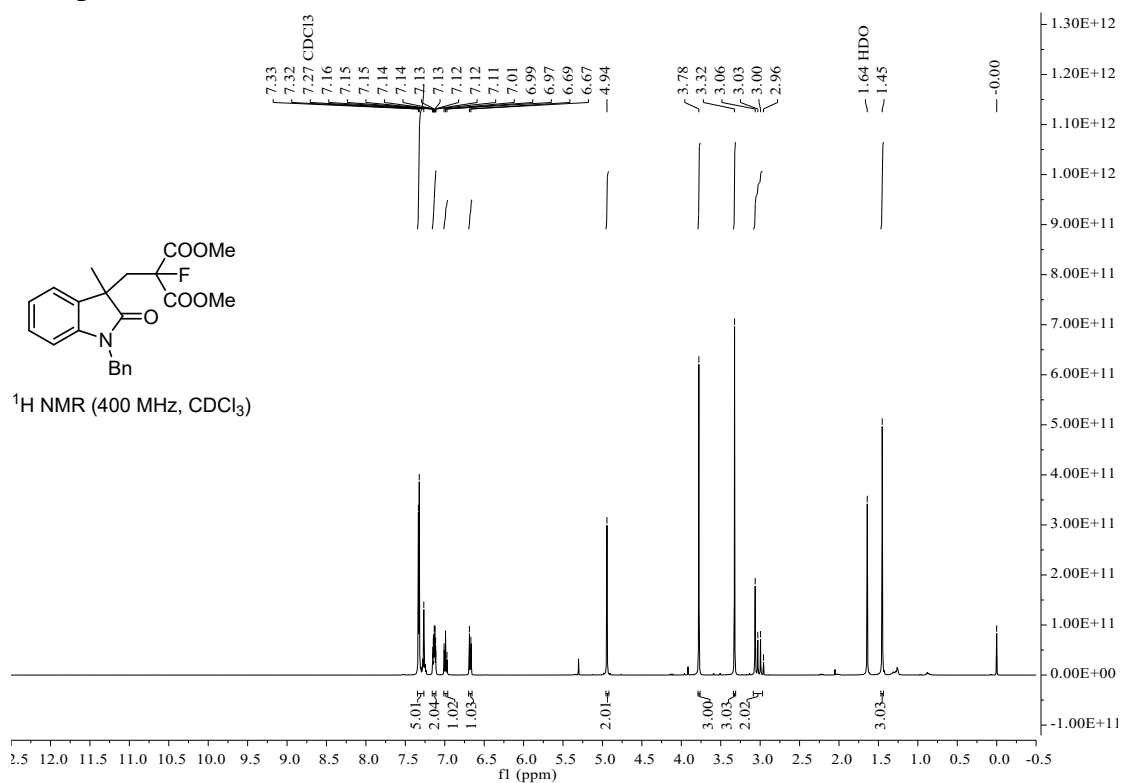


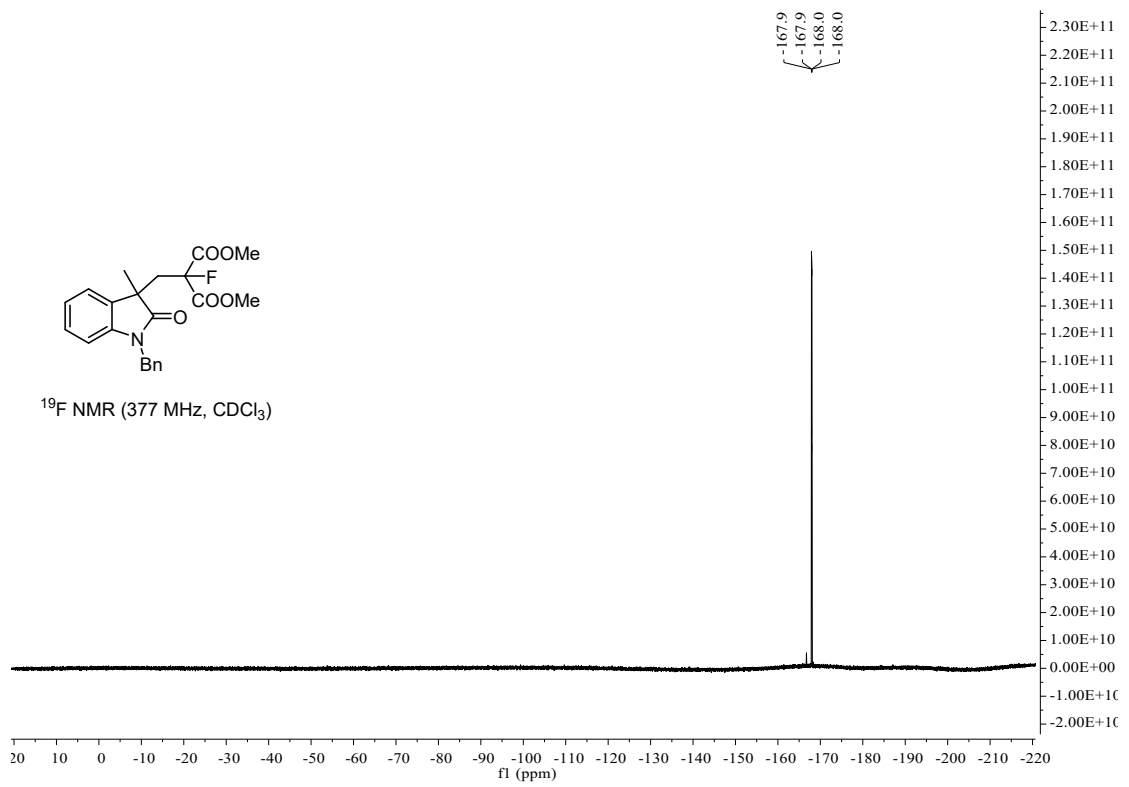
Compound 10



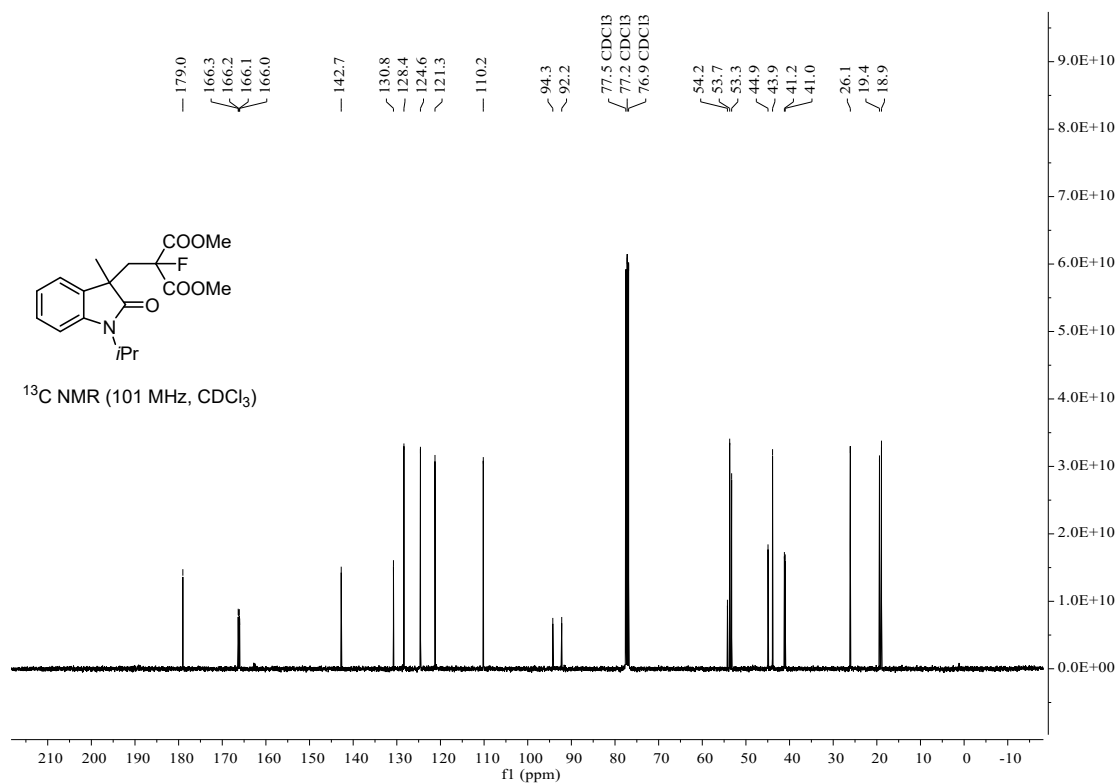
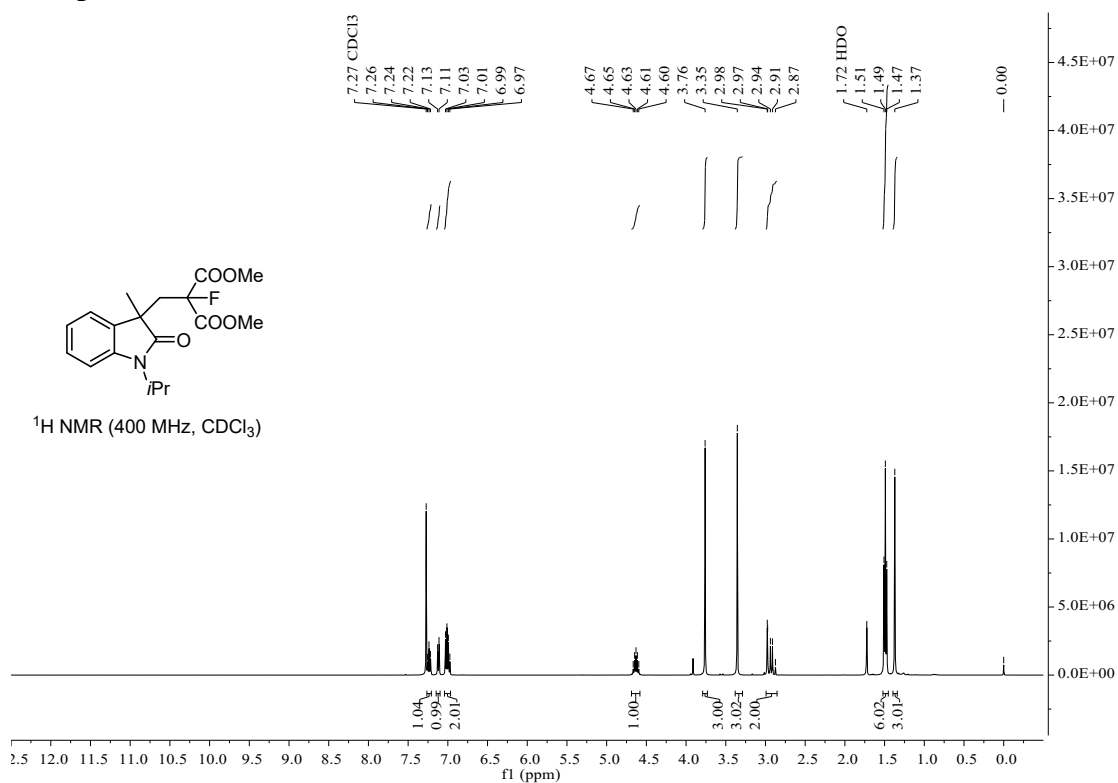


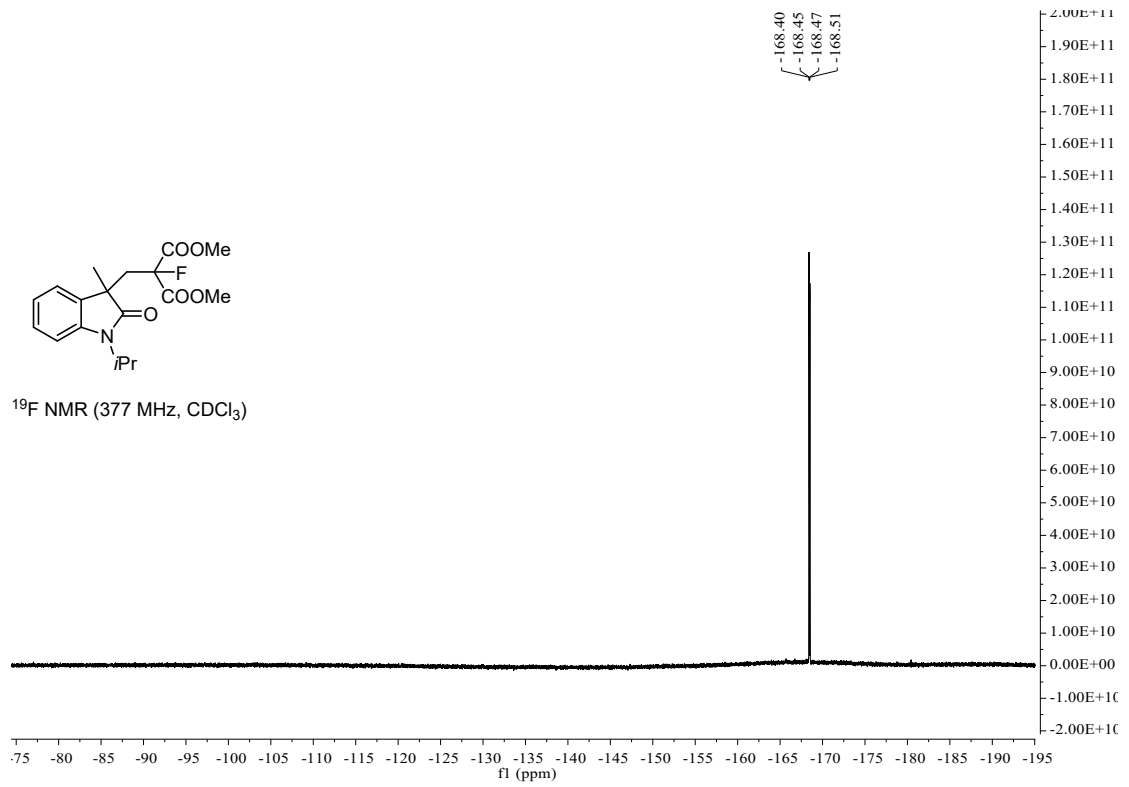
Compound 11



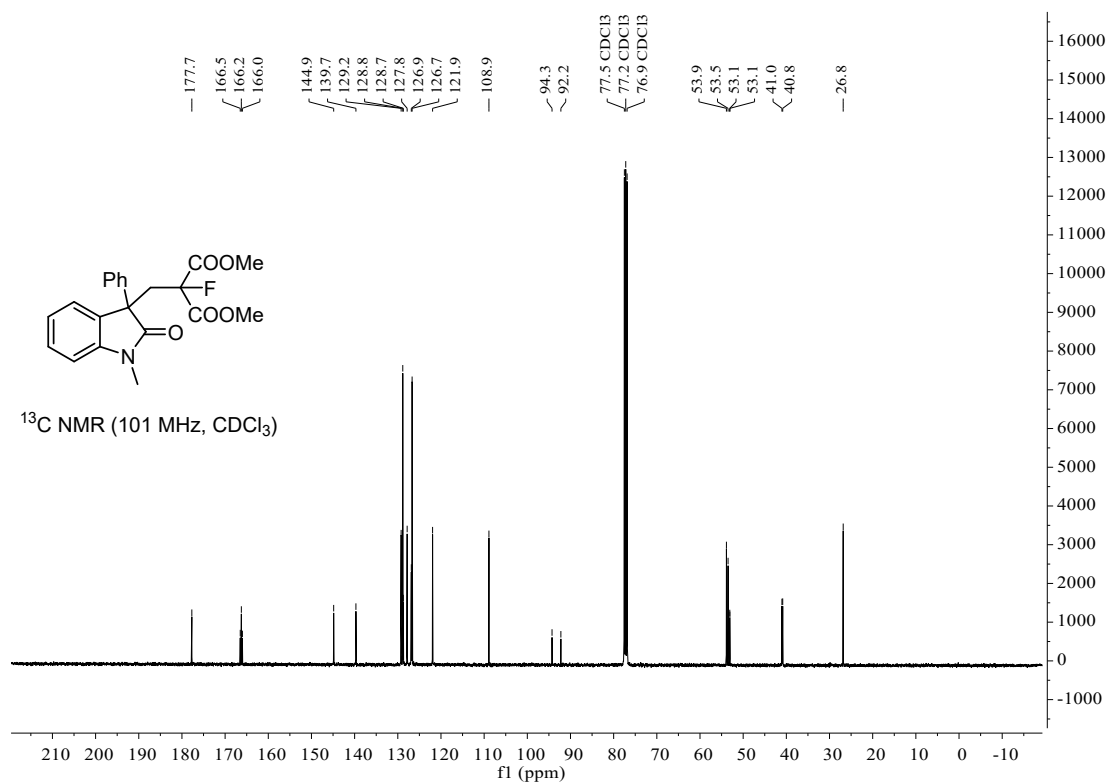
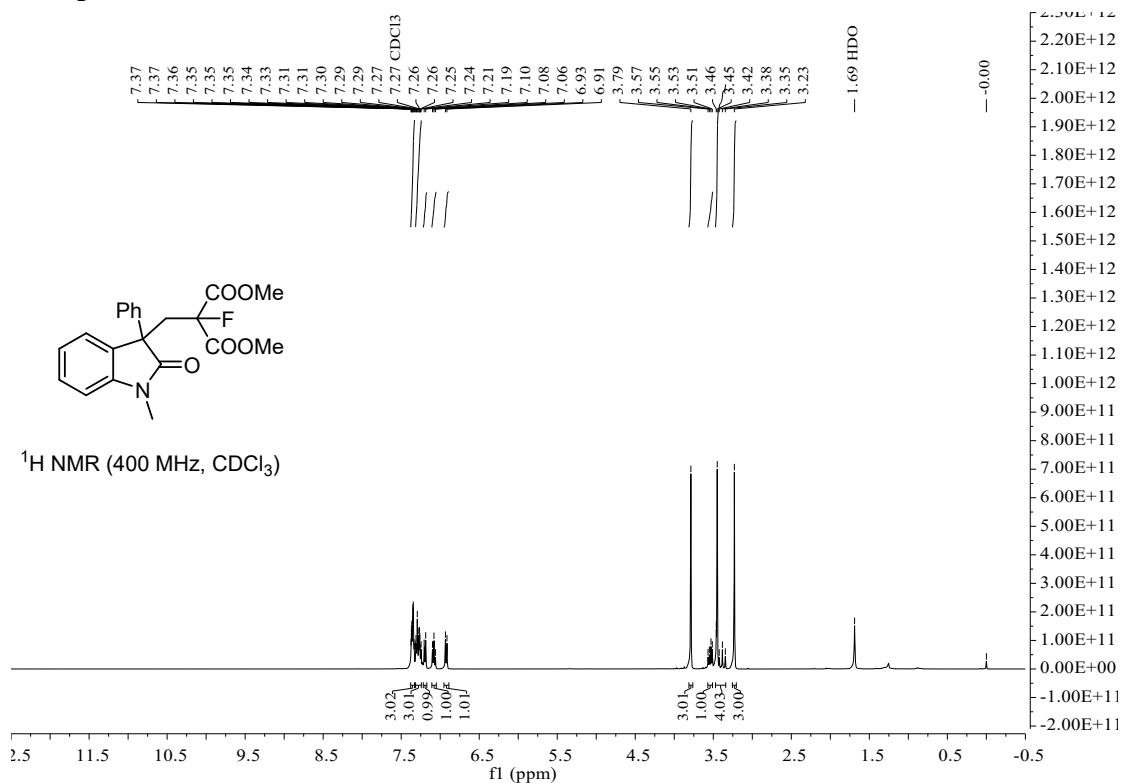


