Silver or copper-catalyzed ring opening [3+2] annulation of 2-polyfluoroalkyl chromones/6-polyfluoroalkyl pyran-4*H*-ones with methylene isocyanides: Regioselective synthesis of 3-polyfluoroalkyl pyrroles

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General information

NMR spectra were recorded on Bruker Avance III-500 (^{1}H, 500 MHz; ^{19}F, 471 MHz; ^{13}C, 126 MHz) and Bruker DRX-400 (^{1}H, 400 MHz; ^{19}F, 376 MHz) spectrometers in $CDCl_3$ or DMSO-*d*6. The chemical shifts (δ) are reported in ppm relative to the internal standard TMS (^{1}H NMR), C_6F_6 (^{19}F NMR), and residual signal of the solvent (^{13}C NMR 77.16 ppm). The HRMS spectra were obtained using the UHR-QqTOF maXis Impact HD (Bruker Daltonics, Billerica, MA, USA) mass spectrometer. Melting points were determined on an SMP40 apparatus. Monitoring of the reaction progress and assessment of the purity of synthesized compounds were carried out by TLC on Sorbfil PTSKh-AF-A-UF plates (eluent EtOAc–hexane 1:3, eluent EtOAc–hexane 1:4). The XRD analyses were carried out using equipment of the Center for Joint Use "Spectroscopy and Analysis of Organic Compounds" at the Postovsky Institute of Organic Synthesis of the Russian Academy of Sciences (Ural Branch). The experiment was accomplished on the automated X-ray diffractometer «Xcalibur 3» with CCD detector on standard procedure (MoKα-irradiation, graphite monochromator, ω-scans with 1o step at T= 295(2) K). Empirical absorption correction was applied. Unless otherwise noted, all solvents and other reagents are commercially available and were used without further purification. All reagents were weighed and handled in air at room temperature. All solvents used were dried and distilled by standard procedures. The starting ethyl isocyanoacetate **1**, chromones **2a-s,** and 4-pyrones **4a-m** were prepared according to described procedures [48, 48, 60-64].

General procedure for synthesis of 3-trifluoromethyl(polyfluoroalkyl)-1H-pyrroles 3a-v

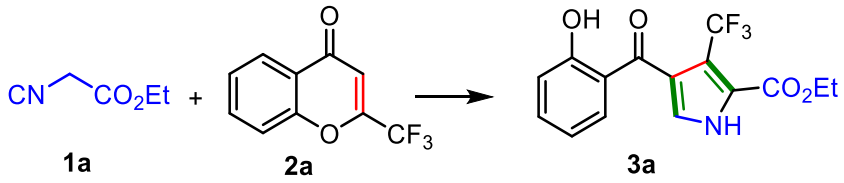
Method A

To 10 mL reaction tube equipped with magnetic stirrer was charged chromone **2a-v** (0.5 mmol), copper iodide (9,5 mg, 0.05 mmol, 10 mol % 0.1 equiv.) 3 mL dry acetonitrile mixture and potassium carbonate (138 mg, 1 mmol, 2.0 equiv.) was stirred at room temperature for 2 min. then ethyl isocyanoacetate **1a** (85 mg, 0.75 mmol 1.5 equiv.), were added and reaction mixture was stirred at room temperature until pyrrole formation was complete. Then mixture was quenched diluted hydrochloric acid (20mL 1M) and extracted with EtOAc (10mL x4), washed brine (10mL x2), dried anhydrous Mg_2SO_4 and evaporated to dryness to yield a crude reaction product, which was purified by silica gel flash chromatography eluted with EtOAc-Hexane, 1:3 to give the product as beige solid.

Method B

To 10 mL reaction tube equipped with magnetic stirrer was charged chromone **2a-v** (0.5 mmol), silver acetate (8,3 mg, 0.05 mmol, 10 mol % 0.1 equiv.) 3 mL dry acetonitrile and potassium carbonate (138 mg, 1.0 mmol, 2.0 equiv. mixture was stirred at room temperature for 2 min. then ethyl isocyanoacetate **1a** (85 mg, 0.75 mmol 1.5 equiv.) were added and reaction mixture was stirred at room temperature until pyrrole formation was complete. Then mixture was quenched diluted hydrochloric acid (20 mL 1M) and extracted with EtOAc (10 mL x 4), washed brine (10 mL x 2), dried anhydrous Mg_2SO_4 and evaporated to dryness to yield a crude reaction product, which was purified by silica gel flash chromatography eluted with EtOAc-Hexane, 1:3 to give the product as beige solid.

Table 1. Optimization of reaction 2-trifluoromethyl chromone with ethyl isocyanoacetate.[a-d]



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

entry	solvent	temperature	Base (equiv.)	catalyst	yield
1[c]	DMF	100	K_2CO_3 (2.0)	-	30
2[c]	DMF	100	DBU (2.0)	-	21
3[d]	DMF	rt	-	AgOAc	47
4[d]	DMF	rt	-	CuI	23
5	DMF	rt	K_2CO_3 (2.0)	AgOAc	92
6	DMF	rt	K_2CO_3 (2.0)	CuI-	90
7	DMF	rt	K_2CO_3 (2.0)	CuBr	77
8	DMF	rt	K_2CO_3 (2.0)	CuCl-	80
9	DMF	rt	K_2CO_3 (2.0)	Cu_2O	60
10	DMF	100	K_2CO_3 (2.0)	CuI	70
11	DMF	100	K_2CO_3 (2.0)	AgOAc	60
12	DMF	rt	DBU (2.0)	AgOAc	90
13	DMF	rt	DBU (2.0)	CuI	81
14	DMF	100	DBU (2.0)	AgOAc	71
15	DMF	100	DBU (2.0)	CuI	90
16[c]	MeCN	rt	K_2CO_3 (2.0)	-	10
17	MeCN	rt	K_2CO_3 (0.1)	AgOAc	56

18	MeCN	rt	K_2CO_3 (1.0)	AgOAc	78
19	MeCN	rt	K_2CO_3 (2.0)	AgOAc	90
20	MeCN	rt	K_2CO_3 (2.0)	CuI	87
21	MeCN	rt	Cs_2CO_3 (0.1)	AgOAc	64
22	MeCN	rt	Cs_2CO_3 (1.0)	AgOAc	86
23	MeCN	rt	Cs_2CO_3 (2.0)	AgOAc	93
24	MeCN	rt	Cs_2CO_3 (2.0)	CuI	89
25[c]	MeCN	rt	DBU (2.0)	-	15
26	MeCN	rt	DBU (0.1)	AgOAc	53
27	MeCN	rt	DBU (1.0)	AgOAc	66
28	MeCN	rt	DBU (2.0)	AgOAc	91
29	MeCN	rt	DBU (2.0)	CuI	83
30	MeCN	reflux	DBU (2.0)	CuI	81
31	MeCN	rt	DABCO (0.1)	AgOAc	57
32	MeCN	rt	DABCO (1.0)	AgOAc	64
33	MeCN	rt	DABCO (2.0)	AgOAc	72
34	THF	rt	K_2CO_3 (2.0)	AgOAc	87
35	NMP	100	DBU (2.0)	CuI	65
36	DMSO	100	DBU (2.0)	CuI	60
37	EtOH	rt	K_2CO_3 (2.0)	AgOAc	71
38	EtOH	rt	K_2CO_3 (2.0)	CuI	79
39	EtOH	rt	DBU (2.0)	CuI	83
40	EtOH	reflux	DBU (2.0)	CuI	85

[a] Reaction conditions: **2a** (0.5 mmol, 1.0 equiv.), **1a** (0.75 mmol, 1.5 equiv.), catalyst (10 mol. %, 0.1 equiv.) base, (1.0 mmol, 2.0 equiv.) and solvent 3 mL. [b] Isolated yields. [c] The reaction was carried out without catalyst. [d] The reaction was carried out without base.

Gram scale preparation of 3a (See **Scheme 1**)

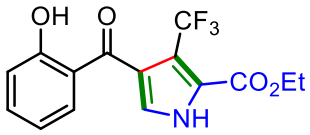
Method A

To 50 mL reaction tube equipped with magnetic stirrer was charged chromone **2a** (1.070 mg 5.0 mmol), copper iodide (95 mg, 0.5 mmol, 10 mol % 0.1 equiv.) 20 mL dry acetonitrile mixture was stirred at room temperature for 2 min. and potassium carbonate (1380 mg, 10 mmol, 2.0 equiv.) then ethyl isocyanoacetate **1a** (850 mg, 7.5 mmol 1.5 equiv.), were added and reaction mixture was stirred at room temperature until pyrrole formation was complete. Then mixture was

quenched diluted hydrochloric acid (90 mL 1M) and extracted with EtOAc (50 mL x 4), washed brine (30 mL x 2), dried anhydrous Mg_2SO_4 and evaporated to dryness to yield a crude reaction product, which was purified by silica gel flash chromatography eluted with EtOAc-Hexane, 1:3 to give the product as a beige solid (1404 mg 85%).

Method B.

To 50 mL reaction tube equipped with magnetic stirrer was charged chromone **2a** (1070 mg, 5 mmol), silver acetate (83 mg, 0.5 mmol, 10 mol % 0.1 equiv.) 20 mL dry acetonitrile and potassium carbonate (1380 mg, 1.0 mmol, 2 equiv.) mixture was stirred at room temperature for 2 min. then ethyl isocyanoacetate **1a** (850 mg, 0.75 mmol 1.5 equiv.), were added and reaction mixture was stirred at room temperature until pyrrole formation was complete. Then mixture was quenched diluted hydrochloric acid (90 mL 1M) and extracted with EtOAc (50 mL x4), washed brine (30 mL x2), dried anhydrous Mg_2SO_4 and evaporated to dryness to yield a crude reaction product, which was purified by silica gel flash chromatography eluted with EtOAc-Hexane, 1:3 to give the product as a beige solid (1422 mg 87%).



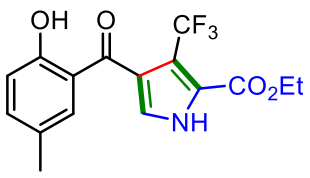
Ethyl 4-(2-hydroxybenzoyl)-3-(trifluoromethyl)-1H-pyrrole-2-carboxylate (**3a**): beige solid, (method A: 142 mg, 87%; method B: 147 mg, 90%), mp 109-111°C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.95 (s, 1H), 9.94 (s, 1H), 7.57 – 7.47 (m, 2H), 7.14 (d, *J* = 3.1 Hz, 1H), 7.04 (dd, *J* = 8.4, 1.2 Hz, 1H), 6.91 – 6.83 (m, 1H), 4.43 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ 107.77.

^{13}C NMR (126 MHz, $CDCl_3$) δ 195.7, 163.0, 159.6, 137.0, 133.1, 123.7 (q, *J* = 2.1 Hz), 123.1, 122.0 (q, *J* = 268.9 Hz), 120.6, 119.1, 118.4, 117.0 (q, *J* = 38.6 Hz), 62.3, 14.1.

HRMS (ESI): m/z calcd for $C_{15}H_{13}F_3NO_4$ $[M + H]^+$, 328.0797; found 328.0789.



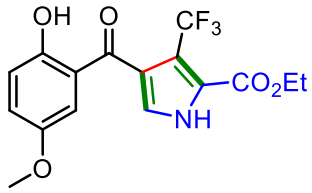
Ethyl 4-(2-hydroxy-5-methylbenzoyl)-3-(trifluoromethyl)-1H-pyrrole-2-carboxylate (**3b**): beige solid, (method A: 138 mg, 81%; method B: 136 mg, 80%), mp 133-135 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.77 (s, 1H), 9.78 (s, 1H), 7.33 (dd, *J* = 8.4, 2.3 Hz, 1H), 7.29 (d, *J* = 2.2 Hz, 1H), 7.14 (d, *J* = 3.1 Hz, 1H), 6.95 (d, *J* = 8.4 Hz, 1H), 4.44 (q, *J* = 7.2 Hz, 2H), 2.25 (s, 3H), 1.41 (t, *J* = 7.1 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ 107.77.

^{13}C NMR (126 MHz, $CDCl_3$) δ 195.7, 160.9, 159.6, 138.1, 132.8, 128.3, 123.8 (q, J = 2.3 Hz), 123.0, 123.0, 122.1 (q, J = 268.9 Hz), 120.2, 118.2, 117.0 (q, J = 38.4 Hz), 62.3, 20.5, 14.1.

HRMS (ESI): m/z calcd for $C_{16}H_{15}F_3NO_5$ $[M + H]^+$, 342.0953; found 342.0945.



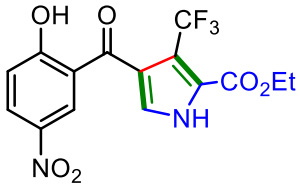
Ethyl 4-(2-hydroxy-5-methoxybenzoyl)-3-(trifluoromethyl)-1H-pyrrole-2-carboxylate (**3c**): light yellow solid, (method A: 134 mg, 75%; method B: 139 mg, 78%), mp 144-146°C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.56 (s, 1H), 9.73 (s, 1H), 7.19 – 7.11 (m, 2H), 7.02 – 6.95 (m, 2H), 4.44 (q, J = 7.2 Hz, 2H), 3.71 (s, 3H), 1.41 (t, J = 7.1 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ 107.84.

^{13}C NMR (126 MHz, $CDCl_3$) δ 195.3, 159.5, 157.4, 151.8, 125.0, 123.8 (q, J = 2.3 Hz), 123.10 (q, J = 3.4 Hz), 123.0, 122.1 (q, J = 269.1 Hz), 120.1, 119.3, 116.9 (q, J = 38.4 Hz), 115.5, 62.3, 56.1, 14.1.

HRMS (ESI): m/z calcd for $C_{16}H_{15}F_3NO_5$ $[M + H]^+$, 358.0902; found 358.0896.



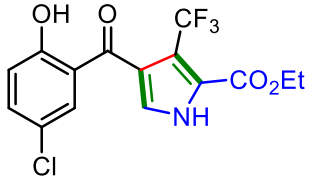
Ethyl 4-(2-hydroxy-5-nitrobenzoyl)-3-(trifluoromethyl)-1H-pyrrole-2-carboxylate (**3d**): white solid, (method A: 158 mg 85%; method B: 160 mg 86%) mp 162-164°C;

^{1}H NMR (500 MHz, $CDCl_3$) δ 12.59 (s, 1H), 10.19 (s, 1H), 8.55 (d, J = 2.7 Hz, 1H), 8.39 (dd, J = 9.2, 2.7 Hz, 1H), 7.16 (d, J = 9.3 Hz, 1H), 4.46 (q, J = 7.2 Hz, 2H), 1.42 (t, J = 7.2 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ 108.00.

^{13}C NMR (126 MHz, $CDCl_3$) δ 194.5, 167.7, 159.3, 139.8, 131.4, 129.1, 124.1 (q, J = 3.7 Hz), 123.8, 122.3 (q, J = 2.3 Hz), 121.9 (q, J = 269.3 Hz), 119.7, 119.4, 117.1 (q, J = 38.7 Hz), 62.6, 14.1.

HRMS (ESI): m/z calcd for $C_{15}H_{12}F_3N_2O_6$ r $[M + H]^+$, 373.0647; found 373.0640.



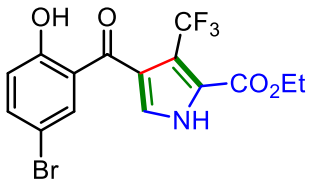
Ethyl 4-(5-chloro-2-hydroxybenzoyl)-3-(trifluoromethyl)-1H-pyrrole-2-carboxylate (**3e**): beige solid, (method A: 148 mg, 82%; method B: 145 mg, 80%), mp 153-155 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.83 (s, 1H), 9.85 (s, 1H), 7.51 (d, J = 2.6 Hz, 1H), 7.46 (dd, J = 8.9, 2.6 Hz, 1H), 7.18 (d, J = 3.1 Hz, 1H), 7.01 (d, J = 8.8 Hz, 1H), 4.45 (q, J = 7.1 Hz, 2H), 1.42 (t, J = 7.1 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ 107.81.

^{13}C NMR (126 MHz, $CDCl_3$) δ 194.6, 161.5, 159.6, 136.8, 131.9, 123.8, 123.5 (q, J = 3.4 Hz), 123.1 (q, J = 2.0 Hz), 123.3, 122.0 (q, J = 269.3 Hz), 121.2, 120.2, 117.0 (q, J = 38.3 Hz), 62.5, 14.1.

HRMS (ESI): m/z calcd for $C_{15}H_{13}F_3NO_4$ $[M + H]^+$, 362.0407; found 362.0398.



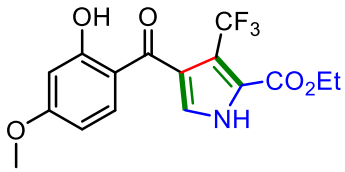
Ethyl 4-(5-bromo-2-hydroxybenzoyl)-3-(trifluoromethyl)-1H-pyrrole-2-carboxylate (**3f**): beige solid (method A: 156 mg, 77%; method B: 152 mg, 75%), mp 163-165 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.86 (s, 1H), 9.99 (s, 1H), 7.65 (d, J = 2.5 Hz, 1H), 7.58 (dd, J = 8.9, 2.5 Hz, 1H), 7.18 (d, J = 3.1 Hz, 1H), 6.96 (d, J = 8.9 Hz, 1H), 4.45 (q, J = 7.2 Hz, 2H), 1.42 (t, J = 7.1 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ 107.84.

^{13}C NMR (126 MHz, $CDCl_3$) δ 194.5, 161.9, 159.5, 139.6, 134.9, 123.5 (d, J = 3.4 Hz), 123.3, 123.1 (d, J = 2.2 Hz), 121.9 (d, J = 269.3 Hz), 121.8, 120.6, 117.0 (d, J = 38.6 Hz), 110.6, 62.5, 14.1.

HRMS (ESI): m/z calcd for $C_{15}H_{12}BrF_3NO_4$ $[M + H]^+$, 405.9902; found 405.9896.



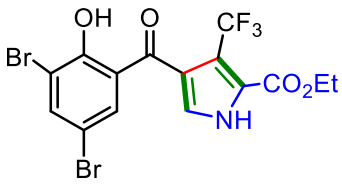
Ethyl 4-(2-hydroxy-4-methoxybenzoyl)-3-(trifluoromethyl)-1H-pyrrole-2-carboxylate (**3g**): beige solid, (method A: 144 mg, 81%; method B: 150 mg, 84%), mp 108-110 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.49 (s, 1H), 9.71 (s, 1H), 7.41 (d, J = 8.9 Hz, 1H), 7.10 (d, J = 2.9 Hz, 1H), 6.49 (d, J = 2.5 Hz, 1H), 6.40 (dd, J = 9.0, 2.5 Hz, 1H), 4.43 (q, J = 7.1 Hz, 2H), 3.86 (s, 3H), 1.41 (t, J = 7.1 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ 107.65.

^{13}C NMR (126 MHz, $CDCl_3$) δ 193.9, 166.8, 166.0, 159.6, 134.8, 123.7 (q, J = 2.2 Hz), 122.7 (q, J = 3.5 Hz), 122.5, 122.0 (q, J = 268.9 Hz), 116.6 (q, J = 38.3 Hz), 114.8, 107.9, 101.0, 62.2, 55.8, 14.1.

HRMS (ESI): m/z calcd for $C_{16}H_{15}F_3NO_5$ $[M + H]^+$, 358.0902; found 358.0895.



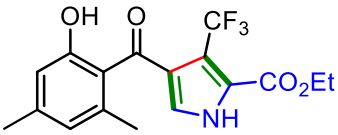
Ethyl 4-(3,5-dibromo-2-hydroxybenzoyl)-3-(trifluoromethyl)-1H-pyrrole-2-carboxylate (**3h**): beige solid, (method A: 170 mg, 70%; method B: 182 mg, 75%), mp 195-197 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.50 (s, 1H), 9.78 (s, 1H), 7.90 (d, *J* = 2.4 Hz, 1H), 7.64 (d, *J* = 2.3 Hz, 1H), 7.19 (d, *J* = 3.1 Hz, 1H), 4.45 (q, *J* = 7.2 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ 107.90.

^{13}C NMR (126 MHz, $CDCl_3$) δ 194.2, 159.4, 158.6, 141.9, 134.3, 123.8 (q, *J* = 3.3 Hz), 123.6, 122.5 (q, *J* = 2.2 Hz), 121.9 (q, *J* = 269.3 Hz), 122.1, 117.0 (q, *J* = 38.7 Hz), 113.3, 110.6, 62.5, 14.1.

HRMS (ESI): m/z calcd for $C_{15}H_{11}Br_2F_3NO_4$ $[M + H]^+$, 483.9007; found 483.9004.



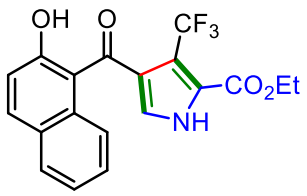
Ethyl 4-(2-hydroxy-4,6-dimethylbenzoyl)-3-(trifluoromethyl)-1H-pyrrole-2-carboxylate (**3i**): beige solid, (method A: 119 mg, 67%; method B: 136, mg 77%), mp 95-97 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.84 (s, 1H), 9.67 (s, 1H), 6.95 (d, *J* = 3.1 Hz, 1H), 6.69 (s, 1H), 6.52 (s, 1H), 4.42 (q, *J* = 7.1 Hz, 2H), 2.30 (s, 3H), 2.02 (s, 3H), 1.40 (t, *J* = 7.2 Hz, 3H).;

^{19}F NMR (376 MHz, $CDCl_3$) δ 107.36.

^{13}C NMR (126 MHz, $CDCl_3$) δ 194.8, 161.6, 159.6, 146.4, 139.7, 128.2 (q, *J* = 2.1 Hz), 124.6, 123.5 (q, *J* = 3.5 Hz), 123.3, 122.1 (q, *J* = 269.3 Hz), 120.4, 115.9 (q, *J* = 38.7 Hz), 116.0, 62.3, 22.9, 21.8, 14.1.

HRMS (ESI): m/z calcd for $C_{17}H_{17}F_3NO_4$ $[M + H]^+$, 356.1110; found 356.1102.



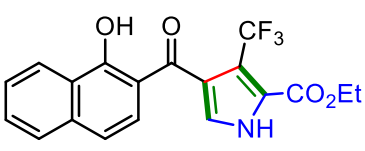
Ethyl 4-(2-hydroxy-1-naphthoyl)-3-(trifluoromethyl)-1H-pyrrole-2-carboxylate (**3j**): beige solid, (method A: 132 mg, 70%; method B: 136 mg, 72%), mp 140-142 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.05 (s, 1H), 9.56 (s, 1H), 7.93 (d, *J* = 9.0 Hz, 1H), 7.74 (dd, *J* = 7.4, 2.0 Hz, 1H), 7.59 – 7.52 (m, 1H), 7.34 – 7.22 (m, 2H), 7.20 (d, *J* = 9.0 Hz, 1H), 6.78 (d, *J* = 3.1 Hz, 1H), 4.43 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ 107.48.

^{13}C NMR (126 MHz, $CDCl_3$) δ 195.5, 163.6, 159.7, 137.7, 130.7, 127.6, 126.7, 126.2, 125.2, 124.7, 123.9 (q, *J* = 2.2 Hz), 122.9 (q, *J* = 3.4 Hz), 122.8, 122.2 (q, *J* = 269.3 Hz), 118.4, 116.9 (q, *J* = 38.5 Hz), 114.1, 62.3, 14.1.

HRMS (ESI): m/z calcd for $C_{19}H_{15}F_3NO_4$ $[M + H]^+$, 378.0953; found 378.0950.



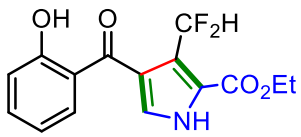
Ethyl 4-(1-hydroxy-2-naphthoyl)-3-(trifluoromethyl)-1H-pyrrole-2-carboxylate (**3k**): light yellow solid, (method A: 132 mg, 70%; method B: 136 mg, 72%), mp 153-155 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 13.77 (s, 1H), 9.74 (s, 1H), 8.51 (d, *J* = 8.4 Hz, 1H), 7.76 (d, *J* = 8.3 Hz, 1H), 7.66 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H), 7.56 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.44 (d, *J* = 8.9 Hz, 1H), 7.22 (d, *J* = 8.7 Hz, 1H), 7.17 (d, *J* = 3.1 Hz, 1H), 4.44 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ 107.69.

^{13}C NMR (126 MHz, $CDCl_3$) δ 193.0, 162.9, 159.6, 137.4, 132.6, 129.0, 128.7, 127.8 (q, *J* = 2.1 Hz), 127.3, 125.5, 124.8, 123.9, 123.7 (q, *J* = 3.4 Hz), 122.1 (q, *J* = 269.3 Hz), 119.4, 116.4 (q, *J* = 39.1 Hz), 114.8, 62.4, 14.1.

HRMS (ESI): m/z calcd for $C_{19}H_{15}F_3NO_4$ $[M + H]^+$, 378.0953; found 378.0945.



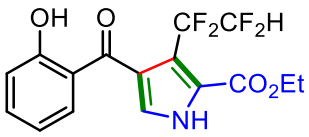
Ethyl 3-(difluoromethyl)-4-(2-hydroxybenzoyl)-1H-pyrrole-2-carboxylate (**3l**): beige solid (method A: 113 mg, 73%; method B: 120 mg, 77%), mp 114-116 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.93 (s, 1H), 9.60 (s, 1H), 7.65 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.51 (ddd, *J* = 8.6, 7.1, 1.7 Hz, 1H), 7.31 (t, *J* = 54.6 Hz, 1H), 7.25 (d, *J* = 3.0 Hz, 1H), 7.05 (dd, *J* = 8.4, 1.1 Hz, 1H), 6.88 (ddd, *J* = 8.2, 7.2, 1.1 Hz, 1H), 4.44 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ 52.83 (d, *J* = 54.6 Hz).

^{13}C NMR (126 MHz, $CDCl_3$) δ 194.9, 162.7, 159.8, 136.4, 132.7, 125.7, 123.1 (t, *J* = 7.1 Hz), 122.9, 122.5 (t, *J* = 27.0 Hz), 120.4, 118.8, 118.3, 109.8 (t, *J* = 234.3 Hz), 62.0, 14.2.

HRMS (ESI): m/z calcd for $C_{15}H_{14}F_2NO_4$ $[M + H]^+$, 310.0891; found 310.0881.



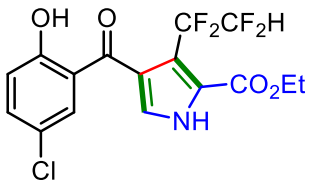
Ethyl 4-(2-hydroxybenzoyl)-3-(1,1,2,2-tetrafluoroethyl)-1H-pyrrole-2-carboxylate (**3m**): beige solid (method A: 134 mg, 75%; method B: 131 mg, 73%), mp 135-137 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.92 (s, 1H), 9.72 (s, 1H), 7.56 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.51 (ddd, *J* = 8.7, 7.2, 1.7 Hz, 1H), 7.13 (d, *J* = 2.9 Hz, 1H), 7.04 (dd, *J* = 8.5, 1.1 Hz, 1H), 6.87 (ddd, *J* = 8.2, 7.2, 1.2 Hz, 1H), 6.59 (td, *J* = 53.9, 5.9 Hz, 1H), 4.42 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ 54.73 (td, *J* = 9.6, 6.0 Hz), 25.39 (t, *J* = 9.1 Hz), 25.25 (dd, *J* = 10.4, 9.0 Hz).

^{13}C NMR (126 MHz, $CDCl_3$) δ 195.9, 163.1, 159.3, 137.0, 133.3, 124.5 (t, *J* = 3.0 Hz), 123.7, 123.2 (t, *J* = 5.3 Hz), 120.5, 119.0, 118.4, 118.4 (t, *J* = 28.4 Hz), 114.4 (tt, *J* = 249.9 Hz, 27.1 Hz), 110.3 (tt, *J* = 251.6, 34.3 Hz).62.3, 14.1.;

HRMS (ESI): m/z calcd for $C_{16}H_{13}ClF_4NO_4$ $[M + H]^+$, 394.0469; found 394.0467.



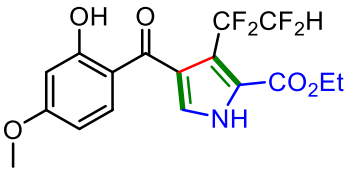
Ethyl 4-(5-chloro-2-hydroxybenzoyl)-3-(1,1,2,2-tetrafluoroethyl)-1H-pyrrole-2-carboxylate (**3n**): beige solid (method A: 137 mg, 70%; method B: 147 mg, 75%), mp 140-142 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.81 (s, 1H), 9.72 (s, 1H), 7.52 (d, *J* = 2.6 Hz, 1H), 7.45 (dd, *J* = 8.9, 2.6 Hz, 1H), 7.16 (d, *J* = 3.1 Hz, 1H), 7.00 (d, *J* = 8.9 Hz, 1H), 6.58 (tt, *J* = 53.7, 5.9 Hz, 1H), 4.43 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H);

^{19}F NMR (376 MHz, $CDCl_3$) δ 54.90 (td, *J* = 9.5, 6.0 Hz), 25.45 (t, *J* = 9.8 Hz), 25.31 (t, *J* = 9.8 Hz);

^{13}C NMR (126 MHz, $CDCl_3$) δ 195.0, 161.6, 159.1, 136.8, 132.1, 123.9 (t, *J* = 3.0 Hz), 123.7, 123.6, 123.4 (t, *J* = 5.9 Hz), 121.2, 120.1, 118.4 (t, *J* = 28.2 Hz), 114.3 (tt, *J* = 249.8 Hz, *J* = 34.1 Hz), 110.19 (tt, *J* = 251.8 Hz, *J* = 34.1 Hz), 62.4, 14.2.;

HRMS (ESI): m/z calcd for $C_{16}H_{13}ClF_4NO_4$ $[M + H]^+$, 394.0464; found 394.0467.



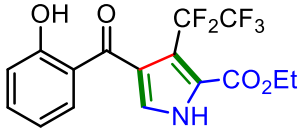
Ethyl 4-(2-hydroxy-4-methoxybenzoyl)-3-(1,1,2,2-tetrafluoroethyl)-1H-pyrrole-2-carboxylate (**3o**): beige solid (method A: 126 mg, 65%; method B: 132 mg, 68%), mp 101-103°C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.48 (s, 1H), 9.67 (s, 1H), 7.44 (d, *J* = 9.0 Hz, 1H), 7.09 (d, *J* = 3.1 Hz, 1H), 6.58 (tt, *J* = 53.5, 6.0 Hz, 1H), 6.48 (d, *J* = 2.4 Hz, 1H), 6.40 (dd, *J* = 9.0, 2.4 Hz, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 3.86 (s, 3H), 1.40 (t, *J* = 7.1 Hz, 3H);

^{19}F NMR (376 MHz, $CDCl_3$) δ 54.44 (td, *J* = 9.5, 5.9 Hz), 25.34 (dd, *J* = 10.3, 9.1 Hz), 25.20 (dd, *J* = 10.3, 9.2 Hz).;

^{13}C NMR (126 MHz, $CDCl_3$) δ 194.2, 166.8, 166.0, 159.4, 135.0, 124.6 (t, *J* = 3.1 Hz), 123.1, 122.8 (t, *J* = 5.4 Hz), 118.2 (t, *J* = 28.7 Hz), 114.7, 114.4 (tt, *J* = 249.8, 26.9 Hz), 110.3 (tt, *J* = 251.2, 33.9 Hz), 107.8, 101.0, 62.2, 55.8, 14.1.;

HRMS (ESI): m/z calcd for $C_{17}H_{16}F_4NO_5$ $[M + H]^+$, 390.0965; found 390.0960.



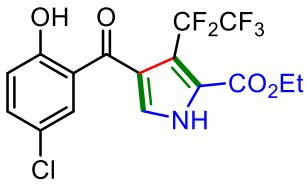
Ethyl 4-(2-hydroxybenzoyl)-3-(perfluoroethyl)-1H-pyrrole-2-carboxylate (**3p**): beige solid (method A: 128 mg, 68%; method B: 137 mg, 73%), mp 109-111°C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.96 (s, 1H), 9.89 (s, 1H), 7.55 – 7.43 (m, 2H), 7.12 (d, *J* = 3.1 Hz, 1H), 7.04 (dd, *J* = 8.4, 1.1 Hz, 1H), 6.85 (ddd, *J* = 8.2, 7.1, 1.1 Hz, 1H), 4.41 (q, *J* = 7.2 Hz, 2H), 1.39 (t, *J* = 7.1 Hz, 3H).;

^{19}F NMR (376 MHz, $CDCl_3$) δ 78.74 (t, *J* = 2.8 Hz), 58.69 (q, *J* = 2.9 Hz).;

^{13}C NMR (126 MHz, $CDCl_3$) δ 195.9, 163.1, 159.5, 137.0, 133.4, 124.7 (t, *J* = 3.2 Hz), 123.9 (t, *J* = 5.0 Hz),123.1, 120.9, 119.2 (dt, *J* = 286.9, 38.9 Hz), 119.0, 118.4, 114.7 (t, *J* = 28.9 Hz), 112.6 (tq, *J* = 254.1, 40.6 Hz).62.3, 14.0.;

HRMS (ESI): m/z calcd for $C_{16}H_{12}F_5NNaO_4$ $[M + Na]^+$, 428.0727; found 428.0724.



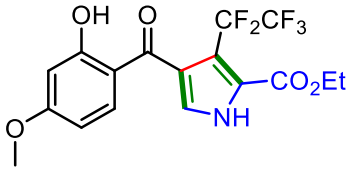
Ethyl 4-(5-chloro-2-hydroxybenzoyl)-3-(perfluoroethyl)-1H-pyrrole-2-carboxylate (**3q**): beige solid (method A: 113 mg, 55%; method B: 119 mg, 58%), mp 138-140°C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.86 (s, 1H), 9.97 (s, 1H), 7.47 – 7.43 (m, 2H), 7.15 (d, *J* = 3.1 Hz, 1H), 7.03 – 6.98 (m, 1H), 4.42 (q, *J* = 7.1 Hz, 2H), 1.40 (t, *J* = 7.2 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ 78.81 (t, *J* = 2.9 Hz), 58.89 (q, *J* = 2.9 Hz);

^{13}C NMR (126 MHz, $CDCl_3$) δ 194.8, 161.6, 159.3, 136.9, 132.1, 124.4 (t, *J* = 5.0 Hz), 124.1 (t, *J* = 3.2 Hz), 123.7, 123.2, 121.5, 120.2, 119.2 (qt, *J* = 287.4, 39.1 Hz), 114.8 (t, *J* = 28.9 Hz), 112.5 (tq, *J* = 254.9, 40.8 Hz), 62.4, 14.0;

HRMS (ESI): m/z calcd for $C_{16}H_{12}ClF_5NO_4$ $[M + H]^+$, 412.0375; found 412.0371.



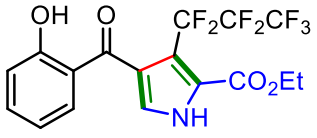
Ethyl 4-(2-hydroxy-4-methoxybenzoyl)-3-(perfluoroethyl)-1H-pyrrole-2-carboxylate (**3r**): beige solid (method A: 132 mg, 65%; method B: 136 mg, 67%), mp 138-140°C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.50 (s, 1H), 9.87 (s, 1H), 7.34 (d, *J* = 9.0 Hz, 1H), 7.08 (d, *J* = 3.0 Hz, 1H), 6.48 (d, *J* = 2.5 Hz, 1H), 6.38 (dd, *J* = 9.0, 2.5 Hz, 1H), 4.40 (q, *J* = 7.1 Hz, 2H), 3.85 (s, 3H), 1.39 (t, *J* = 7.1 Hz, 3H).;

^{19}F NMR (376 MHz, $CDCl_3$) δ 78.64 (t, *J* = 2.8 Hz), 58.39 (d, *J* = 2.9 Hz);

^{13}C NMR (126 MHz, $CDCl_3$) δ 194.2, 166.8, 166.1, 159.4, 135.1, 124.9 (t, *J* = 3.3 Hz), 123.7 (t, *J* = 5.0 Hz), 122.4, 119.2 (dt, *J* = 287.1, 39.2 Hz), 115.1, 114.4 (t, *J* = 28.9 Hz), 112.6 (tq, *J* = 254.0, 40.6 Hz), 107.8, 101.0, 62.2, 55.8, 14.0;

HRMS (ESI): m/z calcd for $C_{17}H_{15}F_5NO_5$ $[M + H]^+$, 408.0865; found 408.0863.



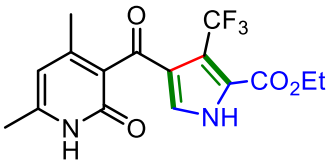
Ethyl 4-(2-hydroxybenzoyl)-3-(perfluoropropyl)-1H-pyrrole-2-carboxylate (**3s**): beige solid (method A: 153 mg, 72%; method B: 158 mg, 74%), mp 98-100°C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.96 (d, *J* = 1.8 Hz, 1H), 9.84 (s, 1H), 7.50 (ddd, *J* = 8.6, 7.1, 1.8 Hz, 1H), 7.45 (dd, *J* = 8.1, 1.7 Hz, 1H), 7.12 (d, *J* = 3.1 Hz, 1H), 7.04 (dd, *J* = 8.4, 1.2 Hz, 1H), 6.85 (td, *J* = 7.6, 1.2 Hz, 1H), 4.41 (q, *J* = 7.2 Hz, 2H), 1.38 (t, *J* = 7.2 Hz, 3H);

^{19}F NMR (376 MHz, $CDCl_3$) δ 81.57 (t, *J* = 10.4 Hz), 61.63 (q, *J* = 10.4 Hz), 38.57 – 38.68 (m);

^{13}C NMR (126 MHz, $CDCl_3$) δ 195.9, 163.1, 159.6, 137.0, 133.4, 124.9 (t, *J* = 3.3 Hz), 124.3 (t, *J* = 5.2 Hz), 122.9, 121.0, 118.9, 118.4, 118.3 (qt, *J* = 288.2, 34.3 Hz), 114.8 (tt, *J* = 254.5, 34.1 Hz), 114.3 (t, *J* = 29.2 Hz), 108.8 (th, *J* = 264.8, 38.5 Hz), 62.4, 13.9;

HRMS (ESI): m/z calcd for $C_{17}H_{13}F_7NO_4$ $[M + H]^+$, 428.0733; found 428.0724.



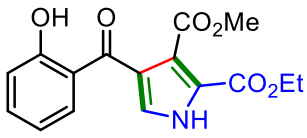
***Ethyl 4-(4,6-dimethyl-2-oxo-1,2-dihydropyridine-3-carbonyl)-3-(trifluoromethyl)-1H-pyrrole-2-carboxylate* (3t):** white solid (method A: 148 mg, 83%; method B: 169 mg, 95%), mp 299-301°C;

^{1}H NMR (400 MHz, DMSO) δ 12.87 (s, 1H), 11.72 (s, 1H), 7.31 (d, *J* = 3.3 Hz, 1H), 5.97 (s, 1H), 4.31 (q, *J* = 7.1 Hz, 2H), 2.17 (s, 3H), 1.98 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H);

^{19}F NMR (376 MHz, DMSO) δ 109.72;

^{13}C NMR (126 MHz, DMSO) δ 188.6, 161.0, 159.0, 149.9, 146.1, 129.1, 126.7, 125.3, 124.1 (q, *J* = 3.4 Hz), 122.3 (q, *J* = 268.5 Hz), 113.5 (q, *J* = 38.2 Hz), 107.3, 61.3, 18.9, 18.4, 13.9;

HRMS (ESI): m/z calcd fo $C_{16}H_{16}F_3N_2O_4$ $[M + H]^+$, 357.1062; found 357.1058.

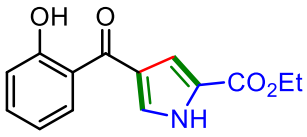


***2-ethyl 3-methyl 4-(2-hydroxybenzoyl)-1H-pyrrole-2,3-dicarboxylate* (3u):** beige solid (method A: 79 mg, 50%; method B: 111 mg, 70%), mp 115-117°C;

^{1}H NMR (500 MHz, $CDCl_3$) δ 11.71 (s, 1H), 9.73 (s, 1H), 7.74 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.49 (ddd, *J* = 8.6, 7.2, 1.7 Hz, 1H), 7.35 (d, *J* = 3.1 Hz, 1H), 7.07 – 7.00 (m, 1H), 6.93 – 6.87 (m, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 3.85 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 4H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 193.0, 165.5, 162.5, 159.9, 136.1, 131.7, 126.1, 124.0, 122.8, 122.7, 120.1, 119.0, 118.5, 77.4, 77.2, 76.9, 61.9, 52.8, 14.2;

HRMS (ESI): m/z calcd for $C_{16}H_{12}ClF_5NO_4$ $[M + H]^+$, 412.0375; found 412.0371.



***Ethyl 4-(2-hydroxybenzoyl)-1H-pyrrole-2-carboxylate* (3v):** beige solid (method A: 53 mg, 41%; method B: 71 mg, 55%), mp 105-107°C;

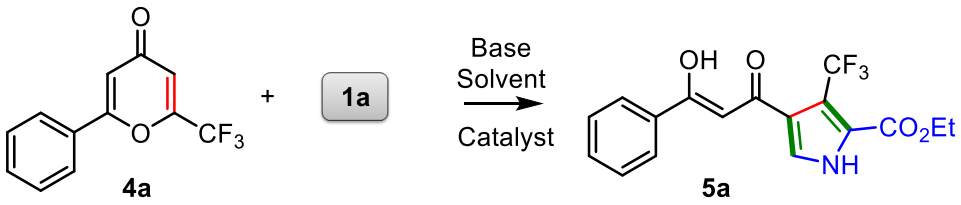
^{1}H NMR (400 MHz, $CDCl_3$) δ 12.03 (s, 1H), 9.56 (s, 1H), 7.90 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.59 (dd, *J* = 3.3, 1.6 Hz, 1H), 7.50 (ddd, *J* = 8.6, 7.2, 1.7 Hz, 1H), 7.37 (dd, *J* = 2.5, 1.6 Hz, 1H), 7.05 (dd, *J* = 8.4, 1.1 Hz, 1H), 6.94 (ddd, *J* = 8.2, 7.2, 1.1 Hz, 1H), 4.38 (q, *J* = 7.2 Hz, 2H), 1.40 (t, *J* = 7.1 Hz, 3H).;

HRMS (ESI): m/z calcd for $C_{14}H_{14}NO_4$ $[M + H]^+$,260.0923; found 260.0918.

General procedure for synthesis of 3-(trifluoromethyl/polyfluoroalkyl)-1H-pyrroles 5a-m

To 10 mL reaction tube equipped with magnetic stirrer was charged pyrone **4a-l** (0.5 mmol), silver acetate (8,3 mg, 0.05 mmol, 10 mol % 0.1 equiv.) 3 mL dry DMF mixture was stirred at room temperature for 2 min and. potassium carbonate (138 mg, 1.0 mmol, 2.0 equiv.) then ethyl isocyanoacetate **1a** (85 mg, 0.75 mmol 1.5 equiv.), were added and reaction mixture was stirred at room temperature until pyrrole formation was complete. Then mixture was quenched diluted hydrochloric acid (20 mL 1M) and extracted with EtOAc (10 mL x4), washed brine (10 mL x 2), dried anhydrous Mg_2SO_4 and evaporated to dryness to yield a crude reaction product, which was purified by silica gel flash chromatography eluted with EtOAc-Hexane, 1:3 to give the product as a beige solid.

Table 2. Optimization of reaction conditions 2-phenyl-6-(trifluoromethyl)-4*H*-pyran-4-one with ethyl isocyaniacetate [a,b]



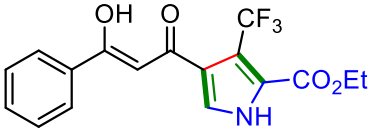
entry	solvent	temperature	Base (equiv.)	catalyst	yield
1	MeCN	rt	K_2CO_3 (2.0)	CuI	65
2	MeCN	rt	K_2CO_3 (0.1)	AgOAc	44
3	MeCN	rt	K_2CO_3 (1.0)	AgOAc	66
4	MeCN	rt	K_2CO_3 (2.0)	AgOAc	75
5	MeCN	rt	Cs_2CO_3 (0.1)	AgOAc	52
6	MeCN	rt	Cs_2CO_3 (1.0)	AgOAc	74
7	MeCN	rt	Cs_2CO_3 (2.0)	AgOAc	80
8	MeCN	rt	DBU (0.1)	AgOAc	45
9	MeCN	rt	DBU (1.0)	AgOAc	60

10	MeCN	rt	DBU (2.0)	AgOAc	75
11	DMF	rt	K_2CO_3 (2.0)	AgOAc	80
12	DMF	rt	DBU (2.0)	AgOAc	75
13	DMF	rt	DABCO (2.0)	AgOAc	50
14	DMF	50	K_2CO_3 (2.0)	AgOAc	70
15	DMF	100	K_2CO_3 (2.0)	AgOAc	57
16	DMF	rt	K_2CO_3 (2.0)	CuI	50
17	DMF	50	K_2CO_3 (2.0)	CuI	53
18	DMF	50	K_2CO_3 (2.0)	CuBr	54
19	DMF	50	K_2CO_3 (2.0)	CuCl	60
20	DMF	100	K_2CO_3 (2.0)	CuCl	67
21	DMSO	rt	K_2CO_3 (2.0)	AgOAc	75
22	THF	rt	K_2CO_3 (2.0)	AgOAc	77

[a] Reaction conditions: **2a** (0.5 mmol, 1.0 equiv.), **1a** (0.75 mmol, 1.5 equiv.), catalyst (10 mol. %, 0.1 equiv) base, (1.0 mmol, 2.0 equiv) and solvent 3 mL. [b] Isolated yields.

Gram scale preparation of 5a (See **Scheme 1**)

To 50 mL reaction tube equipped with magnetic stirrer was charged pyrone **4a** (1070 mg, 5 mmol), silver acetate (83 mg, 0.5 mmol, 10 mol % 0.1 equiv.), 20 mL dry DMF mixture was stirred at room temperature for 2 min. and potassium carbonate (1380 mg, 1.0 mmol, 2.0 equiv.) then ethyl isocyanoacetate **1a** (850 mg, 0.75 mmol 1.5 equiv.), were added and reaction mixture was stirred at room temperature until pyrrole formation was complete. Then mixture was quenched diluted hydrochloric acid (90 mL 1M) and extracted with EtOAc (50 mL x4), washed brine (30 mL x2), dried anhydrous Mg_2SO_4 and evaporated to dryness to yield a crude reaction product, which was purified by silica gel flash chromatography eluted with EtOAc-Hexane, 1:3 to give the product as a beige solid (1230 mg 70%).



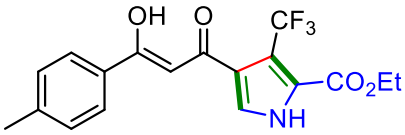
***ethyl (Z)-4-(3-hydroxy-3-phenylacryloyl)-3-(trifluoromethyl)-1H-pyrrole-2-carboxylate* (5a):** beige solid (141 mg, 80%), mp 140-143 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 16.33 (s, 1H), 9.75 (s, 1H), 7.95 – 7.89 (m, 2H), 7.59 – 7.52 (m, 1H), 7.50 – 7.45 (m, 2H), 7.42 (d, *J* = 3.2 Hz, 1H), 6.51 (s, 1H), 4.42 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.2 Hz, 3H).;

^{19}F NMR (376 MHz, $CDCl_3$) δ 108.43.

^{13}C NMR (126 MHz, $CDCl_3$) δ 183.9, 182.7, 159.6, 135.1, 132.6, 128.8 (2C), 127.2 (2C), 124.2, 124.2 (q, *J* = 10.1 Hz), 123.9 (q, *J* = 3.4 Hz), 122.2 (q, *J* = 268.9 Hz), 115.6 (q, *J* = 38.7 Hz), 96.9 (q, *J* = 2.4 Hz), 62.3, 14.1.

HRMS (ESI): m/z calcd for $C_{17}H_{15}F_3NO_4$ $[M + H]^+$, 354.0953; found 354.0950.



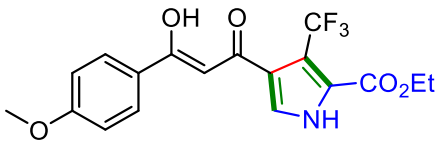
ethyl (Z)-4-(3-hydroxy-3-(p-tolyl)acryloyl)-3-(trifluoromethyl)-1H-pyrrole-2-carboxylate (5b): beige solid (145 mg, 79%), mp 107-110 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 16.39 (s, 1H), 9.74 (s, 1H), 7.82 (d, *J* = 8.3 Hz, 2H), 7.41 (d, *J* = 2.9 Hz, 1H), 7.27 (d, *J* = 8.6 Hz, 2H), 6.48 (s, 1H), 4.42 (q, *J* = 7.2 Hz, 2H), 2.42 (s, 3H), 1.40 (t, *J* = 7.1 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ 108.40.

^{13}C NMR (126 MHz, DMSO) δ 184.4, 180.4, 158.9, 142.9, 131.2, 129.3, 127.5, 126.9, 124.3 (q, *J* = 3.2 Hz), 122.3 (q, *J* = 268.4 Hz), 122.1, 113.6 (q, *J* = 38.0 Hz), 95.1, 61.3, 21.1, 13.9.

HRMS (ESI): m/z calcd for $C_{18}H_{17}F_3NO_4$ $[M + H]^+$, 368.1104; found 368.11106.



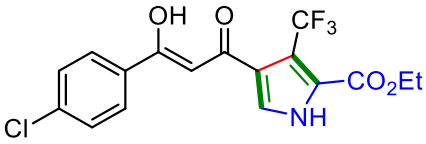
ethyl (Z)-4-(3-hydroxy-3-(4-methoxyphenyl)acryloyl)-3-(trifluoromethyl)-1H-pyrrole-2-carboxylate (5c): beige solid (136 mg, 71%), mp 133-135 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 16.49 (s, 1H), 9.69 (s, 1H), 7.91 (d, *J* = 8.8 Hz, 2H), 7.40 (d, *J* = 2.5 Hz, 1H), 6.97 (d, *J* = 8.8 Hz, 2H), 6.45 (s, 1H), 4.42 (q, *J* = 7.1 Hz, 2H), 3.88 (s, 3H), 1.40 (t, *J* = 7.1 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ 108.40.

^{13}C NMR (126 MHz, DMSO) δ 183.2, 181.2, 162.9, 158.9, 129.1, 127.2, 126.4, 124.1 (q, *J* = 3.2 Hz), 122.3 (q, *J* = 268.4 Hz), 122.0, 114.1, 113.6 (q, *J* = 38.0 Hz), 94.6, 61.3, 55.5, 13.9.

HRMS (ESI): m/z calcd for $C_{18}H_{17}F_3NO_5$ $[M + H]^+$, 384.1053; found 384.1056.



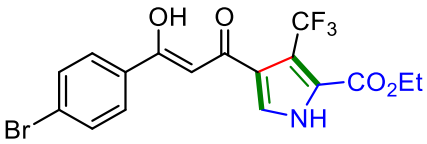
ethyl (Z)-4-(3-(4-chlorophenyl)-3-hydroxyacryloyl)-3-(trifluoromethyl)-1H-pyrrole-2-carboxylate (5d): beige solid (163 mg, 84%), mp 133 135 **°C;**

^{1}H NMR (400 MHz $CDCl_3$) δ 16.28 (s, 1H), 9.73 (s, 1H), 7.85 (d, *J* = 8.7 Hz, 2H), 7.45 (d, *J* = 8.6 Hz, 2H), 7.43 (d, *J* = 3.2 Hz, 1H), 6.47 (s, 1H), 4.42 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ 108.46.

^{13}C NMR (126 MHz, DMSO) δ 185.1, 178.3, 158.9, 137.3, 132.7, 128.8, 128.7, 128.0, 124.5 (q, J = 3.4 Hz), 122.2 (q, J = 268.4 Hz), 121.9, 113.6 (q, J = 38.2 Hz), 95.7, 61.4, 13.9.

HRMS (ESI): m/z calcd for $C_{17}H_{14}ClF_3NO_4$ $[M + H]^+$, 388.0558; found 388.0558.



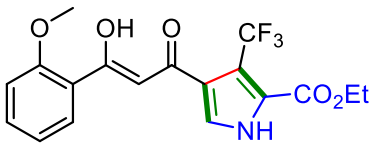
ethyl (Z)-4-(3-(4-bromophenyl)-3-hydroxyacryloyl)-3-(trifluoromethyl)-1H-pyrrole-2-carboxylate (5e): beige solid (166 mg, 77%), mp 145-147 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 16.27 (s, 1H), 9.76 (s, 1H), 7.78 (d, J = 8.6 Hz, 2H), 7.61 (d, J = 8.6 Hz, 2H), 7.43 (d, J = 2.6 Hz, 1H), 6.47 (s, 1H), 4.42 (q, J = 7.2 Hz, 2H), 1.41 (t, J = 7.1 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ 108.46.

^{13}C NMR (126 MHz, DMSO-d_6) δ 185.2, 178.4, 158.9, 131.8, 131.2, 128.8, 128.1, 126.3, 124.5 (q, J = 3.3 Hz), 122.2 (q, J = 268.5 Hz), 122.0, 113.6 (q, J = 38.2 Hz), 95.6, 61.4, 13.9.

HRMS (ESI): m/z calcd for $C_{17}H_{14}BrF_3NO_4$ $[M + H]^+$, 432.0053; found 432.0053.



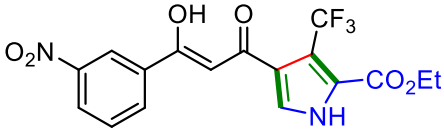
ethyl (Z)-4-(3-hydroxy-3-(2-methoxyphenyl)acryloyl)-3-(trifluoromethyl)-1H-pyrrole-2-carboxylate (5f): beige solid (140 mg, 73%), mp 103-105 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 16.38 (s, 1H), 9.84 (s, 1H), 7.95 (dd, J = 7.8, 1.8 Hz, 1H), 7.46 (ddd, J = 8.8, 7.3, 1.8 Hz, 1H), 7.41 (d, J = 3.1 Hz, 1H), 7.05 (td, J = 7.5, 1.0 Hz, 1H), 6.98 (dd, J = 8.3, 1.0 Hz, 1H), 6.90 (s, 1H), 4.41 (q, J = 7.1 Hz, 2H), 3.92 (s, 3H), 1.40 (t, J = 7.1 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ 108.53.

^{13}C NMR (126 MHz, DMSO-d_6) δ 184.1, 179.9, 158.8, 158.2, 133.5, 129.4, 126.5, 124.2 (q, J = 3.3 Hz), 123.0, 122.4 (q, J = 268.4 Hz), 122.4 (d, J = 1.8 Hz), 120.5, 113.4 (q, J = 37.8 Hz), 112.4, 100.8, 61.3, 55.7, 13.9.

HRMS (ESI): m/z calcd for $C_{18}H_{16}F_3NNaO_5$ $[M + Na]^+$, 406.0873; found 406.0872.



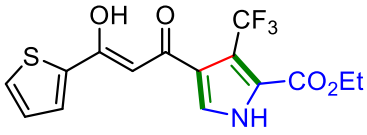
ethyl (Z)-4-(3-hydroxy-3-(3-nitrophenyl)acryloyl)-3-(trifluoromethyl)-1H-pyrrole-2-carboxylate (5g): beige solid (84 mg, 42%), mp 160-163 **°C;**

^{1}H NMR (400 MHz, DMSO-d_6) δ 16.46 (s, 1H), 13.20 (s, 1H), 8.79 (t, J = 2.0 Hz, 1H), 8.50 (dt, J = 8.0, 1.3 Hz, 1H), 8.43 (ddd, J = 8.3, 2.4, 1.0 Hz, 1H), 8.28 (d, J = 3.5 Hz, 1H), 7.85 (t, J = 8.0 Hz, 1H), 7.20 (s, 1H), 4.35 (q, J = 7.1 Hz, 2H), 1.33 (t, J = 7.1 Hz, 3H).

^{19}F NMR (376 MHz, DMSO-d_6) δ 110.01.

^{13}C NMR (126 MHz, DMSO-d_6) δ 185.8, 176.2, 158.9, 148.3, 135.5, 132.9, 130.4, 128.7, 126.6, 124.7 (q, J = 3.4 Hz), 122.2 (q, J = 268.5 Hz), 121.8 (d, J = 1.6 Hz), 121.2, 113.6 (q, J = 38.1 Hz), 96.3, 61.4, 13.9.

