Substrate-directed chemo- and regioselective synthesis of polyfunctionalized trifluoromethylarenes via organoctalytic benzannulation

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Supplementary Information

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1. General experimental information

- Unless otherwise noted, all commercially available reagents were used without further purification. All of the solvents were treated according to known methods.
- Column chromatography was performed on silica gel (200-300 mesh). All reactions were monitored by thin layer chromatography (TLC) with silica gel-coated plates and products were visualized using UV light and I_2.
- Melting points were determined on a Mel-Temp apparatus and were not corrected.
- NMR data were obtained for ^1H at 400 MHz, 600 MHz or 700 MHz, and for ^{13}C at 100 MHz, 150 MHz or 175 MHz. Chemical shifts were reported in ppm from tetramethylsilane using solvent resonance in $CDCl_3$ solution as the internal standard.
- High resolution mass spectra (HRMS) were recorded on a Waters SYNAPT G2 or Agilent G1969-85000 using an electrospray (ESI) ionization source.
- 2-benzylidenemalononitriles **1** were synthesized following the literature procedure.[1] Tri-substituted CF_3-alkenes **2** were synthesized following the literature procedure.[2] (E)-2-Nitroallylic acetates **4** were synthesized following the literature procedure.[3]
- The relative configuration of compounds **3k**, **5g** and **Int. E** were determined unequivocally according to the X-ray diffraction analysis, and those of other products were deduced on the basis of these results.

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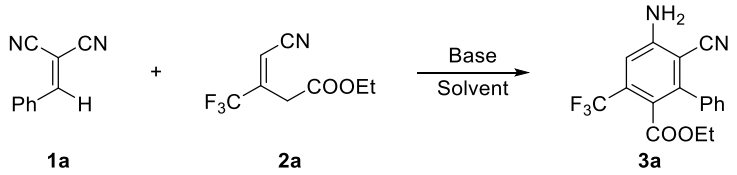
1. G. Kaupp, M. Reza Naimi-Jamal and J. Schmeyers, *Tetrahedron*, 2003, **59**, 3753.
2. X. H. He, L. Yang, Y. L. Ji, Q. Zhao, M. C. Yang, W. Huang, C. Peng and B. Han, *Chem. Eur. J.*, 2018, **24**, 1947.
3. (*a*) E. Gopi and I. N. Namboothiri, *J. Org. Chem.*, 2014, **79**, 7468; (*b*) W. Xiao, X. Yin, Z. Zhou, W. Du and Y. C. Chen, *Org. Lett.*, 2016, **18**, 116; (*c*) Y. Zheng, L. Cui, Y. Wang and Z. *J.* Zhou, *Org. Chem.*, 2016, **81**, 4340; (*d*) J. Y. Liu, J. Zhao, J. L. Zhang and P. F. Xu, *Org. Lett.*, 2017, **19**, 1846; (*e*) J. Zhang, G. Yin, Y. Du, Z. Yang, Y. Li and L. Chen, *J. Org. Chem.*, 2017, **82**, 13594; (*f*) D. Enders, L. Zhao and G. Raabe, *Synthesis*, 2018, **51**, 1391.

2. Optimization of the reaction condition of 1a and CF_3-alkene 2a

Table S1. Optimization of the reaction of **1a** and CF_3-alkene **2a**[a]



1a **2a** **3a**

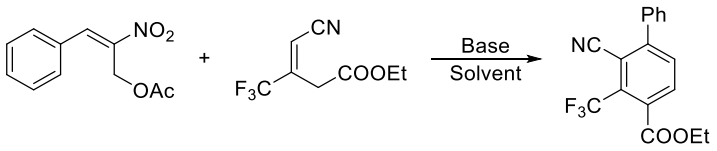
entry	solvent	base	yield (%)[b]
1	**DCM**	**DABCO**	**85**
2	EtOH	DABCO	78
3	Tol	DABCO	60
4	MeCN	DABCO	74
5	DCM	DIPEA	67
6	DCM	TEA	58
7	DCM	DBU	69
8	DCM	DMAP	80
9	DCM	PPh_3	48
10	DCM	K_2CO_3	27
11	DCM	Cs_2CO_3	37
12	DCM	$NaHCO_3$	12
13	DCM	K_2HPO_4	10
14[c]	DCM	DABCO	67
15[d]	DCM	DABCO	58
16[e]	DCM	DABCO	75
17[f]	DCM	DABCO	68

[a] Unless indicated otherwise, the reaction was performed with 0.2 mmol of **1a**, 0.24 mmol of **2a**, and 0.04 mmol of base in 1 mL solvent at room temperature (monitored by TLC). [b] Yield of isolated **3a**. [c] 0.02 mol DABCO was used. [d] 0.08 mol DABCO was used. [e] The reaction was performed at 0 °C. [f] The reaction was performed at 60 °C.

Initially, 2-benzylidenemalononitriles **1** and CF_3-alkenes **2** were chosen as model substrates to investigate the feasibility of this protocol (Table S1). Conducting the reaction in dichloromethane at room temperature catalyzed by DABCO efficiently afforded the desired penta-substituted trifluoromethylarene **3a** in 85% yield (entry 1). Screening other solvents in the presence of DABCO gave inferior results (entries 2-4). Next, we screened a series of bases employing dichloromethane as solvent to improve yield. Many kinds of organic bases could promote the reaction to offer the desired product in 48-80% yields (entries 5-9), which were lower than that using DABCO. Inorganic base is also available for the assembly of penta-substituted CF_3-benzene **3a**, but low yield was observed (entries 10-13). The influence of different catalyst loading or reaction temperature on the [4+2] aromatization reaction was also investigated, but no better results was obtained. Thus, conducting the reaction in DCM at room temperature with 20 mol% DABCO as catalyst was chosen as the optimal reaction condition, and this optimal condition was used for the substrate scope investigation.

3. Optimization of the reaction condition of 4a and CF_3-alkene 2a

Table S2. Optimization of the reaction of **4a** and CF_3-alkene **2a**[a]



4a **2a** **5a**

entry	solvent	base	yield (%)[b]
1	DCM	DABCO	21
2	MeCN	DABCO	40
3	Tol	DABCO	18
4	EtOH	DABCO	44
5	THF	DABCO	38
6	DMF	DABCO	36
7	EtOH	TEA	33
8	EtOH	DBU	35
9	EtOH	PPh_3	38
10	EtOH	DMAP	57
11	EtOH	K_2CO_3	-
12	EtOH	Cs_2CO_3	-
13	EtOH	$NaHCO_3$	-
14	EtOH	K_2HPO_4	-
15[c]	EtOH	DMAP	70
16[d]	EtOH	DMAP	65
17[c,e]	EtOH	DMAP	60
18[c,f]	**EtOH**	**DMAP**	**77**

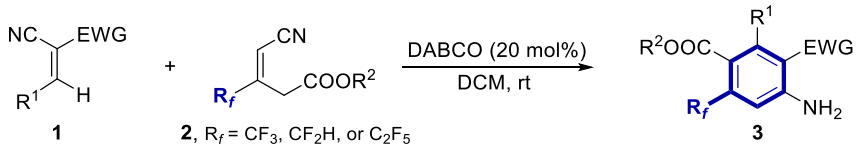
[a] Unless indicated otherwise, the reaction was performed with 0.2 mmol of 4**a**, 0.3 mmol of **2a**, and 0.04 mmol of base in 1 mL solvent at room temperature (monitored by TLC). [b] Yield of isolated 5**a**. [c] 0.08 mol DMAP was used. [d] 0.12 mol DMAP was used. [e] The reaction was performed at 0 °C. [f] The reaction was performed at 60 °C.

2-nitroallylic acetate **4a** was carefully selected as the dielectrophilic reaction partner to undergo [3+3] aromatization reaction with CF_3-alkenes **2a**. Unfortunately, the optimal reaction conditions for the aforementioned [4+2] aromatization did not efficiently delivery our desired aromatized CF_3-benzene **5a** (Table S2, entry 1). In order to further explore the feasibility of our protocol, various solvents were screened using 20 mol% DABCO as catalyst at room temperature (entries 2-6). Fortunately, acetonitrile, ethanol, tetrahydrofuran and dimethyl formamide were proved to be effective solvents for the [3+3] aromatization reaction, with ethanol showing the higher efficiency (entry 4). The screening of bases revealed that DMAP was the best choice providing target product **5a** in 57% yield (entries 7-14). Remarkably, Inorganic bases led to complex mixtures from which we fail to purify the expected compounds (entries 11-14). Thinking of the elimination of acetic acid during the reaction, we increased the catalyst loading to improve the reaction efficiency, and 40 mol% DMAP was the best

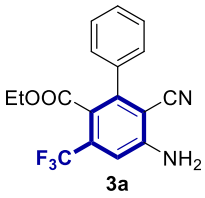
choice (entries 15-16). By screening the reaction temperature, further improvement of the reaction efficiency was achieved (entries 17-18). Thus, conducting the reaction in EtOH at 60 °C with 40 mol% DMAP as catalyst was chosen as the optimal reaction condition, and this optimal condition was used for the substrate scope investigation.

4. General procedure for the preparation of trifluoromethylarenes 3 and 5

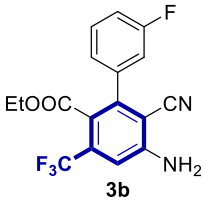
4.1 General procedure for the preparation of trifluoromethylarenes 3



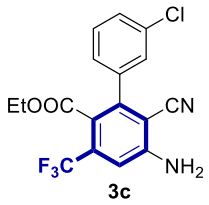
The reaction was carried out with **1** (0.20 mmol) and **2** (0.24 mmol), and DABCO (0.04 mmol) in DCM (1mL) at room temperature. The reaction was monitored by TLC until the reaction was completion. Then the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) to give the desired penta-substituted trifluoromethylarenes **3**, which was further analyzed by ^{1}H NMR, ^{13}C HMR, HRMS analysis.



3a: Obtained as a white solid; yield: 85% (56.8 mg) after flash chromatography. mp 155-157 °C, ^{1}H NMR (400 MHz, CDCl3): δ = 7.45-7.34 (m, 5H), 7.04 (s, 1H), 4.89 (s, 2H), 3.96 (q, J = 7.2 Hz, 2H), 0.94 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CDCl3): δ = 165.95, 150.20, 145.96, 135.94, 132.37 (q, J_{CF} = 32.3 Hz), 129.28, 128.70, 128.49, 122.62 (d, J_{CF} = 273.2 Hz), 122.04, 115.151, 111.29 (q, J_{CF} = 5.2 Hz), 99.64, 61.83, 13.42 ppm. ESI HRMS: calcd. For C17H13F3N2O2+Na 357.0827, found 357.0824.

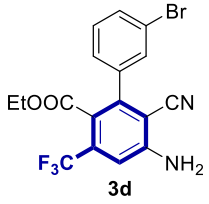


3b: Obtained as a white solid; yield: 80% (56.4 mg) after flash chromatography. mp 141-143 °C, ^{1}H NMR (400 MHz, CDCl3): δ = 7.45-7.40 (m, 1H), 7.18-7.07 (m, 4H), 4.92 (s, 2H), 4.01 (q, J = 7.2 Hz, 2H), 1.00 (t, J = 6.8 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CDCl3): δ = 165.63, 162.39 (d, J_{CF} = 246.7 Hz), 150.22, 144.40 (d, J_{CF} = 1.9 Hz), 137.79 (d, J_{CF} = 8.0 Hz), 132.54 (q, J_{CF} = 32.2 Hz), 130.27 (d, J_{CF} = 8.3 Hz), 124.70 (d, J_{CF} = 3.1 Hz), 122.52 (d, J_{CF} = 273.2 Hz), 122.01 (d, J_{CF} = 1.7 Hz), 116.37 (d, J_{CF} = 20.8 Hz), 116.12 (d, J_{CF} = 22.8 Hz), 114.83, 111.74 (q, J_{CF} = 5.0 Hz), 99.40, 61.98, 13.47 ppm. ESI HRMS: calcd. For C17H12F4N2O2+Na 375.0733, found 375.0732.



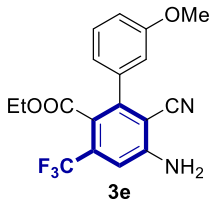
3c

3c: Obtained as a white solid; yield: 81% (59.7 mg) after flash chromatography. mp 125-127 °C, ^{1}H NMR (600 MHz, CDCl3): δ = 7.43-7.41 (m, 1H), 7.38 (t, *J* = 7.8 Hz, 1H), 7.34 (t, *J* = 1.8 Hz, 1H), 7.25-7.23 (m, 1H), 7.05 (s, 1H), 4.94 (s, 2H), 4.01 (q, *J* = 7.2 Hz, 2H), 1.00 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (150 MHz, CDCl3): δ = 165.73, 150.35, 144.32, 137.57, 134.54, 132.60 (q, J_{CF} = 32.4 Hz), 129.94, 129.56, 128.93, 127.13, 122.57 (q, J_{CF} = 273.3 Hz), 121.99, 114.94, 111.84 (q, J_{CF} = 5.3 Hz), 99.34, 62.12, 13.58 ppm. ESI HRMS: calcd. For C17H12ClF3N2O2+Na 391.0437, found 391.0429.



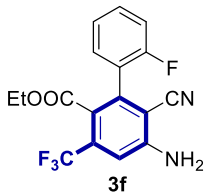
3d

3d: Obtained as a white solid; yield: 80% (66.1 mg) after flash chromatography. mp 113-115 °C, ^{1}H NMR (600 MHz, CDCl3): δ = 7.59-7.57 (m, 1H), 7.50 (t, *J* = 1.8 Hz, 1H), 7.34-7.29 (m, 2H), 7.05 (s, 1H), 4.92 (s, 2H), 4.02 (q, *J* = 7.2 Hz, 2H), 1.01 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (150 MHz, CDCl3): δ = 165.69, 150.30, 144.21, 137.80, 132.61 (d, J_{CF} = 32.1 Hz), 132.48, 131.74, 130.16, 127.59, 122.56 (d, J_{CF} = 273.2 Hz), 122.54, 122.06, 114.92, 111.83 (q, J_{CF} = 5.3 Hz), 99.39, 62.13, 13.62 ppm. ESI HRMS: calcd. For C17H12BrF3N2O2+Na 434.9932, found 434.9931.



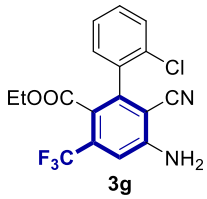
3e

3e: Obtained as a white solid; yield: 82% (59.7 mg) after flash chromatography. mp 145-147 °C, ^{1}H NMR (600 MHz, CDCl3): δ = 7.36 (t, *J* = 7.8 Hz, 1H), 7.06 (s, 1H), 7.00-6.89 (m, 3H), 4.92 (s, 2H), 4.03-3.99 (m, 2H), 3.83(s, 3H), 0.99 (t, *J* = 7.8 Hz, 3H) ppm; ^{13}C NMR (150 MHz, CDCl3): δ = 165.98, 159.40, 150.18, 145.73, 137.06, 132.33 (q, J_{CF} = 32.4 Hz), 129.64, 122.59 (d, J_{CF} = 273.3 Hz), 121.90, 121.08, 115.26, 115.15, 114.04, 111.28 (q, J_{CF} = 5.3 Hz), 99.50, 61.89, 55.35, 13.47 ppm. ESI HRMS: calcd. For C18H15F3N2O3+Na 387.0932, found 387.0927.



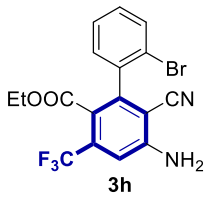
3f

3f: Obtained as a white solid; yield: 84% (59.2 mg) after flash chromatography. mp 137-139 °C, ^{1}H NMR (600 MHz, CDCl3): δ = 7.48-7.44 (m, 1H), 7.28-7.19 (m, 3H), 7.09 (s, 1H), 4.9 (s, 2H), 4.02-3.97 (m, 2H), 0.976 (t, J = 6.6 Hz, 3H) ppm; ^{13}C NMR (150 MHz, CDCl3): δ = 165.51, 159.38 (d, J_{CF} = 247.2 Hz), 150.12, 140.10, 132.72 (q, J_{CF} = 32.4 Hz), 131.58 (d, J_{CF} = 8.3 Hz), 130.69 (d, J_{CF} = 2.7 Hz), 124.21 (d, J_{CF} = 4.1 Hz), 123.59 (d, J_{CF} = 16.4 Hz), 122.51 (q, J_{CF} = 273.0 Hz), 122.40, 115.94 (d, J_{CF} = 21.3 Hz), 114.73, 112.22 (q, J_{CF} = 5.3 Hz), 100.21, 61.90, 13.42 ppm. ESI HRMS: calcd. For C17H12F4N2O2+Na 375.0733, found 375.0732.



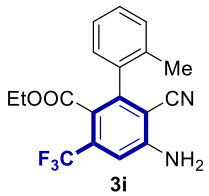
3g

3g: Obtained as a white solid; yield: 78% (57.5 mg) after flash chromatography. mp 130-132 °C, ^{1}H NMR (400 MHz, CDCl3): δ = 7.51-7.49 (m, 1H), 7.42-7.24 (m, 3H), 7.09 (s, 1H), 4.91 (s, 2H), 3.97 (q, J = 7.2 Hz, 2H), 0.95 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CDCl3): δ = 165.29, 150.05, 143.39, 134.82, 133.45, 132.74 (d, J_{CF} = 32.5 Hz), 130.72, 130.54, 129.75, 126.74, 122.55 (d, J_{CF} = 273.0 Hz), 122.05 (d, J_{CF} = 1.8 Hz), 114.55, 112.22 (q, J_{CF} = 5.1 Hz), 100.17, 61.81, 13.38 ppm. ESI HRMS: calcd. For C17H12ClF3N2O2+Na 391.0437, found 391.0437.



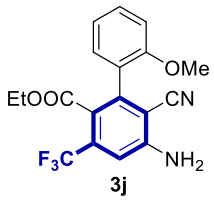
3h

3h: Obtained as a white solid; yield: 86% (71.1 mg) after flash chromatography. mp 115-117 °C, ^{1}H NMR (400 MHz, CDCl3): δ = 7.69 (dd, J_1 = 7.6 Hz, J_2 = 0.4 Hz, 1H), 7.40-7.24 (m, 3H), 7.09 (s, 1H), 4.92 (s, 2H), 3.97 (q, J = 7.2 Hz, 2H), 0.96 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CDCl3): δ = 165.23, 150.03, 144.86, 136.84, 132.91, 132.40 (d, J_{CF} = 32.5 Hz), 130.78, 130.52, 127.30, 123.23, 122.55 (d, J_{CF} = 273.1 Hz), 121.86 (d, J_{CF} = 1.9 Hz), 114.53, 112.22 (q, J_{CF} = 5.2 Hz), 100.16, 61.80, 13.39 ppm. ESI HRMS: calcd. For C17H12BrF3N2O2+Na 434.9932, found 434.9930.



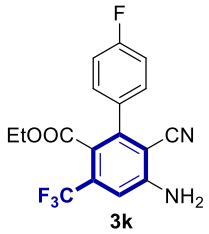
3i

3i: Obtained as a white solid; yield: 81% (56.4 mg) after flash chromatography. mp 127-129 °C, ^{1}H NMR (400 MHz, CDCl3): δ = 7.35-7.28 (m, 2H), 7.24-7.20 (m, 1H), 7.11-7.09 (m, 1H), 7.05 (s, 1H), 4.85 (s, 2H), 3.92 (q, *J* = 7.2 Hz, 2H), 2.17 (s, 3H), 0.90 (s, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CDCl3): δ = 165.60, 149.88, 145.95, 136.34, 135.29, 132.43 (d, J_{CF} = 32.4 Hz), 130.19, 129.37, 128.83, 125.67, 122.63 (d, J_{CF} = 273.0 Hz), 122.21 (d, J_{CF} = 1.8 Hz), 114.75, 111.38 (q, J_{CF} = 5.1 Hz), 100.09, 61.67, 19.61, 13.34 ppm. ESI HRMS: calcd. For C18H15F3N2O2+Na 371.0983, found 371.0980.



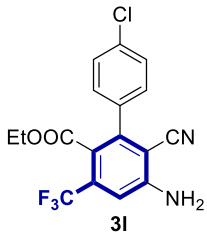
3j

3j: Obtained as a white solid; yield: 87% (63.4 mg) after flash chromatography. mp 127-129 °C, ^{1}H NMR (600 MHz, CDCl3): δ = 7.41-7.38 (m, 1H), 7.12 (dd, J_1 = 7.2 Hz, J_2 = 1.8 Hz, 1H), 7.01 (s, 1H), 7.00-6.97 (m, 2H), 4.84 (s, 2H), 3.95 (q, *J* = 7.2 Hz, 2H), 3.81 (s, 3H), 0.93 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (150 MHz, CDCl3): δ = 165.98, 156.64, 150.02, 143.31, 132.58 (q, J_{CF} = 32.3 Hz), 132.56, 131.06, 130.22, 124.93, 122.76 (d, J_{CF} = 273.2 Hz), 122.33, 120.63, 111.57 (q, J_{CF} = 5.3 Hz), 111.30, 100.85, 61.71, 55.81, 13.52 ppm. ESI HRMS: calcd. For C18H15F3N2O3+Na 387.0932, found 387.0930.



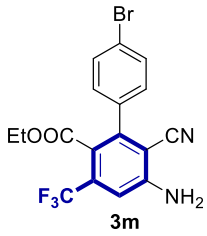
3k

3k: Obtained as a white solid; yield: 87% (61.3 mg) after flash chromatography. mp 121-123 °C, ^{1}H NMR (600 MHz, CDCl3): δ = 7.36-7.33 (m, 2H), 7.17-7.13 (m, 2H), 7.05 (s, 1H), 4.92 (s, 2H), 4.00 (q, *J* = 7.2 Hz, 2H), 1.00 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (150 MHz, CDCl3): δ = 165.84, 163.27 (d, J_{CF} = 248.1 Hz), 150.21, 144.83, 132.44 (q, J_{CF} = 32.4 Hz), 131.84 (d, J_{CF} = 3.6 Hz), 130.74 (d, J_{CF} = 8.6 Hz), 122.55 (d, J_{CF} = 273.2 Hz), 122.16 (d, J_{CF} = 2.1 Hz), 115.69 (d, J_{CF} = 21.8 Hz), 115.04, 111.50 (q, J_{CF} = 5.3 Hz), 99.65, 61.95, 13.52 ppm. ESI HRMS: calcd. For C17H12F4N2O2+Na 375.0733, found 375.0728.



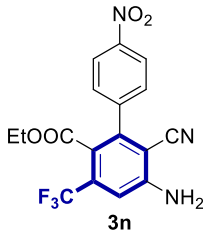
3l

3l: Obtained as a white solid; yield: 78% (57.5 mg) after flash chromatography. mp 175-177 °C, ^{1}H NMR (400 MHz, CDCl3): δ = 7.43 (d, *J* = 8.8 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 2H), 7.06 (s, 1H), 4.90 (s, 2H), 4.01 (q, *J* = 7.2 Hz, 2H), 1.01 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CDCl3): δ = 165.69, 150.20, 144.64, 135.64, 134.28, 132.53 (d, J_{CF} = 32.1 Hz), 130.15, 128.83, 122.52 (d, J_{CF} = 273.3 Hz), 122.07 (d, J_{CF} = 2.0 Hz), 144.93, 111.61 (q, J_{CF} = 5.2 Hz), 99.49, 61.99, 13.50 ppm. ESI HRMS: calcd. For C17H12ClF3N2O2+Na 391.0437, found 391.0437.



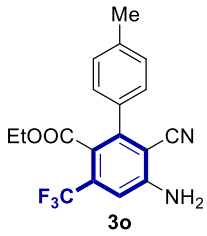
3m

3m: Obtained as a white solid; yield: 86% (71.1 mg) after flash chromatography. mp 187-189 °C, ^{1}H NMR (600 MHz, CDCl3): δ = 7.58 (d, *J* = 8.4 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 2H), 7.05 (s, 1H), 4.92 (s, 2H), 4.00 (q, *J* = 7.2 Hz, 2H), 1.00 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (150 MHz, CDCl3): δ = 165.80, 150.33, 144.71, 134.84, 132.61 (q, J_{CF} = 32.6 Hz), 131.86, 130.44, 123.94, 122.58 (d, J_{CF} = 273.5 Hz), 121.97, 115.05, 111.71 (q, J_{CF} = 5.4 Hz), 99.36, 62.11, 13.58 ppm. ESI HRMS: calcd. For C17H12BrF3N2O2+Na 434.9932, found 434.9938.



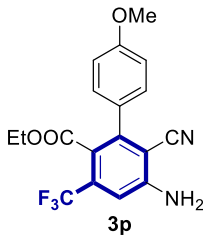
3n

3n: Obtained as a white solid; yield: 83% (63.0 mg) after flash chromatography. mp 195-197 °C, ^{1}H NMR (600 MHz, CDCl3): δ = 8.33-8.30 (m, 2H), 7.56-7.54 (m, 2H), 7.12 (s, 1H), 5.02 (s, 2H), 3.99 (q, *J* = 7.2 Hz, 2H), 1.00 (t, *J* = 6.6 Hz, 3H) ppm; ^{13}C NMR (150 MHz, CDCl3): δ = 165.42, 150.52, 148.39, 143.58, 142.47, 132,95 (q, J_{CF} = 32.6 Hz), 130.15, 123.81, 122.46 (q, J_{CF} = 273.3 Hz), 121.69, 114.68, 112.51 (q, J_{CF} = 5.3 Hz), 98.82, 62.30, 13.61 ppm. ESI HRMS: calcd. For C17H12F3N3O4+Na 402.0678, found 402.0670.



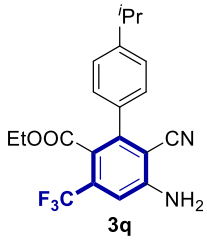
3o

3o: Obtained as a white solid; yield: 84% (58.5 mg) after flash chromatography. mp 129-131 °C, ^{1}H NMR (400 MHz, CDCl3): δ = 7.24 (s, 4H), 7.02 (s, 1H), 4.85 (s, 2H), 3.99 (q, *J* = 7.2 Hz, 2H), 2.39 (s, 3H), 0.98 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CDCl3): δ = 166.01, 150.10, 146.13, 139.25, 132.97, 132.31 (d, J_{CF} = 32.2 Hz), 129.18, 128.56, 122.64 (d, J_{CF} = 273.1 Hz), 122.17 (d, J_{CF} = 1.5 Hz), 115.27, 111.05 (q, J_{CF} = 5.1 Hz), 99.85, 61.79, 21.34, 13.46 ppm. ESI HRMS: calcd. For C18H15F3N2O2+Na 371.0983, found 371.0983.



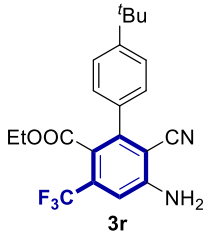
3p

3p: Obtained as a white solid; yield: 75% (54.6 mg) after flash chromatography. mp 139-141 °C, ^{1}H NMR (600 MHz, CDCl3): δ = 7.29-7.26 (m, 2H), 7.00 (s, 1H), 6.96-6.93 (m, 2H), 4.88 (s, 2H), 4.00 (q, *J* = 7.2 Hz, 2H), 3.83 (s, 3H), 0.99 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (150 MHz, CDCl3): δ = 166.26, 160.38, 150.27, 145.82, 132.31 (q, J_{CF} = 32.3 Hz), 130.14, 128.17, 122.71 (d, J_{CF} = 273.2 Hz), 122.22, 115.47, 114.01, 111.05 (q, J_{CF} = 5.3 Hz), 99.90, 61.93, 55.39, 13.65 ppm. ESI HRMS: calcd. For C18H15F3N2O3+Na 387.0932, found 387.0924.



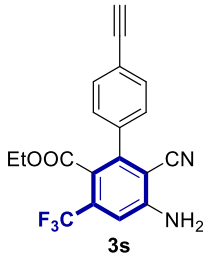
3q

3q: Obtained as a white solid; yield: 84% (63.2 mg) after flash chromatography. mp 183-185 °C, ^{1}H NMR (400 MHz, CDCl3): δ = 7.30-7.28 (m, 4H), 7.03 (s, 1H), 4.86 (s, 2H), 3.96 (q, *J* = 6.8 Hz, 2H), 2.95 (m, 1H), 1.27 (d, *J* = 7.2 Hz, 6H), 0.88 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CDCl3): δ = 166.04, 150.15, 150.09, 146.12, 133.29, 132.32 (d, J_{CF} = 32.2 Hz), 128.66, 126.54, 122.63 (d, J_{CF} = 273.2 Hz), 122.23 (d, J_{CF} = 1.9 Hz), 115.28, 111.02 (q, J_{CF} = 5.1 Hz), 99.73, 61.72, 33.95, 23.86, 13.33 ppm. ESI HRMS: calcd. For C20H19F3N2O2+Na 399.1296, found 399.1285.



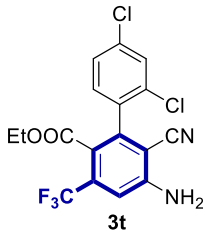
3r

3r: Obtained as a white solid; yield: 81% (63.2 mg) after flash chromatography. mp 203-205 °C, ^{1}H NMR (600 MHz, CDCl3): δ = 7.46-7.44 (m, 2H), 7.29-7.26 (m, 2H), 7.03 (s, 1H), 4.89 (s, 2H), 3.95 (q, *J* = 7.2Hz, 2H), 1.34 (s, 9H), 0.85 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (150 MHz, CDCl3): δ = 166.10, 152.34, 150.19, 146.06, 132.92, 132.31 (q, J_{CF} = 32.3 Hz), 128.37, 125.39, 122.61 (d, J_{CF} = 273.3 Hz), 122.15, 115.33, 111.02 (q, J_{CF} = 5.4 Hz), 99.58, 61.73, 34.74, 31.25, 13.28 ppm. ESI HRMS: calcd. For C21H21F3N2O2+Na 413.1453, found 413.1453.



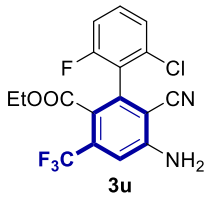
3s

3s: Obtained as a white solid; yield: 85% (60.9 mg) after flash chromatography. mp 131-133 °C, ^{1}H NMR (600 MHz, CDCl3): δ = 7.58-7.56 (m, 2H), 7.34-7.32 (m, 2H), 7.06 (s, 1H), 4.93 (s, 2H), 3.99 (q, *J* = 7.2 Hz, 2H), 3.16 (s, 1H), 0.99 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (150 MHz, CDCl3): δ = 165.74, 150.27, 145.05, 136.29, 132.52 (d, J_{CF} = 32.1 Hz), 132.22, 128.79, 123.32, 122.53 (d, J_{CF} = 273.3 Hz), 121.89 (d, J_{CF} = 2.1 Hz), 114.96, 111.61 (q, J_{CF} = 5.3 Hz), 99.29, 82.87, 78.70, 61.99, 13.48 ppm. ESI HRMS: calcd. For C19H13F3N2O2+Na 381.0827, found 381.0830.



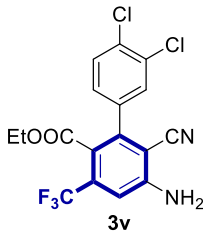
3t

3t: Obtained as a white solid; yield: 78% (62.9 mg) after flash chromatography. mp 161-162 °C, ^{1}H NMR (400 MHz, CDCl3): δ = 7.53 (d, *J* = 2.0 Hz, 1H), 7.33 (dd, J_1 = 8.4 Hz, J_2 = 2.0 Hz, 1H), 7.20 (d, *J* = 8.0 Hz, 1H), 7.10 (s, 1H), 4.93 (s, 2H), 4.01 (q, *J* = 7.2 Hz, 2H), 1.03 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CDCl3): δ = 165.08, 150.09, 142.31, 136.21, 136.21, 134.38, 133.33, 132.91 (d, J_{CF} = 32.6 Hz), 131.34, 129.73, 127.20, 122.46 (d, J_{CF} = 273.1 Hz), 122.06 (d, J_{CF} = 1.8 Hz), 114.36, 112.52 (q, J_{CF} = 5.1 Hz), 100.01, 61.98, 13.47 ppm. ESI HRMS: calcd. For C17H11Cl2F3N2O2+Na 425.0047, found 425.0048.



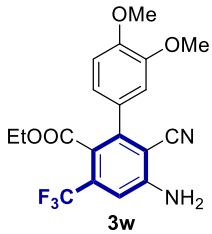
3u

3u: Obtained as a white solid; yield: 78% (60.3 mg) after flash chromatography. mp 108-110 °C, ^{1}H NMR (600 MHz, CDCl3): δ = 7.56-7.54 (m, 1H), 7.40 (dd, J_1 = 6.0 Hz, J_2 = 2.4 Hz, 1H), 7.10-7.07 (m, 2H), 4.94 (s, 2H), 4.08-4.04 (m, 2H), 1.05 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (150 MHz, CDCl3): δ = 165.24, 159.46, 157.81, 150.23, 138.54, 134.53, 134.47, 133.39, 133.38, 133.00 (q, J_{CF} = 32.4 Hz), 125.63, 125.51, 122.48 (q, J_{CF} = 273.3 Hz), 122.44, 117.92, 117.77, 116.69, 116.66, 114.53, 112.73 (q, J_{CF} = 5.3 Hz), 100.01, 62.21, 13.63 ppm. ESI HRMS: calcd. For C17H11ClF4N2O2+Na 409.0343, found 409.0346.



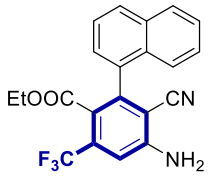
3v

3v: Obtained as a white solid; yield: 82% (66.1 mg) after flash chromatography. mp 158-160 °C, ^{1}H NMR (600 MHz, CDCl3): δ = 7.53 (d, J = 8.4 Hz, 1H), 7.54 (d, J = 2.4 Hz, 1H), 7.21 (dd, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 1H), 7.07 (s, 1H), 4.94 (s, 2H), 4.05 (q, J = 7.2 Hz, 2H), 1.06 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (150 MHz, CDCl3): δ = 165.57, 150.37, 143.26, 135.66, 134.02, 132.98, 132.73 (d, J_{CF} = 32.4 Hz), 130.78, 130.73, 128.28, 122.50 (d, J_{CF} = 273.3 Hz), 121.97, 114.82, 112.09 (q, J_{CF} = 5.3 Hz), 99.21, 62.26, 13.66 ppm. ESI HRMS: calcd. For C17H11Cl2F3N2O2+Na 425.0047, found 425.0036.



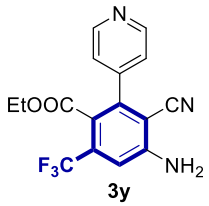
3w

3w: Obtained as a white solid; yield: 79% (62.3 mg) after flash chromatography. mp 159-161 °C, ^{1}H NMR (600 MHz, CDCl3): δ = 7.01 (s, 1H), 6.94-6.92 (m, 2H), 6.86 (d, J = 1.8 Hz, 1H), 4.89 (s, 2H), 4.00 (q, J = 7.2 Hz, 2H), 3.91 (s, 3H), 3.87 (s, 3H), 1.00 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (150 MHz, CDCl3): δ = 166.31, 150.28, 149.82, 148.77, 145.74, 132.33 (q, J_{CF} = 32.1 Hz), 128.31, 122.69 (d, J_{CF} = 273.2 Hz), 122.18, 121.63, 115.46, 111.96, 111.07 (q, J_{CF} = 5.3 Hz), 110.98, 99.82, 62.00, 56.06, 55.98, 13.69 ppm. ESI HRMS: calcd. For C19H17F3N2O4+Na 417.1038, found 417.1037.



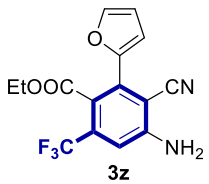
3x

3x: Obtained as a white solid; yield: 71% (54.6 mg) after flash chromatography. mp 185-187 °C, ^{1}H NMR (400 MHz, CDCl3): δ = 7.94-7.88 (m, 2H), 7.53-7.45 (m, 4H), 7.38 (dd, J_1 = 7.2 Hz, J_2 = 1.2 Hz, 1H), 7.12 (s, 1H), 4.88 (s, 2H), 3.69 (q, J = 7.2 Hz, 2H), 0.53 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CDCl3): δ = 165.54, 150.04, 144.79, 133.38, 133.27, 132.54 (d, J_{CF} = 32.2 Hz), 131.43, 129.73, 128.34, 127.26, 126.76, 126.31, 125.32, 124.92, 123.02 (d, J_{CF} = 1.8 Hz), 114.76, 122.66 (d, J_{CF} = 273.0 Hz), 111.79 (q, J_{CF} = 5.1 Hz), 100.88, 61.49, 12.95 ppm. ESI HRMS: calcd. For C21H15F3N2O2+Na 407.0983, found 407.0984.



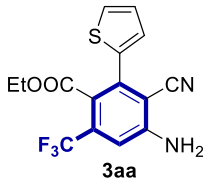
3y

3y: Obtained as a white solid; yield: 74% (49.6 mg) after flash chromatography. mp 256-258 °C, ^{1}H NMR (600 MHz, (CD3)2SO): δ = 8.69 (dd, J_1 = 4.2 Hz, J_2 = 1.2 Hz, 2H), 7.38 (dd, J_1 = 4.2 Hz, J_2 = 1.2 Hz, 2H), 7.14 (s, 2H), 3.87 (q, J = 7.2 Hz, 2H), 0.83 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (150 MHz, (CD3)2SO): δ = 165.12, 152.75, 149.74, 144.20, 143.20, 130.67 (q, J_{CF} = 31.5 Hz), 123.57, 122.75 (d, J_{CF} = 273.0 Hz), 120.02, 119.60, 112.59 (d, J_{CF} = 6.0 Hz), 96.10, 61.42, 13.10 ppm. ESI HRMS: calcd. For C16H12F3N3O2+Na 358.0779, found 358.0772.



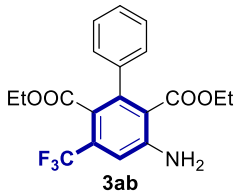
3z

3z: Obtained as a white solid; yield: 72% (46.7 mg) after flash chromatography. mp 124-126 °C, ^{1}H NMR (600 MHz, CDCl3): δ = 7.56 (d, J = 1.2 Hz, 1H), 7.02 (s, 1H), 6.93 (d, J = 3.0 Hz, 1H), 6.56 (dd, J_1 = 3.6 Hz, J_2 = 1.8 Hz, 1H), 4.97 (s, 2H), 4.24 (q, J = 7.2 Hz, 2H), 1.22 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (150 MHz, CDCl3): δ = 166.17, 150.72, 147.37, 144.12, 133.88, 132.90 (q, J_{CF} = 32.3 Hz), 122.46 (q, J_{CF} = 273.3 Hz), 120.64, 115.43, 112.81, 112.00, 111.63 (q, J_{CF} = 5.4 Hz), 96.78, 62.21, 13.80 ppm. ESI HRMS: calcd. For C15H11F3N2O3+Na 347.0619, found 347.0615.



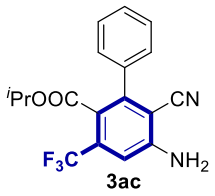
3aa

3aa: Obtained as a white solid; yield: 71% (48.3 mg) after flash chromatography. mp 142-144 °C, ^{1}H NMR (400 MHz, CDCl3): δ = 7.48 (dd, J_1 = 4.8 Hz, J_2 = 1.2 Hz, 1H), 7.18 (dd, J_1 = 3.2 Hz, J_2 = 0.8 Hz, 1H), 7.12-7.10 (m, 1H), 7.05 (s, 1H), 4.91 (s, 2H), 4.08 (q, J = 6.8 Hz, 2H), 1.08 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CDCl3): δ = 165.74, 150.24, 138.54, 135.14, 132.32 (d, J_{CF} = 32.5 Hz), 129.56, 128.21, 127.27, 122.49 (d, J_{CF} = 273.2 Hz), 123.14 (d, J_{CF} = 1.5 Hz), 114.96, 111.98 (q, J_{CF} = 5.1 Hz), 100.45, 62.07, 13.55 ppm. ESI HRMS: calcd. For C15H11F3N2O2S+Na 363.0391, found 363.0391.



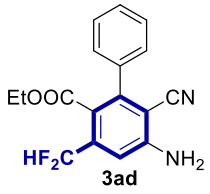
3ab

3ab: Obtained as a white solid; yield: 78% (59.5 mg) after flash chromatography. mp 128-130 °C, ^{1}H NMR (600 MHz, CDCl3): δ = 7.33-7.32 (m, 3H), 7.23-7.21 (m, 2H), 6.99 (s, 1H), 5.23 (s, 2H), 3.91 (q, J = 7.2 Hz, 2H), 3.84 (q, J = 7.2 Hz, 2H), 0.93 (t, J = 7.2 Hz, 3H), 0.68 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (150 MHz, CDCl3): δ = 167.83, 166.88, 147.85, 142.76, 139.05, 130.12 (q, J_{CF} = 31.8 Hz), 128.60, 127.70, 127.64, 123.0 (q, J_{CF} = 272.1 Hz), 122.09, 117.64, 112.80 (q, J_{CF} = 4.5 Hz), 61.42, 61.01, 13.46, 13.08 ppm. ESI HRMS: calcd. For C19H18F3NO4+Na 404.1086, found 404.1088.

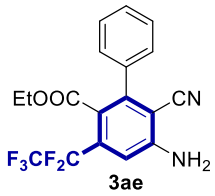


3ac

3ac: Obtained as a white solid; yield: 78% (54.3 mg) after flash chromatography. mp 130-132 °C, ^{1}H NMR (600 MHz, CDCl3): δ = 7.51-7.46 (m, 3H), 7.35-7.33 (m, 2H), 7.26 (s, 1H), 5.63 (s, 2H), 4.85-4.79 (m, 1H), 0.94 (d, J = 6.6 Hz, 6H) ppm; ^{13}C NMR (150 MHz, CDCl3): δ =163.83, 152.07, 149.66, 134.37, 133.22 (d, J_{CF} = 32.3 Hz), 130.14, 128.70, 128.51, 124.35, 121.48 (d, J_{CF} = 275.4 Hz), 113.64, 112.74, 101.85, 93.41, 70.58, 20.93 ppm. ESI HRMS: calcd. For C18H15F3N2O2+Na 371.0983, found 371.0980.

