SUPPORTING INFORMATON

Pyrazolium-Ylide [3+2] Cycloaddition/Oxidative Aromatization for the Construction of 1*H*-pyrrolo[1,2-*b*]pyrazoles

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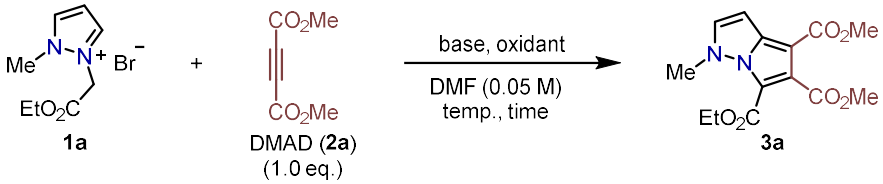
General information

All air and/or moisture sensitive reactions were carried out in anhydrous solvents under an Ar atmosphere in flame-dried glassware. All commercially available starting materials and reagents were used as received without further purification. Reactions were monitored by thin-layer chromatography (TLC) using Merck silica gel 60 F_{254} plate, and column chromatography was carried out by using Wako gel C-200 as adsorbent. Medium-pressure column chromatography with Biotage Selekt® was carried out by using Wako gel C-200 or Santai Technologies, Inc. SepaFlash™ Standard Series as absorbent. Melting point (m.p.) was measured using an Olympus BX53 microscope (Tokyo, Japan) equipped with heating stages (10,002 L, Linkam Scientific Instruments, Surrey, UK). Infrared spectra (IR) were determined in a liquid film on a NaCl plate or KBr method with a JASCO FT/IR-4100 type spectrometer, and reported in wave number (cm^{-1}). High-resolution mass spectra (HRMS) were taken on a JEOL JMS-700MS spectrometer by fast atom bombardment (FAB) methods. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) were measured on a Bruker AVANCE III 400 NMR spectrometer, and chemical shifts were reported in parts per million (ppm, δ) using the residual solvents peaks. Coupling constants (*J*) were reported in hertz (Hz). ^{19}F NMR (376 MHz) was also measured on the Bruker AVANCE III 400 NMR spectrometer, and chemical shifts were reported ppm using hexafluorobenzene (C_6F_6) as an internal standard. ^{1}H NMR spectra of the crude materials were used for determining the yield of the starting material with triphenylmethane.

Detailed information on optimization study

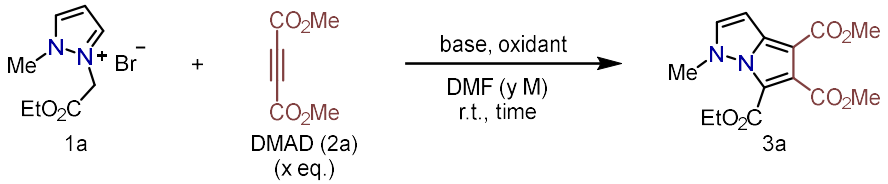
Table S1. Initial screening



entry	base	oxidant	temp./°C	time/h	Yield[a]/% of **3a**
1	K_2HPO_4 (2.0 eq.)	MnO_2 (20.0 eq.)	50	18	28
2	K_2HPO_4 (2.0 eq.)	I_2 (1.2 eq.)	50	18	2
3	K_2HPO_4 (2.0 eq.)	mCPBA (1.2 eq.)	50	18	trace
4	K_2HPO_4 (2.0 eq.)	H_2O_2 (1.2 eq.)	50	18	11
5	K_2HPO_4 (3.0 eq.)	MnO_2 (20.0 eq.)	50	18	10
6	K_2HPO_4 (5.0 eq.)	MnO_2 (20.0 eq.)	50	18	12
7	K_2HPO_4 (2.0 eq.)	MnO_2 (20.0 eq.)	r.t.	18	27
8	K_2HPO_4 (2.0 eq.)	MnO_2 (20.0 eq.)	r.t.	24	28

a) Determined by ^{1}H NMR using triphenylmethane as an internal standard.

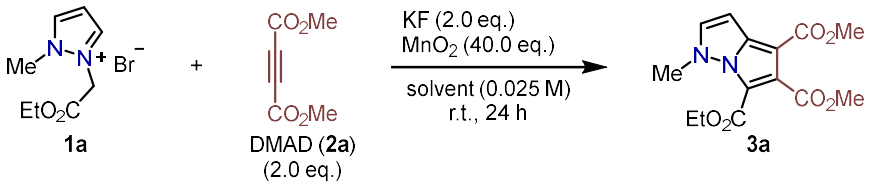
Table S2. Investigation of bases and stoichiometric ratio



entry	x	y	base	oxidant	time/h	Yield[a]/% of **3a**
1	1	0.05	CsF (2.0 eq.)	MnO_2 (20.0 eq.)	24	21
2	1	0.05	NaF (2.0 eq.)	MnO_2 (20.0 eq.)	24	3
3	1	0.05	KH_2PO_4 (2.0 eq.)	MnO_2 (20.0 eq.)	24	2
4	1	0.05	K_3PO_4 (2.0 eq.)	MnO_2 (20.0 eq.)	24	27
5	1	0.05	KOtBu (2.0 eq.)	MnO_2 (20.0 eq.)	24	trace
6	1	0.05	KF (2.0 eq.)	MnO_2 (20.0 eq.)	24	34
7	2	0.05	KF (2.0 eq.)	MnO_2 (20.0 eq.)	24	40
8	4	0.05	KF (2.0 eq.)	MnO_2 (20.0 eq.)	24	26
9	2	0.1	KF (2.0 eq.)	MnO_2 (20.0 eq.)	24	10
10	2	0.025	KF (2.0 eq.)	MnO_2 (20.0 eq.)	24	44
11	2	0.025	KF (2.0 eq.)	MnO_2 (40.0 eq.)	24	61
12	2	0.025	KF (2.0 eq.)	MnO_2 (60.0 eq.)	24	55
13	2	0.025	KF (3.0 eq.)	MnO_2 (40.0 eq.)	24	62
14	2	0.025	KF (4.0 eq.)	MnO_2 (40.0 eq.)	24	62
15	3	0.025	KF (2.0 eq.)	MnO_2 (40.0 eq.)	24	53
16	4	0.025	KF (2.0 eq.)	MnO_2 (40.0 eq.)	24	54
17	2	0.025	KF (2.0 eq.)	MnO_2 (40.0 eq.)	48	56

a) Determined by ^{1}H NMR using triphenylmethane as an internal standard.

Table S3. Investigation of solvents



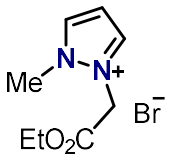
entry	solvent	Yield[a]/% of **3a**
1	toluene	10
2	THF	12
3	DCM	14
4	NMP	35
5	DMF	61
6	DMA	56
7	DMPU	11
8	DMSO	22

a) Determined by ^{1}H NMR using triphenylmethane as an internal standard.

General procedure for the synthesis of pyrazolium salts

1a, **1c**, **1k**, **1m**, and **1q** were synthesized according to previous report.[1]

To the solution of pyrazole (1.0 equiv) in acetonitrile (1.0 M) was added the alkylating agent (1.5 equiv). The mixture was stirred at reflux for 24 h. After the mixture was cooled to room temperature, diethyl ether was added, and the resulting precipitate was filtered and washed with ether to afford pyrazolium salts. If product was not precipitated, purification by silica gel column chromatography (CH_2Cl_2/MeOH) was conducted to afford pyrazolium salts.



1a

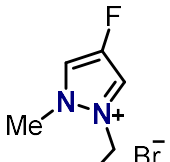
Synthesized from 1-methylpyrazole (84.2 mg, 1.03 mmol);

Yield: 229 mg, 90% (isolated yield); White solid; m.p.: 134.0-135.2 °C;

^{1}H NMR (400 MHz, DMSO-d6) δ 8.62 (d, *J* = 2.9 Hz, 1H, Ar*H*), 8.52 (dd, *J* = 2.9, 0.96 Hz, 1H, Ar*H*), 6.94 (t, *J* = 2.9 Hz, 1H, Ar*H*), 5.68 (s, 2H, NCH_2), 4.23 (q, *J* = 7.1 Hz, 2H, CO_2CH_2), 4.09 (s, 3H, NCH_3), 1.24 (t, *J* = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, DMSO-d6) δ 165.9 (CO_2), 139.1 (Ar), 139.0 (Ar), 107.6 (Ar), 62.4 (NCH_2), 50.0 (CO_2CH_2), 36.8 (NCH_3), 13.9 (CH_2CH_3);

IR (KBr) *v* 3105, 3039, 1752, 1543, 1443, 1321, 1296, 1110, 1022, 792;

HRMS (FAB) m/z calcd for $C_8H_{13}N_2O_2Br$ $[M\text{-}Br]^+$ 169.0977, found 169.0984.



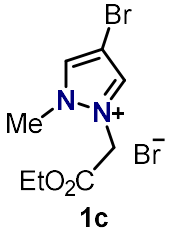
1b

Synthesized from 4-fluoro-1-methylpyrazole (200 mg, 2.00 mmol);

Yield: 81.2 mg, 15% (isolated yield); Brown solid; m.p.: 162.8-163.2 °C;

^{1}H NMR (400 MHz, DMSO-d6): δ 8.93 (s, 1H, Ar*H*), 8.77 (s, 1H, Ar*H*), 5.64 (s, 2H, NCH_2), 4.24 (q, *J* = 7.1 Hz, 2H, CO_2CH_2), 4.08 (s, 3H, NCH_3), 1.25 (t, *J* = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, DMSO-d6) δ 165.45 (CO_2), 145.4 (d, *J* = 241.4 Hz, Ar), 127.1 (d, *J* = 24.5 Hz, Ar), 126.1 (d, *J* = 24.5 Hz, Ar), 62.5 (NCH_2), 50.6 (CO_2CH_2), 37.59 (NCH_3), 13.8 (CH_2CH_3); ^{19}F NMR (376 MHz, DMSO-d6, C_6F_6) δ –170.91 (s, 1F, C*F*);

HRMS (FAB) m/z calcd for $C_8H_{12}BrFN_2O_2$ $[M\text{-}Br]^+$ 187.0883, found 187.0873.



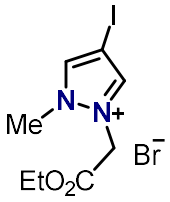
1c

Synthesized from 4-bromo-1-methylpyrazole (805 mg, 5.00 mmol);

Yield: 311 mg, 19% (isolated yield); White solid; m.p.: 151.7-152.3 °C;

^{1}H NMR (400 MHz, DMSO-d6) δ 8.94 (d, *J* = 0.88 Hz, 1H, Ar*H*), 8.80 (d, *J* = 0.88 Hz, 1H, Ar*H*), 5.67 (s, 2H, NCH_2), 4.24 (q, *J* = 7.12 Hz, 2H, CO_2CH_2), 4.10 (s, 3H, NCH_3), 1.25 (t, *J* = 7.12 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, DMSO-d6) δ 165.9 (CO_2), 139.8 (Ar), 139.3 (Ar), 94.7 (Ar), 63.1 (NCH_2), 51.0 (CO_2CH_2), 38.0 (NCH_3), 14.3 (CH_2CH_3);

HRMS (FAB) m/z calcd for $C_8H_{12}Br_2N_2O_2$ [M-Br]$^+$ 247.0082, found 247.0075.



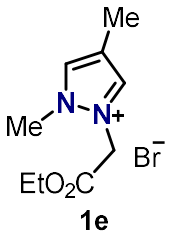
1d

Synthesized from 4-iodo-1-methylpyrazole (1.04 g, 5.00 mmol);

Yield: 817 mg, 50% (isolated yield); White solid; m.p.: 215.6-216.4 °C;

^{1}H NMR (400 MHz, DMSO-d6) δ 8.82 (d, *J* = 0.80 Hz, 1H, Ar*H*), 8.68 (d, *J* = 0.80 Hz, 1H, Ar*H*), 5.64 (s, 2H, NCH_2), 4.23 (q, *J* = 7.11 Hz, 2H, CO_2CH_2), 4.08 (s, 3H, NCH_3), 1.25 (t, *J* = 7.11 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, DMSO-d6) δ 165.6 (CO_2), 143.2 (Ar), 142.8 (Ar), 62.5 (Ar), 61.2 (NCH_2), 50.2 (CO_2CH_2), 37.1 (NCH_3), 13.9 (CH_2CH_3);

HRMS (FAB) m/z calcd for $C_8H_{12}BrN_2O_2I$ [M-Br]$^+$ 294.9943, found 294.9938.



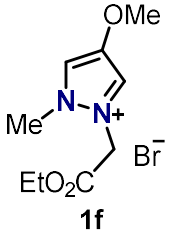
1e

Synthesized from 1,4-dimethylpyrazole (480 mg, 4.99 mmol);

Yield: 1.31 g, quant (isolated yield); White solid; m.p.: 56.8-57.8 °C;

^{1}H NMR (400 MHz, DMSO-d6): δ 8.41 (s, 1H, Ar*H*), 8.29 (s, 1H, Ar*H*), 5.59 (s, 2H, NCH_2), 4.18 (q, *J* = 7.12 Hz, 2H, CO_2CH_2), 4.00 (s, 3H, NCH_3), 2.08 (s, 3H, CH_3), 1.19 (t, *J* = 7.12 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, DMSO-d6) δ 165.9 (CO_2), 138.1 (Ar), 137.4 (Ar), 117.1 (Ar), 62.3 (NCH_2), 49.8 (CO_2CH_2), 36.6 (NCH_3), 13.8 (CH_2CH_3), 8.3 (CH_3);

HRMS (FAB) m/z calcd for $C_9H_{15}BrN_2O_2$ [M-Br]$^+$ 183.1134, found 183.1139.



1f

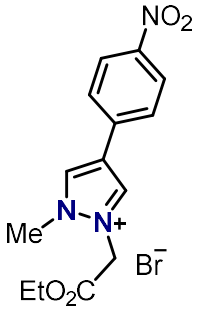
Synthesized from 4-methoxy-1-methylpyrazole (133 mg, 1.19 mmol);

Yield: 205 mg, 62% (isolated yield); Colorless oil;

^{1}H NMR (400 MHz, DMSO-d6): δ 8.54 (d, *J* = 1.4 Hz, 1H, Ar*H*), 8.35 (d, *J* = 1.4 Hz, 1H, Ar*H*), 5.57 (s, 2H, NC*H*$_2$), 4.23 (q, *J* = 7.1 Hz, 2H, CO$_2$C*H*$_2$), 4.02 (s, 3H, NC*H*$_3$), 3.82 (s, 3H, OC*H*$_3$), 1.24 (t, *J* = 7.1 Hz, 3H, CH$_2$C*H*$_3$)

^{13}C NMR (100 MHz, DMSO-d6) δ 165.7 (*C*O$_2$), 144.0 (Ar), 125.9 (Ar), 124.4 (Ar), 62.4 (N*C*H$_2$), 59.3 (O*C*H$_3$), 50.2 (CO$_2$*C*H$_2$), 37.0 (N*C*H$_3$), 13.9 (CH$_2$*C*H$_3$);

HRMS (FAB) m/z calcd for $C_9H_{15}BrN_2O_3$ [M-Br]$^+$ 199.1083, found 199.1086.



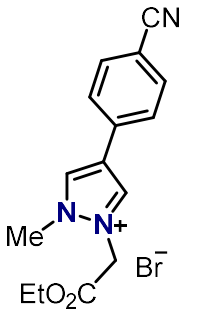
1g

Synthesized from 1-methyl-4-(4-nitrophenyl)-1*H*-pyrazole (204 mg, 1.00 mmol);

Yield: 219 mg, 59% (isolated yield); Brown solid; m.p.: 152.8-153.7 °C;

^{1}H NMR (400 MHz, DMSO-d6): δ 9.33 (s, 1H, Ar*H*), 9.17 (s, 1H, Ar*H*), 8.34 (d, 2H, *J* = 8.8 Hz, Ar*H*), 7.96 (d, 2H, *J* = 8.8 Hz Ar*H*), 5.73 (s, 2H, NC*H*$_2$), 4.26 (q, *J* = 7.1 Hz, 2H, CO$_2$C*H*$_2$), 4.16 (s, 3H, NC*H3*), 1.27 (t, *J* = 7.1 Hz, 3H, CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, DMSO-d6) δ 165.7 (*C*O$_2$), 147.2 (Ar), 137.0 (Ar), 136.4 (Ar), 134.5 (Ar), 126.8 (Ar), 124.7 (Ar), 120.2 (Ar), 62.6 (N*C*H$_2$), 50.7 (CO$_2$*C*H$_3$), 37.6 (N*C*H$_2$), 13.9 (CH$_2$*C*H$_3$);

HRMS (FAB) m/z calcd for $C_{14}H_{16}BrN_3O_4$ [M-Br]$^+$ 290.1141, found 290.1141.



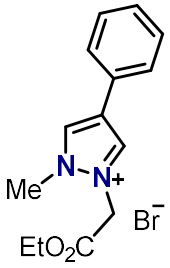
1h

Synthesized from 4-(1-methyl-1*H*-pyrazol-4-yl)benzonitrile (129 mg, 0.70 mmol);

Yield: 192 mg, 78% (isolated yield); White solid; m.p.: 166.0-166.4 °C;

^{1}H NMR (400 MHz, DMSO-d6): δ 9.28 (s, 1H, Ar*H*), 9.12 (s, 1H, Ar*H*), 8.01 (d, *J* = 8.4 Hz, 2H, Ar*H*), 7.90 (d, *J* = 8.4 Hz, 2H, Ar*H*), 5.72 (s, 2H, NC*H*$_2$), 4.26 (q, *J* = 7.1 Hz, 2H, CO$_2$C*H*$_2$), 4.15 (s, 2H, NC*H*$_2$), 1.26 (t, *J* = 7.1 Hz, 3H, CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, DMSO-d6) δ 165.6 (*C*O$_2$), 136.7 (Ar), 136.1 (Ar), 133.4 (Ar), 132.5 (Ar), 126.4 (Ar), 120.6 (Ar), 118.5 (Ar), 111.0 (*C*N), 62.6 (N*C*H$_2$), 50.5 (CO$_2$*C*H$_3$), 37.5 (N*C*H$_3$), 13.9 (CH$_2$*C*H$_3$),

HRMS (FAB) m/z calcd for $C_{15}H_{16}BrN_3O_2$ [M-Br]$^+$ 270.1243, found 270.1249.



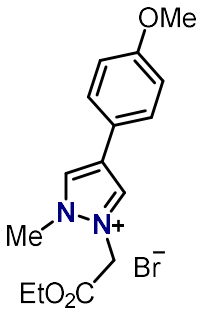
1i

Synthesized from 1-methyl-4-phenylpyrazole (321 mg, 2.03 mmol);

Yield: 634 mg, 96% (isolated yield); White solid; 164.8-165.3 °C;

^{1}H NMR (400 MHz, DMSO-d6): δ 9.17 (d, *J* = 0.96 Hz, 1H, Ar*H*), 9.01 (d, *J* = 0.96 Hz, 1H, Ar*H*), 7.66-7.70 (m, 2H, Ar*H*), 7.49-7.54 (m, 2H, Ar*H*), 7.42 (tt, *J* = 7.3, 1.4 Hz, 1H, Ar*H*), 5.71 (s, 2H, NCH_2), 4.26 (q, *J* = 7.1 Hz, 2H, CO_2CH_2), 4.14 (s, 3H, NCH_3), 1.26 (t, *J* = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, DMSO-d6) δ 165.8 (CO_2), 135.9 (Ar), 135.2 (Ar), 129.5 (Ar), 128.8 (Ar), 127.8 (Ar), 125.7 (Ar), 122.3 (Ar), 62.6 (NCH_2), 50.4 (CO_2CH_2), 37.3 (NCH_3), 13.9 (CH_2CH_3);

HRMS (FAB) m/z calcd for $C_{14}H_{17}BrN_2O_2$ [M-Br]$^+$ 245.1290, found 245.1280.



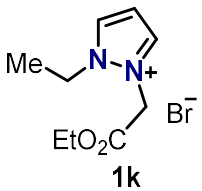
1j

Synthesized from 4-(4-methoxyphenyl)-1-methyl-1*H*-pyrazole (180 mg, 0.96 mmol);

Yield: 187 mg, 55% (isolated yield); Yellow oil;

^{1}H NMR (400 MHz, DMSO-d6): δ 9.11 (s, 1H, Ar*H*), 8.95 (s, 1H, Ar*H*), 7.56 (d, *J* = 8.6 Hz, 2H, Ar*H*), 7.02 (d, *J* = 8.6 Hz, 2H, Ar*H*), 5.69 (s, 2H, NCH_2), 4.20 (q, *J* = 7.1 Hz, 2H, CO_2CH_2), 4.09 (s, 3H, NCH_3), 3.74 (s, 3H, OCH_3), 1.21 (t, *J* = 7.10 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, DMSO-d6) δ 165.8 (CO_2), 159.5 (Ar), 135.3 (Ar), 134.5 (Ar), 127.1 (Ar), 122.12(Ar), 120.1 (Ar), 114.8 (Ar), 62.5 (NCH_2), 55.3 (OCH_3), 50.3 (CO_2CH_2), 37.2 (NCH_3), 13.9 (CH_2CH_3);

HRMS (FAB) m/z calcd for $C_{15}H_{19}BrN_2O_3$ [M-Br]$^+$ 275.1396, found 275.1402.



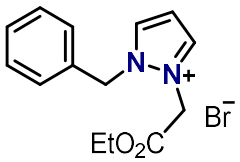
1k

Synthesized from 1-ethylpyrazole (480 mg, 4.99 mmol);

Yield: 853 mg, 65% (isolated yield); Brown solid; m.p.: 136.9-137.3 °C;

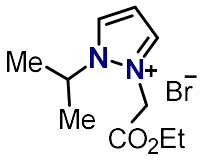
^{1}H NMR (400 MHz, DMSO-d6): δ 8.71 (dd, *J* = 2.9, 0.90 Hz, 1H, Ar*H*), 8.53 (dd, *J* = 2.9, 0.90 Hz, 1H, Ar*H*), 7.00 (t, *J* = 2.9 Hz, 1H, Ar*H*), 5.68 (s, 2H, NCH_2), 4.44 (q, *J* = 7.2 Hz, 2H, NCH_2), 4.22 (q, *J* = 7.1 Hz, 2H, CO_2CH_2), 1.43 (t, *J* = 7.2 Hz, 3H,

CH_2CH_2), 1.24 (t, J = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, DMSO-d6) δ 166.0 (CO_2), 139.2 (Ar), 137.6 (Ar), 107.9 (Ar), 62.4 (NCH_2), 50.1 (CO_2CH_2), 45.1 (NCH_2), 14.0 (CH_2CH_3), 13.9 (CH_2CH_3);
HRMS (FAB) m/z calcd for $C_9H_{15}BrN_2O_2$ $[M\text{-}Br]^+$ 183.1134, found 183.1140.



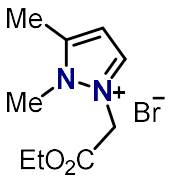
1l

Synthesized from 1-benzylpyrazole (2.37 g, 15.0 mmol);
Yield: 2.47 g, 51% (isolated yield); White solid; m.p.: 178.0-178.8 °C;
^{1}H NMR (400 MHz, DMSO-d6): δ 8.85 (d, J = 2.2 Hz, 1H, ArH), 8.63 (d, J = 2.1 Hz, ArH), 7.38-7.44 (m, 3H, ArH), 7.33-7.38 (m, 2H, ArH), 7.06 (t, J=, 3.0 Hz, 1H, ArH), 5.89 (s, 2H, NCH_2), 5.68 (s, 2H, NCH_2), 3.87 (q, J = 7.1 Hz, 2H, CO_2CH_2), 1.08 (t, J = 7.1 Hz, 3H, CH_2CH_3), ^{13}C NMR (100 MHz, DMSO-d6) δ 165.1 (CO_2), 140.3 (Ar), 139.3 (Ar), 132.0 (Ar), 129.0 (Ar), 129.0 (Ar), 128.2 (Ar), 108.1 (Ar), 62.1 (NCH_2), 52.5 (NCH_2), 50.2 (CO_2CH_3), 13.7 (CH_2CH_3);
HRMS (FAB) m/z calcd for $C_{14}H_{17}BrN_2O_2I$ $[M\text{-}Br]^+$ 245.1290, found 245.1295.



1m

Synthesized from 1-isopropylpyrazole (960 mg, 8.71 mmol);
Yield: 2.09 g, 86% (isolated yield); White solid; m.p.: 52.5-53.6 °C;
^{1}H NMR (400 MHz, DMSO-d6): δ 8.87 (d, J = 2.8 Hz, 1H, ArH), 8.51 (d, J = 2.8 Hz, 1H, ArH), 7.03 (t, J = 2.8 Hz, 1H, ArH), 5.60 (s, 2H, NCH_2), 4.90 (sep, J = 6.6 Hz, 1H, NCH), 1.49 (d, J = 6.6 Hz, 6H, $CH(CH_3)_2$); ^{13}C NMR (100 MHz, DMSO-d6) δ 166.0 (CO_2), 138.8 (Ar), 135.7 (Ar), 108.3 (Ar), 62.4 (NCH_2), 53.1 (NCH), 50.2 (CO_2CH_3), 22.2 ($CH(CH_3)_2$), 13.9 (CH_2CH_3);
HRMS (FAB) m/z calcd for $C_{10}H_{17}BrN_2O_2$ $[M\text{-}Br]^+$ 197.1290, found 197.1288.

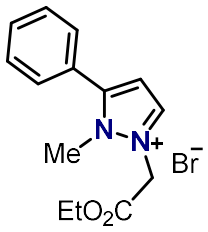


1n

Synthesized from 1,5-dimethylpyrazole (962 mg, 10.0 mmol);
Yield: 1.02 g, 39% (isolated yield); White solid; m.p.: 122.0-123.1°C;
^{1}H NMR (400 MHz, DMSO-d6) δ 8.43 (d, J = 2.9 Hz, 1H, ArH), 6.81 (d, J = 2.9 Hz, 1H, ArH), 5.68 (s, 2H, NCH_2), 4.21 (q, J = 7.1 Hz, 2H, CO_2CH_2), 3.92 (s, 3H, NCH_3), 2.50 (s, 3H, CCH_3), 1.23 (t, J = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, DMSO-d6) δ 166.1 (CO_2), 148.1 (Ar), 137.9 (Ar), 107.8 (Ar), 62.3 (NCH_2), 50.2 (CO_2CH_2), 33.7 (NCH_3), 13.9 (CH_2CH_3),

11.8 (C*C*H$_3$);

HRMS (FAB) m/z calcd for $C_9H_{15}BrN_2O_2$ [M-Br]$^+$ 183.1134, found 183.1125.



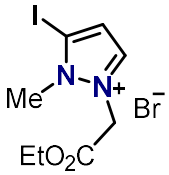
1o

Synthesized from 1-methyl-5-phenylpyrazole (157 mg, 0.99 mmol);

Yield: 65.0 mg, 20% (isolated yield); Colorless oil;

^{1}H NMR (400 MHz, DMSO-d6): δ 8.65 (d, *J* = 3.05 Hz, 1H, Ar*H*), 7.69 (m, 5H, Ar*H*), 7.21 (d, *J* = 3.1 Hz, 1H, Ar*H*), 5.78 (s, 2H, NC*H*$_2$), 4.26 (q, *J* = 7.1 Hz, 2H, CO$_2$C*H*$_2$), 4.02 (s, 3H, NC*H*$_3$), 1.27 (t, *J* = 7.1 Hz, 3H, CH$_2$C*H*$_3$);^{13}C NMR (100 MHz, DMSO-d6) δ 166.3 (*C*O$_2$), 149.3 (Ar), 138.7 (Ar), 131.4 (Ar), 129.49 (Ar), 129.45 (Ar), 125.9 (Ar), 108.1 (Ar), 62.5 (N*C*H$_2$), 50.8 (CO$_2$*C*H$_3$), 35.4 (N*C*H$_3$), 14.0 (CH$_2$*C*H$_3$);

HRMS (FAB) m/z calcd for $C_{14}H_{17}BrN_2O_2$ [M-Br]$^+$ 245.1290, found 245.1285.



