

# Metal-free Catalytic De Nove Construction of Multi-functionalized Trifluoromethylarenes Through [3+3] Benzannulation at Low Catalyst Loadings

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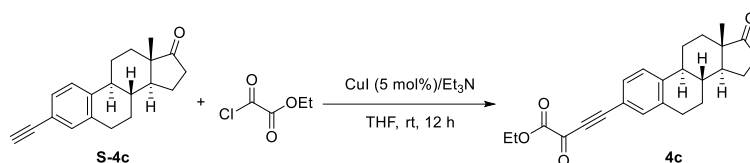
## 1. General information

The products were purified by column chromatography on silica gel (300-400 mesh). For thin-layer chromatography (TLC) analysis, silica gel plates (HSGF254) were used. Visualization of the developed TLC plates was performed with ultraviolet irradiation (254 nm) or staining potassium permanganate solution followed by heating using a heat gun. Reaction temperatures above room temperature refer to oil-bath temperature. High resolution mass spectra on a Bruker Apex IV RTMS spectrometer.  $^1\text{H}$ ,  $^{13}\text{C}$  and  $^{19}\text{F}$  NMR spectra (decoupled) were recorded on Bruker AVANCE-400 (400 MHz) spectrometer or Bruker AVANCE-500 (600 MHz) spectrometer. Chemical shifts were reported in parts per million (ppm), and the residual solvent peak was used as an internal reference: proton (chloroform  $\delta$  7.26), carbon (chloroform  $\delta$  77.0) or tetramethylsilane (TMS  $\delta$  0.00) was used as a reference. Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet), bs (broad singlet). Coupling constants were reported in Hertz (Hz). Melting points were determined on a SGW X-4 melting apparatus. Ynone substrates **1**<sup>1</sup> and **4**<sup>1</sup> as well as alkene substrates **2**<sup>2</sup> were synthesized according to the literature procedures.

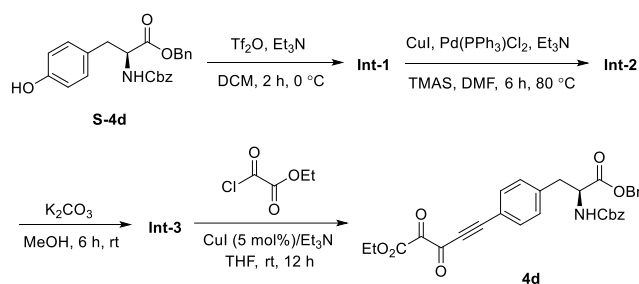
(1) a) Sheng, C.; Ling, Z.; Luo, Y.; Zhang, W. Cu-catalyzed asymmetric addition of alcohols to  $\beta,\gamma$ -alkynyl- $\alpha$ -imino esters for the construction of linear chiral *N,O*-ketals. *Nat Commun.* **2021**, *12*, 928; b) Sharma, A.; Jamwal, P.; Gurubrahamam, R. Synthesis of Tetrasubstituted 1,4-Dicarbonyl (*Z*)-2,3-Dihaloalkenes via Electrophilic Halogenation of Alkynyl Hydrazones. *Org. Lett.* **2023**, *25*, 7236–7241.

(2) a) Peng, F.; Zhao, Q.; Haung, W.; Liu, S.-J.; Zhong, Y.-J.; Mao, Q.; Zhang, N.; He, G.; Han, B. Amine-catalyzed and functional group-controlled chemo- and regioselective synthesis of multi functionalized CF<sub>3</sub>-benzene via a metal-free process. *Green Chem.* **2019**, *21*, 6179–6186; b) Ji, Y.-L.; He, X.-H.; Li, G.; Ai, Y.-Y.; Li, H.-P.; Peng, C.; Han, B. Substrate-directed chemo- and regioselective synthesis of polyfunctionalized trifluoromethylarenes via organocatalytic benzannulation. *Org. Chem. Front.* **2020**, *7*, 563–570.

## 2. General Procedure for 4c and 4d.



An oven-dried Schlenk tube/two-neck round bottom flask equipped with a magnetic stir bar was evacuated and backfilled with nitrogen three times. The tube/flask was charged in sequence with CuI (5 mol%), triethylamine (2 equiv.), and THF (0.25 M). Once a colorless clear solution formed, the alkyne **S-4c** (2 mmol, 556 mg, 1 equiv.) and mono oxalyl chloride (4 mmol, 2 equiv.) were added and the reaction was allowed to stir at room temperature. The reaction was monitored through TLC and quenched with saturated aqueous NaHCO<sub>3</sub> solution upon completion and diluted with ethyl acetate. The contents were allowed to partition, and the organic phase was separated. The aqueous layer was back extracted with ethyl acetate and the combined organic extracts were washed with brine, and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. The contents were filtered and concentrated on a rotary evaporator. The residue was purified by flash column chromatography to obtain the ketoester **4c**: white solid in 62% yield (468 mg); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.47–7.43 (m, 2H), 7.35 (d, *J* = 8.0 Hz, 1H), 4.41 (q, *J* = 7.2 Hz, 2H), 2.95–2.97 (m, 2H), 2.56–2.49 (m, 1H), 2.46–2.31 (m, 2H), 2.21–1.97 (m, 4H), 1.70–1.46 (m, 6H), 1.43 (t, *J* = 7.2 Hz, 3H), 0.92 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 169.6, 159.4, 144.7, 137.4, 134.5, 131.2, 126.0, 116.3, 99.0, 87.2, 63.3, 50.5, 47.9, 44.7, 37.7, 35.8, 31.5, 29.0, 26.1, 25.5, 21.6, 14.0, 13.8.



To **S-4d** (5 mmol, 1.0 equiv.) in dry DCM (20 mL) at 0 °C was added Et<sub>3</sub>N (10.0 mmol, 2.0 equiv.) and trifluoromethanesulfonic anhydride (6 mmol, 1.2 equiv.). The reaction was stirred at 0 °C for 2 h before the addition of water. The phases were

separated and the aqueous phase was extracted with DCM ( $3 \times 10$  mL). The combined organic phases are washed with brine and dried over  $\text{Na}_2\text{SO}_4$ . The filtrate was concentrated in vacuo and the residue was purified by flash column chromatography on silica gel to obtain the intermediate **Int-1**.

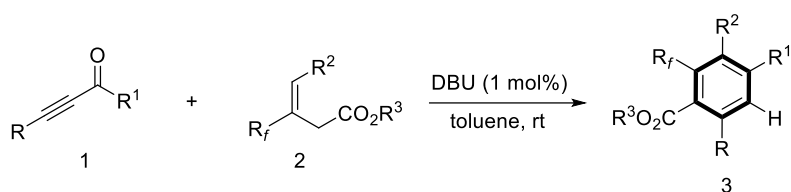
And then, to a mixture of the intermediate **Int-1** (4.7 mmol),  $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$  (5 mol%, 0.05 equiv.) and  $\text{CuI}$  (10 mol%, 0.1 equiv.) in DMF (30 mL) was added  $\text{Et}_3\text{N}$  (3.0 equiv.), and trimethylsilylacetylene (7.1 mmol, 1.5 equiv.), then the reaction was stirred at  $80^\circ\text{C}$  for 6 h. Monitored by TLC, when the reaction was completed, the mixture was quenched with water and extracted with  $\text{EtOAc}$  (20 mL  $\times$  3). The combined organic phases were washed with brine and dried over  $\text{Na}_2\text{SO}_4$ . The filtrate was concentrated in vacuo and the residue was purified by flash column chromatography on silica gel to obtain the intermediate **Int-2**.

And then, to **Int-2** (4.0 mmol) in MeOH (20 mL) was added  $\text{K}_2\text{CO}_3$  (8.0 mmol). The reaction mixture was stirred at  $25^\circ\text{C}$  for 6 h. Monitored by TLC, when the reaction was completed, the mixture was quenched with water and extracted with  $\text{EtOAc}$  (20 mL  $\times$  3). The combined organic phases are washed with brine and dried over  $\text{Na}_2\text{SO}_4$ . The filtrate was concentrated in vacuo and the residue was purified by flash column chromatography to afford **Int-3** as a white solid.

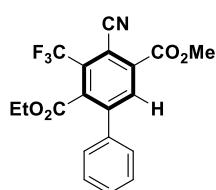
And then, an oven-dried Schlenk tube/two-neck round bottom flask equipped with a magnetic stir bar was evacuated and backfilled with nitrogen three times. The tube/flask was charged in sequence with  $\text{CuI}$  (5 mol%), triethylamine (2 equiv.), and THF (0.25 M). Once a colorless clear solution formed, the alkyne **Int-3** (2 mmol, 1 equiv.) and mono oxalyl chloride (4 mmol, 2 equiv.) were added and the reaction was allowed to stir at room temperature. The reaction was monitored through TLC and quenched with saturated aqueous  $\text{NaHCO}_3$  solution upon completion and diluted with ethyl acetate. The contents were allowed to partition, and the organic phase was separated. The aqueous layer was back extracted with ethyl acetate and the combined organic extracts were washed with brine, and dried over anhydrous  $\text{Na}_2\text{SO}_4$ . The contents were filtered and concentrated on a rotary evaporator. The residue was purified

by flash column chromatography to obtain the ketoester **4d**: light yellow solid in 46% yield (498 mg);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.46 (d,  $J = 8.4$  Hz, 2H), 7.38–7.26 (m, 10H), 7.01 (d,  $J = 7.6$  Hz, 2H), 5.29 (d,  $J = 8.0$  Hz, 1H), 5.21–5.05 (m, 4H), 4.71 (d,  $J = 6.4$  Hz, 1H), 4.41 (d,  $J = 7.2$  Hz, 2H), 3.21–3.06 (m, 2H), 1.43 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  170.8, 169.6, 159.2, 155.5, 140.3, 136.1, 134.8, 134.0, 133.9, 129.9, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 117.7, 97.9, 87.5, 67.5, 67.1, 63.3, 54.5, 38.4, 14.0.

### 3. General procedure for preparation of $\text{CF}_3$ -arenes **3**.



Yrones **1** (0.1 mmol, 1.0 equiv.), alkenes **2** (0.12 mmol, 1.2 equiv.) and catalyst DBU (0.001 mmol, 0.01 equiv.) were stirred in redistilled toluene (1.0 mL) at rt. The reaction mixture was monitored by TLC until the material **1** disappear completely. And then the reaction mixture was concentrated under reduced pressure and the residue was subjected to column chromatography directly using petroleum ether/EtOAc (most use v/v = 20/1 to 8:1) as eluent to afford the desired product **3**.

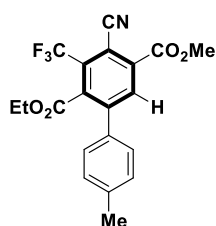


#### *2-ethyl 5-methyl 4-cyano-3-(trifluoromethyl)-[1,1'-biphenyl]-*

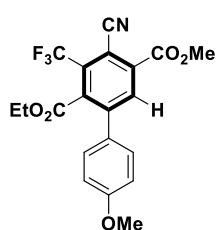
*2,5-dicarboxylate (3a)*: Purified by silica gel column chromatography (eluent: petroleum ether/EtOAc (v/v) = 10:1).

White solid in 99% yield (37.3 mg); mp. 87–89 °C;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.24 (s, 1H), 7.49–7.44 (m, 3H), 7.36–7.34 (m, 2H), 4.11 (q,  $J = 7.2$  Hz, 2H), 4.04 (s, 3H), 1.05 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  165.0, 163.4, 145.2, 136.6, 136.4 (d,  $^3J_{\text{CF}} = 3.2$  Hz), 135.6, 135.4, 131.9 (q,  $^2J_{\text{CF}} = 32.5$  Hz), 129.4, 128.7, 128.5, 121.8 (q,  $^1J_{\text{CF}} = 276.5$  Hz), 113.0, 110.0, 62.7, 53.6, 13.5;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -57.00; HRMS (ESI-TOF)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for

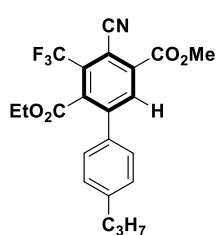
$[\text{C}_{20}\text{H}_{16}\text{F}_3\text{NO}_4+\text{Na}]^+$  414.0924; Found 414.0935.



**2-ethyl 5-methyl 4-cyano-4'-methyl-3-(trifluoromethyl)-[1,1'-biphenyl]-2,5-dicarboxylate (3b):** Purified by silica gel column chromatography (eluent: petroleum ether/EtOAc (v/v) = 10:1). White solid in 95% yield (37.2 mg); mp. 80–82 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.22 (s, 1H), 7.27–7.23 (m, 4H), 4.13 (q,  $J = 7.2$  Hz, 2H), 4.04 (s, 3H), 2.41 (s, 3H), 1.10 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  165.1, 163.5, 145.3, 139.6, 136.3, 135.6, 135.4, 133.7, 131.8 (q,  $^2J_{\text{CF}} = 31.7$  Hz), 129.4, 128.3, 121.8 (q,  $^1J_{\text{CF}} = 274.9$  Hz), 113.1, 109.7, 62.6, 53.5, 21.3, 13.5;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -56.94; HRMS (ESI-TOF) m/z:  $[\text{M}+\text{Na}]^+$  Calcd for  $[\text{C}_{20}\text{H}_{16}\text{F}_3\text{NO}_4+\text{Na}]^+$  414.0924; Found 414.0928.

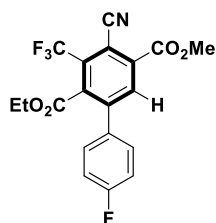


**2-ethyl 5-methyl 4-cyano-4'-methoxy-3-(trifluoromethyl)-[1,1'-biphenyl]-2,5-dicarboxylate (3c):** Purified by silica gel column chromatography (eluent: petroleum ether/EtOAc (v/v) = 10:1). White solid in 93% yield (37.9 mg); mp. 83–85 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.21 (s, 1H), 7.32–7.28 (m, 2H), 6.99–6.95 (m, 2H), 4.16 (q,  $J = 7.2$  Hz, 2H), 4.04 (s, 3H), 3.86 (s, 3H), 1.11 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  165.2, 163.5, 160.6, 145.0, 136.3, 135.6, 135.4, 132.0, 131.4 (q,  $^2J_{\text{CF}} = 31.6$  Hz), 129.9, 128.8, 121.8 (q,  $^1J_{\text{CF}} = 275.0$  Hz), 114.2, 113.1, 109.4, 62.6, 55.4, 53.5, 13.6;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -56.96; HRMS (ESI-TOF) m/z:  $[\text{M}+\text{Na}]^+$  Calcd for  $[\text{C}_{20}\text{H}_{16}\text{F}_3\text{NO}_5+\text{Na}]^+$  430.0873; Found 430.0873.



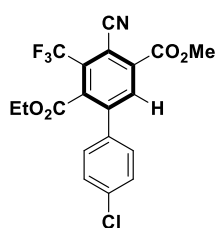
**2-ethyl 5-methyl 4-cyano-4'-propyl-3-(trifluoromethyl)-[1,1'-biphenyl]-2,5-dicarboxylate (3d):** Purified by silica gel column chromatography (eluent: petroleum ether/EtOAc (v/v) = 12:1). White solid in 99% yield (41.4 mg); mp. 68–70 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.16 (s, 1H), 7.21–7.16 (m, 4H), 4.06 (q,  $J = 6.8$  Hz, 2H), 3.96 (s, 3H), 2.59–2.55 (m, 2H), 1.64–1.55 (m, 2H), 0.98 (t,  $J = 6.8$  Hz, 3H), 0.88

(t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  165.1, 163.5, 145.4, 144.3, 136.3 (d,  $^3J_{\text{CF}} = 2.3$  Hz), 135.5, 135.4, 133.9, 131.8 (q,  $^2J_{\text{CF}} = 31.8$  Hz), 128.8, 128.4, 121.8 (q,  $^1J_{\text{CF}} = 274.8$  Hz), 113.1, 109.6 (d,  $^3J_{\text{CF}} = 2.2$  Hz), 62.6, 53.5, 37.7, 24.4, 13.7, 13.5;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -57.05; HRMS (ESI-TOF)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $[\text{C}_{22}\text{H}_{20}\text{F}_3\text{NO}_4+\text{Na}]^+$  442.1237; Found 442.1274.



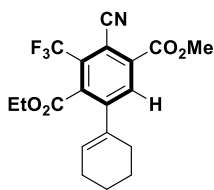
**2-ethyl 5-methyl 4-cyano-4'-fluoro-3-(trifluoromethyl)-[1,1'-biphenyl]-2,5-dicarboxylate (3e):** Purified by silica gel column chromatography (eluent: petroleum ether/EtOAc (v/v) = 12:1). White solid in 99% yield (39.1 mg); mp. 105–107 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.22 (s, 1H), 7.37–7.34 (m, 2H), 7.18–7.14 (m, 2H),

4.13 (q,  $J = 7.2$  Hz, 2H), 4.05 (s, 3H), 1.10 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  164.9, 163.4 (d,  $^1J_{\text{CF(F)}} = 249.0$  Hz), 163.3, 144.1, 136.4, 135.7, 135.4, 132.5 (d,  $^3J_{\text{CF(CF}_3)} = 3.5$  Hz), 131.4 (q,  $^2J_{\text{CF(CF}_3)} = 31.9$  Hz), 130.6, 130.5, 122.0 (q,  $^1J_{\text{CF(CF}_3)} = 275.1$  Hz), 115.9 (d,  $^2J_{\text{CF(F)}} = 21.7$  Hz), 112.9, 110.2 (d,  $^3J_{\text{CF(CF}_3)} = 2.1$  Hz), 62.8, 53.6, 13.5;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -57.06, -111.12; HRMS (ESI-TOF)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $[\text{C}_{19}\text{H}_{13}\text{F}_4\text{NO}_4+\text{Na}]^+$  418.0673; Found 418.0688.

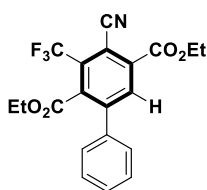


**2-ethyl 5-methyl 4'-chloro-4-cyano-3-(trifluoromethyl)-[1,1'-biphenyl]-2,5-dicarboxylate (3f):** Purified by silica gel column chromatography (eluent: petroleum ether/EtOAc (v/v) = 12:1). White solid in 98% yield (40.3 mg); mp. 93–95 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.21 (s, 1H), 7.46–7.43 (m, 2H), 7.32–7.29 (m, 2H),

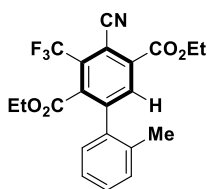
4.15 (q,  $J = 7.2$  Hz, 2H), 4.05 (s, 3H), 1.11 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  164.8, 163.2, 143.9, 136.3 (d,  $^3J_{\text{CF}} = 2.5$  Hz), 135.9, 135.7, 135.2, 134.9, 131.9 (q,  $^2J_{\text{CF}} = 32.0$  Hz), 129.9, 129.0, 121.8 (q,  $^1J_{\text{CF}} = 275.0$  Hz), 112.9, 110.0 (d,  $^3J_{\text{CF}} = 2.2$  Hz), 62.8, 53.6, 13.6;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -57.07; HRMS (ESI-TOF)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $[\text{C}_{19}\text{H}_{13}\text{F}_3\text{ClNO}_4+\text{Na}]^+$  434.0377; Found 434.0398.



**2-ethyl 5-methyl 4-cyano-3-(trifluoromethyl)-2',3',4',5'-tetrahydro-[1,1'-biphenyl]-2,5-dicarboxylate (3g):** Purified by silica gel column chromatography (eluent: petroleum ether/EtOAc (v/v) = 14:1). Light yellow oil in 97% yield (37.0 mg);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.07 (s, 1H), 5.77–5.74 (m, 1H), 4.33 (q,  $J = 7.2$  Hz, 2H), 4.04 (s, 3H), 2.27–2.23 (m, 2H), 2.16–2.12 (m, 2H), 1.79–1.73 (m, 2H), 1.68–1.63 (m, 2H), 1.35 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  165.3, 163.6, 147.8, 136.0 (d,  $^3J_{\text{CF}} = 2.2$  Hz), 135.4, 134.6, 134.0, 131.9 (q,  $^2J_{\text{CF}} = 31.7$  Hz), 130.7, 121.8 (q,  $^1J_{\text{CF}} = 264.7$  Hz), 113.1, 109.1 (d,  $^3J_{\text{CF}} = 2.2$  Hz), 62.5, 53.4, 29.7, 25.3, 22.6, 21.4, 14.0;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -57.09; HRMS (ESI-TOF)  $m/z$ :  $[\text{M}+\text{H}]^+$  Calcd for  $[\text{C}_{19}\text{H}_{18}\text{F}_3\text{NO}_4+\text{Na}]^+$  404.1080; Found 404.1083.



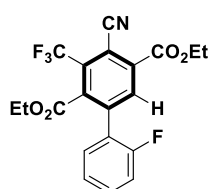
**Diethyl 4-cyano-3-(trifluoromethyl)-[1,1'-biphenyl]-2,5-dicarboxylate (3h):** Purified by silica gel column chromatography (eluent: petroleum ether/EtOAc (v/v) = 10:1). White solid in 98% yield (38.3 mg); mp. 69–71 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.23 (s, 1H), 7.48–7.43 (m, 3H), 7.38–7.34 (m, 2H), 4.51 (q,  $J = 7.2$  Hz, 2H), 4.11 (q,  $J = 7.2$  Hz, 2H), 1.46 (t,  $J = 7.2$  Hz, 3H), 1.05 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  165.0, 163.0, 145.1, 136.6, 136.3 (d,  $^3J_{\text{CF}} = 2.4$  Hz), 136.0, 135.3, 131.9 (q,  $^2J_{\text{CF}} = 31.8$  Hz), 129.4, 128.7, 128.5, 121.8 (q,  $^1J_{\text{CF}} = 270.0$  Hz), 113.1, 110.0 (d,  $^3J_{\text{CF}} = 2.1$  Hz), 63.2, 62.6, 14.0, 13.5;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -57.00; HRMS (ESI-TOF)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $[\text{C}_{20}\text{H}_{16}\text{F}_3\text{NO}_4+\text{Na}]^+$  414.0924; Found 414.0927.



**Diethyl 4-cyano-2'-methyl-3-(trifluoromethyl)-[1,1'-biphenyl]-2,5-dicarboxylate (3i):** Purified by silica gel column chromatography (eluent: petroleum ether/EtOAc (v/v) = 12:1). White solid in 97% yield (39.3 mg); mp. 51–53 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.14 (s, 1H), 7.37–7.33 (m, 1H), 7.29–7.21 (m, 2H), 7.10–7.08 (m, 1H), 4.50 (q,  $J = 7.2$  Hz, 2H), 4.04–3.96 (m, 2H), 2.10 (s, 3H), 1.45 (t,  $J = 7.2$  Hz, 3H), 0.96 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  164.6, 163.0, 145.1, 137.0 (d,  $^3J_{\text{CF}}$

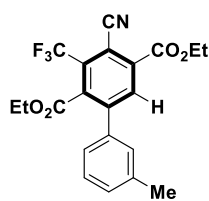


= 2.3 Hz), 136.1, 135.7, 135.6, 135.3, 131.6 (q,  $^2J_{CF} = 31.9$  Hz), 130.2, 129.5, 129.0, 125.5, 121.8 (q,  $^1J_{CF} = 275.0$  Hz), 113.0, 110.0 (d,  $^3J_{CF} = 2.1$  Hz), 63.2, 62.4, 20.1, 14.0, 13.4;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -57.03; HRMS (ESI-TOF)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $[\text{C}_{21}\text{H}_{18}\text{F}_3\text{NO}_4+\text{Na}]^+$  428.1080; Found 428.1082.



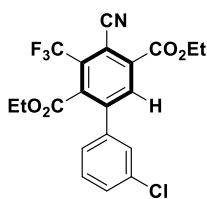
**Diethyl 4-cyano-2'-fluoro-3-(trifluoromethyl)-[1,1'-biphenyl]-2,5-dicarboxylate (3j):** Purified by silica gel column chromatography (eluent: petroleum ether/EtOAc (v/v) = 12:1). White solid in 91% yield (37.2 mg); mp. 53–55 °C;  $^1\text{H}$  NMR (400

MHz,  $\text{CDCl}_3$ )  $\delta$  8.25 (s, 1H), 7.50–7.44 (m, 1H), 7.29–7.17 (m, 3H), 4.51 (q,  $J = 7.2$  Hz, 2H), 4.10 (q,  $J = 7.2$  Hz, 2H), 1.46 (t,  $J = 7.2$  Hz, 3H), 1.05 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  164.6, 162.8, 159.0 (d,  $^1J_{CF(F)} = 247.7$  Hz), 139.1, 137.1, 136.0, 135.8, 132.0 (q,  $^2J_{CF(CF_3)} = 32.1$  Hz), 131.6 (d,  $^3J_{CF(F)} = 7.9$  Hz), 130.7 (d,  $^4J_{CF(F)} = 2.0$  Hz), 124.1 (d,  $^4J_{CF(F)} = 3.8$  Hz), 124.0, 123.8, 122.0 (q,  $^1J_{CF(CF_3)} = 274.9$  Hz), 116.0 (d,  $^2J_{CF(F)} = 21.3$  Hz), 112.9, 110.8 (d,  $^3J_{CF(CF_3)} = 2.2$  Hz), 63.3, 62.7, 14.0, 13.5;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -57.09, -114.15; HRMS (ESI-TOF)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $[\text{C}_{20}\text{H}_{15}\text{F}_4\text{NO}_4+\text{Na}]^+$  432.0829; Found 432.0833.



**Diethyl 4-cyano-3'-methyl-3-(trifluoromethyl)-[1,1'-biphenyl]-2,5-dicarboxylate (3k):** Purified by silica gel column chromatography (eluent: petroleum ether/EtOAc (v/v) = 14:1). Light yellow oil in 92% yield (37.3 mg);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$

8.21 (s, 1H), 7.36–7.32 (m, 1H), 7.29–7.26 (m, 1H), 7.16–7.14 (m, 2H), 4.51 (q,  $J = 7.2$  Hz, 2H), 4.13 (q,  $J = 7.2$  Hz, 2H), 2.40 (s, 3H), 1.45 (t,  $J = 7.2$  Hz, 3H), 1.08 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  165.0, 163.0, 145.3, 138.5, 136.6, 136.2 (d,  $^3J_{CF} = 2.5$  Hz), 135.9, 135.2, 131.7 (q,  $^2J_{CF} = 31.9$  Hz), 130.1, 129.1, 128.6, 125.5, 121.8 (q,  $^1J_{CF} = 274.9$  Hz), 113.1, 109.7 (d,  $^3J_{CF} = 2.1$  Hz), 63.2, 62.6, 21.4, 14.0, 13.5;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -57.25; HRMS (ESI-TOF)  $m/z$ :  $[\text{M}+\text{H}]^+$  Calcd for  $[\text{C}_{21}\text{H}_{18}\text{F}_3\text{NO}_4+\text{Na}]^+$  428.1080; Found 428.1099.

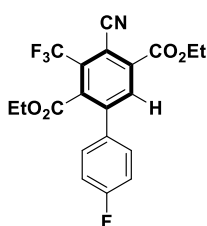


**Diethyl 3'-chloro-4-cyano-3-(trifluoromethyl)-[1,1'-biphenyl]-2,5-dicarboxylate (3l):** Purified by silica gel column

chromatography (eluent: petroleum ether/EtOAc (v/v) = 12:1).

White solid in 98% yield (41.6 mg); mp. 72–74 °C; <sup>1</sup>H NMR (400

MHz, CDCl<sub>3</sub>) δ 8.20 (s, 1H), 7.48–7.37 (m, 3H), 7.26–7.24 (m, 1H), 4.52 (q, *J* = 7.2 Hz, 2H), 4.16 (q, *J* = 7.2 Hz, 2H), 1.46 (t, *J* = 7.2 Hz, 3H), 1.13 (t, *J* = 7.2 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 164.7, 162.8, 143.5, 138.2, 136.2 (d, <sup>3</sup>*J*<sub>CF</sub> = 2.5 Hz), 136.1, 135.1, 134.7, 131.9 (q, <sup>2</sup>*J*<sub>CF</sub> = 31.8 Hz), 130.0, 129.6, 128.6, 126.8, 121.8 (q, <sup>1</sup>*J*<sub>CF</sub> = 275.0 Hz), 112.9, 110.5 (d, <sup>3</sup>*J*<sub>CF</sub> = 2.1 Hz), 63.4, 62.9, 14.0, 13.6; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ -57.06; HRMS (ESI-TOF) *m/z*: [M+Na]<sup>+</sup> Calcd for [C<sub>20</sub>H<sub>15</sub>F<sub>3</sub>NO<sub>4</sub>+Na]<sup>+</sup> 448.0534; Found 448.0569.

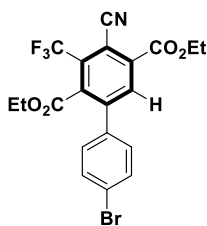


**Diethyl 4-cyano-4'-fluoro-3-(trifluoromethyl)-[1,1'-biphenyl]-2,5-dicarboxylate (3m):** Purified by silica gel column

chromatography (eluent: petroleum ether/EtOAc (v/v) = 12:1).

White solid in 92% yield (37.6 mg); mp. 83–85 °C; <sup>1</sup>H NMR (400

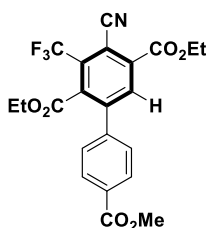
MHz, CDCl<sub>3</sub>) δ 8.20 (s, 1H), 7.38–7.33 (m, 2H), 7.19–7.13 (m, 2H), 4.51 (q, *J* = 7.2 Hz, 2H), 4.13 (q, *J* = 7.2 Hz, 2H), 1.46 (t, *J* = 7.2 Hz, 3H), 1.10 (t, *J* = 7.2 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 164.6, 163.5 (d, <sup>1</sup>*J*<sub>CF(F)}</sub> = 202.1 Hz), 162.1, 144.0, 136.3, 136.0, 135.3, 132.5 (d, <sup>3</sup>*J*<sub>CF(F)}</sub> = 3.4 Hz), 131.8 (q, <sup>2</sup>*J*<sub>CF(CF<sub>3</sub>)}</sub> = 32.0 Hz), 130.6 (d, <sup>3</sup>*J*<sub>CF(F)}</sub> = 8.5 Hz), 122.0 (q, <sup>1</sup>*J*<sub>CF(CF<sub>3</sub>)}</sub> = 275.0 Hz), 115.8 (d, <sup>2</sup>*J*<sub>CF(F)}</sub> = 22.7 Hz), 112.9, 110.1, 63.3, 62.7, 14.0, 13.5; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ -57.04, -111.18; HRMS (ESI-TOF) *m/z*: [M+Na]<sup>+</sup> Calcd for [C<sub>20</sub>H<sub>15</sub>F<sub>4</sub>NO<sub>4</sub>+Na]<sup>+</sup> 432.0829; Found 432.0836.



**Diethyl 4'-bromo-4-cyano-3-(trifluoromethyl)-[1,1'-biphenyl]-2,5-dicarboxylate (3n):**

Purified by silica gel column chromatography (eluent: petroleum ether/EtOAc (v/v) = 14:1). White solid in 98% yield (46.0 mg); mp. 77–79 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.19 (s, 1H), 7.61–7.59 (m, 2H), 7.25–7.23 (m, 2H),

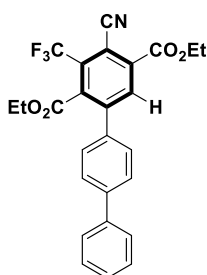
4.52 (q, *J* = 7.2 Hz, 2H), 4.15 (q, *J* = 7.2 Hz, 2H), 1.46 (t, *J* = 7.2 Hz, 3H), 1.11 (t, *J* = 7.2 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 164.8, 162.8, 143.8, 136.2 (d, <sup>3</sup>*J*<sub>CF</sub> = 2.4 Hz), 136.1, 135.4, 135.1, 131.9, 131.8 (q, <sup>2</sup>*J*<sub>CF</sub> = 32.0 Hz), 130.1, 124.1, 121.8 (q, <sup>1</sup>*J*<sub>CF</sub> = 275.0 Hz), 112.9, 110.3 (d, <sup>3</sup>*J*<sub>CF</sub> = 2.1 Hz), 63.3, 62.8, 14.0, 13.6; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ -57.04; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ -57.04; HRMS (ESI-TOF) *m/z*: [M+ Na]<sup>+</sup> Calcd for [C<sub>20</sub>H<sub>15</sub>F<sub>3</sub>BrNO<sub>4</sub>+ Na]<sup>+</sup> 492.0029; Found 492.0033.



**2,5-diethyl 4'-methyl 4-cyano-3-(trifluoromethyl)-[1,1'-biphenyl]-2,4',5-tricarboxylate (3o):**

Purified by silica gel column chromatography (eluent: petroleum ether/EtOAc (v/v) = 8:1). White solid in 98% yield (44.0 mg); mp. 93–94 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.22 (s, 1H), 8.14–8.11 (m, 2H), 7.46–7.43 (m, 2H), 4.52

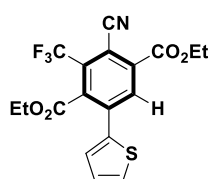
(q, *J* = 7.2 Hz, 2H), 4.11 (q, *J* = 7.2 Hz, 2H), 3.97 (s, 3H), 1.46 (t, *J* = 7.2 Hz, 3H), 1.08 (t, *J* = 7.2 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 166.3, 164.7, 162.8, 144.0, 140.9, 136.2 (d, <sup>3</sup>*J*<sub>CF</sub> = 2.3 Hz), 136.1, 131.8 (q, <sup>2</sup>*J*<sub>CF</sub> = 32.1 Hz), 131.1, 129.9, 128.7, 121.8 (q, <sup>1</sup>*J*<sub>CF</sub> = 275.0 Hz), 112.9, 110.5 (d, <sup>3</sup>*J*<sub>CF</sub> = 2.2 Hz), 63.4, 62.8, 52.5, 14.0, 13.5; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ -57.02; HRMS (ESI-TOF) *m/z*: [M+H]<sup>+</sup> Calcd for [C<sub>22</sub>H<sub>18</sub>F<sub>3</sub>NO<sub>6</sub>+Na]<sup>+</sup> 472.0978; Found 472.1003.



**Diethyl 4-cyano-3-(trifluoromethyl)-[1,1':4',1''-terphenyl]-2,5-dicarboxylate (3p):**

Purified by silica gel column chromatography (eluent: petroleum ether/EtOAc (v/v) = 10:1). Light yellow solid in 96% yield (44.8 mg); mp. 96–97 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.27 (s, 1H), 7.71–7.67 (m, 2H), 7.64–7.61 (m, 2H),

7.50–7.38 (m, 5H), 4.52 (q,  $J = 7.2$  Hz, 2H), 4.15 (q,  $J = 7.2$  Hz, 2H), 1.46 (t,  $J = 7.2$  Hz, 3H), 1.09 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  165.1, 163.0, 144.8, 142.3, 139.9, 136.2 (d,  $^3J_{\text{CF}} = 2.2$  Hz), 136.0, 135.5, 135.3, 132.0 (q,  $^2J_{\text{CF}} = 31.9$  Hz), 129.1, 129.0, 128.0, 127.3, 127.1, 121.8 (q,  $^1J_{\text{CF}} = 275.0$  Hz), 113.1, 110.0 (d,  $^3J_{\text{CF}} = 2.1$  Hz), 63.3, 62.7, 14.0, 13.5;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -57.27; HRMS (ESI-TOF)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $[\text{C}_{26}\text{H}_{20}\text{F}_3\text{NO}_4+\text{Na}]^+$  490.1237; Found 490.1240.

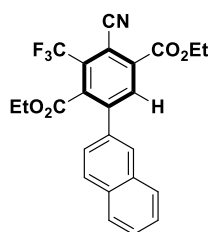


**Diethyl**

**2-cyano-5-(thiophen-2-yl)-3-**

**(trifluoromethyl)terephthalate (3q):** Purified by silica gel column chromatography (eluent: petroleum ether/EtOAc (v/v) = 14:1). Light yellow solid in 83% yield (32.9 mg); mp. 84–85 °C;  $^1\text{H}$  NMR (400

MHz,  $\text{CDCl}_3$ )  $\delta$  8.33 (s, 1H), 7.53–7.52 (m, 1H), 7.26–7.24 (m, 1H), 7.14–7.12 (m, 1H), 4.52 (q,  $J = 7.2$  Hz, 2H), 4.26 (q,  $J = 7.2$  Hz, 2H), 1.47 (t,  $J = 7.2$  Hz, 3H), 1.21 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  165.1, 162.8, 137.8, 136.9, 136.0, 135.8 (d,  $^3J_{\text{CF}} = 2.1$  Hz), 135.5, 132.2 (q,  $^2J_{\text{CF}} = 31.8$  Hz), 129.3, 129.1, 128.1, 121.8 (q,  $^1J_{\text{CF}} = 275.2$  Hz), 113.0, 109.9 (d,  $^3J_{\text{CF}} = 2.1$  Hz), 63.3, 62.9, 14.0, 13.6;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -56.96; HRMS (ESI-TOF)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $[\text{C}_{18}\text{H}_{14}\text{F}_3\text{NSO}_4+\text{Na}]^+$  420.0488; Found 420.0498.



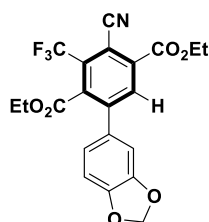
**Diethyl**

**2-cyano-5-(naphthalen-2-yl)-3-**

**(trifluoromethyl)terephthalate (3r):** Purified by silica gel column chromatography (eluent: petroleum ether/EtOAc (v/v) = 10:1). White solid in 98% yield (43.2 mg); mp. 107–108 °C;  $^1\text{H}$  NMR (400

MHz,  $\text{CDCl}_3$ )  $\delta$  8.32 (s, 1H), 7.94–7.85 (m, 4H), 7.61–7.54 (m, 2H), 7.47–7.44 (m, 1H), 4.52 (q,  $J = 7.2$  Hz, 2H), 4.07 (q,  $J = 7.2$  Hz, 2H), 1.46 (t,  $J = 7.2$  Hz, 3H), 1.00 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  165.1, 163.0, 145.2, 144.0, 140.9, 136.5 (d,  $^3J_{\text{CF}} = 2.6$  Hz), 136.0, 135.5, 133.9, 133.2, 132.8, 131.8 (q,  $^2J_{\text{CF}} = 31.8$  Hz), 128.6, 128.3, 127.8, 127.4, 127.1, 125.6, 121.8 (q,  $^1J_{\text{CF}} = 275.0$  Hz), 113.1, 110.0 (d,  $^3J_{\text{CF}} = 2.3$  Hz), 63.3, 62.7, 14.0, 13.5;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -56.92;

HRMS (ESI-TOF)  $m/z$ :  $[M+H]^+$  Calcd for  $[C_{24}H_{18}F_3NO_4+Na]^+$  464.1080; Found 464.1131.