HRMS (ESI): m/z calcd for $C_{17}H_{13}F_3N_2NaO_6$ [M + Na]$^+$, 421.0618; found 421.0623.



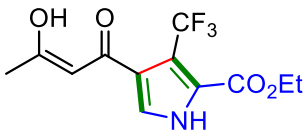
ethyl (Z)-4-(3-hydroxy-3-(thiophen-2-yl)acryloyl)-3-(trifluoromethyl)-1H-pyrrole-2-carboxylate (5h): beige solid (113 mg, 63%), mp 135-137 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 15.88 (s, 1H), 9.70 (s, 1H), 7.74 (dd, J = 3.8, 1.2 Hz, 1H), 7.63 (dd, J = 4.9, 1.1 Hz, 1H), 7.40 (d, J = 3.1 Hz, 1H), 7.16 (dd, J = 5.0, 3.8 Hz, 1H), 6.38 (s, 1H), 4.42 (q, J = 7.2 Hz, 2H), 1.40 (t, J = 7.1 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ 108.27.

^{13}C NMR (126 MHz, DMSO-d_6) δ 179.8, 179.2, 158.8, 140.6, 134.0, 131.5, 128.8, 126.8, 124.1 (q, J = 3.3 Hz), 122.3 (q, J = 268.3 Hz), 120.6, 113.5 (q, J = 38.0 Hz), 95.1, 61.3, 13.9.

HRMS (ESI): m/z calcd for $C_{15}H_{13}F_3NO_4S$ [M + H]$^+$, 360.0512; found 360.0511.



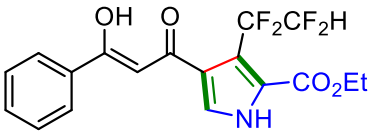
ethyl (Z)-4-(3-hydroxybut-2-enoyl)-3-(trifluoromethyl)-1H-pyrrole-2-carboxylate (5i): beige solid (66 mg, 45%), mp 73-75 **°C;**

^{1}H NMR (400 MHz, $CDCl_3$) δ 15.69 (s, 1H), 9.67 (s, 1H), 7.32 (d, J = 3.2 Hz, 1H), 5.82 (s, 1H), 4.40 (q, J = 7.2 Hz, 2H), 2.14 (s, 3H), 1.39 (t, J = 7.2 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ 108.21.

^{13}C NMR (126 MHz, DMSO-d_6) δ 188.1, 182.9, 158.8, 129.6, 126.6, 124.1 (d, J = 3.4 Hz), 122.3 (q, J = 268.4 Hz), 121.6 (q, J = 1.4 Hz), 113.5 (q, J = 38.0 Hz), 99.1, 61.3, 23.7, 13.8 (d, J = 1.8 Hz).

HRMS (ESI): m/z calcd for $C_{12}H_{12}F_3NNaO_4$ [M + Na]$^+$, 314.0611; found 314.0612.



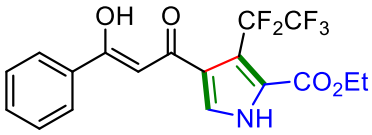
ethyl (Z)-4-(3-hydroxy-3-phenylacryloyl)-3-(1,1,2,2-tetrafluoroethyl)-1H-pyrrole-2-carboxylate(5j): beige solid (119 mg, 62%), mp 125-127 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 16.27 (s, 1H), 9.78 (s, 1H), 7.94 – 7.88 (m, 2H), 7.57 – 7.51 (m, 1H), 7.50 – 7.44 (m, 2H), 7.41 (d, J = 2.4 Hz, 1H), 6.86 – 6.53 (m, 1H), 6.53 (s, 1H), 4.40 (q, J = 7.2 Hz, 2H), 1.40 (t, J = 7.1 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ 55.29 (td, J = 10.2, 6.0 Hz), 25.52 – 25.41 (m), 25.32 (dd, J = 10.9, 9.5 Hz).

^{13}C NMR (126 MHz, DMSO-d_6) δ 186.2, 178.8, 159.3, 133.7, 132.4, 128.7, 128.3, 126.8, 124.8 (t, J = 4.1 Hz), 122.7, 116.5 (t, J = 26.8 Hz), 115.1 (t, J = 27.7 Hz), 114.5 (tt, J = 248.8, 27.4 Hz), 110.2 (tt, J = 251.3, 33.1 Hz), 108.2 (dt, J = 250.1, 32.7 Hz), 95.6, 61.3, 13.8.

HRMS (ESI): m/z calcd for $C_{18}H_{16}F_4NO_4$ $[M + H]^+$, 386.1003; found 386.1010.



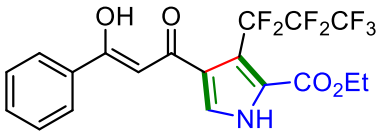
ethyl (Z)-4-(3-hydroxy-3-phenylacryloyl)-3-(perfluoroethyl)-1H-pyrrole-2-carboxylate(5k): beige solid (135 mg, 67%), mp 133-135 **°C;**

^{1}H NMR (400 MHz, $CDCl_3$) δ 16.34 (s, 1H), 9.92 (s, 1H), 7.93 – 7.91 (m, 1H), 7.91 – 7.88 (m, 1H), 7.57 – 7.51 (m, 1H), 7.50 – 7.44 (m, 2H), 7.42 (d, J = 3.2 Hz, 1H), 6.50 (s, 1H), 4.40 (q, J = 7.2 Hz, 2H), 1.39 (t, J = 7.1 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ 79.24 (t, J = 3.2 Hz), 59.80 (q, J = 3.2 Hz).

^{13}C NMR (126 MHz, DMSO-d_6) δ 185.2, 179.7, 158.7, 134.0, 132.4, 128.7 (2C), 128.5, 126.9 (2C), 125.4 (t, J = 4.5 Hz), 123.1, 119.1 (qt, J = 287.8, 39.6 Hz), 112.6 (tq, J = 253.5, 40.1 Hz), 111.8 (t, J = 27.8 Hz), 95.9, 61.3, 13.8.

HRMS (ESI): m/z calcd for $C_{18}H_{14}F_5NNaO_4$ $[M + Na]^+$, 426.0735; found 426.0739.



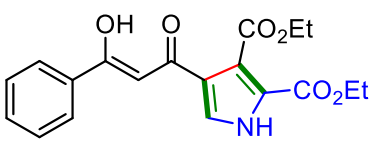
ethyl (Z)-4-(3-hydroxy-3-phenylacryloyl)-3-(perfluoropropyl)-1H-pyrrole-2-carboxylate (5l): beige solid (147 mg, 65%), mp 113-115 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 16.36 (s, 1H), 9.95 (s, 1H), 7.93 – 7.91 (m, 1H), 7.91 – 7.88 (m, 1H), 7.57 – 7.52 (m, 1H), 7.49 – 7.44 (m, 2H), 7.43 (d, J = 3.1 Hz, 1H), 6.50 (s, 1H), 4.39 (q, J = 7.2 Hz, 2H), 1.38 (t, J = 7.2 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$) δ 81.66 (t, J = 10.3 Hz), 62.73 (q, J = 10.4 Hz), 40.28 – 38.11 (m).

^{13}C NMR (126 MHz, DMSO-d_6) δ 185.0, 179.9, 158.7, 134.0, 132.4, 128.6, 128.4, 128.4, 126.8, 125.6 (t, J = 4.6 Hz), 123.1 (t, J = 2.1 Hz), 118.0 (qt, J = 288.7, 34.5 Hz), 114.8 (tt, J = 253.3, 33.4 Hz), 111.5 (t, J = 28.2 Hz), 108.6 (tq, J = 265.1, 37.4 Hz), 95.9, 61.2, 13.6.

HRMS (ESI): m/z calcd for $C_{19}H_{15}F_7NNaO_4$ $[M + Na]^+$, 476.0703; found 476.0708.



diethyl (Z)-4-(3-hydroxy-3-phenylacryloyl)-1H-pyrrole-2,3-dicarboxylate (5m): beige solid (71 mg, 40%), mp 115-117 °C;

^{1}H NMR (500 MHz, $CDCl_3$) δ 16.35 (s, 1H), 9.69 (s, 1H), 7.92 – 7.86 (m, 2H), 7.55 – 7.49 (m, 2H), 7.49 – 7.41 (m, 2H), 6.48 (s, 1H), 4.46 (q, *J* = 7.2 Hz, 2H), 4.34 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.2 Hz, 3H), 1.35 (t, *J* = 7.2 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 183.5, 181.6, 166.2, 159.9, 134.8, 132.2, 128.7 (2C), 126.9 (2C), 124.5, 123.0, 122.1, 121.9, 93.7, 62.1, 61.7, 14.3, 14.2;

HRMS (ESI): m/z calcd for $C_{19}H_{20}NO_6$ $[M + H]^+$, 358.1291; found 358.1286.

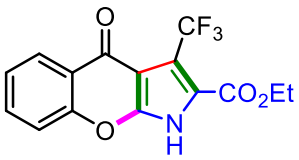
General procedure for synthesis of 7

Method A (From 3-chloro-2-trifluoromethyl-3-chlorochromone 6a)

To a 10 mL reaction tube equipped with magnetic stirrer was charged chromone **6a** (124 mg 0.5 mmol, 1 equiv.), copper iodide (9.5 mg, 0.05 mmol, 0.1 equiv., 10 mol %) 3 mL dry DMF and potassium carbonate (138 mg, 1.0 mmol, 2 equiv mixture was stirred at room temperature for 2 min. then benzyl isocyanide **1a** (88 mg, 0.75 mmol 1.5 equiv),) were added and reaction mixture was stirred at 70 °C until pyrrole formation was complete. Then mixture was quenched diluted hydrochloric acid (20 mL 1M) filtered, washed water (2 mL x3) dried under air at room temperature yield a crude reaction product, which was purified by silica gel column chromatography eluted with EtOAc-Hexane, 1:1 to give the product as white solid.

Method B (From pyrrole 3a)

To a 25 mL two necked round bottom flask with magnetic stirrer reflux condenser and bubbler was charged pyrrole **3a** (327 mg, 1 mmol, 1.0 equiv.), potassium carbonate (276 mg, 2 mmol, 2.0 equiv.) copper iodide (19 mg 0.1 mmol, 0.1equiv. 10 mol%) and 10mL DMF reaction mixture was heated at 100 °C 10 h. Then mixture was quenched into hydrochloric acid (20 mL 1M) filtered, washed water (2 mL x3) dried under air at room tem yield a crude reaction product, which was purified by silica gel column chromatography eluted with EtOAc-Hexane, 1:1 to give the product as white solid.



ethyl 4-oxo-3-(trifluoromethyl)-1,4-dihydrochromeno[2,3-b]pyrrole-2-carboxylate (7): white solid (method A: 41 mg, 25%; method B: 140 mg, 43%), mp 235-237 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 14.10 (s, 1H), 8.19 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.83 (ddd, *J* = 8.4, 7.2, 1.6 Hz, 1H), 7.68 (d, *J* = 8.4 Hz, 0H), 7.52 (t, *J* = 7.2 Hz, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 1.33 (t, *J* = 7.1 Hz, 3H).

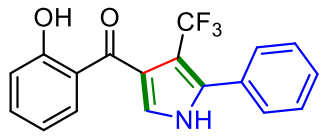
^{19}F NMR (376 MHz, DMSO-d_6) δ 110.41.

^{13}C NMR (126 MHz, DMSO-d_6) δ 170.82, 158.71, 153.26, 150.13, 134.00, 126.17, 125.03, 122.60, 121.86 (q, J = 269.1 Hz), 118.85 (d, J = 3.7 Hz), 117.56, 110.36 (q, J = 40.0 Hz), 104.06, 61.66, 13.83.

HRMS (ESI): m/z calcd for $C_{15}H_{11}F_3NO_4$ $[M + H]^+$, 332.0635; found 326.0633.

General procedure for the synthesis of 2-phenylpyrroles 9a-b.

10 mL reaction tube equipped with magnetic stirrer was charged chromone **2a** (0.5 mmol), silver acetate (8,3 mg, 0.05 mmol, 10 mol % 0.1 equiv.) 3 mL dry acetonitrile and potassium carbonate (138 mg, 1.0 mmol, 2.0 equiv.) mixture was stirred at room temperature for 2 min. then benzyl isocyanide **1a** (88 mg, 0.75 mmol 1.5 equiv.), were added and reaction mixture was stirred at 70 until pyrrole formation was complete. Then mixture was quenched diluted hydrochloric acid (20 mL 1M) and extracted with EtOAc (10 mL x4), washed brine (10 mL x2), dried anhydrous Mg_2SO_4 and evaporated to dryness to yield a crude reaction product, which was purified by silica gel column chromatography eluted with EtOAc-Hexane, 1:4 to give the product as beige solid.



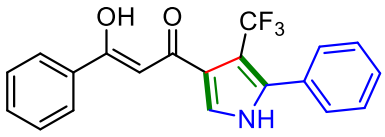
(2-hydroxyphenyl)(5-phenyl-4-(trifluoromethyl)-1H-pyrrol-3-yl)methanone **(9a):** beige solid (61 mg, 37%), mp 133-135 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.03 (s, 1H), 8.74 (s, 1H), 7.83 (dd, J = 8.0, 1.7 Hz, 1H), 7.56 – 7.43 (m, 6H), 7.16 (s, 1H), 7.04 (dd, J = 8.4, 1.1 Hz, 1H), 6.95 – 6.87 (m, 1H).

^{19}F NMR (376 MHz, $CDCl_3$) δ 109.12.

^{13}C NMR (126 MHz, $CDCl_3$) δ 194.8, 162.9, 136.3, 135.6 (q, J = 4.0 Hz), 132.9, 130.4, 129.5, 128.9 (4C), 124.0, 123.3 (q, J = 268.2 Hz), 122.4 (q, J = 1.9 Hz), 120.6, 118.9, 118.4, 110.7 (q, J = 36.6 Hz).

HRMS (ESI): m/z calcd for $C_{18}H_{13}F_3NO_2$ $[M + H]^+$, 332.0898; found 332.0891.



(Z)-3-hydroxy-3-phenyl-1-(5-phenyl-4-(trifluoromethyl)-1H-pyrrol-3-yl)prop-2-en-1-one **(9b):** beige solid (100 mg, 56%), mp 185-187°C;

^{1}H NMR (500 MHz, DMSO) δ 16.74 (s, 1H), 12.46 (s, 1H), 8.28 (d, J = 3.2 Hz, 1H), 8.09 – 8.05 (m, 2H), 7.63 – 7.58 (m, 1H), 7.57 – 7.53 (m, 2H), 7.52 – 7.45 (m, 5H), 7.06 (s, 1H).

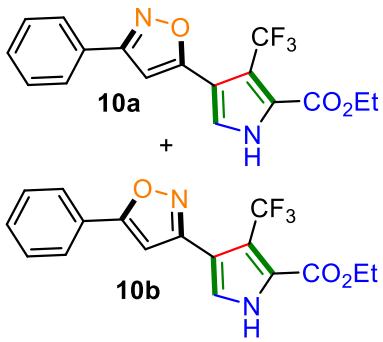
^{19}F NMR (376 MHz, DMSO) δ 111.28.

^{13}C NMR (126 MHz, DMSO) δ 186.3, 177.5, 136.1 (q, J = 4.2 Hz),134.1, 132.1, 130.9, 129.4 (2C), 128.8, 128.7 (2C), 128.2 (2C), 127.3, 126.6 (2C), 123.6 (d, J = 267.4 Hz), 121.0, 107.1 (q, J = 35.6 Hz), 94.4.

HRMS (ESI): m/z calcd for $C_{20}H_{15}F_3NO_2$ $[M + H]^+$, 358.1055; found 358.1047.

General procedure for the synthesis of isoxazoles **10a-b.**

10 mL reaction tube equipped with magnetic stirrer was charged diketone **5a** (0.5 mmol), 5 mL ethanol and NH_2OH*HCl (0.75 mmol, 1.5 equiv.) were added and reaction mixture was stirred at relux until isoxazoles formation was complete (8h). Then mixture was evaporated to dryness to yield a crude reaction product, washed with water and purified by silica gel column chromatography eluted with EtOAc-Hexane, 1:4 to give the product as beige solid.



***ethyl 4-(3-phenylisoxazol-5-yl)-3-(trifluoromethyl)-1H-pyrrole-2-carboxylate* (10a) (90%) *and ethyl 4-(5-phenylisoxazol-3-yl)-3-(trifluoromethyl)-1H-pyrrole-2-carboxylate* (10b) (10%):** beige solid (105 mg, 60%), mp 159-162 °C.

^{1}H NMR (500 MHz, CDCl3) δ 9.74 (s, 1H), 7.88 – 7.80 (m, 2H), 7.52 – 7.42 (m, 4H), 6.72 (q, J = 1.5 Hz, 1H), 4.43 (q, J = 7.1 Hz, 2H), 1.41 (t, J = 7.1 Hz, 3H).

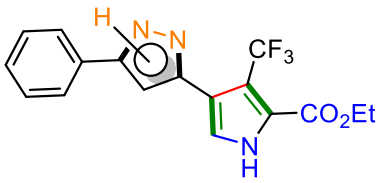
^{19}F NMR (471 MHz, CDCl3) δ 108.29 (d, *J* = 1.4 Hz) (10b), 107.72 (d, *J* = 1.4 Hz) (10a).

^{13}C NMR (126 MHz, CDCl3) δ 163.9, 163.1, 159.6, 159.5, 132.6, 130.4, 130.2, 129.1, 129.1, 129.1, 128.8, 127.5, 127.2, 127.0, 126.0, 123.4 (q, J = 3.4 Hz), 122.5 (q, J = 268.7 Hz), 122.6, 122.3, 114.7 (q, J = 38.5 Hz), 113.4 (q, J = 2.5 Hz), 101.00 (q, J = 4.0 Hz), 100.80 (q, J = 4.4 Hz), 62.2, 62.0, 14.1, 14.1.

HRMS (ESI): m/z calcd for $C_{17}H_{14}F_3N_2O_3$ $[M + H]^+$, 351.0951; found 351.0954.

General procedure for the synthesis of pyrazoles **11a, 12a-b.**

10 mL reaction tube equipped with magnetic stirrer was charged diketone **5a** (0.5 mmol), 5 mL ethanol and sodium acetate (0.75 mmol, 1.5 equiv.) and $PhNHNH_2$*HCl or NH_2NH_2*2HCl, were added and reaction mixture was stirred at reflux until isoxazoles (pyrazoles) formation was complete (8h). Then mixture was evaporated to dryness to yield a crude reaction product, washed with water and purified by silica gel column chromatography eluted with EtOAc-Hexane, 1:4 to give the product as beige solid.



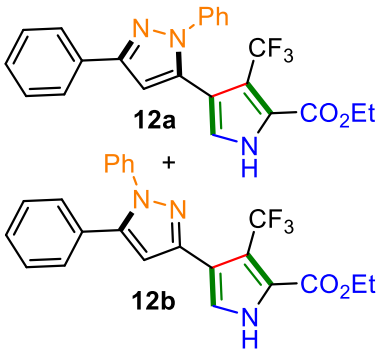
***ethyl 4-(3-phenyl-1H-pyrazol-5-yl)-3-(trifluoromethyl)-1H-pyrrole-2-carboxylate* (11a):** beige solid (126 mg, 72%), mp 227-230 °C.

^{1}H NMR (500 MHz, DMSO) δ 13.06 (br. s, 1H), 12.85 (br. s, 1H), 7.81 (d, *J* = 7.6 Hz, 2H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.33 (d, *J* = 6.1 Hz, 2H), 6.73 (s, 1H), 4.33 (q, *J* = 7.1 Hz, 2H), 1.32 (t, *J* = 7.1 Hz, 3H).

^{19}F NMR (471 MHz, $CDCl_3$) δ 110.42.

^{13}C NMR (126 MHz, $CDCl_3$) δ 158.7, 150.3, 142.8, 135.6, 133.3, 128.7, 127.5, 125.0, 123.0 (q, J = 268.7 Hz), 122.8, 121.6, 113.7 (q, J = 36.2 Hz), 102.5, 60.7, 13.9.

HRMS (ESI): m/z calcd for $C_{17}H_{15}F_3N_3O_2$ $[M + H]^+$, 350.1111; found 350.1115.



***ethyl 4-(1,3-diphenyl-1H-pyrazol-5-yl)-3-(trifluoromethyl)-1H-pyrrole-2-carboxylate* (12a) (74%) *and ethyl 4-(1,5-diphenyl-1H-pyrazol-3-yl)-3-(trifluoromethyl)-1H-pyrrole-2-carboxylate* (12b) (26%):** beige solid (110 mg, 52%), mp 125-128 °C.

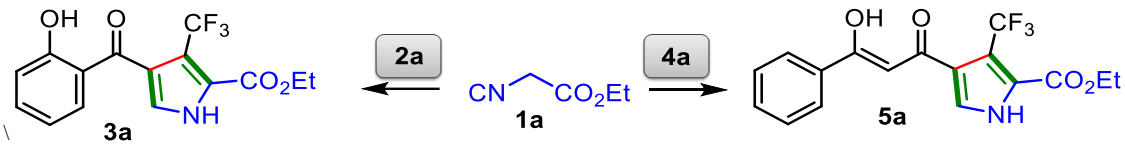
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.72 (br s, 1H), 7.95 – 7.87 (m, 2H), 7.49 – 7.38 (m, 3H), 7.38 – 7.24 (m, 10H), 6.83 (d, *J* = 3.0 Hz, 1H), 6.76 (s, 1H), 6.67 (q, *J* = 1.5 Hz, 1H), 4.40 (d, *J* = 5.5 Hz, 1H), 4.37 (d, *J* = 7.1 Hz, 2H), 1.41 (d, *J* = 7.1 Hz, 1H), 1.36 (t, *J* = 7.2 Hz, 3H).

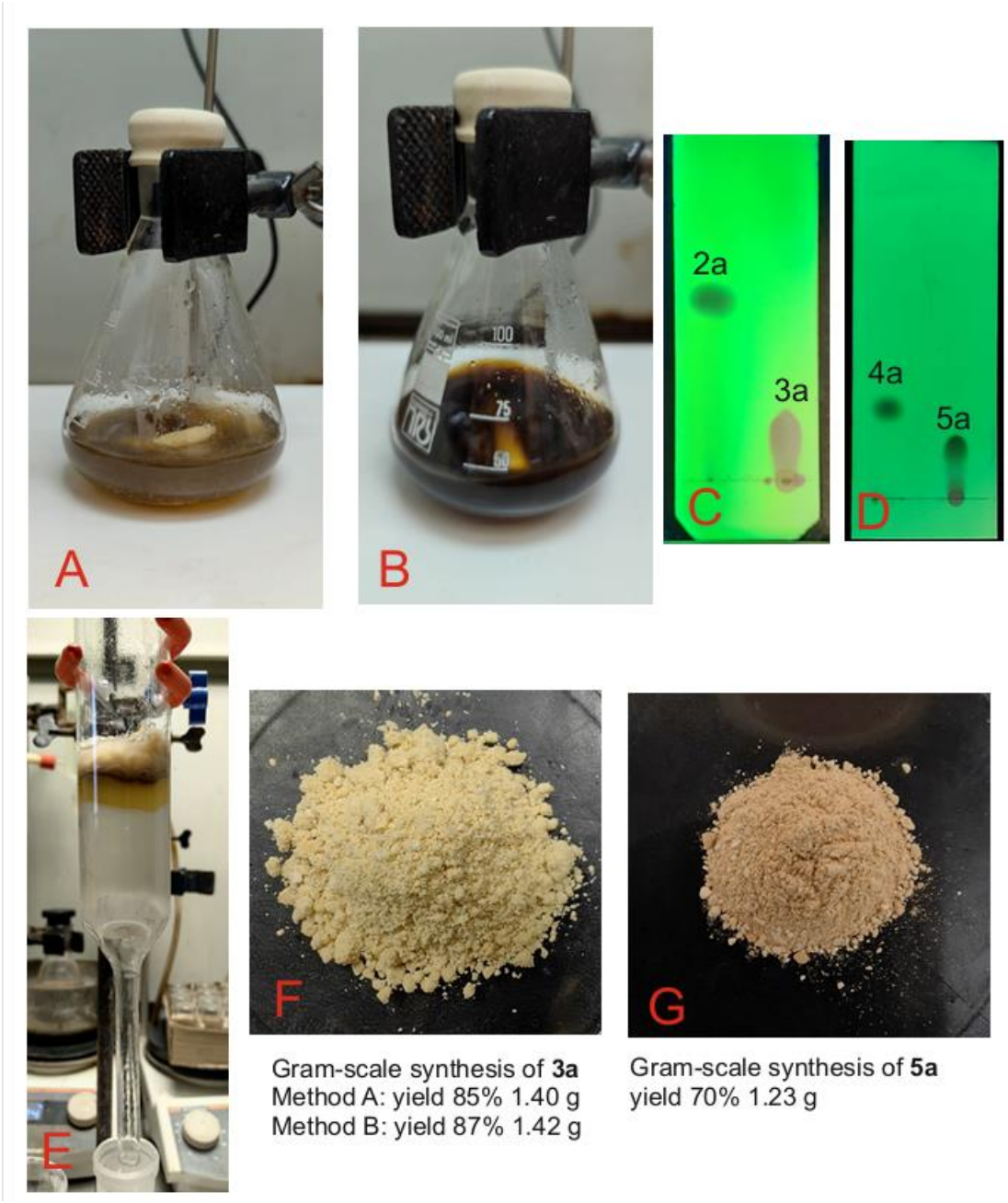
^{19}F NMR (376 MHz, $CDCl_3$) δ 108.47 (d, J = 1.5 Hz), 106.78.

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.9, 159.6, 151.7, 145.5, 143.8, 140.0, 135.9, 133.1, 130.4, 129.0, 128.9, 128.9, 128.8, 128.6, 128.4, 128.1, 127.6, 127.4, 125.9, 125.4, 124.8, 123.0 (q, J = 269.0 Hz), 122.6, 122.4 (q, J = 3.1 Hz), 122.3 (q, J = 269.3 Hz), 122.1 (q, J = 2.9 Hz), 121.8, 119.2 (1, J = 2.1 Hz), 117.0 (q, J = 36.7 Hz), 115.7 (q, J = 37.5 Hz), 115.2 (q, J = 2.7 Hz), 108.7 (q, J = 2.9 Hz), 107.4, 61.9, 61.7, 14.2, 14.1.

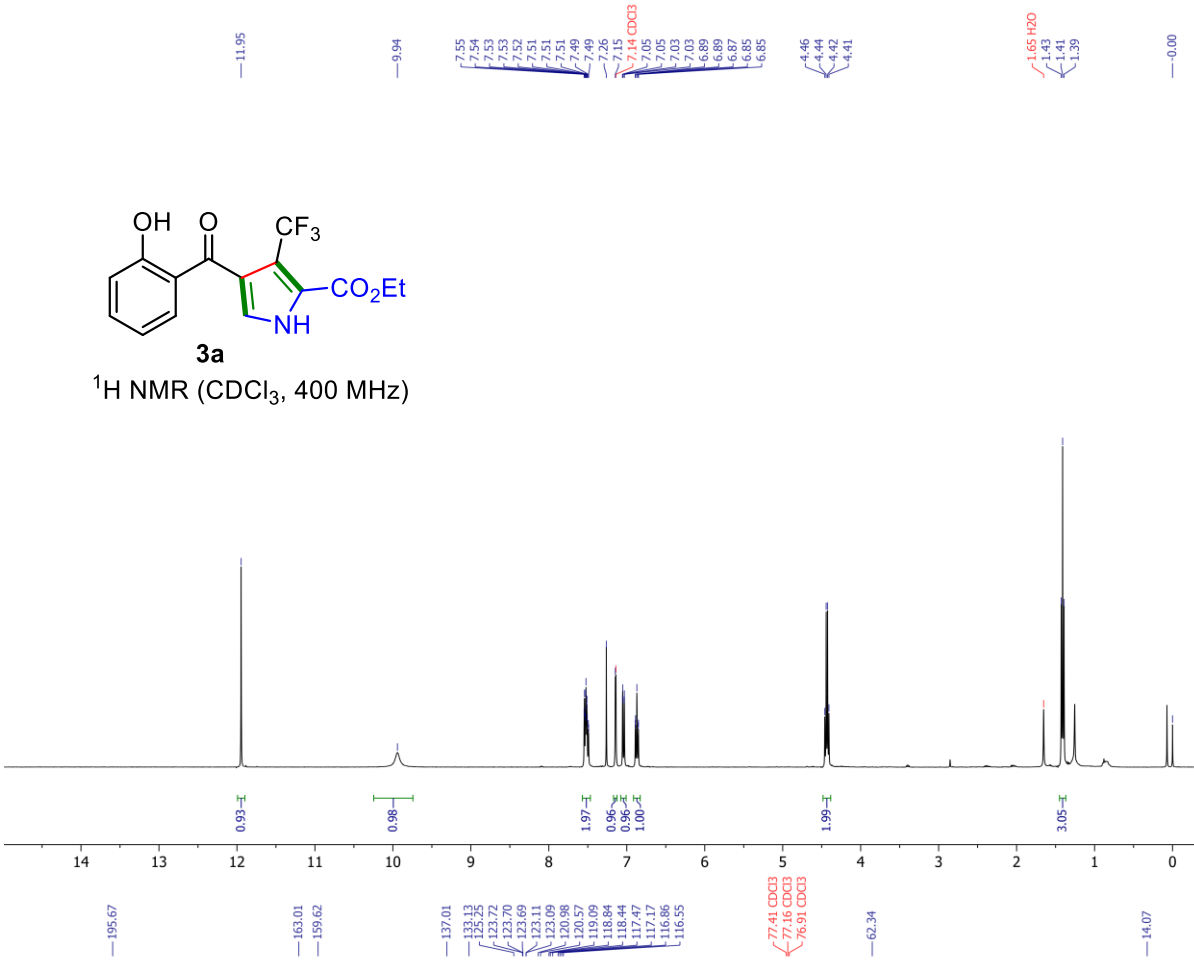
HRMS (ESI): m/z calcd for $C_{23}H_{19}F_3N_3O_2$+ $[M + H]^+$, 426.1424; found 426.1430.

Scheme 1. Gram scale preparation of 3a and 5a



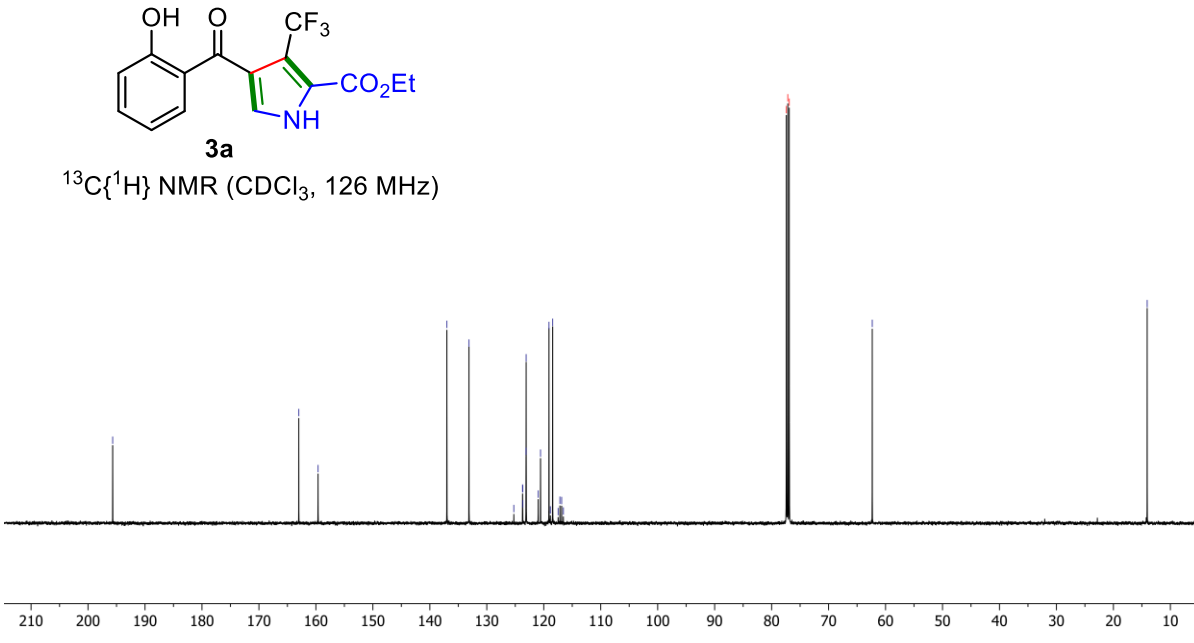


A: reaction mixture before addition of ethyl isocyanoacetate (**1a**) addition; **B**: reaction mixture after addition of isocyanoacetate (**1a**) addition; **C**: TLC analysis of reaction with chromone **2a** in within 6-12 h after ethyl isocyanoacetate (**1a**) addition. **D**: TLC analysis of reaction with pyrone **4a** in within 6-12 h after ethyl isocyanoacetate (**1a**) addition**.** **E**: Column purification of pyrrole **3a**. **F**: Isolated pyrrole **3a. G**: Isolated pyrrole **5a**



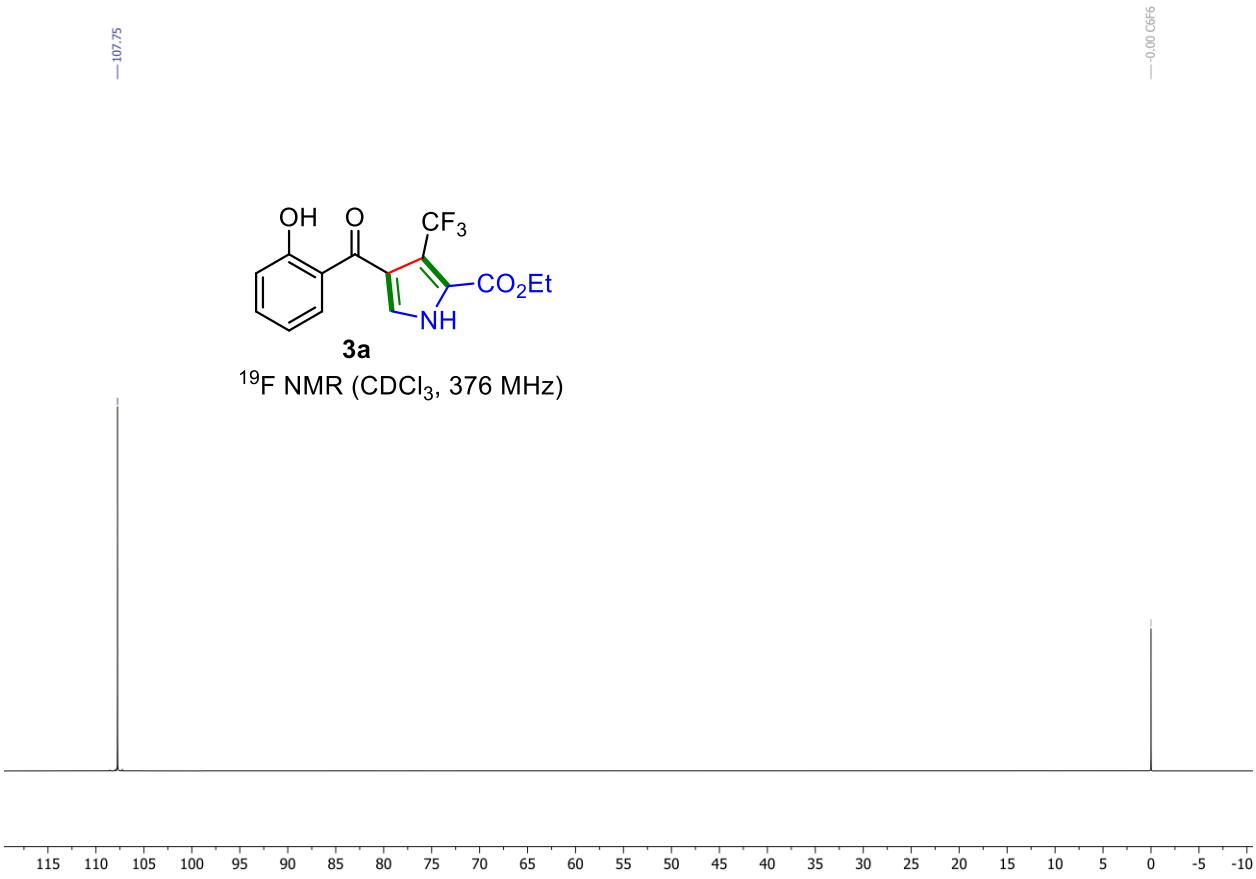
3a

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



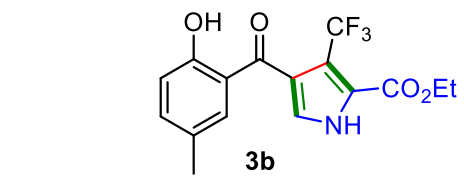
3a

$^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



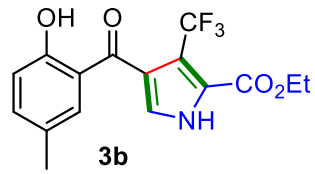
3a

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



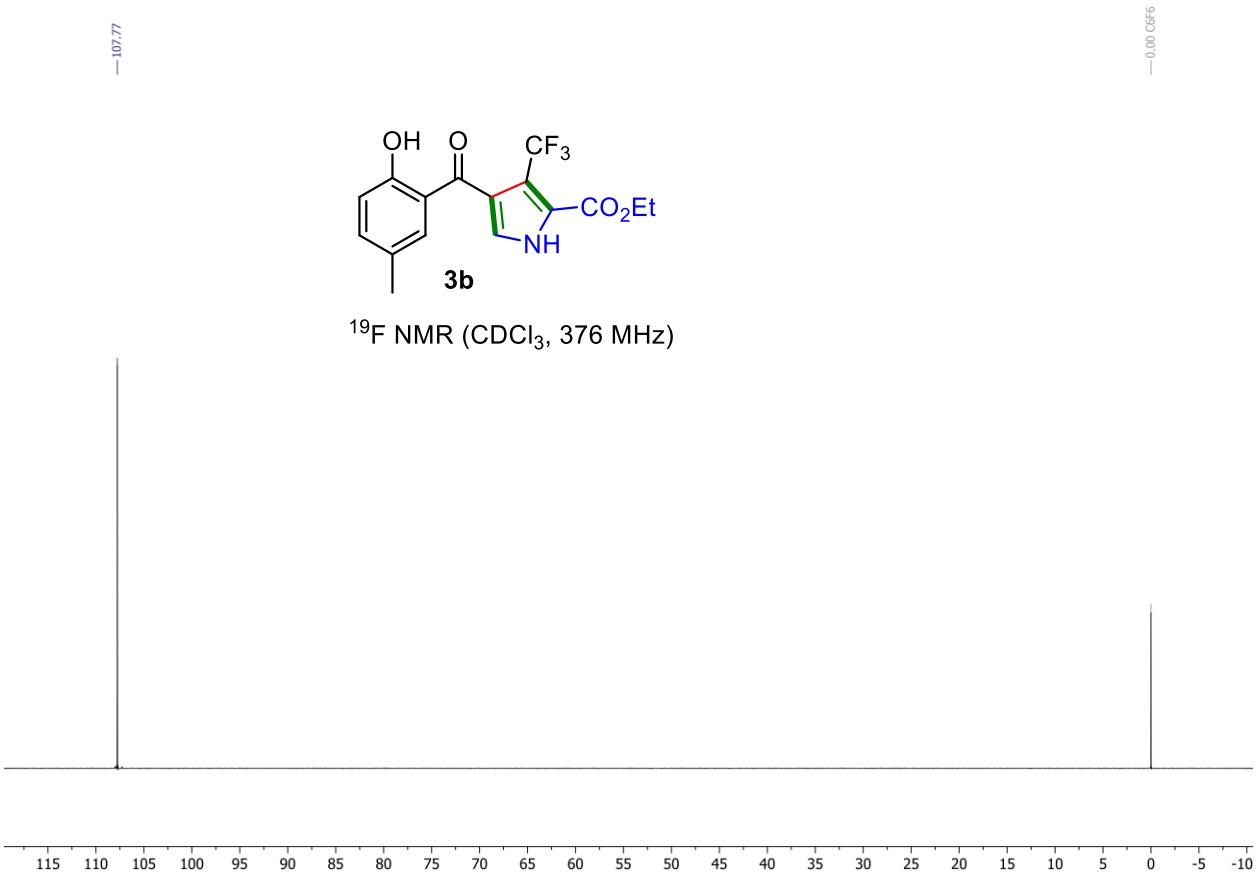
3b

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



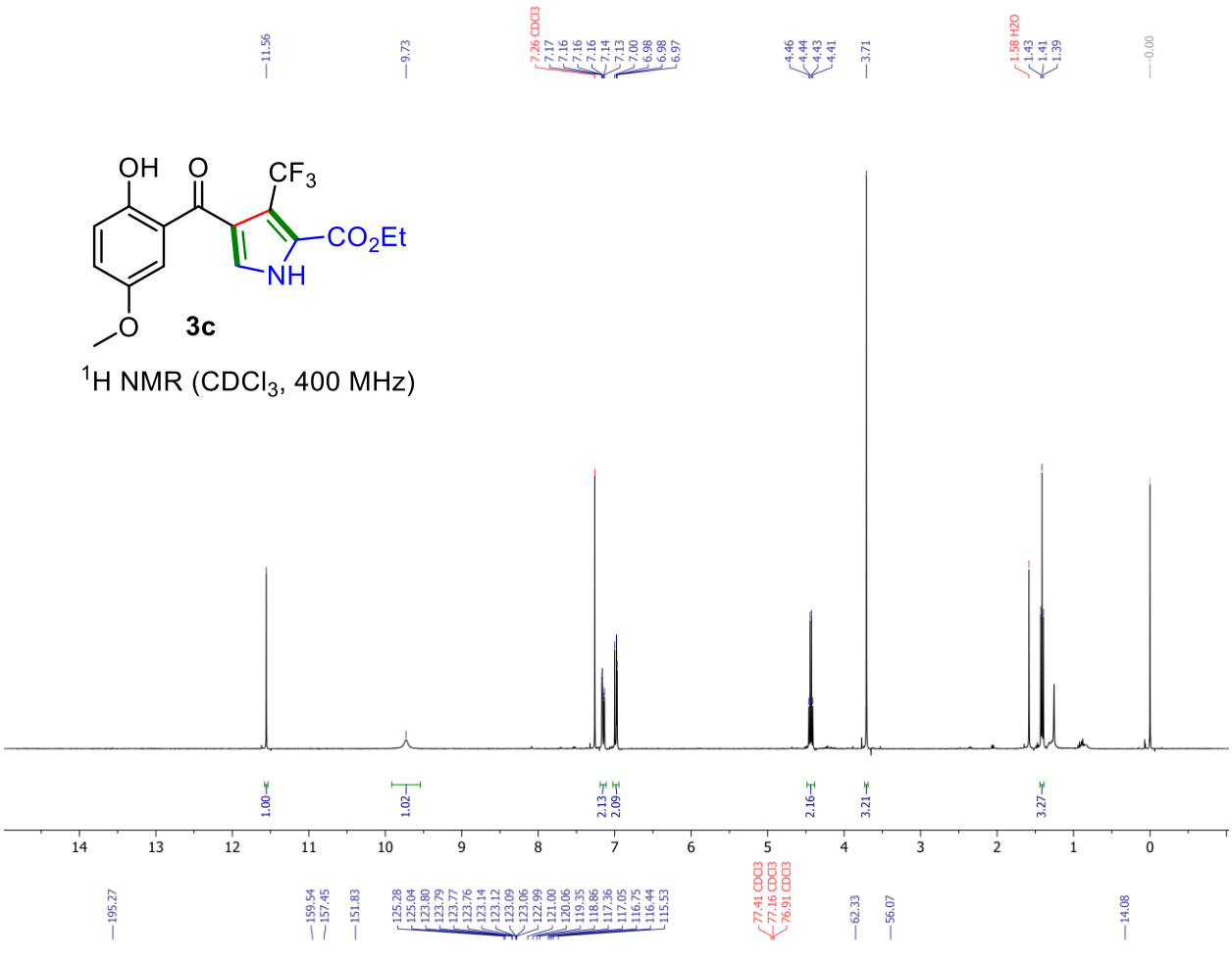
3b

$^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)

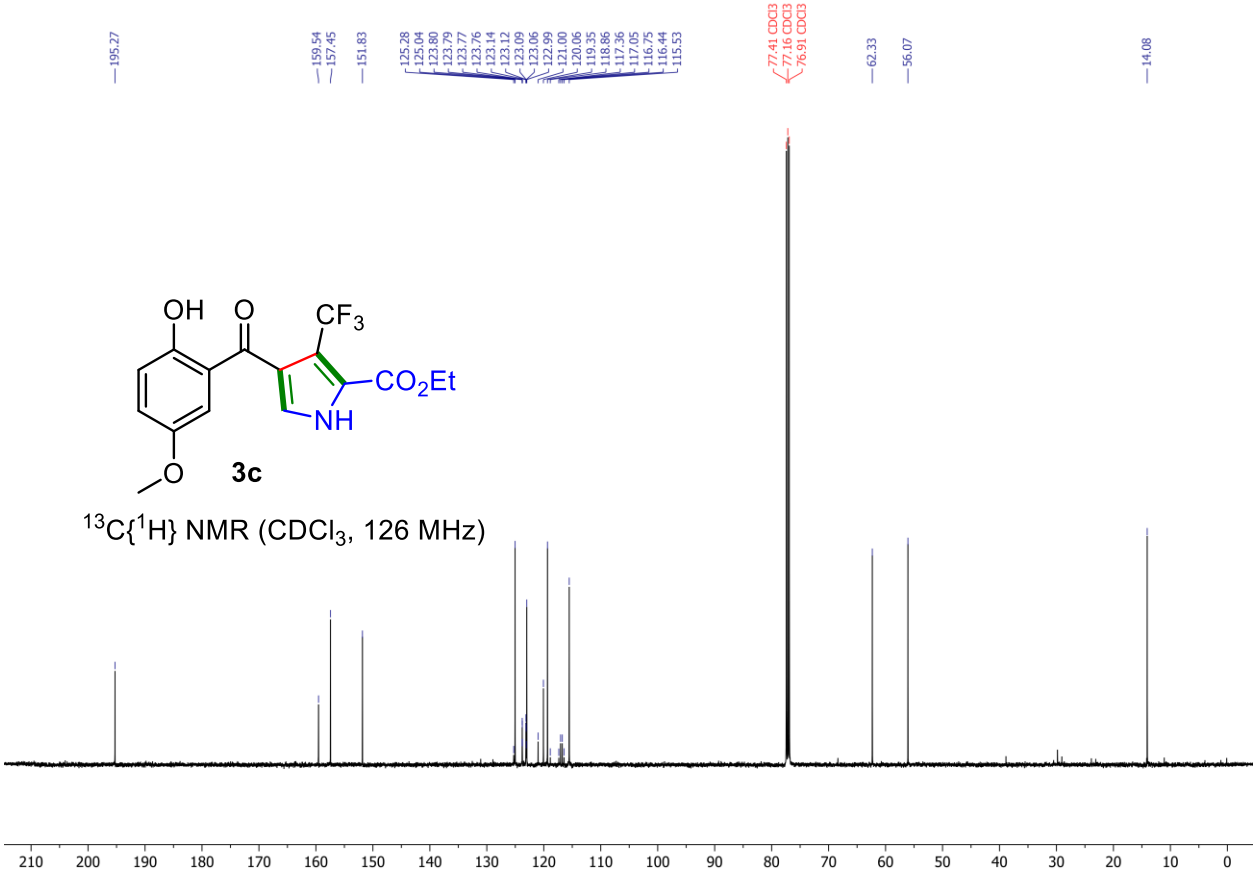


3b

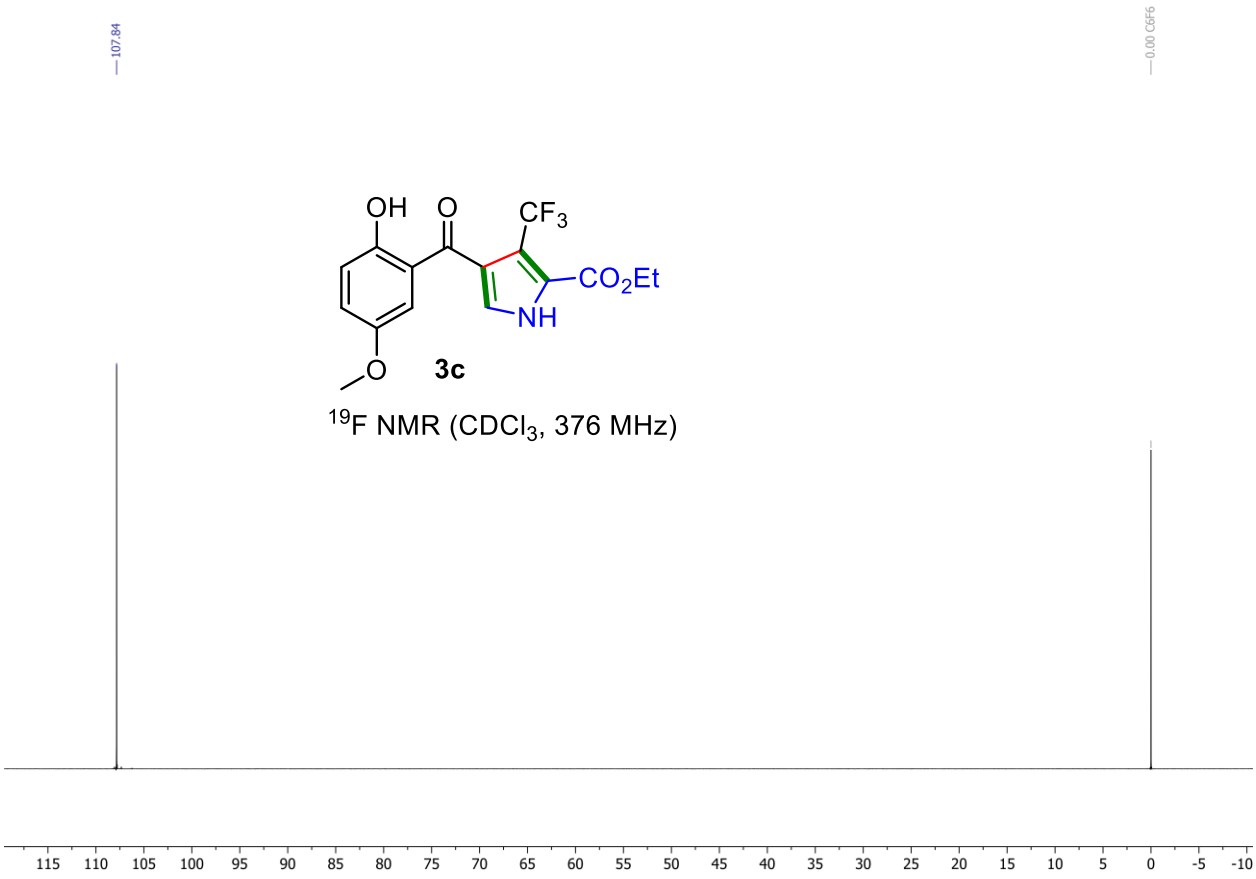
^{19}F NMR ($CDCl_3$, 376 MHz)



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

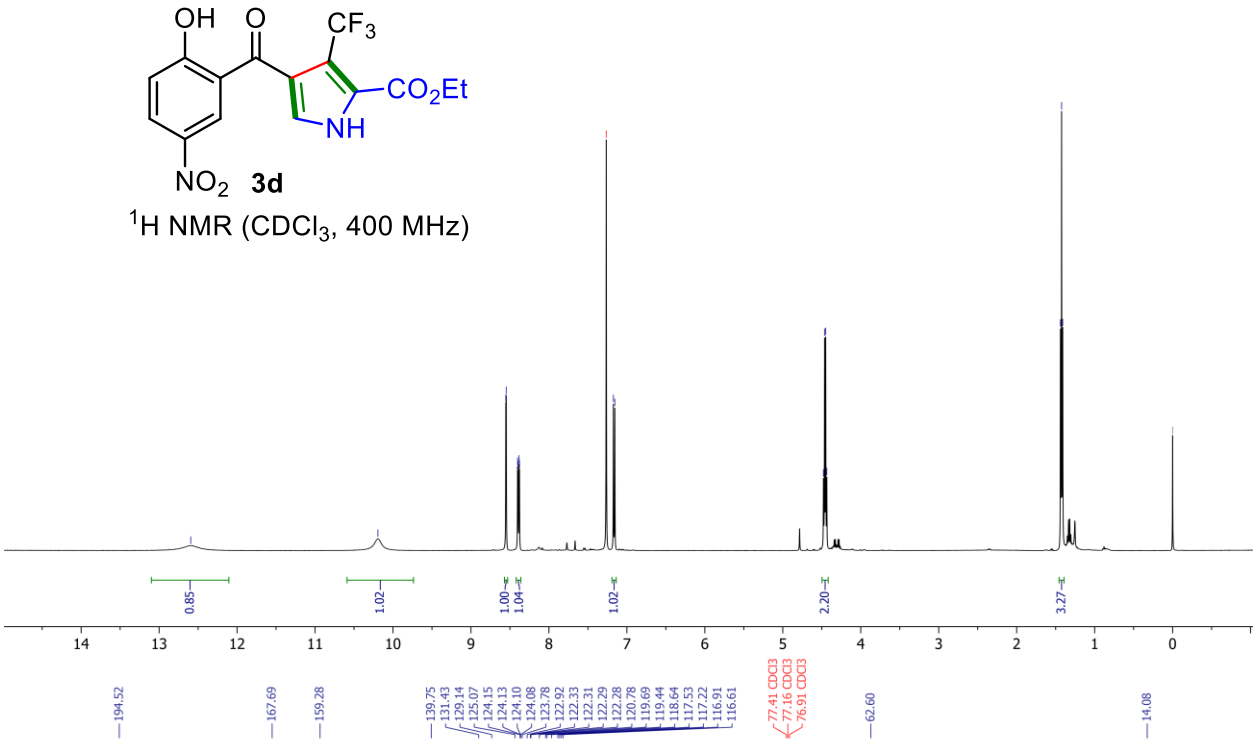


$^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)