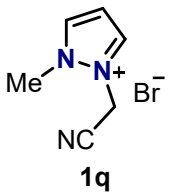
1p

Synthesized from 5-iodo-1-methylpyrazole (253mg, 1.22 mmol);

Yield: 226 mg, 50% (isolated yield); Brown solid; m.p.: 84.2-85.9;

^{1}H NMR (400 MHz, DMSO–d6): δ 8.47 (d, *J* = 3.1 Hz, 1H, Ar*H*), 7.28 (d, *J* = 3.1 Hz, 1H, Ar*H*), 5.73 (s, 2H, NC*H*$_2$), 4.22 (q, *J* = 7.1 Hz, 2H, CO$_2$C*H*$_2$), 4.07 (s, 3H, NC*H*$_3$), 1.24 (t, *J* = 7.1 Hz, 3H, CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, DMSO-d6) δ 165.8 (*C*O$_2$), 139.5 (Ar), 116.8 (Ar), 106.2 (Ar), 62.4 (N*C*H$_2$), 51.5 (CO$_2$*C*H$_3$), 37.7 (N*C*H$_3$), 13.9 (CH$_2$*C*H$_3$)

HRMS (FAB) m/z calcd for $C_8H_{12}BrN_2O_2I$ [M-Br]$^+$ 294.9943, found 294.9942.



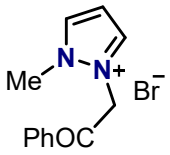
1q

Synthesized from 1-methylpyrazole (663 mg, 8.07 mmol);

Yield: 1.18 g, 72% (isolated yield); White solid; m.p.: 163.0-163.9 °C;

^{1}H NMR (400 MHz, DMSO-d6): δ 8.72 (d, *J* = 2.8 Hz, 1H, Ar*H*), 8.70 (d, *J* = 2.8 Hz, 1H, Ar*H*), 6.97 (t, *J* =2.8 Hz, 1H, Ar*H*), 6.12 (s, 2H, NC*H*$_2$), 4.24 (s, 3H, NC*H*$_3$); ^{13}C NMR (100 MHz, DMSO-d6) δ 140.1 (Ar), 138.7 (Ar), 113.3 (*C*N), 108.1 (Ar), 37.5 (N*C*H$_2$), 37.3 (N*C*H$_3$);

HRMS (FAB) m/z calcd for $C_6H_8BrN_3$ [M-Br]$^+$ 122.0718, found 122.0708.



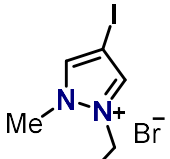
1r

Synthesized from 1-methylpyrazole (832 mg, 10.1 mmol);

Yield: 1.65 g, 58% (isolated yield); White solid; m.p.: 215.5-216.0 °C;

^{1}H NMR (400 MHz, DMSO-d6): δ 8.65 (d, *J* = 2.8 Hz, 1H, Ar*H*), 8.48 (dd, *J* = 2.8, 1.02 Hz, 1H, Ar*H*), 8.07-8.05 (m, 2H, Ar*H*), 7.79 (tt, *J* = 1.9, 0.35 Hz, 1H, Ar*H*), 7.68-7.64 (m, 2H, Ar*H*), 6.98 (t, *J* = 2.8 Hz, 1H, Ar*H*), 6.49 (s, 2H, NCH_2), 4.06 (s, 3H, NCH_3), ^{13}C NMR (100 MHz, DMSO-d6) δ 191.0 (*C*O), 138.9 (Ar), 138.8 (Ar), 134.8 (Ar), 133.3 (Ar), 129.0 (Ar), 128.4 (Ar), 107.5 (Ar), 56.0 (N*C*H$_2$), 36.7 (N*C*H$_3$);

HRMS (FAB) m/z calcd for $C_{12}H_{13}BrN_2O$ $[M\text{-}Br]^+$ 201.1028, found 201.1032.



1s

Synthesized from 4-iodo-1-methylpyrazole (434 mg, 2.09 mmol);

Yield: 640 mg, 75% (isolated yield); White solid; m.p.: 221.3-221.8 °C;

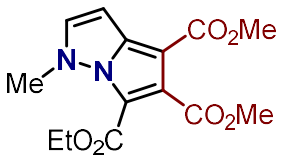
^{1}H NMR (400 MHz, DMSO-d6): δ 8.86 (s, 1H, Ar*H*), 8.62 (d, *J* = 1.1 Hz, 1H, Ar*H*), 8.42 (dd, *J* = 7.9, 1.3 Hz, 2H, Ar*H*), 7.80 (t, *J* = 7.9 Hz, 1H, Ar*H*), 7.66 (t, *J* = 7.9 Hz, 2H, Ar*H*), 6.45 (s, 2H, NCH_2), 4.04 (s, 3H, NCH_3); ^{13}C NMR (100 MHz, DMSO-d6) δ 190.7 (*C*O), 143.0 (Ar), 142.8 (Ar), 134.9 (Ar), 133.3 (Ar), 129.1 (Ar), 128.5 (Ar), 60.9 (Ar), 56.3 (N*C*H$_2$), 37.2 (N*C*H$_3$);

HRMS (FAB) m/z calcd for $C_{12}H_{12}BrIN_2O$ $[M\text{-}Br]^+$ 326.9994, found 326.9994.

General procedure for the synthesis of 1*H*-pyrrolo[1,2-*b*]pyrazole derivatives

To the solution of pyrazolium salt (0.20 mmol) in DMF (0.025 M, 8 mL) was added alkyne (2.0 equiv), KF (2.0 equiv) and MnO_2 (40 equiv). After stirred at room temperature for 24 h, the mixture was filtered through Celite®. The filtrate was evaporated in vacuo, which was analyzed by ^{1}H NMR spectroscopy for calculating NMR yield. Then, purification by silica gel chromatography (Hexane/EtOAc) was conducted to afford 1*H*-pyrrolo[1,2-*b*]pyrazole derivative.

Note: In all experiments, manganese(IV) oxide (powder, 85%; Wako 1st Grade) supplied by FUJIFILM Wako Pure Chemical Corporation was used. The reagent was dried under vacuum at 40 °C for more than 10 h prior to use.



3a

Synthesized from **1a** (49.9 mg, 0.20 mmol);

Yield: 31.9 mg, 53% (isolated yield); Yellow solid; m.p.: 123.5-124.4 °C;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23 (d, *J* = 3.5 Hz, 1H, Ar*H*), 6.48 (d, *J* = 3.5 Hz, 1H, Ar*H*), 4.27 (q, *J* = 7.1 Hz, 2H, CO_2CH_2), 4.08 (s, 3H, CO_2CH_3), 3.96 (s, 3H, CO_2CH_3), 3.83 (s, 3H, NCH_3), 1.34 (t, *J* = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8 (CO_2), 163.2 (CO_2), 158.7 (CO_2), 140.6 (Ar), 136.9 (Ar), 129.2 (Ar), 110.3 (Ar), 96.4 (Ar), 95.4 (Ar), 60.6 (CO_2CH_2), 52.5 (CO_2CH_3), 51.2 (CO_2CH_3), 39.9 (NCH_3), 13.9 (CH_2CH_3);

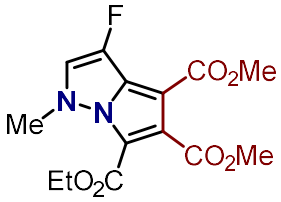
IR (KBr) *v* 3164, 2982, 1700, 1692, 1453, 1239, 1190, 1117, 1033, 668;

HRMS (FAB) m/z calcd for $C_{14}H_{16}N_2O_6$ $[M]^+$ 308.1008, found 308.1010.

Scale-up procedure for the synthesis of 3a

To the solution of pyrazolium salt **1a** (259 mg, 1.0 mmol) in DMF (40 mL) was added DMAD (245 μL, 2.0 mmol), KF (116 mg, 2.0 mmol) and MnO_2 (348 mg, 40 mmol). After stirred at room temperature for 24 h, the mixture was diluted with ether. The resulting solution was washed with water, dried over Na_2SO_4, and filtered. The filtrate was evaporated in vacuo and the residue was purified by silica gel chromatography (Hexane/EtOAc) was conducted to afford 1*H*-pyrrolo[1,2-*b*]pyrazole derivative **3a** (142 mg, 44%).

Note: This liquid–liquid separation procedure gave 53% NMR yield when **1a** (49.9 mg, 0.20 mmol) was used.



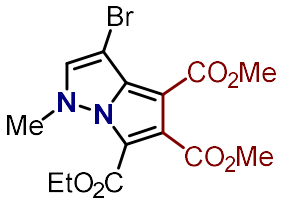
3b

Synthesized from **1b** (54.6 mg, 0.20 mmol);

Yield: 225 mg, 34% (isolated yield); Yellow solid; m.p.: 80.1-80.7 °C;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.11 (d, *J* = 2.9 Hz, 1H, Ar*H*), 4.29 (q, *J* = 7.1 Hz, 2H, CO_2CH_2), 3.96 (s, 3H, CO_2CH_3), 3.85 (s, 3H, NCH_3), 3.84 (s, 3H, CO_2CH_3), 1.34 (t, *J* = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5 (CO_2), 162.7 (CO_2), 158.6 (CO_2), 139.5 (d, *J* = 248.7 Hz, Ar), 130.3 (d, *J* = 26.4 Hz, Ar), 129.5 (Ar), 122.7 (d, *J* = 23.5 Hz, Ar), 112.3 (Ar), 96.9 (d, *J* = 3.12 Hz, Ar), 61.2 (CO_2CH_2), 52.9 (CO_2CH_3), 51.7 (CO_2CH_3), 40.9 (NCH_3), 14.2 (CH_2CH_3); ^{19}F NMR (376 MHz, $CDCl_3$, C_6F_6) δ -173.53 (d, *J* = 2.72, 1F, C*F*);

HRMS (FAB) m/z calcd for $C_{14}H_{15}FN_2O_6$ $[M]^+$ 326.0914, found 326.0905.



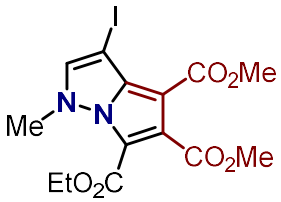
3c

Synthesized from **1c** (68.0 mg, 0.21 mmol);

Yield: 46.2 mg, 58% (isolated yield); Brown solid; m.p.: 97.2-98.0 °C;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (s, 1H, Ar*H*), 4.27 (q, *J* = 7.1 Hz, 2H, CO_2CH_2), 3.99 (s, 3H, CO_2CH_3), 3.94 (s, 3H, CO_2CH_3), 3.82 (s, 3H, NCH_3), 1.32 (t, *J* = 7.1 Hz, 3H, CH_2CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7 (CO_2), 162.8 (CO_2), 158.5 (CO_2), 137.8 (Ar), 137.2 (Ar), 130.3 (Ar), 110.6 (Ar), 96.9 (Ar), 84.5 (Ar), 61.1 (CO_2CH_2), 52.8 (CO_2CH_3), 51.2 (CO_2CH_3), 40.6 (NCH_3), 14.1 (CH_2CH_3);

HRMS (FAB) m/z calcd for $C_{14}H_{15}BrN_2O_6$ $[M]^+$ 386.0113, found 386.0120.



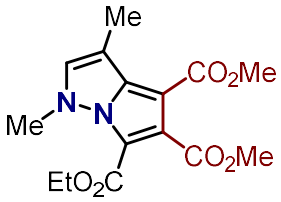
3d

Synthesized from **1d** (76.1 mg, 0.20 mmol);

Yield: 58.9 mg, 67% (isolated yield); Brown solid; m.p.: 102.0-102.8 °C;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 (s, 1H, Ar*H*), 4.25 (q, *J* = 7.1 Hz, 2H, CO_2CH_2), 4.01 (s, 3H, CO_2CH_3), 3.92 (s, 3H, CO_2CH_3), 3.82 (s, 3H, NCH_3), 1.31 (t, *J* = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9 (CO_2), 163.0 (CO_2), 158.4 (CO_2), 143.0 (Ar), 139.1 (Ar), 130.4 (Ar), 110.3 (Ar), 96.9 (Ar), 61.1 (CO_2CH_2), 52.8 (CO_2CH_3), 50.9 (CO_2CH_3), 45.6 (Ar), 40.5 (NCH_3), 14.1 (CH_2CH_3);

HRMS (FAB) m/z calcd for $C_{14}H_{15}IN_2O_6$ $[M]^+$ 433.9975, found 433.9983.



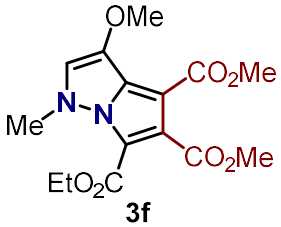
3e

Synthesized from **1e** (51.4 mg, 0.20 mmol);

Yield: 32.9 mg, 52% (isolated yield); Brown solid; m.p.: 73.8-74.6 °C;

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.97 (d, *J* = 1.0 Hz, 1H, Ar*H*), 4.26 (q, *J* = 7.1 Hz, 2H, CO_2CH_2), 3.94 (s, 3H, CO_2CH_3), 3.86 (s, 3H, CO_2CH_3), 3.80 (s, 3H, NCH_3), 2.32 (d, *J* = 1.0 Hz, 3H, $ArCH_3$), 1.32 (t, *J* = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4 (CO_2), 163.4 (CO_2), 158.8 (CO_2), 140.5 (Ar), 136.8 (Ar), 129.7 (Ar), 110.4 (Ar), 108.5 (Ar), 96.9 (Ar), 60.8 (CO_2CH_2), 52.7 (CO_2CH_3), 51.3 (CO_2CH_3), 40.0 (NCH_3), 14.2 (CH_2CH_3), 10.6 ($ArCH_3$);

HRMS (FAB) m/z calcd for $C_{15}H_{18}N_2O_6$ $[M]^+$ 322.1165, found 322.1171.



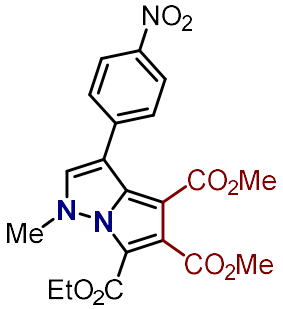
3f

Synthesized from **1f** (54.1 mg, 0.19 mmol);

Yield: 11.0 mg, 17% (isolated yield); Red oil;

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.70 (s, 1H, Ar*H*), 4.28 (q, *J* = 7.1 Hz, 2H, CO_2CH_2), 3.94 (s, 3H, CO_2CH_3), 3.86 (s, 3H, OCH_3), 3.82 (s, 3H, CO_2CH_3), 3.68 (s, 3H, NCH_3), 1.33 (t, *J* = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0 (CO_2), 163.0 (CO_2), 158.7 (CO_2), 138.1 (Ar), 133.1 (Ar), 129.0 (Ar), 120.6 (Ar), 111.9 (Ar), 98.0 (Ar), 61.0 (CO_2CH_2), 59.3 (OCH_3), 52.8 (CO_2CH_3), 51.7 (CO_2CH_3), 41.2 (NCH_3), 14.2 (CH_2CH_3);

HRMS (FAB) m/z calcd for $C_{15}H_{18}N_2O_7$ $[M]^+$ 338.1114, found 338.1104.



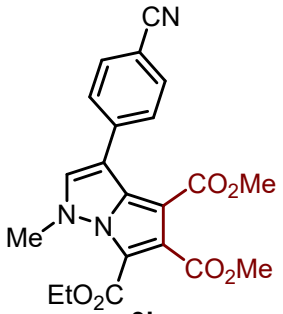
3g

Synthesized from **1g** (72.8 mg, 0.20 mmol);

Yield: 53.2 mg, 63% (isolated yield); Yellow solid; m.p. 178.3-179.0 °C;

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (d, 2H, *J* = 8.8 Hz, Ar*H*), 7.51 (d, 2H, *J* = 8.8 Hz, Ar*H*), 7.36 (s, 1H, Ar*H*), 4.30 (q, *J* = 7.1 Hz, 2H, CO_2CH_2), 4.15 (s, 3H, CO_2CH_3), 3.95 (s, 3H, CO_2CH_3), 3.53 (s, 3H, NCH_3), 1.35 (t, *J* = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0 (CO_2), 162.7 (CO_2), 158.7 (CO_2), 147.0 (Ar), 138.1 (Ar), 136.6 (Ar), 136.1 (Ar), 130.5 (Ar), 130.2 (Ar), 122.9 (Ar), 111.5 (Ar), 110.3 (Ar), 96.8 (Ar), 61.2 (CO_2CH_2), 52.9 (CO_2CH_3), 51.0 (CO_2CH_3), 40.7 (NCH_3), 14.2 (CH_2CH_3);

HRMS (FAB) m/z calcd for $C_{20}H_{19}N_3O_8$ $[M]^+$ 429.1172, found .429.1168.



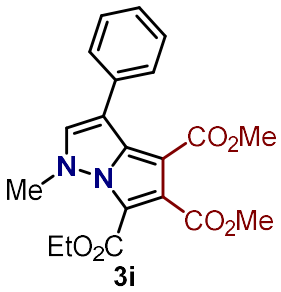
3h

Synthesized from **1h** (70.7 mg, 0.20 mmol);

Yield: 66.8 mg, 81% (isolated yield); White solid; m.p.:218.0-218.5 °C;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65–7.69 (m, 2H, Ar*H*), 7.45–7.49 (m, 2H, Ar*H*), 7.30 (s, 1H, Ar*H*), 4.31 (q, *J* = 7.14 Hz, 2H, CO_2CH_2), 4.14 (s, 3H, CO_2CH_3), 3.96 (s, 3H, CO_2CH_3), 3.52 (s, 3H, NCH_3), 1.35 (t, *J* = 7.14 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.98 (CO_2), 162.76 (CO_2), 158.77 (CO_2), 136.75 (Ar), 136.18 (Ar), 135.96 (Ar), 131.43 (Ar), 130.60 (Ar), 130.26 (Ar), 119.00 (Ar), 112.10 (*C*N), 111.13 (Ar), 110.38 (Ar), 96.92 (Ar), 61.20 (CO_2CH_2), 52.85 (CO_2CH_3), 50.98 (CO_2CH_3), 40.67 (NCH_3), 14.21 (CH_2CH_3);

HRMS (FAB) m/z calcd for $C_{21}H_{19}N_3O_6$ $[M]^+$ 409.1274, found 409.1267.



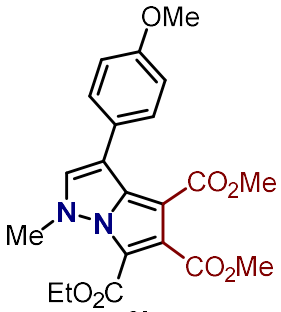
3i

Synthesized from **1i** (69.3 mg, 0.21 mmol);

Yield: 58.8 mg, 72% (isolated yield); White solid; m.p.:133.8-134.2 °C;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33-7.38 (m, 5H, Ar*H*), 7.22 (s, 1H, Ar*H*), 4.30 (q, *J* = 7.1 Hz, 2H, CO_2CH_2), 4.07 (s, 3H, CO_2CH_3), 3.96 (s, 3H, CO_2CH_3), 3.41 (s, 3H, NCH_3), 1.35 (t, *J* = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2 (CO_2), 163.1 (CO_2), 158.9 (CO_2), 137.6 (Ar), 136.1 (Ar), 131.3 (Ar), 130.6 (Ar), 129.7 (Ar), 127.6 (Ar), 127.6 (Ar), 114.2 (Ar), 110.2 (Ar), 97.0 (Ar), 61.0 (CO_2CH_2), 52.8 (CO_2CH_3), 50.6 (CO_2CH_3), 40.4 (NCH_3), 14.2 (CH_2CH_3);

HRMS (FAB) m/z calcd for $C_{20}H_{20}N_2O_6$ $[M]^+$ 384.1321, found 384.1322.



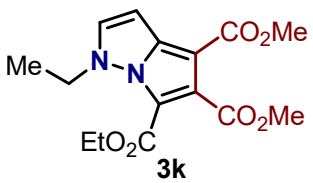
3j

Synthesized from **1j** (55.8 mg, 0.16 mmol);

Yield: 50.7 mg, 78% (isolated yield); Brown solid; m.p.: 139.5-149.5 °C;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24-7.28 (m, 2H, Ar*H*), 7.17 (s, 1H, Ar*H*), 6.88-6.92 (m, 2H, Ar*H*), 4.29 (q, *J* = 7.1 Hz, 2H, CO_2CH_2), 4.03 (s, 3H, OCH_3), 3.95 (s, 3H, CO_2CH_3), 3.82 (s, 3H, CO_2CH_3), 3.46 (s, 3H, NCH_3), 1.34 (t, *J* = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3 (CO_2), 163.1 (CO_2), 159.2 (CO_2), 158.8 (Ar), 137.7 (Ar), 136.0 (Ar), 130.9 (Ar), 130.5 (Ar), 123.6 (Ar), 113.8 (Ar), 113.0 (Ar), 110.1 (Ar), 97.0 (Ar), 60.9 (CO_2CH_2), 55.4 (OCH_3), 52.7 (CO_2CH_3), 50.8 (CO_2CH_3), 40.3 (NCH_3), 14.2 (CH_2CH_3);

HRMS (FAB) m/z calcd for $C_{21}H_{22}N_2O_7$ $[M]^+$ 414.1427, found 414.1415.



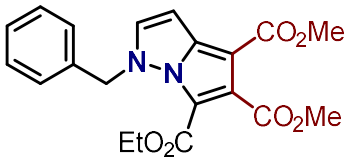
3k

Synthesized from **1k** (53.8 mg, 0.20 mmol);

Yield: 43.4 mg, 66% (isolated yield); Yellow solid; m.p.: 117.2-118.8 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ7.28 (d, *J* = 3.5 Hz, 1H, Ar*H*), 6.50 (d, *J* = 3.5 Hz, 1H, Ar*H*), 4.69 (q, *J* = 7.1 Hz, 2H, NCH_2), 4.28 (q, *J* = 7.1 Hz, 2H, CO_2CH_2), 3.96 (s, 3H, CO_2CH_3), 3.83 (s, 3H, CO_2CH_3), 1.33 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.16 (t, *J* = 7.1 Hz, 3H, NCH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2 (CO_2), 163.5 (CO_2), 159.0 (CO_2), 141.5 (Ar), 136.1 (Ar), 129.7 (Ar), 111.2 (Ar), 97.6 (Ar), 96.0 (Ar), 60.9 (CO_2CH_2), 52.8 (CO_2CH_3), 51.5 (CO_2CH_3), 47.9 (NCH_2), 14.3 (CH_2CH_3), 13.3 (CH_2CH_3);

HRMS (FAB) m/z calcd for $C_{15}H_{18}N_2O_6$ $[M]^+$ 322.1165, found 322.1163.



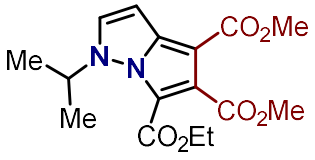
3l

Synthesized from **1l** (66.6 mg, 0.21mmol);

Yield: 32.3 mg, 41% (isolated yield); Yellow solid; m.p.: 89.0-89.9 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, *J* = 3.5 Hz, 1H, Ar*H*), 7.24-7.28 (m, 3H, Ar*H*), 7.03-7.07 (m, 2H, Ar*H*), 6.52 (d, *J* = 3.5 Hz, 1H, Ar*H*), 5.78 (s, 2H, NCH_2), 4.27 (q, *J* = 7.1 Hz, 2H, CO_2CH_2), 3.93 (s, 3H, CO_2C_3), 3.81 (s, 3H, CO_2CH_3), 1.31 (t, *J* = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1 (CO_2), 163.4 (CO_2), 159.0 (CO_2), 141.4 (Ar), 137.1 (Ar), 134.0 (Ar), 129.4 (Ar), 129.0 (Ar), 128.6 (Ar), 128.0 (Ar), 111.5 (Ar), 97.9 (Ar), 96.0 (Ar), 61.0 (CO_2CH_2), 55.6 (NCH_2), 52.8 (CO_2CH_3), 51.5 (CO_2CH_3), 14.2 (CH_2CH_3);

HRMS (FAB) m/z calcd for $C_{20}H_{20}N_2O_6$ $[M]^+$ 384.1321, found 384.1313.



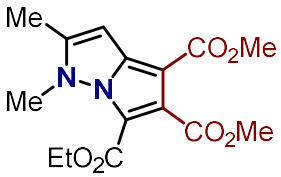
3m

Synthesized from **1m** (55.4 mg, 0.20 mmol);

Yield: 104 mg, 16% (isolated yield); Yellow oil;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (d, *J* = 3.6 Hz, 1H, Ar*H*), 6.55 (d, *J* = 3.6 Hz, 1H, Ar*H*), 5.86 (sep, *J* = 6.6 Hz, 1H, NC*H*), 4.27 (q, *J* = 7.0 Hz, 2H, CO_2CH_2), 3.96 (s, 3H, CO_2CH_3), 3.83 (s, 3H, CO_2CH_3), 1.34 (t, *J* = 7.0 Hz, 3H, CH_2CH_3), 1.31 (d, *J* = 6.6 Hz, 6H, $CH(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3 (CO_2), 163.5 (CO_2), 159.0 (CO_2), 141.4 (Ar), 132.4 (Ar), 130.0 (Ar), 111.3 (Ar), 98.4 (Ar), 95.9 (Ar), 61.0 (CO_2CH_2), 53.9 (NCH), 52.8 (CO_2CH_3), 51.5 (CO_2CH_3), 20.8 ($CH(CH_3)_2$), 14.2 (CH_2CH_3);

HRMS (FAB) m/z calcd for $C_{16}H_{20}N_2O_6$ $[M]^+$ 336.1321, found 336.1313.



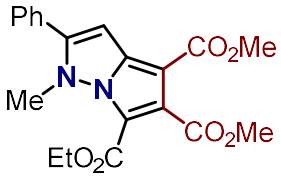
3n

Synthesized from **1n** (52.8 mg, 0.20 mmol);

Yield: 149 mg, 23% (isolated yield); Yellow solid; m.p.: 127.0-127.9 °C;

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.28 (d, *J* = 0.82 Hz, 1H, Ar*H*), 4.27 (q, *J* = 7.1 Hz, 2H, CO_2CH_2), 3.95 (s, 3H, CO_2CH_3), 3.93 (s, 3H, NCH_3), 3.81 (s, 3H, CO_2CH_3), 2.36 (d, *J* = 0.82 Hz, 3H, $ArCH_3$), 1.33 (t, *J* = 7.13 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3 (CO_2), 163.6 (CO_2), 159.0 (CO_2), 146.7 (Ar), 140.1 (Ar), 129.1 (Ar), 110.8 (Ar), 96.5 (Ar), 95.3 (Ar), 60.8 (CO_2CH_2), 52.8 (CO_2CH_3), 51.4 (CO_2CH_3), 37.1 (NCH_3), 14.2 (CH_2CH_3), 13.1 ($ArCH_3$);

HRMS (FAB) m/z calcd for $C_{15}H_{18}N_2O_6$ $[M]^+$ 322.1165, found .322.1161.



