Supporting Information

BF_3-Enabled unusual (3 + 2) cycloaddition of bicyclobutanes with aldimine ester: access to 2-azabicyclo[2.1.1]hexanes

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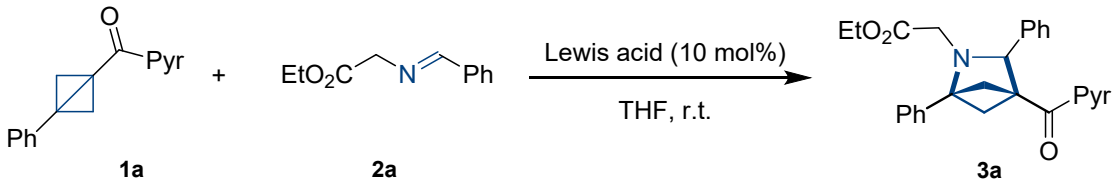
1. General information

Commercially available reagents were used without further purification unless otherwise stated. All reactions were carried out under argon atmosphere with dry solvents under anhydrous conditions, all solvents were purchased from Energy Chemical and stored over molecular sieves. Analytical thin-layer chromatography (TLC) was conducted with TLC plates (Silica gel 60 F254, Qingdao Haiyang) and visualization on TLC was achieved by UV light or Phosphomolybdic acid. Flash column chromatography was performed on silica gel 200-300 mesh with freshly distilled solvents. Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker 600, 400 and JEOL 400 MHz in $CDCl_3$ solvent. All chemical shifts in ^1H NMR spectra were given in parts per million (ppm) relative to the residual or $CDCl_3$ (7.26 ppm) as internal standards and coupling constants (*J*) were given in Hertz (Hz). ^{13}C NMR chemical shifts were reported in ppm relative to the central peak of $CDCl_3$ (77.16 ppm) as internal standards. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, q = quartet, m = multiplet, dd = doublet of doublets, dt = doublet of triplets), coupling constant (Hz), and integration. HRMS data were obtained by ESI or APCI method with Bruker mass spectrometer (MAXIS). The absolute configurations of **3a** were assigned by the X-ray analysis and the configurations of other cycloaddition products were assigned by analogy. The X-ray single-crystal determination was performed on Bruker D8 VENTURE X-ray single crystal diffractometer.

1a-1r were prepared according to the literature procedure.[1] **1s-1y** were prepared according to the literature procedure.[2]

2. Optimization of reaction conditions

Table S1. The screening of Lewis acid.[a]

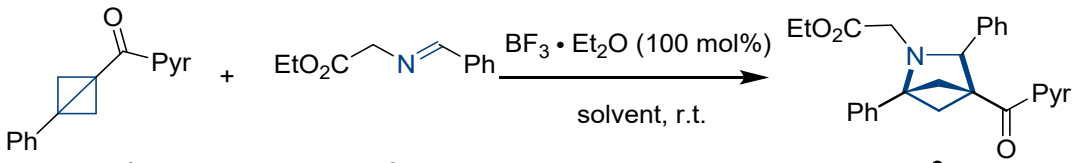


entry	Lewis acid (10 mol%)	yield (%)
1	$Sc(OTf)_3$	trace
2	$Cu(OTf)_2$	trace
3	$Zn(OTf)_2$	NR
4	$Mg(OTf)_2$	NR
5	$Eu(OTf)_3$	NR

6	$Cu(MeCN)_4PF_6$	trace
7	$Bi(OTf)_3$	trace
8	Ag(OTf)	NR
9	$Yb(OTf)_3$	trace
10	$La(OTf)_3$	trace
11	$Ga(OTf)_3$	trace
12	$BF_3 \cdot OEt_2$ (1 equiv.)	16

[a] Standard conditions: **1a** (0.1 mmol), **2a** (0.3 mmol), Lewis acid (10 mol%), THF (1 mL), Ar atmosphere, r.t., 16 h. Yields were determined by ^{1}H NMR spectroscopy with CH_2Br_2 as an internal standard.

Table S2. The screening of solvent.[a]

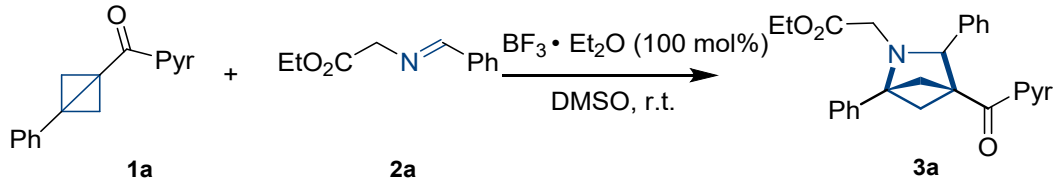


1a **2a** **3a**

entry	solvent	yield (%)
1	THF	16
2	DME	19
3	DCM	trace
4	DCE	10
5	MeCN	trace
6	DMF	34
7	DMA	39
8	NMP	48
9	DMSO	48
10	dioxane	trace

[a] Standard conditions: **1a** (0.1 mmol), **2a** (0.3 mmol), $BF_3 \cdot OEt_2$ (1 equiv.), solvent (1 mL), Ar atmosphere, r.t., 16 h. Yields were determined by ^{1}H NMR spectroscopy with CH_2Br_2 as an internal standard.

Table S3. The screening of material ratio.[a]



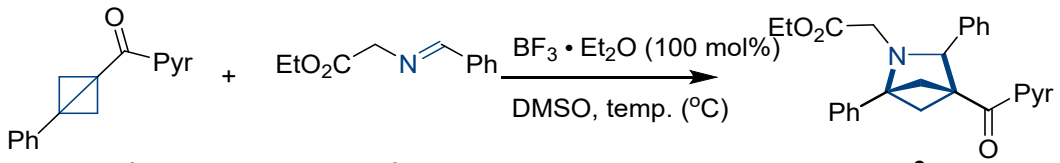
1a **2a** **3a**

entry	**1a** : **2a** (equiv ratio)	yield (%)

1	3:1	40
2	2:1	43
3	1:1	33
4	1:1.5	44
5	1:2	48
6	1:3	48
7	1:5	50

[a] Standard conditions: **1a** (x mmol), **2a** (y mmol), $BF_3{\cdot}OEt_2$ (1 equiv.), DMSO (1 mL), Ar atmosphere, T °C, 16 h. Yields were determined by ^1H NMR spectroscopy with CH_2Br_2 as an internal standard.

Table S4. Investigation of reaction temperature.[a]

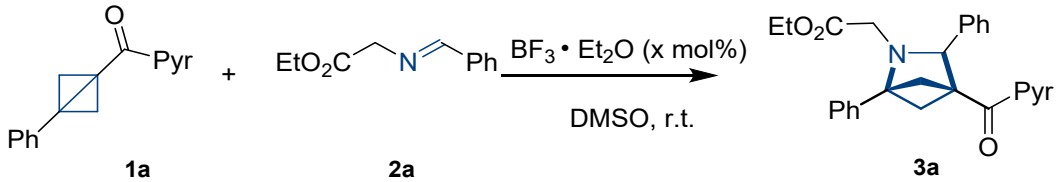


1a **2a** **3a**

entry	temp.(°C)	yield (%)
1	0	34
2	r.t.	48
3	30	47
6	40	36
7	50	19

[a] Standard conditions: **1a** (x mmol), **2a** (y mmol), $BF_3{\cdot}OEt_2$ (1 equiv.), DMSO (1 mL), Ar atmosphere, r.t., 16 h. Yields were determined by ^1H NMR spectroscopy with CH_2Br_2 as an internal standard.

Table S5. The screening amount of $BF_3{\cdot}OEt_2$.[a]



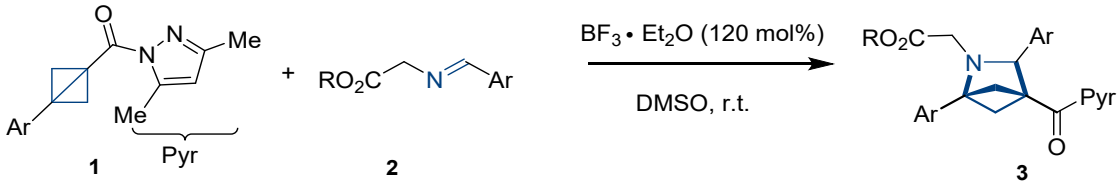
1a **2a** **3a**

entry	$BF_3{\cdot}OEt_2$ (x mol%)	yield (%)
1	10 mol%	--
2	30 mol%	9
3	50 mol%	26
4	70 mol%	43
5	80 mol%	44

6	90 mol%	46
7	100 mol%	48
8	120 mol%	53 (52[b])
9	150 mol%	54
10	200 mol%	54

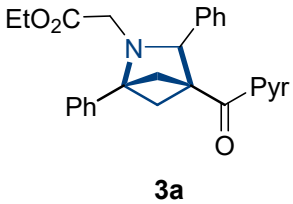
[a] Standard conditions: **1a** (0.1 mmol), **2a** (0.3 mmol), $BF_3{\cdot}OEt_2$ (x equiv.), DMSO (1 mL), Ar atmosphere, r.t., 16 h. Yields were determined by ^1H NMR spectroscopy with CH_2Br_2 as an internal standard. [b] Isolated yield.

3. General procedure for reactions



To a 10 mL reaction vial equipped with a magnetic stir bar was added compounds **1** (0.2 mmol, 1.0 equiv), **2** (0.6 mmol, 3.0 equiv), $BF_3{\cdot}OEt_2$ (BF_3 46.5%) (120 mol%), and the tube was evacuated and backfilled with argon three times. DMSO (2 mL) was added under argon atmosphere. The mixture was then stirred rapidly for 16 hours. Upon completion of the reaction, the aqueous phases were extracted with EtOAc (3 × 10 mL). The combined organic phases were washed with saturated brine (20 mL), then dried over Na_2SO_4, concentrated under reduced pressure. The crude product was purified by silica gel chromatography to afford the products **3a-3y**.

ethyl 2-(4-(3,5-dimethyl-1*H*-pyrazole-1-carbonyl)-1,3-diphenyl-2-azabicyclo[2.1.1]hexan-2-yl)acetate 3a

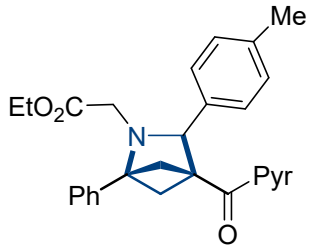


3a

The crude product was purified by column chromatography on silica gel (*n*-Hexane/acetone = 100:1). Colorless oil, 46.0 mg, 52% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.5 Hz, 2H), 7.38 (t, *J* = 7.4 Hz, 2H), 7.30 (d, *J* = 7.9 Hz, 3H), 7.26 – 7.12 (m, 3H), 5.99 (s, 1H), 4.88 (s, 1H), 3.85 – 3.67 (m, 2H), 3.43 (d, *J* = 15.2 Hz, 1H), 3.27 (d, *J* = 15.2 Hz, 1H), 3.03 (t, *J* = 8.6 Hz, 1H), 2.60 (d, *J* = 7.3 Hz, 1H), 2.54 (t, *J* = 8.6 Hz, 1H), 2.44 (s, 3H), 2.29 (s, 3H), 1.92 (d, *J* = 7.5 Hz, 1H), 0.90 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.2, 171.1, 152.6, 144.1, 141.0, 138.2, 128.5, 127.9, 127.8, 127.4, 127.4, 127.1, 110.8, 73.9, 71.2, 60.3, 57.5, 55.0, 45.0, 42.8, 14.2, 14.1, 13.7. **HRMS** (APCI-TOF) m/z: $[M + H]^+$

Calcd for $C_{27}H_{30}N_3O_3$ 444.2282, found 444.2287.

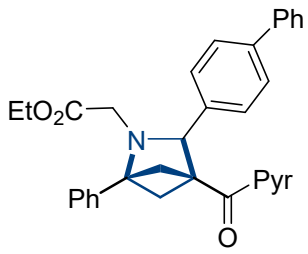
ethyl 2-(4-(3,5-dimethyl-1*H*-pyrazole-1-carbonyl)-1-phenyl-3-(*p*-tolyl)-2-azabicyclo[2.1.1]hexan-2-yl)acetate 3b



3b

The crude product was purified by column chromatography on silica gel (*n*-Hexane/acetone = 100:1). Colorless oil, 15.5 mg, 17% yield. **^{1}H NMR** (400 MHz, $CDCl_3$): δ ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.1 Hz, 2H), 7.39 (t, *J* = 7.4 Hz, 2H), 7.32 (t, *J* = 7.2 Hz, 1H), 7.18 (d, *J* = 7.9 Hz, 2H), 7.04 (d, *J* = 7.8 Hz, 2H), 6.01 (s, 1H), 4.83 (s, 1H), 4.00 – 3.68 (m, 2H), 3.43 (d, *J* = 15.3 Hz, 1H), 3.27 (d, *J* = 15.3 Hz, 1H), 3.10 – 2.80 (m, 1H), 2.60 (d, *J* = 7.4 Hz, 1H), 2.57 – 2.49 (m, 1H), 2.46 (s, 3H), 2.31 (s, 3H), 2.29 (s, 3H), 1.91 (d, *J* = 7.4 Hz, 1H), 0.95 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.4, 171.3, 152.7, 144.2, 138.4, 138.0, 136.5, 128.6, 128.6, 127.9, 127.6, 127.3, 110.8, 73.8, 71.3, 60.4, 57.5, 55.1, 45.1, 43.0, 21.3, 14.3, 14.2, 13.9. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{28}H_{32}N_3O_3$ 458.2438, found 458.2437.

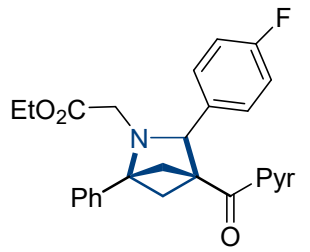
ethyl 2-(3-([1,1'-biphenyl]-4-yl)-4-(3,5-dimethyl-1*H*-pyrazole-1-carbonyl)-1-phenyl-2-azabicyclo[2.1.1]hexan-2-yl)acetate 3c



3c

The crude product was purified by column chromatography on silica gel (*n*-Hexane/acetone = 100:1). White solid, 32.2 mg, 31% yield. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.57 (d, *J* = 7.6 Hz, 2H), 7.53 – 7.45 (m, 4H), 7.45 – 7.38 (m, 5H), 7.38 – 7.29 (m, 3H), 6.03 (s, 1H), 4.92 (s, 1H), 4.02 – 3.72 (m, 2H), 3.47 (d, *J* = 15.3 Hz, 1H), 3.31 (d, *J* = 15.3 Hz, 1H), 3.06 (t, *J* = 8.6 Hz, 1H), 2.64 (d, *J* = 7.3 Hz, 1H), 2.59 (t, *J* = 8.6 Hz, 1H), 2.49 (s, 3H), 2.32 (s, 3H), 1.98 (d, *J* = 7.4 Hz, 1H), 1.05 – 0.86 (m, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.32, 171.3, 152.8, 144.3, 141.4, 140.2, 139.9, 138.3, 128.8, 128.6, 128.0, 127.9, 127.5, 127.2, 127.1, 126.64, 110.9, 73.8, 71.4, 60.5, 57.6, 55.2, 45.1, 43.1, 14.3, 14.2, 13.8. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{33}H_{34}N_3O_3$ 520.2595, found 520.2592.

ethyl 2-(4-(3,5-dimethyl-1*H*-pyrazole-1-carbonyl)-3-(4-fluorophenyl)-1-phenyl-2-azabicyclo[2.1.1]hexan-2-yl)acetate 3d

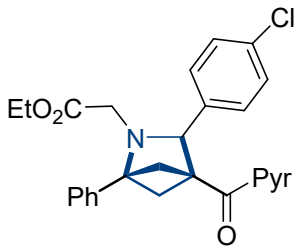


3d

The crude product was purified by column chromatography on silica gel (*n*-Hexane/acetone = 100:1). Colorless oil, 38.8

mg, 42% yield. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.45 (d, *J* = 7.1 Hz, 2H), 7.39 (t, *J* = 7.5 Hz, 2H), 7.33 (d, *J* = 7.2 Hz, 1H), 7.28 (td, *J* = 8.2, 2.5 Hz, 2H), 6.92 (t, *J* = 8.7 Hz, 2H), 6.00 (s, 1H), 4.84 (s, 1H), 3.92 – 3.67 (m, 2H), 3.42 (d, *J* = 15.3 Hz, 1H), 3.26 (d, *J* = 15.3 Hz, 1H), 3.00 (dd, *J* = 9.7, 7.6 Hz, 1H), 2.60 (d, *J* = 7.5 Hz, 1H), 2.53 – 2.47 (m, 1H), 2.46 (s, 3H), 2.30 (s, 3H), 1.93 (d, *J* = 7.6 Hz, 1H), 0.94 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.31, 171.3, 162.3 (d, *J* = 244.5 Hz), 153.0, 144.4, 138.2, 136.9, 129.1 (d, *J* = 7.9 Hz), 128.7, 128.2, 127.6, 114.8 (d, *J* = 21.2 Hz), 111.1, 73.4, 71.5, 60.6, 57.7, 55.1, 45.2, 43.0, 14.4, 14.3, 14.0. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -116.20. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{29}FN_3O_3$ 462.2187, found 462.2189.

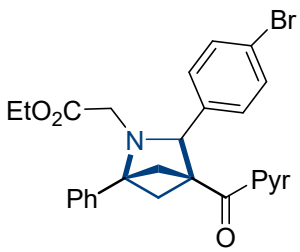
ethyl 2-(3-(4-chlorophenyl)-4-(3,5-dimethyl-1*H*-pyrazole-1-carbonyl)-1-phenyl-2-azabicyclo[2.1.1]hexan-2-yl)acetate 3e



3e

The crude product was purified by column chromatography on silica gel (*n*-Hexane/acetone = 100:1). Colorless oil, 49.7 mg, 52% yield. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.44 (d, *J* = 7.1 Hz, 2H), 7.39 (t, *J* = 7.4 Hz, 2H), 7.32 (t, *J* = 7.1 Hz, 1H), 7.28 – 7.23 (m, 2H), 7.20 (d, *J* = 8.5 Hz, 2H), 6.01 (s, 1H), 4.83 (s, 1H), 3.81 (q, *J* = 7.1 Hz, 2H), 3.42 (d, *J* = 15.4 Hz, 1H), 3.26 (d, *J* = 15.4 Hz, 1H), 3.00 (dd, *J* = 9.6, 7.8 Hz, 1H), 2.60 (d, *J* = 7.5 Hz, 1H), 2.54 – 2.41 (m, 4H), 2.29 (s, 3H), 1.93 (d, *J* = 7.6 Hz, 1H), 0.95 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.1, 171.0, 152.9, 144.3, 139.7, 138.0, 132.9, 128.9, 128.6, 128.1, 128.0, 127.5, 111.0, 73.4, 71.4, 60.5, 57.5, 55.0, 45.0, 42.9, 14.3, 14.2, 13.9. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{29}ClN_3O_3$ 478.1892, found 478.1897.

ethyl 2-(3-(4-bromophenyl)-4-(3,5-dimethyl-1*H*-pyrazole-1-carbonyl)-1-phenyl-2-azabicyclo[2.1.1]hexan-2-yl)acetate 3f

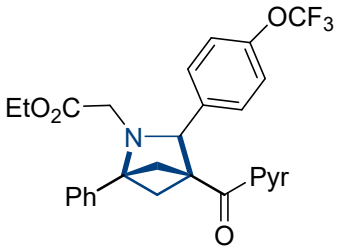


3f

The crude product was purified by column chromatography on silica gel (*n*-Hexane/acetone = 100:1). Colorless oil, 50.0 mg, 48% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.0 Hz, 2H), 7.43 – 7.32 (m, 5H), 7.24 – 7.17 (m, 2H), 6.02 (s, 1H), 4.83 (s, 1H), 3.83 (q, *J* = 7.2 Hz, 2H), 3.44 (dd, *J* = 15.5, 1.8 Hz, 1H), 3.27 (dd, *J* = 15.4, 1.8 Hz, 1H), 3.01 (t, *J* = 8.8 Hz, 1H), 2.62 (d, *J* = 7.5 Hz, 1H), 2.52 – 2.43 (m, 4H), 2.30 (s, 3H), 1.95 (d, *J* = 7.6 Hz, 1H), 1.00 – 0.91 (m, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.1, 170.9, 152.9,

144.3, 140.2, 138.0, 130.9, 129.3, 128.6, 128.1, 127.4, 121.1, 111.0, 73.4, 71.4, 60.5, 57.5, 54.9, 45.0, 42.9, 14.3, 14.2, 13.9. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{29}BrN_3O_3$ 522.1387, found 522.1386.

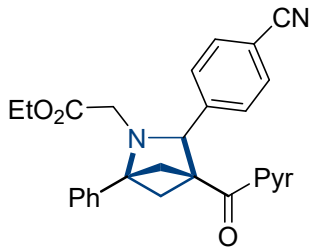
ethyl 2-(4-(3,5-dimethyl-1*H*-pyrazole-1-carbonyl)-1-phenyl-3-(4-(trifluoromethoxy)phenyl)-2-azabicyclo[2.1.1]hexan-2-yl)acetate 3g



3g

The crude product was purified by column chromatography on silica gel (*n*-Hexane/acetone = 100:1). Colorless oil, 37.9 mg, 36% yield. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.50 – 7.43 (m, 2H), 7.40 (t, *J* = 7.4 Hz, 2H), 7.38 – 7.30 (m, 3H), 7.09 (d, *J* = 8.2 Hz, 2H), 6.01 (s, 1H), 4.87 (s, 1H), 3.80 (q, *J* = 6.9 Hz, 2H), 3.44 (d, *J* = 15.4 Hz, 1H), 3.27 (d, *J* = 15.4 Hz, 1H), 3.01 (dd, *J* = 9.7, 7.7 Hz, 1H), 2.62 (d, *J* = 7.5 Hz, 1H), 2.53 – 2.48 (m, 1H), 2.47 (s, 3H), 2.29 (s, 3H), 1.97 (d, *J* = 7.6 Hz, 1H), 0.91 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.2, 171.0, 152.9, 148.4 (d, *J* = 1.7 Hz), 144.3, 139.9, 138.0, 128.9, 128.7, 128.1, 127.5, 120.6 (q, *J* = 256.5 Hz), 120.3, 111.1, 73.3, 71.4, 60.6, 57.5, 55.1, 45.1, 43.0, 14.3, 14.2, 13.7. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -57.79. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{28}H_{29}F_3N_3O_4$ 528.2105, found 528.2109.

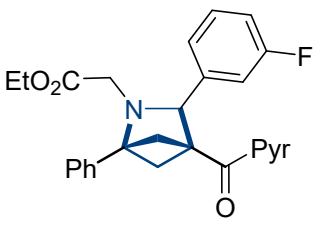
ethyl 2-(3-(4-cyanophenyl)-4-(3,5-dimethyl-1*H*-pyrazole-1-carbonyl)-1-phenyl-2-azabicyclo[2.1.1]hexan-2-yl)acetate 3h



3h

The crude product was purified by column chromatography on silica gel (*n*-Hexane/acetone = 50:1). Colorless oil, 41.2 mg, 44% yield. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.54 (d, *J* = 8.2 Hz, 2H), 7.51 – 7.37 (m, 6H), 7.34 (t, *J* = 6.8 Hz, 1H), 6.03 (s, 1H), 4.89 (s, 1H), 3.83 (q, *J* = 6.8 Hz, 2H), 3.44 (d, *J* = 15.8 Hz, 1H), 3.27 (d, *J* = 15.8 Hz, 1H), 3.01 (dd, *J* = 9.5, 8.0 Hz, 1H), 2.63 (d, *J* = 7.6 Hz, 1H), 2.54 – 2.37 (m, 4H), 2.29 (s, 3H), 1.96 (d, *J* = 7.7 Hz, 1H), 0.95 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.0, 170.6, 153.1, 147.0, 144.4, 137.6, 131.7, 128.7, 128.3, 128.2, 127.4, 119.3, 111.2, 110.9, 73.6, 71.5, 60.6, 57.7, 54.8, 45.0, 42.9, 14.30, 14.2, 13.9. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{28}H_{29}N_4O_3$ 469.2234, found 469.2234.

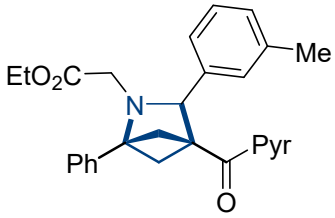
ethyl 2-(4-(3,5-dimethyl-1*H*-pyrazole-1-carbonyl)-3-(3-fluorophenyl)-1-phenyl-2-azabicyclo[2.1.1]hexan-2-yl)acetate 3i



3i

The crude product was purified by column chromatography on silica gel (*n*-Hexane/acetone = 100:1). Colorless oil, 48.8 mg, 53% yield. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.46 (dd, *J* = 8.2, 1.3 Hz, 2H), 7.41 (dd, *J* = 10.1, 4.7 Hz, 2H), 7.37 – 7.30 (m, 1H), 7.18 (ddd, *J* = 13.9, 9.2, 6.4 Hz, 2H), 6.96 – 6.84 (m, 2H), 6.02 (d, *J* = 0.5 Hz, 1H), 4.87 (s, 1H), 3.83 (qd, *J* = 7.1, 1.1 Hz, 2H), 3.44 (d, *J* = 15.3 Hz, 1H), 3.27 (d, *J* = 15.3 Hz, 1H), 3.02 (dd, *J* = 9.8, 7.6 Hz, 1H), 2.62 (d, *J* = 7.5 Hz, 1H), 2.52 – 2.48 (m, 1H), 2.47 (d, *J* = 0.6 Hz, 3H), 2.31 (s, 3H), 0.96 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.2, 171.0, 162.8 (d, *J* = 244.4 Hz), 152.9, 144.3, 144.0 (d, *J* = 6.9 Hz), 138.0, 129.2 (d, *J* = 8.2 Hz), 128.7, 128.1, 127.5, 122.8 (d, *J* = 2.7 Hz), 114.8 (d, *J* = 22.4 Hz), 114.0 (d, *J* = 21.4 Hz), 111.1, 73.4 (d, *J* = 1.9 Hz), 71.4, 60.6, 57.6, 55.0, 45.1, 42.9, 14.3, 14.2, 13.8. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -113.79 – -113.91 (m). **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{29}FN_3O_3$ 462.2187, found 462.2189.

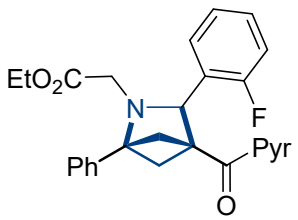
ethyl 2-(4-(3,5-dimethyl-1*H*-pyrazole-1-carbonyl)-1-phenyl-3-(*m*-tolyl)-2-azabicyclo[2.1.1]hexan-2-yl)acetate 3j



3j

The crude product was purified by column chromatography on silica gel (*n*-Hexane/acetone = 100:1). Colorless oil, 18.3 mg, 20% yield. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.51 – 7.45 (m, 2H), 7.40 (t, *J* = 7.4 Hz, 2H), 7.36 – 7.29 (m, 1H), 7.16 – 7.10 (m, 1H), 7.08 (d, *J* = 7.7 Hz, 1H), 7.04 (s, 1H), 7.00 (d, *J* = 7.1 Hz, 1H), 6.02 (s, 1H), 4.80 (s, 1H), 4.05 – 3.73 (m, 2H), 3.44 (d, *J* = 15.2 Hz, 1H), 3.27 (d, *J* = 15.2 Hz, 1H), 3.04 (dd, *J* = 9.7, 7.6 Hz, 1H), 2.62 (d, *J* = 7.4 Hz, 1H), 2.53 (dd, *J* = 9.7, 7.5 Hz, 1H), 2.46 (s, 3H), 2.32 (s, 3H), 2.28 (s, 3H), 1.93 (d, *J* = 7.4 Hz, 1H), 0.94 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.4, 171.3, 152.7, 144.2, 140.9, 138.3, 137.1, 128.6, 128.0, 128.0, 127.9, 127.7, 127.6, 124.6, 110.8, 73.9, 71.3, 60.4, 57.5, 55.2, 45.1, 42.9, 21.7, 14.2, 14.2, 13.8. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{28}H_{32}N_3O_3$ 458.2438, found 458.2444.

ethyl 2-(4-(3,5-dimethyl-1*H*-pyrazole-1-carbonyl)-3-(2-fluorophenyl)-1-phenyl-2-azabicyclo[2.1.1]hexan-2-yl)acetate 3k

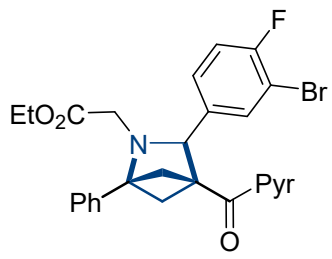


3k

The crude product was purified by column chromatography on silica gel (*n*-Hexane/acetone = 100:1). Colorless oil, 45.2

mg, 49% yield. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 8.34 – 8.13 (m, 1H), 7.48 (d, *J* = 7.2 Hz, 2H), 7.40 (t, *J* = 7.5 Hz, 2H), 7.33 (t, *J* = 7.2 Hz, 1H), 7.25 – 7.12 (m, 2H), 6.90 – 6.76 (m, 1H), 5.95 (s, 1H), 4.87 (s, 1H), 3.91 – 3.69 (m, 2H), 3.45 (d, *J* = 15.5 Hz, 1H), 3.31 (d, *J* = 15.5 Hz, 1H), 3.11 (dd, *J* = 9.7, 8.1 Hz, 1H), 2.67 (d, *J* = 7.8 Hz, 1H), 2.59 (dd, *J* = 9.7, 7.8 Hz, 1H), 2.50 (s, 3H), 2.22 (s, 3H), 1.94 (d, *J* = 7.6 Hz, 1H), 0.93 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.3, 171.1, 160.5 (d, *J* = 244.7 Hz), 152.0, 144.0, 138.0, 131.8 (d, *J* = 4.6 Hz), 128.7 (d, *J* = 8.2 Hz), 128.6 , 128.0, 127.8 (d, *J* = 13.8 Hz), 127.6, 123.6 (d, *J* = 3.1 Hz), 114.2 (d, *J* = 21.7 Hz), 110.6, 71.1, 68.7, 60.5, 56.5, 54.9, 44.8, 44.2, 14.4, 14.1, 13.8. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -118.28 – -118.48 (m). **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{29}FN_3O_3$ 462.2187, found 462.2184.

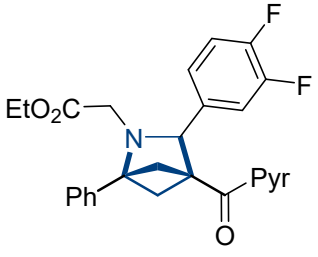
ethyl 2-(3-(3-bromo-4-fluorophenyl)-4-(3,5-dimethyl-1*H*-pyrazole-1-carbonyl)-1-phenyl-2-azabicyclo[2.1.1]hexan-2-yl)acetate 3l



3l

The crude product was purified by column chromatography on silica gel (*n*-Hexane/acetone = 100:1). Colorless oil, 43.1 mg, 40% yield. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.54 (dd, *J* = 6.8, 1.9 Hz, 1H), 7.43 (dt, *J* = 14.8, 4.6 Hz, 4H), 7.38 – 7.30 (m, 1H), 7.19 – 7.08 (m, 1H), 6.98 (t, *J* = 8.4 Hz, 1H), 6.03 (s, 1H), 4.79 (s, 1H), 3.85 (q, *J* = 7.1 Hz, 2H), 3.43 (d, *J* = 15.5 Hz, 1H), 3.25 (d, *J* = 15.5 Hz, 1H), 3.00 (dd, *J* = 9.7, 7.7 Hz, 1H), 2.63 (d, *J* = 7.6 Hz, 1H), 2.48 (s, 3H), 2.44 (dd, *J* = 9.7, 7.9 Hz, 1H), 2.30 (s, 3H), 1.96 (d, *J* = 7.7 Hz, 1H), 1.00 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.1, 170.9, 158.3 (d, *J* = 246.4 Hz), 153.1, 144.4, 138.7 (d, *J* = 3.3 Hz), 137.8, 132.7, 128.7, 128.2, 127.8 (d, *J* = 7.2 Hz), 127.4, 115.8 (d, *J* = 22.2 Hz), 111.2, 108.5 (d, *J* = 20.9 Hz), 72.8, 71.5, 60.6, 57.6, 54.9, 45.0, 42.8, 14.3, 14.2, 14.0. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -110.15 – -110.34 (m). **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{28}BrFN_3O_3$ 540.1293, found 540.1282.

ethyl 2-(3-(3,4-difluorophenyl)-4-(3,5-dimethyl-1*H*-pyrazole-1-carbonyl)-1-phenyl-2-azabicyclo[2.1.1]hexan-2-yl)acetate 3m

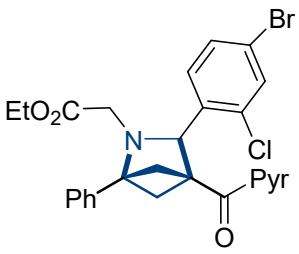


3m

The crude product was purified by column chromatography on silica gel (*n*-Hexane/acetone = 100:1). Colorless oil, 48.8 mg, 51% yield. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.43 (dt, *J* = 14.8, 4.6 Hz, 4H), 7.38 – 7.27

(m, 2H), 7.11 – 6.94 (m, 1H), 6.94 – 6.81 (m, 1H), 6.03 (s, 1H), 4.83 (s, 1H), 3.85 (q, *J* = 7.1 Hz, 2H), 3.43 (d, *J* = 15.5 Hz, 1H), 3.26 (d, *J* = 15.5 Hz, 1H), 3.00 (dd, *J* = 9.7, 7.7 Hz, 1H), 2.62 (d, *J* = 7.5 Hz, 1H), 2.48 (s, 3H), 2.45 (dd, *J* = 9.8, 7.9 Hz, 1H), 2.30 (s, 3H), 1.96 (d, *J* = 7.7 Hz, 1H), 1.00 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.2, 171.0, 153.2, 151.1 (dd, *J* = 48.6, 12.7 Hz), 148.7 (dd, *J* = 48.5, 12.8 Hz), 144.5, 138.5 (dd, *J* = 5.0, 3.6 Hz), 137.9, 128.8, 128.3, 127.5, 123.1 (dd, *J* = 6.2, 3.4 Hz), 116.9 (d, *J* = 18.2 Hz), 116.6 (d, *J* = 17.1 Hz), 111.3, 73.0, 71.5, 60.7, 57.7, 55.0, 45.2, 42.9, 14.4, 14.3, 14.0. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -138.34 – -138.51 (m), -140.67 – -140.85 (m). **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{28}F_2N_3O_3$ 480.2093, found 480.2101.