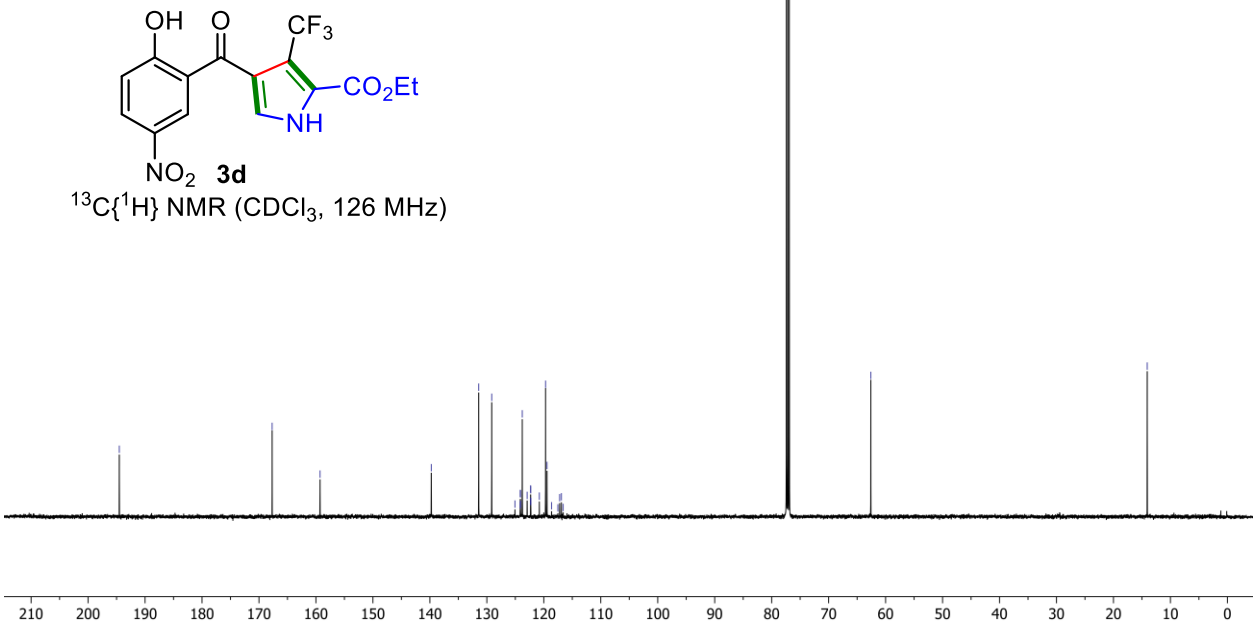


3c

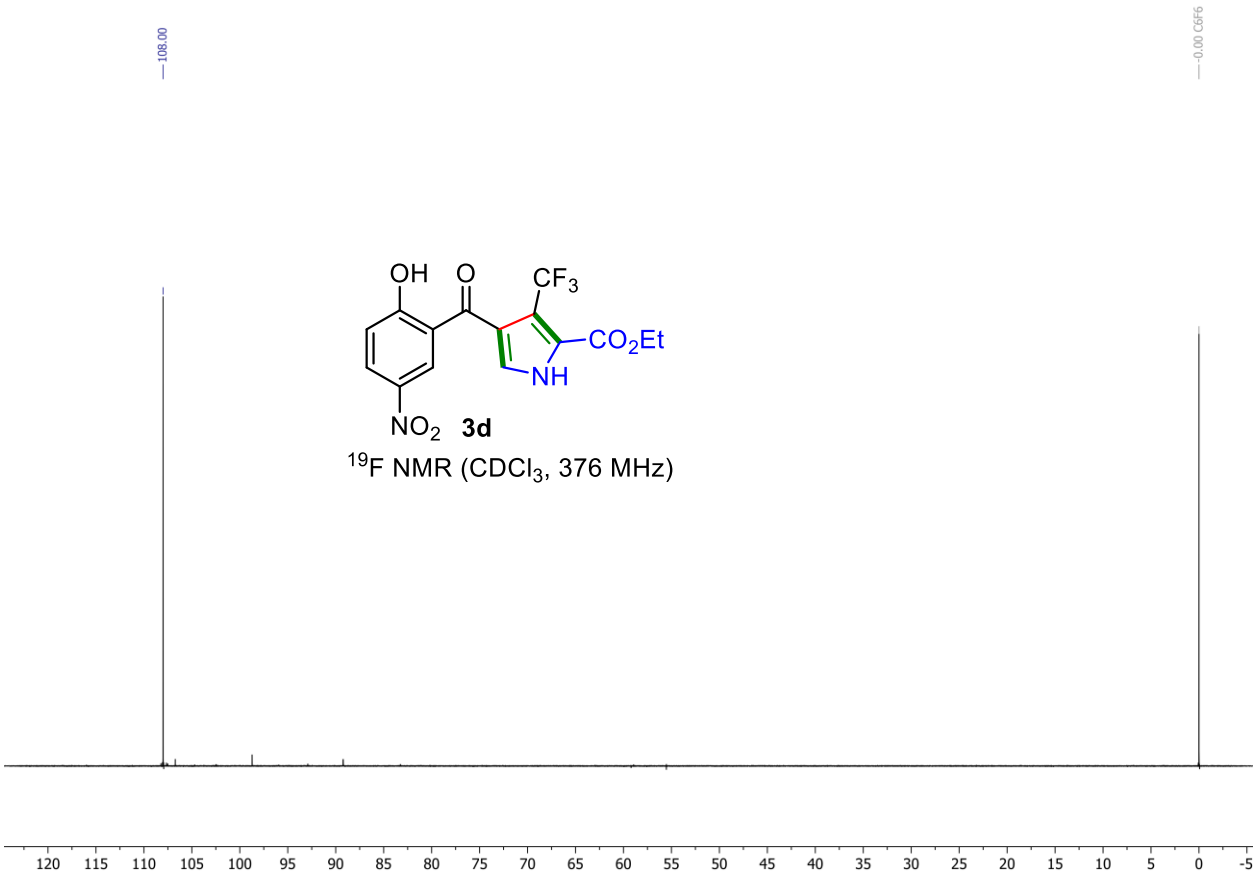
^{19}F NMR ($CDCl_3$, 376 MHz)



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

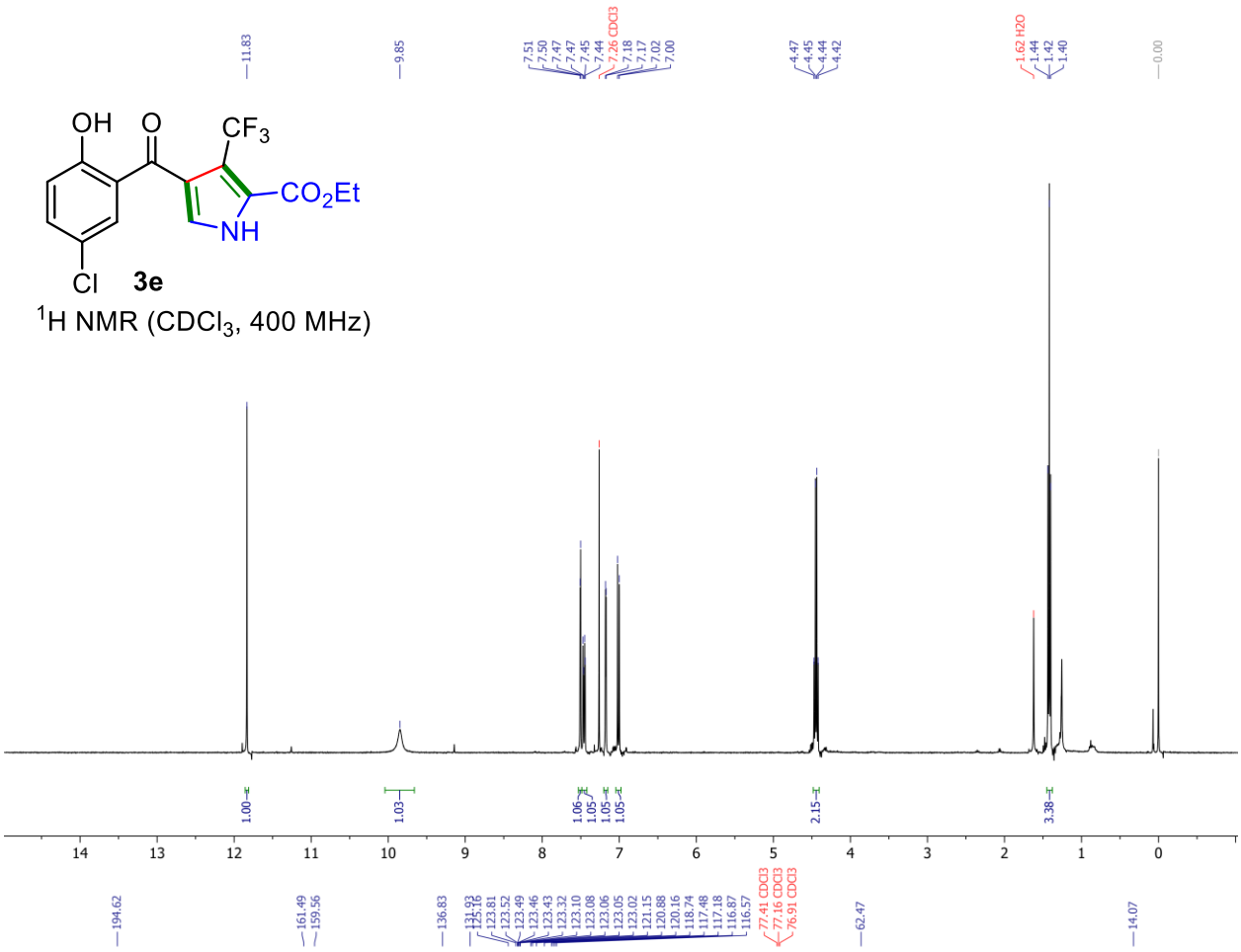


$^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)

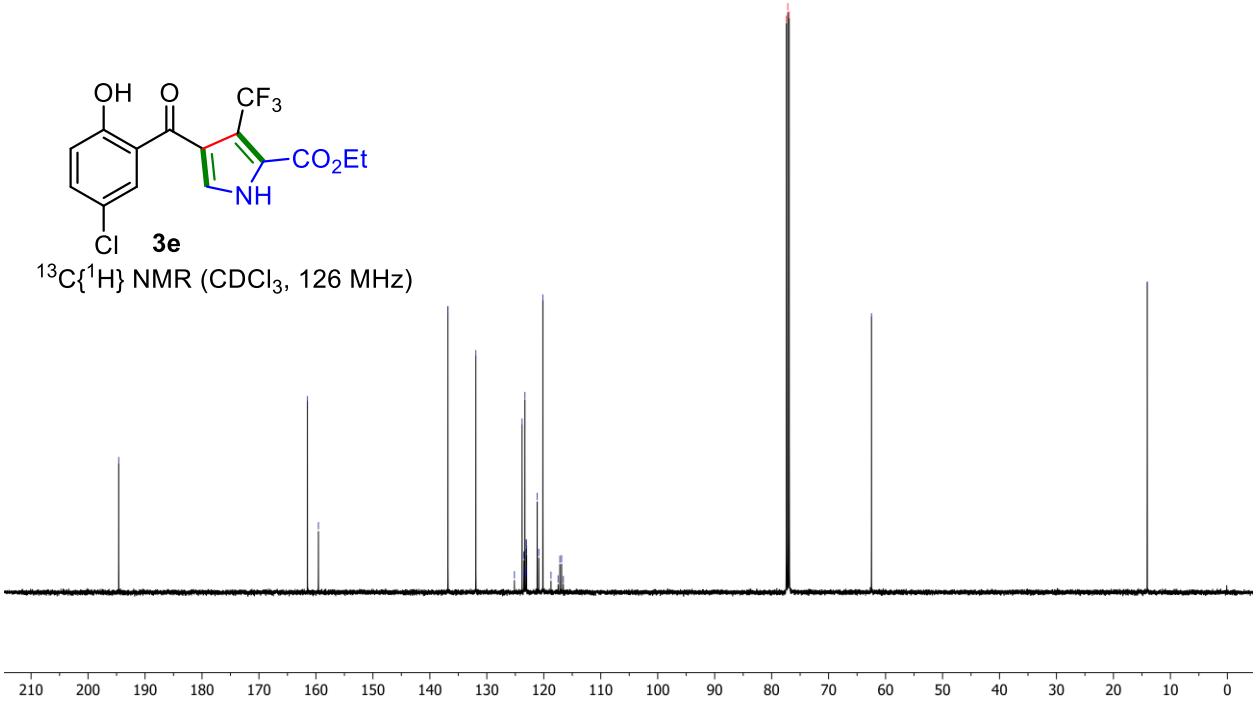


3d

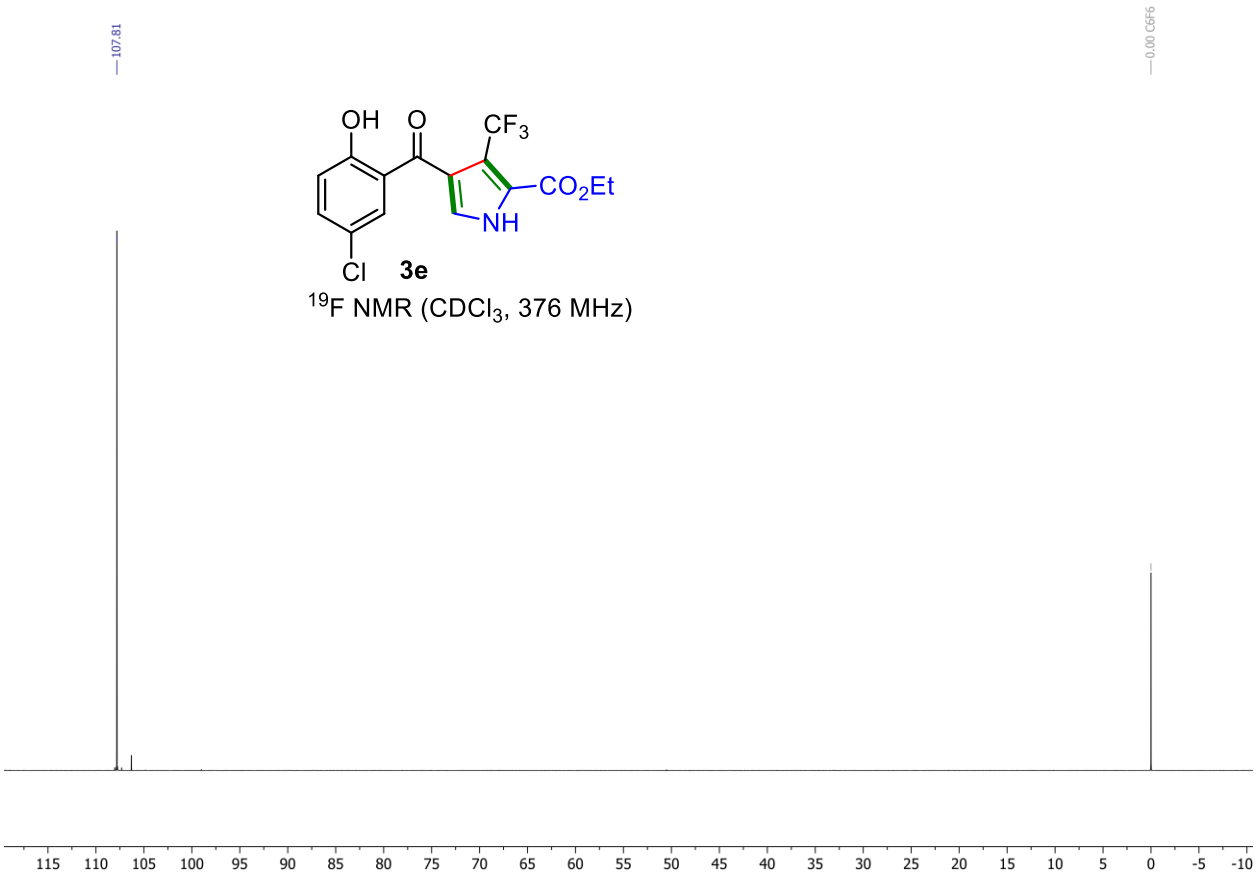
^{19}F NMR ($CDCl_3$, 376 MHz)



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

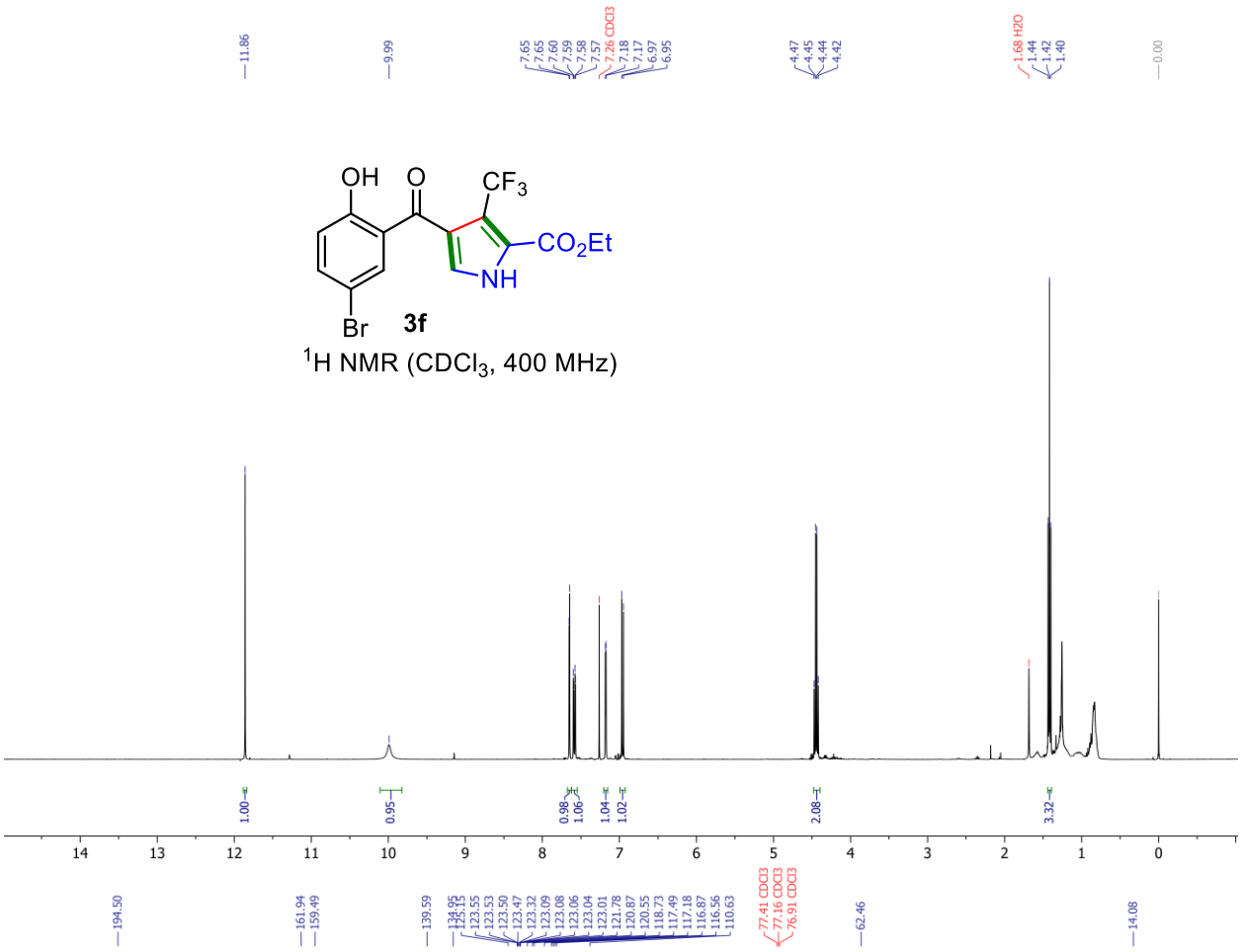


$^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)

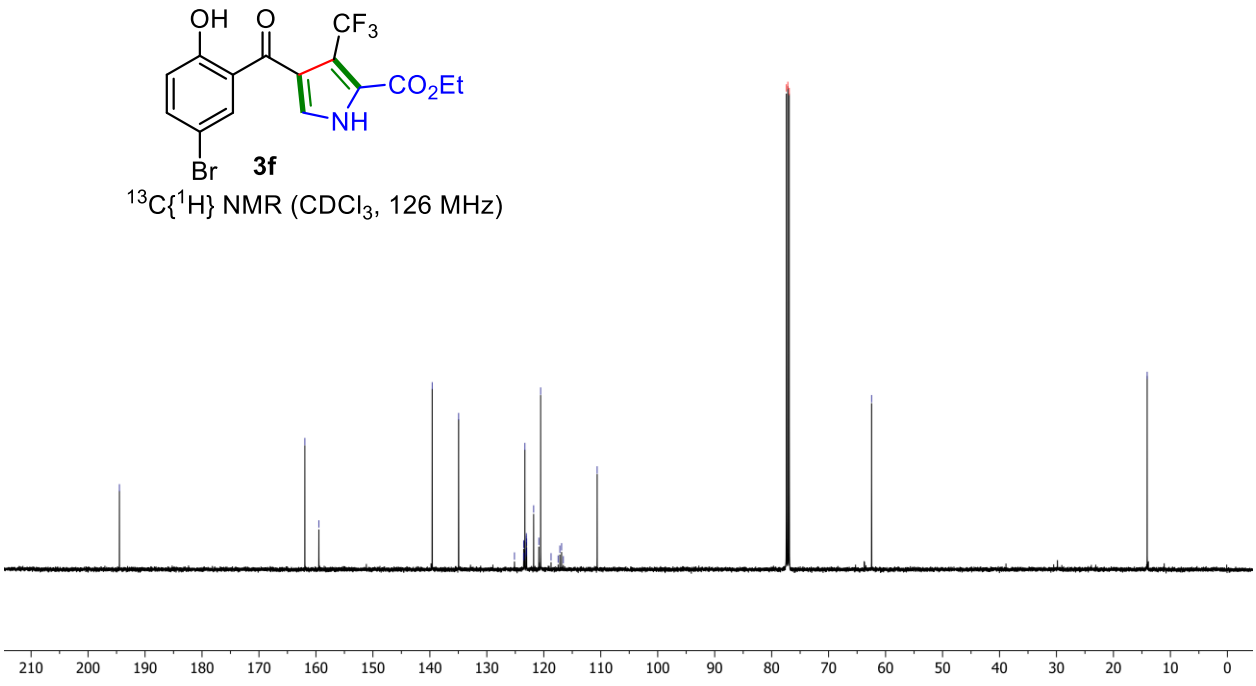


3e

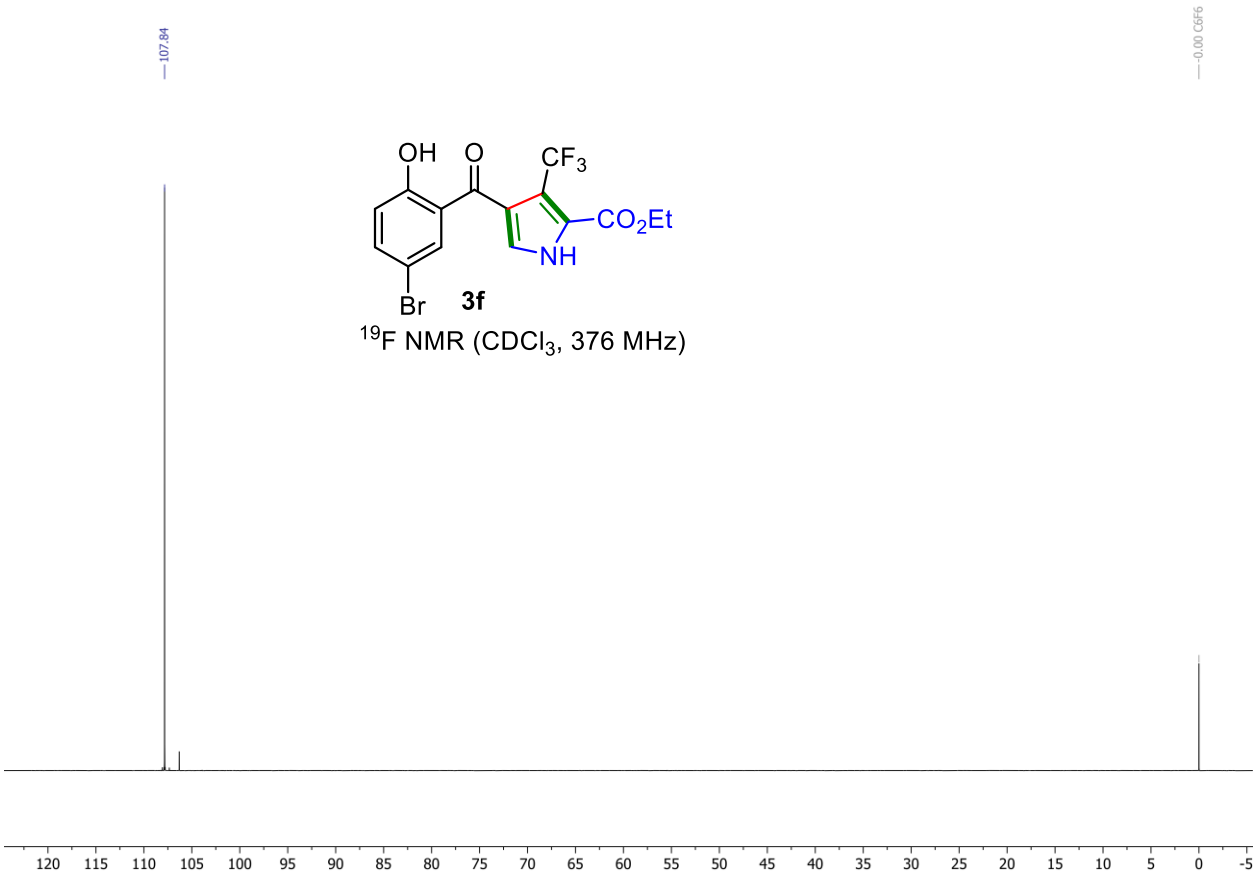
^{19}F NMR ($CDCl_3$, 376 MHz)



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

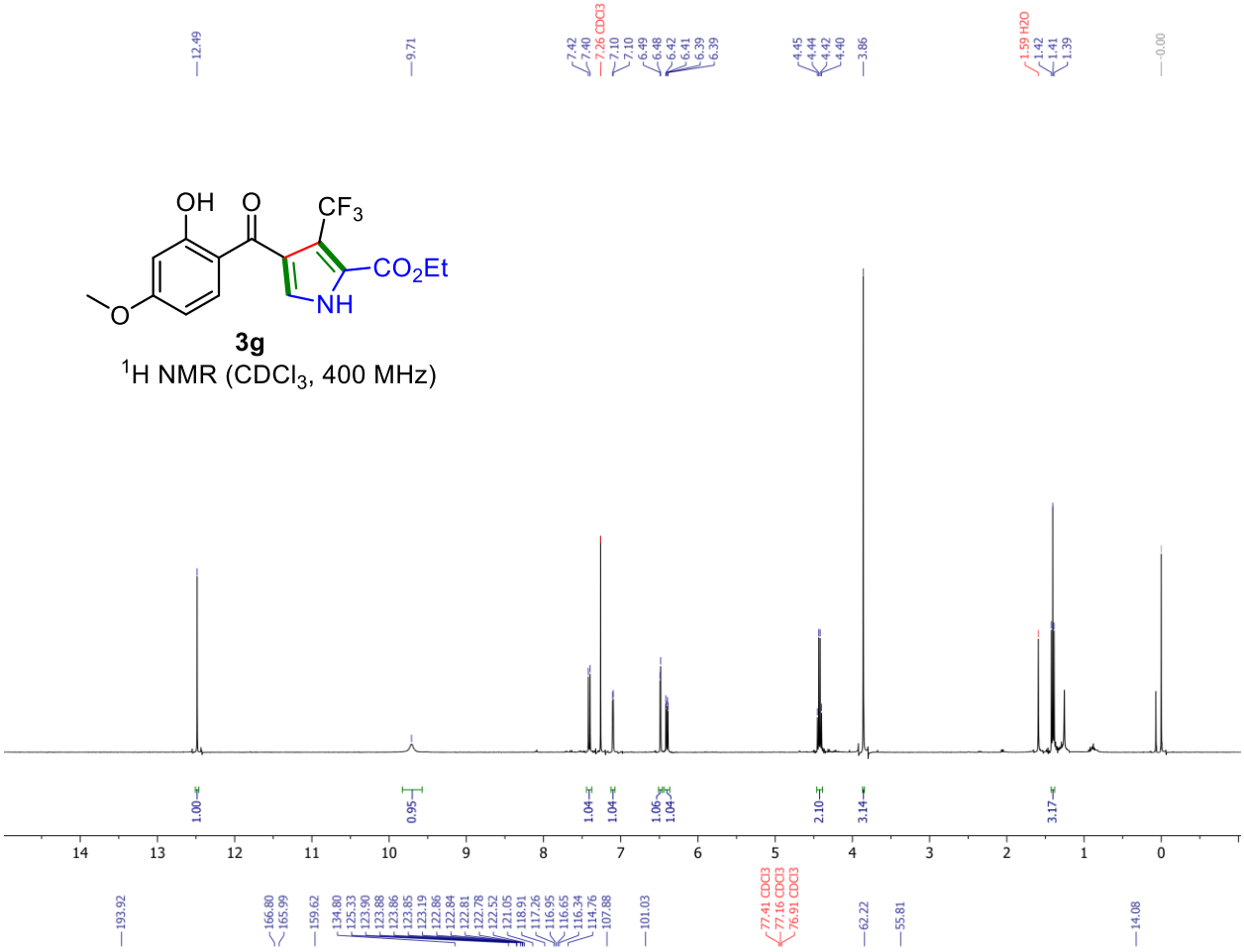


$^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



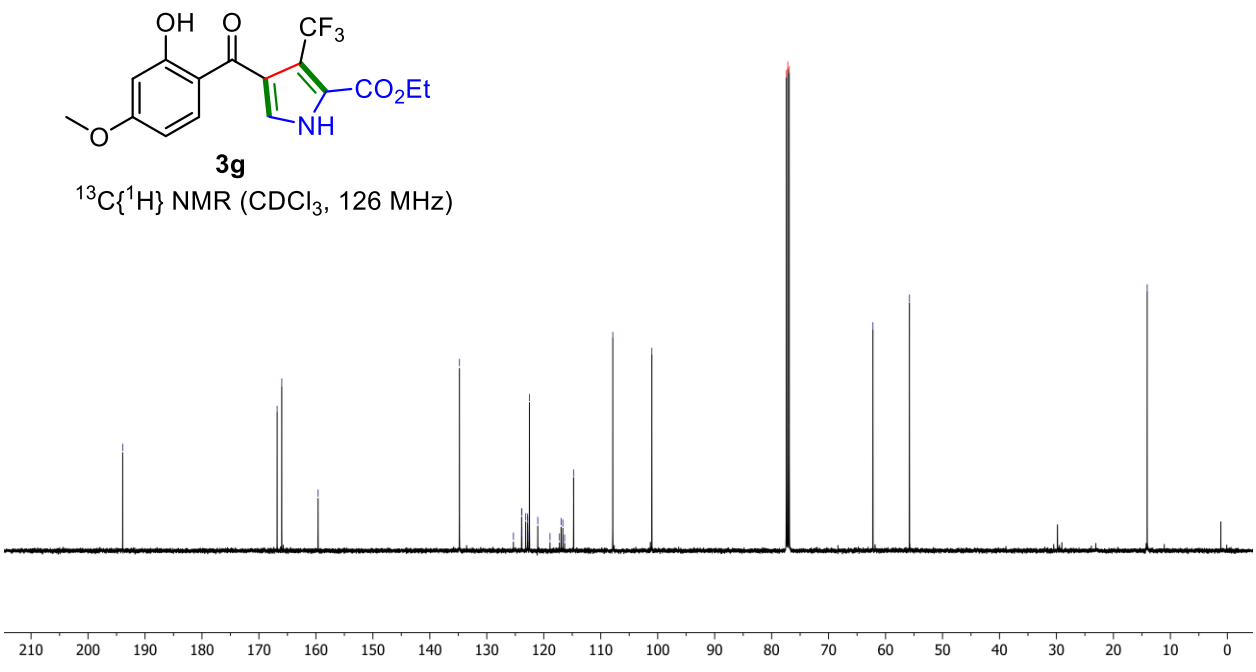
3f

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



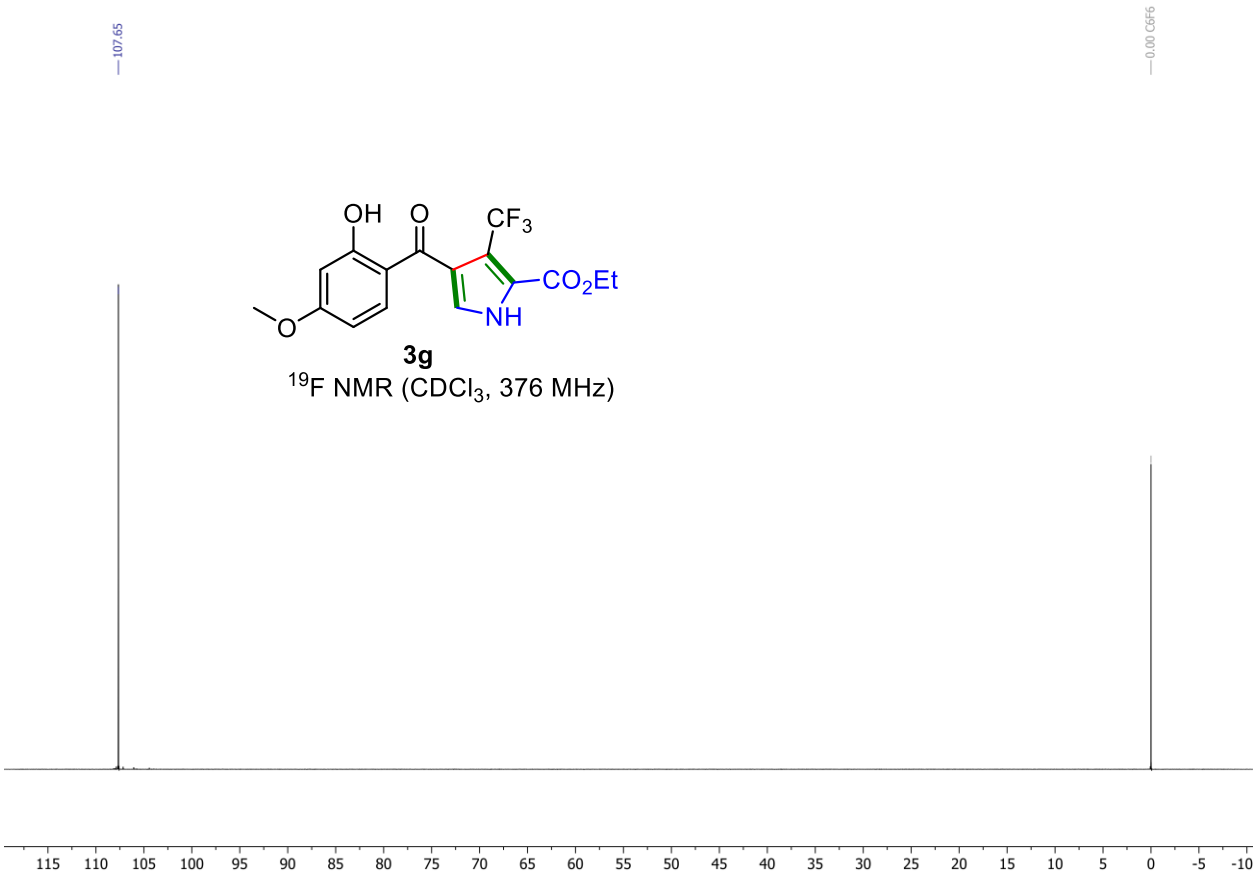
3g

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



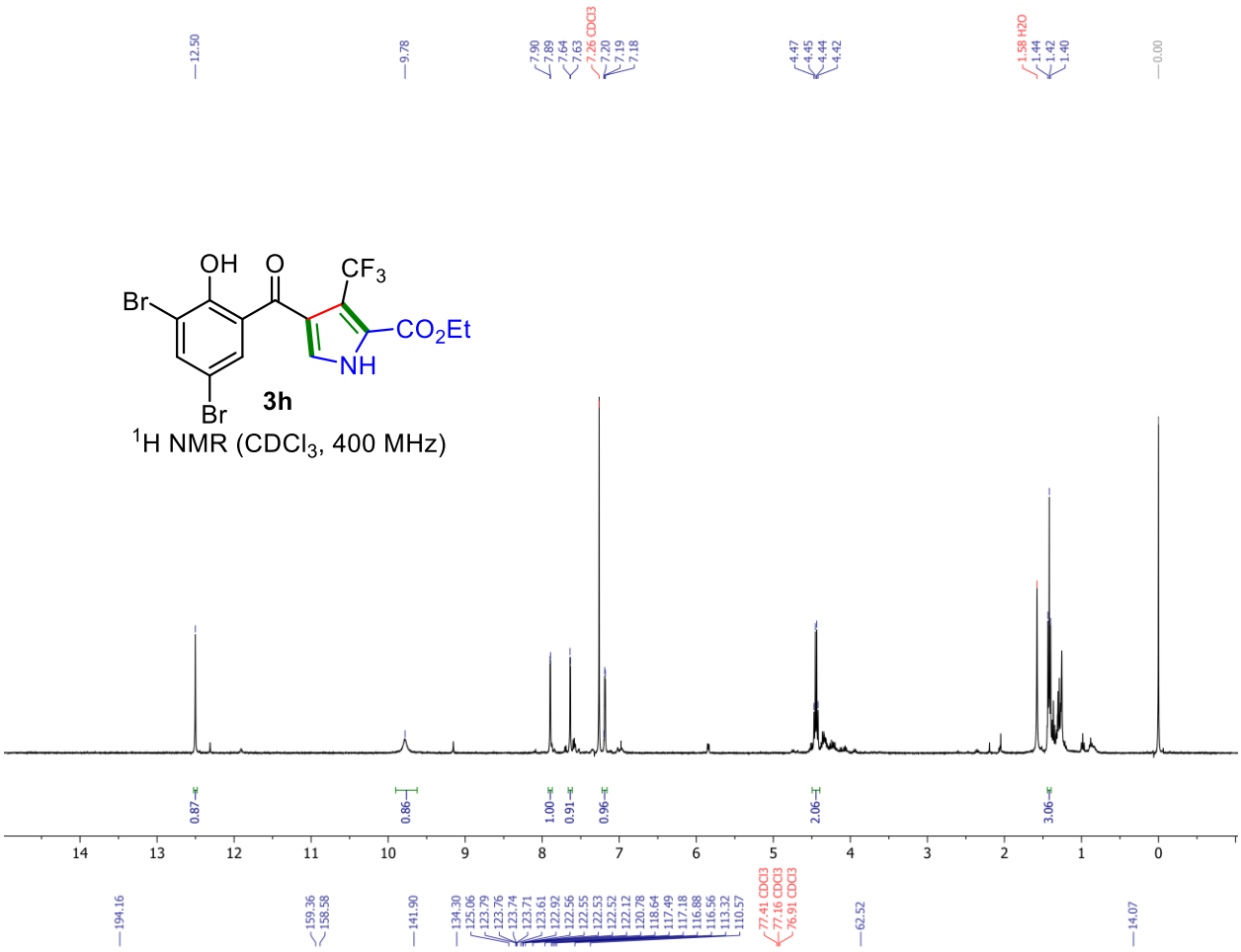
3g

$^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)

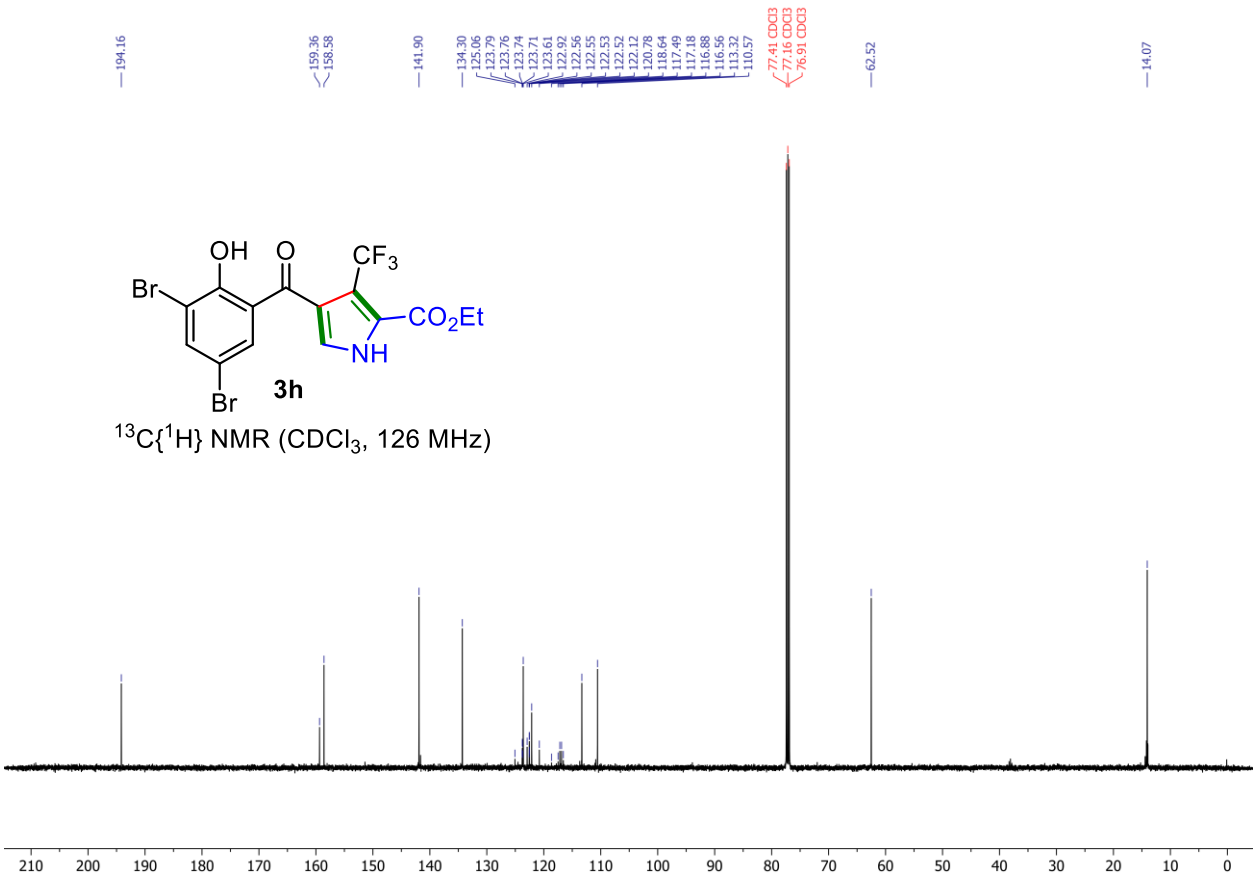


3g

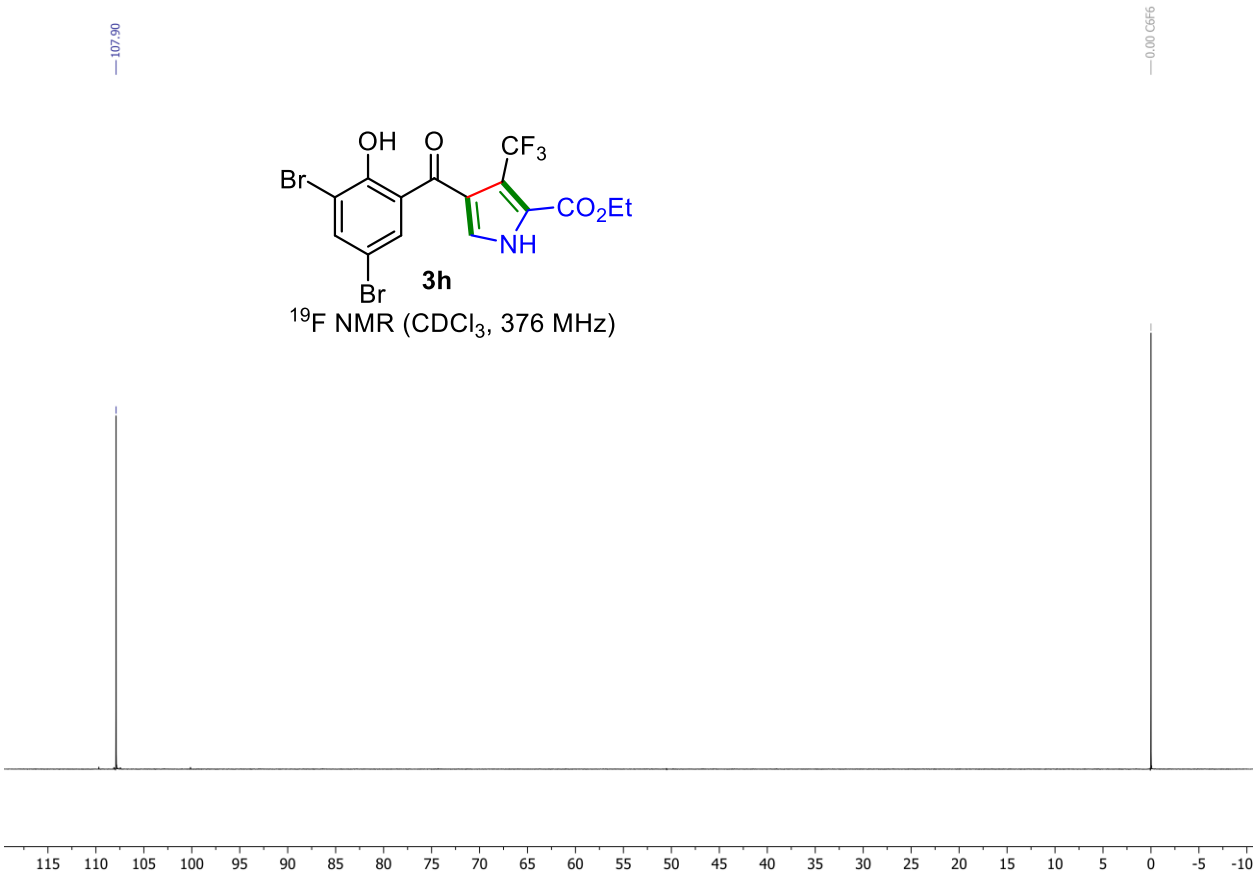
^{19}F NMR ($CDCl_3$, 376 MHz)

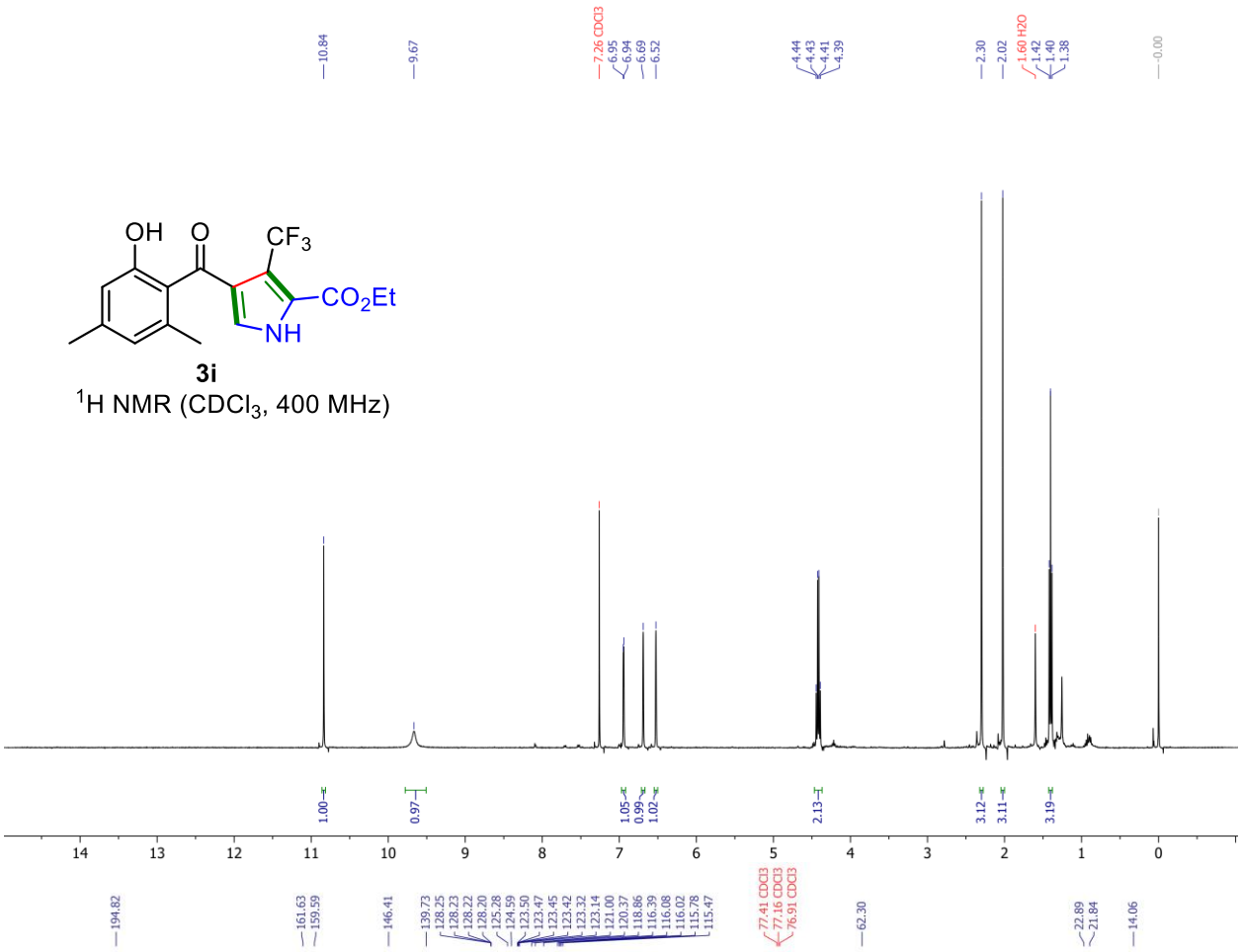


^{1}H NMR ($CDCl_3$, 400 MHz)



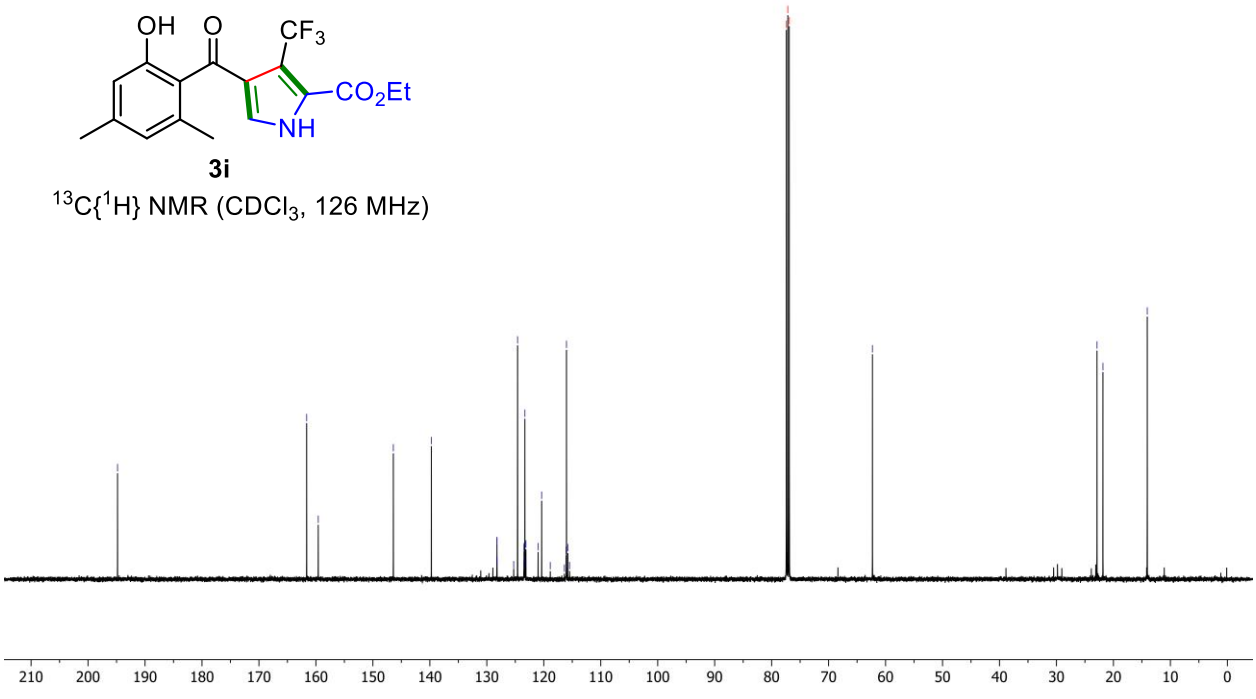
$^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)


107.90
0.00 C6F6
OH
O
CF3
Br
CO2Et
NH
Br
3h
19F NMR (CDCl3, 376 MHz)
115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0 -5 -10



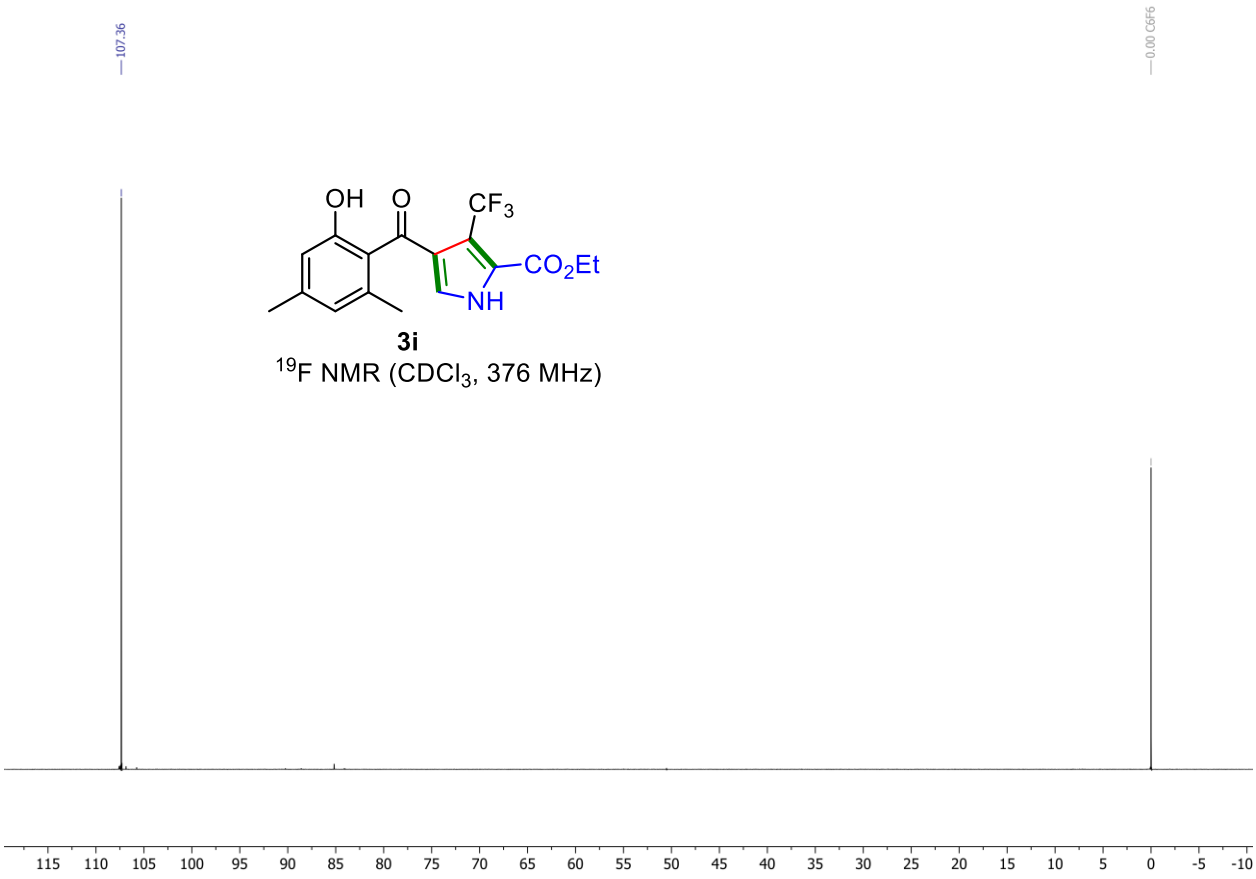
3i

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



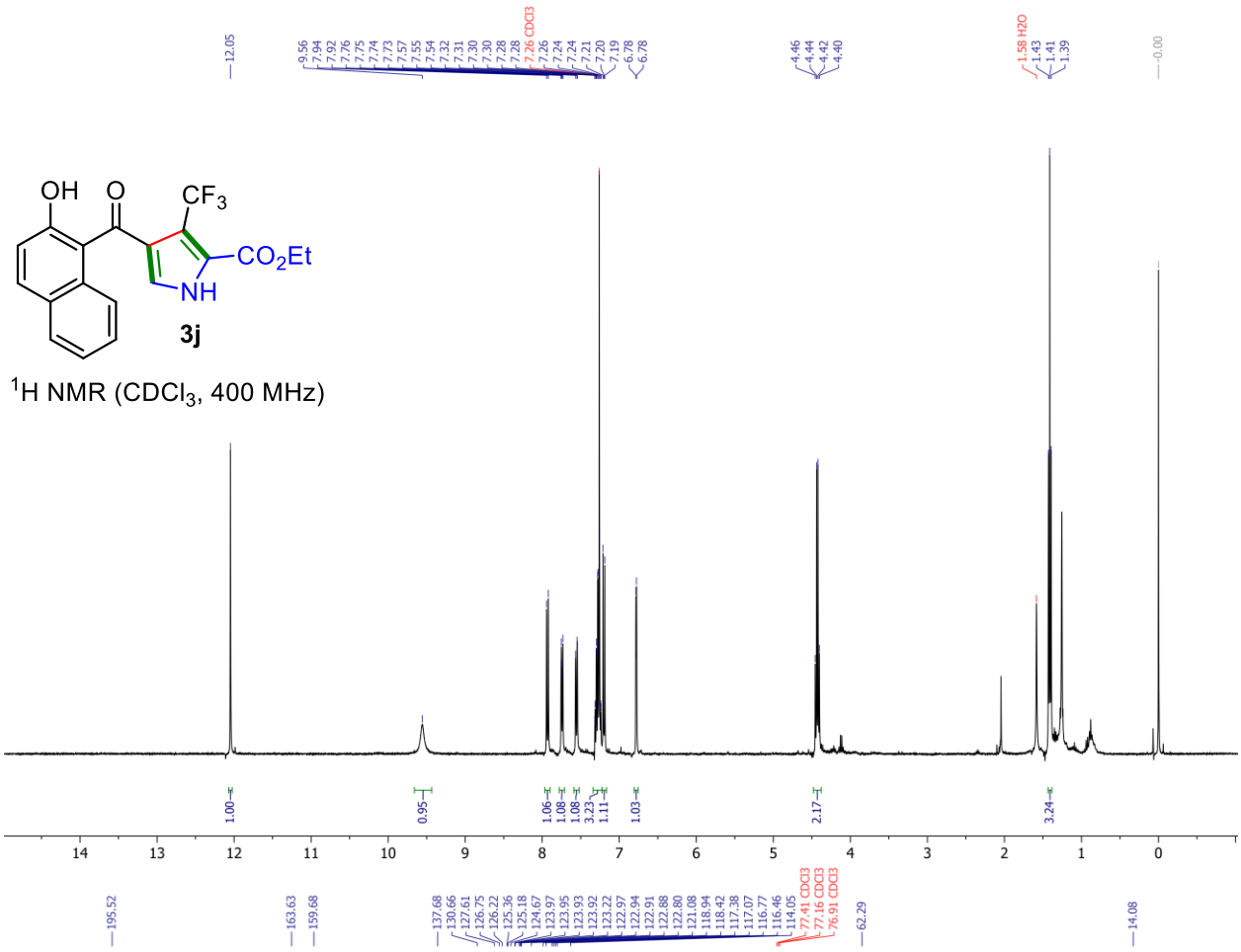
3i

$^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)