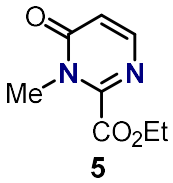
3o

Synthesized from **1o** (69.5 mg, 0.21 mmol);

Yield: 11.7 mg, 14% (isolated yield); Yellow oil;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47-7.58 (m, 5H, Ar*H*), 6.68 (s, 1H, Ar*H*), 4.31 (q, *J* = 7.1 Hz, 2H, CO_2CH_2), 3.97 (s, 3H, CO_2CH_3), 3.85 (s, 3H, NCH_3), 3.77 (s, 3H, CO_2CH_3), 1.36 (t, *J* = 7.13 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1 (CO_2), 163.4 (CO_2), 158.8 (CO_2), 154.0 (Ar), 140.1 (Ar), 130.0 (Ar), 129.3 (Ar), 128.8 (Ar), 128.7 (Ar), 111.4 (Ar), 97.8 (Ar), 96.7 (Ar), 61.0 (CO_2CH_2), 52.8 (CO_2CH_3), 51.5 (CO_2CH_3), 40.8 (NCH_3), 14.2 (CH_2CH_3).

HRMS (FAB) m/z calcd for $C_{20}H_{20}N_2O_6$ $[M]^+$ 384.1321, found384.1332.



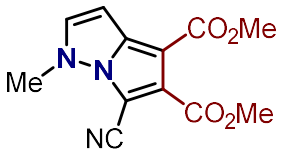
5

Synthesized from **1p** (78.7 mg, 0.21 mmol);

Yield: 16.0 mg, 42% (isolated yield); Red oil;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, *J* = 6.6 Hz, 1H, NC*H*), 6.52 (d, *J* = 6.6 Hz, 1H, COC*H*), 4.47 (q, *J* = 7.2 Hz, 2H, CO_2CH_2), 3.57 (s, 3H, NCH_3), 1.43 (t, *J* = 7.2 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0 (*C*O), 160.8 (*C*O), 151.9 (N*C*H or *C*=N). 151.61 (N*C*H or *C*=N), 116.9 (CO*C*H), 63.6 (CO_2CH_2), 32.3 (NCH_3), 14.1 (CH_2CH_3);

HRMS (FAB) m/z calcd for $C_8H_{10}N_2O_3$ $[M+H]^+$ 183.0770, found 183.0780.



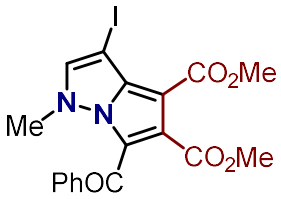
3q

Synthesized from **1q** (40.8 mg, 0.20 mmol);

Yield: 24.7 mg, 47% (isolated yield); Brown solid; m.p.: 158.9-159.9 °C;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29 (d, *J* = 3.5 Hz, 1H, Ar*H*), 6.45 (d, *J* = 3.5 Hz, 1H, Ar*H*), 4.08 (s, 3H, NC*H*$_3$), 3.95 (s, 3H, CO_2CH_3), 3.84 (s, 3H, CO_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.62 (*C*O_2), 162.59 (*C*O_2), 140.1 (Ar), 135.1 (Ar), 128.8 (Ar), 112.4 (Ar), 97.5 (Ar), 96.6 (Ar), 91.3 (*C*N), 52.8 (CO_2CH_3), 51.6 (CO_2CH_3), 37.0 (N*C*H$_3$);

HRMS (FAB) m/z calcd for $C_{12}H_{11}N_3O_4$ $[M]^+$ 261.0750, found 261.0751.



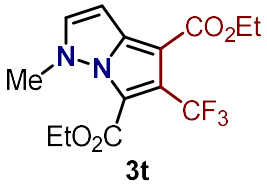
3s

Synthesized from **1s** (82.9 mg, 0.20 mmol);

Yield: 23.8 mg, 25% (isolated yield); Brown solid; m.p.: 96.5-97.1 °C;

^{1}H NMR (400 MHz, $CDCl_3$): δ7.79 (d, *J* = 8.4 Hz, 1H, Ar*H*), 7.78 (s, 1H, Ar*H*), 7.56 (tt, *J* = 7.5, 1.6 Hz, 1H, Ar*H*), 7.48-7.43 (m, 3H, Ar*H*), 3.92 (s, 3H, CO_2CH_3), 3.83 (s, 3H, CO_2CH_3), 3.26 (s, 3H, NC*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.7 (*C*O), 165.0 (*C*O_2), 163.1 (*C*O_2), 141.5 (Ar), 138.9 (Ar), 138.7 (Ar), 132.6 (Ar), 131.1 (Ar), 129.3 (Ar), 128.3 (Ar), 118.5 (Ar), 97.8 (Ar), 52.3 (CO_2CH_3), 51.0 (CO_2CH_3), 45.0 (Ar), 40.0 (N*C*H$_3$);

HRMS (FAB) m/z calcd for $C_{14}H_{16}N_2O_6$ $[M]^+$ 466.0026, found 466.0037.



3t

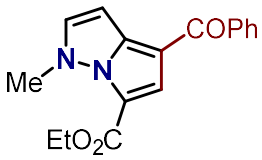
Synthesized from **1a** (50.6 mg, 0.20 mmol);

Yield: 16.6 mg, 25% (isolated yield); Brown solid; m.p. 64.1-64.7°C;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20 (d, *J* = 3.5 Hz, 1H, Ar*H*), 6.47 (d, *J* = 3.5 Hz, 1H, Ar*H*), 4.38 (q, *J* = 7.2 Hz, 2H, CO_2CH_2), 4.32 (q, *J* = 7.1 Hz, 2H, CO_2CH_2), 3.82 (s, 3H, NC*H*$_3$), 1.39 (t, *J* = 7.2 Hz, 3H, CH_2CH_3), 1.36 (t, *J* = 7.1 Hz, 3H, CH_2CH_3);

^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8 (*C*O_2), 160.3 (*C*O_2), 140.6 (Ar), 136.8 (Ar), 122.2 (q, *J* = 270.5 Hz, *C*F_3), 119.8 (q, *J* = 38.1 Hz, Ar), 112.7 (q, *J* = 4.1 Hz, Ar), 97.1 (Ar), 96.5 (Ar), 62.1 (CO_2CH_2), 60.3 (CO_2CH_2), 39.3 (N*C*H$_3$), 14.5 (CH_2CH_3), 14.0 (CH_2CH_3); ^{19}F NMR (376 MHz, $CDCl_3$, C_6F_6) δ -54.78 (s, 3F, C*F*$_3$);

HRMS (FAB) m/z calcd for $C_{14}H_{15}F_3N_2O_4$ $[M]^+$ 332.0984, found 332.0990.



3v

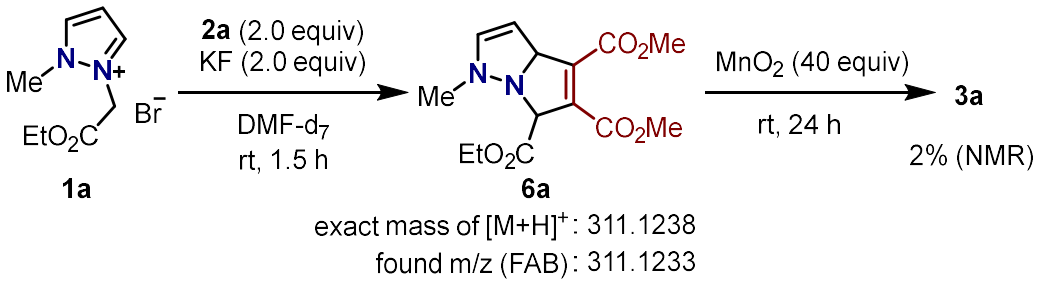
Synthesized from **1a** (50.0 mg, 0.20 mmol);

Yield: 10.2 mg, 17% (isolated yield); Brown solid; m.p.: 67.8-68.2 °C;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (s, 1H, Ar*H*), 7.82 (d, *J* = 8.2 Hz, 1H, Ar*H*), 7.54-7.46 (m, 4H, Ar*H*), 7.29 (d, *J* = 3.3 Hz, 1H, Ar*H*), 6.66 (d, *J* = 3.3 Hz, 1H, Ar*H*), 4.29 (q, *J* = 7.1 Hz, 2H, CO_2CH_2), 4.19 (s, 3H, NCH_3), 1.35 (t, *J* = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.0 (*C*O), 160.1 (CO_2), 143.3 (Ar), 140.3 (Ar), 136.5 (Ar), 131.1 (Ar), 128.8 (Ar), 128.4 (Ar), 125.3 (Ar), 113.5 (Ar), 106.8 (Ar), 97.4 (Ar), 60.4 (CO_2CH_2), 40.0 (NCH_3), 14.6 (CH_2CH_3);

HRMS (FAB) m/z calcd for $C_{17}H_{17}N_2O_3$ $[M+H]^+$ 297.1239, found 297.1241.

Conformation of a reaction intermediate

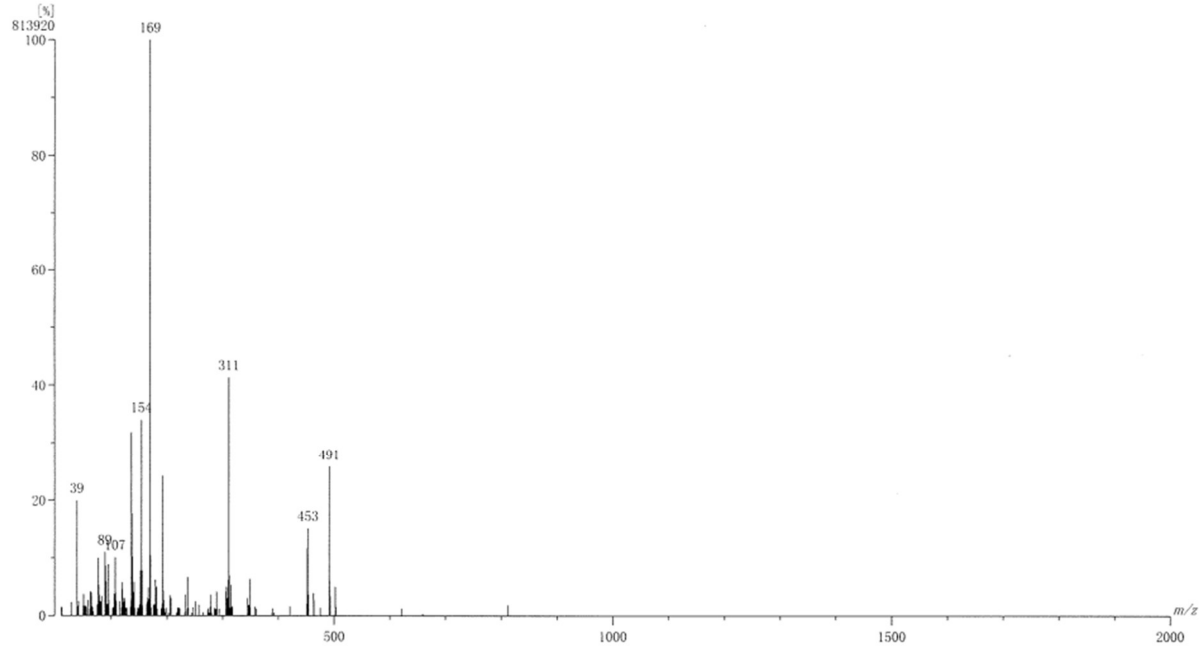


exact mass of $[M+H]^+$: 311.1238

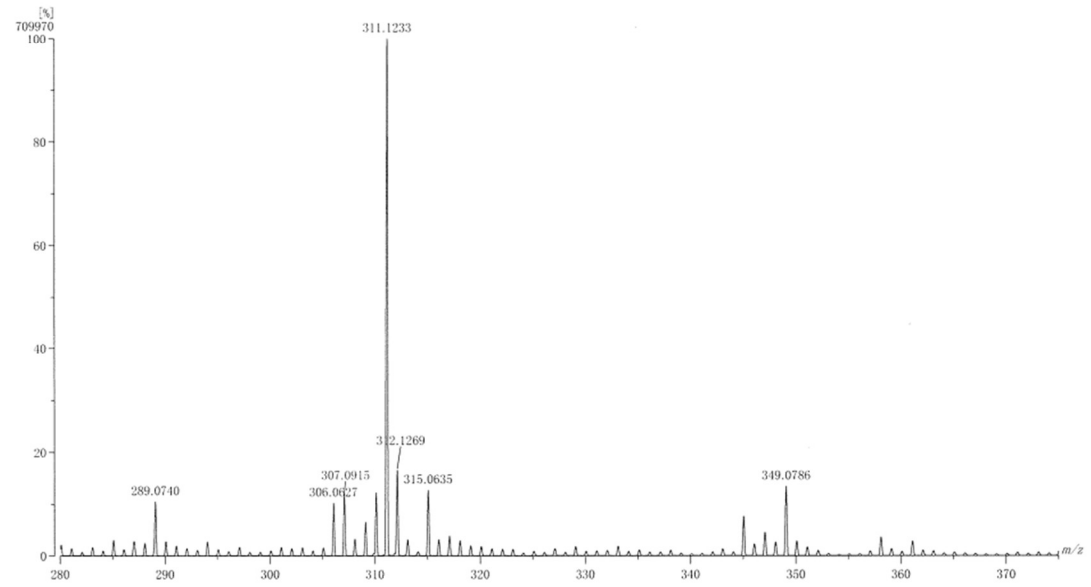
found m/z (FAB): 311.1233

To the solution of **1a** (6.4 mg, 0.026 mmol) in DMF-d7 (0.025M, 1 mL) were added dimethyl acetylenedicarboxylate (2.0 equiv) and KF (2.0 equiv). After stirred at room temperature for 1.5 h, the reaction mixture was analyzed by FAB-HMRS. Then, to the reaction mixture was added MnO_2 (40 equiv). The mixture was stirred at room temperature for 24 h. The resulting mixture was filtered by Celite®, and the filtrate was evaporated in vacuo. The residue was analyzed by ^{1}H NMR spectroscopy to determine the NMR yield using triphenylmethane (3.8 mg, 0.015 mmol).

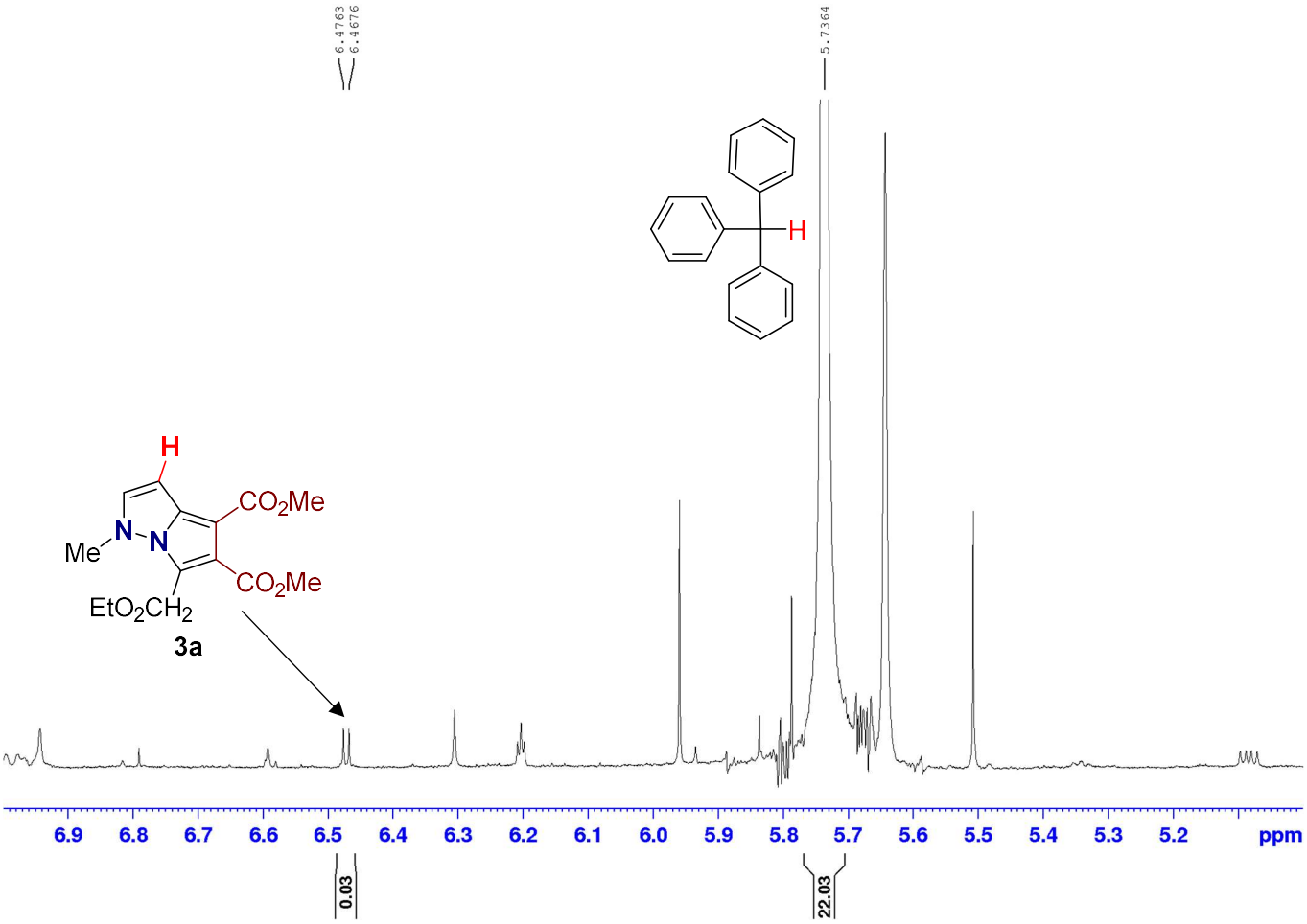
[Mass Spectrum]
Data : 251121-007 Date : 21-Nov-2025 15:13
Instrument : MStation
Sample : Rxn 678(310)/(matrix m-NBA)
Note : R1000, 8kV [JEOL JMS-700(MStation)]
Inlet : Direct Ion Mode : FAB+
Spectrum Type : Normal Ion [MF-Linear]
RT : 0.61 min Scan# : (6,7) Temp : 3276.7 deg.C
BP : m/z 169 Int. : 77.62 (813920)
Output m/z range : 10 to 2000 Cut Level : 0.00 %

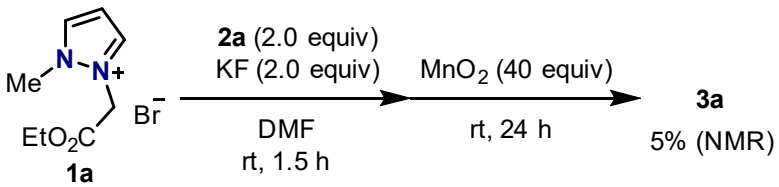


[Mass Spectrum]
Data : 251121-008 Date : 21-Nov-2025 15:16
Instrument : MStation
Sample : Rxn 678(M+ 310.1165)/(matrix m-NBA)
Note : R1000, ESTD(PEG200 + PEG400) [JEOL JMS-700(MStation)]
Inlet : Direct Ion Mode : FAB+
Spectrum Type : Normal Ion [EF-Linear]
RT : 1.85 min Scan# : (13,14) Temp : 3276.7 deg.C
BP : m/z 311.1233 Int. : 67.71 (709970)
Output m/z range : 280 to 375 Cut Level : 0.00 %



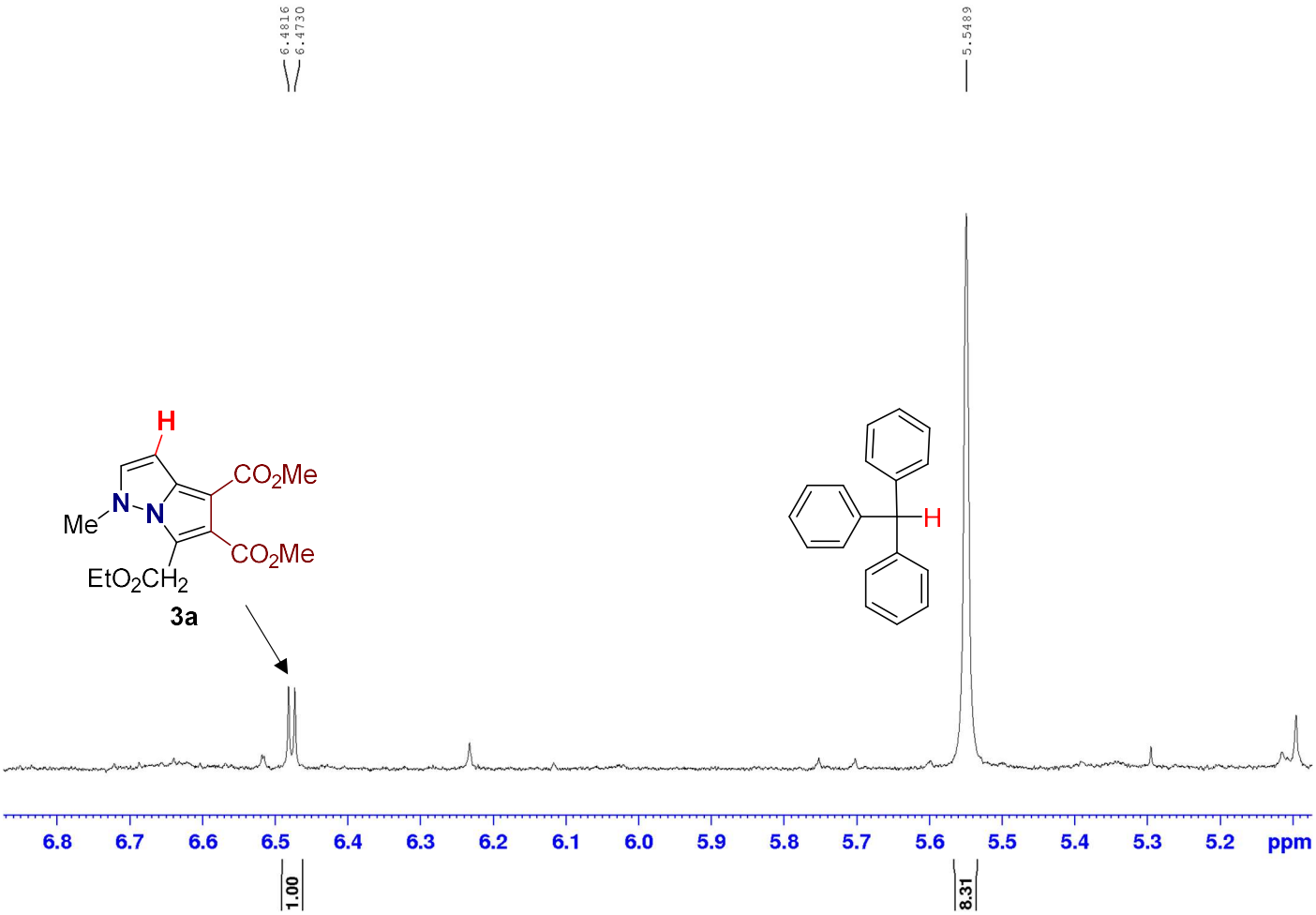
^{1}H NMR (400 MHz, DMF-d7)





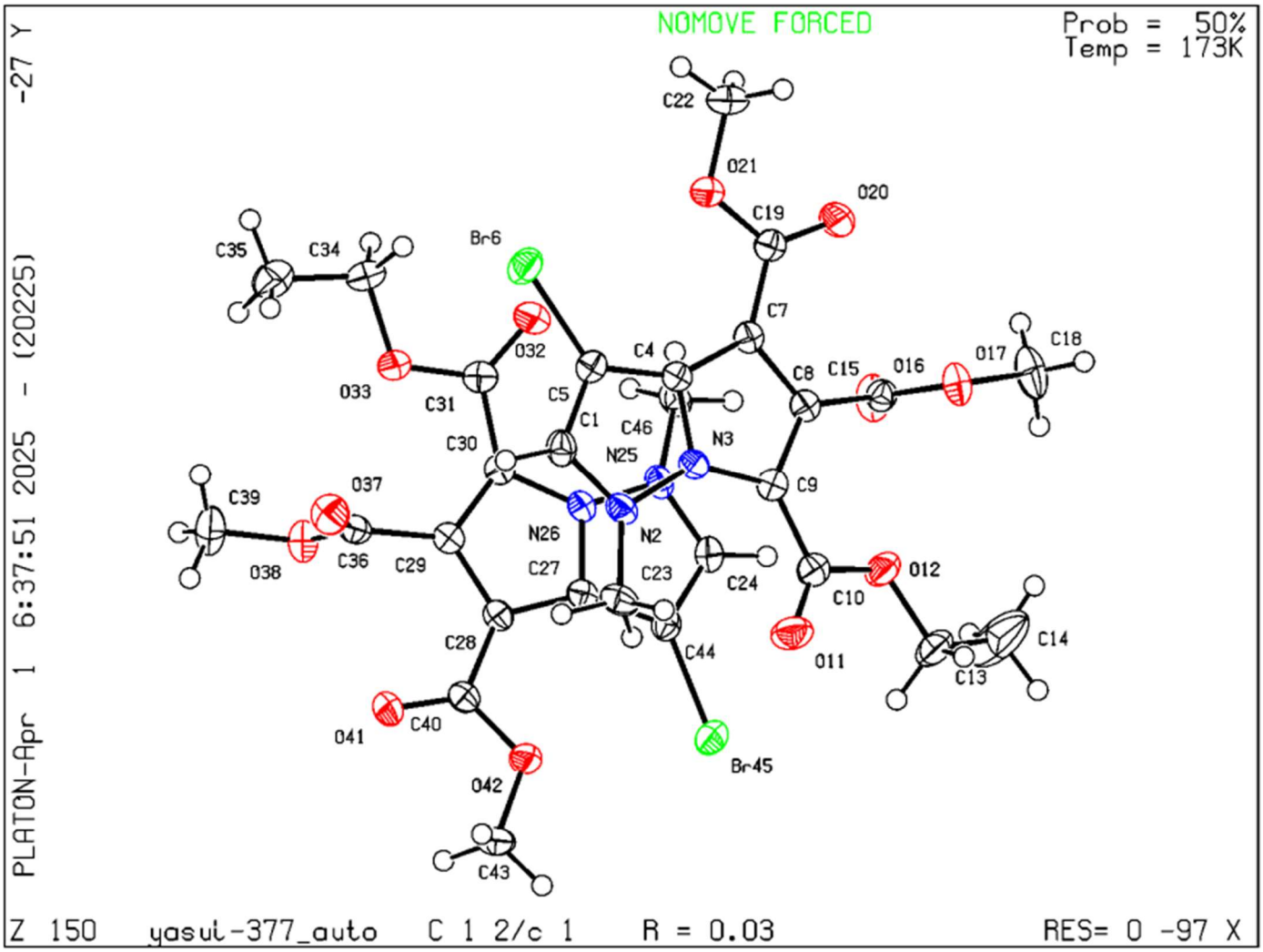
To the solution of **1a** (7.7 mg, 0.031 mmol) in DMF (0.025 M, 1 mL) were added dimethyl acetylenedicarboxylate (2.0 equiv) and KF (2.0 equiv). After the mixture was stirred at room temperature for 1.5 h, MnO_2 (40 equiv) was added to the reaction mixture. After stirred at room temperature for 24 h, the resulting mixture was filtered by Celite® and the filtrate was evaporated. The residue was analyzed by ^{1}H NMR spectroscopy to determine the NMR yield using triphenylmethane (2.9 mg, 0.012 mmol).

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



X-ray crystallographic data

X-ray structure of compound **3c**



ORTEP of **3c** with ellipsoid shown at the 50% contour percent probability level (CCDC 2443840).

Single crystals of **3c** ($C_{14}H_{15}BrN_2O_6$) were prepared by vapor diffusion from hexane/dichloromethane. A suitable crystal was selected and measured on a XtaLAB AFC10 (RCD3): quarter-chi single diffractometer. The crystal was kept at 173 K during data collection. Using Olex2 [1], the structure was solved with the ShelXT [2] structure solution program using Intrinsic Phasing and refined with the ShelXL [3] refinement package using Least Squares minimization.

[1] Dolomanov, O.V., Bourhis, L.J., Gildea, R.J, Howard, J.A.K. & Puschmann, H. (**2009**), *J. Appl. Cryst.* 42, 339-341.