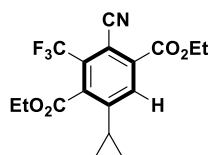


**Diethyl 5-(benzo[d][1,3]dioxol-5-yl)-2-cyano-3-**

**(trifluoromethyl)terephthalate (3s):** Purified by silica gel column chromatography (eluent: petroleum ether/EtOAc (v/v) = 12:1).

White solid in 97% yield (42.2 mg); mp. 109–111 °C;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  8.19 (s, 1H), 6.89–6.82 (m, 3H), 6.04 (s, 2H), 4.51

(q,  $J = 7.2$  Hz, 2H), 4.20 (q,  $J = 7.2$  Hz, 2H), 1.46 (t,  $J = 7.2$  Hz, 3H), 1.17 (t,  $J = 7.2$  Hz, 3H);  $^{13}C$  NMR (101 MHz,  $CDCl_3$ )  $\delta$  165.1, 163.0, 148.7, 148.0, 144.7, 136.2 (d,  $^3J_{CF} = 2.6$  Hz), 136.0, 135.3, 132.0 (q,  $^2J_{CF} = 31.8$  Hz), 130.2, 122.7, 121.8 (q,  $^1J_{CF} = 274.9$  Hz), 113.1, 109.7 (d,  $^3J_{CF} = 2.3$  Hz), 109.0, 108.5, 101.7, 63.3, 62.7, 14.0, 13.6;  $^{19}F$  NMR (376 MHz,  $CDCl_3$ )  $\delta$  -56.95; HRMS (ESI-TOF)  $m/z$ :  $[M+Na]^+$  Calcd for  $[C_{21}H_{16}F_3NO_6+Na]^+$  458.0822; Found 458.0829.

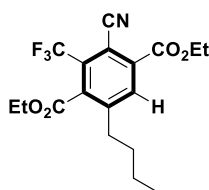


**Diethyl 2-cyano-5-cyclopropyl-3-**

**(trifluoromethyl)terephthalate (3t):** Purified by silica gel column chromatography (eluent: petroleum ether/EtOAc (v/v) = 14:1).

White solid in 83% yield (29.4 mg); mp. 68–70 °C;  $^1H$  NMR (400

MHz,  $CDCl_3$ )  $\delta$  7.79 (s, 1H), 4.52–4.43 (m, 4H), 2.04–1.97 (m, 1H), 1.46 (t,  $J = 7.2$  Hz, 3H), 1.40 (t,  $J = 7.2$  Hz, 3H), 1.18–1.13 (m, 2H), 0.91–0.87 (m, 2H);  $^{13}C$  NMR (101 MHz,  $CDCl_3$ )  $\delta$  165.6, 163.3, 147.0, 137.4 (d,  $^3J_{CF} = 2.6$  Hz), 136.2, 131.2 (q,  $^2J_{CF} = 31.7$  Hz), 130.4, 121.8 (q,  $^1J_{CF} = 274.7$  Hz), 113.2, 108.0 (d,  $^3J_{CF} = 2.2$  Hz), 63.1, 62.8, 14.0, 13.9, 13.7, 9.8;  $^{19}F$  NMR (376 MHz,  $CDCl_3$ )  $\delta$  -57.26; HRMS (ESI-TOF)  $m/z$ :  $[M+Na]^+$  Calcd for  $[C_{17}H_{16}F_3NO_4+Na]^+$  378.0924; Found 378.0941.

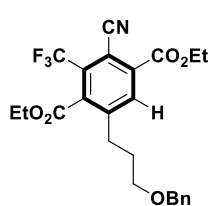


**Diethyl 5-butyl-2-cyano-3-(trifluoromethyl)terephthalate**

**(3u):** Purified by silica gel column chromatography (eluent: petroleum ether/EtOAc (v/v) = 20:1). Light yellow oil in 86% yield

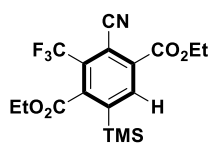
(31.9 mg);  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  8.13 (s, 1H), 4.51 (q,  $J =$

7.2 Hz, 2H), 4.44 (q,  $J = 7.2$  Hz, 2H), 2.72–2.68 (m, 2H), 1.68–1.60 (m, 2H), 1.47 (t,  $J = 7.2$  Hz, 3H), 1.43–1.38 (m, 5H), 0.95 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  165.5, 163.2, 146.1, 136.4 (d,  $^3J_{\text{CF}} = 2.6$  Hz), 135.9, 134.6, 131.5 (q,  $^2J_{\text{CF}} = 31.5$  Hz), 121.9 (q,  $^1J_{\text{CF}} = 274.9$  Hz), 113.2, 108.6 (d,  $^3J_{\text{CF}} = 2.2$  Hz), 63.1, 62.8, 33.4, 32.8, 22.5, 14.0, 13.8, 13.7;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -57.21; HRMS (ESI-TOF)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $[\text{C}_{18}\text{H}_{20}\text{F}_3\text{NO}_4+\text{Na}]^+$  394.1237; Found 394.1238.



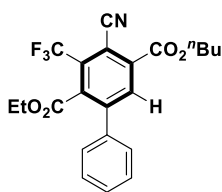
**Diethyl 5-(3-(benzyloxy)propyl)-2-cyano-3-(trifluoromethyl)terephthalate (3v):** Purified by silica gel column chromatography (eluent: petroleum ether/EtOAc (v/v) = 14:1). Light yellow oil in 85% yield (39.3 mg);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$

8.15 (s, 1H), 7.37–7.27 (m, 5H), 4.52–4.46 (m, 4H), 4.39 (q,  $J = 7.2$  Hz, 2H), 3.50 (t,  $J = 6.0$  Hz, 2H), 2.85–2.81 (m, 2H), 1.98–1.91 (m, 2H), 1.44 (t,  $J = 7.2$  Hz, 3H), 1.35 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  165.5, 163.1, 145.4, 138.1, 136.5 (d,  $^3J_{\text{CF}} = 2.5$  Hz), 135.9, 134.9, 131.7 (q,  $^2J_{\text{CF}} = 31.6$  Hz), 128.4, 127.7, 127.6, 121.8 (q,  $^1J_{\text{CF}} = 274.7$  Hz), 113.1, 110.0 (d,  $^3J_{\text{CF}} = 2.0$  Hz), 73.0, 68.7, 63.1, 62.9, 30.7, 30.6, 14.0, 13.8;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -56.93; HRMS (ESI-TOF)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $[\text{C}_{24}\text{H}_{24}\text{F}_3\text{NO}_5+\text{Na}]^+$  486.1499; Found 486.1527.



**Diethyl 2-cyano-3-(trifluoromethyl)-5-(trimethylsilyl)terephthalate (3w):** Purified by silica gel column chromatography (eluent: petroleum ether/EtOAc (v/v) = 15:1). White solid in 88% yield (34.0 mg); mp. 46–48 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.21

(s, 1H), 4.30 (q,  $J = 7.2$  Hz, 2H), 4.18 (q,  $J = 7.2$  Hz, 2H), 1.26 (t,  $J = 7.2$  Hz, 3H), 1.18 (t,  $J = 7.2$  Hz, 3H), 0.16 (s, 9H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  167.7, 164.4, 147.0, 142.4 (d,  $^3J_{\text{CF}} = 2.2$  Hz), 140.5, 135.6, 131.6 (q,  $^2J_{\text{CF}} = 31.4$  Hz), 123.1 (q,  $^1J_{\text{CF}} = 274.9$  Hz), 114.1, 112.1 (d,  $^3J_{\text{CF}} = 2.2$  Hz), 63.9, 63.7, 14.8, 14.5;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -56.97; HRMS (ESI-TOF)  $m/z$ :  $[\text{M}+\text{H}]^+$  Calcd for  $[\text{C}_{17}\text{H}_{20}\text{F}_3\text{SiNO}_4+\text{Na}]^+$  410.1006; Found 410.0981.

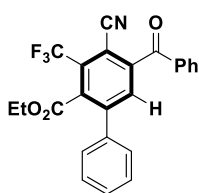


**5-butyl 2-ethyl 4-cyano-3-(trifluoromethyl)-[1,1'-biphenyl]-**

**2,5-dicarboxylate (3x):** Purified by silica gel column chromatography (eluent: petroleum ether/EtOAc (v/v) = 14:1).

Light yellow oil in 95% yield (39.8 mg);  $^1\text{H}$  NMR (400 MHz,

$\text{CDCl}_3$ )  $\delta$  8.25 (s, 1H), 7.48–7.47 (m, 3H), 7.38–7.36 (m, 2H), 4.46 (t,  $J = 6.4$  Hz, 2H), 4.11 (q,  $J = 7.2$  Hz, 2H), 1.85–1.80 (m, 2H), 1.53–1.46 (m, 2H), 1.05 (t,  $J = 6.4$  Hz, 3H), 0.98 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  165.0, 163.0, 145.1, 136.6, 136.3 (d,  $^3J_{\text{CF}} = 2.5$  Hz), 136.0, 135.3, 131.6 (q,  $^2J_{\text{CF}} = 31.9$  Hz), 129.4, 128.7, 128.5, 121.8 (q,  $^1J_{\text{CF}} = 275.1$  Hz), 113.1, 109.8 (d,  $^3J_{\text{CF}} = 1.9$  Hz), 67.1, 62.6, 30.4, 19.1, 13.6, 13.4;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -56.99; HRMS (ESI-TOF)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $[\text{C}_{22}\text{H}_{20}\text{F}_3\text{NO}_4+\text{Na}]^+$  442.1237; Found 442.1239.

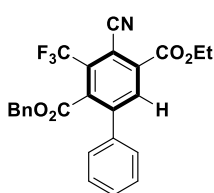


**Ethyl 5-benzoyl-4-cyano-3-(trifluoromethyl)-[1,1'-biphenyl]-**

**2-carboxylate (3y):** Purified by silica gel column chromatography (eluent: petroleum ether/EtOAc (v/v) = 15:1). Light yellow solid in

97% yield (41.0 mg); mp. 85–87 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$

7.75–7.73 (m, 2H), 7.64 (s, 1H), 7.60–7.56 (m, 1H), 7.45–7.41 (m, 2H), 7.35–7.34 (m, 3H), 7.28–7.26 (m, 2H), 4.04 (q,  $J = 7.2$  Hz, 2H), 0.97 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  192.3, 165.0, 145.4, 145.2, 136.6, 135.0 (d,  $^3J_{\text{CF}} = 2.5$  Hz), 133.1, 131.0 (q,  $^2J_{\text{CF}} = 32.1$  Hz), 130.4, 129.5, 129.1, 128.8, 128.5, 121.8 (q,  $^1J_{\text{CF}} = 274.8$  Hz), 113.1, 108.4 (d,  $^3J_{\text{CF}} = 2.2$  Hz), 62.7, 13.5;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -56.94; HRMS (ESI-TOF)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $[\text{C}_{24}\text{H}_{16}\text{F}_3\text{NO}_3+\text{Na}]^+$  446.0974; Found 446.0976.

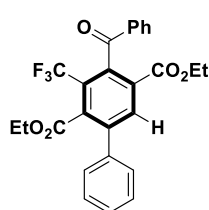


**2-benzyl 5-ethyl 4-cyano-3-(trifluoromethyl)-[1,1'-biphenyl]-**

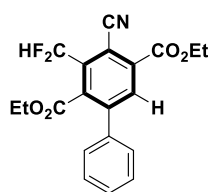
**2,5-dicarboxylate (3z):** Purified by silica gel column chromatography (eluent: petroleum ether/EtOAc (v/v) = 15:1).

Light yellow oil in 95% yield (43.0 mg);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )

$\delta$  8.22 (s, 1H), 7.47–7.06 (m, 8H), 7.04 (d,  $J = 2.0$  Hz, 2H), 5.04 (s, 2H), 4.04 (q,  $J = 7.2$  Hz, 2H), 1.44 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  164.9, 162.9, 145.2, 136.5, 136.1, 135.8 (d,  $^3J_{\text{CF}} = 2.5$  Hz), 135.4, 133.8, 131.9 (q,  $^2J_{\text{CF}} = 31.9$  Hz), 129.5, 128.8, 128.7, 128.6, 128.4, 121.8 (q,  $^1J_{\text{CF}} = 275.0$  Hz), 113.1, 109.9 (d,  $^3J_{\text{CF}} = 2.4$  Hz), 68.6, 63.3, 14.0;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -56.90; HRMS (ESI-TOF)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $[\text{C}_{25}\text{H}_{18}\text{F}_3\text{NO}_4+\text{Na}]^+$  476.1080; Found 476.1085.



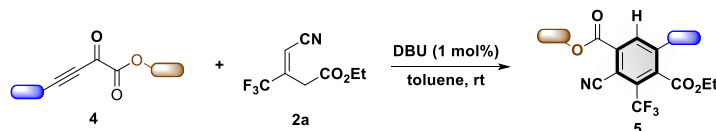
**Diethyl 4-benzoyl-3-(trifluoromethyl)-[1,1'-biphenyl]-2,5-dicarboxylate (3aa):** Purified by silica gel column chromatography (eluent: petroleum ether/EtOAc (v/v) = 12:1). Light yellow solid in 96% yield (45.1 mg); mp. 81–83 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.18 (s, 1H), 7.51–7.39 (m, 3H), 7.27–7.12 (m, 7H), 4.48 (q,  $J = 6.8$  Hz, 2H), 4.41 (q,  $J = 6.8$  Hz, 2H), 1.44–1.37 (m, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  194.5, 166.4, 164.3, 142.2, 141.5 (d,  $^3J_{\text{CF}} = 2.1$  Hz), 137.0, 136.3, 135.1, 133.7, 130.2, 129.3, 129.2, 128.4, 128.3, 128.2, 126.3 (q,  $^2J_{\text{CF}} = 31.9$  Hz), 122.8 (q,  $^1J_{\text{CF}} = 275.1$  Hz), 62.6, 62.4, 14.1, 13.8;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -53.15; HRMS (ESI-TOF)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $[\text{C}_{26}\text{H}_{21}\text{F}_3\text{NO}_5+\text{Na}]^+$  493.1233; Found 493.1230.



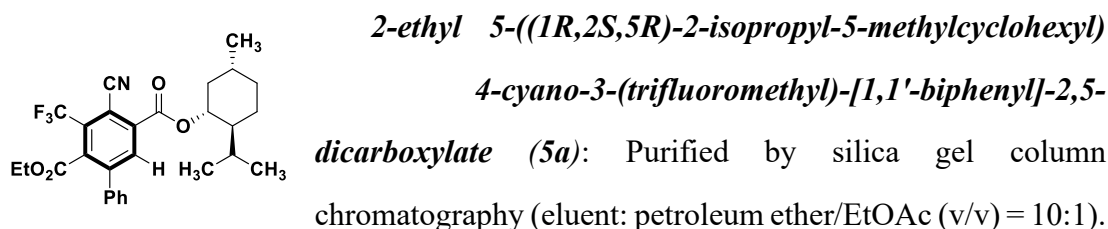
**Diethyl 4-cyano-3-(difluoromethyl)-[1,1'-biphenyl]-2,5-dicarboxylate (3ab):** Purified by silica gel column chromatography (eluent: petroleum ether/EtOAc (v/v) = 15:1). colorless oil in 91% yield (33.9 mg);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.25 (s, 1H), 7.57–7.53 (m, 1H), 7.48–7.46 (m, 2H), 7.39–7.37 (m, 2H), 7.17 (t,  $J = 53.6$  Hz, 1H), 4.52 (q,  $J = 6.8$  Hz, 2H), 4.13 (q,  $J = 6.8$  Hz, 2H), 1.46 (q,  $J = 6.8$  Hz, 3H), 1.02 (q,  $J = 6.8$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  165.5, 163.0, 145.3, 137.2, 136.4, 136.0, 135.4 (t,  $^2J_{\text{CF}} = 23.2$  Hz), 134.6, 133.7, 129.3, 128.8, 128.3, 114.5, 112.0 (t,  $^1J_{\text{CF}} = 241.2$  Hz), 110.5 (t,  $^3J_{\text{CF}} = 4.9$  Hz), 63.1, 62.5, 14.0, 13.5;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -53.15; HRMS (ESI-TOF)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $[\text{C}_{20}\text{H}_{17}\text{F}_2\text{NO}_4+\text{Na}]^+$  396.1018; Found 396.1013.



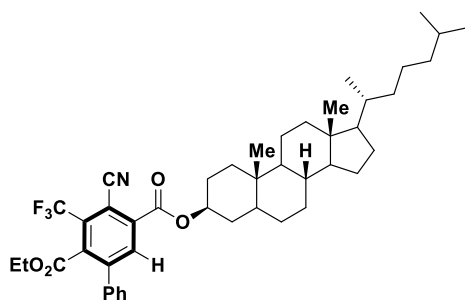
#### 4. Late-stage functionalization of some bioactive molecules.



Ynone **4** (0.1 mmol, 1.0 equiv.), alkenes **2a** (0.12 mmol, 1.2 equiv.) and catalyst DBU (0.001 mmol, 0.01 equiv.) were stirred in redistilled toluene (1.0 mL) at rt. The reaction mixture was monitored by TLC until the material **1** disappear completely. And then the reaction mixture was concentrated under reduced pressure and the residue was subjected to column chromatography directly using petroleum ether/EtOAc (most use v/v = 15/1 to 4:1) as eluent to afford the desired product **5**.



Light yellow solid in 88% yield (44.1 mg); mp. 99–101 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.15 (s, 1H), 7.40–7.37 (m, 3H), 7.29–7.27 (m, 2H), 5.00 (td,  $J = 10.8, 4.4$  Hz, 1H), 4.01 (q,  $J = 7.2$  Hz, 2H), 2.06 (d,  $J = 12.0$  Hz, 1H), 1.89–1.82 (m, 1H), 1.69–1.62 (m, 2H), 1.56–1.42 (m, 2H), 1.20–1.02 (m, 3H), 0.95 (t,  $J = 7.2$  Hz, 3H), 0.87–0.82 (m, 6H), 0.73–0.71 (m, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  165.0, 162.5, 145.1, 136.7, 136.2 (d,  $^3J_{\text{CF}} = 2.3$  Hz), 136.1, 135.2, 131.7 (q,  $^2J_{\text{CF}} = 31.8$  Hz), 129.4, 128.7, 128.5, 121.8 (q,  $^1J_{\text{CF}} = 274.9$  Hz), 113.1, 109.9 (d,  $^3J_{\text{CF}} = 1.9$  Hz), 77.9, 62.6, 46.7, 40.6, 34.0, 31.5, 26.3, 23.3, 22.0, 20.7, 16.2, 13.5;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -56.95; HRMS (ESI-TOF) m/z:  $[\text{M}+\text{Na}]^+$  Calcd for  $[\text{C}_{28}\text{H}_{30}\text{O}_4\text{F}_3+\text{Na}]^+$  524.2019; Found 524.2013.



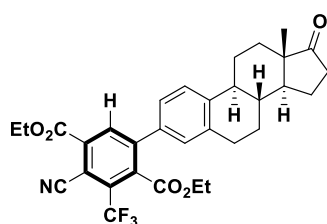
*Ethyl*

*5-benzoyl-4-cyano-3-*

*(trifluoromethyl)-[1,1'-biphenyl]-2-*

*carboxylate (5b)*: Purified by silica gel column chromatography (eluent: petroleum ether/EtOAc (v/v) = 15:1). Light yellow solid in 90% yield (66.0 mg); mp. 56–88 °C; <sup>1</sup>H NMR

(400 MHz, CDCl<sub>3</sub>) δ 8.13 (s, 1H), 7.38–7.36 (m, 3H), 7.29–7.26 (m, 2H), 5.34 (d, *J* = 4.8 Hz, 1H), 4.93–4.84 (m, 1H), 4.01 (q, *J* = 7.2 Hz, 2H), 2.51–2.40 (m, 2H), 2.00–1.69 (m, 6H), 1.52–1.36 (m, 6H), 1.30–1.22 (m, 6H), 1.12–1.00 (m, 7H), 0.97–0.88 (m, 9H), 0.83 (d, *J* = 6.4 Hz, 3H), 0.78 (dd, *J* = 6.4, 2.0 Hz, 6H), 0.60 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 165.0, 162.4, 145.1, 139.0, 136.7, 136.3, 136.1 (d, <sup>3</sup>*J*<sub>CF</sub> = 2.5 Hz), 135.3, 131.5 (q, <sup>2</sup>*J*<sub>CF</sub> = 31.8 Hz), 129.4, 128.7, 128.8, 123.3, 121.8 (q, <sup>1</sup>*J*<sub>CF</sub> = 275.9 Hz), 113.1, 109.8 (d, <sup>3</sup>*J*<sub>CF</sub> = 2.0 Hz), 77.5, 62.6, 56.7, 56.2, 50.0, 42.3, 39.7, 39.5, 37.8, 36.9, 36.6, 36.2, 35.8, 31.9, 31.8, 28.3, 28.0, 27.6, 24.3, 23.9, 22.9, 22.6, 21.1, 19.3, 18.7, 13.5, 11.9; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ -56.94; HRMS (ESI-TOF) *m/z*: [M+Na]<sup>+</sup> Calcd for [C<sub>45</sub>H<sub>58</sub>O<sub>4</sub>F<sub>3</sub>+Na]<sup>+</sup> 756.4210; Found 756.4215.



*3-cyano-6-((8R,9S,13S,14S)-13-methyl-17-oxo-*

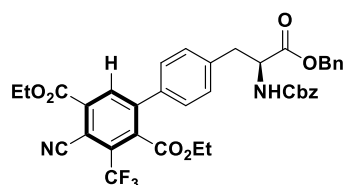
*7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]-*

*phenanthren-3-yl)-2,4-bis(trifluoromethyl)benzoate (5c)*:

Purified by silica gel column chromatography (eluent: petroleum ether/EtOAc (v/v) = 6:1). Light yellow solid in

86% yield (48.8 mg); mp. 140–142 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.15 (s, 1H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.07 (d, *J* = 8.0 Hz, 1H), 7.02 (s, 1H), 4.43 (q, *J* = 8.0 Hz, 2H), 4.11 (q, *J* = 7.2 Hz, 2H), 2.88 (q, *J* = 4.8 Hz, 2H), 2.49–2.25 (m, 3H), 2.12–1.90 (m, 4H), 1.63–1.42 (m, 5H), 1.37 (t, *J* = 8.0 Hz, 3H), 1.18–1.06 (m, 4H), 0.87 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 165.2, 163.0, 145.2, 141.3, 137.2, 136.0 (d, <sup>3</sup>*J*<sub>CF</sub> = 2.5 Hz), 135.9, 135.3, 134.2, 131.7 (q, <sup>2</sup>*J*<sub>CF</sub> = 31.8 Hz), 129.0, 125.8, 125.7, 121.8 (q, <sup>1</sup>*J*<sub>CF</sub> = 275.0 Hz), 113.1, 109.5 (d, <sup>3</sup>*J*<sub>CF</sub> = 2.2 Hz), 63.2, 62.6, 50.5, 47.9, 44.3, 38.0, 35.8, 31.5,

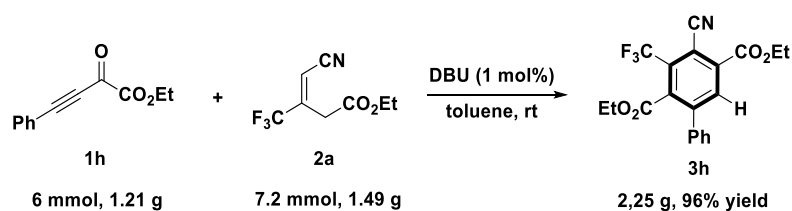
29.3, 26.3, 25.7, 21.6, 14.0, 13.8, 13.6;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -56.94; HRMS (ESI-TOF)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $[\text{C}_{32}\text{H}_{32}\text{F}_3\text{NO}_5+\text{Na}]^+$  590.2125; Found 590.2117.



*Diethyl* *(S)*-4'-(3-(benzyloxy)-2-(((benzyloxy)carbonyl)amino)-3-oxopropyl)-4-cyano-3-(trifluoromethyl)-[1,1'-biphenyl]-2,5-dicarboxylate (**5d**):

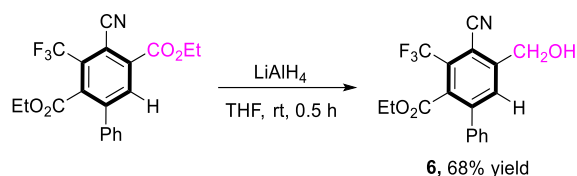
Purified by silica gel column chromatography (eluent: petroleum ether/EtOAc (v/v) = 4:1). Yellow oil in 81% yield (56.9 mg);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.17 (s, 1H), 7.39–7.31 (m, 10H), 7.17 (d,  $J$  = 7.6 Hz, 2H), 7.17 (d,  $J$  = 7.6 Hz, 2H), 5.29–5.08 (m, 5H), 4.75–4.70 (m, 1H), 4.52 (q,  $J$  = 7.6 Hz, 2H), 4.06 (q,  $J$  = 7.6 Hz, 2H), 3.24–3.09 (m, 2H), 1.46 (t,  $J$  = 7.6 Hz, 3H), 1.02 (t,  $J$  = 7.6 Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  171.0, 165.0, 163.0, 155.6, 144.7, 137.2, 136.2, 136.1, 136.0, 135.3, 135.2, 135.0, 131.7 (q,  $^2J_{\text{CF}}$  = 31.9 Hz), 129.7, 128.8, 128.7, 128.6, 128.5, 121.8 (q,  $^1J_{\text{CF}}$  = 275.0 Hz), 113.1, 109.8 (d,  $^4J_{\text{CF}}$  = 1.4 Hz), 67.5, 67.1, 63.3, 62.7, 54.7, 37.8, 29.7, 14.1, 13.5;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -56.95; HRMS (ESI-TOF)  $m/z$ :  $[\text{M}+\text{Na}]^+$  Calcd for  $[\text{C}_{38}\text{H}_{33}\text{F}_3\text{N}_2\text{O}_8+\text{Na}]^+$  725.2081; Found 725.2081.

## 5. Gram-scale reaction.

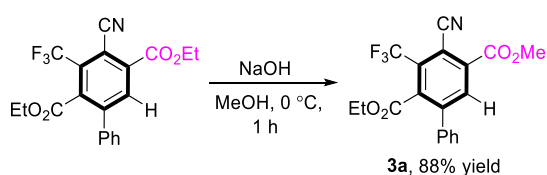


Ynone **1h** (1.21 g, 6.0 mmol, 1.0 equiv.), alkene **2a** (1.49 g, 7.2 mmol, 1.2 equiv.) and DBU (9.1 mg, 0.06 mmol, 0.01 equiv.) were stirred in redistilled toluene (60 mL) at rt. The reaction mixture was monitored by TLC until the material **1h** disappear completely. And then the reaction mixture was concentrated under reduced pressure and the residue was subjected to column chromatography directly using petroleum ether/EtOAc (most use v/v = 12:1) as eluent to afford the desired product **3h** (2.25 g) with 96% yield.

## 6. Synthetic transformations.

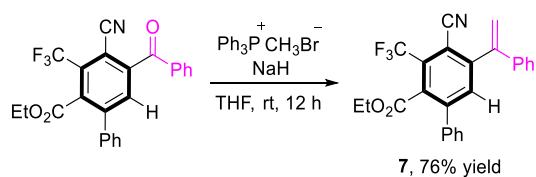


The corresponding compound **3h** (39.1 mg, 0.1 mmol) was dissolved in 1.0 mL of THF and added LiAlH<sub>4</sub> (3.8 mg, 0.1 mmol), then stirred for about 0.5 h at room temperature. The reaction mixture was monitored by TLC until the material **3h** disappear completely. And then the reaction mixture was concentrated under reduced pressure and the residue was dissolved in DCM, and washed with water for several times. The organic phase was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated in vacuo. Then, the residue was subjected to column chromatography using petroleum ether/EtOAc (v/v = 5:1) as eluent to afford the desired product **6** (23.7 mg) with 68% yield: light yellow oil, <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.84 (s, 1H), 7.38–7.35 (m, 3H), 7.29–7.27 (m, 2H), 7.19 (s, 1H), 4.98 (t, *J* = 2.0 Hz, 2H), 4.02 (q, *J* = 7.2 Hz, 2H), 0.97 (t, *J* = 7.2 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 165.6, 147.3, 145.5, 137.6, 132.5 (d, <sup>3</sup>*J*<sub>CF</sub> = 2.4 Hz), 132.1, 129.1, 128.5, 128.4, 121.8 (q, <sup>1</sup>*J*<sub>CF</sub> = 274.5 Hz), 113.3, 107.3 (d, <sup>3</sup>*J*<sub>CF</sub> = 2.4 Hz), 62.4, 29.7, 13.5; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ -57.04; HRMS (ESI-TOF) *m/z*: [M+Na]<sup>+</sup> Calcd for [C<sub>18</sub>H<sub>14</sub>F<sub>3</sub>NO<sub>3</sub>+H]<sup>+</sup> 350.0999; Found 350.1005.



The corresponding compound **3h** (39.1 mg, 0.1 mmol) was dissolved in 1.0 mL of MeOH, and then added NaOH (8.0 mg, 0.2 mmol) at 0 °C, then stirred for about 0.5 h at 0 °C. The reaction mixture was monitored by TLC until the material **3h** disappear completely. And then the reaction mixture was quenched with saturated NH<sub>4</sub>Cl aq, and extraction with DCM (5 mL×3). The combined organic phase was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated in vacuo. Then, the residue was subjected to column chromatography using petroleum ether/EtOAc (v/v = 10:1) as eluent to afford the

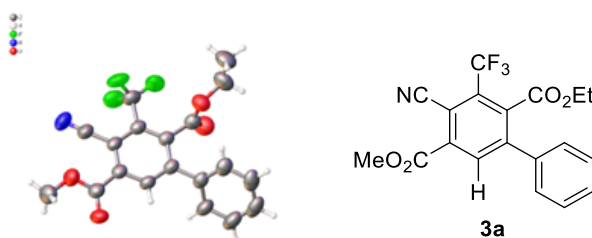
desired product **3a** (33.2 mg) with 88% yield.



To a suspension of methyltriphenylphosphonium bromide (107 mg, 0.3 mmol) in THF (1.0 mL) at 0 °C was added NaH (60%, dispersion in paraffin liquid, 12 mg, 0.3 mmol). The reaction was warmed to ambient temperature and stirred for 0.5 h. The compound **3y** (42.3 mg, 0.1 mmol) was added. The resulting mixture was stirred at room temperature for 12 h. Saturated ammonium chloride (5 mL) was added to quench the reaction. Then extracted with DCM (5 mL×3). The combined organic phase was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated in vacuo. Then, the residue was subjected to column chromatography using petroleum ether/EtOAc (v/v = 20:1) as eluent to afford the desired product **7** (32.0 mg) with 76% yield: white solid, mp. 80–82 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.49 (s, 1H), 7.37–7.33 (m, 3H), 7.32–7.26 (m, 5H), 7.22–7.19 (m, 2H), 5.95 (s, 1H), 5.47 (s, 1H), 4.05 (q, *J* = 7.2 Hz, 2H), 0.99 (t, *J* = 7.2 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 165.7, 149.9, 145.2, 144.8, 138.5, 137.2, 135.0, 130.5 (d, <sup>2</sup>*J*<sub>CF</sub> = 31.7 Hz), 129.1, 128.8, 128.6, 128.5, 127.0, 121.8 (q, <sup>1</sup>*J*<sub>CF</sub> = 274.7 Hz), 119.6, 114.0, 109.7, 62.4, 13.5; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ -56.94; HRMS (ESI-TOF) *m/z*: [M+Na]<sup>+</sup> Calcd for [C<sub>25</sub>H<sub>18</sub>F<sub>3</sub>NO<sub>2</sub>+Na]<sup>+</sup> 444.1182; Found 444.1178.

## 7. Crystal data and structural refinement for **3a**

**Procedure for recrystallization of **3a**:** To a 10 mL tube containing **3a** (100 mg) was added a mixture of DCM, *n*-hexane and EtOAc (1:10:1, about 10 mL). The mixture was heated until a clear solution was formed, which was kept aside overnight at room temperature to obtain crystals. These crystals were subjected for single crystal XRD to determine the absolute configuration of **3a**. The data were collected by an Agilent Gemini equipped with a Cu radiation source ( $K\alpha = 1.54184 \text{ \AA}$ ) at 294.8(3) K. CCDC 2394810 (**3a**) contains the supplementary crystallographic data for this paper.

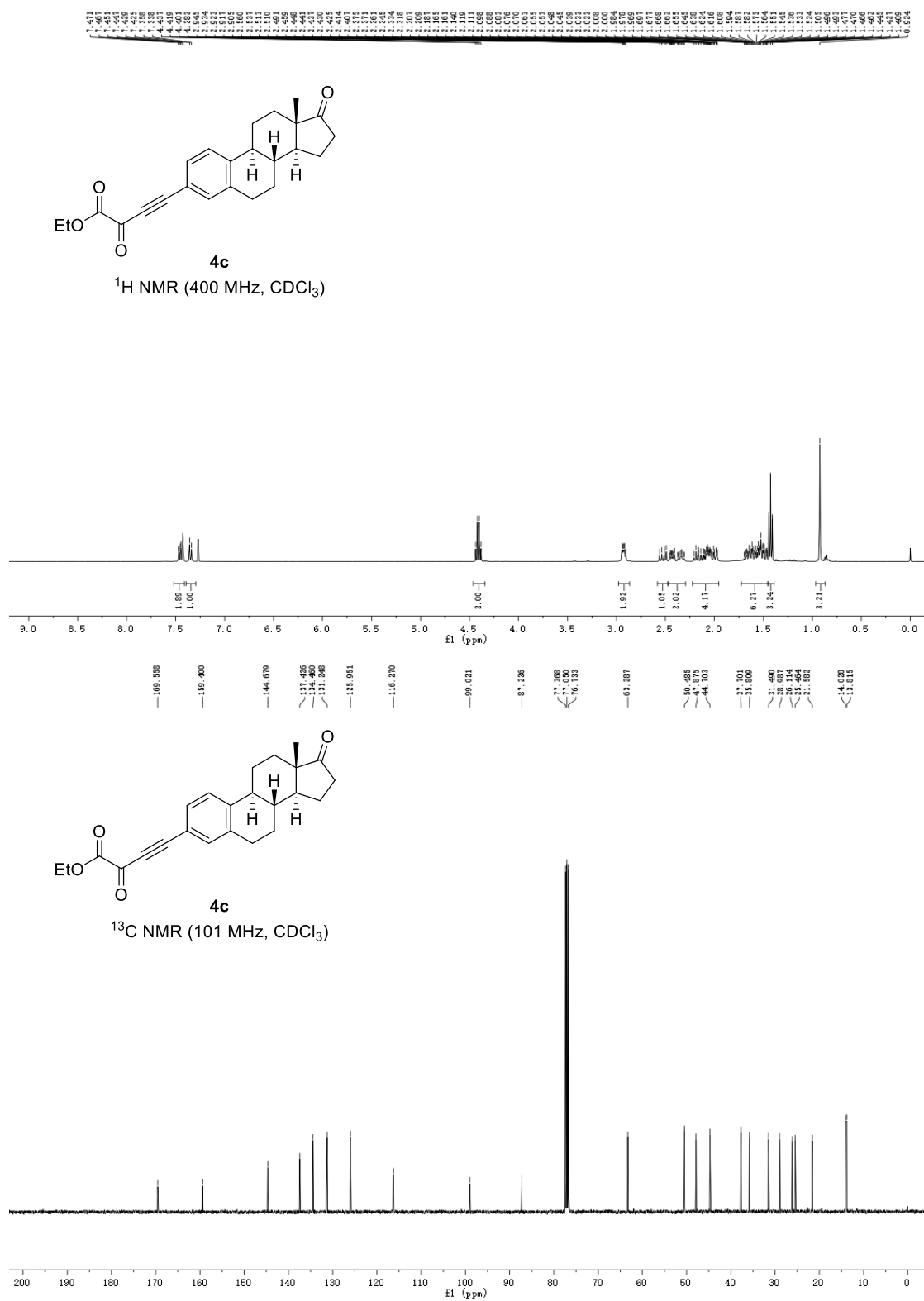


The ellipsoid contour percent probability level: 40%

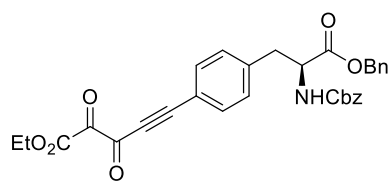
Identification code	<b>3a</b> (CCDC: 2394810)
Empirical formula	$C_{19}H_{14}F_3NO_4$
Formula weight	377.31
Temperature/K	293(2)
Crystal system	monoclinic
Space group	$P2_1/c$
$a/\text{\AA}$	13.4270(9)
$b/\text{\AA}$	11.9465(5)
$c/\text{\AA}$	12.2064(8)
$\alpha/^\circ$	90
$\beta/^\circ$	110.850(8)
$\gamma/^\circ$	90
Volume/ $\text{\AA}^3$	1829.8(2)
Z	4
$\rho_{\text{calc}}/\text{cm}^3$	1.370
$\mu/\text{mm}^{-1}$	1.006
F(000)	776.0

Crystal size/mm <sup>3</sup>	0.43 × 0.33 × 0.23
Radiation	Cu Kα (λ = 1.54184)
2θ range for data collection/	7.044 to 136.49
Index ranges	-16 ≤ h ≤ 14, -14 ≤ k ≤ 10, -14 ≤ l ≤ 14
Reflections collected	13605
Independent reflections	3305 [R <sub>int</sub> = 0.0672, R <sub>sigma</sub> = 0.0492]
Data/restraints/parameters	3305/169/305
Goodness-of-fit on F <sup>2</sup>	1.085
Final R indexes [I ≥ 2σ (I)]	R <sub>1</sub> = 0.0544, wR <sub>2</sub> = 0.1638
Final R indexes [all data]	R <sub>1</sub> = 0.0638, wR <sub>2</sub> = 0.1752