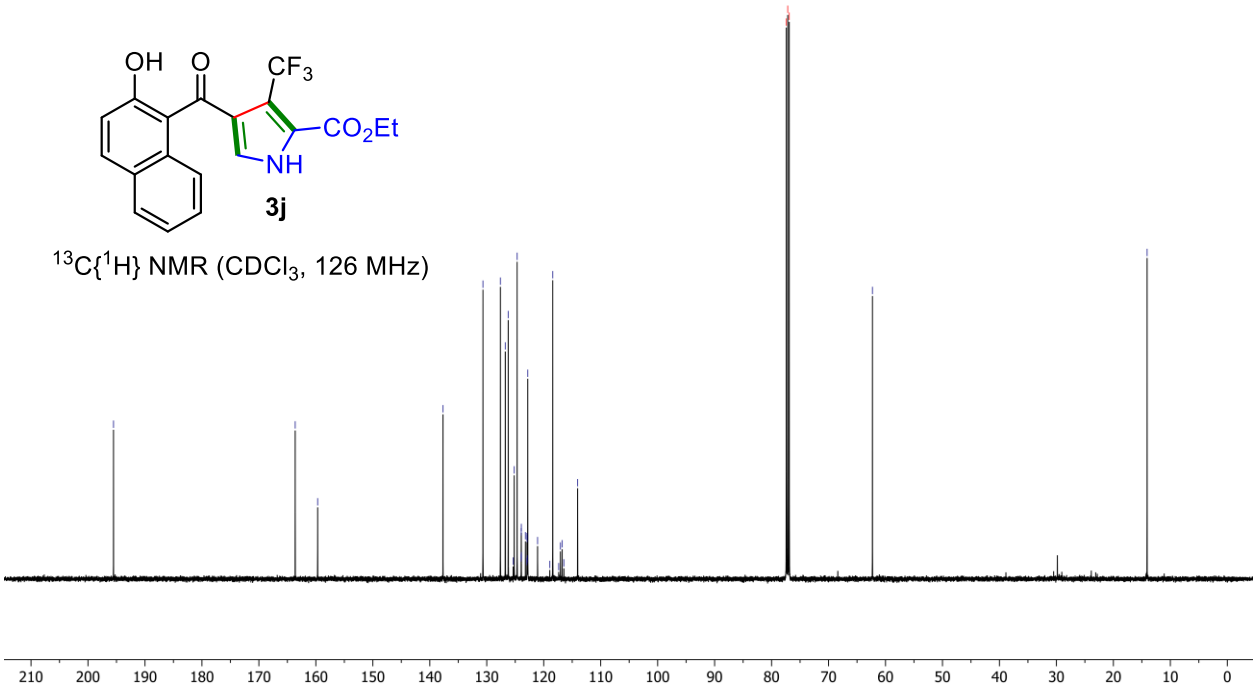


3i

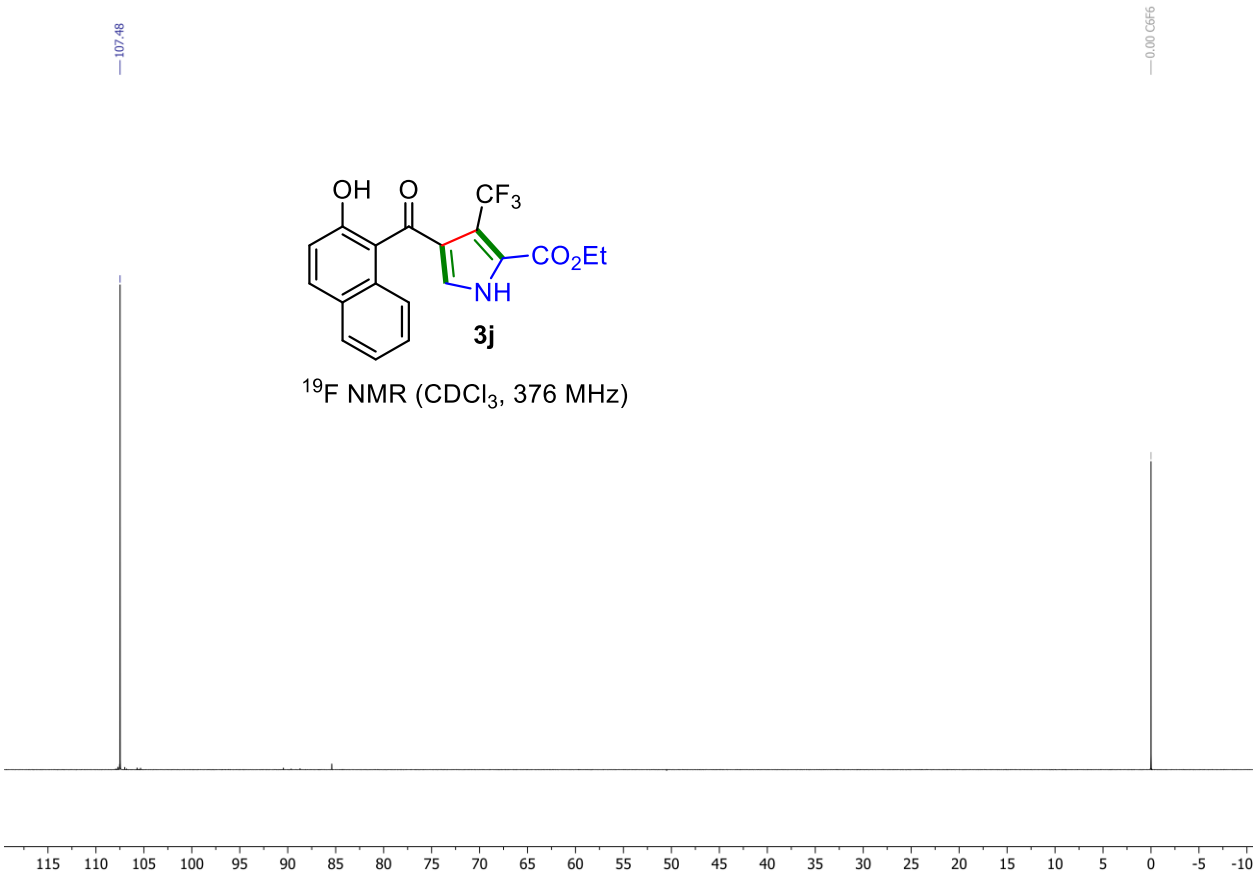
^{19}F NMR ($CDCl_3$, 376 MHz)



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

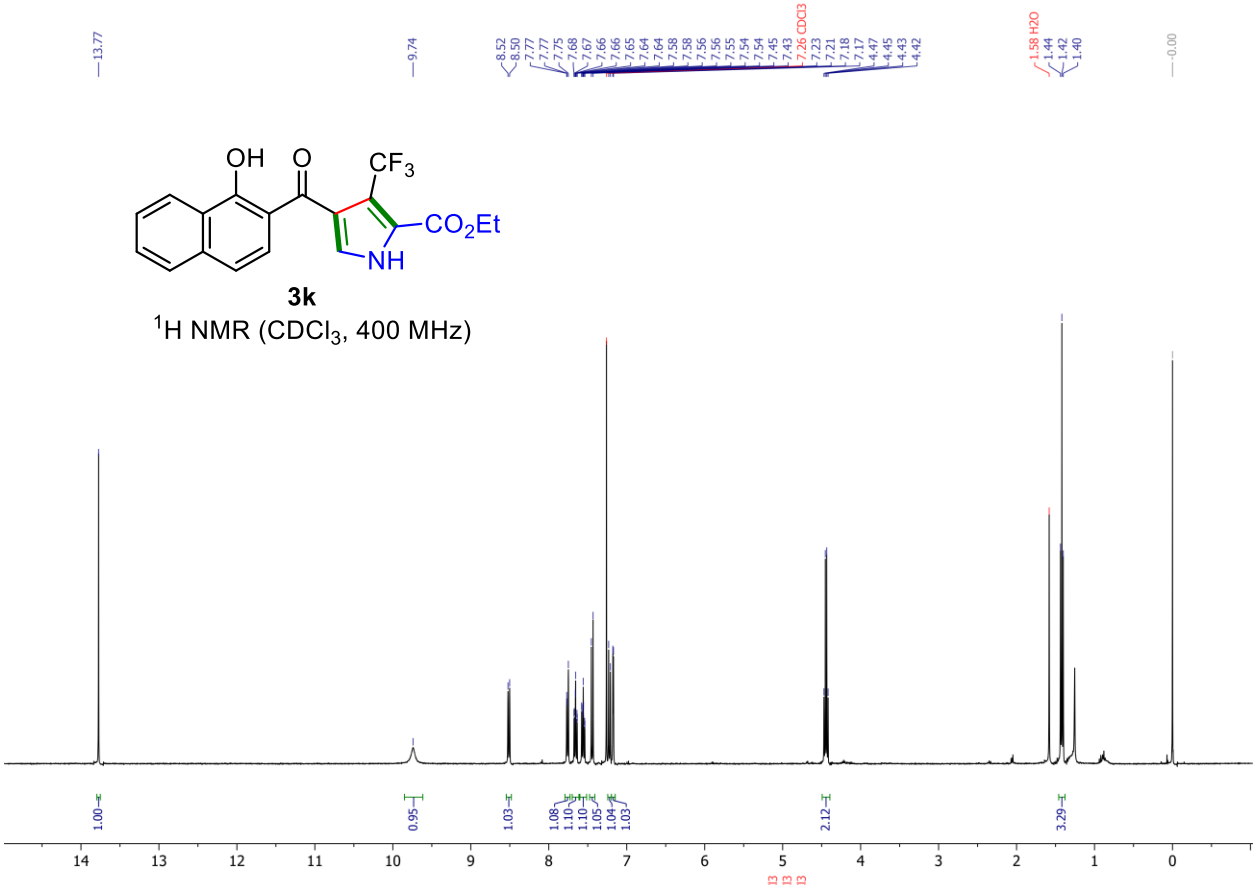


$^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



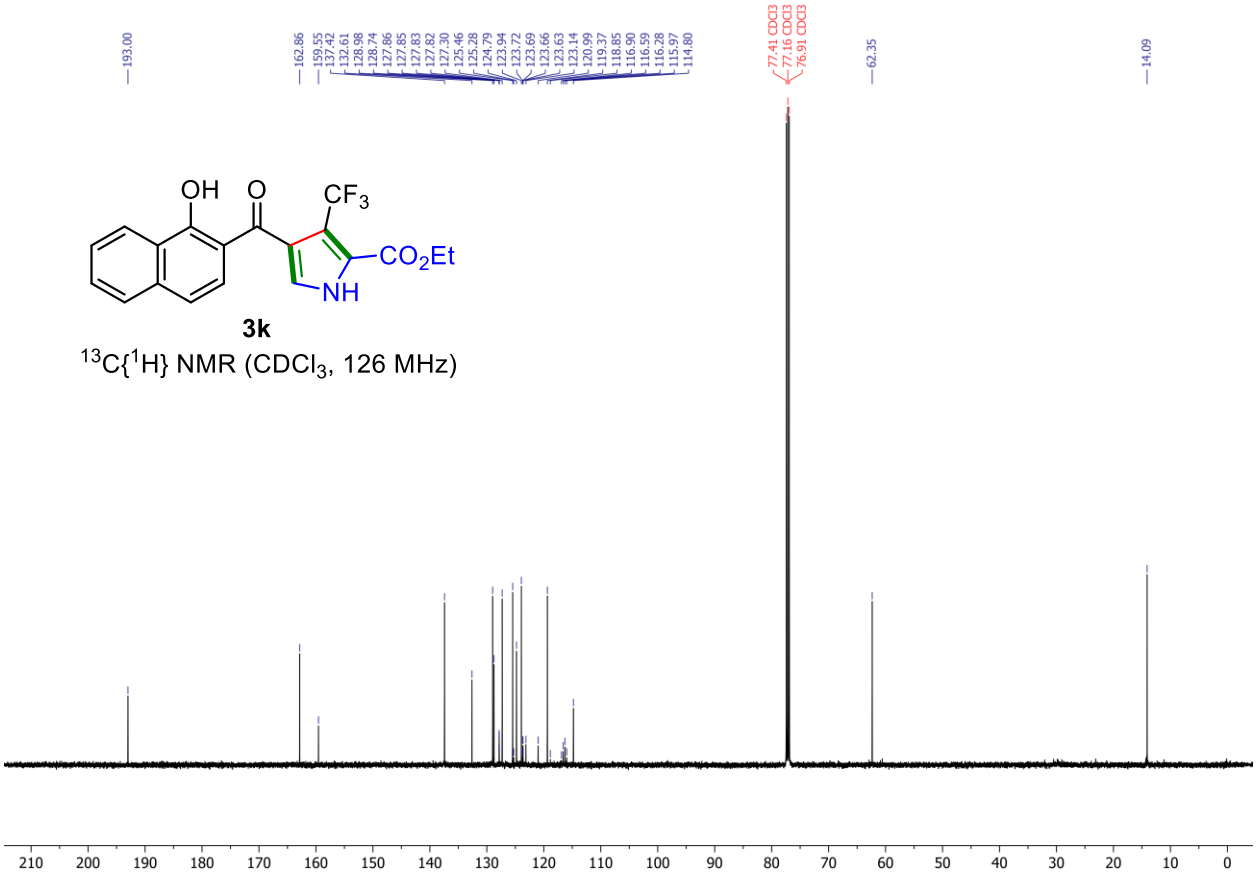
3j

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



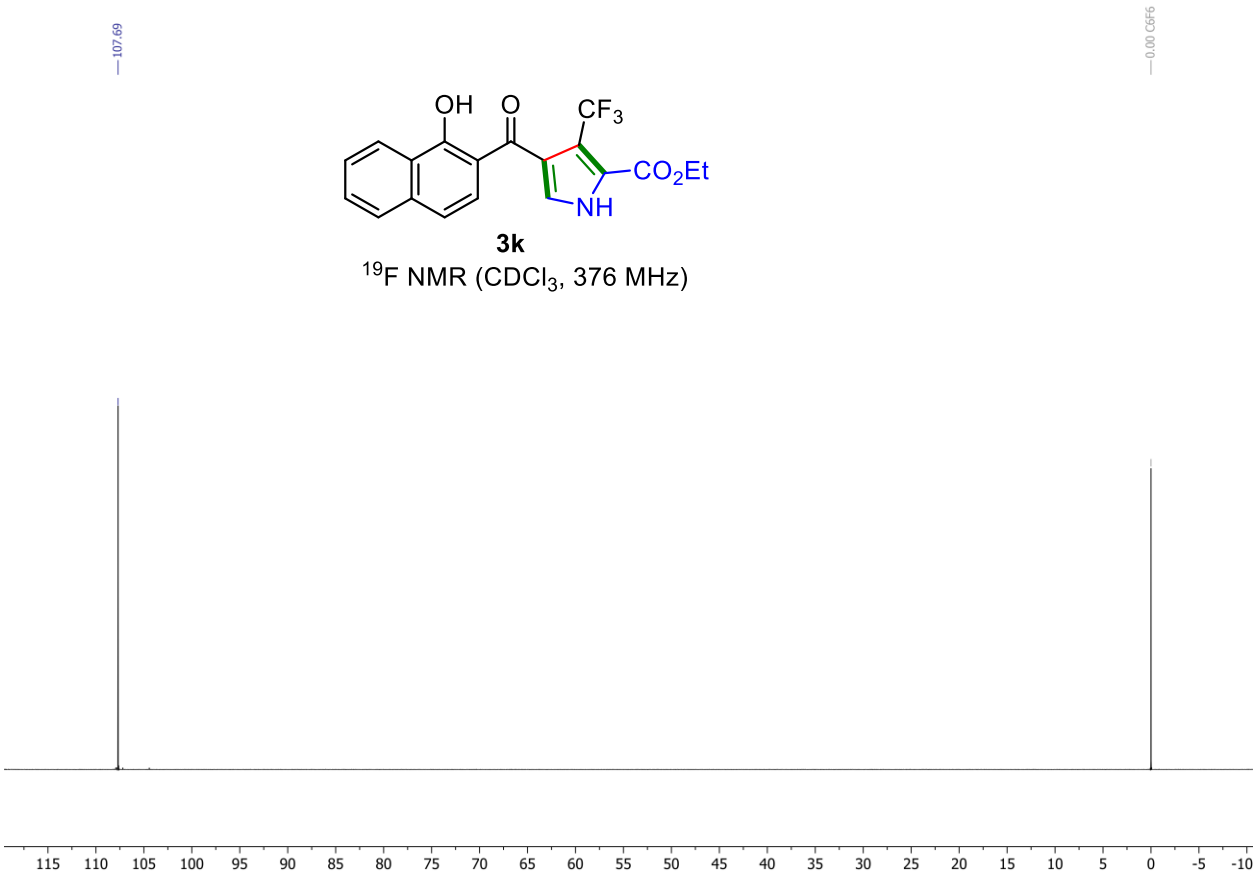
3k

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



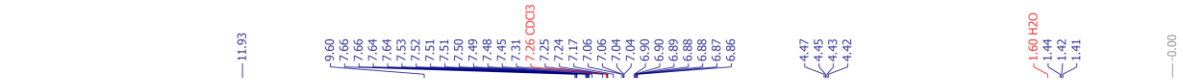
3k

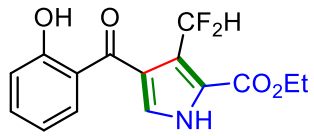
^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz)



3k

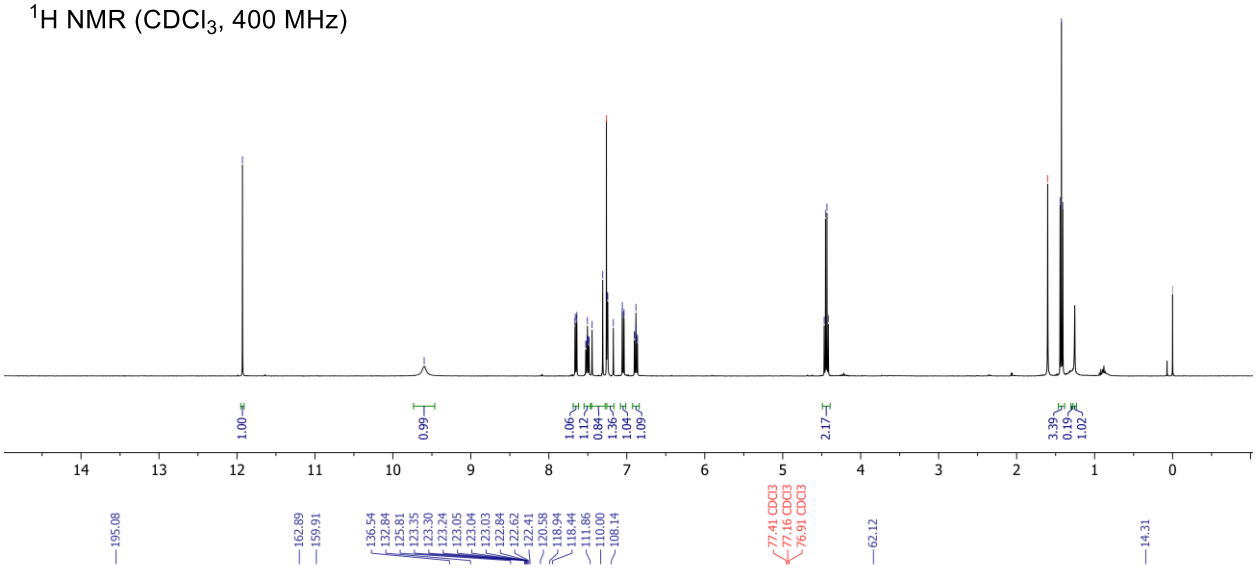
^{19}F NMR ($CDCl_3$, 376 MHz)

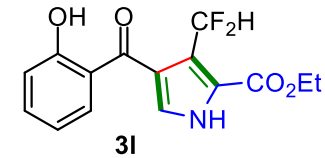




3l

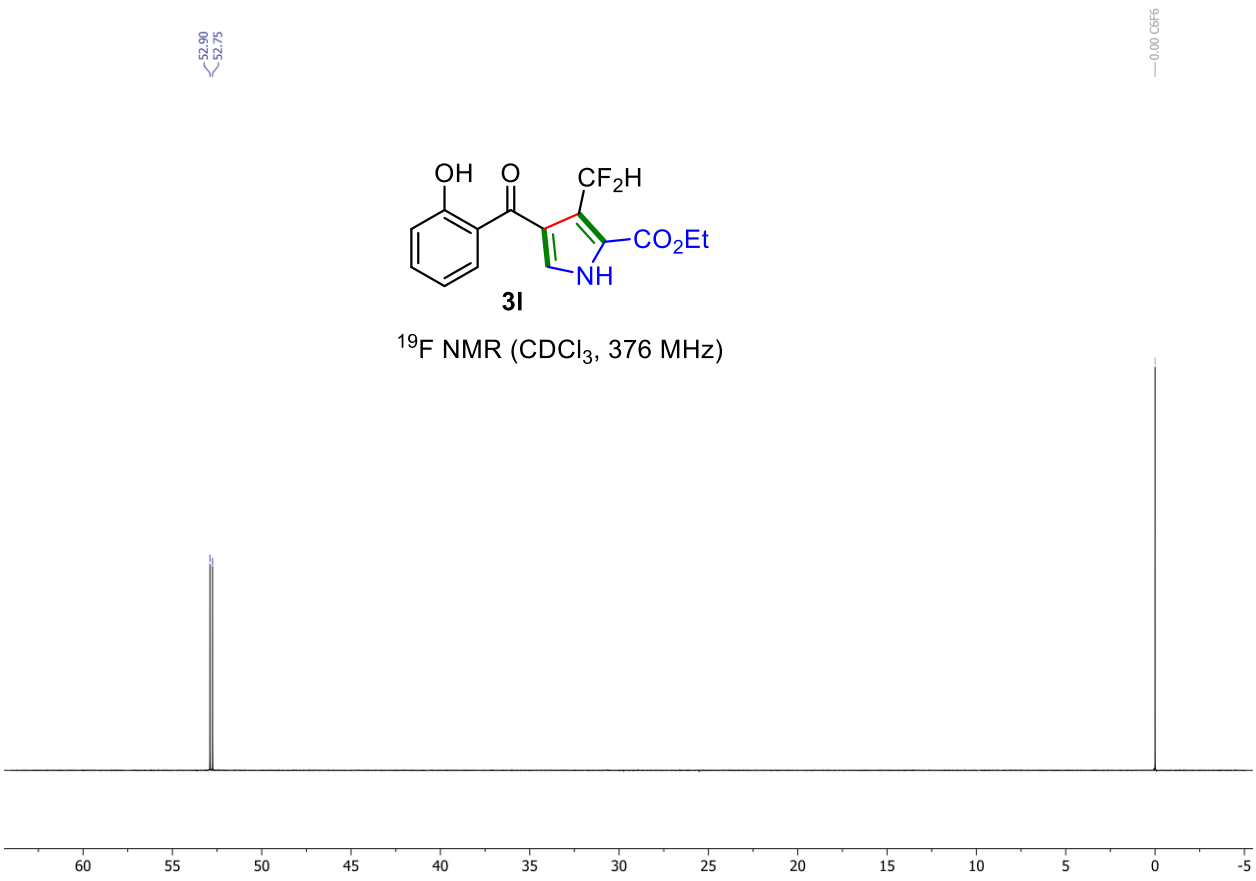
^{1}H NMR ($CDCl_3$, 400 MHz)





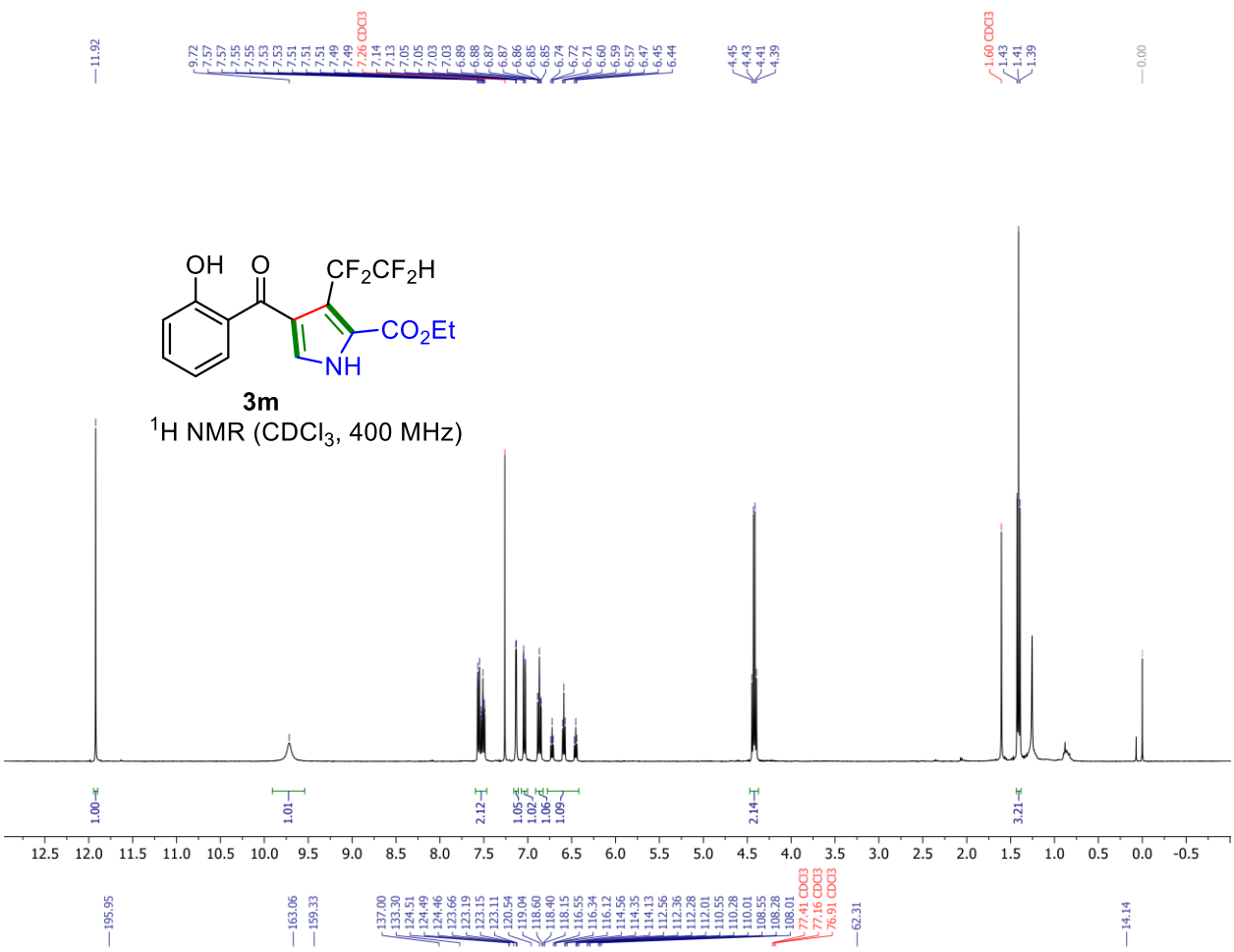
3l

$^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



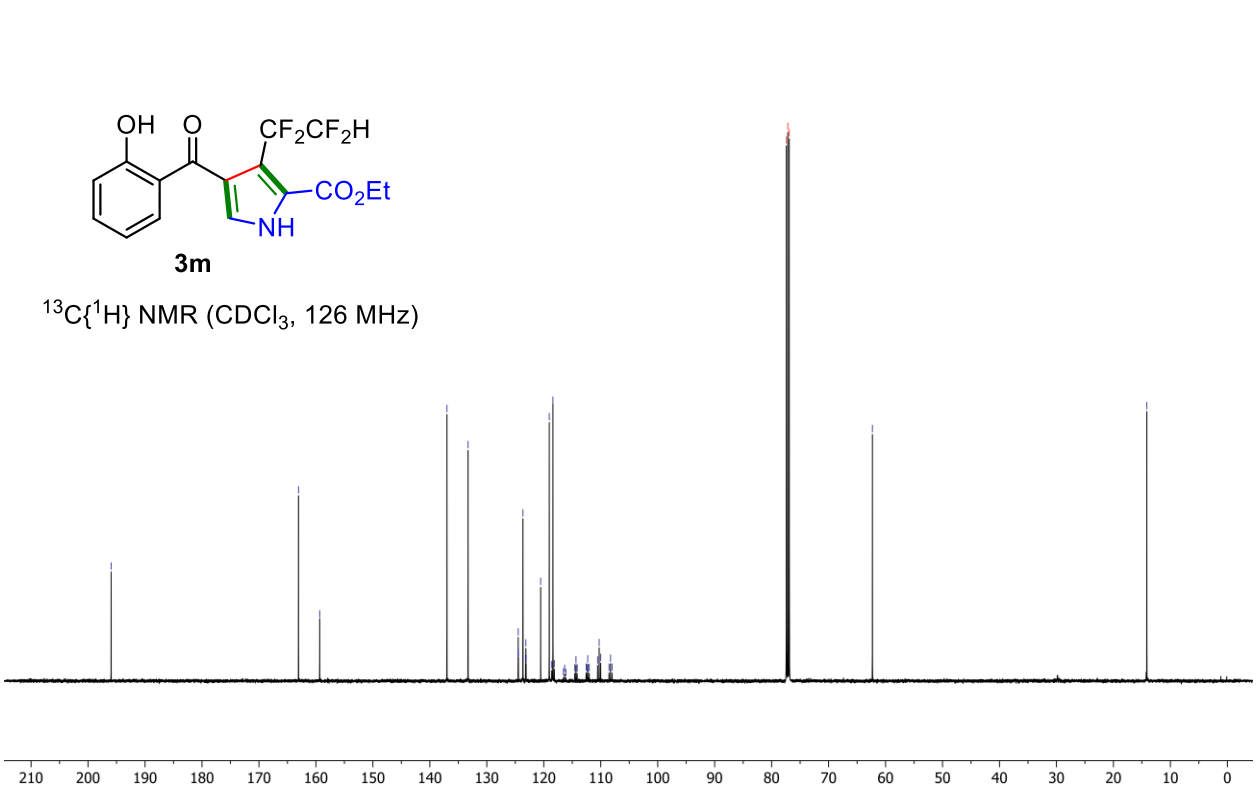
3l

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



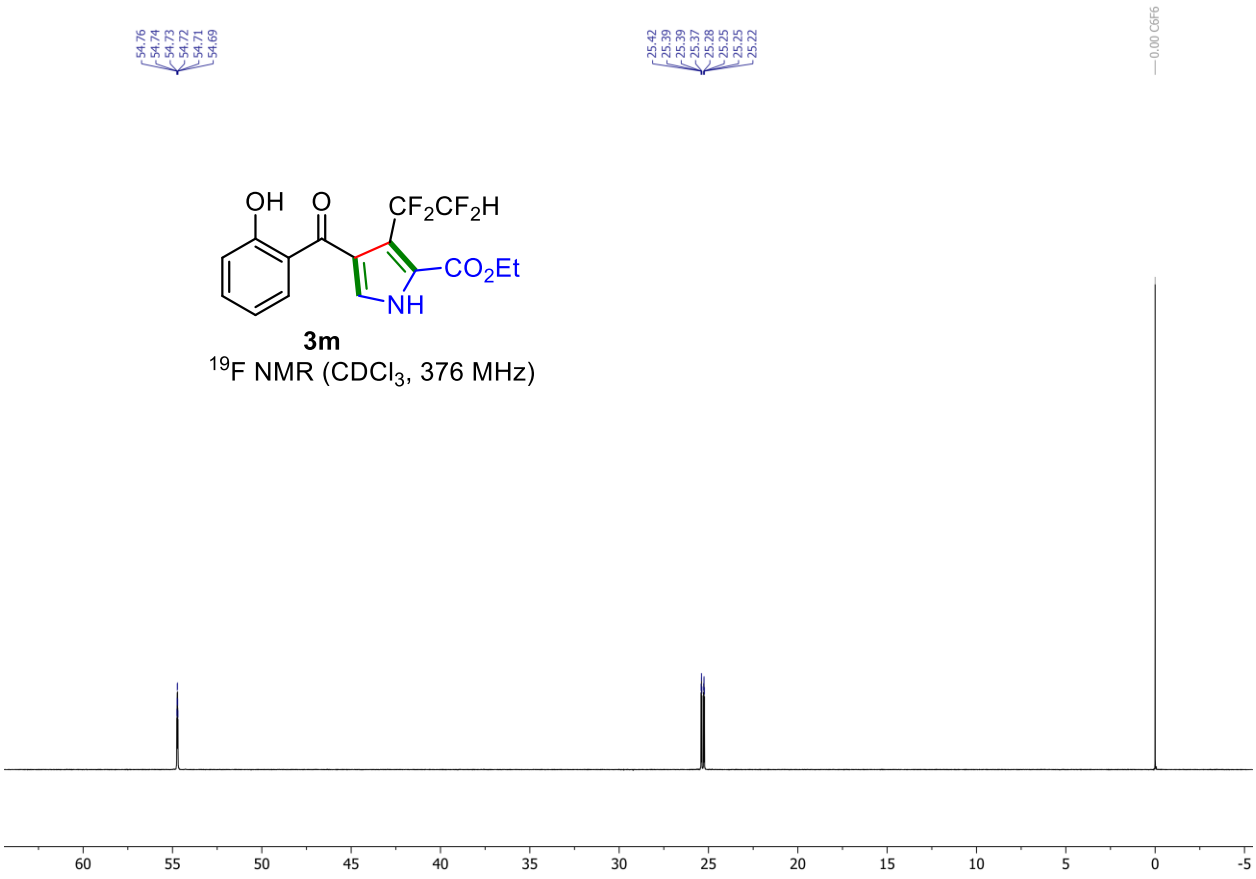
3m

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



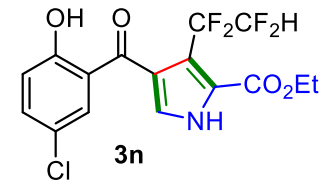
3m

$^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



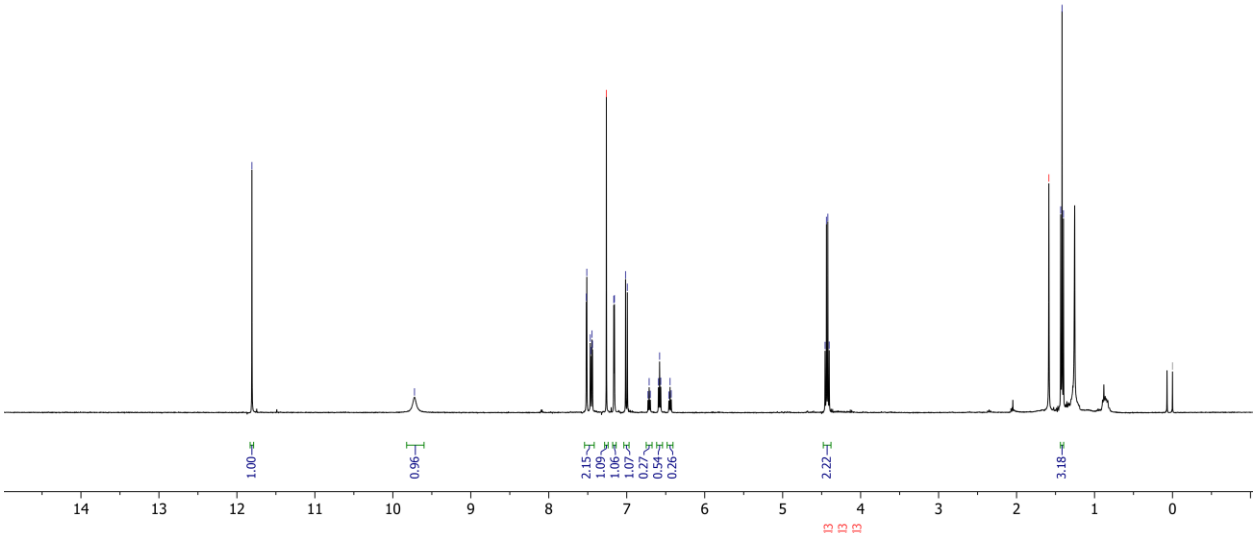
3m

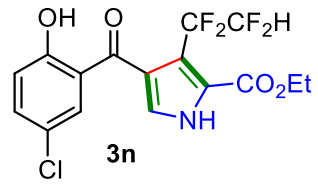
^{19}F NMR ($CDCl_3$, 376 MHz)



3n

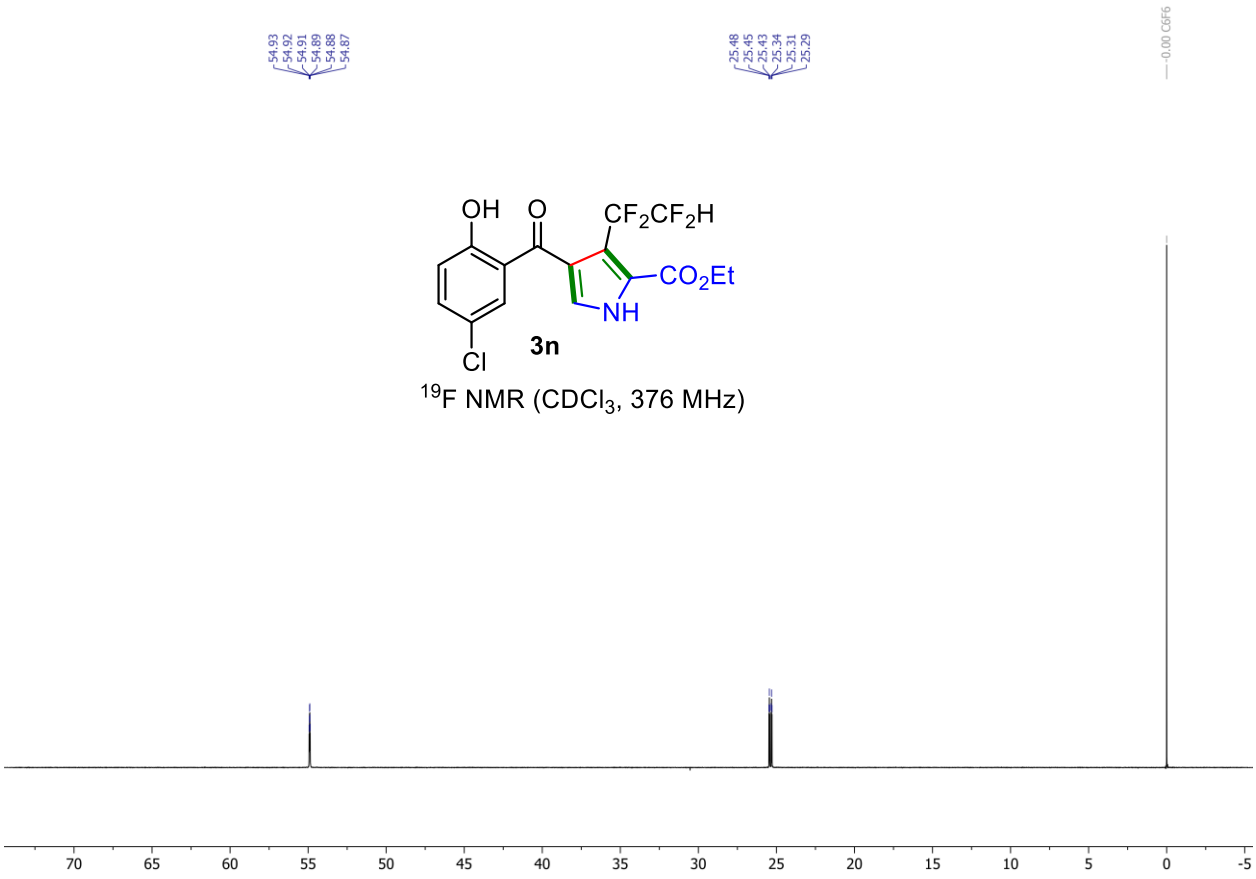
^{1}H NMR ($CDCl_3$, 400 MHz)



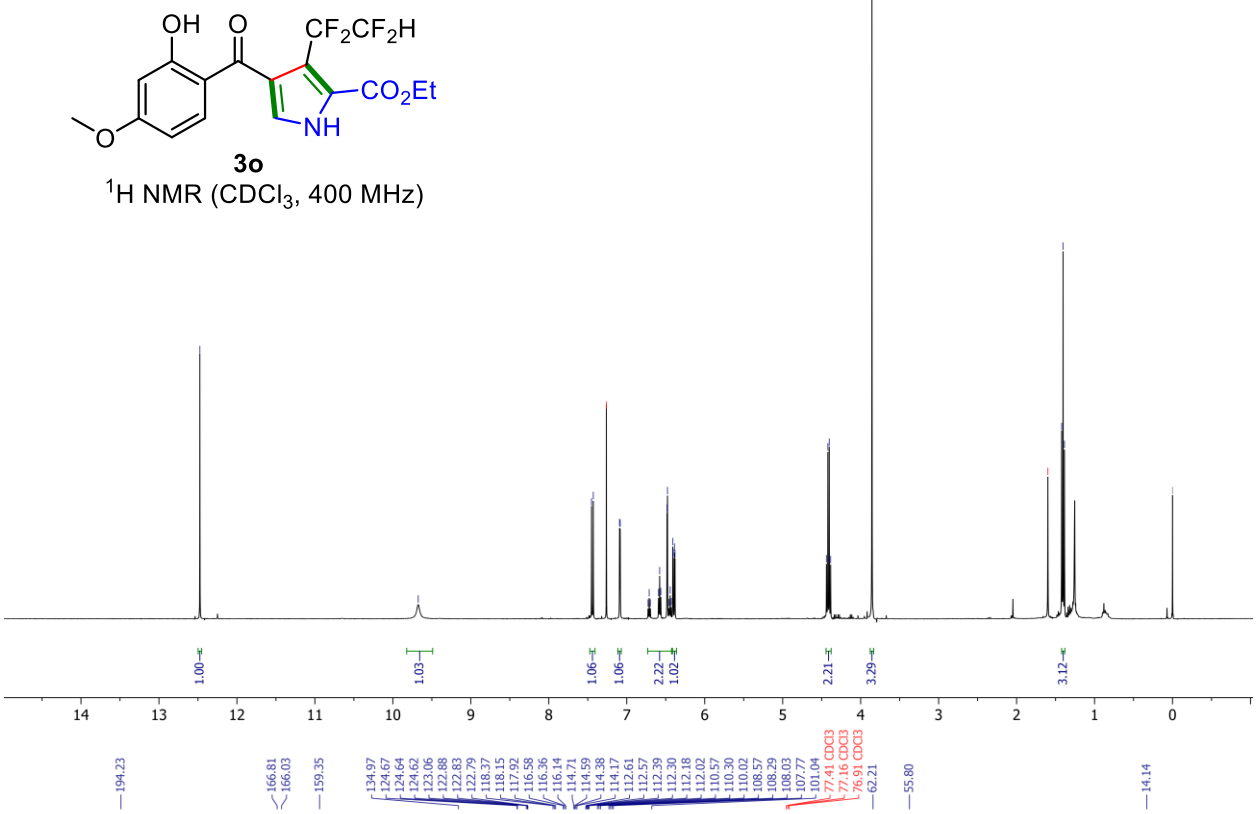


3n

^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz)

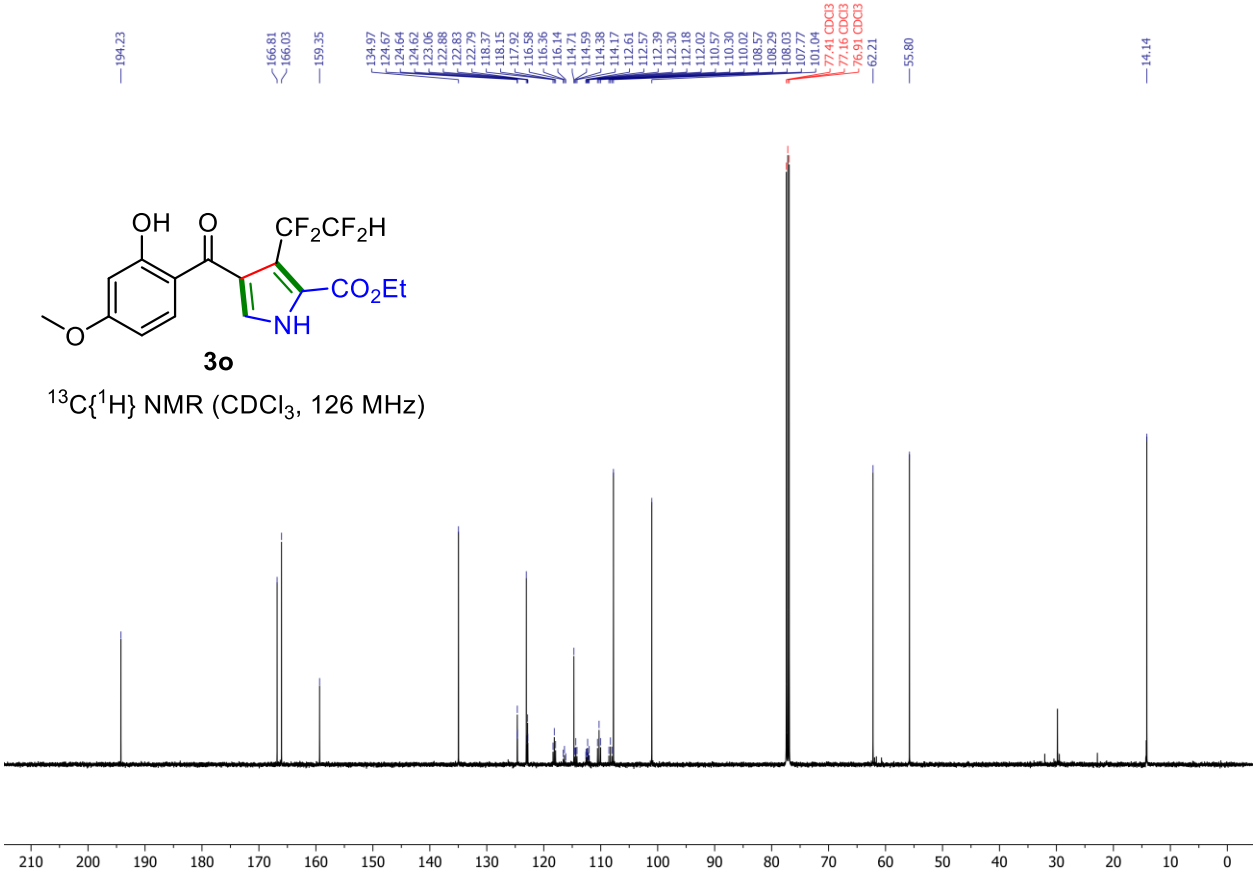


^{19}F NMR ($CDCl_3$, 376 MHz)



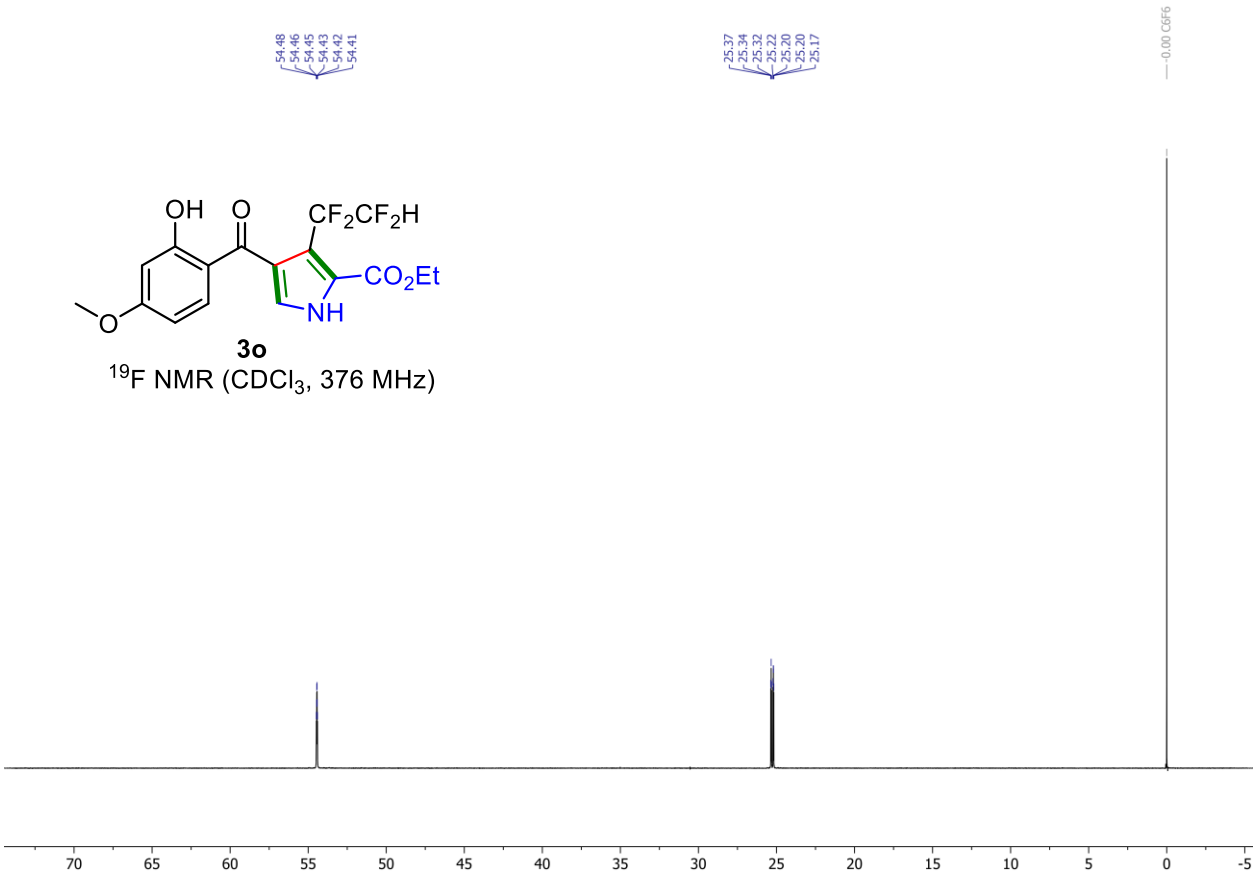
3o

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



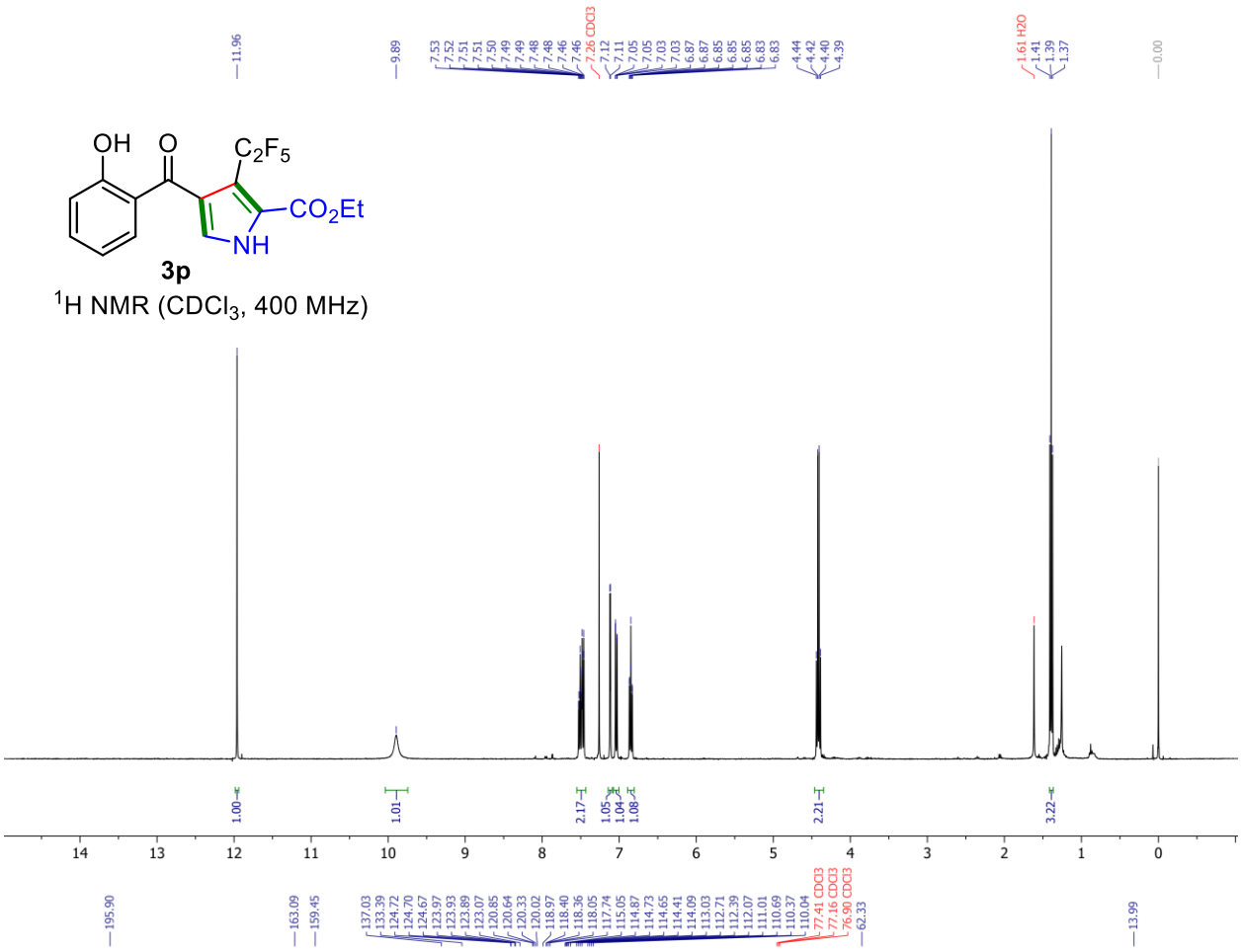
3o

^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz)