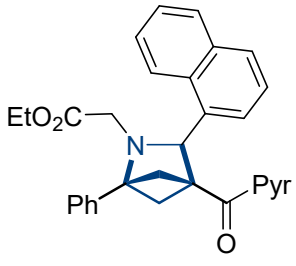
ethyl 2-(3-(4-bromo-2-chlorophenyl)-4-(3,5-dimethyl-1*H*-pyrazole-1-carbonyl)-1-phenyl-2-azabicyclo[2.1.1]hexan-2-yl)acetate 3n



3n

The crude product was purified by column chromatography on silica gel (*n*-Hexane/acetone = 100:1). Colorless oil, 45.5 mg, 41% yield. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 8.19 (d, *J* = 8.4 Hz, 1H), 7.46 (dd, *J* = 8.2, 1.8 Hz, 3H), 7.40 (t, *J* = 7.4 Hz, 2H), 7.37 – 7.30 (m, 1H), 7.30 – 7.22 (m, 1H), 5.87 (s, 1H), 4.73 (s, 1H), 3.90 – 3.70 (m, 2H), 3.39 (d, *J* = 15.5 Hz, 1H), 3.26 (d, *J* = 15.5 Hz, 1H), 3.02 (dd, *J* = 9.7, 8.3 Hz, 1H), 2.77 (dd, *J* = 9.8, 8.1 Hz, 1H), 2.64 (d, *J* = 8.0 Hz, 1H), 2.46 (s, 3H), 2.07 (s, 3H), 1.98 (d, *J* = 7.9 Hz, 1H), 0.92 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.2, 170.8, 151.9, 144.2, 137.9, 137.7, 133.5, 133.4, 131.1, 129.4, 128.7, 128.2, 127.5, 121.2, 110.8, 71.0, 70.7, 60.6, 56.5, 54.7, 45.0, 44.3, 14.5, 13.8, 13.8. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{28}BrClN_3O_3$ 556.0997, found 556.0985.

ethyl 2-(4-(3,5-dimethyl-1*H*-pyrazole-1-carbonyl)-3-(naphthalen-1-yl)-1-phenyl-2-azabicyclo[2.1.1]hexan-2-yl)acetate 3o

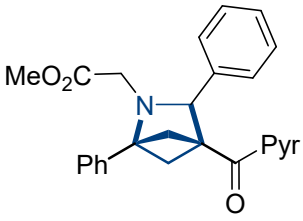


3o

The crude product was purified by column chromatography on silica gel (*n*-Hexane/acetone = 100:1). White solid, 23.7 mg, 24% yield. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 8.45 (d, *J* = 7.2 Hz, 1H), 7.79 – 7.68 (m, 2H), 7.58 – 7.50 (m, 3H), 7.45 – 7.30 (m, 4H), 7.30 – 7.24 (m, 1H), 7.02 – 6.85 (m, 1H), 5.86 (s, 1H), 5.30 (s, 1H), 3.75 – 3.56 (m, 2H), 3.48 (d, *J* = 14.8 Hz, 1H), 3.35 (d, *J* = 14.9 Hz, 1H), 3.23 (dd, *J*

= 9.9, 7.8 Hz, 1H), 2.83 (dd, *J* = 9.9, 7.7 Hz, 1H), 2.74 (d, *J* = 7.7 Hz, 1H), 2.27 (s, 3H), 2.04 (s, 3H), 1.93 (d, *J* = 7.6 Hz, 1H), 0.71 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.2, 171.1, 152.6, 144.6, 138.2, 136.1, 133.4, 131.6, 128.6, 128.5, 127.9, 127.8, 127.7, 127.5, 125.2, 124.7, 124.6, 121.9, 110.6, 70.8, 70.7, 60.3, 56.8, 55.0, 45.3, 44.1, 14.1, 14.0, 13.5. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{31}H_{32}N_3O_3$ 494.2438, found 494.2429.

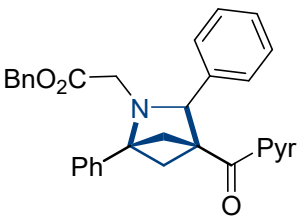
methyl 2-(4-(3,5-dimethyl-1*H*-pyrazole-1-carbonyl)-1,3-diphenyl-2-azabicyclo [2.1.1]hexan-2-yl)acetate 3p



3p

The crude product was purified by column chromatography on silica gel (*n*-Hexane/acetone = 100:1). Colorless oil, 42.9 mg, 50% yield. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.46 (d, *J* = 7.0 Hz, 2H), 7.38 (t, *J* = 7.4 Hz, 2H), 7.35 – 7.27 (m, 3H), 7.24 (t, *J* = 7.4 Hz, 2H), 7.21 – 7.13 (m, 1H), 6.00 (s, 1H), 4.87 (s, 1H), 3.44 (d, *J* = 15.2 Hz, 1H), 3.31 (s, 3H), 3.28 (d, *J* = 15.3 Hz, 1H), 3.05 – 2.99 (m, 1H), 2.61 (d, *J* = 7.4 Hz, 1H), 2.57 – 2.50 (m, 1H), 2.45 (s, 3H), 2.30 (s, 3H), 1.94 (d, *J* = 7.5 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.6, 171.2, 152.7, 144.2, 140.8, 138.2, 128.6, 128.0, 127.8, 127.5, 127.4, 127.1, 110.9, 73.9, 71.2, 57.5, 54.7, 51.3, 45.2, 42.9, 14.3, 14.2. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{26}H_{28}N_3O_3$ 430.2125; Found 430.2132.

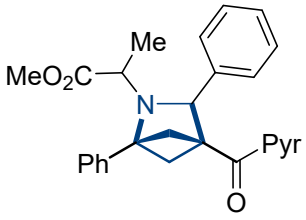
benzyl 2-(4-(3,5-dimethyl-1*H*-pyrazole-1-carbonyl)-1,3-diphenyl-2-azabicyclo [2.1.1]hexan-2-yl)acetate 3q



3q

The crude product was purified by column chromatography on silica gel (*n*-Hexane/acetone = 100:1). Colorless oil, 45.4 mg, 45% yield. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.49 – 7.41 (m, 2H), 7.40 – 7.33 (m, 2H), 7.33 – 7.25 (m, 6H), 7.25 – 7.17 (m, 3H), 7.15 – 7.07 (m, 2H), 6.00 (s, 1H), 4.90 (s, 1H), 4.75 (s, 2H), 3.51 (d, *J* = 15.4 Hz, 1H), 3.33 (d, *J* = 15.4 Hz, 1H), 3.01 (dd, *J* = 9.8, 7.4 Hz, 1H), 2.61 (d, *J* = 7.4 Hz, 1H), 2.52 (dd, *J* = 9.8, 7.5 Hz, 1H), 2.45 (s, 3H), 2.28 (s, 3H), 1.92 (d, *J* = 7.5 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.2, 171.1, 152.7, 144.2, 140.8, 138.2, 135.8, 128.6, 128.5, 128.3, 128.1, 128.0, 127.9, 127.5, 127.4, 127.2, 110.9, 74.0, 71.3, 66.3, 57.5, 55.0, 45.3, 42.9, 14.3, 14.2. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{32}H_{32}N_3O_3$ 506.2438; Found 506.2427.

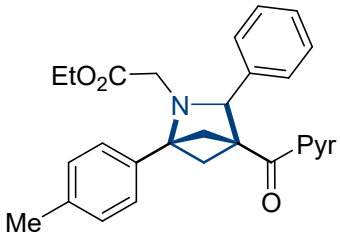
methyl 2-(4-(3,5-dimethyl-1*H*-pyrazole-1-carbonyl)-1,3-diphenyl-2-azabicyclo [2.1.1]hexan-2-yl)propanoate 3r



3r

The crude product was purified by column chromatography on silica gel (*n*-Hexane/acetone = 100:1). Colorless oil, 38.0 mg, 43% yield. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ δ 7.51 – 7.37 (m, 4H), 7.37 – 7.31 (m, 1H), 7.30 – 7.14 (m, 5H), 6.00 (s, 1H), 5.52 (s, 1H), 3.71 (s, 3H), 3.53 (d, *J* = 7.1 Hz, 1H), 2.95 – 2.76 (m, 1H), 2.57 (d, *J* = 7.4 Hz, 1H), 2.49 (s, 1H), 2.42 (s, 3H), 2.33 (s, 3H), 1.85 (d, *J* = 7.3 Hz, 1H), 1.01 (d, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.5, 171.6, 152.6, 144.1, 142.5, 138.6, 128.4, 127.9, 127.8, 127.6, 127.3, 127.2, 110.8, 71.0, 65.7, 56.4, 55.6, 51.3, 46.1, 43.8, 18.2, 14.2, 14.2. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{30}N_3O_3$ 444.2282; Found 444.2286.

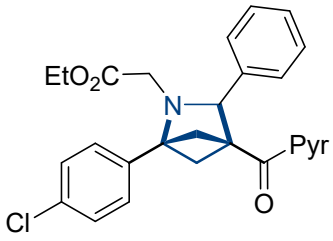
ethyl 2-(4-(3,5-dimethyl-1*H*-pyrazole-1-carbonyl)-3-phenyl-1-(*p*-tolyl)-2-azabicyclo[2.1.1]hexan-2-yl)acetate 3s



3s

The crude product was purified by column chromatography on silica gel (*n*-Hexane/acetone = 100:1). White solid, 53.9 mg, 59% yield. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.35 (d, *J* = 7.7 Hz, 2H), 7.29 (d, *J* = 6.9 Hz, 2H), 7.26 – 7.12 (m, 5H), 5.99 (s, 1H), 4.86 (s, 1H), 3.87 – 3.71 (m, 2H), 3.44 (d, *J* = 15.2 Hz, 1H), 3.26 (d, *J* = 15.2 Hz, 1H), 3.09 – 2.96 (m, 1H), 2.58 (d, *J* = 7.4 Hz, 1H), 2.55 – 2.46 (m, 1H), 2.45 (s, 3H), 2.36 (s, 3H), 2.30 (s, 3H), 1.90 (d, *J* = 7.4 Hz, 1H), 0.91 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.4, 171.3, 152.6, 144.2, 141.1, 137.6, 135.3, 129.2, 127.8, 127.5, 127.4, 127.1, 110.8, 73.9, 71.2, 60.4, 57.5, 55.1, 45.2, 42.8, 21.3, 14.3, 14.2, 13.8. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{28}H_{32}N_3O_3$ 458.2438; Found 458.2437.

ethyl 2-(1-(4-chlorophenyl)-4-(3,5-dimethyl-1*H*-pyrazole-1-carbonyl)-3-phenyl-2-azabicyclo[2.1.1]hexan-2-yl)acetate 3t

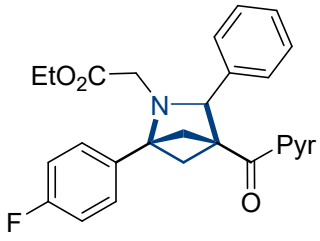


3t

The crude product was purified by column chromatography on silica gel (*n*-Hexane/acetone = 100:1). Colorless oil, 22.9 mg, 24% yield. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.32 (q, *J* = 8.4 Hz, 4H), 7.25 – 7.11 (m, 5H), 5.95 (s, 1H), 4.81 (s, 1H), 3.74 (qd, *J* = 7.1, 2.3 Hz,

2H), 3.33 (d, J = 15.2 Hz, 1H), 3.20 (d, J = 15.2 Hz, 1H), 2.94 (dd, J = 9.5, 7.8 Hz, 1H), 2.53 (d, J = 7.4 Hz, 1H), 2.44 (dd, J = 9.6, 7.8 Hz, 1H), 2.39 (s, 3H), 2.24 (s, 3H), 1.84 (d, J = 7.5 Hz, 1H), 0.87 (t, J = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.1, 171.0, 152.8, 144.3, 140.7, 136.8, 133.8, 129.0, 128.8, 127.9, 127.4, 127.2, 110.9, 74.0, 70.8, 60.5, 57.5, 55.0, 45.1, 43.1, 14.3, 14.2, 13.8. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{29}ClN_3O_3$ 478.1892; Found 478.1885.

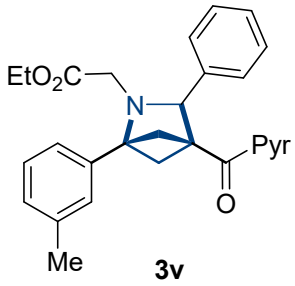
ethyl 2-(4-(3,5-dimethyl-1*H*-pyrazole-1-carbonyl)-1-(4-fluorophenyl)-3-phenyl-2-azabicyclo[2.1.1]hexan-2-yl)acetate 3u



3u

The crude product was purified by column chromatography on silica gel (*n*-Hexane/acetone = 100:1). Colorless oil, 32.2 mg, 35% yield. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.35 (dd, J = 8.2, 5.6 Hz, 2H), 7.24 – 7.09 (m, 5H), 6.99 (t, J = 8.6 Hz, 2H), 5.92 (s, 1H), 4.79 (s, 1H), 3.77 – 3.64 (m, 2H), 3.32 (d, J = 15.2 Hz, 1H), 3.18 (d, J = 15.2 Hz, 1H), 3.03 – 2.87 (m, 1H), 2.51 (d, J = 7.4 Hz, 1H), 2.46 – 2.39 (m, 1H), 2.37 (s, 3H), 2.21 (s, 3H), 1.82 (d, J = 7.4 Hz, 1H), 0.84 (t, J = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.1, 171.0, 162.4 (d, J = 246.5 Hz), 152.7, 144.2, 140.7, 134.0 (d, J = 3.1 Hz), 129.2 (d, J = 8.1 Hz), 127.8, 127.3, 127.1, 115.4 (d, J = 21.4 Hz), 110.8, 73.9, 70.6, 60.4, 57.3, 54.9, 45.2, 42.9, 14.2, 14.1, 13.7. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -114.05 – -114.16 (m). **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{29}FN_3O_3$ 462.2187; Found 462.2193.

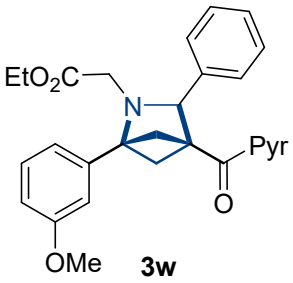
ethyl 2-(4-(3,5-dimethyl-1*H*-pyrazole-1-carbonyl)-3-phenyl-1-(*m*-tolyl)-2-azabicyclo[2.1.1]hexan-2-yl)acetate 3v



3v

The crude product was purified by column chromatography on silica gel (*n*-Hexane/acetone = 100:1). Colorless oil, 32.9 mg, 36% yield. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.33 – 7.22 (m, 7H), 7.21 – 7.11 (m, 2H), 6.00 (s, 1H), 4.85 (s, 1H), 3.85 – 3.73 (m, 2H), 3.44 (d, J = 15.2 Hz, 1H), 3.27 (d, J = 15.3 Hz, 1H), 3.02 (dd, J = 9.8, 7.4 Hz, 1H), 2.59 (d, J = 7.4 Hz, 1H), 2.52 (dd, J = 9.9, 7.5 Hz, 1H), 2.45 (s, 3H), 2.39 (s, 3H), 2.30 (s, 3H), 1.91 (d, J = 7.5 Hz, 1H), 0.91 (t, J = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.4, 171.3, 152.7, 144.2, 141.1, 138.2, 138.2, 128.7, 128.5, 128.1, 127.8, 127.5, 127.1, 124.6, 110.8, 74.0, 71.3, 60.4, 57.5, 55.1, 45.2, 42.84, 21.6, 14.3, 14.2, 13.8. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{28}H_{32}N_3O_3$ 458.2438; Found 458.2436.

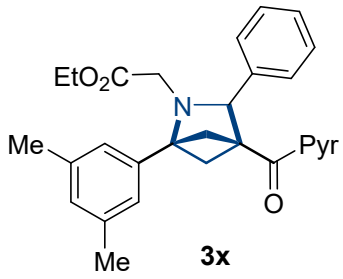
ethyl 2-(4-(3,5-dimethyl-1*H*-pyrazole-1-carbonyl)-1-(3-methoxyphenyl)-3-phenyl-2-azabicyclo[2.1.1]hexan-2-yl)acetate 3w



3w

The crude product was purified by column chromatography on silica gel (*n*-Hexane/acetone = 100:1). Colorless oil, 25.5 mg, 27% yield. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.34 – 7.26 (m, 3H), 7.27 – 7.14 (m, 3H), 7.08 – 7.01 (m, 2H), 6.89 – 6.82 (m, 1H), 6.00 (s, 1H), 4.86 (s, 1H), 3.85 (s, 3H), 3.83 – 3.76 (m, 2H), 3.46 (d, *J* = 15.2 Hz, 1H), 3.27 (d, *J* = 15.3 Hz, 1H), 3.00 (dd, *J* = 9.8, 7.4 Hz, 1H), 2.60 (d, *J* = 7.4 Hz, 1H), 2.55 – 2.48 (m, 1H), 2.45 (s, 3H), 2.30 (s, 3H), 1.92 (d, *J* = 7.5 Hz, 1H), 0.92 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.3, 171.2, 159.9, 152.7, 144.2, 141.0, 139.9, 129.6, 127.8, 127.4, 127.1, 119.8, 113.3, 113.1, 110.9, 74.0, 71.3, 60.4, 57.4, 55.4, 55.1, 45.2, 43.0, 14.3, 14.2, 13.8. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{28}H_{32}N_3O_4$ 474.2387; Found 474.2395.

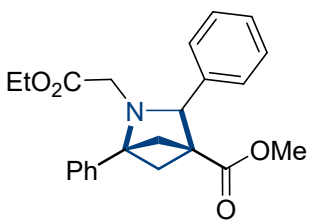
ethyl 2-(4-(3,5-dimethyl-1*H*-pyrazole-1-carbonyl)-1-(3,5-dimethylphenyl)-3-phenyl-2-azabicyclo[2.1.1]hexan-2-yl)acetate 3x



3x

The crude product was purified by column chromatography on silica gel (*n*-Hexane/acetone = 100:1). Colorless oil, 34.8 mg, 37% yield. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.29 (d, *J* = 7.5 Hz, 2H), 7.25 – 7.17 (m, 3H), 7.06 (s, 2H), 6.95 (s, 1H), 5.99 (s, 1H), 4.83 (s, 1H), 3.85 – 3.73 (m, 2H), 3.45 (d, *J* = 15.3 Hz, 1H), 3.26 (d, *J* = 15.3 Hz, 1H), 3.08 – 2.96 (m, 1H), 2.57 (d, *J* = 7.4 Hz, 1H), 2.55 – 2.48 (m, 1H), 2.45 (s, 3H), 2.35 (s, 6H), 2.30 (s, 3H), 1.89 (d, *J* = 7.5 Hz, 1H), 0.91 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.4, 171.3, 152.6, 144.2, 141.2, 138.2, 138.1, 129.6, 127.8, 127.5, 127.1, 125.2, 110.8, 74.0, 71.3, 60.4, 57.6, 55.2, 45.3, 42.8, 21.5, 14.3, 14.2, 13.8. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{29}H_{34}N_3O_3$ 472.2595; Found 472.2589.

methyl 2-(2-ethoxy-2-oxoethyl)-1,3-diphenyl-2-azabicyclo[2.1.1]hexane-4-carboxylate 3y

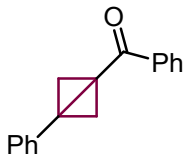


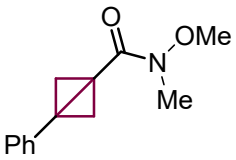
3y

The crude product was purified by column chromatography on silica gel (*n*-Hexane/acetone = 100:1). Colorless oil, 43.2 mg, 57% yield. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.55 (d, *J* = 7.6 Hz, 2H), 7.37 – 7.27 (m, 4H), 7.27 – 7.21 (m, 3H),

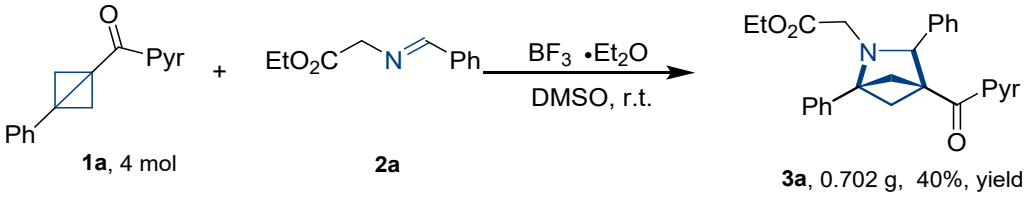
7.20 – 7.12 (m, 1H), 4.27 (s, 1H), 3.73 – 3.61 (m, 2H), 3.56 (d, J = 1.0 Hz, 3H), 3.29 (d, J = 14.9 Hz, 1H), 3.08 (d, J = 14.9 Hz, 1H), 2.63 – 2.51 (m, 1H), 2.39 – 2.32 (m, 2H), 1.83 (d, J = 7.4 Hz, 1H), 0.85 – 0.77 (m, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.4, 170.9, 140.7, 137.8, 128.6, 128.1, 128.0, 127.8, 127.3, 72.4, 71.7, 60.5, 54.7, 54.3, 51.6, 43.0, 42.4, 13.7. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{23}H_{26}NO_4$ 380.1856; Found 380.1862.

Unsuccessful examples:



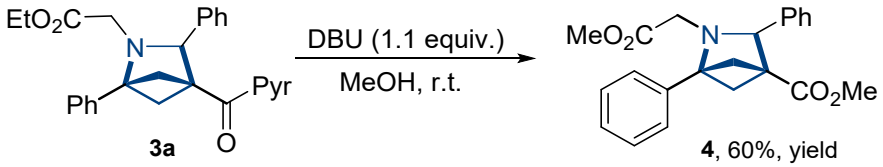


4. Gram-scale reaction



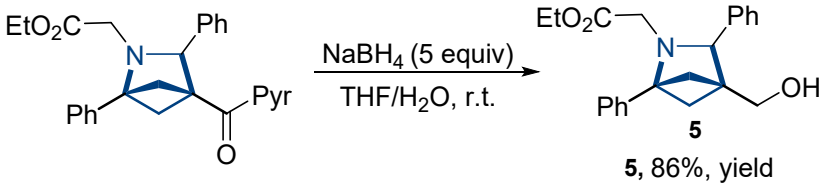
To a 10 mL reaction vial equipped with a magnetic stir bar was added compounds **1** (4.0 mmol, 1.0 equiv), **2** (12.0 mmol, 3.0 equiv), $BF_3{\cdot}Et_2O$ (BF_3 46.5%) (120 mol%), and the tube was evacuated and backfilled with argon three times. DMSO (40 mL) was added under argon atmosphere. The mixture was then stirred rapidly for 16 hours. Upon completion of the reaction, the aqueous phases were extracted with EtOAc (3 × 50 mL). The combined organic phases were washed with saturated brine (50 mL), then dried over Na_2SO_4, concentrated under reduced pressure. The crude product was purified by silica gel chromatography on silica gel (*n*-Hexane/acetone = 100:1) to afford the product **3a** (0.7 g, 40% yield) as a colorless oil.

5. Post-functionalizations

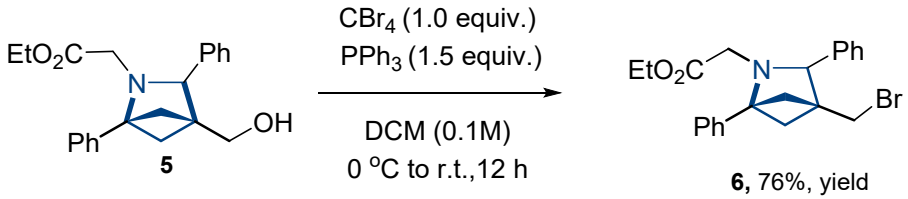


To a solution of **3a** (0.2 mmol, 88.6 mg) in MeOH (2 mL) at room temperature was added DBU (0.22 mmol, 33.5 mg) and the mixture was stirred at room temperature for 16 h. After removal of the solvents under reduced pressure, the product was purified

by silica gel column chromatography (EtOAc/Pentane = 1/5) to afford **4** (43.8 mg, 60%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.62 (d, *J* = 7.5 Hz, 2H), 7.46 – 7.28 (m, 7H), 7.26 (d, *J* = 7.0 Hz, 1H), 4.33 (s, 1H), 3.64 (s, 3H), 3.38 (d, *J* = 14.9 Hz, 1H), 3.29 (s, 3H), 3.17 (d, *J* = 15.0 Hz, 1H), 2.71 – 2.61 (m, 1H), 2.44 (t, *J* = 8.5 Hz, 2H), 1.93 (d, *J* = 7.4 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.4, 171.3, 140.5, 137.7, 128.6, 128.1, 128.0, 127.9, 127.4, 127.3, 72.5, 71.6, 54.4, 54.3, 51.7, 51.4, 43.1, 42.5. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{22}H_{24}NO_4$ 336.1700; Found 336.1699.

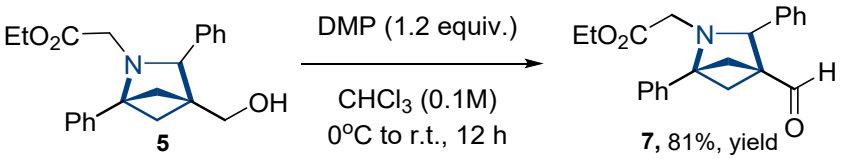


To a solution of **3a** (0.2 mmol, 88.6 mg) in a mixed solvent of THF/H_2O (v/v = 1/1, 6 mL) at room temperature was added $NaBH_4$ (1 mmol, 37.8 mg) in one portion, and stirred for 3 h and then quenched by addition of 4 mL saturated $NaHCO_3$ solution. The mixture was extracted with EtOAc (3×10 mL). The combined organic layer was dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated under reduced pressure and the mixture was purified by silica gel column chromatography (EtOAc/Pentane = 1/4) to afford **5** (60.3 mg, 86%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.65 (d, *J* = 7.5 Hz, 2H), 7.44 (d, *J* = 7.5 Hz, 2H), 7.36 (q, *J* = 7.7 Hz, 4H), 7.32 – 7.20 (m, 2H), 4.00 (s, 1H), 3.78 – 3.68 (m, 2H), 3.66 (d, *J* = 11.5 Hz, 1H), 3.58 (d, *J* = 11.6 Hz, 1H), 3.33 (d, *J* = 14.7 Hz, 1H), 3.11 (d, *J* = 14.7 Hz, 1H), 2.35 – 2.27 (m, 1H), 2.24 – 2.17 (m, 1H), 2.12 (d, *J* = 7.1 Hz, 1H), 1.69 (s, 1H), 1.53 (d, *J* = 7.0 Hz, 1H), 0.87 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.4, 141.3, 138.9, 128.5, 128.4, 127.9, 127.8, 127.4, 126.9, 72.0, 71.7, 62.1, 60.4, 54.7, 53.8, 41.7, 39.1, 13.7. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{22}H_{26}NO_3$ 352.1907; Found 352.1912.

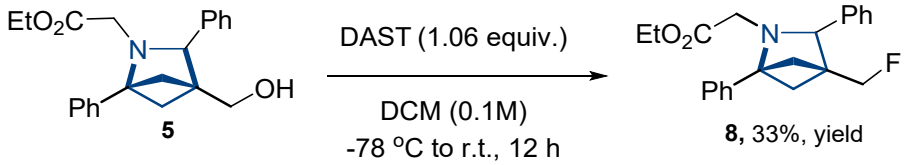


Under N_2 atmosphere, at 0 °C, **5** (70 mg, 0.2 mmol, 1 equiv.), triphenylphosphine (78 mg, 0.3 mmol, 1.5 equiv.) and carbon tetrabromide (73 mg, 0.22 mmol, 1.1 equiv.) were dissolved in DCM (2 mL). The mixture was slowly warmed up to room

temperature and stirred 12 hours. After removal of the solvents under reduced pressure, the product was purified by silica gel column chromatography (EtOAc/Pentane = 1/10) to afford **6** (63 mg, 76%) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.74 (d, *J* = 7.6 Hz, 2H), 7.44 (d, *J* = 6.8 Hz, 2H), 7.41 – 7.34 (m, 4H), 7.34 – 7.26 (m, 2H), 4.03 (s, 1H), 3.83 – 3.65 (m, 2H), 3.47 – 3.36 (m, 2H), 3.32 (d, *J* = 14.9 Hz, 1H), 3.13 (d, *J* = 14.9 Hz, 1H), 2.38 (dd, *J* = 10.1, 7.3 Hz, 1H), 2.30 (dd, *J* = 10.1, 6.9 Hz, 1H), 2.12 (d, *J* = 7.2 Hz, 1H), 1.54 (d, *J* = 6.9 Hz, 1H), 0.88 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.1, 140.5, 138.3, 128.6, 128.3, 128.0, 127.4, 127.2, 71.5, 71.0, 60.4, 54.6, 52.3, 44.1, 41.2, 34.0, 13.8. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{22}H_{25}BrNO_2$ 414.1063; Found 414.1060.

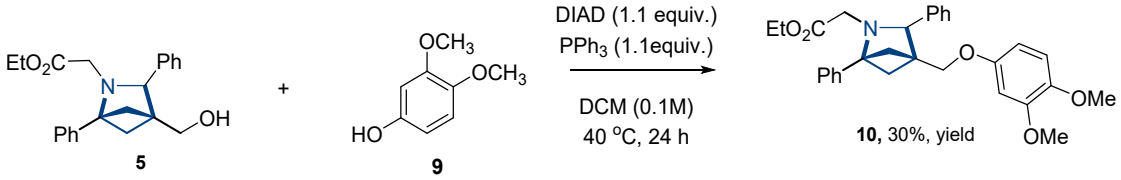


A solution of **5** (70 mg, 0.2 mmol, 1 equiv.) in $CHCl_3$ (2 mL) was ice-cooled under a nitrogen atmosphere, Dess-Martin periodinane (102mg, 1.2 equiv.) was added thereto, and the mixture was stirred at room temperature for 12 hours. Completion of the reaction was monitored by TLC. A mixed solution of saturated aqueous solution of sodium thiosulfate : $NaHCO_3$: water (1:1:1 v:v, 10 mL) was added to quench the reaction, and the resultant mixture was extracted with DCM (3 x 10 mL). The combined organic layers were dried with Na_2SO_4 and concentrated under reduced, the mixture was purified by silica gel column chromatography (EtOAc/Pentane = 1/10) to afford **7** (57 mg, yield 81%) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 9.75 (s, 1H), 7.66 – 7.60 (m, 2H), 7.46 – 7.42 (m, 2H), 7.42 – 7.32 (m, 5H), 7.28 – 7.23 (m, 1H), 4.40 (s, 1H), 3.84 – 3.71 (m, 2H), 3.38 (d, *J* = 14.9 Hz, 1H), 3.16 (d, *J* = 15.0 Hz, 1H), 2.57 (dd, *J* = 10.0, 7.1 Hz, 1H), 2.49 (dd, *J* = 10.0, 7.0 Hz, 1H), 2.41 (d, *J* = 7.0 Hz, 1H), 1.89 (dd, *J* = 7.0, 1.1 Hz, 1H), 0.91 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 200.1, 170.9, 140.4, 137.6, 128.7, 128.3, 128.2, 127.5, 127.3, 72.3, 71.4, 60.6, 60.3, 54.5, 42.3, 40.7, 13.8. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{22}H_{24}NO_3$ 350.1751; Found 350.1748.



To a stirred solution of **5** (70 mg, 0.2 mmol, 1 equiv.) in DCM (2 mL) at -78 °C

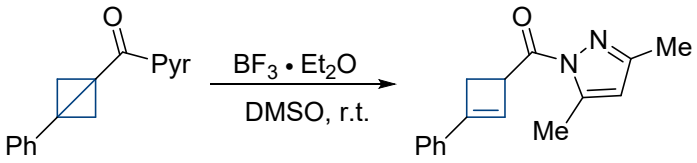
was added dropwise DAST ((34 mg, 0.21 mmol, 1.06 equiv.)). The solution was slowly warmed to room temperature and left overnight. The mixture was washed with a solution K_2CO_3 (63 mg, 0.46 mmol, 2.29 equiv.) in 1 ml of water, water (1 mL), brine (1 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure, the mixture was purified by silica gel column chromatography (EtOAc/Pentane = 1/10) to afford **8** (22.9 mg, yield 33%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ δ 7.63 (d, *J* = 7.6 Hz, 2H), 7.45 (d, *J* = 6.9 Hz, 2H), 7.37 (td, *J* = 7.4, 5.1 Hz, 4H), 7.35 – 7.20 (m, 2H), 4.39 (td, *J* = 47.2, 10.0 Hz, 2H), 4.06 (s, 1H), 3.74 (qq, *J* = 7.1, 3.6 Hz, 2H), 3.34 (d, *J* = 14.8 Hz, 1H), 3.13 (d, *J* = 14.8 Hz, 1H), 2.40 (dd, *J* = 10.2, 7.4 Hz, 1H), 2.22 (dd, *J* = 9.2, 7.2 Hz, 2H), 1.56 (d, *J* = 7.1 Hz, 1H), 0.88 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.2, 140.6, 138.5, 128.6, 128.4, 128.0, 127.9, 127.4, 127.1, 82.4 (d, *J* = 165.3 Hz), 72.4, 71.2 (d, *J* = 2.9 Hz), 60.4, 54.7, 51.8 (d, *J* = 20.9 Hz), 41.5 (d, *J* = 7.8 Hz), 39.5 (d, *J* = 2.2 Hz), 13.8. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -226.15 (t, *J* = 47.3 Hz). **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{22}H_{25}FNO_2$ 354.1864; Found 354.1858.



To a mixture of **5** (70 mg, 0.2 mmol, 1 equiv.), 3,4-dimethoxyphenol (34 mg, 0.22 mmol, 1.1 equiv.), and triphenylphosphine (57 mg, 0.22 mmol, 1.1 equiv.) in dry DCM (1.5 mL) was added dropwise diisopropylazodicarboxylate (73 mg, 0.22 mmol, 1.1 equiv.) at room temperature. The mixture was heated at reflux for 24 hours. The solvent was removed by rotary evaporation and the product was purified by silica gel column chromatography (EtOAc/Pentane = 1/5) to afford **10** (28.0 mg, yield 30%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.69 – 7.60 (m, 2H), 7.47 (d, *J* = 7.0 Hz, 2H), 7.39 (t, *J* = 7.4 Hz, 2H), 7.31 (q, *J* = 7.2 Hz, 3H), 7.28 – 7.20 (m, 1H), 6.76 (d, *J* = 8.7 Hz, 1H), 6.54 (d, *J* = 2.7 Hz, 1H), 6.34 (dd, *J* = 8.7, 2.8 Hz, 1H), 4.17 (s, 1H), 3.92 – 3.79 (m, 8H), 3.80 – 3.70 (m, 2H), 3.37 (d, *J* = 14.7 Hz, 1H), 3.17 (d, *J* = 14.7 Hz, 1H), 2.46 (dd, *J* = 10.1, 7.3 Hz, 1H), 2.29 (dd, *J* = 10.1, 7.0 Hz, 1H), 2.22 (d, *J* = 7.3 Hz, 1H), 1.61 (d, *J* = 7.1 Hz, 1H), 0.89 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.4, 153.7, 145.0, 143.8, 141.0, 138.8, 128.5, 128.4, 127.9, 127.8, 127.4, 126.9, 111.9, 103.8, 100.9, 72.4, 71.5, 67.3, 60.4, 56.6, 56.0, 54.8, 51.6, 42.3, 40.1, 13.8. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{30}H_{34}NO_5$ 488.2431; Found 488.2426.