## 7. NMR Spectra

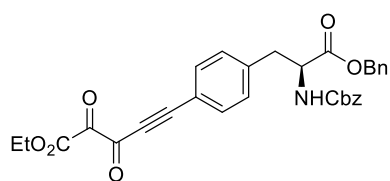
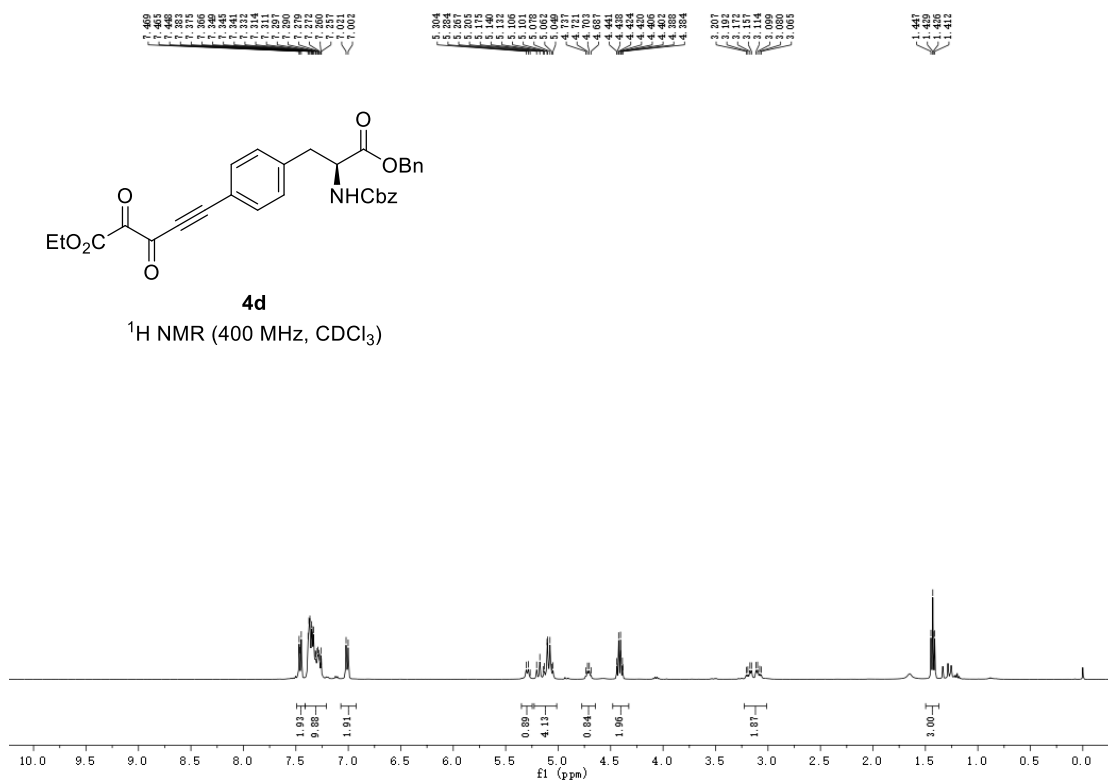






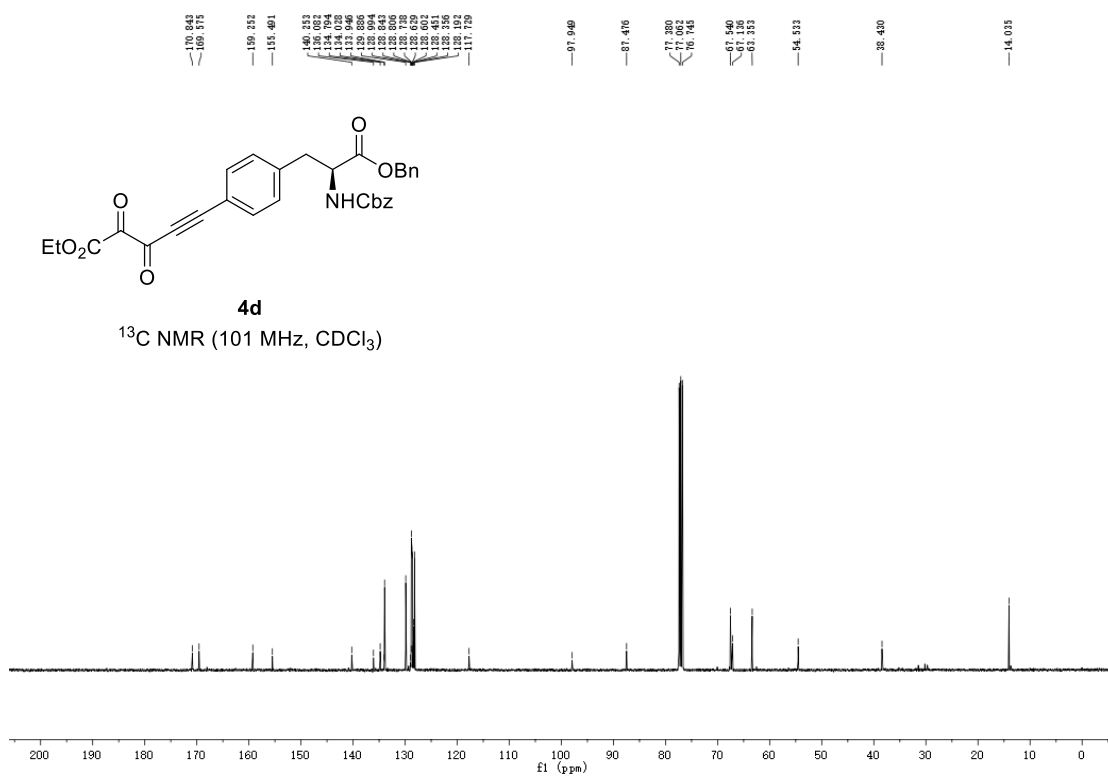
**4d**

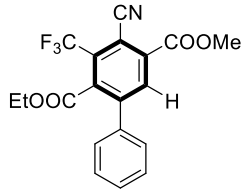
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)



**4d**

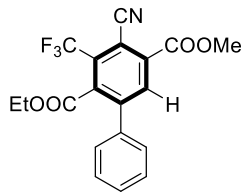
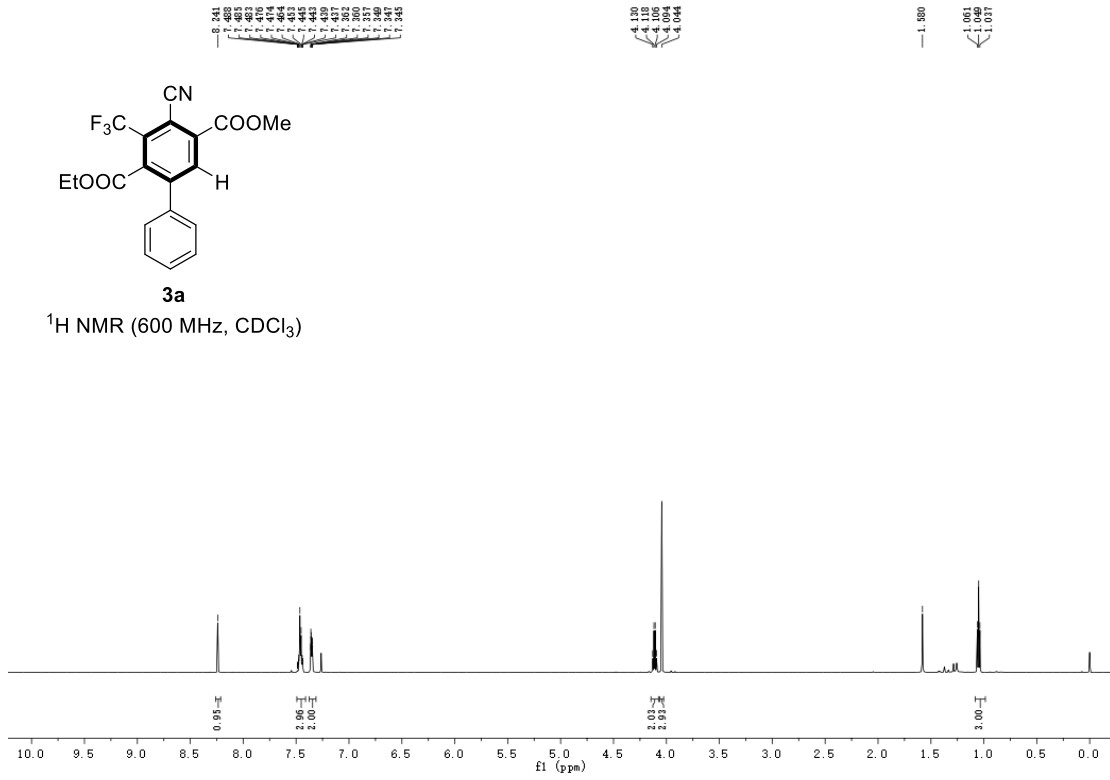
<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)





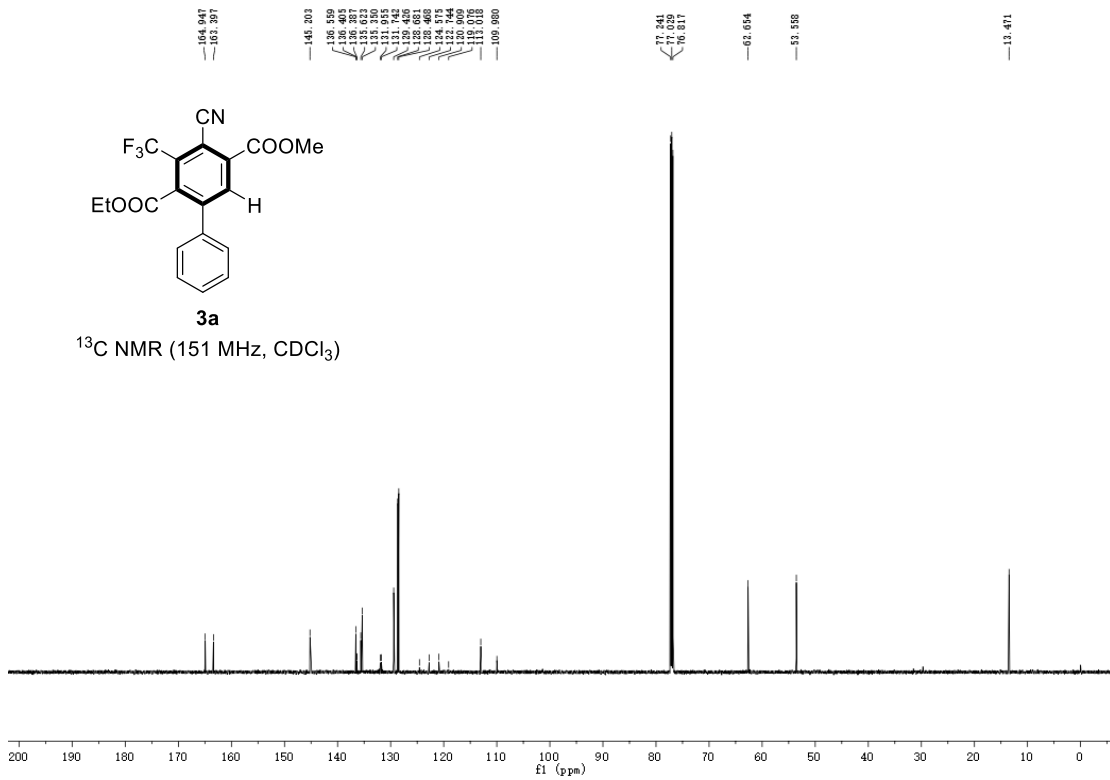
**3a**

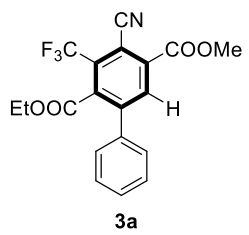
$^1\text{H NMR}$  (600 MHz,  $\text{CDCl}_3$ )



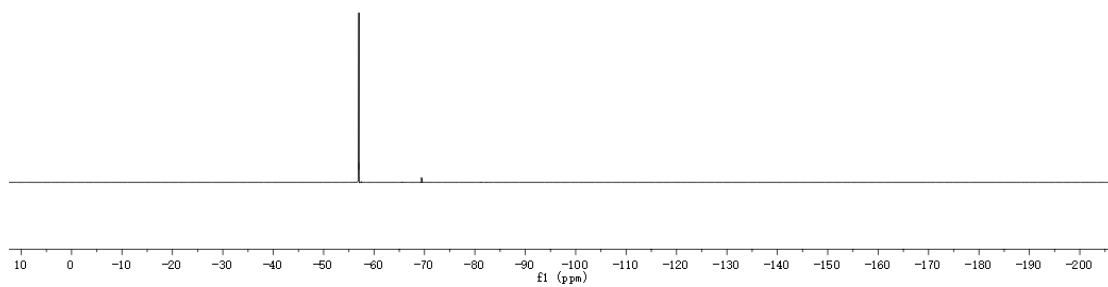
**3a**

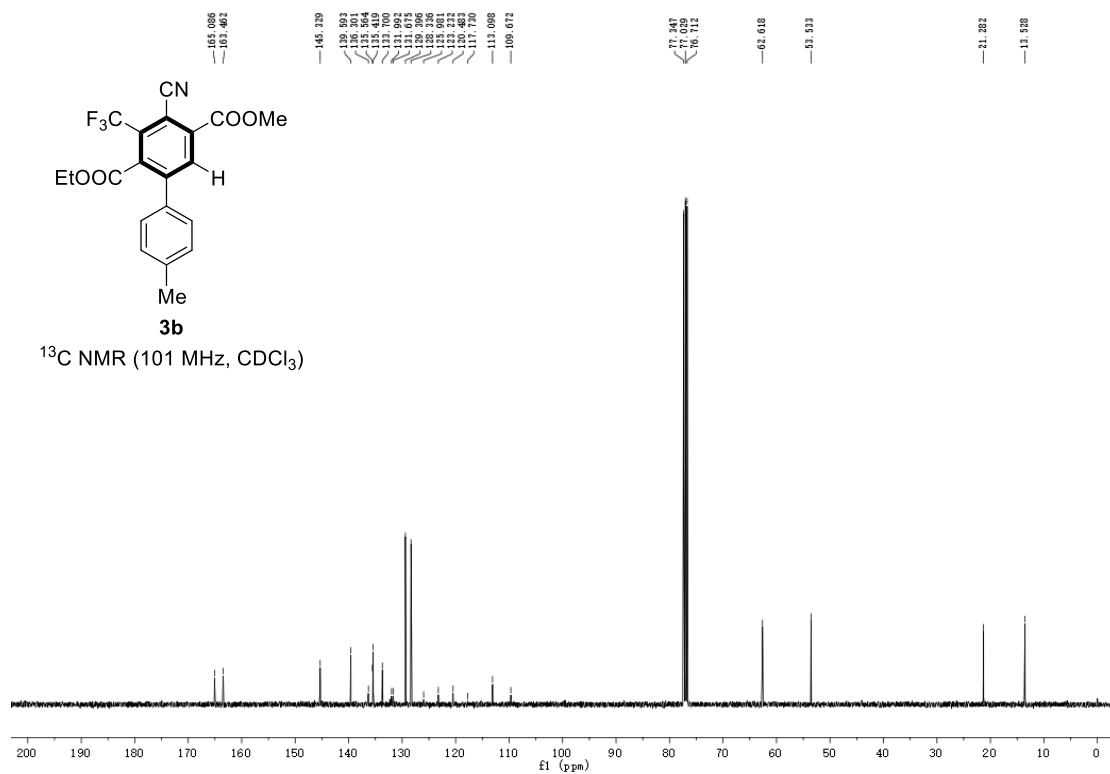
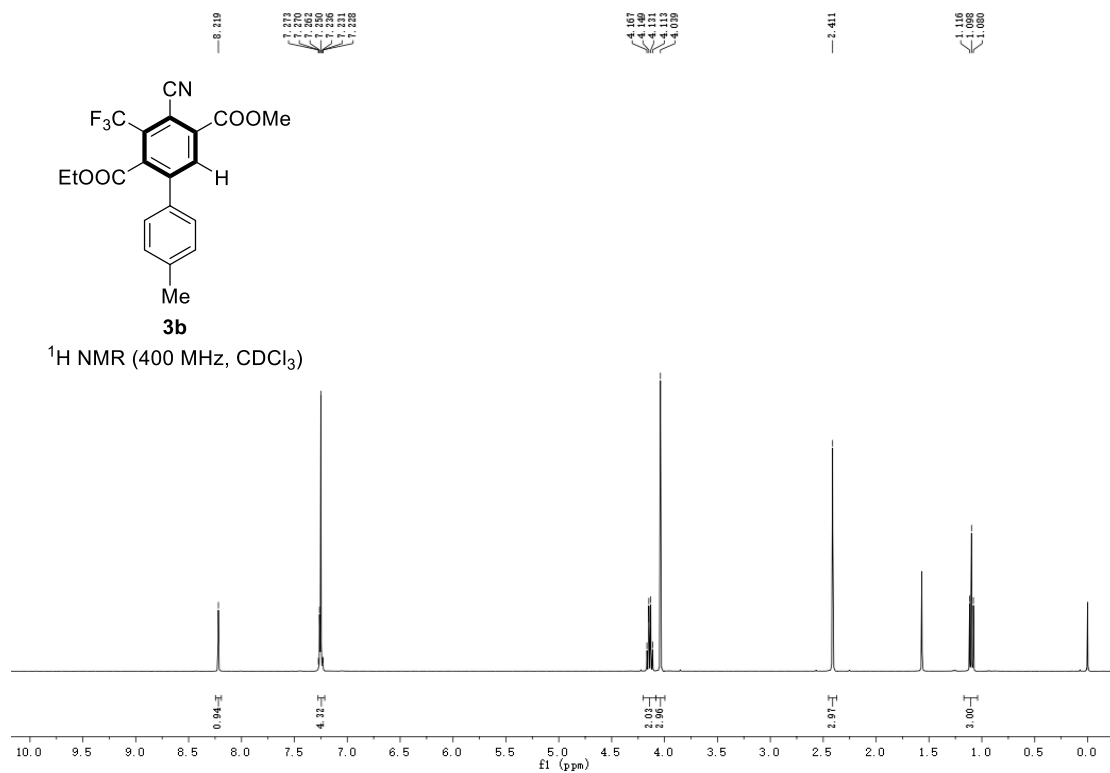
$^{13}\text{C NMR}$  (151 MHz,  $\text{CDCl}_3$ )

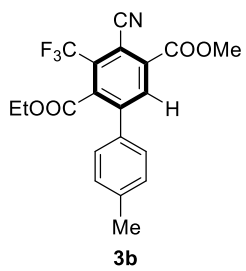




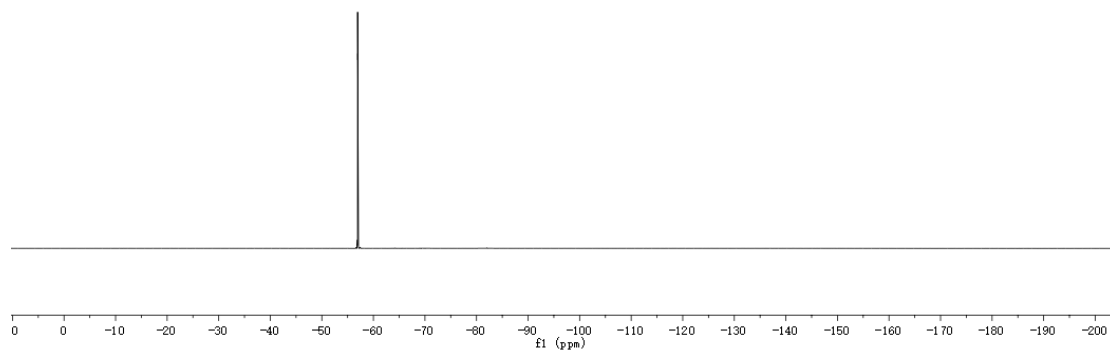
$^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )

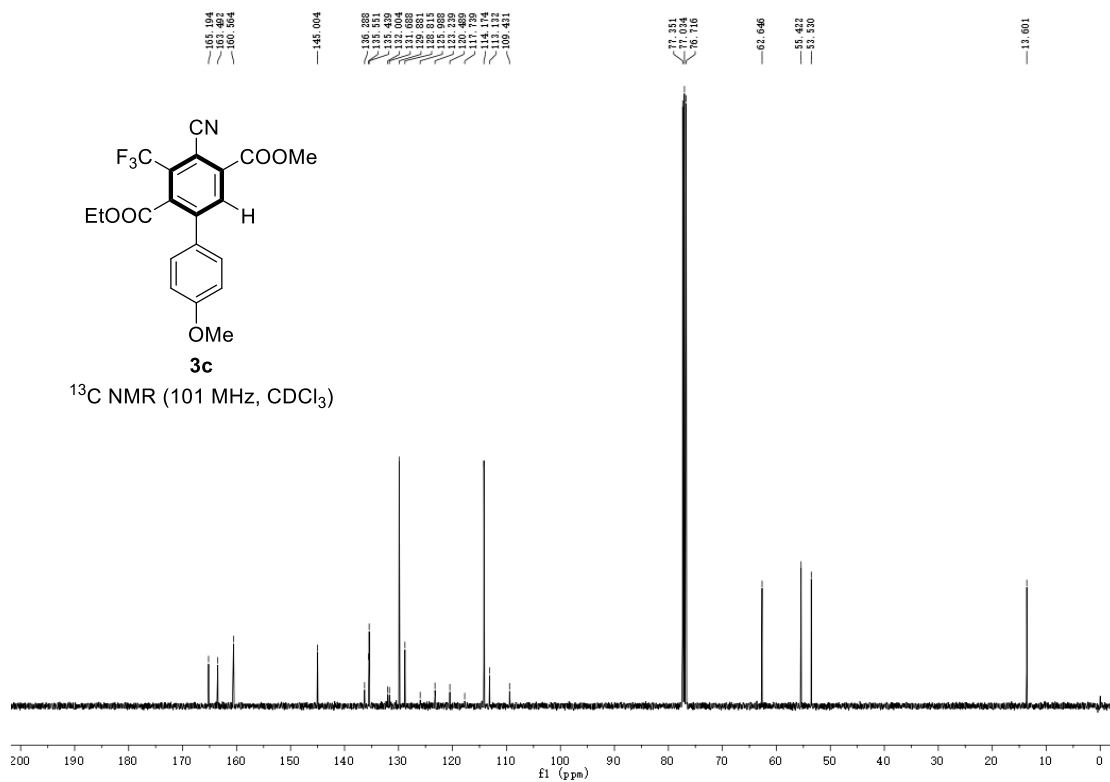
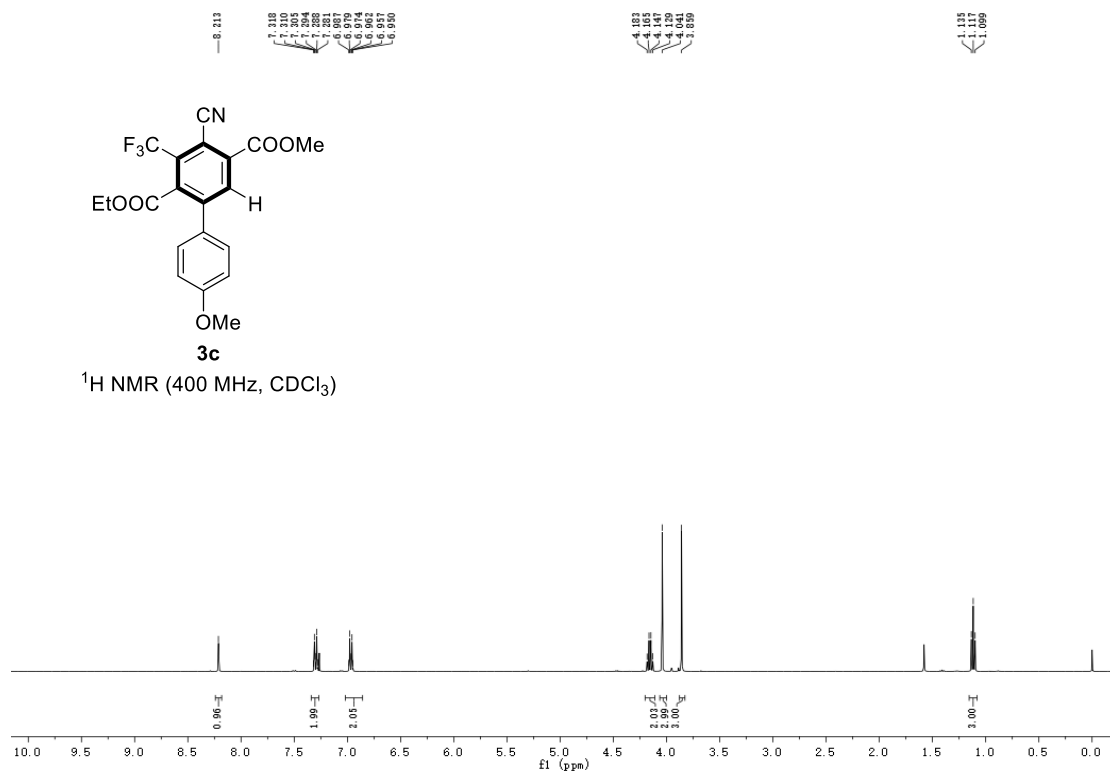


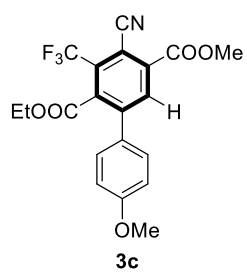




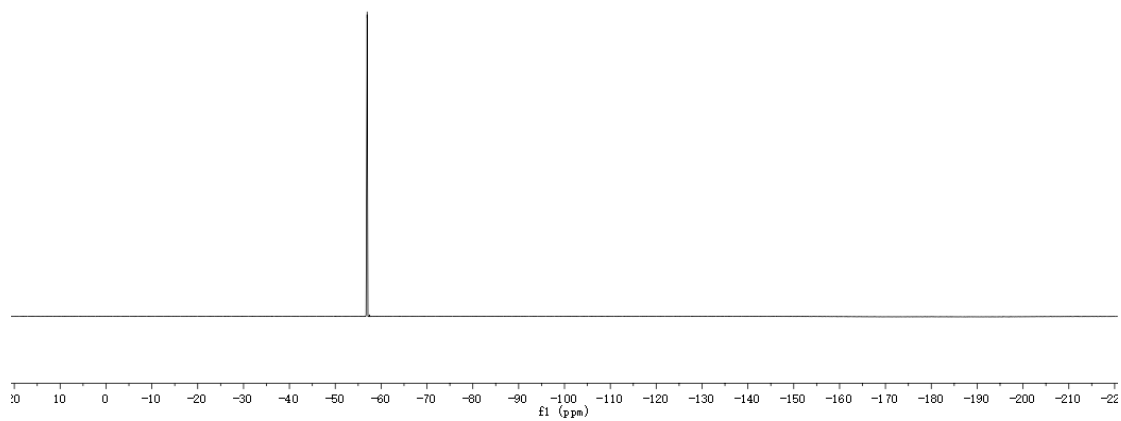
$^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )

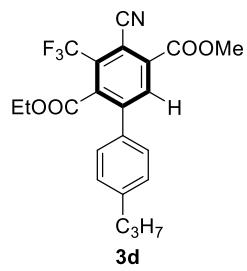




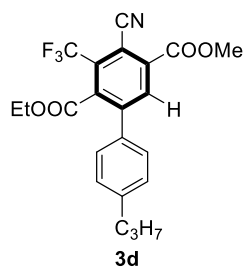
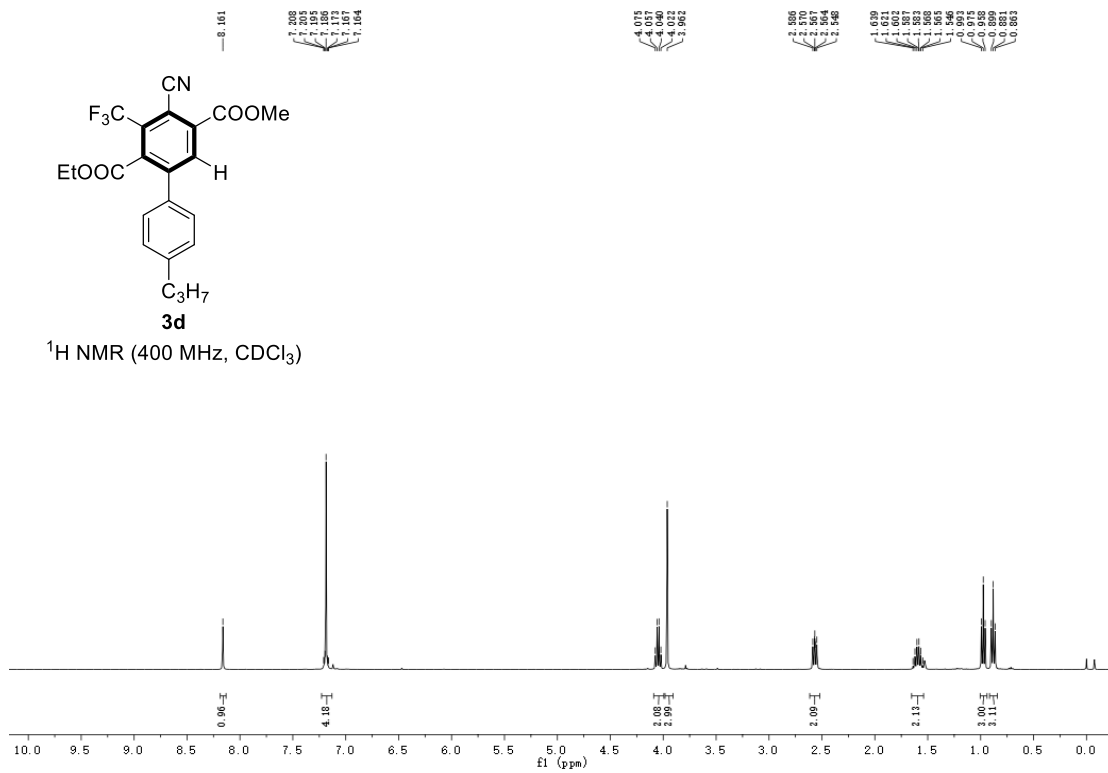


$^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )

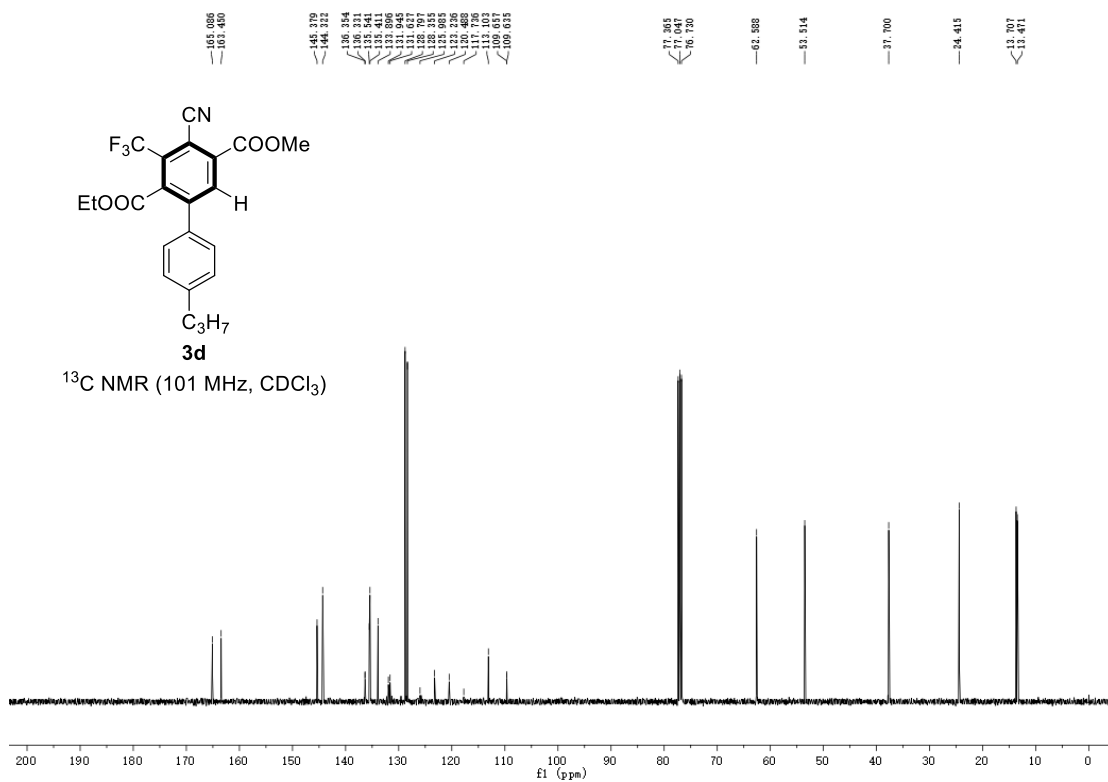




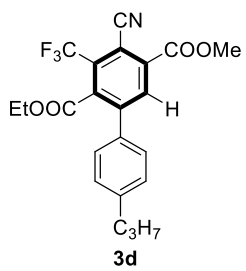
$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )



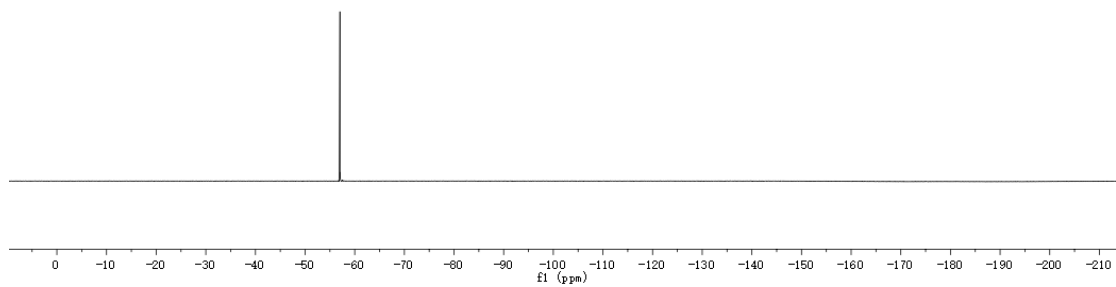
$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )

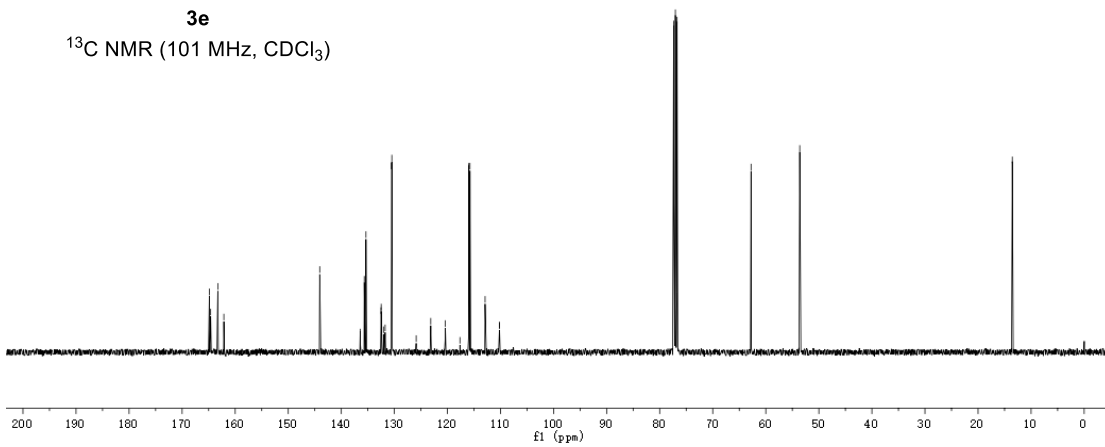
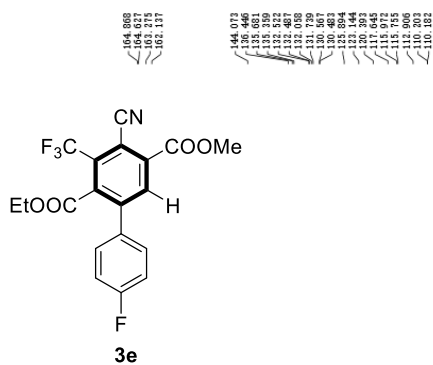
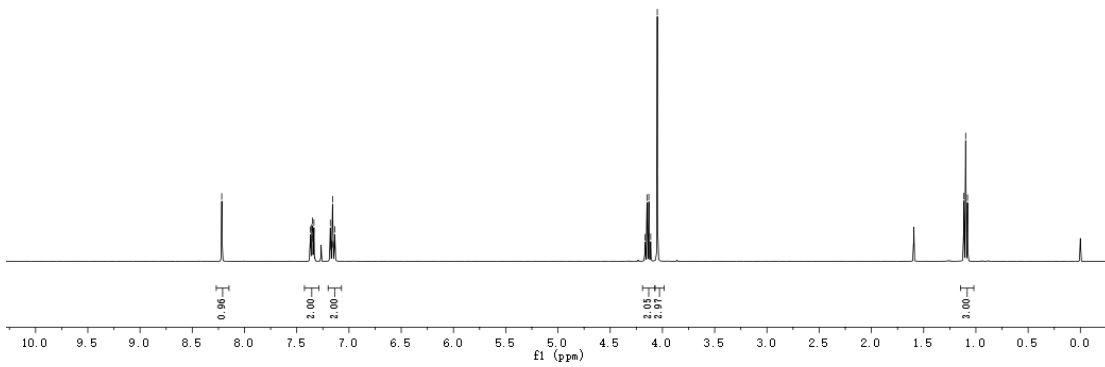
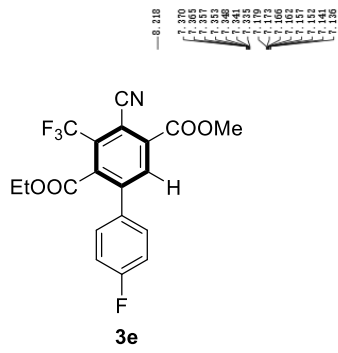


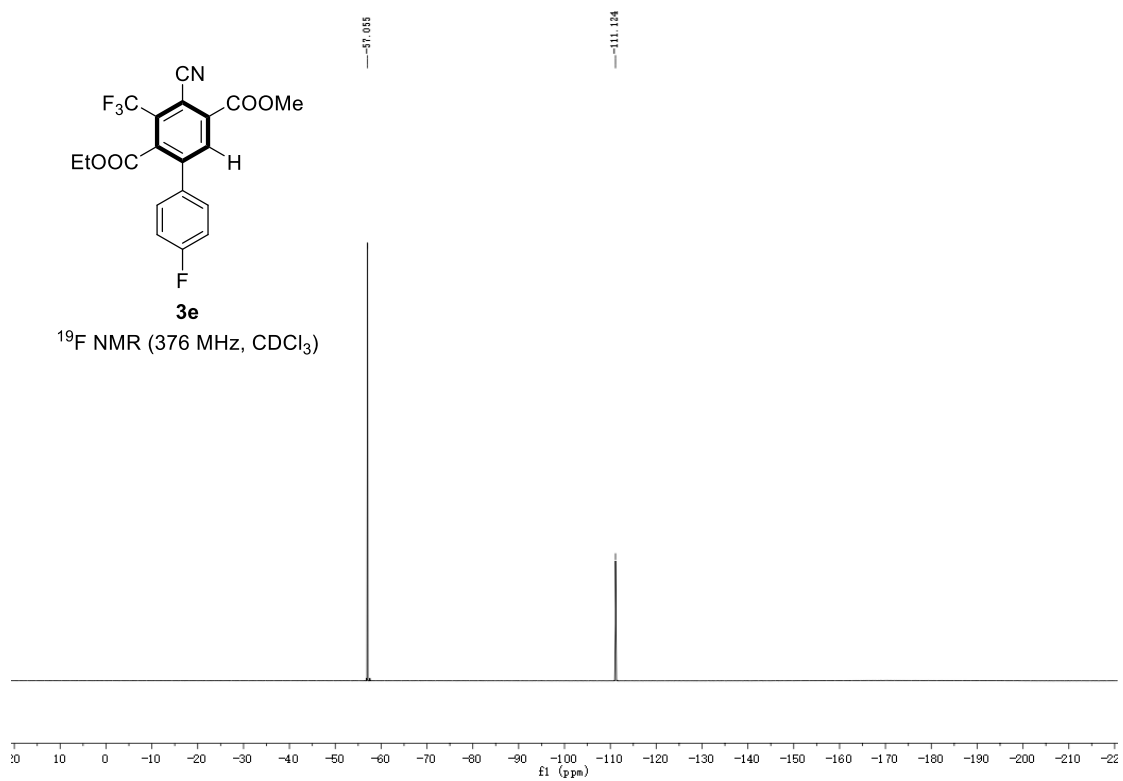


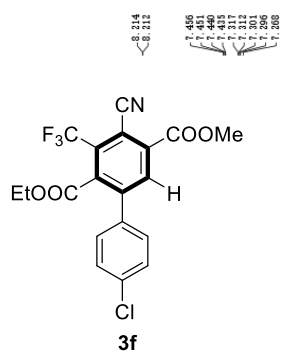


$^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )