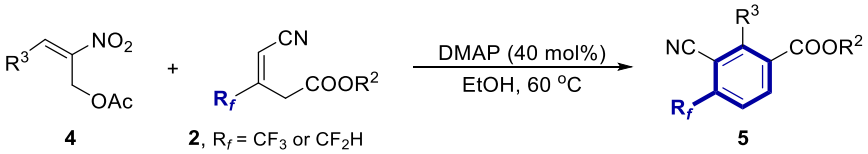


3ad: Obtained as a white solid; yield: 76% (48.1 mg) after flash chromatography. mp 132-134 °C, ^{1}H NMR (600 MHz, CDCl3): δ = 7.45-7.43 (m, 3H), 7.33-7.31 (m, 2H), 7.05 (s, 1H), 7.01 (t, J_{CF} = 55.8 Hz, 1H), 4.90 (s, 2H), 3.91 (q, *J* = 7.2 Hz, 2H), 0.81 (t, *J* = 6.6 Hz, 3H) ppm; ^{13}C NMR (150 MHz, CDCl3): δ = 166.58, 150.90, 146.50, 138.00 (t, J_{CF} = 21.6 Hz), 137.15, 128.92, 128.47, 128.44, 121.50 (t, J_{CF} = 3.5 Hz), 115.57, 111.66 (t, *JCF* = 239.7 Hz), 110.45 (t, J_{CF} = 8.0 Hz), 98.56, 61.53, 13.28 ppm. ESI HRMS: calcd. For C17H14F2N2O2+Na 339.0921, found 339.0920

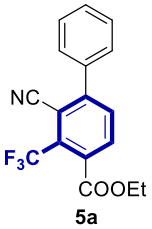


3ae: Obtained as a white solid; yield: 88% (67.6 mg) after flash chromatography. mp 129-131 °C, ^{1}H NMR (700 MHz, CDCl3): δ = 7.44-7.43 (m, 3H), 7.36-7.35 (m, 2H), 6.93 (s, 1H), 4.85 (s, 1H), 3.92 (q, *J* = 7.0 Hz, 2H), 0.93 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (175 MHz, CDCl3): δ = 165.86, 149.66, 145.70, 135.58, 130.34 (t, J_{CF} = 23.3 Hz), 129.32, 128.92, 128.40, 123.41 (t, J_{CF} = 2.5 Hz), 118.61 (dt, J_{CF1} = 285.4 Hz, J_{CF2} = 37.8 Hz), 115.04, 113.0 (tq, J_{CF1} = 255.2 Hz, J_{CF2} = 38.9 Hz), 112.84 (t, J_{CF} = 8.2 Hz), 100.34, 61.73, 13.37 ppm. ESI HRMS: calcd. For C18H13F5N2O2+Na 407.0795, found 407.0793.

4.2 General procedure for the preparation of trifluoromethylarenes 5

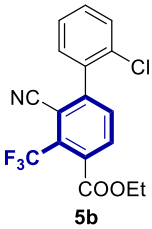


The reaction was carried out with **4** (0.20 zxmmol) and **2** (0.30 mmol), and DMAP (0.08 mmol) in EtOH (1 mL) at 60 °C. The reaction was monitored by TLC until the reaction was completion. Then the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 40:1) to give the final tetra-substituted trifluoromethylated benzenes **5**, which was further analyzed by ^{1}H NMR, ^{13}C HMR, HRMS analysis.



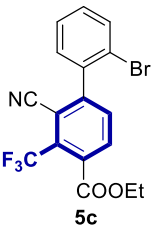
5a

5a: Obtained as a white solid; yield: 76% (48.5 mg) after flash chromatography. mp 68-70 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80 (d, *J* = 8.0 Hz, 1H), 7.72 (d, *J* = 8.4 Hz, 1H), 7.52 (s, 5H), 4.43 (q, *J* = 7.2 Hz, 2H), 1.40 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.42, 149.75, 136.56, 132.95 (d, J_{CF} = 2.5 Hz), 132.18, 131.15 (d, J_{CF} = 32.3 Hz), 129.73, 128.95, 128.93, 122.09 (d, J_{CF} = 274.3 Hz), 114.45, 110.23, 62.91, 13.88 ppm. ESI HRMS: calcd. For $C_{17}H_{12}F_3NO_2$+Na 342.0718, found 342.0714.



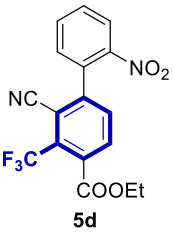
5b

5b: Obtained as a white solid; yield: 75% (53.1 mg) after flash chromatography. mp 68-70 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.83 (d, *J* = 8.0 Hz, 1H), 7.7 (d, *J* = 8.0 Hz, 1H), 7.56 (dd, J_1 = 8.0 Hz, J_2 = 1.2 Hz, 1H), 7.48-7.40 (m, 2H), 7.34 (dd, J_1 = 7.6 Hz, J_2 = 2.0 Hz, 1H), 4.45 (q, *J* = 7.2 Hz, 2H), 1.41 (t, *J* = 6.8Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.26, 147.22, 133.98, 133.56 (d, J_{CF} = 2.5 Hz), 132.82, 132.03, 131.10, 130.80, 130.74 (d, J_{CF} = 32.6 Hz), 130.57, 130.21, 127.23, 121.97 (d, J_{CF} = 274.1 Hz), 113.68, 111.90, 63.00, 13.88 ppm. ESI HRMS: calcd. For $C_{17}H_{11}ClF_3NO_2$+Na 376.0328, found 376.0325.



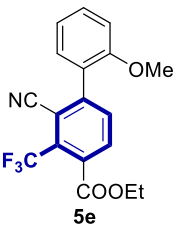
5c

5c: Obtained as a white solid; yield: 71% (56.5 mg) after flash chromatography. mp 96-98 °C, ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.82 (d, *J* = 8.4 Hz, 1H), 7.73 (d, J_1 = 8.4 Hz, J_2 = 1.2 Hz, 1H), 7.66 (d, *J* = 7.8 Hz, 1H), 7.46 (td, J_1 = 8.4 Hz, J_2 = 1.2 Hz, 1H), 7.36 (td, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 1H), 7.31 (dd, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 1H), 4.44 (q, *J* = 7.2 Hz, 2H), 1.40 (t, *J* = 7.2Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 166.36, 137.54, 134.02, 133.60 (d, J_{CF} = 2.3 Hz), 133.43, 133.43, 132.11, 131.27, 130.75, 130.74 (d, J_{CF} = 32.9 Hz), 127.89, 122.57, 122.03 (d, J_{CF} = 274.2 Hz) 113.73, 111.93, 63.10, 13.97 ppm. ESI HRMS: calcd. For $C_{17}H_{11}BrF_3NO_2$+Na 419.9823, found 419.9819.



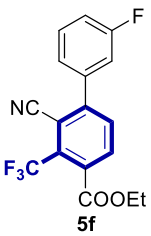
5d

5d: Obtained as a white solid; yield: 80% (58.3 mg) after flash chromatography. mp 74-76 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.29 (dd, J_1 = 8.0 Hz, J_2 = 0.8 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.82-7.71 (m, 2H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.41 (dd, J_1 = 7.6 Hz, J_2 = 1.6 Hz, 1H), 4.45 (q, *J* = 7.2 Hz, 2H), 1.42 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.02, 147.41, 146.86, 133.98, 133.62 (d, J_{CF} = 2.3 Hz), 132.49, 132.07, 132.00, 131.94, 130.97, 130.77 (d, J_{CF} = 32.9 Hz), 125.51, 121.86 (d, J_{CF} = 274.2 Hz), 113.61, 111.14, 63.05, 13.87 ppm. ESI HRMS: calcd. For $C_{17}H_{11}F_3N_2O_4$+Na 387.0569, found 387.0570.



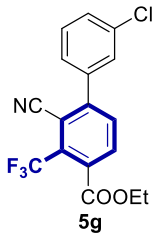
5e

5e: Obtained as a white solid; yield: 75% (52.4 mg) after flash chromatography. mp 86-88 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.77 (d, *J* = 8.0 Hz, 1H), 7.67(d, *J* = 8.0 Hz, 1H), 7.47 (m, 1H), 7.23 (dd, J_1 = 7.6 Hz, J_2 = 1.6 Hz, 1H), 7.08 (t, *J* = 7.2 Hz, 1H), 7.04 (d, *J* = 8.4 Hz, 1H), 4.43 (q, *J* = 7.2 Hz, 2H), 3.83 (s, 3H), 1.40 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.61, 156.41, 147.06, 134.16, 132.63 (d, J_{CF} = 2.5 Hz), 131.86, 131.38, 130.57, 130.46 (d, J_{CF} = 32.2 Hz), 125.54, 122.17 (d, J_{CF} = 274.2 Hz), 120.94, 114.42, 111.54, 62.80, 55.52, 13.89 ppm. ESI HRMS: calcd. For $C_{18}H_{14}F_3NO_3$+Na 372.0823, found 372.0825.



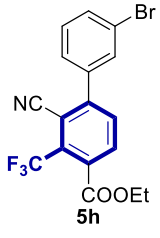
5f

5f: Obtained as a white solid; yield: 75% (50.6 mg) after flash chromatography. mp 95-97 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82 (d, *J* = 8.4 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.54-7.48 (m, 1H), 7.31 (d, *J* = 8.0 Hz, 1H), 7.24-7.20 (m, 2H), 4.44 (q, *J* = 7.2 Hz, 2H), 1.40 (t, *J* = 6.8 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.21, 162.68 (d, J_{CF} = 247.0 Hz), 148.26, 138.44 (d, J_{CF} = 7.8 Hz), 133.45 (d, J_{CF} = 2.5 Hz), 133.26, 132.34, 131.28 (d, J_{CF} = 32.5 Hz), 130.69 (d, J_{CF} = 8.3 Hz), 124.83 (d, J_{CF} = 3.1 Hz), 121.98 (d, J_{CF} = 274.2 Hz), 116.80 (d, J_{CF} = 20.9 Hz), 116.17 (d, J_{CF} = 22.8 Hz), 114.11, 110.39, 63.00, 13.87 ppm. ESI HRMS: calcd. For $C_{17}H_{11}F_4NO_2$+Na 360.0624, found 360.0625.



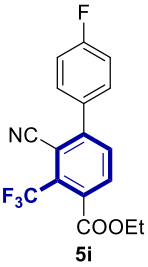
5g

5g: Obtained as a white solid; yield: 80% (56.6 mg) after flash chromatography. mp 89-91 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82 (d, *J* = 8.0 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.51-7.41 (m, 4H), 4.44 (q, *J* = 7.2 Hz, 2H), 1.40 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.19, 148.11, 138.17, 134.96, 133.49 (d, J_{CF} = 2.6 Hz), 133.25, 132.37, 131.27 (d, J_{CF} = 32.3 Hz), 130.23, 129.89, 129.00, 127.213, 121.97 (d, J_{CF} = 274.3 Hz), 114.10, 110.38, 63.01, 13.87 ppm. ESI HRMS: calcd. For $C_{17}H_{11}ClF_3NO_2$+Na 376.0328, found 376.0326.



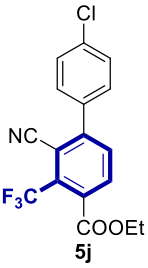
5h

5h: Obtained as a white solid; yield: 76% (60.5 mg) after flash chromatography. mp 102-104 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 8.4 Hz,1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.66 (d, *J* = 8.0 Hz,1H), 7.64 (d, *J* = 1.2 Hz,1H), 7.48 (d, *J* = 7.6 Hz, 1H), 7.40（dd, J_1 = 8.0 Hz, J_2 = 7.6 Hz, 1H）4.44 (q, *J* = 7.2 Hz, 2H), 1.40 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.19, 148.00, 138.42, 133.47 (d, J_{CF} = 2.7 Hz), 133.24, 132.82, 132.36, 131.834, 131.29 (d, J_{CF} = 32.6 Hz), 130.43, 127.66, 122.96, 122.54 (d, J_{CF} = 273.9 Hz), 114.08, 110.25, 63.01, 13.87 ppm. ESI HRMS: calcd. For $C_{17}H_{11}BrF_3NO_2$+Na 419.9823, found 419.9821.



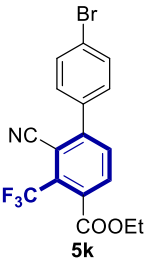
5i

5i: Obtained as a white solid; yield: 71% (47.9 mg) after flash chromatography. mp 44-46 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80 (d, *J* = 8.4 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.51 (dd, J_1 = 8.8 Hz, J_2 = 5.2 Hz, 2H), 7.223 (t, *J* = 8.8 Hz, 2H), 4.43 (q, *J* = 6.8 Hz, 2H), 1.40 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.29, 163.64 (d, J_{CF} = 249.1 Hz), 148.65, 133.29, 133.11 (d, J_{CF} = 2.7 Hz), 132.56 (d, J_{CF} = 3.6 Hz), 132.29, 131.25 (d, J_{CF} = 32.4 Hz), 130.95 (d, J_{CF} = 8.6 Hz), 123.38, 120.73(d, J_{CF} = 277.4 Hz), 116.17 (d, J_{CF} = 21.9 Hz), 112.28, 114.37, 110.32, 62.96, 13.87 ppm. ESI HRMS: calcd. For $C_{17}H_{11}F_4NO_2$+Na 360.0624, found 360.0627.



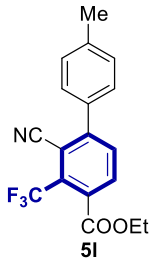
5j

5j: Obtained as a white solid; yield: 77% (54.5 mg) after flash chromatography. mp 94-96 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 8.4 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.51 (dd, J_1 = 6.4, J_2 = 2.0 Hz, 2H), 7.46(dd, J_1 =6.4 Hz, J_2=2.0 Hz, 2H), 4.43(q, *J* = 6.8 Hz, 2H), 1.40(t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.23, 148.45, 136.27, 134.89, 133.29 (d, J_{CF} = 2.4 Hz), 133.20, 132.36, 131.31 (d, J_{CF} = 32.3 Hz), 130.29, 129.28, 121.96 (d, J_{CF} = 268.2 Hz), 114.29, 110.27, 62.99, 13.87 ppm. ESI HRMS: calcd. For $C_{17}H_{11}ClF_3NO_2$+Na 376.0328, found 376.0331.



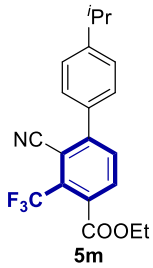
5k

5k: Obtained as a white solid; yield: 70% (55.7 mg) after flash chromatography. mp 101-103 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80 (d, *J* = 8.0 Hz, 1H), 7.70 (d, *J* = 8.4 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.40 (d, *J* = 8.4 Hz, 1H), 4.43 (q, *J* = 7.2 Hz, 2H), 1.40 (t, *J* = 7.2 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.23, 148.46, 135.36, 133.31 (d, J_{CF} = 2.5 Hz), 133.14, 132.38, 132.23, 131.32 (d, J_{CF} = 32.4 Hz), 130.51, 124.52, 121.98 (d, J_{CF} = 274.4 Hz), 114.28, 110.20, 62.99, 13.87 ppm. ESI HRMS: calcd. For $C_{17}H_{11}BrF_3NO_2$+Na 419.9823, found 419.9826.



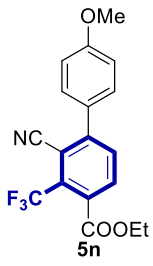
5l

5l: Obtained as a white solid; yield: 80% (53.3 mg) after flash chromatography. mp 62-64 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.77 (d, *J* = 8.0 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.42 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 4.43 (q, *J* = 7.2 Hz, 2H), 2.44 (s, 3H), 1.40 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.48, 149.85, 139.96, 133.68, 133.32, 132.68 (d, J_{CF} = 2.5 Hz), 132.12, 131.13 (d, J_{CF} = 32.3 Hz), 129.64, 128.85, 122.12 (d, J_{CF} = 274.2 Hz), 114.63, 110.12, 62.867, 21.33, 13.88 ppm. ESI HRMS: calcd. For $C_{18}H_{14}F_3NO_2$+Na 356.0874, found 356.0877.



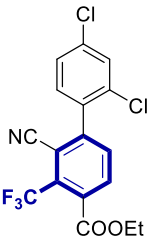
5m

5m: Obtained as a white solid; yield: 71% (51.3 mg) after flash chromatography. mp 58-60 °C, ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.82 (d, J = 7.8 Hz, 1H), 7.76 (d, J = 7.8 Hz, 1H), 7.51-7.49 (m, 2H), 7.43-7.40 (m, 2H), 4.47 (q, *J* = 7.2 Hz, 2H), 3.05-3.01 (m, 1H), 1.44 (t, *J* = 7.2 Hz, 3H), 1.34 (d, *J* = 6.6 Hz, 6H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 166.60, 150.79, 149.87, 133.99, 133.49, 132.70 (d, J_{CF} = 2.9 Hz), 132.20, 131.22 (d, J_{CF} = 32.1 Hz), 129.05, 127.14, 122.20 (d, J_{CF} = 274.2 Hz), 114.74, 110.06, 62.96, 34.06, 23.92, 13.96 ppm. ESI HRMS: calcd. For $C_{20}H_{18}F_3NO_2$+Na 384.1187, found 384.1185.



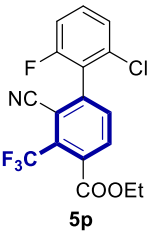
5n

5n: Obtained as a white solid; yield: 85% (59.4 mg) after flash chromatography. mp 101-103 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 8.0 Hz, 1H), 7.70（d, *J* = 8.0 Hz, 1H）, 7.48 (dd, J_1 = 6.8 Hz, J_2 = 2.0 Hz, 2H) , 7.04 (dd, J_1 = 6.8 Hz, J_2 = 2.0 Hz, 2H), 4.42 (q, *J* = 7.2 Hz, 2H), 3.88 (s, 1H), 1.40 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.51, 160.85, 149.51, 133.24, 132.43 (d, J_{CF} = 2.5 Hz), 132.11, 131.19 (d, J_{CF} = 32.2 Hz), 130.40, 128.76, 122.12 (d, J_{CF} = 274.3 Hz), 114.76, 109.93, 62.85, 55.43, 13.88 ppm. ESI HRMS: calcd. For $C_{18}H_{14}F_3NO_3$+Na 372.0823, found 372.0821.



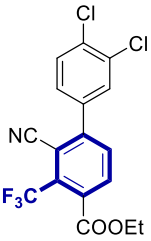
5o

5o: Obtained as a white solid; yield: 77% (59.8 mg) after flash chromatography. mp 110-112 °C, ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.83 (d, *J* = 8.4 Hz, 1H), 7.66 (d, *J* = 8.4 Hz, 1H), 7.58 (d, *J* = 1.8 Hz, 1H), 7.40 (dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1H), 7.27 (d, *J* = 8.4 Hz, 1H), 4.44 (q, *J* = 7.2 Hz, 2H), 1.40 (t, *J* = 7.2 Hz, 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 166.14, 146.15, 136.75, 134.00, 133.95, 133.92, 133.80, 132.28, 131.65, 130.96 (d, J_{CF} = 32.4 Hz), 130.27, 127.80, 121.94 (d, J_{CF} = 274.4 Hz), 113.65, 108.80, 63.17, 13.96 ppm. ESI HRMS: calcd. For $C_{17}H_{10}Cl_2F_3NO_2$+Na 409.9938, found 409.9937.



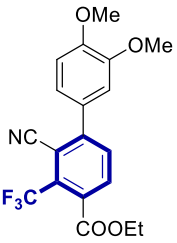
5p

5p: Obtained as a white solid; yield: 75% (55.8 mg) after flash chromatography. mp 65-67 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (d, *J* = 8.0 Hz, 1H), 7.69 (d, *J* = 8.0 Hz, 1H), 7.48-7.38 (m, 2H), 7.21-7.17 (m, 1H), 4.46 (q, *J* = 7.2 Hz, 2H), 1.42 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.10, 161.17, 158.67, 141.09, 134.57, 134.25 (d, J_{CF} = 3.5Hz), 134.14 (d, J_{CF} = 2.5Hz) 132.34, 131.91 (d, J_{CF} = 9.4Hz), 130.94 (d, J_{CF} = 32.8Hz), 125.87 (d, J_{CF} = 18.8 Hz), 121.89 (d, J_{CF} = 274.4 Hz), 114.77 (d, J_{CF} = 21.8 Hz), 113.34, 112.86, 63.06, 13.88 ppm. ESI HRMS: calcd. For $C_{17}H_{10}ClF_4NO_2$+Na 394.0234, found 394.0235.



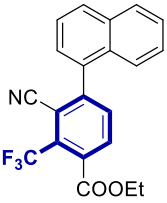
5q

5q: Obtained as a white solid; yield: 77% (59.8 mg) after flash chromatography. mp 118-120 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.83(d, *J* = 8.0 Hz, 1H), 7.70(d, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 8.4 Hz, 1H), 7.59 (d, *J* = 2.0 Hz, 1H), 7.39 (dd, J_1 = 8.0 Hz, J_2 = 2.0 Hz, 1H), 4.44(q, *J* = 6.8 Hz, 2H), 1.40(t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 166.05, 147.04, 136.24, 134.56, 133.74 (d, J_{CF} = 2.6 Hz), 133.10, 132.52, 131.02, 130.82, 128.23, 126.01, 121.86 (d, J_{CF} = 270.6 Hz), 114.012, 110.39, 63.07, 13.87 ppm. ESI HRMS: calcd. For $C_{17}H_{10}Cl_2F_3NO_2$+Na 409.9938, found 409.9941.



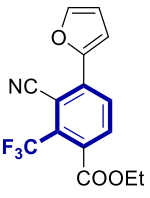
5r

5r: Obtained as a white solid; yield: 79% (60.0 mg) after flash chromatography. mp 128-130 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.77 (d, *J* = 8.4 Hz, 1H), 7.73 (d, *J* = 8.4 Hz, 1H), 7.10 (dd, J_1 = 8.0 Hz, J_2 = 2.0 Hz, 1H), 7.05 (d, *J* = 2.0 Hz, 1H), 7.00 (d, *J* = 8.4 Hz,1H), 4.43 (q, *J* = 7.2 Hz, 2H), 3.95 (s, 1H), 3.95 (s,1H), 1.40 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.48, 150.41, 149.54, 149.11, 133.26, 132.54 (d, J_{CF} = 2.4 Hz), 132.09, 131.22 (d, J_{CF} = 32.1 Hz), 128.95, 122.12 (d, J_{CF} = 275.9 Hz), 121.95, 114.77, 112.16, 111.37, 109.95, 62.86, 56.16, 56.03, 13.88 ppm. ESI HRMS: calcd. For $C_{19}H_{16}F_3NO_4$+Na 402.0929, found 402.0926.



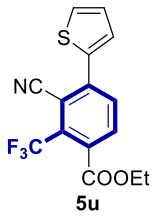
5s

5s: Obtained as a white solid; yield: 83% (61.3 mg) after flash chromatography. mp 99-101 °C, ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.33 (s, 1H), 8.04 (d, *J* = 8.4 Hz, 1H), 7.81 (d, *J* = 8.4 Hz, 1H), 7.61-7.55 (m, 2H), 7.51-7.48 (m, 1H), 7.41 (dd, J_1 = 6.6 Hz, J_2 = 0.6 Hz, 1H), 4.51 (q, *J* = 7.2 Hz, 2H), 1.45 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 164.29, 142.42, 135.26(d, J_{CF} = 2.4 Hz), 133.98 (d, J_{CF} = 33.9 Hz), 133.58, 131.27, 130.76, 129.14, 128.95, 127.91, 127.51, 127.28, 126.97, 125.32, 123.63, 122.11, 121.19 (d, J_{CF} = 274.7 Hz), 116.65, 112.12, 63.99, 13.96 ppm. ESI HRMS: calcd. For $C_{21}H_{14}F_3NO_2$+Na 392.0874, found 392.0876.



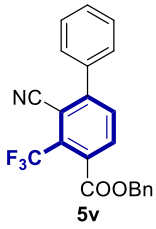
5t

5t: Obtained as a white solid; yield: 68% (42.1 mg) after flash chromatography. mp 86-88 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.15 (d, *J* = 8.4 Hz, 1H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.63 (d, *J* = 1.2 Hz, 1H), 7.58 (d, *J* = 3.6 Hz,1H), 6.63 (dd, J_1 = 3.6 Hz, J_2 = 1.6 Hz, 1H), 4.41 (q, *J* = 7.2 Hz, 2H), 1.39 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.35, 147.82, 144.70, 136.84, 132.42, 131.97 (d, J_{CF} = 2.6 Hz), 131.72 (d, J_{CF} = 32.2 Hz), 129.13, 122.06 (d, J_{CF} = 274.2 Hz), 115.01, 113.77, 112.89, 110.52, 62.85, 13.86 ppm. ESI HRMS: calcd. For $C_{15}H_{10}F_3NO_3$+Na 332.0510, found 332.0515.



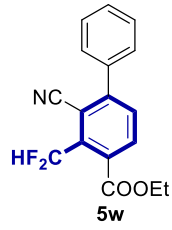
5u

5u: Obtained as a white solid; yield: 70% (45.5 mg) after flash chromatography. mp 98-100 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.83 (d, *J* = 8.0 Hz, 1H), 7.74 (d, *J* = 8.4 Hz, 1H), 7.68 (dd, J_1 = 3.6 Hz, J_2 = 0.8 Hz, 1H), 7.55 (dd, J_1 = 5.2 Hz, J_2 = 1.2 Hz, 1H), 7.21 (dd, J_1 = 5.2 Hz, J_2 = 3.6 Hz, 1H), 4.42 (q, *J* = 7.2 Hz, 2H), 1.39 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.26, 141.84, 137.08, 133.19, 132.77 (d, J_{CF} = 2.5 Hz), 132.30, 131.82 (d, J_{CF} = 32.3 Hz), 129.67, 129.10, 128.54, 121.99 (d, J_{CF} = 274.3 Hz), 114.67, 109.07, 62.93, 13.86 ppm. ESI HRMS: calcd. For $C_{15}H_{10}F_3NO_2S$+Na 348.0282, found 348.0281.



5v

5v: Obtained as a white solid; yield: 76% (65.1 mg) after flash chromatography. mp 91-93 °C, ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.79 (d, *J* = 7.8 Hz, 1H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.53-7.49 (m, 5H), 7.44-7.36 (m, 5H), 5.38 (s, 2H) ppm; ^{13}C NMR (150 MHz, CDCl3): δ = 166.18, 149.85, 136.48, 134.46, 133.40, 132.50, 132.20, 131.21 (q, J_{CF} = 31.5 Hz), 129.75, 128.92, 128.84, 128.74, 128.71, 122.03 (q, J_{CF} = 274.5 Hz), 114.37, 110.31, 68.71 ppm. ESI HRMS: calcd. For C22H14F3NO2+Na 404.0874, found 404.0870.



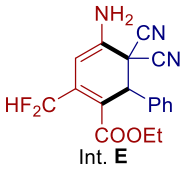
5w

5w: Obtained as a white solid; yield: 73% (50.9 mg) after flash chromatography. mp 96-98 °C, ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.12 (d, *J* = 8.4 Hz, 1H), 7.63 (t, *J* = 53.4 Hz, 1H), 7.66 (d, *J* = 8.4 Hz, 1H), 7.54-7.50 (m, 5H), 4.45 (q, *J* = 7.2 Hz, 2H), 1.43 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (150 MHz, CDCl3): δ =165.09, 151.29, 150.85, 137.7 (t, J_{CF} = 21.5 Hz), 136.80, 133.74, 132.16, 130.31 (t, J_{CF} = 4.5 Hz), 129.65, 128.92, 128.87, 115.13, 110.80 (t, J_{CF} = 239.1 Hz), 62.64, 114.12 ppm. ESI HRMS: calcd. For C17H13F2NO2+Na 324.0812, found 324.0811.

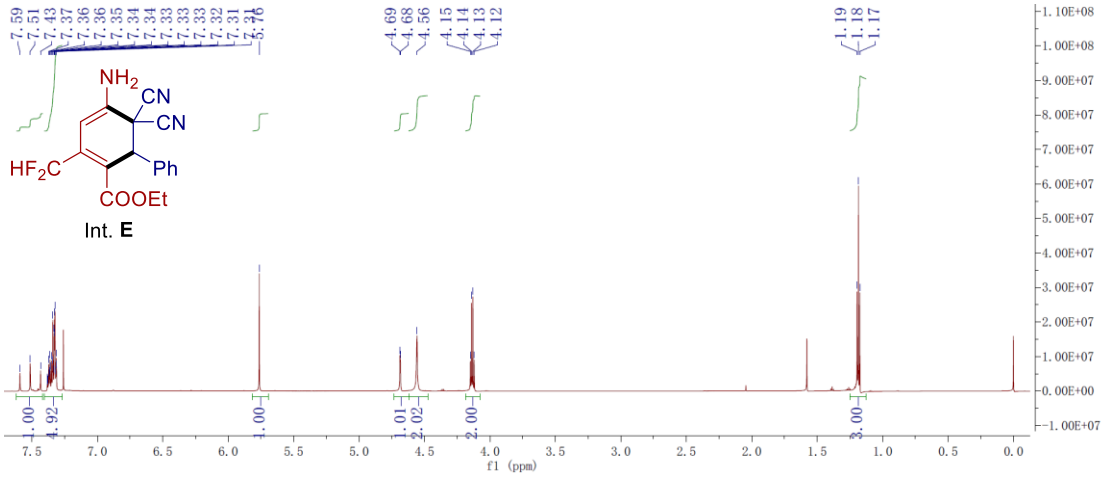
5. Control experiments

5.1 Control experiment of 1a and 2b

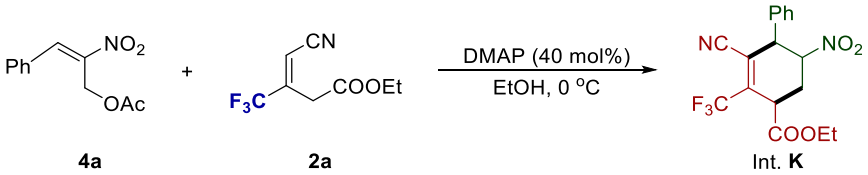
The reaction was carried out with **1a** (0.20 mmol) and **2b** (0.24 mmol), and DABCO (0.04 mmol) in DCM (1 mL) at room temperature. The reaction was monitored by TLC until the reaction produced yellow spots. Stop the reaction immediately, then the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) to give the corresponding Int. **E**, which was further analyzed by ^{1}H NMR, ^{13}C HMR, HRMS and X-ray diffraction analysis.



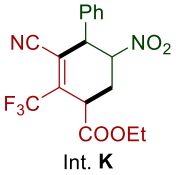
Obtained as a yellow solid; yield: 90% (61.8 mg) after flash chromatography. ^{1}H NMR (700 MHz, CDCl3): δ = 7.51 (t, *J* = 54.6 Hz, 1H), 7.38-7.31 (m, 5H), 5.76 (s, 1H), 4.69 (d, *J* = 2.8 Hz, 1H), 4.56 (s, 2H), 4.14 (q, *J* = 7.0 Hz, 2H), 1.19 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (175 MHz, CDCl3): δ = 163.56, 141.87 (t, J_{CF} = 22.6 Hz), 135.68, 131.61, 129.78, 129.11, 128.97, 117.57 (t, J_{CF} = 7.4 Hz), 112.98, 111.25, 109.98 (t, J_{CF} = 236.6 Hz), 93.06 (t, J_{CF} = 6.0 Hz), 61.65, 48.65, 41.66, 13.87 ppm. ESI HRMS: calcd. For C18H15F2N3O2+Na 366.1030, found 366.1029.



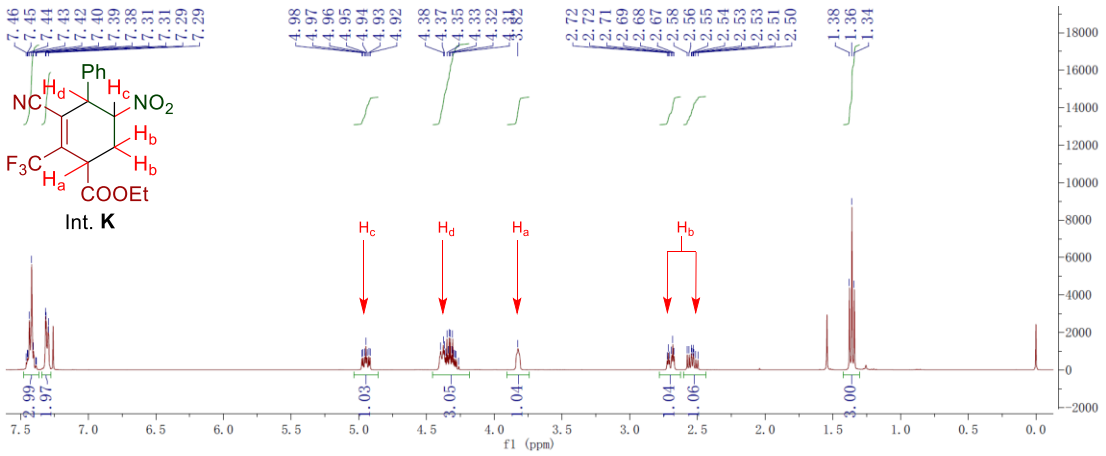
5.2 Control experiment of 4a and 2a



The reaction was carried out with **4a** (0.20 mmol) and **2a** (0.30 mmol), and DMAP (0.08 mmol) in EtOH (1 mL) at 0 °C. The reaction was monitored by TLC until the reaction was completion. Then the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 40:1) to give the Int. **K**, which was further analyzed by ^{1}H NMR, ^{13}C HMR, HRMS analysis.

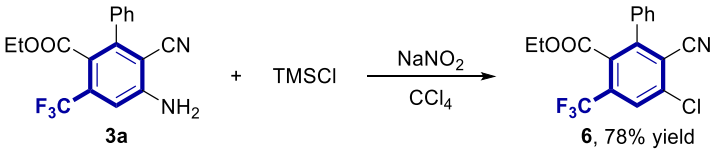


Obtained as a white solid; yield: 86% (63.3 mg) after flash chromatography. ^{1}H NMR (400 MHz, CDCl3): δ = 7.46-7.38 (m, 3H), 7.30-7.29 (m, 2H), 4.98-4.92 (m, 1H), 3.40-4.26 (m, 3H), 3.83 (s, 1H), 2.70 (dt, J_1 = 13.6 Hz, J_2 = 3.6 Hz, 1H), 2.58-2.50 (m, 1H), 1.36 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CDCl3): δ = 169.40, 139.04 (q, J_{CF} = 32.1 Hz), 134.63, 129.82, 129.59, 128.47, 121.09 (d, J_{CF} = 274.7 Hz), 119.93 (q, J_{CF} = 3.2 Hz), 112.72 (d, J_{CF} = 1.4 Hz), 84.22, 63.12, 47.96, 40.40, 29.26, 14.00 ppm. ESI HRMS: calcd. For C17H15F3N2O4+Na 391.0882, found 391.0882.

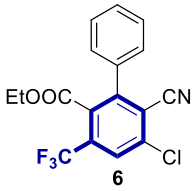


6. Procedures for the transformation

6.1 Transformation of 3a into 6

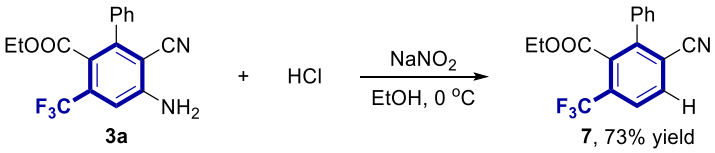


Trifluoromethylated benzene **3a** (0.10 mmol) was added into the mixture of $NaNO_2$ (0.30 mmol) and TMSCl (0.30 mmol) in CCl_4 at 0 °C, and the reaction mixture was stirred at 0 °C for 1.5 hour before warm up to room temperature. The reaction was stirred at room temperature for another 3 hours until the reaction was completion (monitored by TLC). Then, the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 15:1) to give the final ethyl 5-chloro-6-cyano-3-(trifluoromethyl)-[1,1'-biphenyl]-2-carboxylate **6**, which was further analyzed by ^{1}H NMR, ^{13}C HMR, HRMS analysis.



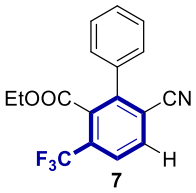
Obtained as a white solid; yield: 78% (27.6 mg) after flash chromatography. mp 131-133 °C, ^{1}H NMR (600 MHz, CDCl3): δ = 7.86 (s, 1H), 7.52-7.47 (m, 3H), 7.38-7.36 (m, 2H), 4.02 (q, J = 7.2 Hz, 2H), 0.96 (t, J = 6.6 Hz, 3H) ppm; ^{13}C NMR (150 MHz, CDCl3): δ = 164.44, 147.03, 138.80, 134.31, 132.11, 131.75 (q, J_{CF} = 33.5 Hz), 129.96, 128.82, 128.71, 126.52 (q, J_{CF} = 5.0 Hz), 121.88 (q, J_{CF} = 273.8 Hz), 118.00, 113.60, 62.51, 13.40 ppm. ESI HRMS: calcd. For C17H11ClF3NO2+Na 376.0328, found 376.0326.

6.2 Transformation of 3a into 7



CF_3-benzene **3a** (0.10 mmol) and $NaNO_2$ (0.30 mmol) were added into 1 mL EtOH at 0 °C, and then one drop of HCl was added to the reaction mixture. The reaction was stirred at room temperature for 3 hours until the reaction was completion (monitored by TLC). When the reaction was completed, the mixture was concentrated in vacuo. The residue was then dissolved in EA, and washed with water for several times. The organic phase was dried over anhydrous Na_2SO_4 and concentrated in vacuo. Then, the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 20:1) to give the target

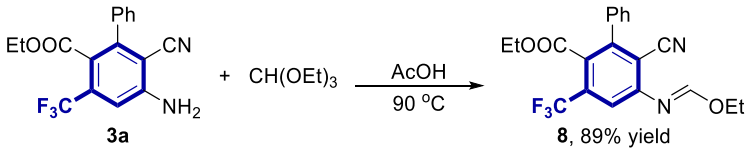
compound **7**, which was further analyzed by ^{1}H NMR, ^{13}C HMR, HRMS analysis.



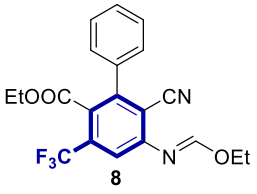
7

Obtained as a white solid; yield: 73% (46.6 mg) after flash chromatography. mp 129-131 °C, ^{1}H NMR (400 MHz, CDCl3): δ = 7.92 (dd, J_1 = 8.4 Hz, J_2 = 0.4 Hz, 1H), 7.81 (d, J = 8.4 Hz, 1H), 7.50-7.44 (m, 3H), 7.39-7.36 (m, 2H), 4.04 (q, J = 7.2 Hz, 2H), 0.98 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CDCl3): δ = 165.10, 144.80, 134.74, 134.02 (q, J_{CF} = 1.9 Hz), 133.79, 131.10 (q, J_{CF} = 33.0 Hz), 129.63, 129.01, 128.61, 125.70 (q, J_{CF} = 4.7 Hz), 122.56 (q, J_{CF} = 273.1 Hz), 117.33, 116.29, 62.33, 13.44 ppm. ESI HRMS: calcd. For C17H12F3NO2+Na 342.0718, found 342.0715.

6.3 Transformation of 3a into 8



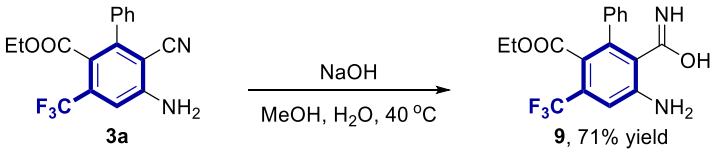
Trifluoromethylated benzene **3a** (0.10 mmol) was added into the mixture of triethyl orthoformate (0.5 mL) and acetic acid (0.2 mL) at 90 °C, and the reaction mixture was stirred for 2 hours until the reaction was completion (monitored by TLC). When the reaction was completed, the mixture was concentrated in vacuo. The residue was then dissolved in CH_2Cl_2, and washed with water for several times. The organic phase was dried over anhydrous Na_2SO_4 and concentrated in vacuo. Then the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 20:1) to give the corresponding compound **8**, which was further analyzed by ^{1}H NMR, ^{13}C HMR, HRMS analysis.



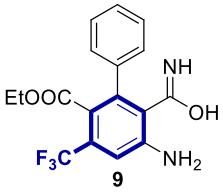
8

Obtained as a white solid; yield: 89% (69.5 mg) after flash chromatography. mp 141-143 °C, ^{1}H NMR (600 MHz, CDCl3): δ = 7.84 (s, 1H), 7.48-7.44 (m, 3H), 7.38-7.36 (m, 2H), 7.29 (s, 1H), 4.45 (q, J = 6.6 Hz, 2H), 4.00 (q, J = 7.2 Hz, 2H), 1.42 (t, J = 6.6 Hz, 3H), 0.96 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (150 MHz, CDCl3): δ =165.52, 157.50, 152.56, 146.17, 135.32, 131.63 (q, J_{CF} = 32.9 Hz), 129.50, 128.98, 128.88, 128.58, 122.58 (q, J_{CF} = 273.3 Hz), 117.54, 114.77, 111.47, 64.19, 62.19, 14.02, 13.50 ppm. ESI HRMS: calcd. For C20H17F3N2O3+Na 413.1089, found 413.1092.

6.4 Transformation of 3a into 9

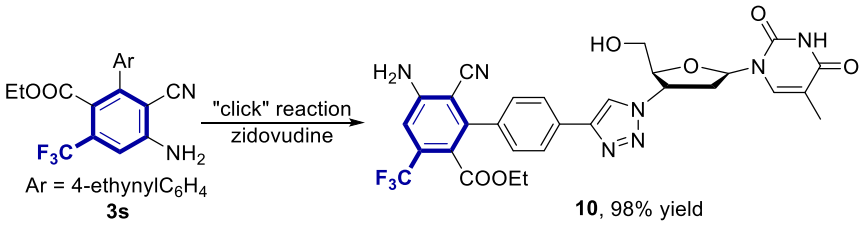


The reaction was carried out with **3a** (0.10 mmol) in the mixture of MeOH (1 mL) and 1M NaOH solution (1 mL) at 40 °C. The reaction mixture was stirred until the reaction was completion (monitored by TLC). The reaction mixture was allowed to cool down to rt, a large number of white solids precipitate. Simple filtration and washing with water gave the desired product **9**, which was further analyzed by ^{1}H NMR, ^{13}C HMR, HRMS analysis.