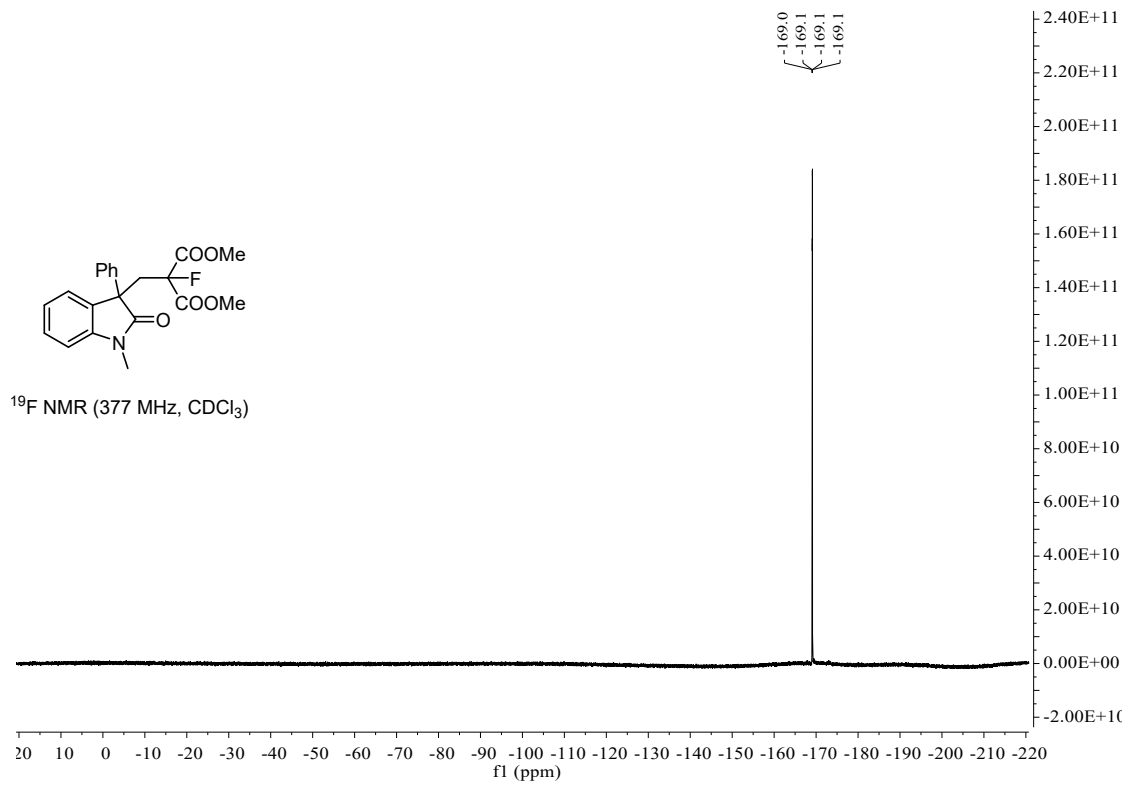
Compound 12



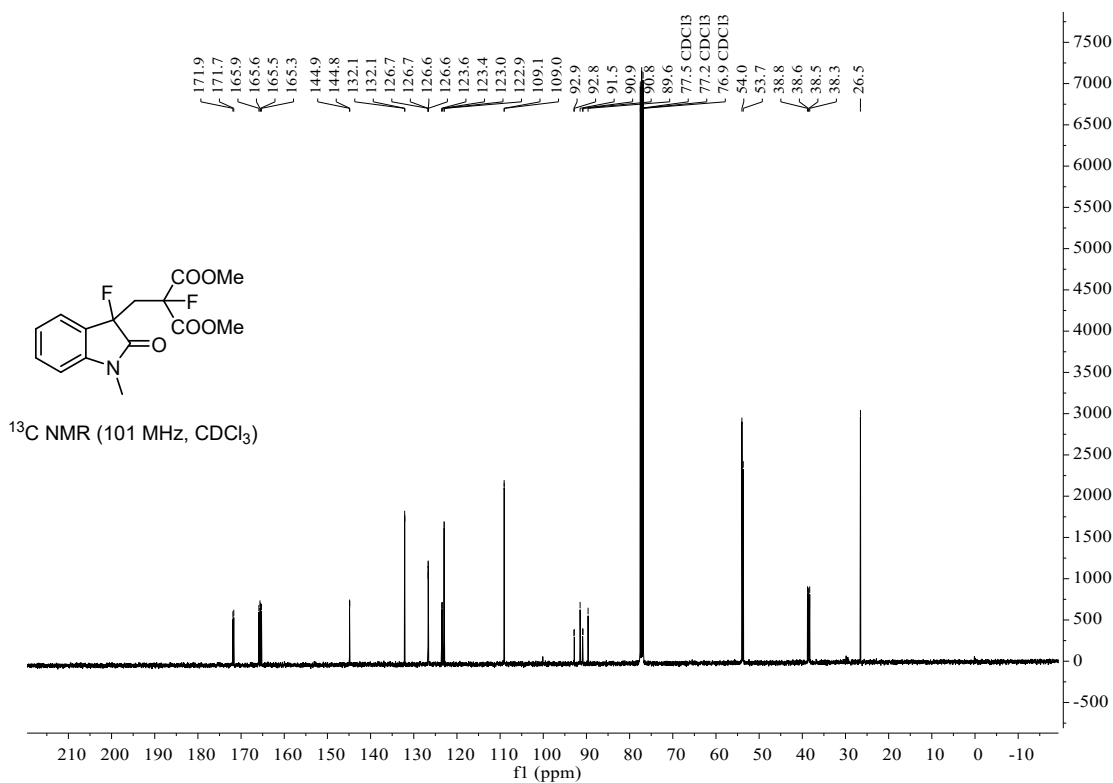
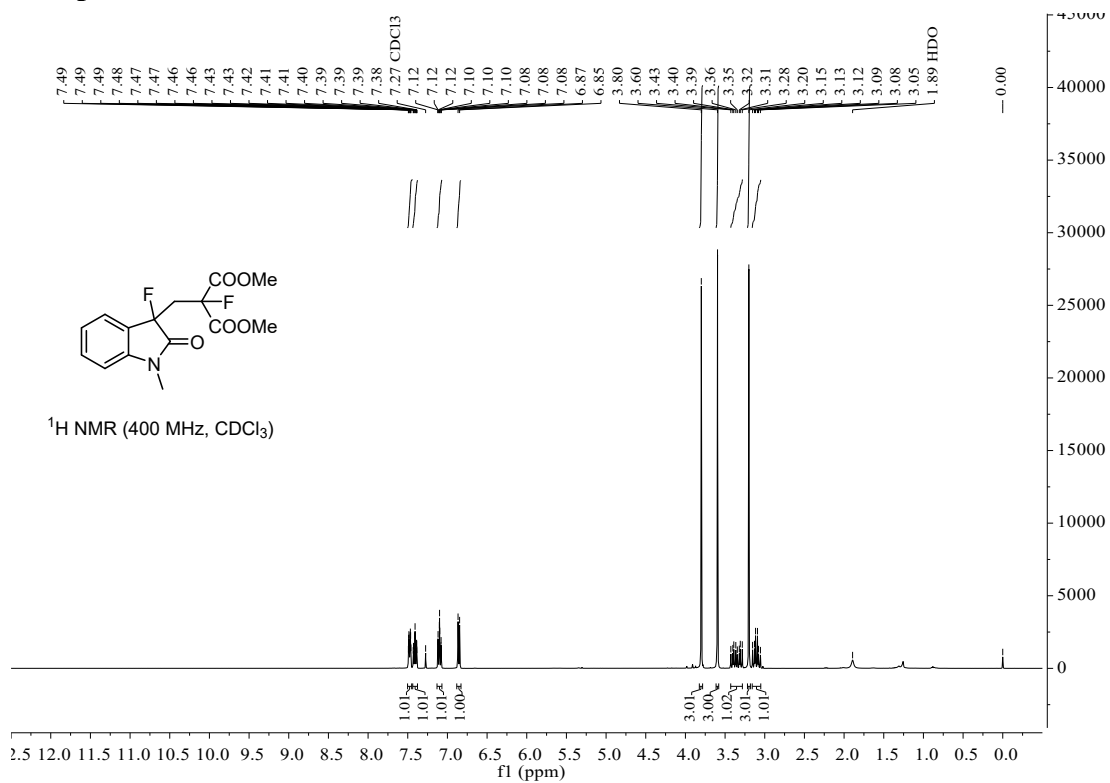


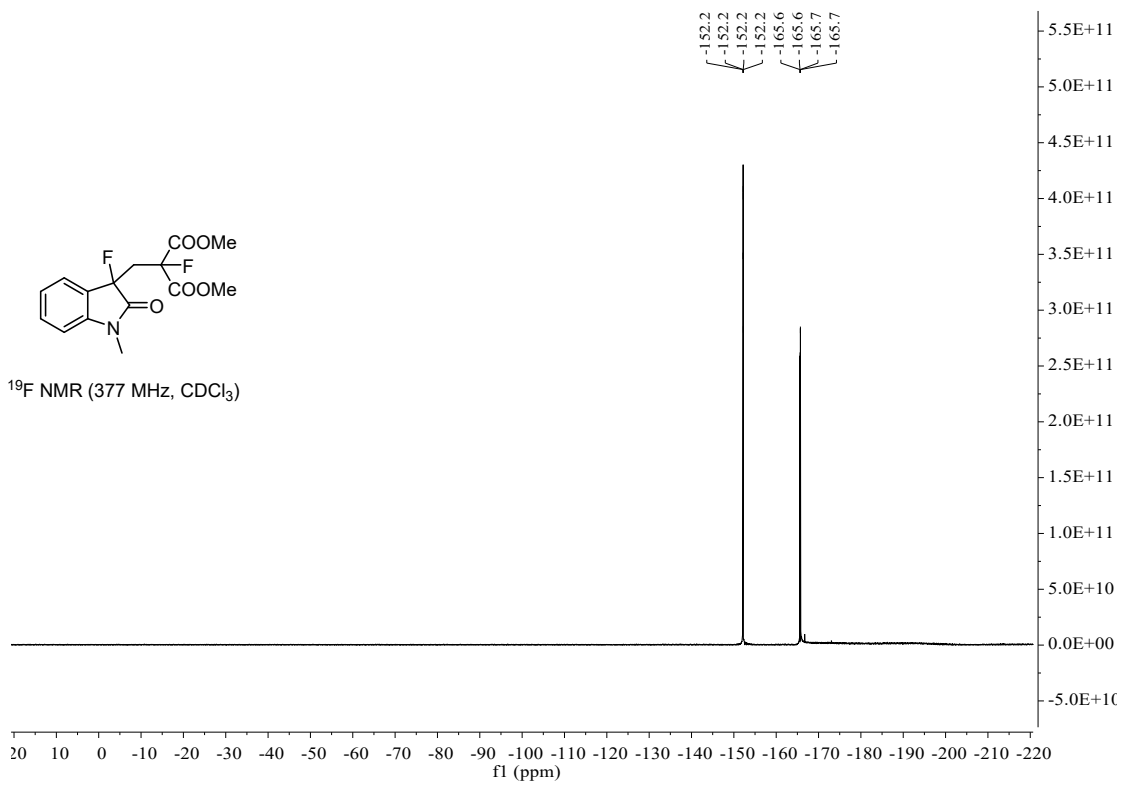
Compound 13



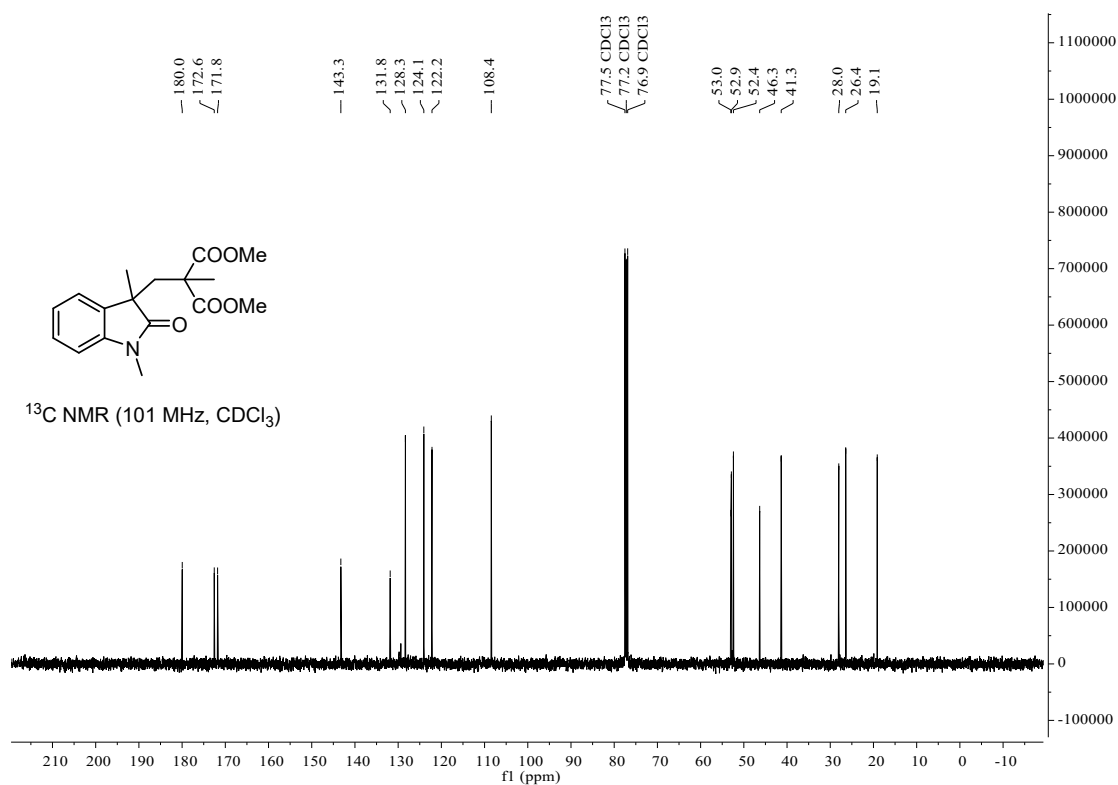
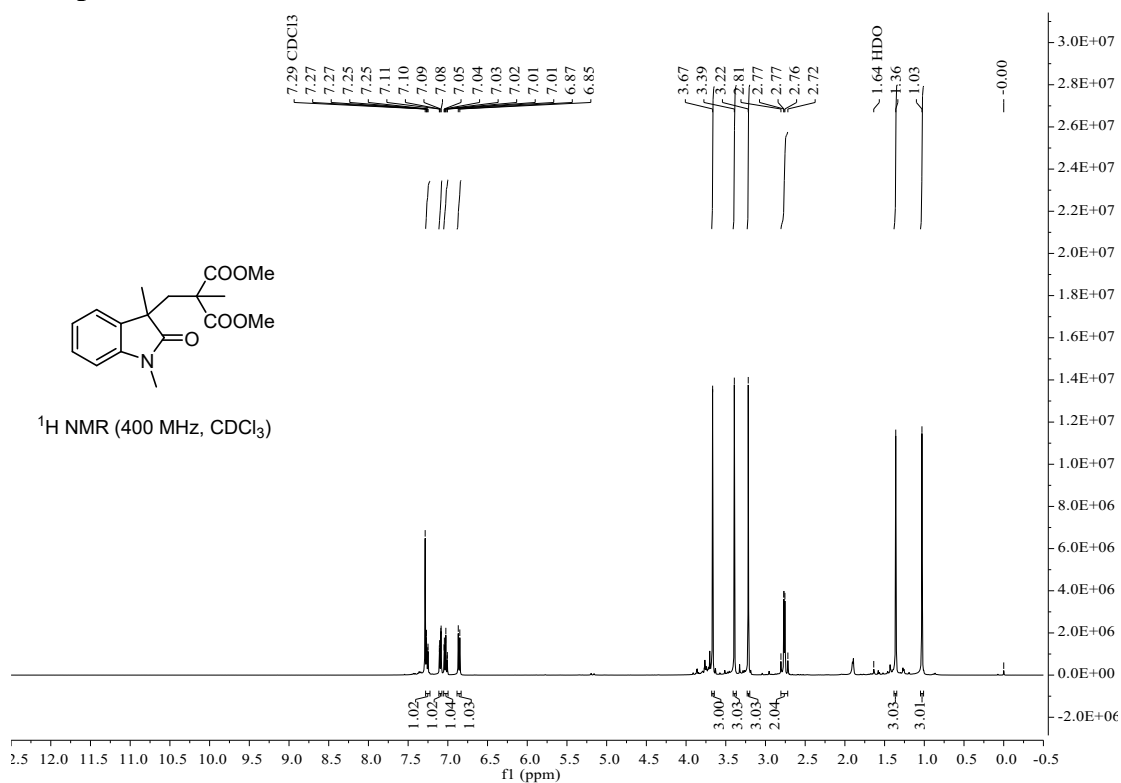