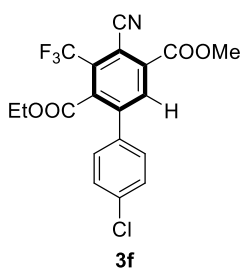
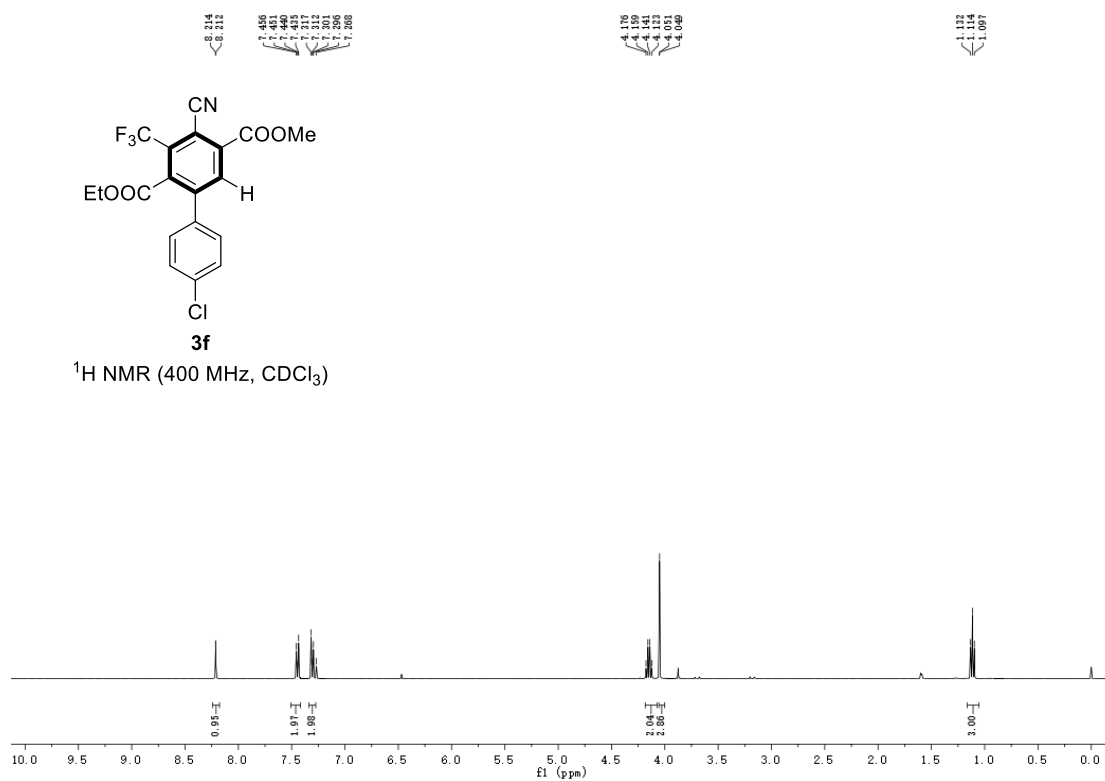




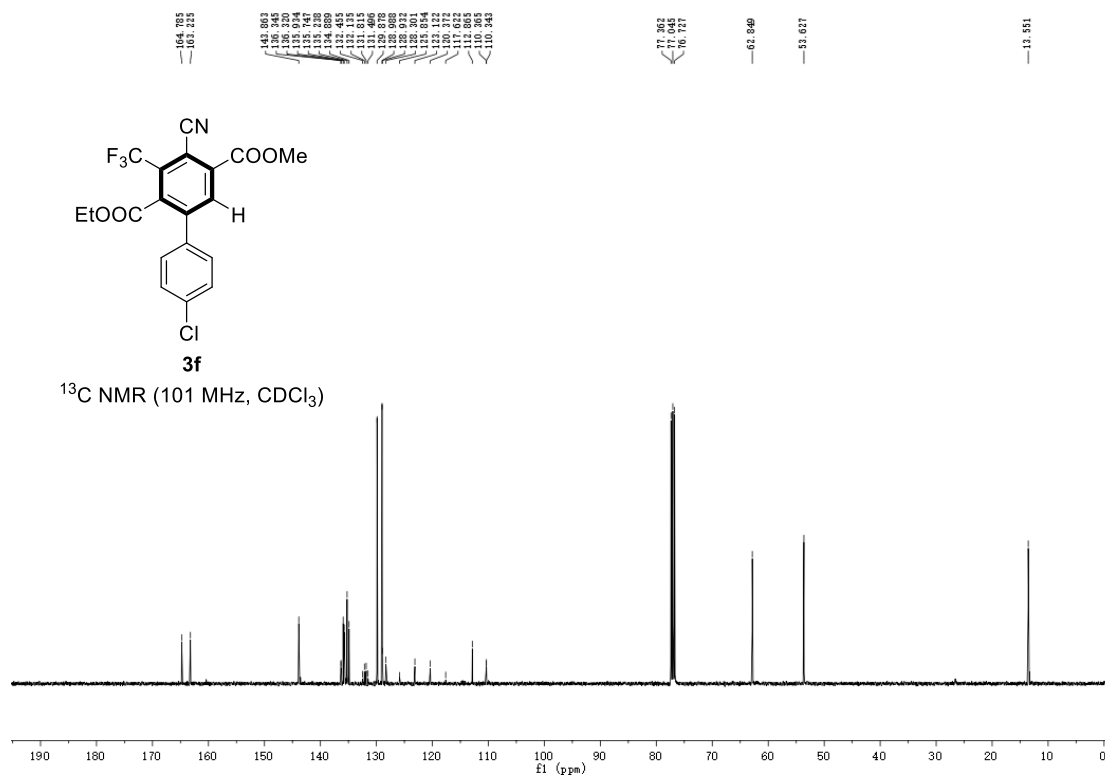


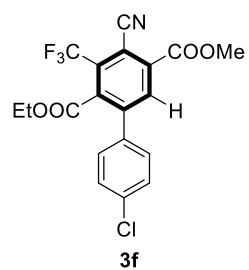


$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )

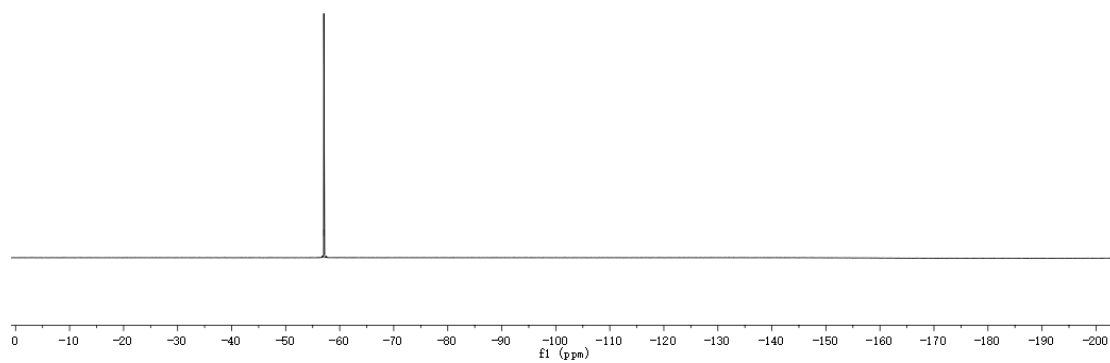


$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )

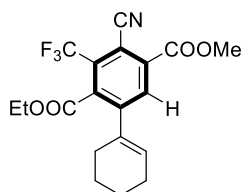




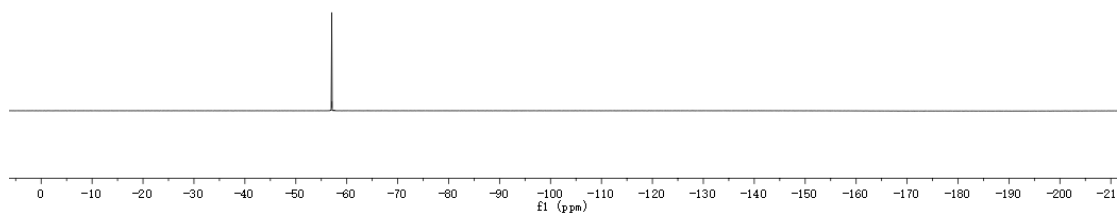
**3f**  
<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>)

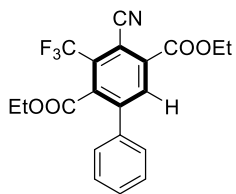






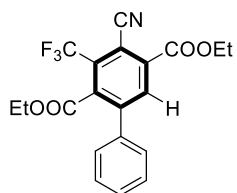
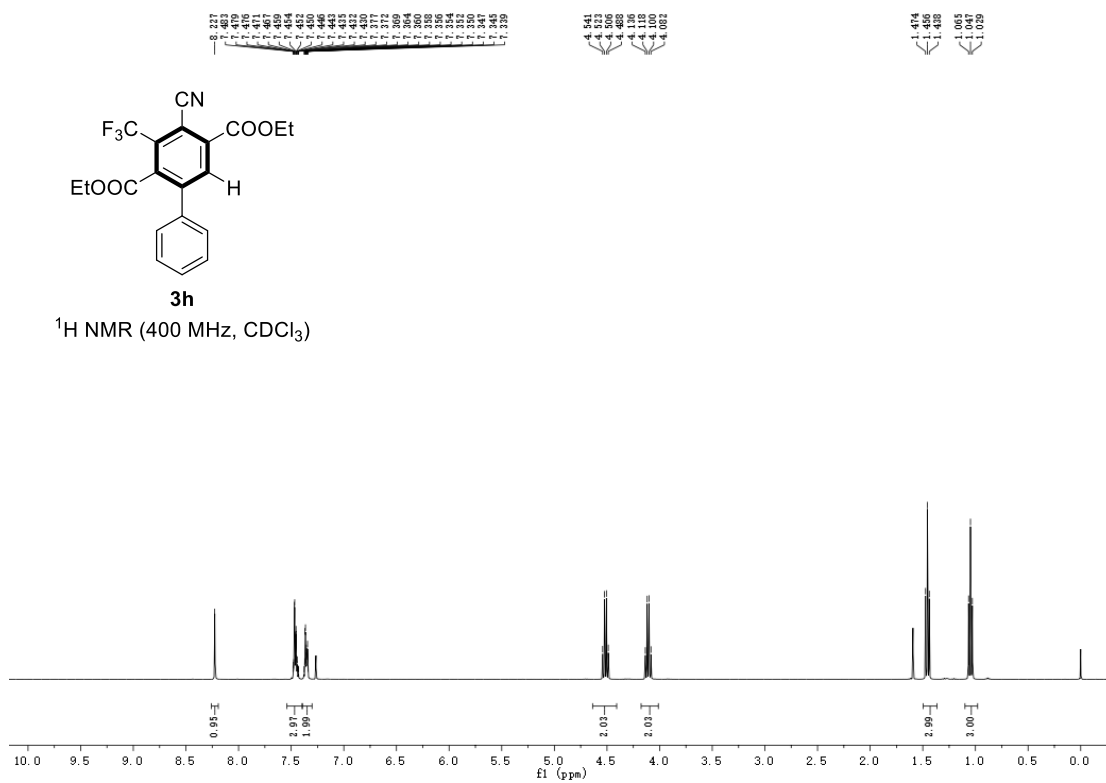
<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>)





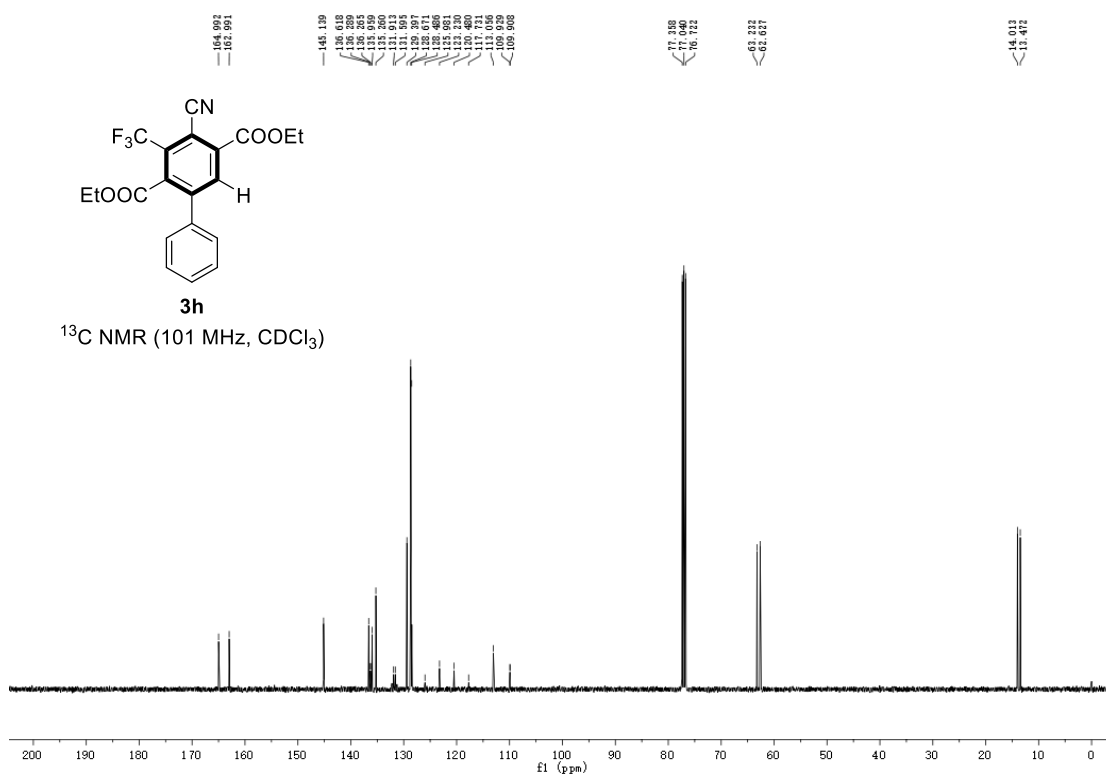
**3h**

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

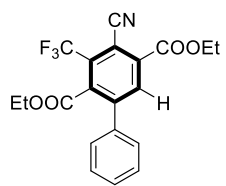


**3h**

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)

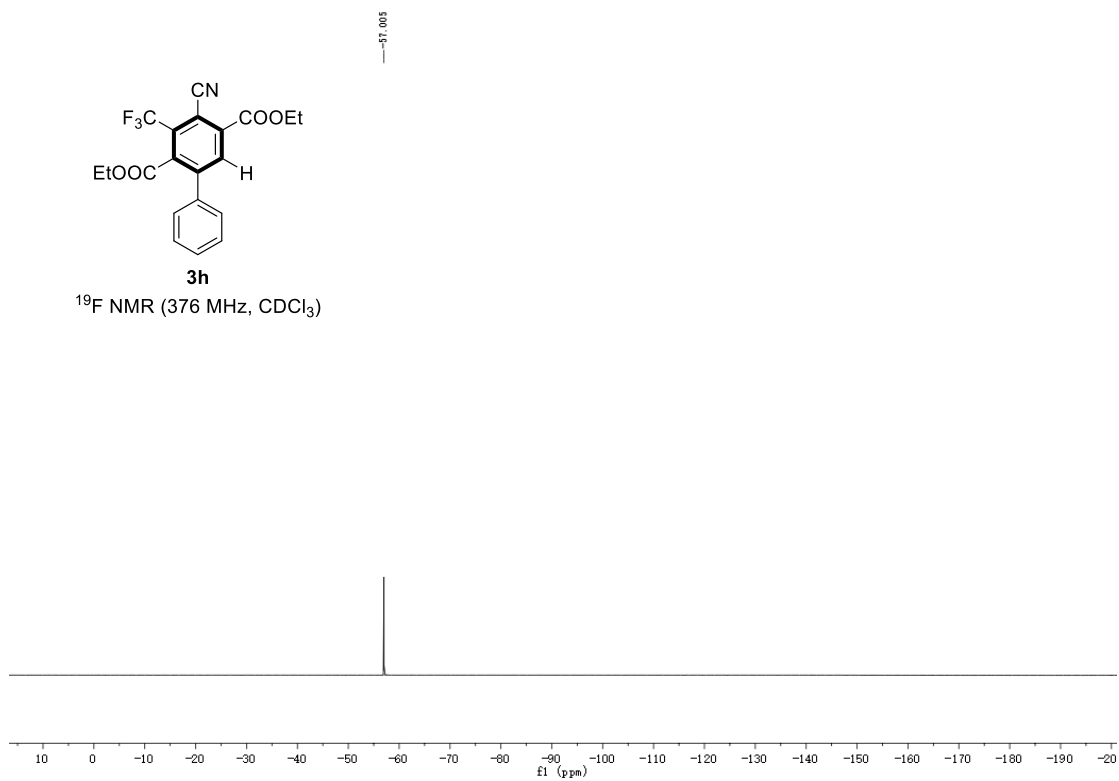


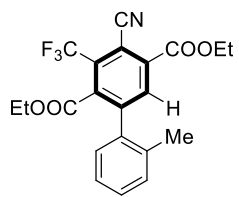




**3h**

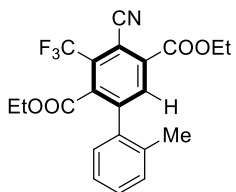
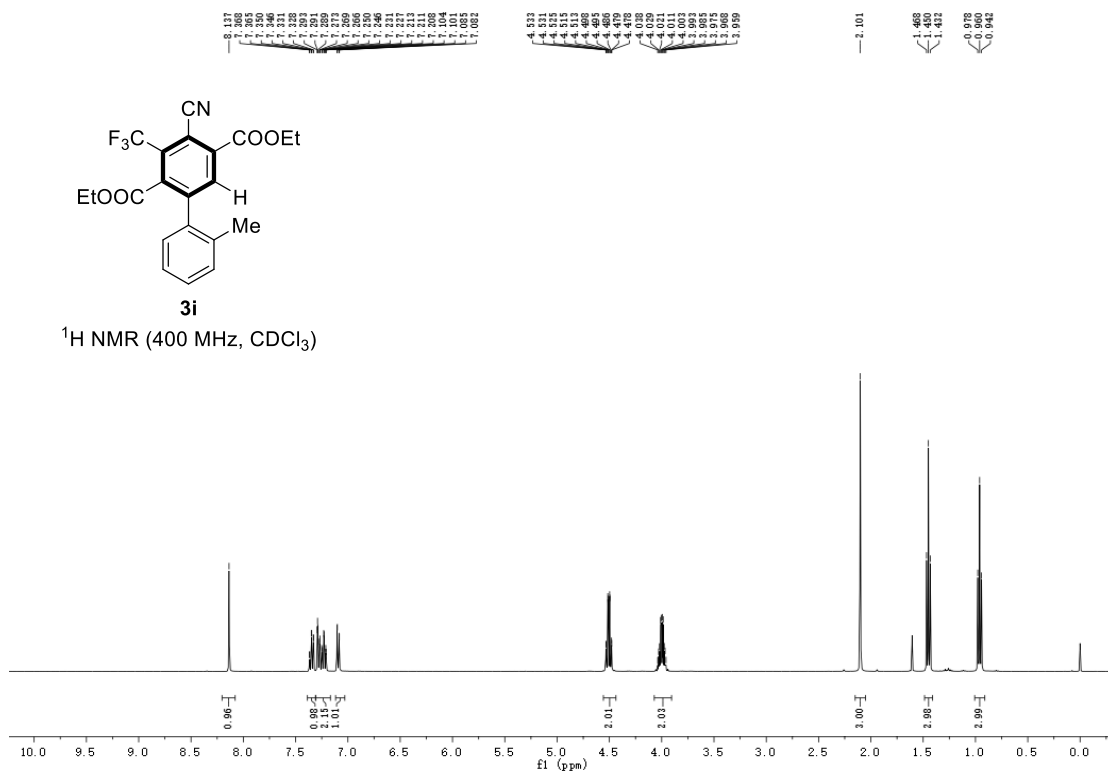
<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>)





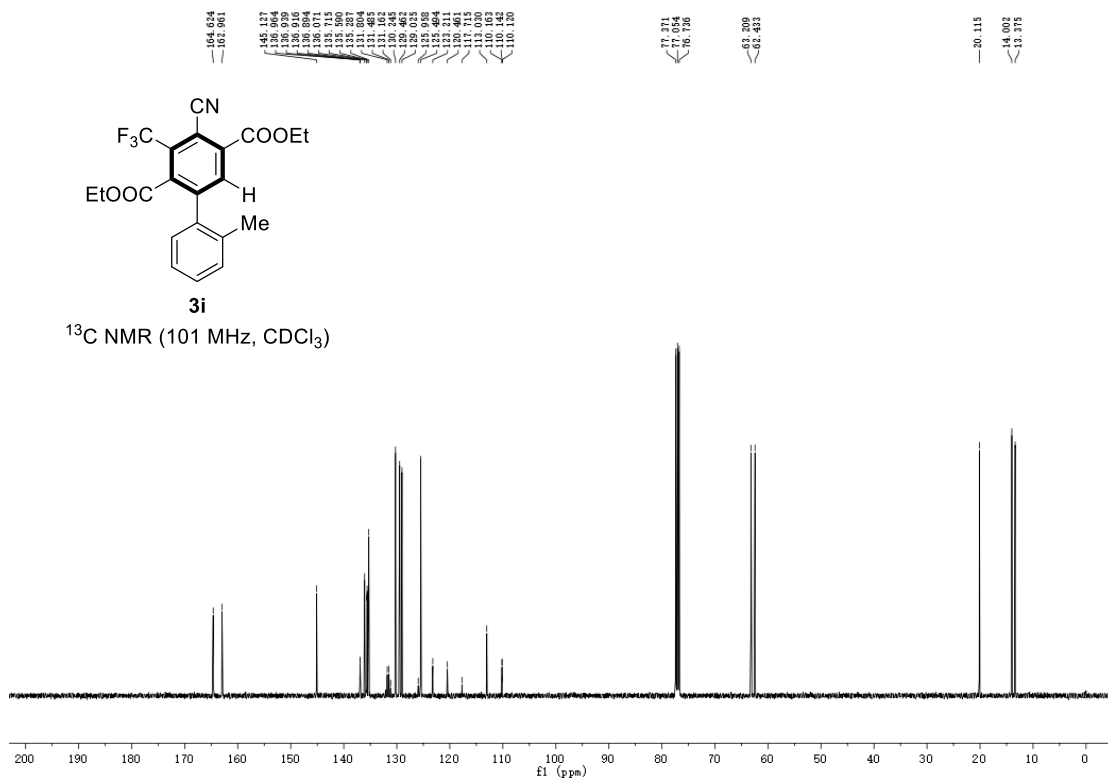
**3i**

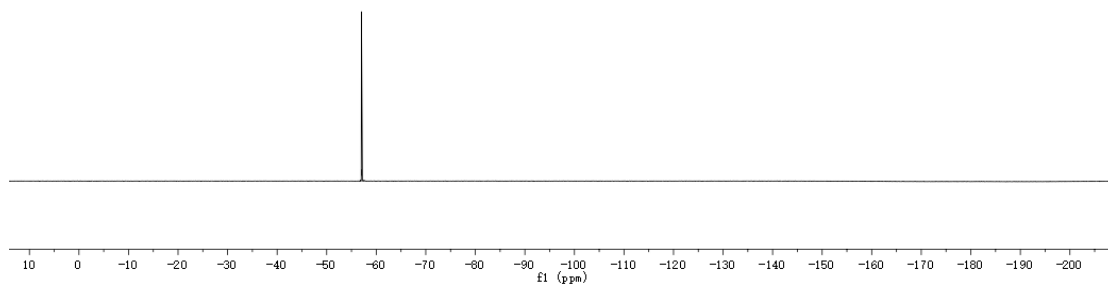
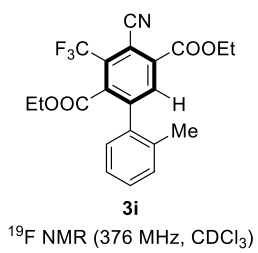
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

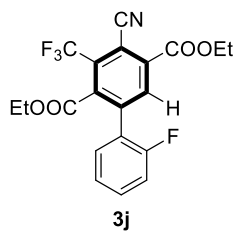


**3i**

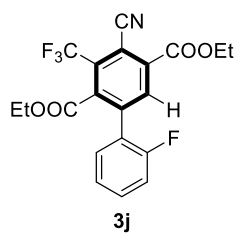
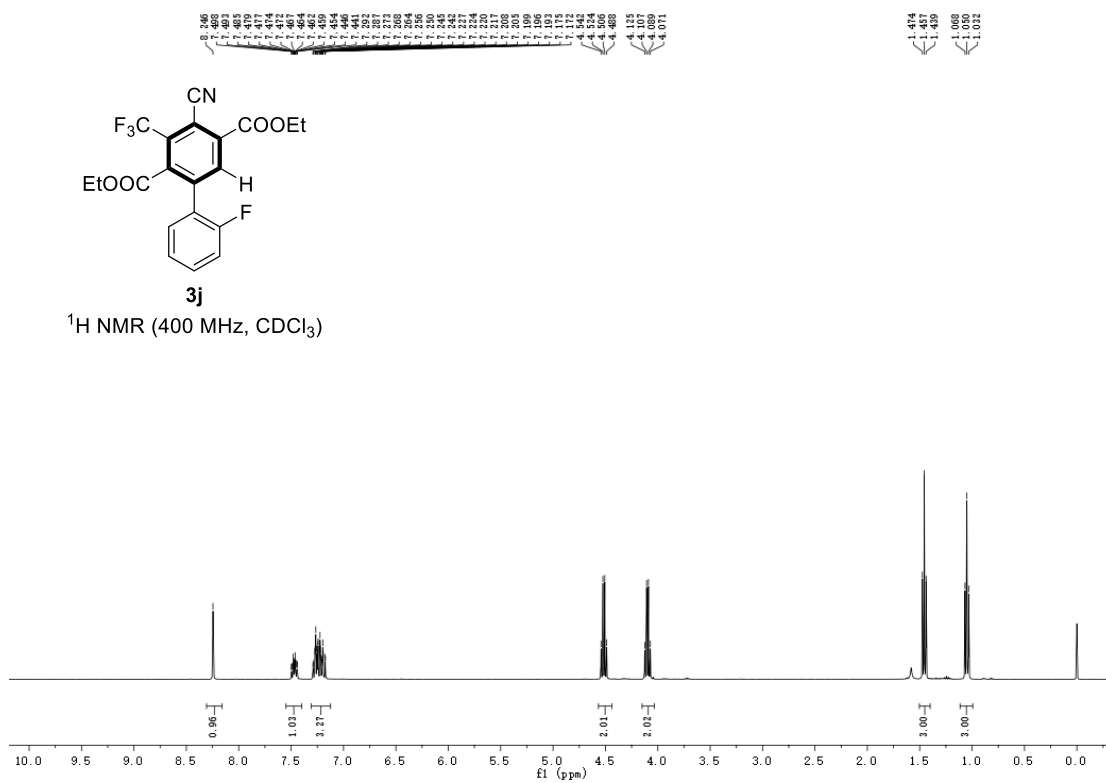
<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)



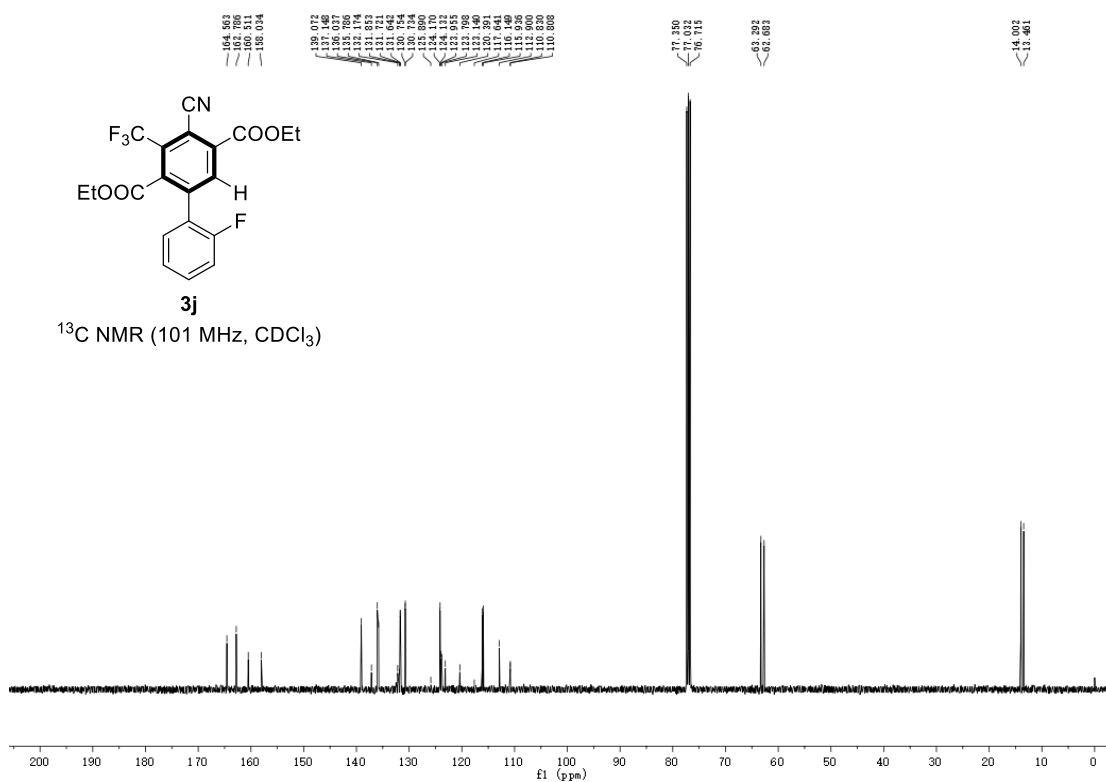


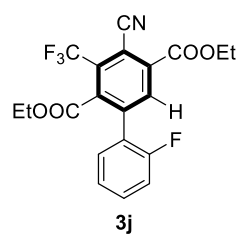


<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

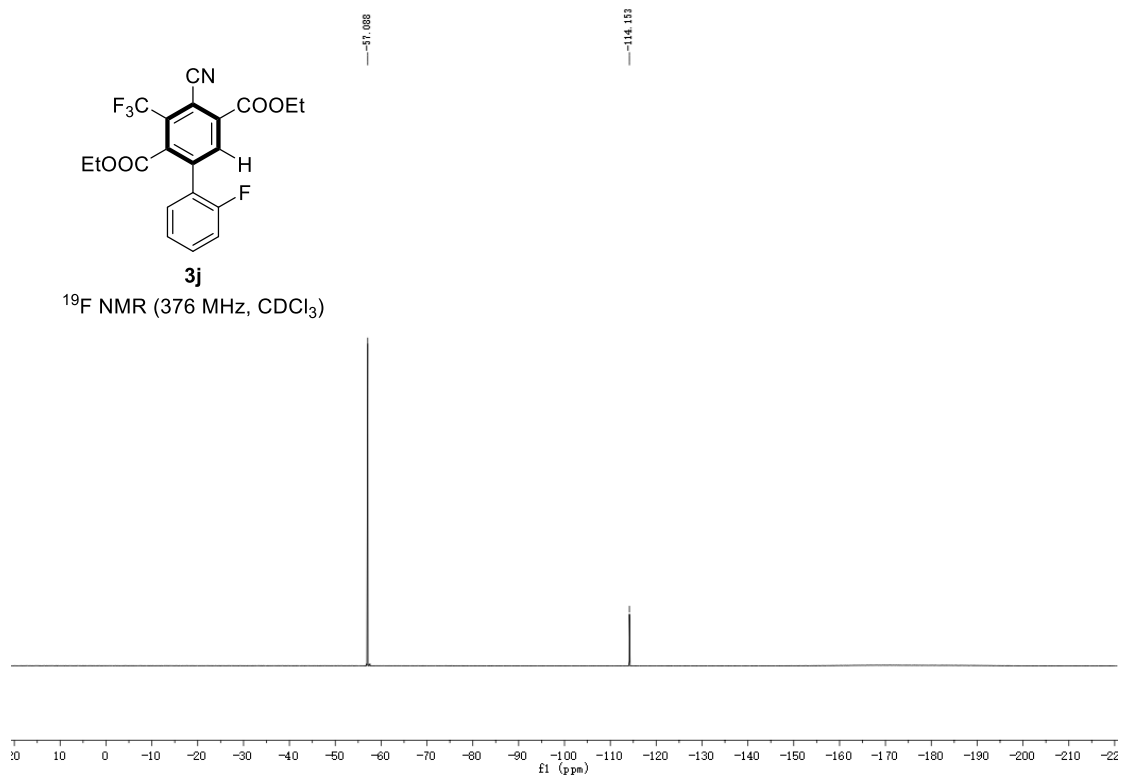


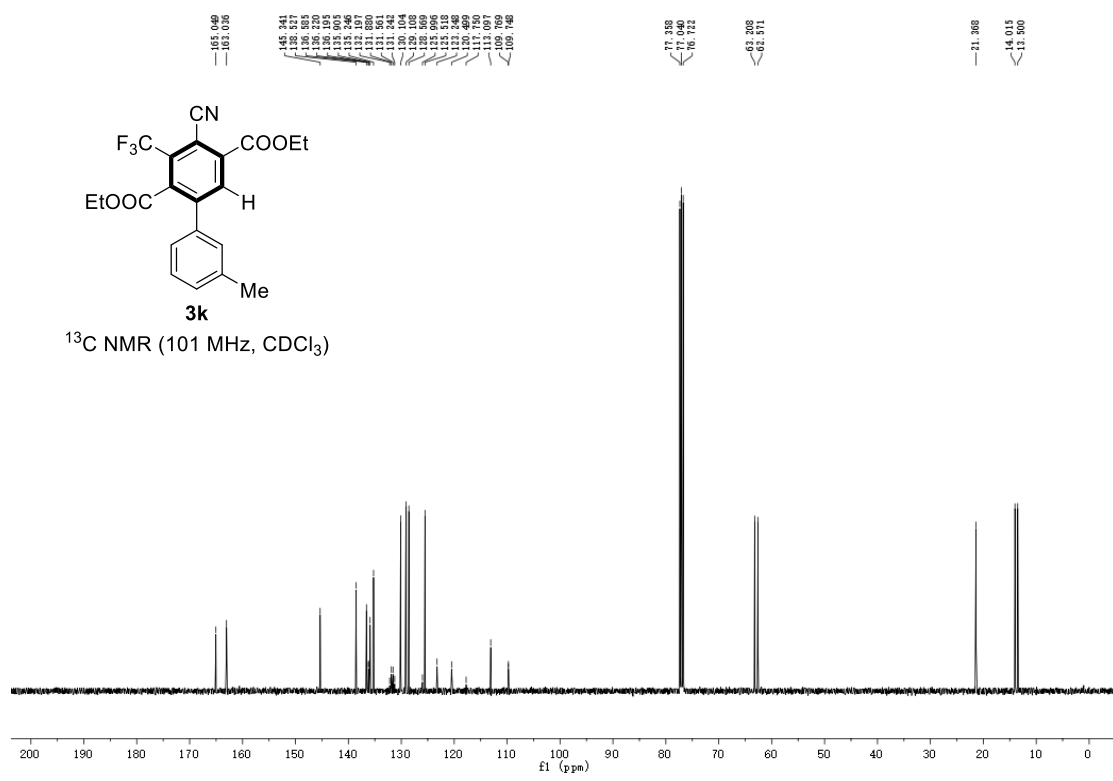
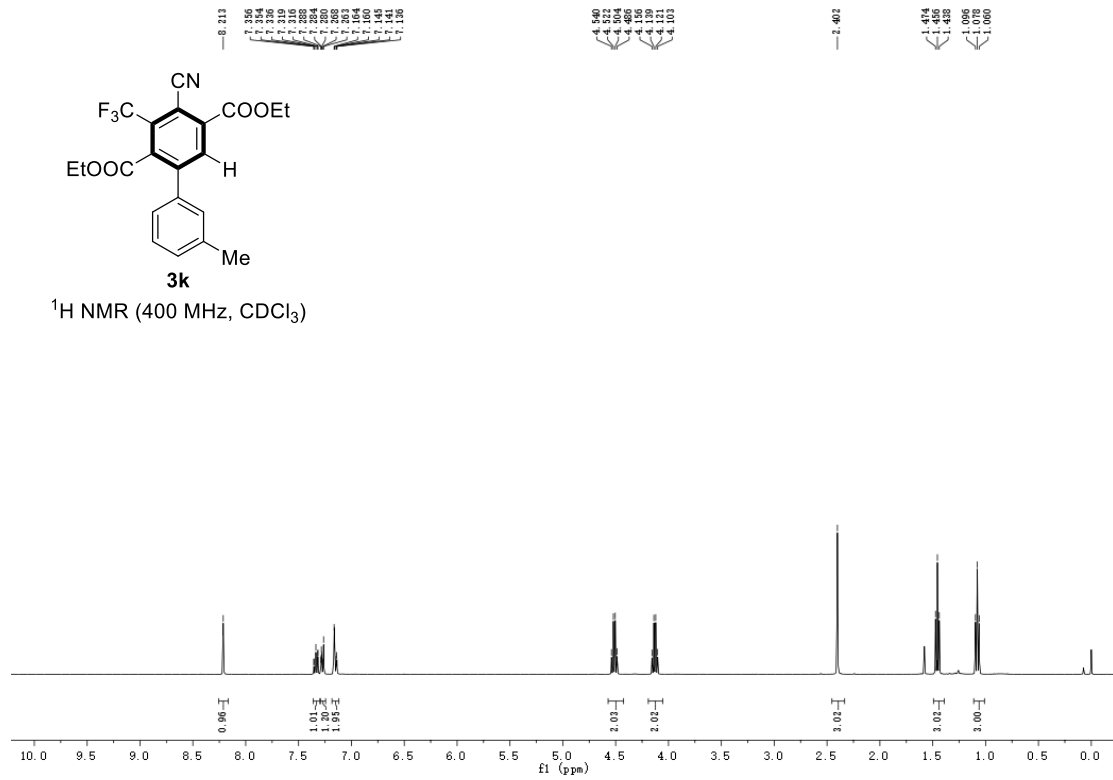
<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)