[2] Sheldrick, G.M. (**2015**). *Acta Cryst.* A71, 3-8.

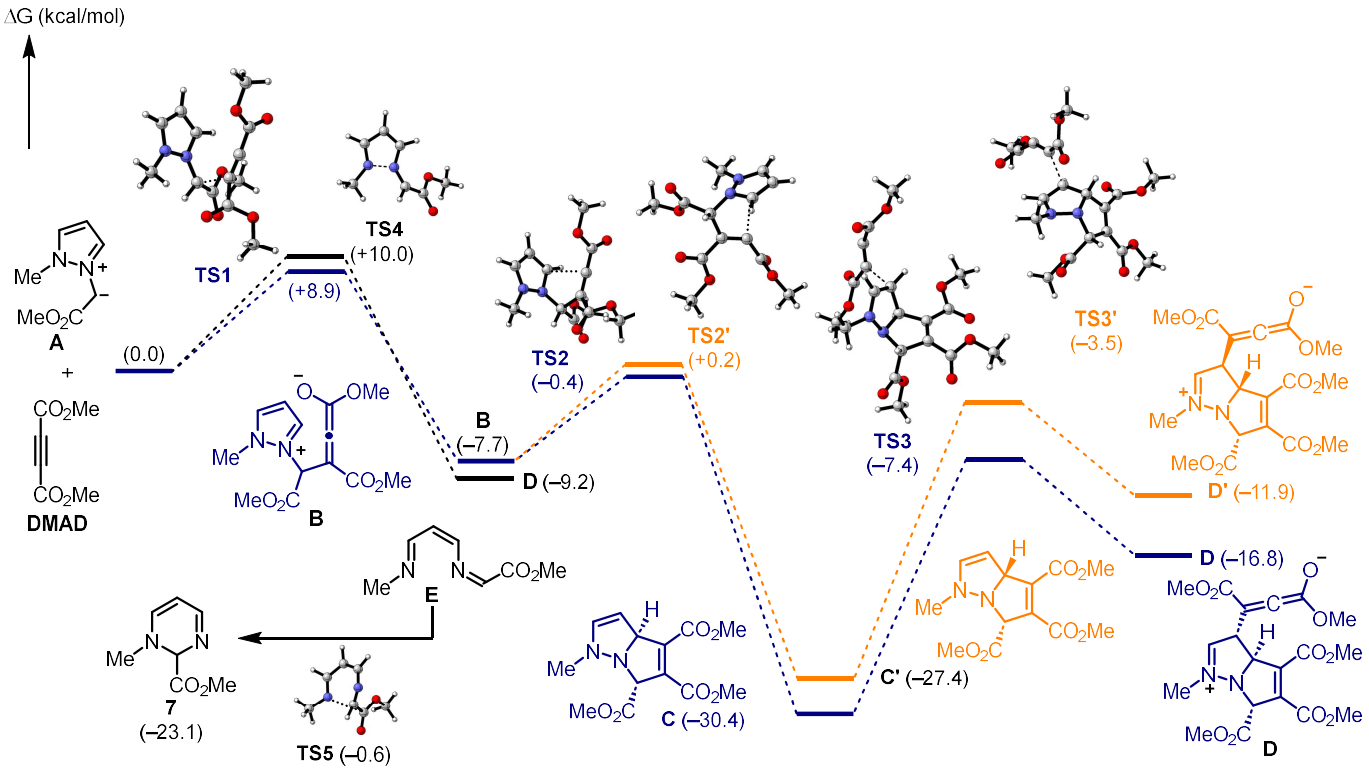
[3] Sheldrick, G.M. (**2015**). *Acta Cryst.* C71, 3-8.

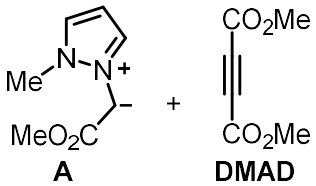
Table S4 Crystal data and structure refinement

Identification code	Yasui-377_auto
Empirical formula	$C_{14}H_{15}BrN_2O_6$
Formula weight	387.19
Temperature/K	173
Crystal system	monoclinic
Space group	C2/c
a/Å	25.6781(10)
b/Å	11.8274(4)
c/Å	22.4137(9)
α/°	90
β/°	115.471(5)
γ/°	90
Volume/Å^3	6145.5(5)
Z	16
ρ_{calc}g/cm^3	1.674
μ/mm^{-1}	2.709
F(000)	3136.0
Crystal size/mm^3	0.46 × 0.3 × 0.26
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	6.104 to 54.966
Index ranges	-24 ≤ h ≤ 33, -11 ≤ k ≤ 15, -29 ≤ l ≤ 29
Reflections collected	22990
Independent reflections	7044 [R_{int} = 0.0314, R_{sigma} = 0.0324]
Data/restraints/parameters	7044/0/423
Goodness-of-fit on F^2	1.026
Final R indexes [I>=2σ (I)]	R_1 = 0.0279, wR_2 = 0.0641
Final R indexes [all data]	R_1 = 0.0388, wR_2 = 0.0671
Largest diff. peak/hole / e Å^{-3}	0.33/-0.28

DFT calculations

The molecular geometries for each transition states were first estimated with the *Reaction plus* software package, based on the nudged elastic band method,[2] and were subsequently re-optimized using the Gaussian 16 software package.[3] Once the stationary points were obtained at B3LYP/6-31G(d,p) level,[4-7] the harmonic vibrational frequencies were calculated at the same level to estimate the Gibbs free energy. The nature of the stationary points was characterized *via* vibrational analysis. All of the Gibbs free energy values reported in this paper were calculated for a temperature of 298.15 K. The transition structure reported was optimized without constraints and the intrinsic reaction coordinate (IRC) route was calculated in both directions toward the corresponding minima for each transition-state structure. The IRC calculation failed to reach the energy minima on the potential energy surface for the transition states, and we therefore carried out geometry optimizations as a continuation of the IRC path. For each optimized structure (potential energy minimum or transition state computed at B3LYP/6-31G(d,p) level, additional single-point energy calculations in the presence of dimethylformamide (smd) were performed at B3LYP/6-311G(d,p) level. The 3D optimized structural figures in this paper were displayed by the CYLview visualization program.[8]





Calculation Type = FREQ

Calculation Method = RB3LYP

Basis Set = 6-31G(d,p)

Charge = 0

Spin = Singlet

Solvation = None

E(RB3LYP) = -1065.7476 Hartree

RMS Gradient Norm = 7.7525e-05 Hartree/Bohr

Imaginary Freq = 0

Dipole Moment = 4.6072481 Debye

Polarizability (?) = 186.38667 a.u.

Point Group = C1

Job cpu time: 0 days 0 hours 14 minutes 3.0 seconds.

Thermo Tab Data Section:

Imaginary Freq = 0

Temperature = 298.15 Kelvin

Pressure = 1 atm

Frequencies scaled by = 1

Electronic Energy (EE) = -1065.7476 Hartree

Zero-point Energy Correction = 0.285895 Hartree

Thermal Correction to Energy = 0.309916 Hartree

Thermal Correction to Enthalpy = 0.31086 Hartree

Thermal Correction to Free Energy = 0.225622 Hartree

EE Zero-point Energy = -1065.4617 Hartree

EE Thermal Energy Correction = -1065.4377 Hartree

EE Thermal Enthalpy Correction = -1065.4367 Hartree

EE Thermal Free Energy Correction = -1065.522 Hartree

E (Thermal) = 194.475 kcal/mol

Heat Capacity (Cv) = 81.305 cal/mol-kelvin

Entropy (S) = 179.398 cal/mol-kelvin

Opt Tab Data Section:

Step number = 1

Maximum force = 0.000222 Converged

RMS force = 7.8e-05 Converged

Maximum displacement = 0.014503 Not converged

RMS displacement = 0.004736 Not converged

Predicted energy change = -1.278342e-06 Hartree

Calculation Type = SP

Calculation Method = RB3LYP

Basis Set = 6-311G(d,p)

Charge = 0

Spin = Singlet

Solvation = scrf=(solvent=generic,read)

E(RB3LYP) = -1066.0341 Hartree

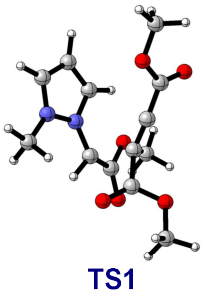
RMS Gradient Norm = Hartree/Bohr

Imaginary Freq =

Dipole Moment = 6.614972 Debye

Point Group = C1

Job cpu time: 0 days 0 hours 10 minutes 21.0 seconds.



Calculation Type = FREQ

Calculation Method = RB3LYP

Basis Set = 6-31G(d,p)

Charge = 0

Spin = Singlet

Solvation = None

E(RB3LYP) = -1065.7341 Hartree

RMS Gradient Norm = 4.149e-06 Hartree/Bohr

Imaginary Freq = 1

Dipole Moment = 6.1090135 Debye

Polarizability (?) = 189.66533 a.u.

Point Group = C1

Job cpu time: 0 days 0 hours 19 minutes 43.0 seconds.

Thermo Tab Data Section:

Imaginary Freq = 1

Temperature = 298.15 Kelvin

Pressure = 1 atm

Frequencies scaled by = 1

Electronic Energy (EE) = -1065.7341 Hartree

Zero-point Energy Correction = 0.286032 Hartree

Thermal Correction to Energy = 0.308842 Hartree

Thermal Correction to Enthalpy = 0.309786 Hartree

Thermal Correction to Free Energy = 0.230857 Hartree

EE Zero-point Energy = -1065.448 Hartree

EE Thermal Energy Correction = -1065.4252 Hartree

EE Thermal Enthalpy Correction = -1065.4243 Hartree

EE Thermal Free Energy Correction = -1065.5032 Hartree

E (Thermal) = 193.801 kcal/mol

Heat Capacity (Cv) = 78.566 cal/mol-kelvin

Entropy (S) = 166.121 cal/mol-kelvin

Opt Tab Data Section:

Step number = 1

Maximum force = 2.8e-05 Converged

RMS force = 5e-06 Converged

Maximum displacement = 0.003034 Not converged

RMS displacement = 0.000717 Converged

Predicted energy change = -2.409838e-08 Hartree

Calculation Type = SP

Calculation Method = RB3LYP

Basis Set = 6-311G(d,p)

Charge = 0

Spin = Singlet

Solvation = scrf=(solvent=generic,read)

E(RB3LYP) = -1066.0252 Hartree

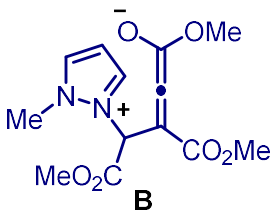
RMS Gradient Norm = Hartree/Bohr

Imaginary Freq =

Dipole Moment = 8.5830107 Debye

Point Group = C1

Job cpu time: 0 days 0 hours 12 minutes 51.0 seconds.



B

Calculation Type = FREQ

Calculation Method = RB3LYP

Basis Set = 6-31G(d,p)

Charge = 0

Spin = Singlet

Solvation = None

E(RB3LYP) = -1065.7589 Hartree

RMS Gradient Norm = 8.176e-06 Hartree/Bohr

Imaginary Freq = 0

Dipole Moment = 11.404192 Debye

Polarizability (?) = 175.23333 a.u.

Point Group = C1

Job cpu time: 0 days 0 hours 21 minutes 10.0 seconds.

Thermo Tab Data Section:

Imaginary Freq = 0

Temperature = 298.15 Kelvin

Pressure = 1 atm

Frequencies scaled by = 1

Electronic Energy (EE) = -1065.7589 Hartree

Zero-point Energy Correction = 0.289225 Hartree

Thermal Correction to Energy = 0.311217 Hartree

Thermal Correction to Enthalpy = 0.312161 Hartree

Thermal Correction to Free Energy = 0.237395 Hartree

EE Zero-point Energy = -1065.4697 Hartree

EE Thermal Energy Correction = -1065.4477 Hartree

EE Thermal Enthalpy Correction = -1065.4468 Hartree

EE Thermal Free Energy Correction = -1065.5216 Hartree

E (Thermal) = 195.291 kcal/mol

Heat Capacity (Cv) = 77.487 cal/mol-kelvin

Entropy (S) = 157.358 cal/mol-kelvin

Opt Tab Data Section:

Step number = 1

Maximum force = 2.7e-05 Converged

RMS force = 4e-06 Converged

Maximum displacement = 0.001452 Converged

RMS displacement = 0.000348 Converged

Predicted energy change = -2.562752e-08 Hartree

Calculation Type = SP

Calculation Method = RB3LYP

Basis Set = 6-311G(d,p)

Charge = 0

Spin = Singlet

Solvation = scrf=(solvent=generic,read)

E(RB3LYP) = -1066.0581 Hartree

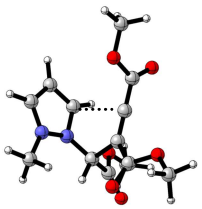
RMS Gradient Norm = Hartree/Bohr

Imaginary Freq =

Dipole Moment = 15.227019 Debye

Point Group = C1

Job cpu time: 0 days 0 hours 11 minutes 24.0 seconds.



TS2

Calculation Type = FREQ

Calculation Method = RB3LYP

Basis Set = 6-31G(d,p)

Charge = 0

Spin = Singlet

Solvation = None

E(RB3LYP) = -1065.7477 Hartree

RMS Gradient Norm = 0.000754205 Hartree/Bohr

Imaginary Freq = 1

Dipole Moment = 7.5251599 Debye

Polarizability (?) = 184.72 a.u.

Point Group = C1

Job cpu time: 0 days 0 hours 21 minutes 54.0 seconds.

Thermo Tab Data Section:

Imaginary Freq = 1

Temperature = 298.15 Kelvin

Pressure = 1 atm

Frequencies scaled by = 1

Electronic Energy (EE) = -1065.7477 Hartree

Zero-point Energy Correction = 0.287707 Hartree

Thermal Correction to Energy = 0.309672 Hartree

Thermal Correction to Enthalpy = 0.310616 Hartree

Thermal Correction to Free Energy = 0.233995 Hartree

EE Zero-point Energy = -1065.46 Hartree

EE Thermal Energy Correction = -1065.4381 Hartree

EE Thermal Enthalpy Correction = -1065.4371 Hartree

EE Thermal Free Energy Correction = -1065.5137 Hartree

E (Thermal) = 194.322 kcal/mol

Heat Capacity (Cv) = 76.566 cal/mol-kelvin

Entropy (S) = 161.262 cal/mol-kelvin

Opt Tab Data Section:

Step number = 1

Maximum force = 5.8e-05 Converged

RMS force = 1.4e-05 Converged

Maximum displacement = 0.01431 Not converged

RMS displacement = 0.003298 Not converged

Predicted energy change = -5.621179e-07 Hartree

Calculation Type = SP

Calculation Method = RB3LYP

Basis Set = 6-311G(d,p)

Charge = 0

Spin = Singlet

Solvation = scrf=(solvent=generic,read)

E(RB3LYP) = -1066.043 Hartree

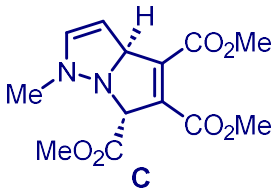
RMS Gradient Norm = Hartree/Bohr

Imaginary Freq =

Dipole Moment = 10.696954 Debye

Point Group = C1

Job cpu time: 0 days 0 hours 11 minutes 56.0 seconds.



Calculation Type = FREQ

Calculation Method = RB3LYP

Basis Set = 6-31G(d,p)

Charge = 0

Spin = Singlet

Solvation = None

E(RB3LYP) = -1065.8155 Hartree

RMS Gradient Norm = 8.263e-06 Hartree/Bohr

Imaginary Freq = 0

Dipole Moment = 2.7747265 Debye

Polarizability (?) = 164.297 a.u.

Point Group = C1

Job cpu time: 0 days 0 hours 19 minutes 14.0 seconds.

Thermo Tab Data Section:

Imaginary Freq = 0

Temperature = 298.15 Kelvin

Pressure = 1 atm

Frequencies scaled by = 1

Electronic Energy (EE) = -1065.8155 Hartree

Zero-point Energy Correction = 0.289839 Hartree

Thermal Correction to Energy = 0.311535 Hartree

Thermal Correction to Enthalpy = 0.312479 Hartree

Thermal Correction to Free Energy = 0.235908 Hartree

EE Zero-point Energy = -1065.5257 Hartree

EE Thermal Energy Correction = -1065.504 Hartree

EE Thermal Enthalpy Correction = -1065.5031 Hartree

EE Thermal Free Energy Correction = -1065.5796 Hartree

E (Thermal) = 195.491 kcal/mol

Heat Capacity (Cv) = 76.048 cal/mol-kelvin

Entropy (S) = 161.159 cal/mol-kelvin

Opt Tab Data Section:

Step number = 1

Maximum force = 4.9e-05 Converged

RMS force = 8e-06 Converged

Maximum displacement = 0.001754 Converged

RMS displacement = 0.000449 Converged

Predicted energy change = -1.796291e-08 Hartree

Calculation Type = SP

Calculation Method = RB3LYP

Basis Set = 6-311G(d,p)

Charge = 0

Spin = Singlet

Solvation = scrf=(solvent=generic,read)

E(RB3LYP) = -1066.0928 Hartree

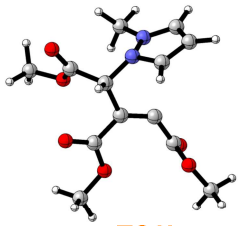
RMS Gradient Norm = Hartree/Bohr

Imaginary Freq =

Dipole Moment = 3.6224315 Debye

Point Group = C1

Job cpu time: 0 days 0 hours 3 minutes 8.0 seconds.



Calculation Type = FREQ

Calculation Method = RB3LYP

Basis Set = 6-31G(d,p)

Charge = 0

Spin = Singlet

Solvation = None

E(RB3LYP) = -1065.7466 Hartree

RMS Gradient Norm = 9.779e-06 Hartree/Bohr

Imaginary Freq = 1

Dipole Moment = 6.1127789 Debye

Polarizability (?) = 180.877 a.u.

Point Group = C1

Job cpu time: 0 days 0 hours 20 minutes 14.0 seconds.

Thermo Tab Data Section:

Imaginary Freq = 1

Temperature = 298.15 Kelvin

Pressure = 1 atm

Frequencies scaled by = 1

Electronic Energy (EE) = -1065.7466 Hartree

Zero-point Energy Correction = 0.288504 Hartree

Thermal Correction to Energy = 0.31004 Hartree

Thermal Correction to Enthalpy = 0.310985 Hartree

Thermal Correction to Free Energy = 0.236421 Hartree

EE Zero-point Energy = -1065.4581 Hartree

EE Thermal Energy Correction = -1065.4366 Hartree

EE Thermal Enthalpy Correction = -1065.4356 Hartree

EE Thermal Free Energy Correction = -1065.5102 Hartree

E (Thermal) = 194.553 kcal/mol

Heat Capacity (Cv) = 75.883 cal/mol-kelvin

Entropy (S) = 156.931 cal/mol-kelvin

Opt Tab Data Section:

Step number = 1

Maximum force = 6.9e-05 Converged

RMS force = 5e-06 Converged

Maximum displacement = 0.003851 Not converged

RMS displacement = 0.000762 Converged

Predicted energy change = -2.776217e-08 Hartree

Calculation Type = SP

Calculation Method = RB3LYP

Basis Set = 6-311G(d,p)

Charge = 0

Spin = Singlet

Solvation = scrf=(solvent=generic,read)

E(RB3LYP) = -1066.0446 Hartree

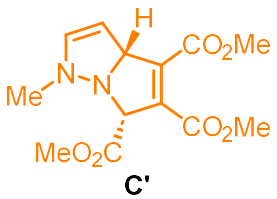
RMS Gradient Norm = Hartree/Bohr

Imaginary Freq =

Dipole Moment = 8.0451498 Debye

Point Group = C1

Job cpu time: 0 days 0 hours 6 minutes 8.0 seconds.



C'

Calculation Type = FREQ

Calculation Method = RB3LYP

Basis Set = 6-31G(d,p)

Charge = 0

Spin = Singlet

Solvation = None

E(RB3LYP) = -1065.8131 Hartree

RMS Gradient Norm = 4.412e-06 Hartree/Bohr

Imaginary Freq = 0

Dipole Moment = 3.2920443 Debye

Polarizability (?) = 163.57633 a.u.

Point Group = C1

Job cpu time: 0 days 0 hours 19 minutes 14.0 seconds.

Thermo Tab Data Section:

Imaginary Freq = 0

Temperature = 298.15 Kelvin

Pressure = 1 atm

Frequencies scaled by = 1

Electronic Energy (EE) = -1065.8131 Hartree

Zero-point Energy Correction = 0.290044 Hartree

Thermal Correction to Energy = 0.311514 Hartree

Thermal Correction to Enthalpy = 0.312458 Hartree

Thermal Correction to Free Energy = 0.237654 Hartree

EE Zero-point Energy = -1065.5231 Hartree

EE Thermal Energy Correction = -1065.5016 Hartree

EE Thermal Enthalpy Correction = -1065.5006 Hartree

EE Thermal Free Energy Correction = -1065.5754 Hartree

E (Thermal) = 195.478 kcal/mol

Heat Capacity (Cv) = 75.957 cal/mol-kelvin

Entropy (S) = 157.438 cal/mol-kelvin

Opt Tab Data Section:

Step number = 1

Maximum force = 1.5e-05 Converged

RMS force = 4e-06 Converged

Maximum displacement = 0.0145 Not converged

RMS displacement = 0.004511 Not converged

Predicted energy change = -1.183362e-07 Hartree

Calculation Type = SP

Calculation Method = RB3LYP

Basis Set = 6-311G(d,p)

Charge = 0

Spin = Singlet

Solvation = scrf=(solvent=generic,read)

E(RB3LYP) = -1066.0899 Hartree

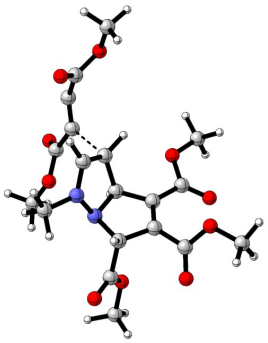
RMS Gradient Norm = Hartree/Bohr

Imaginary Freq =

Dipole Moment = 4.1152026 Debye

Point Group = C1

Job cpu time: 0 days 0 hours 9 minutes 54.0 seconds.



Calculation Type = FREQ

Calculation Method = RB3LYP

Basis Set = 6-31G(d,p)

Charge = 0

Spin = Singlet

Solvation = None

E(RB3LYP) = -1598.8683 Hartree

RMS Gradient Norm = 4.279e-06 Hartree/Bohr

Imaginary Freq = 1

Dipole Moment = 4.6952455 Debye

Polarizability (?) = 269.13667 a.u.

Point Group = C1

Job cpu time: 0 days 0 hours 40 minutes 45.0 seconds.

Thermo Tab Data Section:

Imaginary Freq = 1

Temperature = 298.15 Kelvin

Pressure = 1 atm

Frequencies scaled by = 1

Electronic Energy (EE) = -1598.8683 Hartree

Zero-point Energy Correction = 0.405923 Hartree

Thermal Correction to Energy = 0.439515 Hartree

Thermal Correction to Enthalpy = 0.440459 Hartree

Thermal Correction to Free Energy = 0.334963 Hartree

EE Zero-point Energy = -1598.4624 Hartree

EE Thermal Energy Correction = -1598.4288 Hartree

EE Thermal Enthalpy Correction = -1598.4278 Hartree

EE Thermal Free Energy Correction = -1598.5333 Hartree

E (Thermal) = 275.8 kcal/mol

Heat Capacity (Cv) = 114.771 cal/mol-kelvin

Entropy (S) = 222.034 cal/mol-kelvin

Opt Tab Data Section:

Step number = 1

Maximum force = 4.7e-05 Converged

RMS force = 4e-06 Converged

Maximum displacement = 0.003898 Not converged

RMS displacement = 0.000715 Converged

Predicted energy change = -4.455097e-08 Hartree

Calculation Type = SP

Calculation Method = RB3LYP

Basis Set = 6-311G(d,p)

Charge = 0

Spin = Singlet

Solvation = scrf=(solvent=generic,read)

E(RB3LYP) = -1599.298 Hartree

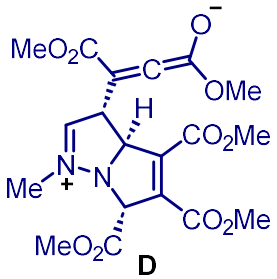
RMS Gradient Norm = Hartree/Bohr

Imaginary Freq =

Dipole Moment = 6.6743518 Debye

Point Group = C1

Job cpu time: 0 days 0 hours 14 minutes 29.0 seconds.



D

Calculation Type = FREQ

Calculation Method = RB3LYP

Basis Set = 6-31G(d,p)

Charge = 0

Spin = Singlet

Solvation = None
E(RB3LYP) = -1598.8772 Hartree
RMS Gradient Norm = 4.978e-06 Hartree/Bohr
Imaginary Freq = 0
Dipole Moment = 9.5692088 Debye
Polarizability (?) = 262.94067 a.u.
Point Group = C1
Job cpu time: 0 days 0 hours 38 minutes 0.0 seconds.

Thermo Tab Data Section:
Imaginary Freq = 0
Temperature = 298.15 Kelvin
Pressure = 1 atm
Frequencies scaled by = 1
Electronic Energy (EE) = -1598.8772 Hartree
Zero-point Energy Correction = 0.407745 Hartree
Thermal Correction to Energy = 0.441182 Hartree
Thermal Correction to Enthalpy = 0.442126 Hartree
Thermal Correction to Free Energy = 0.338203 Hartree
EE Zero-point Energy = -1598.4694 Hartree
EE Thermal Energy Correction = -1598.436 Hartree
EE Thermal Enthalpy Correction = -1598.4351 Hartree
EE Thermal Free Energy Correction = -1598.539 Hartree
E (Thermal) = 276.846 kcal/mol
Heat Capacity (Cv) = 114.987 cal/mol-kelvin
Entropy (S) = 218.724 cal/mol-kelvin

Opt Tab Data Section:
Step number = 1
Maximum force = 1.5e-05 Converged
RMS force = 2e-06 Converged
Maximum displacement = 0.001515 Converged
RMS displacement = 0.000293 Converged
Predicted energy change = -8.710808e-09 Hartree

Calculation Type = SP
Calculation Method = RB3LYP
Basis Set = 6-311G(d,p)
Charge = 0
Spin = Singlet

Solvation = scrf=(solvent=generic,read)

E(RB3LYP) = -1599.3163 Hartree

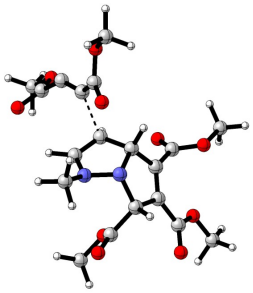
RMS Gradient Norm = Hartree/Bohr

Imaginary Freq =

Dipole Moment = 12.964203 Debye

Point Group = C1

Job cpu time: 0 days 0 hours 41 minutes 52.0 seconds.



TS3'

Calculation Type = FREQ

Calculation Method = RB3LYP

Basis Set = 6-31G(d,p)

Charge = 0

Spin = Singlet

Solvation = None

E(RB3LYP) = -1598.8692 Hartree

RMS Gradient Norm = 4.192e-06 Hartree/Bohr

Imaginary Freq = 1

Dipole Moment = 4.5694047 Debye

Polarizability (?) = 268.33367 a.u.

Point Group = C1

Job cpu time: 0 days 0 hours 35 minutes 14.0 seconds.