Compound 14

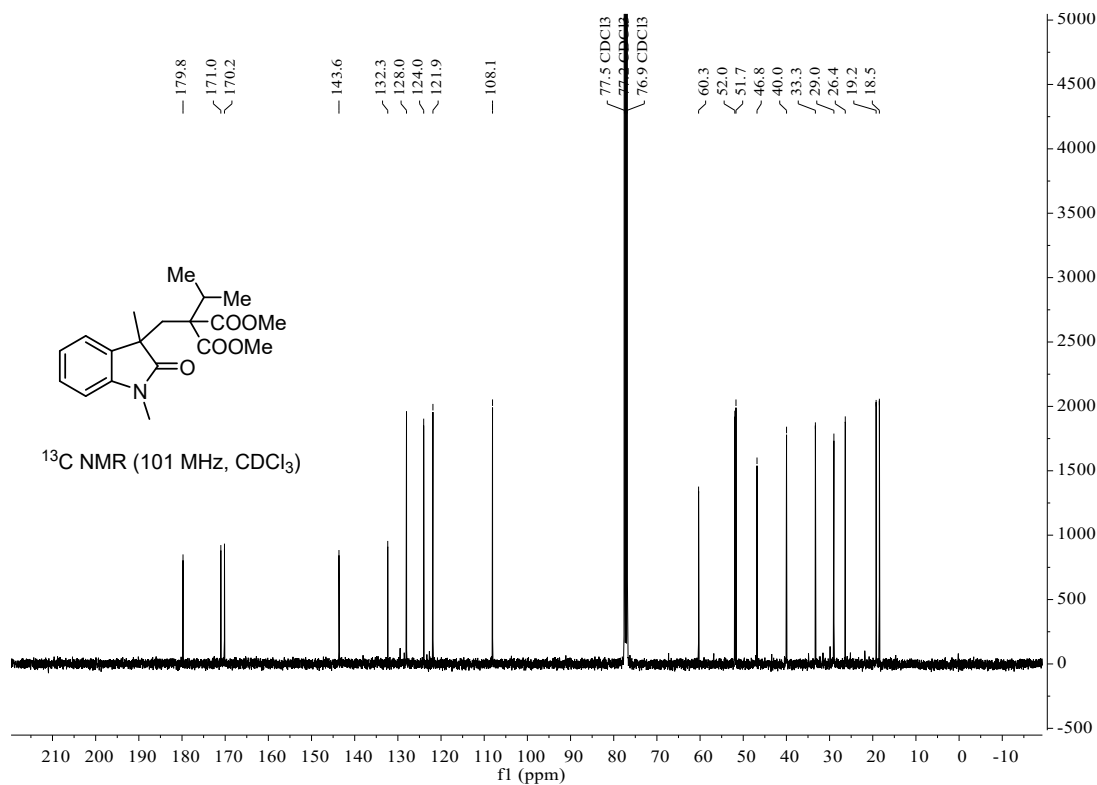
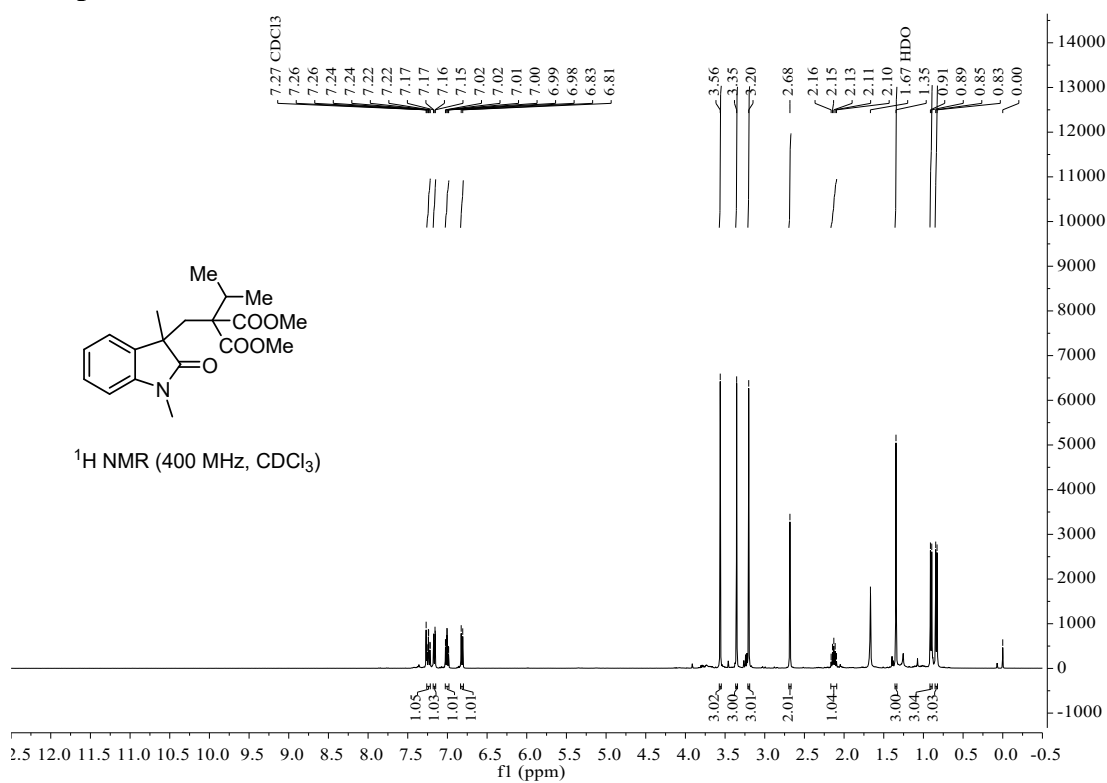




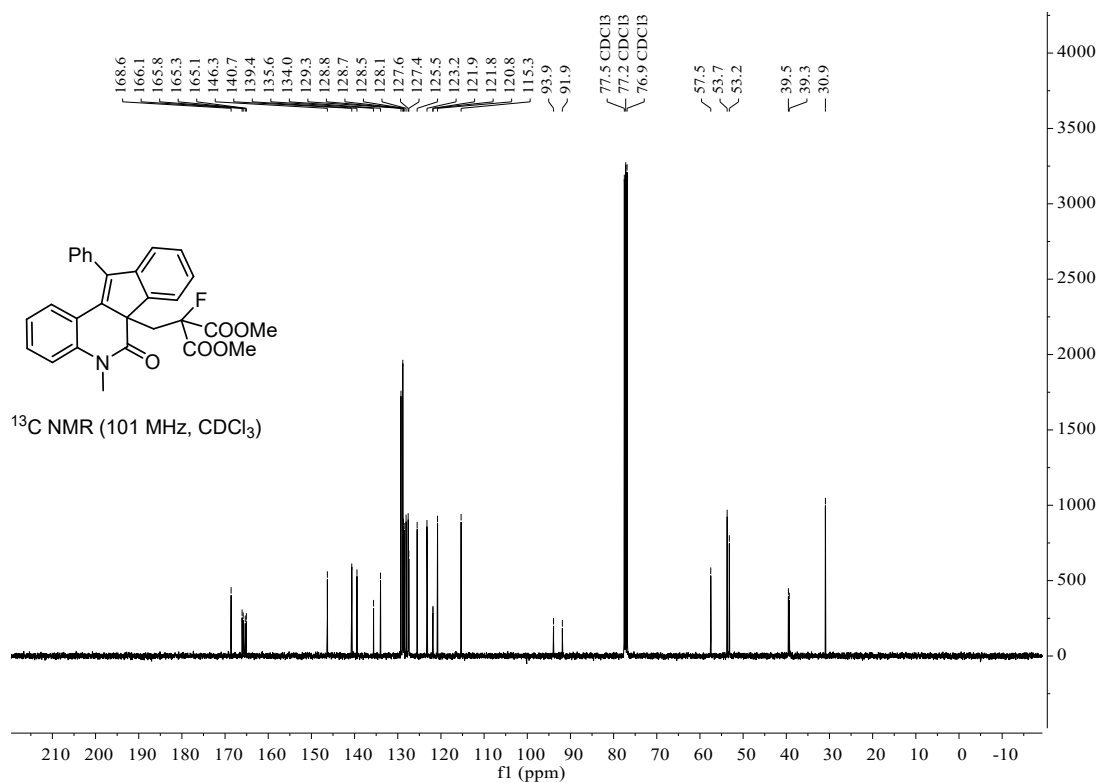
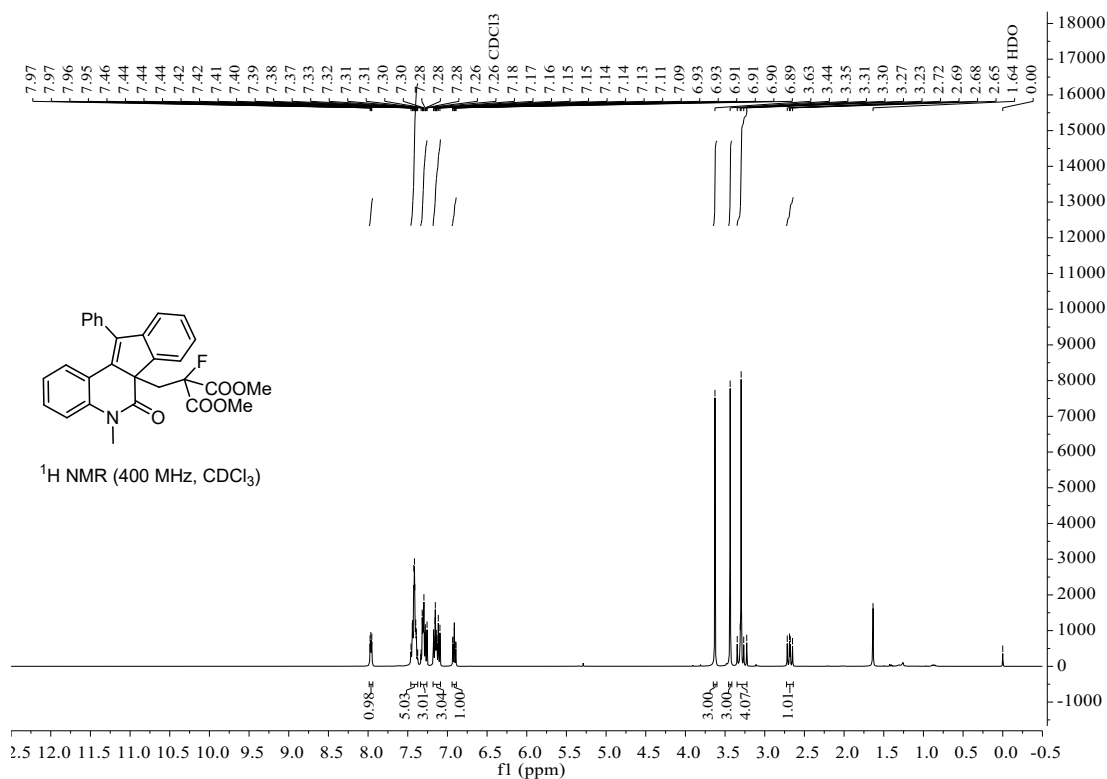
Compound 15

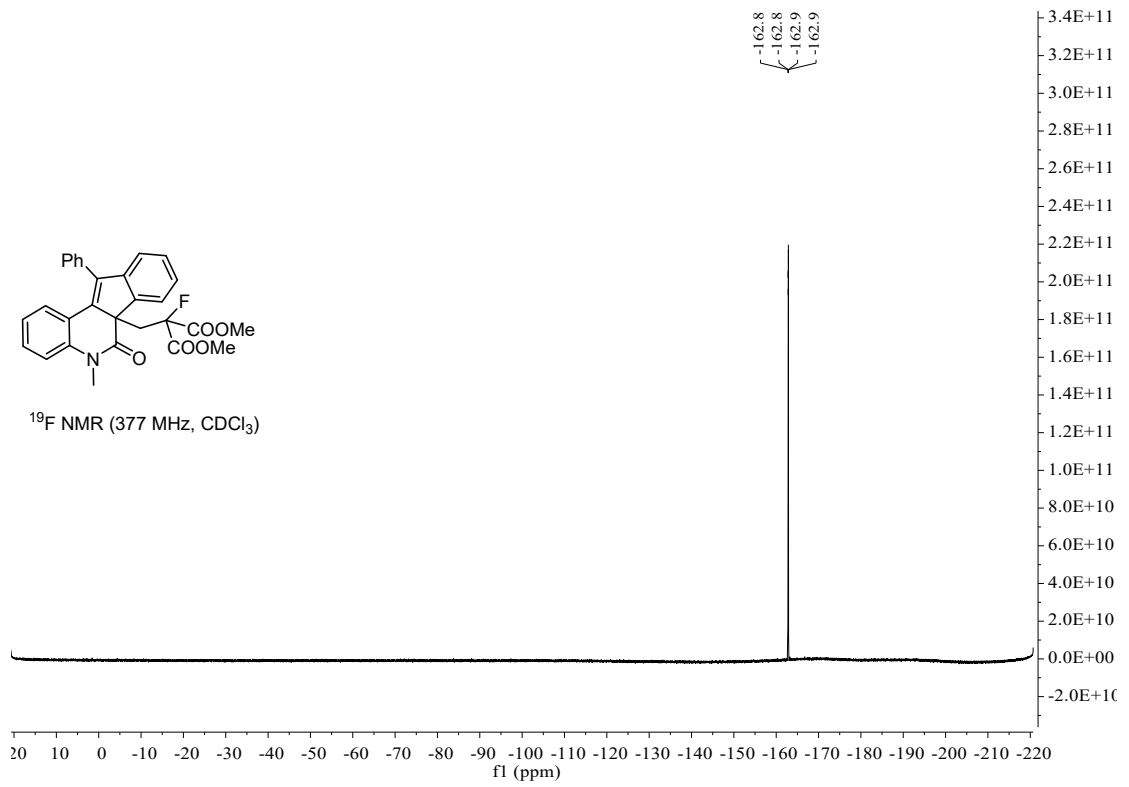


Compound 16

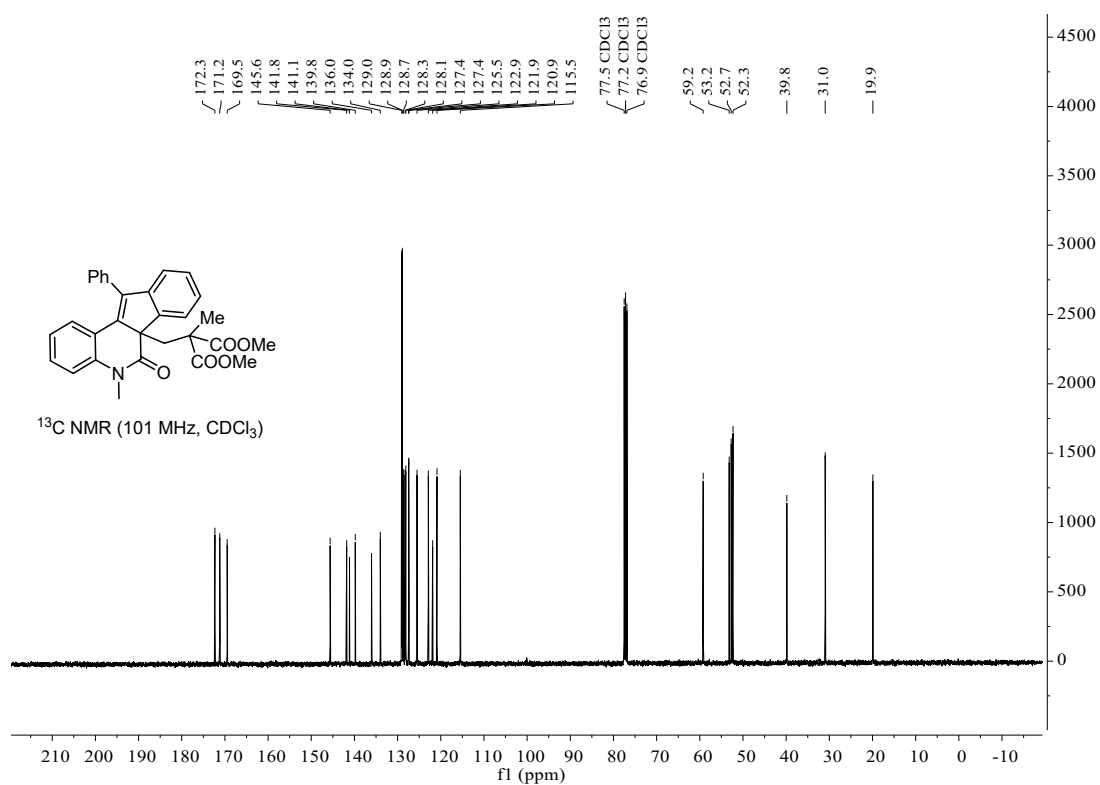
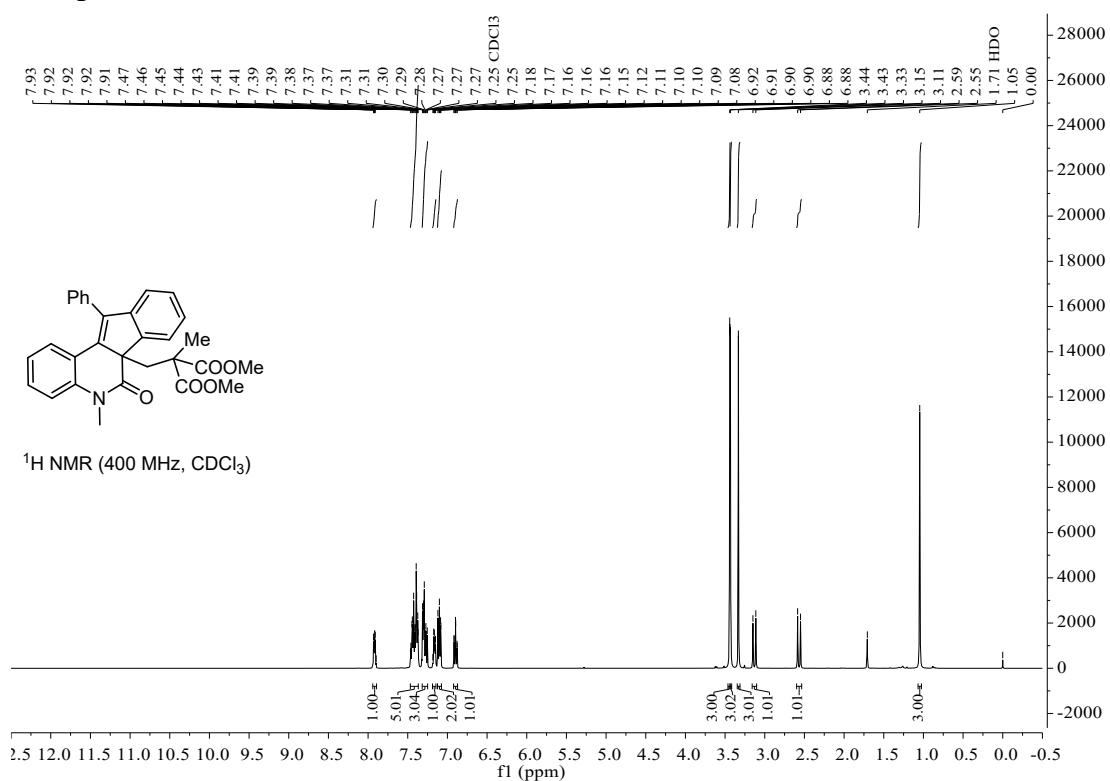