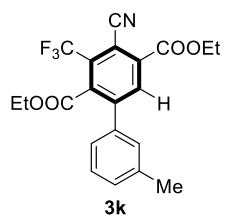




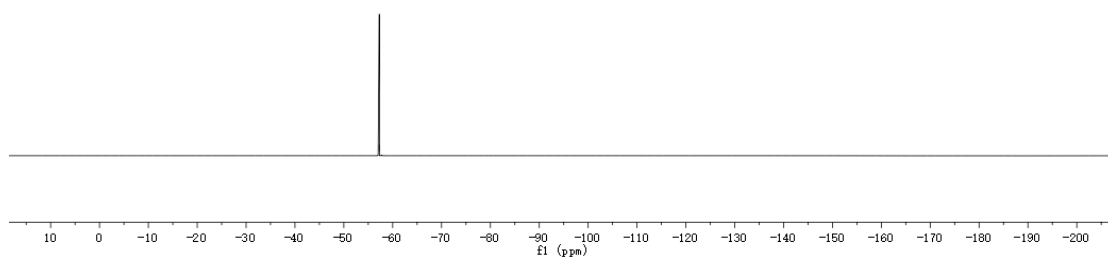
<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>)

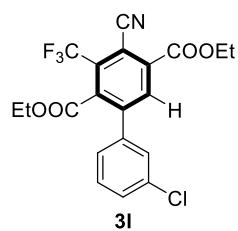




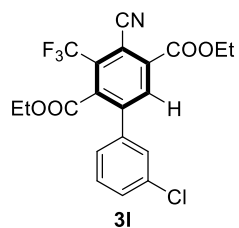
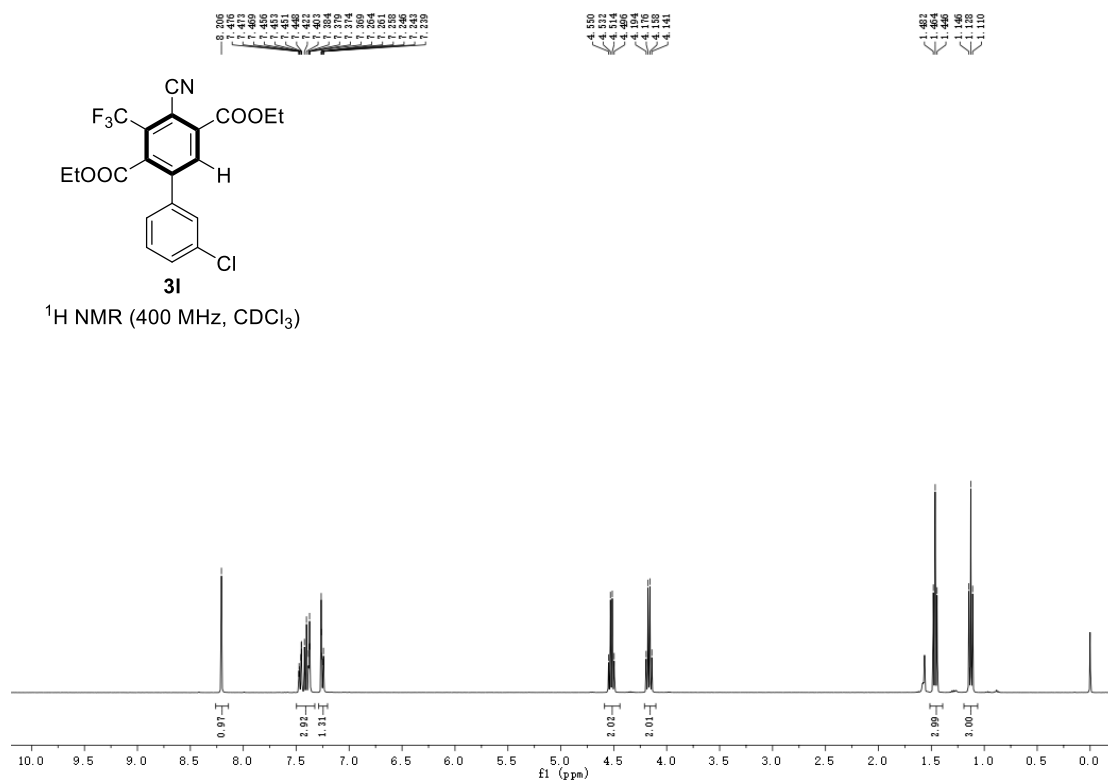


$^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )

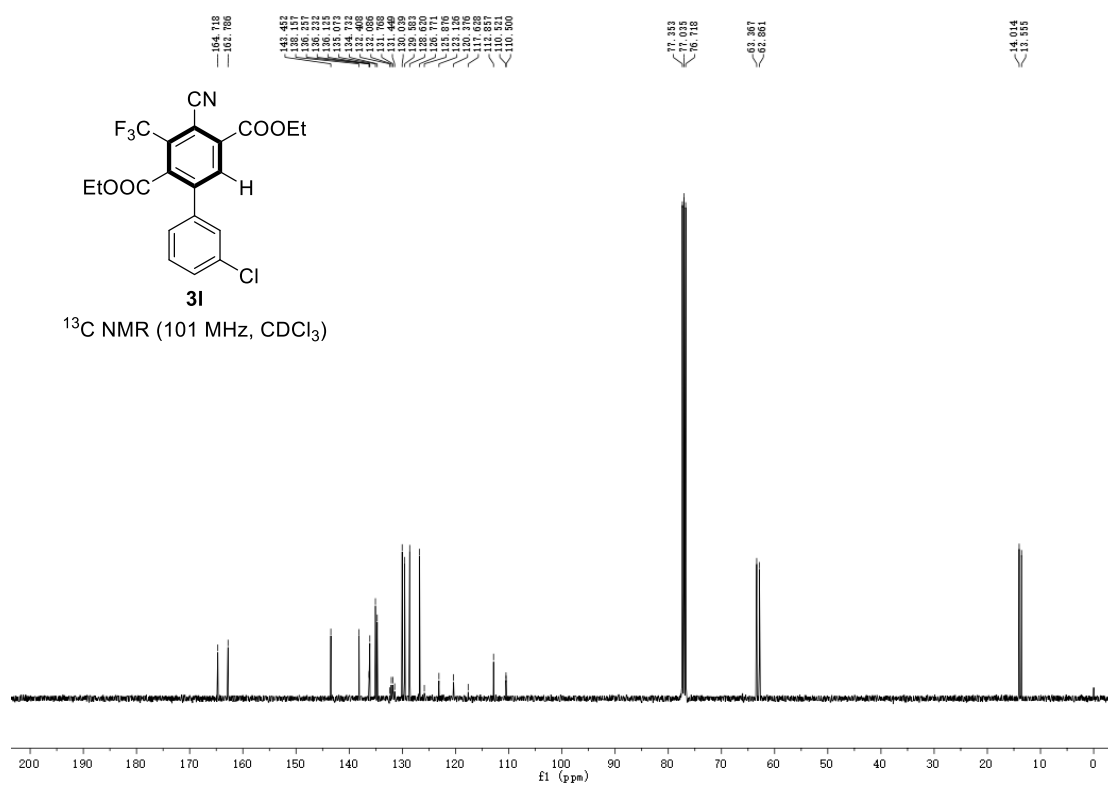




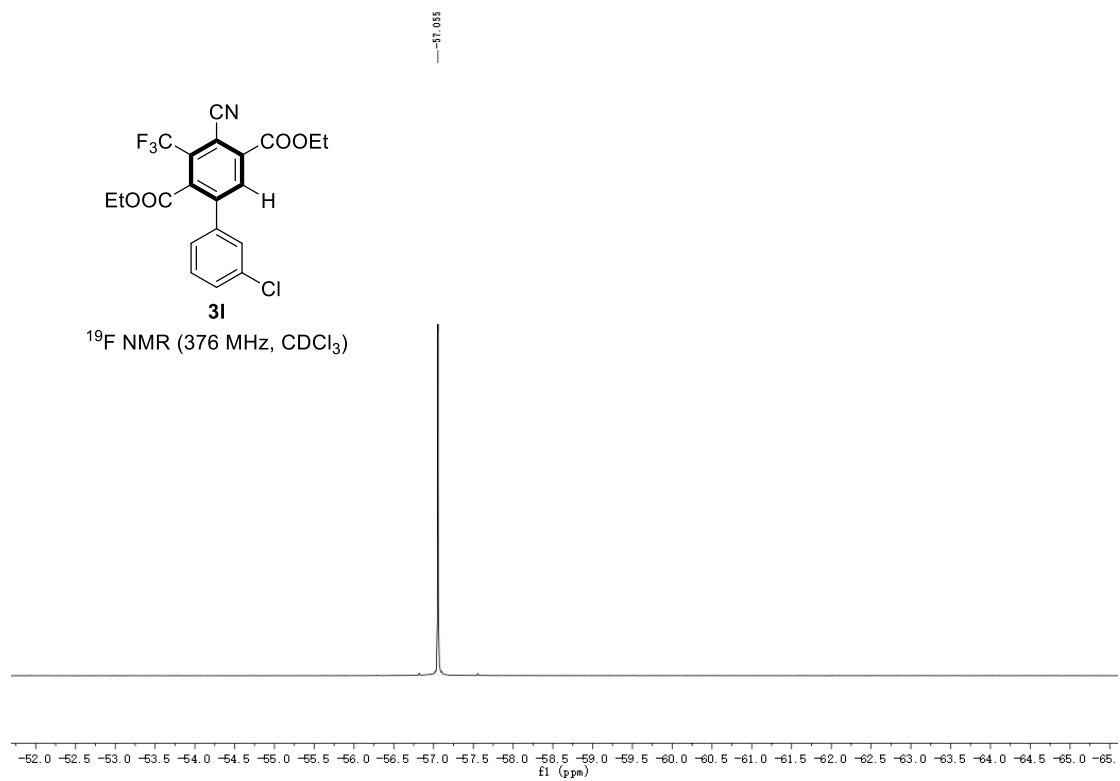
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

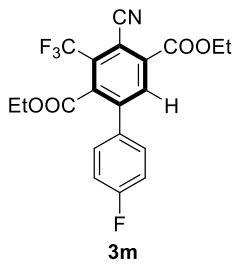


<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)

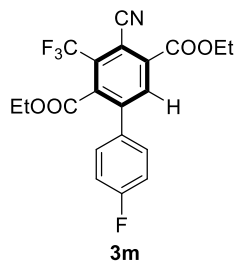
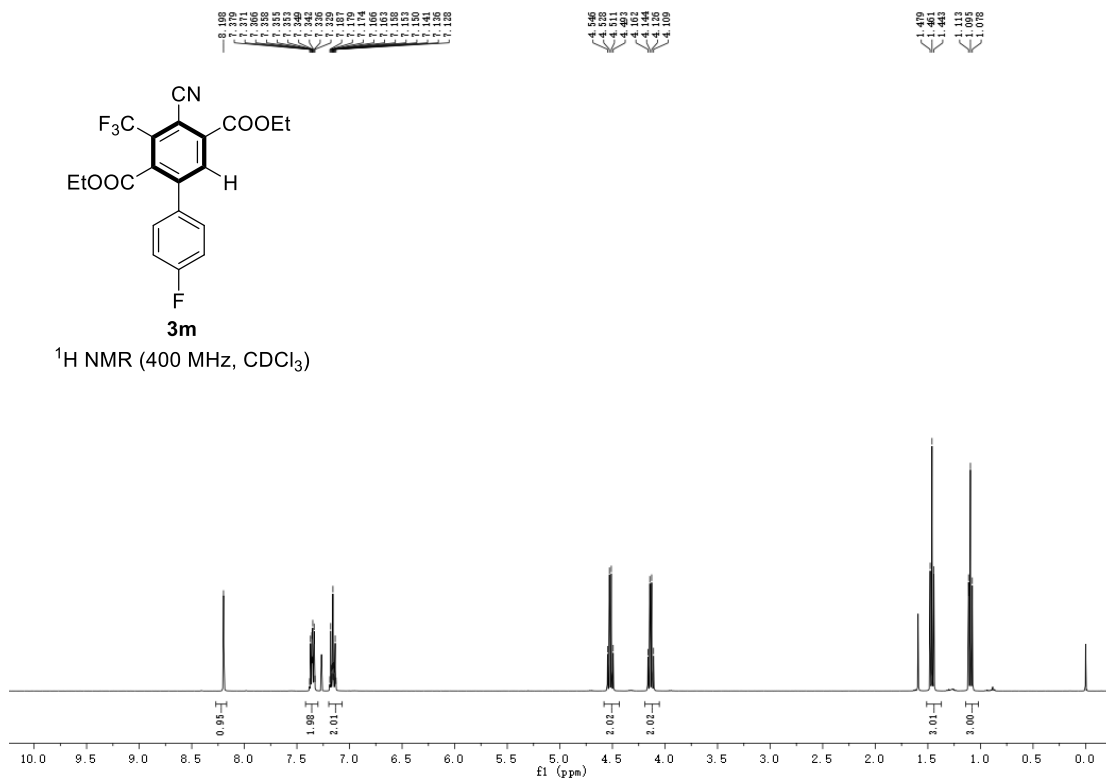




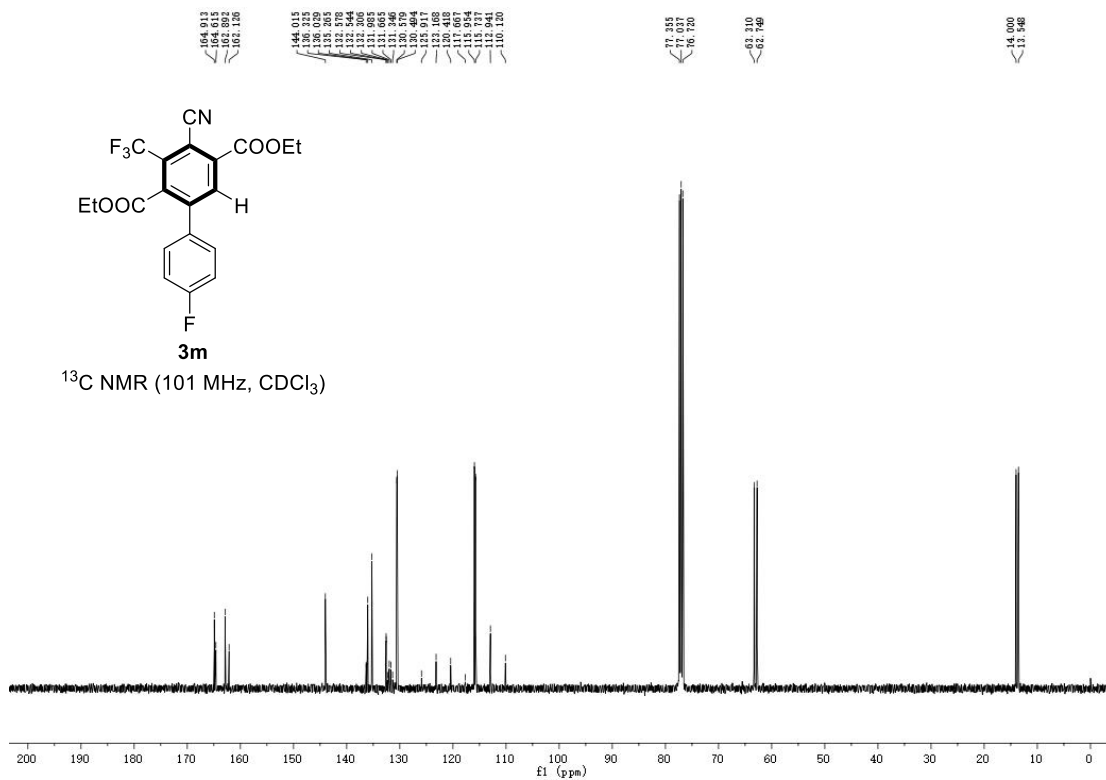


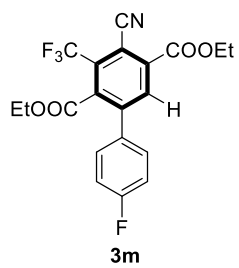


<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

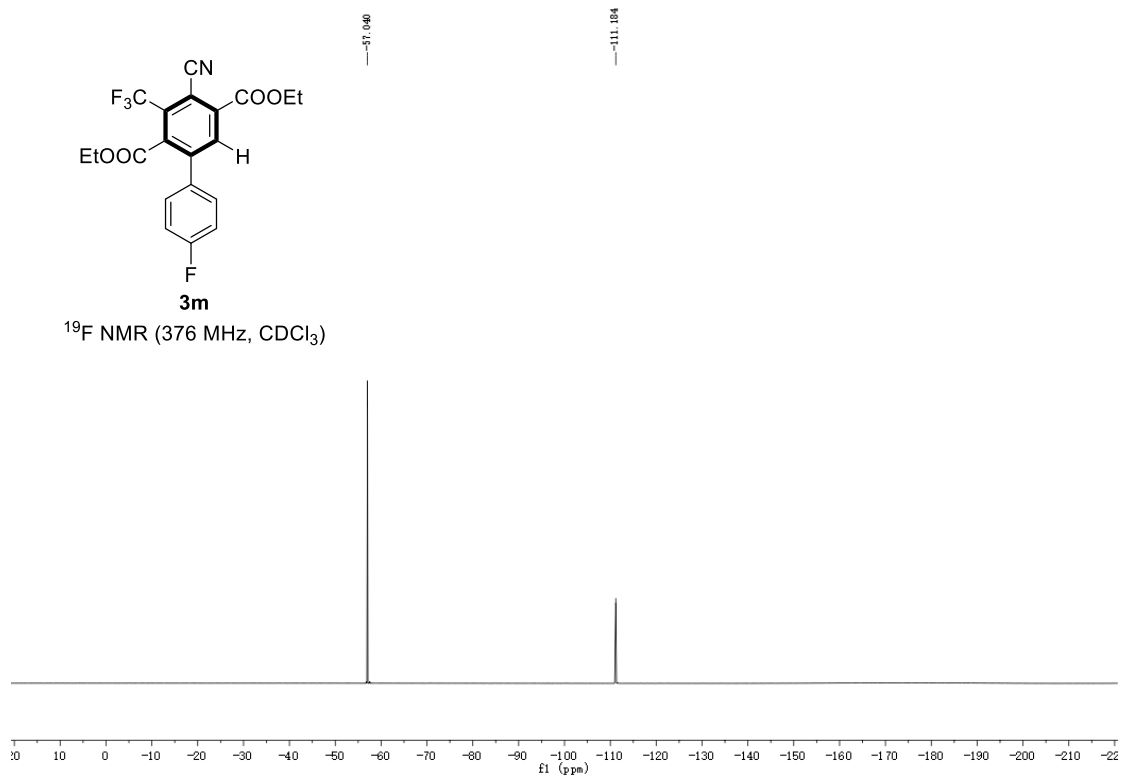


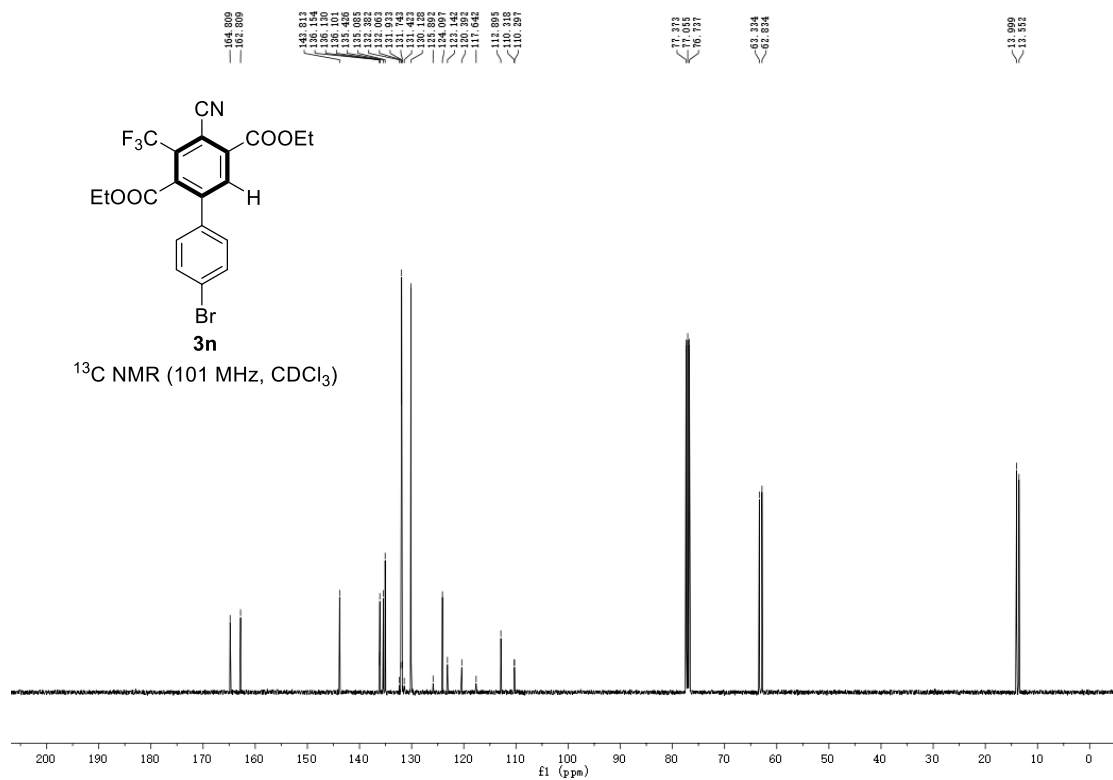
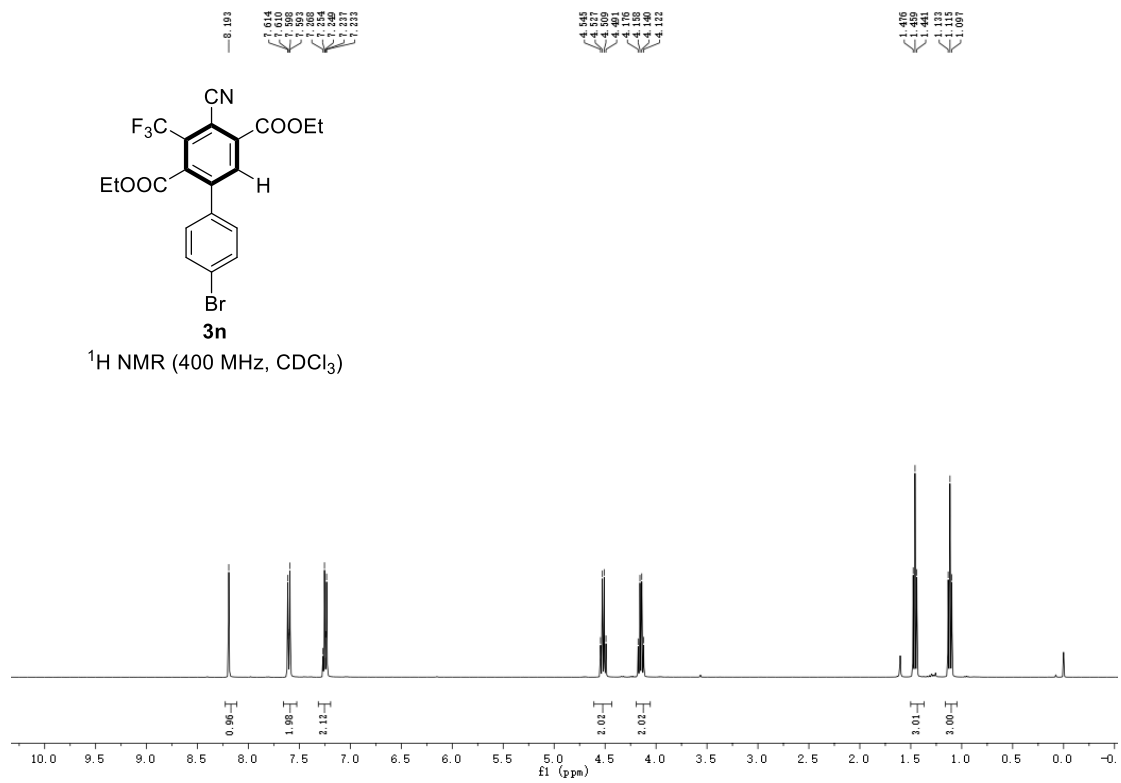
<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)

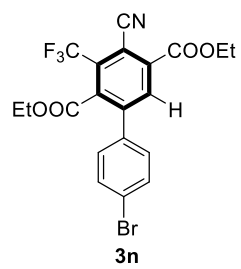




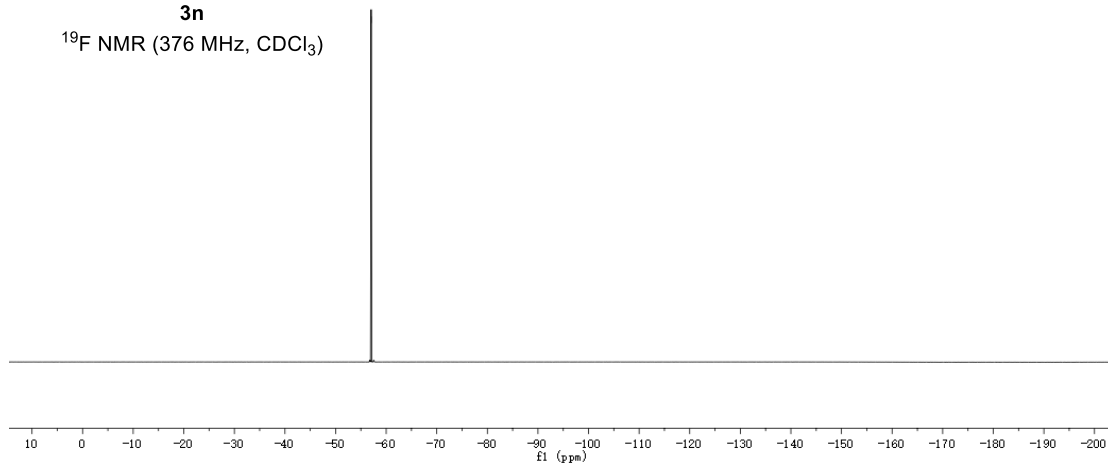
$^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )

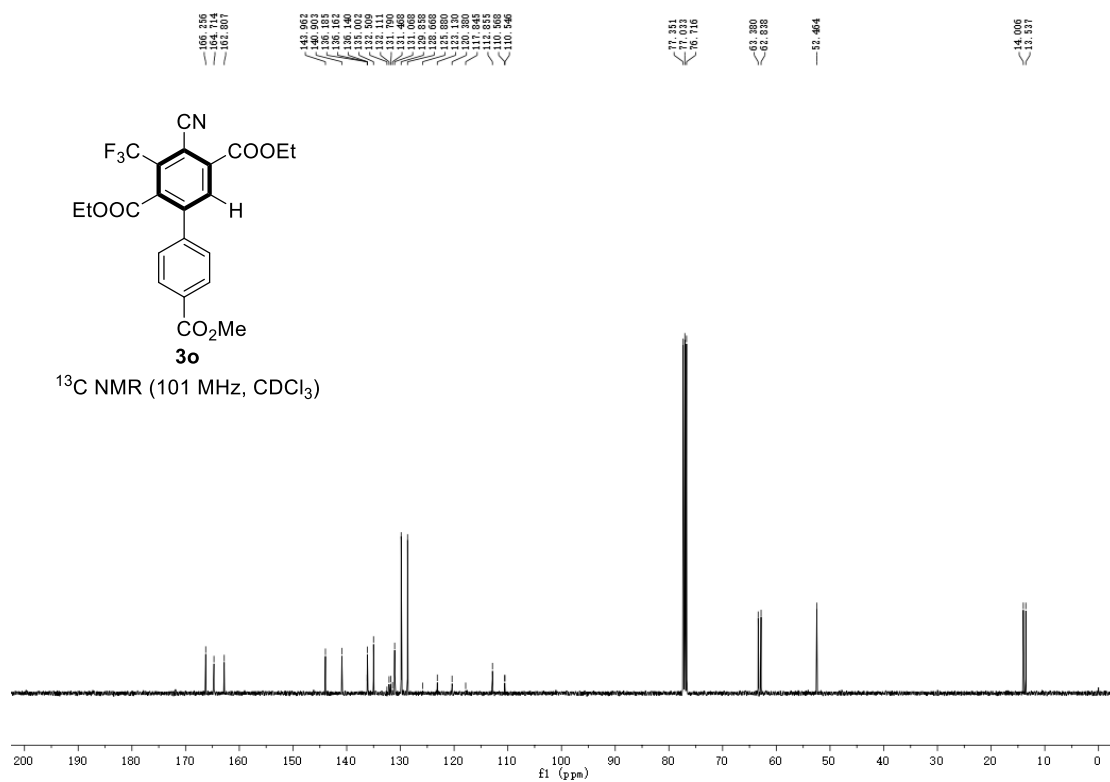
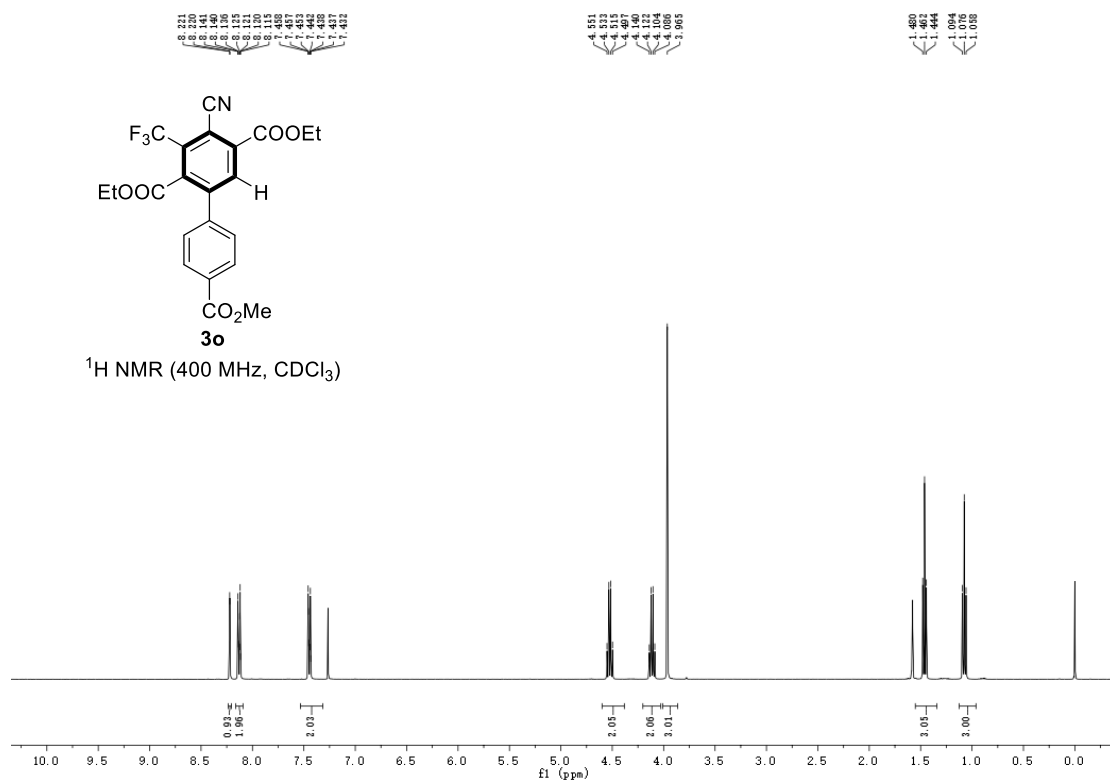


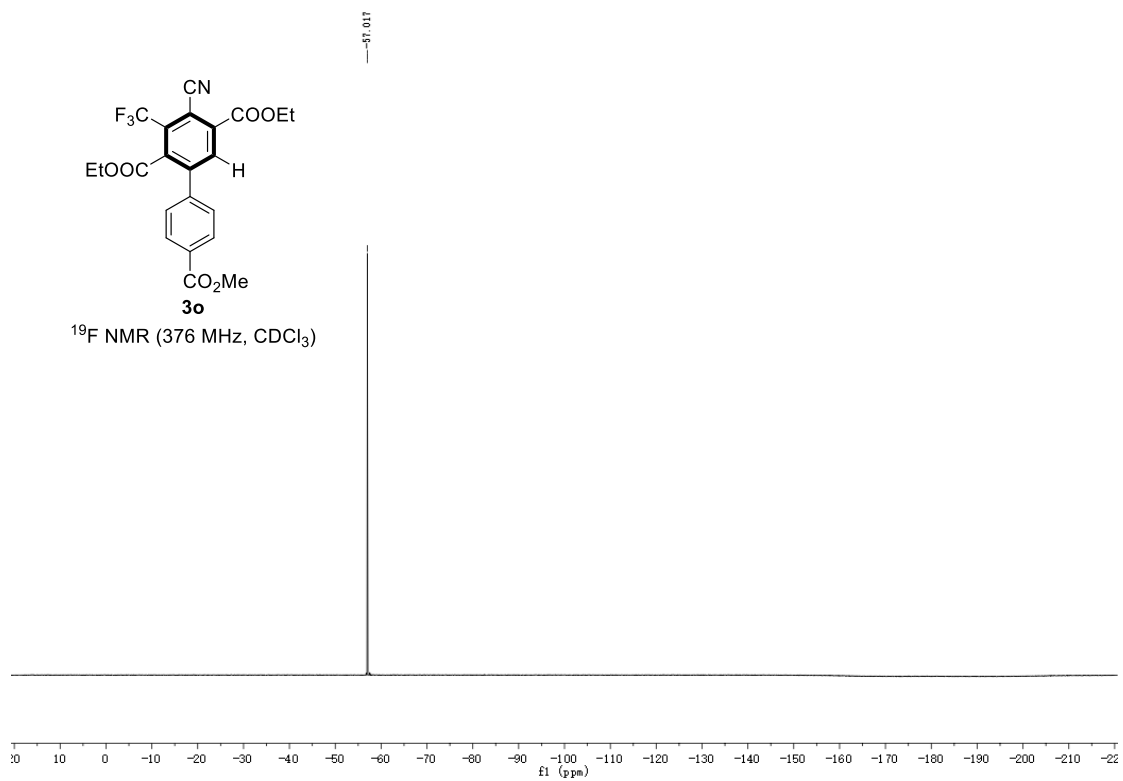


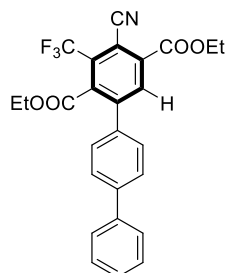


$^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )



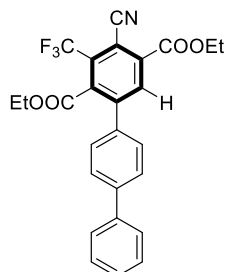
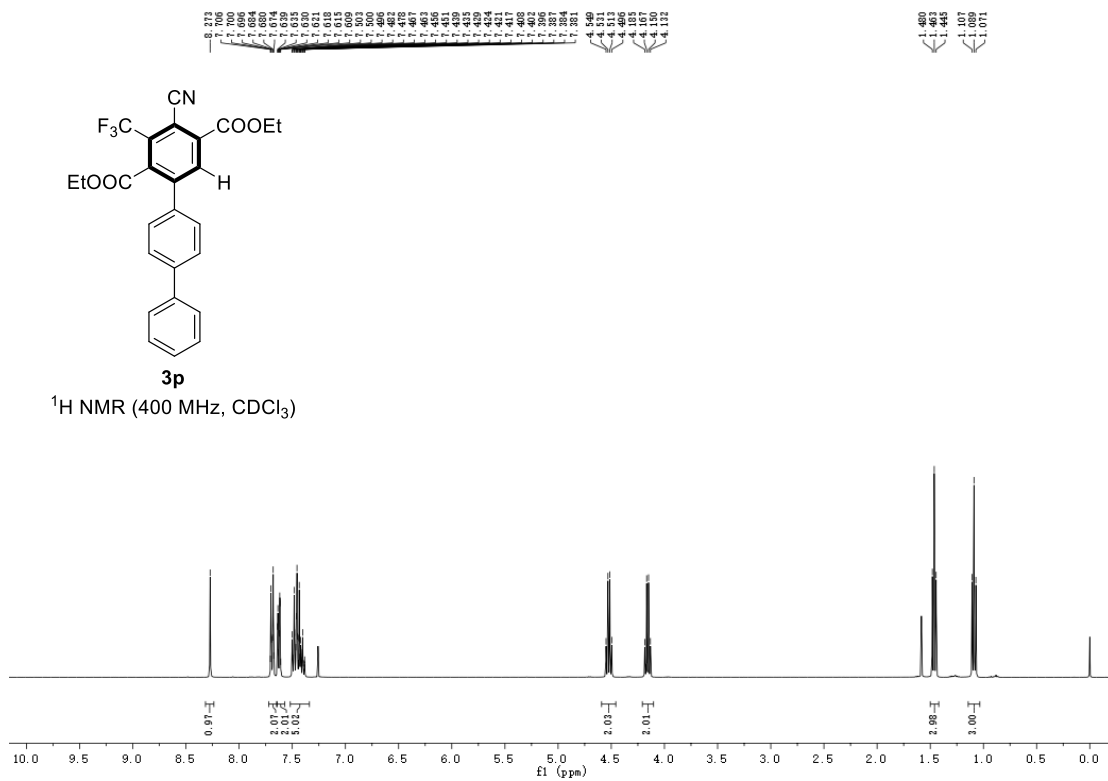