6. Mechanistic studies

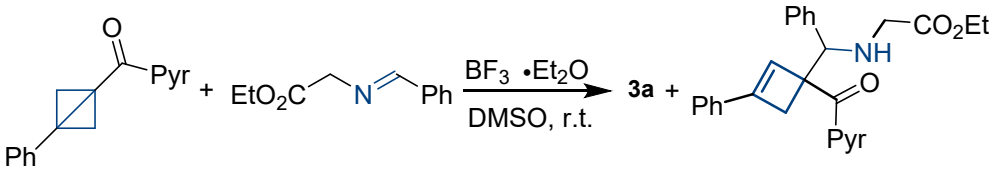
A) Control experiment: reaction without **2a**



1a **11**, 20% yield

To a 10 mL reaction vial equipped with a magnetic stir bar was added compound **1a** (0.1 mmol, 1.0 equiv), $BF_3{\cdot}OEt_2$ (BF_3 46.5%) (120 mol%), and the tube was evacuated and backfilled with argon three times. DMSO (1 mL) were added under argon atmosphere. The mixture was then stirred rapidly for 16 hours. Upon completion of the reaction, the aqueous phases were extracted with EtOAc (3 × 10 mL). The combined organic phases were washed with saturated brine (20 mL), then dried over Na_2SO_4, concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel to afford **11** (5.4 mg, 20% yield) a yellow oil.

B) Detection of the byproduct **12** of the reaction

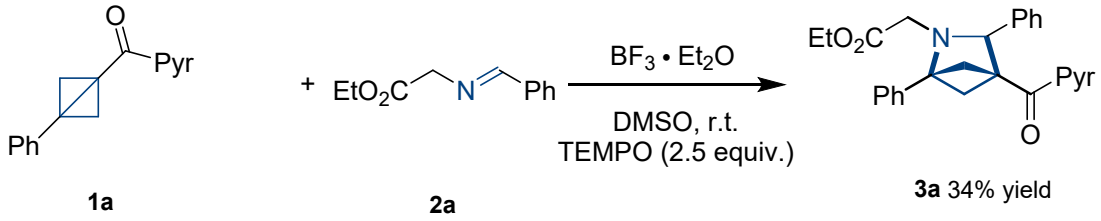


1a **2a** **12**, 10% yield

To a 10 mL reaction vial equipped with a magnetic stir bar was added compound **1a** (4 mmol, 1.0 equiv.), **2a** (12.0 mmol, 3.0 equiv.), $BF_3{\cdot}OEt_2$ (BF_3 46.5%) (120 mol%), and the tube was evacuated and backfilled with argon three times. DMSO (4 mL) were added under argon atmosphere. The mixture was then stirred rapidly for 16 hours. Upon completion of the reaction, the aqueous phases were extracted with EtOAc (3 × 50 mL). The combined organic phases were washed with saturated brine (50 mL), then dried over Na_2SO_4, concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel to afford **12** (177.2 mg, 10% yield, 3.1:1 d.r.) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm) δ 7.35 (d, J = 7.1 Hz, 2H), 7.32 – 7.27 (m, 3H), 7.27 – 7.20 (m, 3H), 7.20 – 7.09 (m, 2H), 6.70 (d, J = 18.2 Hz, 1H), 5.93 (s, 1H), 4.80 (s, 0.21H), 4.68 (s, 70H), 4.10 (q, J = 7.1 Hz, 2H), 3.43 – 3.08 (m, 4H), 2.44 – 2.19 (m, 6H), 1.19 (q, J = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.2 and 172.9, 172.5 and 172.2, 151.7 and 151.5, 148.5 and 147.0, 144.8 and 144.7, 139.2 and 139.1, 133.7 and133.6, 128.4, 128.36 and 128.3, 128.2 and 128.1, 128.0,

127.9 and 127.8, 127.8 and 127.7, 125.2 and 125.1, 110.4, 65.2 and 64.8, 60.8 and 60.7, 59.4 and 58.7, 49.1 and 48.8, 36.5 and 35.6, 14.5 and 14.4, 14.3 and 14.2, 14.1 and 14.0. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{29}N_2O_5$ 444.2282; Found 444.2282.

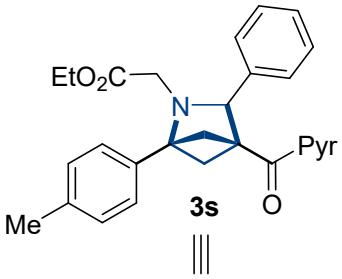
C) TEMPO radical trapping experiment

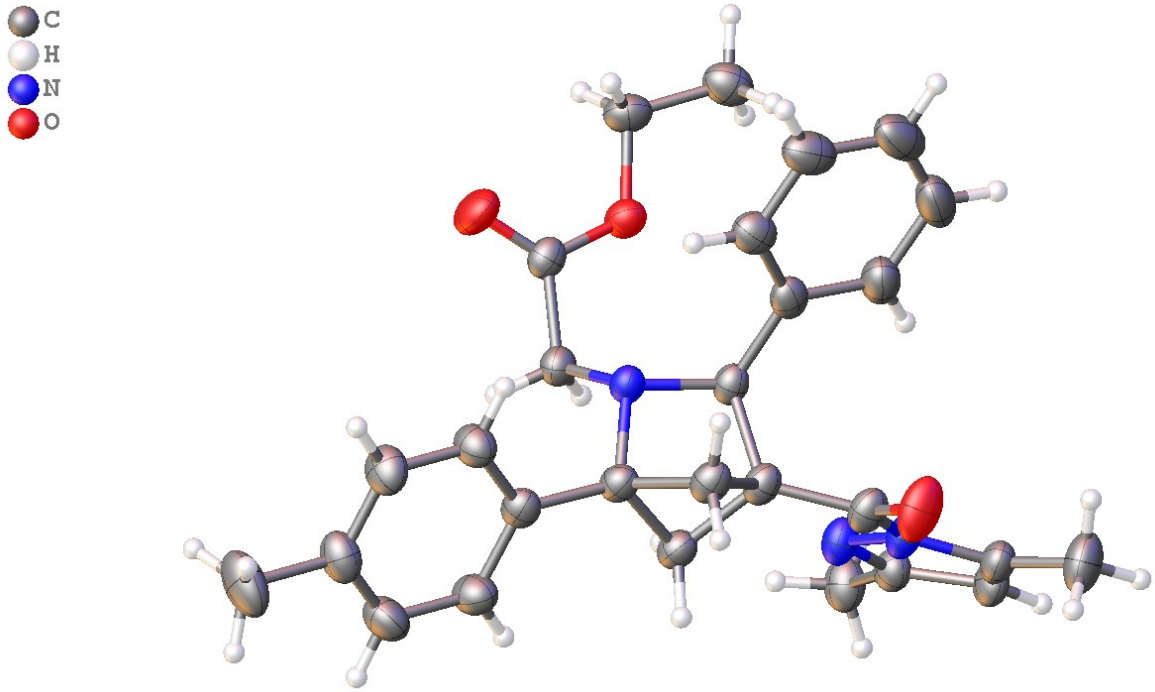


To a 10 mL reaction vial equipped with a magnetic stir bar was added compounds **1a** (0.2 mmol, 1.0 equiv.), **2a** (0.3 mmol, 3.0 equiv.), 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) (0.5 mmol, 2.5 equiv.), $BF_3{\cdot}OEt_2$ (BF_3 46.5%) (120 mol%), and the tube was evacuated and backfilled with argon three times. DMSO (2 mL) was added under argon atmosphere. The mixture was then stirred rapidly for 16 hours. Upon completion of the reaction, the aqueous phases were extracted with EtOAc (3 × 10 mL). The combined organic phases were washed with saturated brine (20 mL), then dried over Na_2SO_4, concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel chromatography on silica gel (*n*-Hexane/acetone = 100:1) to afford **3a** (30.1 mg, 34% yield) a colorless oil.

7. X-ray crystallographic data

The structure of **3s** were determined by the X-ray diffraction analysis of single crystal, which recrystallized from a mixed solution of CH_2Cl_2 and *n*-hexane. CCDC 2427959, contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.





ORTEP of **3s**
(CCDC: 2427959)
Thermal probability ellipsoids shown at the 40% probability level.

Table S6. Crystal data and structure refinement for **3s**.

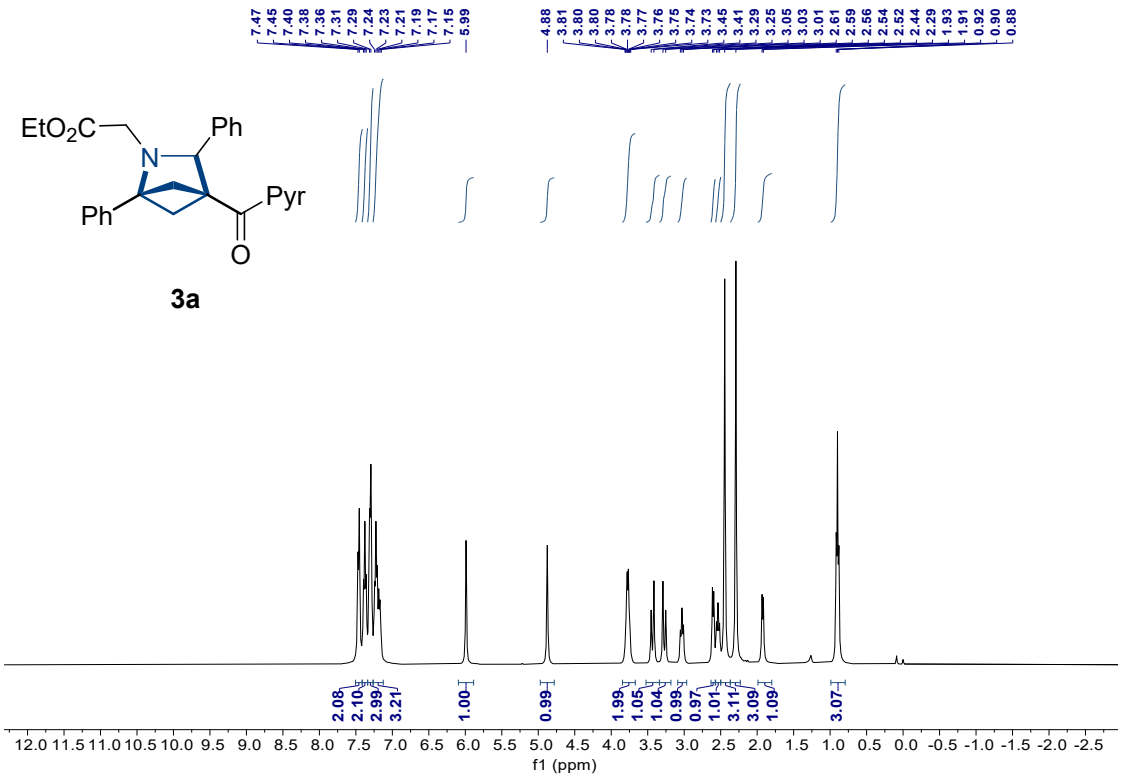
Identification code	**3s**
CCDC Deposit number	2427337
Empirical formula	$C_{28}H_{31}N_3O_3$
Formula weight	457.56
Temperature/K	257.00
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	10.1640(5)
b/Å	12.2391(6)
c/Å	20.0638(9)
α/°	90
β/°	95.683(2)
γ/°	90
Volume/Å^3	2483.6(2)
Z	4
ρ_{calc}g/cm^3	1.224
μ/mm^{-1}	0.639
F(000)	976.0
Crystal size/mm^3	0.3 × 0.2 × 0.1
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	10.188 to 137.344
Index ranges	$-12 \le h \le 12$, $-14 \le k \le 14$, $-23 \le l \le 24$
Reflections collected	36134
Independent reflections	4496 [R_{int} = 0.0340, R_{sigma} = 0.0183]
Data/restraints/parameters	4496/0/311
Goodness-of-fit on F^2	1.050
Final R indexes [I>=2σ (I)]	R_1 = 0.0380, wR_2 = 0.0974
Final R indexes [all data]	R_1 = 0.0400, wR_2 = 0.0990
Largest diff. peak/hole / e Å^{-3}	0.22/-0.14

8. References

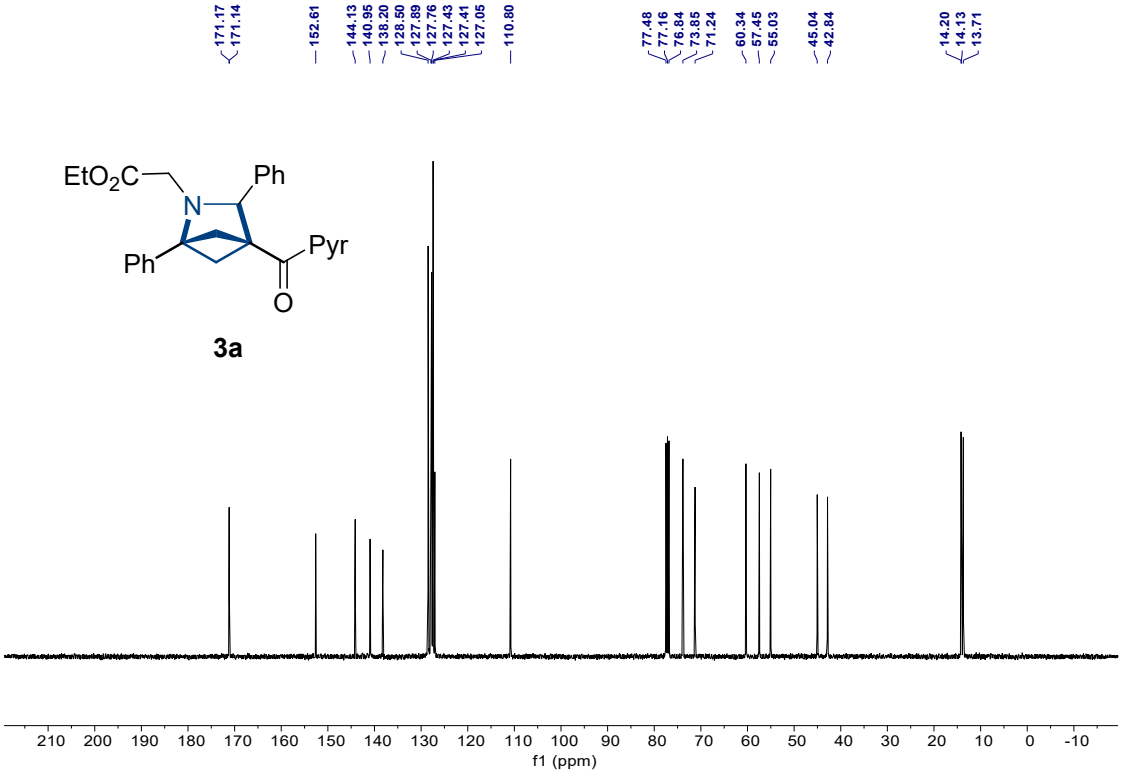
1. C. Zhang; J. Yang, W. Zhou, Q. Tan, Z. Yang, L. He, M. Zhang, Enantioselective Mannich Reaction of Glycine Iminoesters with N-Phosphinoyl Imines: A Bifunctional Approach, *Org. Lett*. 2019, **21**, 8620.
2. Y. Liang, F. Paulus, C. G. Daniliuc, F. Glorius. Catalytic Formal [2π+2σ] Cycloaddition of Aldehydes with Bicyclobutanes: Expedient Access to Polysubstituted 2-Oxabicyclo[2.1.1]hexanes, *Angew. Chem. Int. Ed*. 2023, **62**, e202305043.

9. Copies of NMR spectra of the products

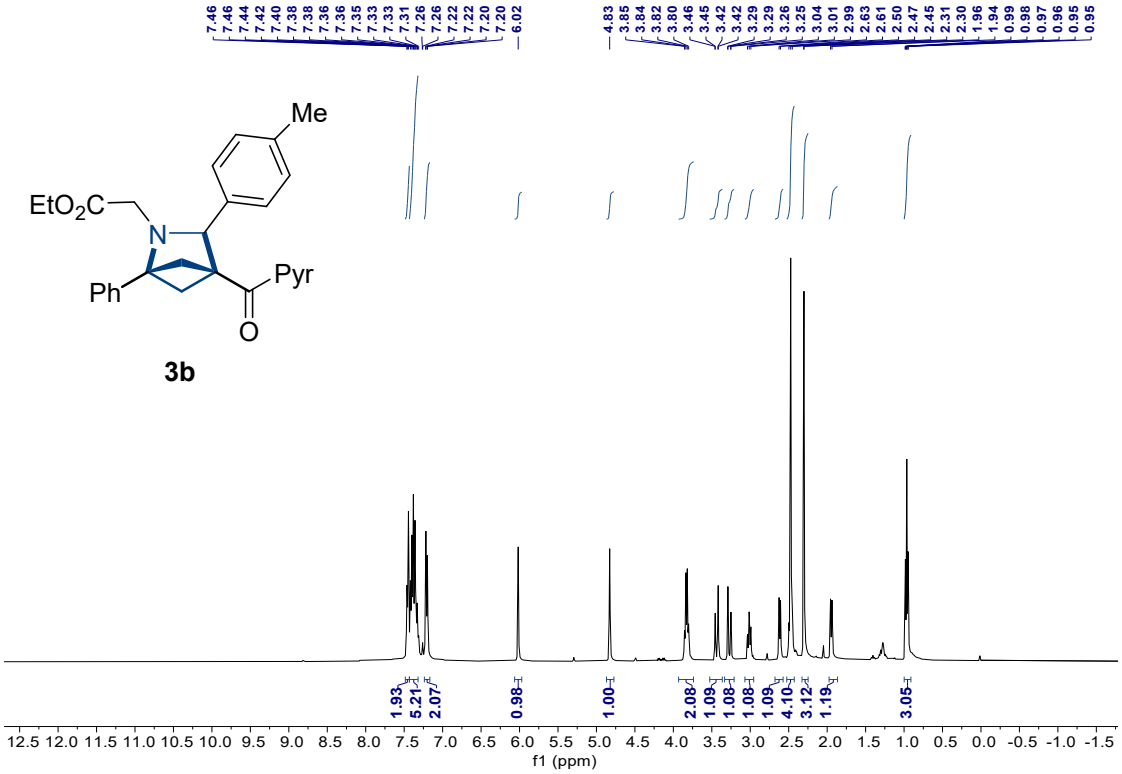
^{1}H NMR (400 MHz, $CDCl_3$) of **3a**



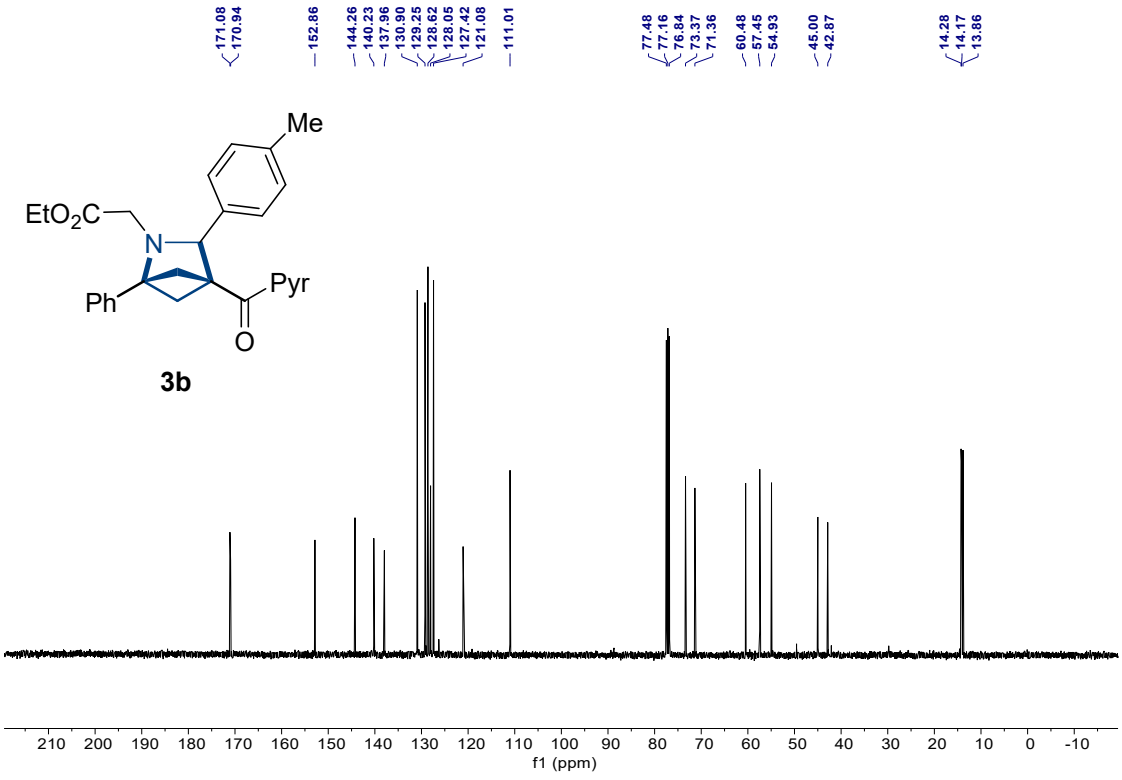
^{13}C NMR (101 MHz, $CDCl_3$) of **3a**



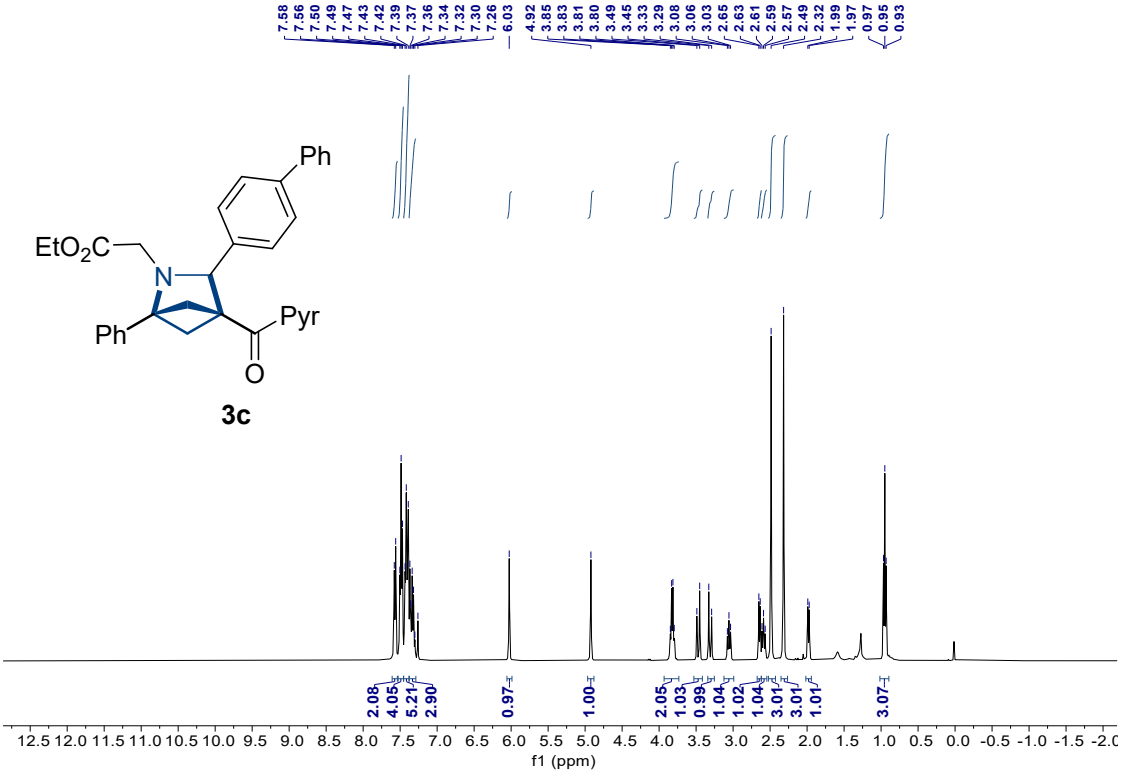
^{1}H NMR (400 MHz, $CDCl_3$) of **3b**



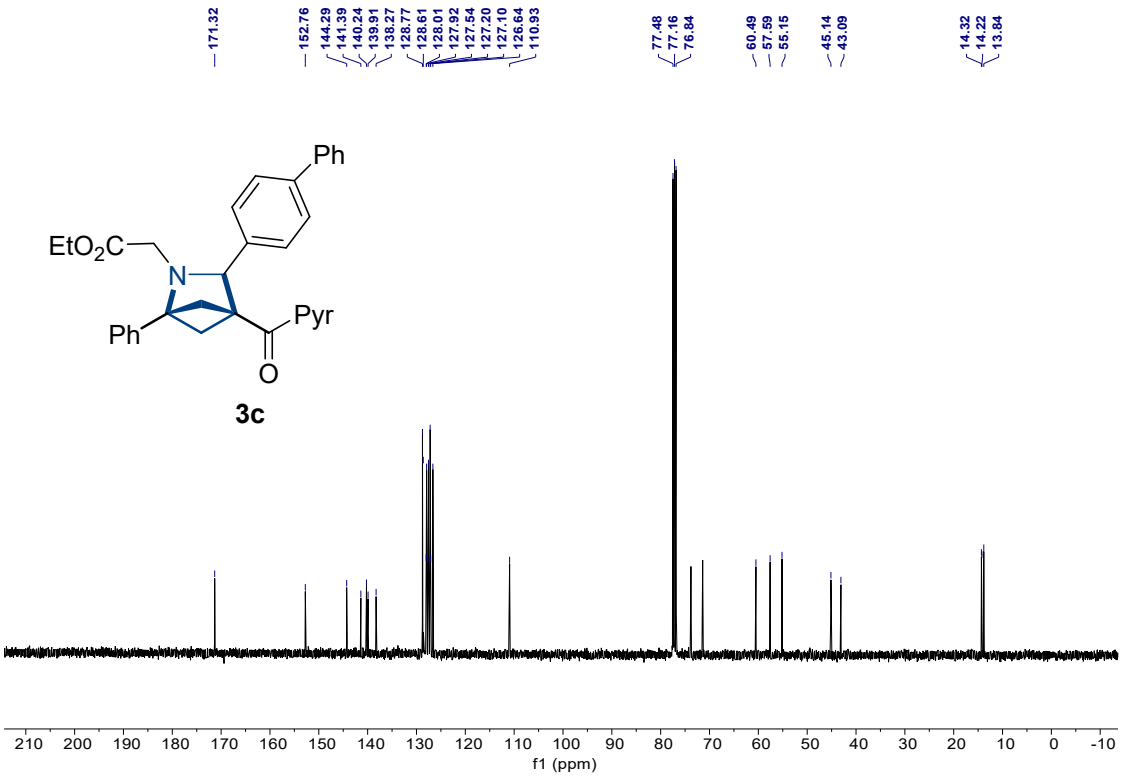
^{13}C NMR (101 MHz, $CDCl_3$) of **3a**



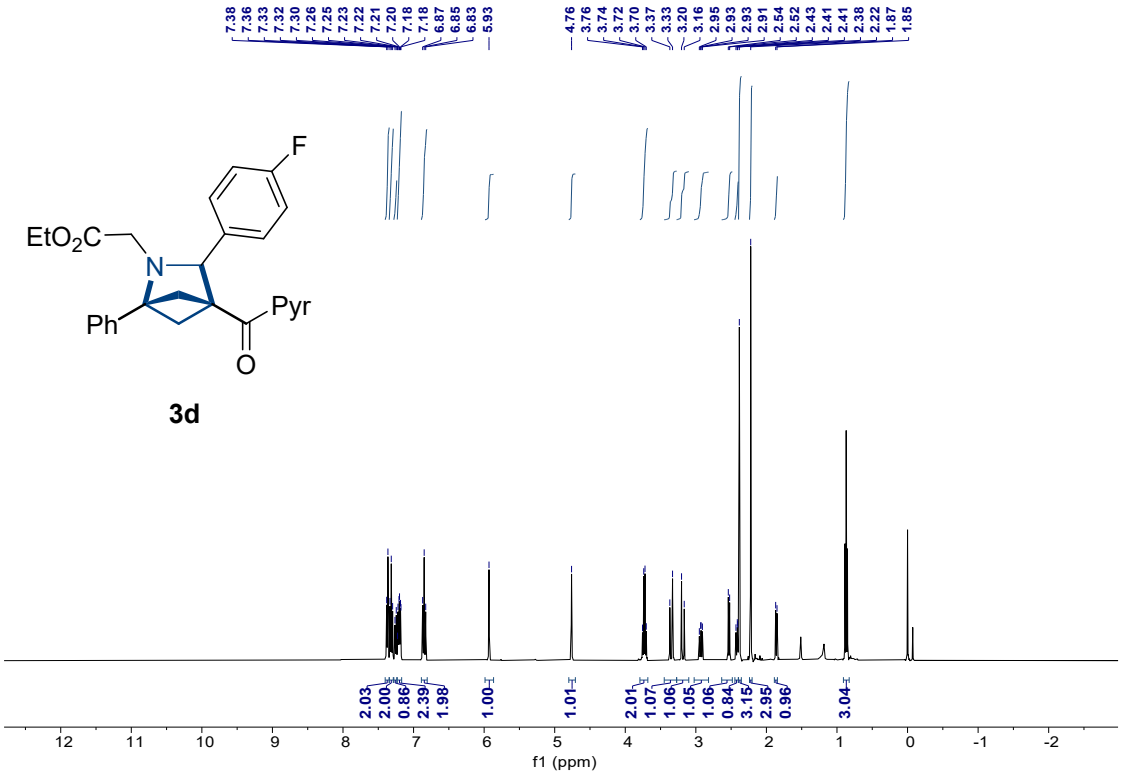
^{1}H NMR (400 MHz, $CDCl_3$) of **3c**



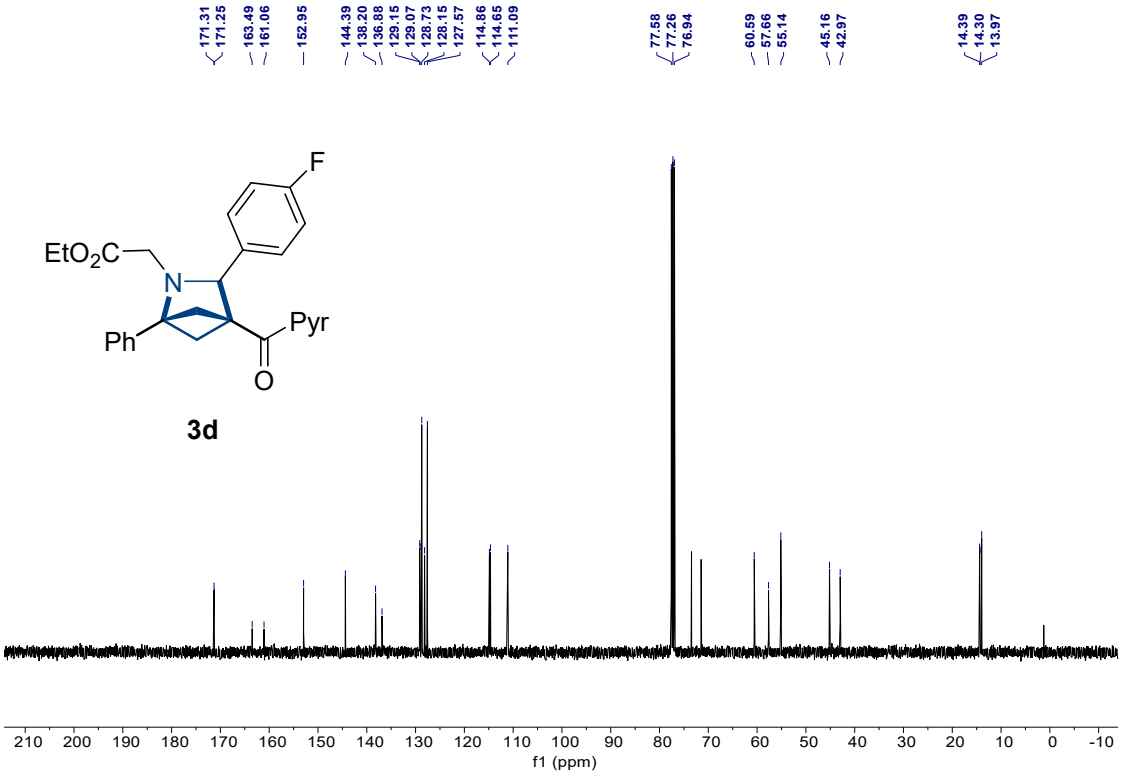
^{13}C NMR (101 MHz, $CDCl_3$) of **3c**