Compound 17

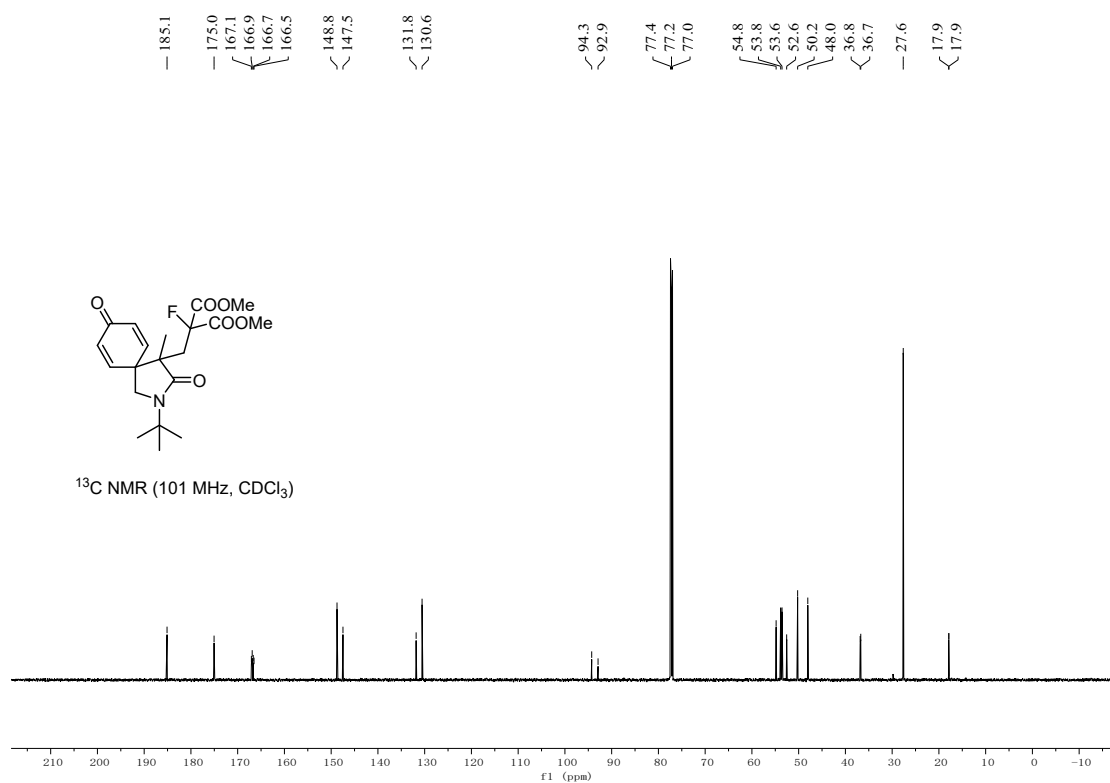
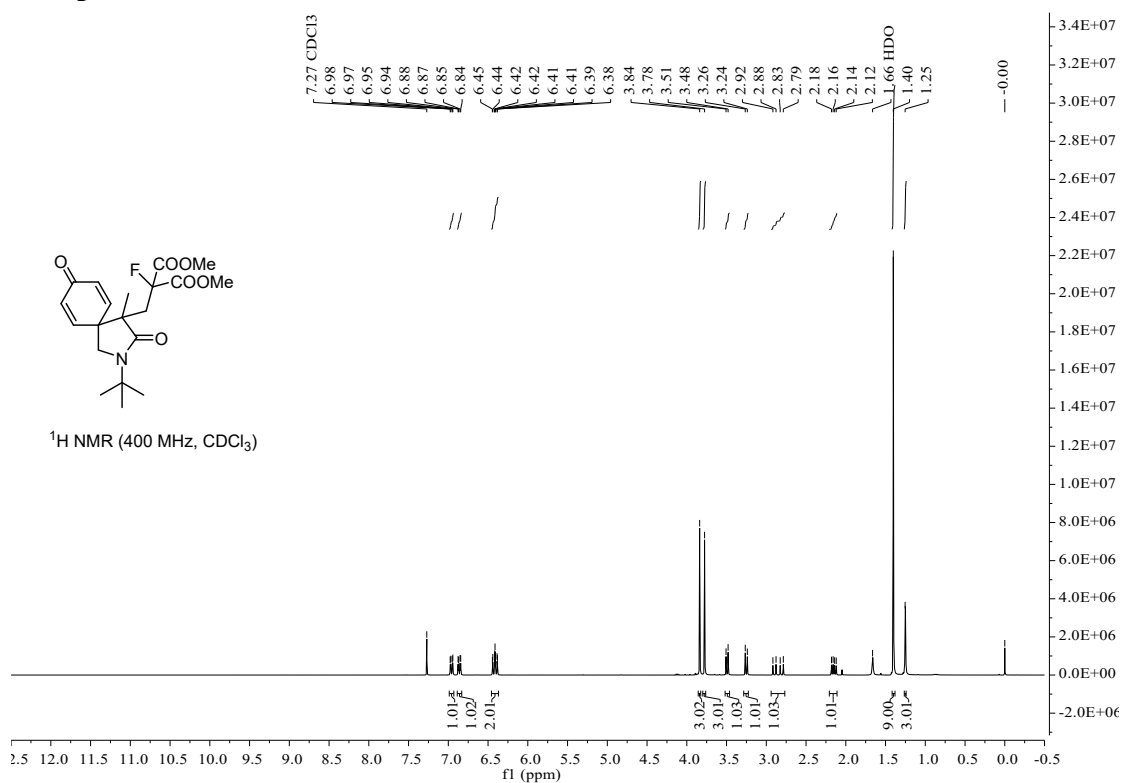


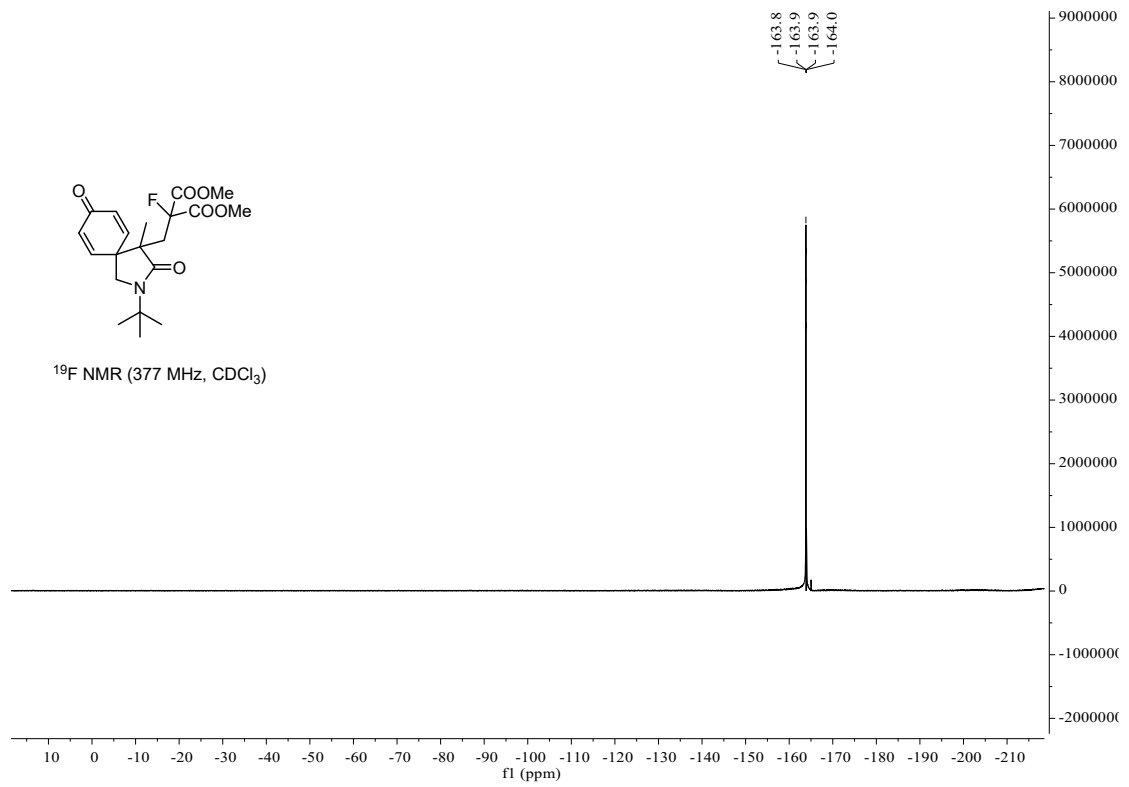


Compound 18

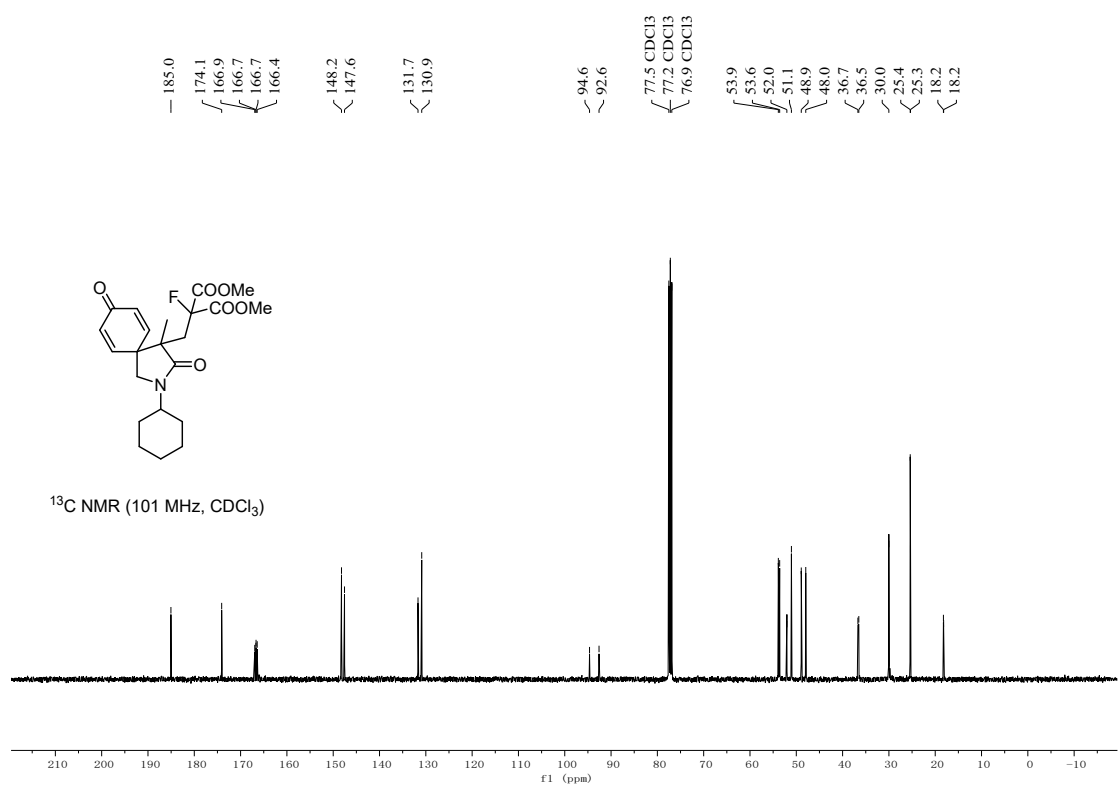
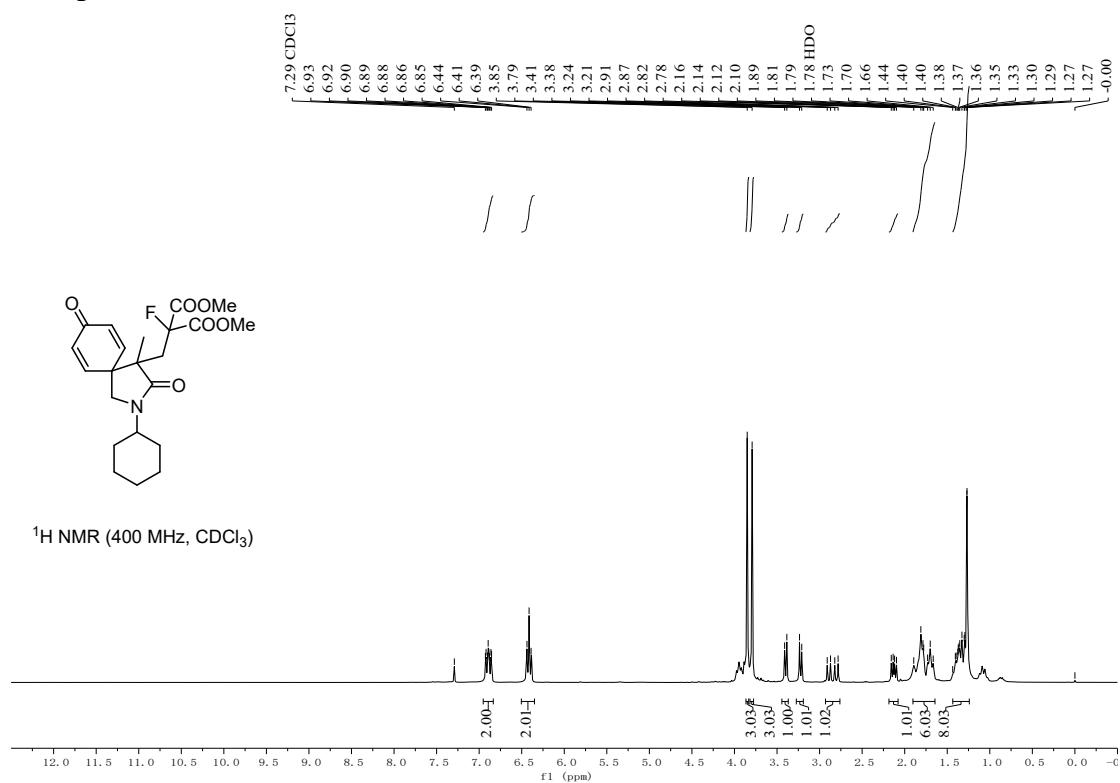


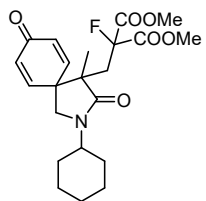
Compound 19



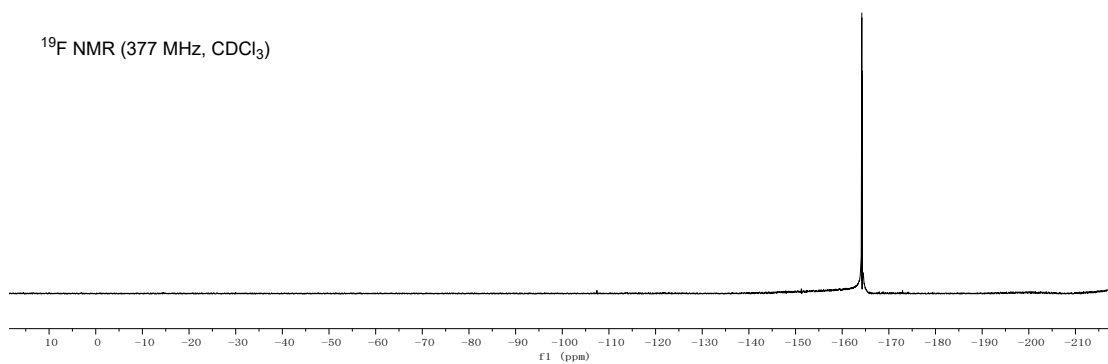


Compound 20

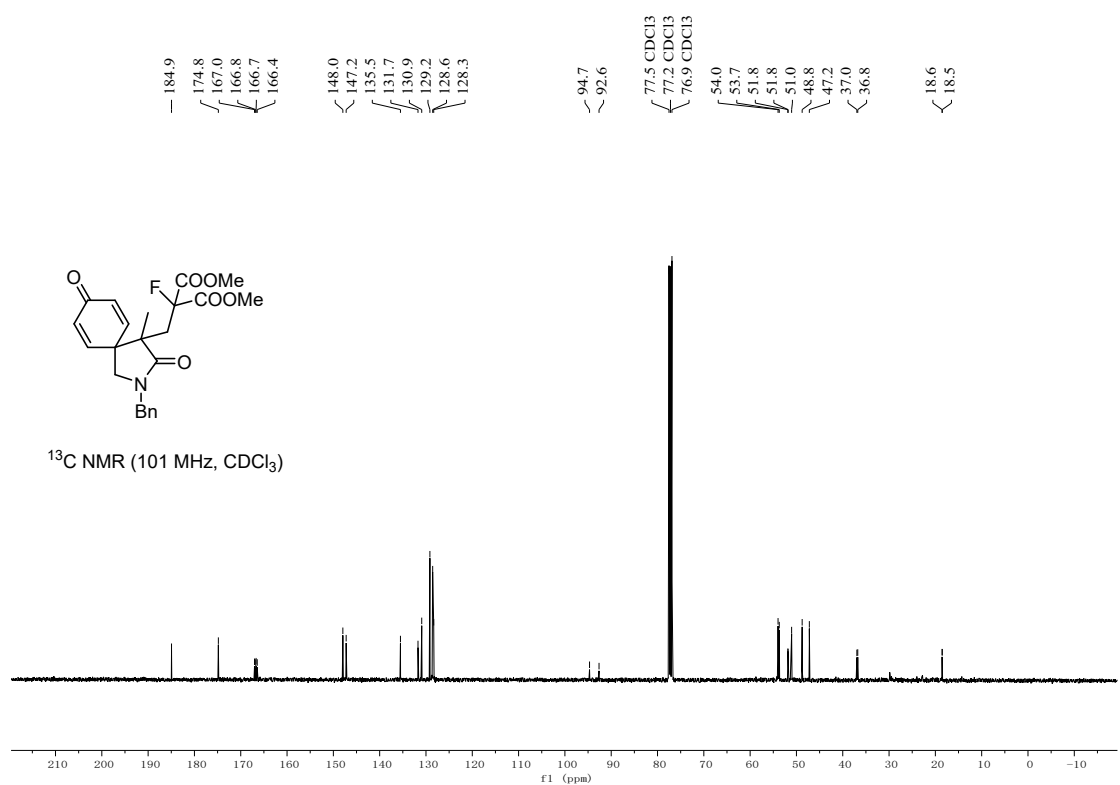
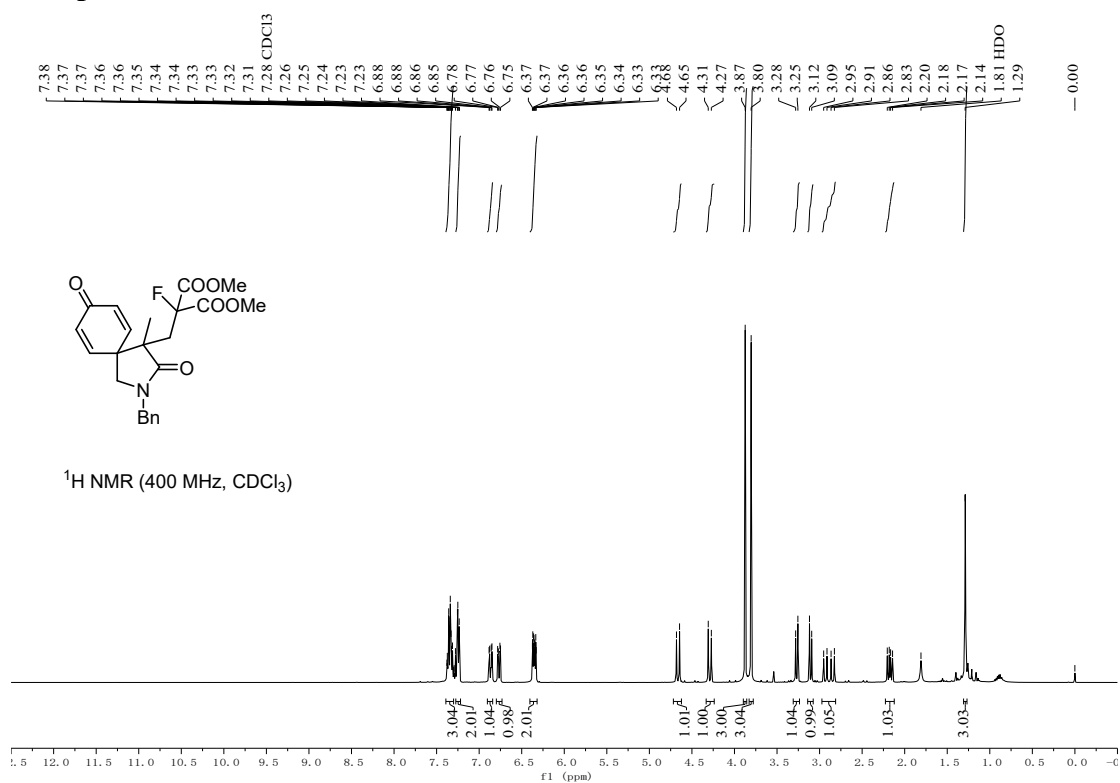


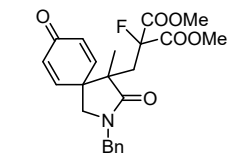


^{19}F NMR (377 MHz, CDCl_3)