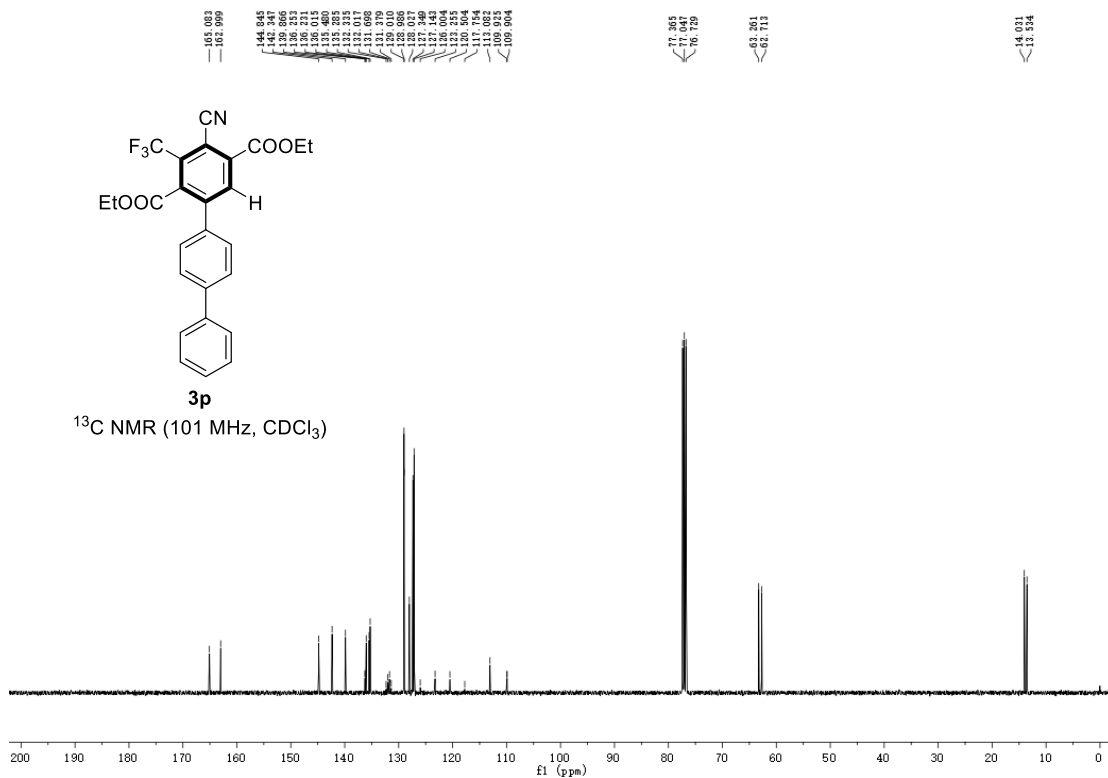
**3p**

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

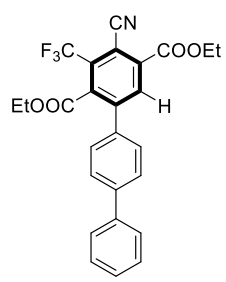


**3p**

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)

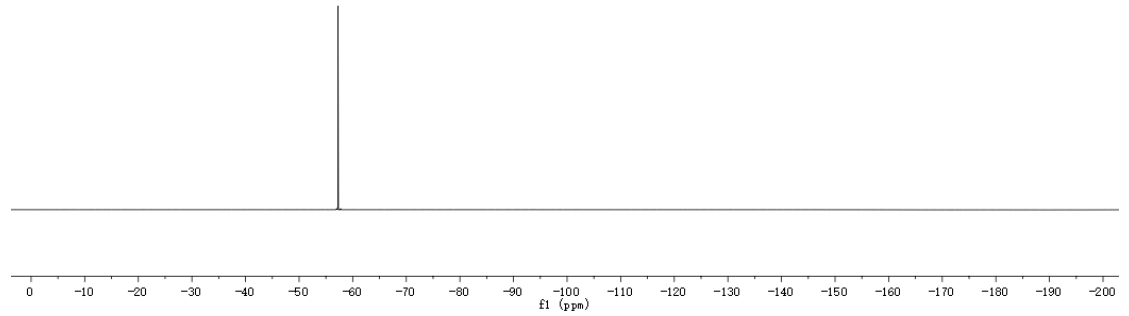


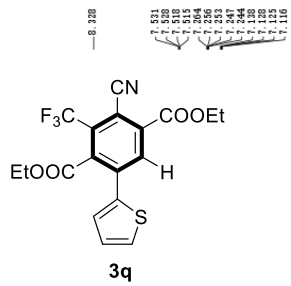




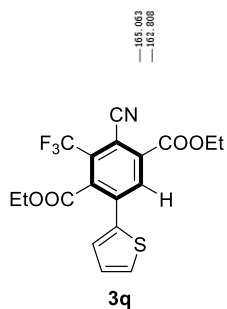
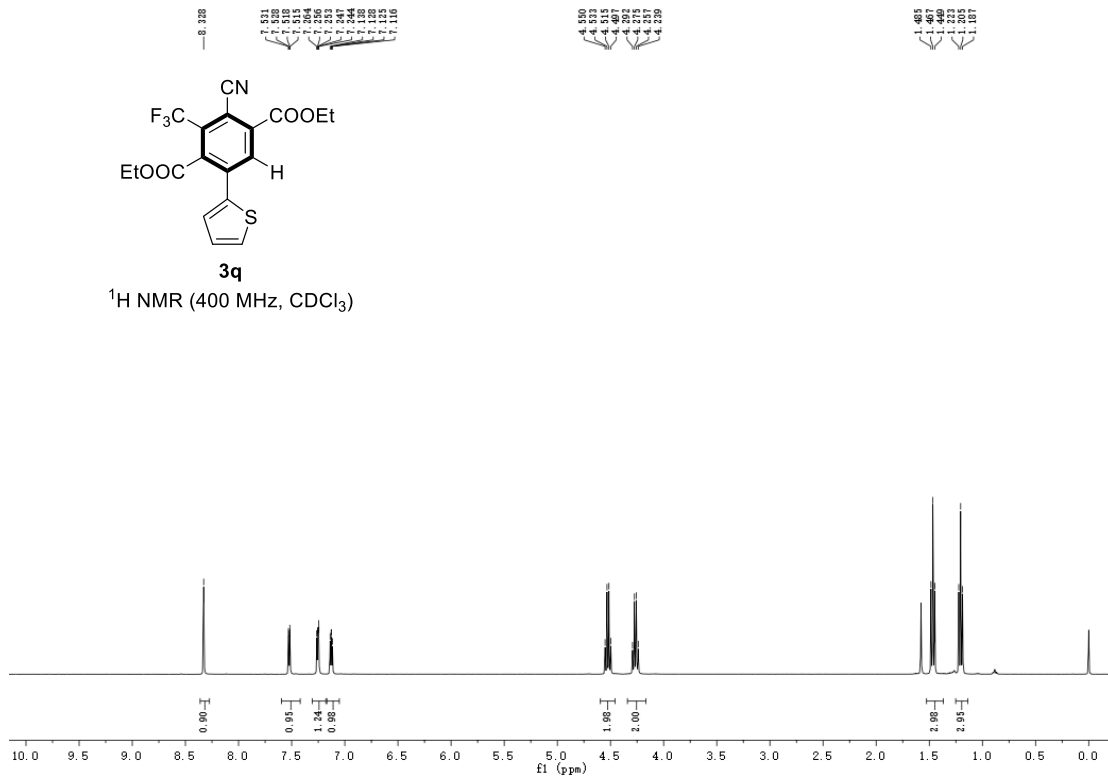
**3p**

<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>)

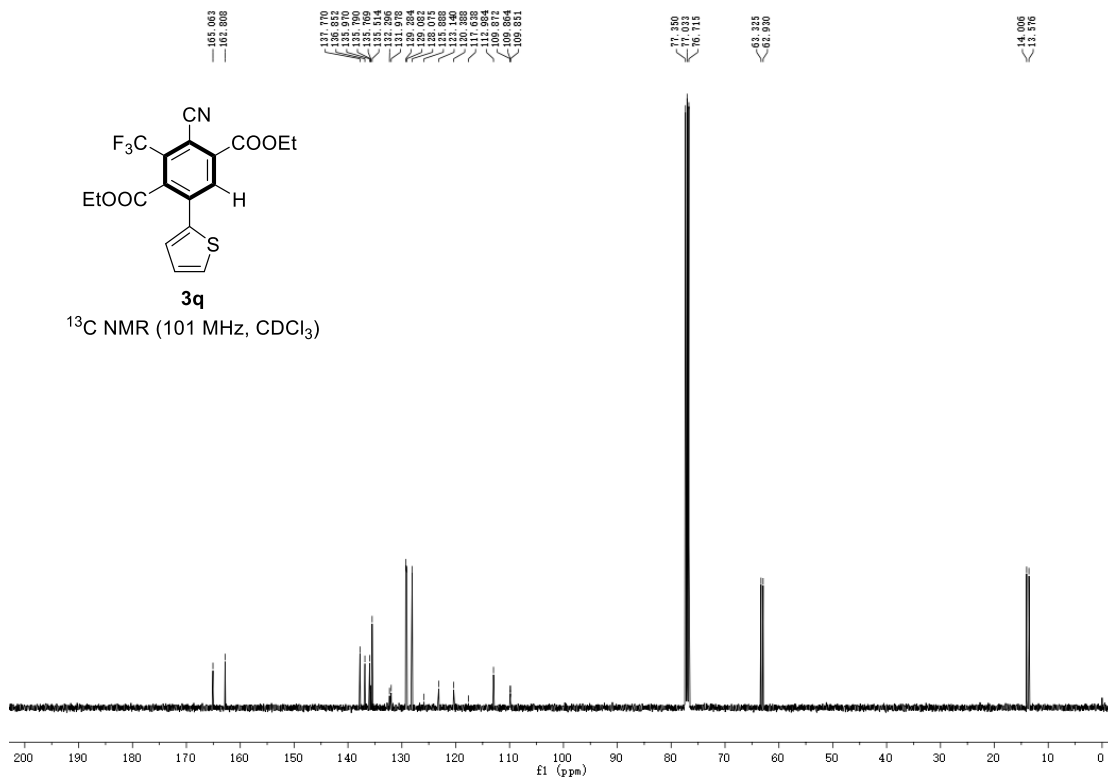


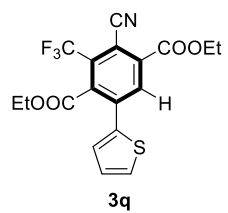


<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

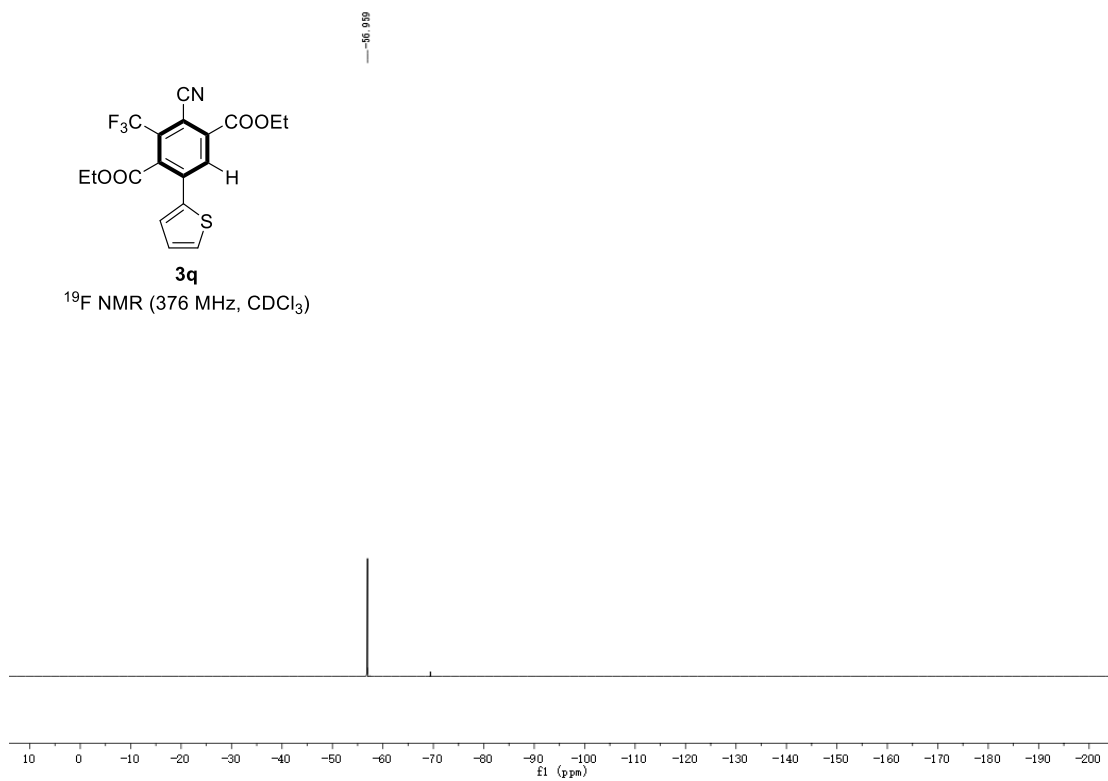


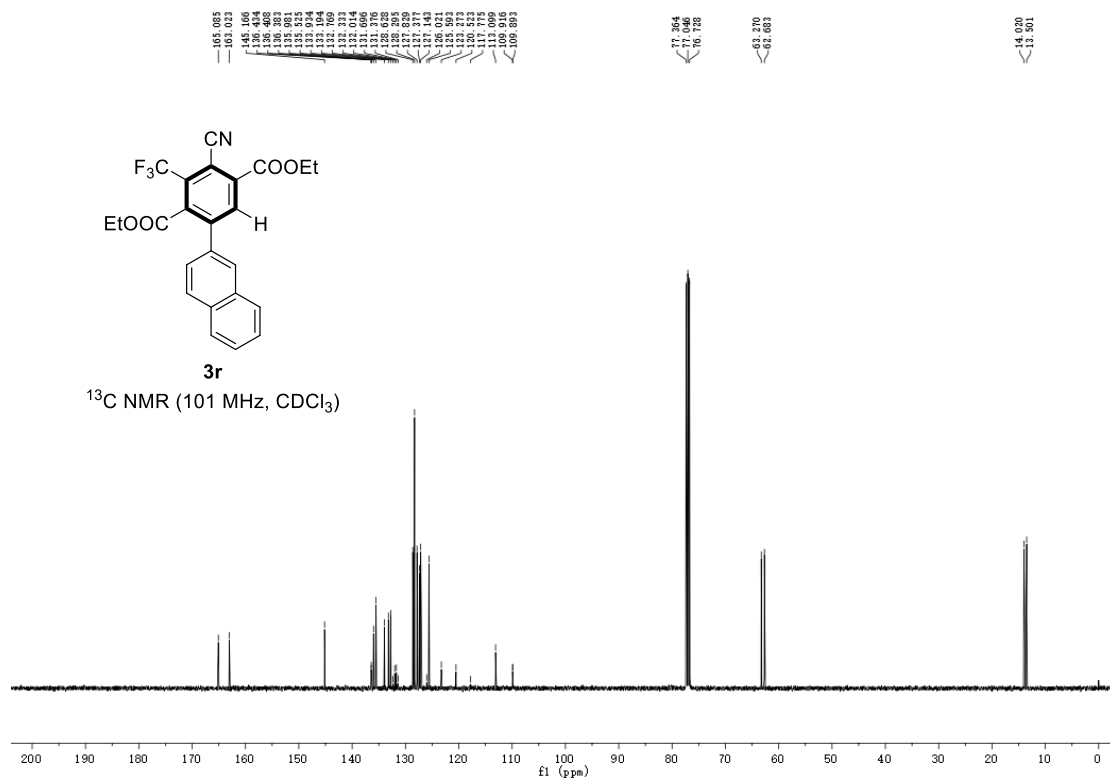
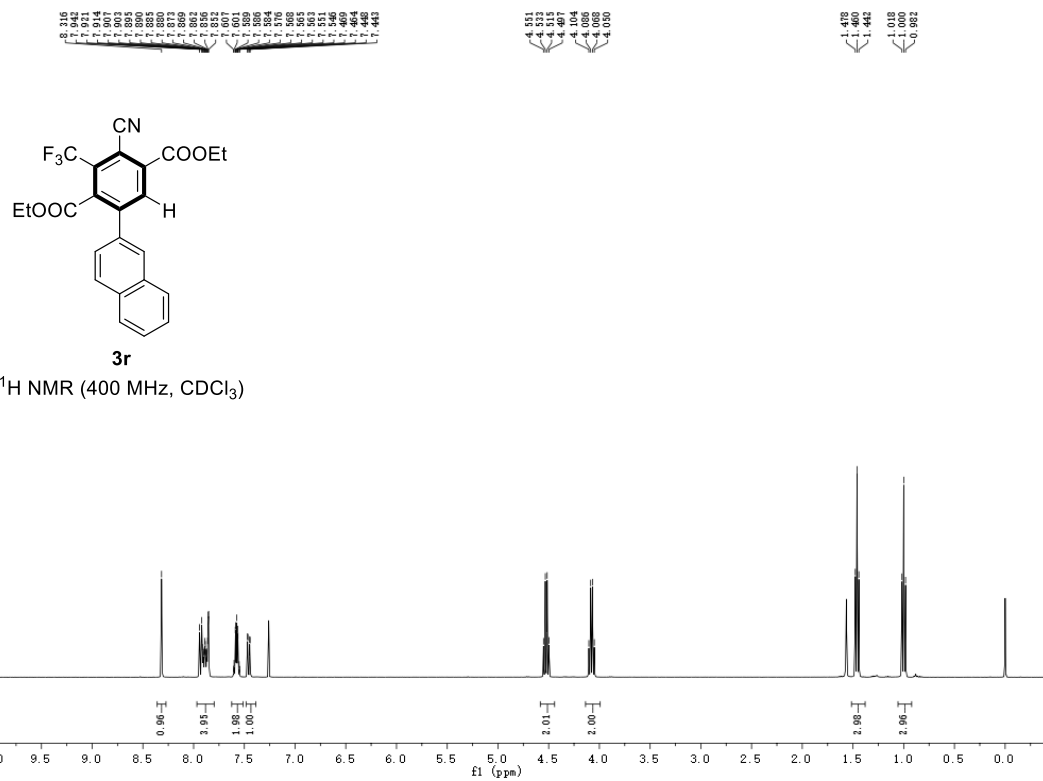
<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)

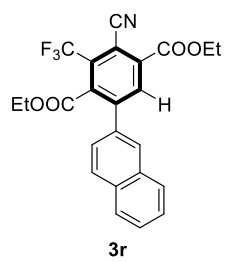




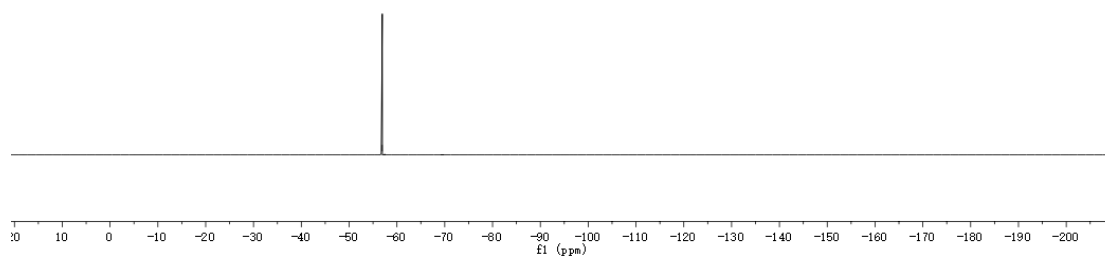
$^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )

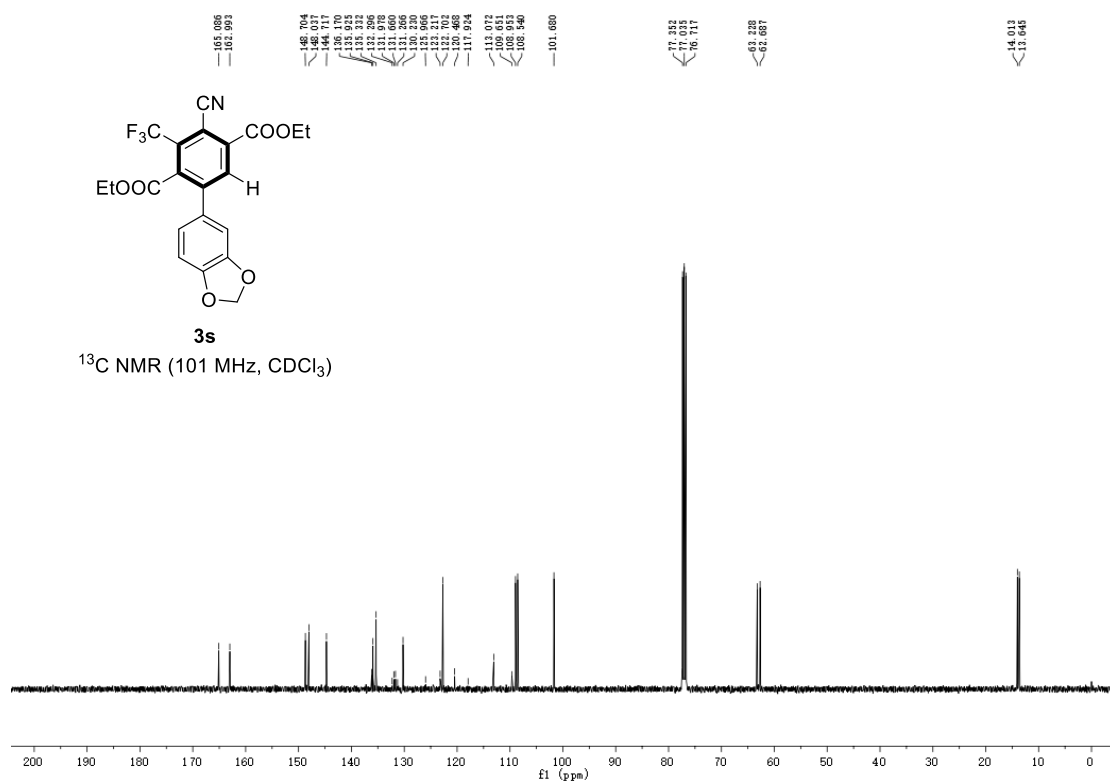
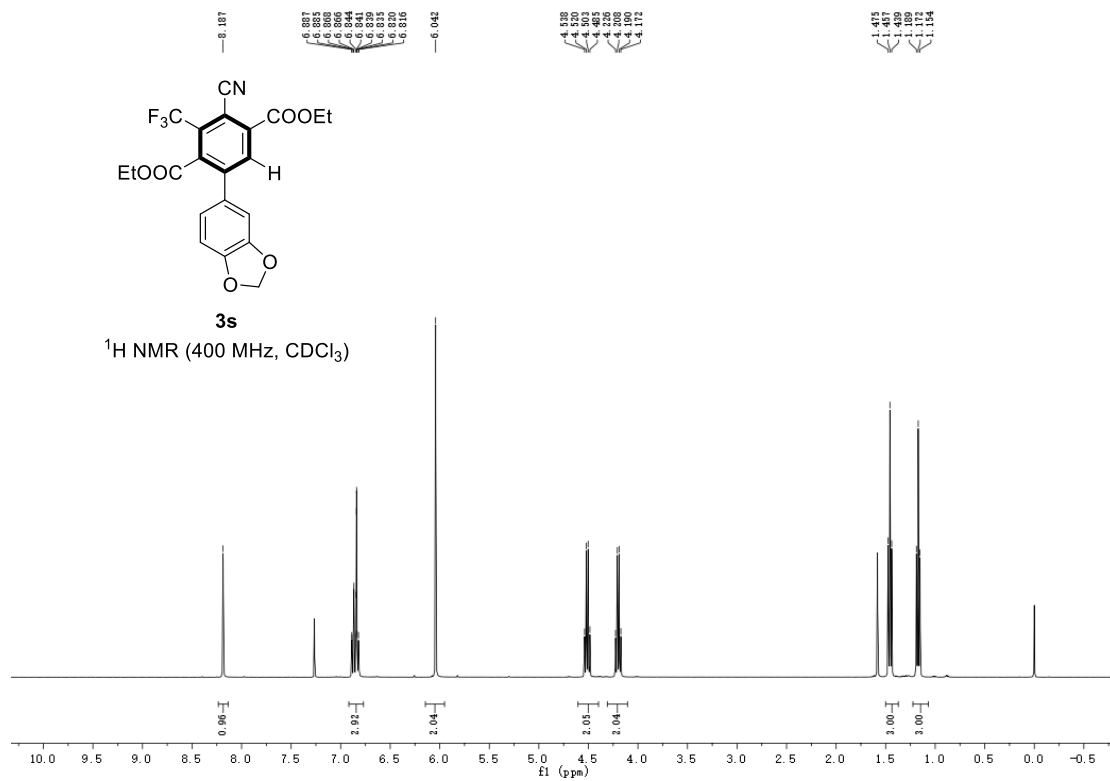


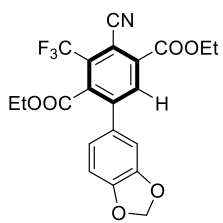




<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>)

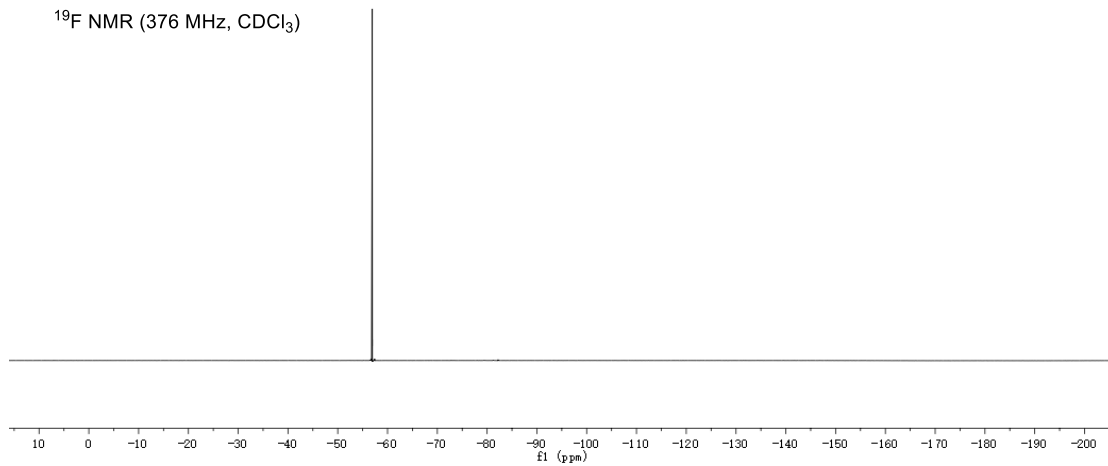


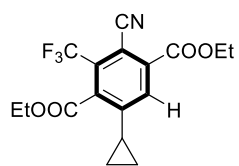




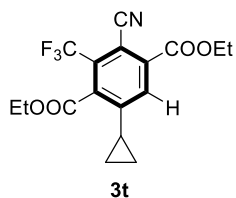
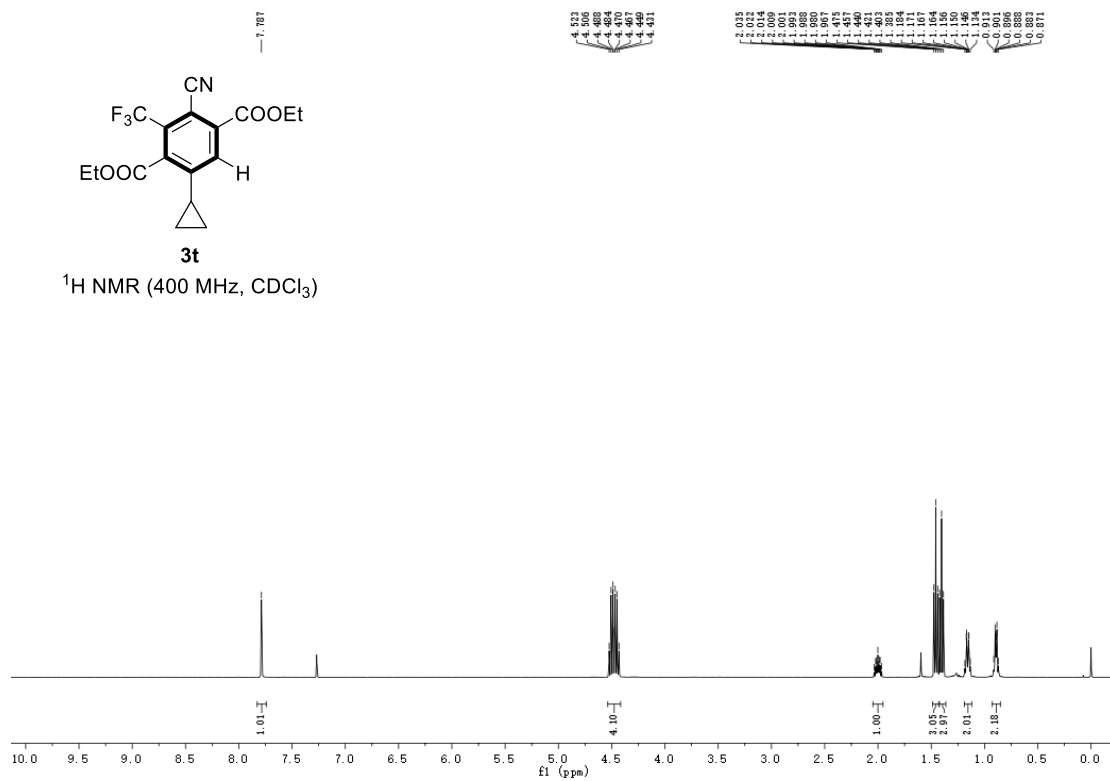
**3s**

<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>)

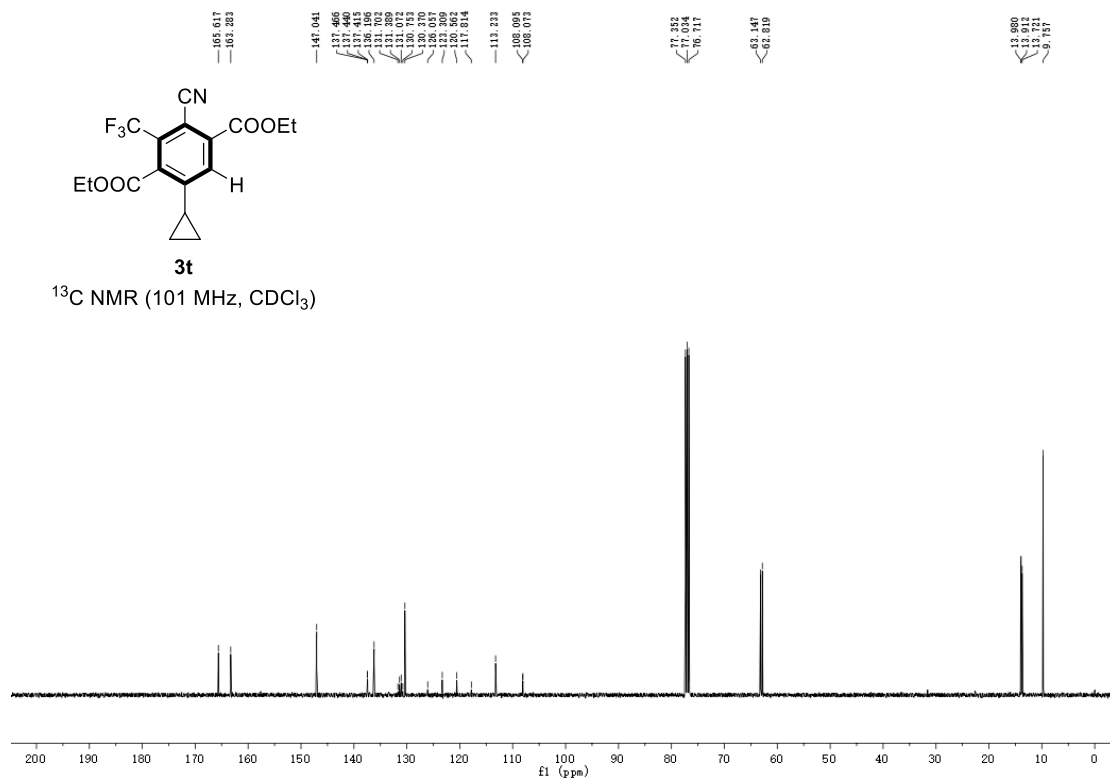




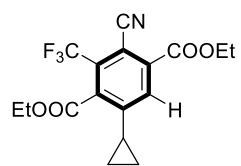
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)



<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)

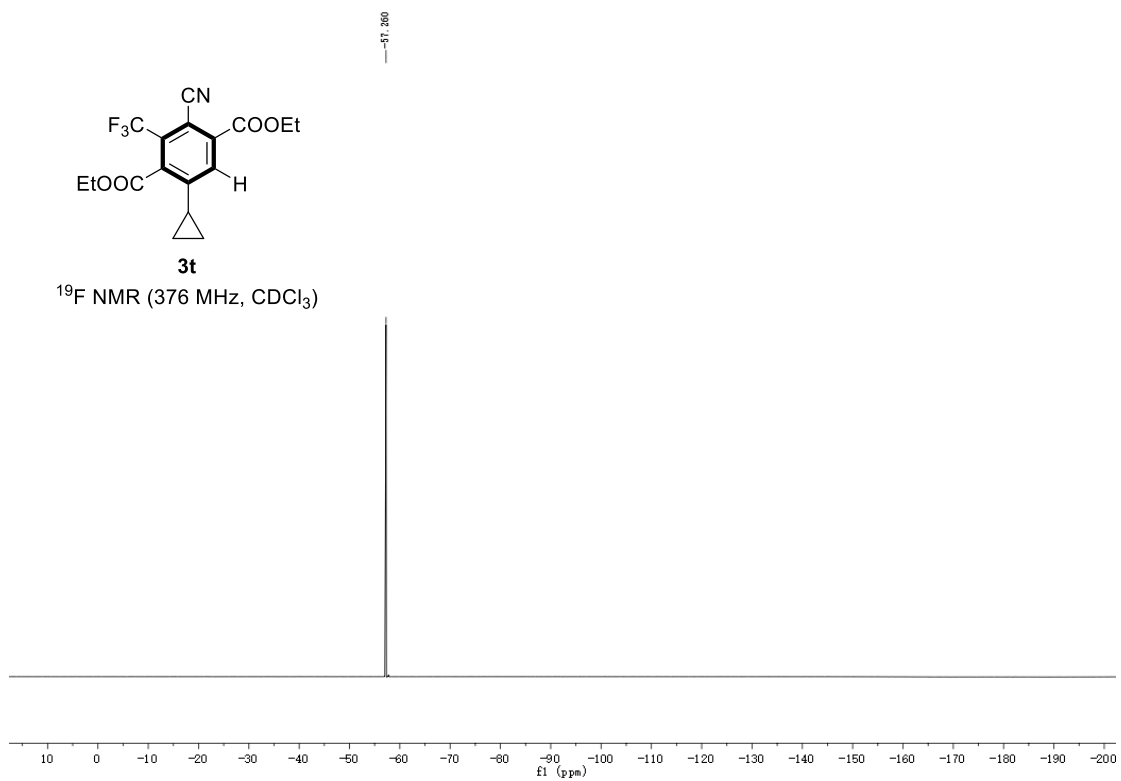


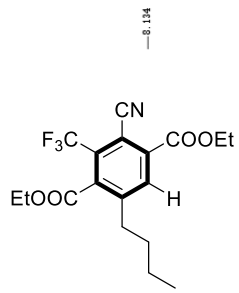




**3t**

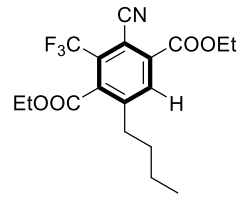
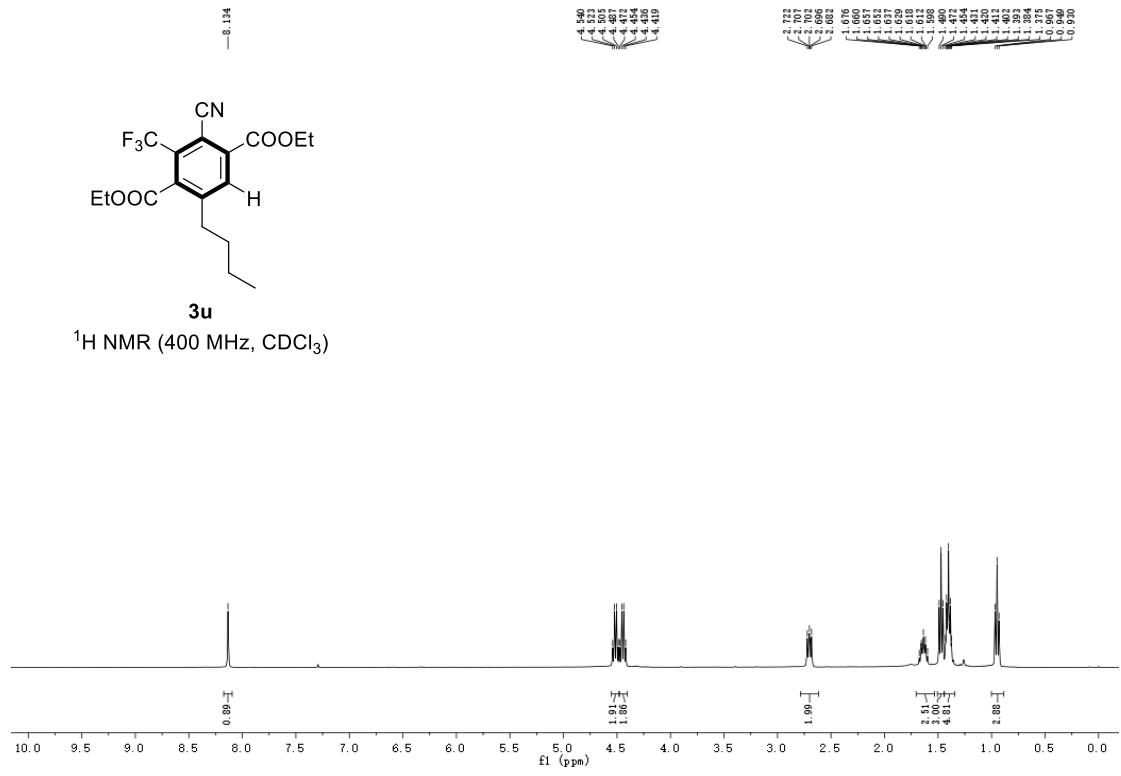
<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>)