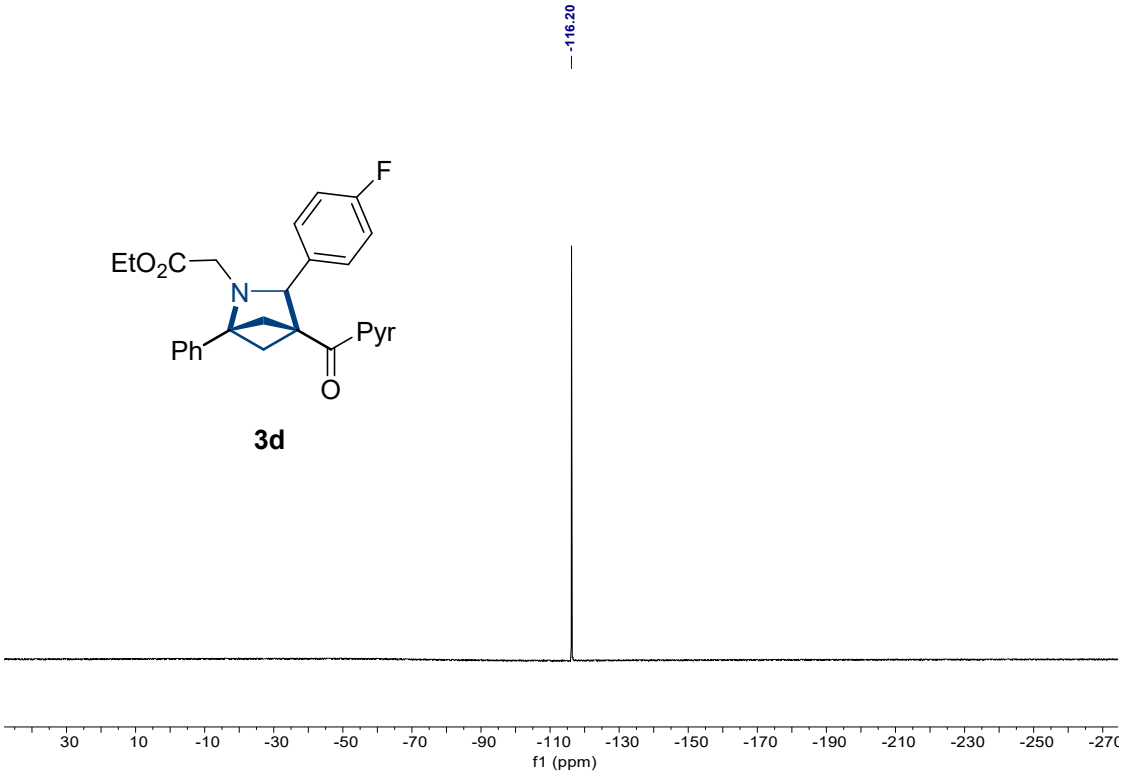
^{1}H NMR (400 MHz, $CDCl_3$) of **3d**



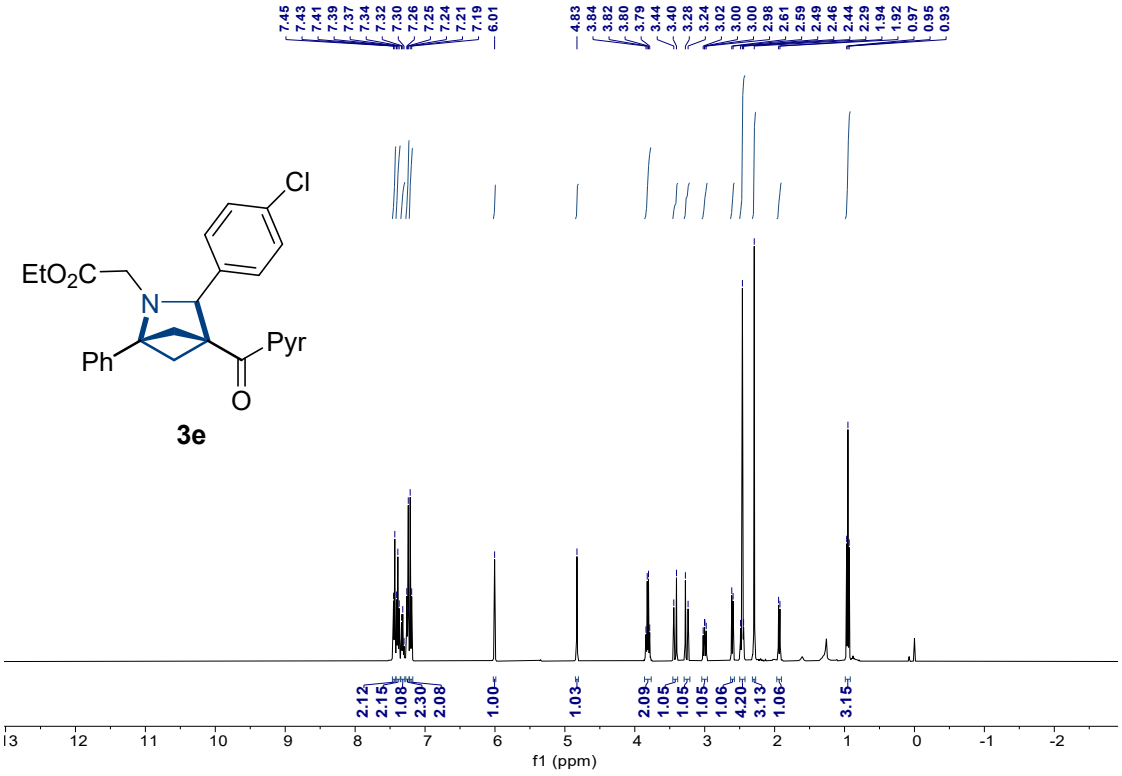
^{13}C NMR (101 MHz, $CDCl_3$) of **3d**



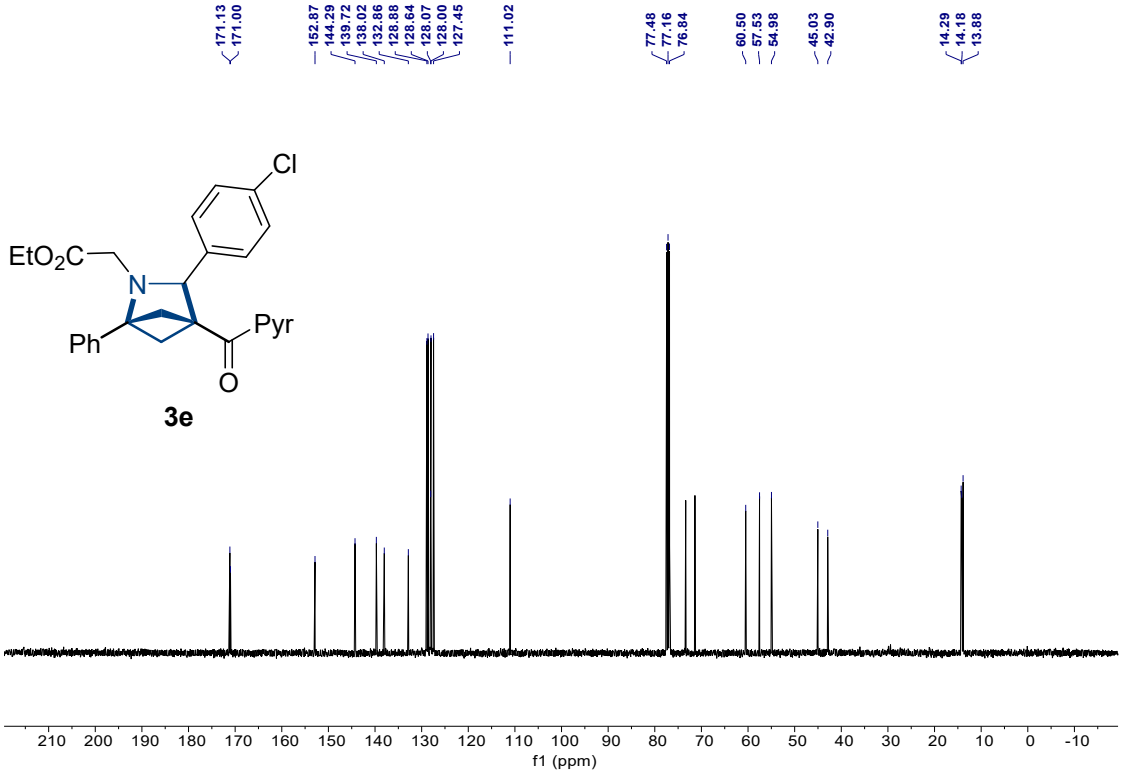
^{19}FNMR (376 MHz, $CDCl_3$) of **3d**


-116.20
F
EtO2C
N
Ph
Pyr
O
3d
30
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
-230
-250
f1 (ppm)

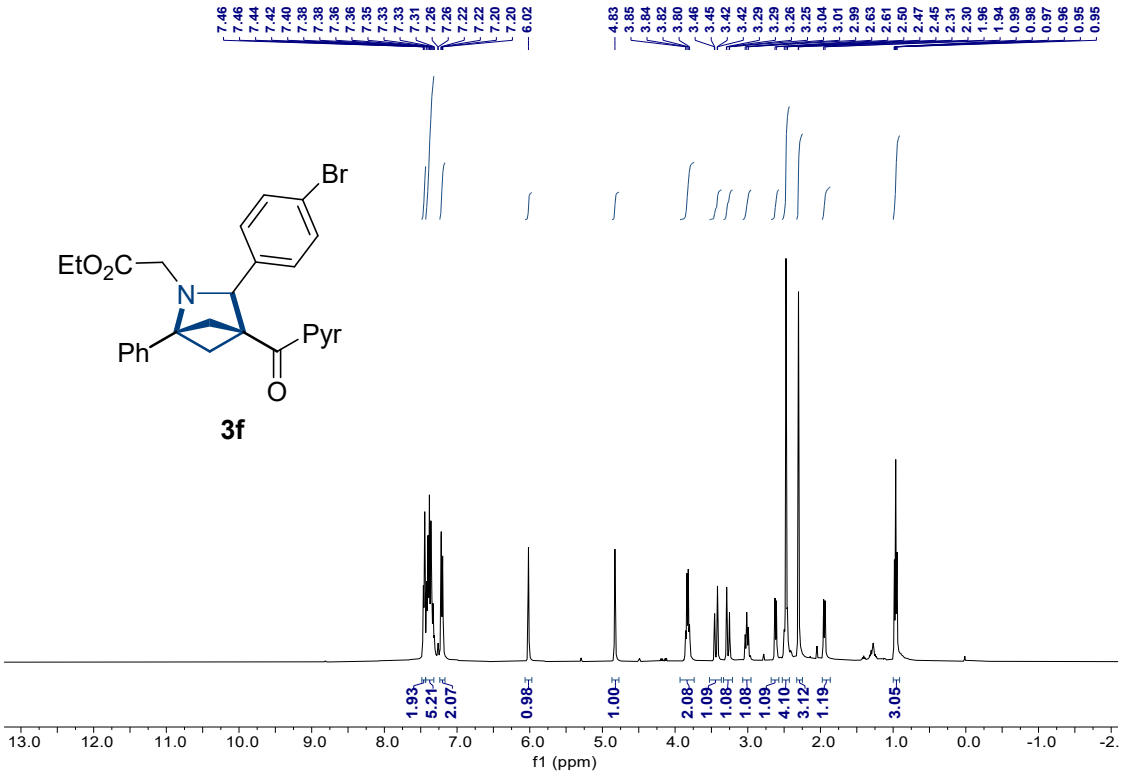
^{1}H NMR (400 MHz, $CDCl_3$) of **3e**



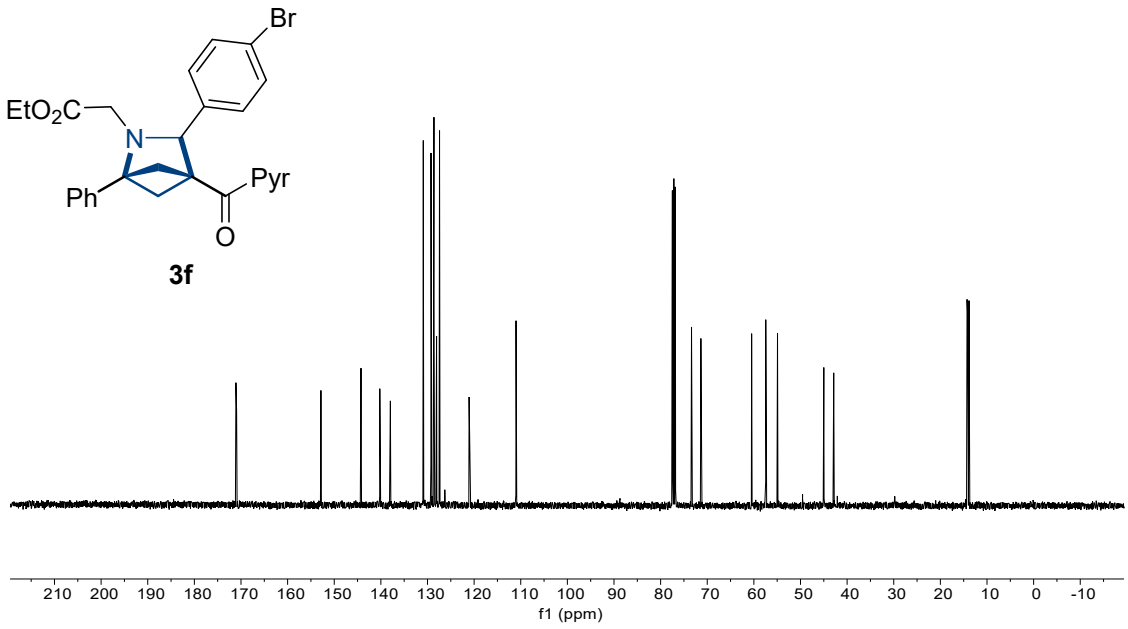
^{13}C NMR (101 MHz, $CDCl_3$) of **3e**



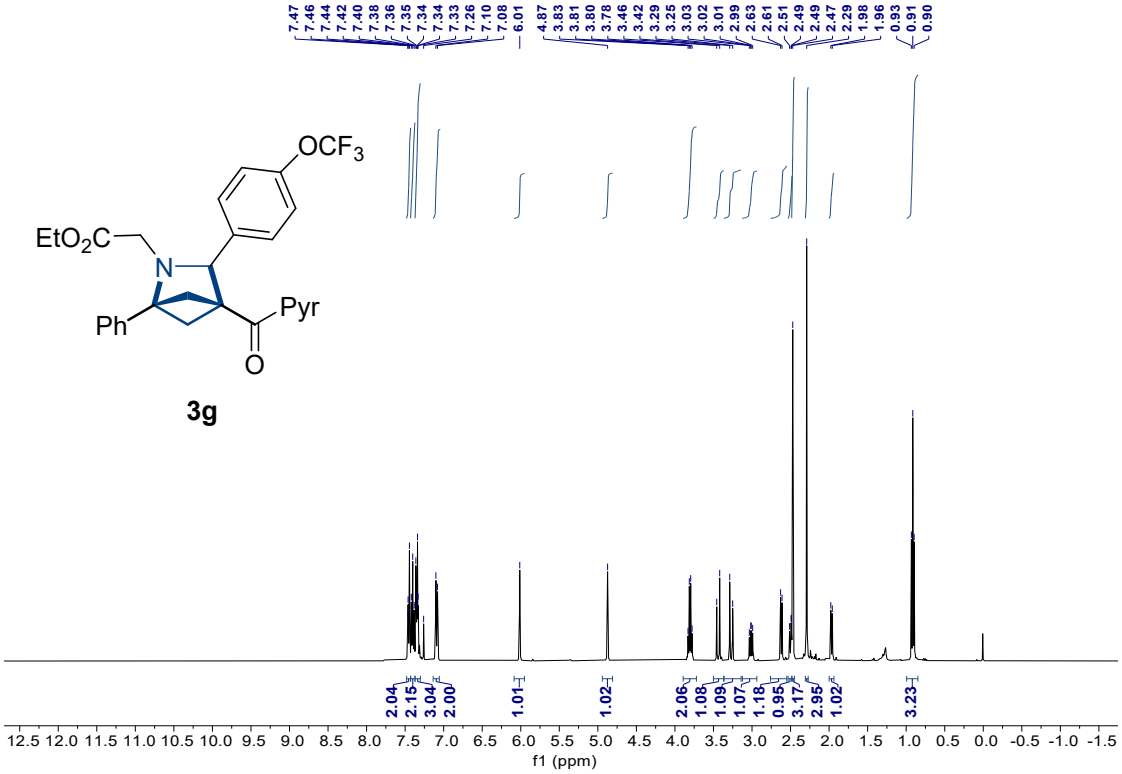
^{1}H NMR (400 MHz, $CDCl_3$) of **3f**



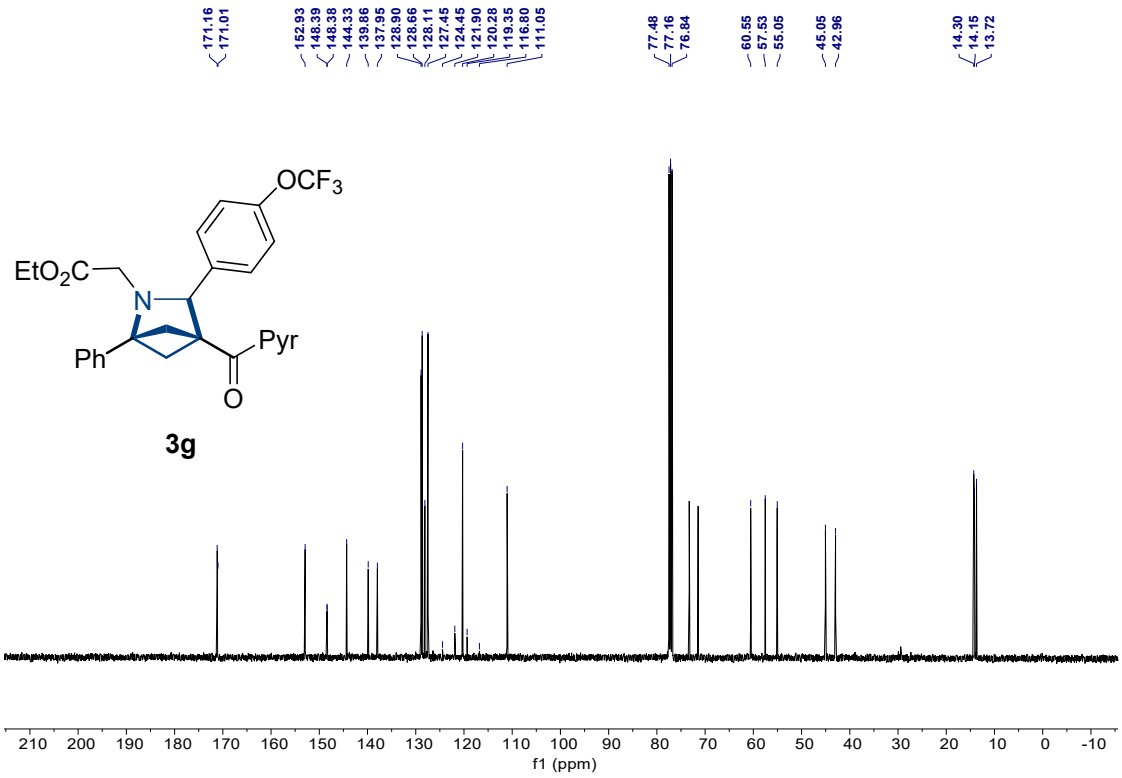
^{13}C NMR (101 MHz, $CDCl_3$) of **3f**



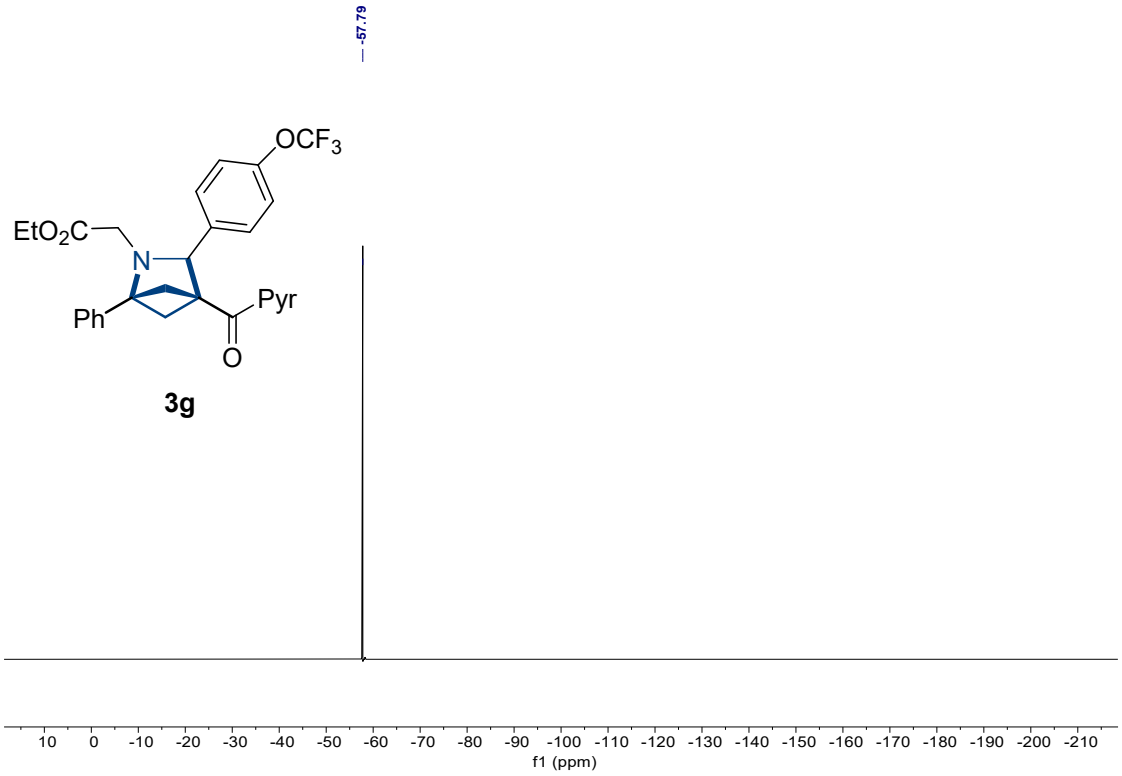
^{1}H NMR (400 MHz, $CDCl_3$) of **3g**



^{13}C NMR (101 MHz, $CDCl_3$) of **3g**

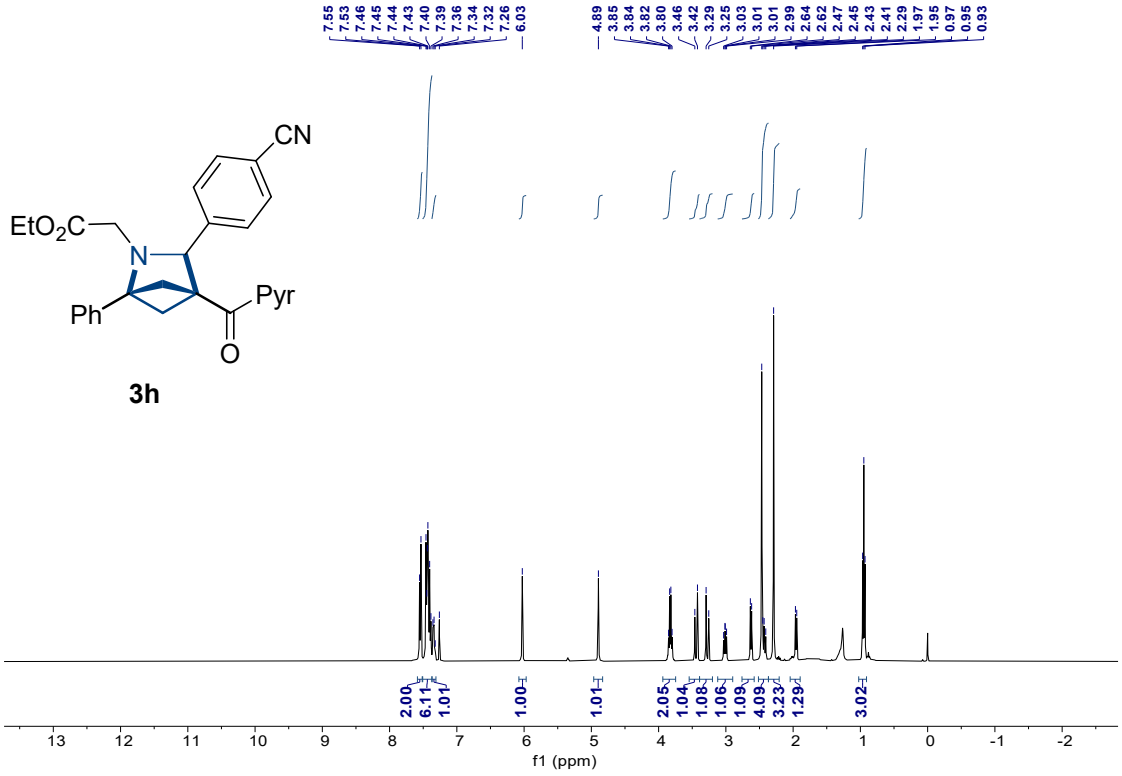


^{19}F NMR (376 MHz, $CDCl_3$) of **3g**

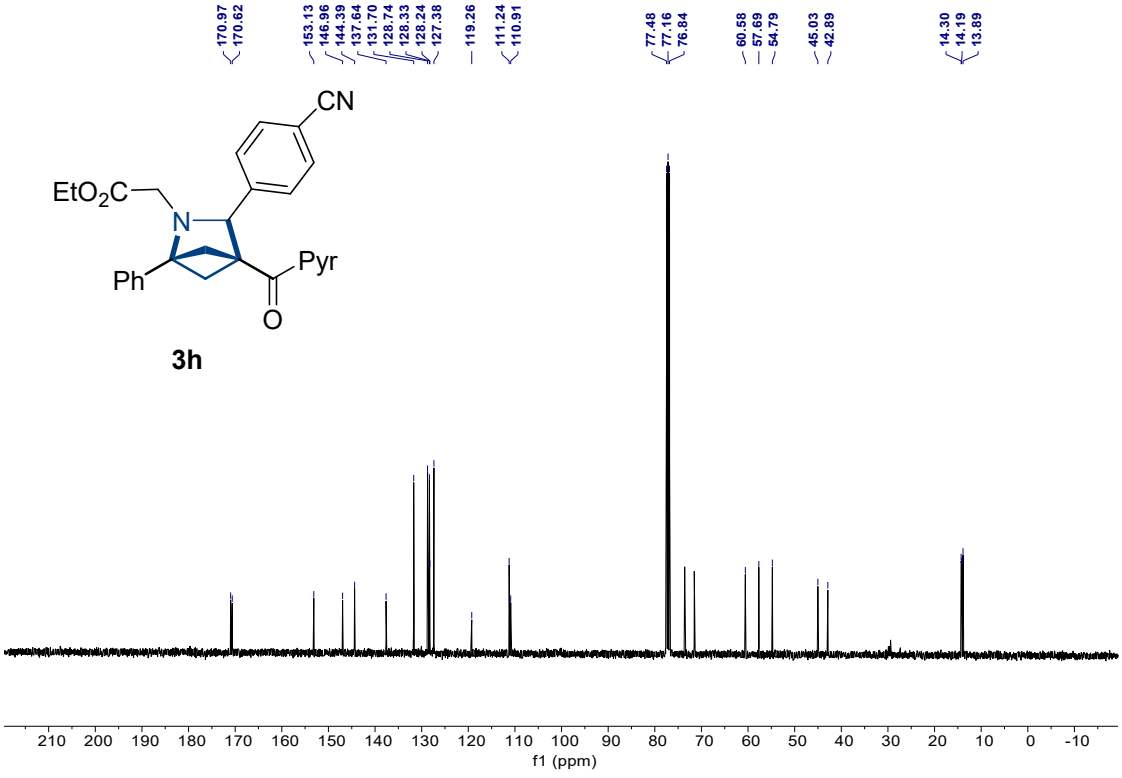

-57.79
OCF3
EtO2C
N
Ph
Pyr
O
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

3g

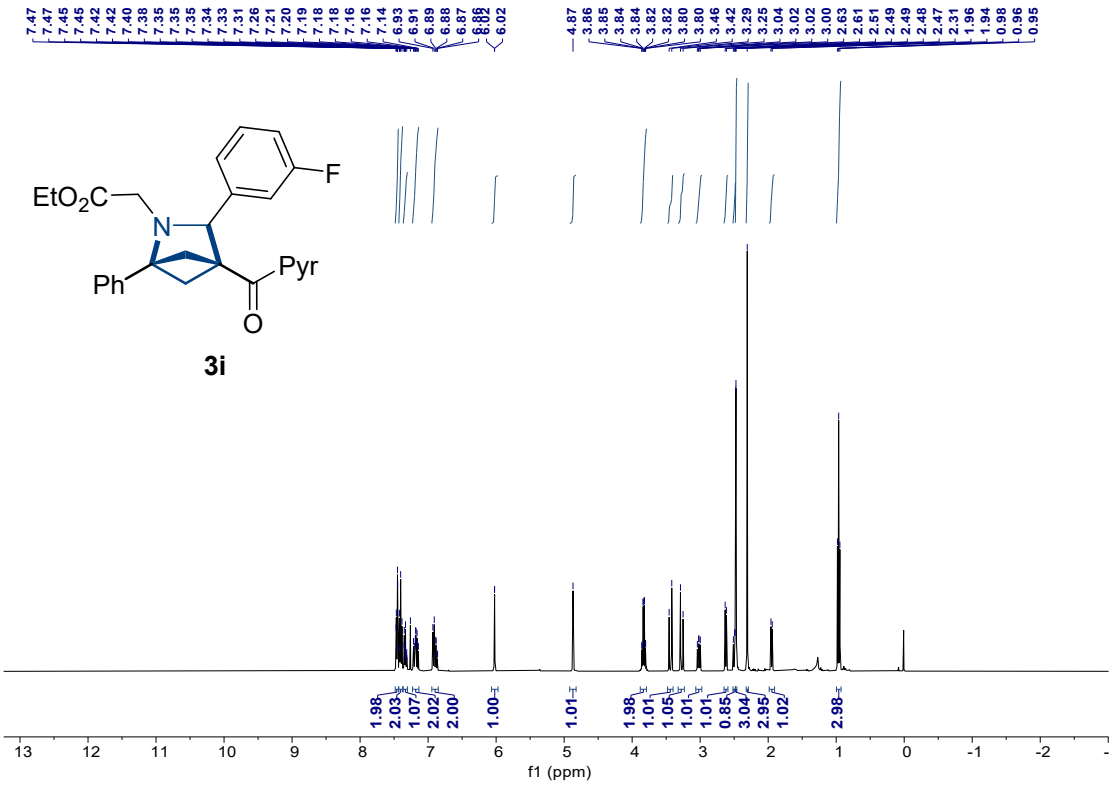
^{1}H NMR (400 MHz, $CDCl_3$) of **3h**



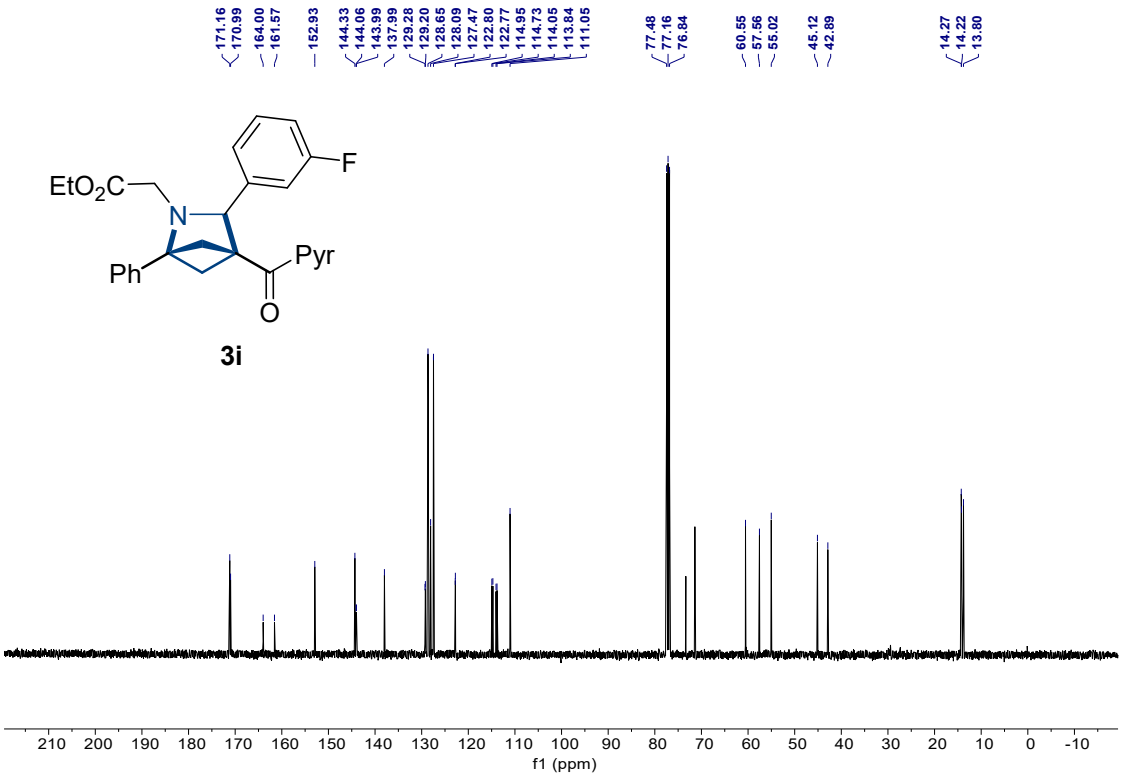
^{13}C NMR (101 MHz, $CDCl_3$) of **3h**



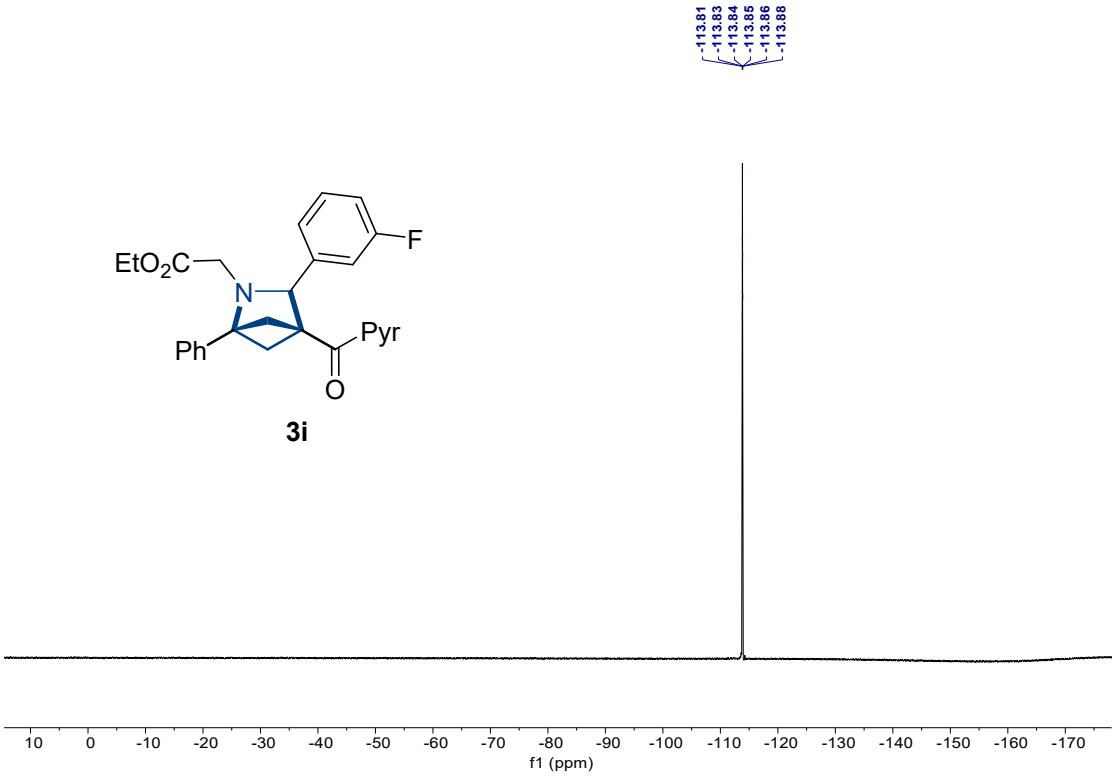
^{1}H NMR (400 MHz, $CDCl_3$) of **3i**



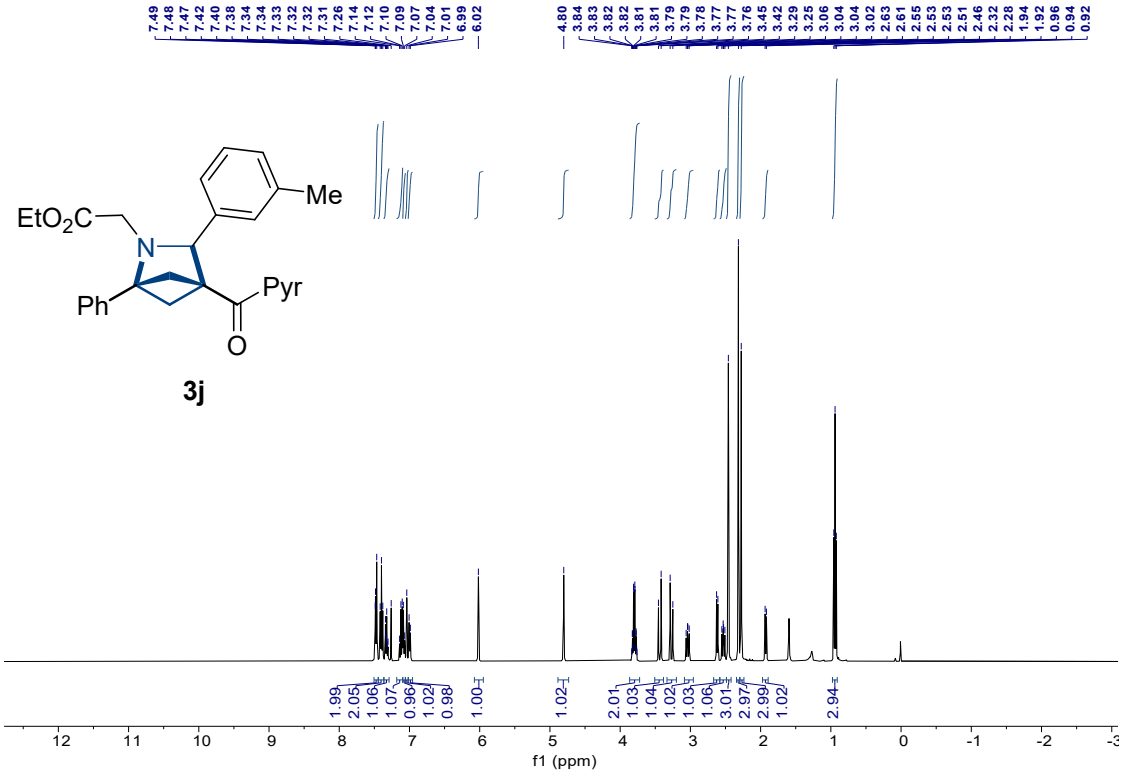
^{13}C NMR (101 MHz, $CDCl_3$) of **3i**