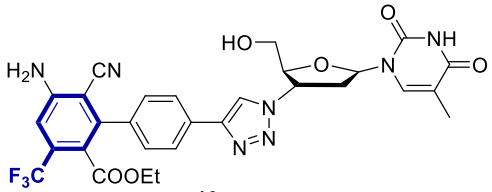


Obtained as a white solid; yield: 71% (25.0 mg) after flash chromatography. mp 128-130 °C, ^{1}H NMR (600 MHz, (CD3)2SO): δ = 7.49 (s, 1H), 7.34-7.32 (m, 3H), 7.29 (s, 1H), 7.23-7.21 (m, 2H), 7.11 (s, 1H), 5.75 (s, 2H), 3.78 (q, J = 6.6 Hz, 2H), 0.79 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (150 MHz, (CD3)2SO): δ = 167.95, 166.74, 146.15, 138.90, 137.43, 129.12, 127.65, 127.45, 126.45, 126.34 (d, J_{CF} = 31.1 Hz), 125.54, 123.57 (d, J_{CF} = 271.8 Hz), 119.15, 110.60 (d, J_{CF} = 4.7 Hz), 60.67, 13.28 ppm. ESI HRMS: calcd. For C17H15F3N2O3+Na 375.0932, found 375.0928.

6.5 Transformation of 3s into 10



The reaction was carried out with **3s** (0.10 mmol) and zidovudine (0.1 mmol) in THF at rt, and the mixed aqueous solution of freshly prepared $CuSO_4$•$5H_2O$ (0.1 mmol) and sodium ascorbate (0.1 mmol) was added. The resulting solution was stirred at room temperature for 2 h. Then the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (dichloromethane/ methanol = 20:1) to give the desire compound **10**, which was further analyzed by ^{1}H NMR, ^{13}C HMR, HRMS analysis.

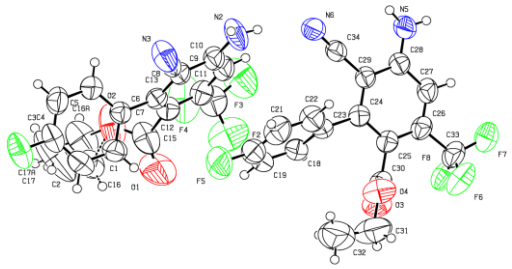


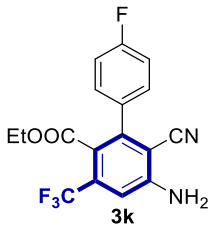
10

Obtained as a white solid; yield: 98% (61.3 mg) after flash chromatography. mp 130-132 °C, ^{1}H NMR (700 MHz, $(CD_3)_2SO$): δ = 11.38 (s, 1H), 8.88 (s, 1H), 7.97-7.6 (m, 2H), 7.86 (s, 1H), 7.42 (d, *J* = 7.7 Hz, 2H), 7.26 (s, 1H), 7.01 (s, 2H), 6.48 (t, *J* = 7.0 Hz, 1H), 5.45-5.43 (m, 1H), 5.33 (s, 1H), 4.31 (d, *J* = 2.8 Hz, 1H), 3.89 (q, *J* = 7.0 Hz, 2H), 3.76 (d, *J* = 11.2 Hz, 1H), 3.70 (d, *J* = 11.2Hz, 1H), 2.85-2.82 (m, 1H), 2.75-2.71 (m, 1H), 1.83 (s, 3H), 0.86 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (150 MHz, CDCl3): δ = 165.57, 163.80, 152.59, 150.50, 145.95, 145.30, 136.32, 135.79, 131.15, 130.38 (q, J_{CF} = 31.7 Hz), 129.38, 125.21, 125.01, 123.65, 121.62, 121.31 (t, J_{CF} = 273.0 Hz), 118.30, 115.48, 111.73 (t, J_{CF} = 6.0 Hz), 109.70, 96.99, 84.49, 83.96, 61.23, 60.79, 59.49, 37.19, 13.31, 12.31 ppm. ESI HRMS: calcd. For C29H26F3N7O6+Na 648.1794, found 648.1790.

7. X-ray crystal data for 3k, 5g, and Int. E.

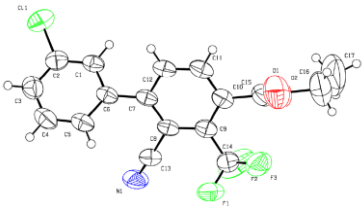
7.1 Crystal data of 3k



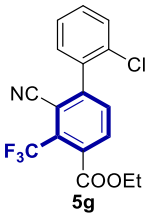


Identification code	lq-hb-hxh5282
Empirical formula	$C_{17}H_{12}F_4N_2O_2$
Formula weight	352.29
Temperature/K	295.4(2)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	12.9910(4)
b/Å	17.6471(7)
c/Å	14.6986(4)
α/°	90
β/°	92.642(3)
γ/°	90
Volume/Å^3	3366.1(2)
Z	8
ρ_{calc}g/cm^3	1.390
μ/mm^{-1}	1.065
F(000)	1440.0
Crystal size/mm^3	0.65 × 0.5 × 0.5
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	7.832 to 145.64
Index ranges	$-15 \leq h \leq 15$, $-21 \leq k \leq 13$, $-16 \leq l \leq 17$
Reflections collected	19165
Independent reflections	6571 [R_{int} = 0.0275, R_{sigma} = 0.0238]
Data/restraints/parameters	6571/2/490
Goodness-of-fit on F^2	1.033
Final R indexes [I>=2σ (I)]	R_1 = 0.0837, wR_2 = 0.2211
Final R indexes [all data]	R_1 = 0.1026, wR_2 = 0.2490
Largest diff. peak/hole / e Å^{-3}	0.31/-0.47

7.2 Crystal data of 5g

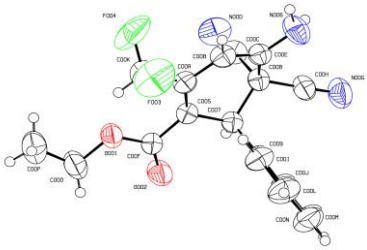


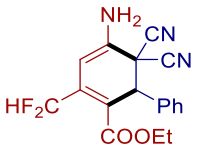
≡



Identification code	lq-hb-hxh5281
Empirical formula	$C_{17}H_{11}ClF_3NO_2$
Formula weight	353.72
Temperature/K	294.9(2)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	16.0338(9)
b/Å	8.0122(3)
c/Å	13.9749(7)
α/°	90
β/°	113.762(6)
γ/°	90
Volume/Å^3	1643.10(16)
Z	4
ρ_{calc}g/cm^3	1.430
μ/mm^{-1}	2.447
F(000)	720.0
Crystal size/mm^3	0.6 × 0.5 × 0.3
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	12.062 to 145.536
Index ranges	-19 ≤ h ≤ 14, -9 ≤ k ≤ 9, -17 ≤ l ≤ 17
Reflections collected	7459
Independent reflections	3219 [R_{int} = 0.0250, R_{sigma} = 0.0260]
Data/restraints/parameters	3219/0/218
Goodness-of-fit on F^2	1.039
Final R indexes [I>=2σ (I)]	R_1 = 0.0798, wR_2 = 0.2008
Final R indexes [all data]	R_1 = 0.0886, wR_2 = 0.2181
Largest diff. peak/hole / e Å^{-3}	0.37/-0.49

7.3 Crystal data of Int. E

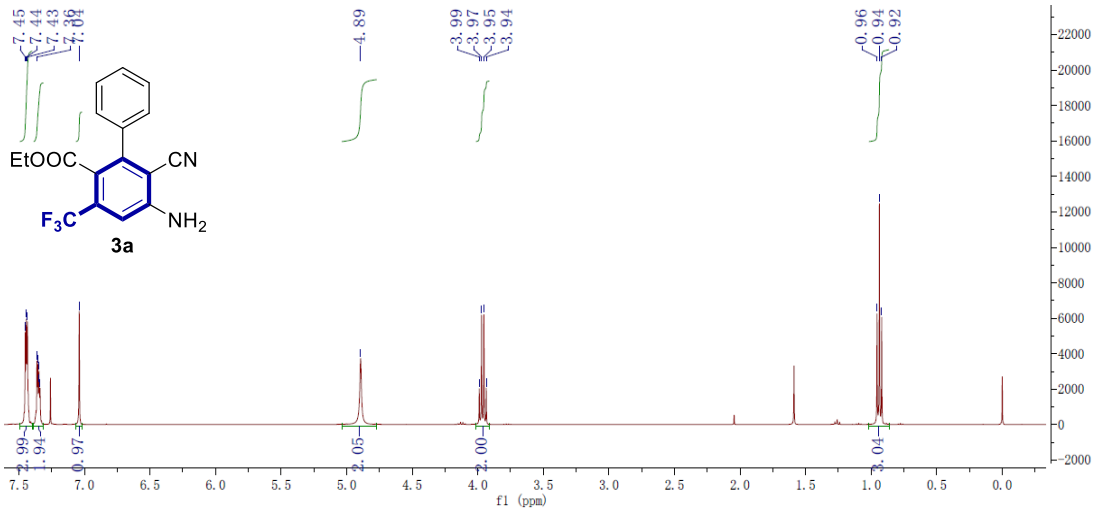


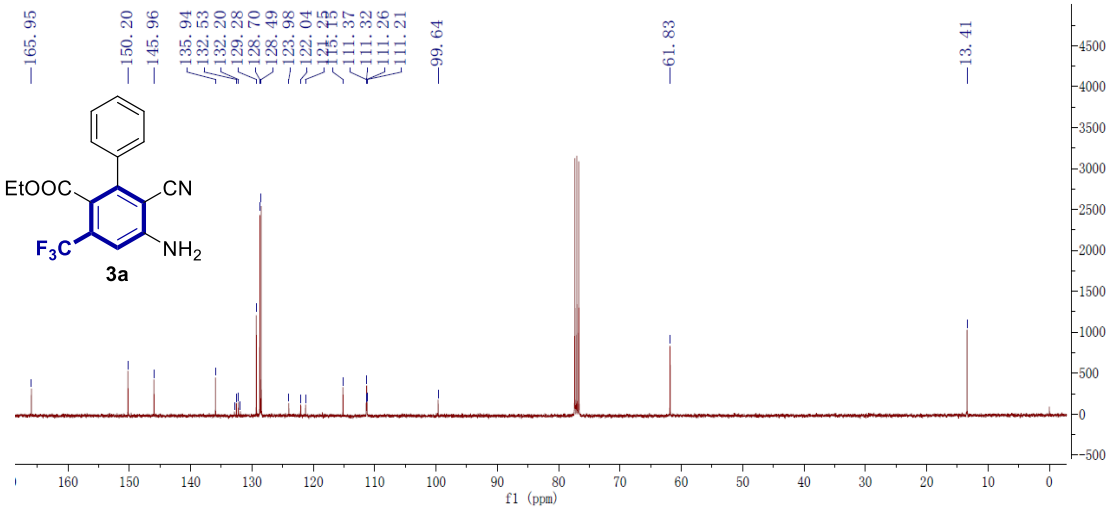


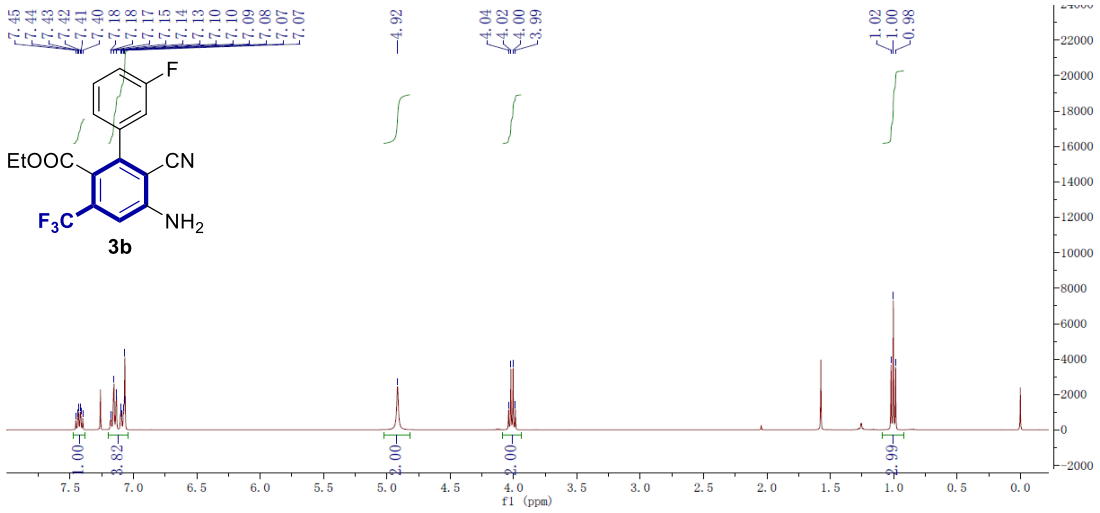
Int. **E**

Identification code	exp_6079
Empirical formula	$C_{18}H_{15}F_2N_3O_2$
Formula weight	343.33
Temperature/K	293.6(3)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	10.2758(5)
b/Å	13.9418(6)
c/Å	13.1480(6)
α/°	90
β/°	111.386(6)
γ/°	90
Volume/Å^3	1753.92(16)
Z	4
ρ_{calc}g/cm^3	1.300
μ/mm^{-1}	0.855
F(000)	712.0
Crystal size/mm^3	0.7 × 0.6 × 0.5
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	9.242 to 143.038
Index ranges	$-12 \leq h \leq 12$, $-16 \leq k \leq 17$, $-15 \leq l \leq 16$
Reflections collected	9507
Independent reflections	3373 [R_{int} = 0.0345, R_{sigma} = 0.0295]
Data/restraints/parameters	3373/0/228
Goodness-of-fit on F^2	1.038
Final R indexes [I>=2σ (I)]	R_1 = 0.0896, wR_2 = 0.2433
Final R indexes [all data]	R_1 = 0.1001, wR_2 = 0.2612
Largest diff. peak/hole / e Å^{-3}	0.53/-0.47

8. NMR spectra



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7.17
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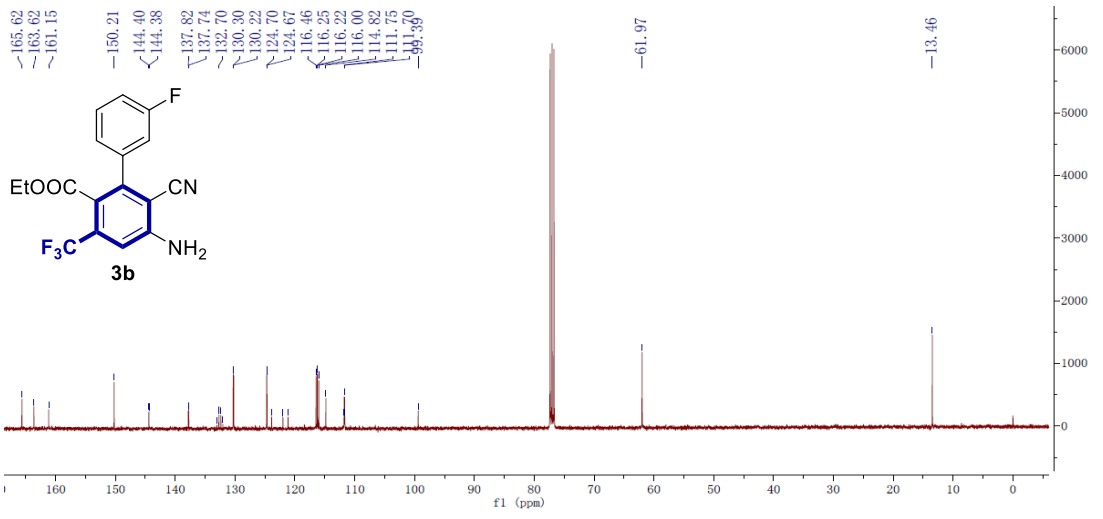
7.14
7.13
7.10
7.09
7.08
7.07
7.07
4.92
4.04
4.02
4.00
3.99
1.02
1.00
0.98
F
EtOOC
CN
F3C
NH2
3b
1.00
3.82
2.00
2.00
2.99
f1 (ppm)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130.30
130.22
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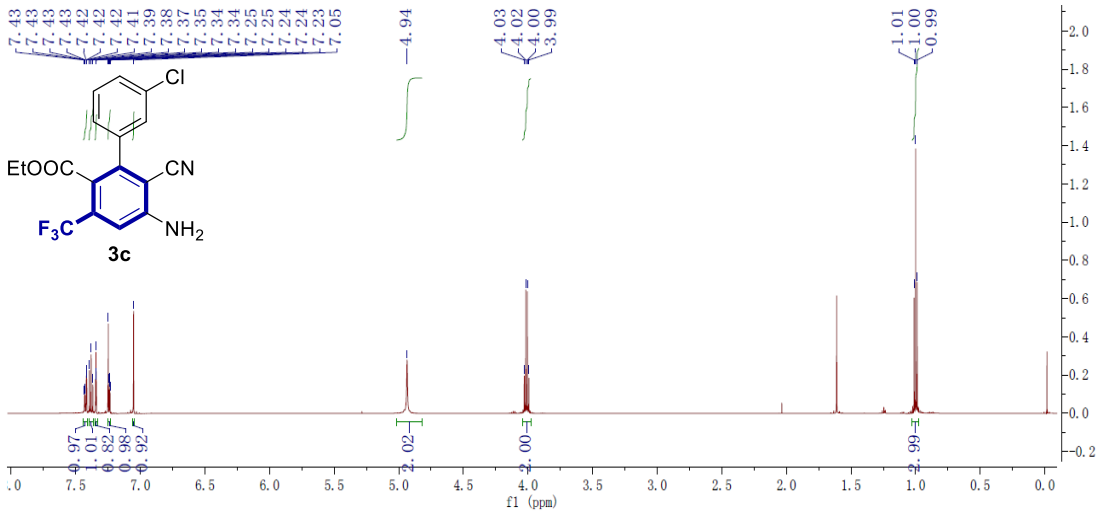
124.67
116.46
116.25
116.22
116.00
114.82
111.75
111.70
99.39
61.97
13.46
F
EtOOC
CN
F3C
NH2
3b
f1 (ppm)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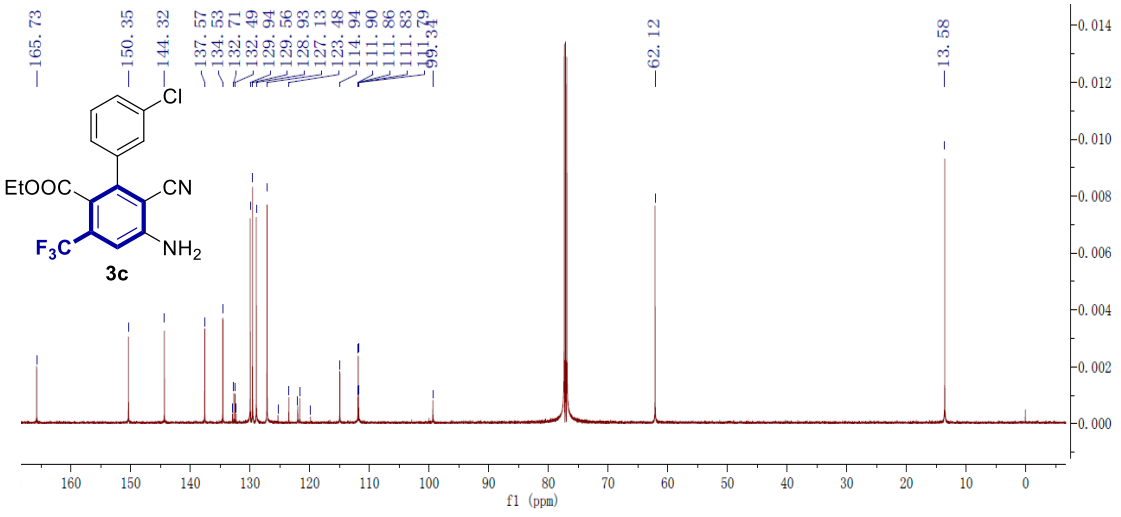
7.25
7.25
7.24
7.24
7.23
7.05
4.94
4.03
4.02
4.00
3.99
1.01
1.00
0.99
Cl
EtOOC
CN
F3C
NH2
3c
0.97
1.01
0.82
0.98
0.92
2.02
2.00
2.99
f1 (ppm)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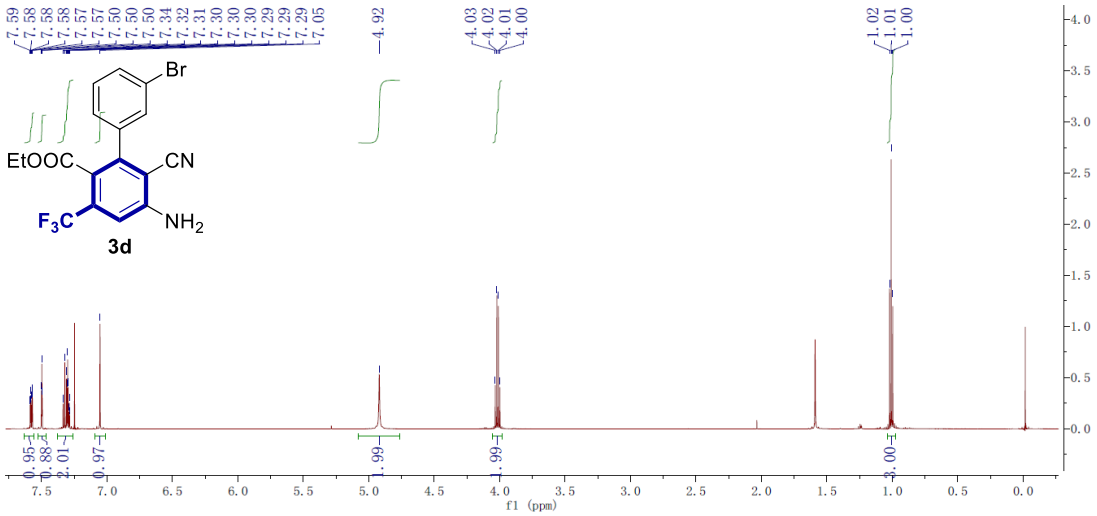
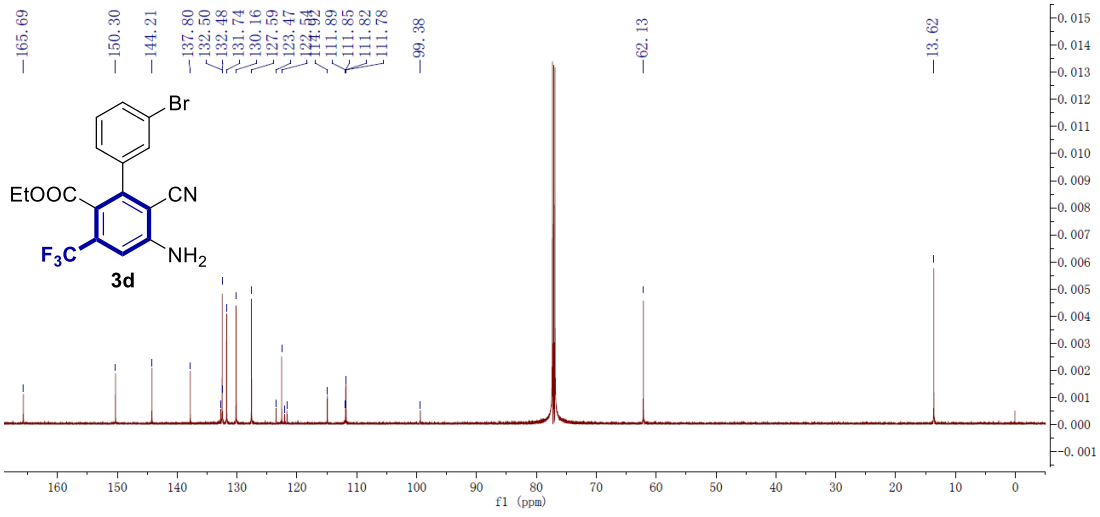
128.93
127.13
123.48
114.94
111.90
111.86
111.83
111.79
99.34
62.12
13.58
Cl
EtOOC
CN
F3C
NH2
3c
f1 (ppm)


Br
EtOOC
CN
F3C
NH2
3d
f1 (ppm)


Br
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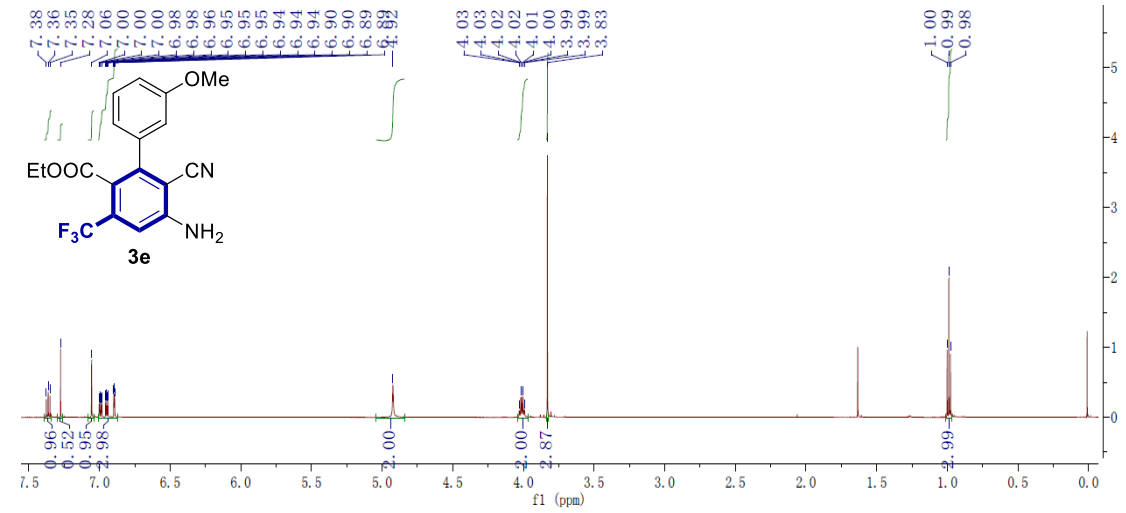
CN
F3C
NH2
3d
f1 (ppm)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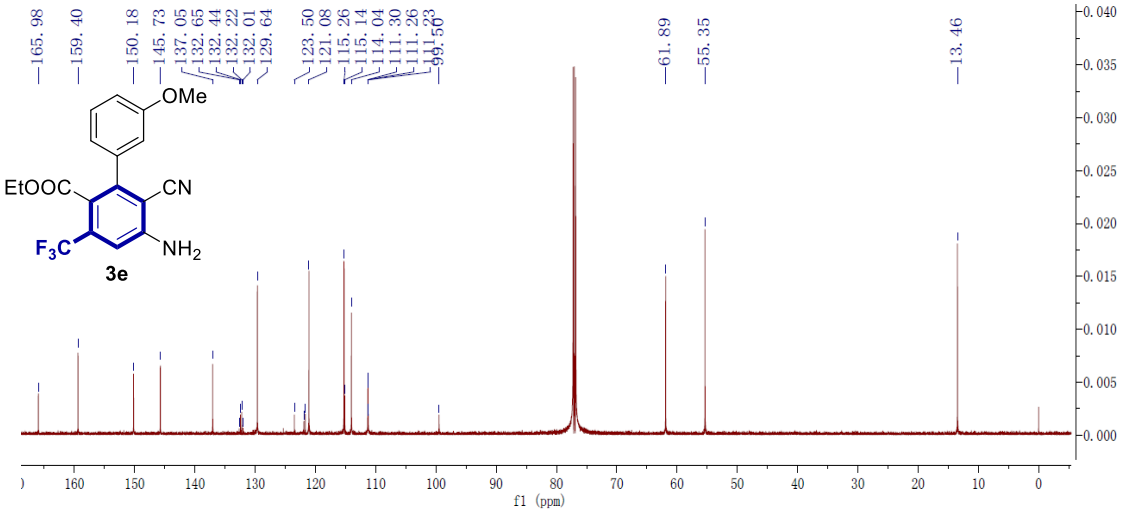
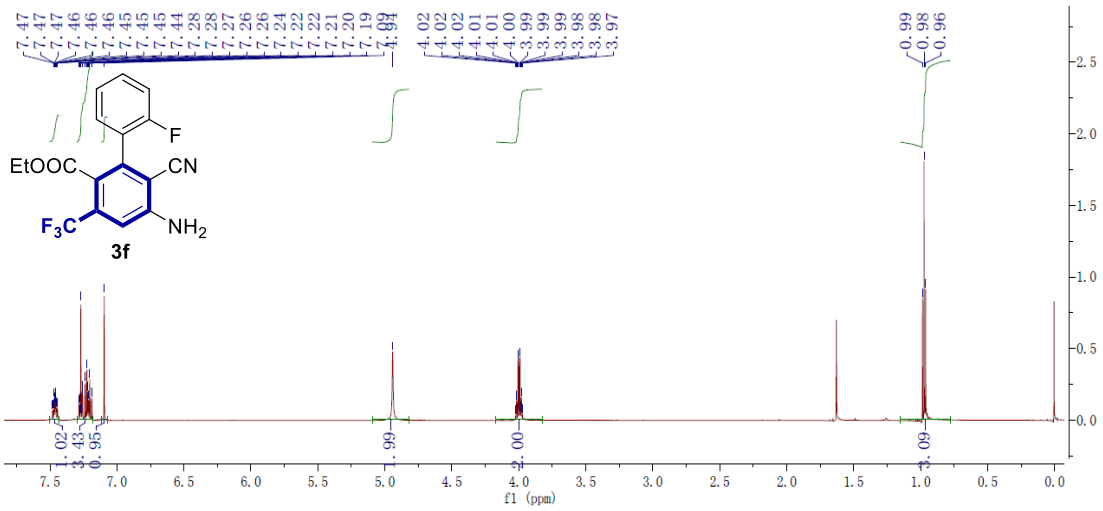
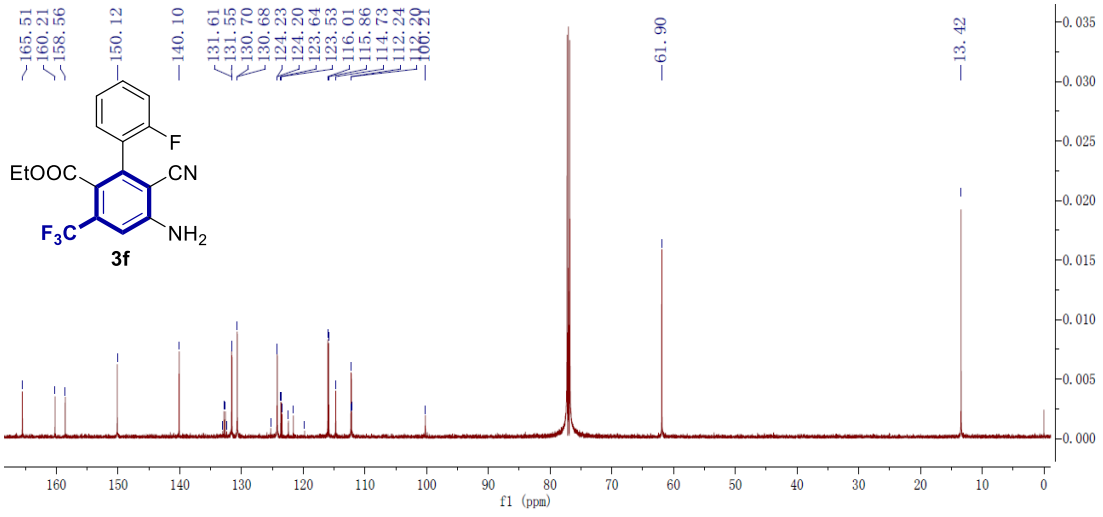
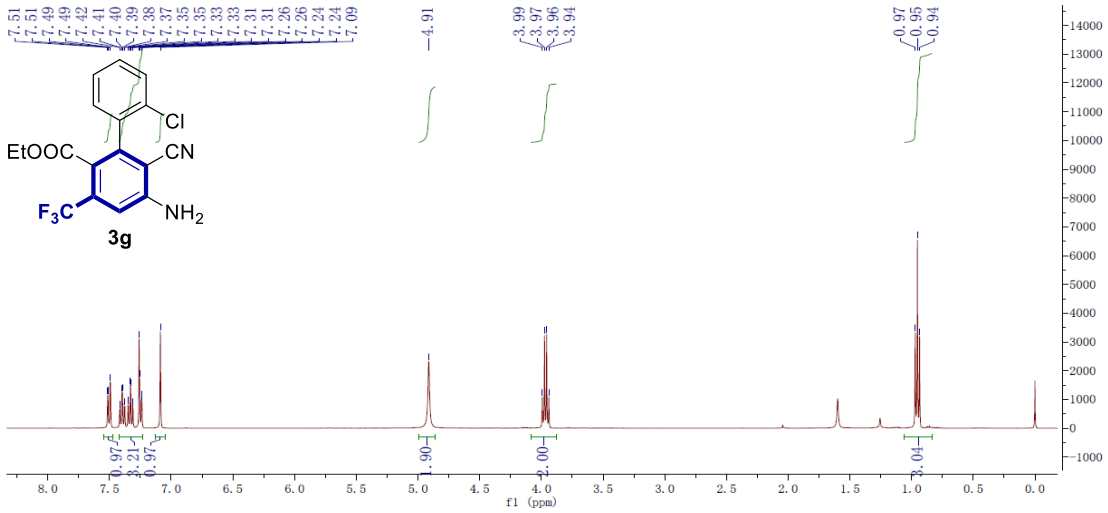
EtOOC
CN
F3C
NH2
3e
f1 (ppm)


OMe
EtOOC
CN
F3C
NH2
3e
f1 (ppm)


F
EtOOC
CN
F3C
NH2
3f
f1 (ppm)


F
EtOOC
CN
F3C
NH2
3f
f1 (ppm)


7.51
7.51
7.49
7.49
7.42
7.41
7.40
7.39
7.38
7.37
7.35
7.35
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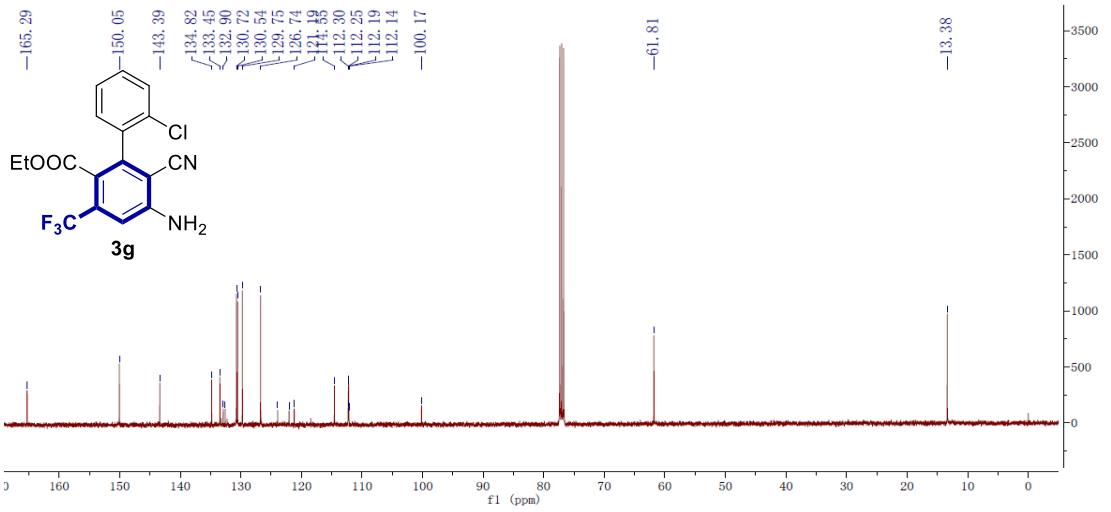
7.31
7.31
7.26
7.24
7.24
7.09
4.91
3.99
3.97
3.96
3.94
0.97
0.95
0.94
Cl
EtOOC
CN
F3C
NH2
3g
0.97
3.21
0.97
1.90
2.00
3.04
f1 (ppm)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143.39
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133.45
132.90
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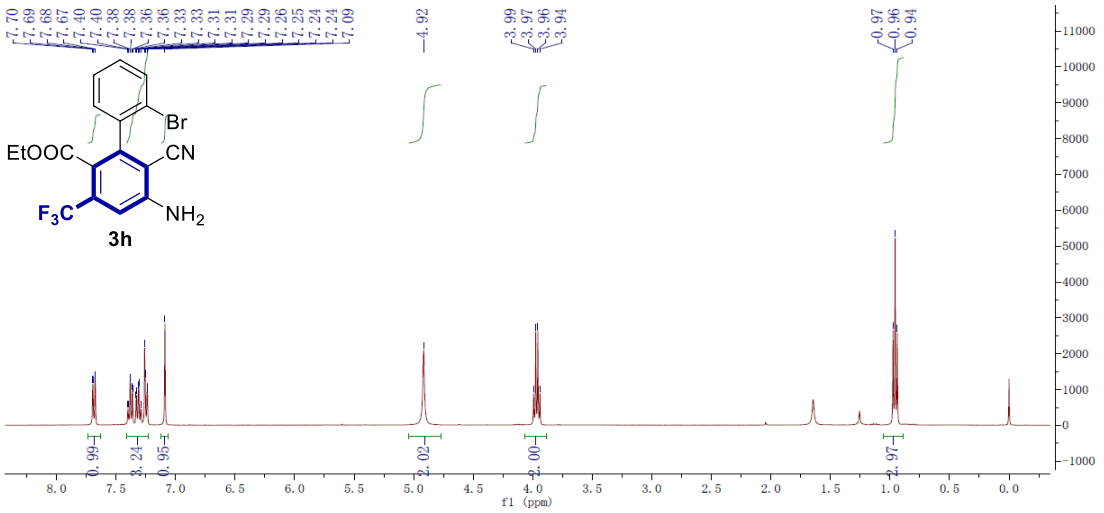
126.74
112.30
112.25
112.19
112.14
100.17
61.81
13.38
Cl
EtOOC
CN
F3C
NH2
3g
f1 (ppm)