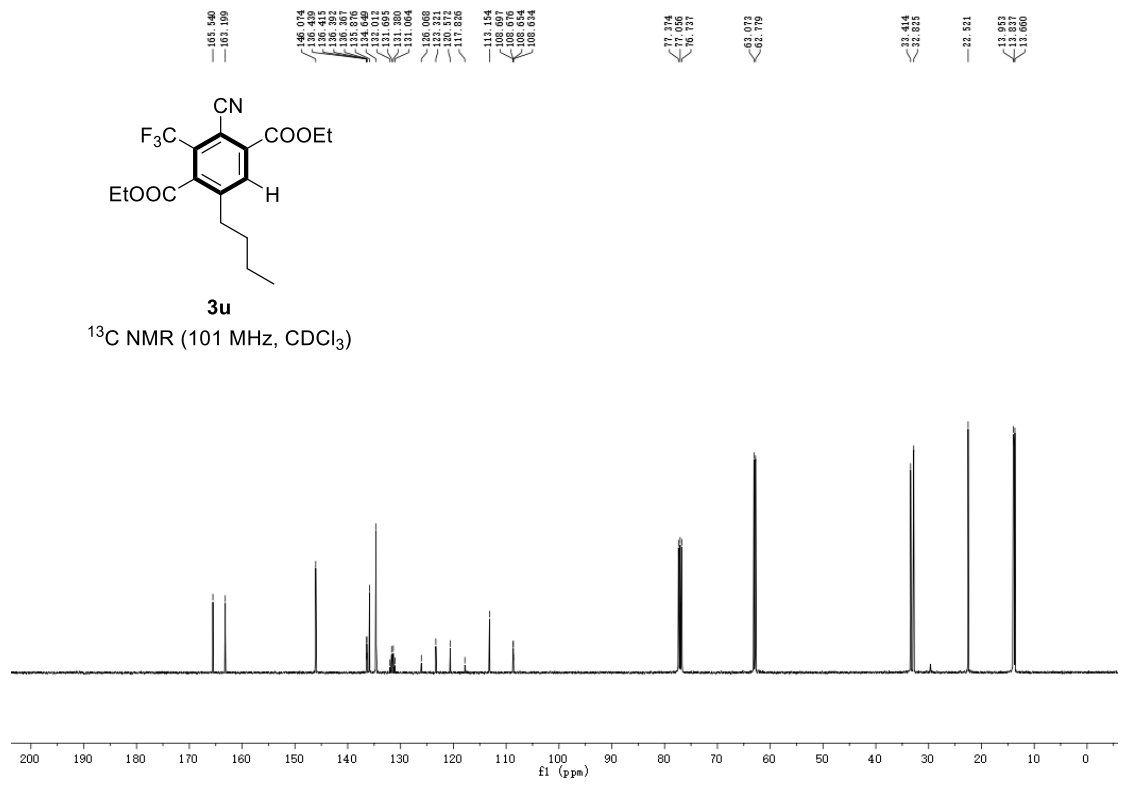
**3u**

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

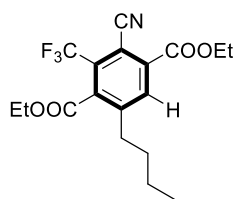


**3u**

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)

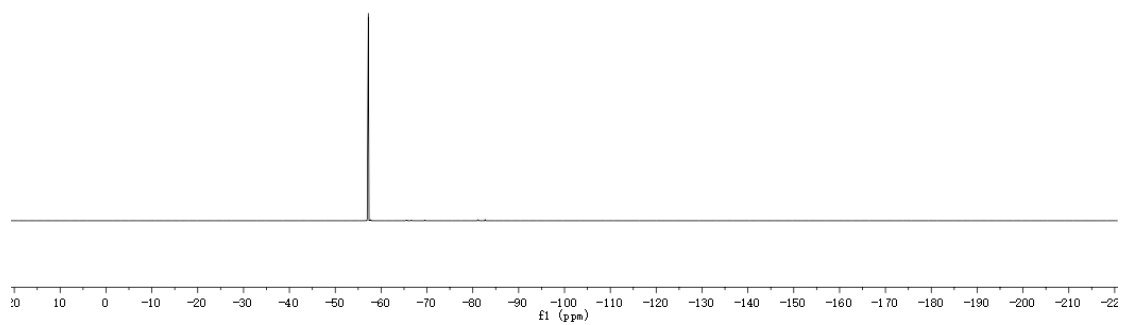


—57. 212



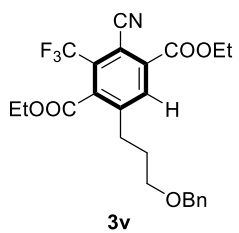
**3u**

$^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )

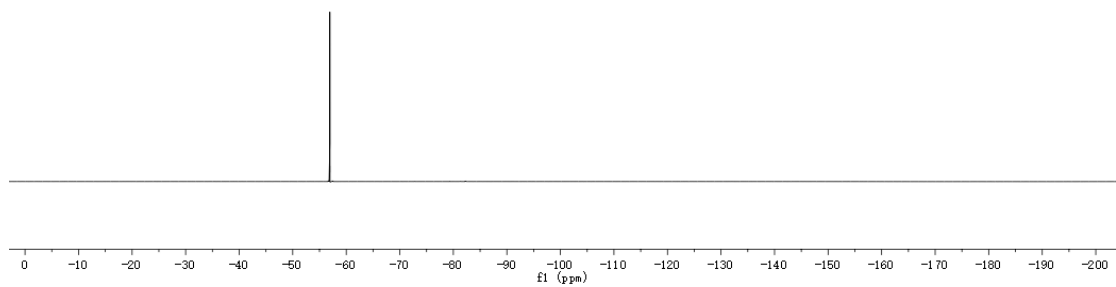


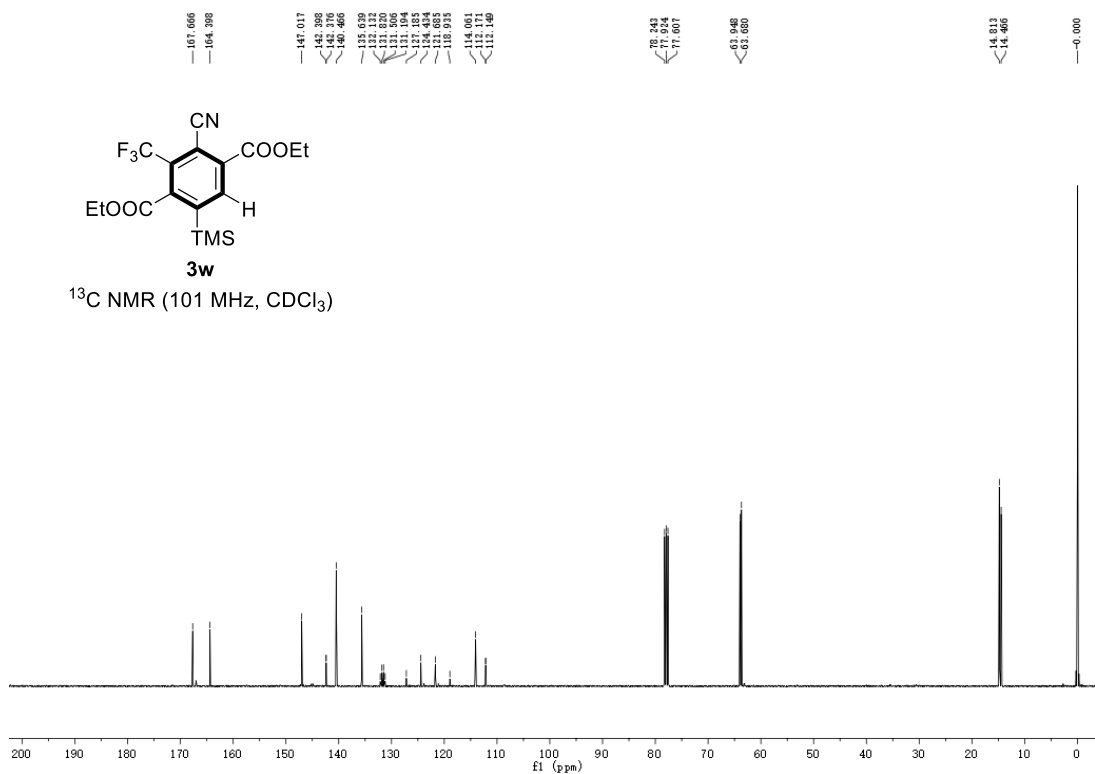
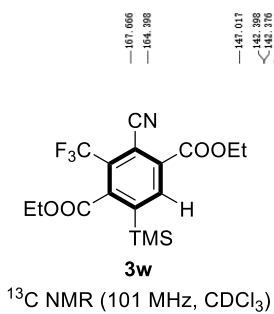
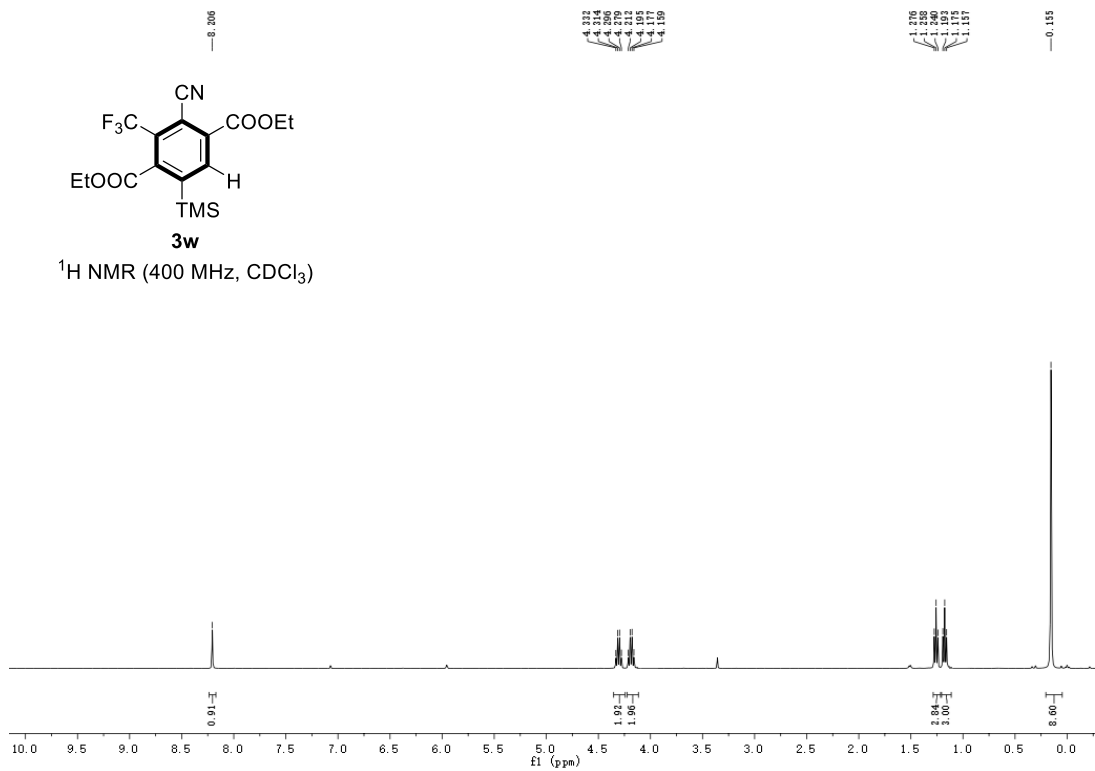
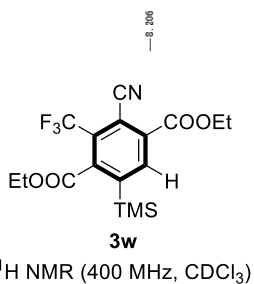


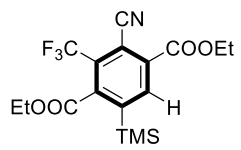
—56.917



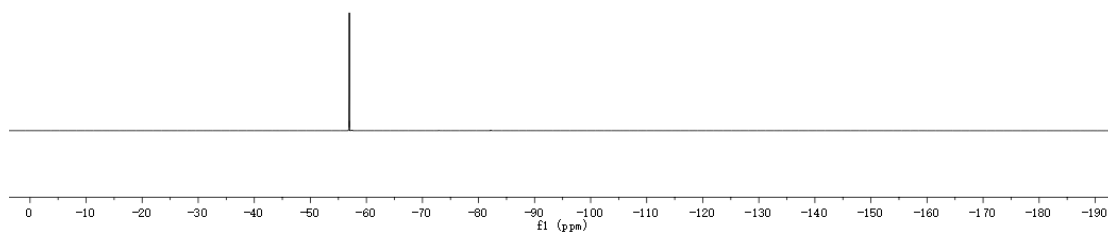
<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>)

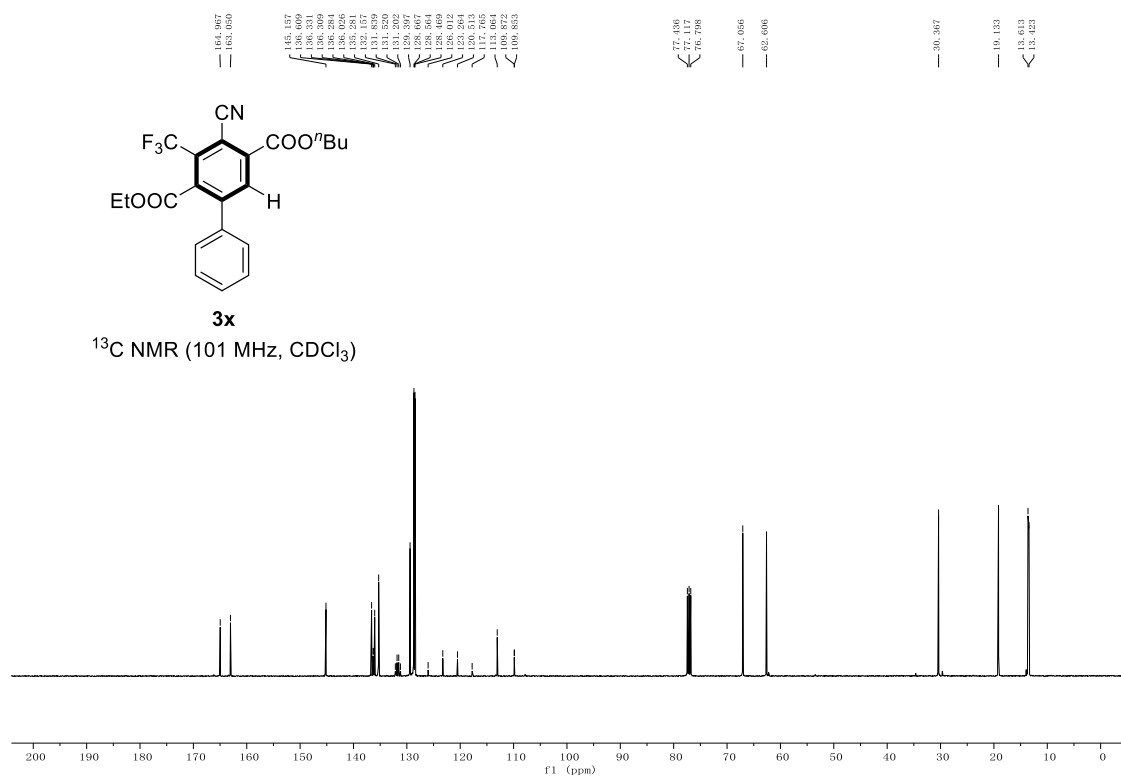




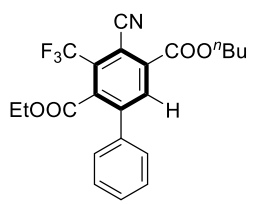


**3w**  
<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>)

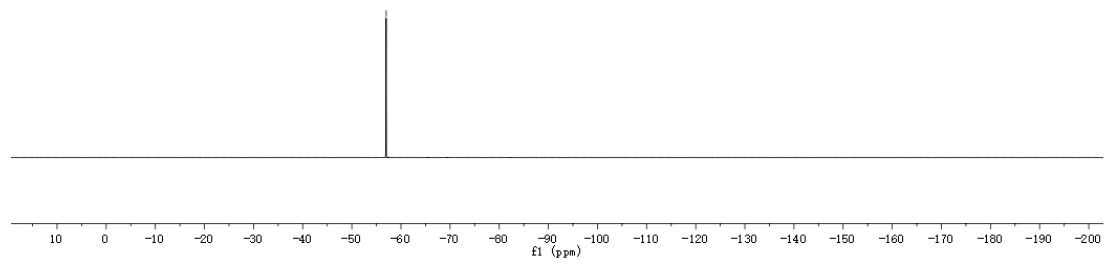


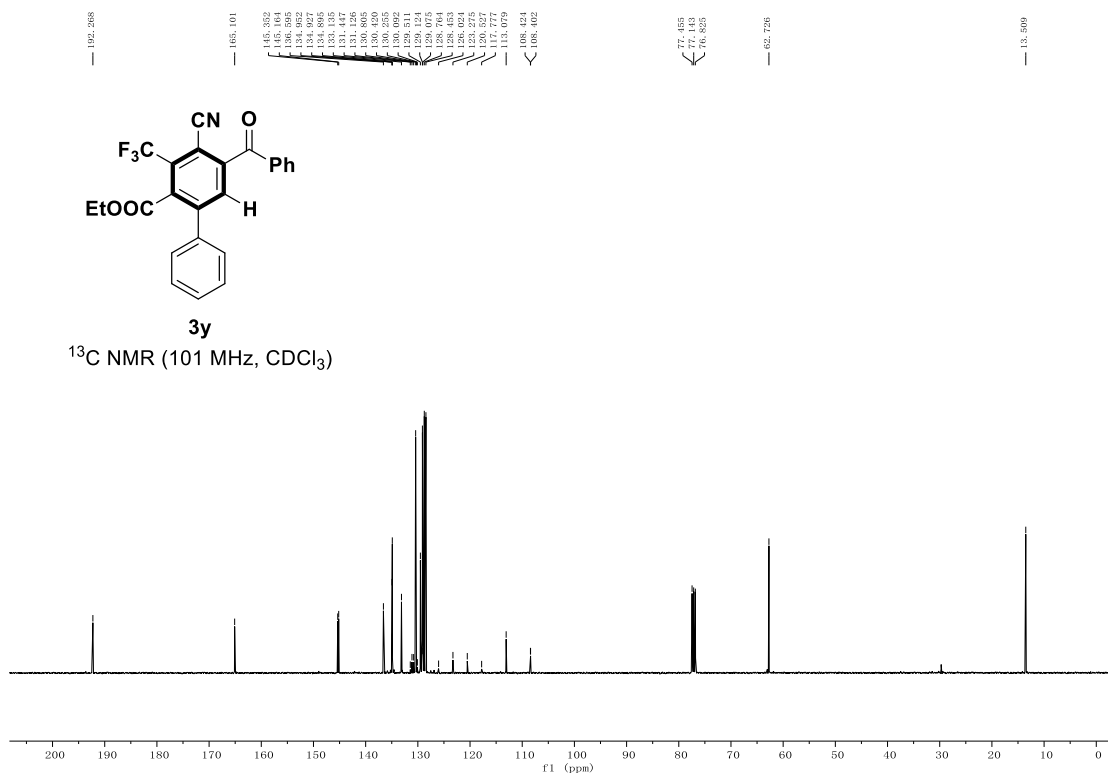
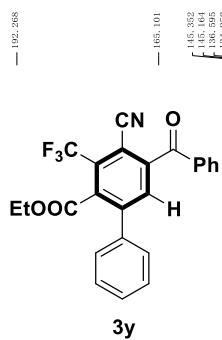
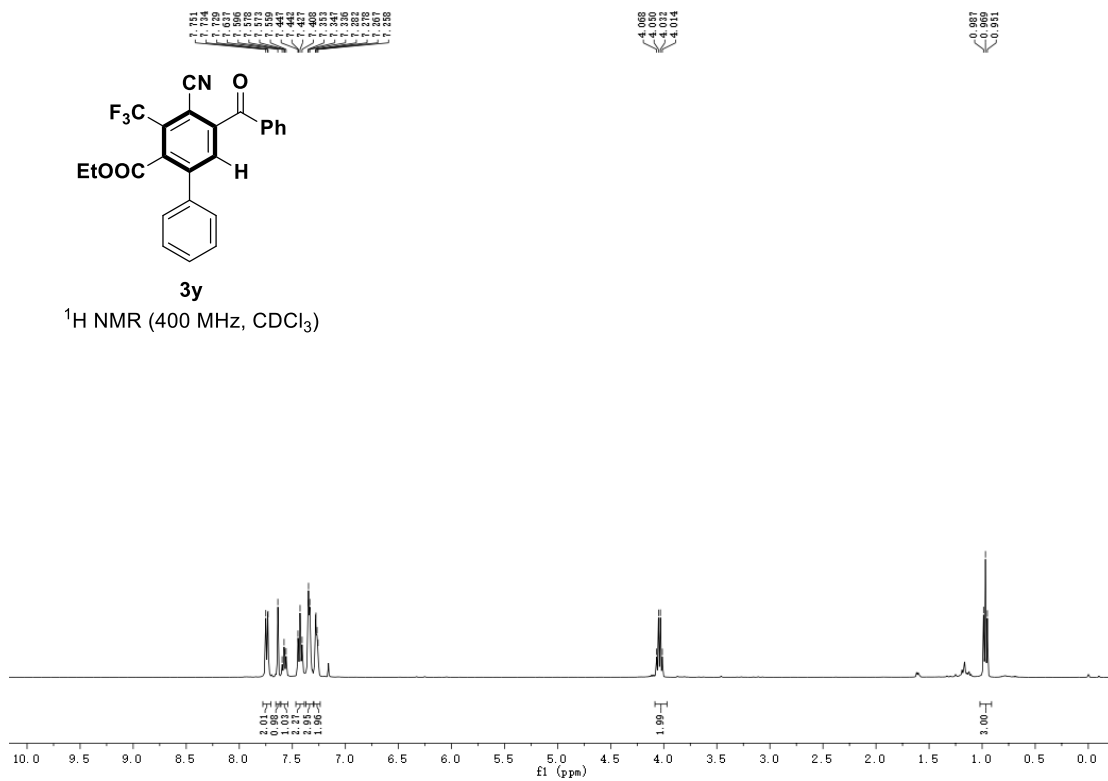
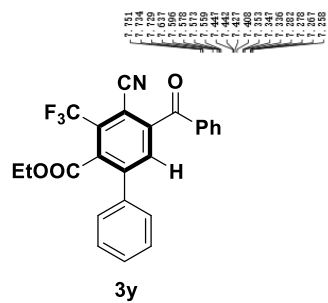


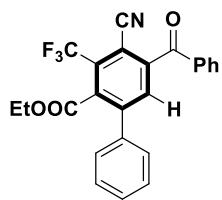




**3x**  
<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>)

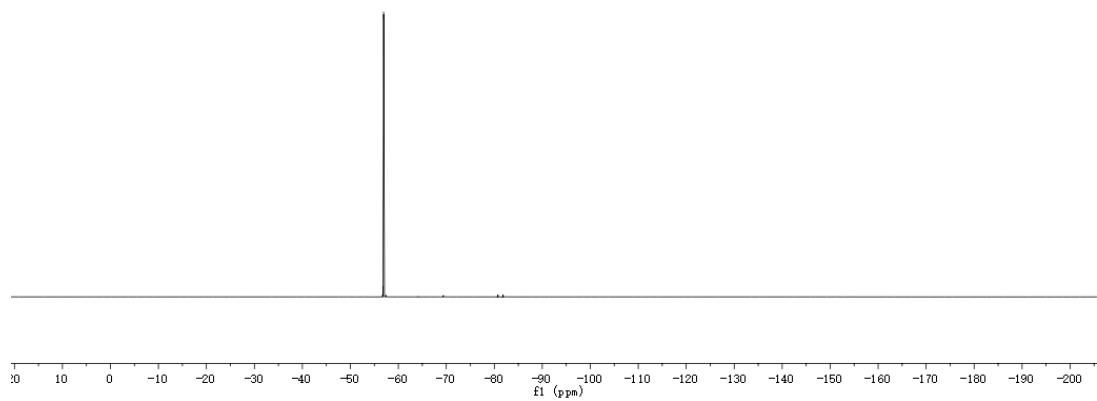




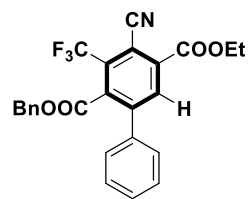


**3y**

<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>)

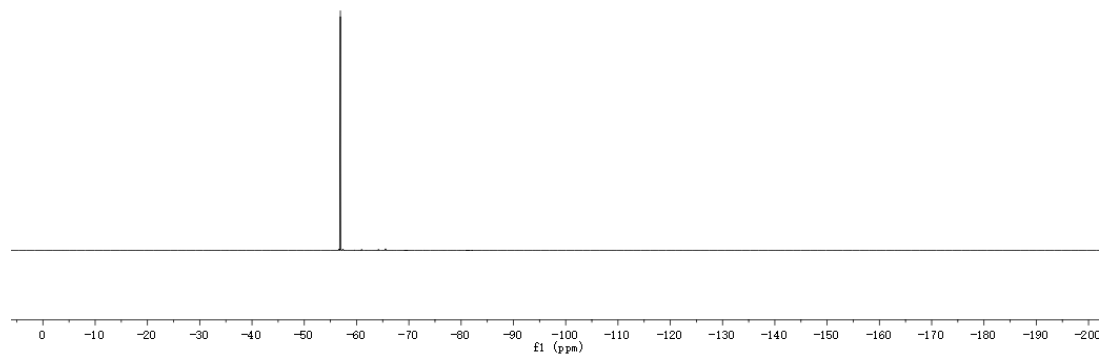






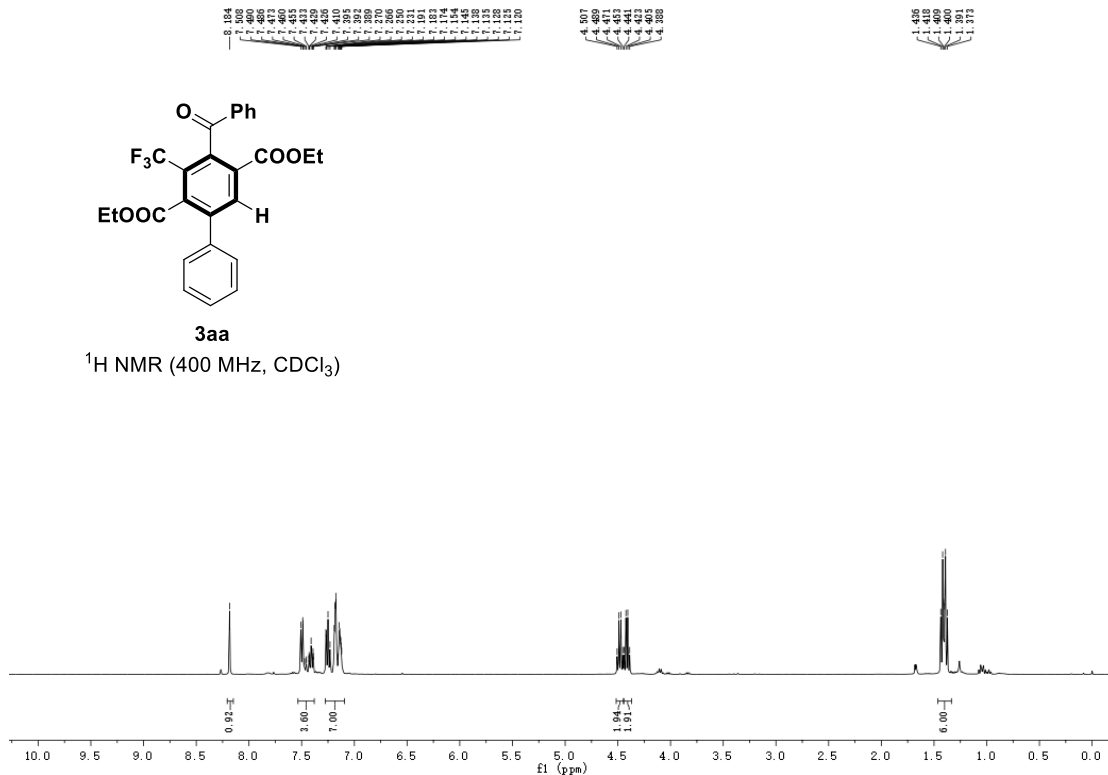
**3z**

<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>)

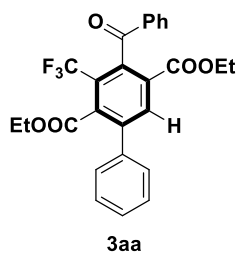




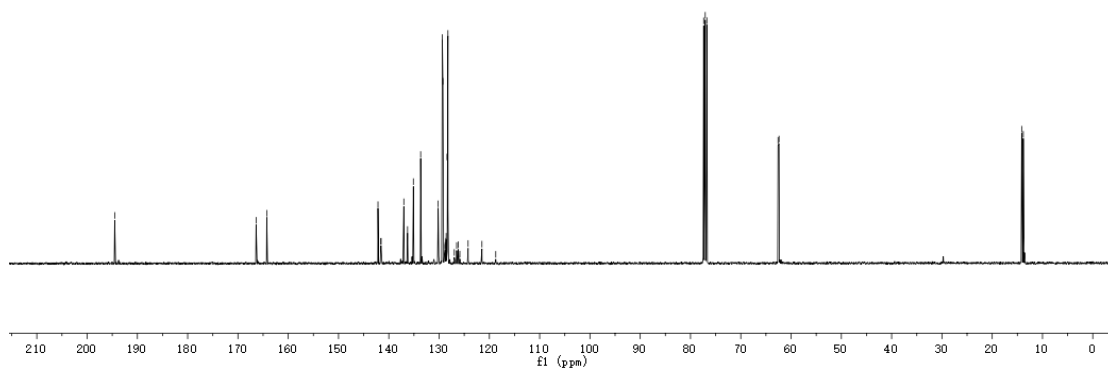
$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )

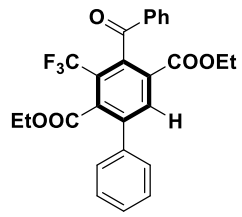


104.510, 106.391, 104.272, 142.151, 141.847, 137.014, 136.315, 133.654, 130.333, 129.240, 128.619, 128.608, 128.543, 126.507, 126.188, 124.232, 121.481, 118.170, 71.030, 70.733, 61.589, 61.294, 14.140, 13.815



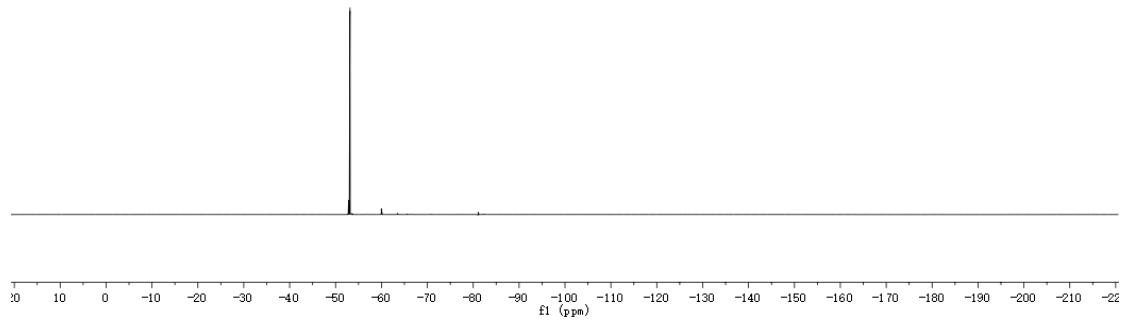
$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )

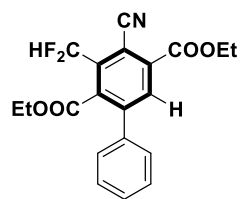




**3aa**

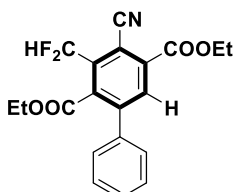
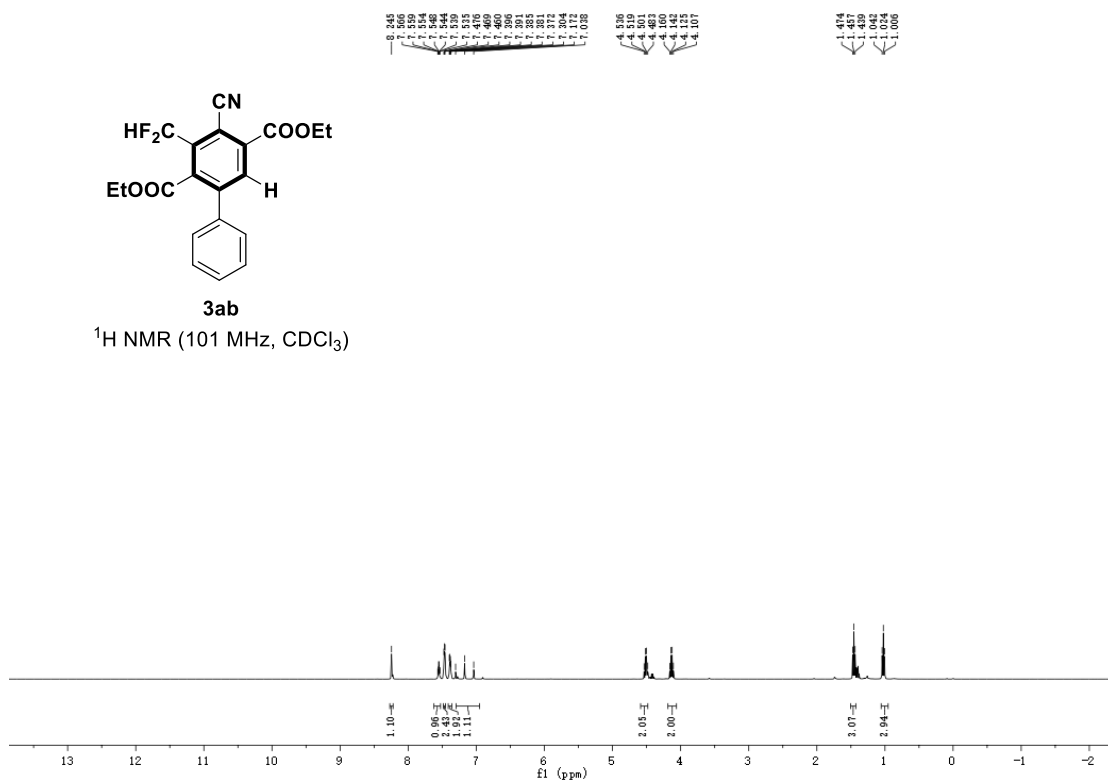
$^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )





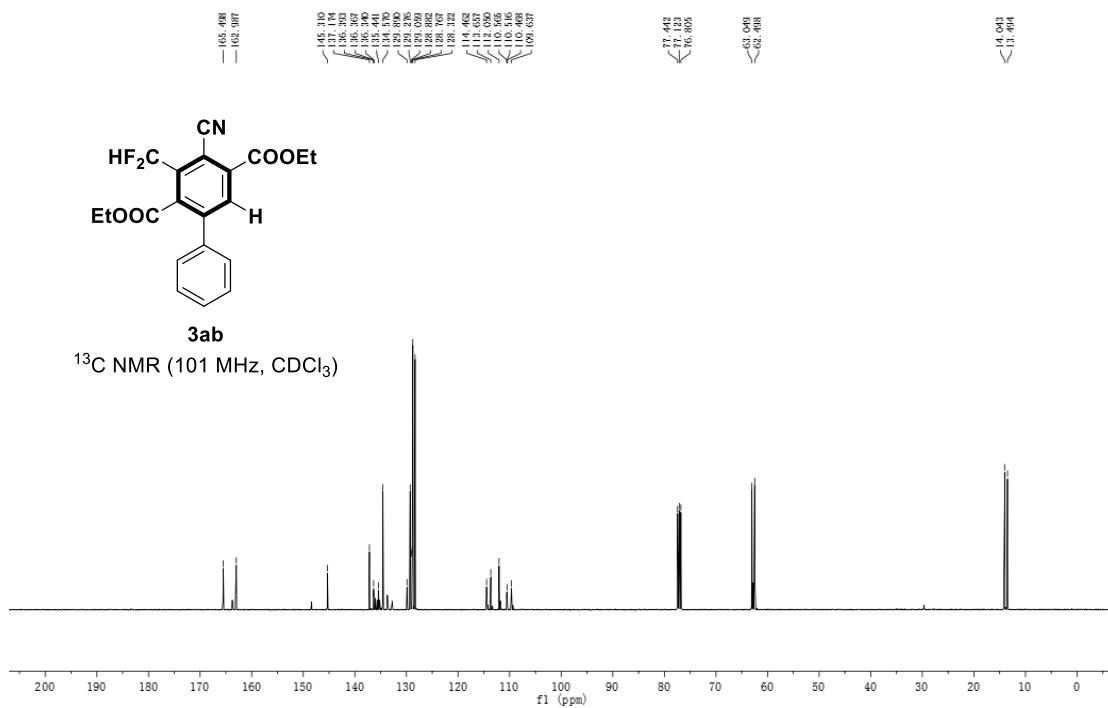
**3ab**

<sup>1</sup>H NMR (101 MHz, CDCl<sub>3</sub>)

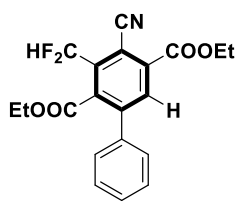


**3ab**

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)

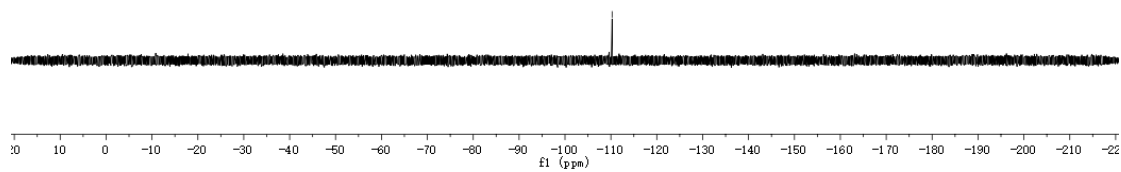


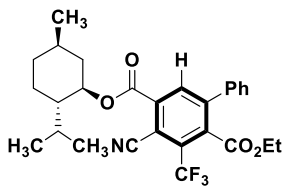




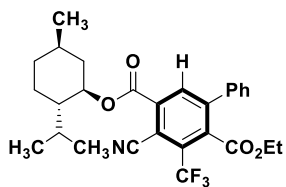
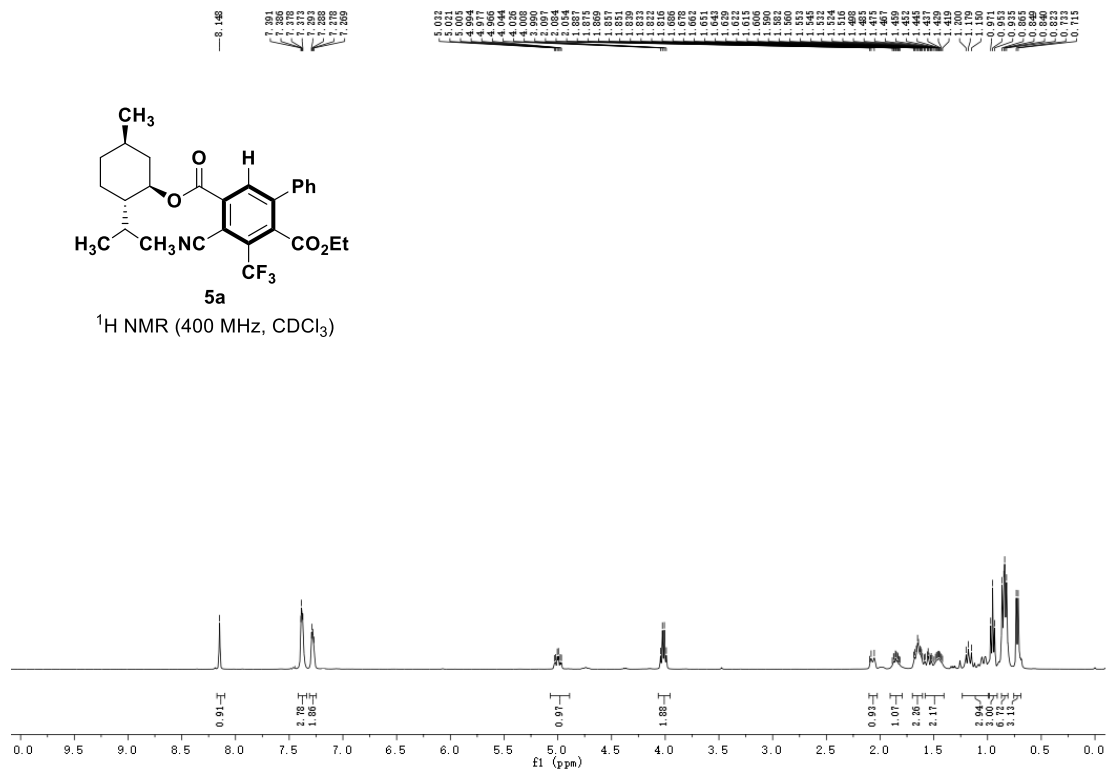
**3ab**