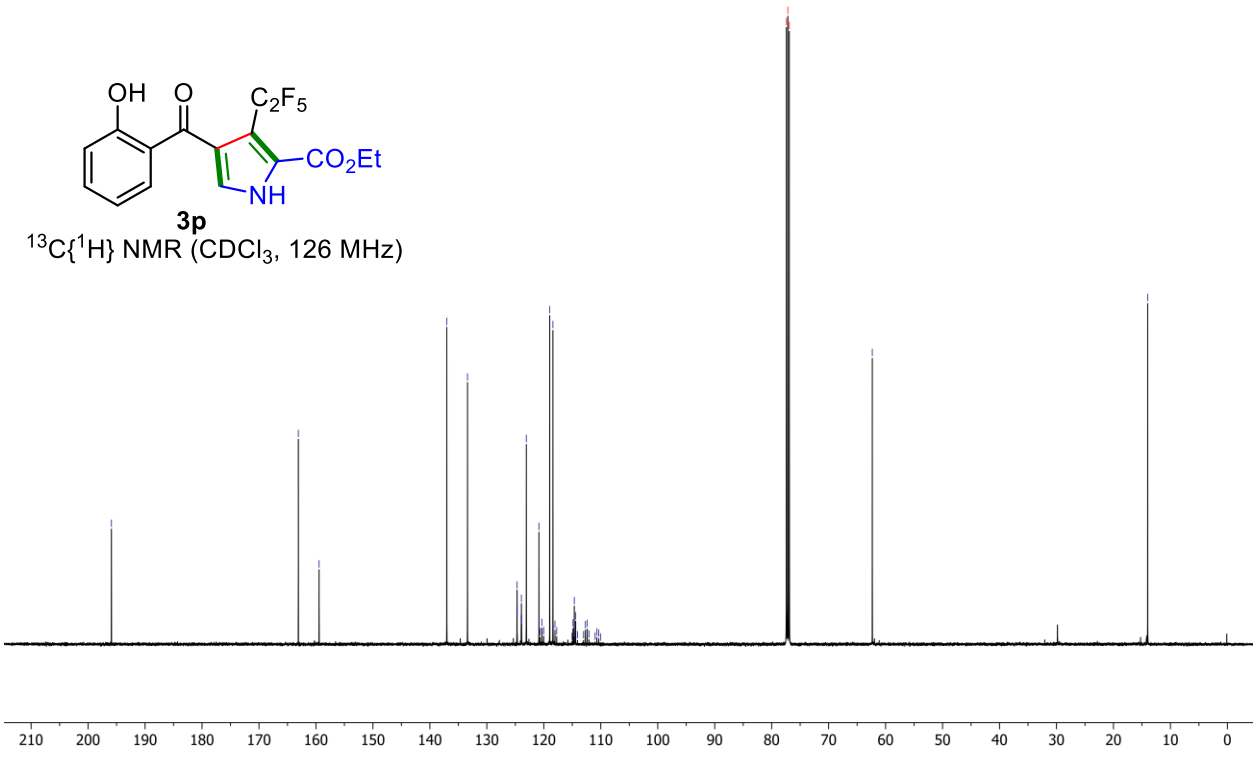
3o

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



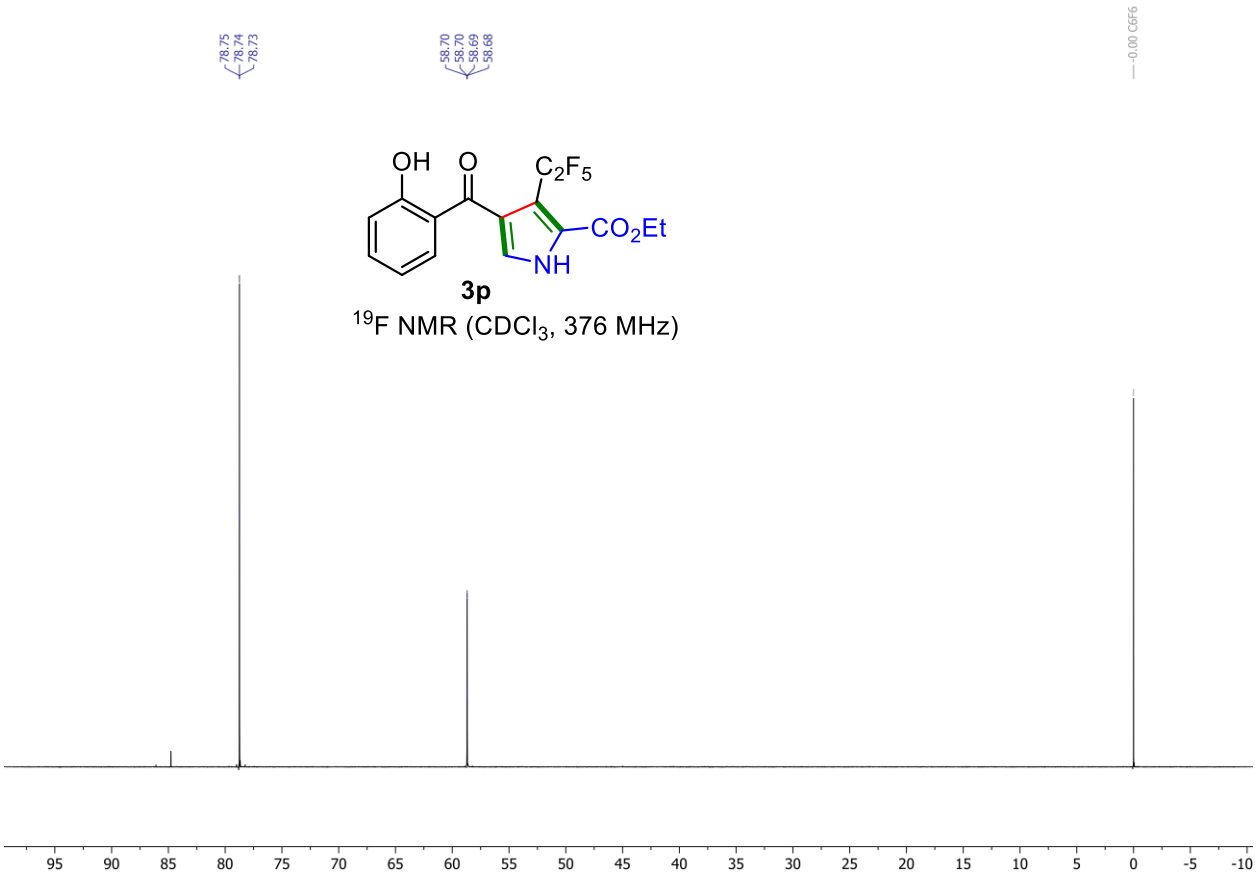
3p

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



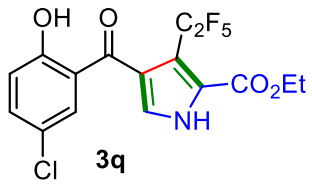
3p

$^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



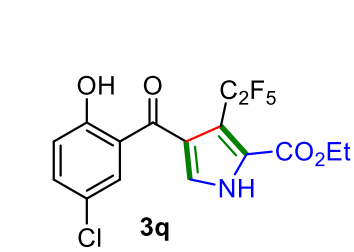
3p

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



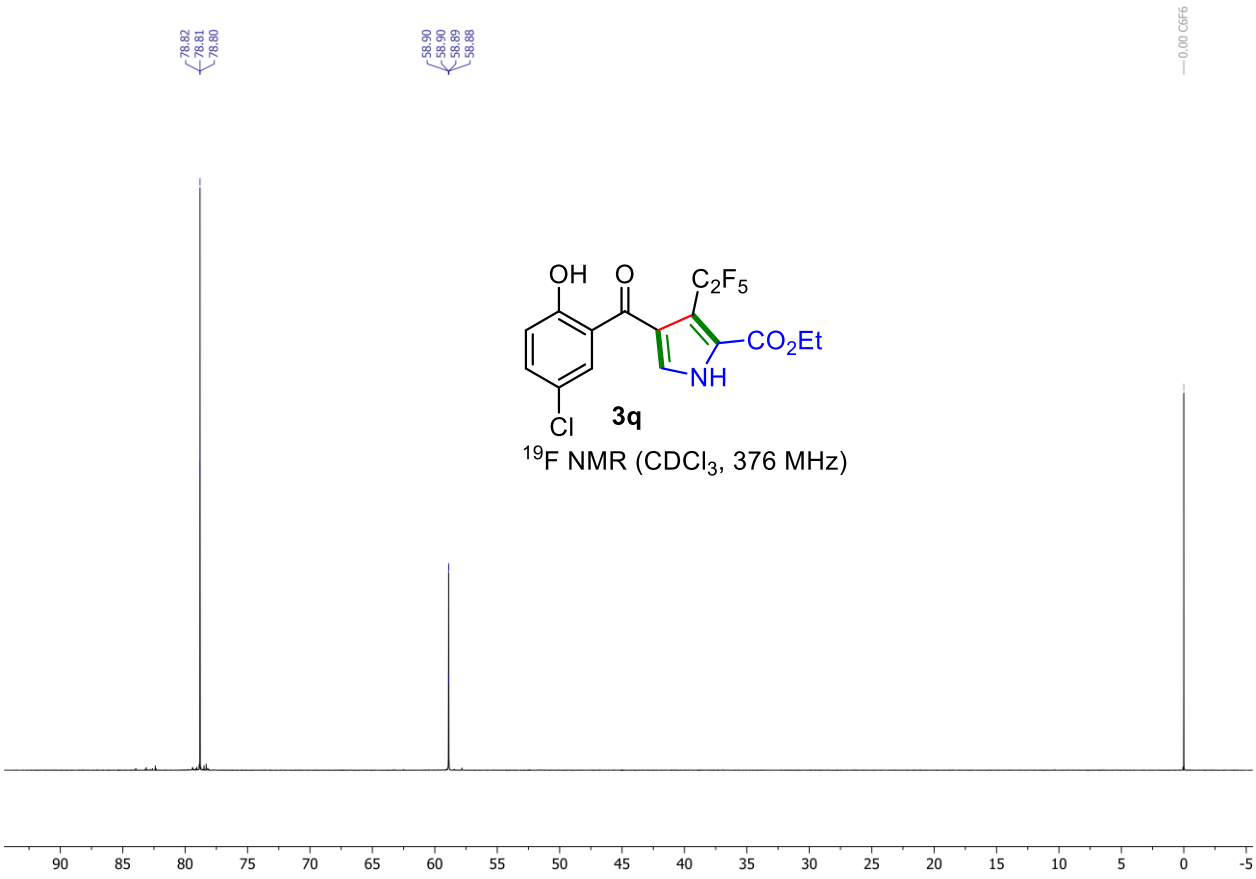
3q

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



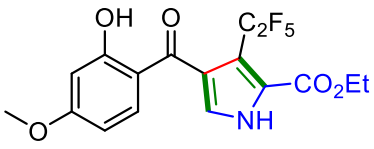
3q

$^{13}C\{^1H\}$ NMR ($CDCl_3$, 126 MHz)



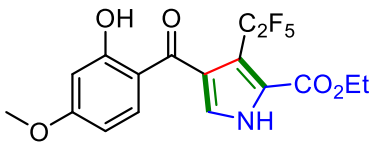
3q

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



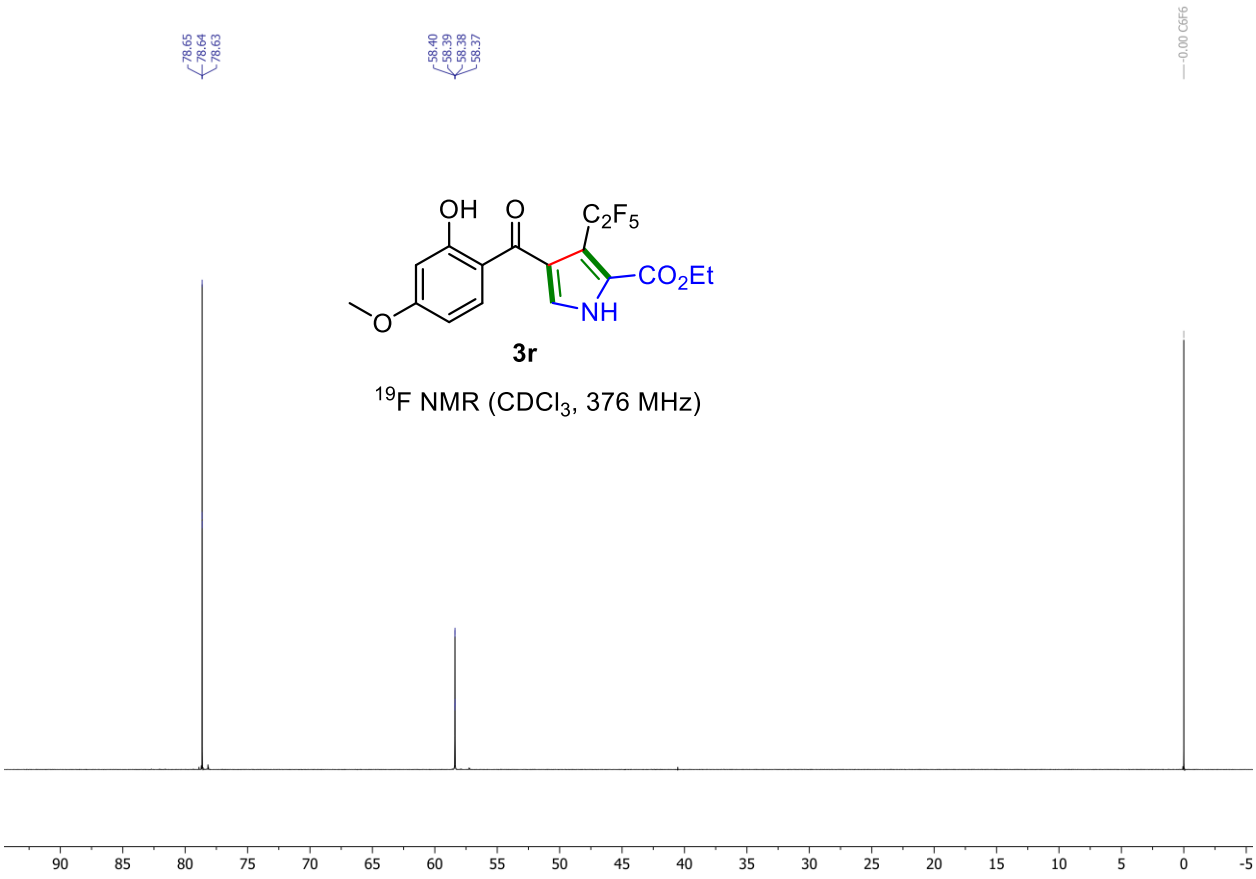
3r

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



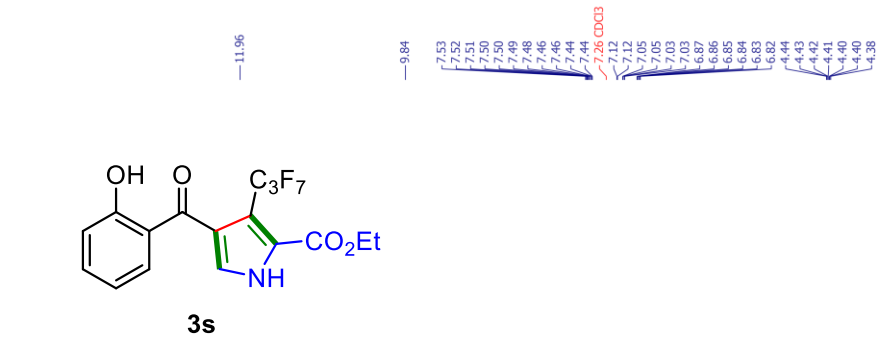
3r

$^{13}C\{^1H\}$ NMR ($CDCl_3$, 126 MHz)



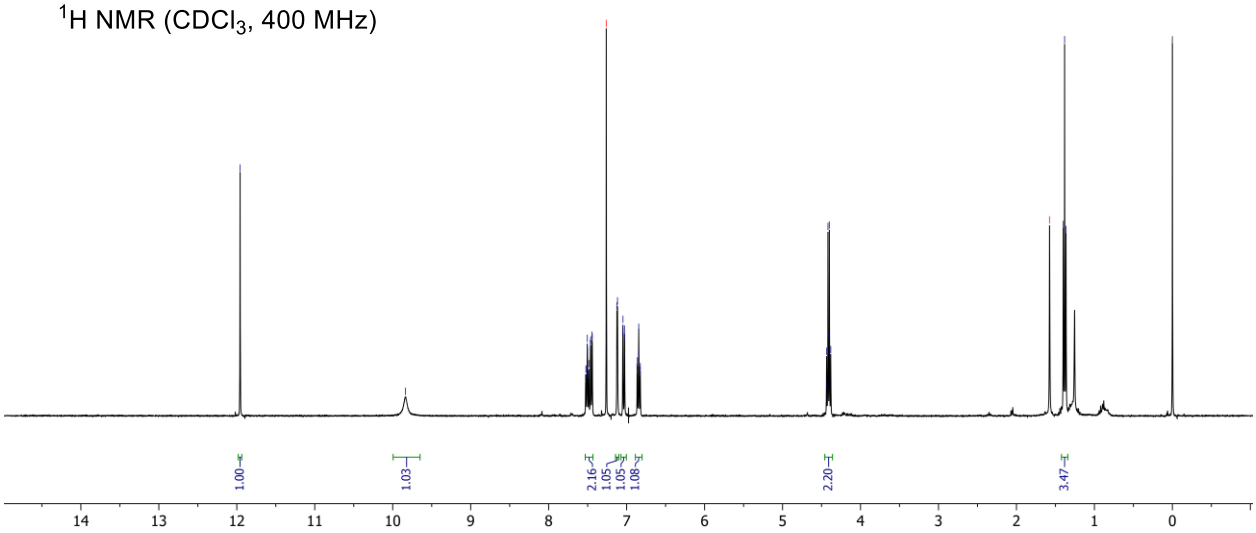
3r

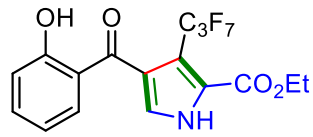
^{19}F NMR ($CDCl_3$, 376 MHz)



3s

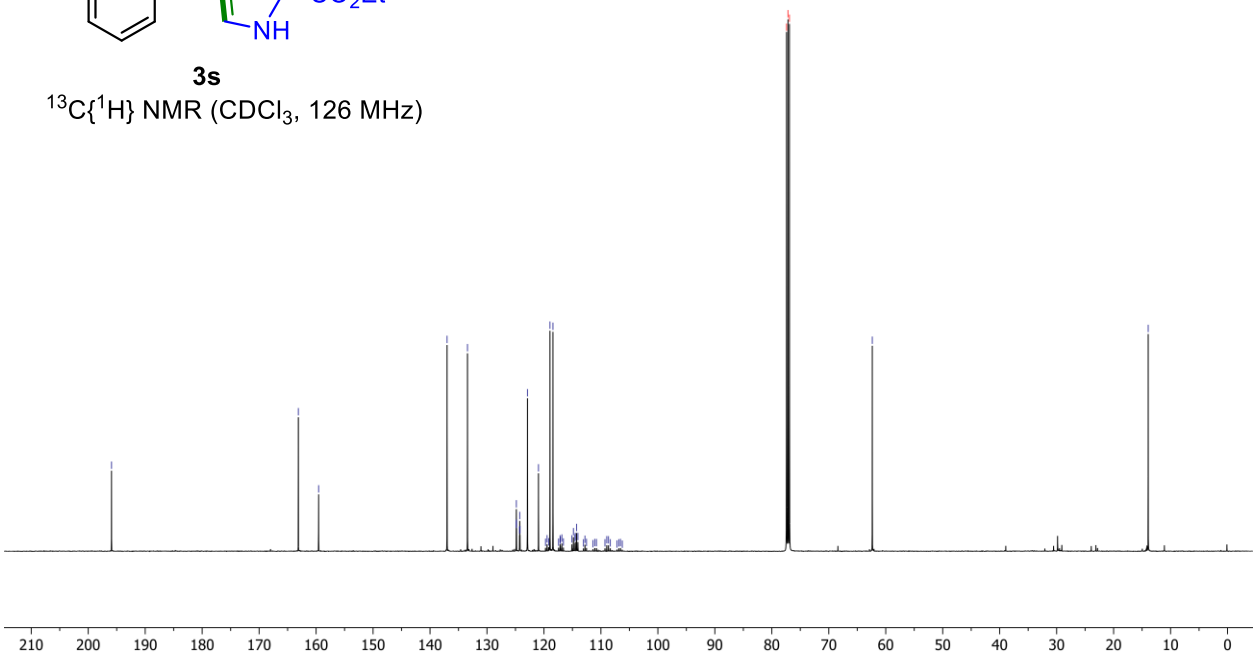
^{1}H NMR ($CDCl_3$, 400 MHz)

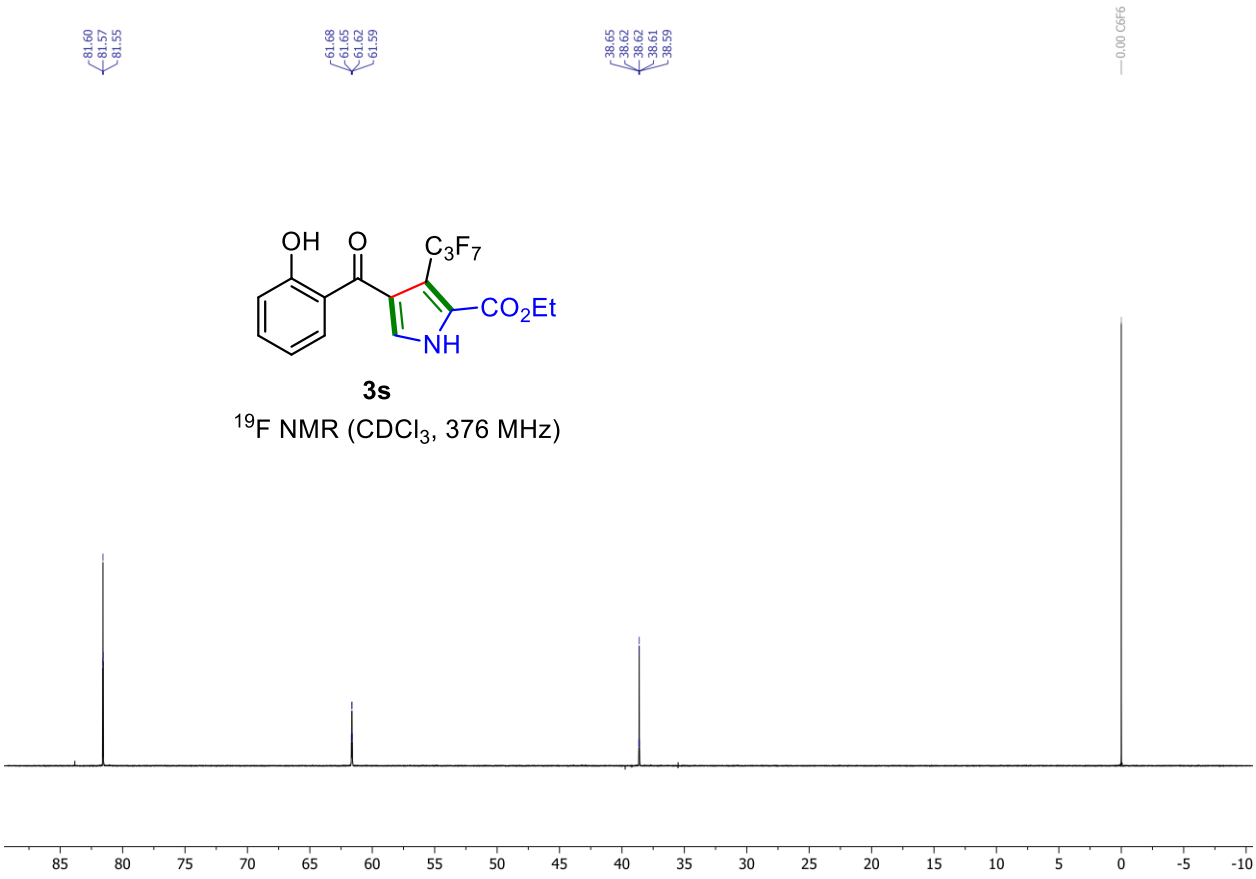




3s

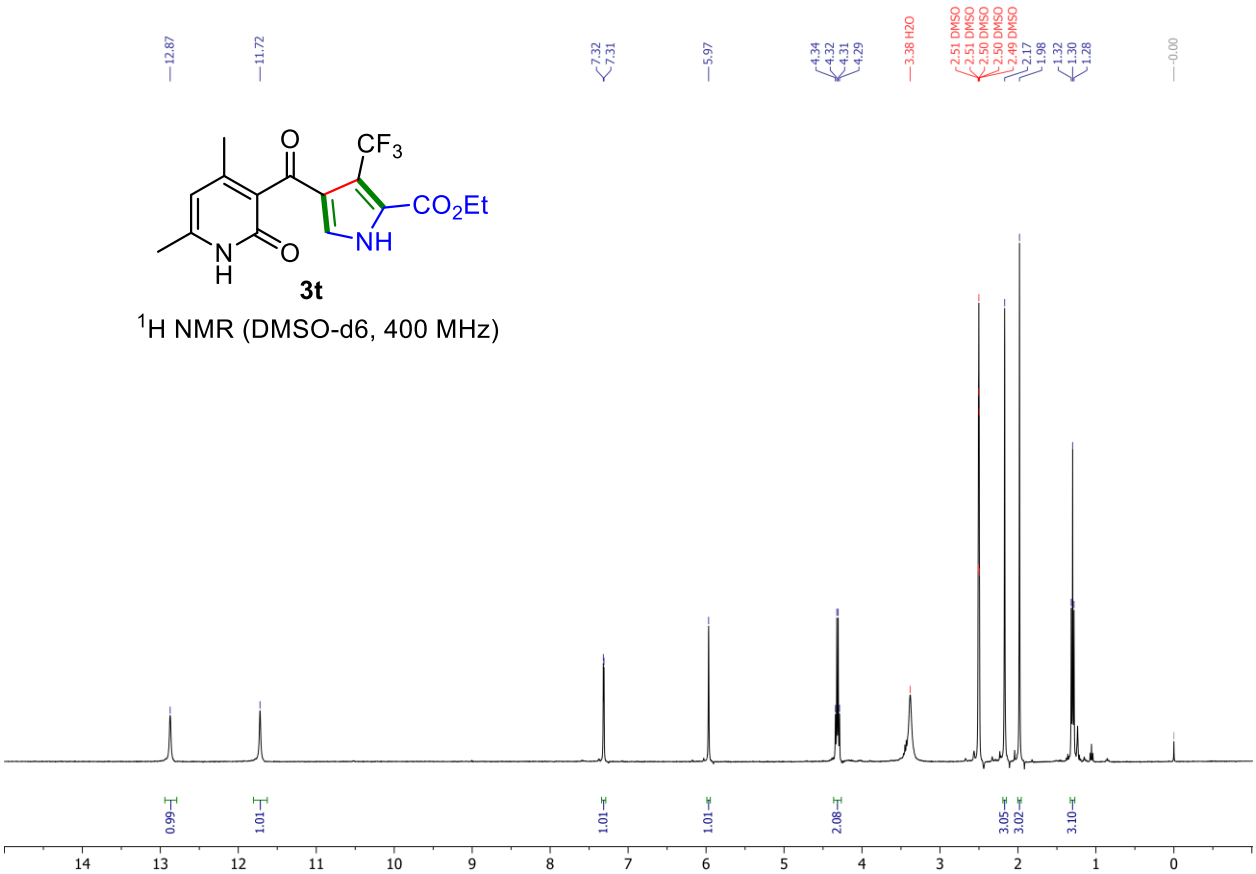
$^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)





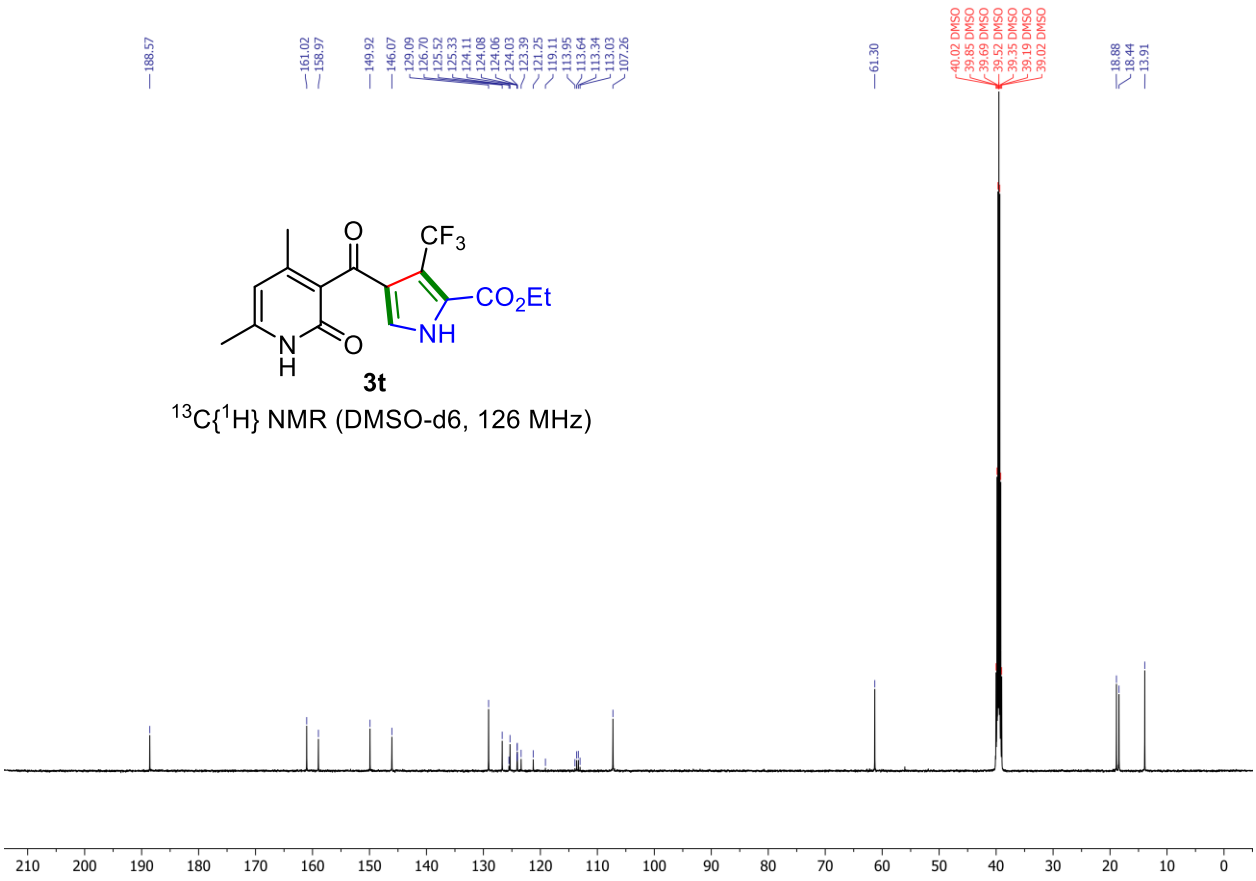
3s

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



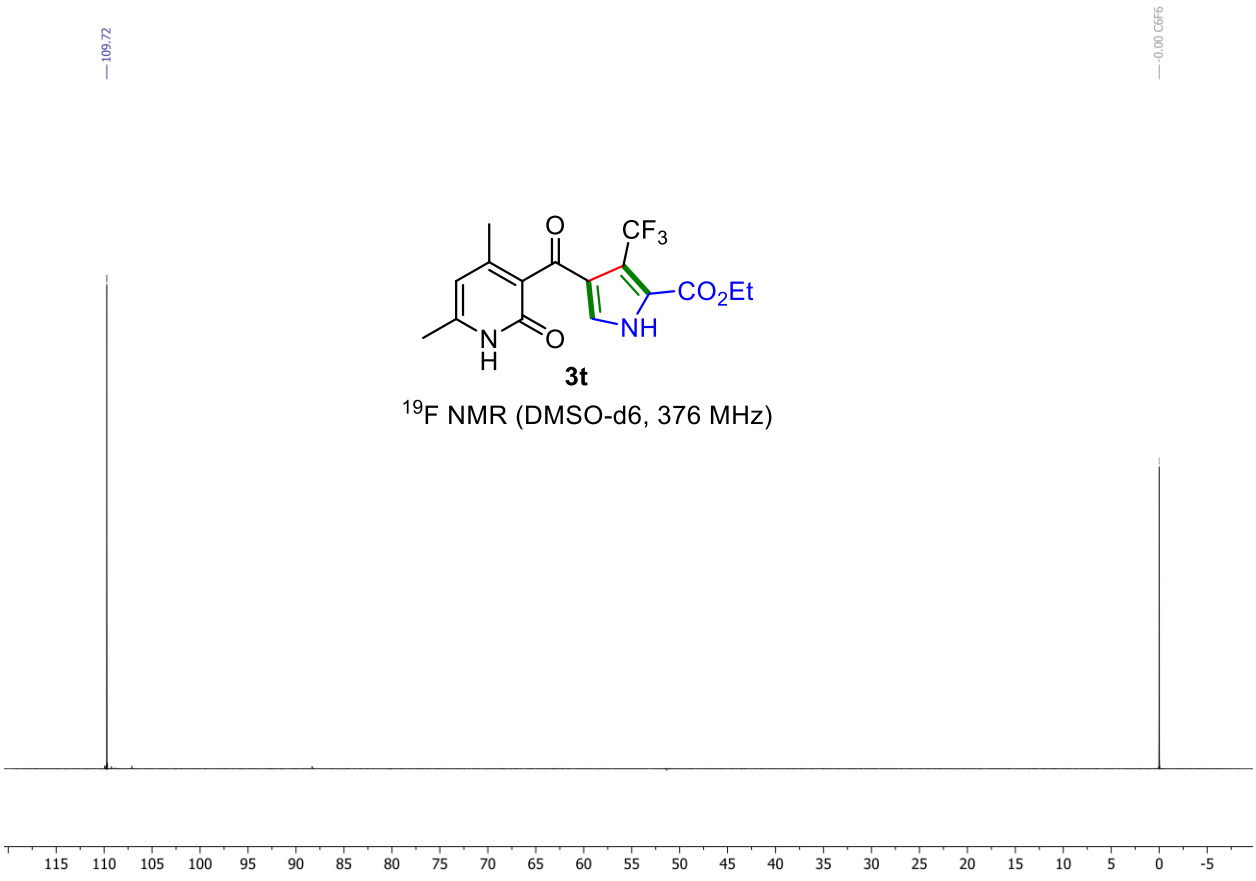
3t

^{1}H NMR (DMSO-d6, 400 MHz)



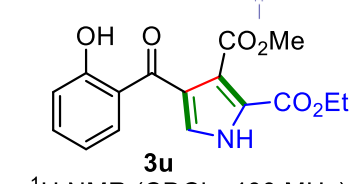
3t

^{13}C{^{1}H} NMR (DMSO-d6, 126 MHz)



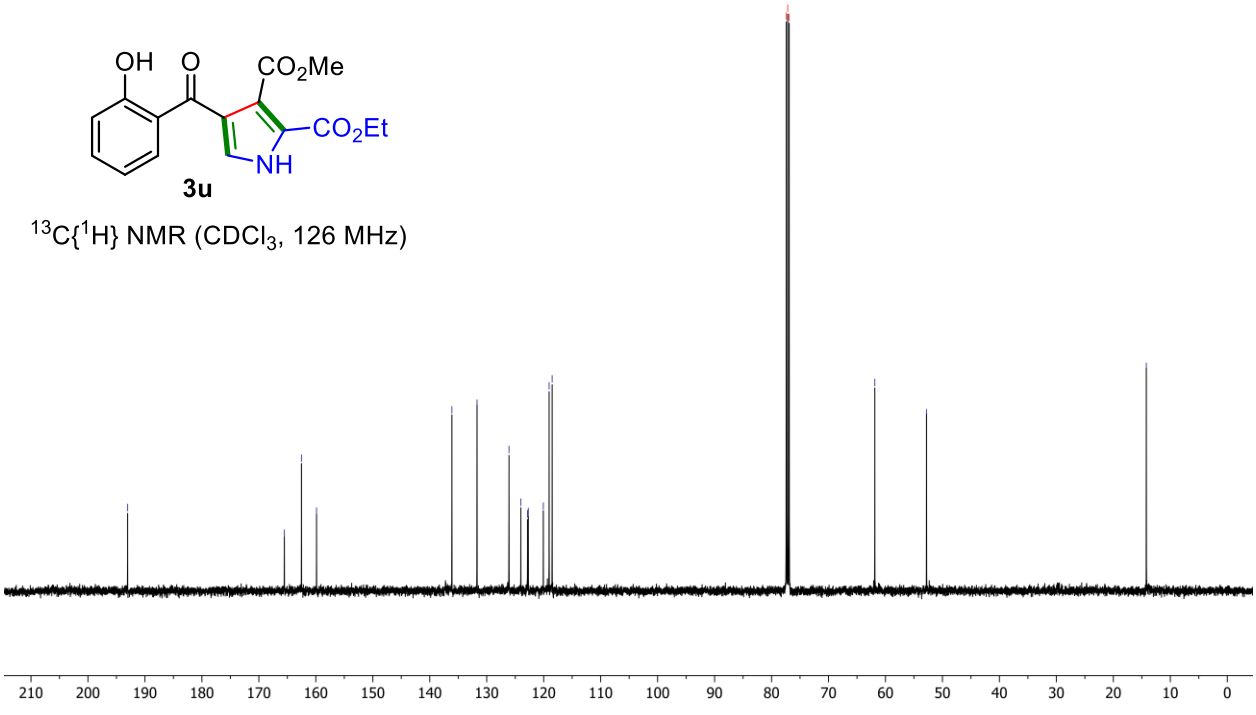
3t

^{19}F NMR (DMSO-d6, 376 MHz)



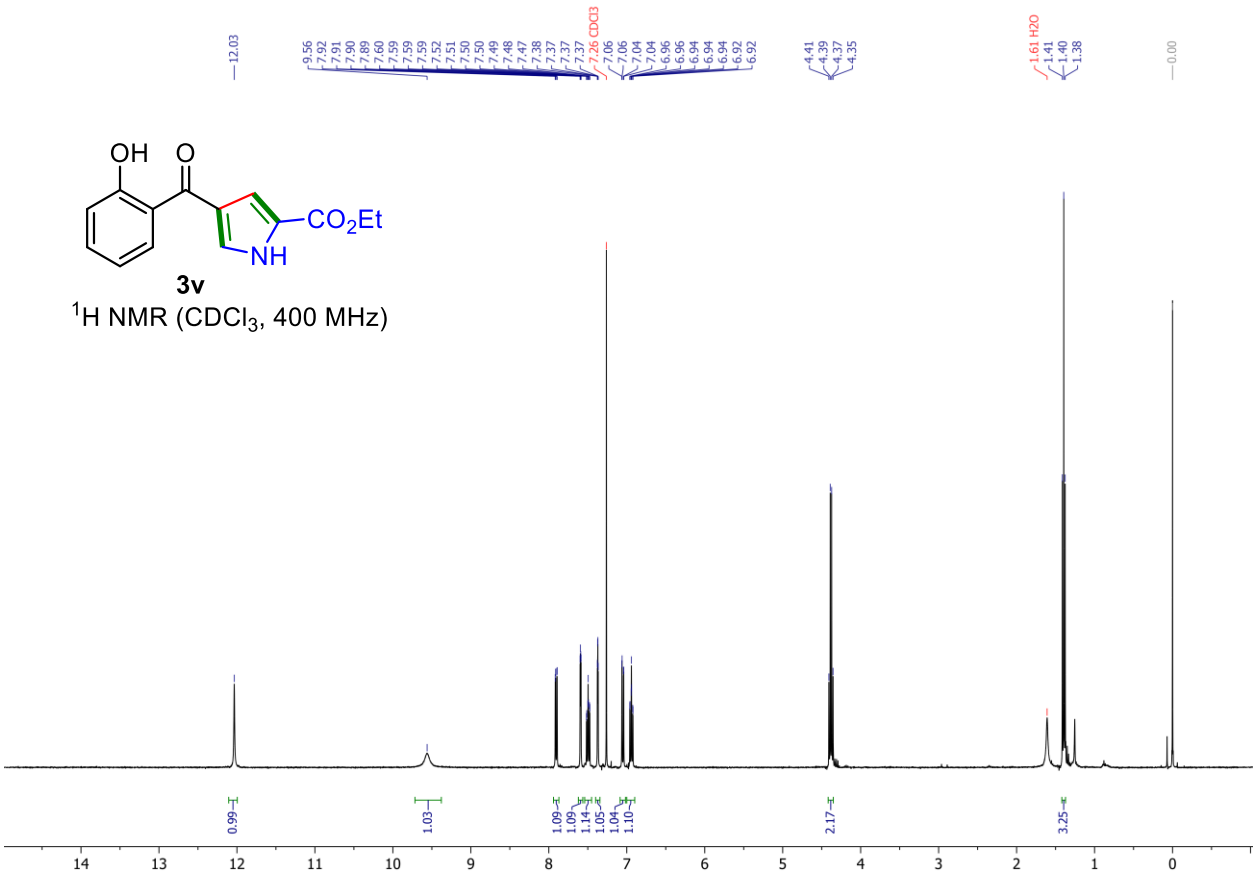
3u

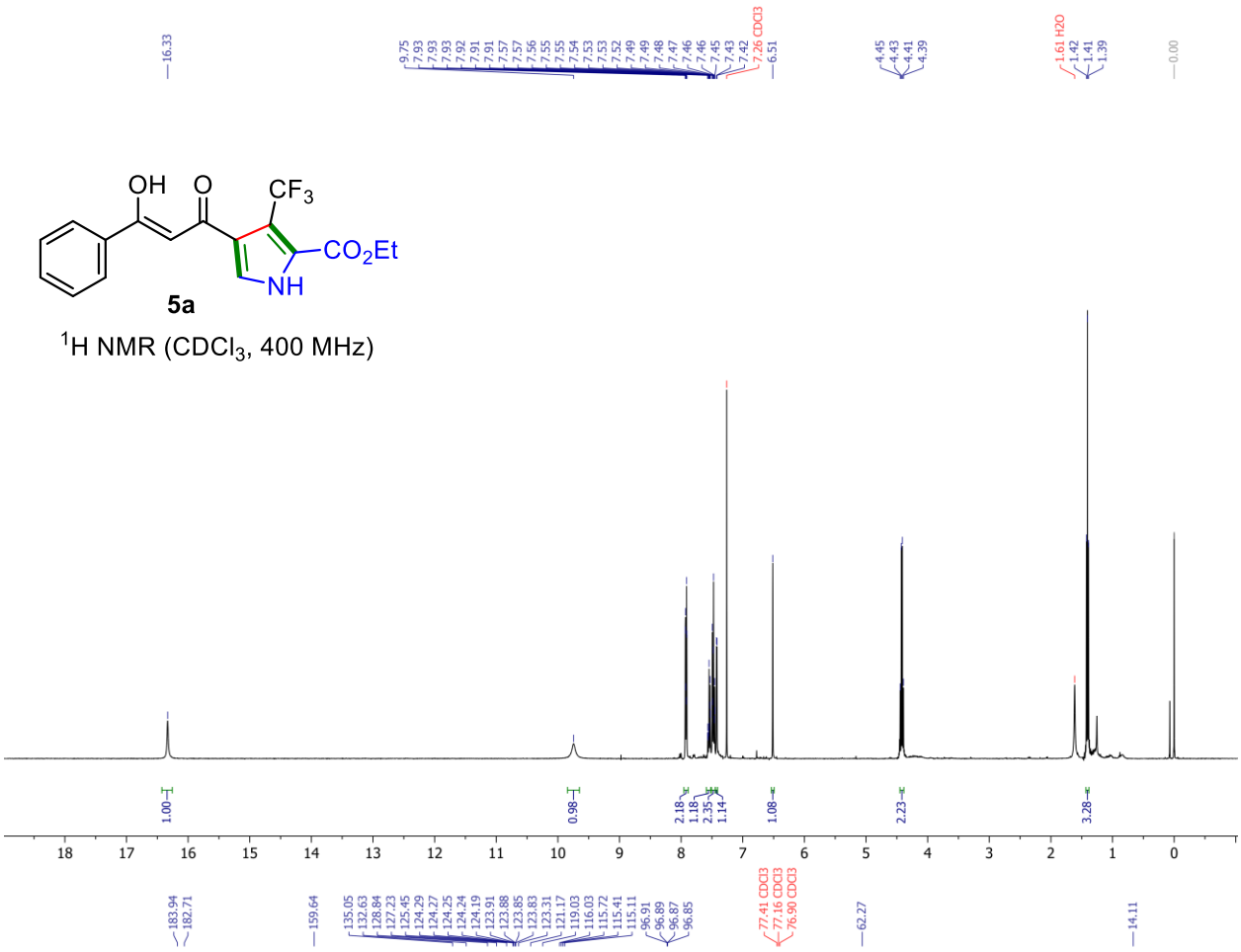
^{1}H NMR ($CDCl_3$, 400 MHz)



3u

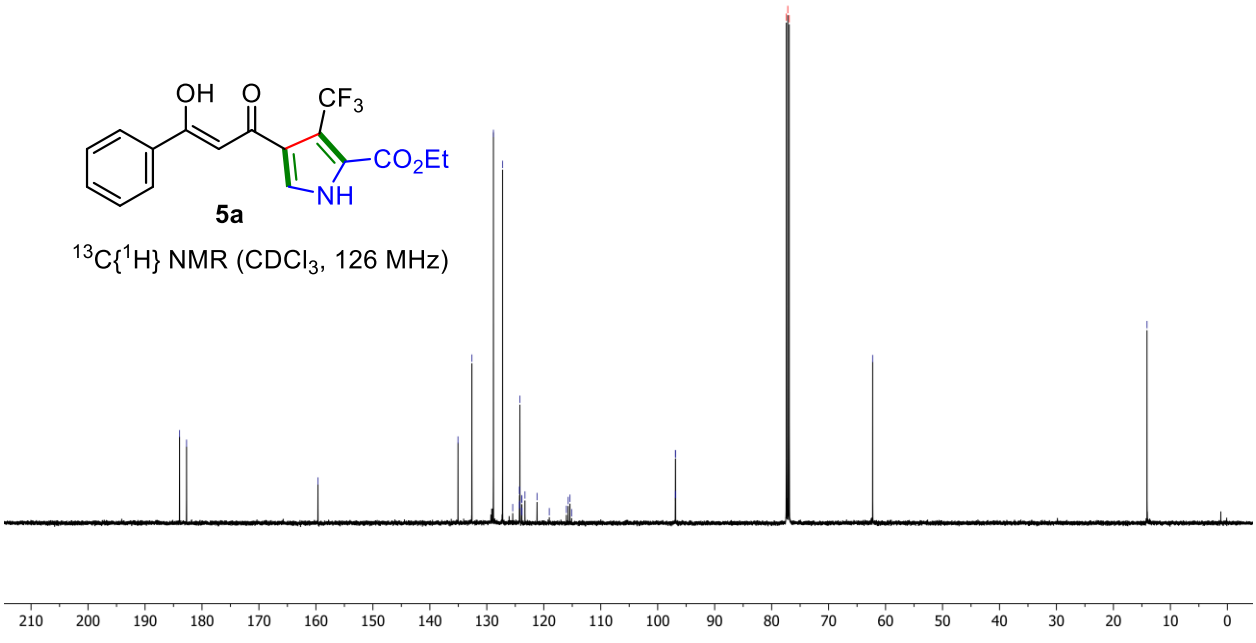
^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz)


OH
O
CO2Et
NH
3v
1H NMR (CDCl3, 400 MHz)



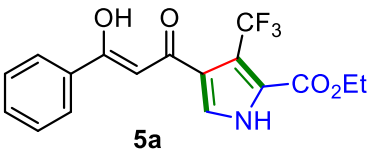
5a

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



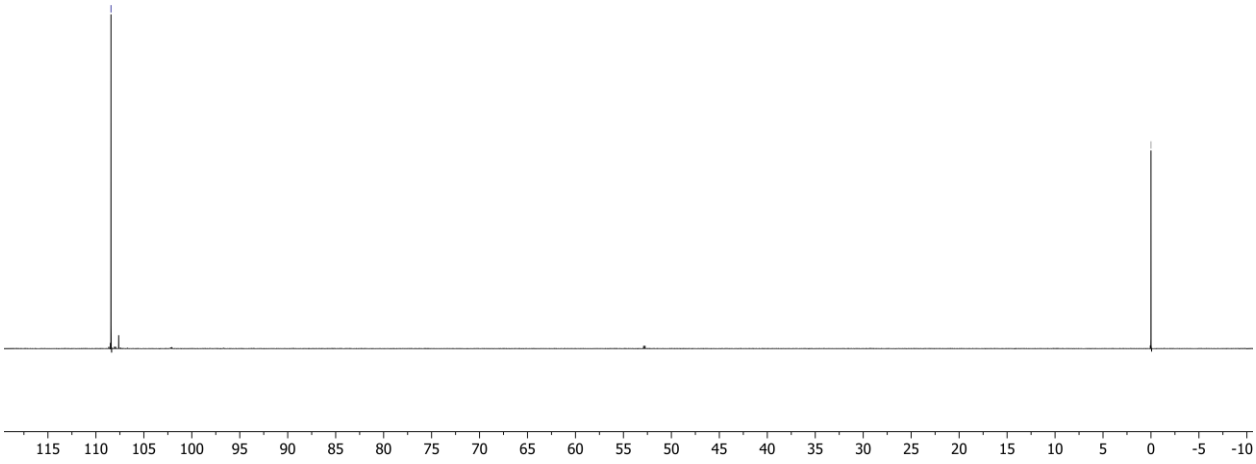
5a

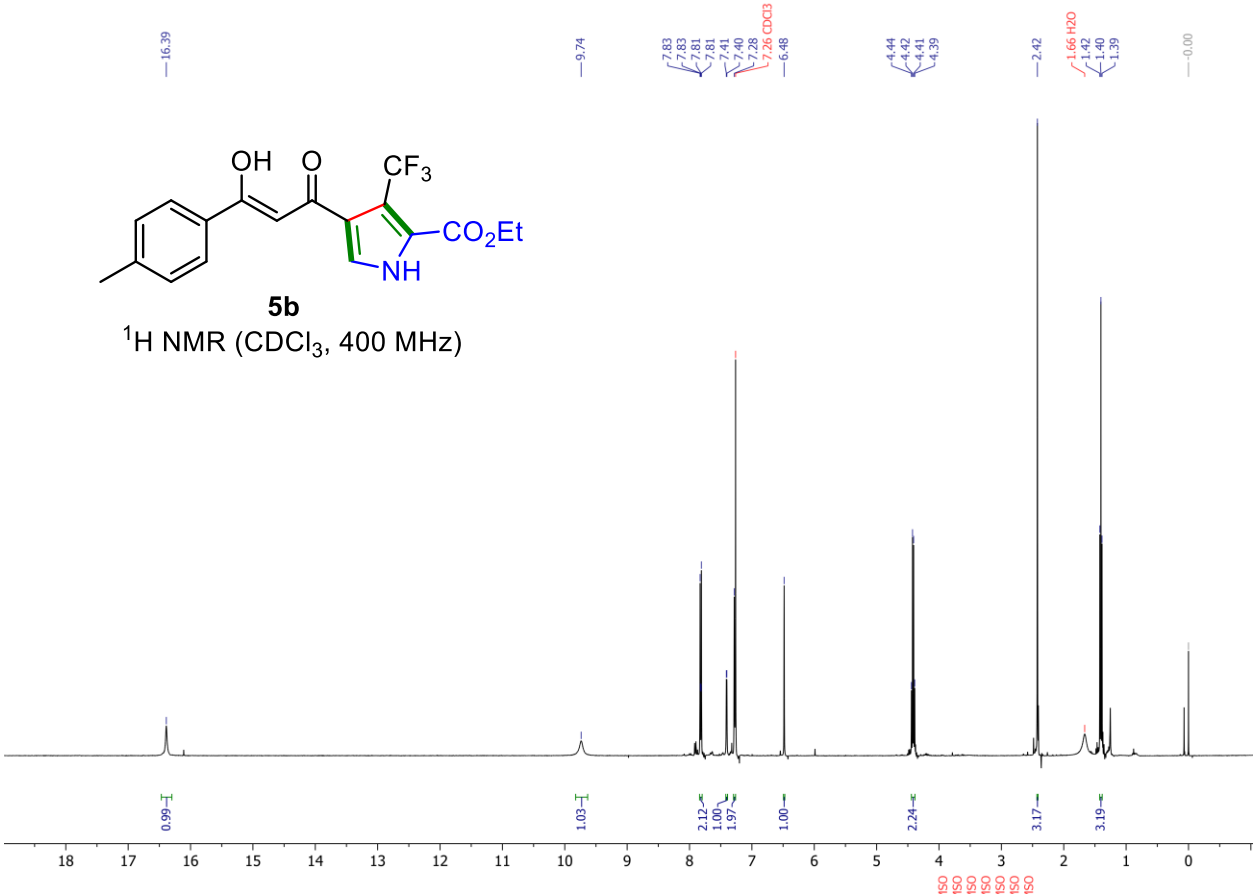
$^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



5a

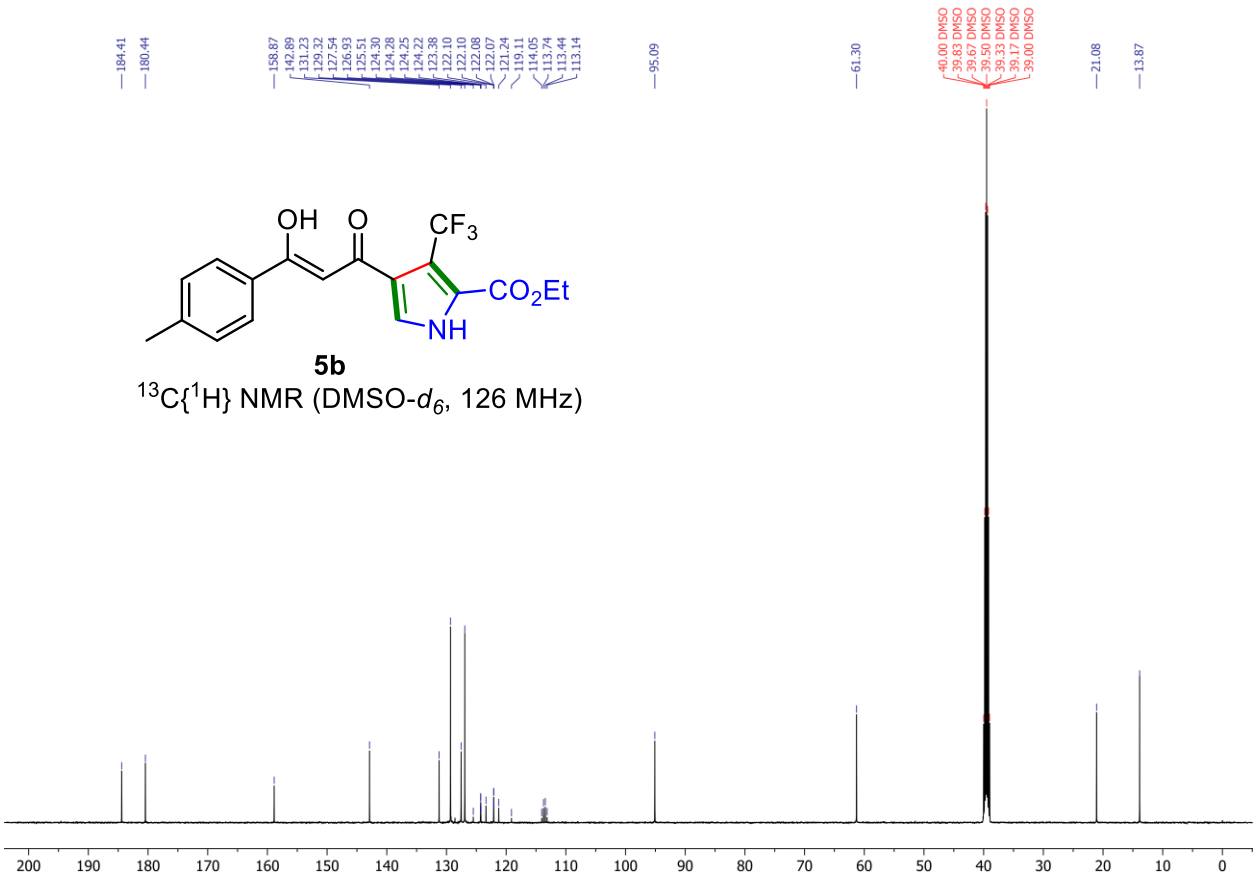
^{19}F NMR ($CDCl_3$, 376 MHz)