7.70
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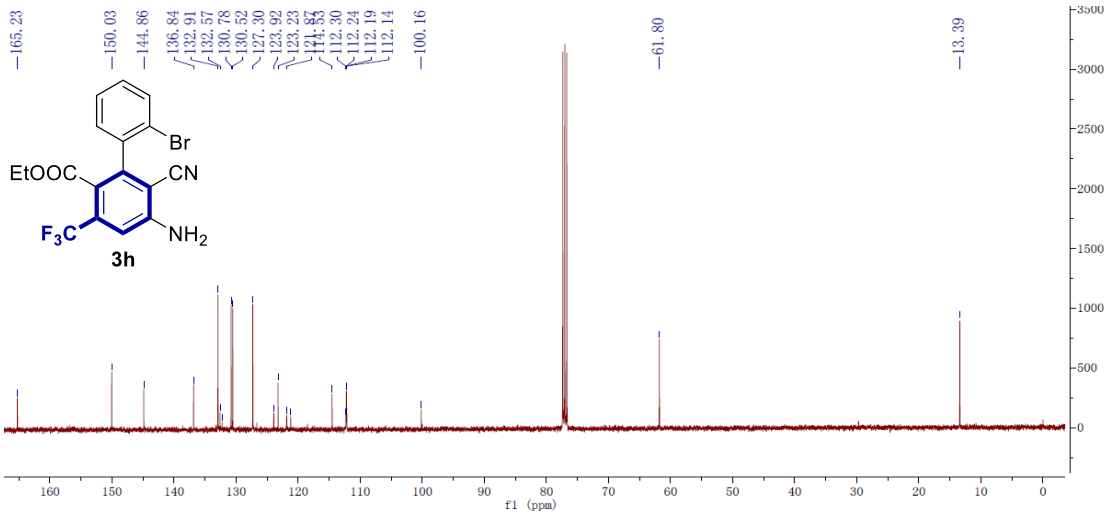
7.33
7.33
7.31
7.31
7.29
7.29
7.26
7.25
7.24
7.24
7.09
4.92
3.99
3.97
3.96
3.94
0.97
0.96
0.94
Br
EtOOC
CN
F3C
NH2
3h
0.99
3.24
0.95
2.02
2.00
2.97
f1 (ppm)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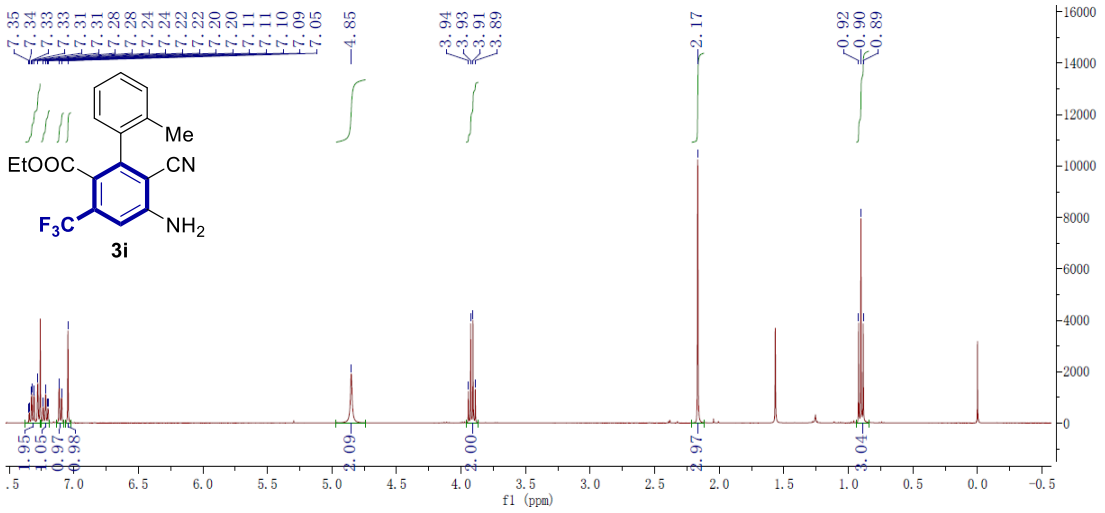
132.91
132.57
130.78
130.52
127.30
123.92
123.23
112.30
112.24
112.19
112.14
100.16
61.80
13.39
Br
EtOOC
CN
F3C
NH2
3h
f1 (ppm)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7.33
7.33
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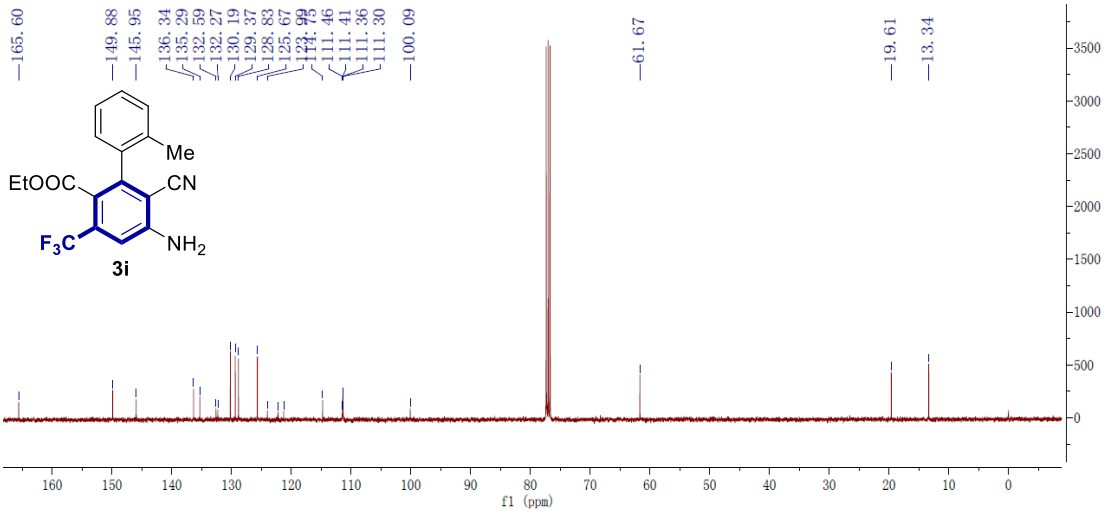
7.31
7.28
7.28
7.24
7.24
7.22
7.22
7.20
7.20
7.11
7.11
7.10
7.09
7.05
4.85
3.94
3.93
3.91
3.89
2.17
0.92
0.90
0.89
Me
EtOOC
CN
F3C
NH2
3i
1.95
1.05
0.97
0.98
2.09
2.00
2.97
3.04
f1 (ppm)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130.19
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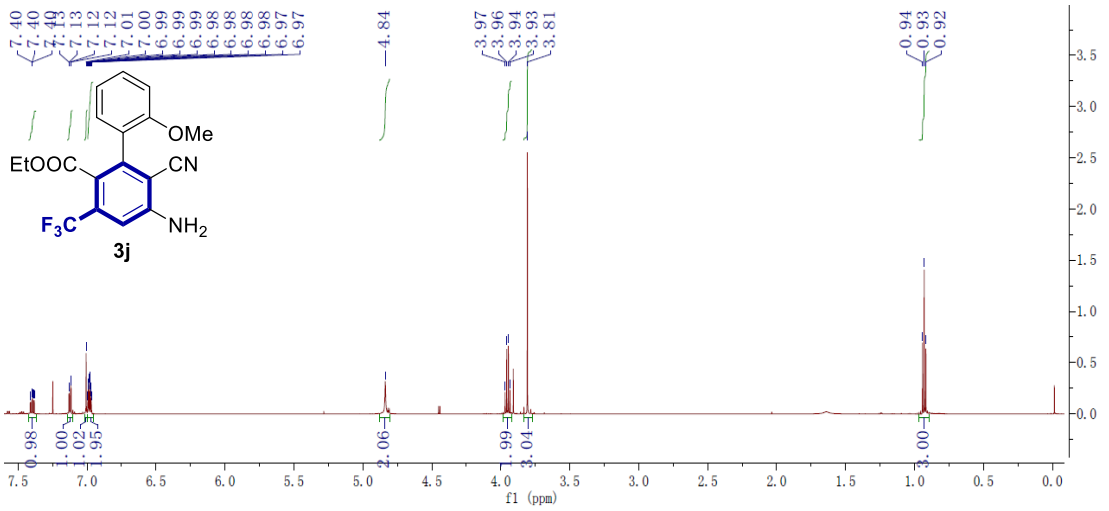
128.83
125.67
111.46
111.41
111.36
111.30
100.09
61.67
19.61
13.34
Me
EtOOC
CN
F3C
NH2
3i
f1 (ppm)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7.00
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6.99
6.98
6.98
6.98
6.97
6.97
4.84
3.97
3.96
3.94
3.93
3.81
0.94
0.93
0.92
OMe
EtOOC
CN
F3C
NH2
3j
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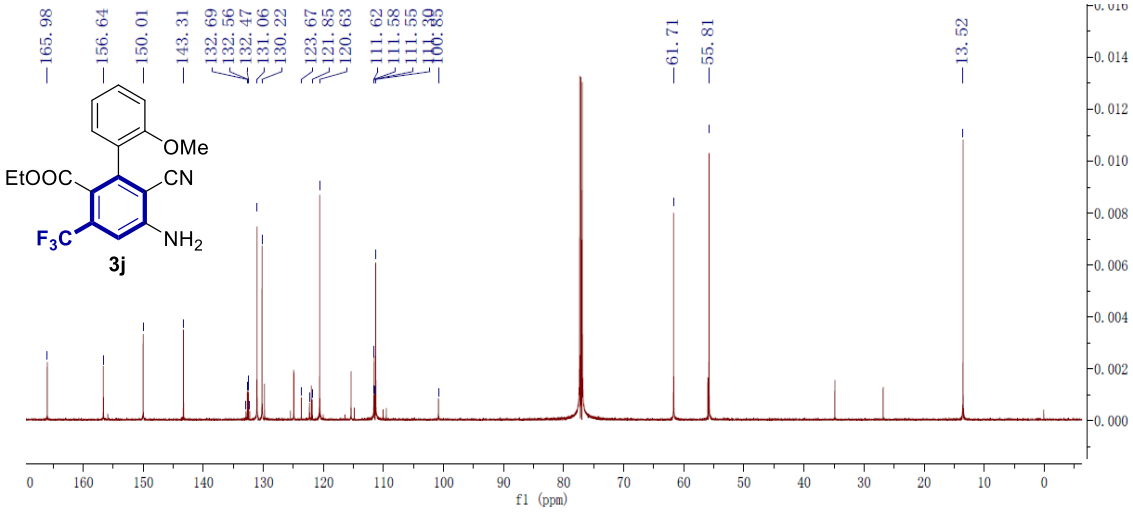
1.02
1.95
2.06
1.99
3.04
3.00
f1 (ppm)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131.06
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123.67
121.85
120.63
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111.58
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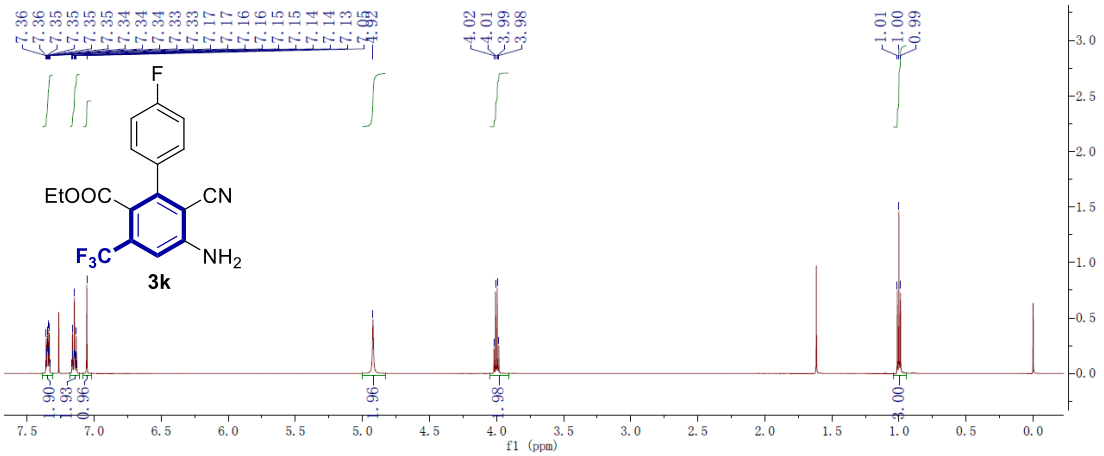
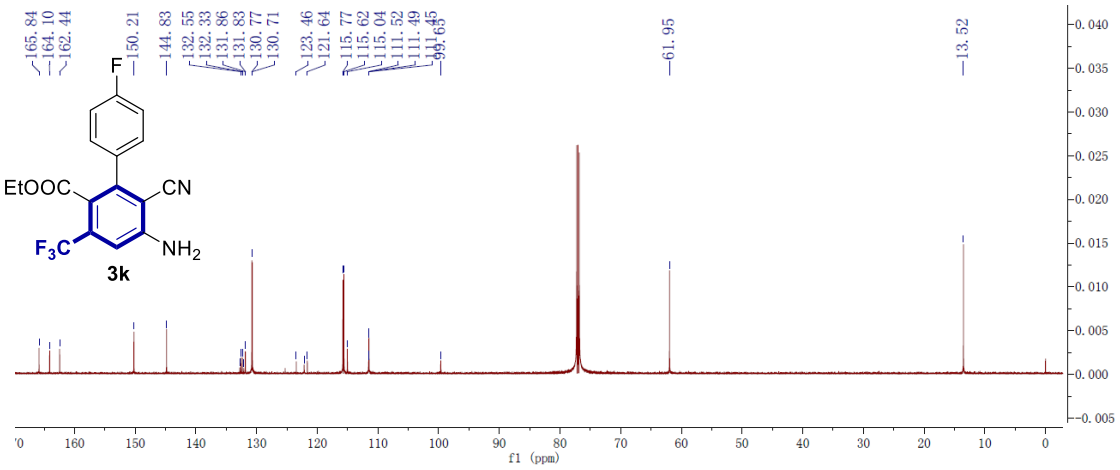
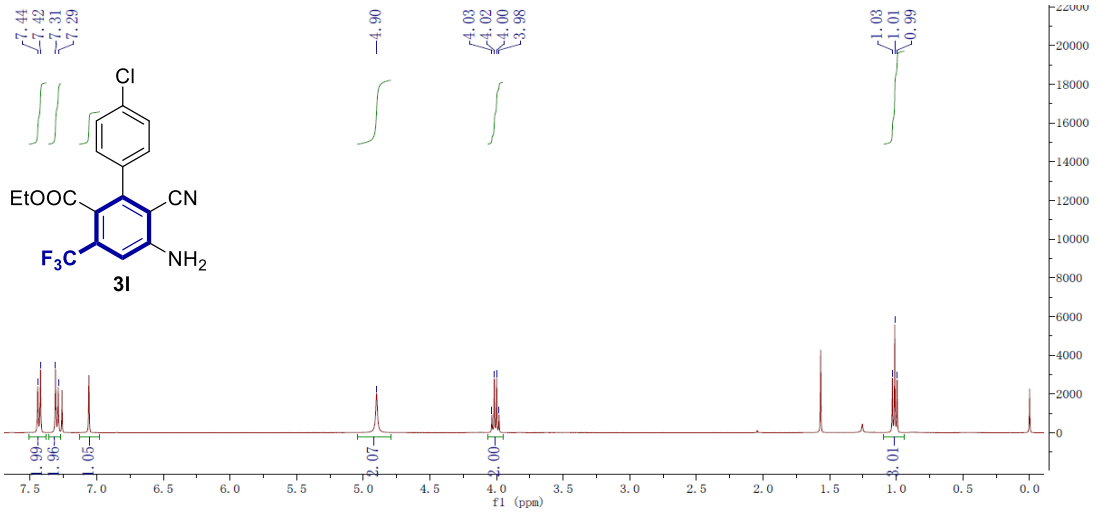
61.71
55.81
13.52
OMe
EtOOC
CN
F3C
NH2
3j
f1 (ppm)


F
EtOOC
CN
F3C
NH2
3k
f1 (ppm)


F
EtOOC
CN
F3C
NH2
3k
f1 (ppm)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7.29
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4.03
4.02
4.00
3.98
1.03
1.01
0.99
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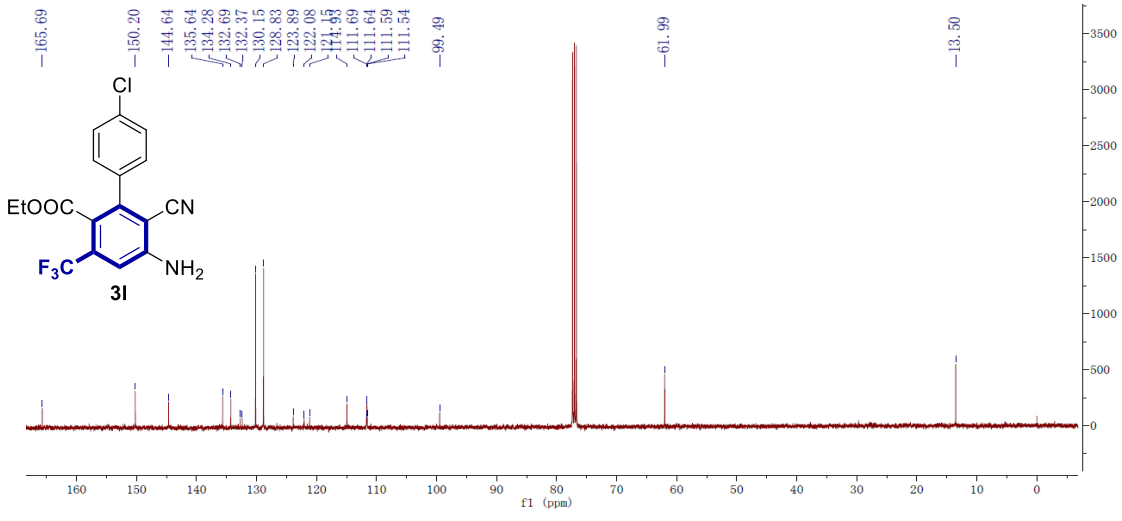
EtOOC
CN
F3C
NH2
3l
1.99
1.96
1.05
2.07
2.00
3.01
f1 (ppm)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132.69
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130.15
128.83
123.89
122.08
111.69
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111.54
99.49
61.99
13.50
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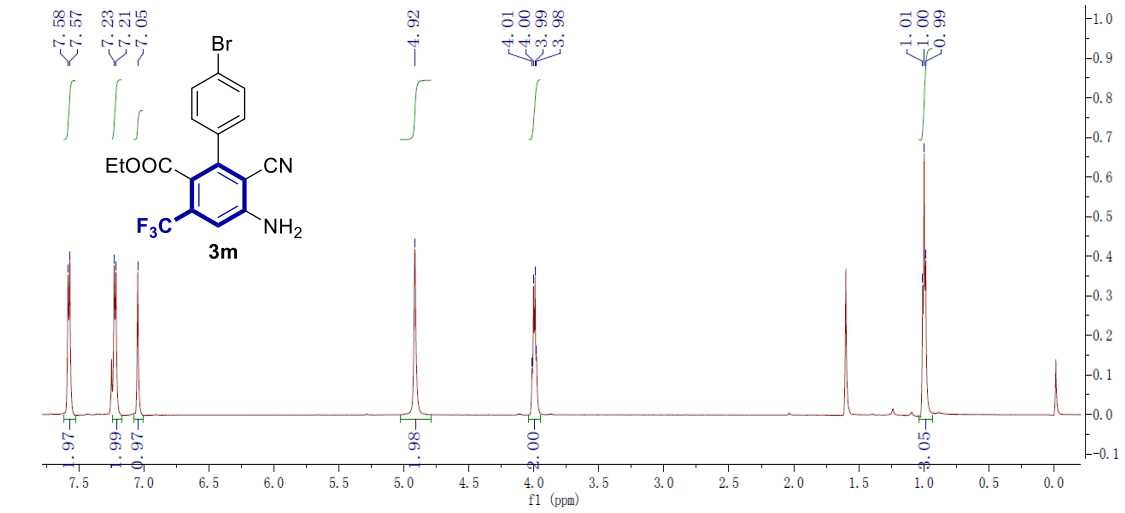
EtOOC
CN
F3C
NH2
3l
f1 (ppm)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7.57
7.23
7.21
7.05
4.92
4.01
4.00
3.99
3.98
1.01
1.00
0.99
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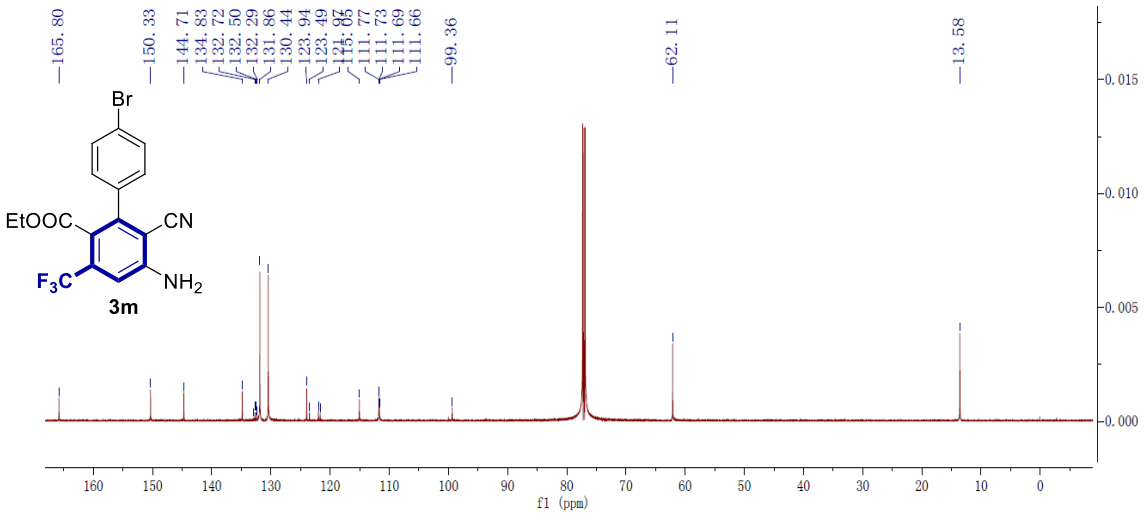
CN
F3C
NH2
3m
1.97
1.99
0.97
1.98
2.00
3.05
f1 (ppm)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130.44
123.94
123.49
111.77
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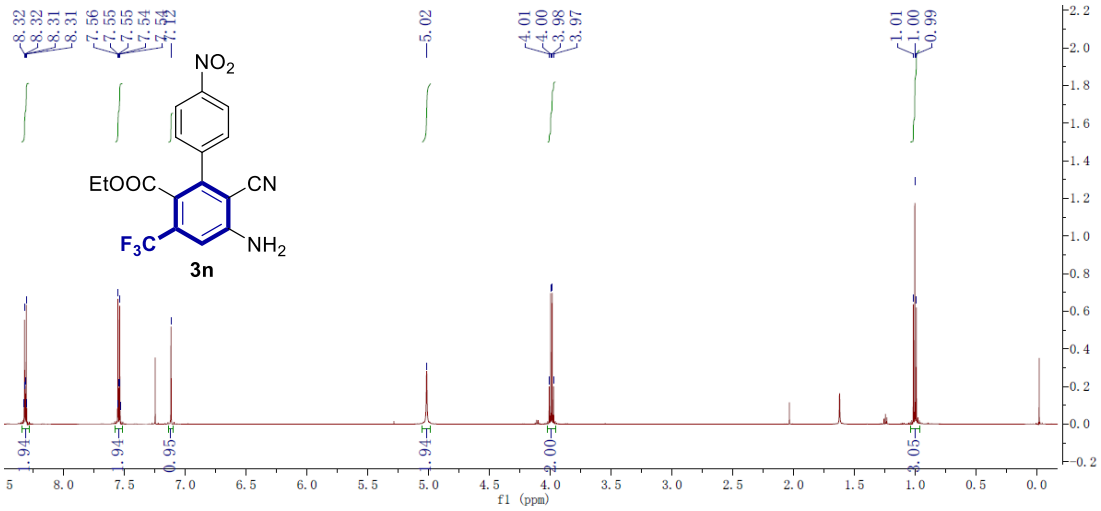
111.69
111.66
99.36
62.11
13.58
Br
EtOOC
CN
F3C
NH2
3m
f1 (ppm)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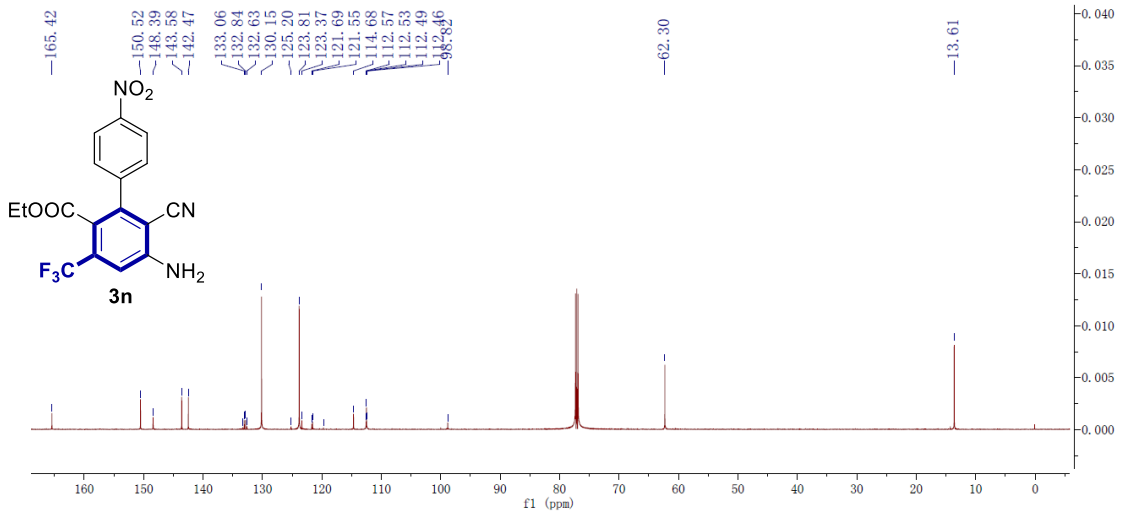
7.55
7.55
7.54
7.54
7.12
5.02
4.01
4.00
3.98
3.97
1.01
1.00
0.99
NO2
EtOOC
CN
F3C
NH2
3n
1.94
1.94
0.95
1.94
2.00
3.05
f1 (ppm)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125.20
123.81
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121.69
121.55
114.68
112.57
112.53
112.49
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98.82
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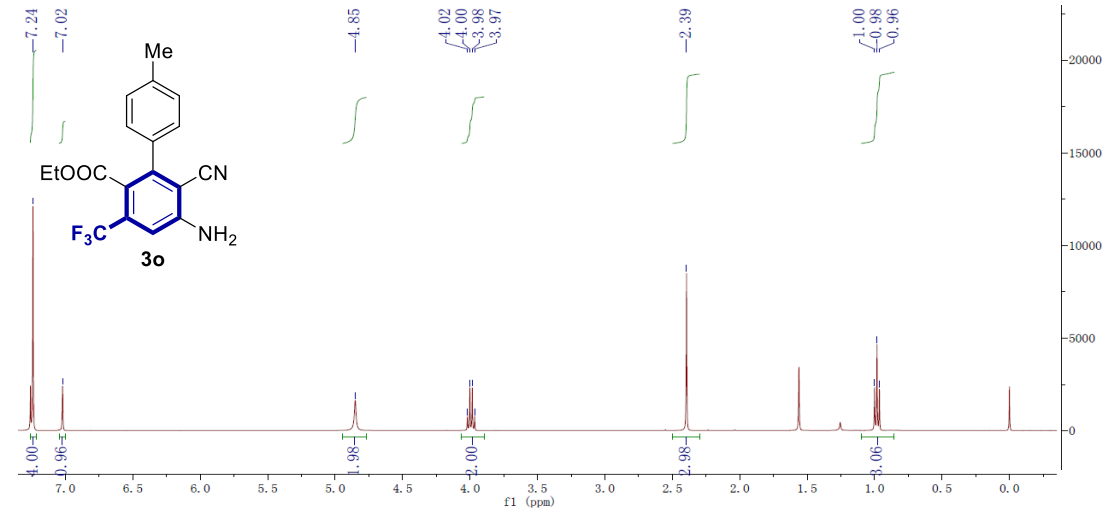
13.61
NO2
EtOOC
CN
F3C
NH2
3n
f1 (ppm)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7.02
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4.02
4.00
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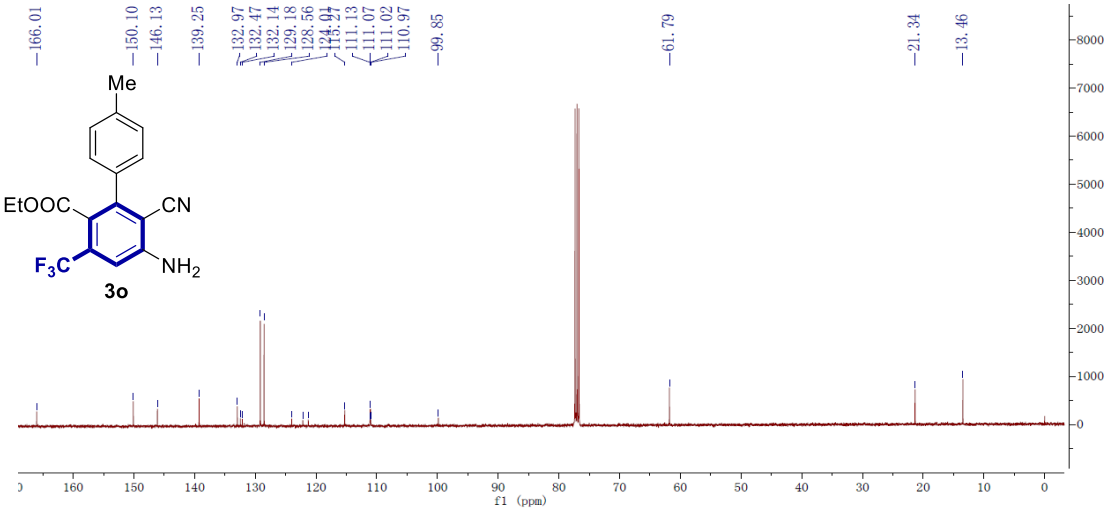
3.97
2.39
1.00
0.98
0.96
Me
EtOOC
CN
F3C
NH2
3o
4.00
0.96
1.98
2.00
2.98
3.06
f1 (ppm)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129.18
128.56
111.13
111.07
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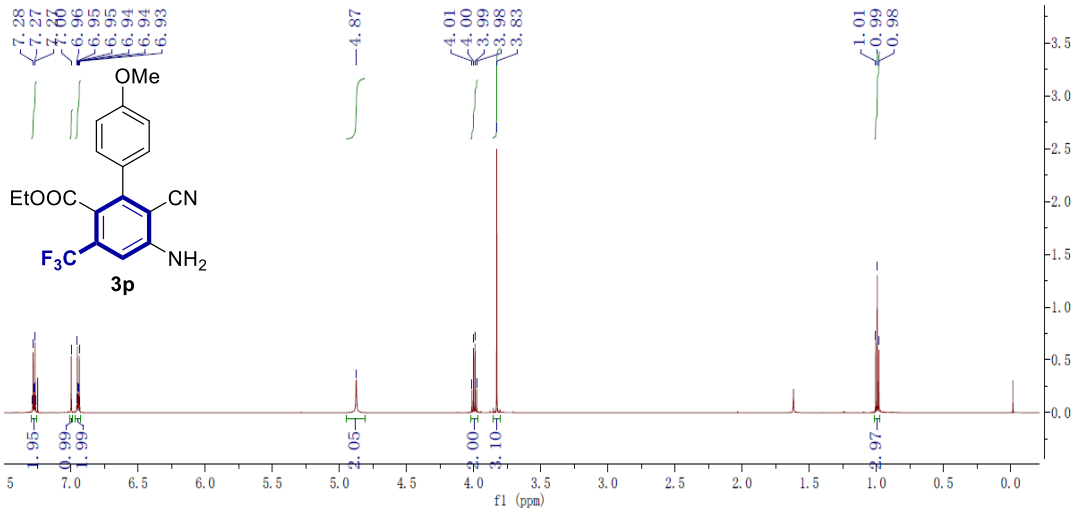
61.79
21.34
13.46
Me
EtOOC
CN
F3C
NH2
3o
f1 (ppm)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6.93
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4.00
3.99
3.98
3.83
1.01
0.99
0.98
OMe
EtOOC
CN
F3C
NH2
3p
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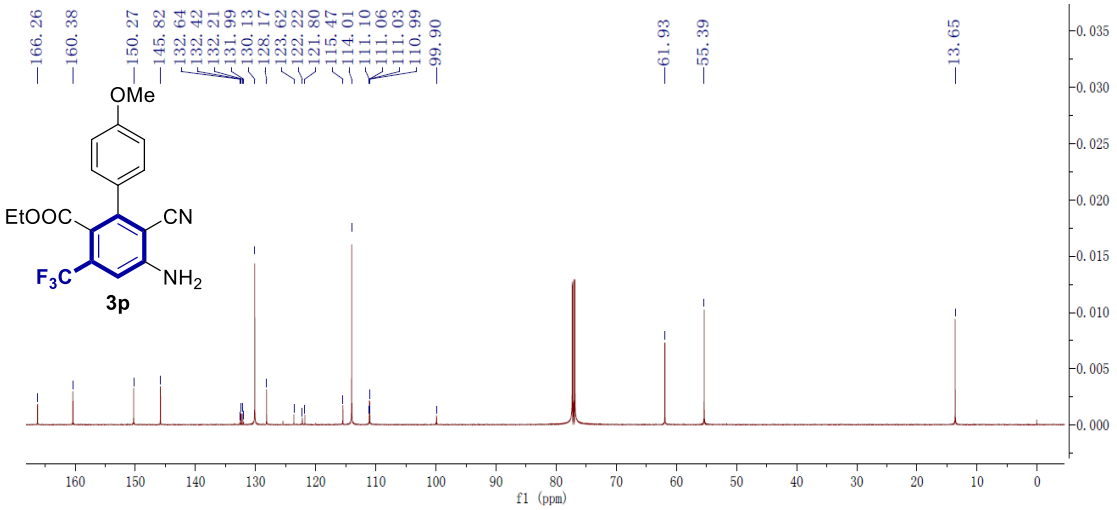
0.99
1.99
2.05
2.00
3.10
2.97
f1 (ppm)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122.22
121.80
115.47
114.01
111.10
111.06
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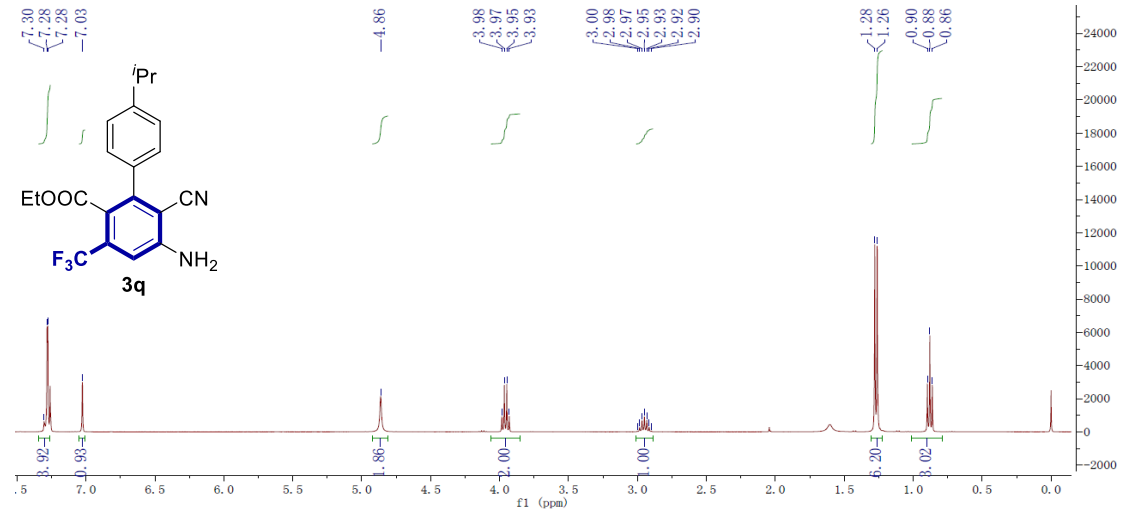
99.90
61.93
55.39
13.65
OMe
EtOOC
CN
F3C
NH2
3p
f1 (ppm)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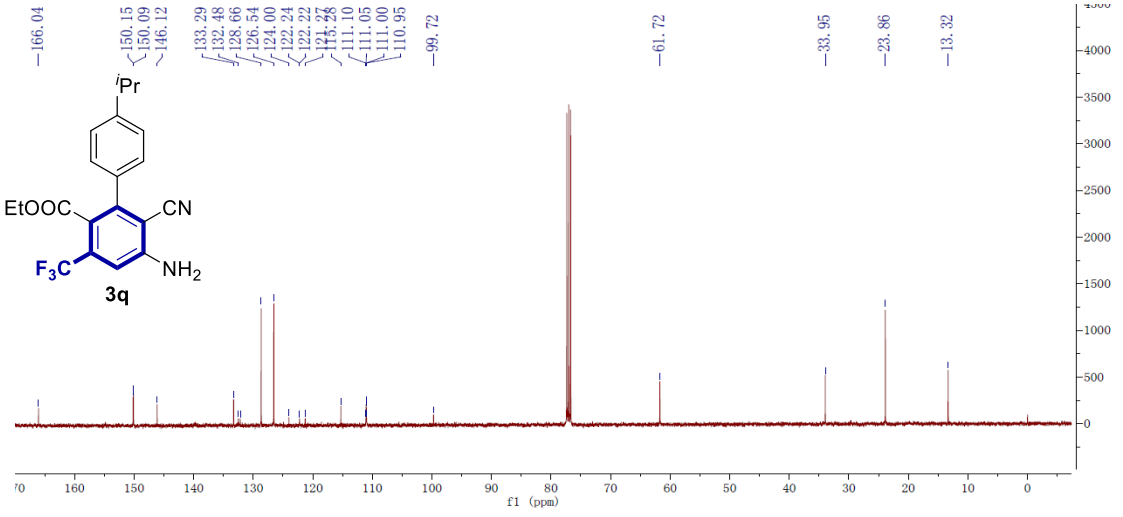
3.97
3.95
3.93
3.00
2.98
2.97
2.95
2.93
2.92
2.90
1.28
1.26
0.90
0.88
0.86
iPr
EtOOC
CN
F3C
NH2
3q
3.92
0.93
1.86
2.00
1.00
6.20
3.02
f1 (ppm)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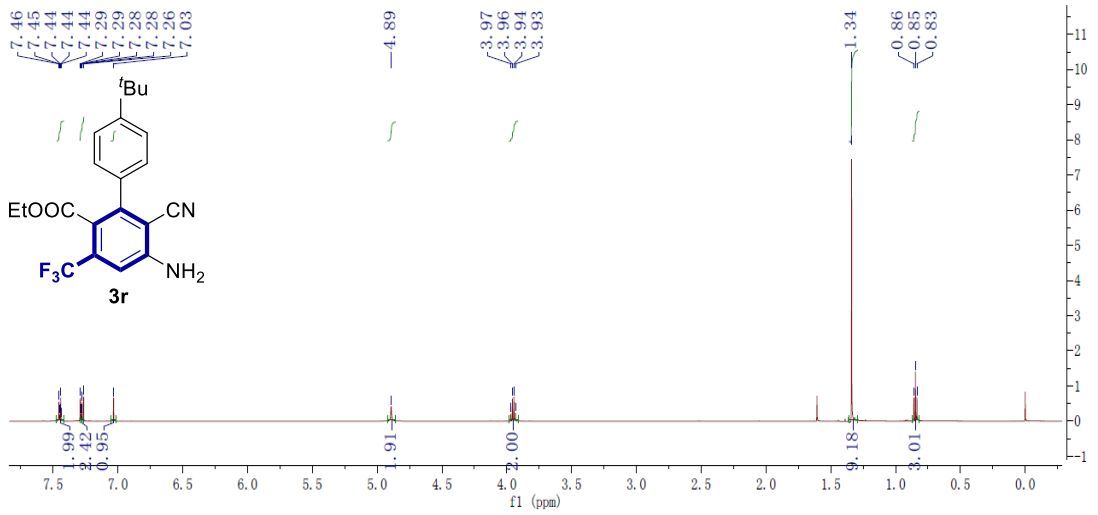
126.54
124.00
122.24
122.22
111.10
111.05
111.00
110.95
99.72
61.72
33.95
23.86
13.32
iPr
EtOOC
CN
F3C
NH2
3q
f1 (ppm)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7.28
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7.26
7.03
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3.96
3.94
3.93
1.34
0.86
0.85
0.83
tBu
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CN
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NH2
3r
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2.42
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2.00
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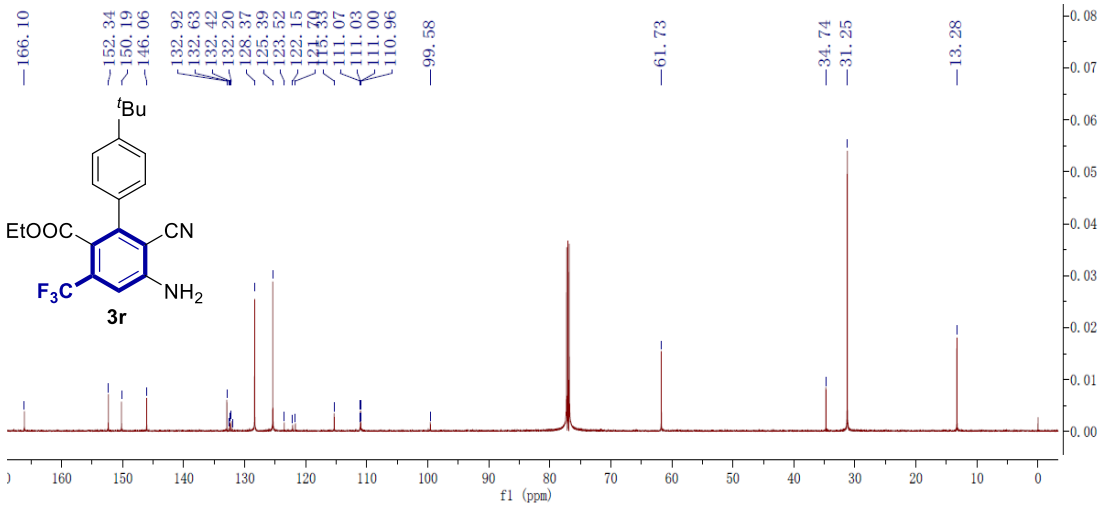
3.01
f1 (ppm)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125.39
123.52
122.15
111.07
111.03
111.00
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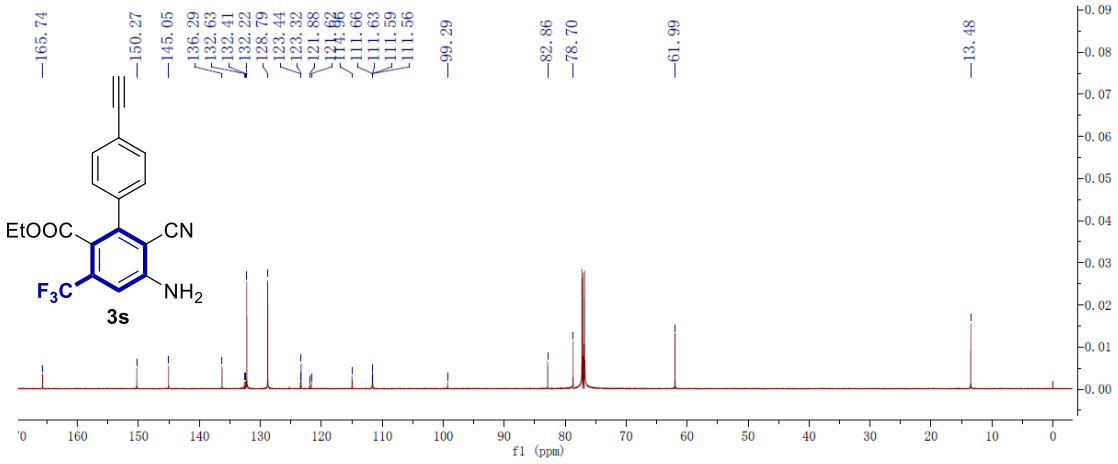
34.74
31.25
13.28
tBu
EtOOC
CN
F3C
NH2
3r
f1 (ppm)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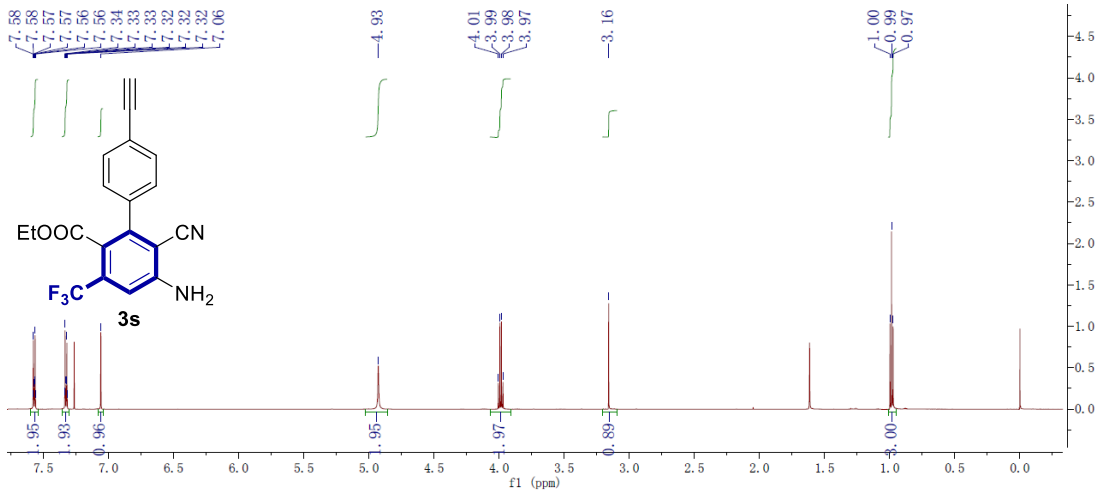
CN
F3C
NH2
3s
f1 (ppm)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7.56
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7.32
7.32
7.32
7.06
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4.01
3.99
3.98
3.97
3.16
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0.99
0.97
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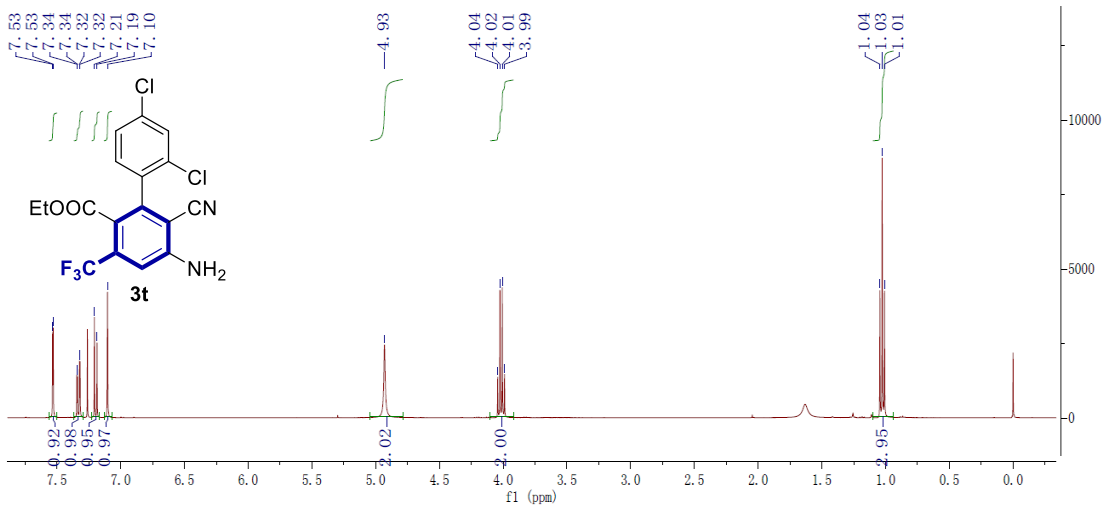
1.95
1.97
0.89
3.00
EtOOC
CN
F3C
NH2
3s
f1 (ppm)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4.93
4.04
4.02
4.01
3.99
1.04
1.03
1.01
Cl
Cl
EtOOC
CN
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NH2
3t
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0.98
0.95
0.97
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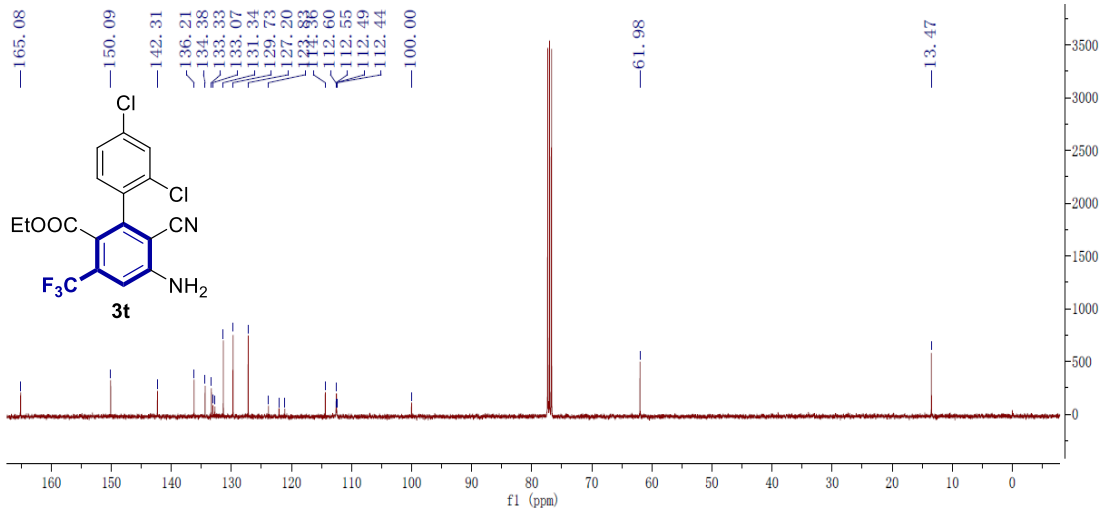
2.95
f1 (ppm)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127.20
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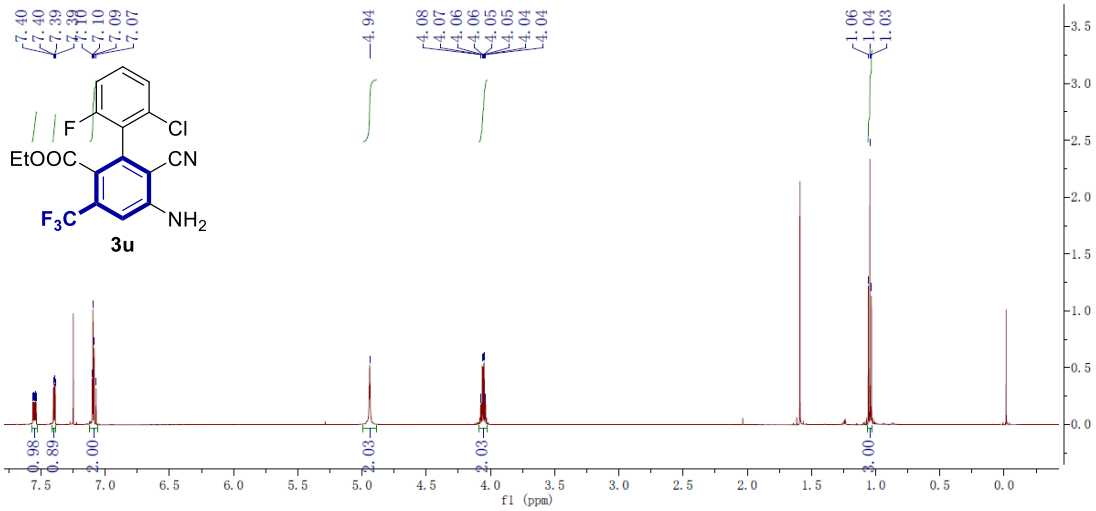
Cl
Cl
EtOOC
CN
F3C
NH2
3t
f1 (ppm)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4.07
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4.06
4.05
4.05
4.04
4.04
1.06
1.04
1.03
F
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NH2
3u
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0.89
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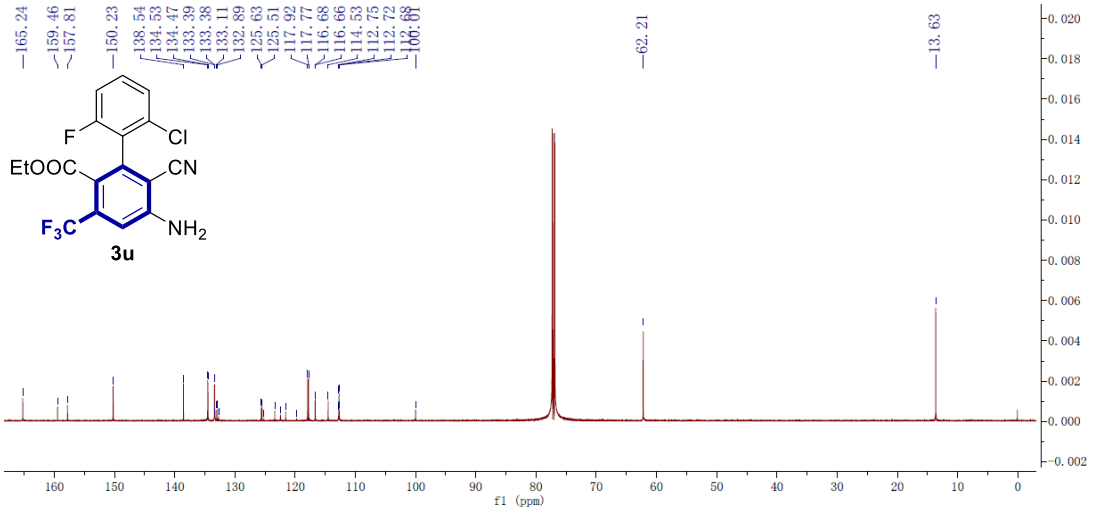
2.03
2.03
3.00
f1 (ppm)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125.51
117.92
117.77
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116.66
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62.21
13.63
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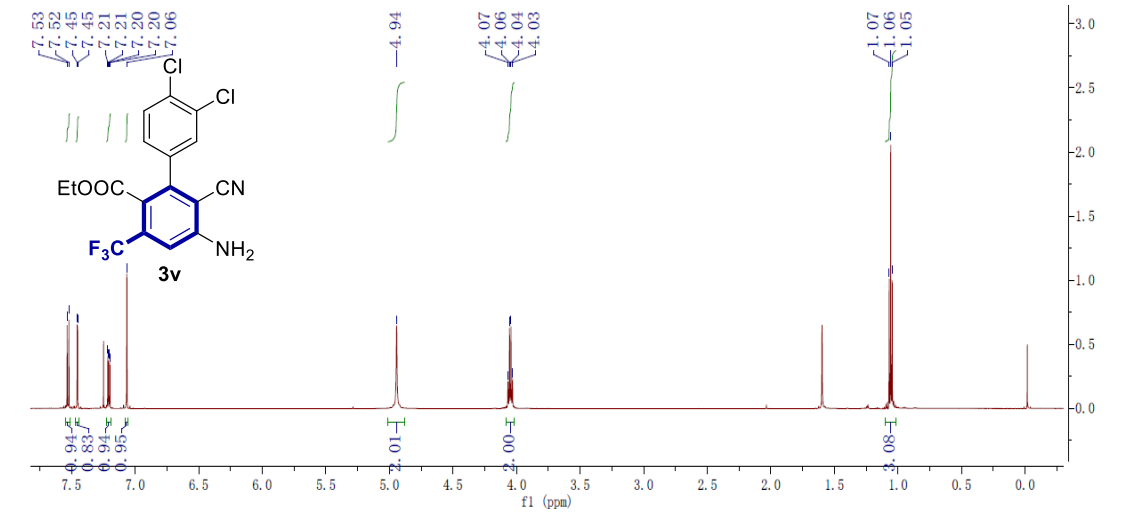
EtOOC
CN
F3C
NH2
3u
f1 (ppm)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7.21
7.20
7.20
7.06
4.94
4.07
4.06
4.04
4.03
1.07
1.06
1.05
Cl
Cl
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3v
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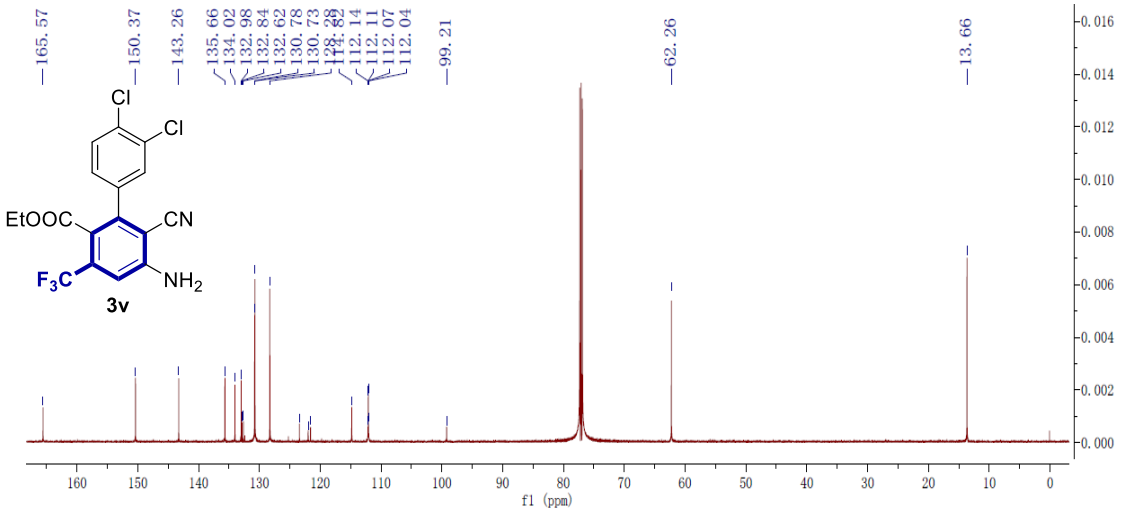
0.95
2.01
2.00
3.08
f1 (ppm)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132.98
132.84
132.62
130.78
130.73
112.14
112.11
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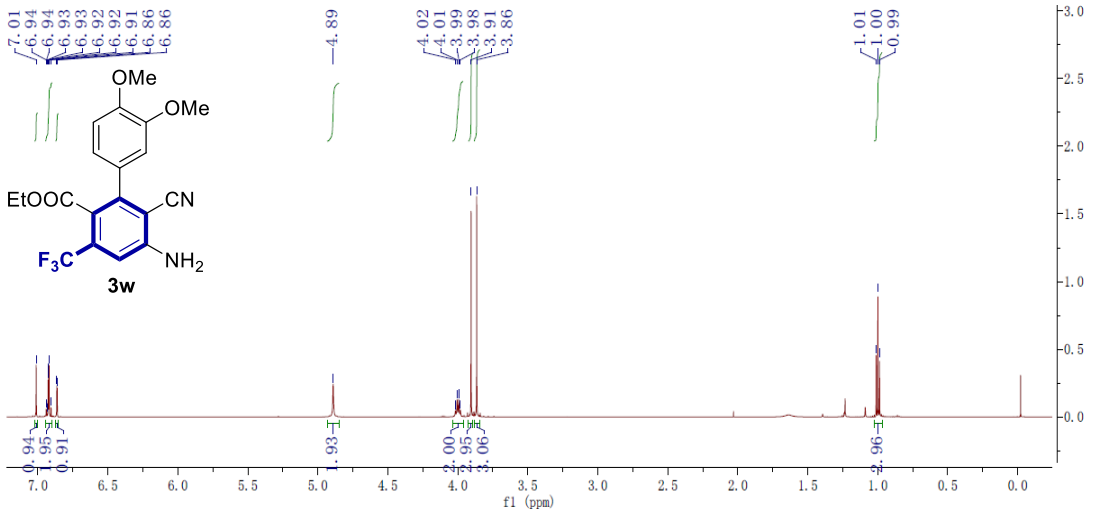
112.04
99.21
62.26
13.66
Cl
Cl
EtOOC
CN
F3C
NH2
3v
f1 (ppm)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6.94
6.94
6.93
6.93
6.92
6.92
6.91
6.86
6.86
4.89
4.02
4.01
3.99
3.98
3.91
3.86
1.01
1.00
0.99
OMe
OMe
EtOOC
CN
F3C
NH2
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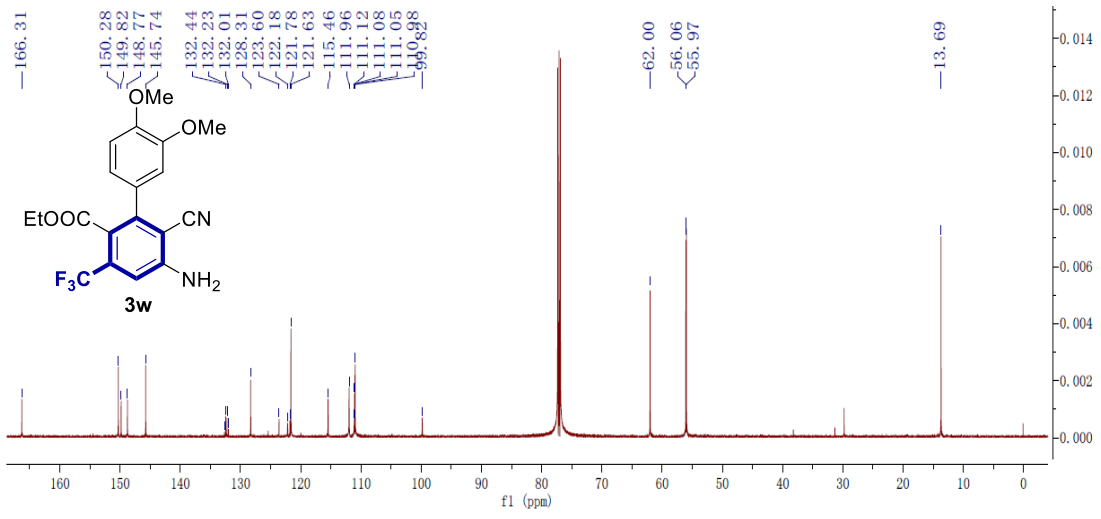
1.95
0.91
1.93
2.00
2.95
3.06
2.96
f1 (ppm)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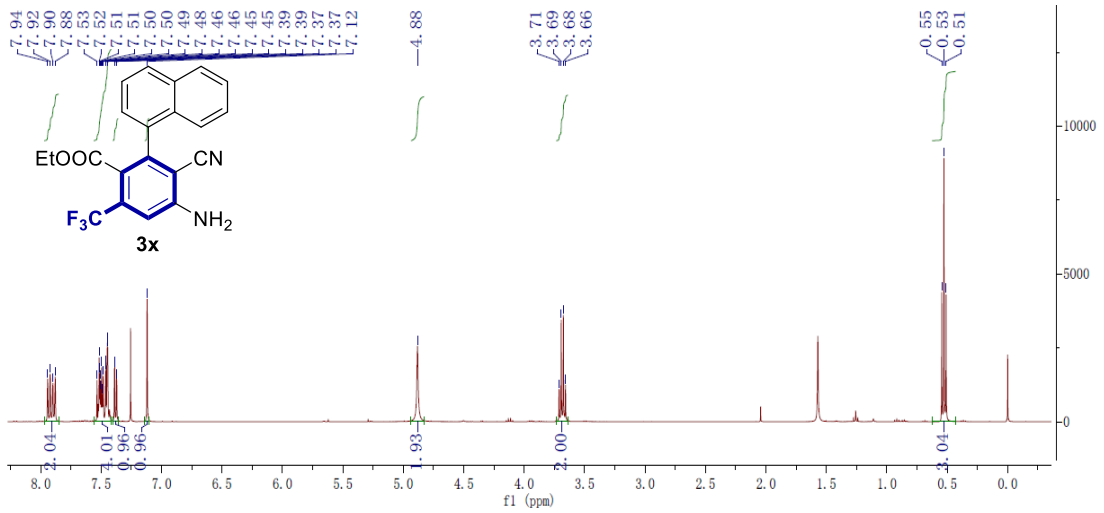
122.18
121.78
121.63
115.46
111.96
111.12
111.08
111.05
110.98
99.82
62.00
56.06
55.97
13.69
OMe
OMe
EtOOC
CN
F3C
NH2
3w
f1 (ppm)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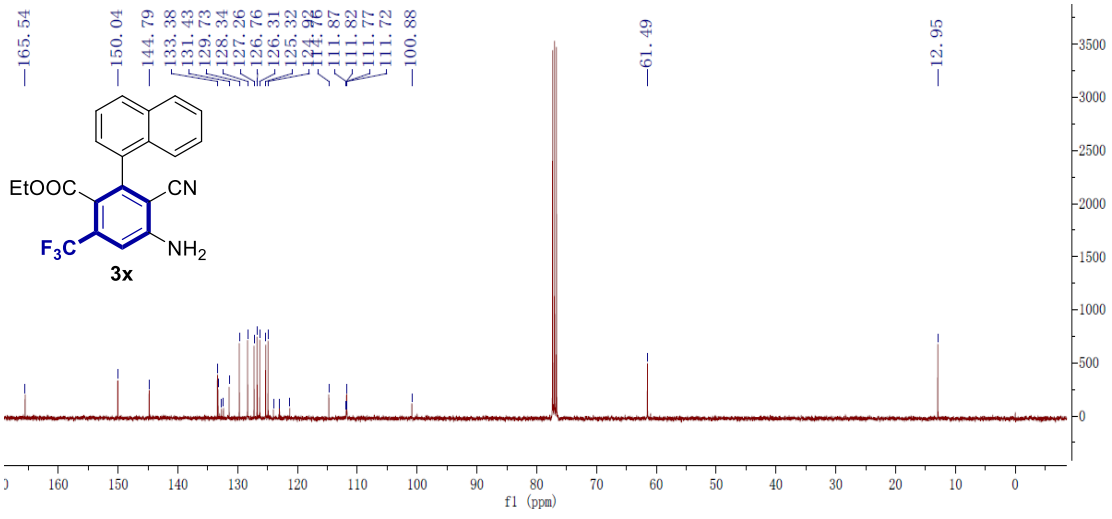
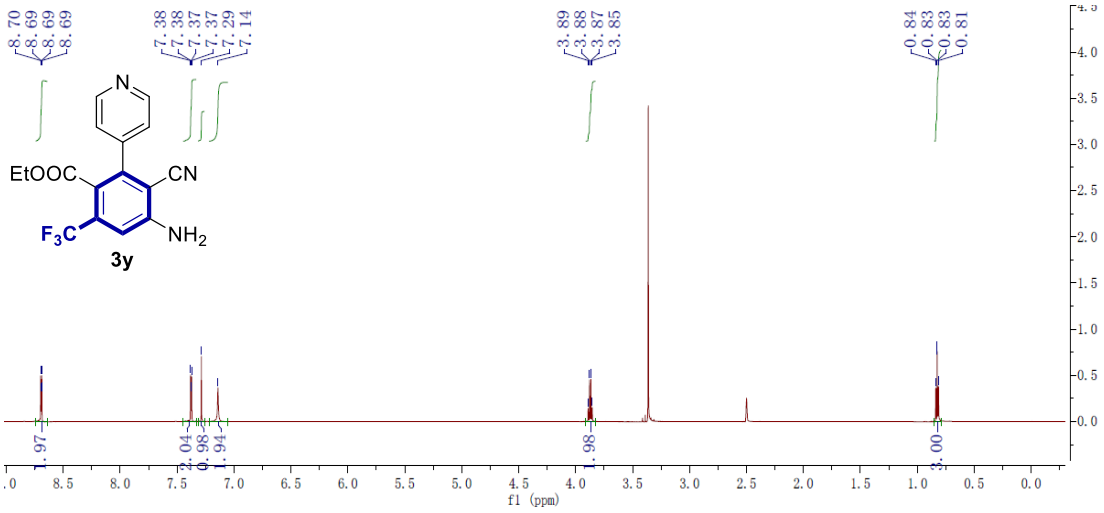
7.92
7.90
7.88
7.53
7.52
7.51
7.51
7.50
7.50
7.49
7.48
7.46
7.46
7.45
7.45
7.39
7.37
7.37
7.12
4.88
3.71
3.69
3.68
3.66
0.55
0.53
0.51
EtOOC
CN
F3C
NH2
3x
10000
5000
0
2.04
2.01
0.96
0.96
1.93
2.00
3.04
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