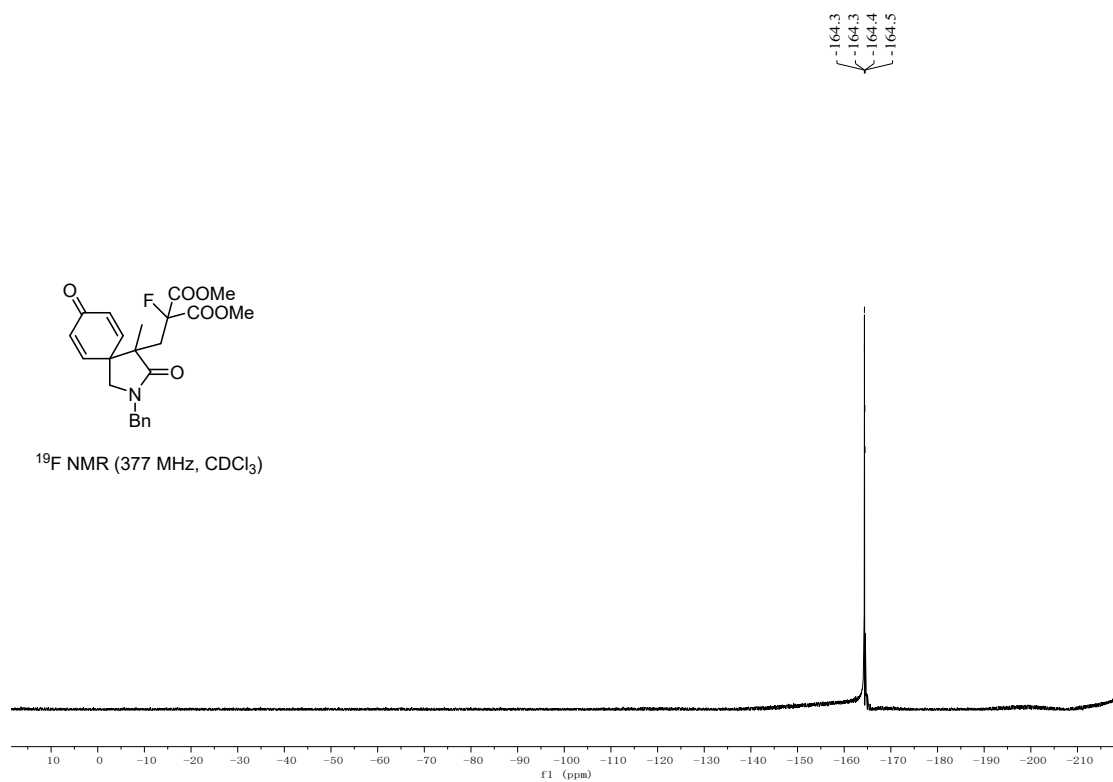


Compound 21

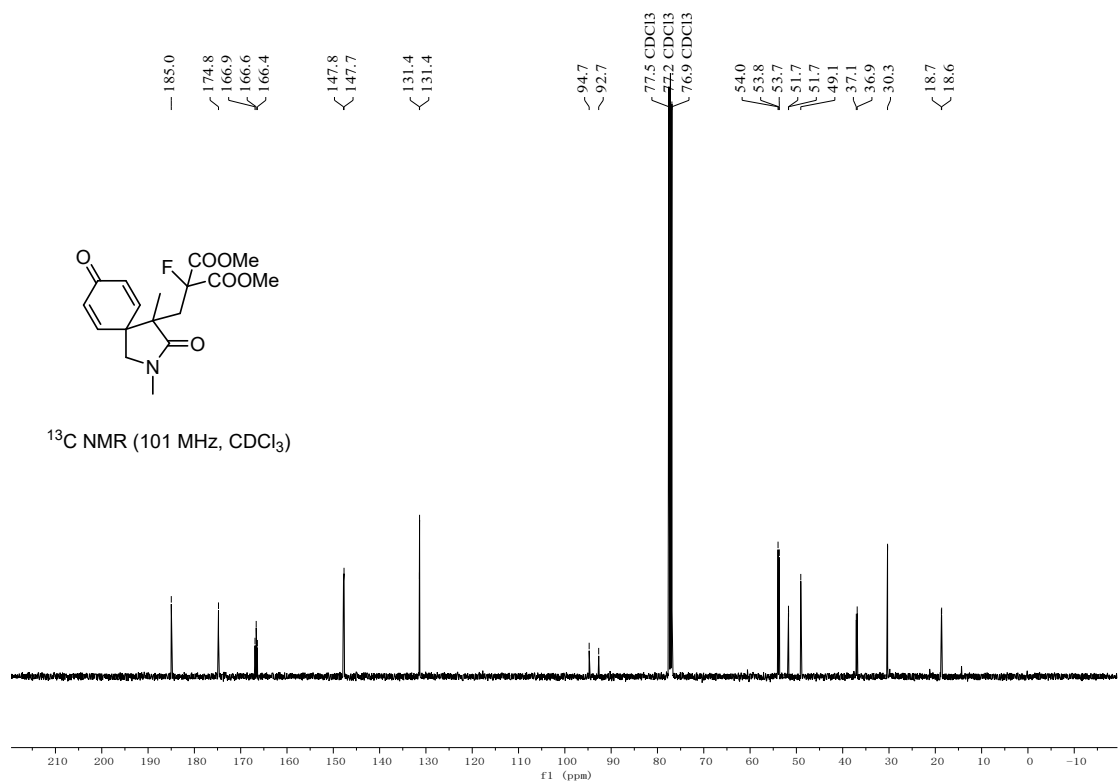
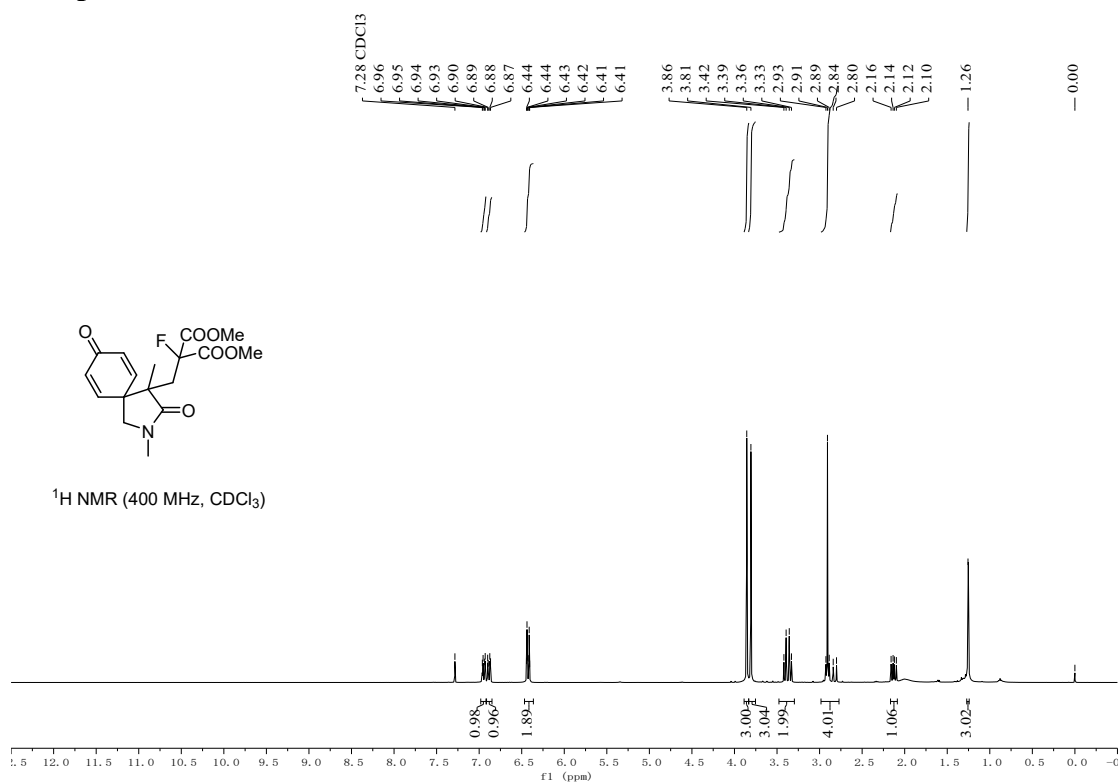


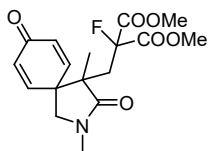


^{19}F NMR (377 MHz, CDCl_3)

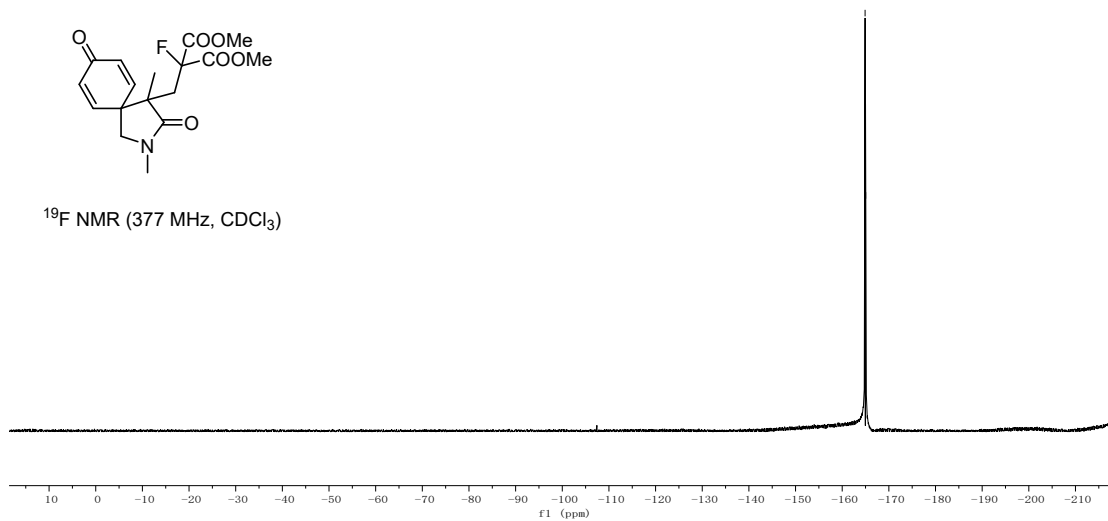


Compound 22

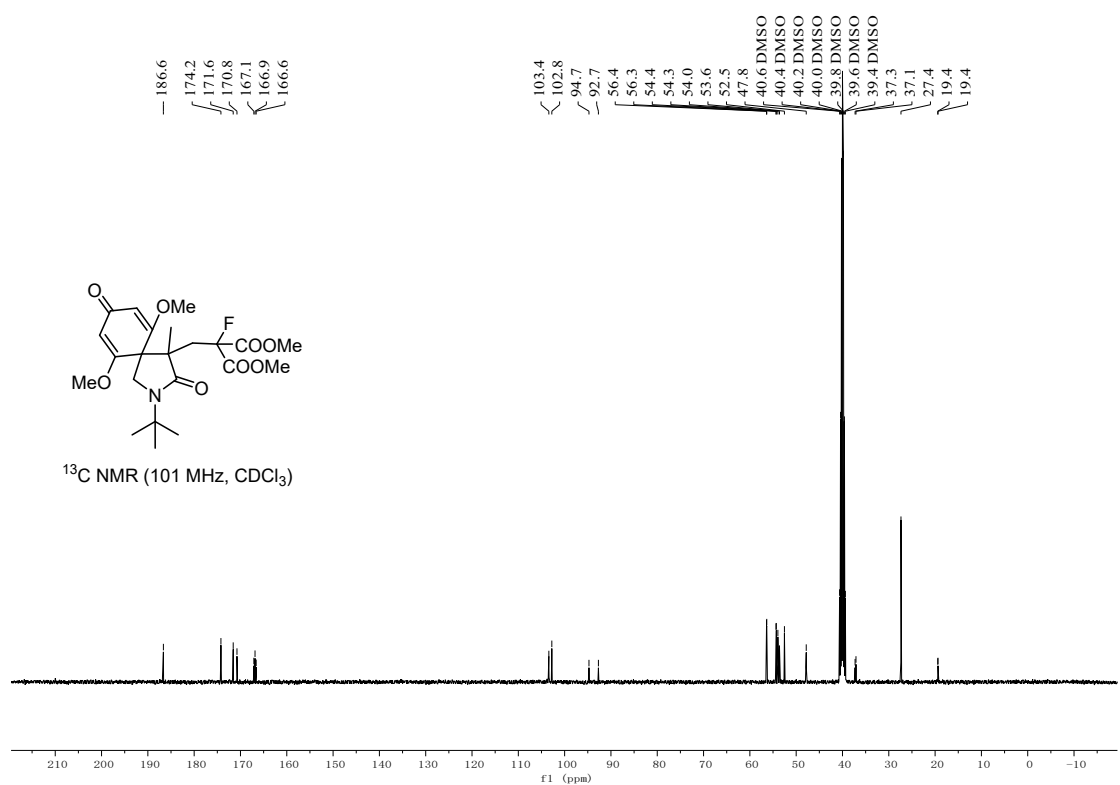
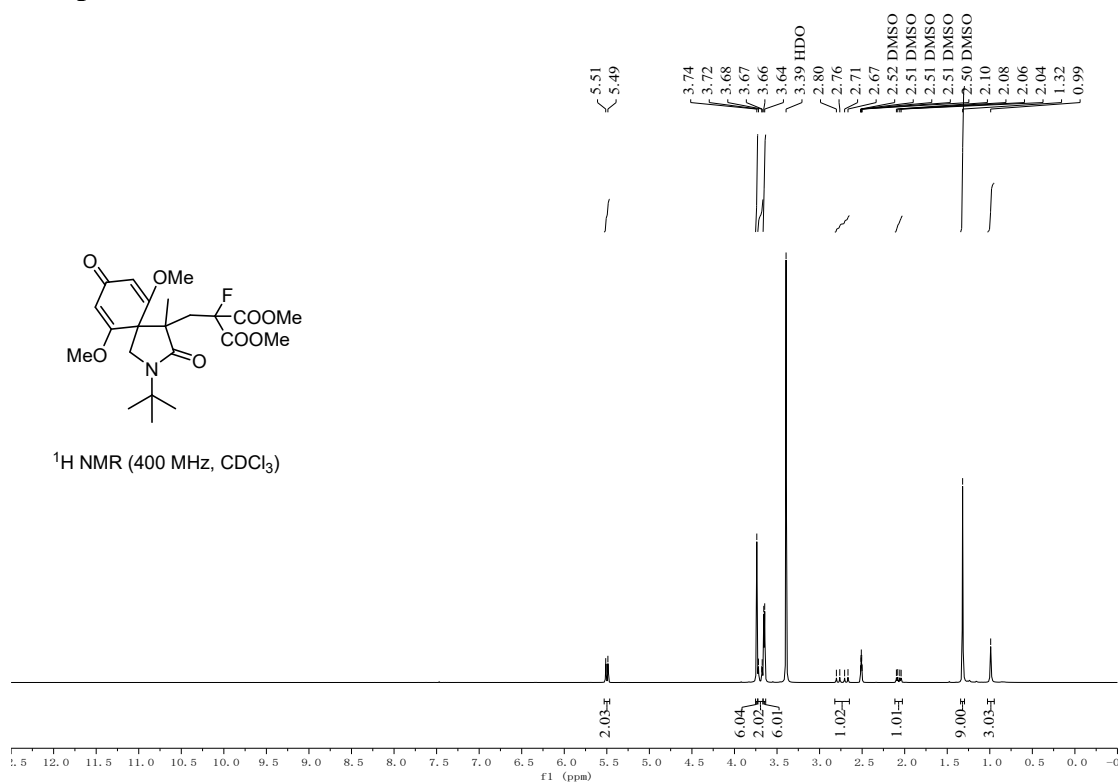


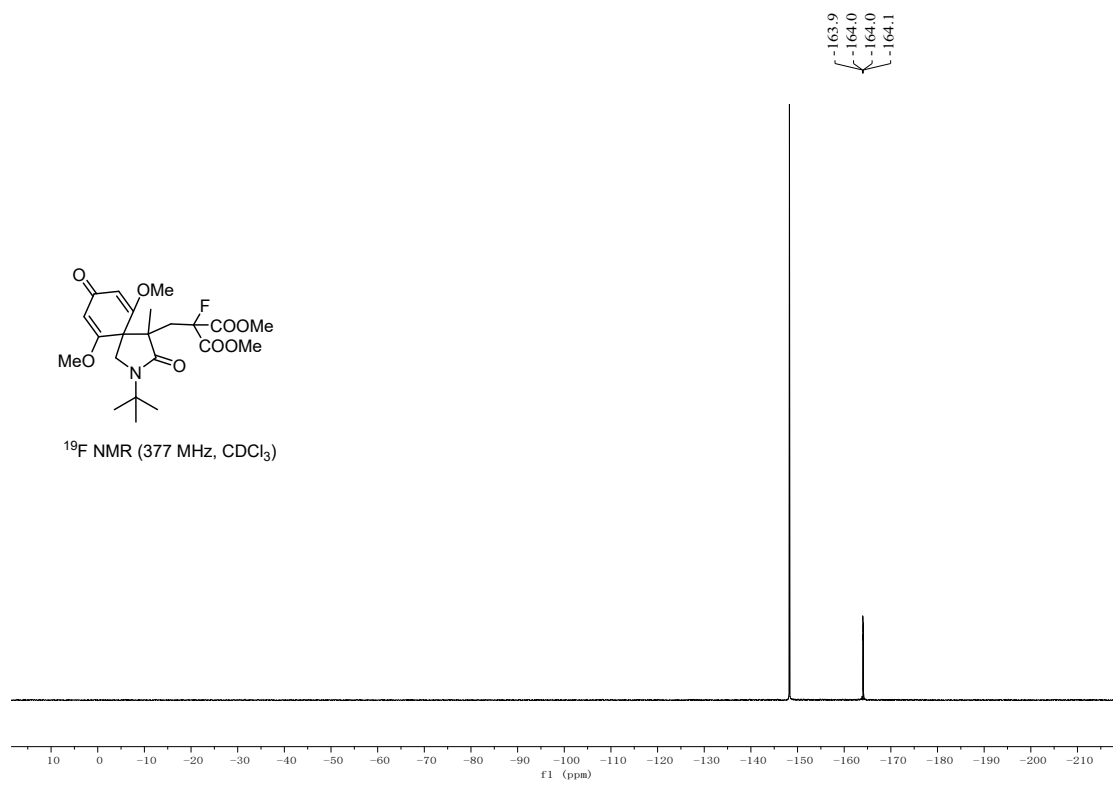


^{19}F NMR (377 MHz, CDCl_3)