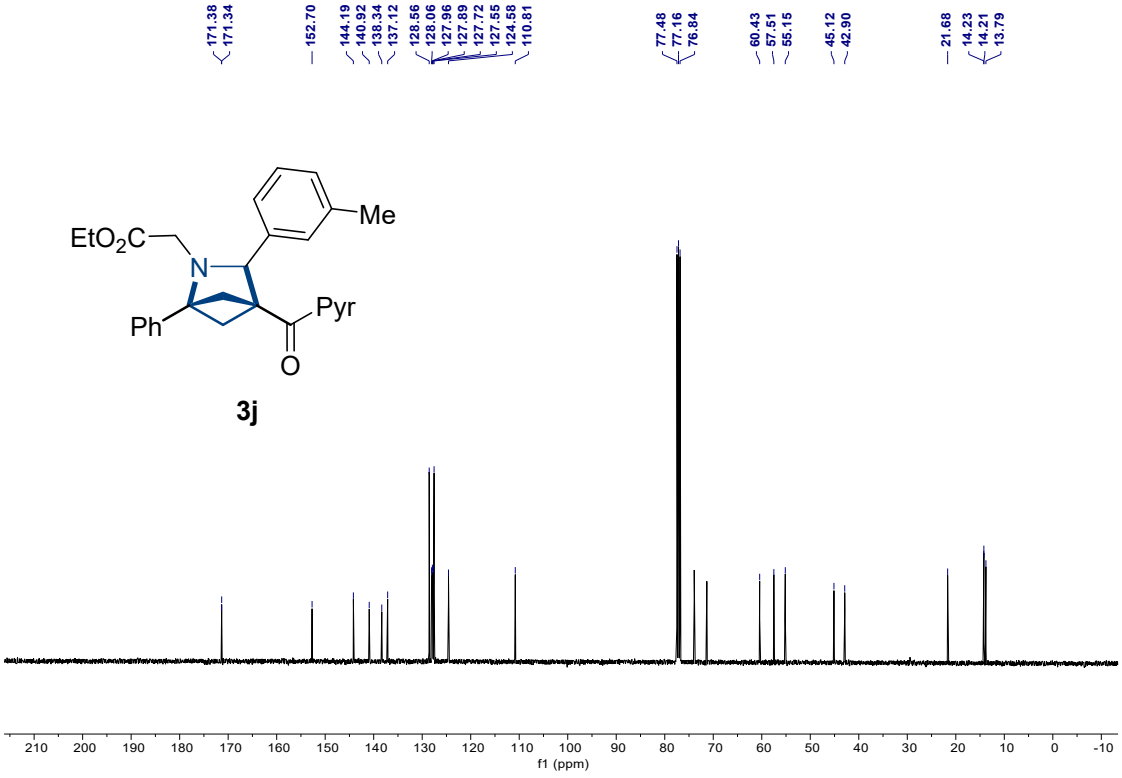
^{19}F NMR (376 MHz, $CDCl_3$) of **3i**



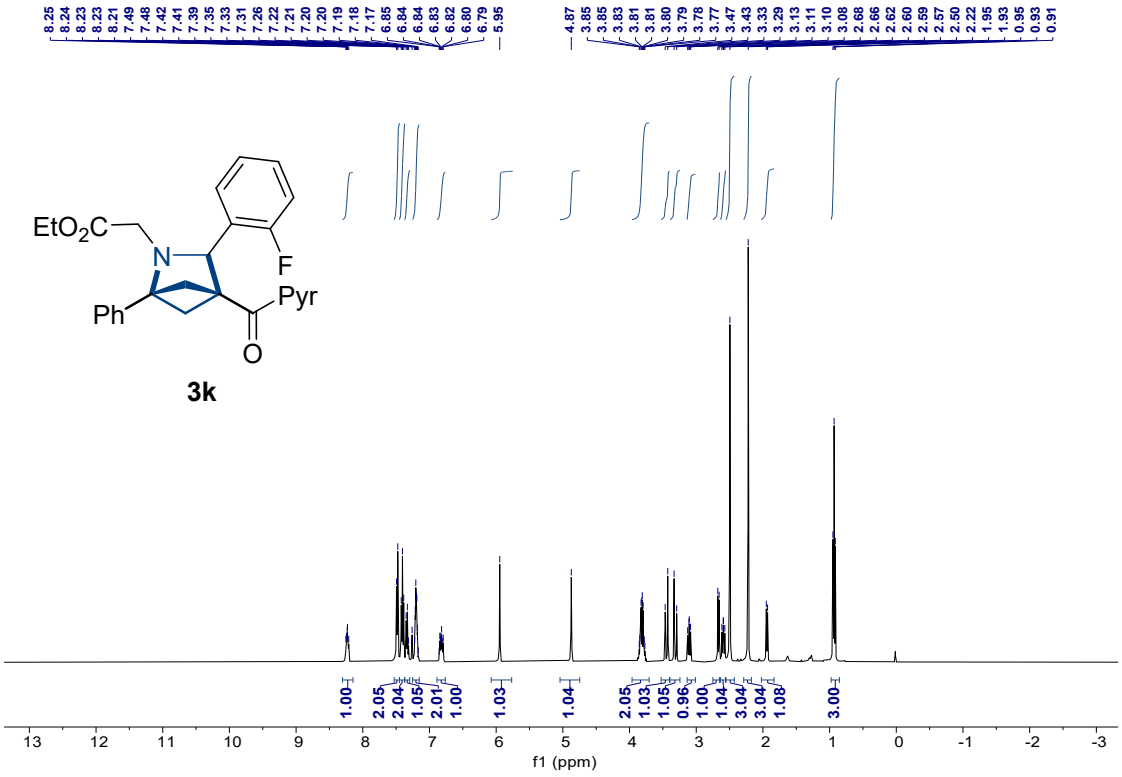
^{1}H NMR (400 MHz, $CDCl_3$) of **3j**



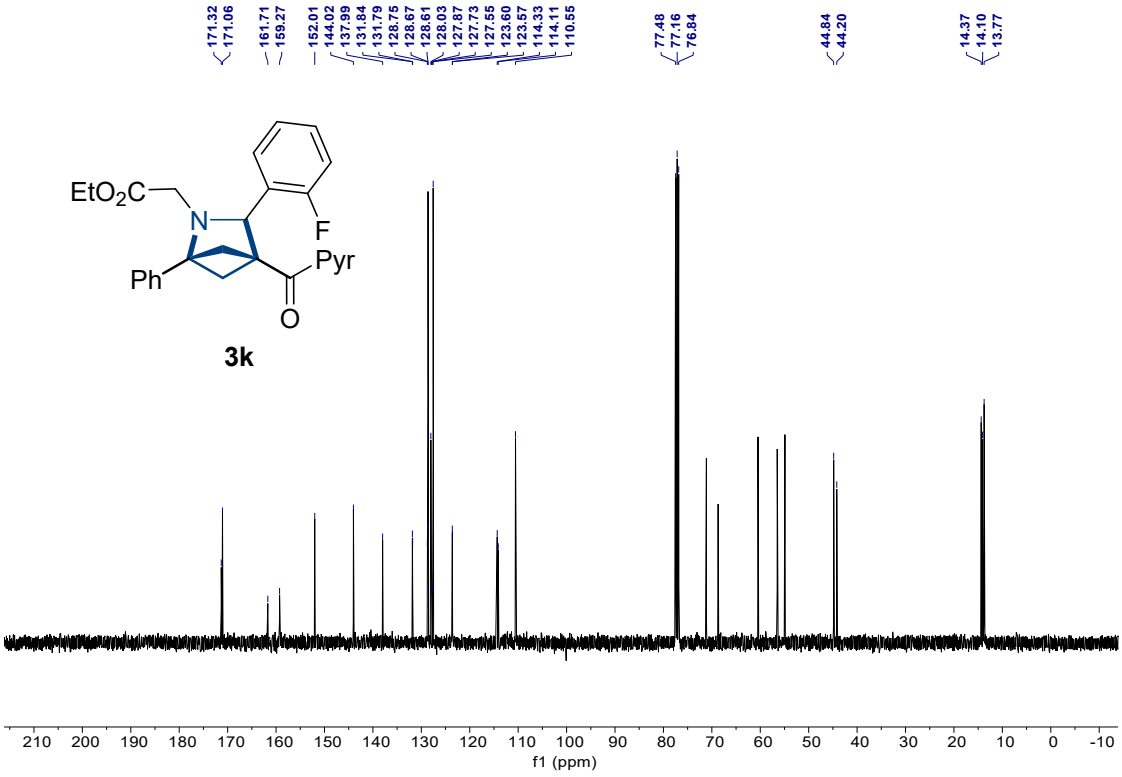
^{13}C NMR (101 MHz, $CDCl_3$) of **3j**



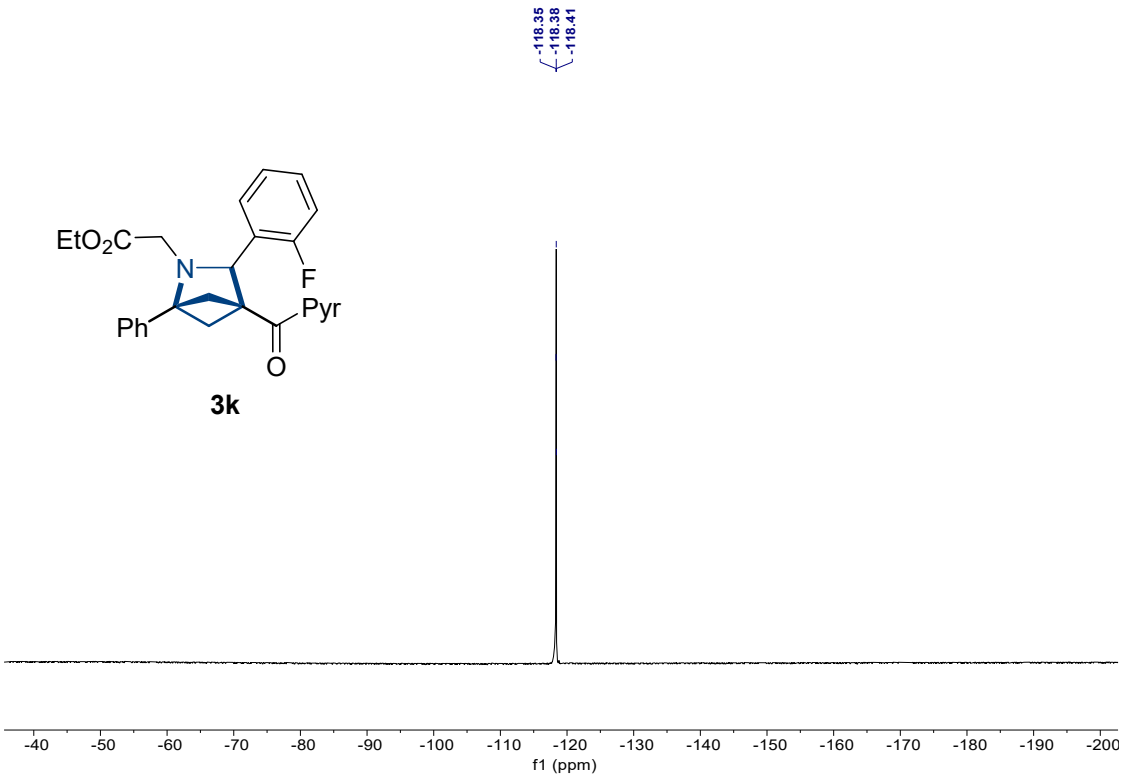
^{1}H NMR (400 MHz, $CDCl_3$) of **3k**



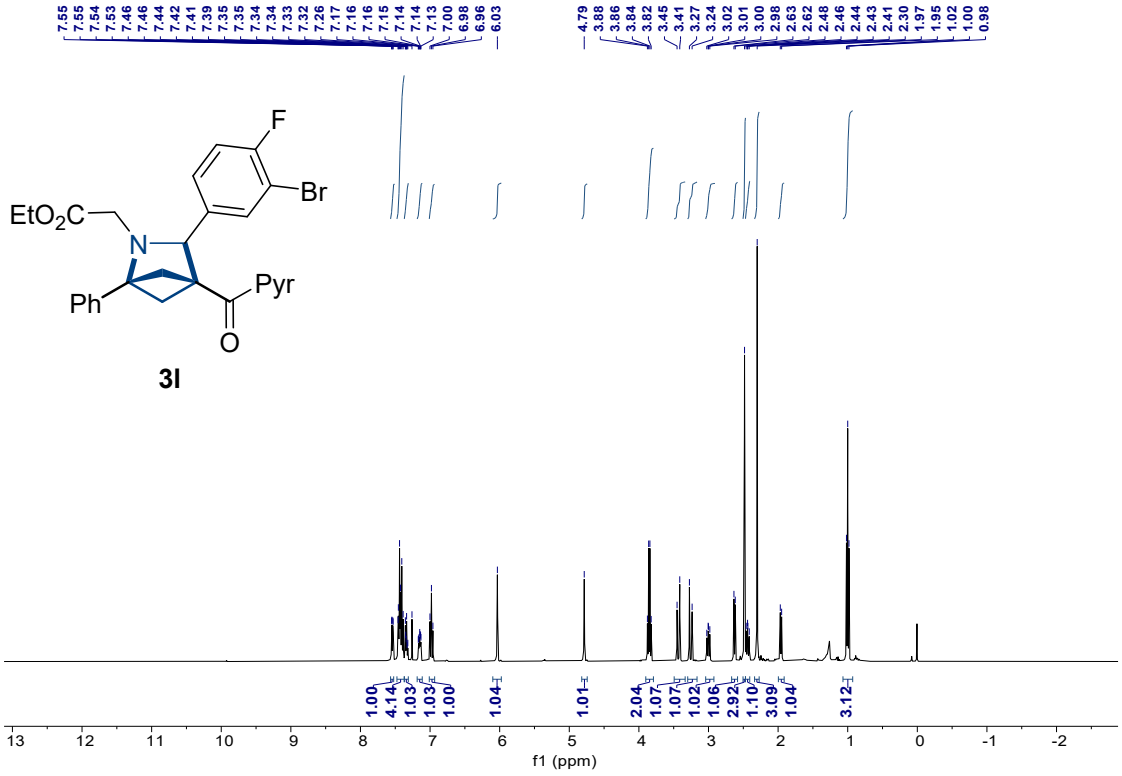
^{13}C NMR (101 MHz, $CDCl_3$) of **3k**



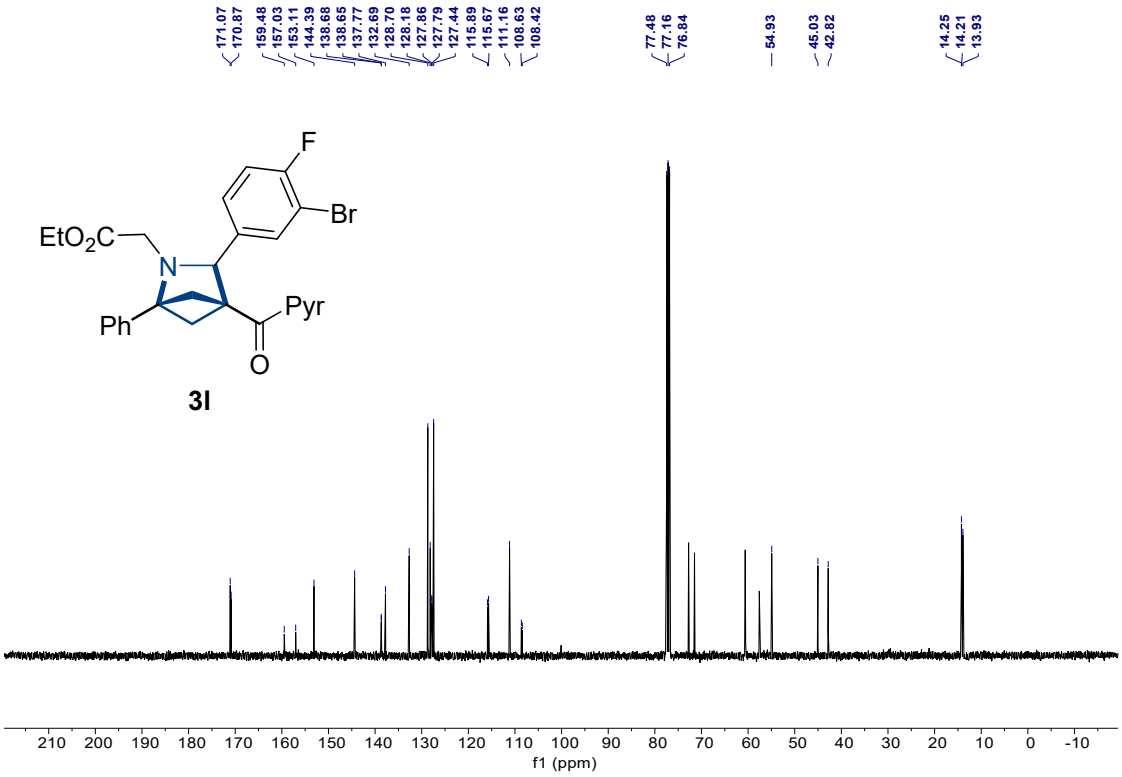
^{19}F NMR (376 MHz, $CDCl_3$) of **3k**



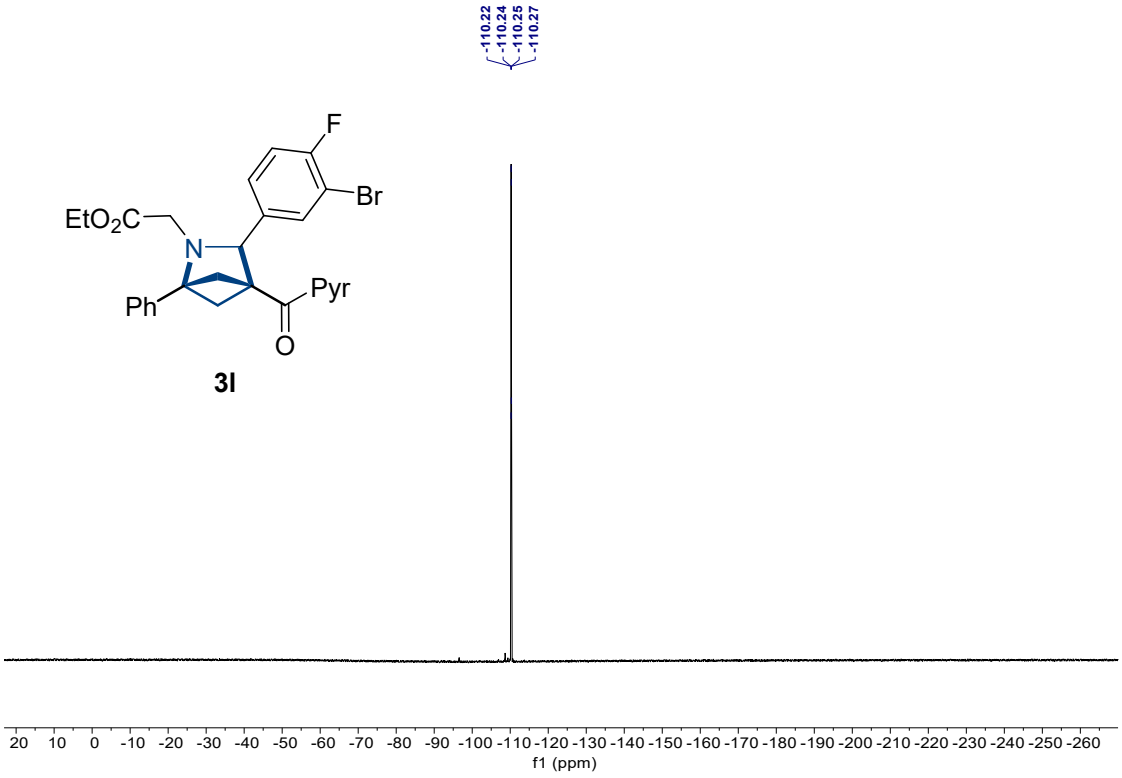
^{1}H NMR (400 MHz, $CDCl_3$) of **3l**



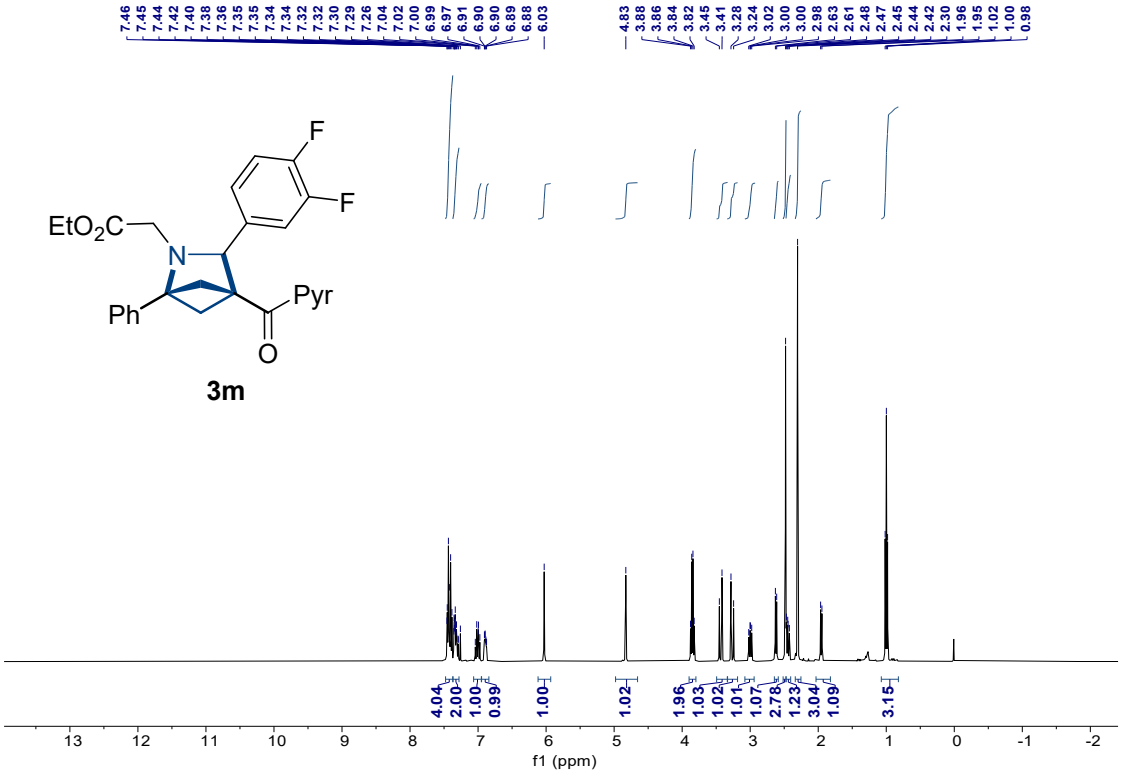
^{13}C NMR (101 MHz, $CDCl_3$) of **3l**



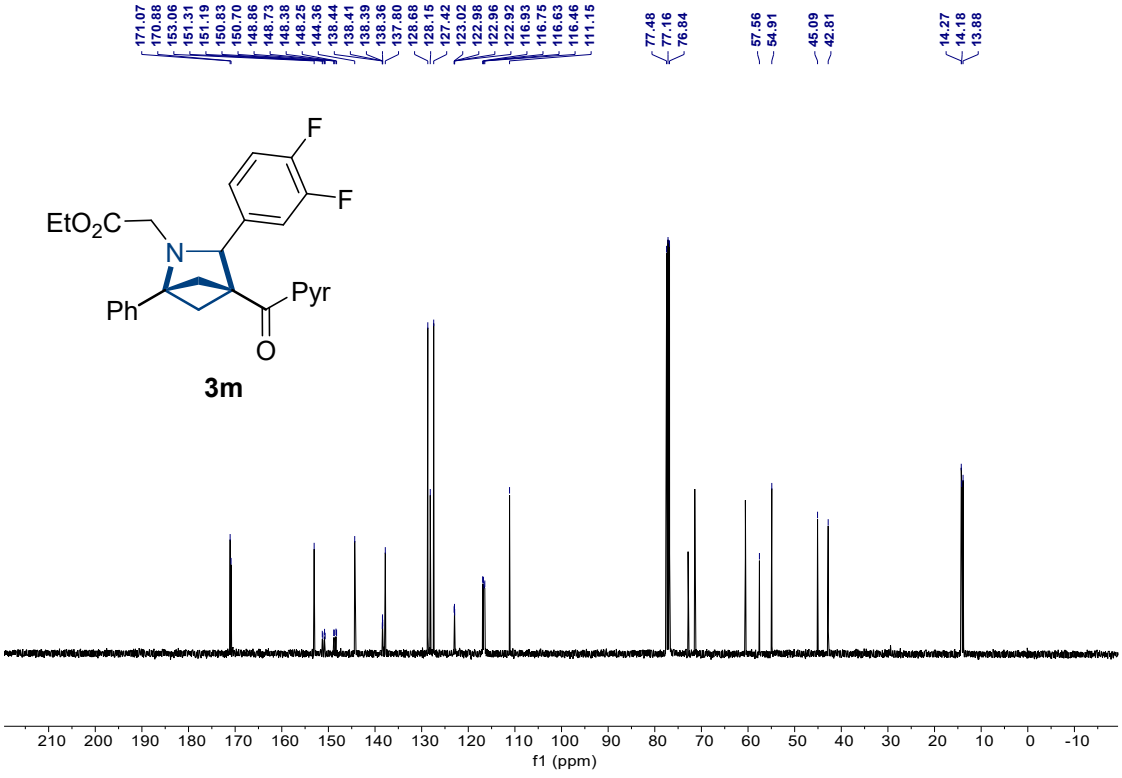
^{19}F NMR (376 MHz, $CDCl_3$) of **3l**



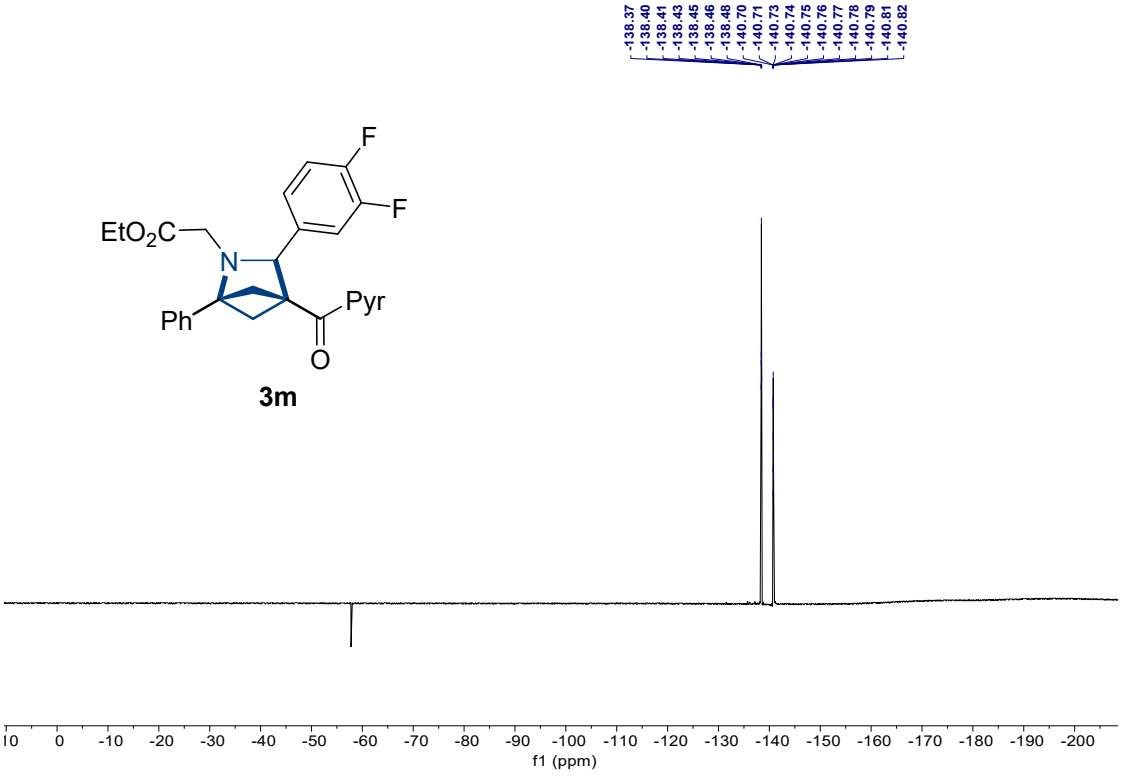
^{1}H NMR (400 MHz, $CDCl_3$) of **3m**



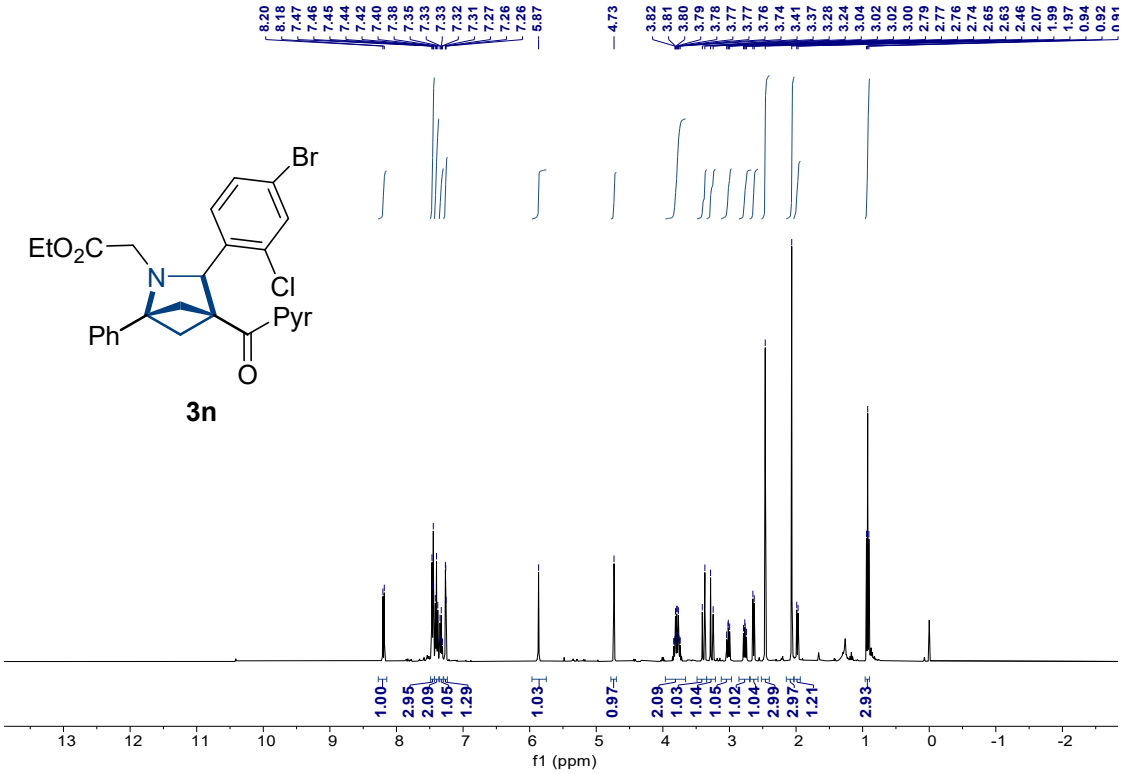
^{13}C NMR (101 MHz, $CDCl_3$) of **3m**