165.54
150.04
144.79
133.38
131.43
129.73
128.34
127.26
126.76
126.31
125.32
111.87
111.82
111.77
111.72
100.88
61.49
12.95
EtOOC
CN
F3C
NH2
3x
3500
3000
2500
2000
1500
1000
500
0
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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8.69
8.69
8.69
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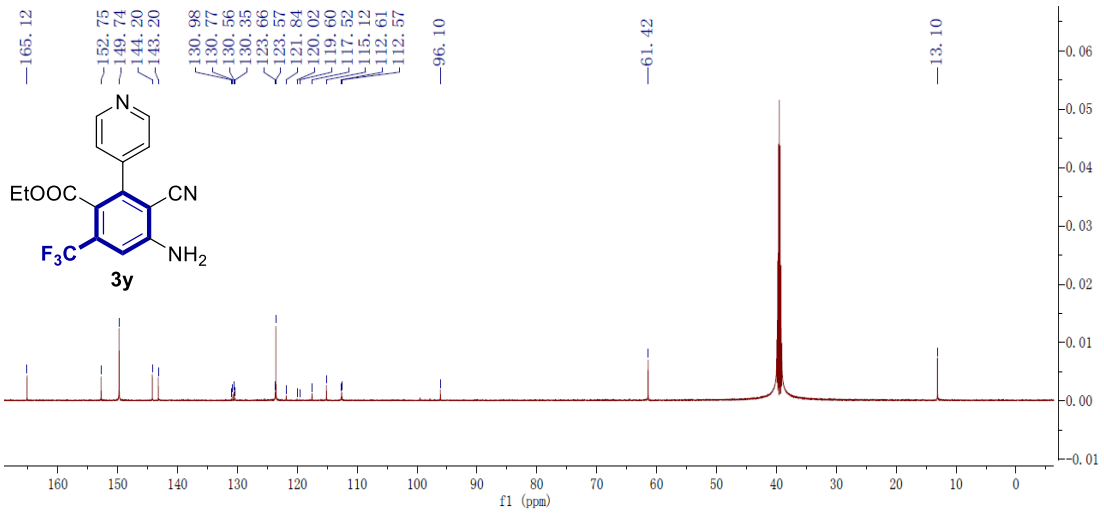
7.38
7.37
7.37
7.29
7.14
3.89
3.88
3.87
3.85
0.84
0.83
0.83
0.81
N
EtOOC
CN
F3C
NH2
3y
1.97
2.04
0.98
1.94
1.98
3.00
f1 (ppm)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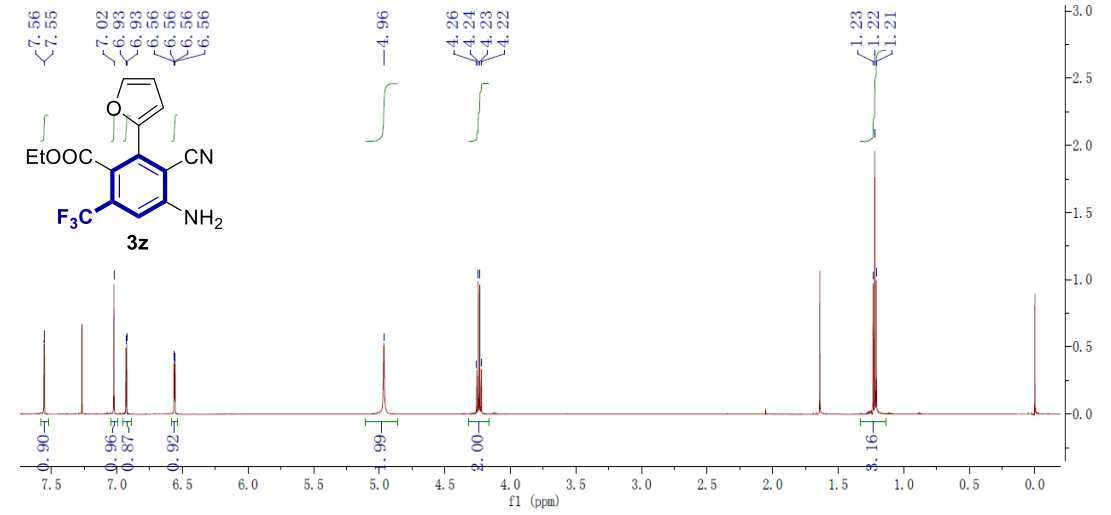
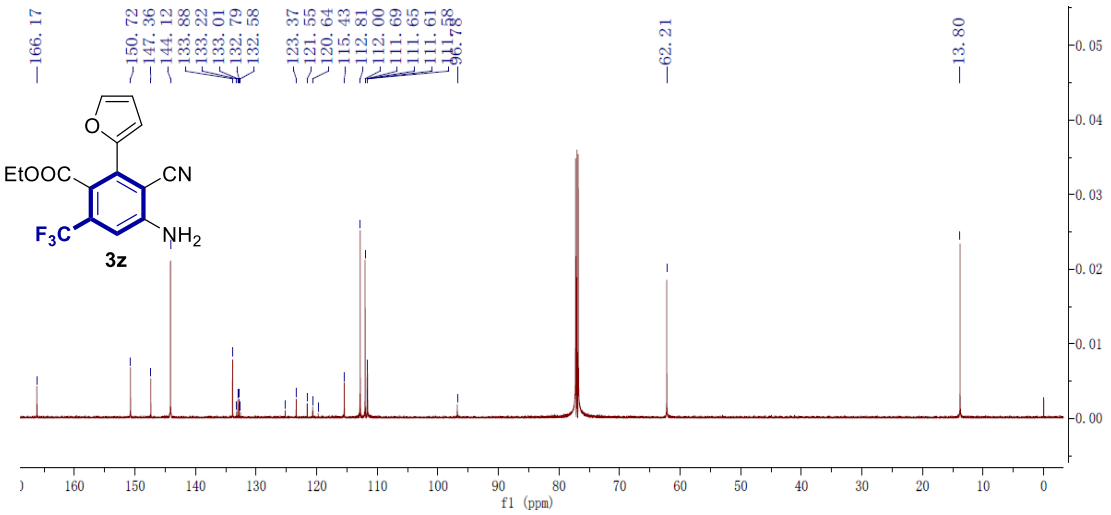
152.75
149.74
144.20
143.20
130.98
130.77
130.56
130.35
123.66
123.57
121.84
120.02
119.60
117.52
115.12
112.61
112.57
96.10
61.42
13.10
N
EtOOC
CN
F3C
NH2
3y
f1 (ppm)


7.56
7.55
7.02
6.93
6.93
6.56
6.56
6.56
6.56
4.96
4.26
4.24
4.23
4.22
1.23
1.22
1.21
EtOOC
CN
F3C
NH2
3z
0.90
0.96
0.87
0.92
1.99
2.00
3.16
f1 (ppm)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133.22
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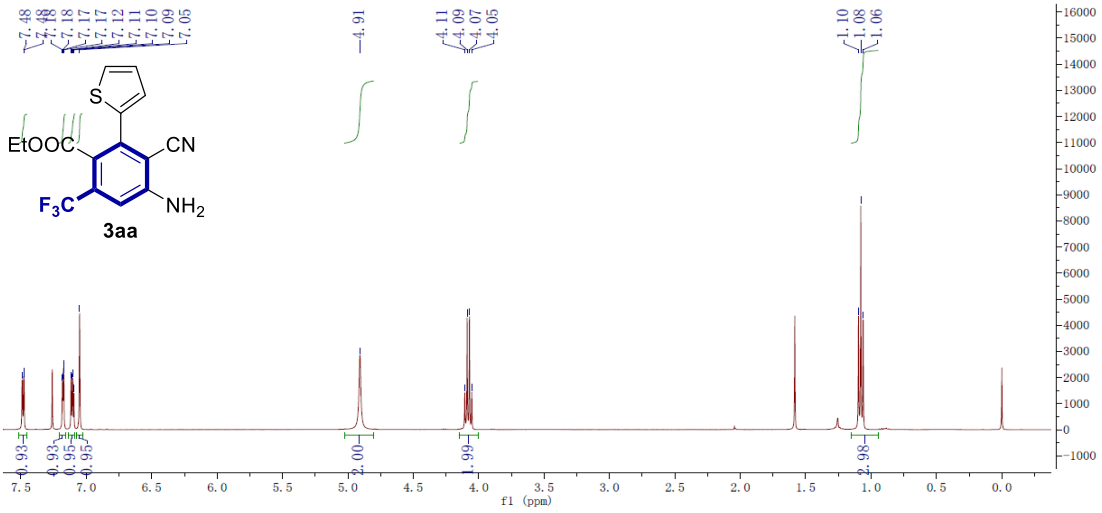
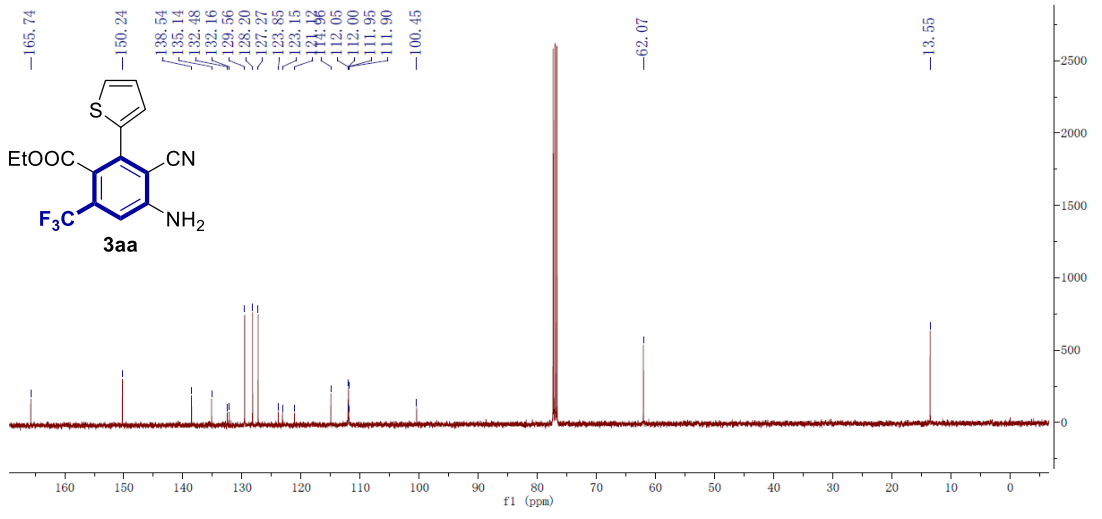
132.79
132.58
123.37
121.55
120.64
115.43
112.81
112.00
111.69
111.65
111.61
96.78
62.21
13.80
EtOOC
CN
F3C
NH2
3z
f1 (ppm)


7.48
7.48
7.18
7.17
7.17
7.12
7.11
7.10
7.09
7.05
4.91
4.11
4.09
4.07
4.05
1.10
1.08
1.06
S
EtOOC
CN
F3C
NH2
3aa
0.93
0.93
0.95
0.95
2.00
1.99
2.98
f1 (ppm)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150.24
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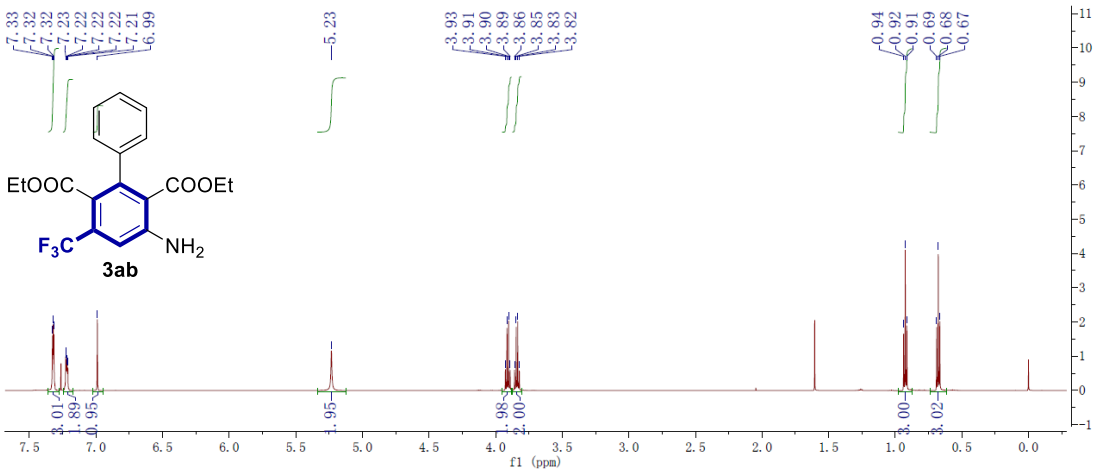
135.14
132.48
132.16
129.56
128.20
127.27
123.85
123.15
112.05
112.00
111.95
111.90
100.45
62.07
13.55
S
EtOOC
CN
F3C
NH2
3aa
f1 (ppm)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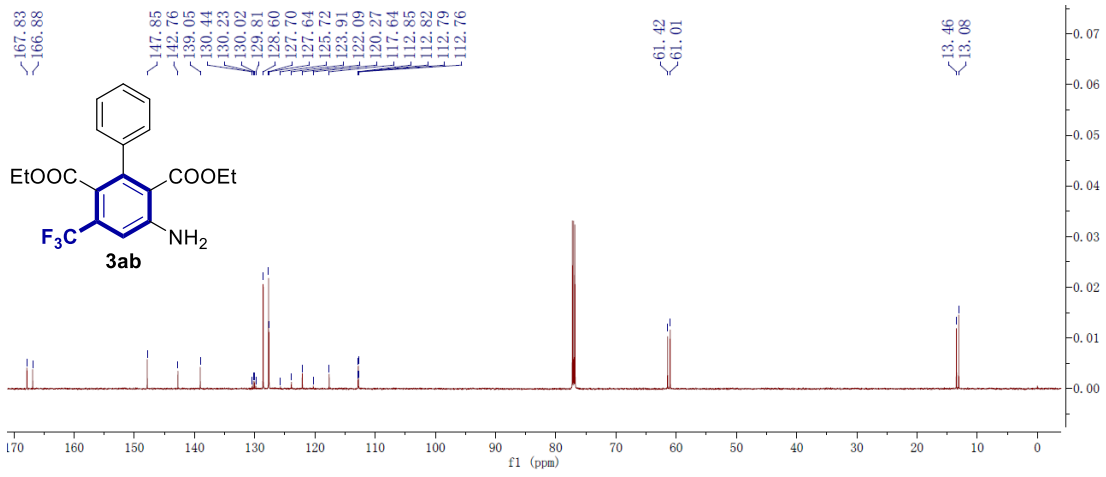
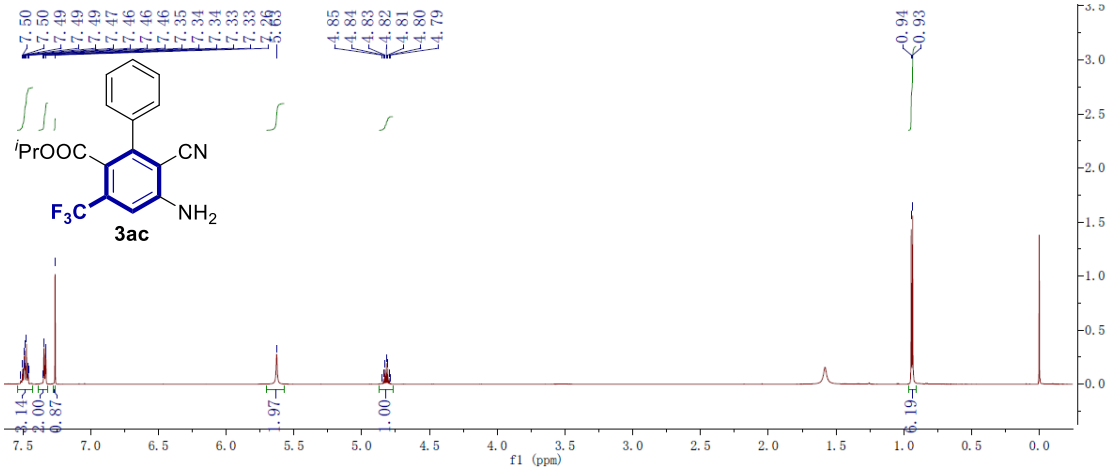
7.32
7.32
7.23
7.22
7.22
7.22
7.21
6.99
5.23
3.93
3.91
3.90
3.89
3.86
3.85
3.83
3.82
0.94
0.92
0.91
0.69
0.68
0.67
EtOOC
COOEt
F3C
NH2
3ab
3.01
1.89
0.95
1.95
1.98
2.00
3.00
3.02
f1 (ppm)