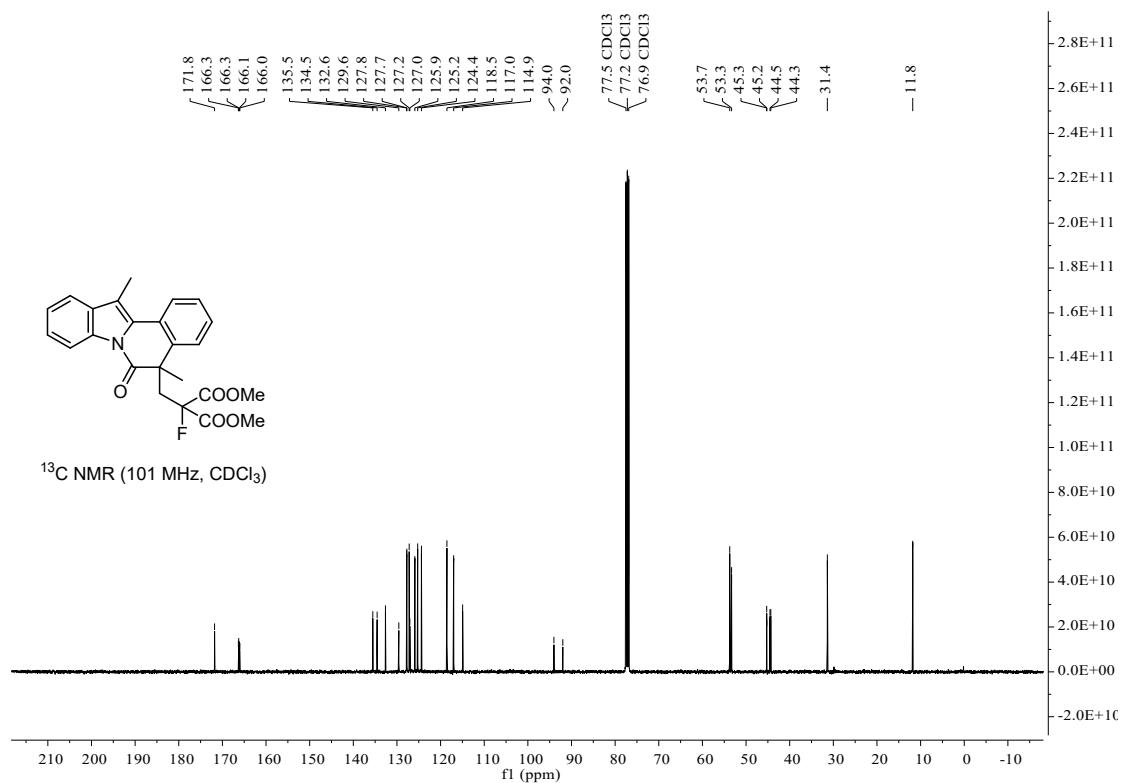
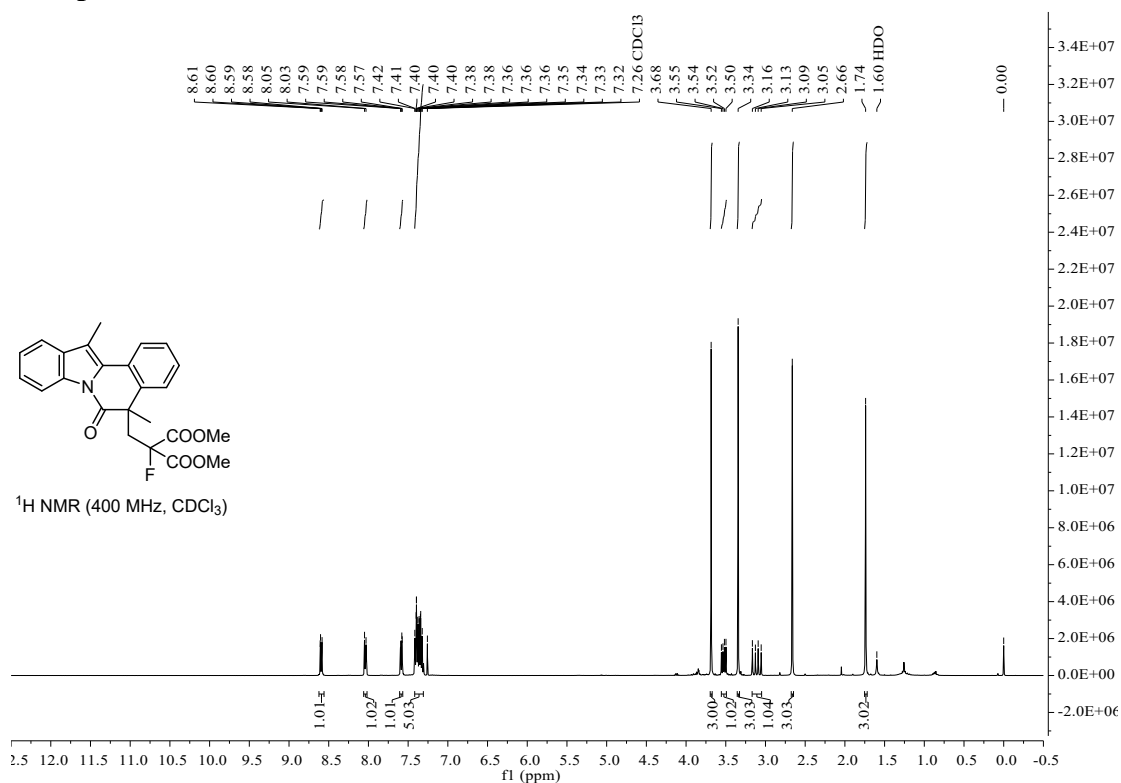


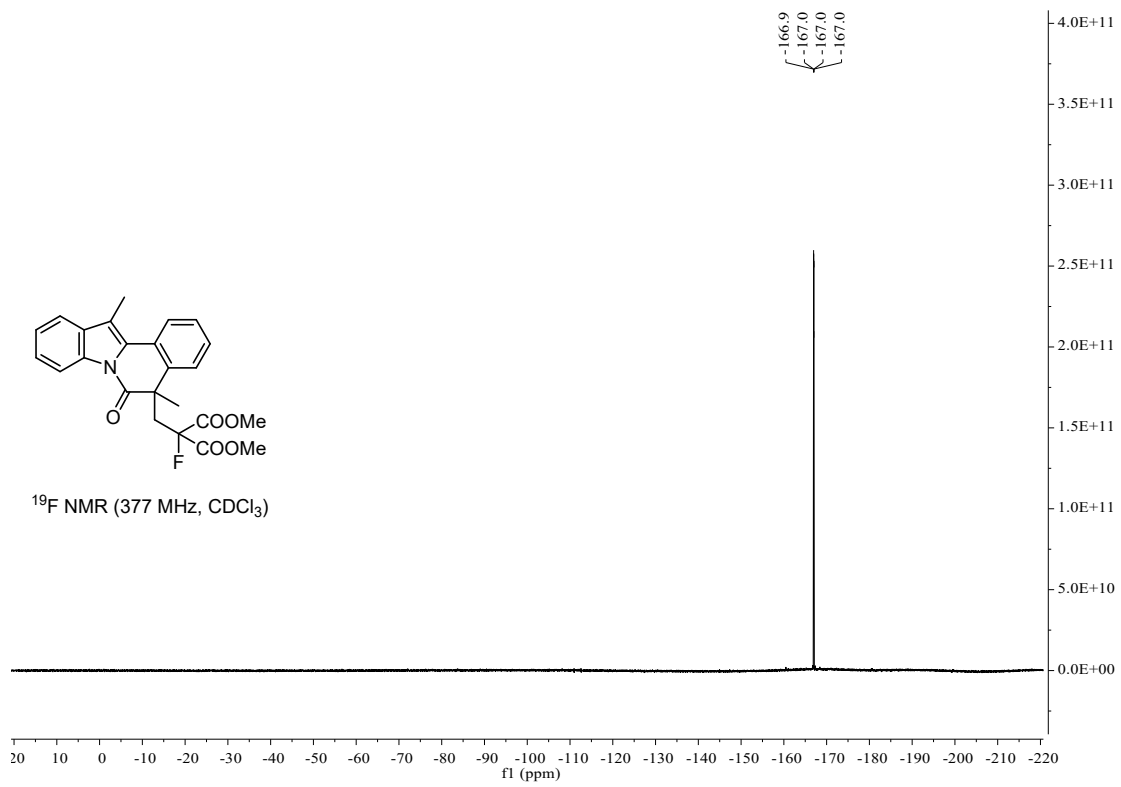
Compound 23



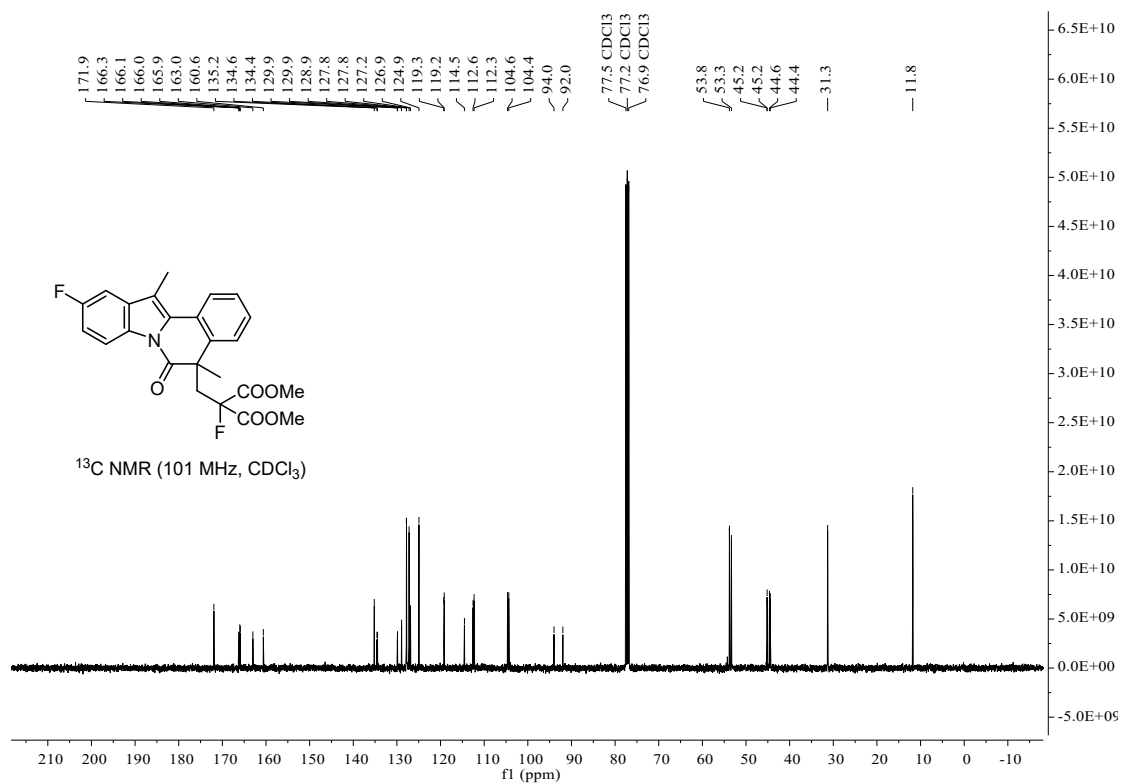
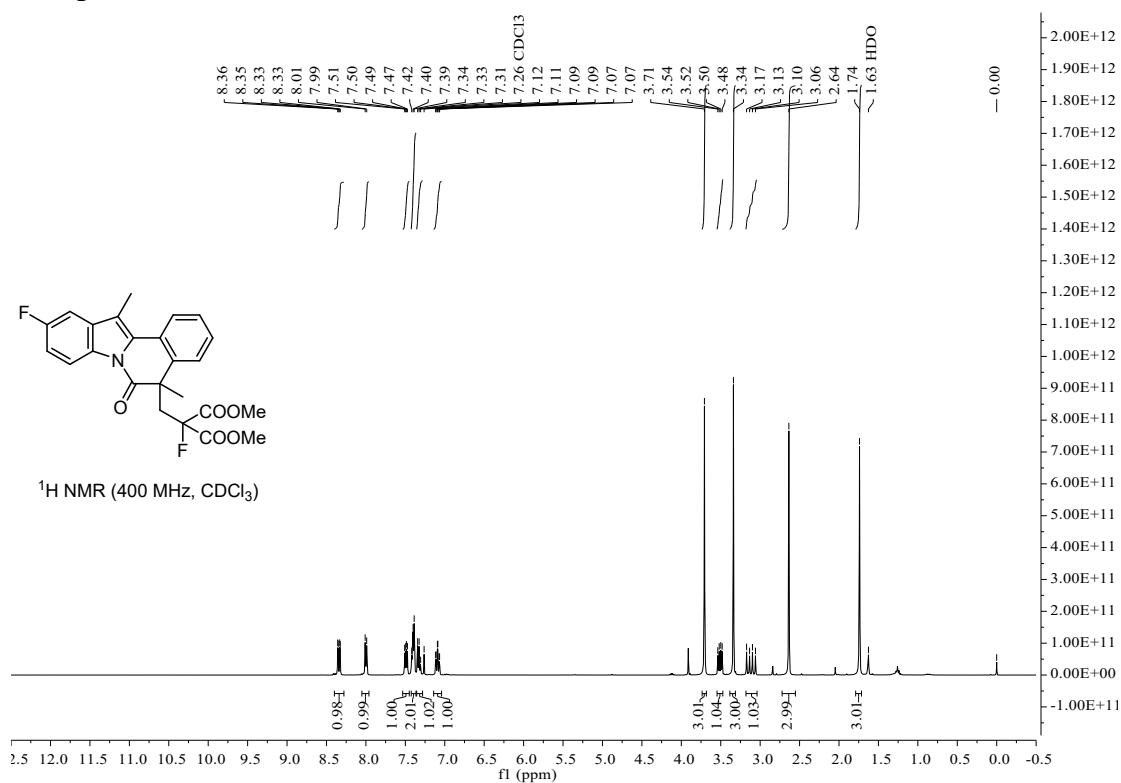


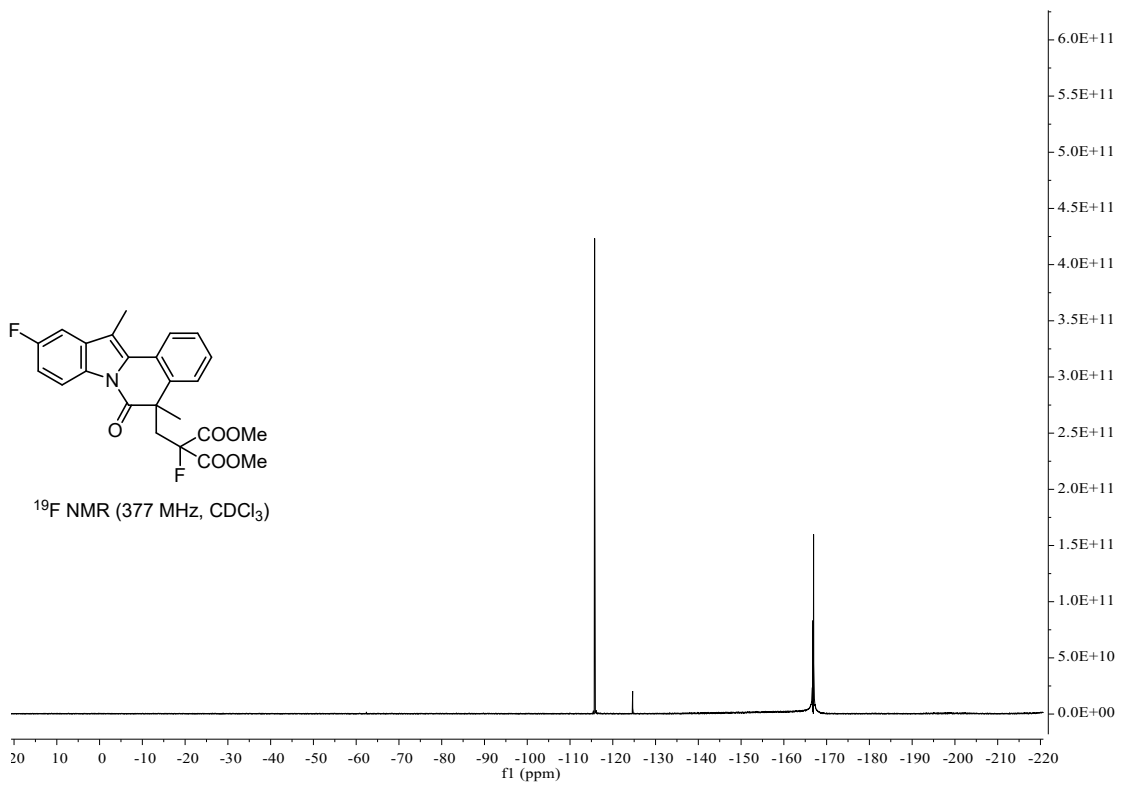
Compound 24



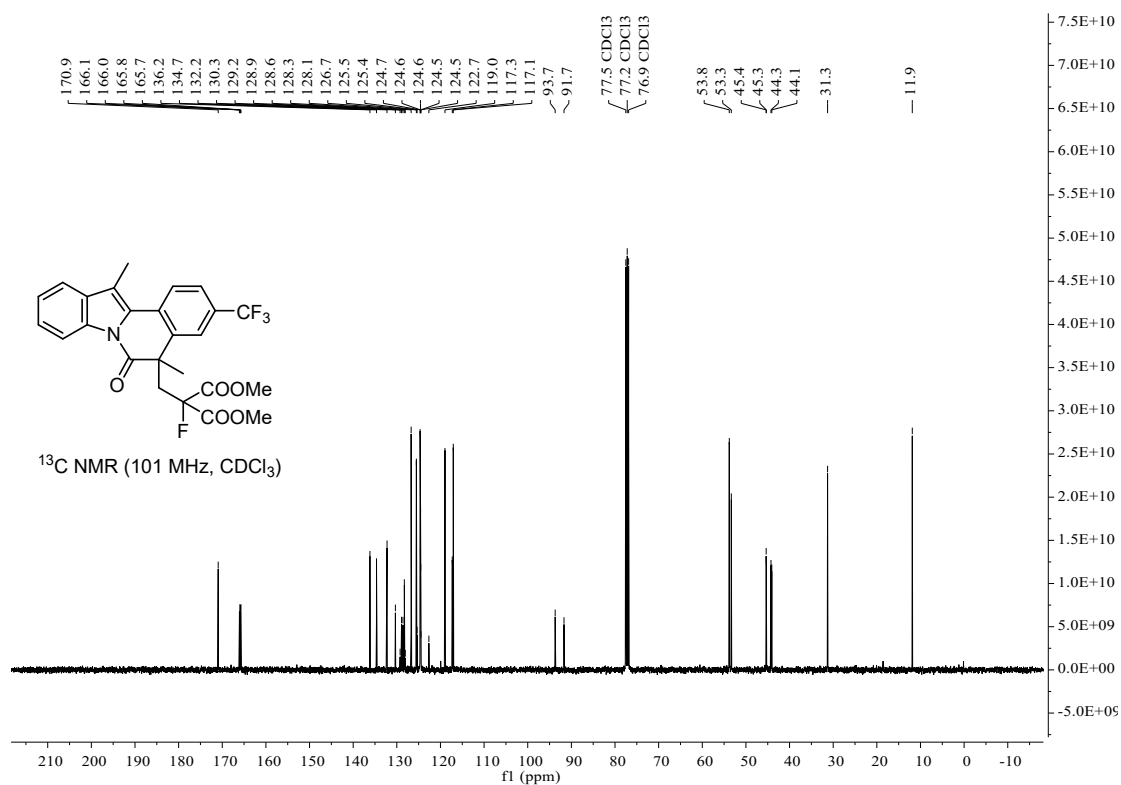
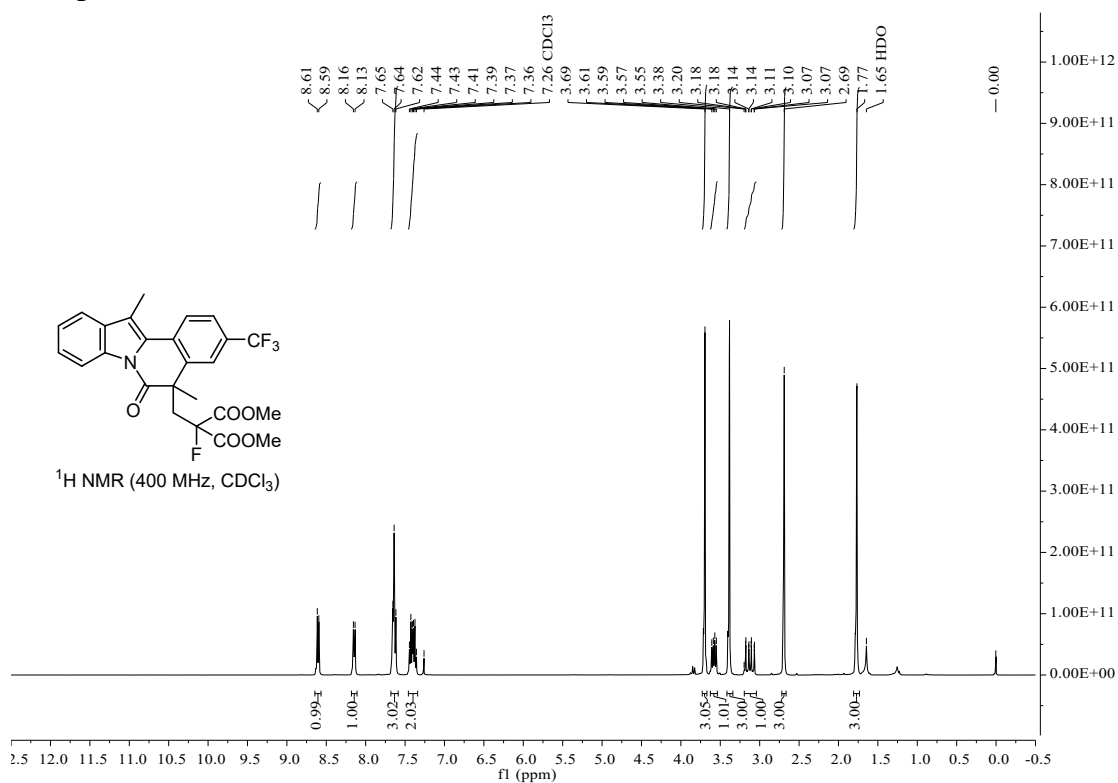