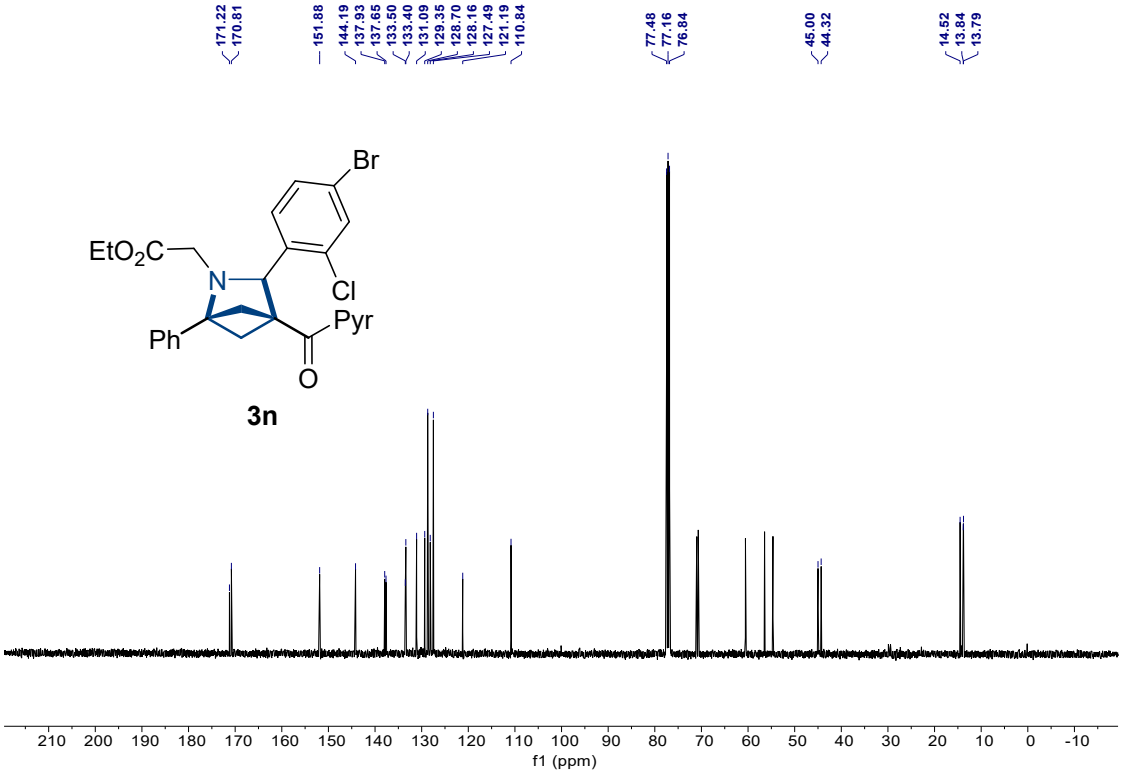
^{19}F NMR (376 MHz, $CDCl_3$) of **3m**



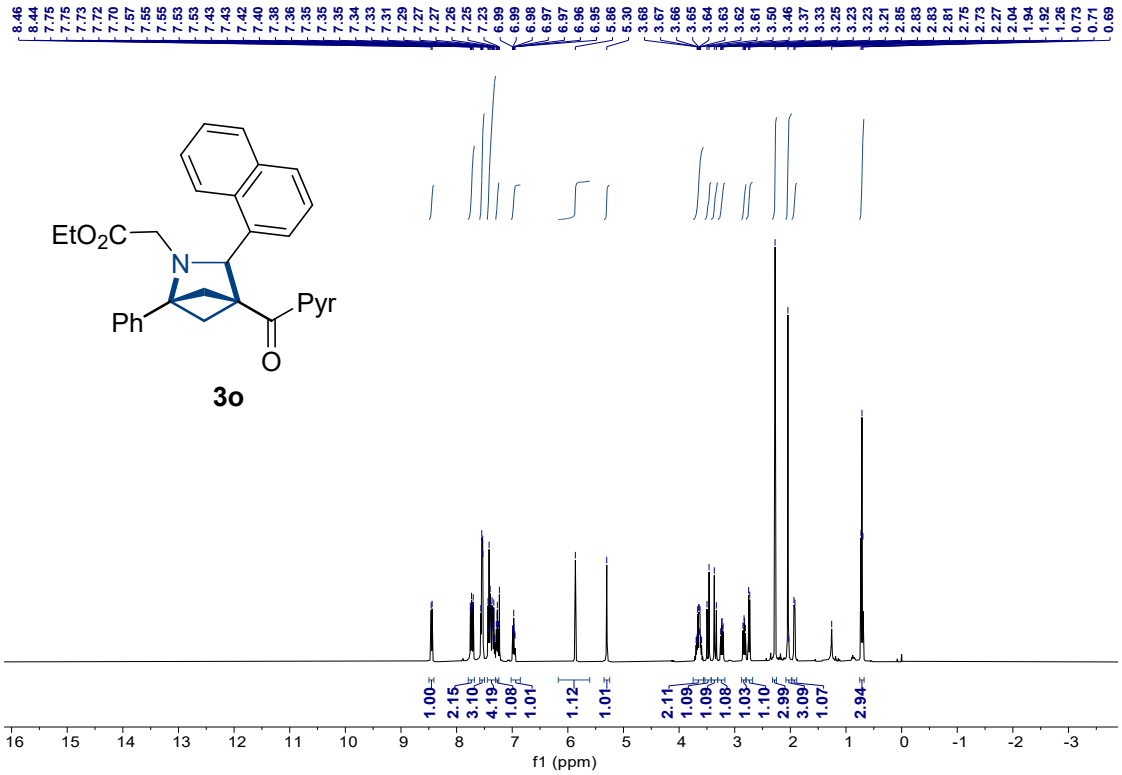
^{1}H NMR (400 MHz, $CDCl_3$) of **3n**



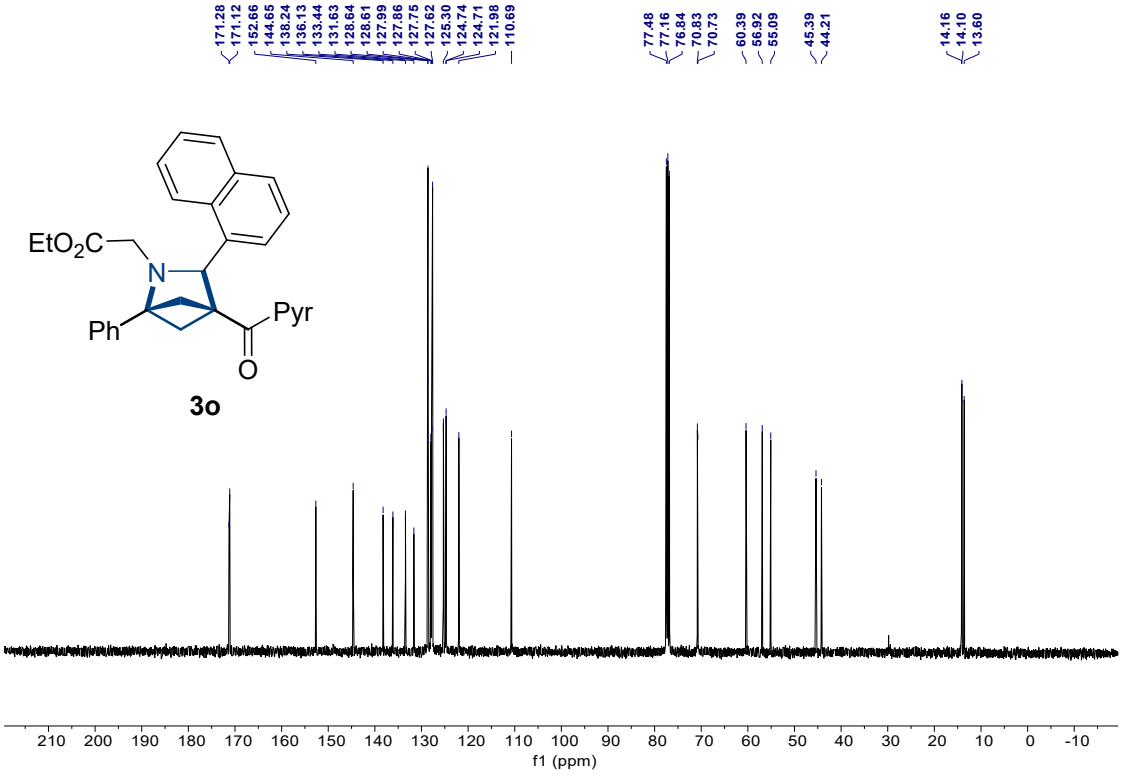
^{13}C NMR (101 MHz, $CDCl_3$) of **3n**



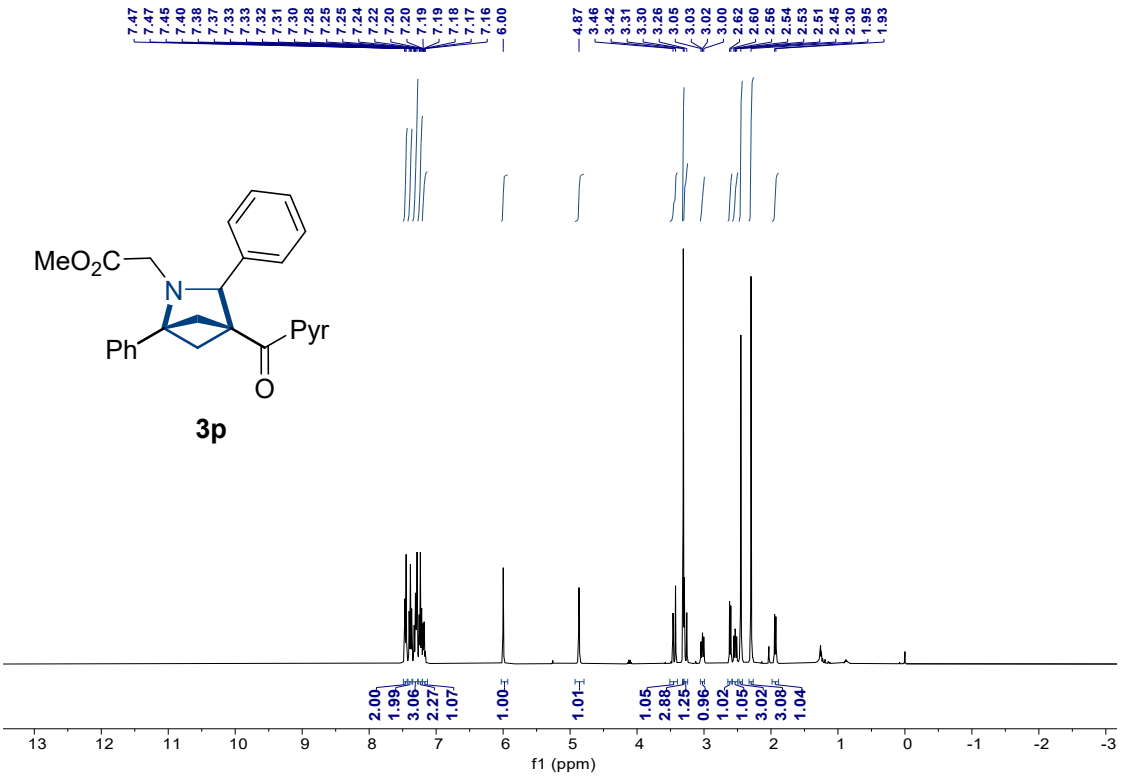
^{1}H NMR (400 MHz, $CDCl_3$) of **3o**



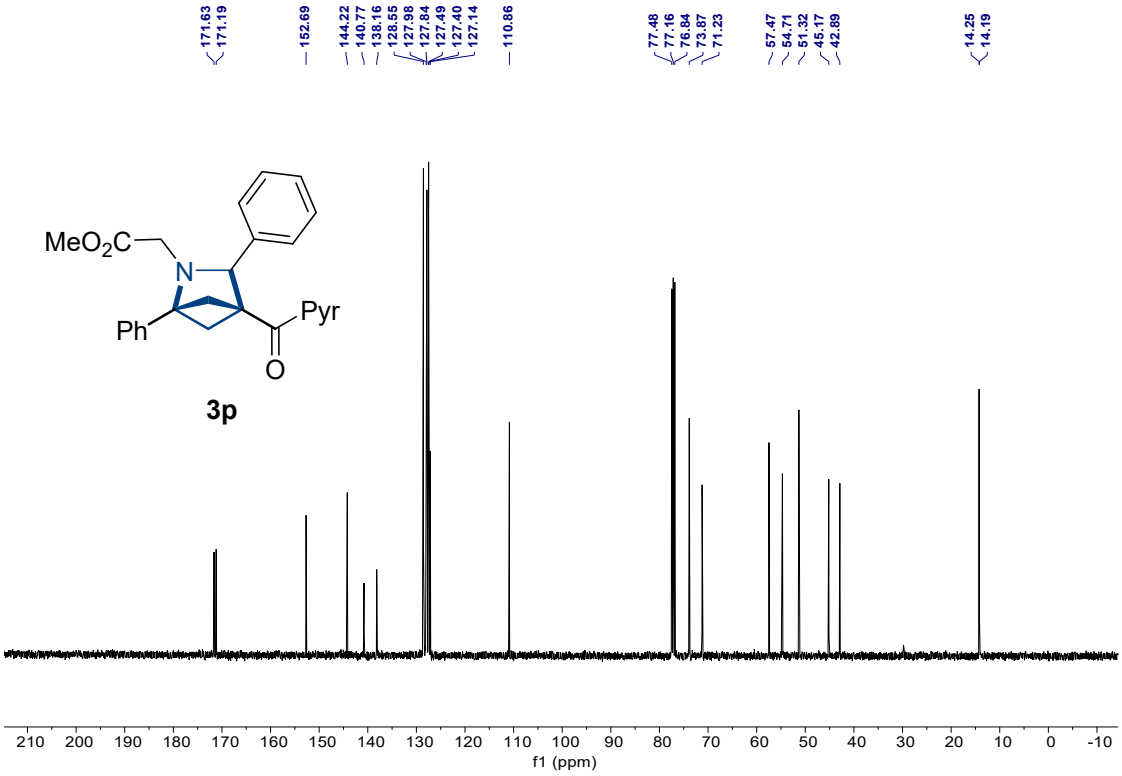
^{13}C NMR (101 MHz, $CDCl_3$) of **3o**



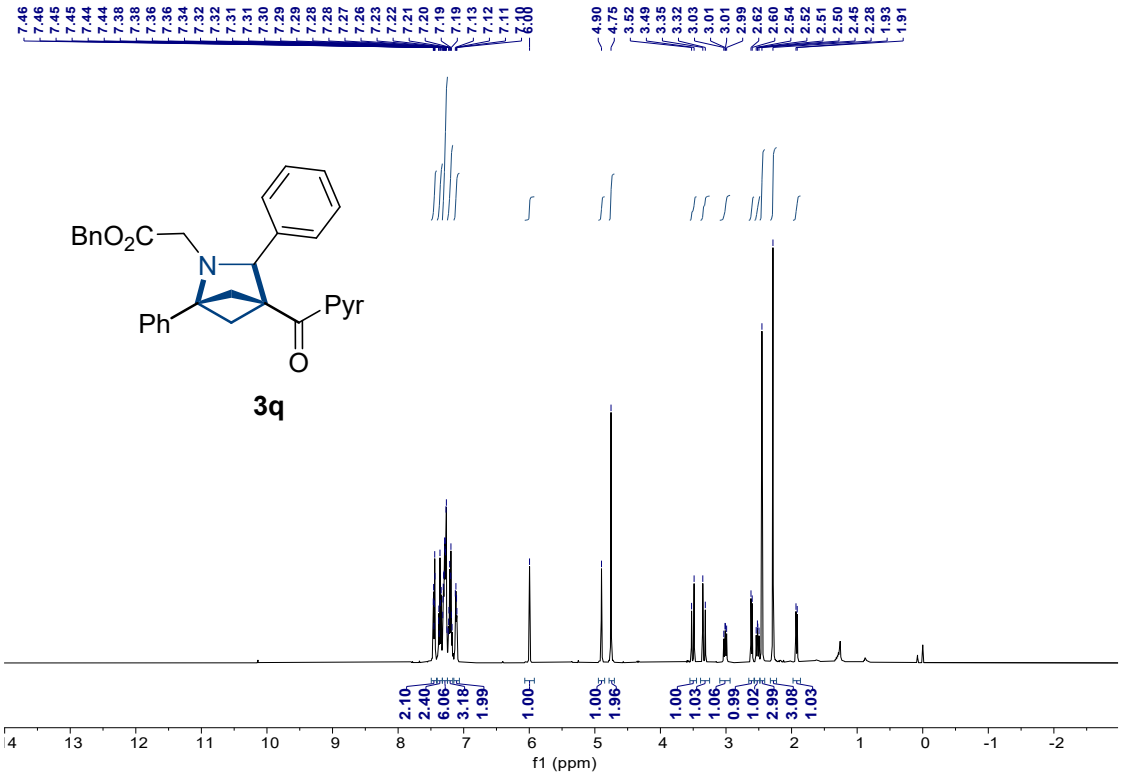
^{1}H NMR (400 MHz, $CDCl_3$) of **3p**



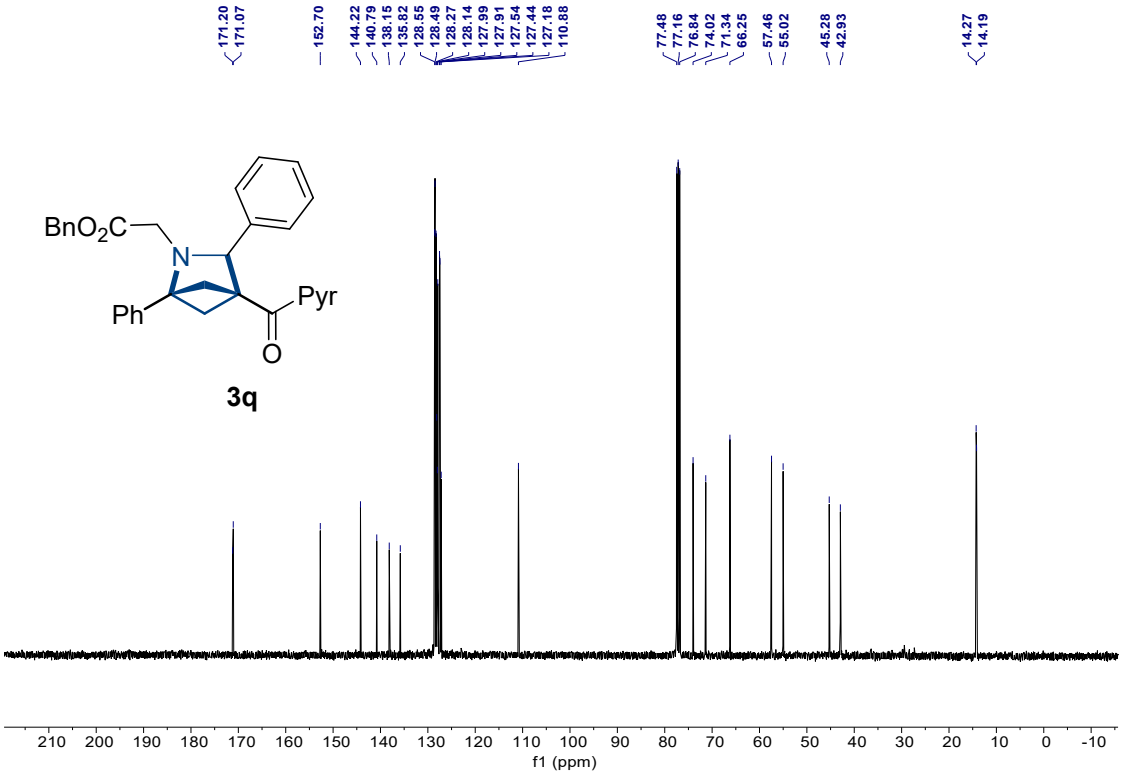
^{13}C NMR (101 MHz, $CDCl_3$) of **3p**



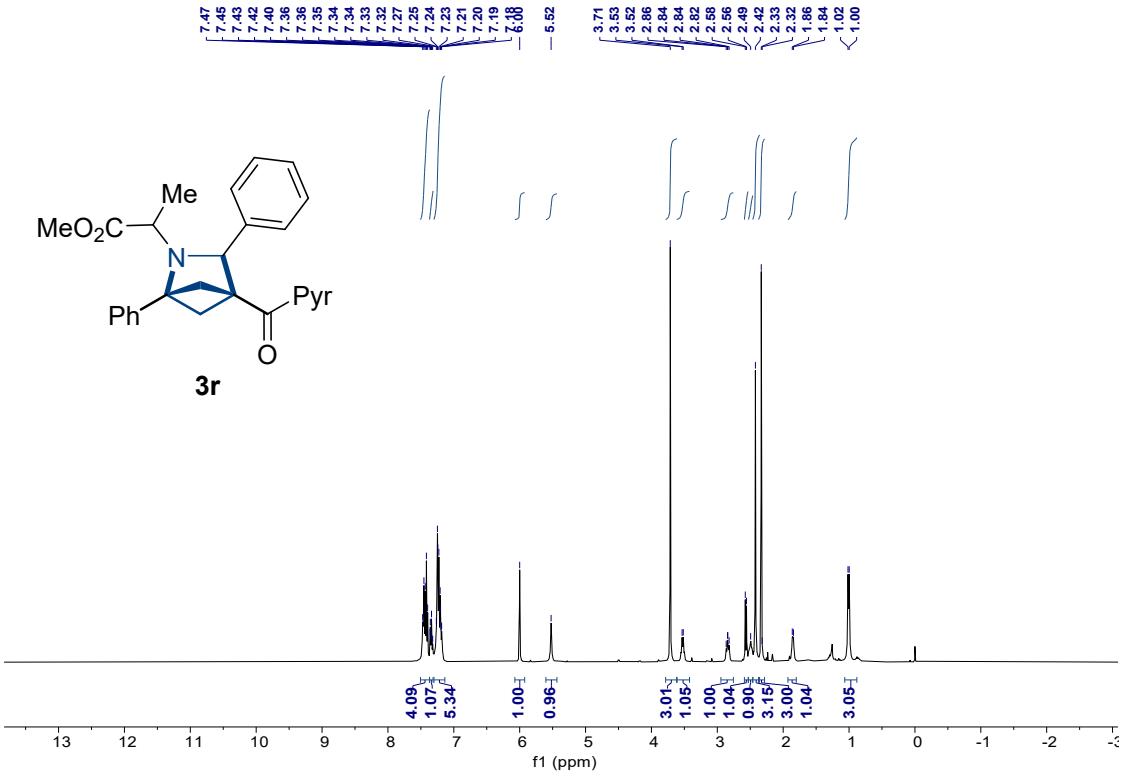
^{1}H NMR (400 MHz, $CDCl_3$) of **3q**



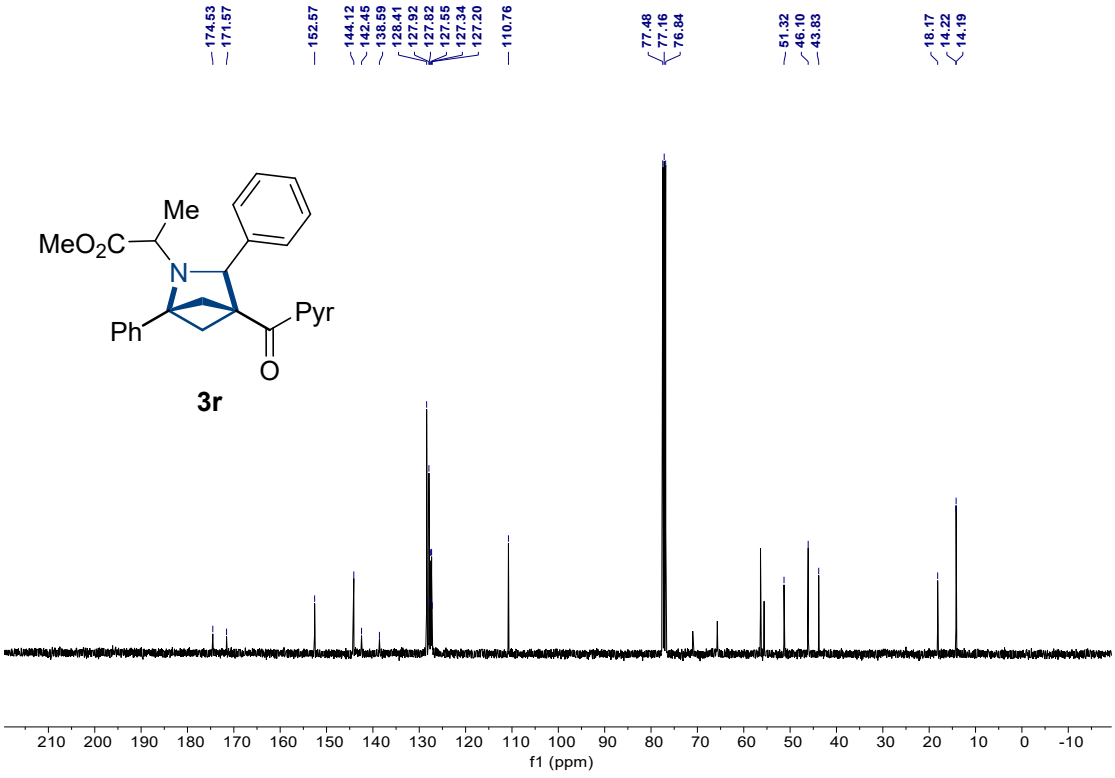
^{13}C NMR (101 MHz, $CDCl_3$) of **3q**



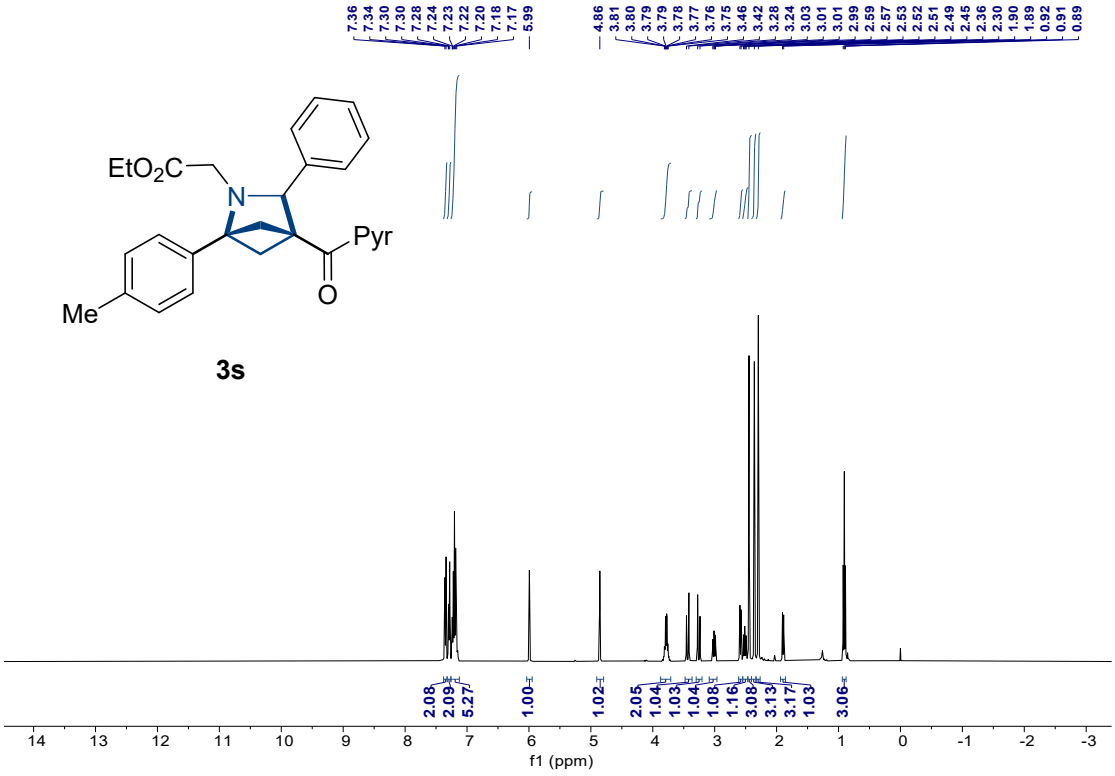
^{1}H NMR (400 MHz, $CDCl_3$) of **3r**



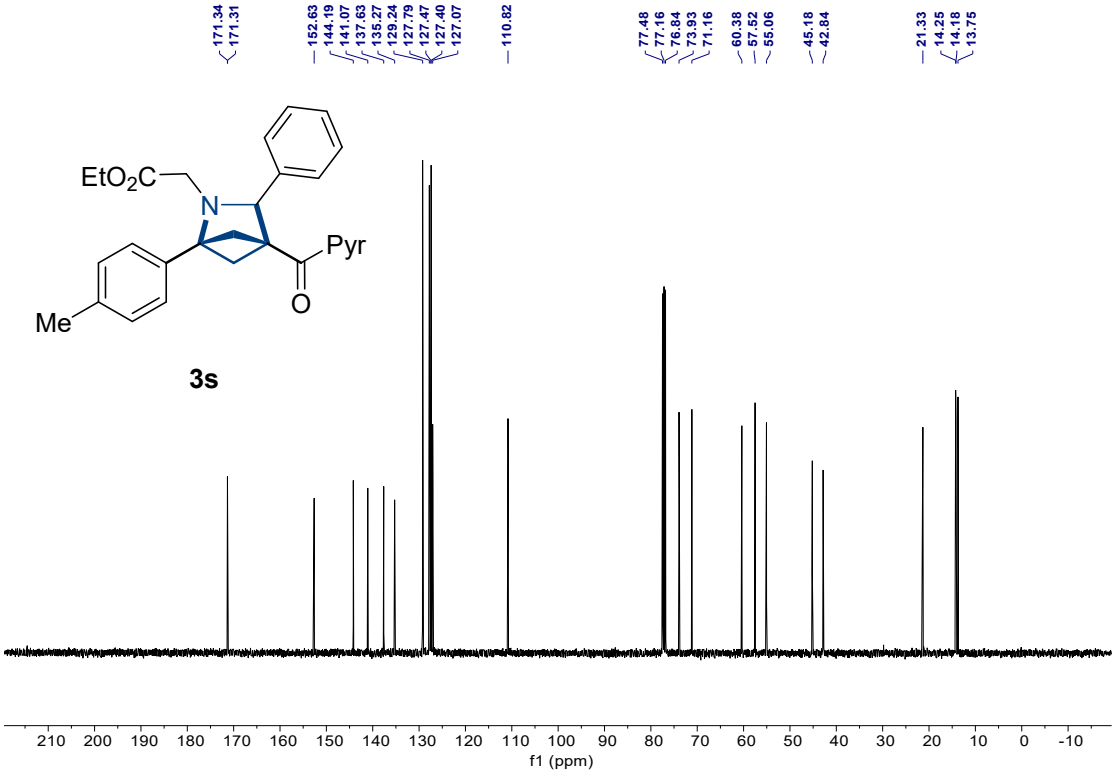
^{13}C NMR (101 MHz, $CDCl_3$) of **3r**



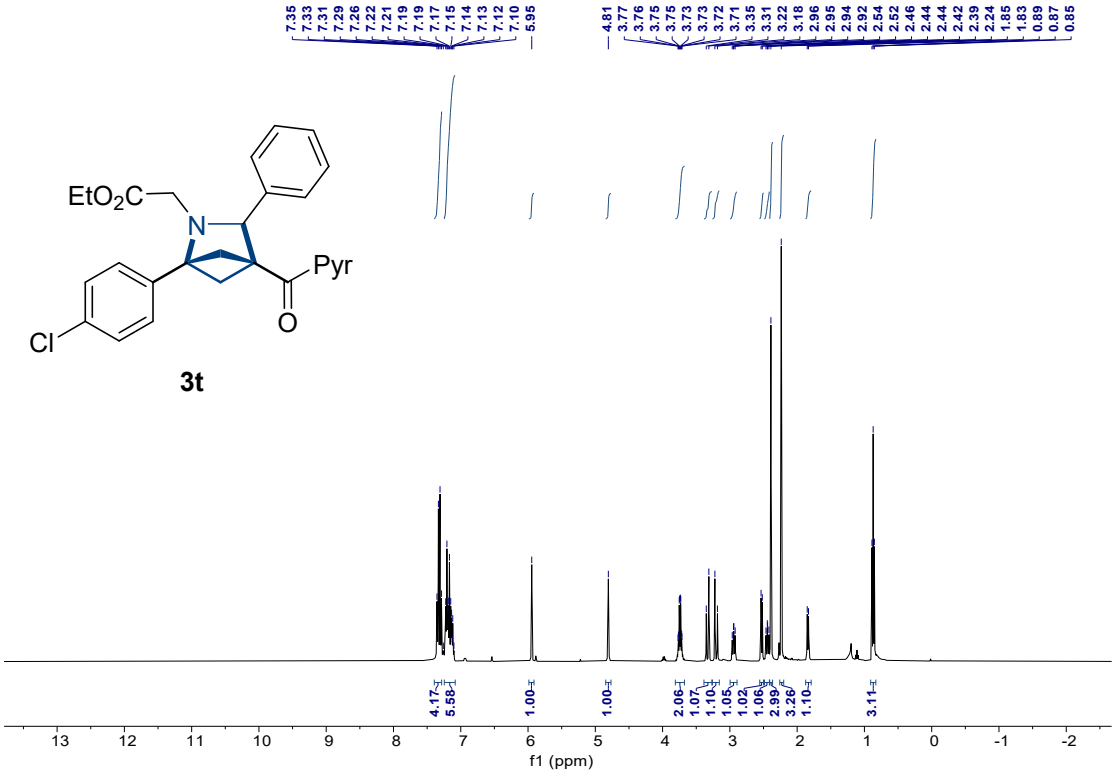
^{1}H NMR (400 MHz, $CDCl_3$) of **3s**



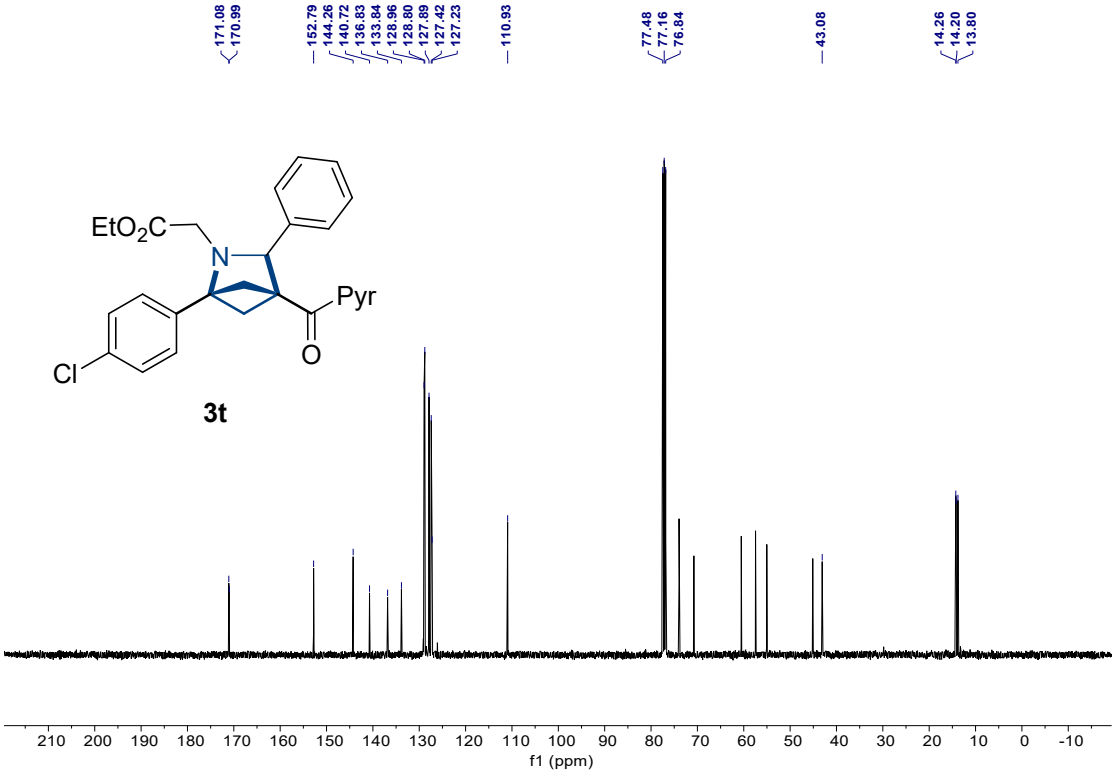
^{13}C NMR (101 MHz, $CDCl_3$) of **3s**