167.83
166.88
147.85
142.76
139.05
130.44
130.23
130.02
129.81
128.60
127.70
127.64
125.72
123.91
122.09
120.27
117.64
112.85
112.82
112.79
112.76
61.42
61.01
13.46
13.08
EtOOC
COOEt
F3C
NH2
3ab
f1 (ppm)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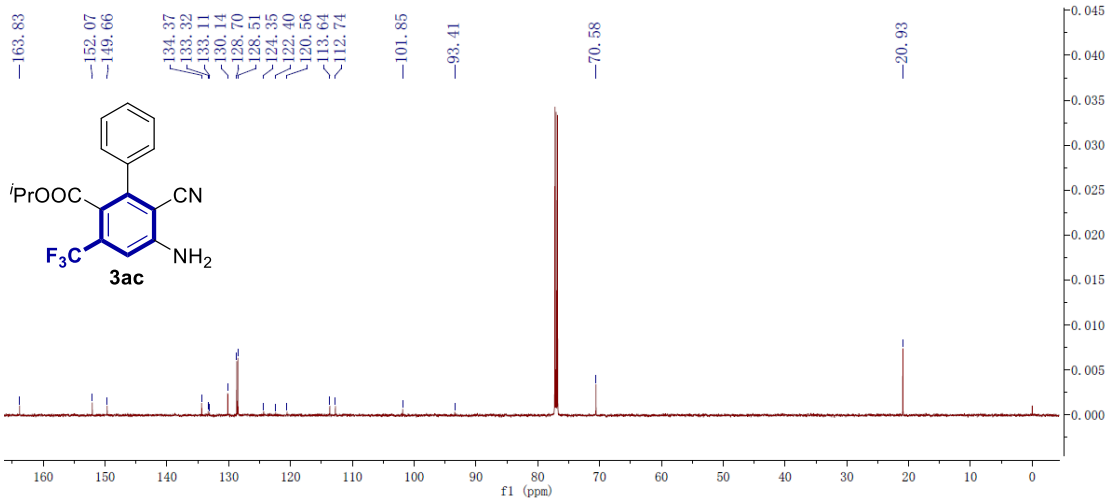
7.50
7.49
7.49
7.49
7.47
7.46
7.46
7.46
7.35
7.34
7.34
7.33
7.33
7.26
5.63
4.85
4.84
4.83
4.82
4.81
4.80
4.79
0.94
0.93
iPrOOC
CN
F3C
NH2
3ac
3.14
2.00
0.87
1.97
1.00
6.19
f1 (ppm)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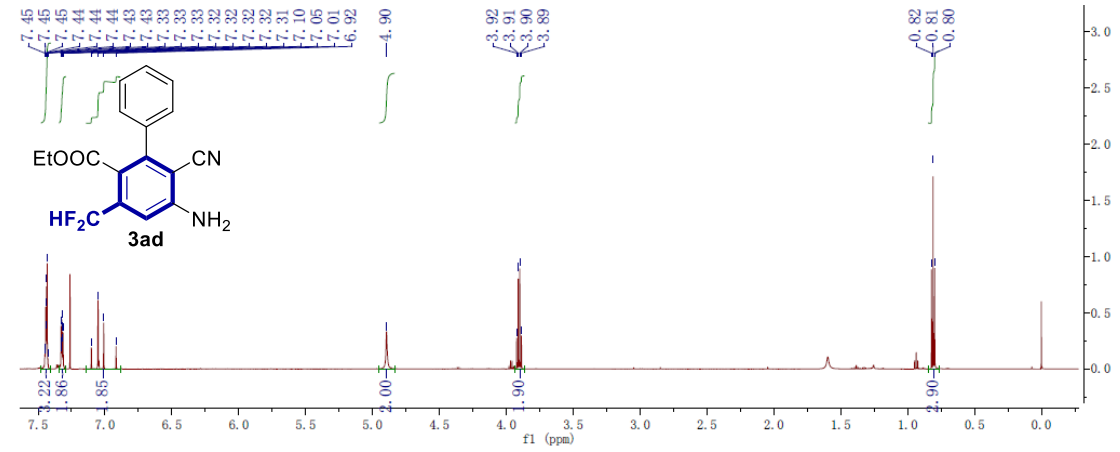
152.07
149.66
134.37
133.32
133.11
130.14
128.70
128.51
124.35
122.40
120.56
113.64
112.74
101.85
93.41
70.58
20.93
iPrOOC
CN
F3C
NH2
3ac
f1 (ppm)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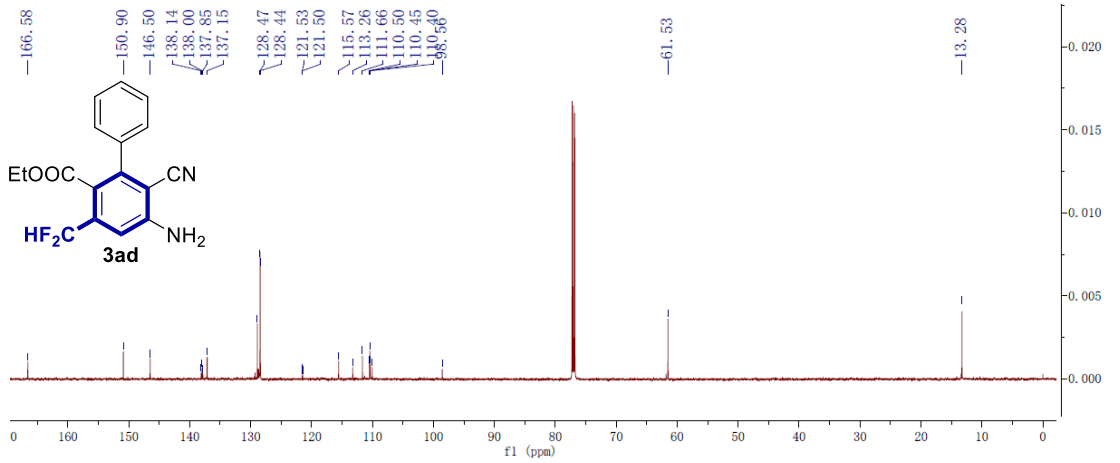
7.45
7.45
7.44
7.44
7.44
7.43
7.43
7.33
7.33
7.32
7.32
7.32
7.32
7.31
7.10
7.05
7.01
6.92
4.90
3.92
3.91
3.90
3.89
0.82
0.81
0.80
EtOOC
CN
HF2C
NH2
3ad
2.22
1.86
1.85
2.00
1.90
2.90
f1 (ppm)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146.50
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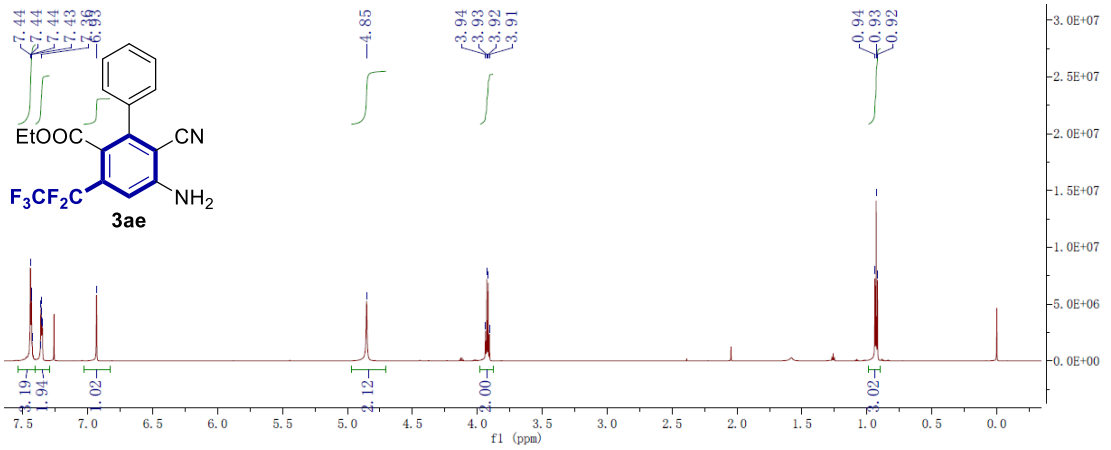
138.00
137.85
137.15
128.47
128.44
121.53
121.50
115.57
113.26
111.66
110.50
110.45
110.40
98.56
61.53
13.28
EtOOC
CN
HF2C
NH2
3ad
f1 (ppm)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7.44
7.44
7.43
7.36
6.93
4.85
3.94
3.93
3.92
3.91
0.94
0.93
0.92
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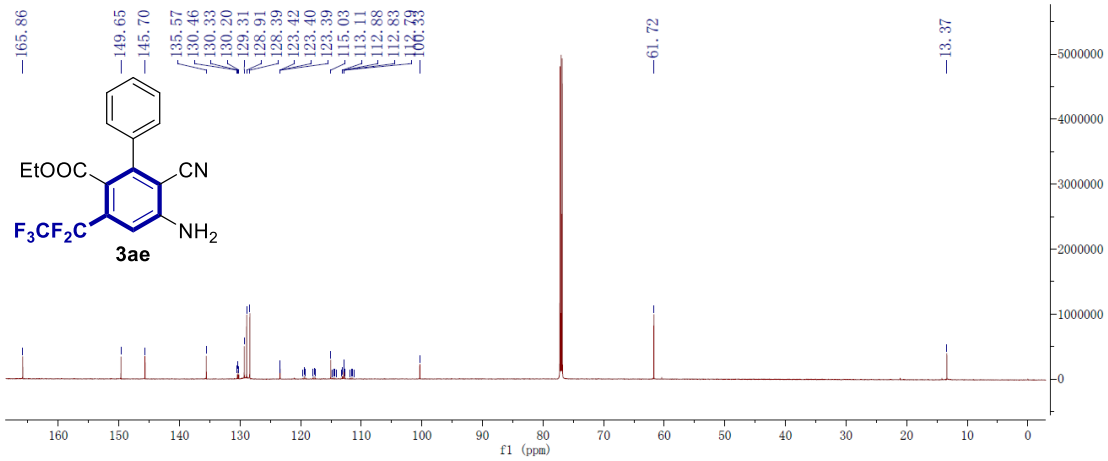
CN
F3CF2C
NH2
3ae
2.19
1.94
1.02
2.12
2.00
3.02
f1 (ppm)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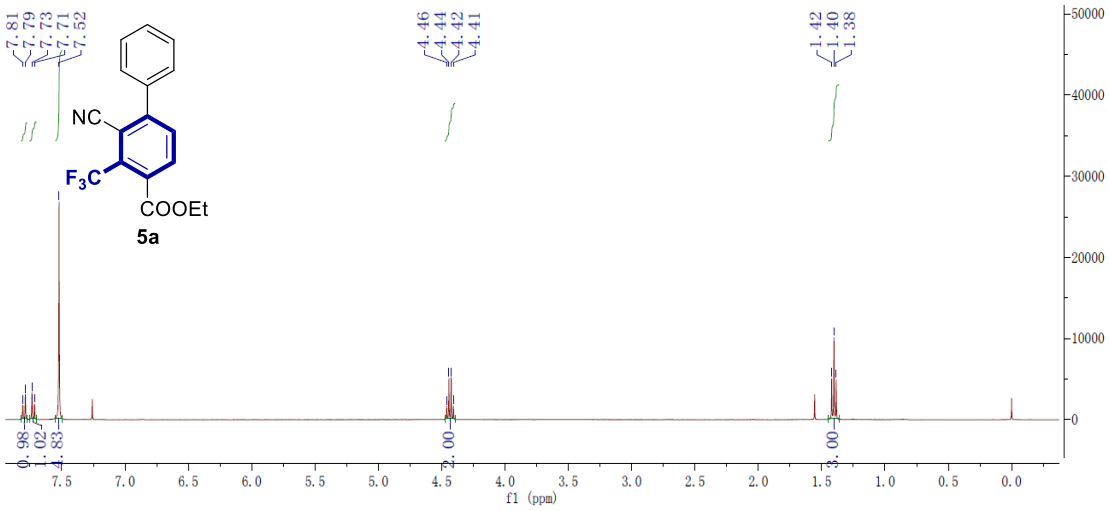
149.65
145.70
135.57
130.46
130.33
130.20
129.31
128.91
128.39
123.42
123.40
123.39
115.03
113.11
112.88
112.83
61.72
13.37
EtOOC
CN
F3CF2C
NH2
3ae
f1 (ppm)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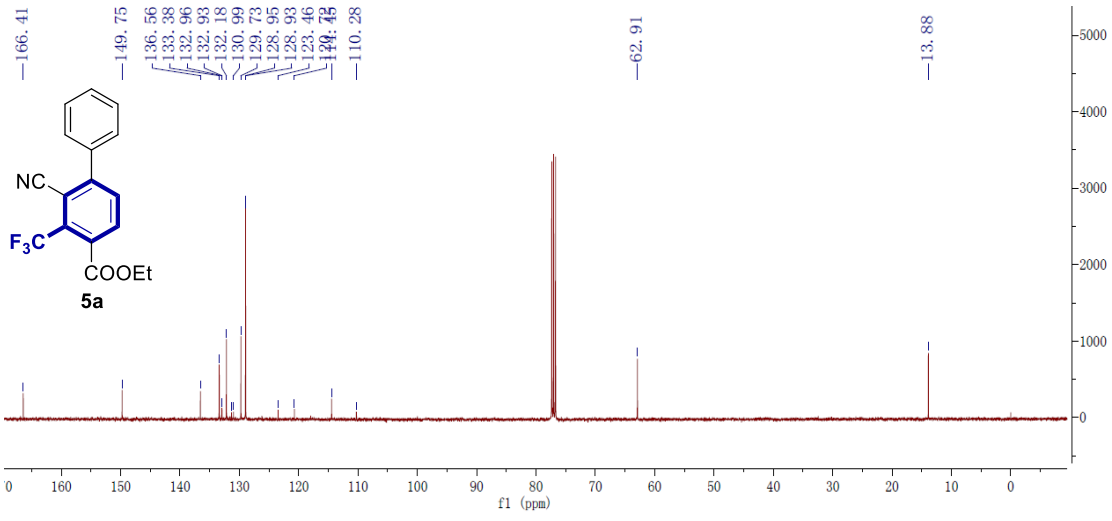
7.79
7.73
7.71
7.52
4.46
4.44
4.42
4.41
1.42
1.40
1.38
NC
F3C
COOEt
5a
0.98
1.02
4.83
2.00
3.00
f1 (ppm)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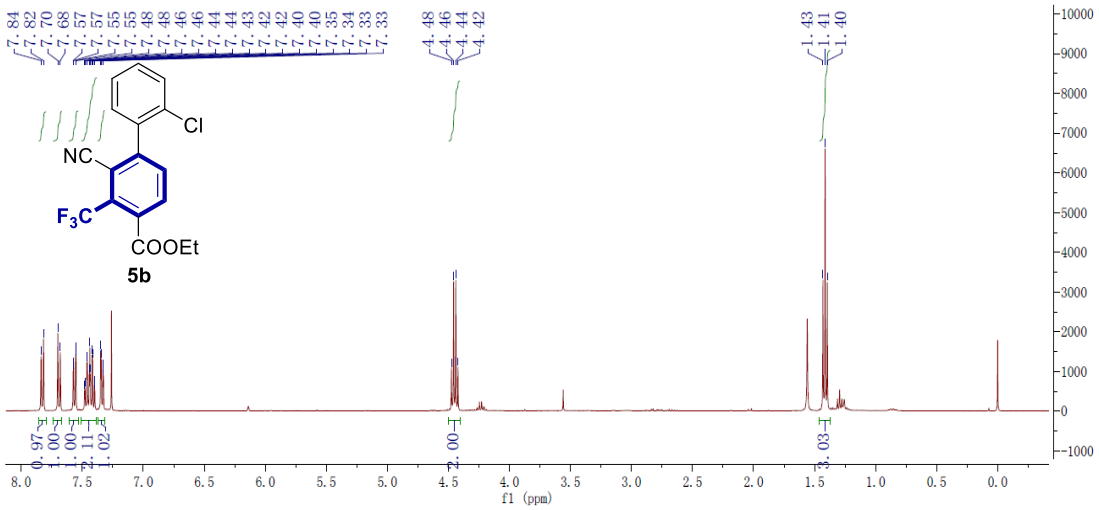
133.38
132.96
132.93
132.18
130.99
129.73
128.95
128.93
123.46
110.28
62.91
13.88
NC
F3C
COOEt
5a
f1 (ppm)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7.68
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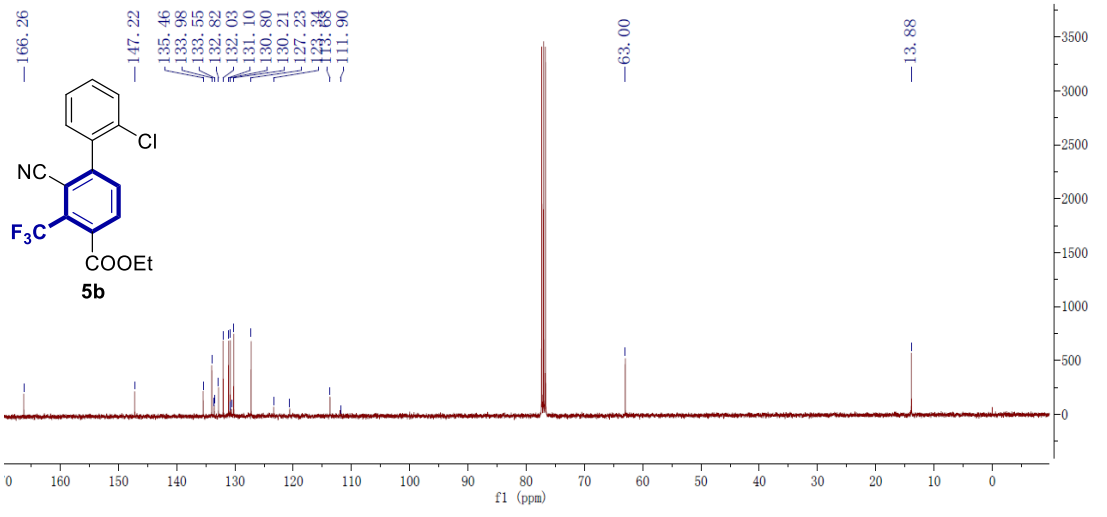
7.57
7.55
7.55
7.48
7.48
7.46
7.46
7.44
7.44
7.43
7.42
7.42
7.40
7.40
7.35
7.34
7.33
7.33
4.48
4.46
4.44
4.42
1.43
1.41
1.40
Cl
NC
F3C
COOEt
5b
0.97
1.00
1.00
2.11
1.02
2.00
3.03
f1 (ppm)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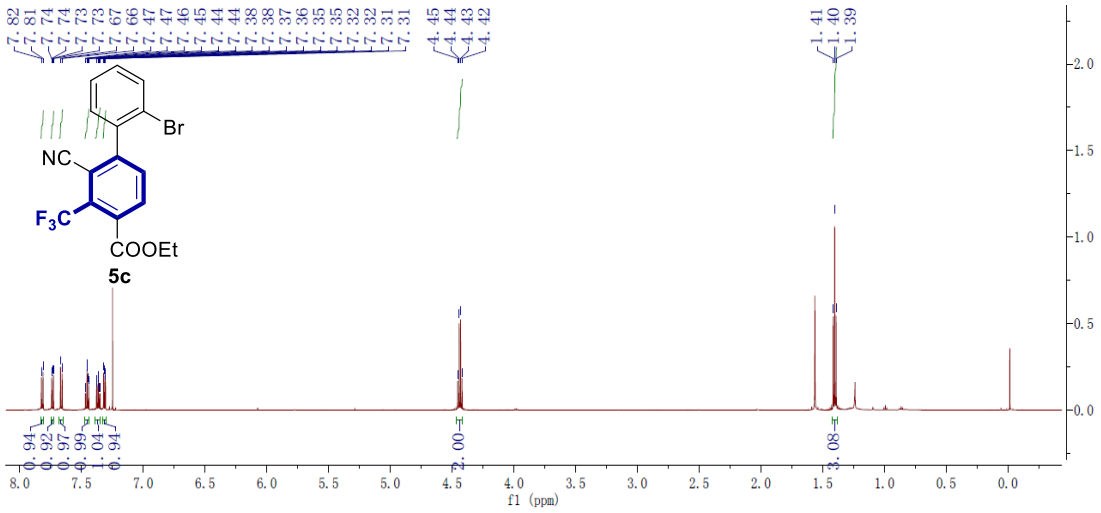
133.98
133.55
132.82
132.03
131.10
130.80
130.21
127.23
123.34
113.68
111.90
63.00
13.88
Cl
NC
F3C
COOEt
5b
f1 (ppm)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7.66
7.47
7.47
7.46
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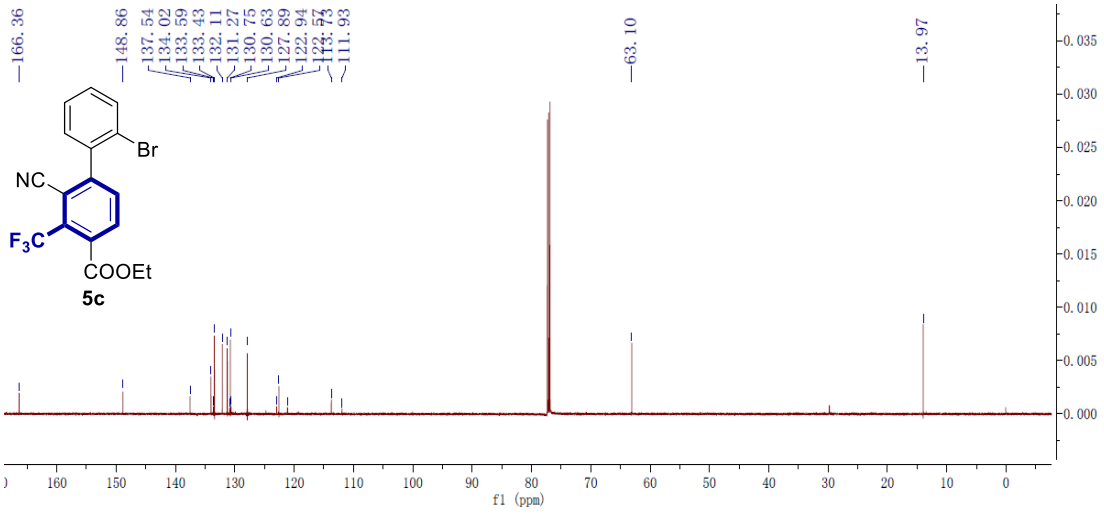
7.44
7.38
7.38
7.37
7.36
7.35
7.35
7.32
7.31
7.31
4.45
4.44
4.43
4.42
1.41
1.40
1.39
Br
NC
F3C
COOEt
5c
0.94
0.92
0.97
0.99
1.04
0.94
2.00
3.08
f1 (ppm)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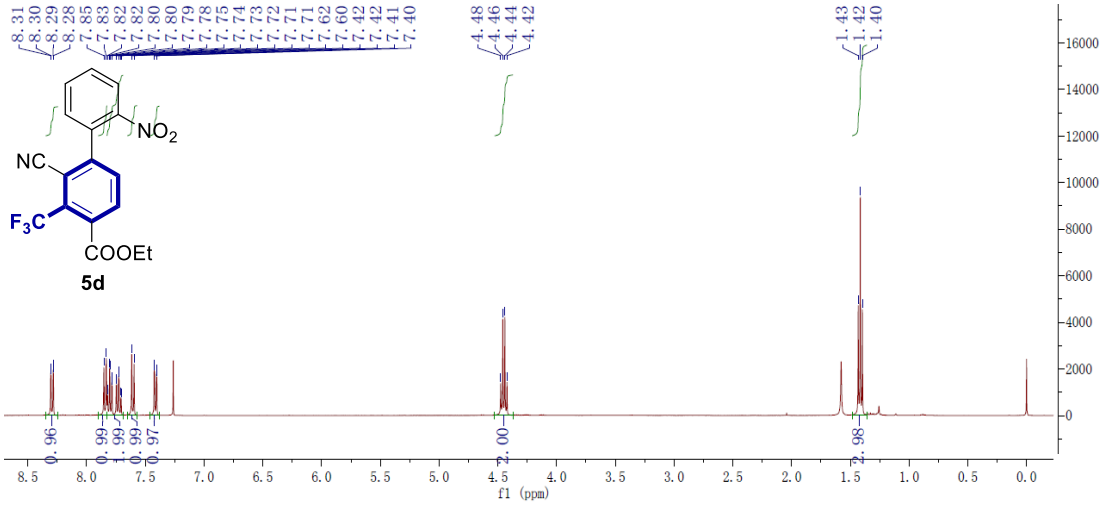
132.11
131.27
130.75
130.63
127.89
122.94
122.57
113.73
111.93
63.10
13.97
Br
NC
F3C
COOEt
5c
f1 (ppm)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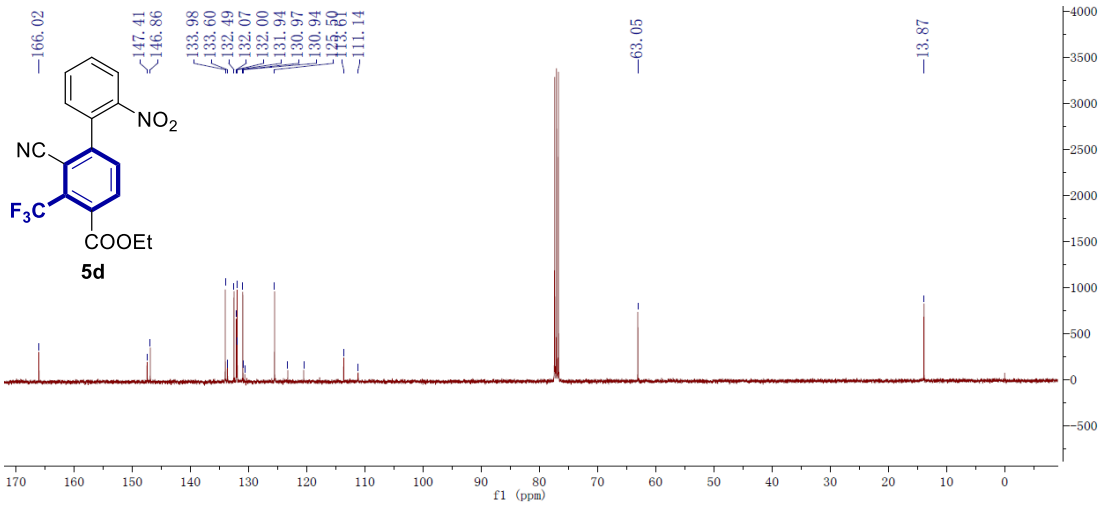
7.82
7.82
7.80
7.80
7.79
7.78
7.75
7.74
7.73
7.72
7.71
7.71
7.62
7.60
7.42
7.42
7.41
7.40
4.48
4.46
4.44
4.42
1.43
1.42
1.40
NO2
NC
F3C
COOEt
5d
0.96
0.99
1.99
0.99
0.97
2.00
2.98
f1 (ppm)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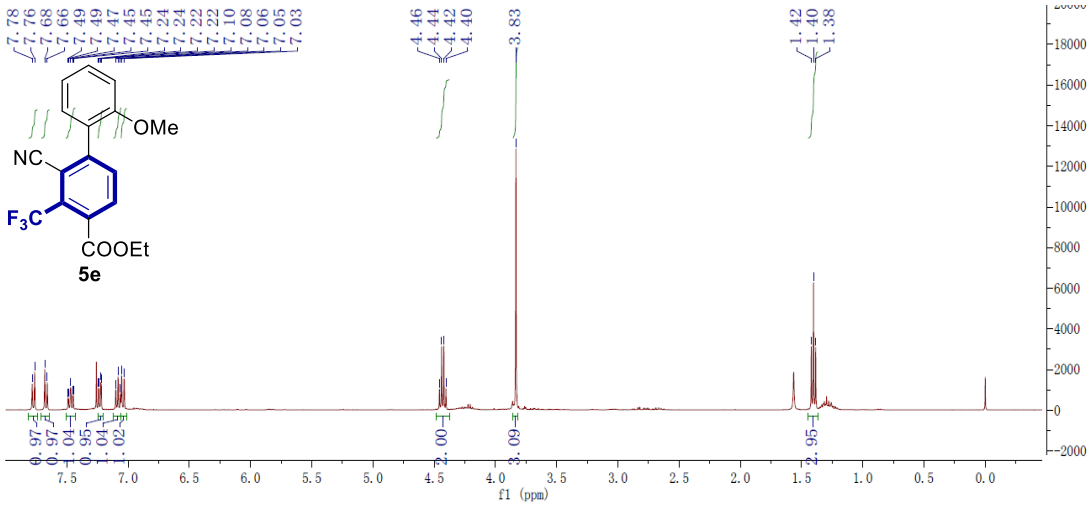
133.60
132.49
132.07
132.00
131.94
130.97
130.94
125.50
113.61
111.14
63.05
13.87
NO2
NC
F3C
COOEt
5d
f1 (ppm)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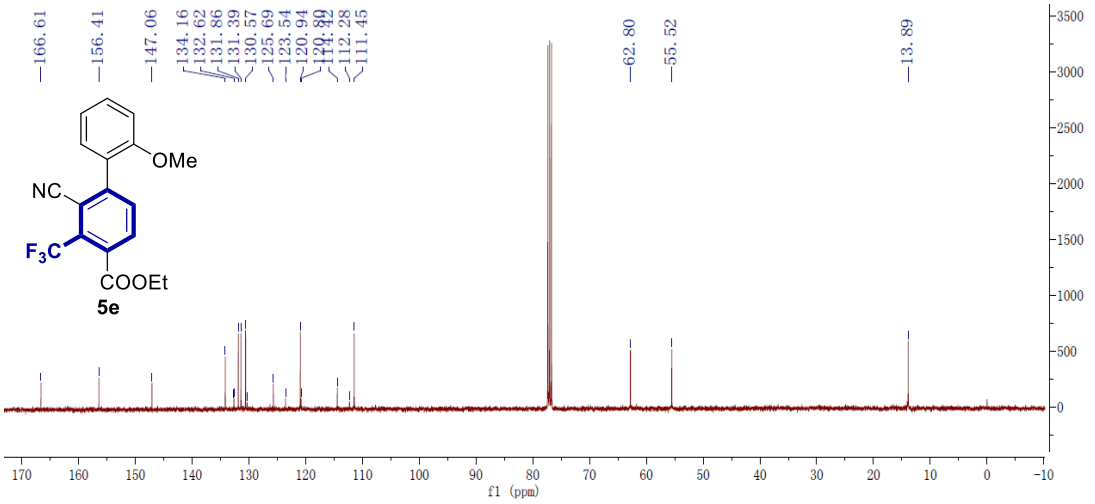
7.45
7.45
7.24
7.24
7.22
7.10
7.08
7.06
7.05
7.03
4.46
4.44
4.42
4.40
3.83
1.42
1.40
1.38
OMe
NC
F3C
COOEt
5e
0.97
0.97
1.04
0.95
1.04
1.02
2.00
3.09
2.95
f1 (ppm)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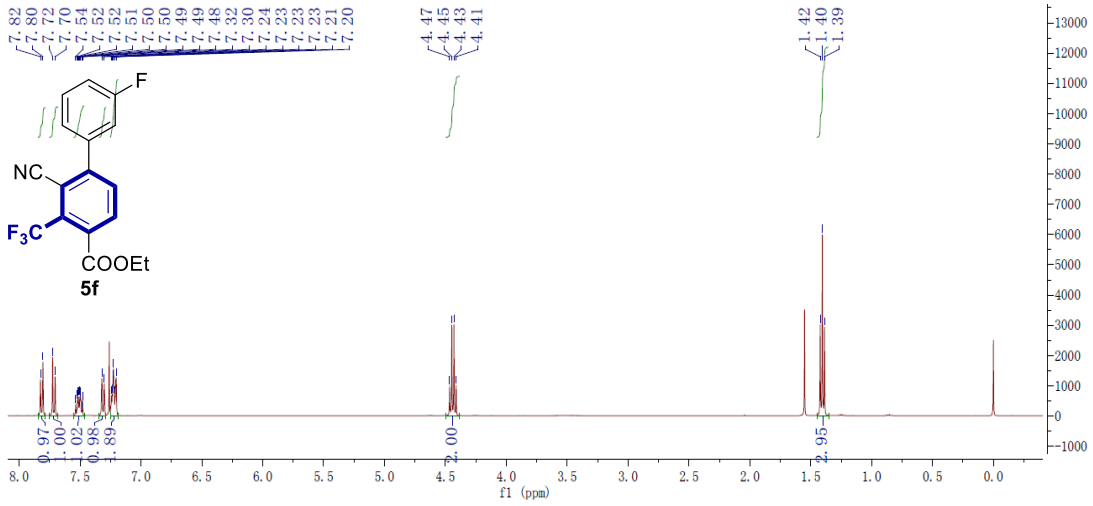
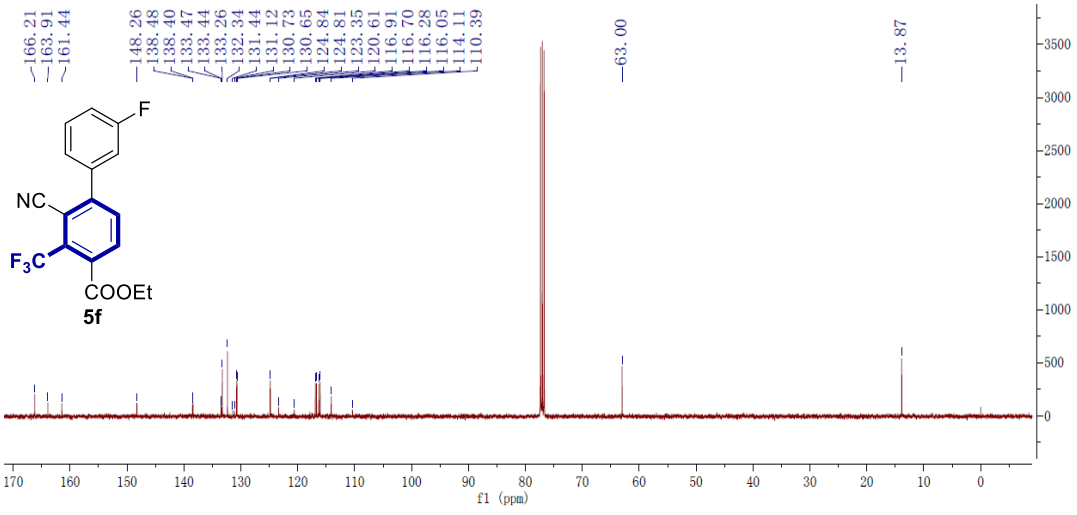
147.06
134.16
132.62
131.86
131.39
130.57
125.69
123.54
120.94
112.28
111.45
62.80
55.52
13.89
OMe
NC
F3C
COOEt
5e
f1 (ppm)


7.82
7.80
7.72
7.70
7.54
7.52
7.52
7.51
7.50
7.50
7.49
7.49
7.48
7.32
7.30
7.24
7.23
7.23
7.21
7.20
4.47
4.45
4.43
4.41
1.42
1.40
1.39
F
NC
F3C
COOEt
5f
0.97
1.00
1.02
0.98
1.89
2.00
2.95
f1 (ppm)