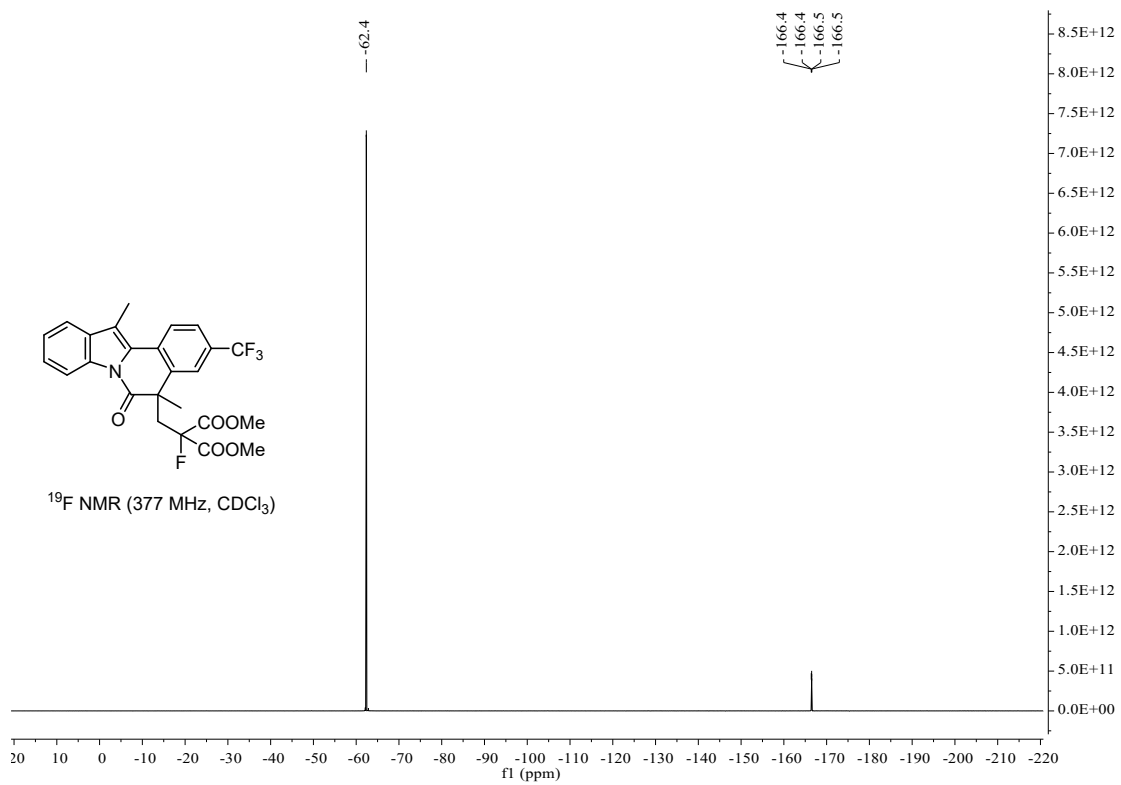
Compound 25



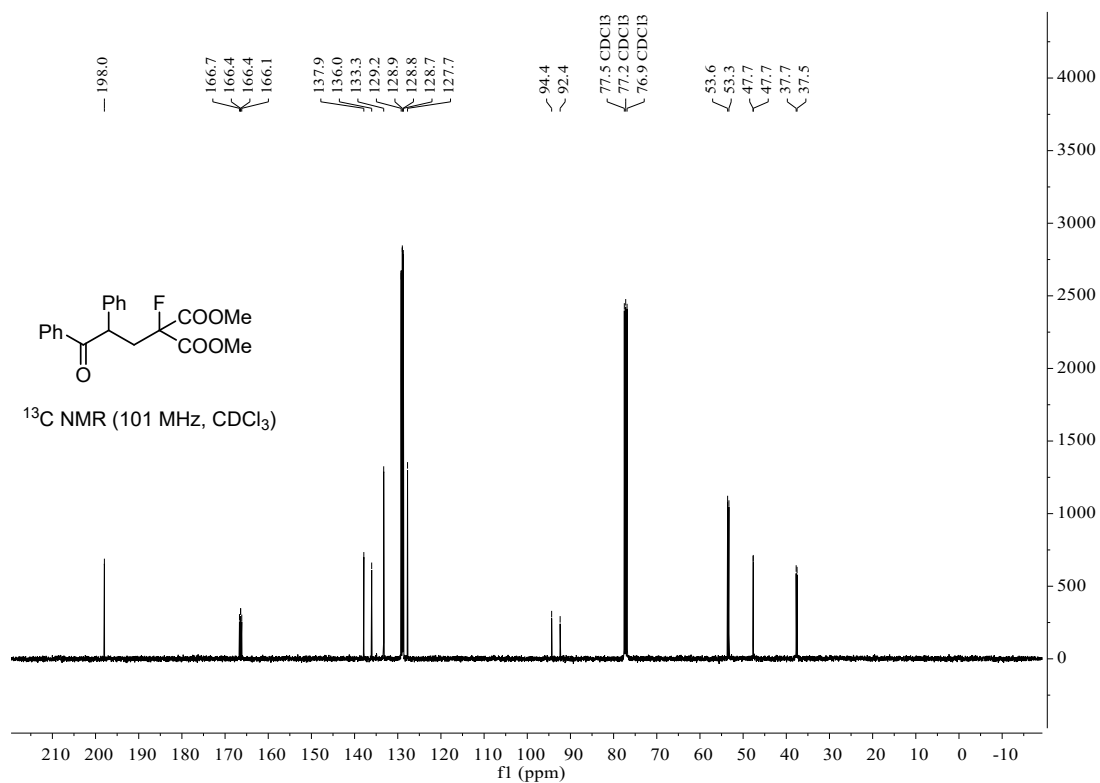
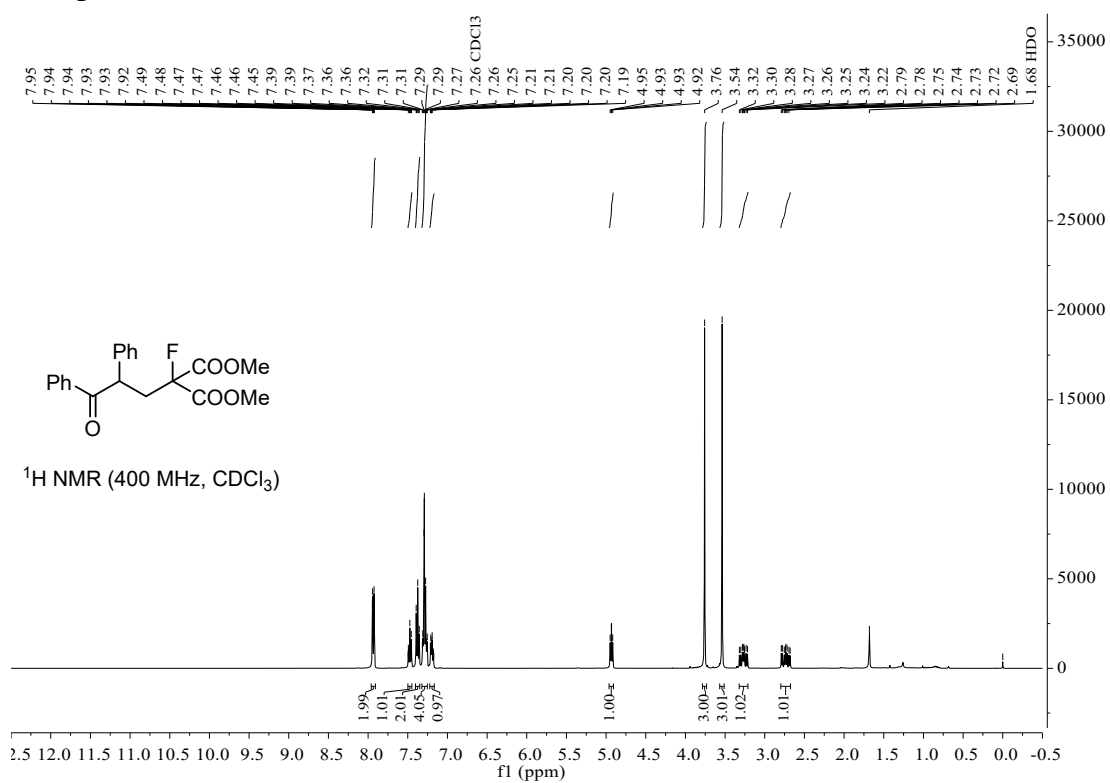


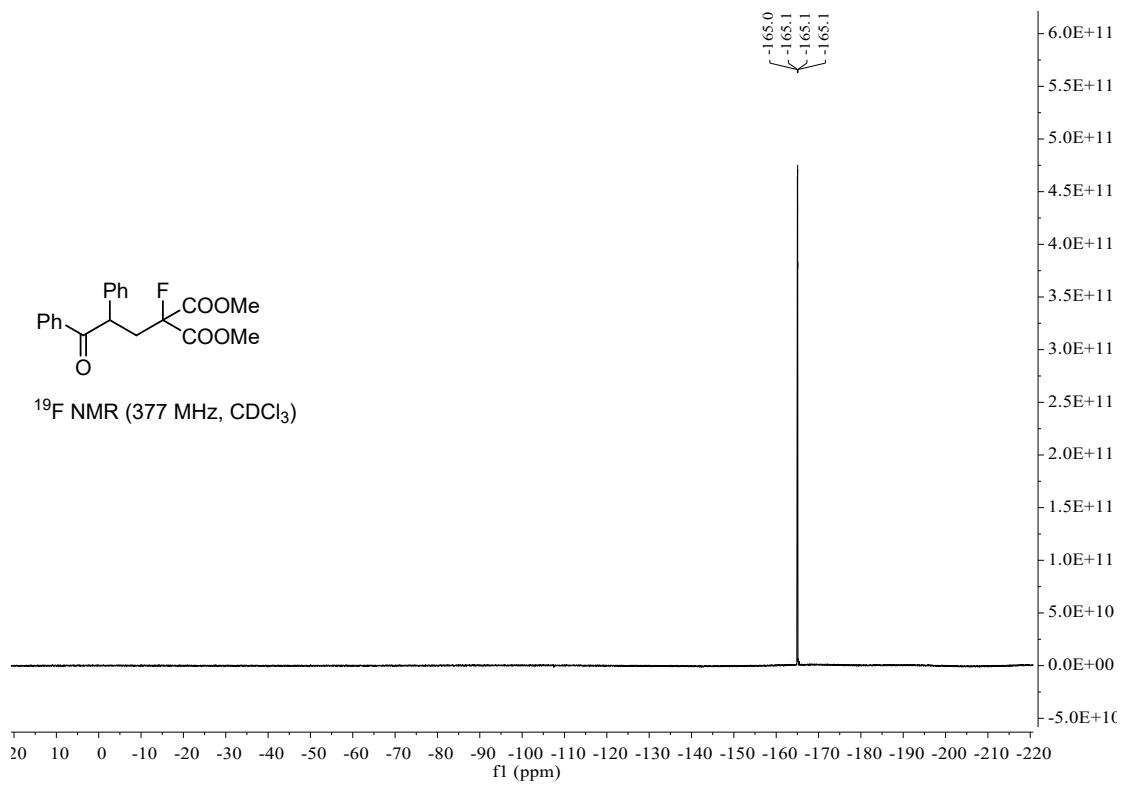
Compound 26



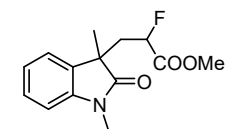
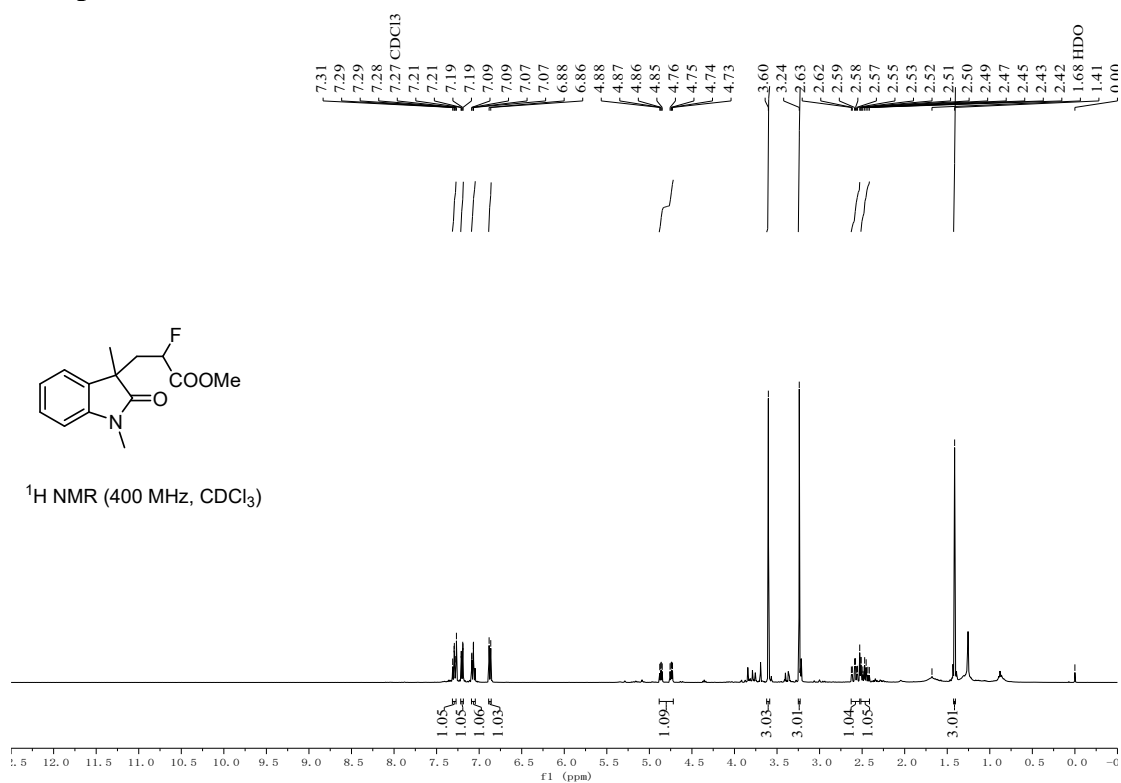


Compound 28

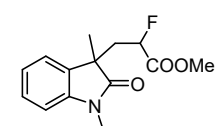
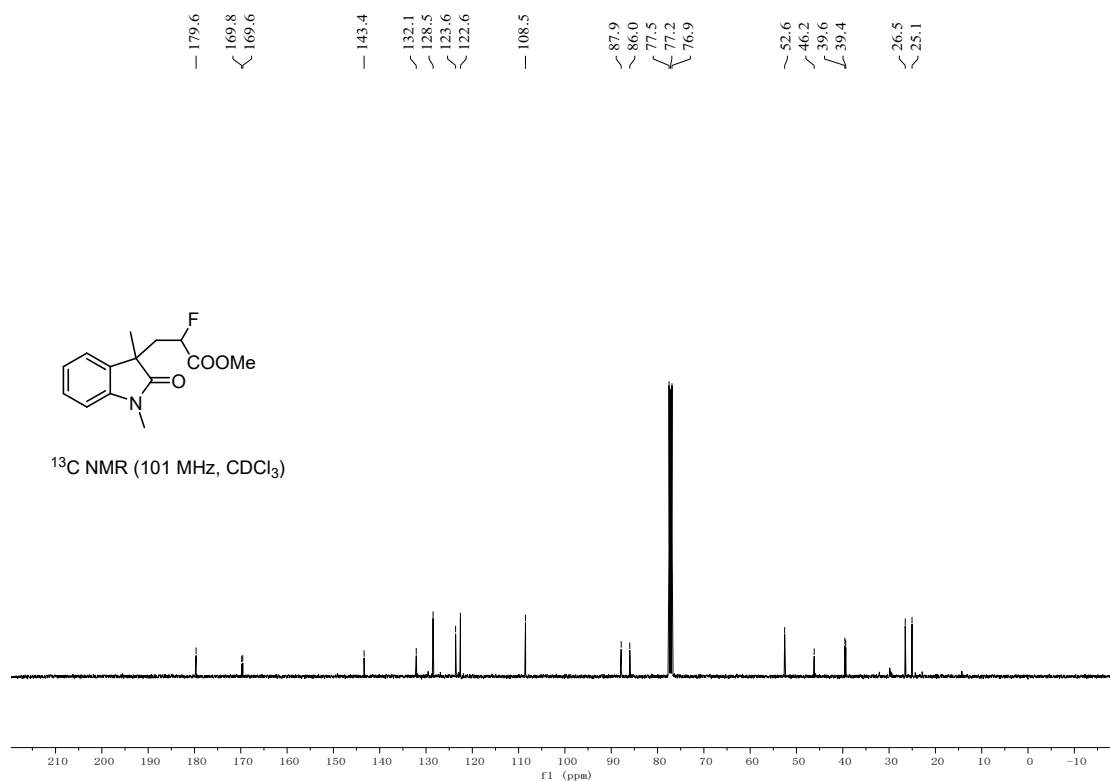




Compound 29

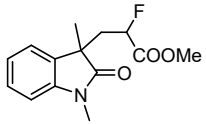


¹H NMR (400 MHz, CDCl₃)

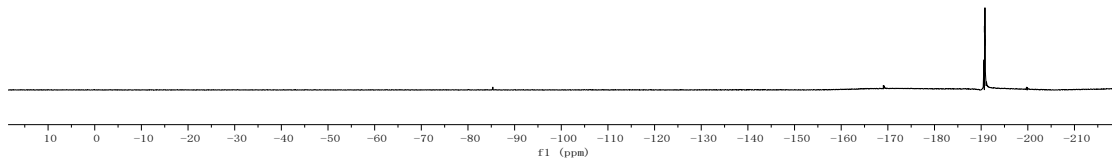


¹³C NMR (101 MHz, CDCl₃)