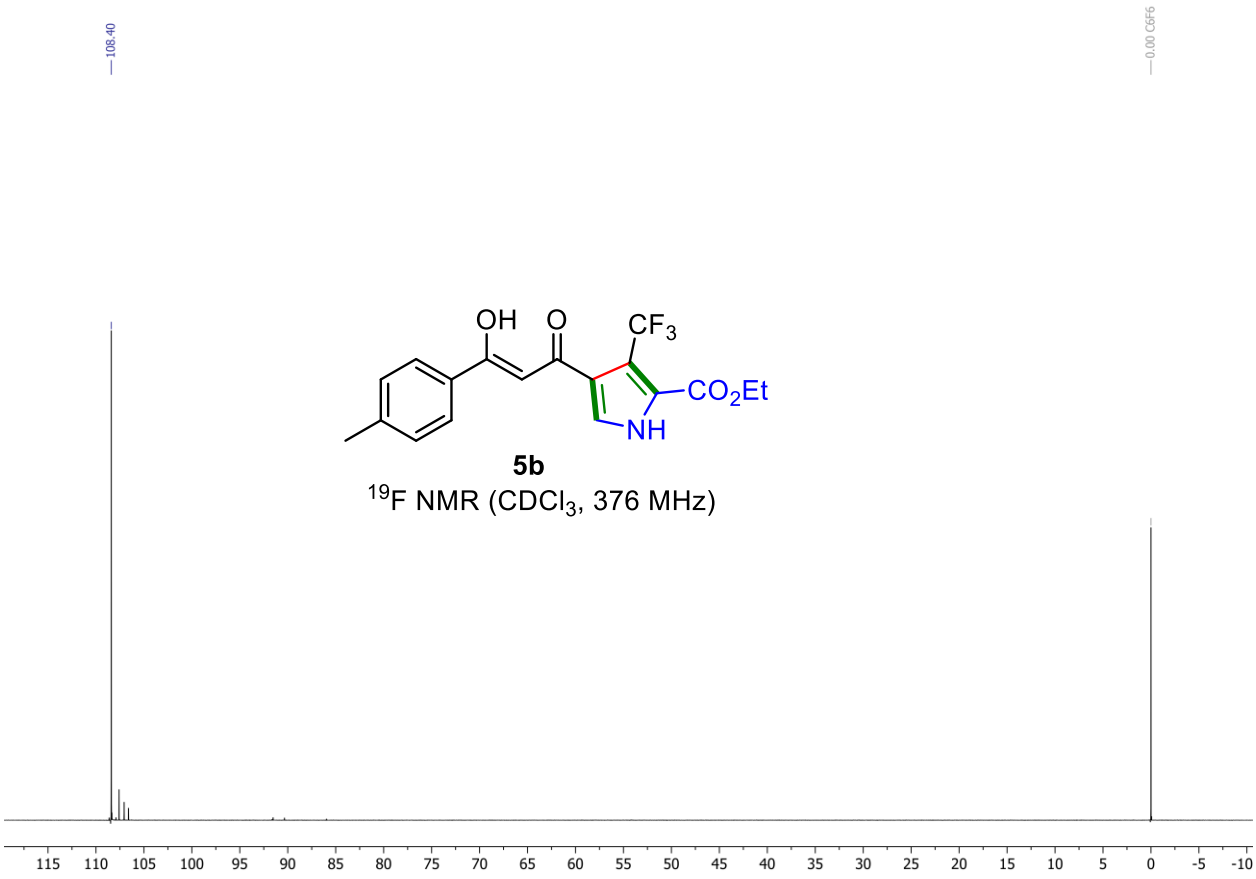
5b

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



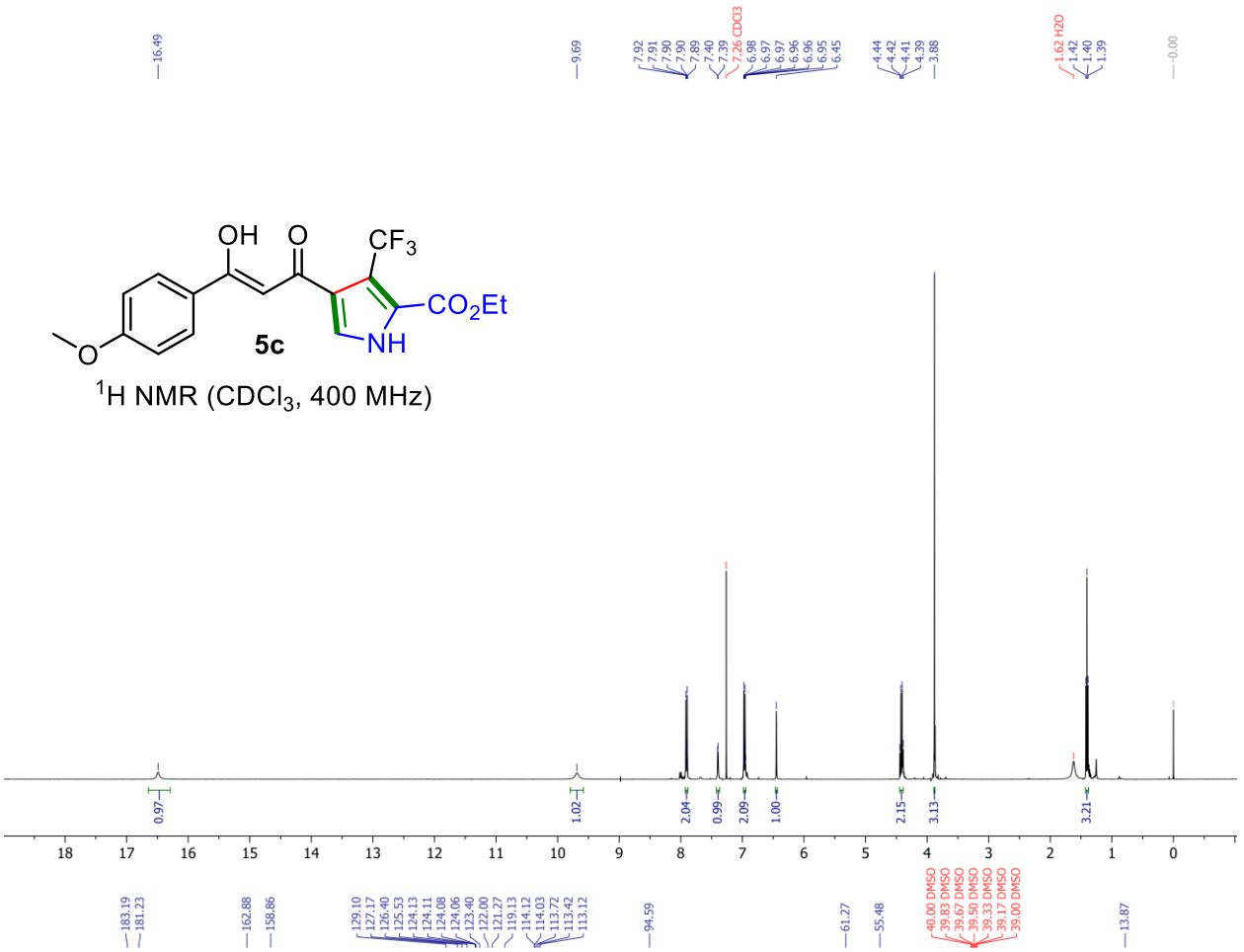
5b

$^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 126 MHz)

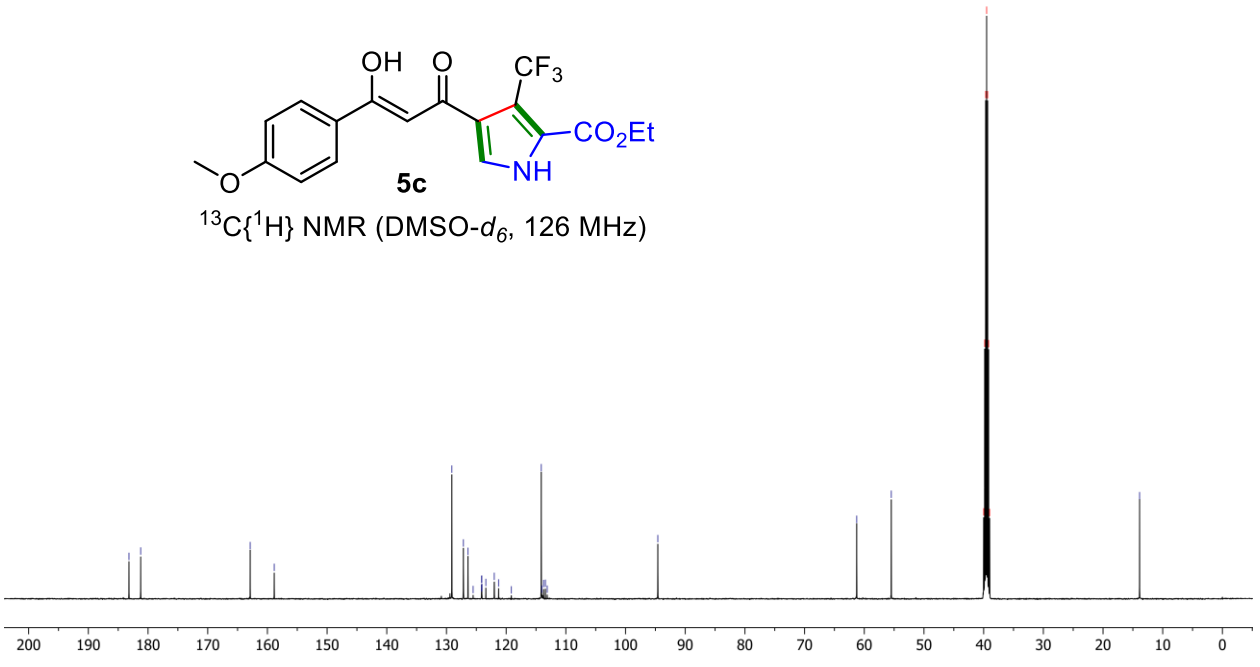


5b

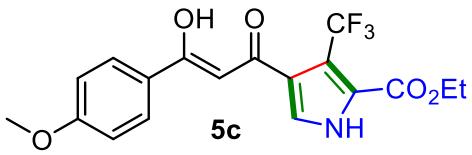
^{19}F NMR ($CDCl_3$, 376 MHz)



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

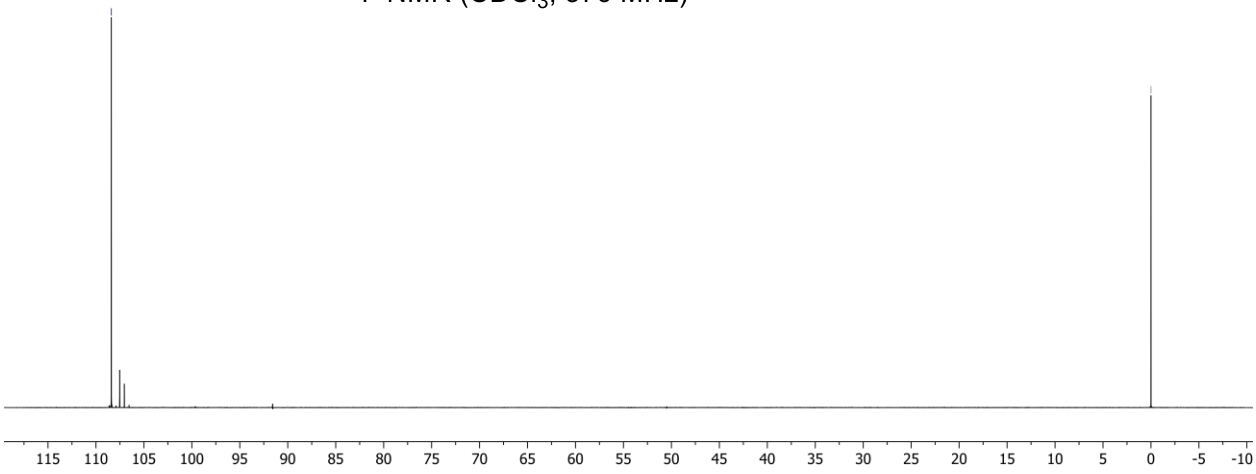


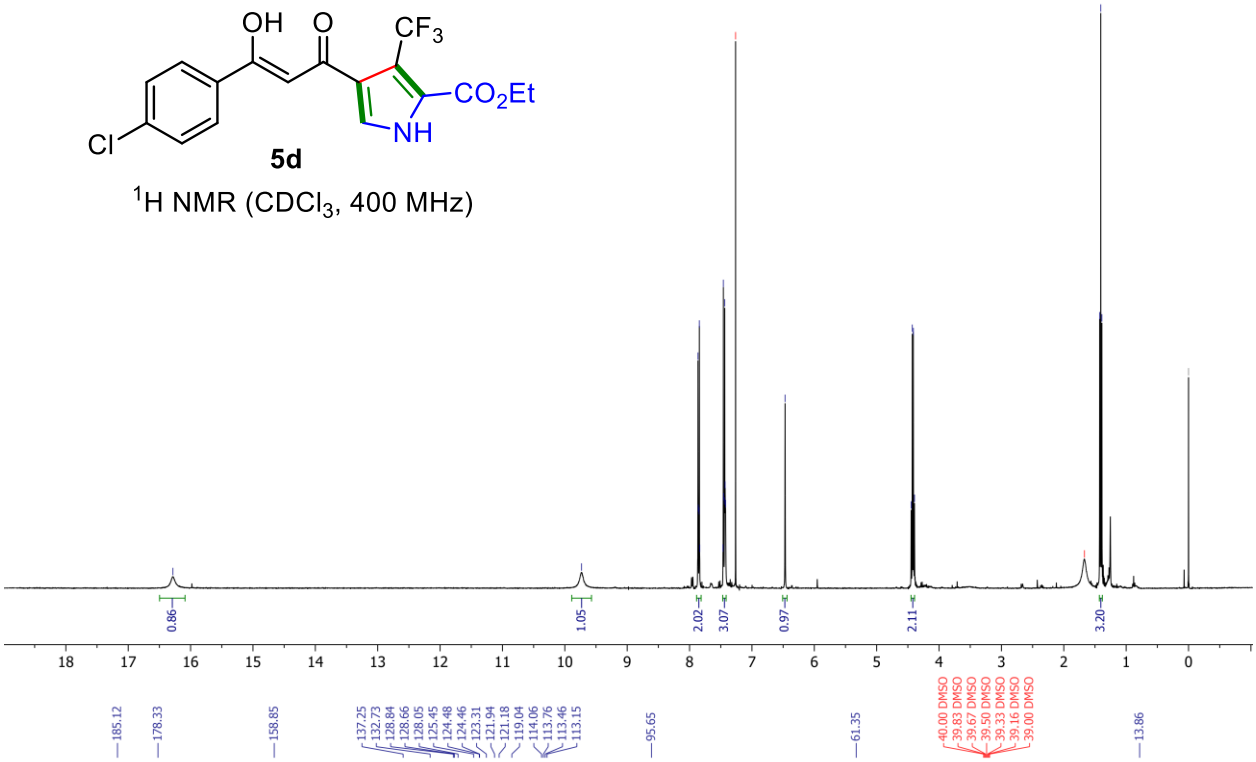
^{13}C{^{1}H} NMR (DMSO-d_6, 126 MHz)



5c

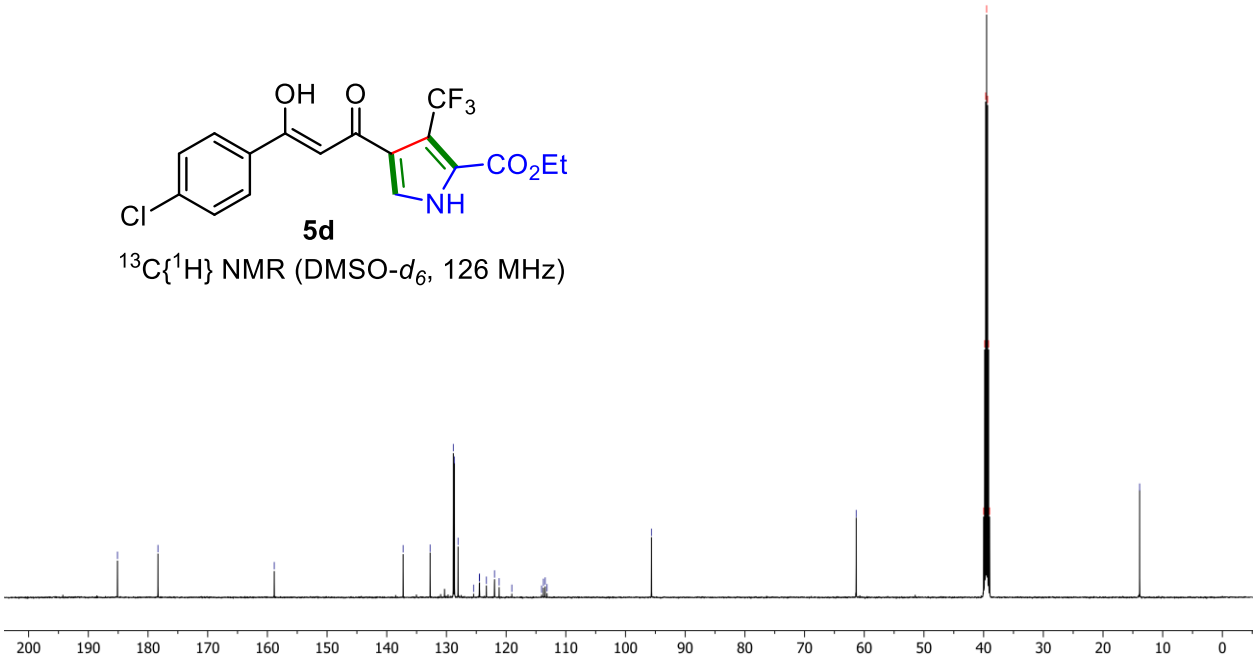
^{19}F NMR ($CDCl_3$, 376 MHz)





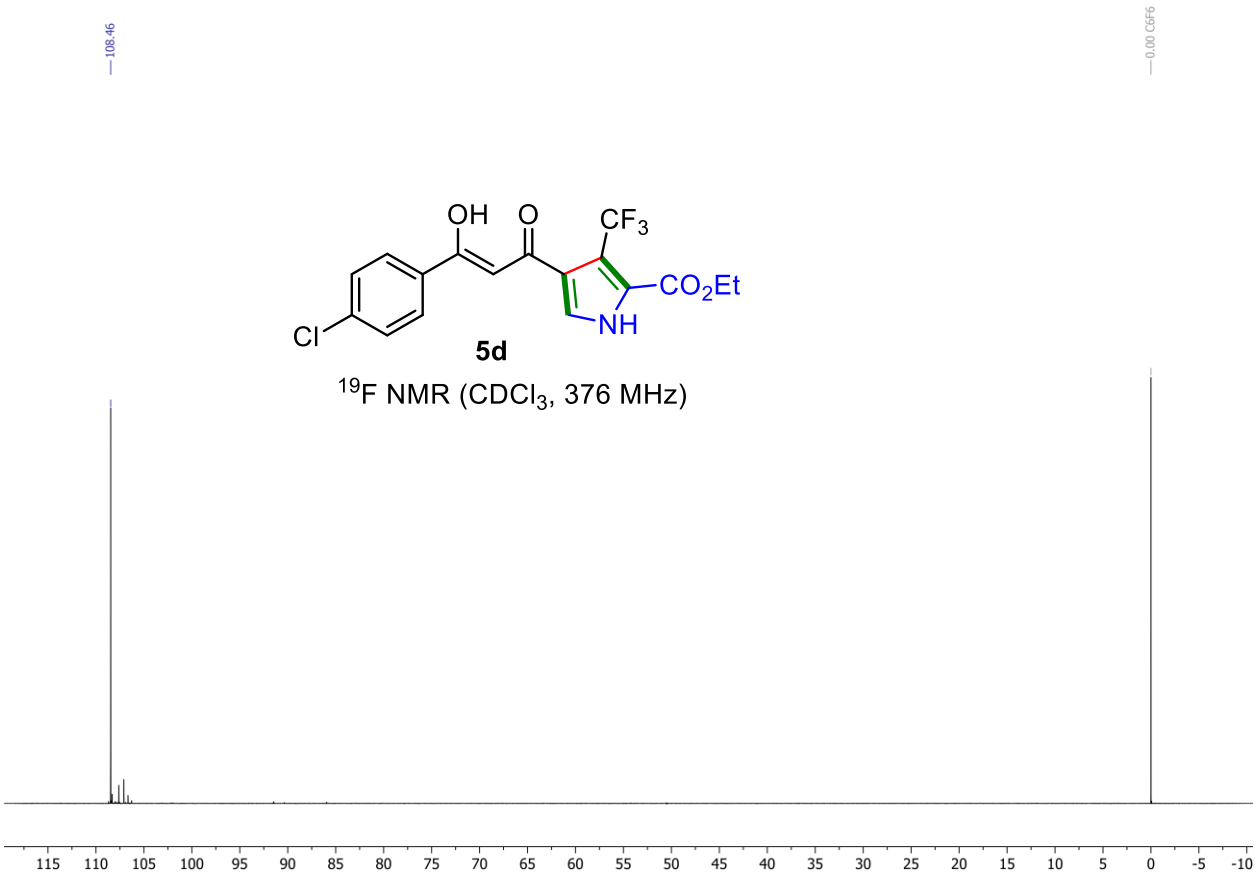
5d

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



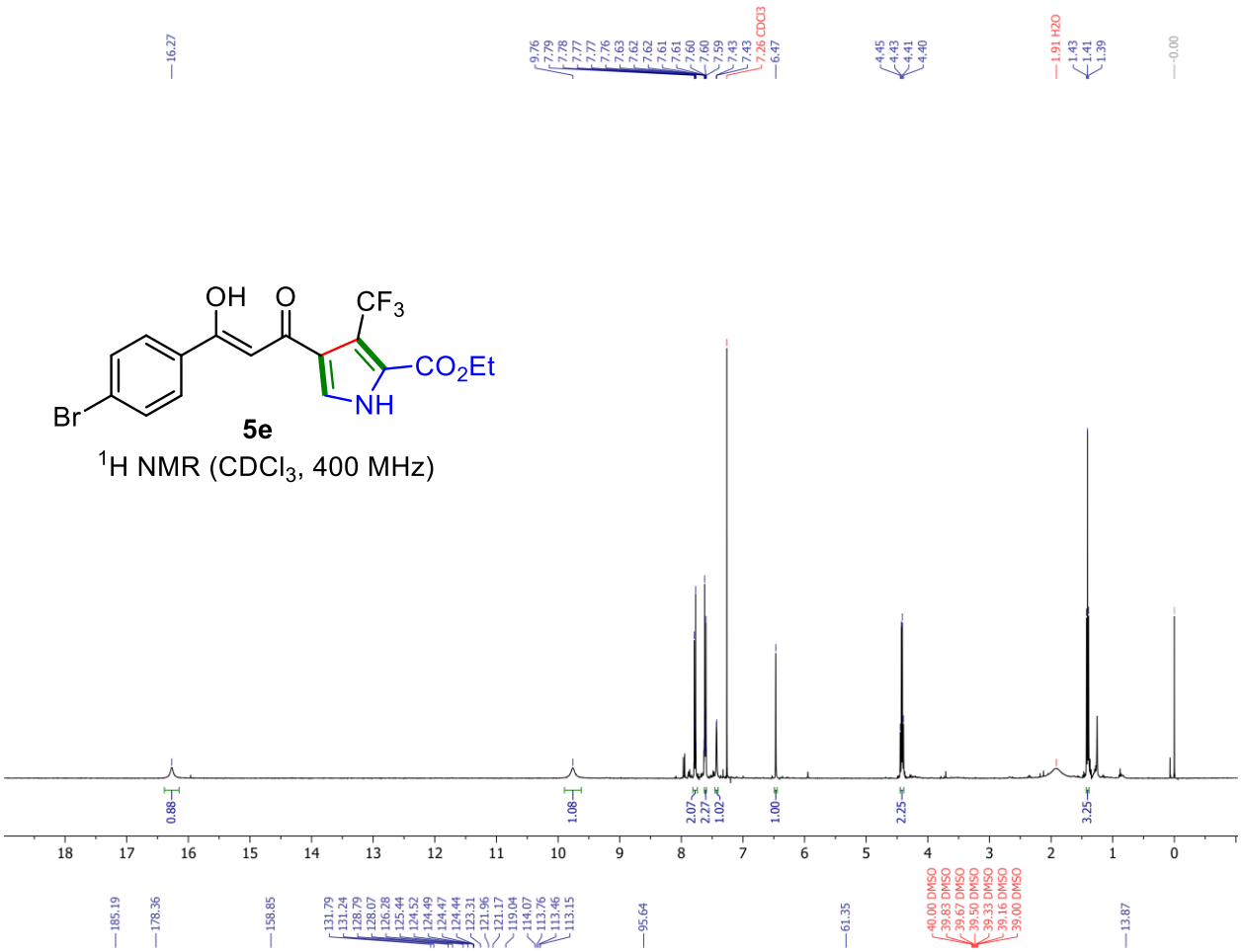
5d

$^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 126 MHz)



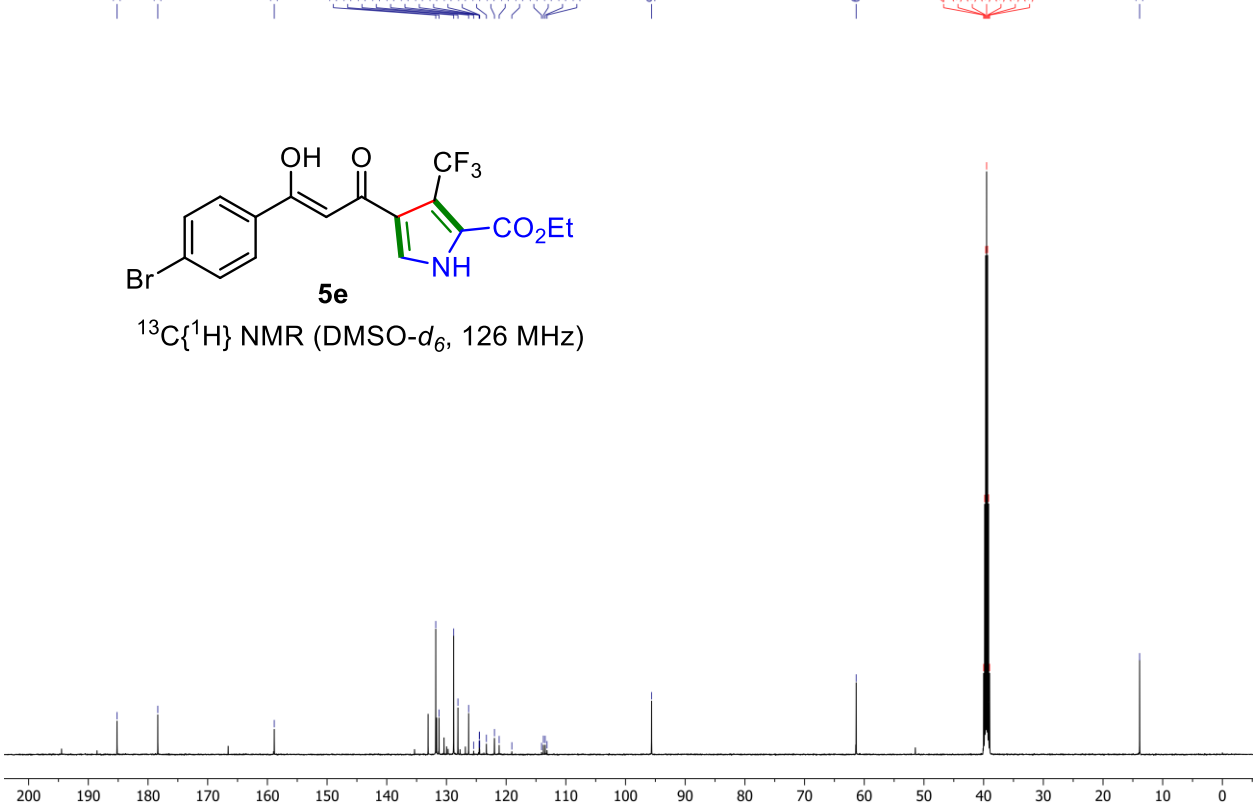
5d

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



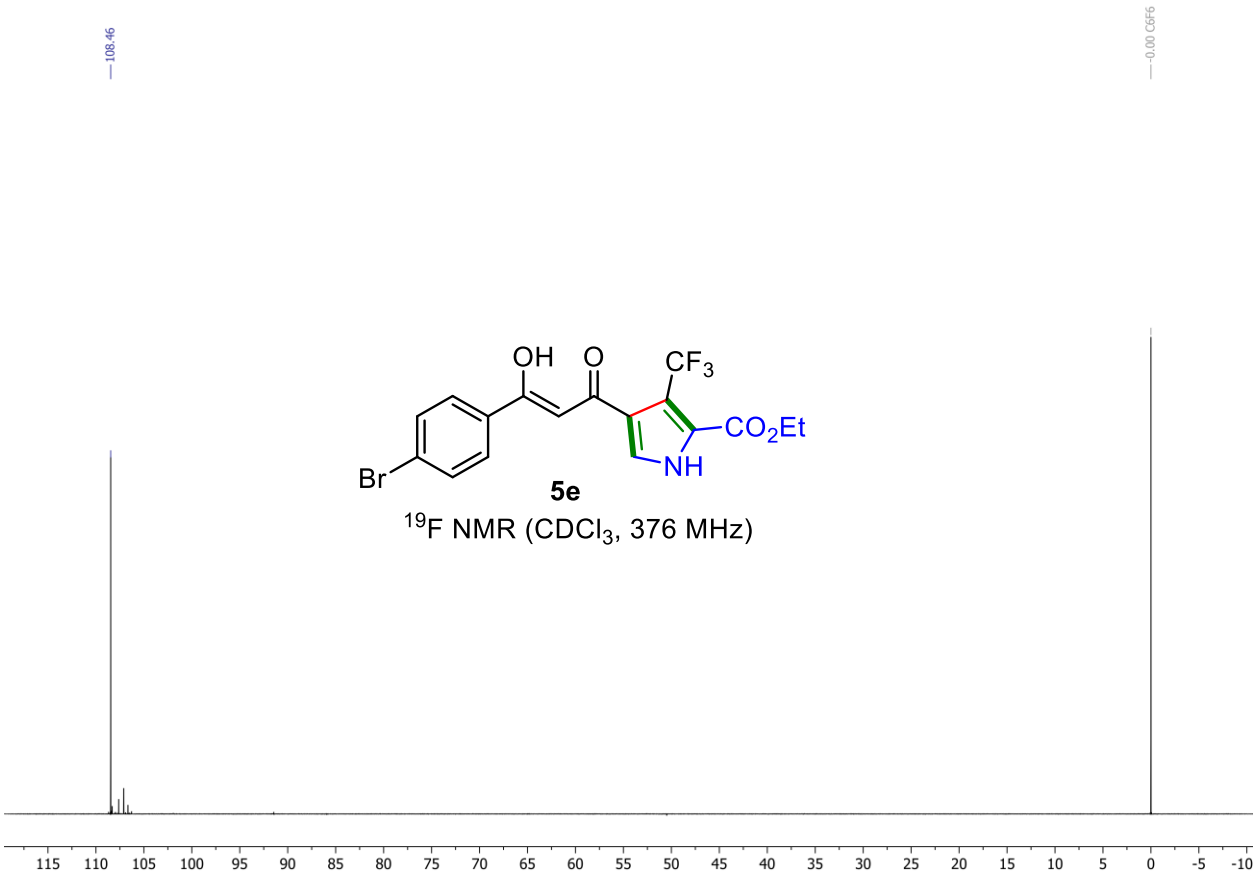
5e

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



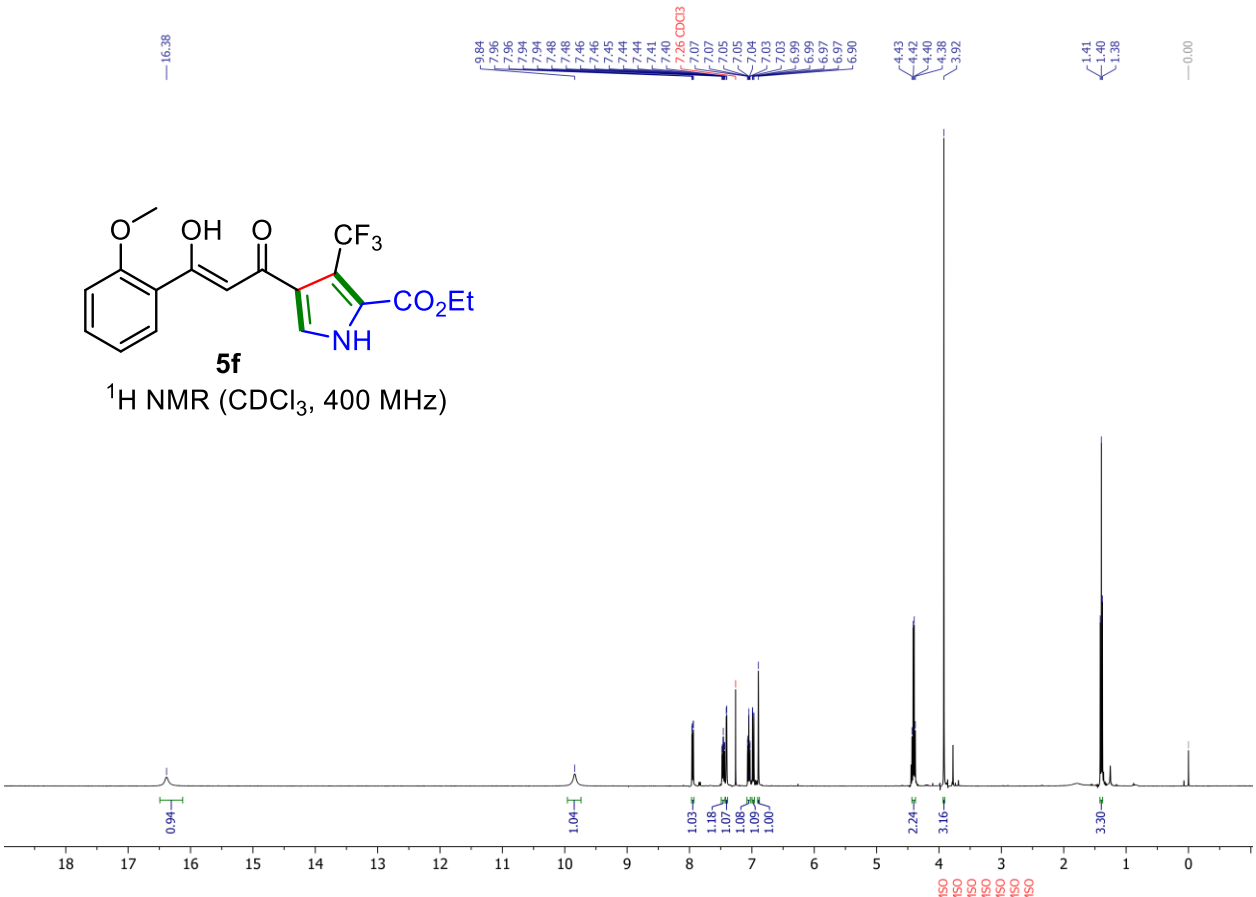
5e

^{13}C{^{1}H} NMR (DMSO-d_6, 126 MHz)



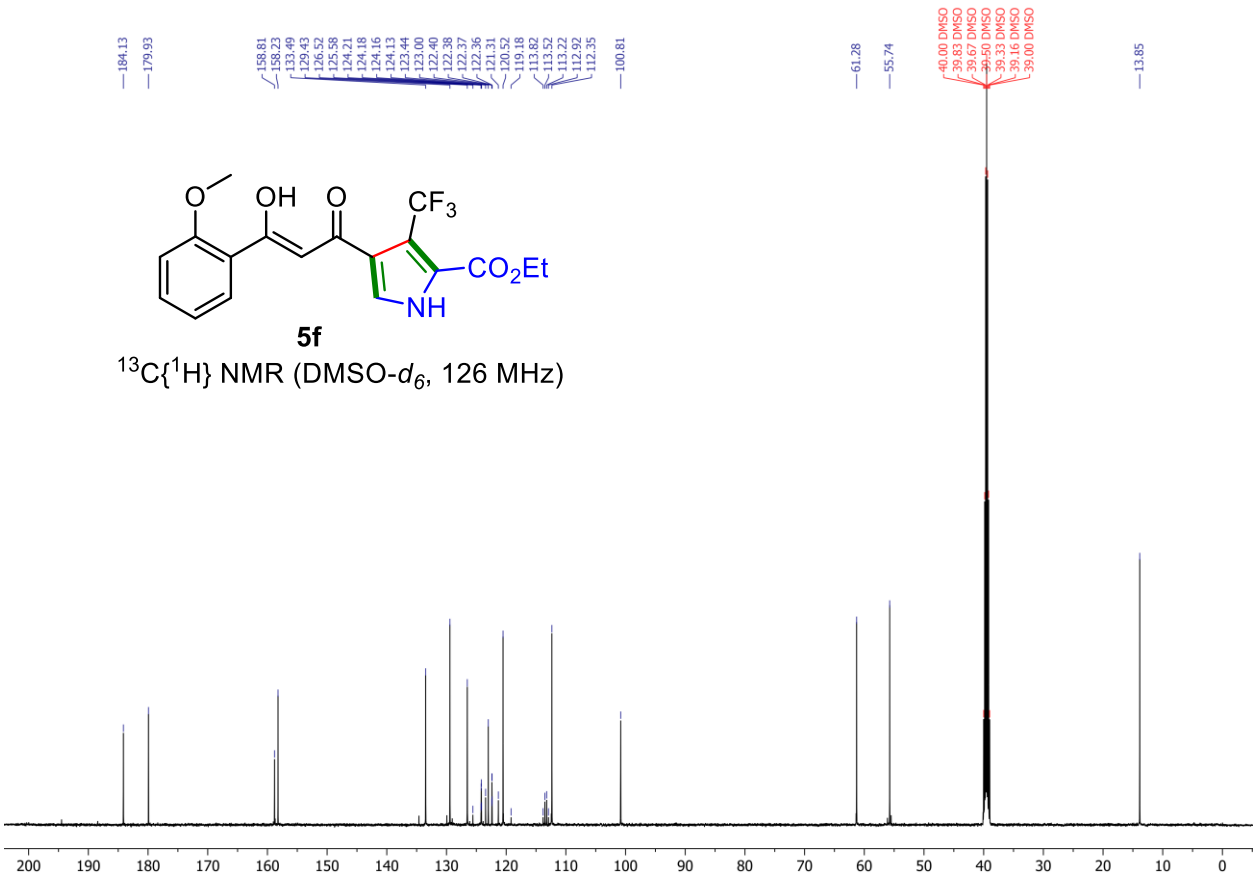
5e

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



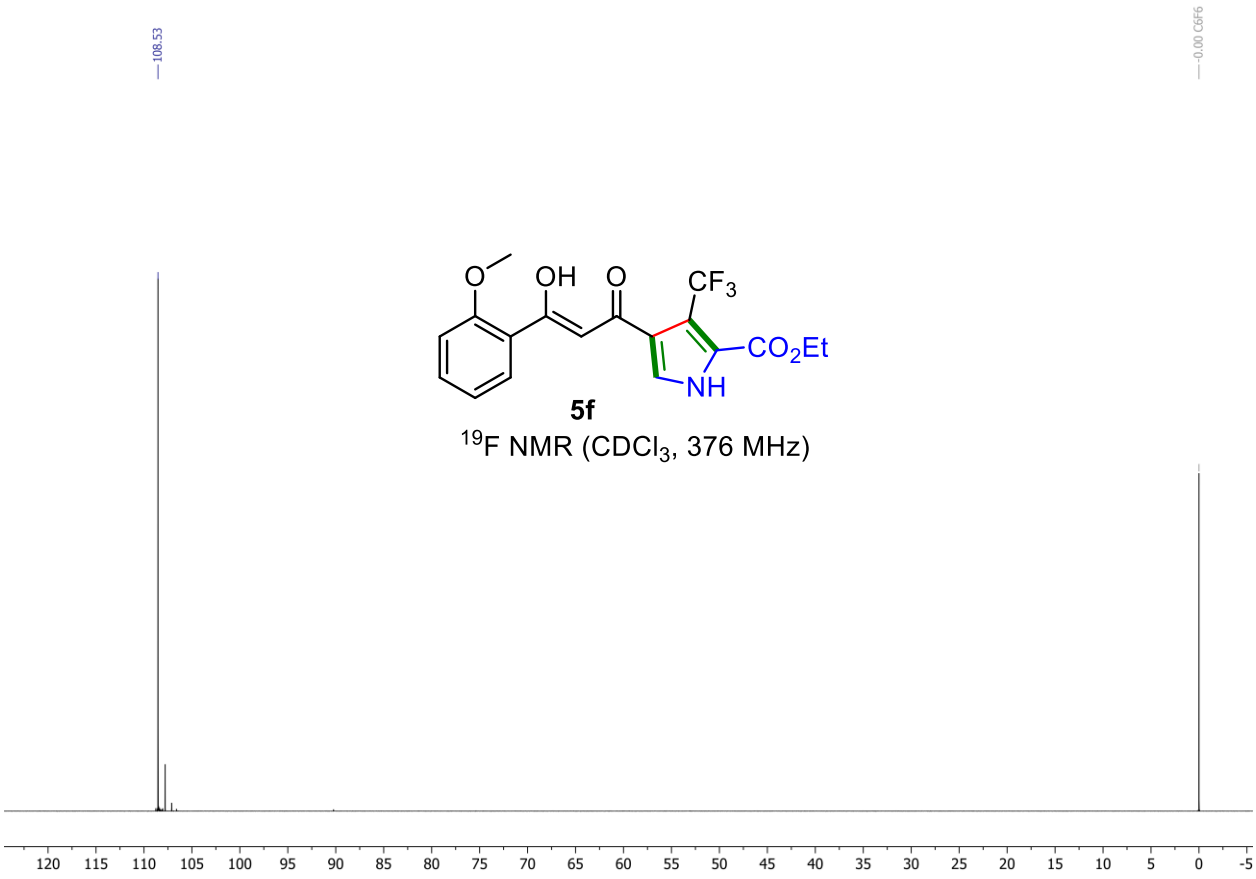
5f

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



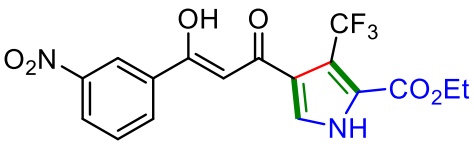
5f

^{13}C{^{1}H} NMR (DMSO-d_6, 126 MHz)



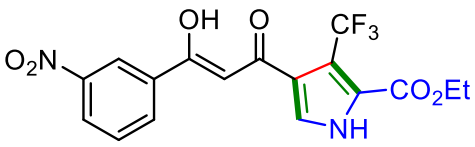
5f

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



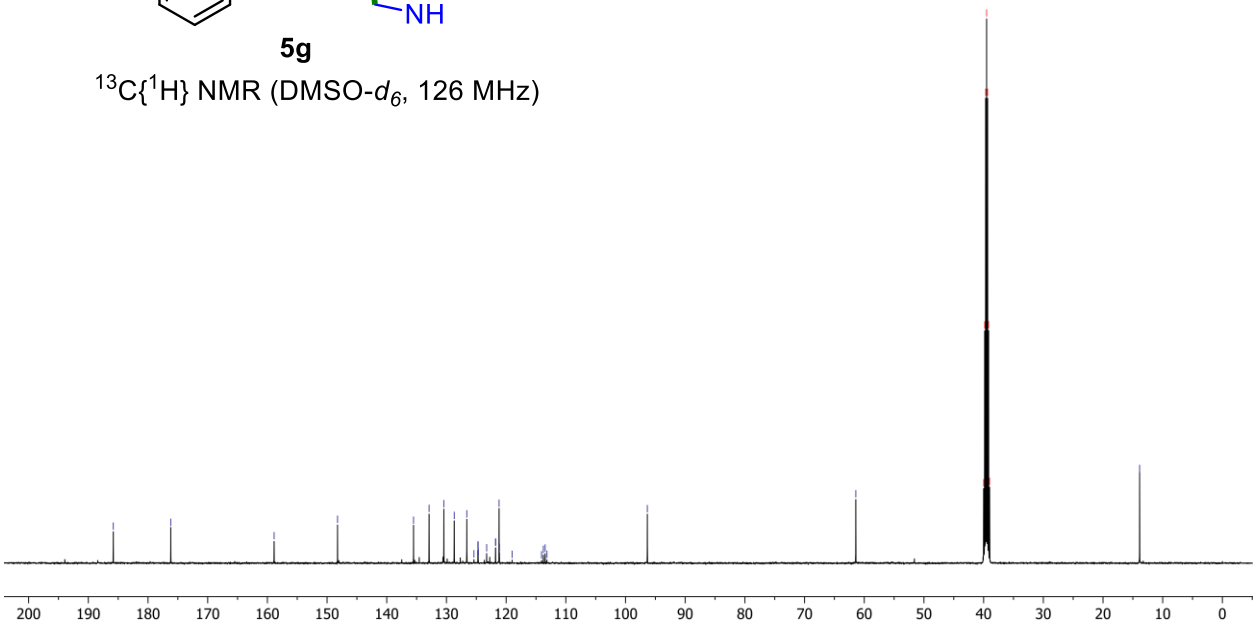
5g

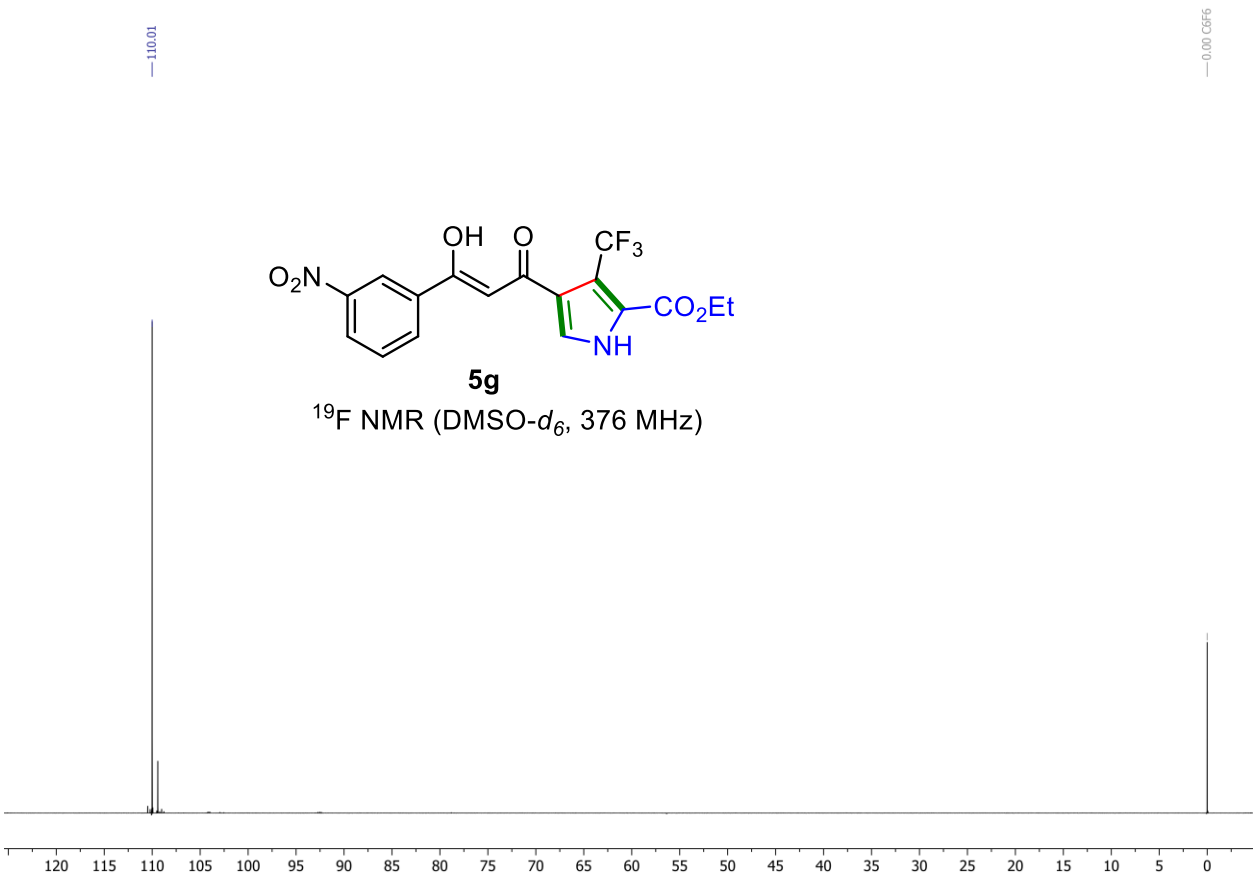
^{1}H NMR (DMSO-d_6, 400 MHz)



5g

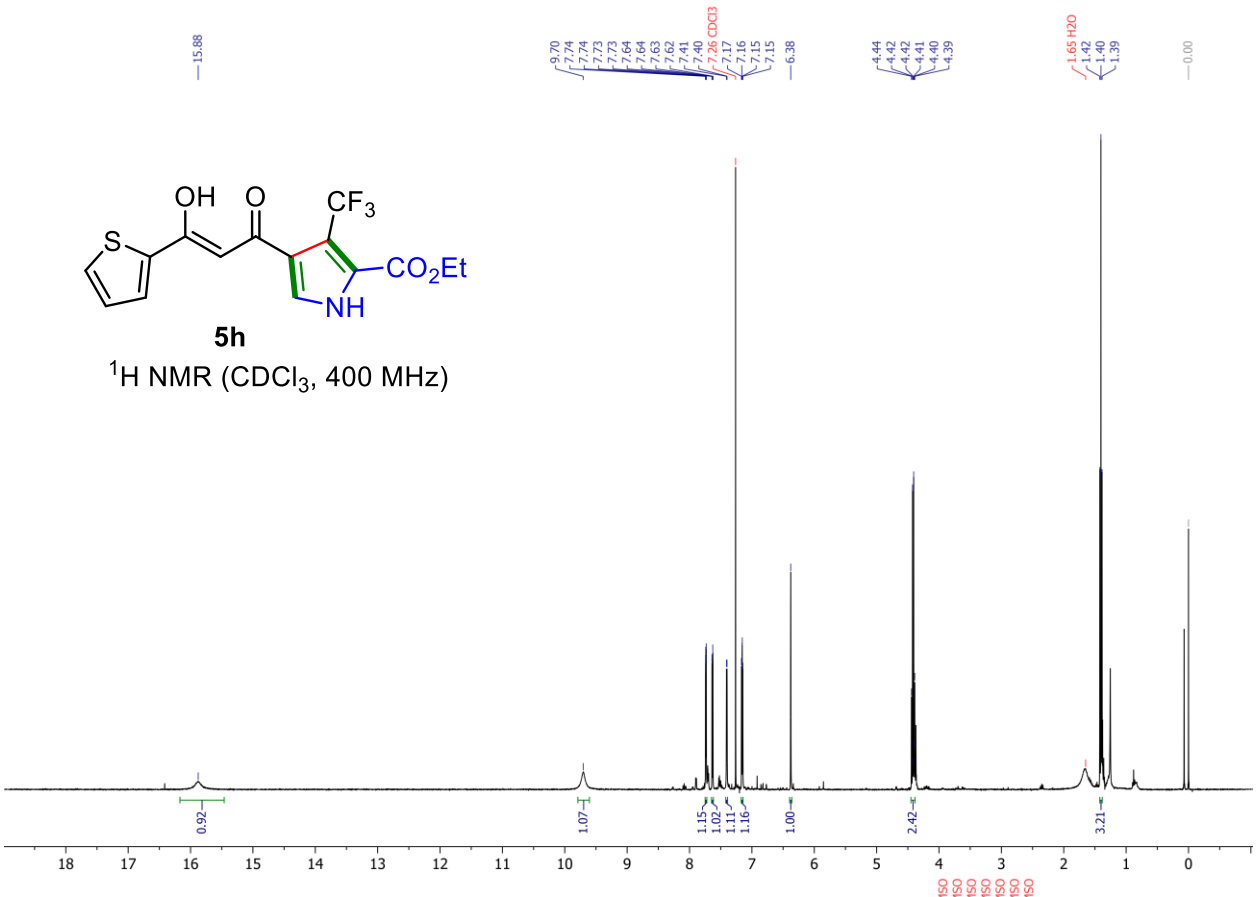
^{13}C{^{1}H} NMR (DMSO-d_6, 126 MHz)





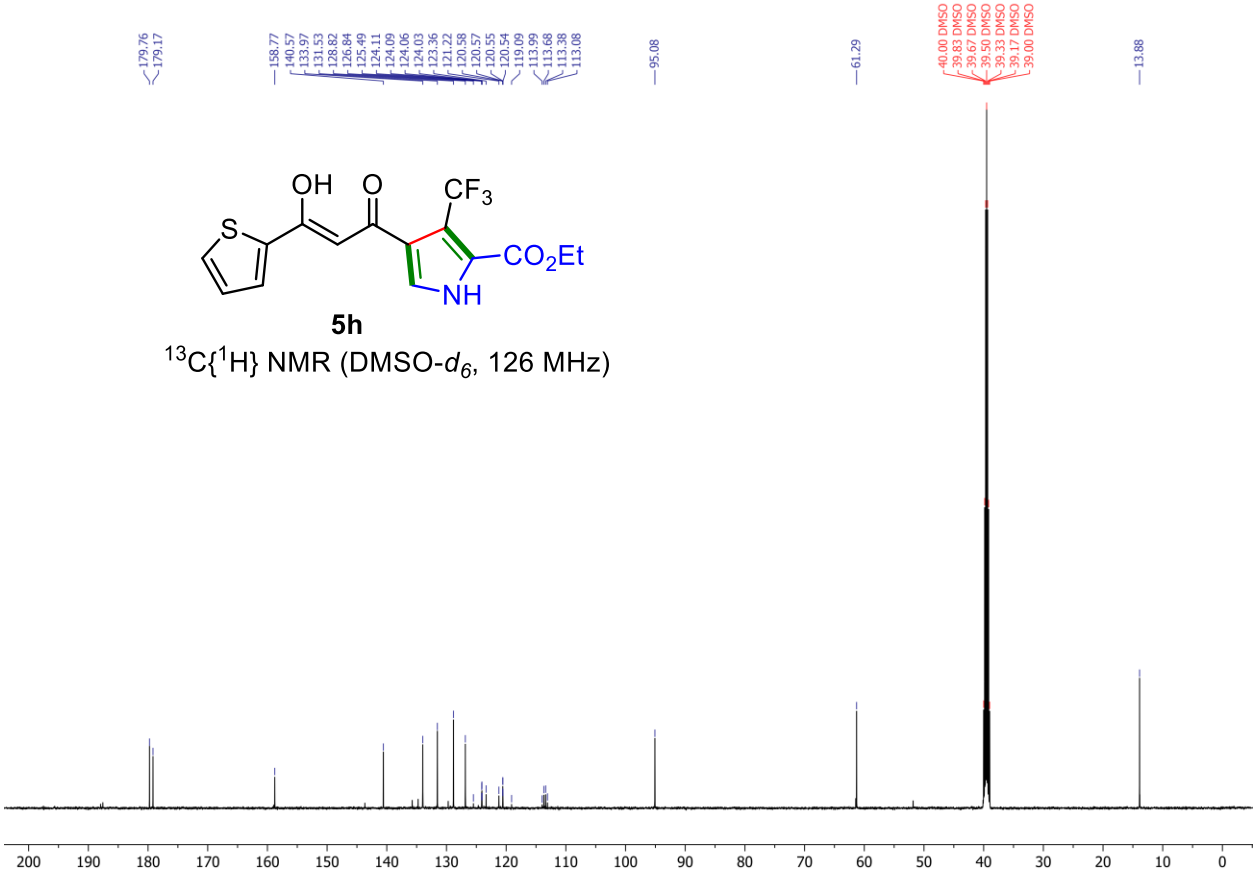
5g

^{19}F NMR (DMSO-d_6, 376 MHz)