166.21
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161.44
148.26
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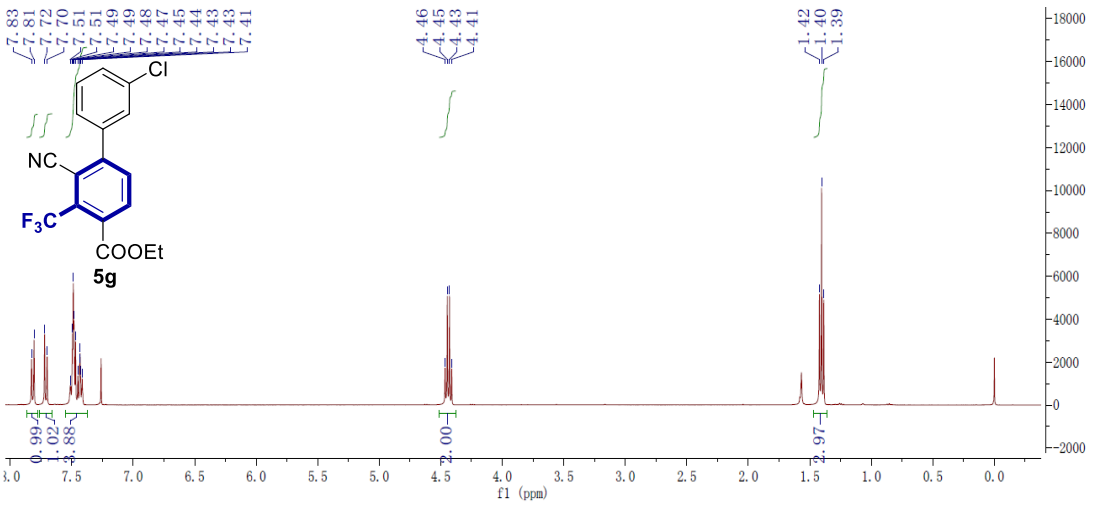
131.44
131.12
130.73
130.65
124.84
124.81
123.35
120.61
116.91
116.70
116.28
116.05
114.11
110.39
63.00
13.87
F
NC
F3C
COOEt
5f
f1 (ppm)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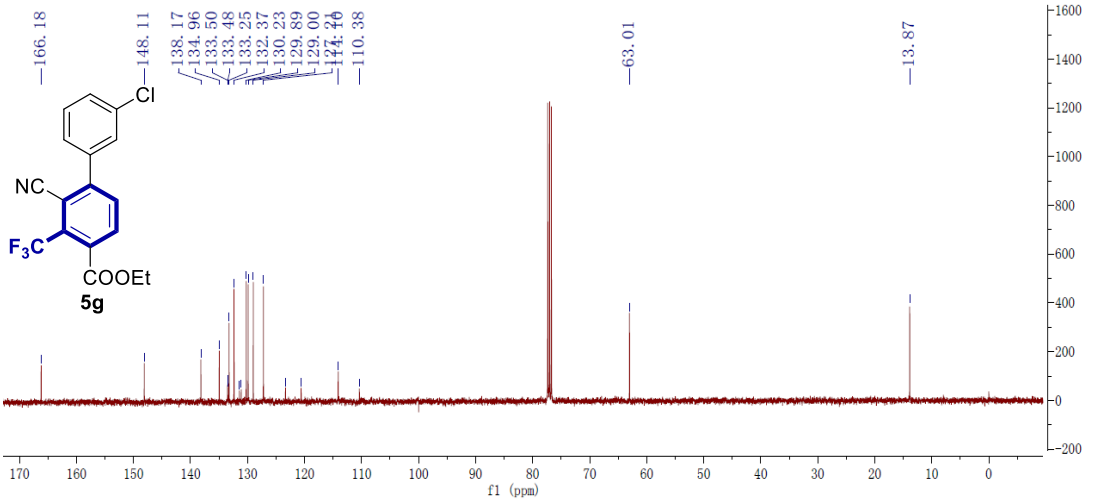
7.51
7.49
7.49
7.48
7.47
7.45
7.44
7.43
7.43
7.41
4.46
4.45
4.43
4.41
1.42
1.40
1.39
Cl
NC
F3C
COOEt
5g
0.99
1.02
3.88
2.00
2.97
f1 (ppm)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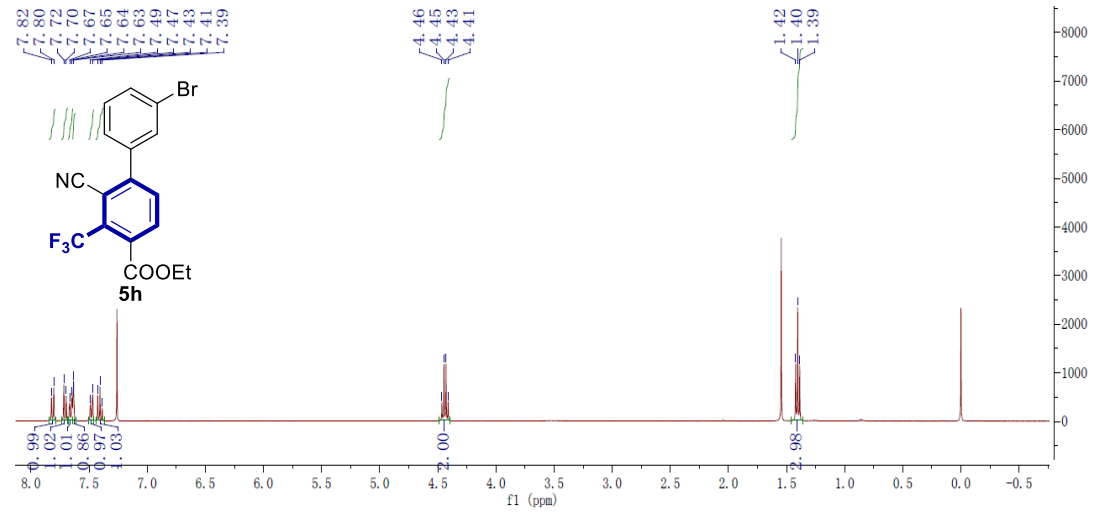
133.50
133.48
133.25
132.37
130.23
129.89
129.00
110.38
63.01
13.87
Cl
NC
F3C
COOEt
5g
f1 (ppm)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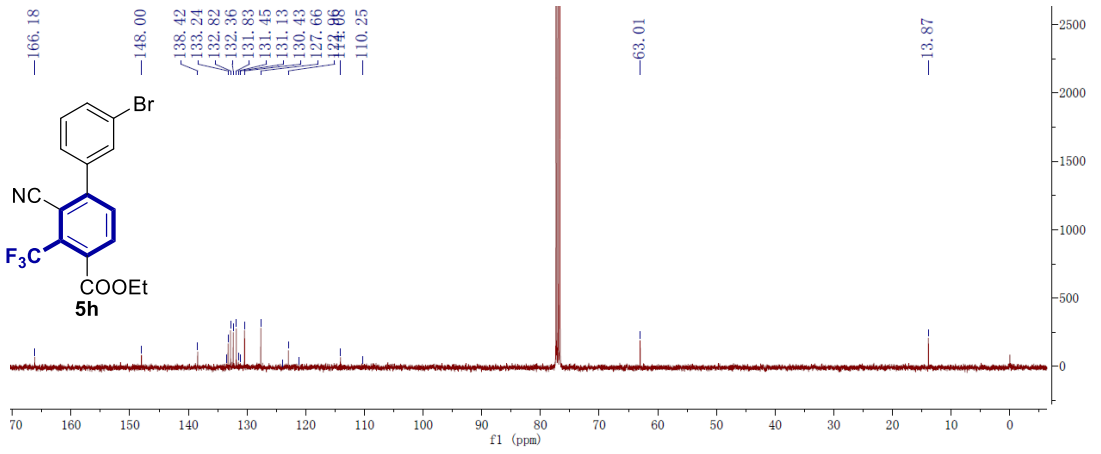
7.63
7.49
7.47
7.43
7.41
7.39
4.46
4.45
4.43
4.41
1.42
1.40
1.39
Br
NC
F3C
COOEt
5h
0.99
1.02
1.01
0.86
0.97
1.03
2.00
2.98
f1 (ppm)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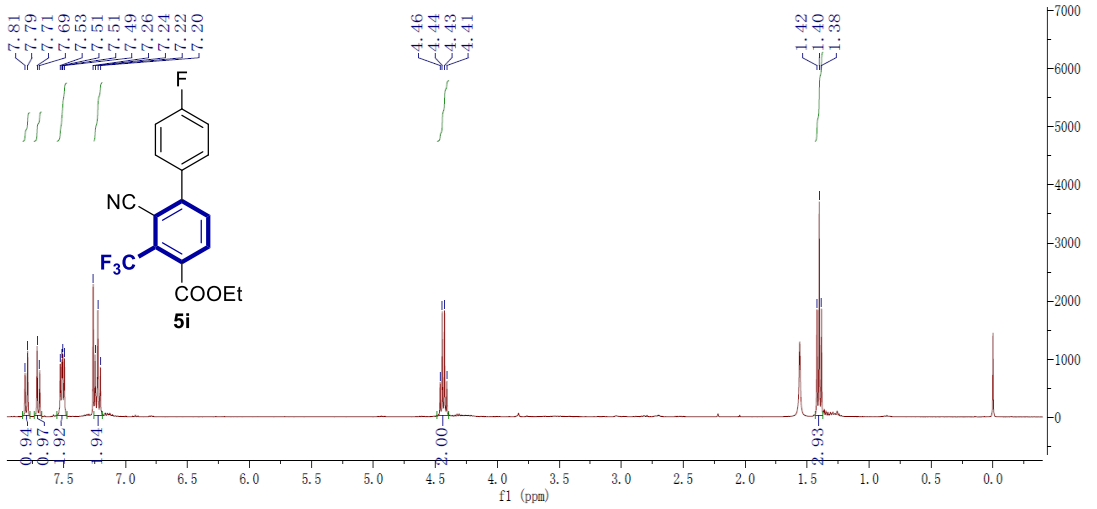
110.25
63.01
13.87
Br
NC
F3C
COOEt
5h
f1 (ppm)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7.20
4.46
4.44
4.43
4.41
1.42
1.40
1.38
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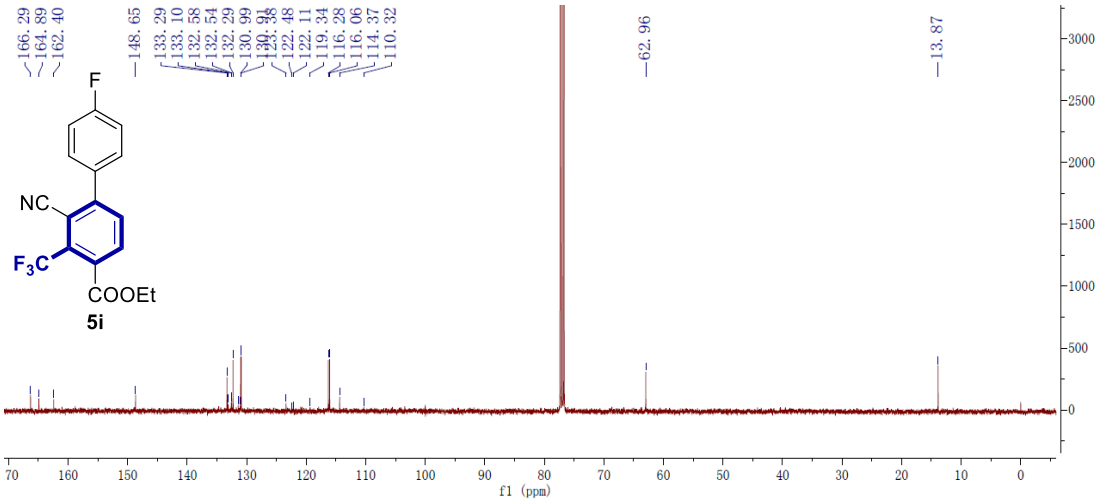
F3C
COOEt
5i
0.94
0.97
1.92
1.94
2.00
2.93
f1 (ppm)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123.38
122.48
122.11
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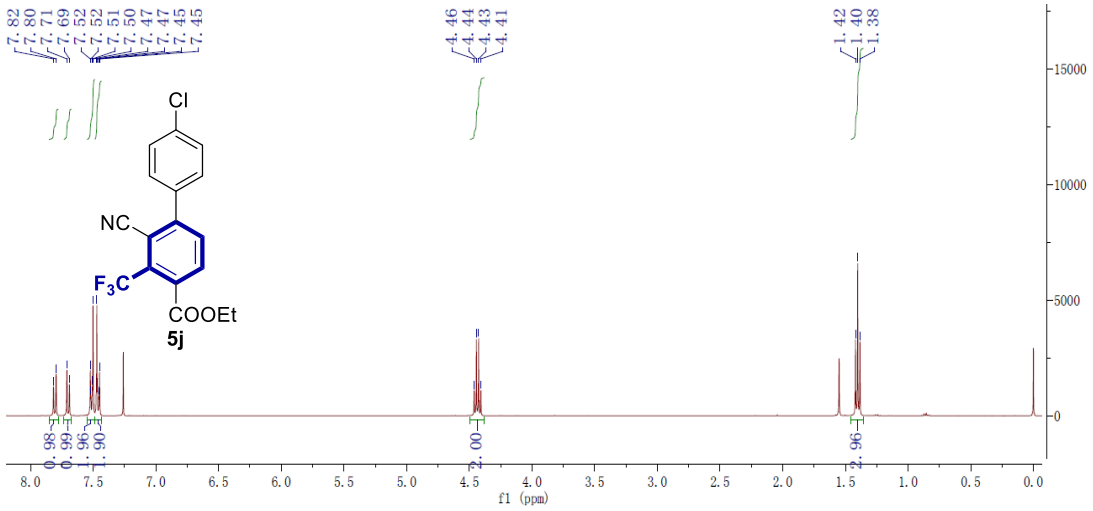
114.37
110.32
62.96
13.87
F
NC
F3C
COOEt
5i
f1 (ppm)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7.50
7.47
7.45
4.46
4.44
4.43
4.41
1.42
1.40
1.38
Cl
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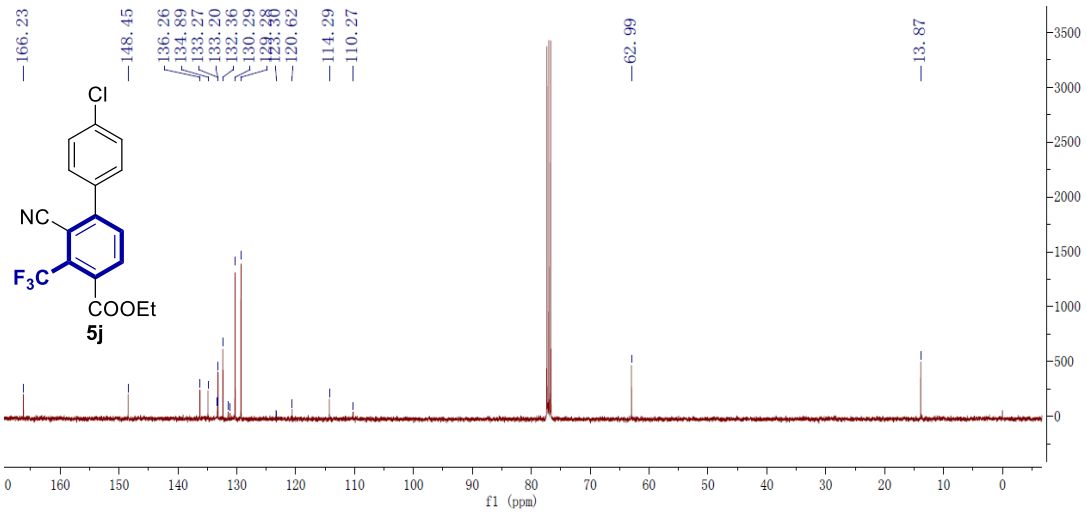
F3C
COOEt
5j
0.98
0.99
1.96
1.90
2.00
2.96
f1 (ppm)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133.27
133.20
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130.29
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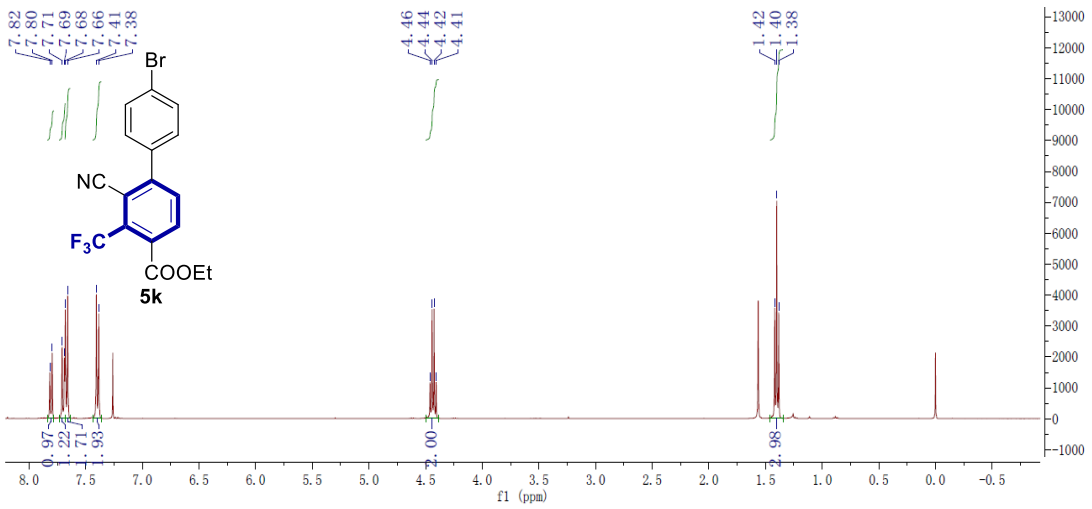
114.29
110.27
62.99
13.87
Cl
NC
F3C
COOEt
5j
f1 (ppm)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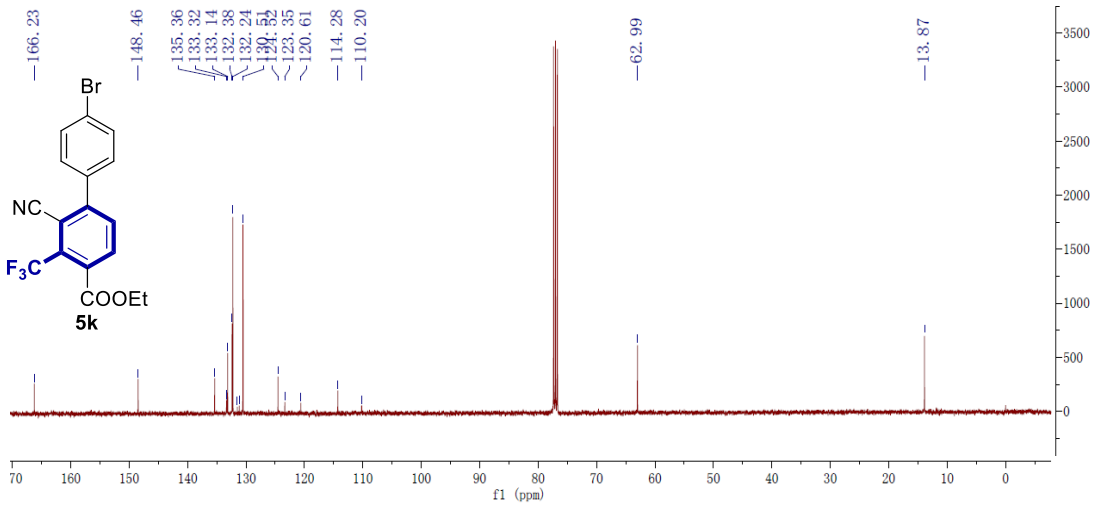
7.66
7.41
7.38
4.46
4.44
4.42
4.41
1.42
1.40
1.38
Br
NC
F3C
COOEt
5k
0.97
1.22
1.71
1.93
2.00
2.98
f1 (ppm)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133.32
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132.38
132.24
123.35
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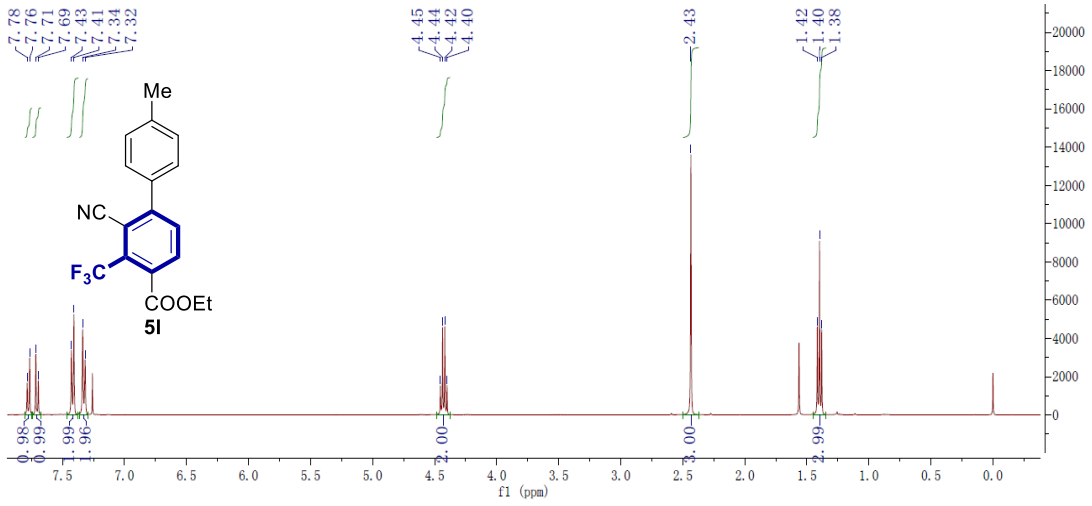
114.28
110.20
62.99
13.87
Br
NC
F3C
COOEt
5k
f1 (ppm)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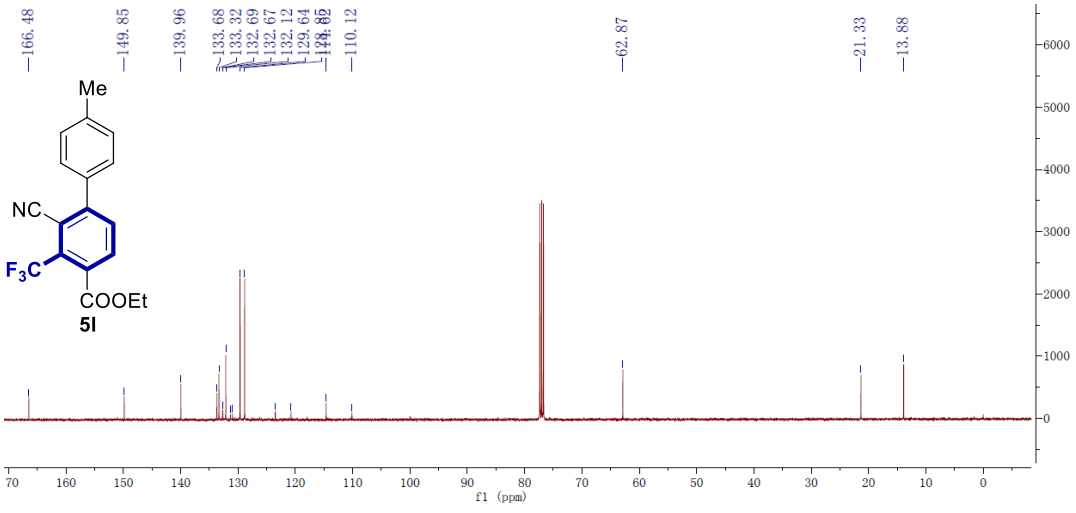
7.34
7.32
4.45
4.44
4.42
4.40
2.43
1.42
1.40
1.38
Me
NC
F3C
COOEt
5l
0.98
0.99
1.99
1.96
2.00
3.00
2.99
f1 (ppm)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132.69
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110.12
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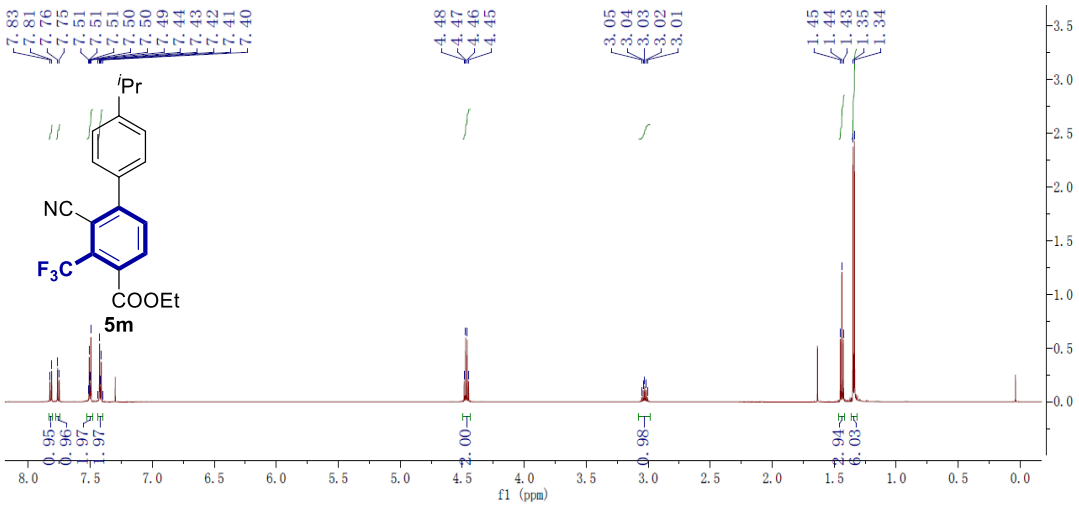
21.33
13.88
Me
NC
F3C
COOEt
5l
f1 (ppm)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7.50
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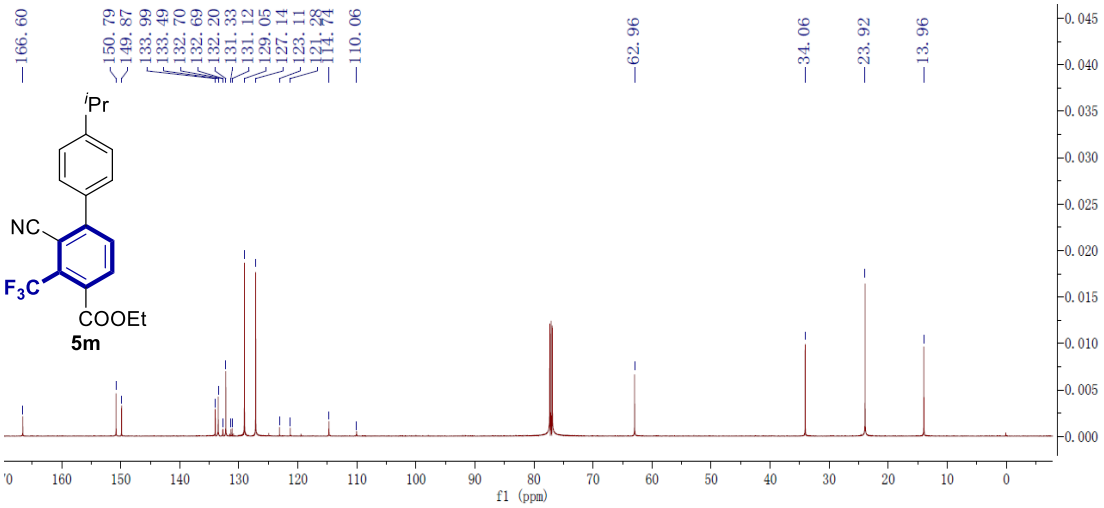
7.49
7.44
7.43
7.42
7.41
7.40
4.48
4.47
4.46
4.45
3.05
3.04
3.03
3.02
3.01
1.45
1.44
1.43
1.35
1.34
iPr
NC
F3C
COOEt
5m
0.95
0.96
1.97
1.97
2.00
0.98
2.94
6.03
f1 (ppm)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132.69
132.20
131.33
131.12
129.05
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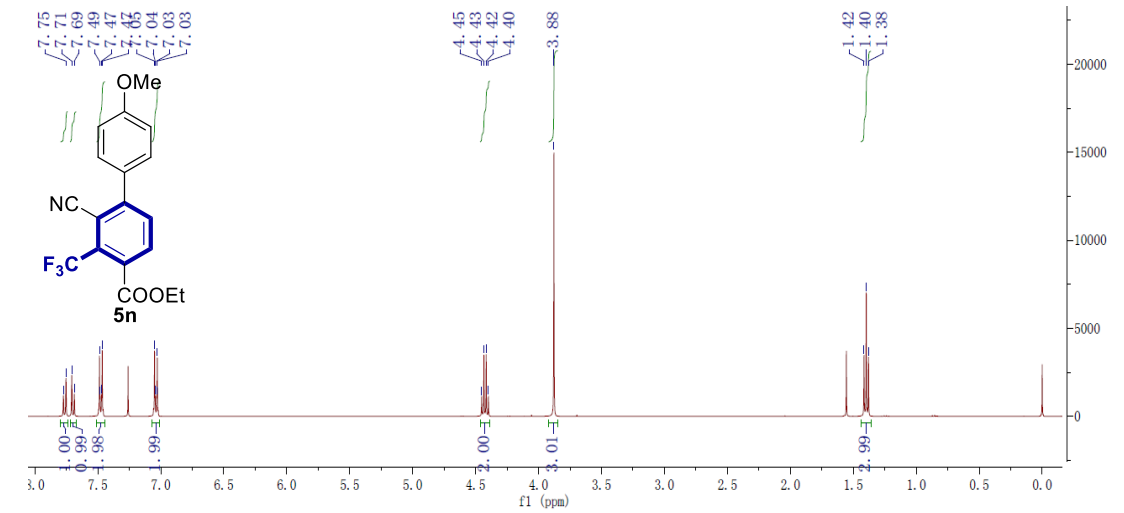
110.06
62.96
34.06
23.92
13.96
iPr
NC
F3C
COOEt
5m
f1 (ppm)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7.03
7.03
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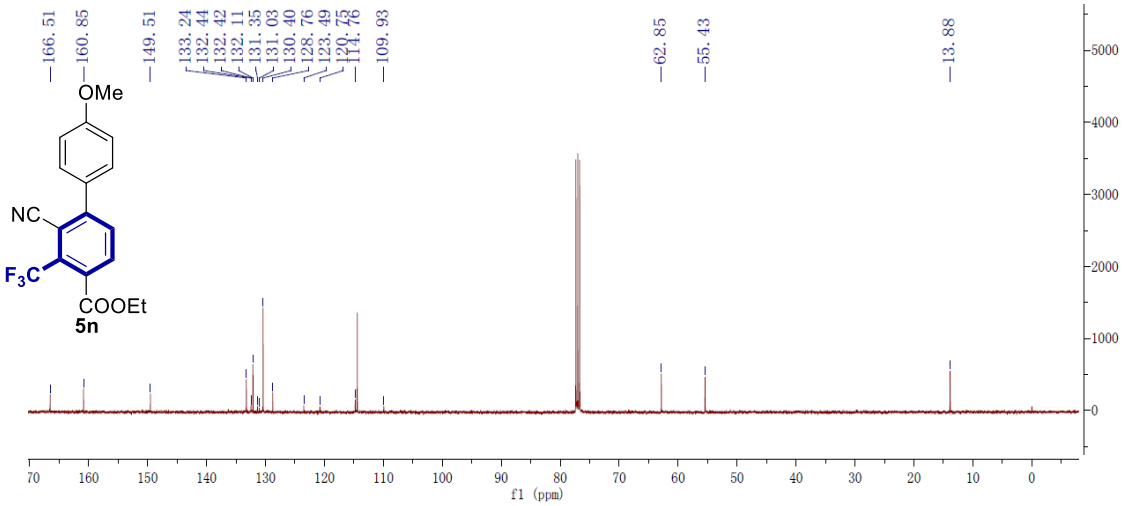
4.43
4.42
4.40
3.88
1.42
1.40
1.38
OMe
NC
F3C
COOEt
5n
1.00
0.99
1.98
1.99
2.00
3.01
2.99
f1 (ppm)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130.40
128.76
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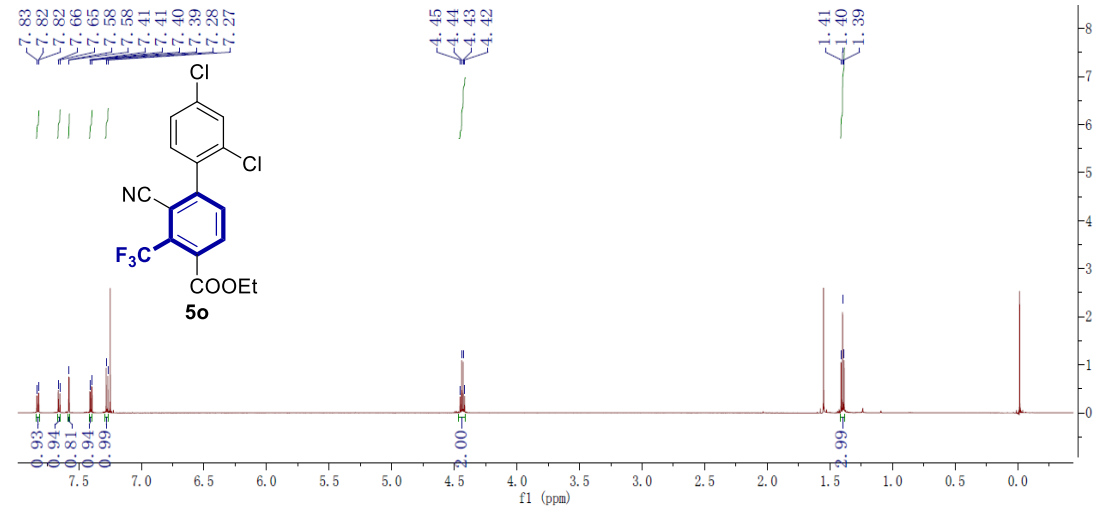
109.93
62.85
55.43
13.88
OMe
NC
F3C
COOEt
5n
f1 (ppm)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7.39
7.28
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4.44
4.43
4.42
1.41
1.40
1.39
Cl
Cl
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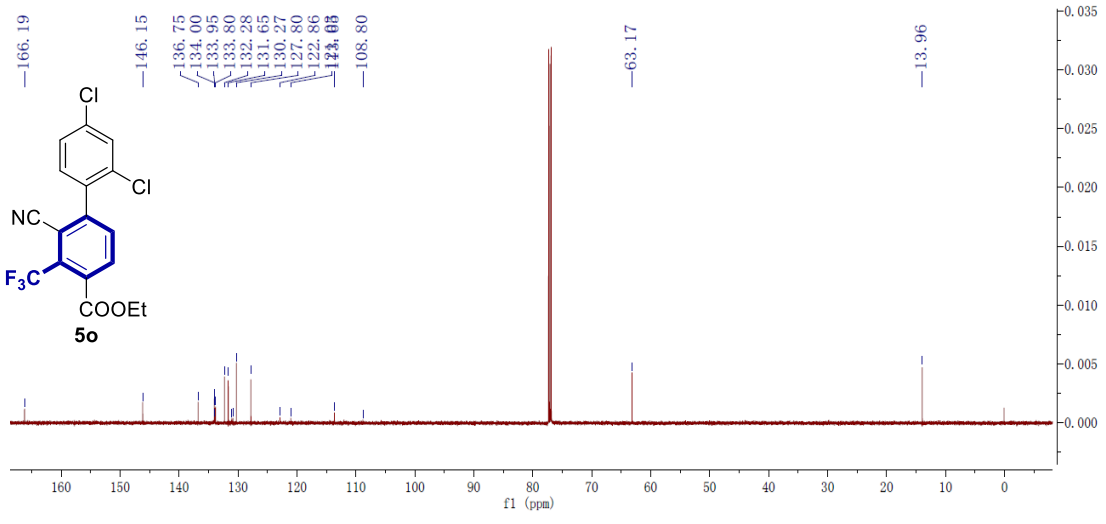
F3C
COOEt
5o
0.93
0.94
0.81
0.94
0.99
2.00
2.99
f1 (ppm)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131.65
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108.80
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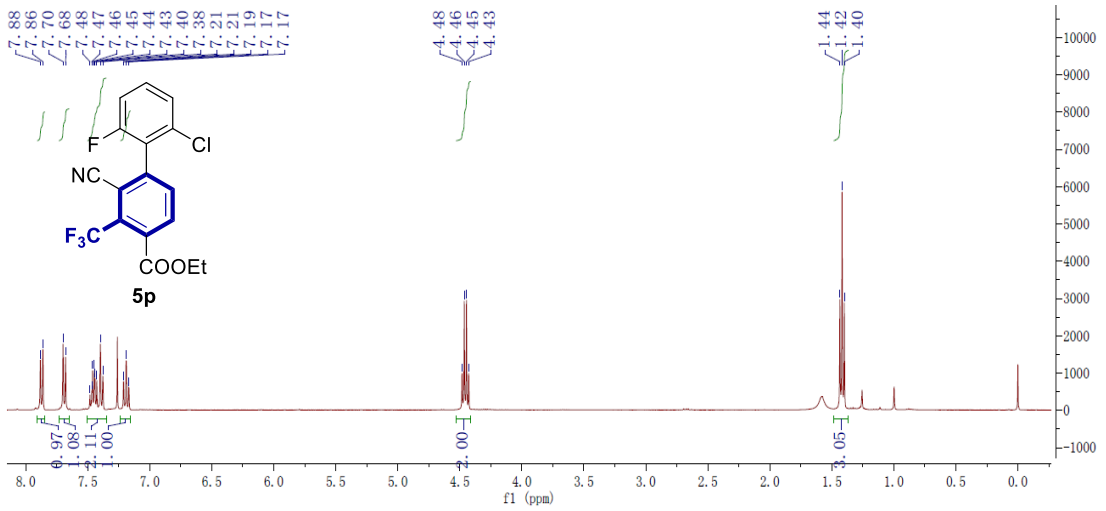
13.96
Cl
Cl
NC
F3C
COOEt
5o
f1 (ppm)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4.48
4.46
4.45
4.43
1.44
1.42
1.40
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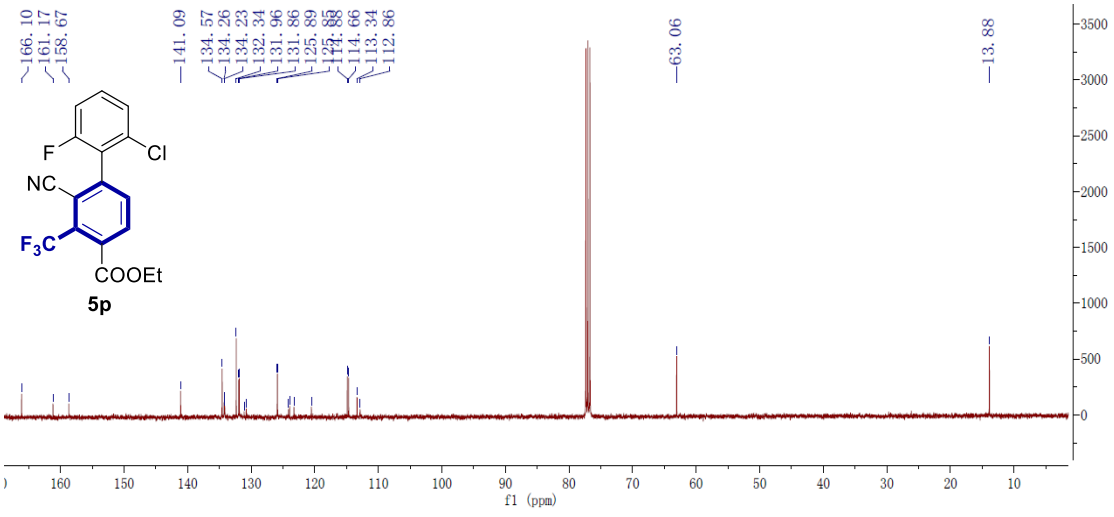
F3C
COOEt
5p
0.97
1.08
2.11
1.00
2.00
3.05
f1 (ppm)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134.23
132.34
131.96
131.86
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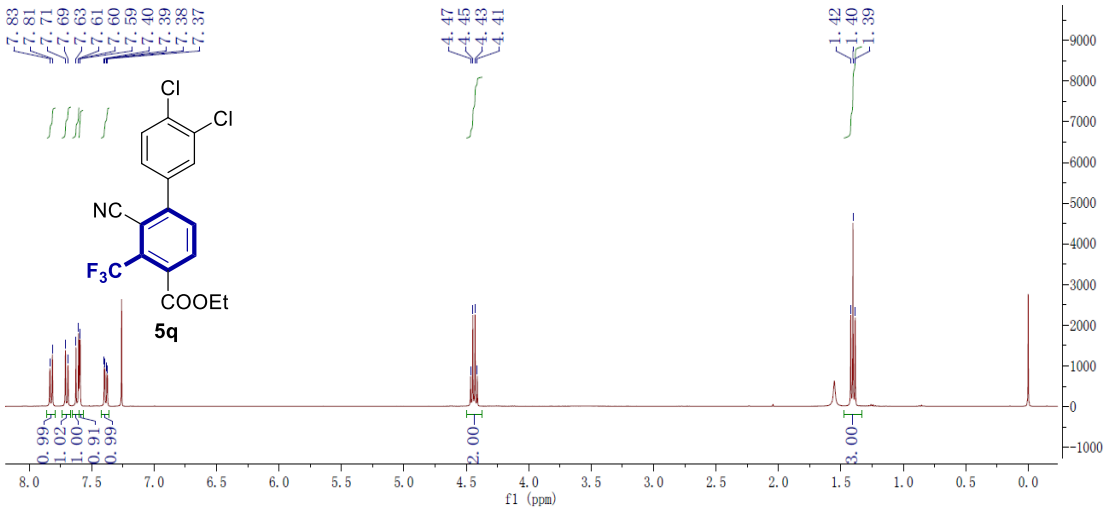
114.66
113.34
112.86
63.06
13.88
F
Cl
NC
F3C
COOEt
5p
f1 (ppm)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7.59
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7.39
7.38
7.37
4.47
4.45
4.43
4.41
1.42
1.40
1.39
Cl
Cl
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F3C
COOEt
5q
0.99
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1.00
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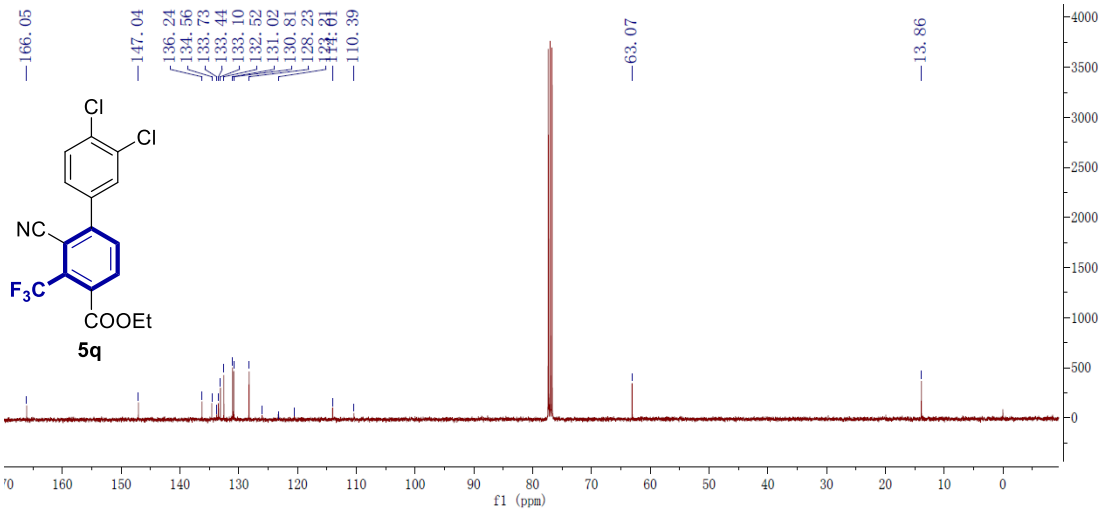
0.99
2.00
3.00
f1 (ppm)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133.10
132.52
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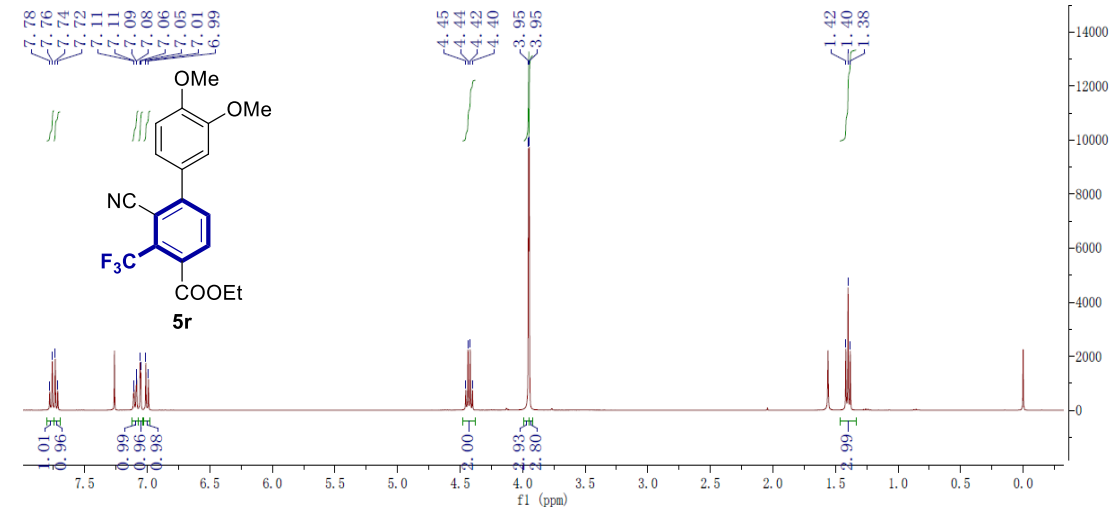
128.23
110.39
63.07
13.86
Cl
Cl
NC
F3C
COOEt
5q
f1 (ppm)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7.06
7.05
7.01
6.99
4.45
4.44
4.42
4.40
3.95
3.95
1.42
1.40
1.38
OMe
OMe
NC
F3C
COOEt
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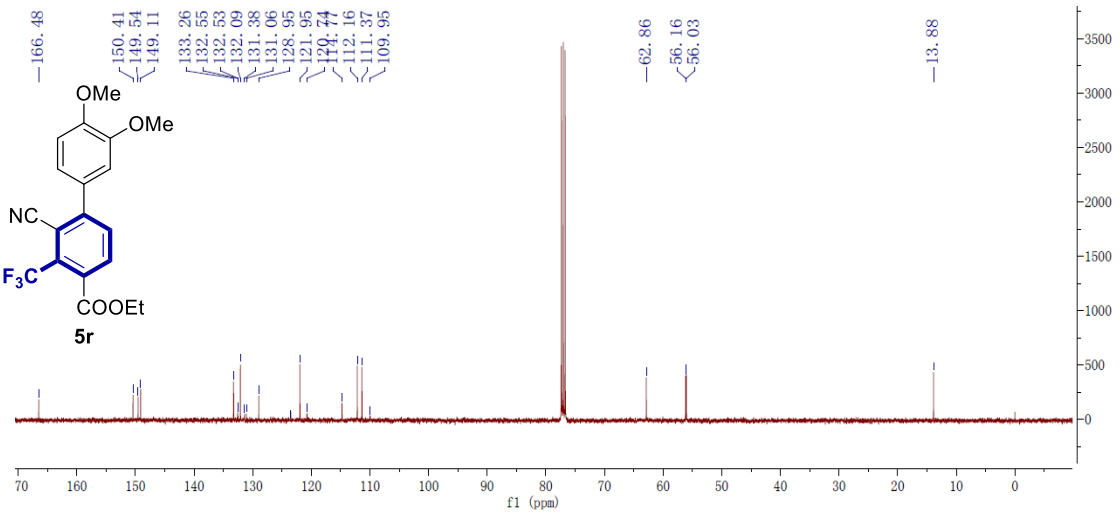
0.99
0.96
0.98
2.00
2.93
2.80
2.99
f1 (ppm)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132.09
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131.06
128.95
121.95
112.16
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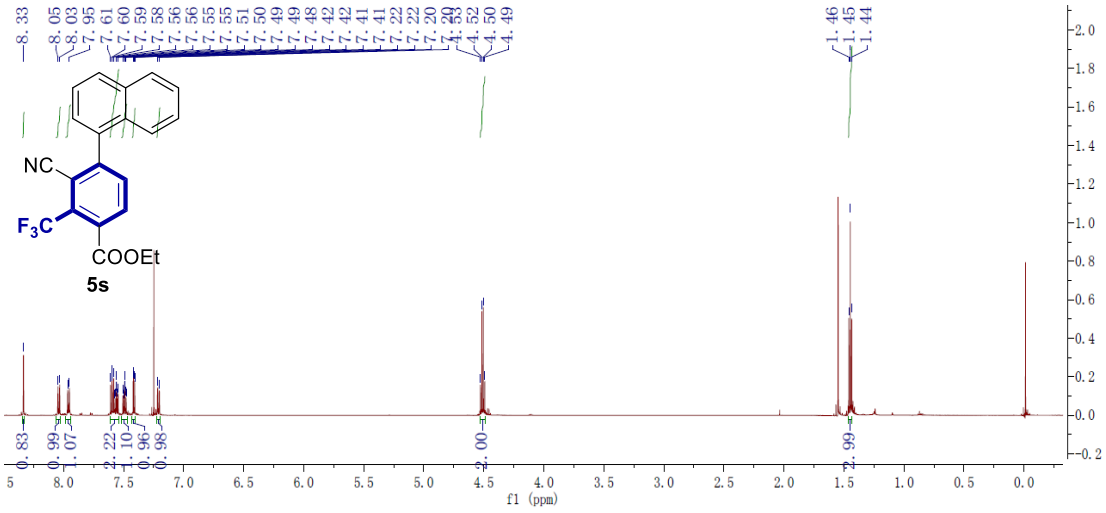
62.86
56.16
56.03
13.88
OMe
OMe
NC
F3C
COOEt
5r
f1 (ppm)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7.56
7.56
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7.50
7.49
7.49
7.48
7.42
7.42
7.41
7.41
7.22
7.22
7.20
7.20
4.53
4.52
4.50
4.49
1.46
1.45
1.44
NC
F3C
COOEt
5s
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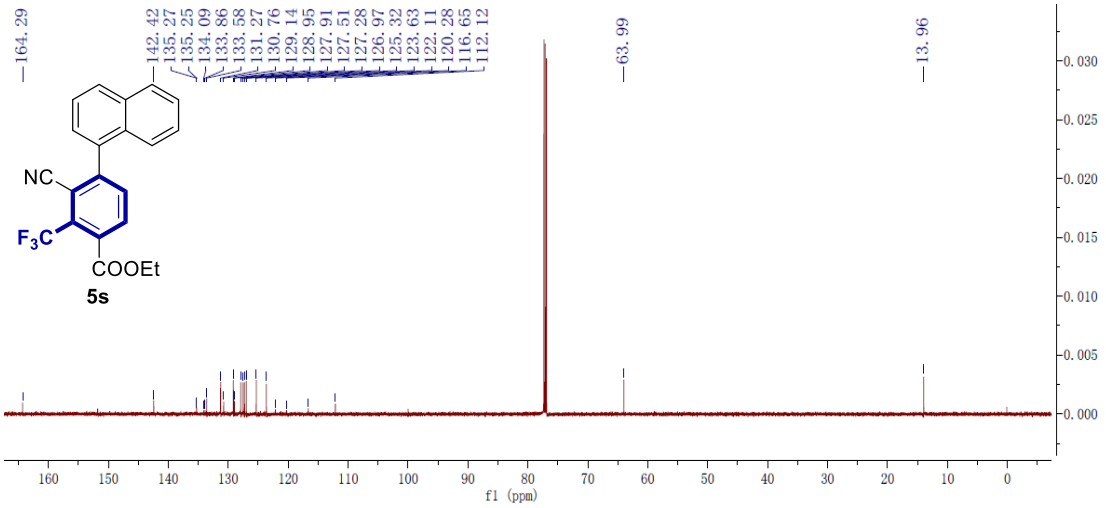
0.99
1.07
2.22
1.10
0.96
0.98
2.00
2.99
f1 (ppm)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127.28
126.97
125.32
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120.28
116.65
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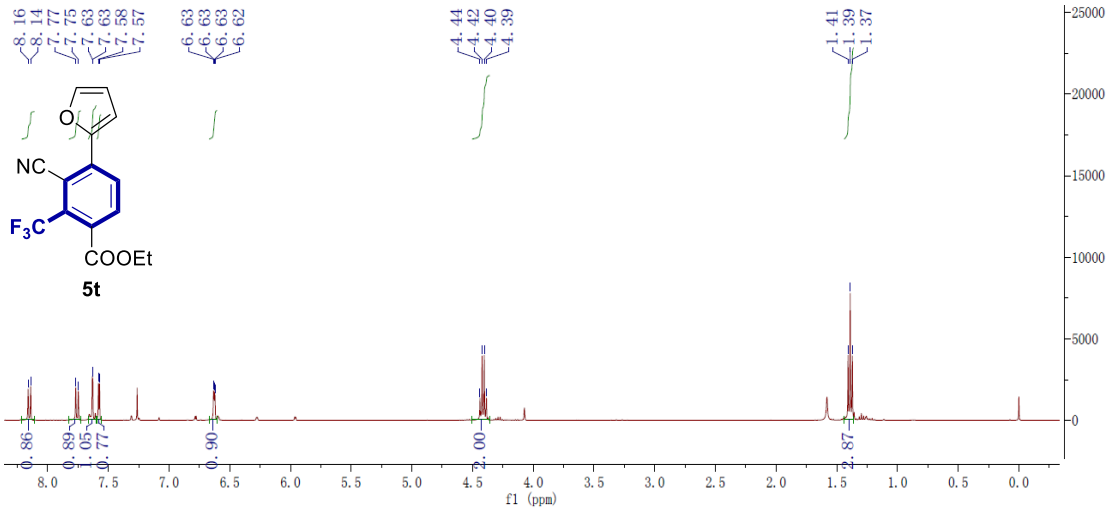
63.99
13.96
NC
F3C
COOEt
5s
f1 (ppm)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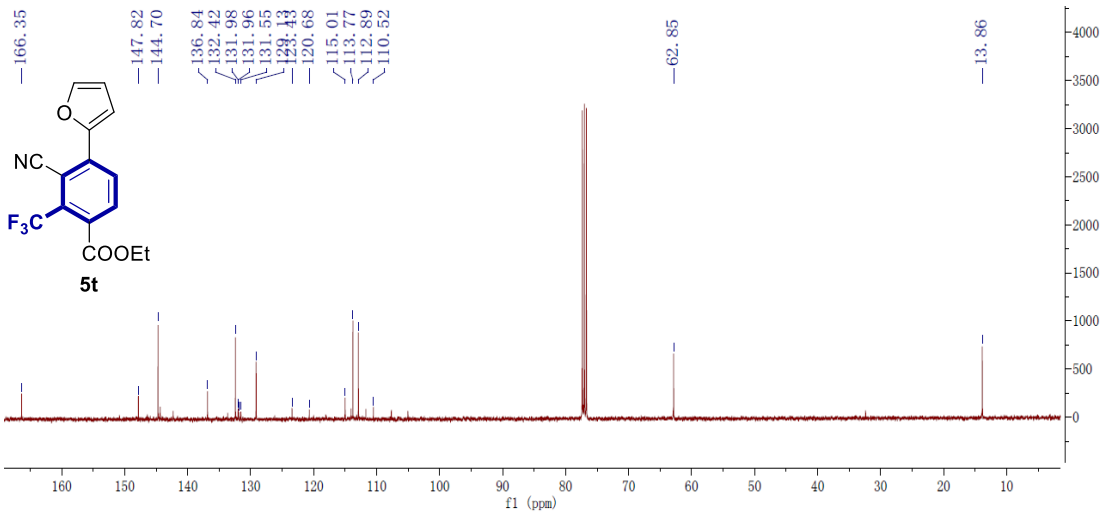
6.63
6.63
6.62
4.44
4.42
4.40
4.39
1.41
1.39
1.37
O
NC
F3C
COOEt
5t
0.86
0.89
1.05
0.77
0.90
2.00
2.87
f1 (ppm)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131.96
131.55
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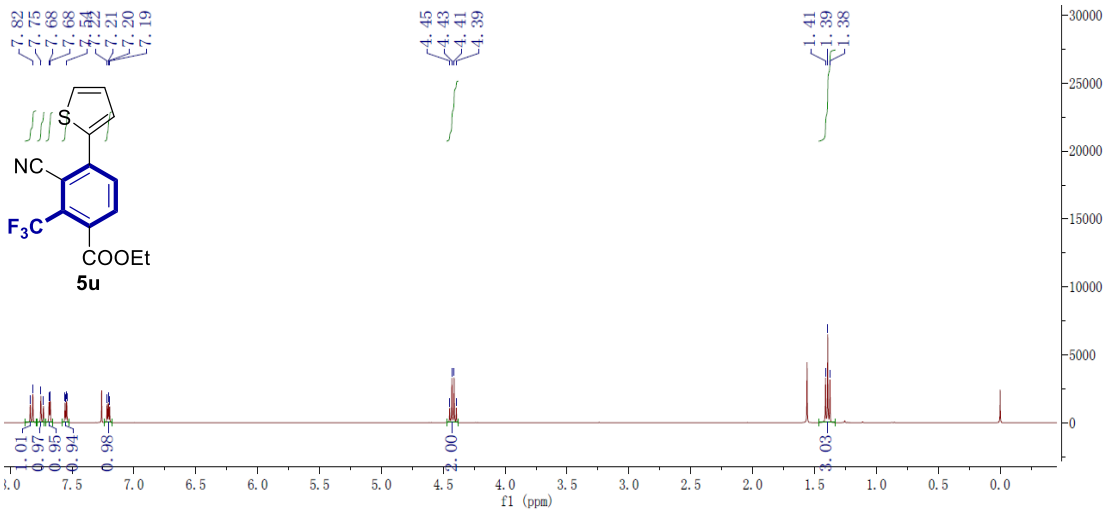
112.89
110.52
62.85
13.86
O
NC
F3C
COOEt
5t
f1 (ppm)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7.75
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7.68
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7.21
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7.19
4.45
4.43
4.41
4.39
1.41
1.39
1.38
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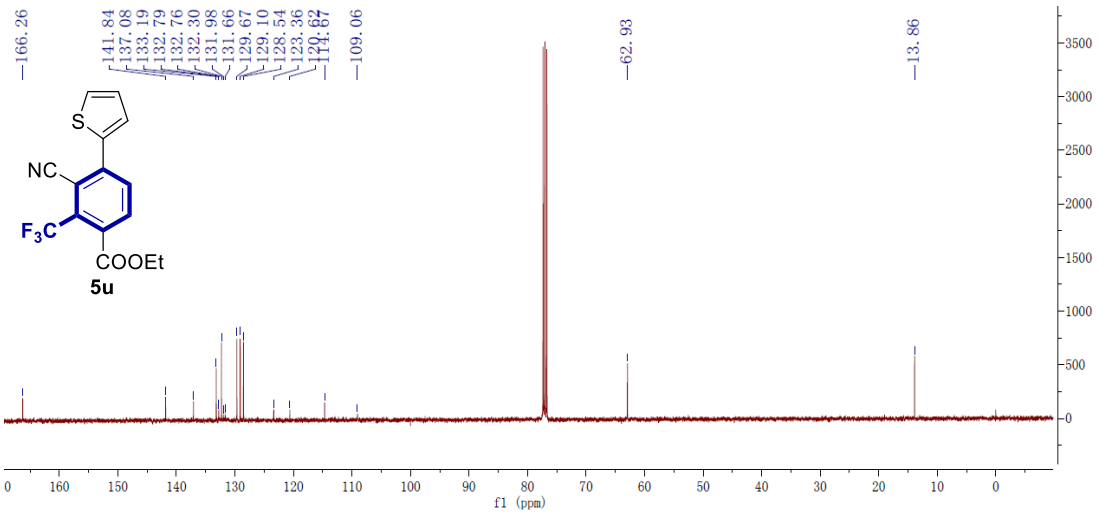
NC
F3C
COOEt
5u
1.01
0.97
0.95
0.94
0.98
2.00
3.03
f1 (ppm)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131.66
129.67
129.10
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123.36
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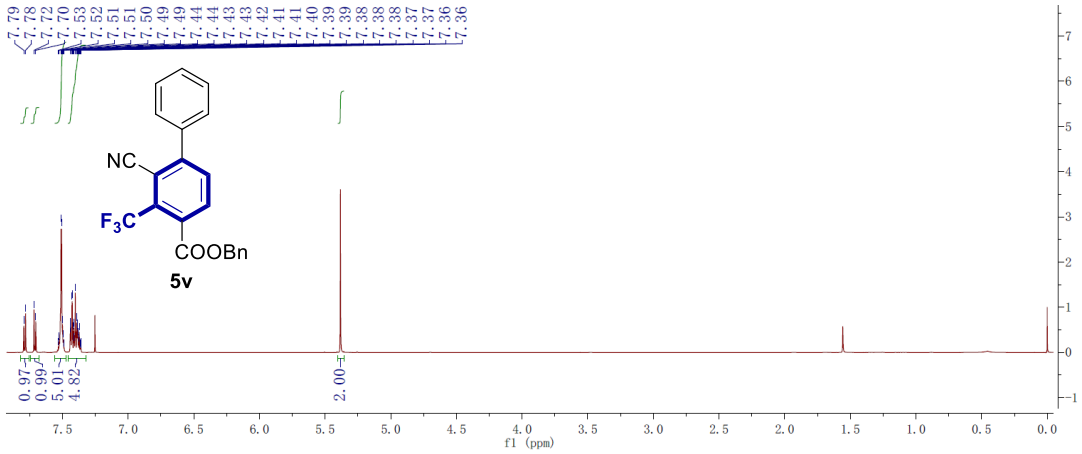
114.87
109.06
62.93
13.86
S
NC
F3C
COOEt
5u
f1 (ppm)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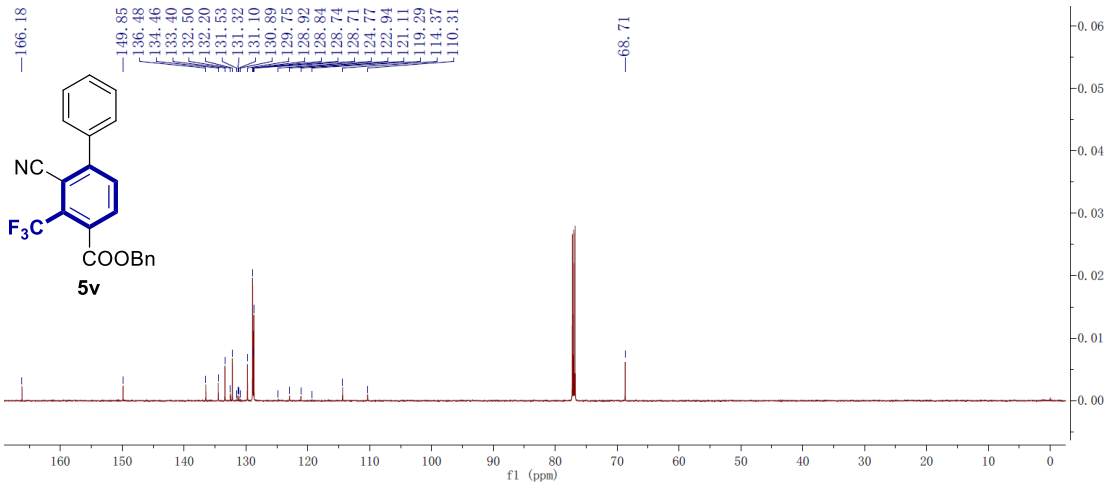
7.72
7.70
7.53
7.52
7.51
7.51
7.50
7.49
7.49
7.44
7.44
7.43
7.43
7.42
7.41
7.41
7.40
7.39
7.39
7.38
7.38
7.38
7.37
7.37
7.36
7.36
NC
F3C
COOBn
5v
0.97
0.99
5.01
4.82
2.00
f1 (ppm)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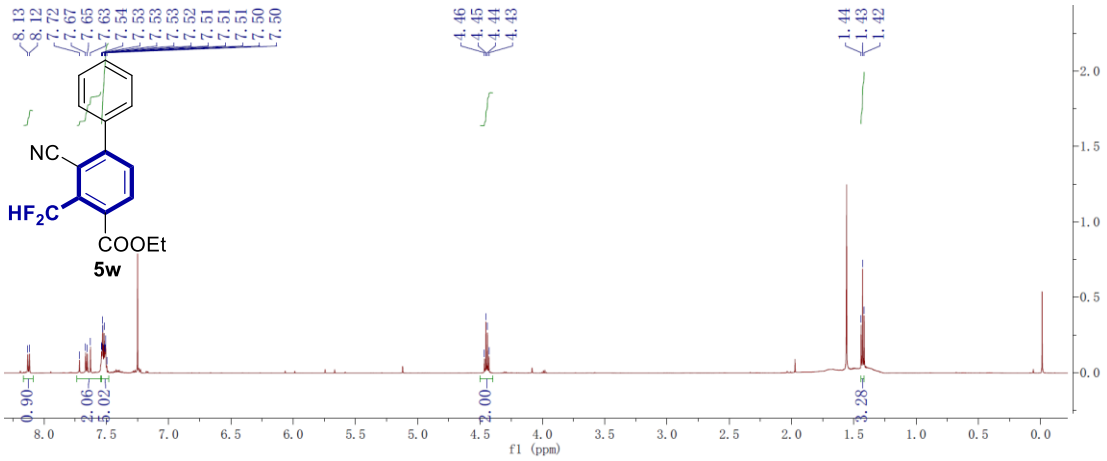
149.85
136.48
134.46
133.40
132.50
132.20
131.53
131.32
131.10
130.89
129.75
128.92
128.84
128.74
128.71
124.77
122.94
121.11
119.29
114.37
110.31
68.71
NC
F3C
COOBn
5v
f1 (ppm)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8.12
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7.54
7.53
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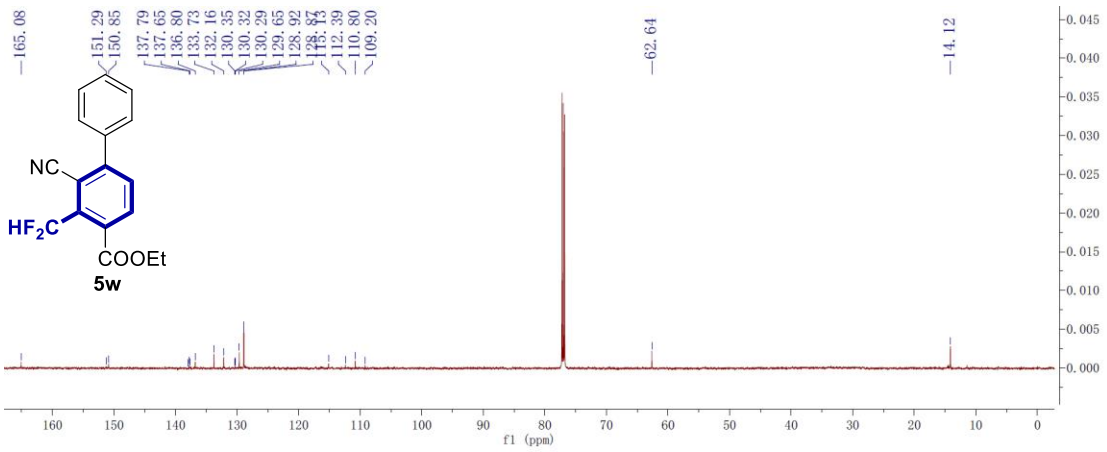
7.53
7.52
7.51
7.51
7.51
7.50
7.50
4.46
4.45
4.44
4.43
1.44
1.43
1.42
NC
HF2C
COOEt
5w
0.90
2.06
5.02
2.00
3.28
f1 (ppm)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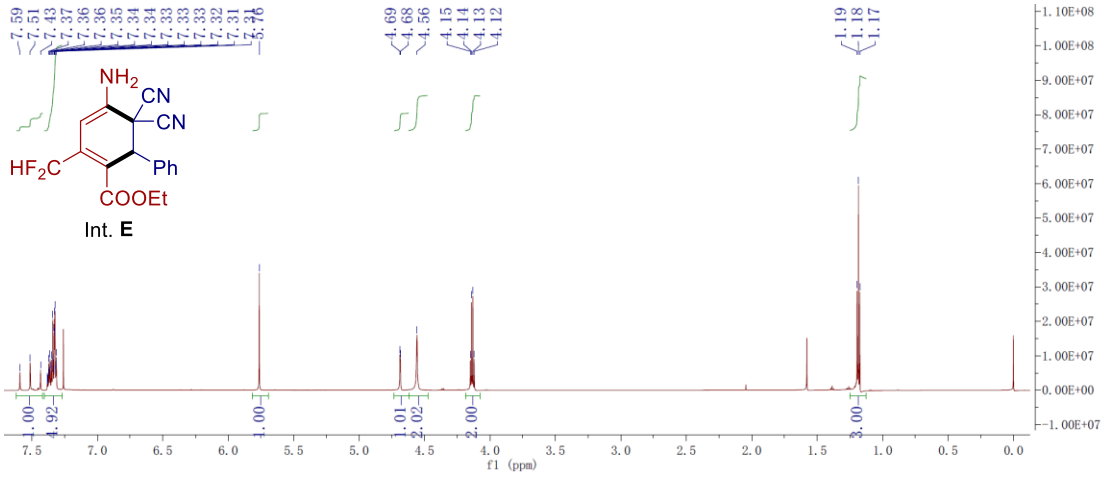
151.29
150.85
137.79
137.65
136.80
133.73
132.16
130.35
130.32
130.29
129.65
128.92
112.39
110.80
109.20
62.64
14.12
NC
HF2C
COOEt
5w
f1 (ppm)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7.43
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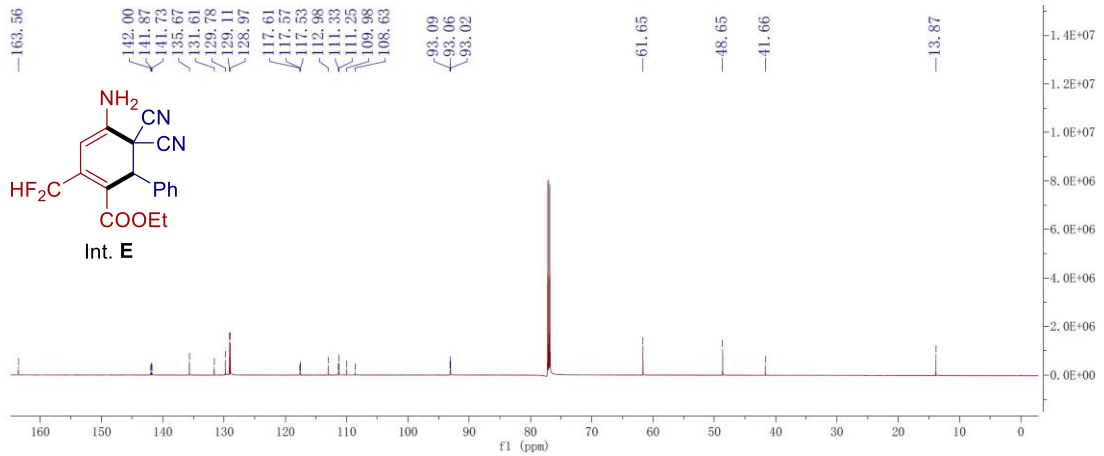
7.36
7.35
7.34
7.34
7.33
7.33
7.33
7.32
7.31
7.31
5.76
4.69
4.68
4.56
4.15
4.14
4.13
4.12
1.19
1.18
1.17
NH2
CN
CN
Ph
HF2C
COOEt
Int. E
1.00
4.92
1.00
1.01
2.02
2.00
3.00
f1 (ppm)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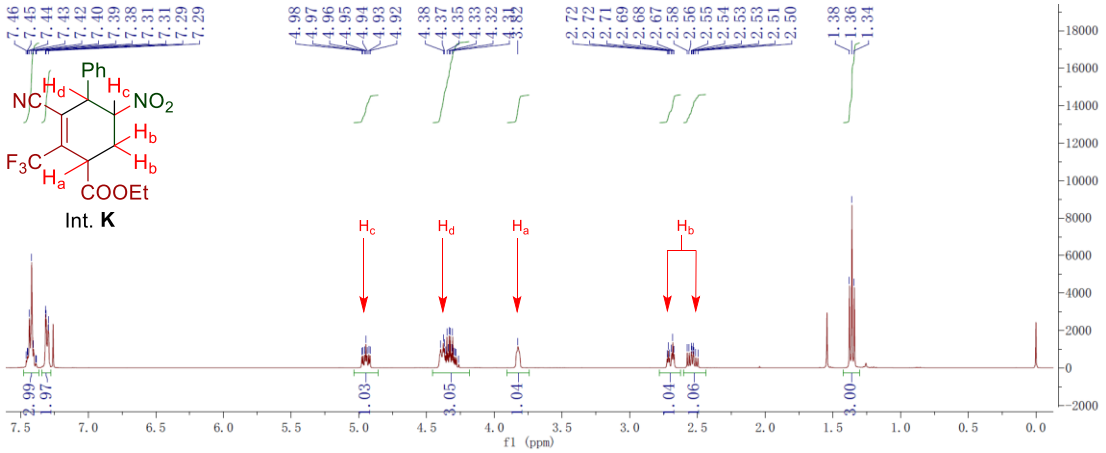
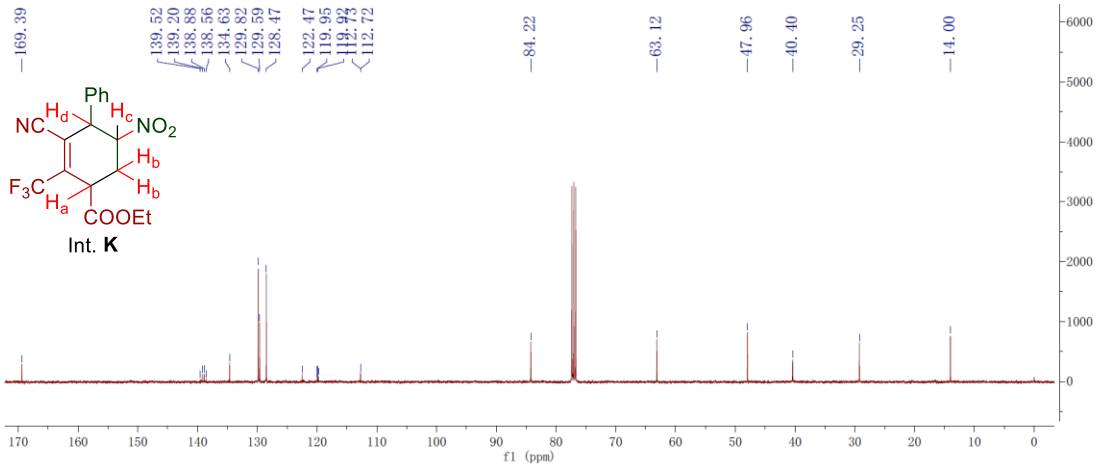
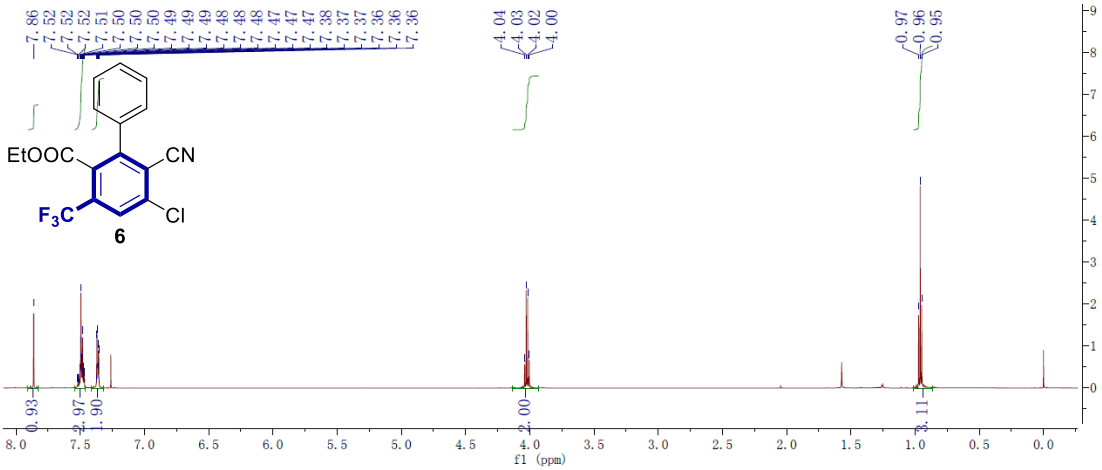
129.11
128.97
117.61
117.57
117.53
112.98
111.33
111.25
109.98
108.63
93.09
93.06
93.02
61.65
48.65
41.66
13.87
NH2
CN
CN
Ph
HF2C
COOEt
Int. E
f1 (ppm)