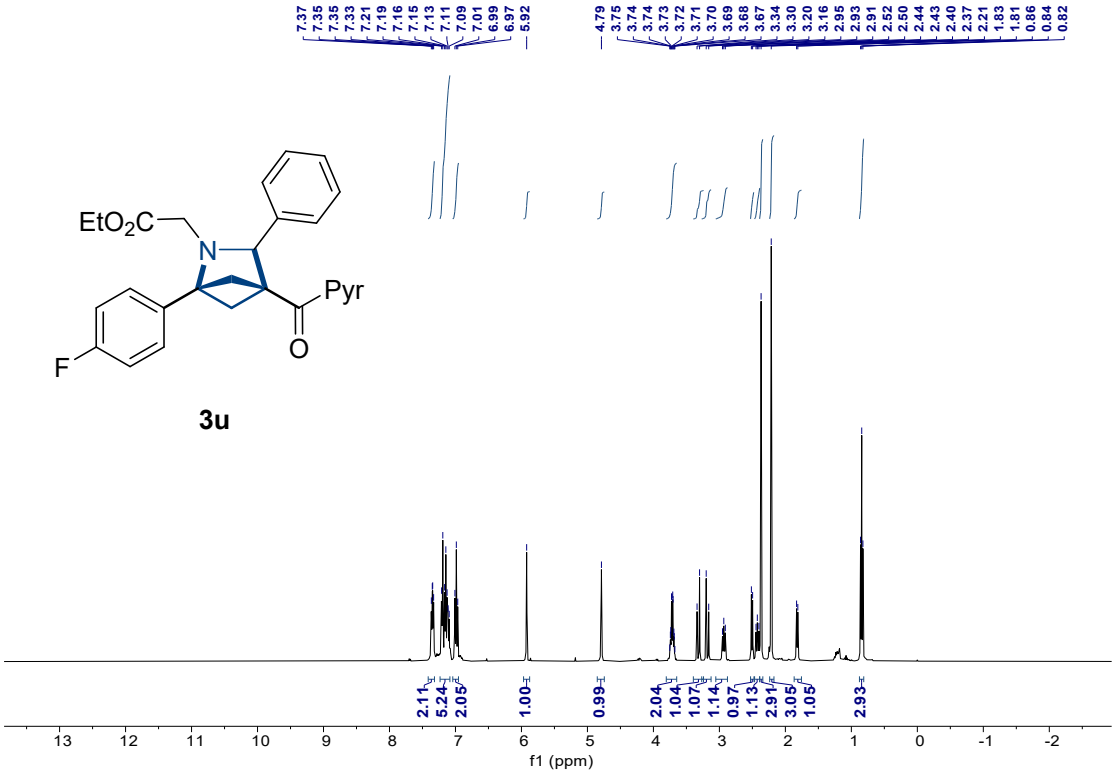
^{1}H NMR (400 MHz, $CDCl_3$) of **3t**



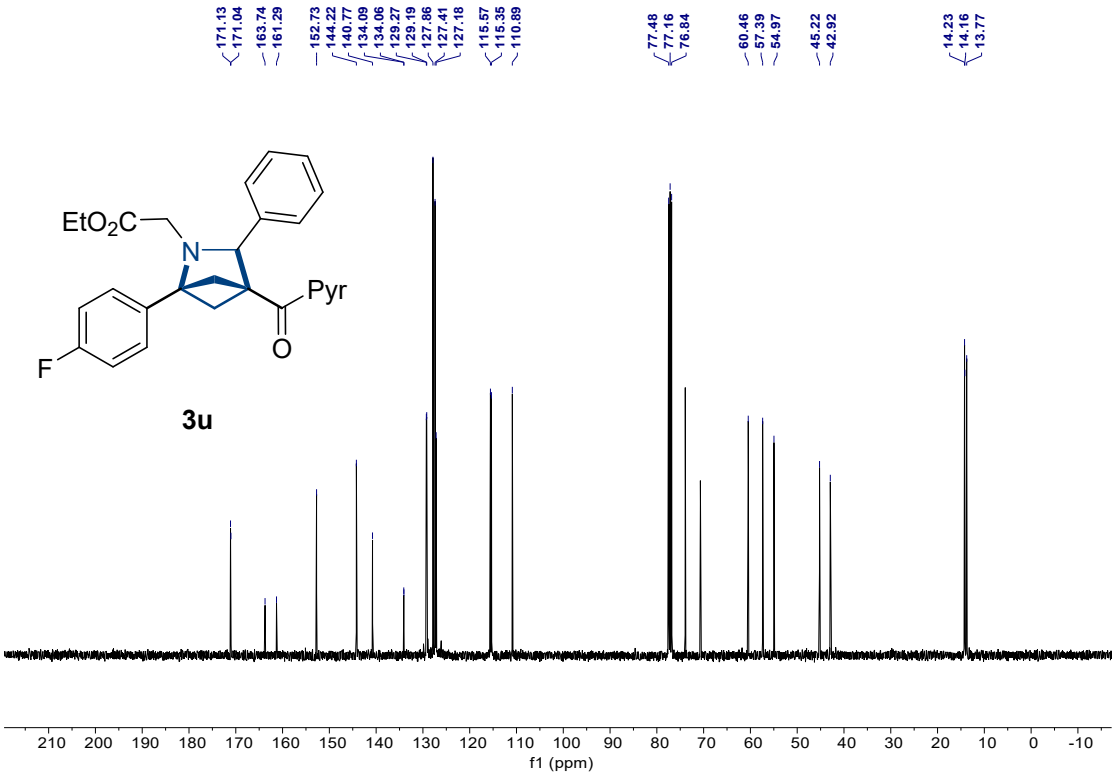
^{13}C NMR (101 MHz, $CDCl_3$) of **3t**



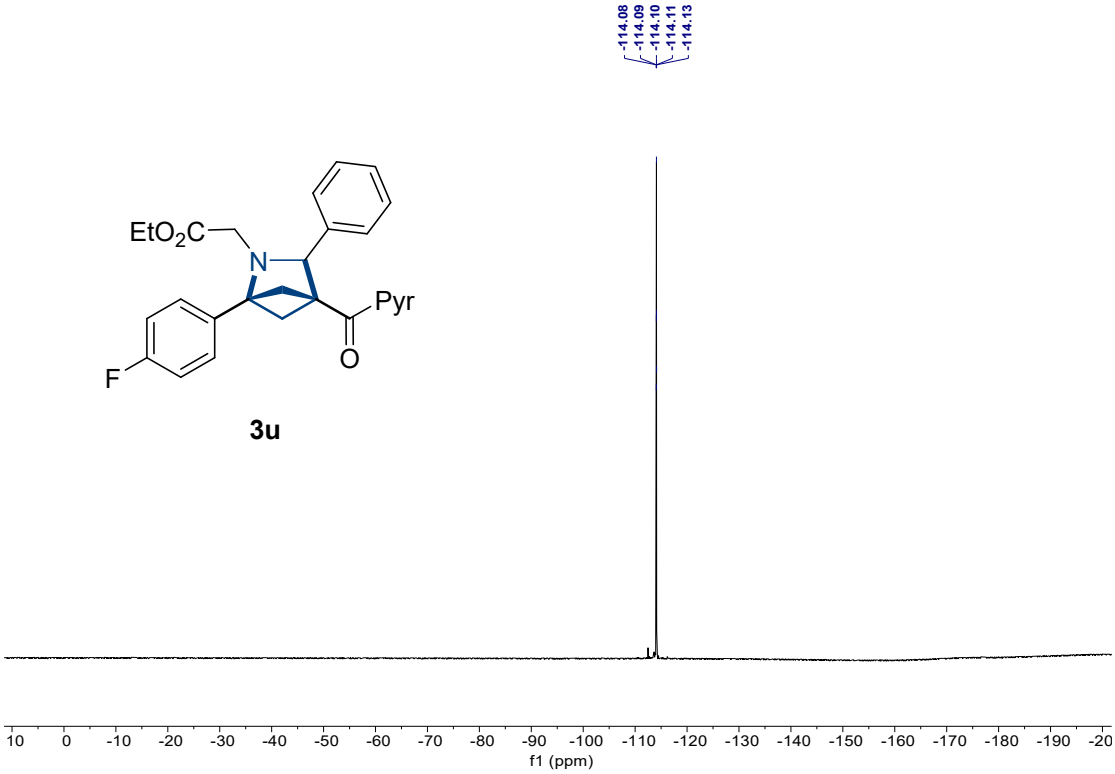
^{1}H NMR (400 MHz, $CDCl_3$) of **3u**



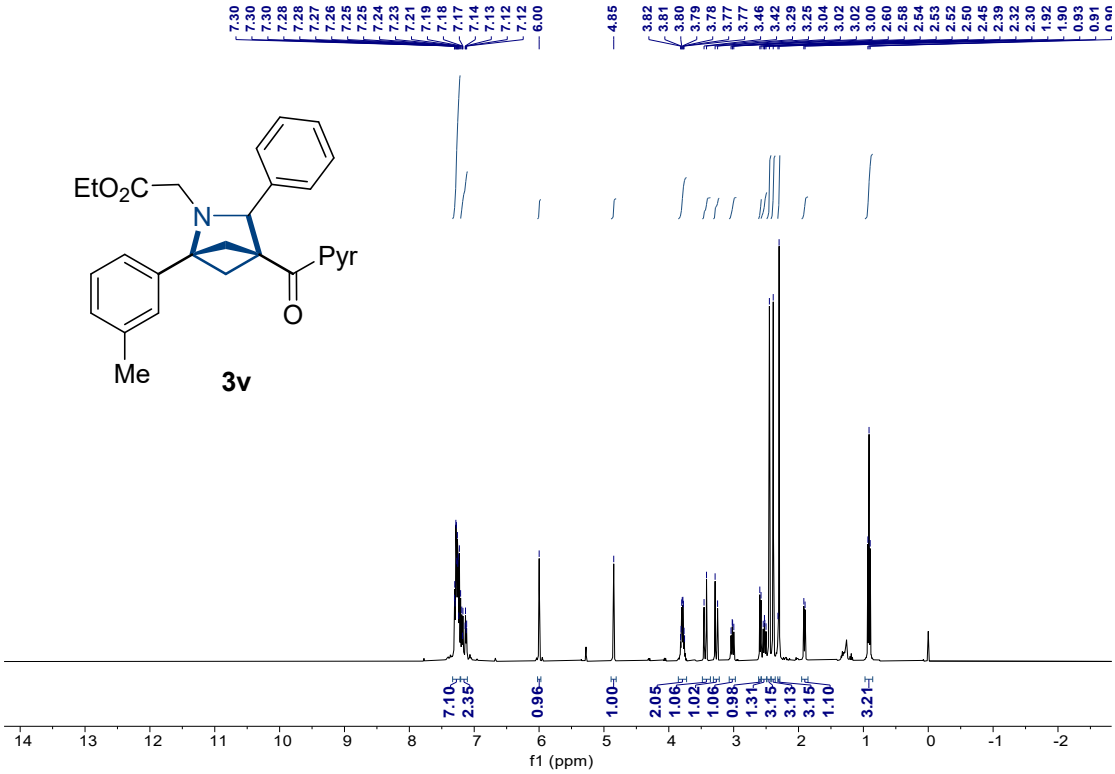
^{13}C NMR (101 MHz, $CDCl_3$) of **3u**



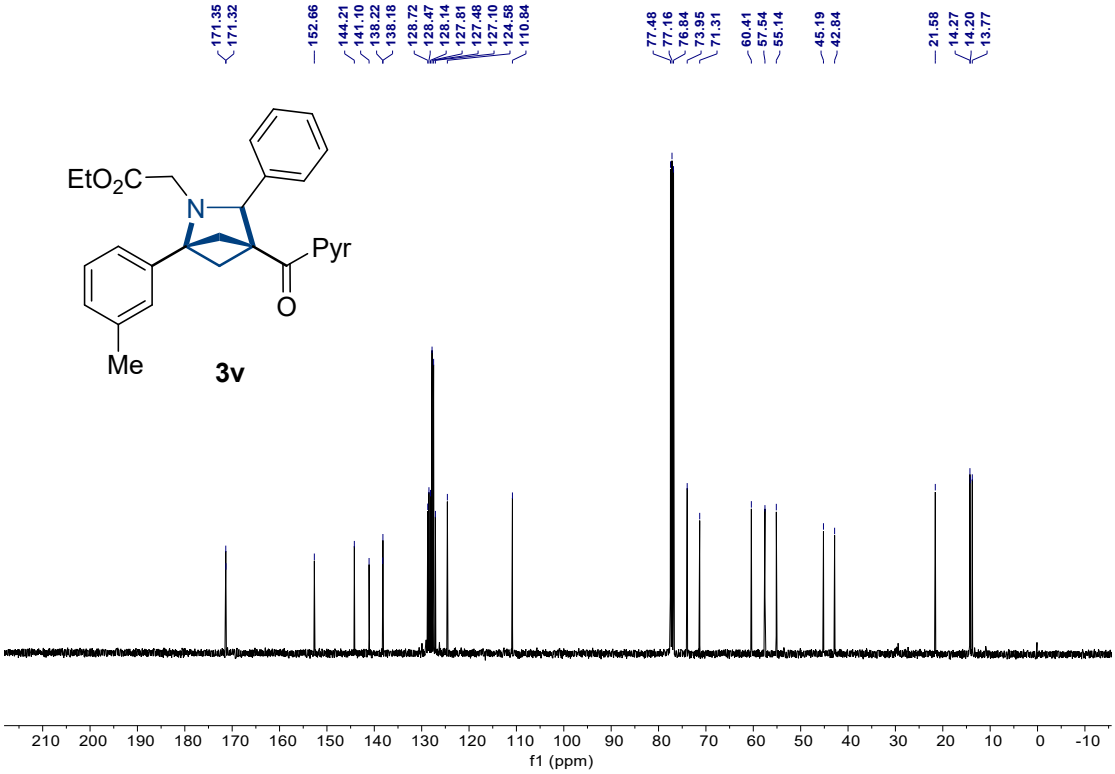
^{19}F NMR (376 MHz, $CDCl_3$) of **3u**



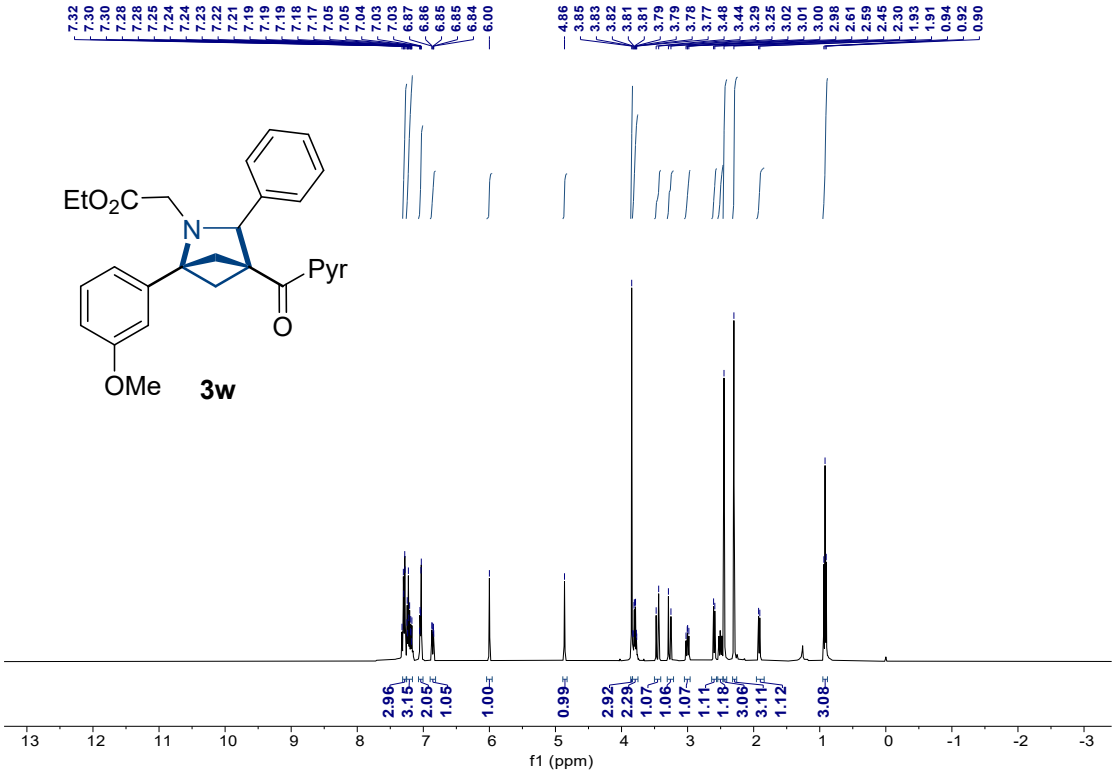
^{1}H NMR (400 MHz, $CDCl_3$) of **3v**



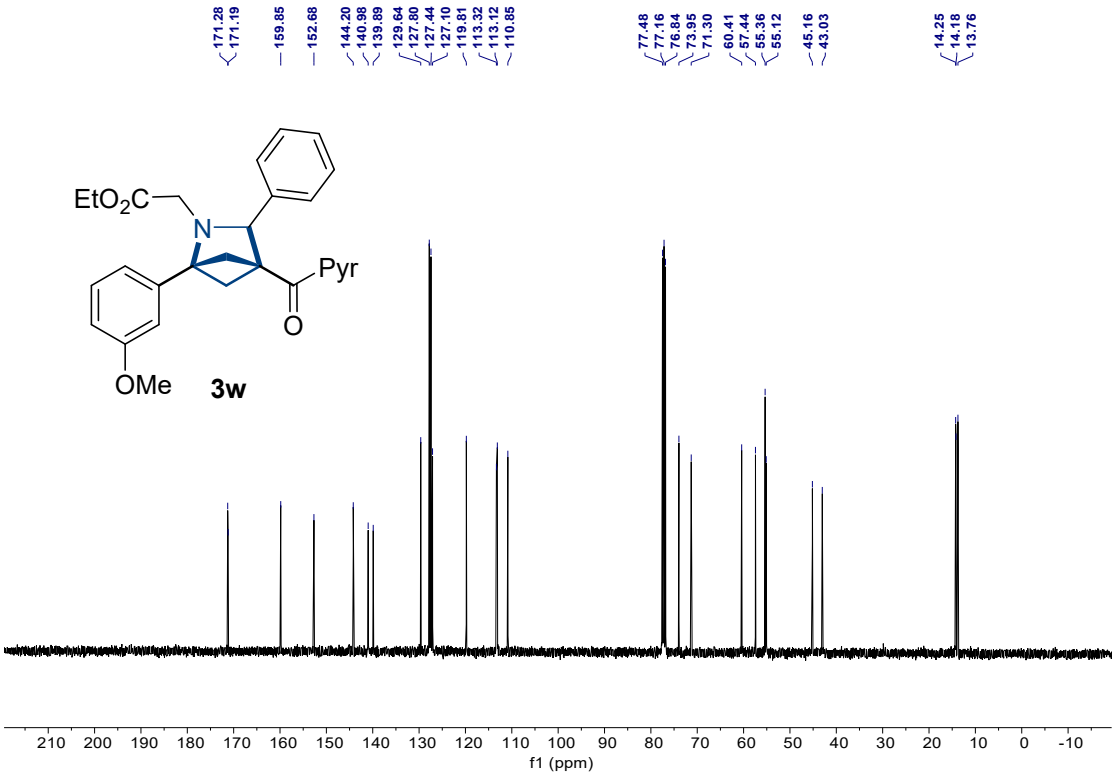
^{13}C NMR (101 MHz, $CDCl_3$) of **3v**



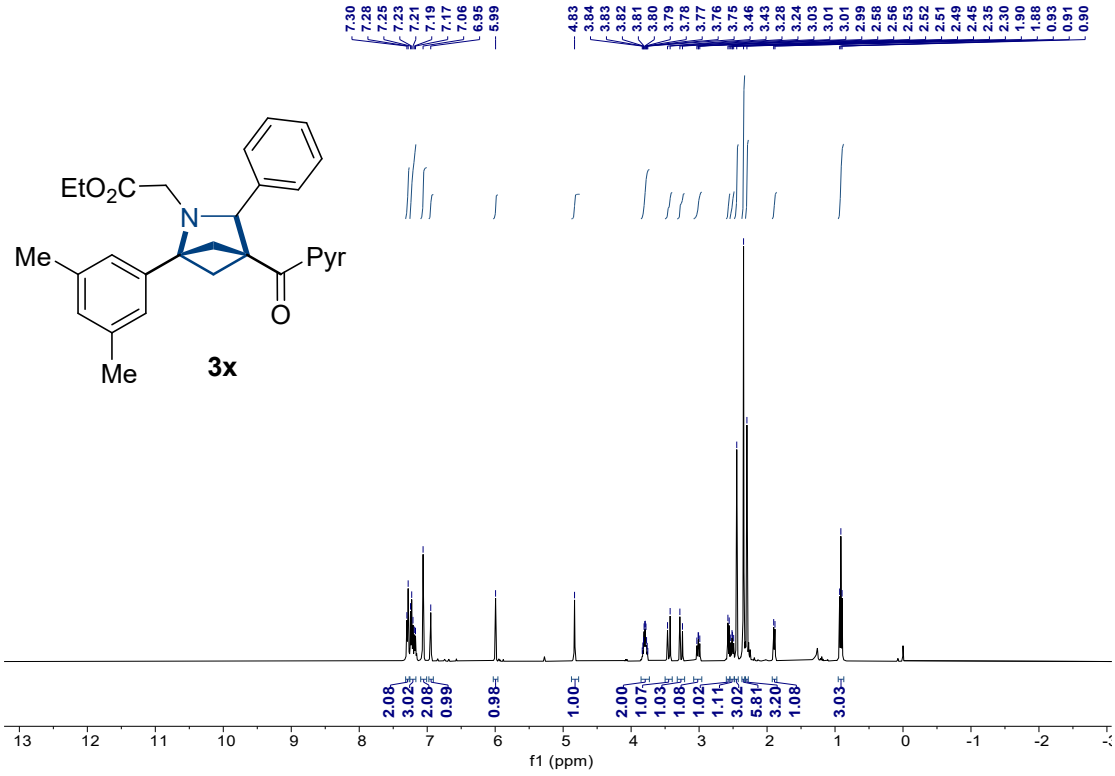
^{1}H NMR (400 MHz, $CDCl_3$) of **3w**



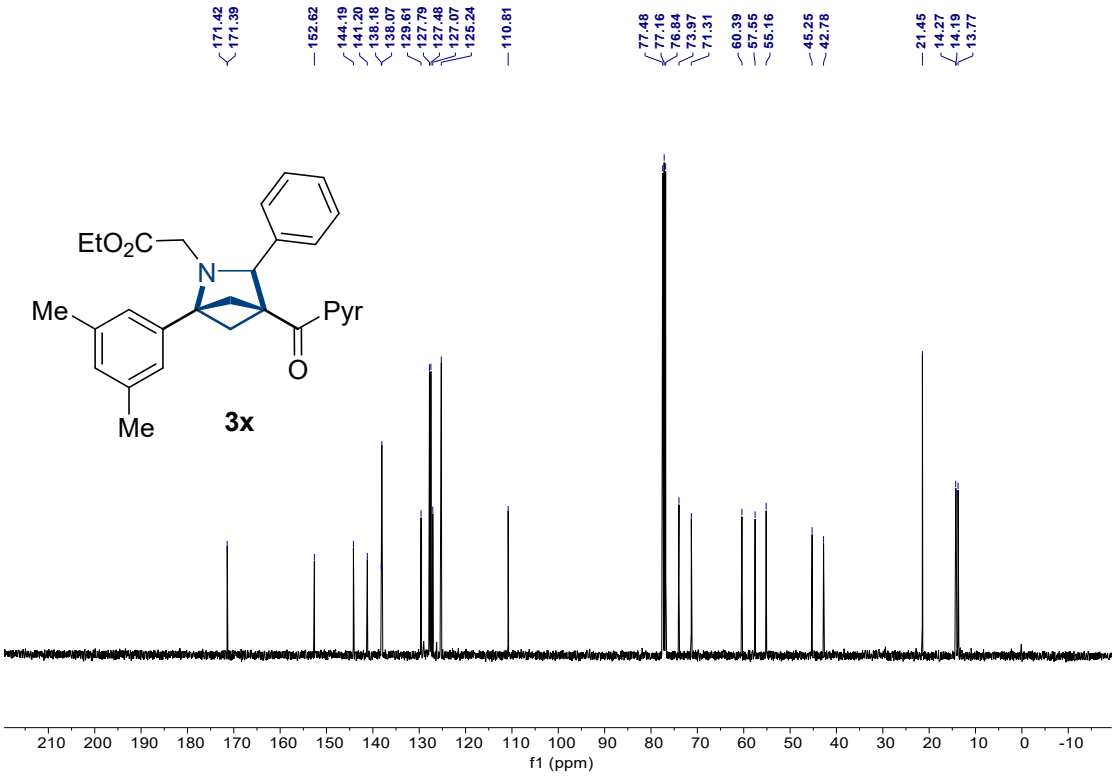
^{13}C NMR (101 MHz, $CDCl_3$) of **3w**



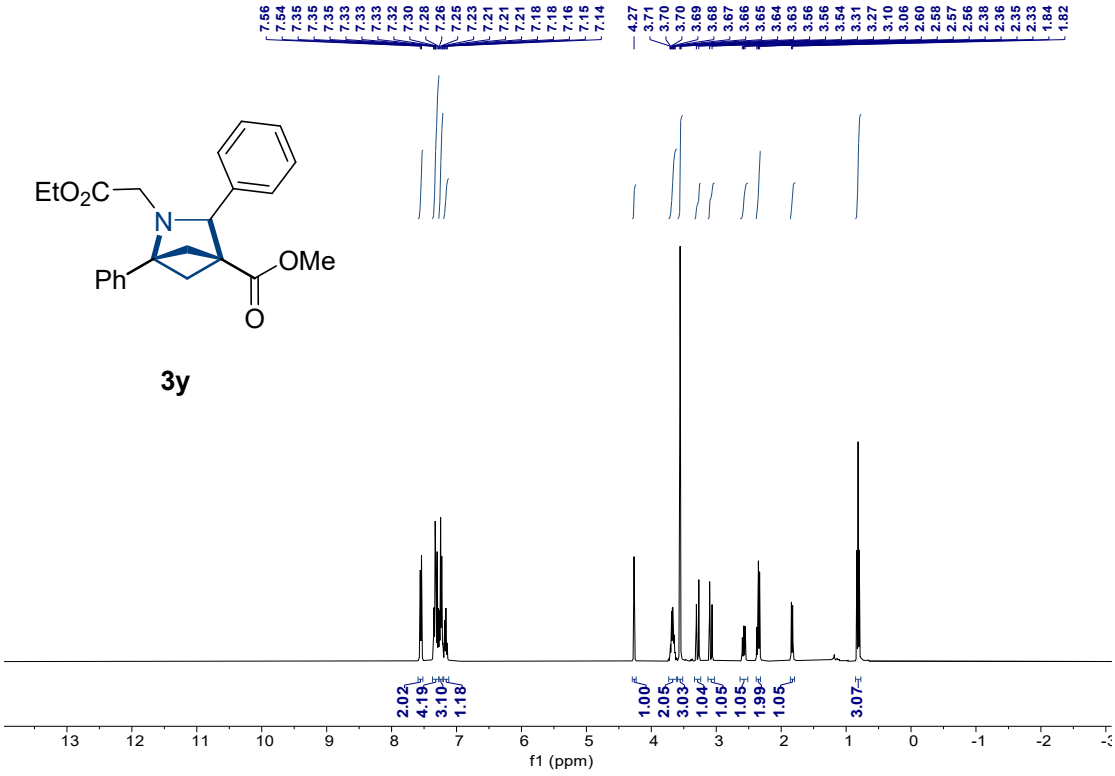
^{1}H NMR (400 MHz, $CDCl_3$) of **3x**



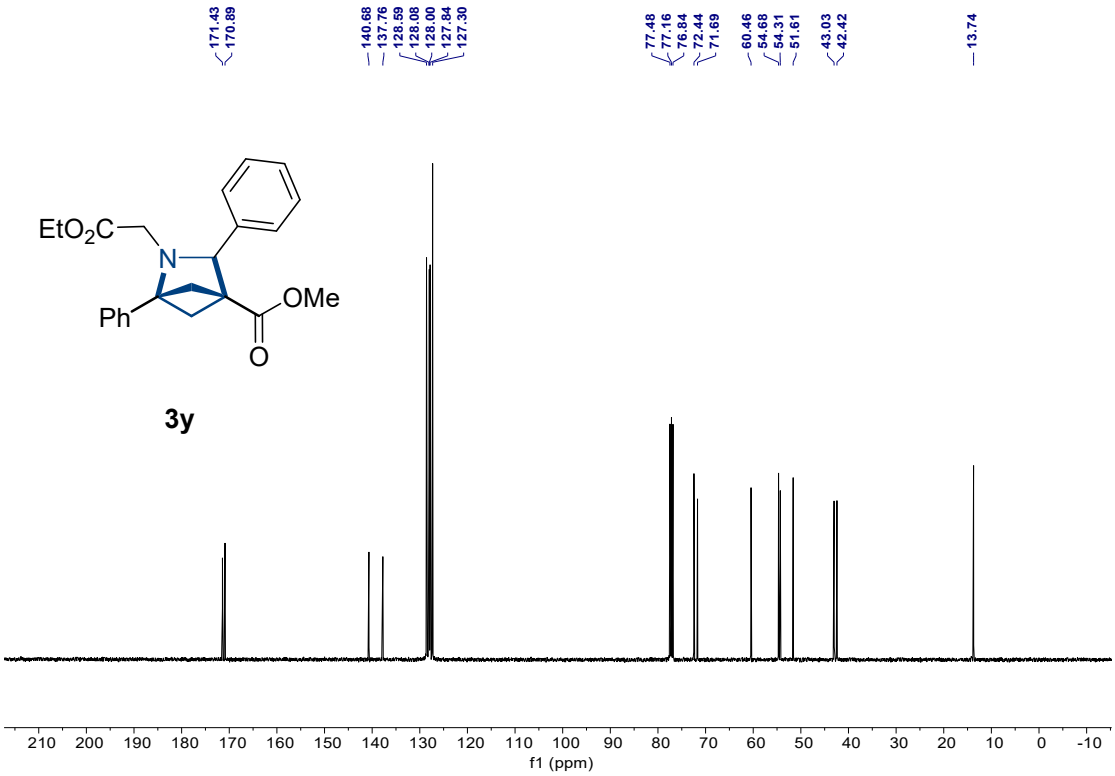
^{13}C NMR (101 MHz, $CDCl_3$) of **3x**



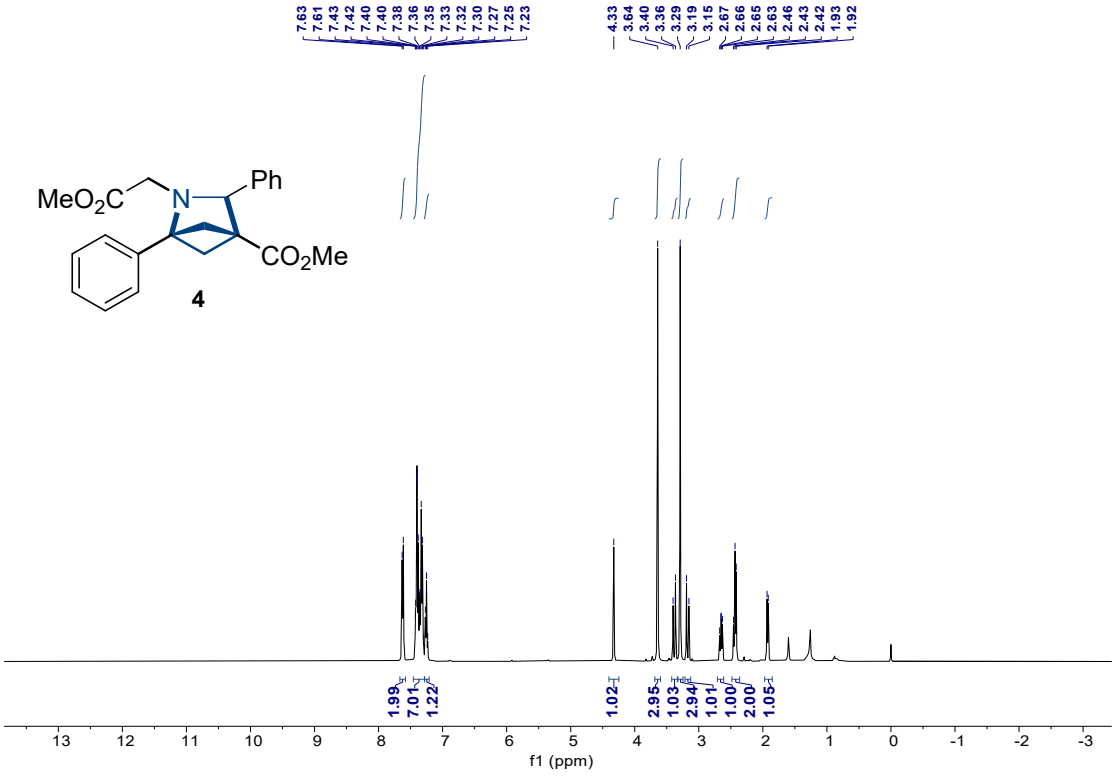
^{1}H NMR (400 MHz, $CDCl_3$) of **3y**



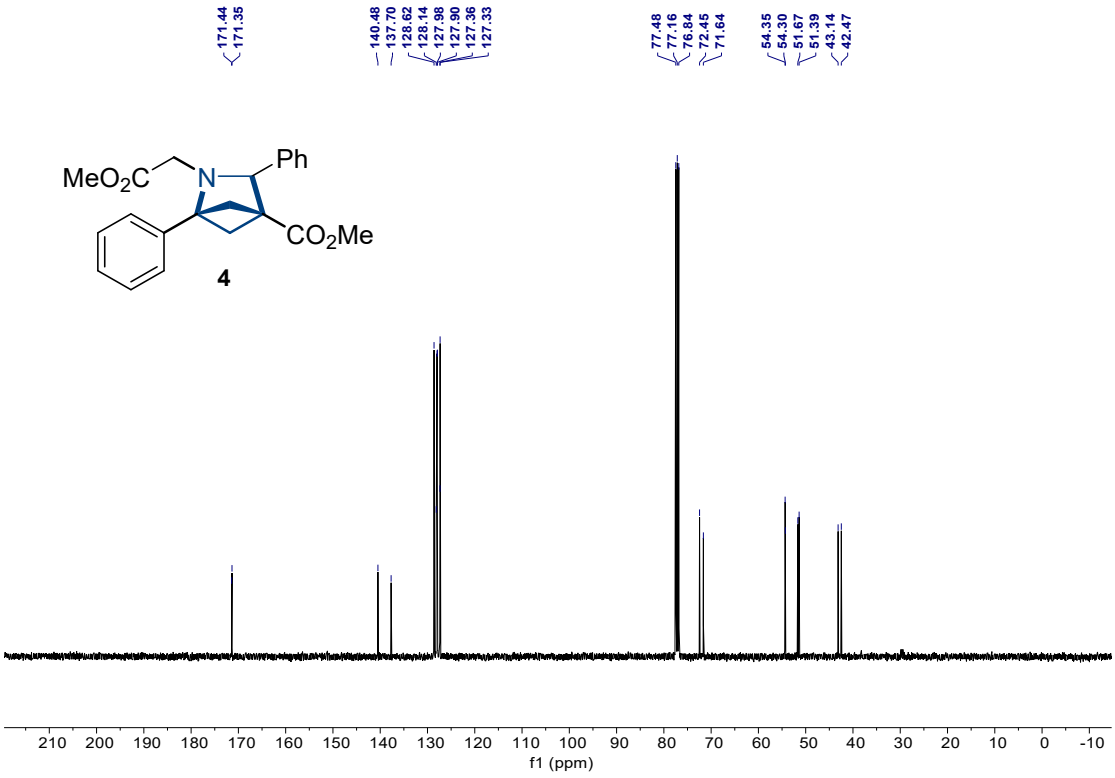
^{13}C NMR (101 MHz, $CDCl_3$) of **3y**