Thermo Tab Data Section:

Imaginary Freq = 1

Temperature = 298.15 Kelvin

Pressure = 1 atm

Frequencies scaled by = 1

Electronic Energy (EE) = -1598.8692 Hartree

Zero-point Energy Correction = 0.406061 Hartree

Thermal Correction to Energy = 0.439451 Hartree

Thermal Correction to Enthalpy = 0.440396 Hartree

Thermal Correction to Free Energy = 0.335906 Hartree

EE Zero-point Energy = -1598.4632 Hartree

EE Thermal Energy Correction = -1598.4298 Hartree

EE Thermal Enthalpy Correction = -1598.4288 Hartree

EE Thermal Free Energy Correction = -1598.5333 Hartree

E (Thermal) = 275.76 kcal/mol

Heat Capacity (Cv) = 114.695 cal/mol-kelvin

Entropy (S) = 219.918 cal/mol-kelvin

Opt Tab Data Section:

Step number = 1

Maximum force = 3.3e-05 Converged

RMS force = 3e-06 Converged

Maximum displacement = 0.001514 Converged

RMS displacement = 0.000241 Converged

Predicted energy change = -4.23147e-09 Hartree

Calculation Type = SP

Calculation Method = RB3LYP

Basis Set = 6-311G(d,p)

Charge = 0

Spin = Singlet

Solvation = scrf=(solvent=generic,read)

E(RB3LYP) = -1599.2946 Hartree

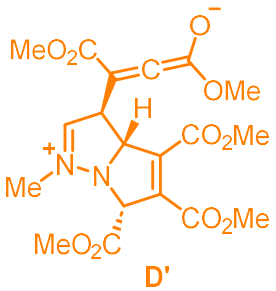
RMS Gradient Norm = Hartree/Bohr

Imaginary Freq =

Dipole Moment = 5.9362062 Debye

Point Group = C1

Job cpu time: 0 days 0 hours 9 minutes 59.0 seconds.



D'

Calculation Type = FREQ

Calculation Method = RB3LYP

Basis Set = 6-31G(d,p)

Charge = 0

Spin = Singlet

Solvation = None

E(RB3LYP) = -1598.8787 Hartree

RMS Gradient Norm = 7.568e-06 Hartree/Bohr

Imaginary Freq = 0

Dipole Moment = 6.4480543 Debye

Polarizability (?) = 261.048 a.u.

Point Group = C1

Job cpu time: 0 days 0 hours 35 minutes 11.0 seconds.

Thermo Tab Data Section:

Imaginary Freq = 0

Temperature = 298.15 Kelvin

Pressure = 1 atm

Frequencies scaled by = 1

Electronic Energy (EE) = -1598.8787 Hartree

Zero-point Energy Correction = 0.40816 Hartree

Thermal Correction to Energy = 0.441378 Hartree

Thermal Correction to Enthalpy = 0.442322 Hartree

Thermal Correction to Free Energy = 0.339172 Hartree

EE Zero-point Energy = -1598.4706 Hartree

EE Thermal Energy Correction = -1598.4374 Hartree

EE Thermal Enthalpy Correction = -1598.4364 Hartree

EE Thermal Free Energy Correction = -1598.5396 Hartree

E (Thermal) = 276.969 kcal/mol

Heat Capacity (Cv) = 114.732 cal/mol-kelvin

Entropy (S) = 217.097 cal/mol-kelvin

Opt Tab Data Section:

Step number = 1

Maximum force = 2.2e-05 Converged

RMS force = 4e-06 Converged

Maximum displacement = 0.001759 Converged

RMS displacement = 0.000307 Converged

Predicted energy change = -1.705109e-08 Hartree

Calculation Type = SP

Calculation Method = RB3LYP

Basis Set = 6-311G(d,p)

Charge = 0

Spin = Singlet

Solvation = scrf=(solvent=generic,read)

E(RB3LYP) = -1599.3112 Hartree

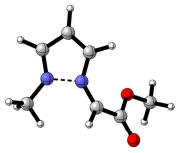
RMS Gradient Norm = Hartree/Bohr

Imaginary Freq =

Dipole Moment = 8.7246936 Debye

Point Group = C1

Job cpu time: 0 days 0 hours 5 minutes 56.0 seconds.



TS4

Calculation Type = FREQ

Calculation Method = RB3LYP

Basis Set = 6-31G(d,p)

Charge = 0

Spin = Singlet

Solvation = None

E(RB3LYP) = -532.63612 Hartree

RMS Gradient Norm = 1.436e-06 Hartree/Bohr

Imaginary Freq = 1

Dipole Moment = 5.1193241 Debye

Polarizability (?) = 105.53533 a.u.

Point Group = C1

Job cpu time: 0 days 0 hours 6 minutes 8.0 seconds.

Thermo Tab Data Section:

Imaginary Freq = 1

Temperature = 298.15 Kelvin

Pressure = 1 atm

Frequencies scaled by = 1

Electronic Energy (EE) = -532.63612 Hartree

Zero-point Energy Correction = 0.166522 Hartree

Thermal Correction to Energy = 0.177589 Hartree

Thermal Correction to Enthalpy = 0.178533 Hartree

Thermal Correction to Free Energy = 0.128872 Hartree

EE Zero-point Energy = -532.4696 Hartree

EE Thermal Energy Correction = -532.45853 Hartree

EE Thermal Enthalpy Correction = -532.45758 Hartree

EE Thermal Free Energy Correction = -532.50725 Hartree

E (Thermal) = 111.438 kcal/mol

Heat Capacity (Cv) = 39.38 cal/mol-kelvin

Entropy (S) = 104.521 cal/mol-kelvin

Opt Tab Data Section:

Step number = 1

Maximum force = 4e-06 Converged

RMS force = 1e-06 Converged

Maximum displacement = 0.000426 Converged

RMS displacement = 0.000114 Converged

Predicted energy change = -8.823603e-10 Hartree

Calculation Type = SP

Calculation Method = RB3LYP

Basis Set = 6-311G(d,p)

Charge = 0

Spin = Singlet

Solvation = scrf=(solvent=generic,read)

E(RB3LYP) = -532.77686 Hartree

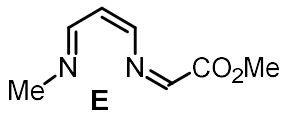
RMS Gradient Norm = Hartree/Bohr

Imaginary Freq =

Dipole Moment = 7.1108935 Debye

Point Group = C1

Job cpu time: 0 days 0 hours 9 minutes 12.0 seconds.



Calculation Type = FREQ

Calculation Method = RB3LYP

Basis Set = 6-31G(d,p)

Charge = 0

Spin = Singlet

Solvation = None

E(RB3LYP) = -532.66653 Hartree

RMS Gradient Norm = 6.896e-06 Hartree/Bohr

Imaginary Freq = 0

Dipole Moment = 2.8450068 Debye

Polarizability (?) = 105.842 a.u.

Point Group = C1

Job cpu time: 0 days 0 hours 13 minutes 20.0 seconds.

Thermo Tab Data Section:

Imaginary Freq = 0

Temperature = 298.15 Kelvin

Pressure = 1 atm

Frequencies scaled by = 1

Electronic Energy (EE) = -532.66653 Hartree

Zero-point Energy Correction = 0.166889 Hartree

Thermal Correction to Energy = 0.178999 Hartree

Thermal Correction to Enthalpy = 0.179943 Hartree

Thermal Correction to Free Energy = 0.126982 Hartree

EE Zero-point Energy = -532.49964 Hartree

EE Thermal Energy Correction = -532.48753 Hartree

EE Thermal Enthalpy Correction = -532.48658 Hartree

EE Thermal Free Energy Correction = -532.53954 Hartree

E (Thermal) = 112.323 kcal/mol

Heat Capacity (Cv) = 41.463 cal/mol-kelvin

Entropy (S) = 111.466 cal/mol-kelvin

Opt Tab Data Section:

Step number = 1

Maximum force = 1.8e-05 Converged

RMS force = 5e-06 Converged

Maximum displacement = 0.001995 Not converged

RMS displacement = 0.000695 Converged

Predicted energy change = -2.80592e-08 Hartree

Calculation Type = SP

Calculation Method = RB3LYP

Basis Set = 6-311G(d,p)

Charge = 0

Spin = Singlet

Solvation = scrf=(solvent=generic,read)

E(RB3LYP) = -532.80552 Hartree

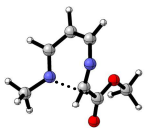
RMS Gradient Norm = Hartree/Bohr

Imaginary Freq =

Dipole Moment = 3.6952227 Debye

Point Group = C1

Job cpu time: 0 days 0 hours 10 minutes 2.0 seconds.



TS5

Calculation Type = FREQ

Calculation Method = RB3LYP

Basis Set = 6-31G(d,p)

Charge = 0

Spin = Singlet

Solvation = None

E(RB3LYP) = -532.65701 Hartree

RMS Gradient Norm = 4.096e-06 Hartree/Bohr

Imaginary Freq = 1

Dipole Moment = 2.3839978 Debye

Polarizability (?) = 95.543 a.u.

Point Group = C1

Job cpu time: 0 days 0 hours 11 minutes 27.0 seconds.

Thermo Tab Data Section:

Imaginary Freq = 1

Temperature = 298.15 Kelvin

Pressure = 1 atm

Frequencies scaled by = 1

Electronic Energy (EE) = -532.65701 Hartree

Zero-point Energy Correction = 0.167136 Hartree

Thermal Correction to Energy = 0.178211 Hartree

Thermal Correction to Enthalpy = 0.179155 Hartree

Thermal Correction to Free Energy = 0.129872 Hartree

EE Zero-point Energy = -532.48987 Hartree

EE Thermal Energy Correction = -532.4788 Hartree

EE Thermal Enthalpy Correction = -532.47785 Hartree

EE Thermal Free Energy Correction = -532.52714 Hartree

E (Thermal) = 111.829 kcal/mol

Heat Capacity (Cv) = 39.061 cal/mol-kelvin

Entropy (S) = 103.724 cal/mol-kelvin

Opt Tab Data Section:

Step number = 1

Maximum force = 1.5e-05 Converged

RMS force = 3e-06 Converged

Maximum displacement = 0.002505 Not converged

RMS displacement = 0.000789 Converged

Predicted energy change = -1.986184e-08 Hartree

Calculation Type = SP

Calculation Method = RB3LYP

Basis Set = 6-311G(d,p)

Charge = 0

Spin = Singlet

Solvation = scrf=(solvent=generic,read)

E(RB3LYP) = -532.79477 Hartree

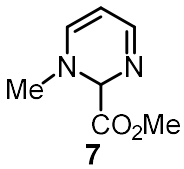
RMS Gradient Norm = Hartree/Bohr

Imaginary Freq =

Dipole Moment = 3.1766783 Debye

Point Group = C1

Job cpu time: 0 days 0 hours 2 minutes 34.0 seconds.



7

Calculation Type = FREQ

Calculation Method = RB3LYP

Basis Set = 6-31G(d,p)

Charge = 0

Spin = Singlet

Solvation = None

E(RB3LYP) = -532.69449 Hartree

RMS Gradient Norm = 3.928e-06 Hartree/Bohr

Imaginary Freq = 0

Dipole Moment = 1.8534361 Debye

Polarizability (?) = 88.875667 a.u.

Point Group = C1

Job cpu time: 0 days 0 hours 9 minutes 53.0 seconds.

Thermo Tab Data Section:

Imaginary Freq = 0

Temperature = 298.15 Kelvin

Pressure = 1 atm

Frequencies scaled by = 1

Electronic Energy (EE) = -532.69449 Hartree

Zero-point Energy Correction = 0.170383 Hartree

Thermal Correction to Energy = 0.181367 Hartree

Thermal Correction to Enthalpy = 0.182312 Hartree

Thermal Correction to Free Energy = 0.132542 Hartree

EE Zero-point Energy = -532.5241 Hartree

EE Thermal Energy Correction = -532.51312 Hartree

EE Thermal Enthalpy Correction = -532.51218 Hartree

EE Thermal Free Energy Correction = -532.56195 Hartree

E (Thermal) = 113.81 kcal/mol

Heat Capacity (Cv) = 38.926 cal/mol-kelvin

Entropy (S) = 104.748 cal/mol-kelvin

Opt Tab Data Section:

Step number = 1

Maximum force = 1.2e-05 Converged

RMS force = 2e-06 Converged

Maximum displacement = 0.004118 Not converged

RMS displacement = 0.000949 Converged

Predicted energy change = -1.559738e-08 Hartree

Calculation Type = SP

Calculation Method = RB3LYP

Basis Set = 6-311G(d,p)

Charge = 0

Spin = Singlet

Solvation = scrf=(solvent=generic,read)

E(RB3LYP) = -532.83335 Hartree

RMS Gradient Norm = Hartree/Bohr

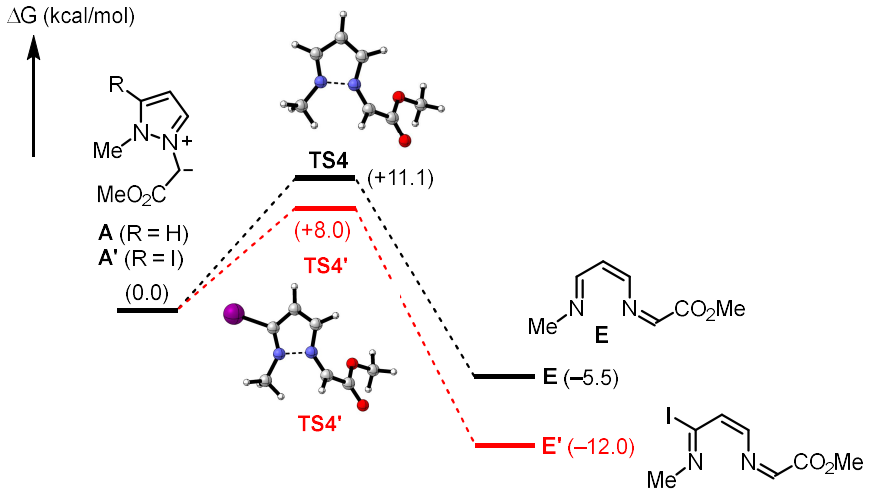
Imaginary Freq =

Dipole Moment = 2.5581601 Debye

Point Group = C1

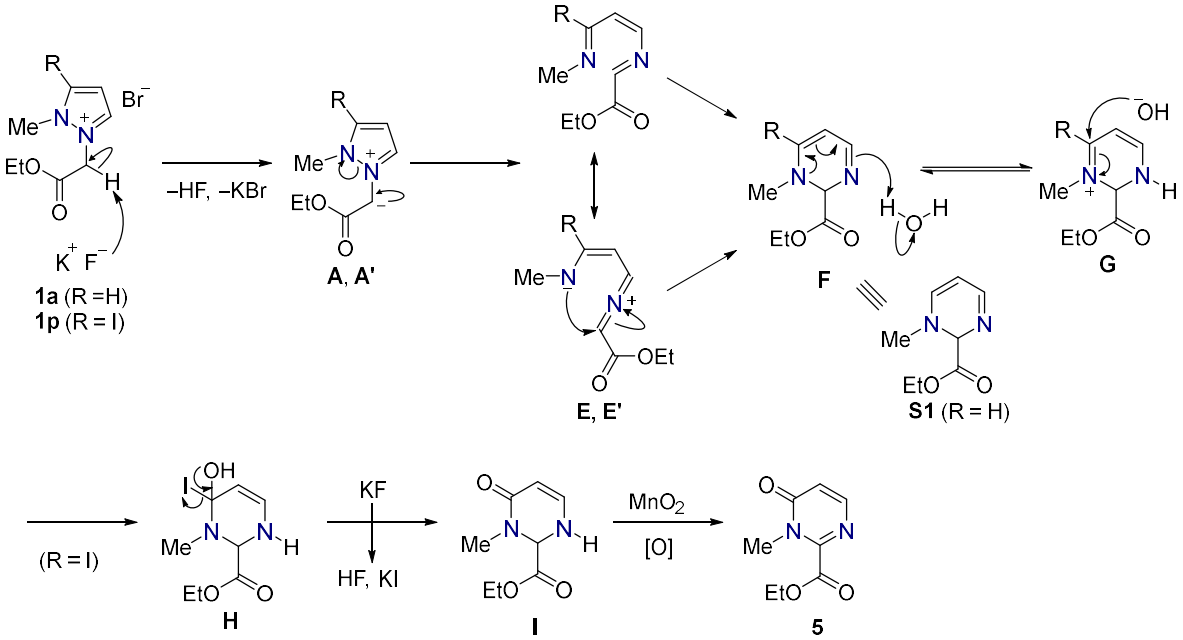
Job cpu time: 0 days 0 hours 2 minutes 13.0 seconds.

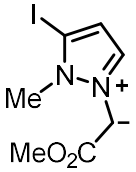
To clarify to obtain pyrimidinone **5**, we calculated the activation energy for the ring-opening step at the wB97XD/Lanl2DZ (for I) and wB97XD/6-311G+(d,p) level (for the other atoms, SMD, solvent = DMF)//wB97XD/Lanl2DZ (for I) and wB97XD/6-31G+(d,p) (for the other atoms, gas phase). The results indicate that the iodinated ylide **A′** undergoes ring-opening more readily than the corresponding non-iodinated species. Furthermore, the ring-opened diazatriene **E′** is significantly more stable than **E**. We attribute these effects to stabilization of both the transition state and the product by the iodine substituent. In particular, the high polarizability of iodine likely enhances stabilization of the more conjugated electronic structure involved in the ring-opening process.



wB97XD/Lanl2DZ (for I) and wB97XD/6-311G+(d,p) level (for the other atoms, SMD, solvent = DMF)
//wB97XD/Lanl2DZ (for I) and wB97XD/6-31G+(d,p) (for the other atoms, gas phase)

In addition, the iodinated 1,4-dihydropyrimidine intermediate was found to be readily hydrolyzed by trace amounts of H_2O, affording pyrimidinone **5** after oxidation. In contrast, compound **S1** (R = H) was too polar to be isolated.





A'

Calculation Type = FREQ

Calculation Method = RwB97XD

Basis Set = Gen

Charge = 0

Spin = Singlet

Solvation = None

E(RwB97XD) = -543.0732 Hartree

RMS Gradient Norm = 6.562e-06 Hartree/Bohr

Imaginary Freq = 0

Dipole Moment = 6.1580857 Debye

Polarizability (?) = 122.26567 a.u.

Point Group = C1

Job cpu time: 0 days 0 hours 2 minutes 24.0 seconds.

Thermo Tab Data Section:

Imaginary Freq = 0

Temperature = 298.15 Kelvin

Pressure = 1 atm

Frequencies scaled by = 1

Electronic Energy (EE) = -543.0732 Hartree

Zero-point Energy Correction = 0.162258 Hartree

Thermal Correction to Energy = 0.174649 Hartree

Thermal Correction to Enthalpy = 0.175593 Hartree

Thermal Correction to Free Energy = 0.120912 Hartree

EE + Zero-point Energy = -542.91094 Hartree

EE + Thermal Energy Correction = -542.89855 Hartree

EE + Thermal Enthalpy Correction = -542.8976 Hartree

EE + Thermal Free Energy Correction = -542.95229 Hartree

E (Thermal) = 109.594 kcal/mol

Heat Capacity (Cv) = 43.215 cal/mol-kelvin

Entropy (S) = 115.087 cal/mol-kelvin

Opt Tab Data Section:

Step number = 1

Maximum force = 1.4e-05 Converged

RMS force = 4e-06 Converged

Maximum displacement = 0.002613 Not converged

RMS displacement = 0.000673 Converged

Predicted energy change = -1.688787e-08 Hartree

Calculation Type = SP

Calculation Method = RwB97XD

Basis Set = Gen

Charge = 0

Spin = Singlet

Solvation = scrf=(solvent=generic,read)

E(RwB97XD) = -543.2147 Hartree

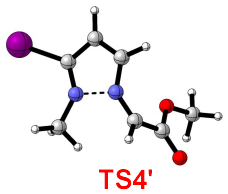
RMS Gradient Norm = Hartree/Bohr

Imaginary Freq =

Dipole Moment = 8.9750081 Debye

Point Group = C1

Job cpu time: 0 days 0 hours 1 minutes 17.0 seconds.



Calculation Type = FREQ

Calculation Method = RwB97XD

Basis Set = Gen

Charge = 0

Spin = Singlet

Solvation = None

E(RwB97XD) = -543.06328 Hartree

RMS Gradient Norm = 1.195e-06 Hartree/Bohr

Imaginary Freq = 1

Dipole Moment = 3.2184892 Debye

Polarizability (?) = 131.295 a.u.

Point Group = C1

Job cpu time: 0 days 0 hours 1 minutes 37.0 seconds.

Thermo Tab Data Section:

Imaginary Freq = 1

Temperature = 298.15 Kelvin

Pressure = 1 atm

Frequencies scaled by = 1

Electronic Energy (EE) = -543.06328 Hartree

Zero-point Energy Correction = 0.159253 Hartree

Thermal Correction to Energy = 0.171778 Hartree

Thermal Correction to Enthalpy = 0.172723 Hartree

Thermal Correction to Free Energy = 0.117342 Hartree

EE + Zero-point Energy = -542.90403 Hartree

EE + Thermal Energy Correction = -542.8915 Hartree

EE + Thermal Enthalpy Correction = -542.89056 Hartree

EE + Thermal Free Energy Correction = -542.94594 Hartree

E (Thermal) = 107.793 kcal/mol

Heat Capacity (Cv) = 42.933 cal/mol-kelvin

Entropy (S) = 116.559 cal/mol-kelvin

Opt Tab Data Section:

Step number = 1

Maximum force = 7e-06 Converged

RMS force = 1e-06 Converged

Maximum displacement = 0.000808 Converged

RMS displacement = 0.000184 Converged

Predicted energy change = -1.955735e-09 Hartree

Calculation Type = SP

Calculation Method = RwB97XD

Basis Set = Gen

Charge = 0

Spin = Singlet

Solvation = scrf=(solvent=generic,read)

E(RwB97XD) = -543.19835 Hartree

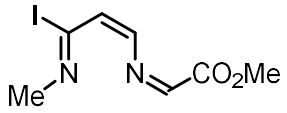
RMS Gradient Norm = Hartree/Bohr

Imaginary Freq =

Dipole Moment = 4.9526919 Debye

Point Group = C1

Job cpu time: 0 days 0 hours 1 minutes 47.0 seconds.



E'

Calculation Type = FREQ

Calculation Method = RwB97XD

Basis Set = Gen

Charge = 0

Spin = Singlet

Solvation = None

E(RwB97XD) = -543.09647 Hartree

RMS Gradient Norm = 6.985e-06 Hartree/Bohr

Imaginary Freq = 0

Dipole Moment = 2.466873 Debye

Polarizability (?) = 113.402 a.u.

Point Group = C1

Job cpu time: 0 days 0 hours 1 minutes 49.0 seconds.

Thermo Tab Data Section:

Imaginary Freq = 0

Temperature = 298.15 Kelvin

Pressure = 1 atm

Frequencies scaled by = 1

Electronic Energy (EE) = -543.09647 Hartree

Zero-point Energy Correction = 0.159425 Hartree

Thermal Correction to Energy = 0.173077 Hartree

Thermal Correction to Enthalpy = 0.174021 Hartree

Thermal Correction to Free Energy = 0.115946 Hartree

EE + Zero-point Energy = -542.93704 Hartree

EE + Thermal Energy Correction = -542.92339 Hartree

EE + Thermal Enthalpy Correction = -542.92245 Hartree

EE + Thermal Free Energy Correction = -542.98052 Hartree

E (Thermal) = 108.608 kcal/mol

Heat Capacity (Cv) = 45.568 cal/mol-kelvin

Entropy (S) = 122.231 cal/mol-kelvin

Opt Tab Data Section:

Step number = 1

Maximum force = 2.2e-05 Converged

RMS force = 5e-06 Converged

Maximum displacement = 0.002243 Not converged

RMS displacement = 0.000503 Converged

Predicted energy change = -1.083466e-08 Hartree

Calculation Type = SP

Calculation Method = RwB97XD

Basis Set = Gen

Charge = 0

Spin = Singlet

Solvation = scrf=(solvent=generic,read)

E(RwB97XD) = -543.22878 Hartree

RMS Gradient Norm = Hartree/Bohr

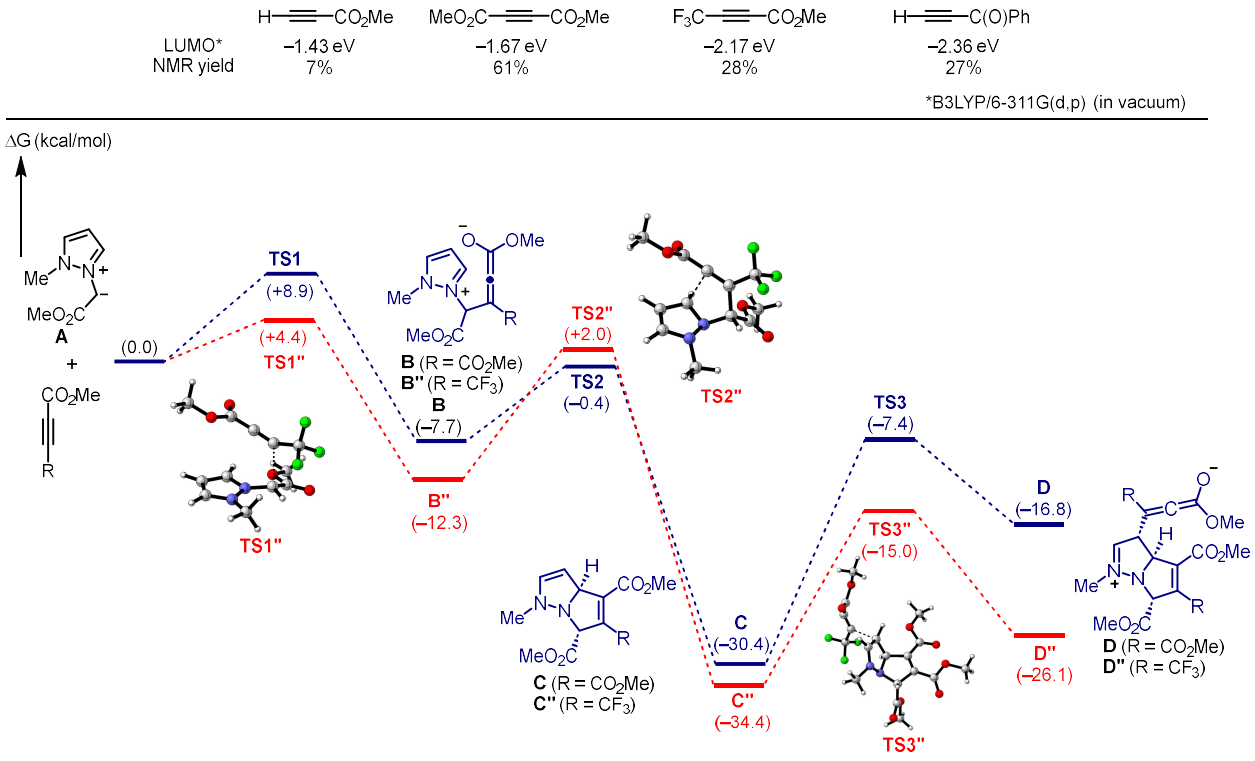
Imaginary Freq =

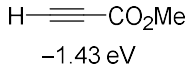
Dipole Moment = 2.8190513 Debye

Point Group = C1

Job cpu time: 0 days 0 hours 1 minutes 38.0 seconds.

Calculation of the LUMO energies of the corresponding alkynes was conducted, indicating that a lower LUMO energy does not necessarily correlate with the yield of the desired product. The calculations for the CF_3-substituted alkyne suggest that it is highly reactive in the initial step and prone to excessive electrophilic addition to the cycloadduct intermediate, while the cyclization step is relatively sluggish. Therefore, the decrease in yield is presumed to arise from decomposition of the unstable intermediate and/or formation of excess adducts.





Calculation Type = FREQ

Calculation Method = RB3LYP

Basis Set = 6-311G(d,p)

Charge = 0

Spin = Singlet

Solvation = None

E(RB3LYP) = -305.28954 Hartree

RMS Gradient Norm = 8.5953e-05 Hartree/Bohr

Imaginary Freq = 0

Dipole Moment = 1.764287 Debye

Polarizability (?) = 46.53 a.u.