<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>)

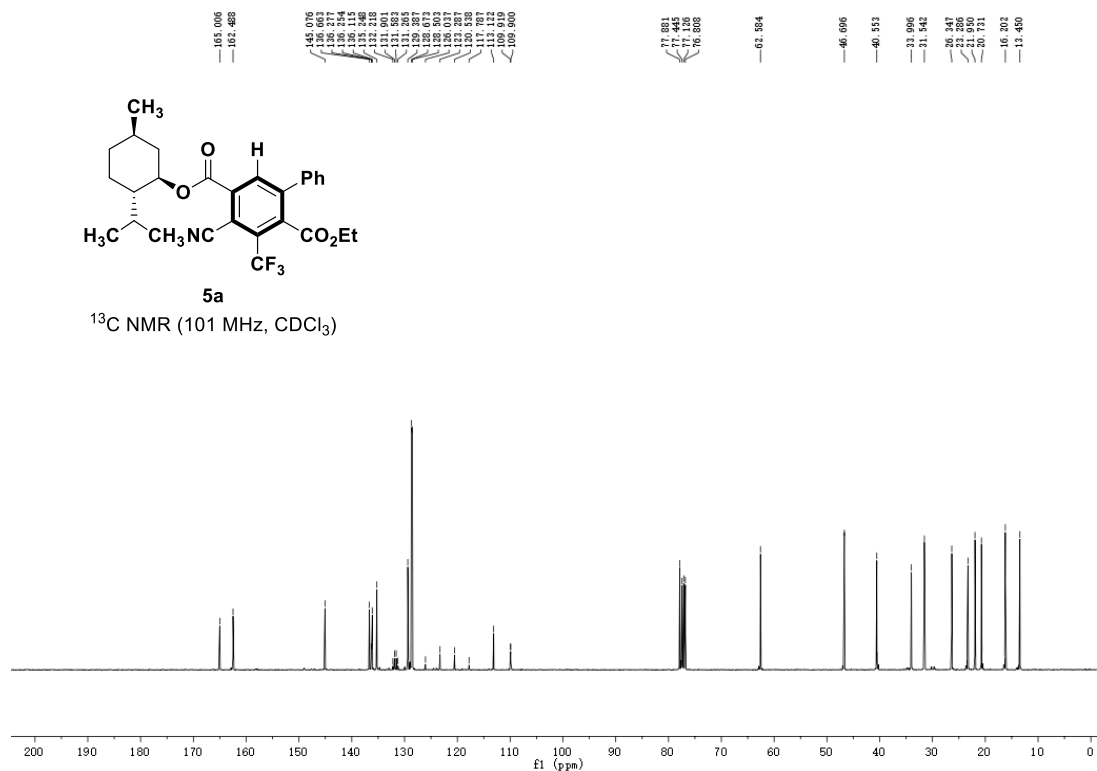


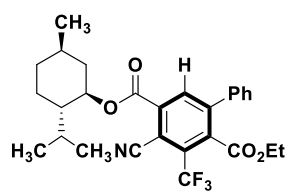


<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

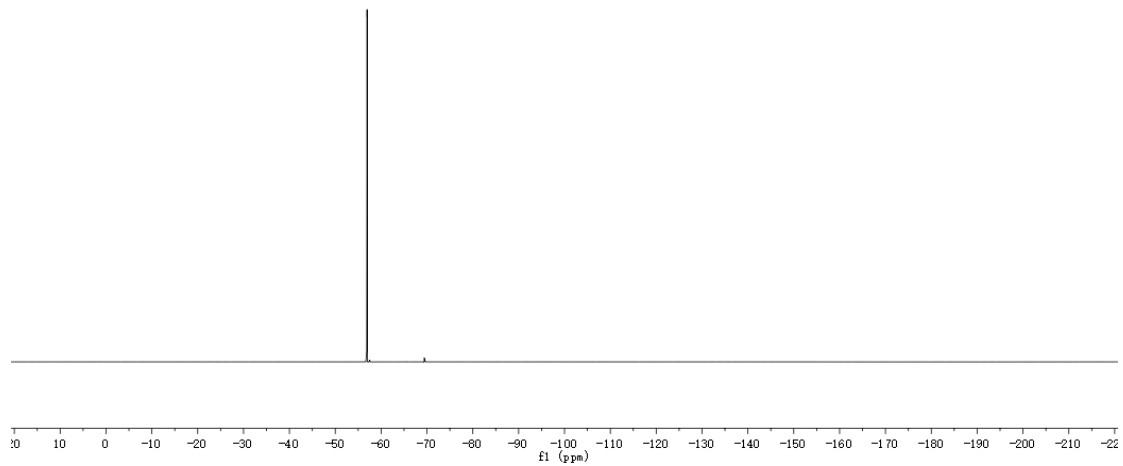


<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)

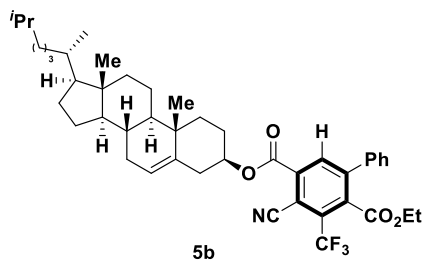




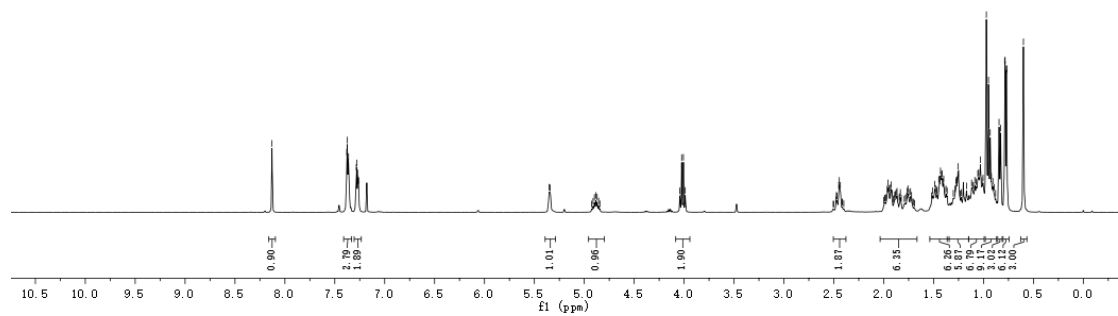
$^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )



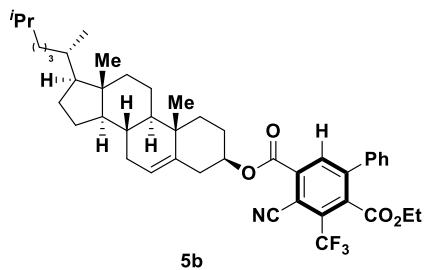
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4.042  
4.035  
3.989  
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2.451  
2.467  
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1.999  
1.993  
1.975  
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1.892  
1.889  
1.874  
1.874  
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1.841  
1.824  
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1.761  
1.757  
1.728  
1.721  
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1.480  
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1.464  
1.448  
1.431  
1.432  
1.400  
1.399  
1.375  
1.375  
1.364  
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1.286  
1.286  
1.264  
1.264  
1.256  
1.256  
1.224  
1.223  
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1.110  
1.109  
1.081  
1.081  
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1.047  
1.031  
1.015  
1.015  
0.971  
0.950  
0.921  
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0.879  
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0.844  
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0.783  
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0.761  
0.600



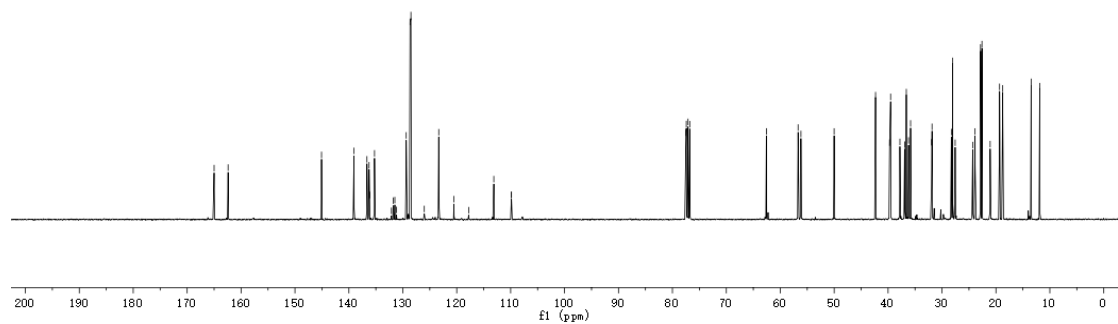
$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )

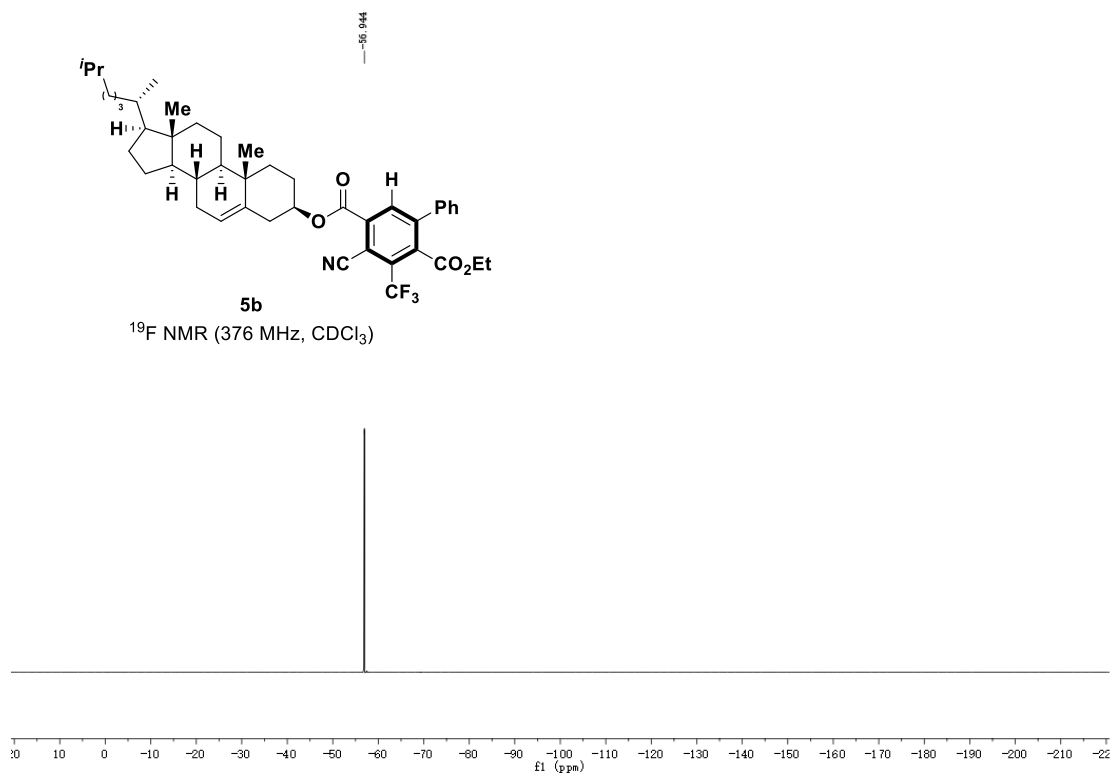


155.000  
152.404  
148.076  
136.655  
136.360  
136.360  
136.172  
136.172  
133.248  
133.248  
131.702  
131.702  
131.474  
131.474  
130.370  
130.370  
128.633  
128.496  
128.496  
123.328  
123.328  
123.268  
123.268  
117.768  
117.768  
113.321  
113.321  
109.849  
109.849  
77.505  
77.423  
77.341  
76.787  
62.574  
56.089  
56.102  
50.010  
44.238  
44.238  
39.535  
37.806  
36.934  
36.934  
36.207  
36.207  
31.838  
31.838  
31.850  
31.850  
28.205  
28.205  
27.558  
24.306  
24.306  
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21.889  
19.325  
19.325  
18.741  
18.741  
11.875  
11.875

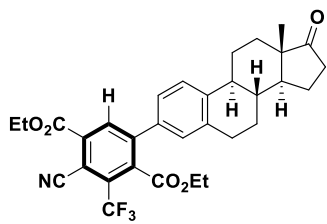


$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )



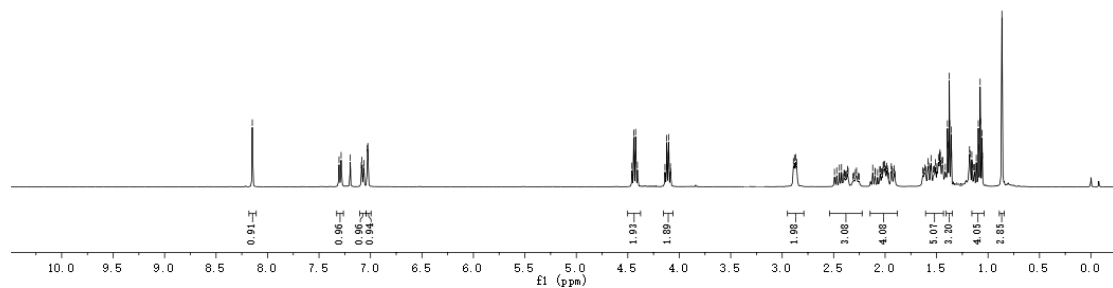


8.148  
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6.888  
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6.439  
6.431  
6.430  
6.432  
6.410  
6.400  
6.391  
6.385  
6.380  
6.366  
6.365  
6.359  
6.359  
6.350  
6.330  
6.278  
6.278  
6.205  
6.205  
6.202  
6.202  
6.204  
6.204  
6.212  
6.212  
6.195  
6.195  
6.192  
6.192  
6.175  
6.175  
6.164  
6.164  
6.154  
6.154  
6.151  
6.151  
6.137  
6.137  
6.134  
6.134  
6.130  
6.130  
6.122  
6.122  
6.117  
6.117  
6.105  
6.105  
6.085  
6.085  
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1.464  
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1.446  
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1.391  
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1.394  
1.375  
1.375  
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1.359  
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1.320  
1.175  
1.175  
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0.985

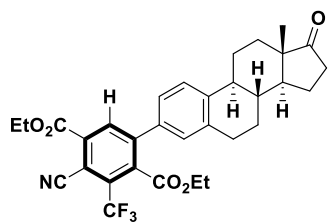


5c

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

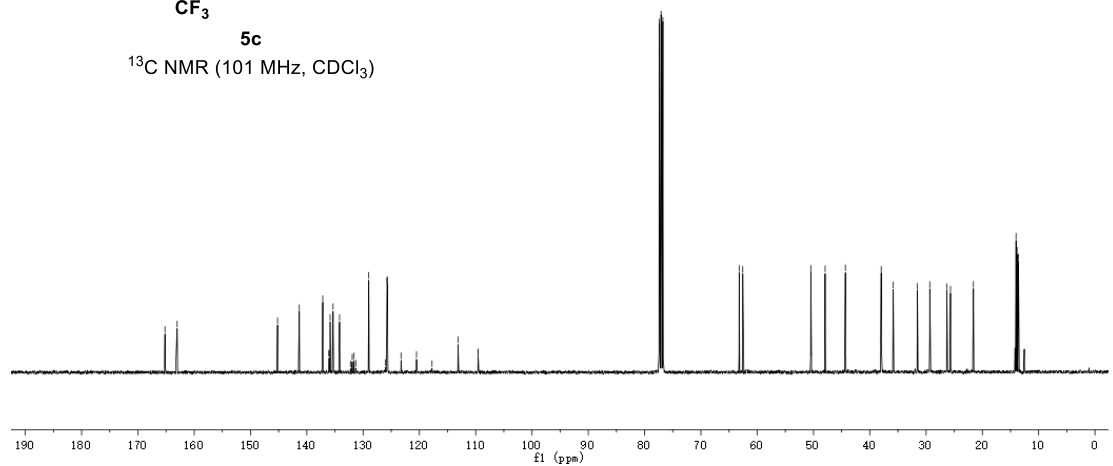


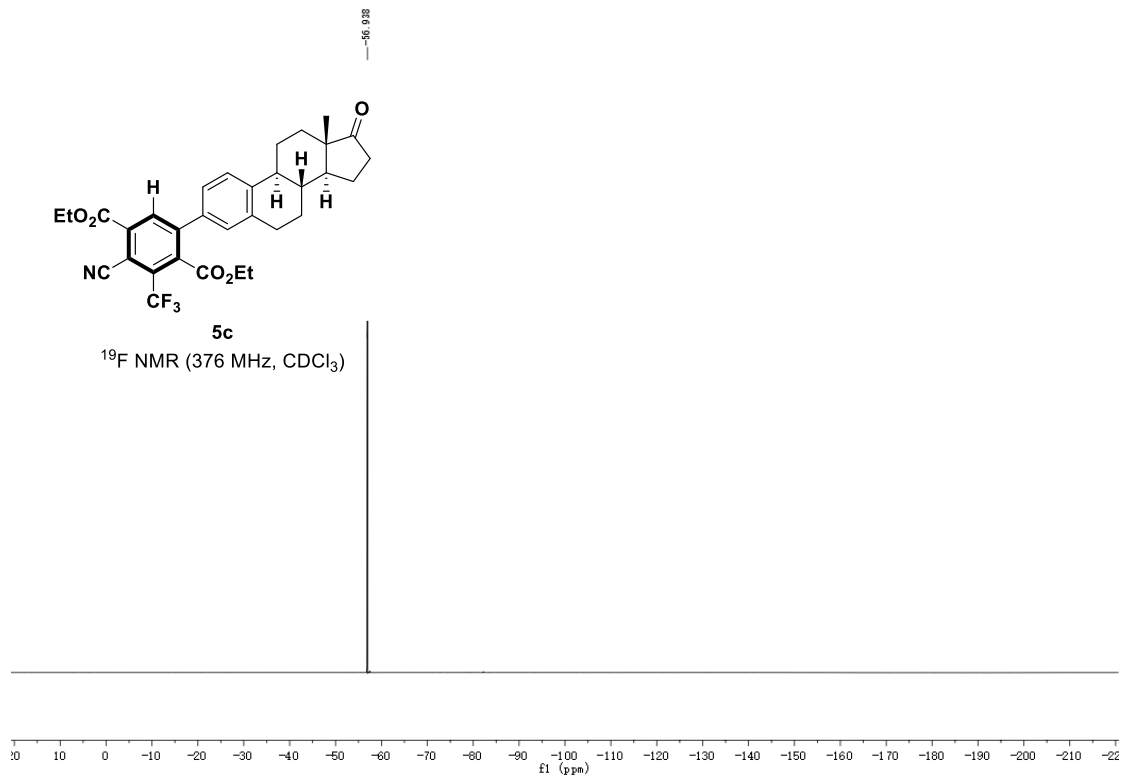
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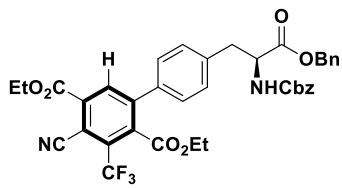


5c

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)

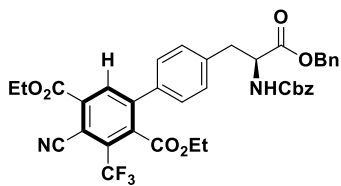
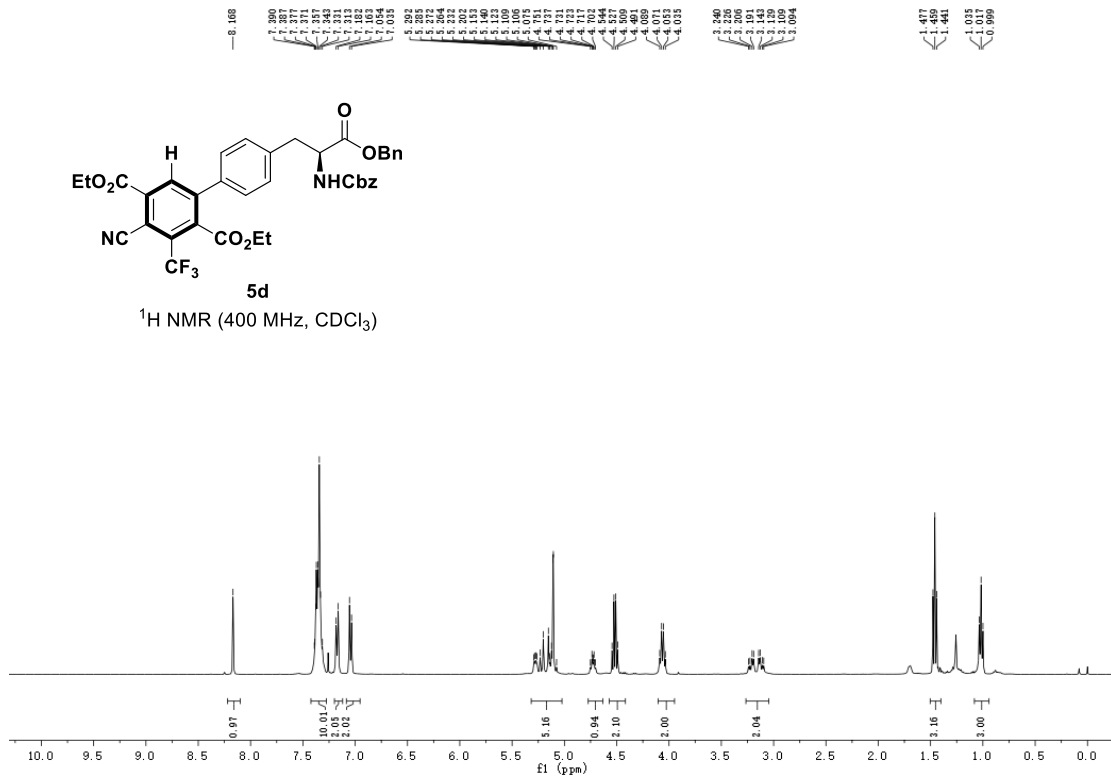






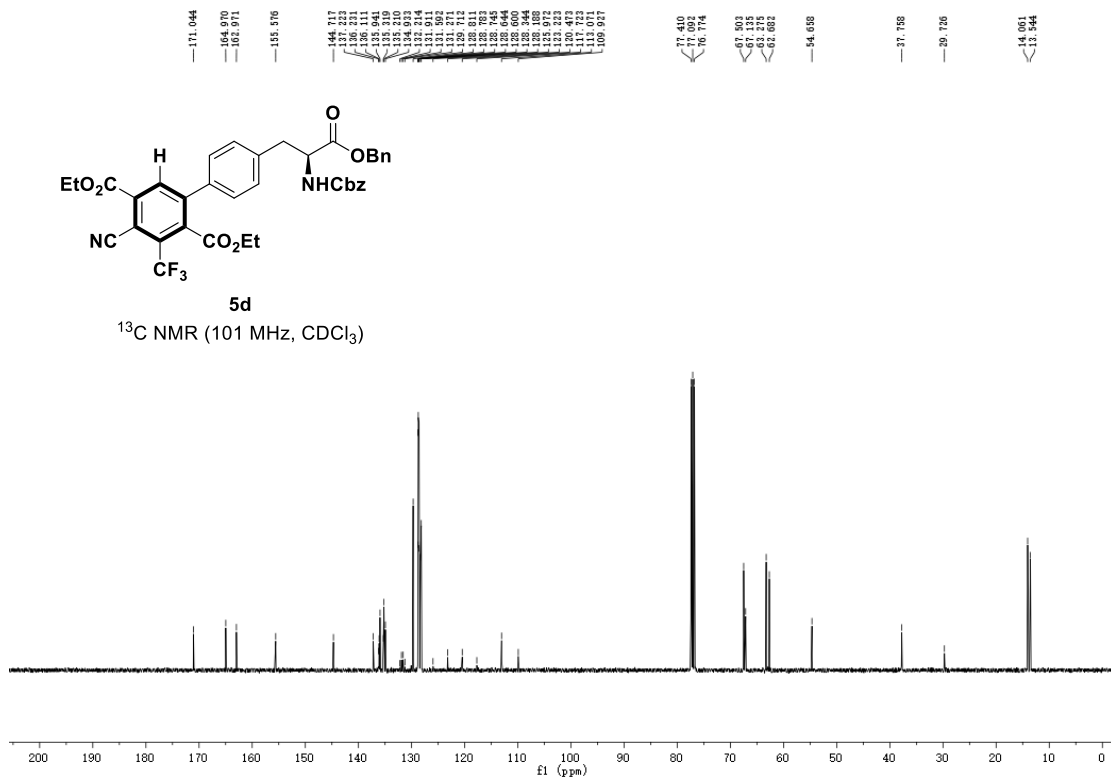
**5d**

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

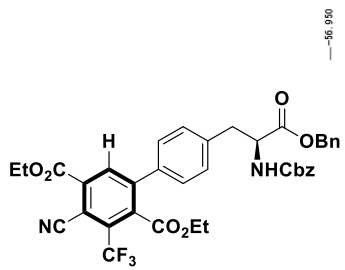


**5d**

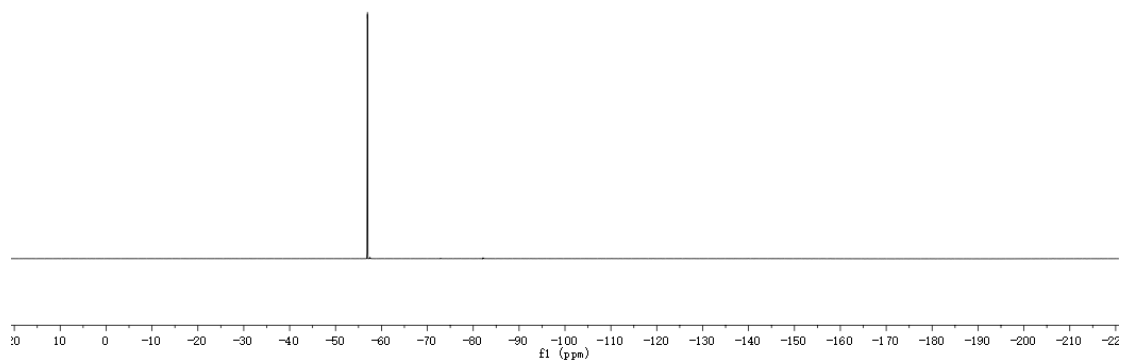
<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)

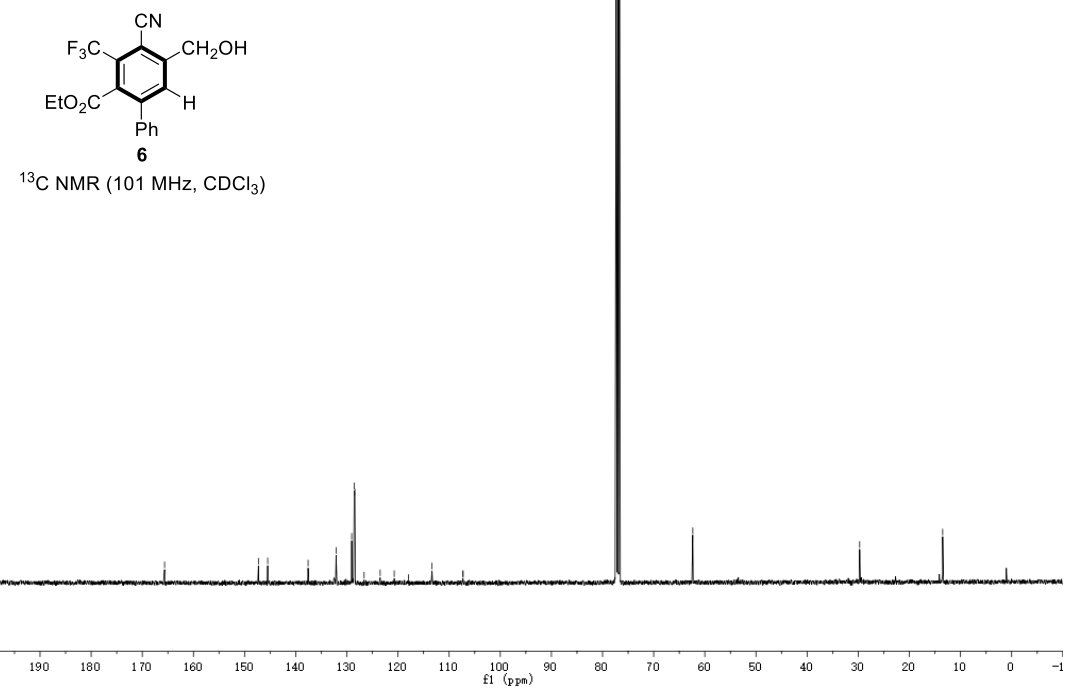
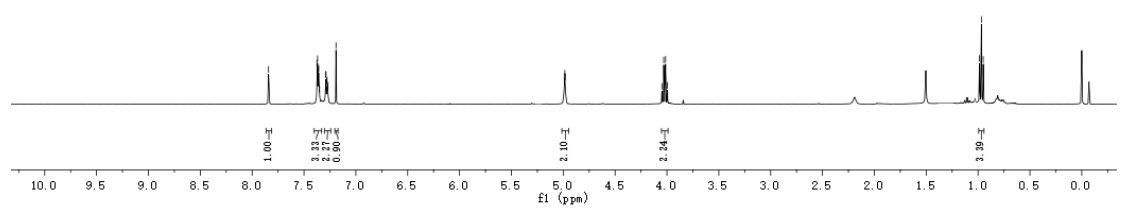
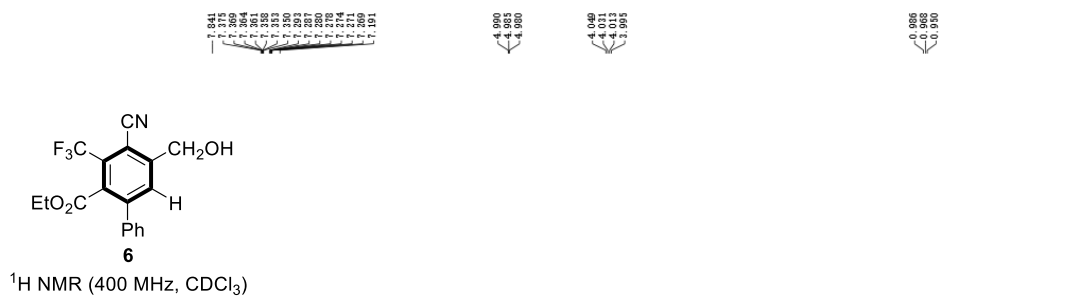


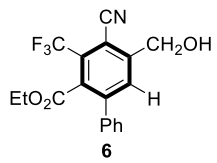




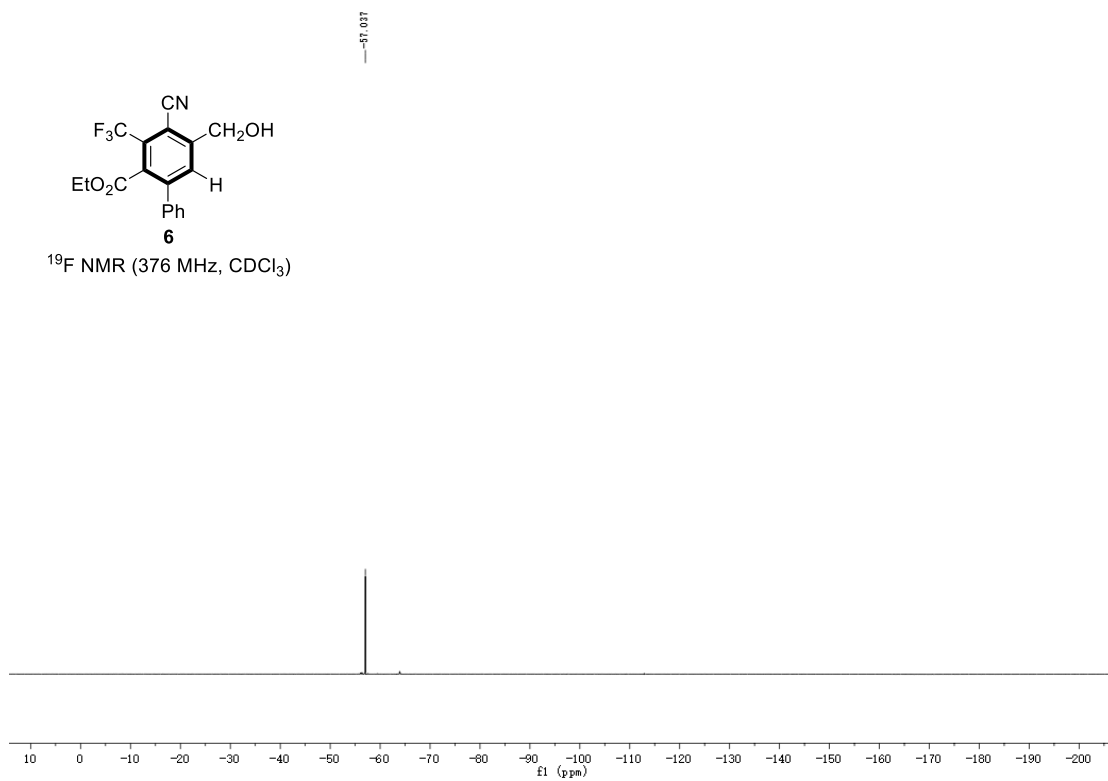
<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>)

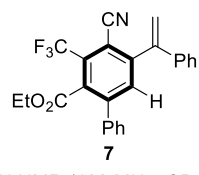




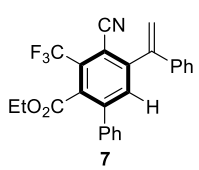
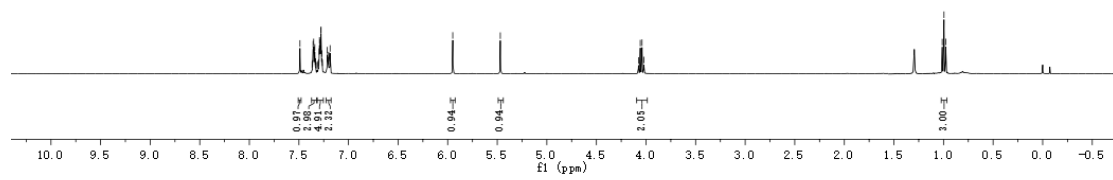


$^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )

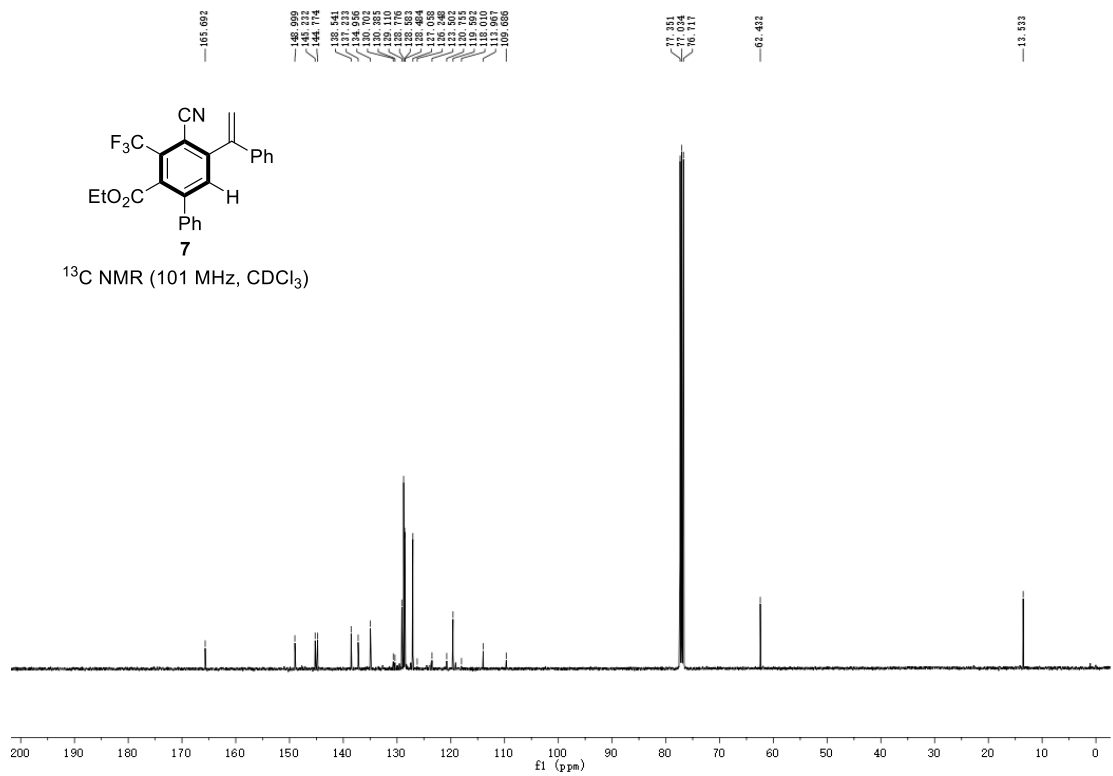


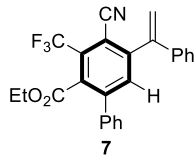


<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)



<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)





$^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )