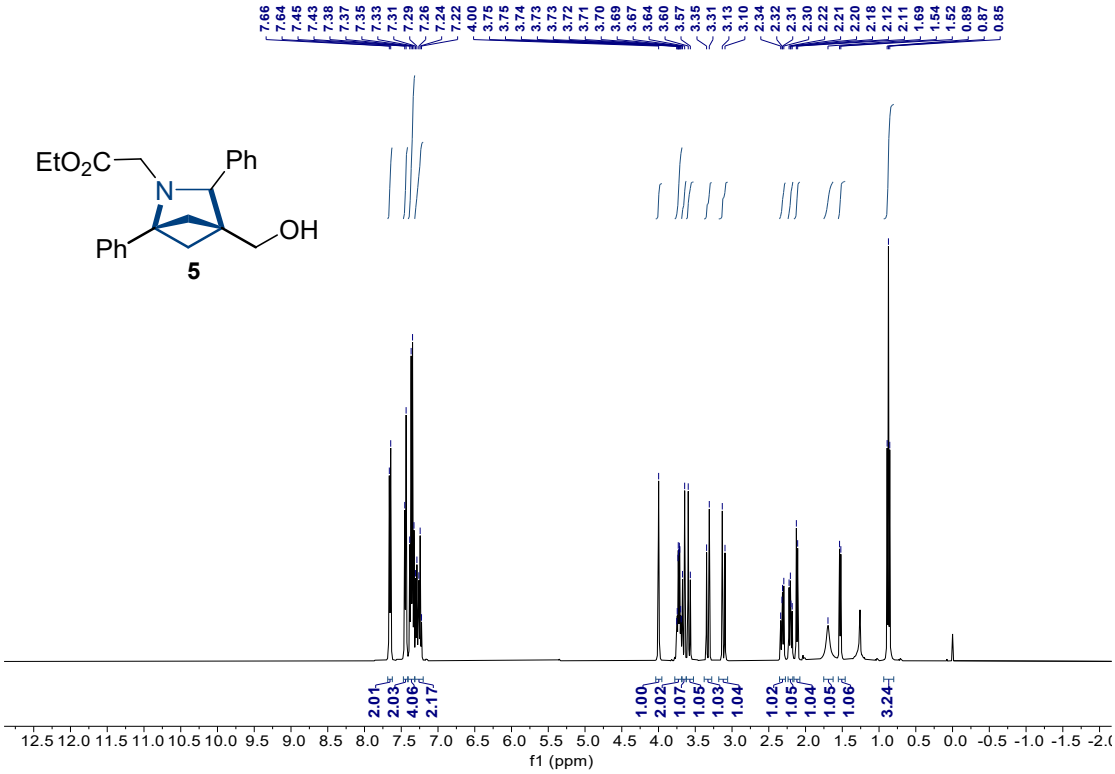
^{1}H NMR (400 MHz, $CDCl_3$) of **4**



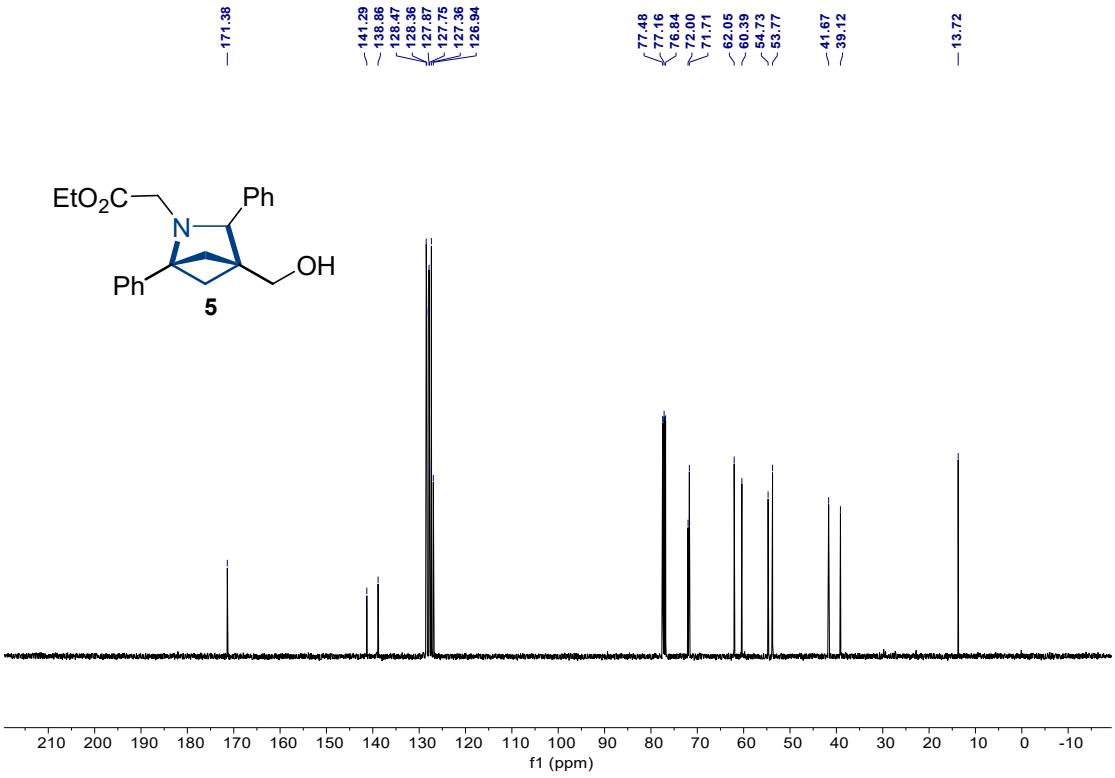
^{13}C NMR (101 MHz, $CDCl_3$) of **4**



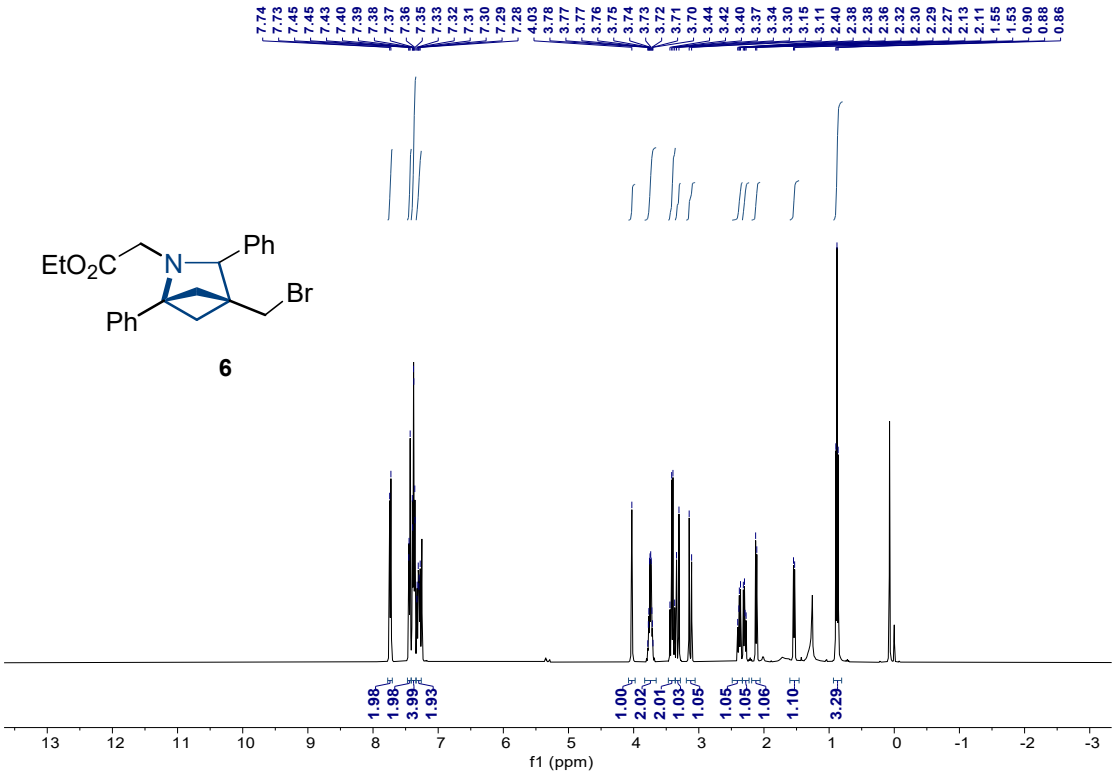
^{1}H NMR (400 MHz, $CDCl_3$) of **5**



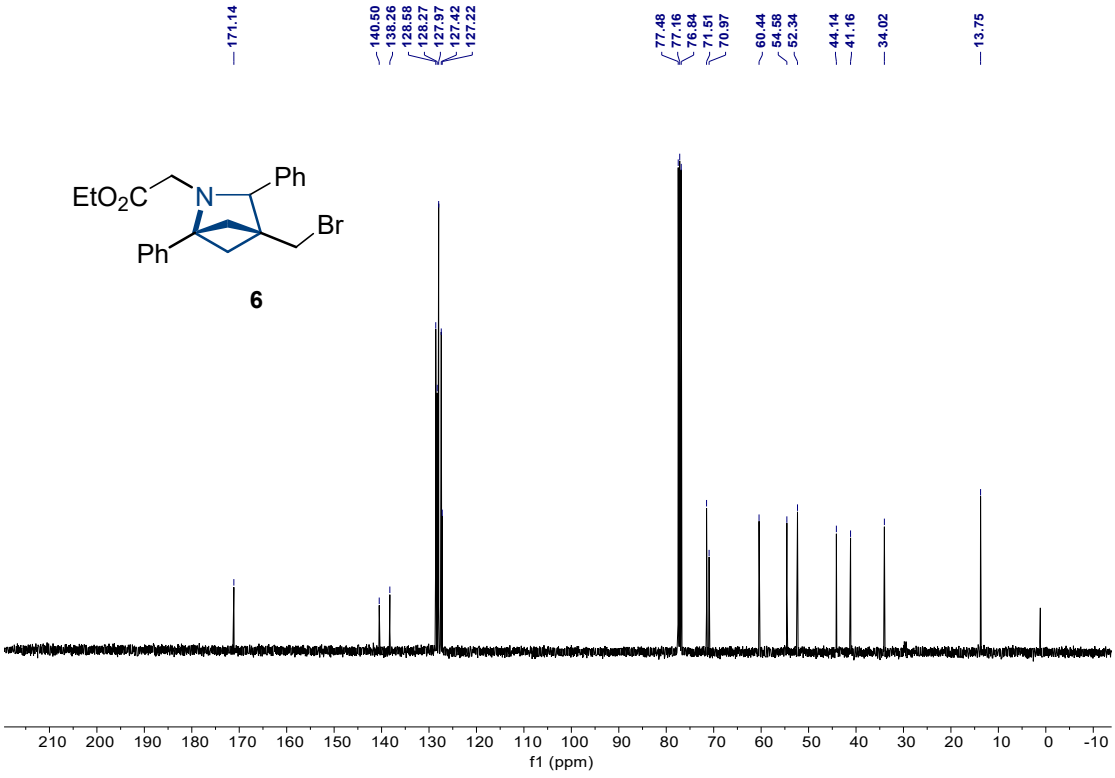
^{13}C NMR (101 MHz, $CDCl_3$) of **5**



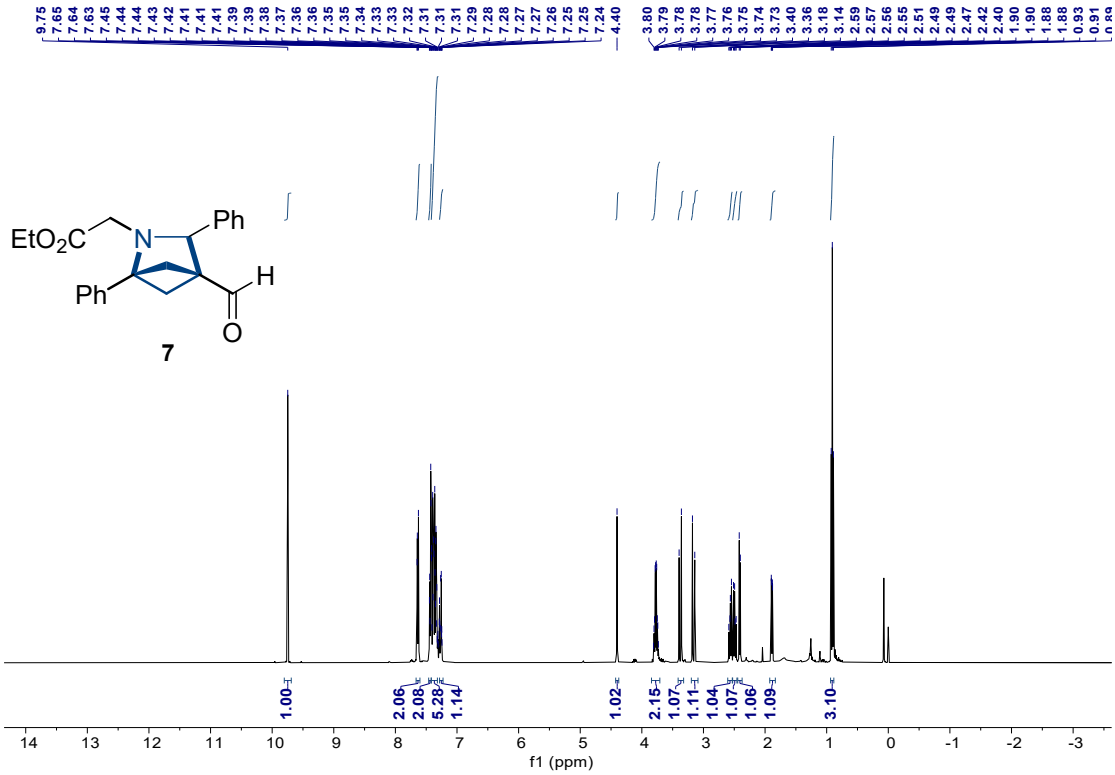
^{1}H NMR (400 MHz, $CDCl_3$) of **6**



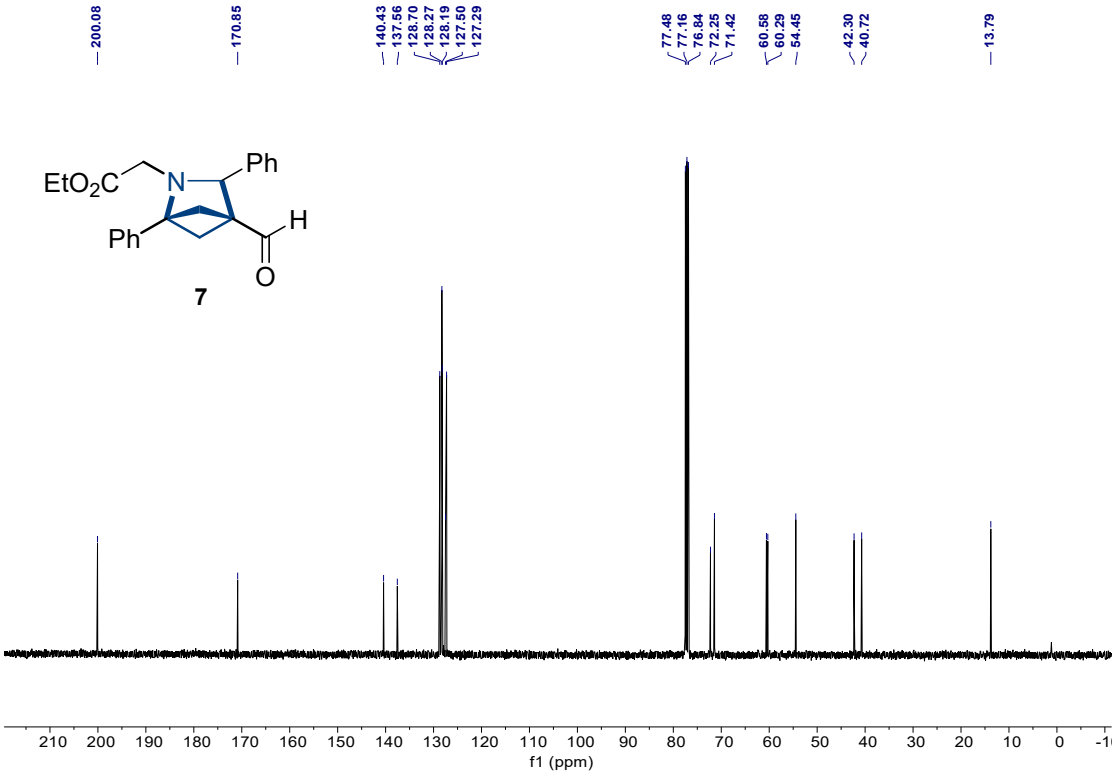
^{13}C NMR (101 MHz, $CDCl_3$) of **6**



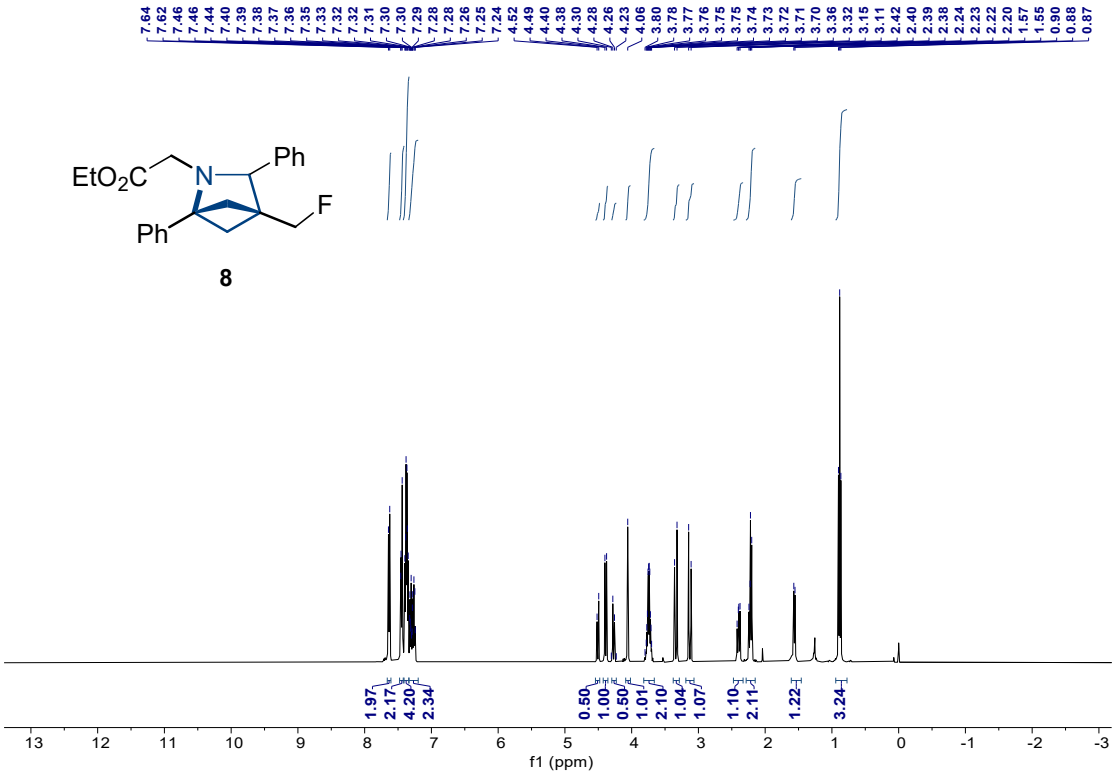
^{1}H NMR (400 MHz, $CDCl_3$) of **7**



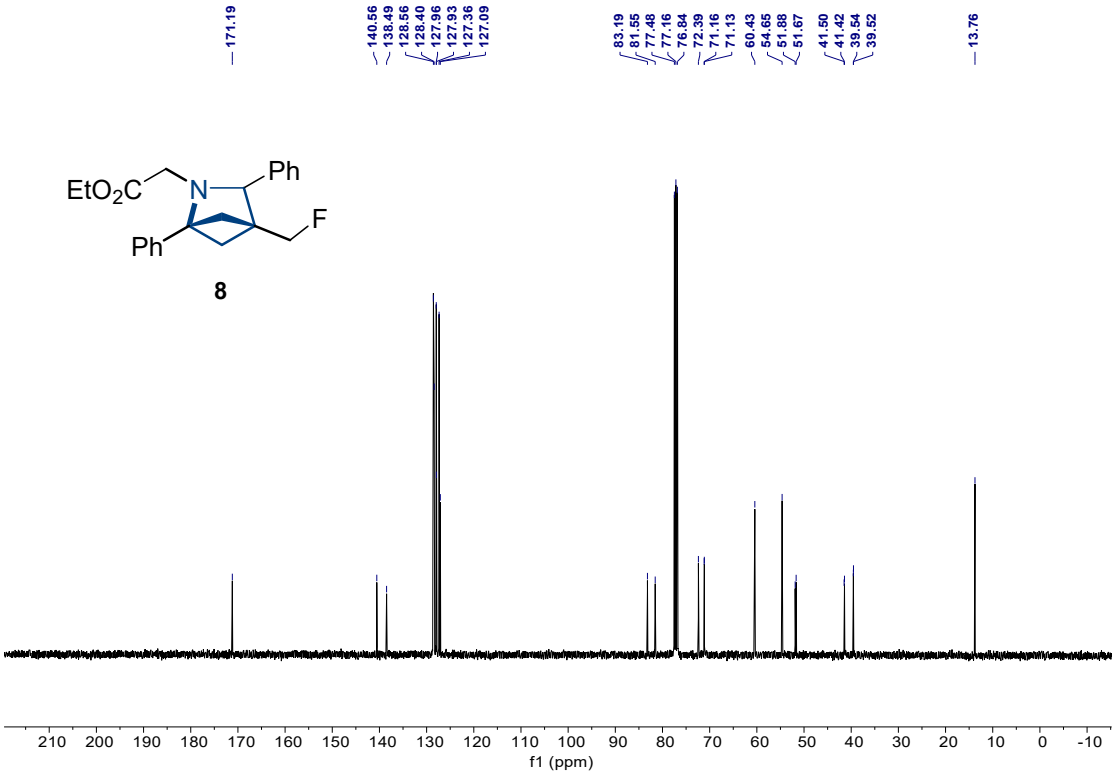
^{13}C NMR (101 MHz, $CDCl_3$) of **7**



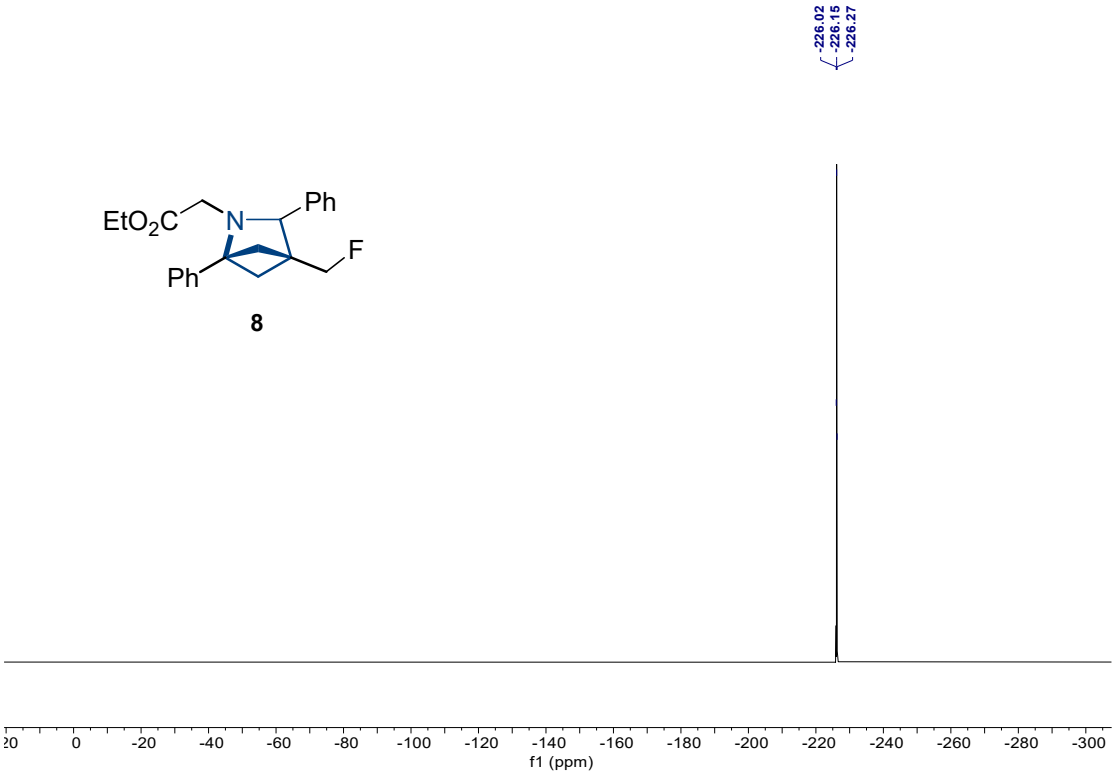
^{1}H NMR (400 MHz, $CDCl_3$) of **8**



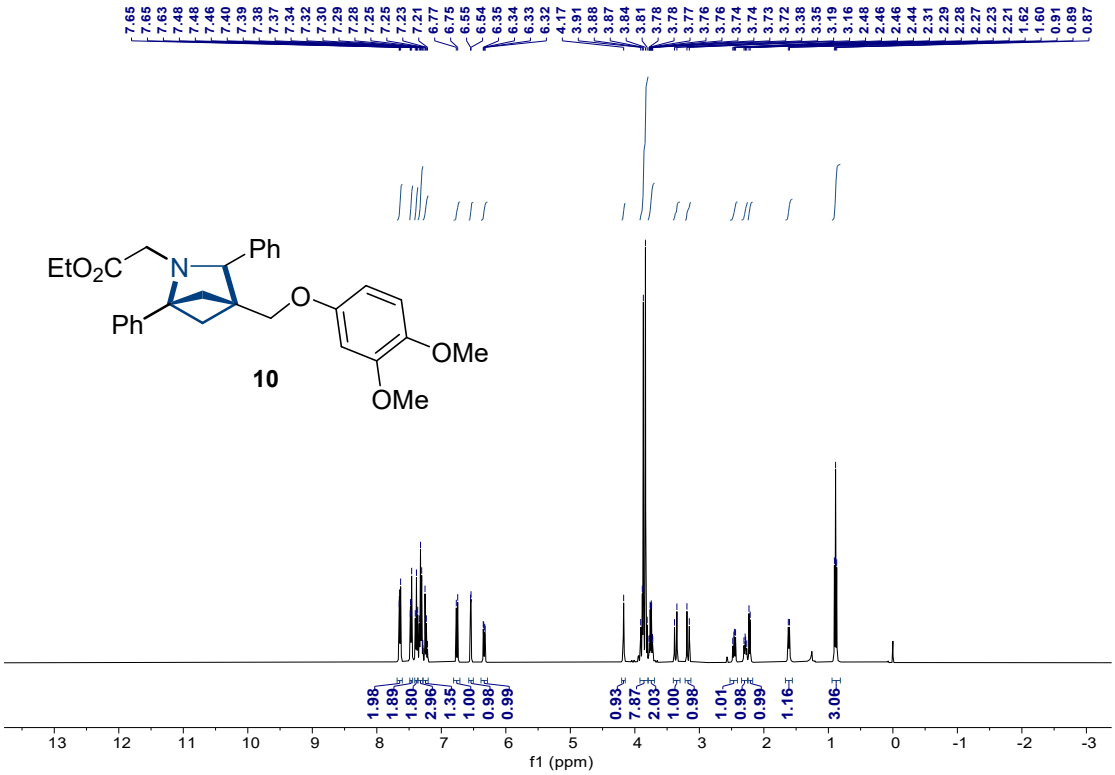
^{13}C NMR (101 MHz, $CDCl_3$) of **8**



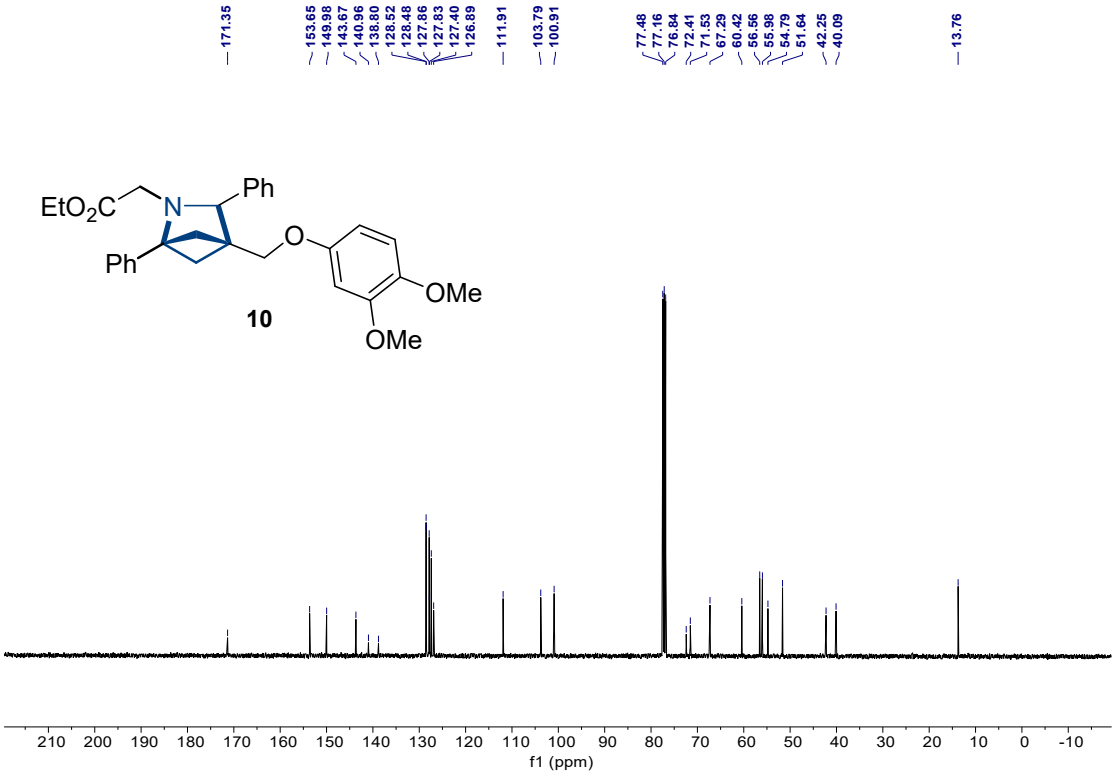
^{19}F NMR (376 MHz, $CDCl_3$) of **8**



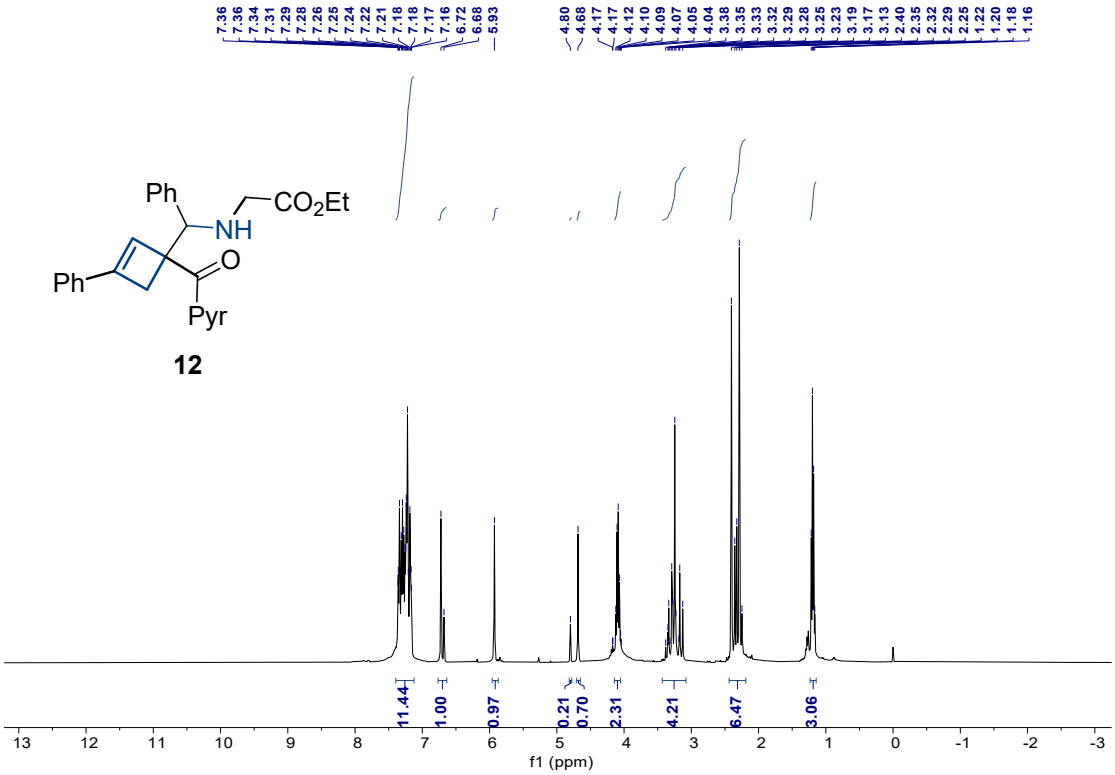
^{1}H NMR (400 MHz, $CDCl_3$) of **10**



^{13}C NMR (101 MHz, $CDCl_3$) of **10**



^{1}H NMR (400 MHz, $CDCl_3$) of **12**



^{13}C NMR (101 MHz, $CDCl_3$) of **12**