Point Group = C1

Job cpu time: 0 days 0 hours 0 minutes 53.0 seconds.

Thermo Tab Data Section:

Imaginary Freq = 0

Temperature = 298.15 Kelvin

Pressure = 1 atm

Frequencies scaled by = 1

Electronic Energy (EE) = -305.28954 Hartree

Zero-point Energy Correction = 0.070978 Hartree

Thermal Correction to Energy = 0.07744 Hartree

Thermal Correction to Enthalpy = 0.078384 Hartree

Thermal Correction to Free Energy = 0.040847 Hartree

EE + Zero-point Energy = -305.21856 Hartree

EE + Thermal Energy Correction = -305.2121 Hartree

EE + Thermal Enthalpy Correction = -305.21115 Hartree

EE + Thermal Free Energy Correction = -305.24869 Hartree

E (Thermal) = 48.594 kcal/mol

Heat Capacity (Cv) = 21.302 cal/mol-kelvin

Entropy (S) = 79.003 cal/mol-kelvin

Opt Tab Data Section:

Step number = 1

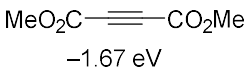
Maximum force = 0.000284 Converged

RMS force = 8.6e-05 Converged

Maximum displacement = 0.007536 Not converged

RMS displacement = 0.003136 Not converged

Predicted energy change = -1.843548e-06 Hartree



Calculation Type = FREQ

Calculation Method = RB3LYP

Basis Set = 6-311G(d,p)

Charge = 0

Spin = Singlet

Solvation = None

E(RB3LYP) = -533.22445 Hartree

RMS Gradient Norm = 1.0647e-05 Hartree/Bohr

Imaginary Freq = 0

Dipole Moment = 2.4726065 Debye

Polarizability (?) = 80.534667 a.u.

Point Group = C1

Job cpu time: 0 days 0 hours 1 minutes 47.0 seconds.

Thermo Tab Data Section:

Imaginary Freq = 0

Temperature = 298.15 Kelvin

Pressure = 1 atm

Frequencies scaled by = 1

Electronic Energy (EE) = -533.22445 Hartree

Zero-point Energy Correction = 0.114463 Hartree

Thermal Correction to Energy = 0.125491 Hartree

Thermal Correction to Enthalpy = 0.126435 Hartree

Thermal Correction to Free Energy = 0.075693 Hartree

EE + Zero-point Energy = -533.10999 Hartree

EE + Thermal Energy Correction = -533.09896 Hartree

EE + Thermal Enthalpy Correction = -533.09802 Hartree

EE + Thermal Free Energy Correction = -533.14876 Hartree

E (Thermal) = 78.747 kcal/mol

Heat Capacity (Cv) = 35.714 cal/mol-kelvin

Entropy (S) = 106.795 cal/mol-kelvin

Opt Tab Data Section:

Step number = 1

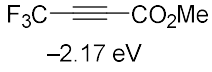
Maximum force = 4.1e-05 Converged

RMS force = 1.1e-05 Converged

Maximum displacement = 0.003525 Not converged

RMS displacement = 0.001271 Not converged

Predicted energy change = -3.084513e-08 Hartree



Calculation Type = FREQ

Calculation Method = RB3LYP

Basis Set = 6-311G(d,p)

Charge = 0

Spin = Singlet

Solvation = None

E(RB3LYP) = -642.41952 Hartree

RMS Gradient Norm = 7.721e-05 Hartree/Bohr

Imaginary Freq = 0

Dipole Moment = 3.1548654 Debye

Polarizability (?) = 60.069333 a.u.

Point Group = C1

Job cpu time: 0 days 0 hours 3 minutes 51.0 seconds.

Thermo Tab Data Section:

Imaginary Freq = 0

Temperature = 298.15 Kelvin

Pressure = 1 atm

Frequencies scaled by = 1

Electronic Energy (EE) = -642.41952 Hartree

Zero-point Energy Correction = 0.076507 Hartree

Thermal Correction to Energy = 0.086549 Hartree

Thermal Correction to Enthalpy = 0.087494 Hartree

Thermal Correction to Free Energy = 0.037152 Hartree

EE + Zero-point Energy = -642.34301 Hartree

EE + Thermal Energy Correction = -642.33297 Hartree

EE + Thermal Enthalpy Correction = -642.33202 Hartree

EE + Thermal Free Energy Correction = -642.38237 Hartree

E (Thermal) = 54.311 kcal/mol

Heat Capacity (Cv) = 32.985 cal/mol-kelvin

Entropy (S) = 105.953 cal/mol-kelvin

Opt Tab Data Section:

Step number = 1

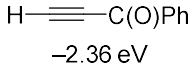
Maximum force = 0.000317 Converged

RMS force = 7.7e-05 Converged

Maximum displacement = 0.138468 Not converged

RMS displacement = 0.046302 Not converged

Predicted energy change = -1.149012e-06 Hartree



Calculation Type = FREQ

Calculation Method = RB3LYP

Basis Set = 6-311G(d,p)

Charge = 0

Spin = Singlet

Solvation = None

E(RB3LYP) = -421.82416 Hartree

RMS Gradient Norm = 0.000126929 Hartree/Bohr

Imaginary Freq = 0

Dipole Moment = 3.292449 Debye

Polarizability (?) = 94.977333 a.u.

Point Group = C1

Job cpu time: 0 days 0 hours 2 minutes 8.0 seconds.

Thermo Tab Data Section:

Imaginary Freq = 0

Temperature = 298.15 Kelvin

Pressure = 1 atm

Frequencies scaled by = 1

Electronic Energy (EE) = -421.82416 Hartree

Zero-point Energy Correction = 0.11888 Hartree

Thermal Correction to Energy = 0.127217 Hartree

Thermal Correction to Enthalpy = 0.128161 Hartree

Thermal Correction to Free Energy = 0.085137 Hartree

EE + Zero-point Energy = -421.70528 Hartree

EE + Thermal Energy Correction = -421.69695 Hartree

EE + Thermal Enthalpy Correction = -421.696 Hartree

EE + Thermal Free Energy Correction = -421.73903 Hartree

E (Thermal) = 79.83 kcal/mol

Heat Capacity (Cv) = 31.537 cal/mol-kelvin

Entropy (S) = 90.552 cal/mol-kelvin

Opt Tab Data Section:

Step number = 1

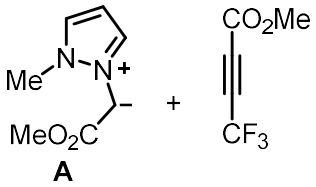
Maximum force = 0.000413 Converged

RMS force = 0.000127 Converged

Maximum displacement = 0.006303 Not converged

RMS displacement = 0.002544 Not converged

Predicted energy change = -4.120403e-06 Hartree



A

Calculation Type = FREQ

Calculation Method = RB3LYP

Basis Set = 6-31G(d,p)

Charge = 0

Spin = Singlet

Solvation = None

E(RB3LYP) = -1174.8983 Hartree

RMS Gradient Norm = 6.443e-06 Hartree/Bohr

Imaginary Freq = 0

Dipole Moment = 3.2790702 Debye

Polarizability (?) = 161.47667 a.u.

Point Group = C1

Job cpu time: 0 days 0 hours 19 minutes 20.0 seconds.

Thermo Tab Data Section:

Imaginary Freq = 0

Temperature = 298.15 Kelvin

Pressure = 1 atm

Frequencies scaled by = 1

Electronic Energy (EE) = -1174.8983 Hartree

Zero-point Energy Correction = 0.247831 Hartree

Thermal Correction to Energy = 0.270796 Hartree

Thermal Correction to Enthalpy = 0.271741 Hartree

Thermal Correction to Free Energy = 0.19076 Hartree

EE + Zero-point Energy = -1174.6505 Hartree

EE + Thermal Energy Correction = -1174.6275 Hartree

EE + Thermal Enthalpy Correction = -1174.6265 Hartree

EE + Thermal Free Energy Correction = -1174.7075 Hartree

E (Thermal) = 169.927 kcal/mol

Heat Capacity (Cv) = 78.71 cal/mol-kelvin

Entropy (S) = 170.438 cal/mol-kelvin

Opt Tab Data Section:

Step number = 1

Maximum force = 4.4e-05 Converged

RMS force = 6e-06 Converged

Maximum displacement = 0.062348 Not converged

RMS displacement = 0.019613 Not converged

Predicted energy change = -6.703367e-07 Hartree

Calculation Type = SP

Calculation Method = RB3LYP

Basis Set = 6-311G(d,p)

Charge = 0

Spin = Singlet

Solvation = scrf=(solvent=generic,read)

E(RB3LYP) = -1175.2248 Hartree

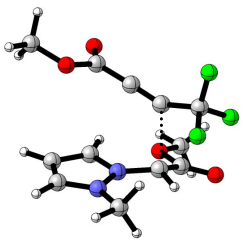
RMS Gradient Norm = Hartree/Bohr

Imaginary Freq =

Dipole Moment = 4.9700887 Debye

Point Group = C1

Job cpu time: 0 days 0 hours 4 minutes 40.0 seconds.



TS1"

Calculation Type = FREQ

Calculation Method = RB3LYP

Basis Set = 6-31G(d,p)

Charge = 0

Spin = Singlet

Solvation = None

E(RB3LYP) = -1174.8883 Hartree

RMS Gradient Norm = 2.96e-06 Hartree/Bohr

Imaginary Freq = 1

Dipole Moment = 8.1829227 Debye

Polarizability (?) = 170.70833 a.u.

Point Group = C1

Job cpu time: 0 days 0 hours 19 minutes 52.0 seconds.

Thermo Tab Data Section:

Imaginary Freq = 1

Temperature = 298.15 Kelvin

Pressure = 1 atm

Frequencies scaled by = 1

Electronic Energy (EE) = -1174.8883 Hartree

Zero-point Energy Correction = 0.24793 Hartree

Thermal Correction to Energy = 0.269737 Hartree

Thermal Correction to Enthalpy = 0.270682 Hartree

Thermal Correction to Free Energy = 0.194075 Hartree

EE + Zero-point Energy = -1174.6404 Hartree

EE + Thermal Energy Correction = -1174.6185 Hartree

EE + Thermal Enthalpy Correction = -1174.6176 Hartree

EE + Thermal Free Energy Correction = -1174.6942 Hartree

E (Thermal) = 169.263 kcal/mol

Heat Capacity (Cv) = 76.028 cal/mol-kelvin

Entropy (S) = 161.232 cal/mol-kelvin

Opt Tab Data Section:

Step number = 1

Maximum force = 6e-06 Converged

RMS force = 2e-06 Converged

Maximum displacement = 0.000652 Converged

RMS displacement = 0.000158 Converged

Predicted energy change = -6.237434e-09 Hartree

Calculation Type = SP

Calculation Method = RB3LYP

Basis Set = 6-311G(d,p)

Charge = 0

Spin = Singlet

Solvation = scrf=(solvent=generic,read)

E(RB3LYP) = -1175.2211 Hartree

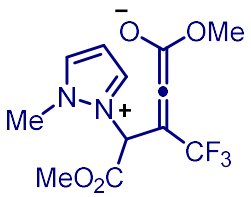
RMS Gradient Norm = Hartree/Bohr

Imaginary Freq =

Dipole Moment = 11.057389 Debye

Point Group = C1

Job cpu time: 0 days 0 hours 3 minutes 52.0 seconds.



B"

Calculation Type = FREQ

Calculation Method = RB3LYP

Basis Set = 6-31G(d,p)

Charge = 0

Spin = Singlet

Solvation = None

E(RB3LYP) = -1174.9092 Hartree

RMS Gradient Norm = 9.114e-06 Hartree/Bohr

Imaginary Freq = 0

Dipole Moment = 12.958134 Debye

Polarizability (?) = 156.521 a.u.

Point Group = C1

Job cpu time: 0 days 0 hours 18 minutes 6.0 seconds.

Thermo Tab Data Section:

Imaginary Freq = 0

Temperature = 298.15 Kelvin

Pressure = 1 atm

Frequencies scaled by = 1

Electronic Energy (EE) = -1174.9092 Hartree

Zero-point Energy Correction = 0.250874 Hartree

Thermal Correction to Energy = 0.272016 Hartree

Thermal Correction to Enthalpy = 0.27296 Hartree

Thermal Correction to Free Energy = 0.199751 Hartree

EE + Zero-point Energy = -1174.6584 Hartree

EE + Thermal Energy Correction = -1174.6372 Hartree

EE + Thermal Enthalpy Correction = -1174.6363 Hartree

EE + Thermal Free Energy Correction = -1174.7095 Hartree

E (Thermal) = 170.692 kcal/mol

Heat Capacity (Cv) = 75.085 cal/mol-kelvin

Entropy (S) = 154.081 cal/mol-kelvin

Opt Tab Data Section:

Step number = 1

Maximum force = 3.3e-05 Converged

RMS force = 5e-06 Converged

Maximum displacement = 0.0009 Converged

RMS displacement = 0.000235 Converged

Predicted energy change = -1.404972e-08 Hartree

Calculation Type = SP

Calculation Method = RB3LYP

Basis Set = 6-311G(d,p)

Charge = 0

Spin = Singlet

Solvation = scrf=(solvent=generic,read)

E(RB3LYP) = -1175.2534 Hartree

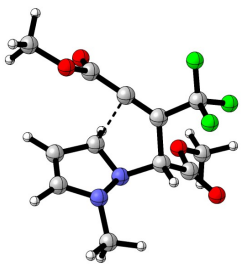
RMS Gradient Norm = Hartree/Bohr

Imaginary Freq =

Dipole Moment = 16.980161 Debye

Point Group = C1

Job cpu time: 0 days 0 hours 4 minutes 18.0 seconds.



TS2"

Calculation Type = FREQ

Calculation Method = RB3LYP

Basis Set = 6-31G(d,p)

Charge = 0

Spin = Singlet

Solvation = None

E(RB3LYP) = -1174.9056 Hartree

RMS Gradient Norm = 0.005310641 Hartree/Bohr

Imaginary Freq = 1

Dipole Moment = 5.563294 Debye

Polarizability (?) = 158.767 a.u.

Point Group = C1

Job cpu time: 0 days 0 hours 20 minutes 4.0 seconds.

Thermo Tab Data Section:

Imaginary Freq = 1

Temperature = 298.15 Kelvin

Pressure = 1 atm

Frequencies scaled by = 1

Electronic Energy (EE) = -1174.9056 Hartree

Zero-point Energy Correction = 0.24998 Hartree

Thermal Correction to Energy = 0.270583 Hartree

Thermal Correction to Enthalpy = 0.271527 Hartree

Thermal Correction to Free Energy = 0.198766 Hartree

EE + Zero-point Energy = -1174.6557 Hartree

EE + Thermal Energy Correction = -1174.6351 Hartree

EE + Thermal Enthalpy Correction = -1174.6341 Hartree

EE + Thermal Free Energy Correction = -1174.7069 Hartree

E (Thermal) = 169.793 kcal/mol

Heat Capacity (Cv) = 73.17 cal/mol-kelvin

Entropy (S) = 153.137 cal/mol-kelvin

Opt Tab Data Section:

Step number = 1

Maximum force = 0.000279 Converged

RMS force = 3.2e-05 Converged

Maximum displacement = 0.004449 Not converged

RMS displacement = 0.000571 Converged

Predicted energy change = 5.614685e-05 Hartree

Calculation Type = SP

Calculation Method = RB3LYP

Basis Set = 6-311G(d,p)

Charge = 0

Spin = Singlet

Solvation = scrf=(solvent=generic,read)

E(RB3LYP) = -1175.2296 Hartree

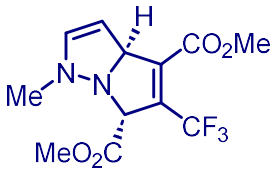
RMS Gradient Norm = Hartree/Bohr

Imaginary Freq =

Dipole Moment = 7.5636267 Debye

Point Group = C1

Job cpu time: 0 days 0 hours 4 minutes 45.0 seconds.



C''

Calculation Type = FREQ

Calculation Method = RB3LYP

Basis Set = 6-31G(d,p)

Charge = 0

Spin = Singlet

Solvation = None

E(RB3LYP) = -1174.9726 Hartree

RMS Gradient Norm = 4.831e-06 Hartree/Bohr

Imaginary Freq = 0

Dipole Moment = 1.4787245 Debye

Polarizability (?) = 147.69133 a.u.

Point Group = C1

Job cpu time: 0 days 0 hours 14 minutes 37.0 seconds.

Thermo Tab Data Section:

Imaginary Freq = 0

Temperature = 298.15 Kelvin

Pressure = 1 atm

Frequencies scaled by = 1

Electronic Energy (EE) = -1174.9726 Hartree

Zero-point Energy Correction = 0.252015 Hartree

Thermal Correction to Energy = 0.272552 Hartree

Thermal Correction to Enthalpy = 0.273496 Hartree

Thermal Correction to Free Energy = 0.20055 Hartree

EE + Zero-point Energy = -1174.7206 Hartree

EE + Thermal Energy Correction = -1174.7001 Hartree

EE + Thermal Enthalpy Correction = -1174.6991 Hartree

EE + Thermal Free Energy Correction = -1174.7721 Hartree

E (Thermal) = 171.029 kcal/mol

Heat Capacity (Cv) = 73.263 cal/mol-kelvin

Entropy (S) = 153.529 cal/mol-kelvin

Opt Tab Data Section:

Step number = 1

Maximum force = 1.2e-05 Converged

RMS force = 2e-06 Converged

Maximum displacement = 0.002422 Not converged

RMS displacement = 0.000487 Converged

Predicted energy change = -2.089327e-08 Hartree

Calculation Type = SP

Calculation Method = RB3LYP

Basis Set = 6-311G(d,p)

Charge = 0

Spin = Singlet

Solvation = scrf=(solvent=generic,read)

E(RB3LYP) = -1175.2894 Hartree

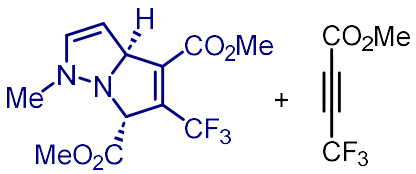
RMS Gradient Norm = Hartree/Bohr

Imaginary Freq =

Dipole Moment = 1.848597 Debye

Point Group = C1

Job cpu time: 0 days 0 hours 4 minutes 57.0 seconds.



C''

Calculation Type = FREQ

Calculation Method = RB3LYP

Basis Set = 6-31G(d,p)

Charge = 0

Spin = Singlet

Solvation = None

E(RB3LYP) = -1708.0552 Hartree

RMS Gradient Norm = 8.0278e-05 Hartree/Bohr

Imaginary Freq = 0

Dipole Moment = 6.6985067 Debye

Polarizability (?) = 224.556 a.u.

Point Group = C1

Job cpu time: 0 days 0 hours 48 minutes 8.0 seconds.

Thermo Tab Data Section:

Imaginary Freq = 0

Temperature = 298.15 Kelvin

Pressure = 1 atm

Frequencies scaled by = 1

Electronic Energy (EE) = -1708.0552 Hartree

Zero-point Energy Correction = 0.367658 Hartree

Thermal Correction to Energy = 0.401673 Hartree

Thermal Correction to Enthalpy = 0.402617 Hartree

Thermal Correction to Free Energy = 0.291826 Hartree

EE + Zero-point Energy = -1707.6876 Hartree

EE + Thermal Energy Correction = -1707.6535 Hartree

EE + Thermal Enthalpy Correction = -1707.6526 Hartree

EE + Thermal Free Energy Correction = -1707.7634 Hartree

E (Thermal) = 252.054 kcal/mol

Heat Capacity (Cv) = 114.777 cal/mol-kelvin

Entropy (S) = 233.179 cal/mol-kelvin

Opt Tab Data Section:

Step number = 1

Maximum force = 0.000245 Converged

RMS force = 8e-05 Converged

Maximum displacement = 0.017792 Not converged

RMS displacement = 0.004077 Not converged

Predicted energy change = -6.025117e-06 Hartree

Calculation Type = SP

Calculation Method = RB3LYP

Basis Set = 6-311G(d,p)

Charge = 0

Spin = Singlet

Solvation = scrf=(solvent=generic,read)

E(RB3LYP) = -1708.52 Hartree

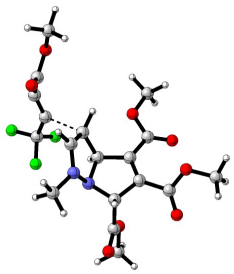
RMS Gradient Norm = Hartree/Bohr

Imaginary Freq =

Dipole Moment = 8.3497898 Debye

Point Group = C1

Job cpu time: 0 days 0 hours 6 minutes 52.0 seconds.



TS3''

Calculation Type = FREQ

Calculation Method = RB3LYP

Basis Set = 6-31G(d,p)

Charge = 0

Spin = Singlet

Solvation = None

E(RB3LYP) = -1708.0292 Hartree

RMS Gradient Norm = 6.421e-06 Hartree/Bohr

Imaginary Freq = 1

Dipole Moment = 4.1611915 Debye

Polarizability (?) = 252.90767 a.u.

Point Group = C1

Job cpu time: 0 days 0 hours 35 minutes 47.0 seconds.

Thermo Tab Data Section:

Imaginary Freq = 1

Temperature = 298.15 Kelvin

Pressure = 1 atm

Frequencies scaled by = 1

Electronic Energy (EE) = -1708.0292 Hartree

Zero-point Energy Correction = 0.368257 Hartree

Thermal Correction to Energy = 0.400714 Hartree

Thermal Correction to Enthalpy = 0.401658 Hartree

Thermal Correction to Free Energy = 0.299173 Hartree

EE + Zero-point Energy = -1707.6609 Hartree

EE + Thermal Energy Correction = -1707.6285 Hartree

EE + Thermal Enthalpy Correction = -1707.6275 Hartree

EE + Thermal Free Energy Correction = -1707.73 Hartree

E (Thermal) = 251.452 kcal/mol

Heat Capacity (Cv) = 112.007 cal/mol-kelvin

Entropy (S) = 215.698 cal/mol-kelvin

Opt Tab Data Section:

Step number = 1

Maximum force = 5.2e-05 Converged

RMS force = 6e-06 Converged

Maximum displacement = 0.002498 Not converged

RMS displacement = 0.000451 Converged

Predicted energy change = -1.88505e-08 Hartree

Calculation Type = SP

Calculation Method = RB3LYP

Basis Set = 6-311G(d,p)

Charge = 0

Spin = Singlet

Solvation = scrf=(solvent=generic,read)

E(RB3LYP) = -1708.4964 Hartree

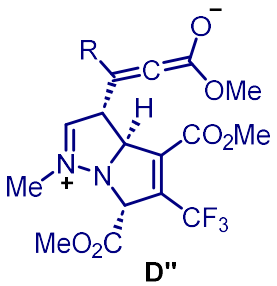
RMS Gradient Norm = Hartree/Bohr

Imaginary Freq =

Dipole Moment = 5.5650251 Debye

Point Group = C1

Job cpu time: 0 days 0 hours 12 minutes 17.0 seconds.



D"

Calculation Type = FREQ

Calculation Method = RB3LYP

Basis Set = 6-31G(d,p)

Charge = 0

Spin = Singlet

Solvation = None

E(RB3LYP) = -1708.0403 Hartree

RMS Gradient Norm = 2.628e-06 Hartree/Bohr

Imaginary Freq = 0

Dipole Moment = 8.6724788 Debye

Polarizability (?) = 244.01833 a.u.

Point Group = C1

Job cpu time: 0 days 0 hours 34 minutes 32.0 seconds.

Thermo Tab Data Section:

Imaginary Freq = 0

Temperature = 298.15 Kelvin

Pressure = 1 atm

Frequencies scaled by = 1

Electronic Energy (EE) = -1708.0403 Hartree

Zero-point Energy Correction = 0.370169 Hartree

Thermal Correction to Energy = 0.402477 Hartree

Thermal Correction to Enthalpy = 0.403422 Hartree

Thermal Correction to Free Energy = 0.301941 Hartree

EE + Zero-point Energy = -1707.6702 Hartree

EE + Thermal Energy Correction = -1707.6378 Hartree

EE + Thermal Enthalpy Correction = -1707.6369 Hartree

EE + Thermal Free Energy Correction = -1707.7384 Hartree

E (Thermal) = 252.558 kcal/mol

Heat Capacity (Cv) = 112.095 cal/mol-kelvin

Entropy (S) = 213.583 cal/mol-kelvin

Opt Tab Data Section:

Step number = 1

Maximum force = 7e-06 Converged

RMS force = 1e-06 Converged

Maximum displacement = 0.000809 Converged

RMS displacement = 0.000209 Converged

Predicted energy change = -3.103835e-09 Hartree

Calculation Type = SP

Calculation Method = RB3LYP

Basis Set = 6-311G(d,p)

Charge = 0

Spin = Singlet

Solvation = scrf=(solvent=generic,read)

E(RB3LYP) = -1708.5168 Hartree

RMS Gradient Norm = Hartree/Bohr

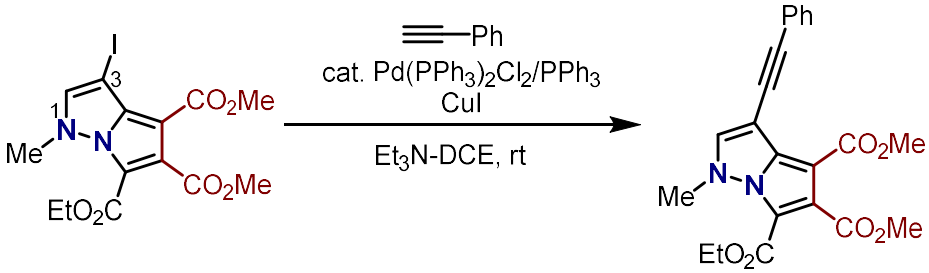
Imaginary Freq =

Dipole Moment = 11.436412 Debye

Point Group = C1

Job cpu time: 0 days 0 hours 12 minutes 52.0 seconds.

Transformation of 1*H*-pyrrolo[1,2-*b*]pyrazole derivatives



3d **8**: 50%

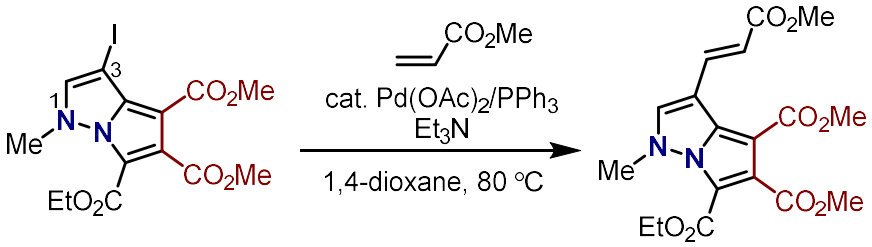
To the solution of **3d** (89.9 mg, 0.21 mmol) in DCE/Et_3N=1:1 (0.1 M, 2 mL) was added ethynylbenzene (53.7 mg, 0.53 mmol), $Pd(PPh_3)_2Cl_2$ (7.9 mg, 0.011 mmol), PPh_3 (5.2 mg, 0.020 mmol) and CuI (4.1 mg, 0.022 mmol). The mixture was stirred at room temperature for 24 h. Then, the resulting mixture was filtered through Celite® and the filtrate was evaporated. After diluted with EtOAc (10 mL) and water (10 mL), the mixture was transferred to a separatory funnel, where it was extracted with EtOAc three times. The organic extracts were combined, dried over Na_2SO_4, filtered and concentrated in vacuo using a rotatory evaporator. The residue was purified by silica gel column chromatography (Hexane/EtOAc) to afford alkyne **8**.