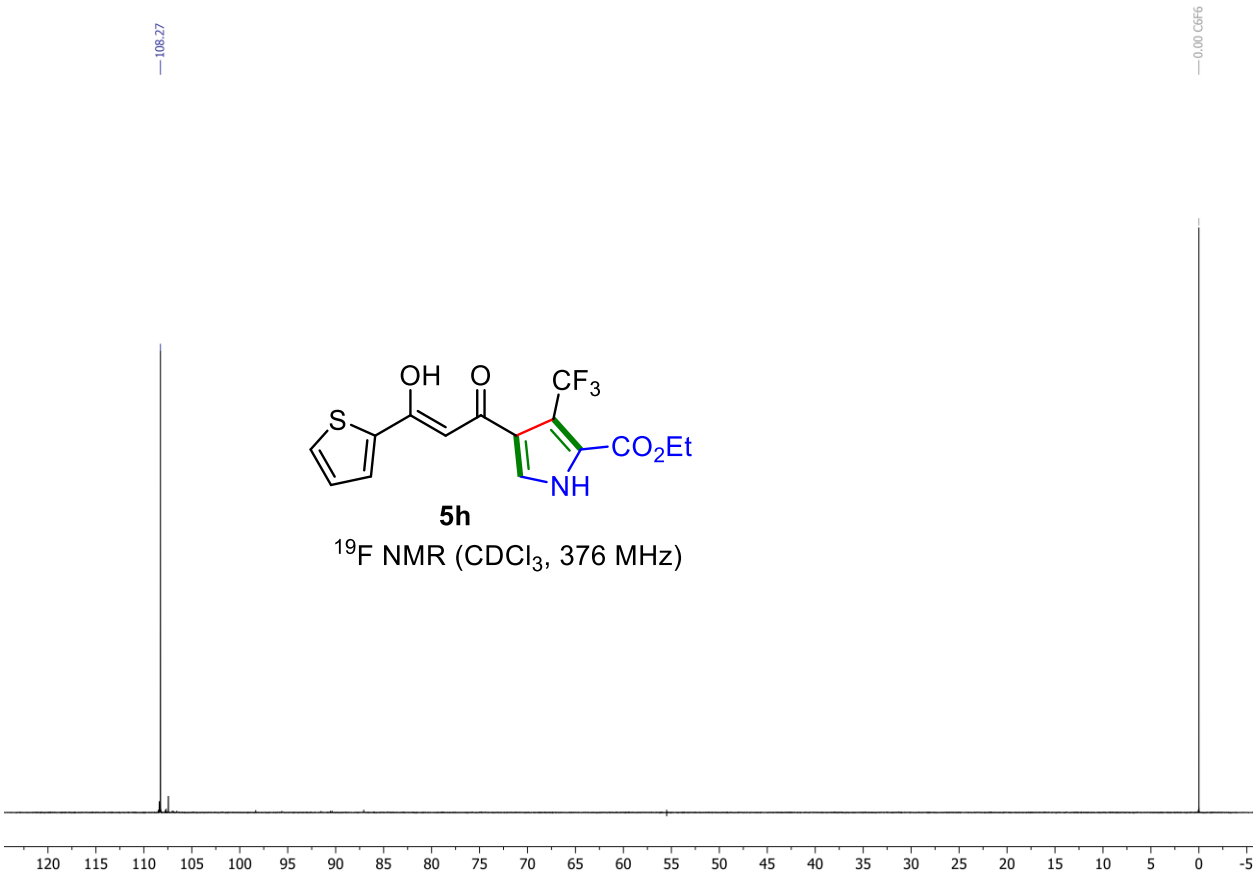
5h

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



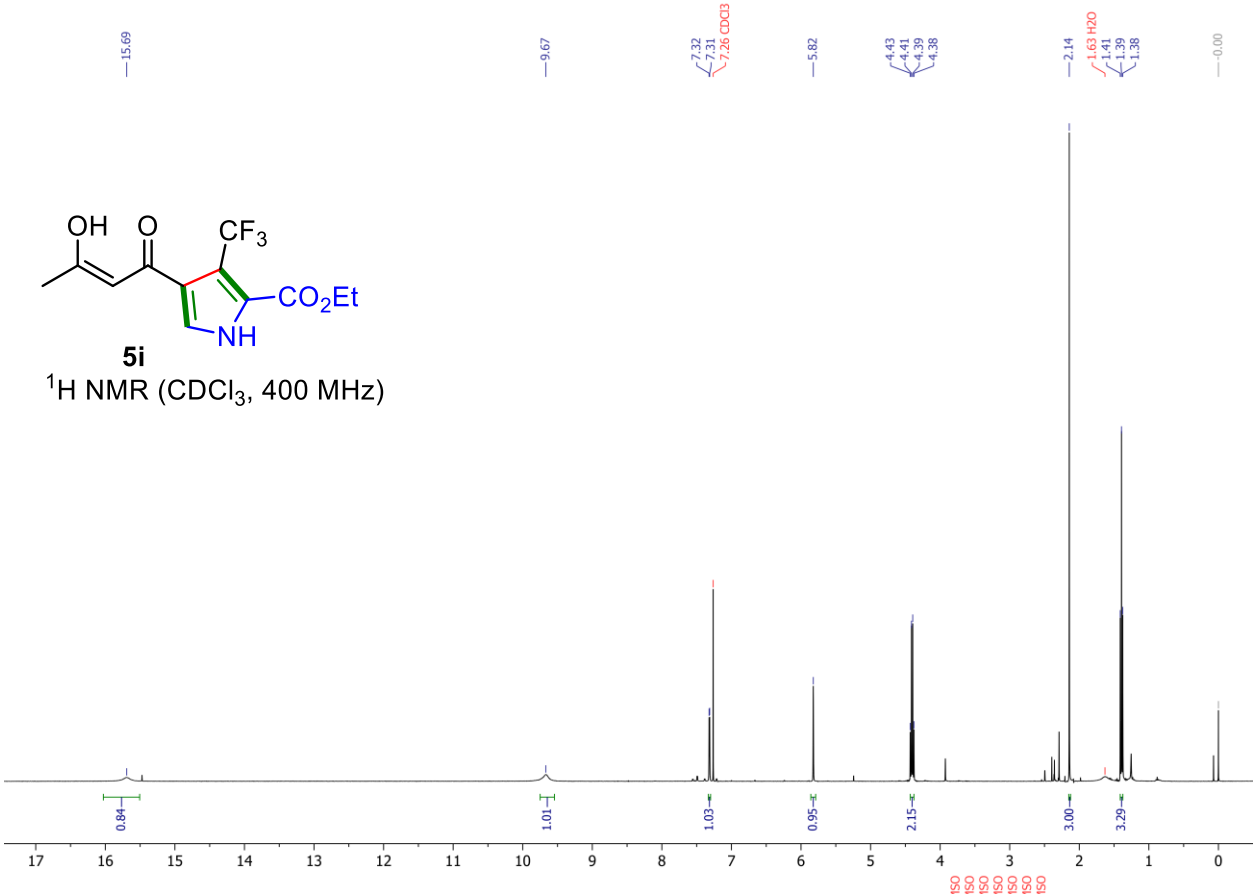
5h

$^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 126 MHz)



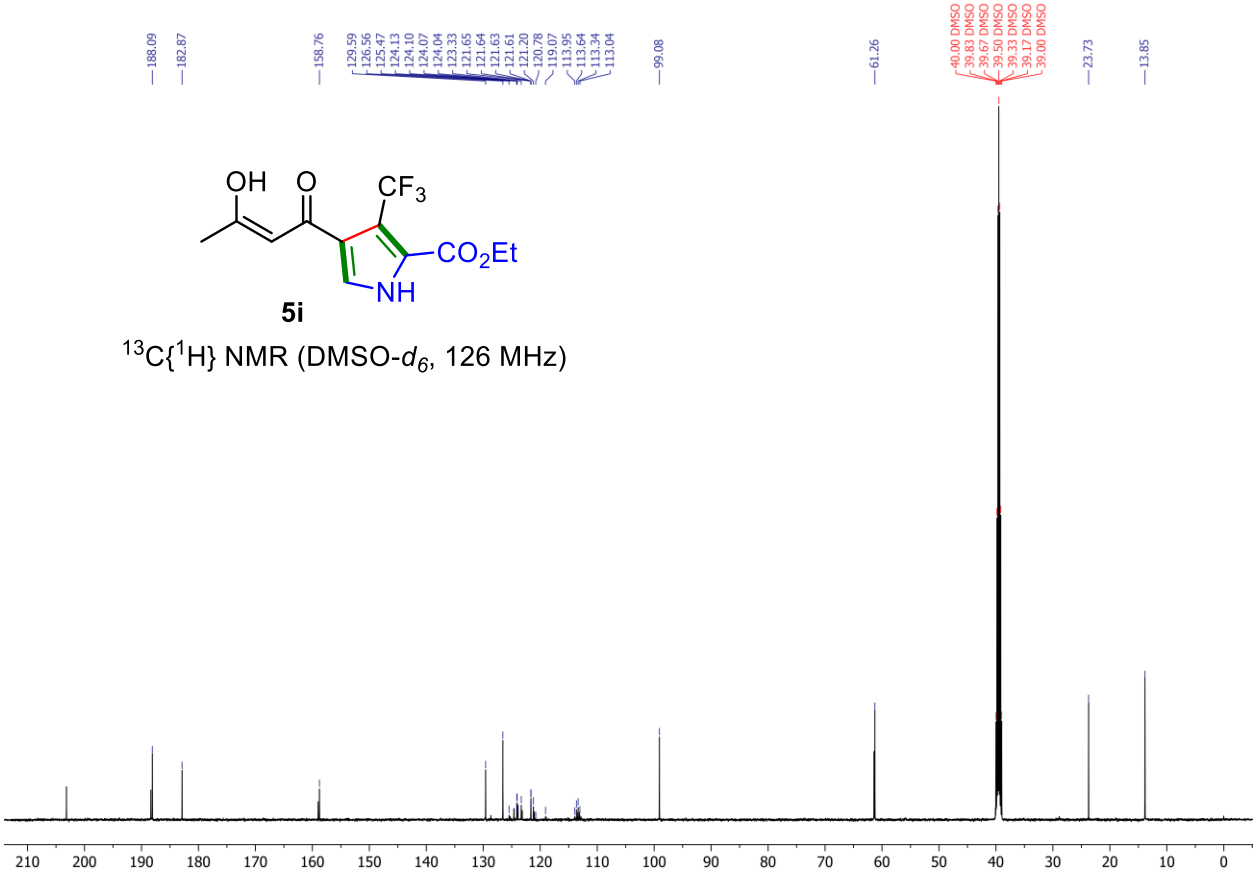
5h

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



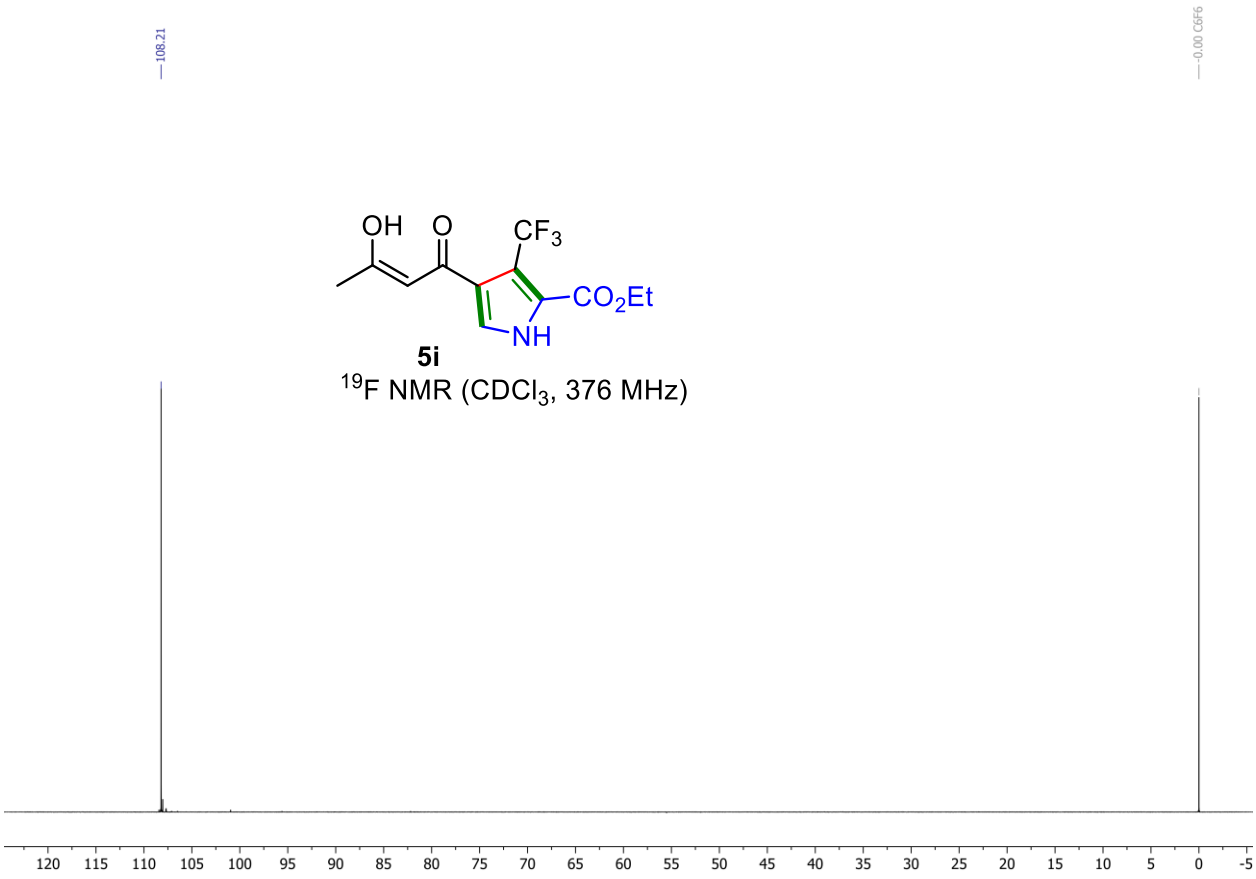
5i

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



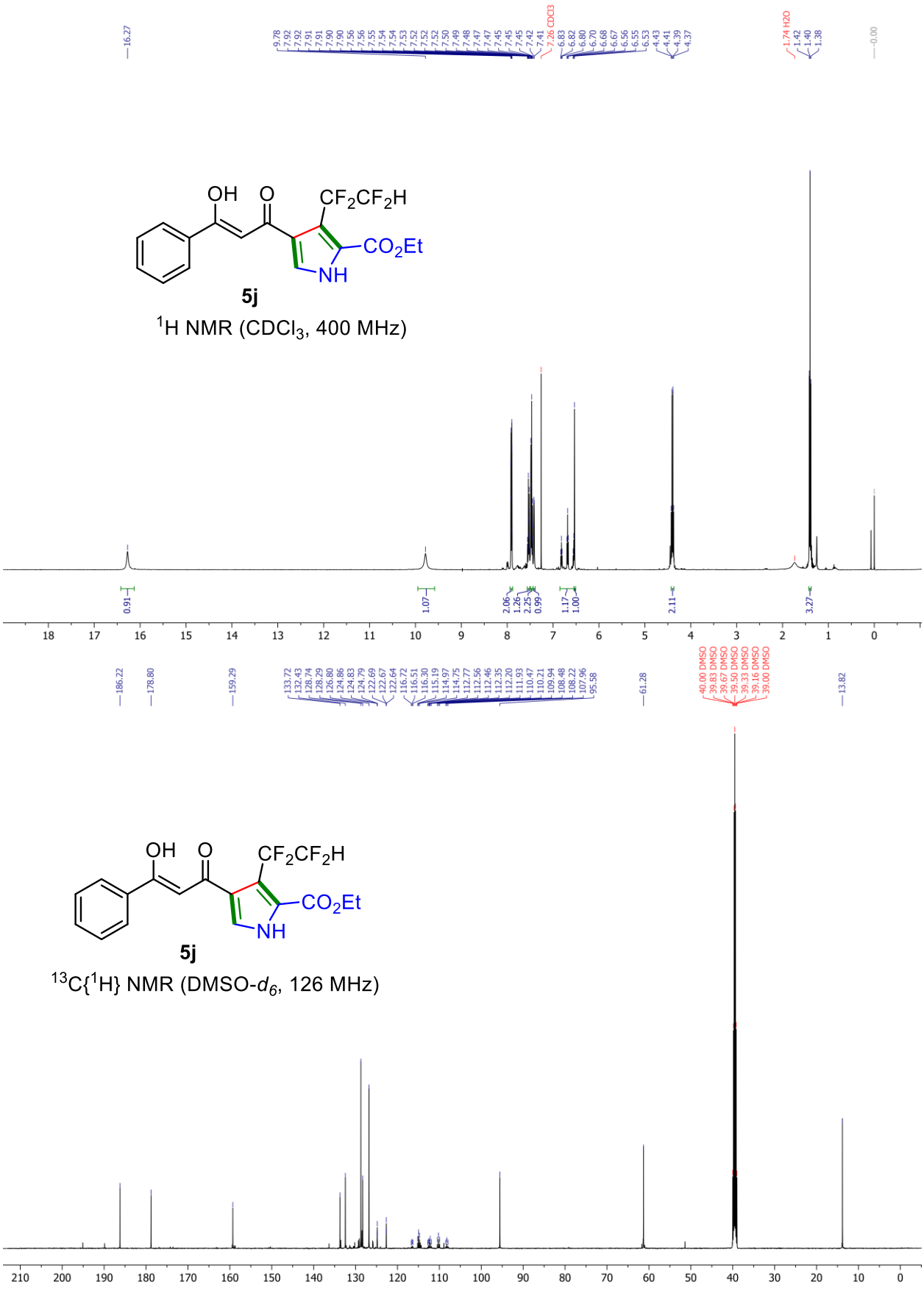
5i

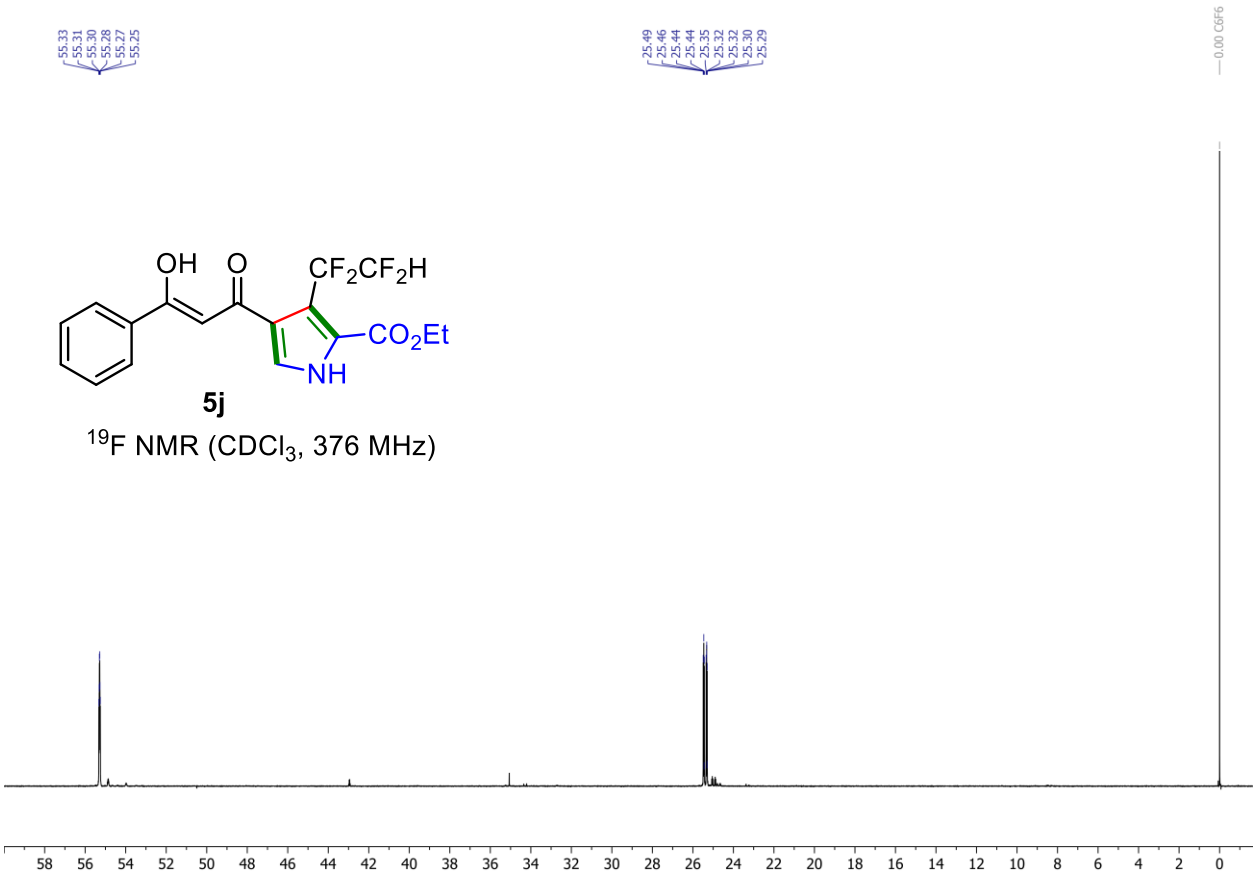
^{13}C{^{1}H} NMR (DMSO-d_6, 126 MHz)



5i

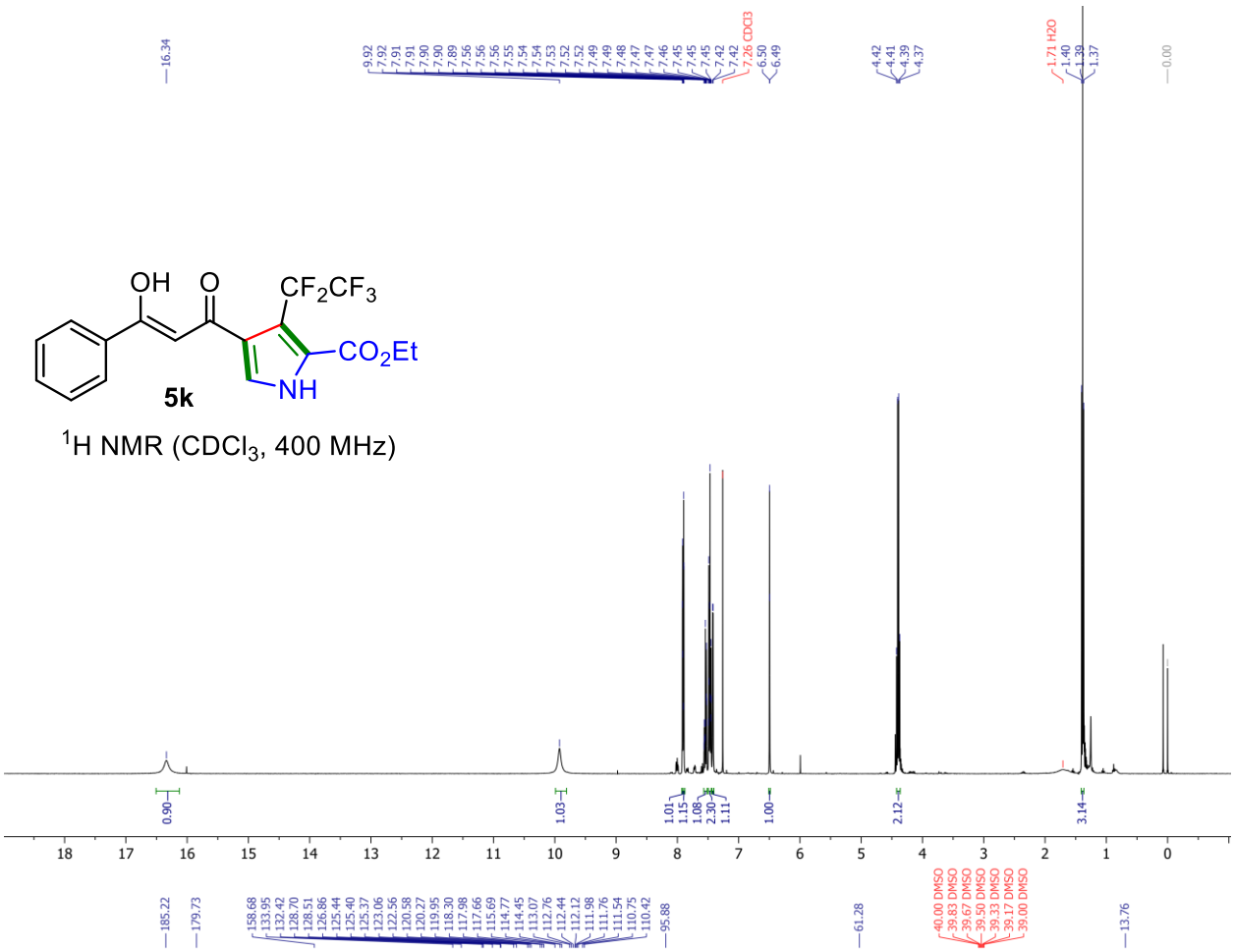
^{19}F NMR ($CDCl_3$, 376 MHz)


OH
O
CF2CF2H
CO2Et
NH
5j
1H NMR (CDCl3, 400 MHz)
13C{1H} NMR (DMSO-d6, 126 MHz)

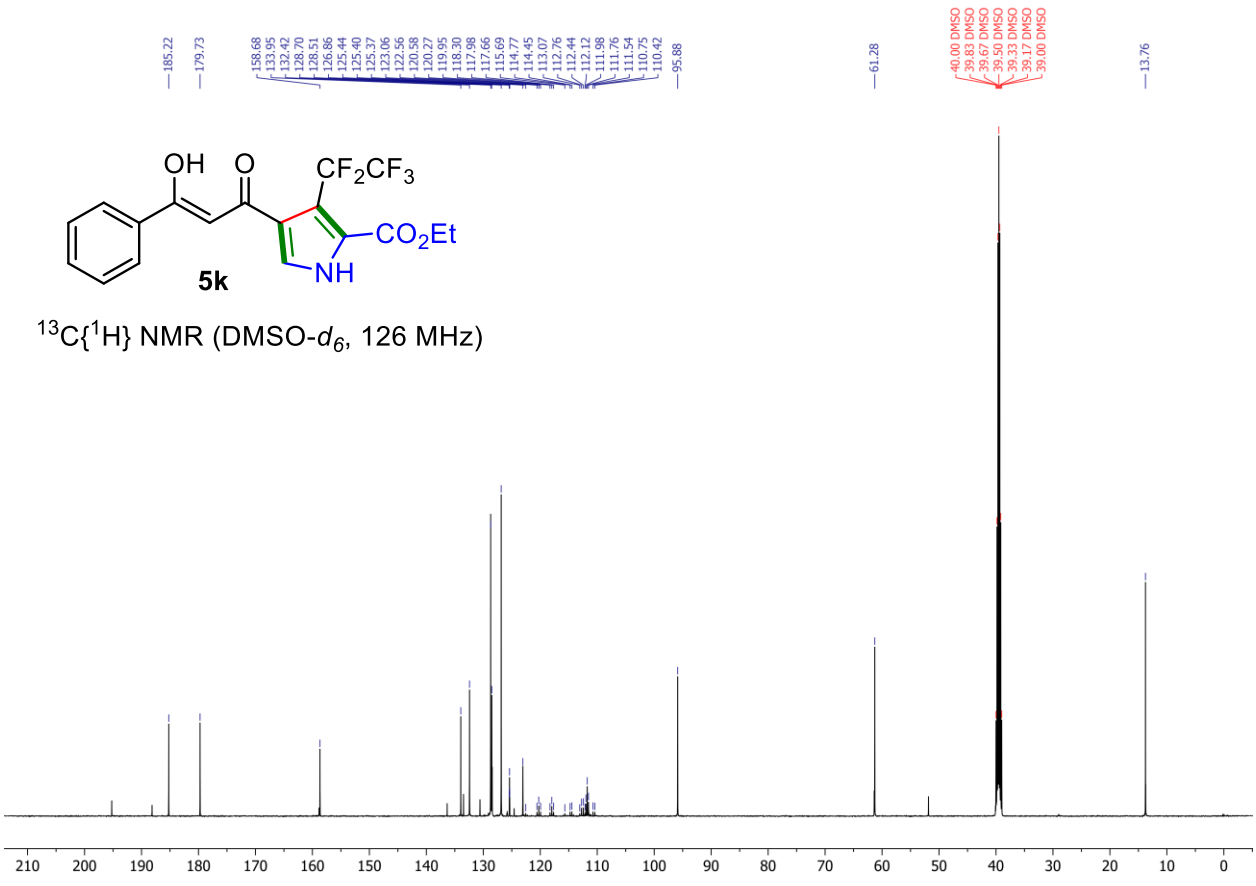


5j

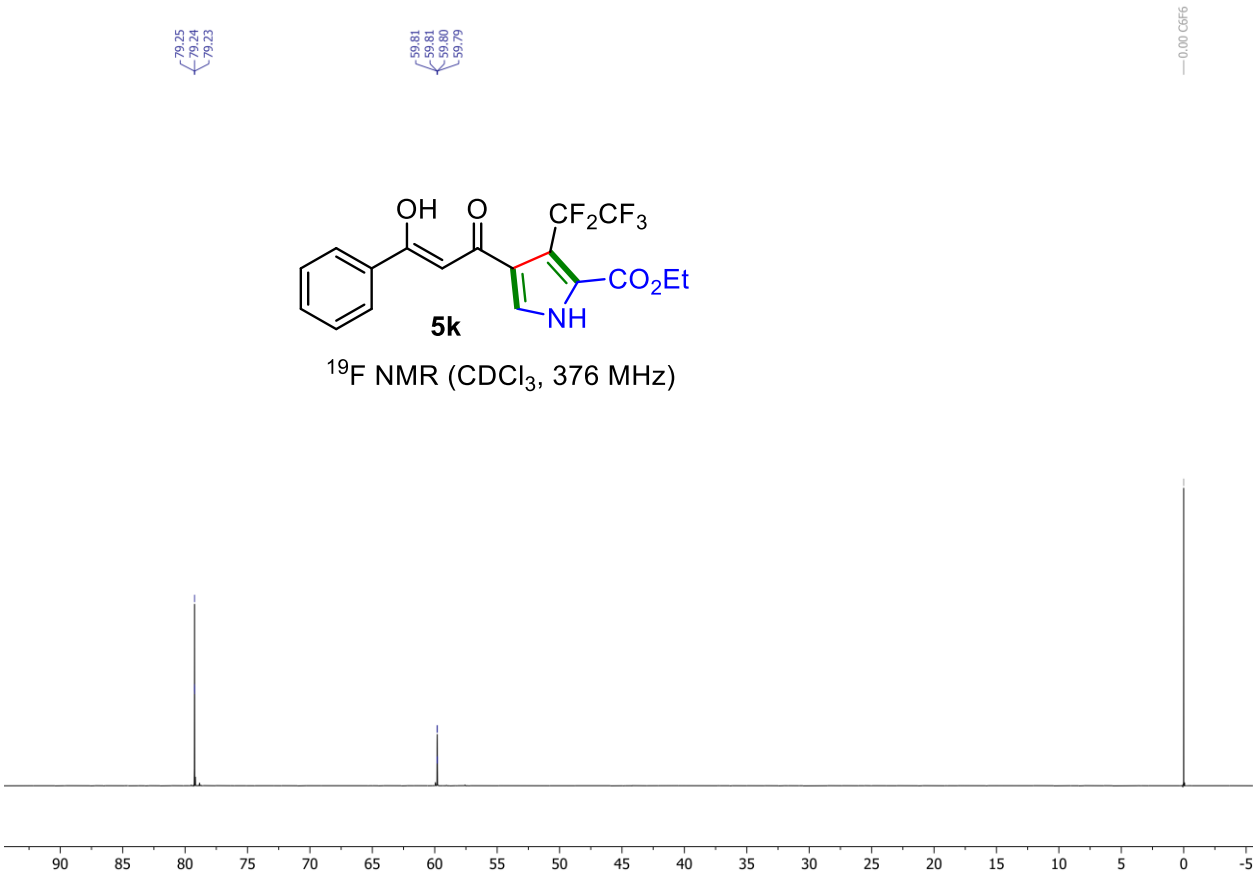
^{19}F NMR ($CDCl_3$, 376 MHz)



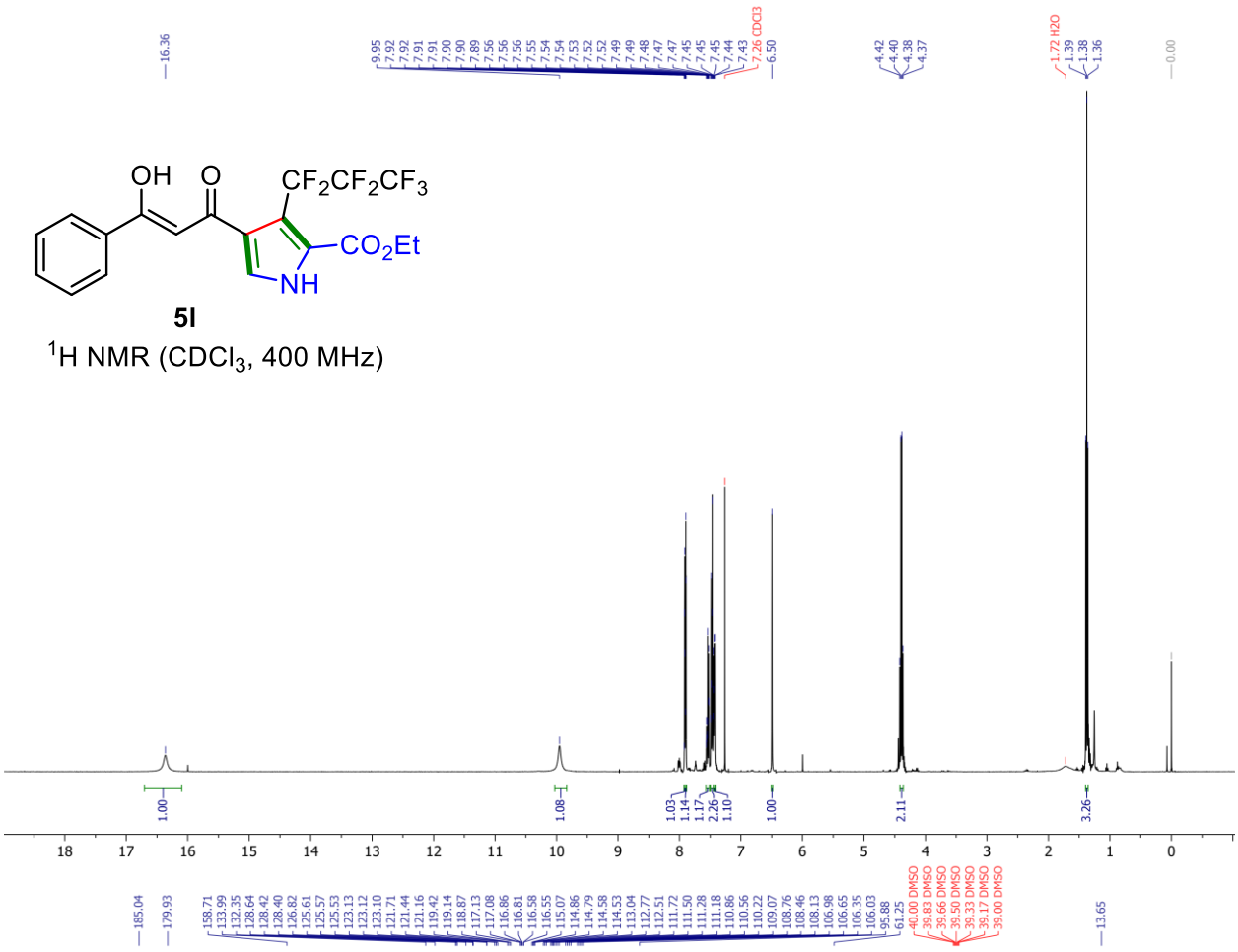
^{1}H NMR ($CDCl_3$, 400 MHz)



$^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 126 MHz)

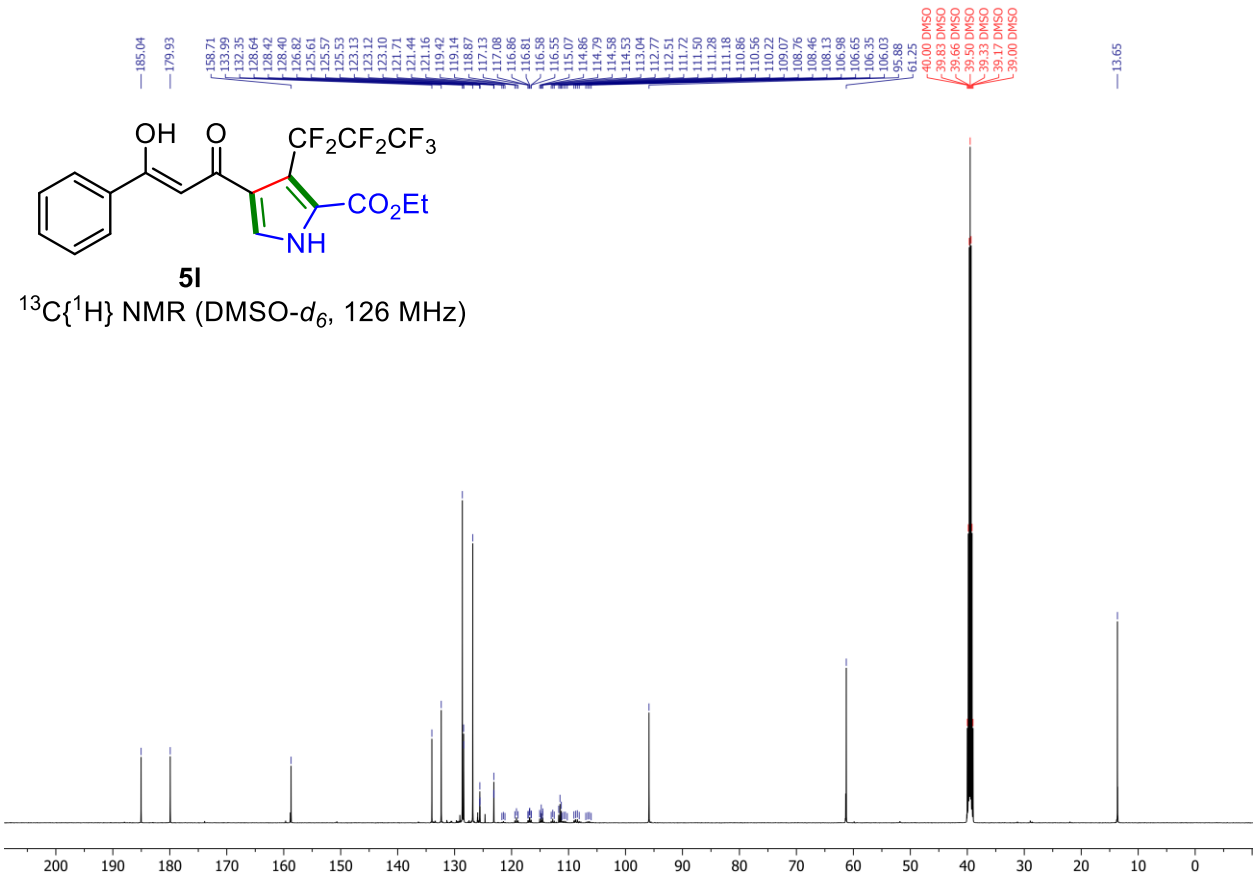


^{19}F NMR ($CDCl_3$, 376 MHz)



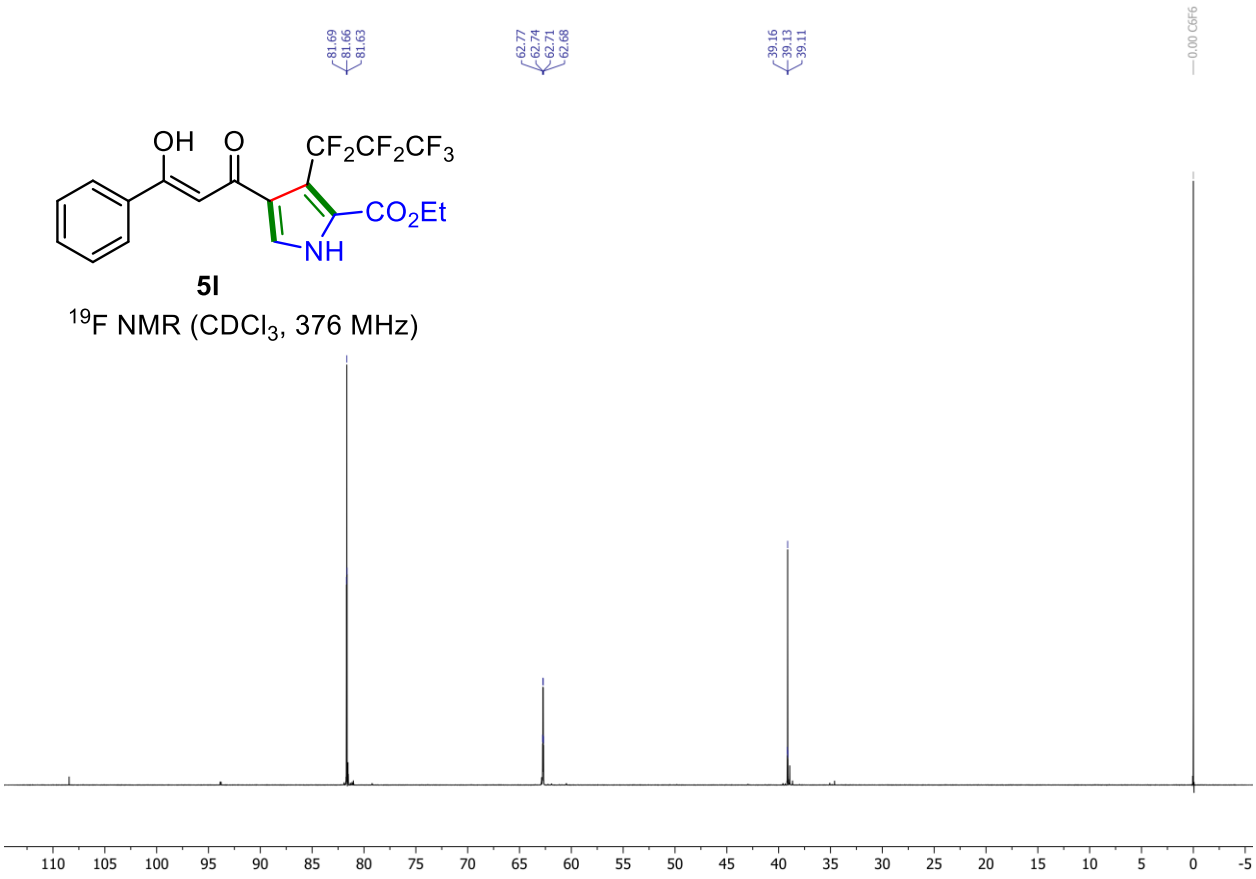
5l

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



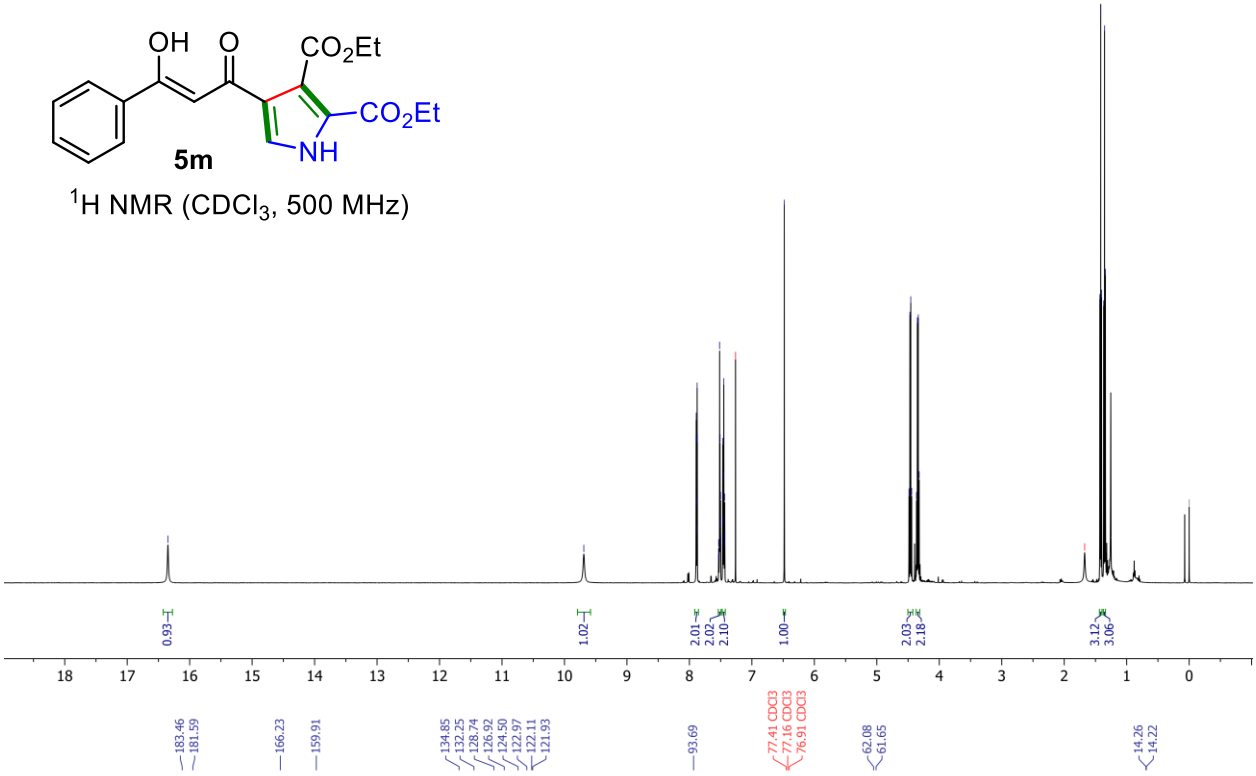
5l

$^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 126 MHz)

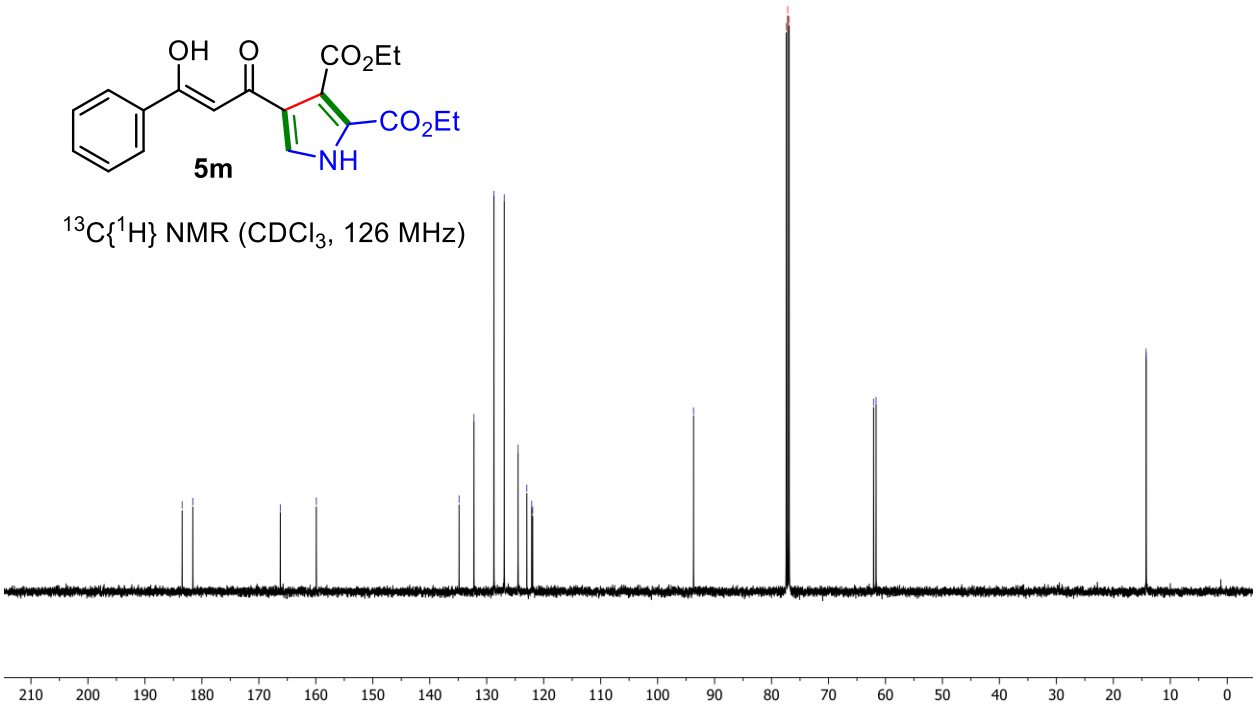


5l

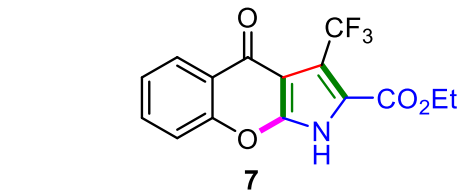
^{19}F NMR ($CDCl_3$, 376 MHz)



^{1}H NMR ($CDCl_3$, 500 MHz)

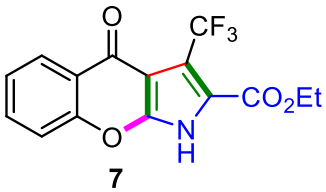


$^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



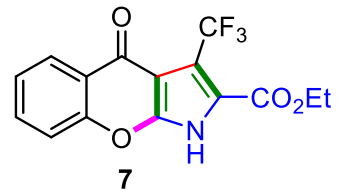
7

^{1}H NMR (DMSO-d_6, 400 MHz)



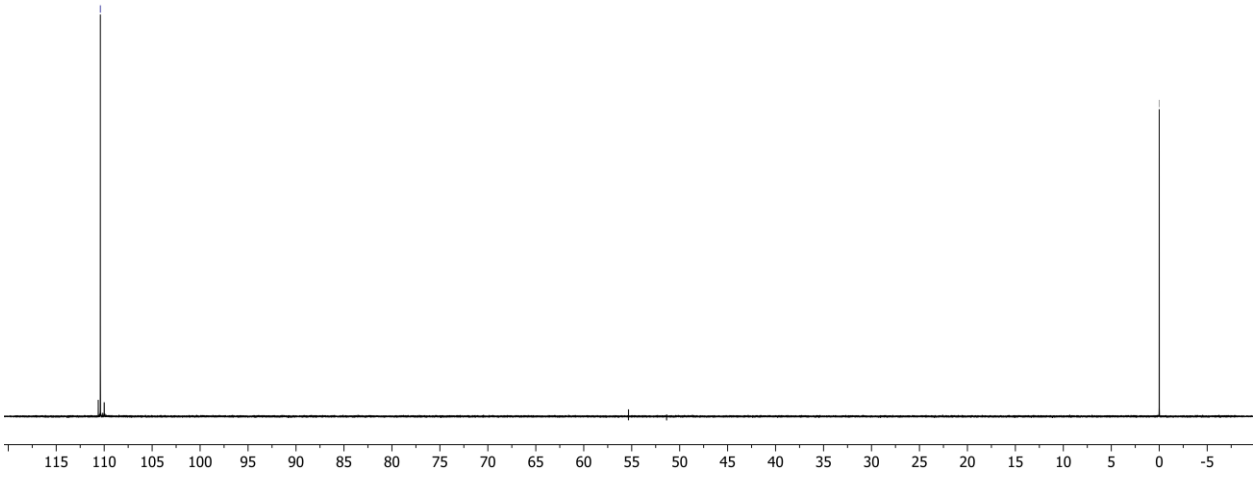
7

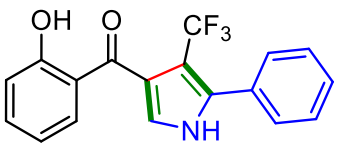
^{13}C{^{1}H} NMR (DMSO-d_6, 126 MHz)



7

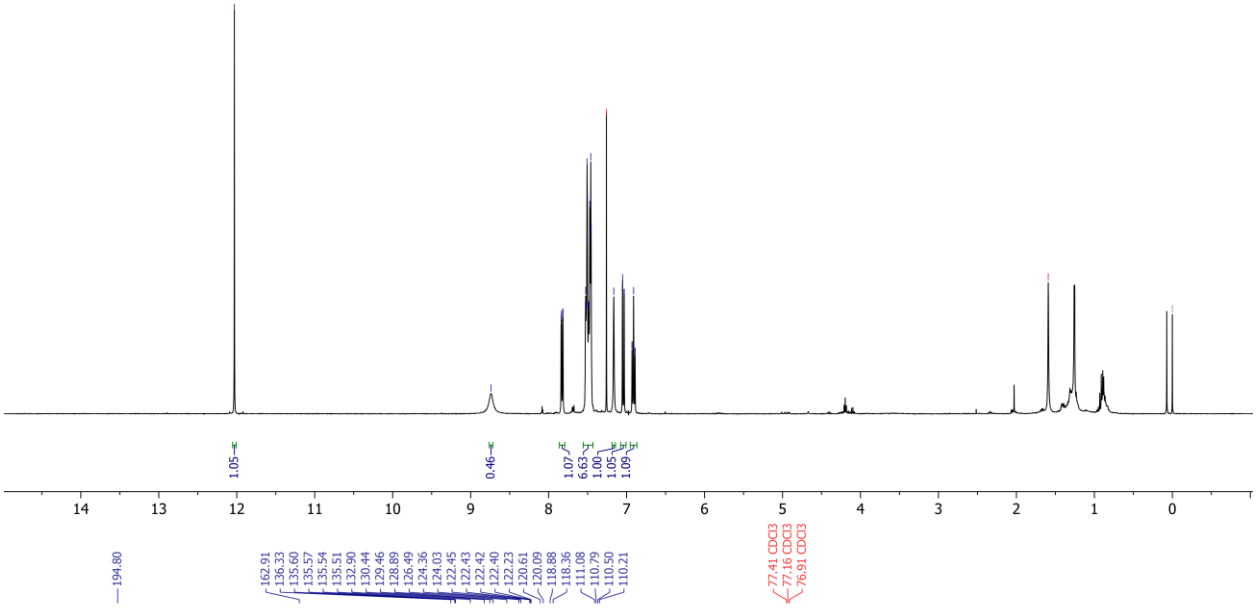
^{19}F NMR (DMSO-d_6, 376 MHz)