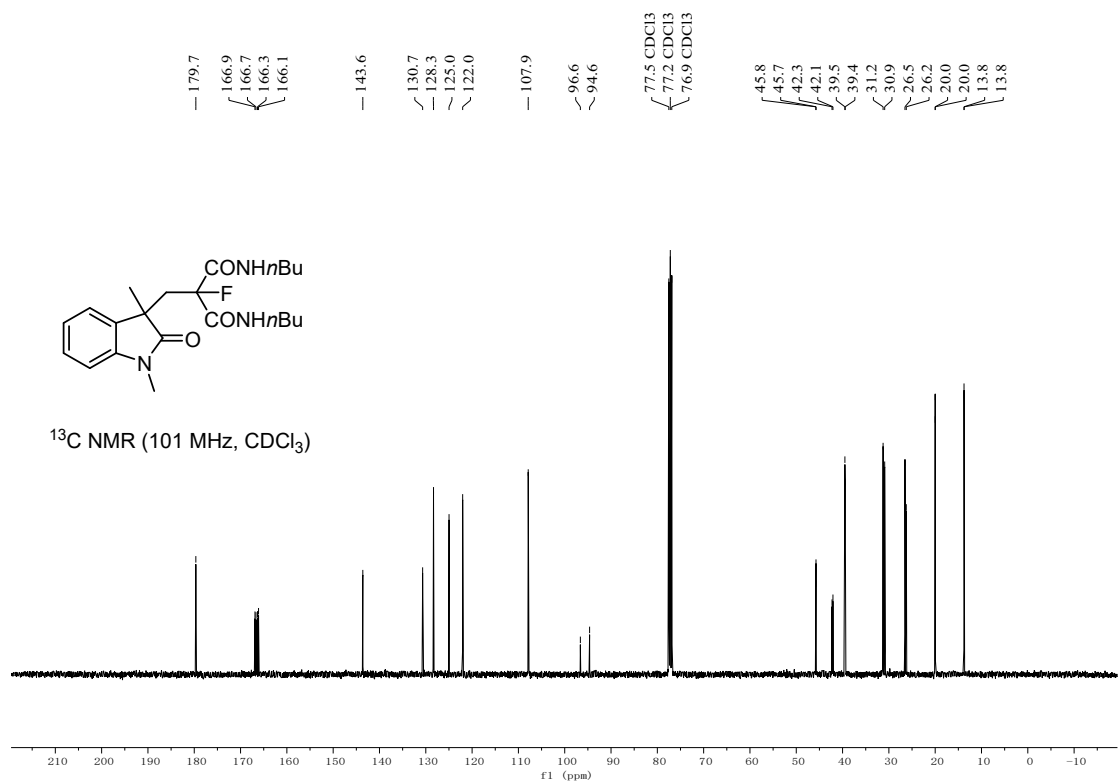
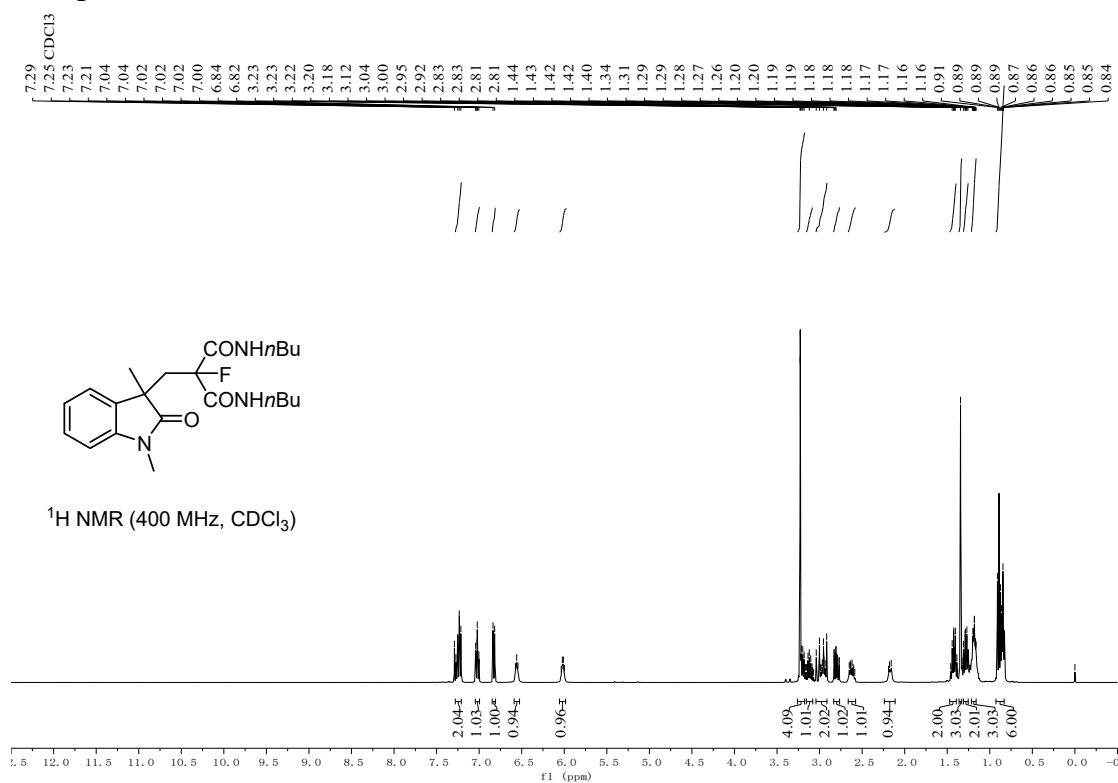
-190.7
-190.7
-190.8
-190.9

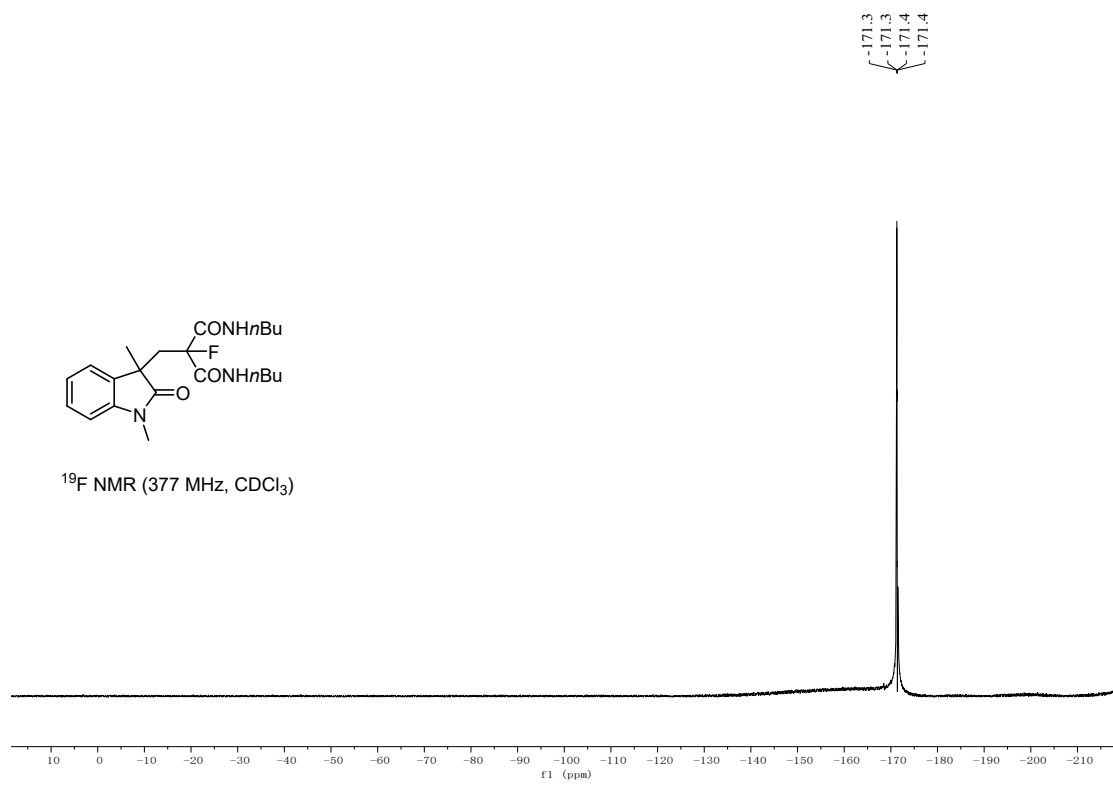


^{19}F NMR (377 MHz, CDCl_3)

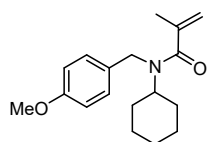


Compound 30

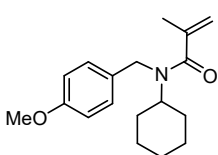
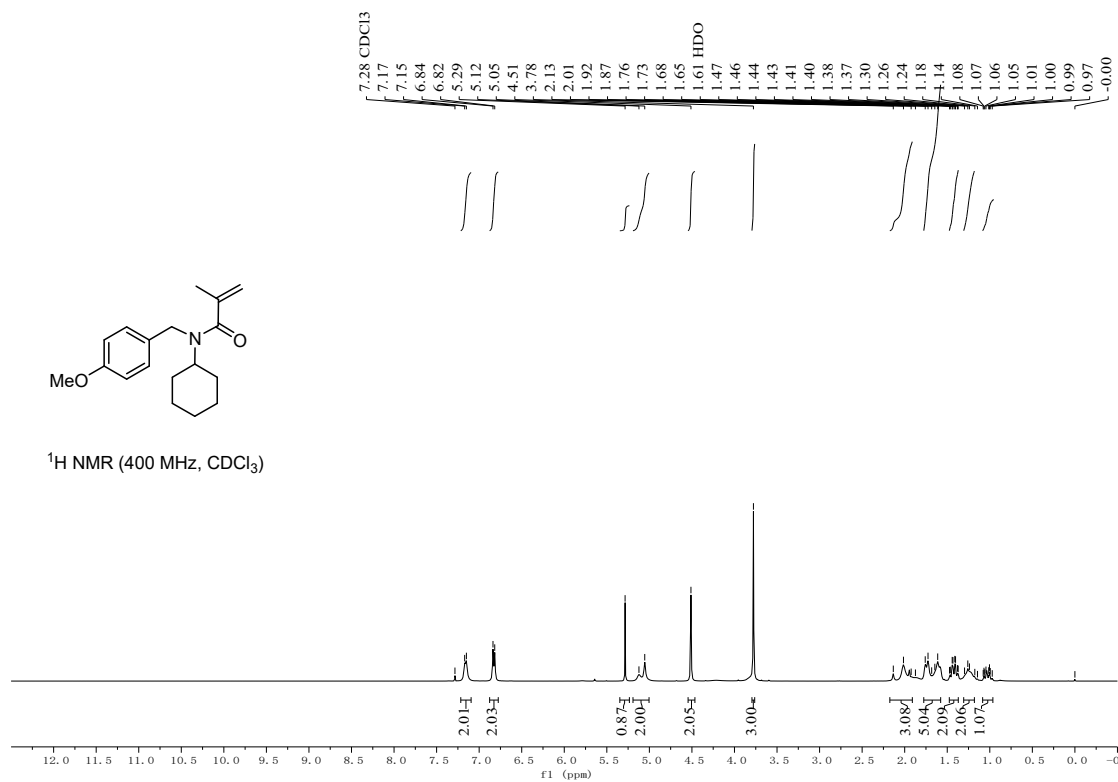




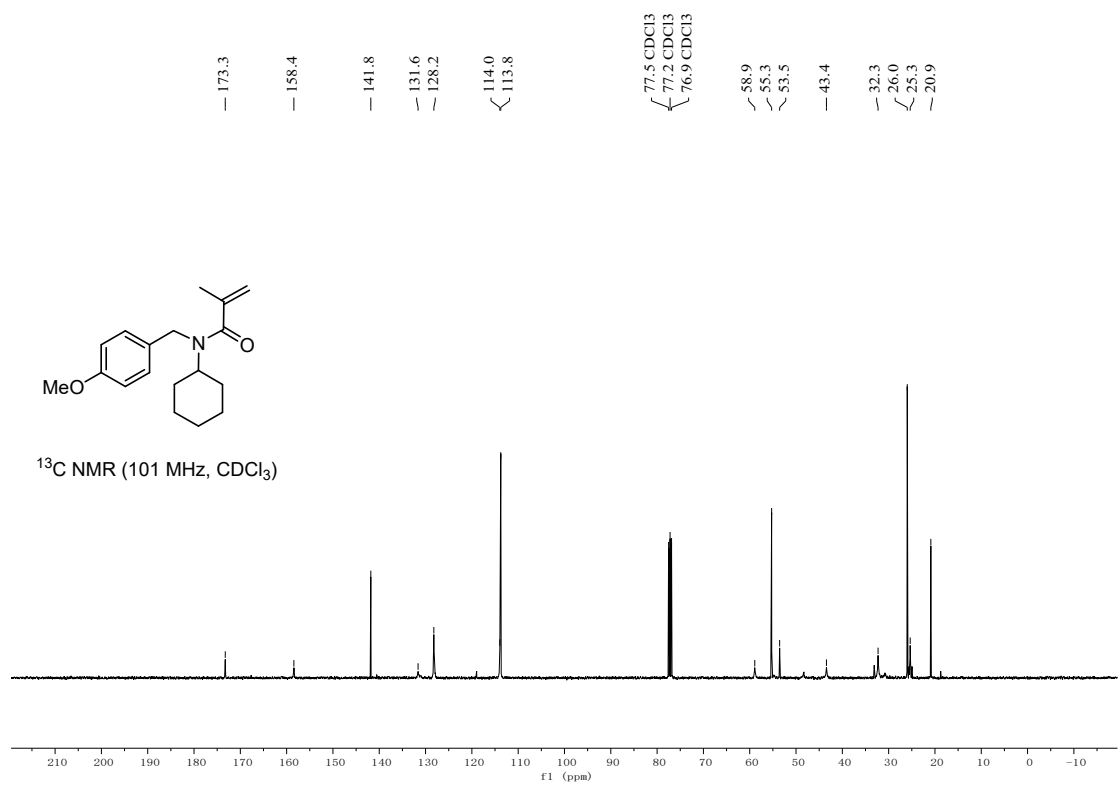
Compound S1



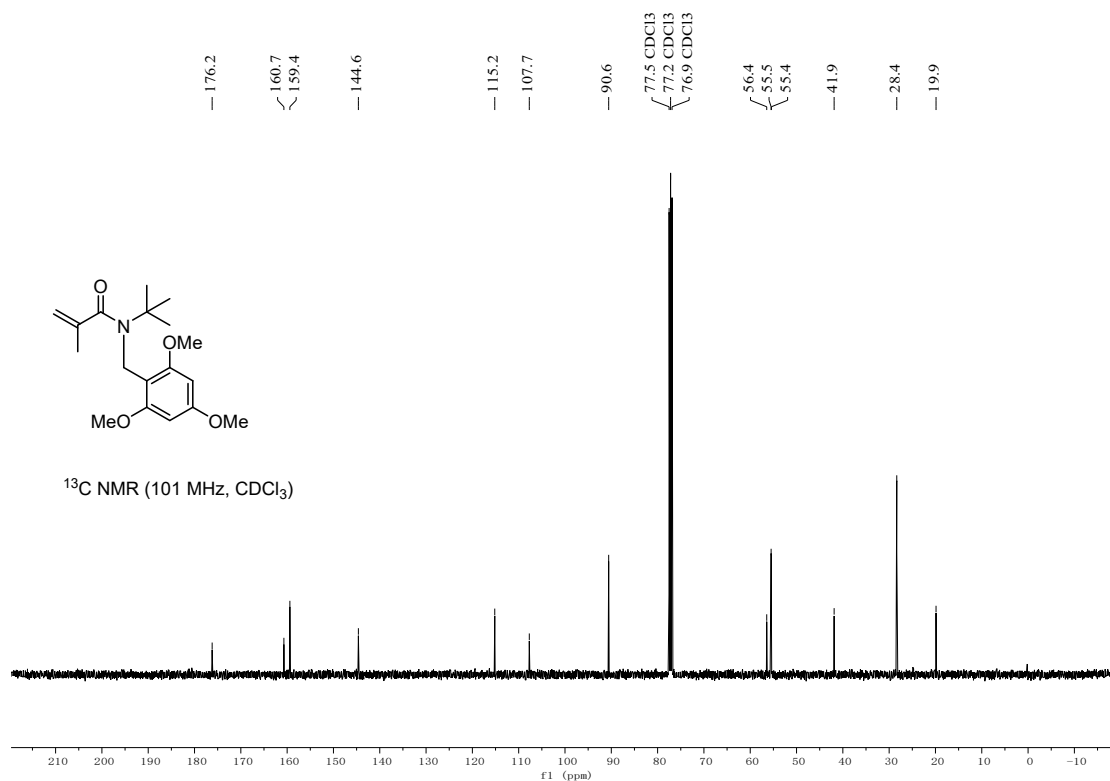
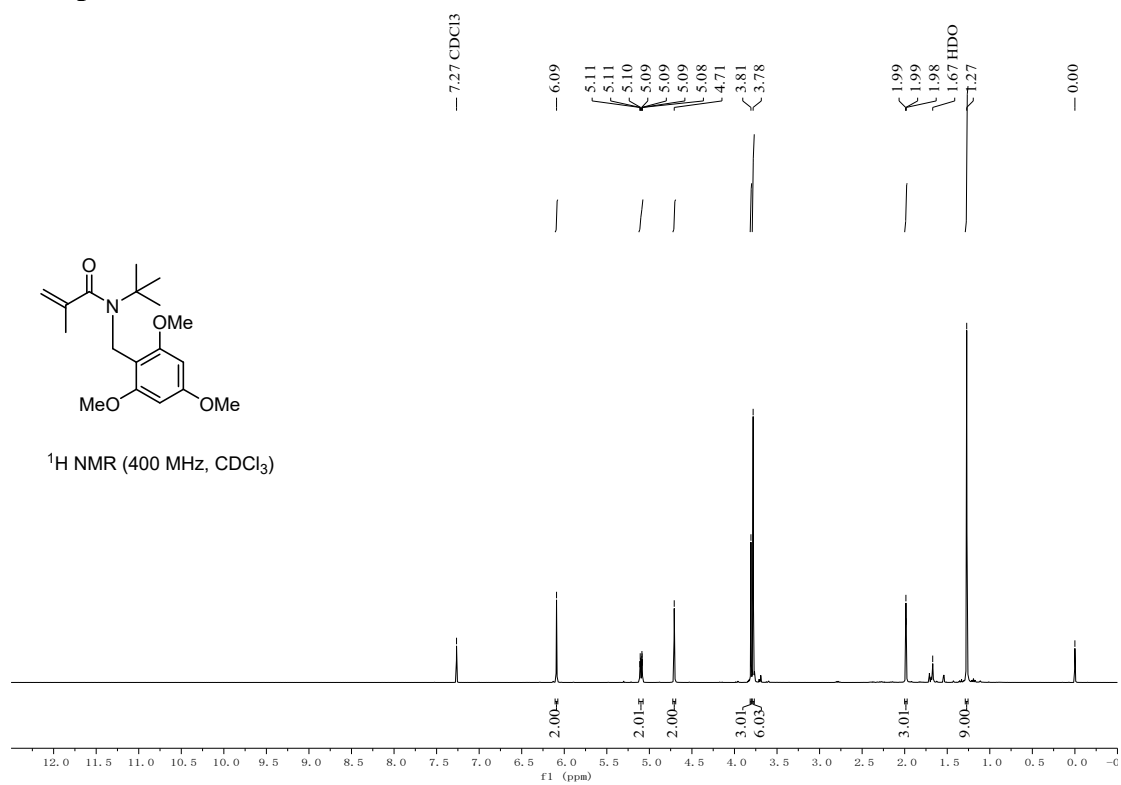
¹H NMR (400 MHz, CDCl₃)



¹³C NMR (101 MHz, CDCl₃)



Compound S2



Compound S3