Yield: 42.2 mg, 50% (isolated yield); Brown solid; m.p.: 186.5-186.9 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55-7.51 (m, 2H, Ar*H*), 7.48 (s, 1H, Ar*H*), 7.38-7.32 (m, 3H, Ar*H*), 4.28 (q, *J* = 7.1 Hz, 2H, CO_2CH_2), 4.11 (s, 3H, NCH_3), 3.97 (s, 3H, CO_2CH_3), 3.83 (s, 3H, CO_2CH_3), 1.34 (t, *J* = 7.14 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8 (CO_2), 163.2 (CO_2), 158.7 (CO_2), 140.0 (Ar), 137.9 (Ar), 131.4 (Ar), 130.4 (Ar), 128.5 (Ar), 128.4 (Ar), 123.3 (Ar), 110.4 (Ar), 97.3 (C≡C), 94.1 (C≡C), 91.9 (Ar), 79.4 (Ar), 61.1 (CO_2CH_2), 52.8 (CO_2CH_3), 51.3 (CO_2CH_3), 40.6 (NCH_3), 14.1 (CH_2CH_3);

IR (KBr) *v* 2949, 2336, 2219, 1684, 1546, 1453, 1418, 1281, 1205, 749;

HRMS (FAB) m/z calcd for $C_{22}H_{20}N_2O_6$ $[M]^+$ 408.1321, found 408.1328.



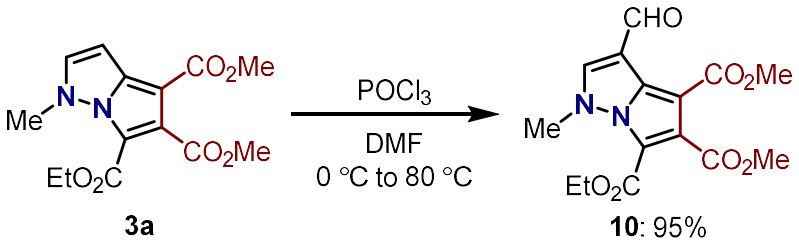
3d **9**: 60%

To the solution of **3d** (87.2 mg, 0.20 mmol) in 1,4-dioxane (0.13 M, 1.5 mL) were added methyl acrylate (86.4 mg, 1.0 mmol), $Pd(OAc)_2$ (2.3 mg, 0.010 mmol), PPh_3 (5.3 mg, 0.020 mmol) and Et_3N (6.6 mg, 0.65 mmol). The mixture was stirred at 80 °C for 24 h. After cooled to room temperature, the mixture was filtered through Celite® and the filtrate was evaporated. After diluted with EtOAc and water, the mixture was transferred to a separatory funnel, where it was extracted with EtOAc three times. The organic extracts were combined, dried over Na_2SO_4, filtered and concentrated in vacuo using a rotatory evaporator. The residue was purified by silica gel column chromatography (Hexane/EtOAc) to afford alkene **9**.

Yield: 45.9 mg, 60% (isolated yield); Brown solid; m.p.: 187.8-189.1°C;

^{1}H NMR (400 MHz, $CDCl_3$) 8.36 (dd, J = 16.2, 0.47 Hz, 1H, ArC*H*), 7.58 (s, 1H, Ar*H*), 6.14 (d, J = 16.2 Hz, 1H, CH=C*H*), 4.26 (q, J = 7.1 Hz, 2H, CO_2CH_2), 4.15 (s, 3H, NCH_3), 3.94 (s, 3H, CO_2CH_3), 3.86 (s, 3H, CO_2CH_3), 3.78 (s, 3H, CO_2CH_3), 1.32 (t, J = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3 (CO_2), 165.9 (CO_2), 163.0 (CO_2), 158.7 (CO_2), 137.8 (Ar), 135.2 (Ar), 134.0 (Ar), 130.7 (Ar), 116.6 (Ar), 110.2 (Ar), 107.7 (CH=*C*H), 97.0 (CH=*C*H), 61.2 (CO_2CH_2), 52.8 (CO_2CH_3), 51.8 (CO_2CH_3), 51.6 (CO_2CH_3), 40.9 (NCH_3), 14.2 (CH_2CH_3);

HRMS (FAB) m/z calcd for $C_{18}H_{20}N_2O_8$ $[M]^+$ 392.1220, found 392.1222



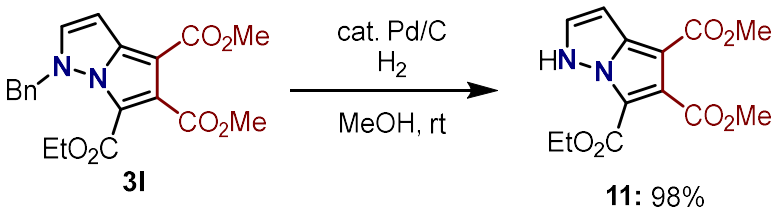
3a **10**: 95%

Phosphorus oxychloride (82.3 mg, 0.54 mmol) was cooled to 0 °C and then it was added dropwise to DMF (0.1 M, 1 mL) at 0 °C. The mixture was stirred for 30 minutes and then **3a** (30.3 mg, 0.098 mmol) was added at 0 °C. Then, the mixture was heated to 80 °C and stirred for 24 h. After cooled to room temperature, the resulting mixture was then quenched by sat. aq. Na_2CO_3 and diluted with EtOAc. The mixture was extracted with EtOAc three times. The organic extracts were combined, dried over Na_2SO_4, filtered and concentrated in vacuo using a rotatory evaporator. The residue was purified by silica gel column chromatography (Hexane/EtOAc) to afford aldehyde **10**.

Yield: 31.6 mg, 95% (isolated yield); White solid; m.p.: 168.5-170.3°C;

^{1}H NMR (400 MHz, $CDCl_3$): δ 10.5 (s, 1H, C*H*O), 7.96 (s, 1H, Ar*H*), 4.30 (s, 3H, NCH_3), 4.29 (q, 2H, J = 7.1 Hz, CO_2CH_2), 3.96 (s, 3H, CO_2CH_3), 3.86 (s, 3H, CO_2CH_3), 1.35 (t, 3H, J = 7.1 Hz, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.3 (*C*HO), 165.5 (CO_2), 163.2 (CO_2), 158.7 (CO_2), 137.7 (Ar), 137.2 (Ar), 130.6 (Ar), 111.5 (Ar), 110.5 (Ar), 96.8 (Ar), 61.4 (CO_2CH_2), 52.9 (CO_2CH_3), 51.8 (CO_2CH_3), 41.5 (NCH_3), 14.2 (CH_2CH_3);

HRMS (FAB) m/z calcd for $C_{15}H_{16}N_2O_7$ $[M^+H]^+$ 337.1035, found 337.1054.



3l **11:** 98%

To the solution of **3l** (36.2 mg, 0.094 mmol) in MeOH (0.05 M, 2 mL) was added Pd/C (Pd 10%, 5.9 mg, 0.0055 mmol) under argon. The mixture was purged with hydrogen three times. After stirred at room temperature for 2 hours, the mixture was filtered by Celite®. The filtrate was evaporated and the residue was purified by silica gel chromatography (Hexane/EtOAc) to afford deprotected product **11**.

Yield: 27.1 mg, 98% (isolated yield); White solid; m.p.: 179.2-180.1 °C;

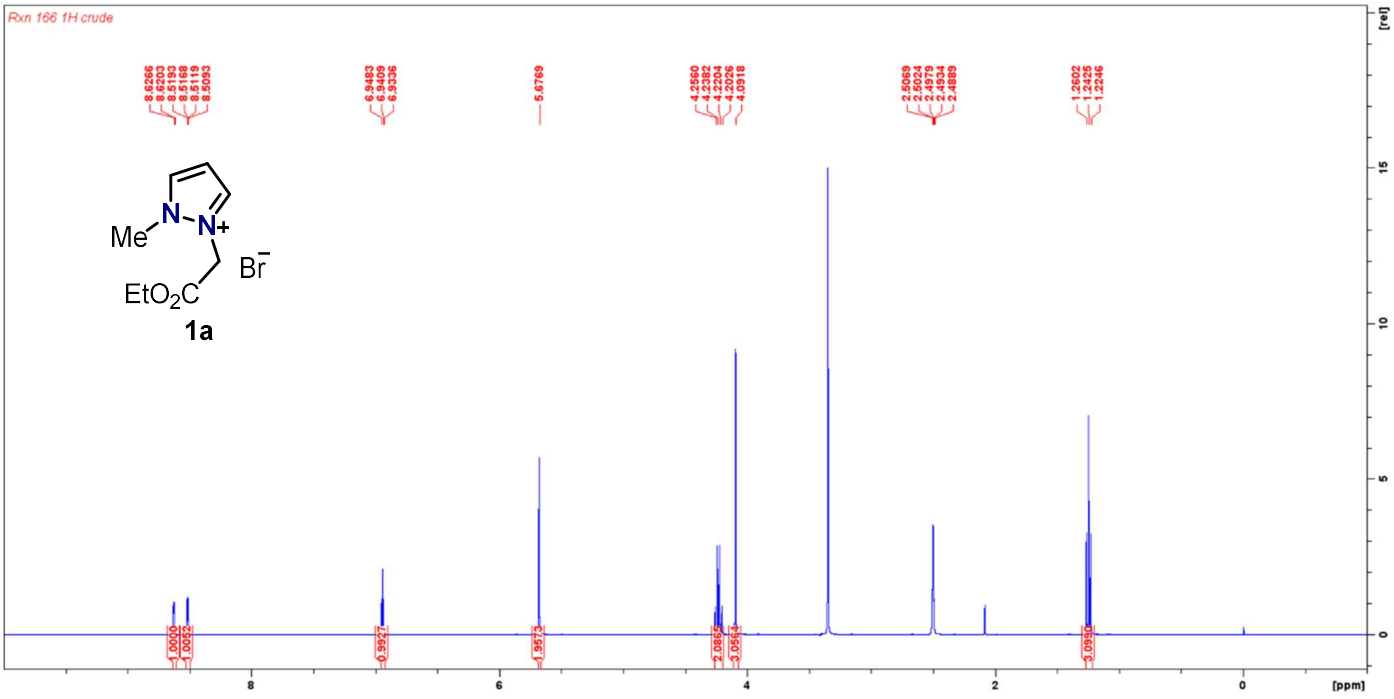
^{1}H NMR (400 MHz, $CDCl_3$): δ 11.24 (br, 1H, N*H*), 7.48 (d, *J* = 3.5 Hz, 1H, Ar*H*), 6.47 (d, *J* = 3.5 Hz, 1H, Ar*H*), 4.32 (q, *J* = 7.1 Hz, 2H, CO_2CH_2), 3.96 (s, 3H, CO_2CH_3), 3.84 (s, 3H, CO_2CH_3), 1.35 (t, *J* = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8 (CO_2), 163.7 (CO_2), 160.7 (CO_2), 137.3 (Ar), 129.4 (Ar), 126.2 (Ar), 107.8 (Ar), 96.5 (Ar), 95.9 (Ar), 61.1 (CO_2CH_2), 52.9 (CO_2CH_3), 51.5 (CO_2CH_3), 14.3 (CH_2CH_3);

IR (KBr) *v* 3260, 2957, 2360, 1743, 1708, 1663, 1250, 1156, 1021, 629;

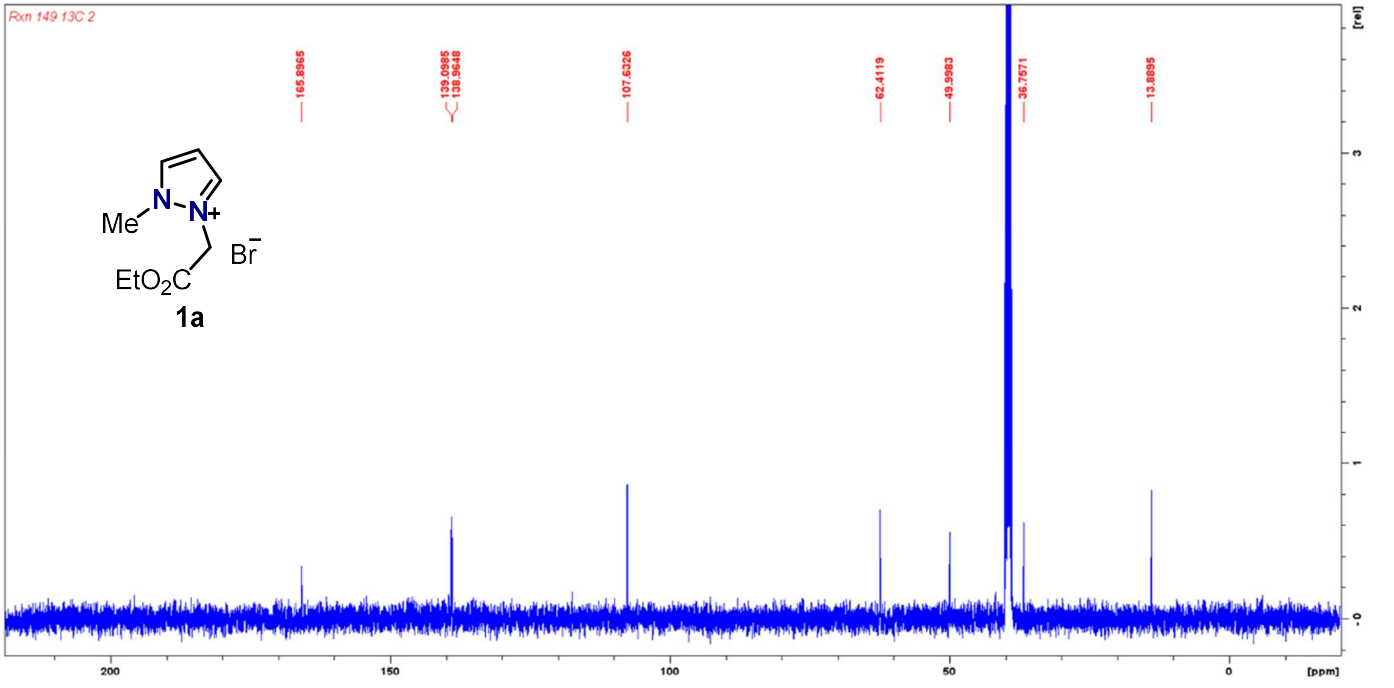
HRMS (FAB) m/z calcd for $C_{13}H_{14}N2O_6$ $[M+H]^+$ 295.0930, found 295.0925.

NMR spectra

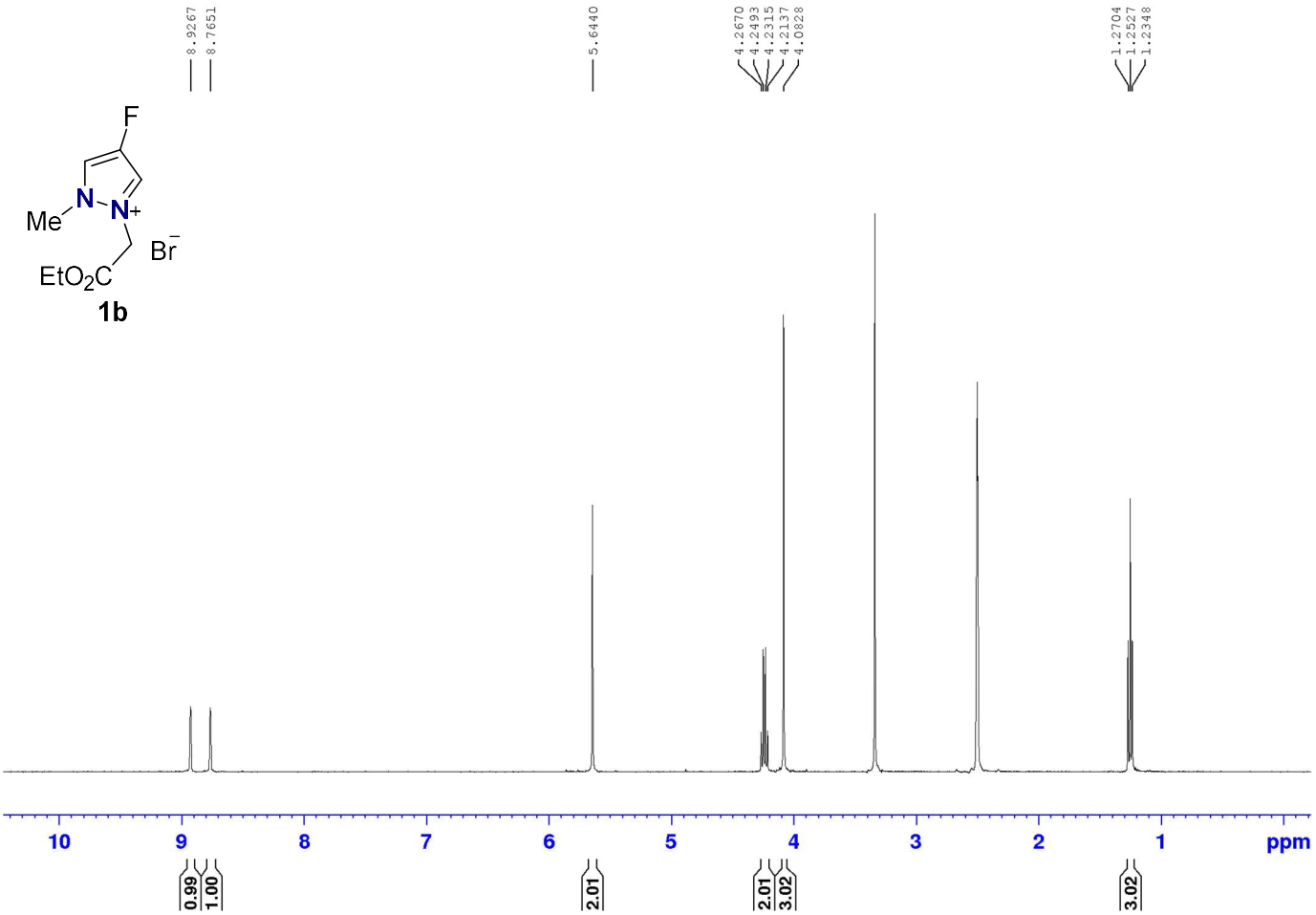
^{1}H NMR (400 MHz, DMSO-d6)



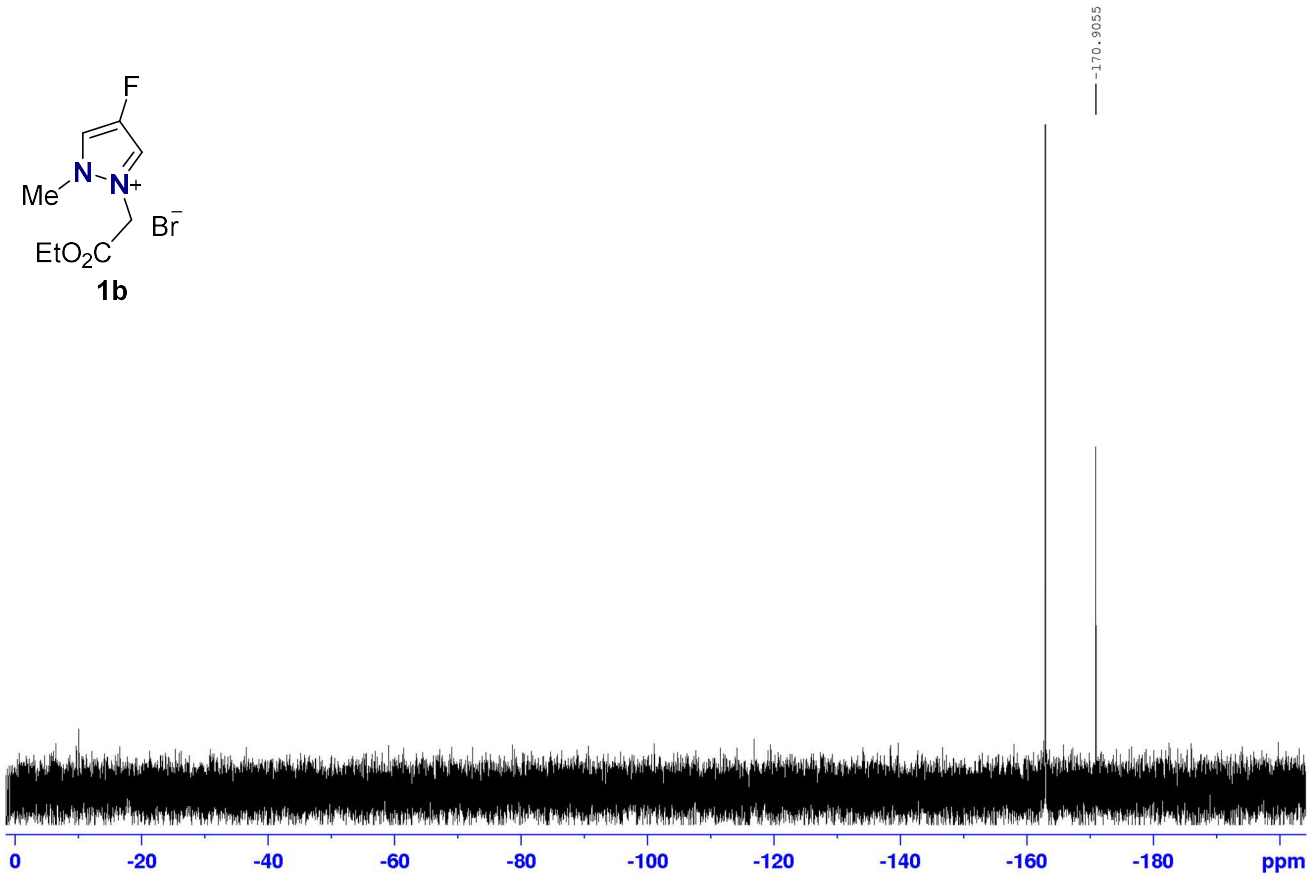
^{13}C NMR (100 MHz, DMSO-d6)



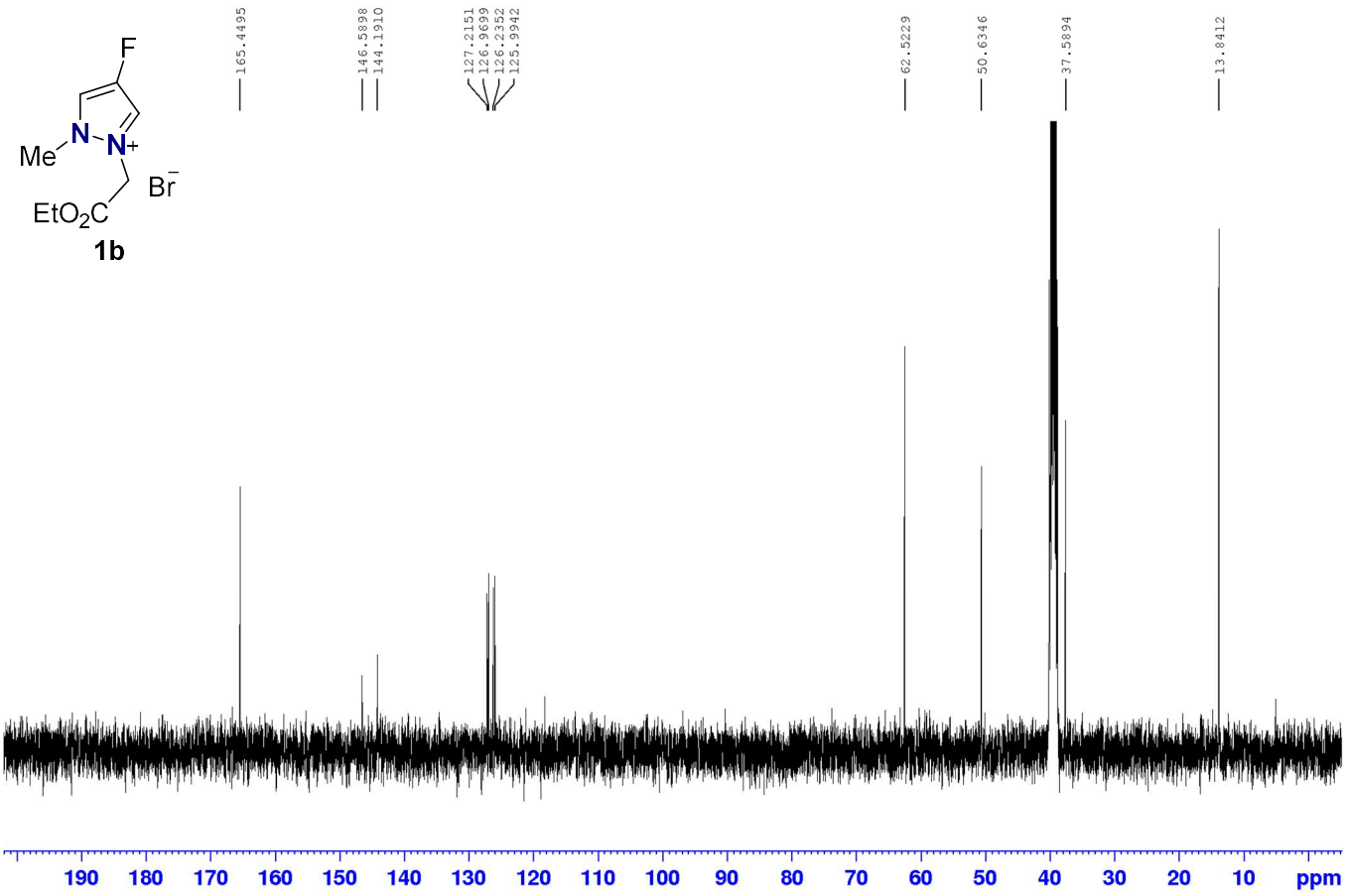
^{1}H NMR (400 MHz, DMSO-d6)



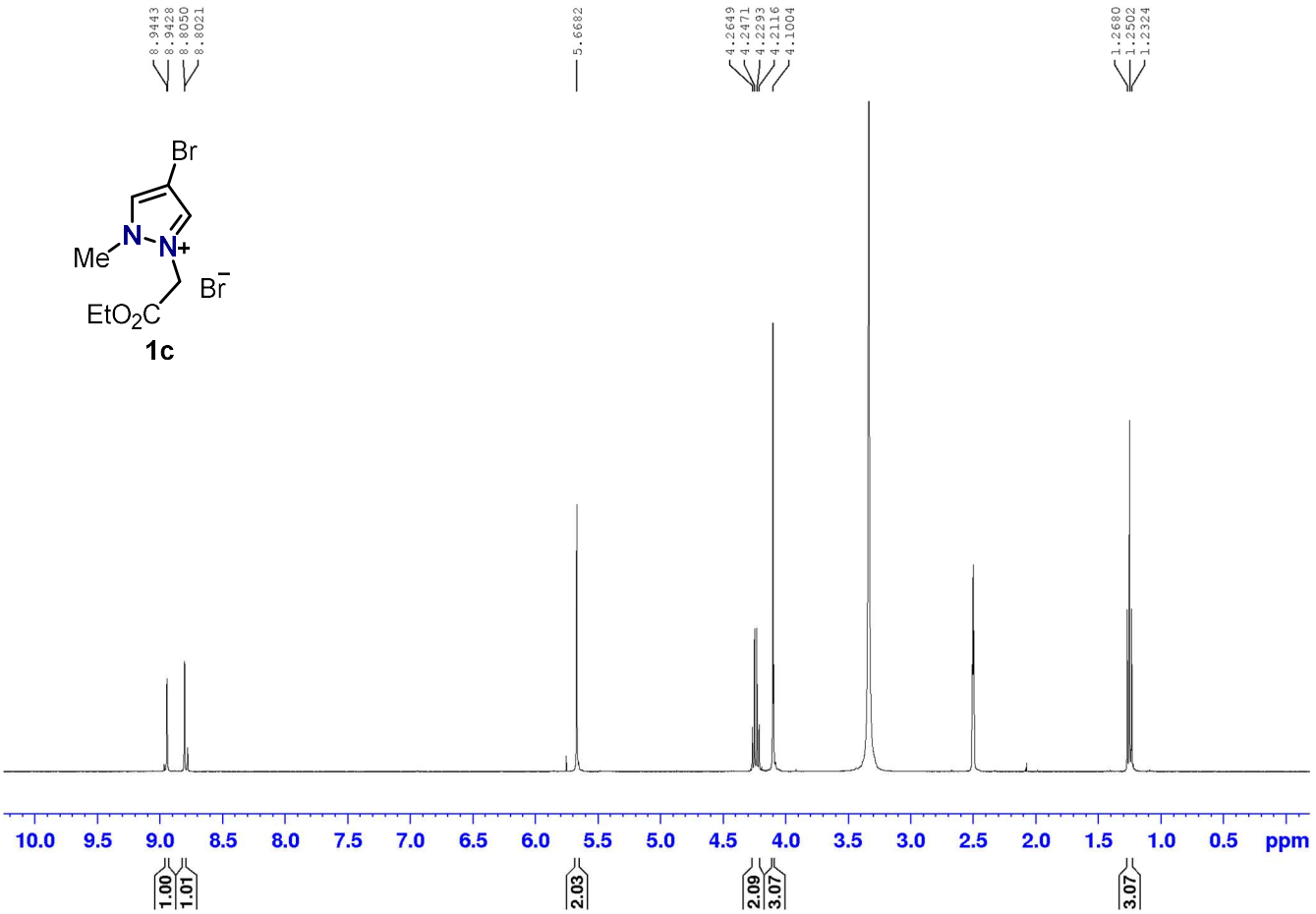
^{19}F NMR (376 MHz, DMSO-d6, C_6F_6)