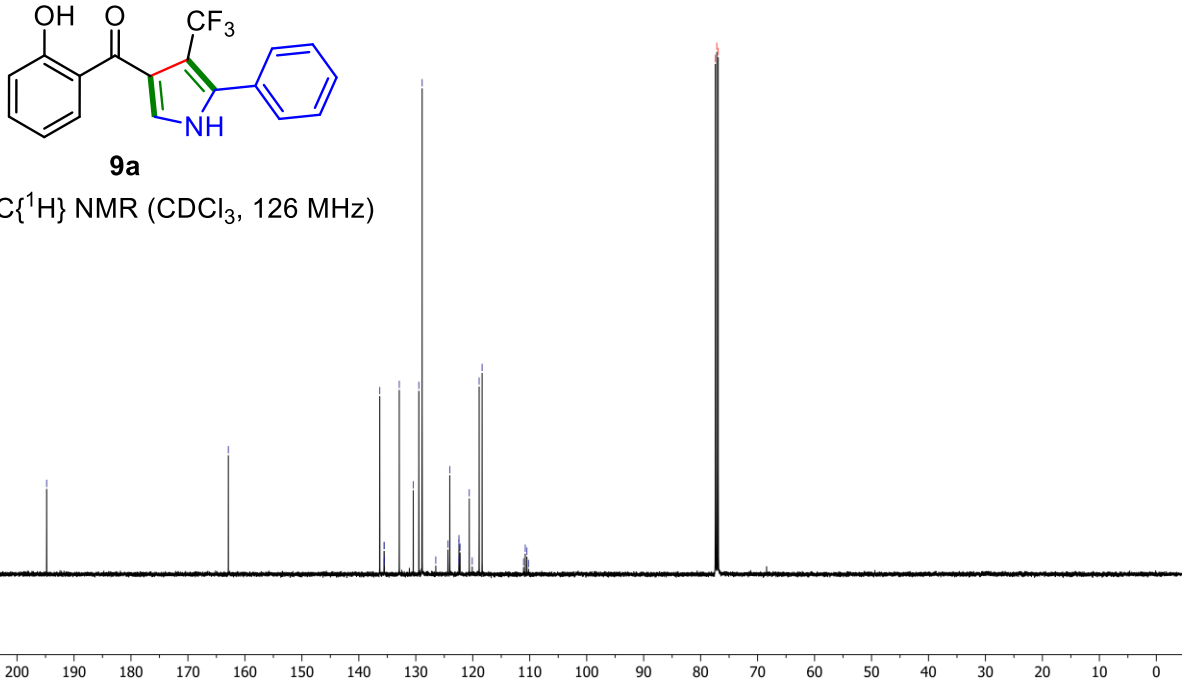




9a

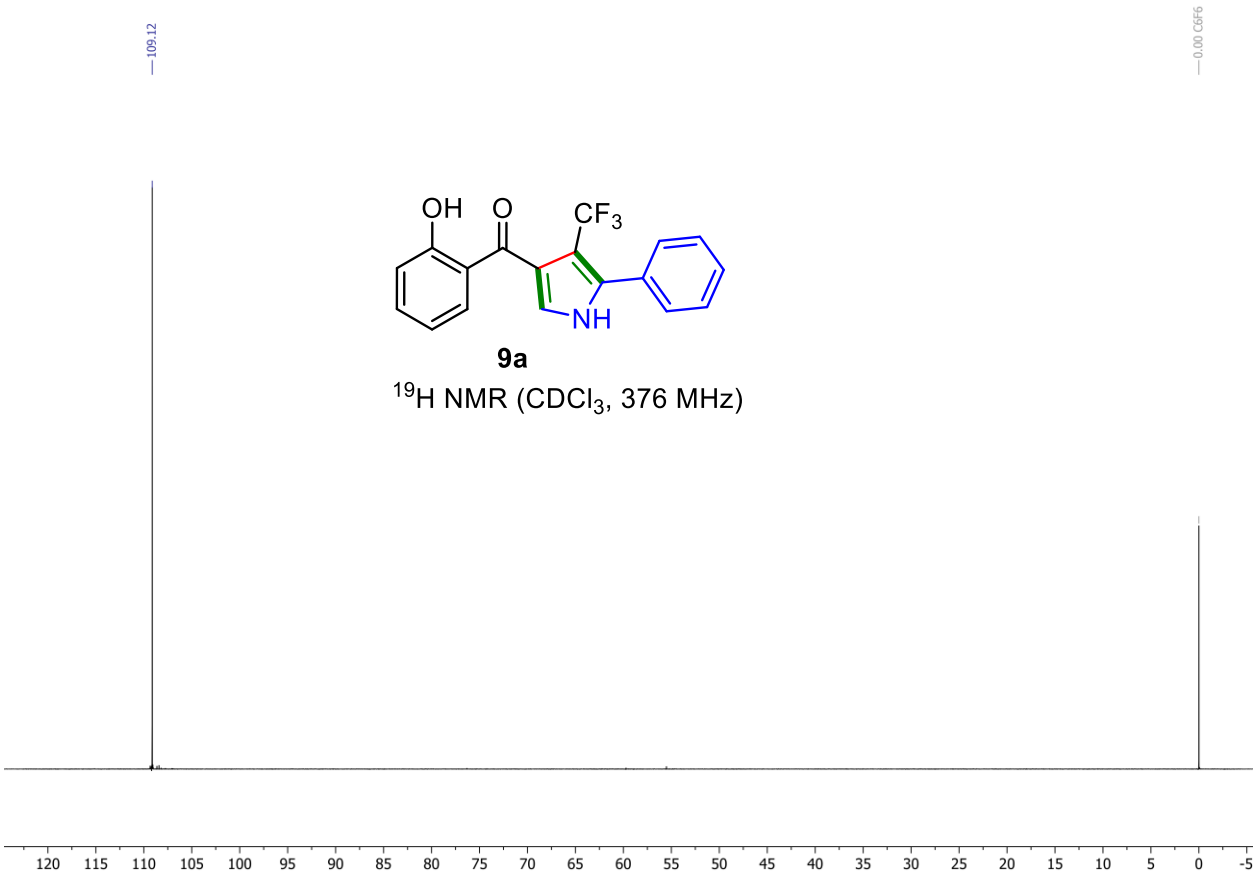
^{1}H NMR ($CDCl_3$, 400 MHz)





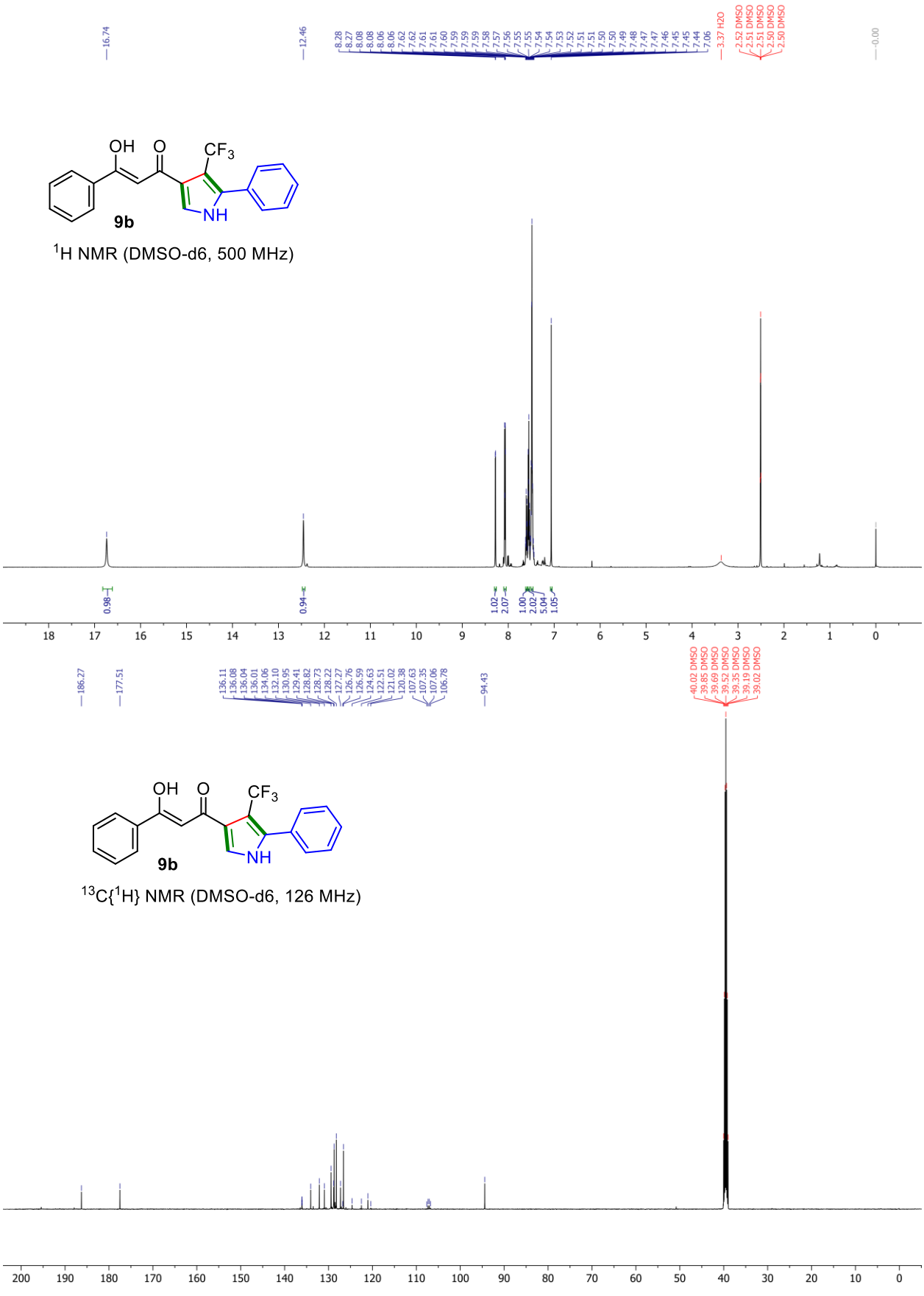
9a

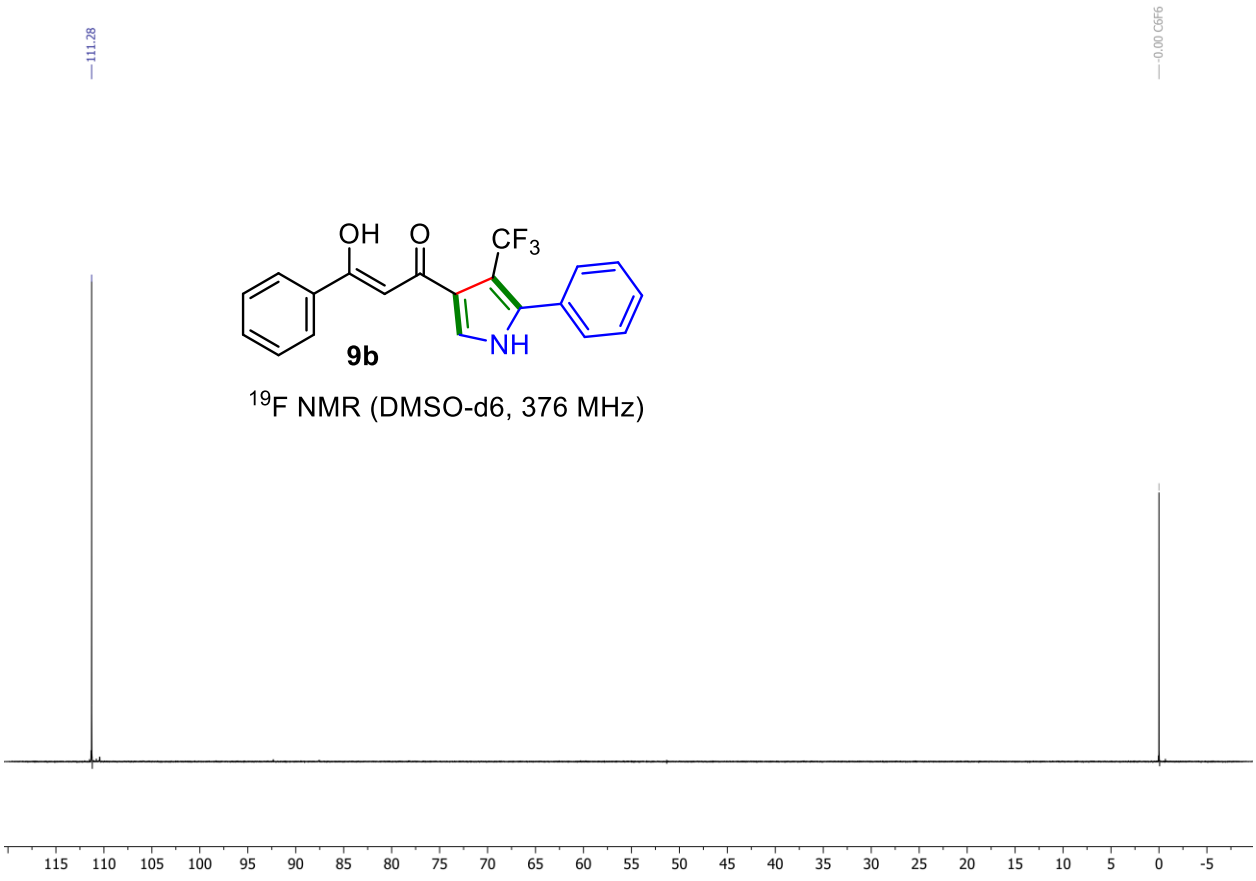
$^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



9a

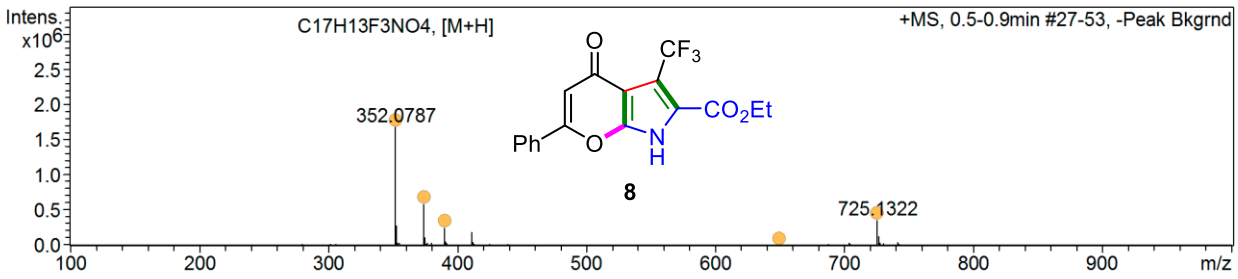
^{19}H NMR ($CDCl_3$, 376 MHz)


OH
O
CF3
NH
9b
1H NMR (DMSO-d6, 500 MHz)
13C{1H} NMR (DMSO-d6, 126 MHz)

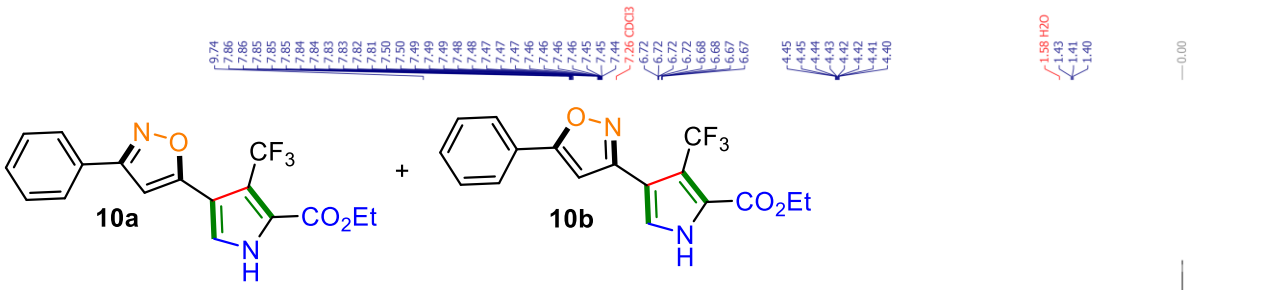


9b

^{19}F NMR (DMSO-d6, 376 MHz)

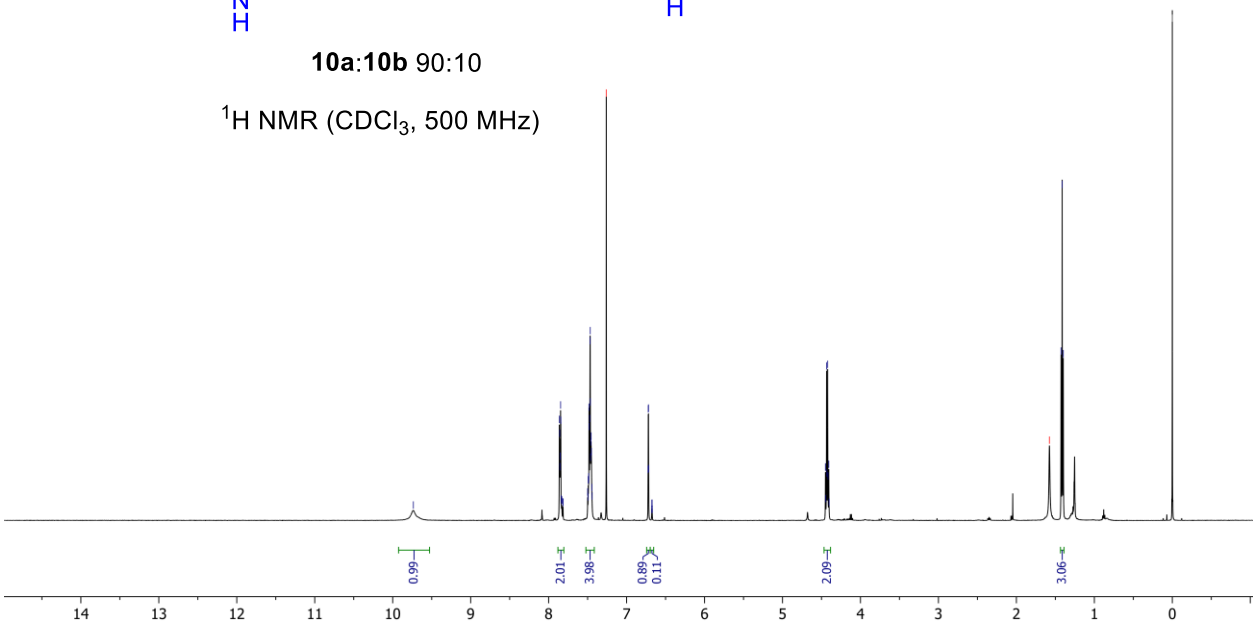


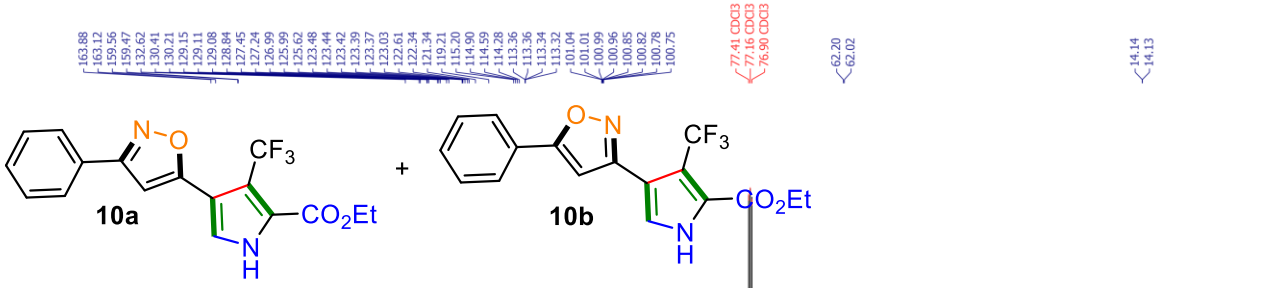
Ion Formula	Meas. m/z	m/z	err [ppm]	mSigma
$C_{17}H_{13}F_3NO_4$	352.0787	352.0791	1.1	13.1
$C_{17}H_{12}F_3NNaO_4$	374.0604	374.0611	1.7	6.4
$C_{17}H_{12}F_3KNO_4$	390.0344	390.0350	1.6	6.0
$C_{34}H_{24}F_6N_2NaO_8$	725.1322	725.1329	1.0	11.2



10a:**10b** 90:10

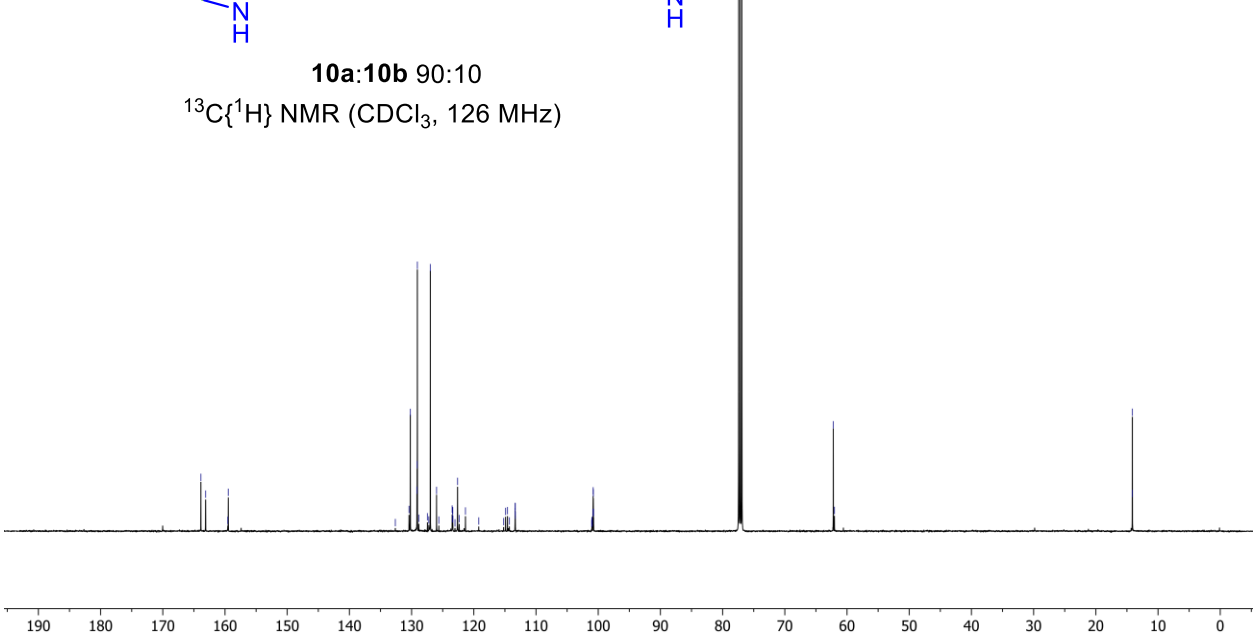
^{1}H NMR ($CDCl_3$, 500 MHz)

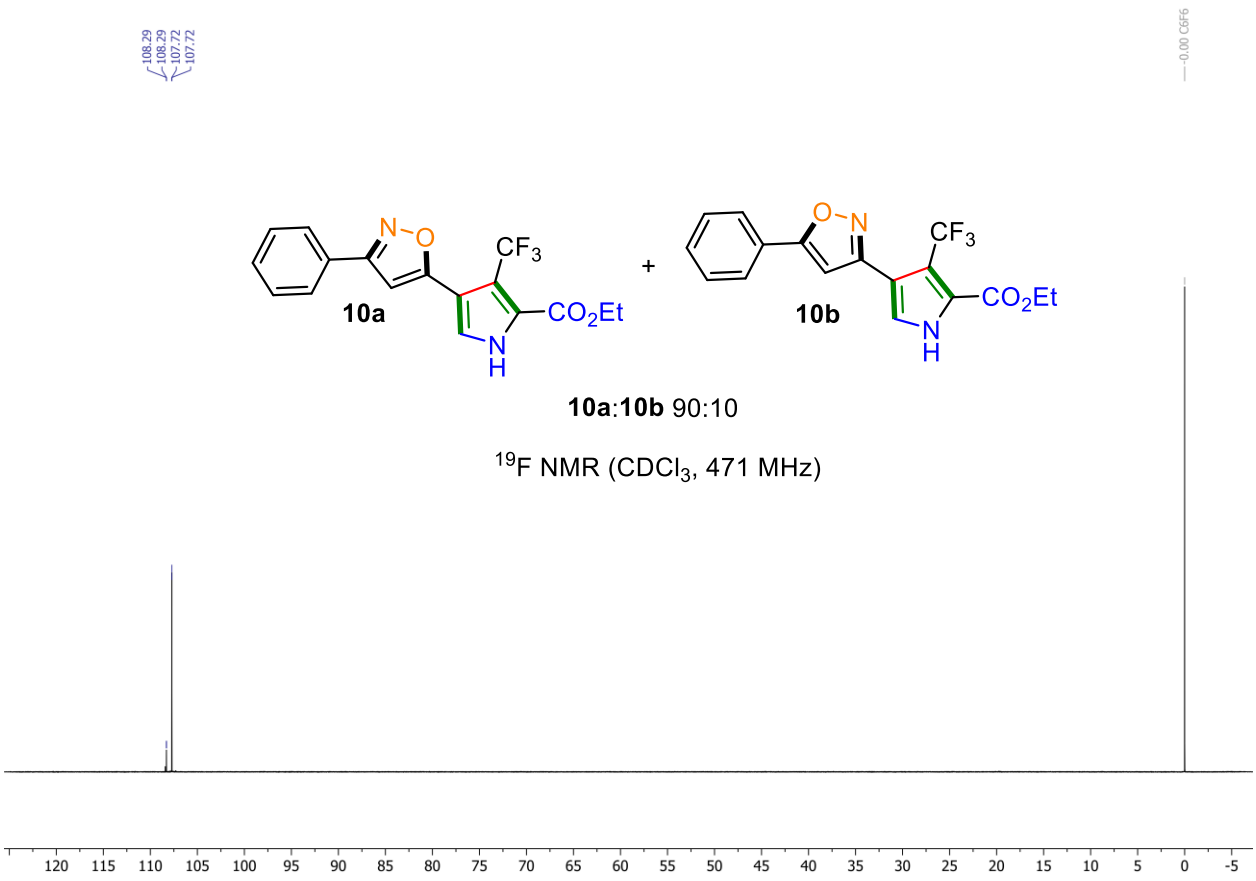


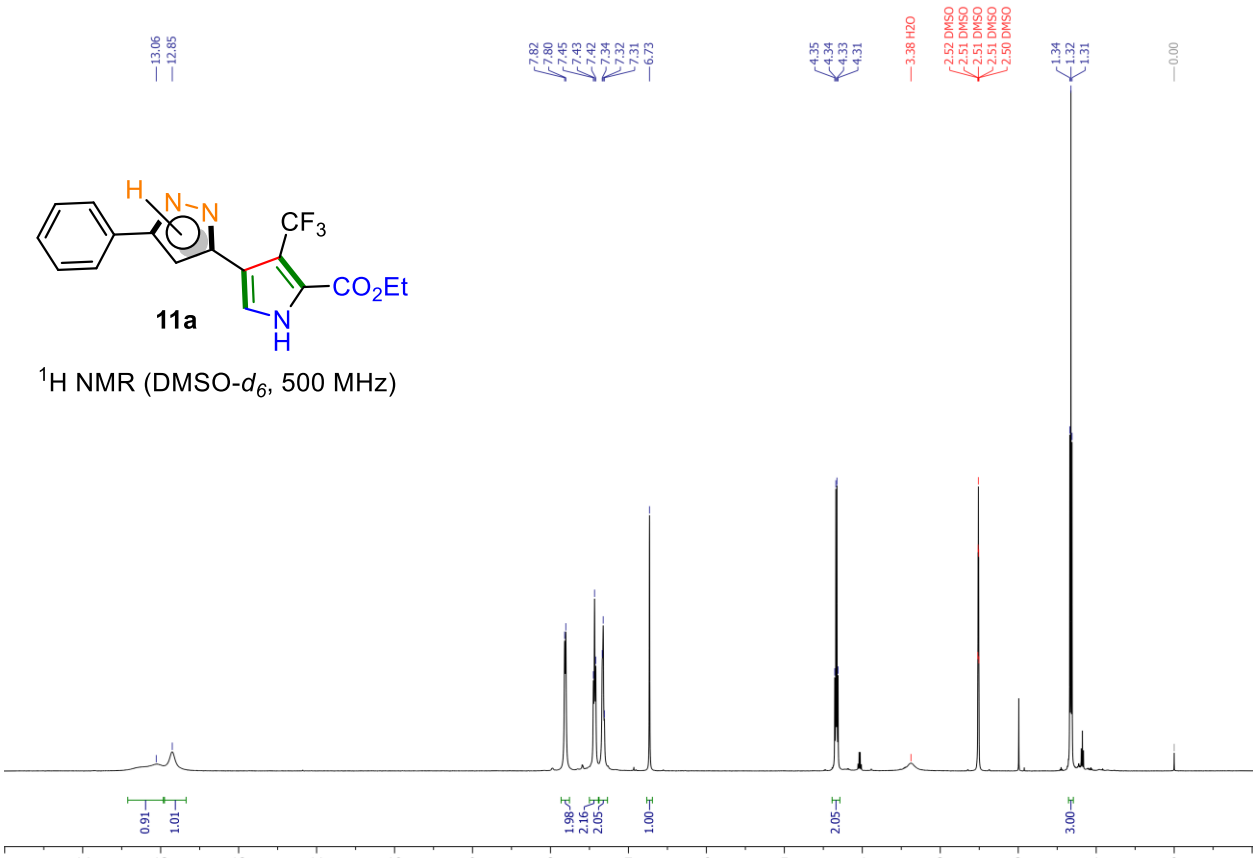


10a:**10b** 90:10

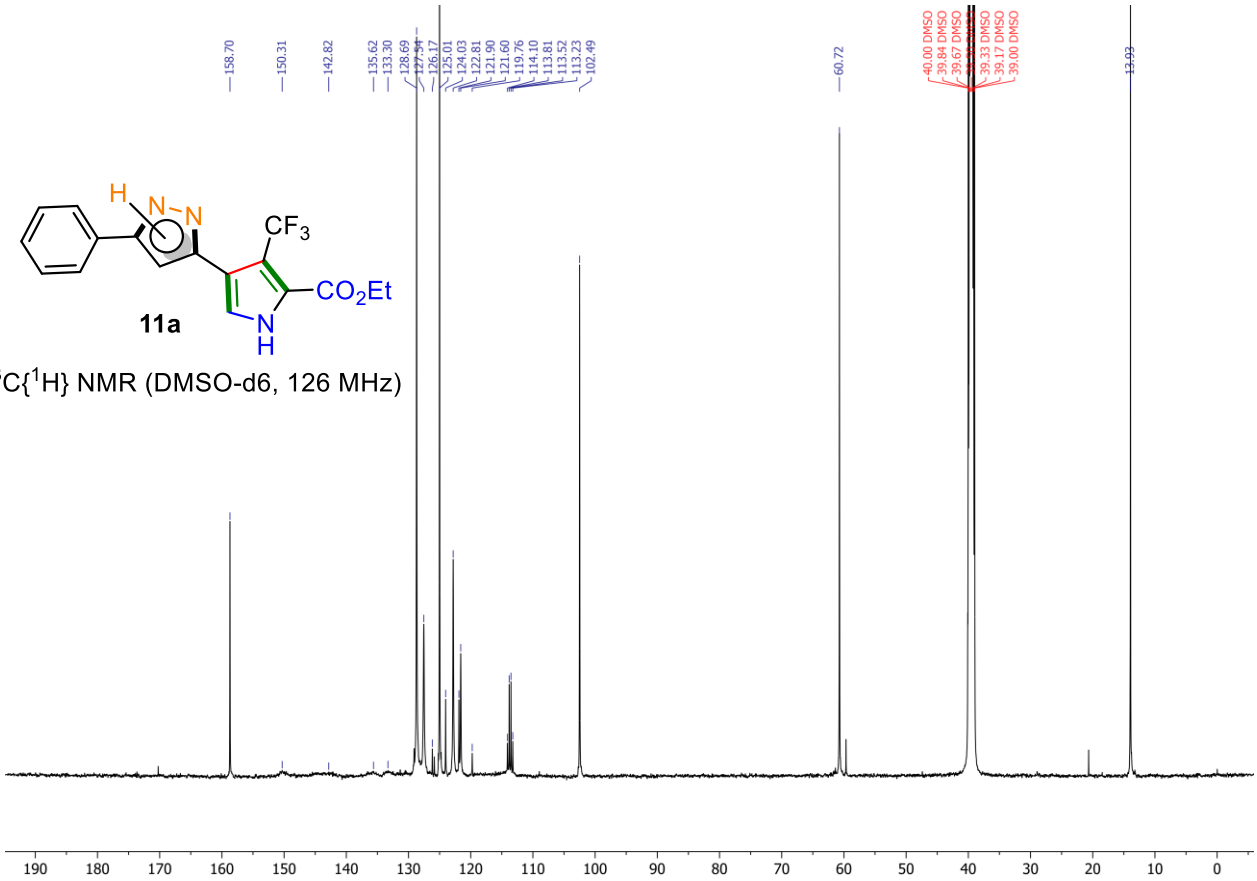
$^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz)



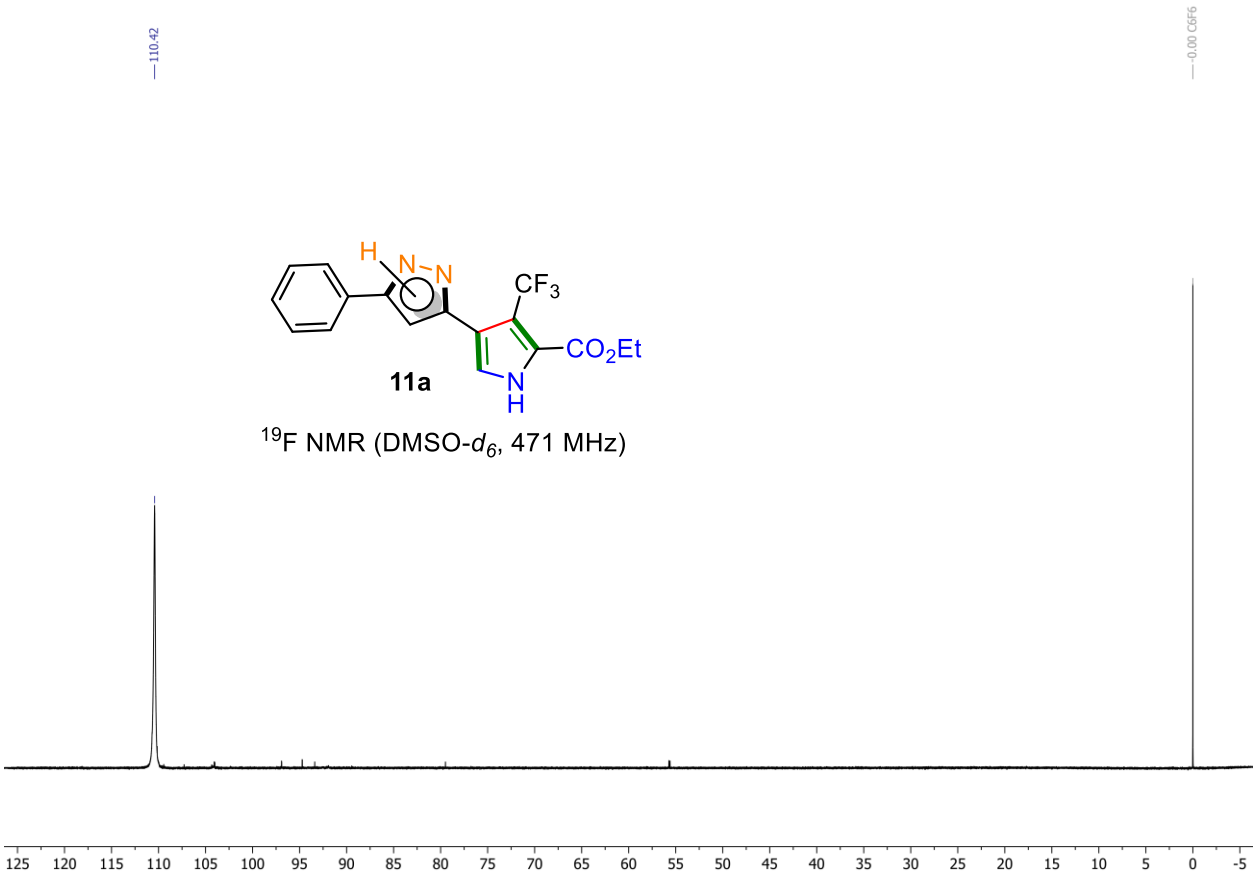

108.29
108.29
107.72
107.72
0.00 C6F6
N
O
CF3
CO2Et
N
H
10a
+
O
N
CF3
CO2Et
N
H
10b
10a:10b 90:10
19F NMR (CDCl3, 471 MHz)
120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0 -5

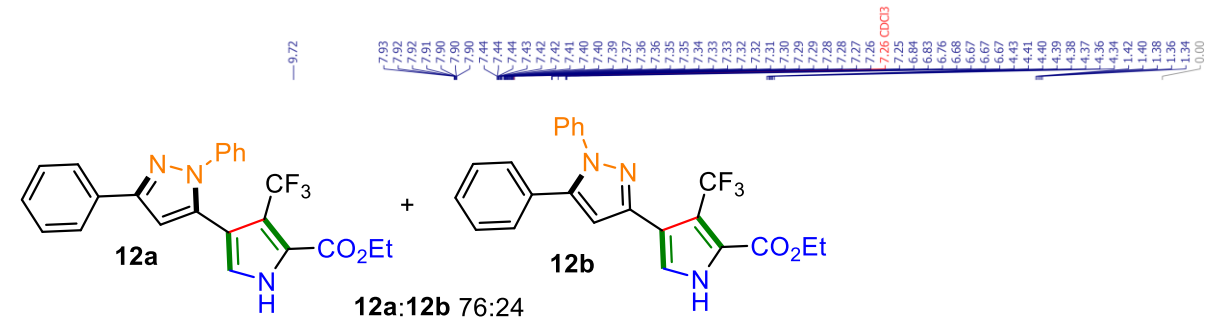


^{1}H NMR (DMSO-d_6, 500 MHz)

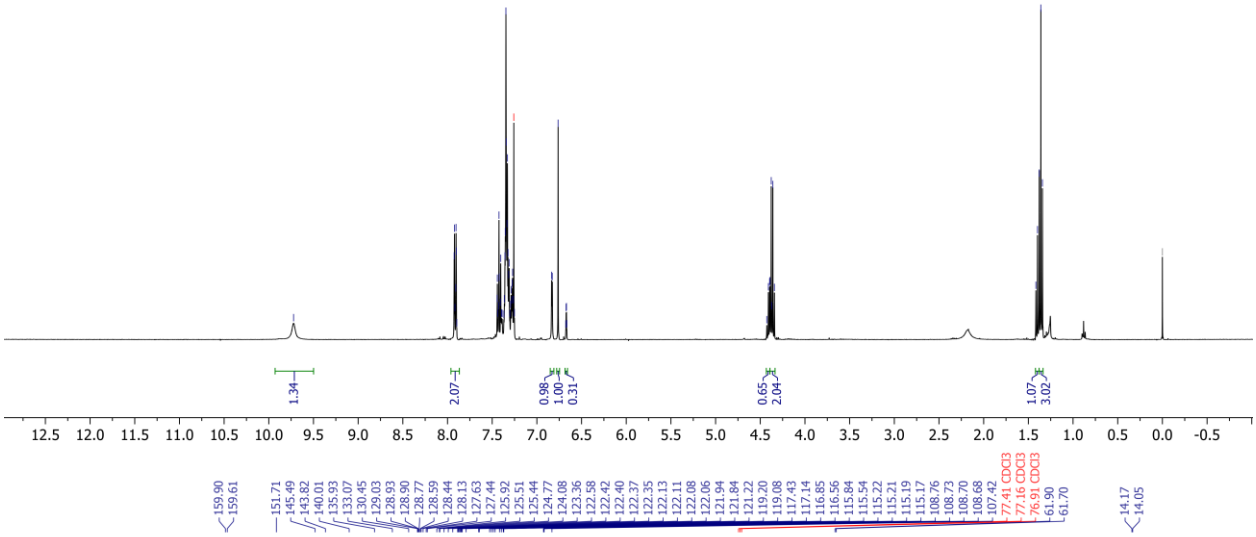


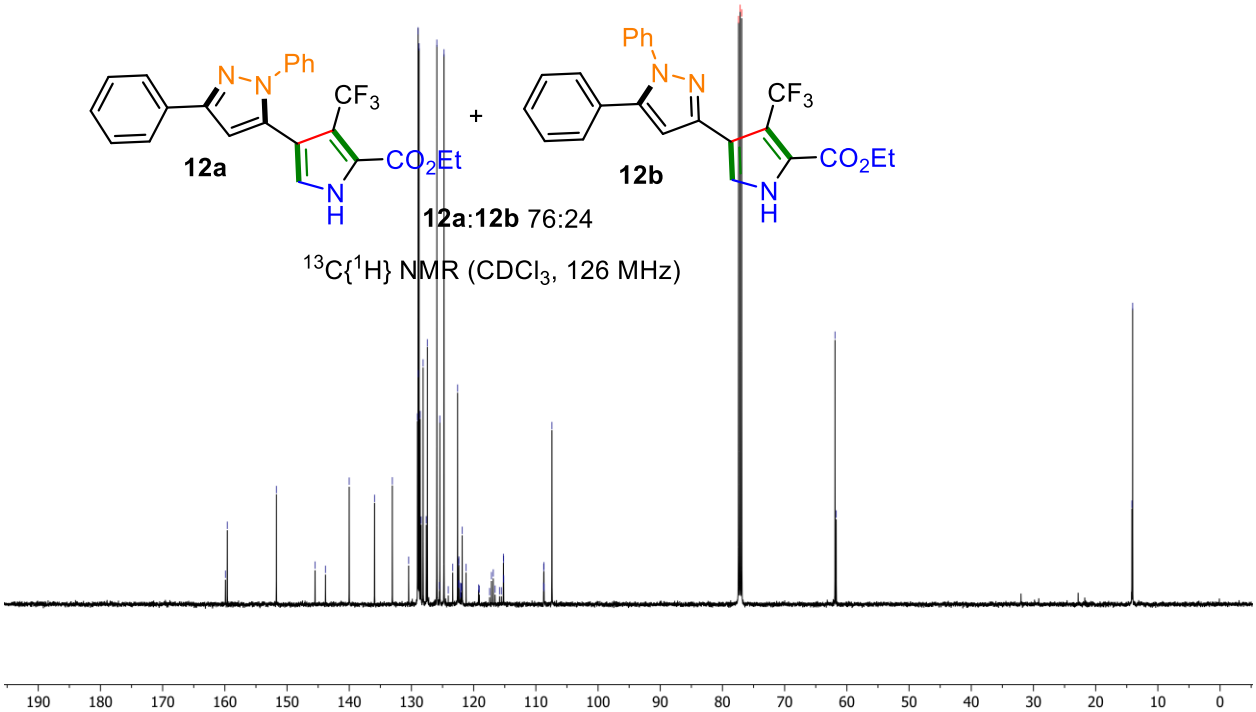
^{13}C{^{1}H} NMR (DMSO-d6, 126 MHz)


110.42
0.00 C6F6
H
N
N
CF3
CO2Et
N
H
11a
19F NMR (DMSO-d6, 471 MHz)
125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0 -5

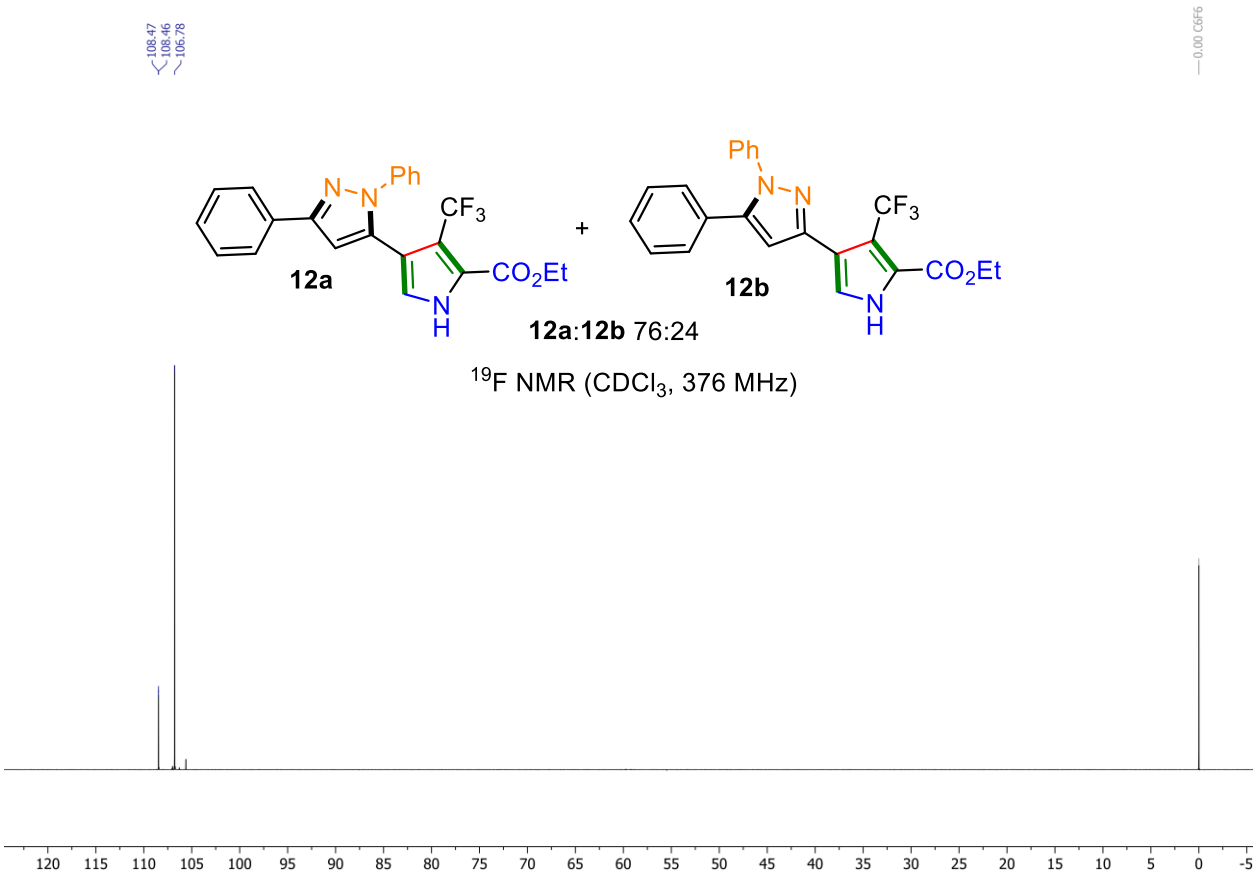


^{1}H NMR ($CDCl_3$, 400 MHz)

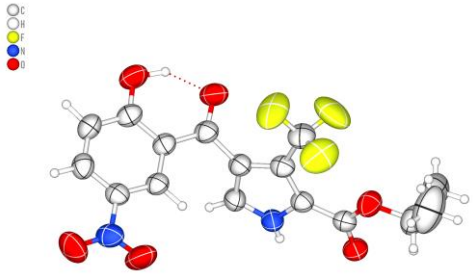




^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz)


108.47
108.46
106.78
0.00 C6F6
Ph
N
N
CF3
CO2Et
N
H
12a
+
Ph
N
N
CF3
CO2Et
N
H
12b
12a:12b 76:24
19F NMR (CDCl3, 376 MHz)
120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0 -5

10. **X-ray crystal data for 3d**



CCDC 2297091

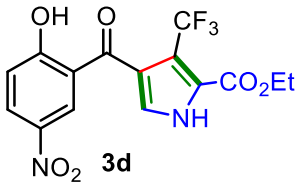
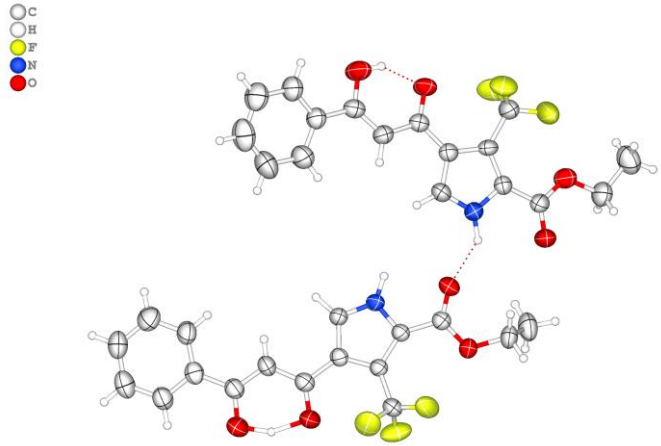


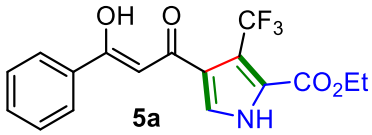
Table S1 Crystal data and structure refinement for 3d

Identification code	exp_351 / 2297091
Empirical formula	$C_{15}H_{11}F_3N_2O_6$
Formula weight	372.26
Temperature/K	295(2)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å, b/Å, c/Å	7.6176(7), 11.1985(9), 18.9787(18)
α/°, β/°, γ/°	90, 95.657(10), 90
Volume/Å3	1611.1(3)
Z	4
ρ_{calc}g/cm^3	1.535
μ/mm^{-1}	0.141
F(000)	760.0
Crystal size/mm^3	0.47 × 0.31 × 0.19
Radiation	MoKα (λ= 0.71073)
2Θ range for data collection/°	7.426 to 60.956
Index ranges	-10 ≤ h ≤ 10, -15 ≤ k ≤ 14, -25 ≤ l ≤ 26
Reflections collected	12656
Independent reflections	4307 [R_{int} = 0.0549, R_{sigma} = 0.0656]
Data/restraints/parameters	4307/12/271
Goodness-of-fit on F^2	1.010
Final R indexes [I>=2σ (I)]	R_1 = 0.0643, wR_2 = 0.1690
Final R indexes [all data]	R_1 = 0.1495, wR_2 = 0.2370
Largest diff. peak/hole / e Å^{-3}	0.24/-0.24

Crystal Data for $C_{15}H_{11}F_3N_2O_6$ (*M* =372.26 g/mol): monoclinic, space group $P2_1/c$ (no. 14), *a* = 7.6176(7) Å, *b* = 11.1985(9) Å, *c* = 18.9787(18) Å, *V* = 11611.1(3) Å3, *Z* = 4, *T* = 295(2) K, μ(MoKα) = 0.141 mm^{-1}, D_{calc} = 1.535 g/cm^3, 12656 reflections measured (7.426° ≤2Θ ≤ 60.956°), 4307 unique (R_{int} = 0.0549, R_{sigma} = 0.0656) which were used in all calculations. The final R_1 was 0.0643 (I > 2σ(I)) and wR_2 was 0.2370 (all data).

11. **X-ray crystal data for 5a**





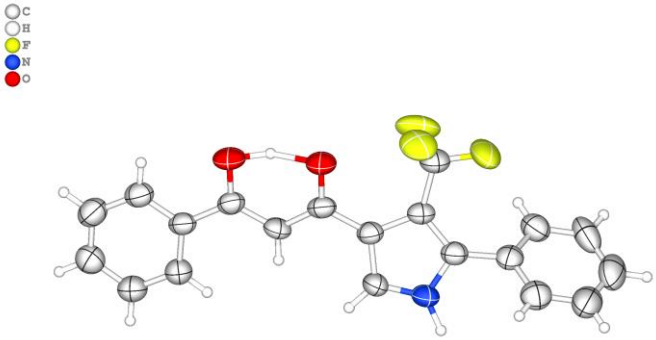
CCDC 2454280

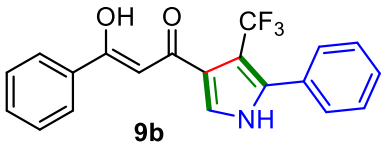
Table S2 Crystal data and structure refinement for 5a

Identification code	exp_411 / 2454280
Empirical formula	$C_{17}H_{14}F_3NO_4$
Formula weight	353.29
Temperature/K	295(2)
Crystal system	triclinic
Space group	P-1
a/Å, b/Å, c/Å	7.7224(7), 14.8067(13), 15.0191(11)
α/°, β/°, γ/°	107.418(7), 97.252(7), 95.632(7)
Volume/Å3	1608.6(2)
Z	4
ρ_{calc}g/cm^3	1.459
μ/mm^{-1}	0.126
F(000)	728.0
Crystal size/mm^3	0.48 × 0.35 × 0.19
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	7.34 to 59.128
Index ranges	-9 ≤ h ≤ 10, -19 ≤ k ≤ 20, -19 ≤ l ≤ 20
Reflections collected	15647
Independent reflections	8513 [R_{int} = 0.0603, R_{sigma} = 0.1365]
Data/restraints/parameters	8513/0/482
Goodness-of-fit on F^2	0.959
Final R indexes [I>=2σ (I)]	R_1 = 0.0743, wR_2 = 0.1746
Final R indexes [all data]	R_1 = 0.2098, wR_2 = 0.2658
Largest diff. peak/hole / e Å^{-3}	0.49/-0.40

Crystal Data for $C_{17}H_{14}F_3NO_4$ (M = 353.29 g/mol): triclinic, space group P-1 (no. 1), a = 7.7224(7) Å, b = 14.8067(13) Å, c = 15.0191(11) Å, V = 1608.6(2) Å3, Z = 4, T = 295(2) K, μ(MoKα) = 0.126 mm^{-1}, D_{calc} = 1.459 g/cm^3, 15647 reflections measured (7.34° ≤ 2Θ ≤ 59.128°), 8513 unique (R_{int} = 0.0603, R_{sigma} = 0.1365) which were used in all calculations. The final R_1 was 0.0743 (I > 2σ(I)) and wR_2 was 0.2658 (all data).

12. **X-ray crystal data for 9b**





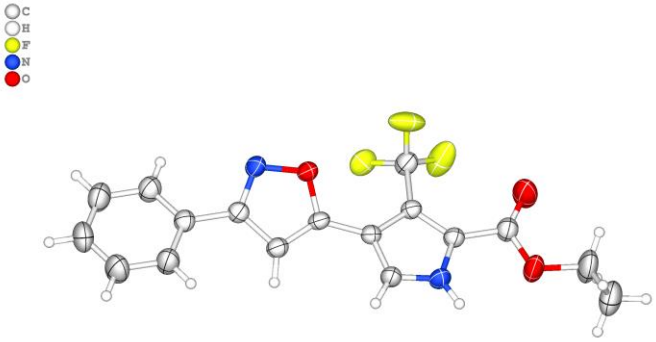
CCDC 2297093

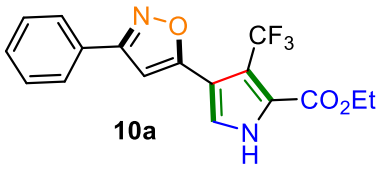
Table S3 Crystal data and structure refinement for 9b

Identification code	exp_1224 / 2297093
Empirical formula	$C_{20}H_{14}F_3NO_2$
Formula weight	357.32
Temperature/K	293(2)
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å, b/Å, c/Å	5.2062(6), 13.1121(8), 24.064(2)
α/°, β/°, γ/°	90.00, 90.00, 90.00
Volume/Å3	1642.7(3)
Z	4
ρ_{calc}g/cm^3	1.445
μ/mm^{-1}	0.116
F(000)	736.0
Crystal size/mm^3	0.47 × 0.21 × 0.06
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	3.54 to 56.56
Index ranges	-6 ≤ h ≤ 6, -17 ≤ k ≤ 9, -15 ≤ l ≤ 31
Reflections collected	4701
Independent reflections	3431 [R_{int} = 0.0450, R_{sigma} = 0.0974]
Data/restraints/parameters	3431/0/244
Goodness-of-fit on F^2	0.999
Final R indexes [I>=2σ (I)]	R_1 = 0.0639, wR_2 = 0.1336
Final R indexes [all data]	R_1 = 0.1292, wR_2 = 0.1895
Largest diff. peak/hole / e Å^{-3}	0.21/-0.19

Crystal Data for $C_{20}H_{14}F_3NO_2$ (*M* =357.32 g/mol): orthorhombic, space group $P2_12_12_1$ (no. 19), *a* = 5.2062(6) Å, *b* = 13.1121(8) Å, *c* = 24.064(2) Å, *V* = 1642.7(3) Å3, *Z* = 4, *T* = 293(2) K, μ(MoKα) = 0.116 mm^{-1}, D_{calc} = 1.445 g/cm^3, 4701 reflections measured (3.54° ≤ 2Θ ≤ 56.56°), 3431 unique (R_{int} = 0.0450, R_{sigma} = 0.0974) which were used in all calculations. The final R_1 was 0.0639 (I > 2σ(I)) and wR_2 was 0.1895 (all data).

13. **X-ray crystal data for 10a**





CCDC 2491605

Table S4 Crystal data and structure refinement for10a

Identification code	exp_1812 / 2491605
Empirical formula	$C_{17}H_{13}F_3N_2O_3$
Formula weight	350.29
Temperature/K	295(2)
Crystal system	orthorhombic
Space group	Pbca
a/Å, b/Å, c/Å	13.0298(7), 7.5259(7), 31.6005(19)
α/°, β/°, γ/°	90, 90, 90
Volume/Å3	3098.8(4)
Z	8
ρ_{calc}g/cm^3	1.502
μ/mm^{-1}	0.128
F(000)	1440.0
Crystal size/mm^3	0.48 × 0.17 × 0.06
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	6.03 to 62.352
Index ranges	-18 ≤ h ≤ 16, -7 ≤ k ≤ 10, -33 ≤ l ≤ 45
Reflections collected	8639
Independent reflections	4226 [R_{int} = 0.0450, R_{sigma} = 0.0997]
Data/restraints/parameters	4226/0/239
Goodness-of-fit on F^2	0.976
Final R indexes [I>=2σ (I)]	R_1 = 0.0631, wR_2 = 0.0990
Final R indexes [all data]	R_1 = 0.1781, wR_2 = 0.1361
Largest diff. peak/hole / e Å^{-3}	0.20/-0.20

Crystal Data for $C_{17}H_{13}F_3N_2O_3$ (*M* = 350.29 g/mol): orthorhombic, space group Pbca (no. 61), *a* = 13.0298(7) Å, *b* = 7.5259(7) Å, *c* = 31.6005(19) Å, *V* = 3098.8(4) Å3, *Z* = 8, *T* = 295(2) K, μ(MoKα) = 0.128 mm^{-1}, D_{calc} = 1.502 g/cm^3, 8639 reflections measured (6.03° ≤ 2Θ ≤ 62.352°), 4226 unique (R_{int} = 0.0450, R_{sigma} = 0.0997) which were used in all calculations. The final R_1 was 0.0631 (I > 2σ(I)) and wR_2 was 0.1361 (all data).

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