Ph
NC
Hd
Hc
NO2
Hb
Hb
F3C
Ha
COOEt
Int. K
Hc
Hd
Ha
Hb
f1 (ppm)


Ph
NC
Hd
Hc
NO2
Hb
Hb
F3C
Ha
COOEt
Int. K
f1 (ppm)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7.49
7.48
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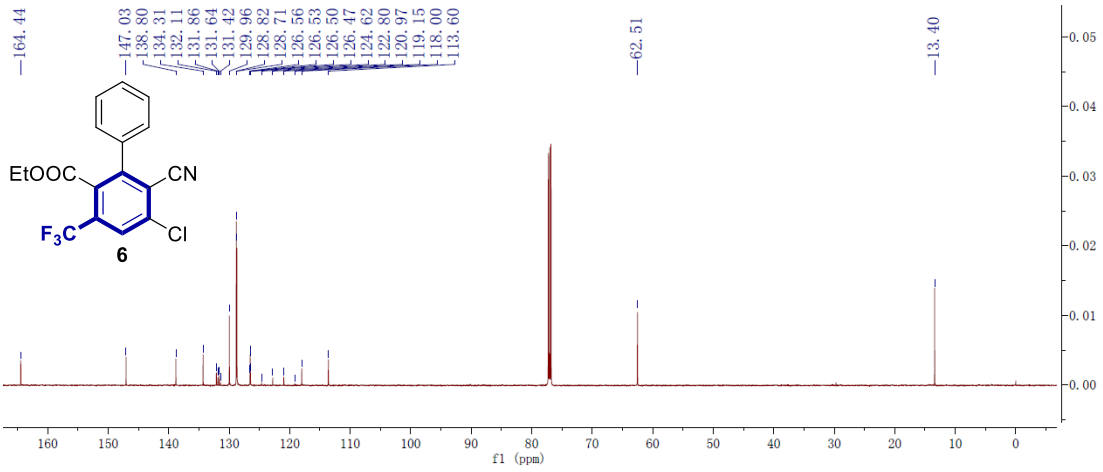
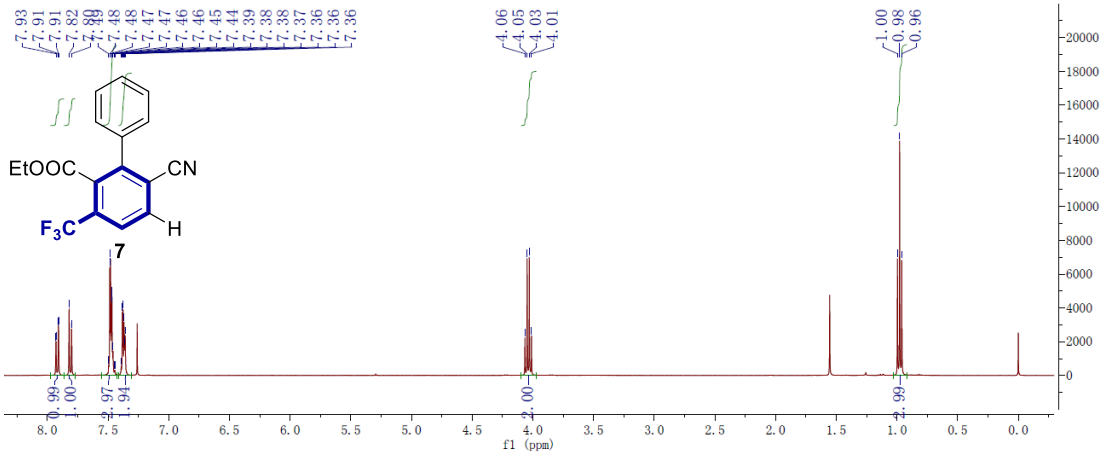
7.48
7.47
7.47
7.47
7.38
7.37
7.36
7.36
7.36
4.04
4.03
4.02
4.00
0.97
0.96
0.95
EtOOC
CN
F3C
Cl
6
0.93
2.97
1.90
2.00
3.11
f1 (ppm)


164.44
147.03
138.80
134.31
132.11
131.86
131.64
131.42
129.96
128.82
128.71
126.56
126.53
126.50
126.47
124.62
122.80
120.97
119.15
118.00
113.60
62.51
13.40
EtOOC
CN
F3C
Cl
6
f1 (ppm)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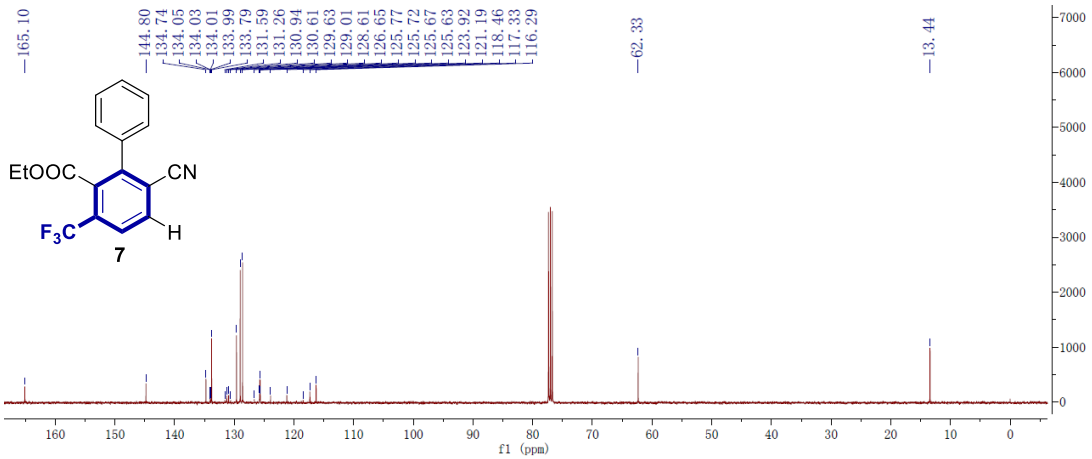
7.91
7.91
7.82
7.48
7.47
7.47
7.46
7.46
7.45
7.44
7.39
7.38
7.38
7.37
7.36
7.36
7.36
4.06
4.05
4.03
4.01
1.00
0.98
0.96
EtOOC
CN
F3C
H
7
0.99
1.00
2.97
1.94
2.00
2.99
f1 (ppm)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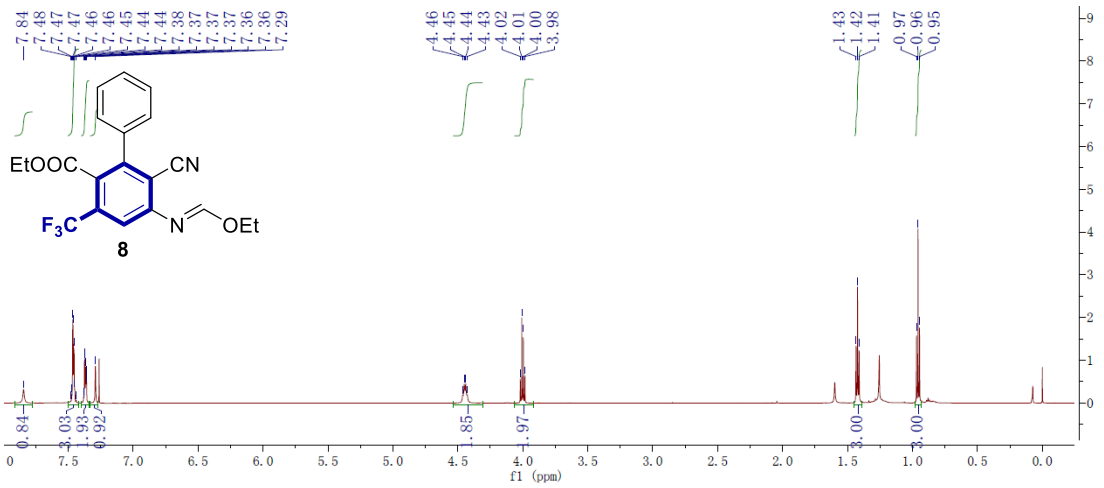
144.80
134.74
134.05
134.03
134.01
133.99
133.79
131.59
131.26
130.94
130.61
129.63
129.01
128.61
126.65
125.77
125.72
125.67
125.63
123.92
121.19
118.46
117.33
116.29
62.33
13.44
EtOOC
CN
F3C
H
7
f1 (ppm)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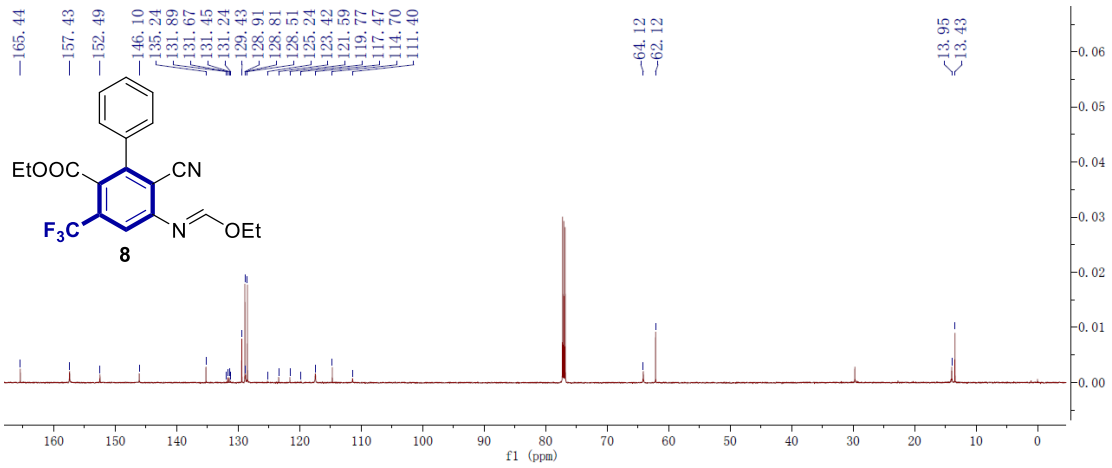
7.46
7.45
7.44
7.44
7.38
7.37
7.37
7.37
7.36
7.36
7.29
4.46
4.45
4.44
4.43
4.02
4.01
4.00
3.98
1.43
1.42
1.41
0.97
0.96
0.95
EtOOC
CN
F3C
N
OEt
8
0.84
3.03
1.93
0.92
1.85
1.97
3.00
3.00
f1 (ppm)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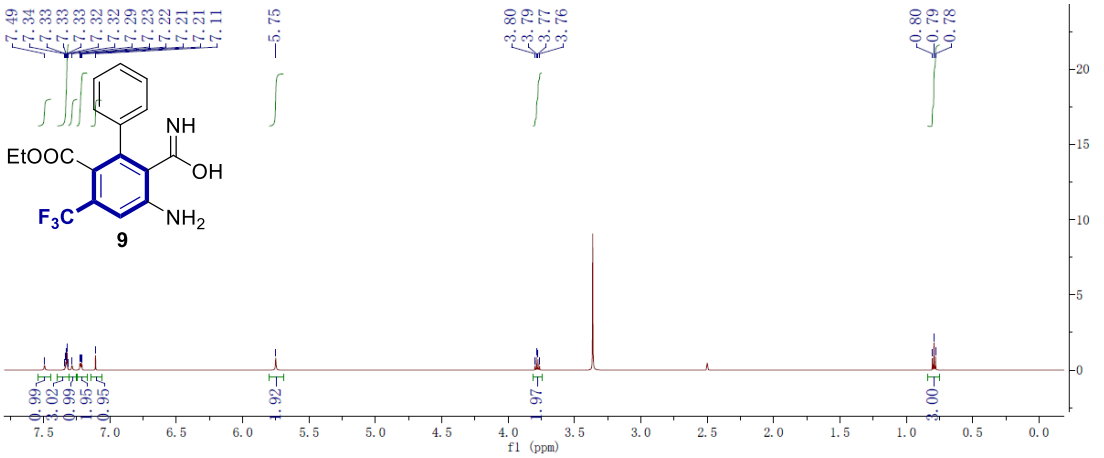
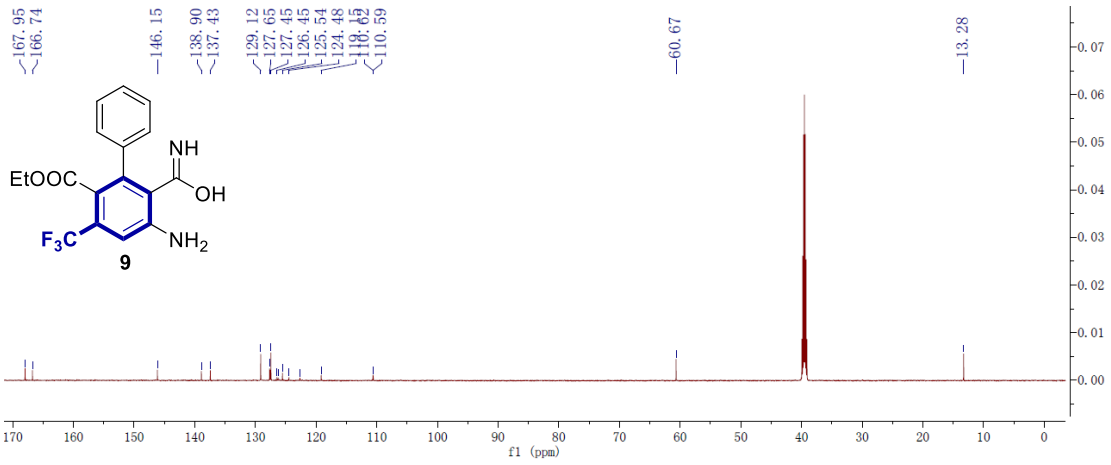
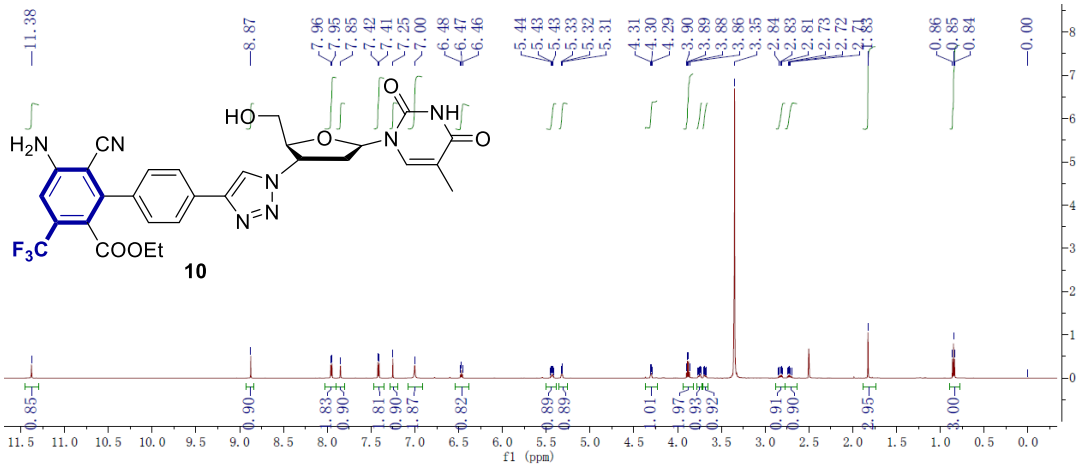
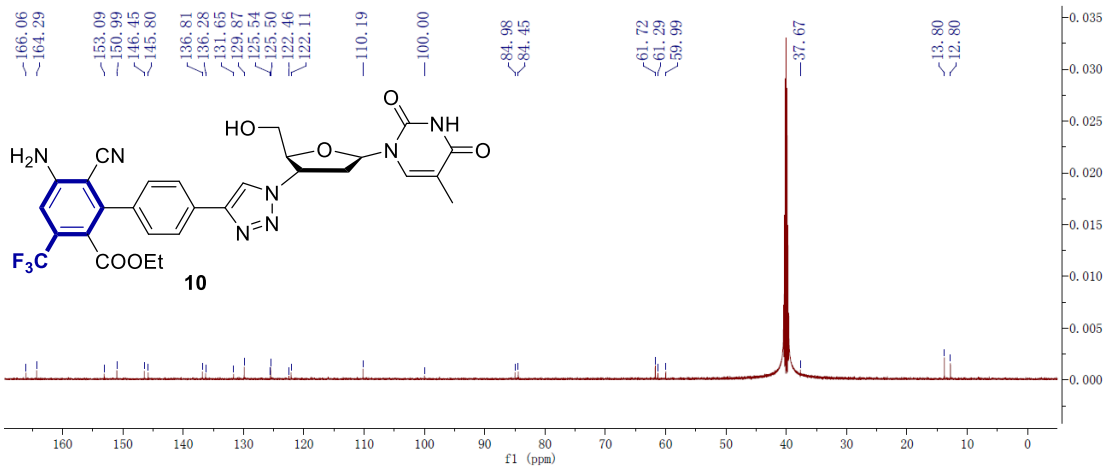
157.43
152.49
146.10
135.24
131.89
131.67
131.45
131.24
129.43
128.91
128.81
128.51
125.24
123.42
121.59
119.77
117.47
114.70
111.40
64.12
62.12
13.95
13.43
EtOOC
CN
F3C
N
OEt
8
f1 (ppm)


7.49
7.34
7.33
7.33
7.33
7.32
7.32
7.29
7.23
7.22
7.21
7.21
7.11
5.75
3.80
3.79
3.77
3.76
0.80
0.79
0.78
NH
EtOOC
OH
F3C
NH2
9
0.99
3.02
0.99
1.95
0.95
1.92
1.97
3.00
f1 (ppm)


167.95
166.74
146.15
138.90
137.43
129.12
127.65
127.45
126.45
125.54
124.48
110.59
60.67
13.28
NH
EtOOC
OH
F3C
NH2
9
f1 (ppm)


HO
O
NH
N
O
H2N
CN
F3C
COOEt
N
N
N
10
f1 (ppm)


HO
O
NH
N
O
H2N
CN
F3C
COOEt
N
N
N
10
f1 (ppm)