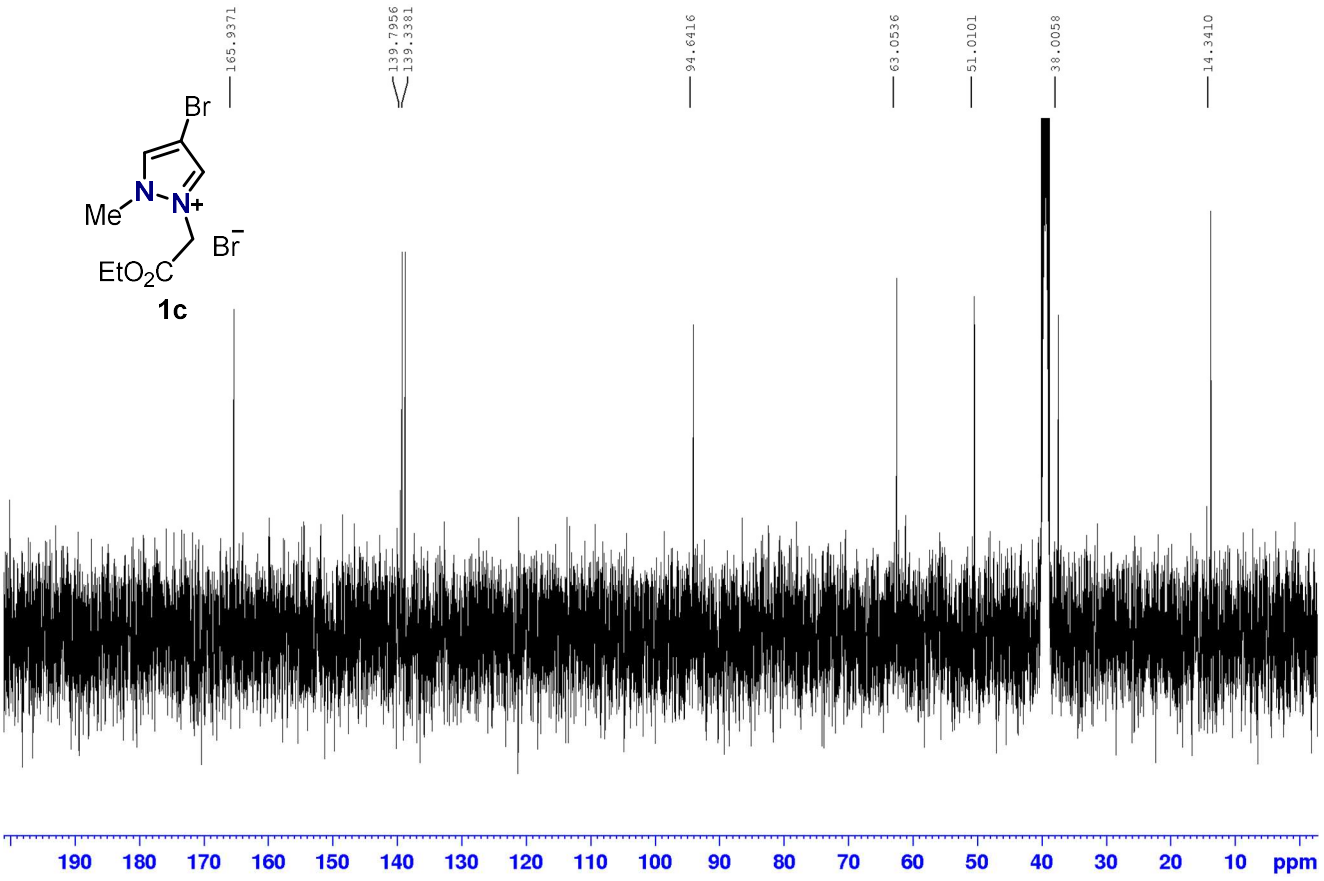
^{13}C NMR (100 MHz, DMSO-d6)



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



^{13}C NMR (100 MHz, DMSO-d6)



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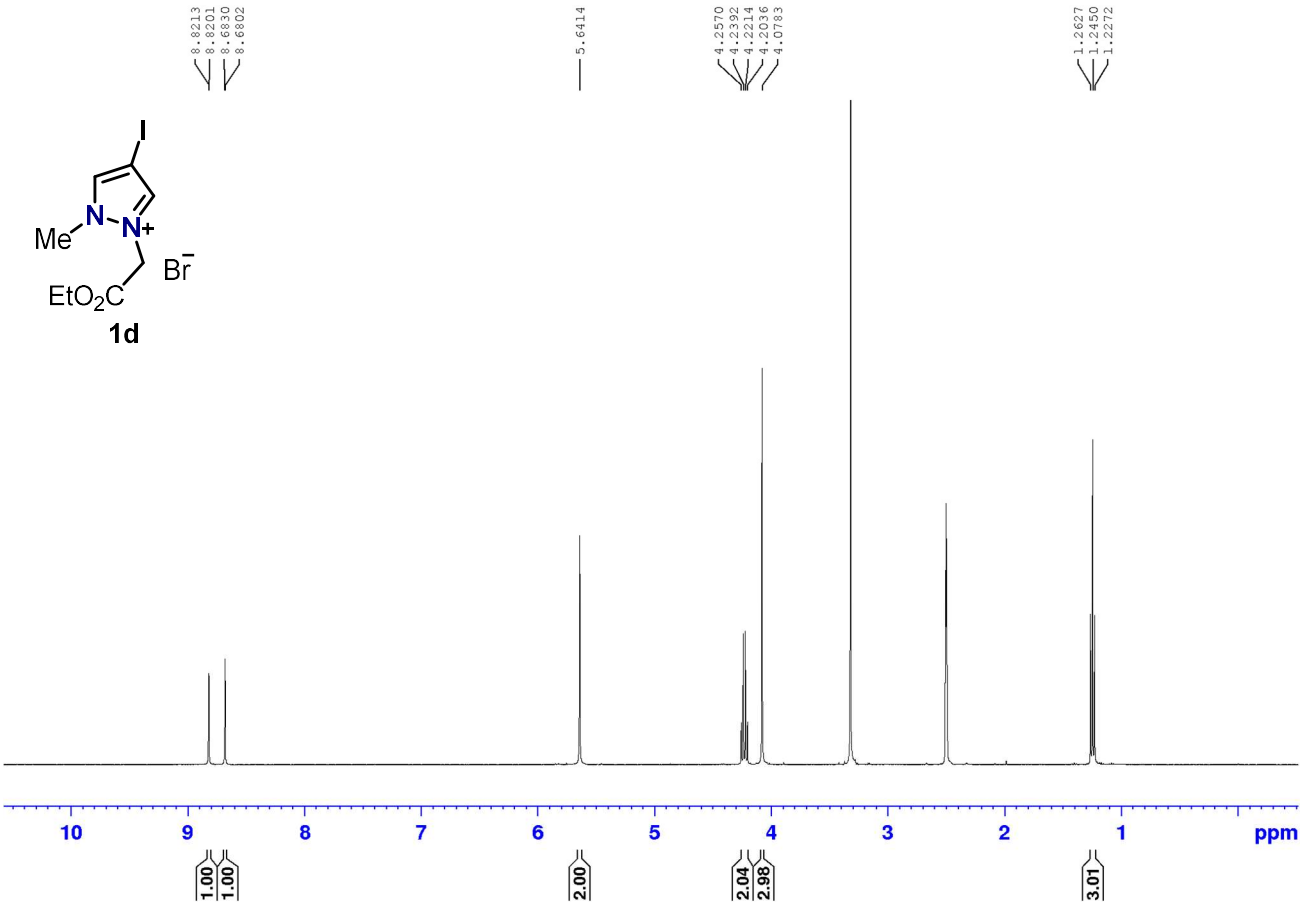
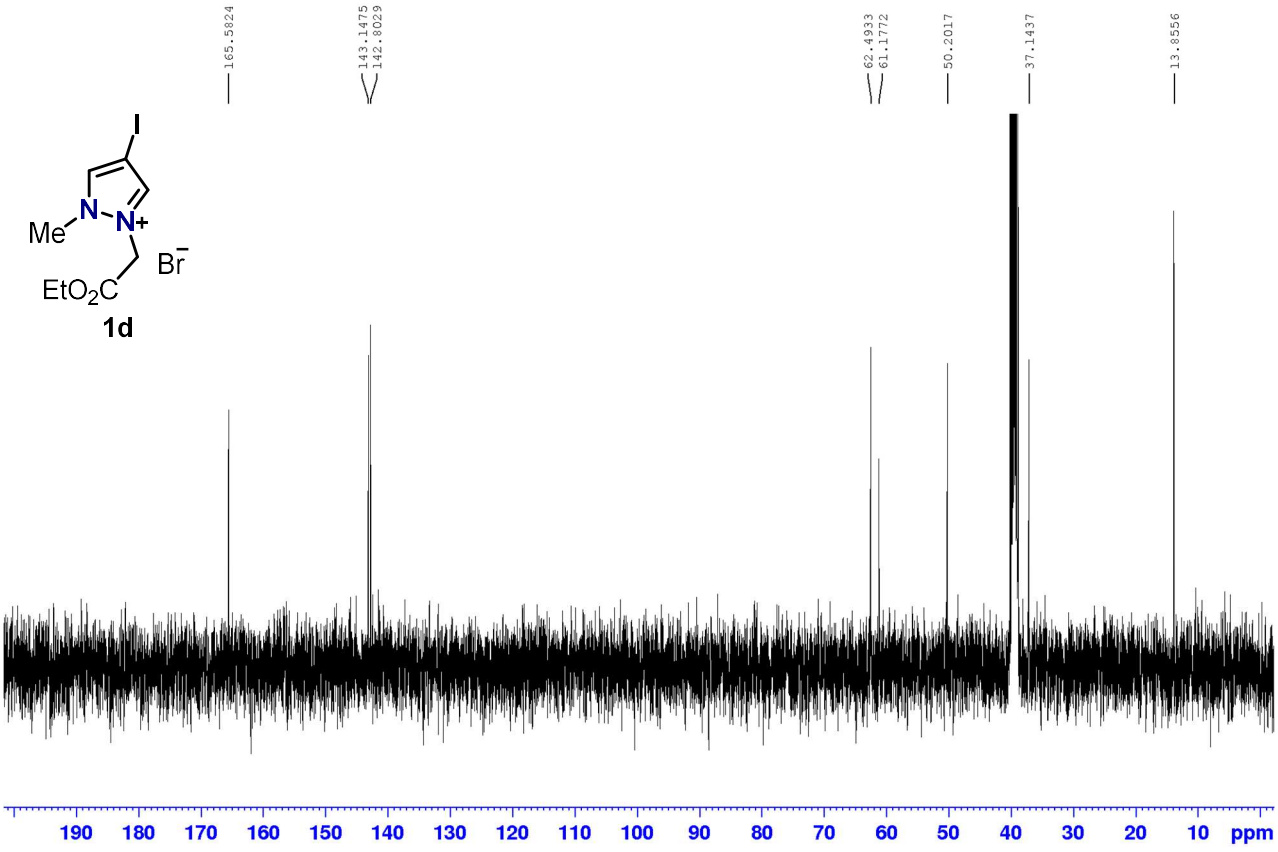


^{13}C NMR (100 MHz, DMSO-d6)



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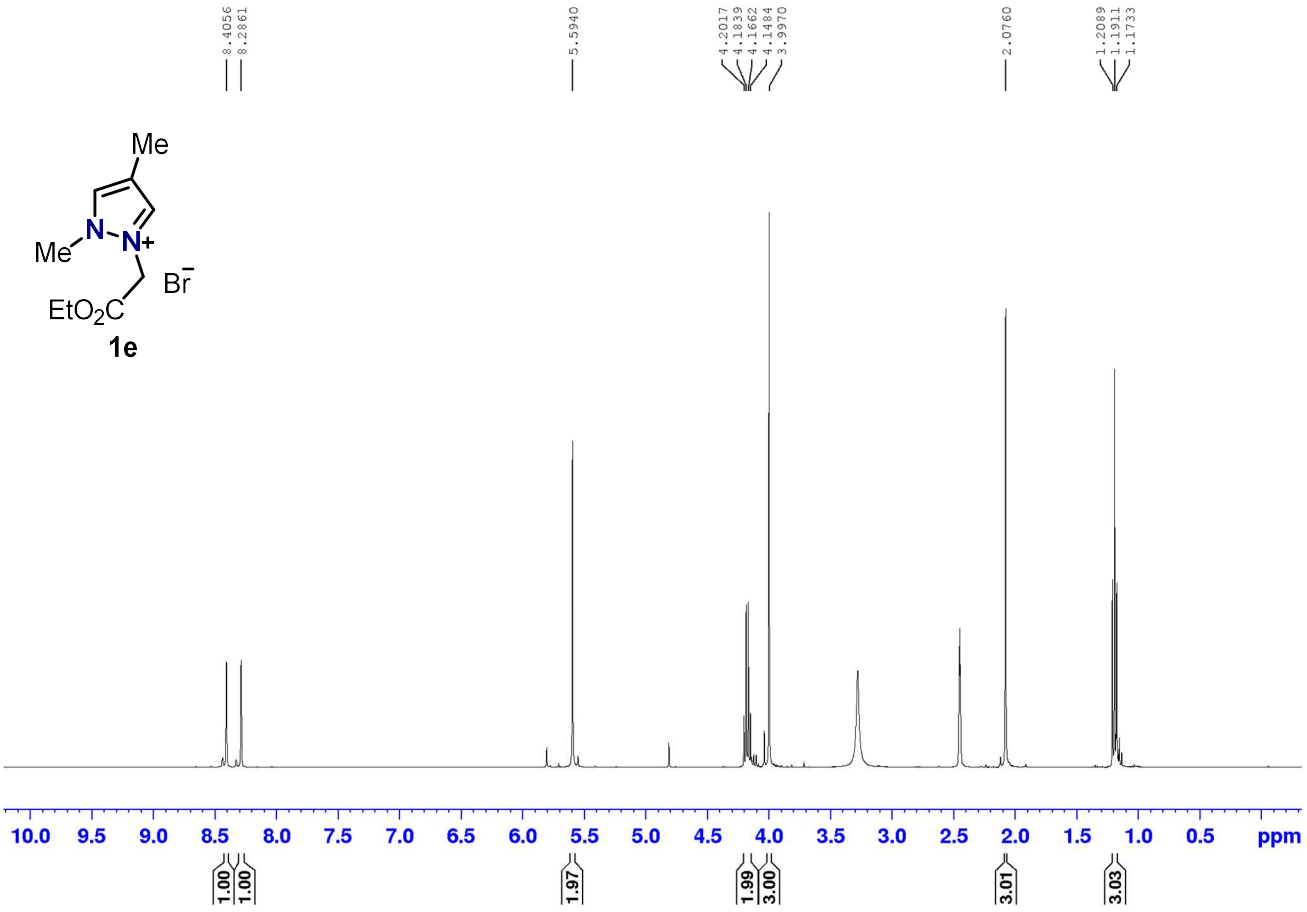
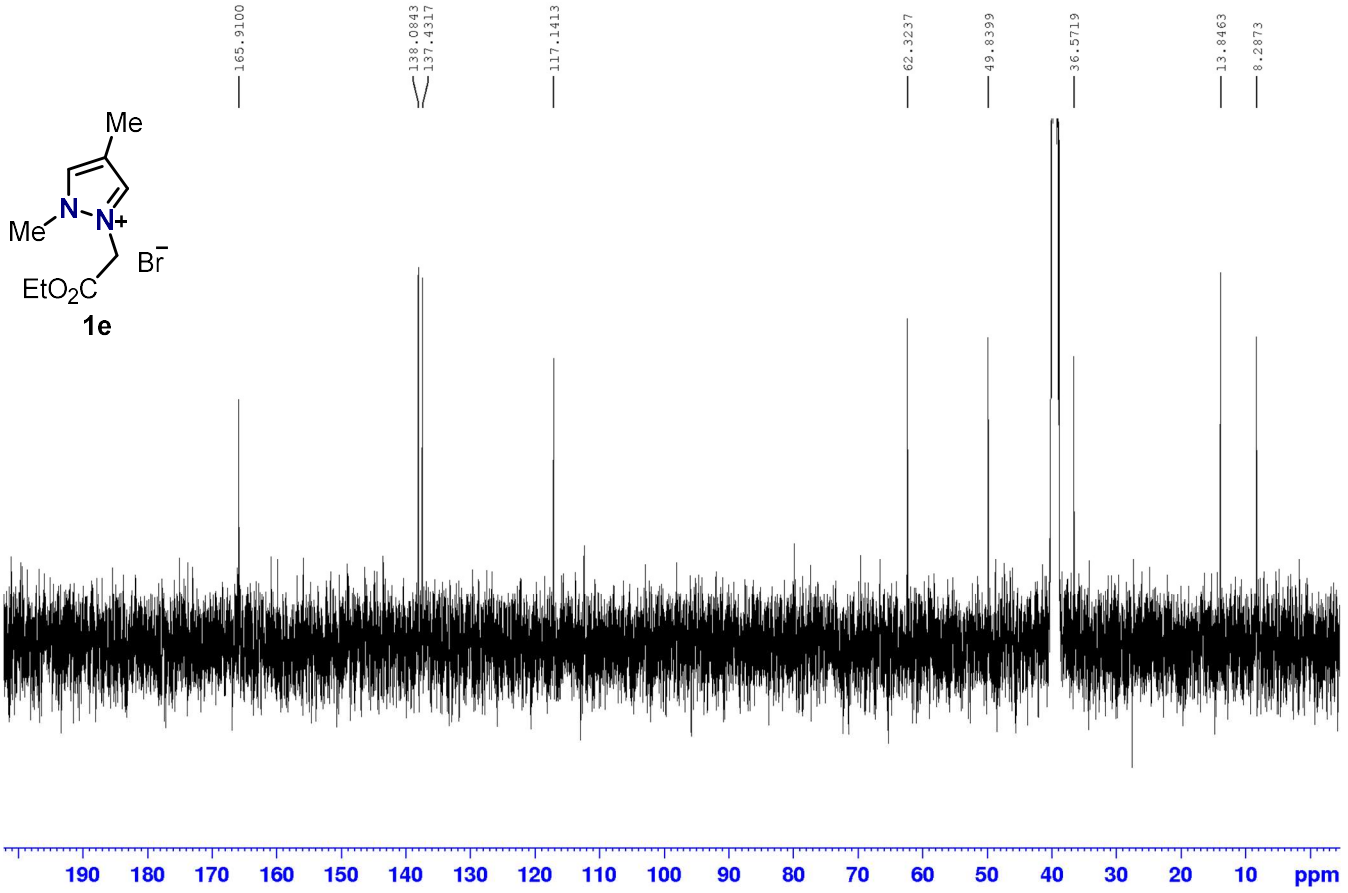
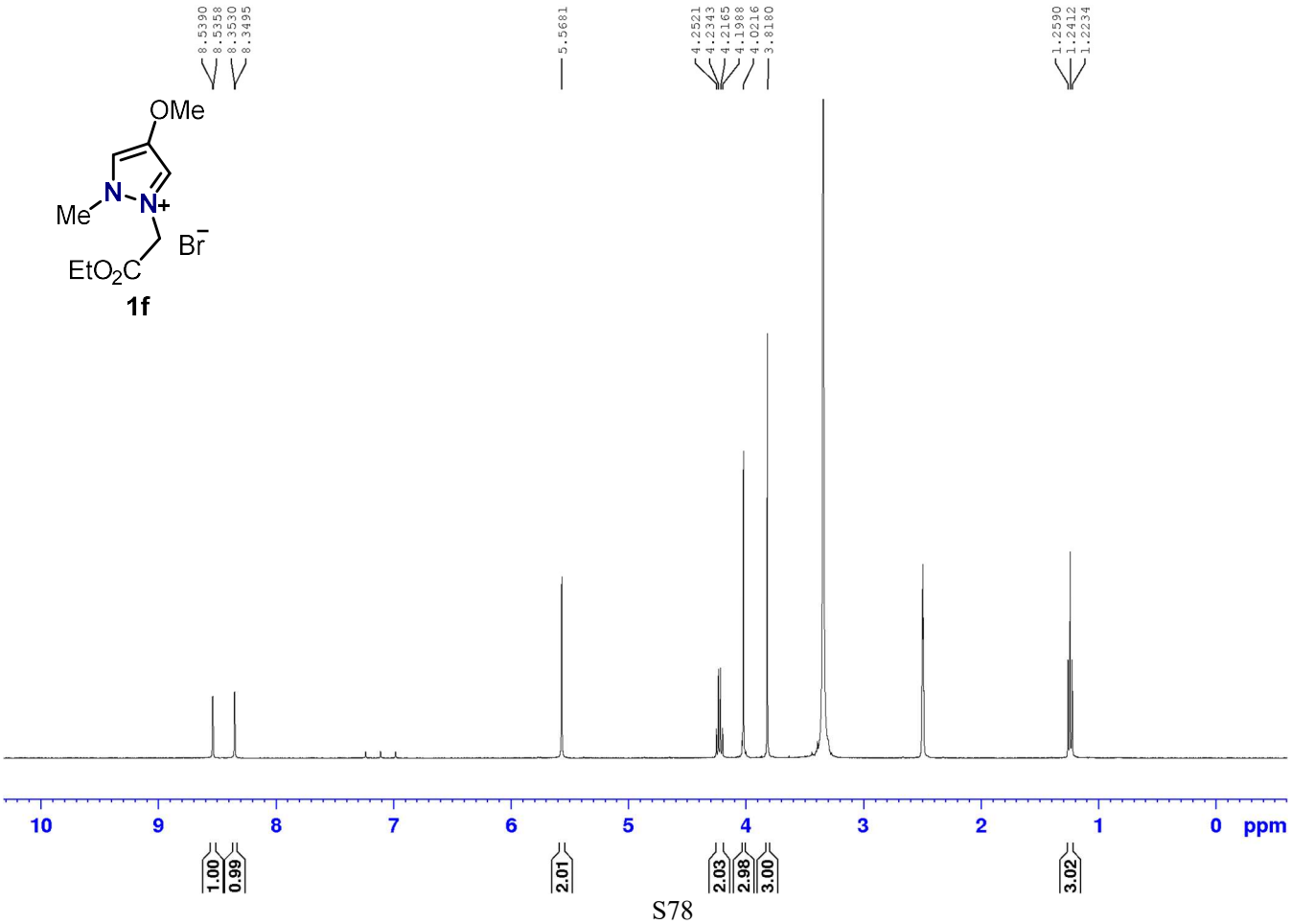


^{13}C NMR (100 MHz, DMSO-d6)



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



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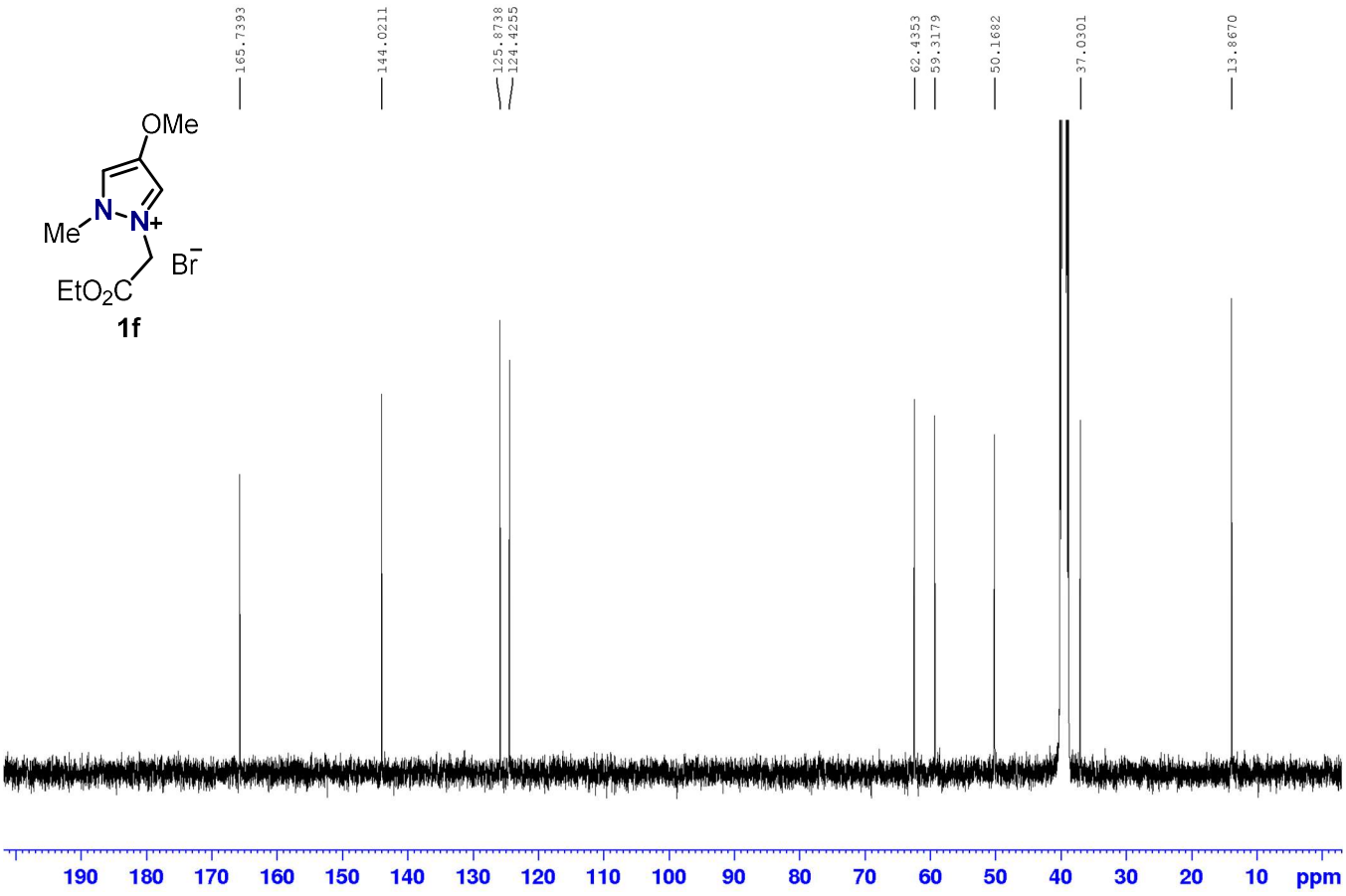
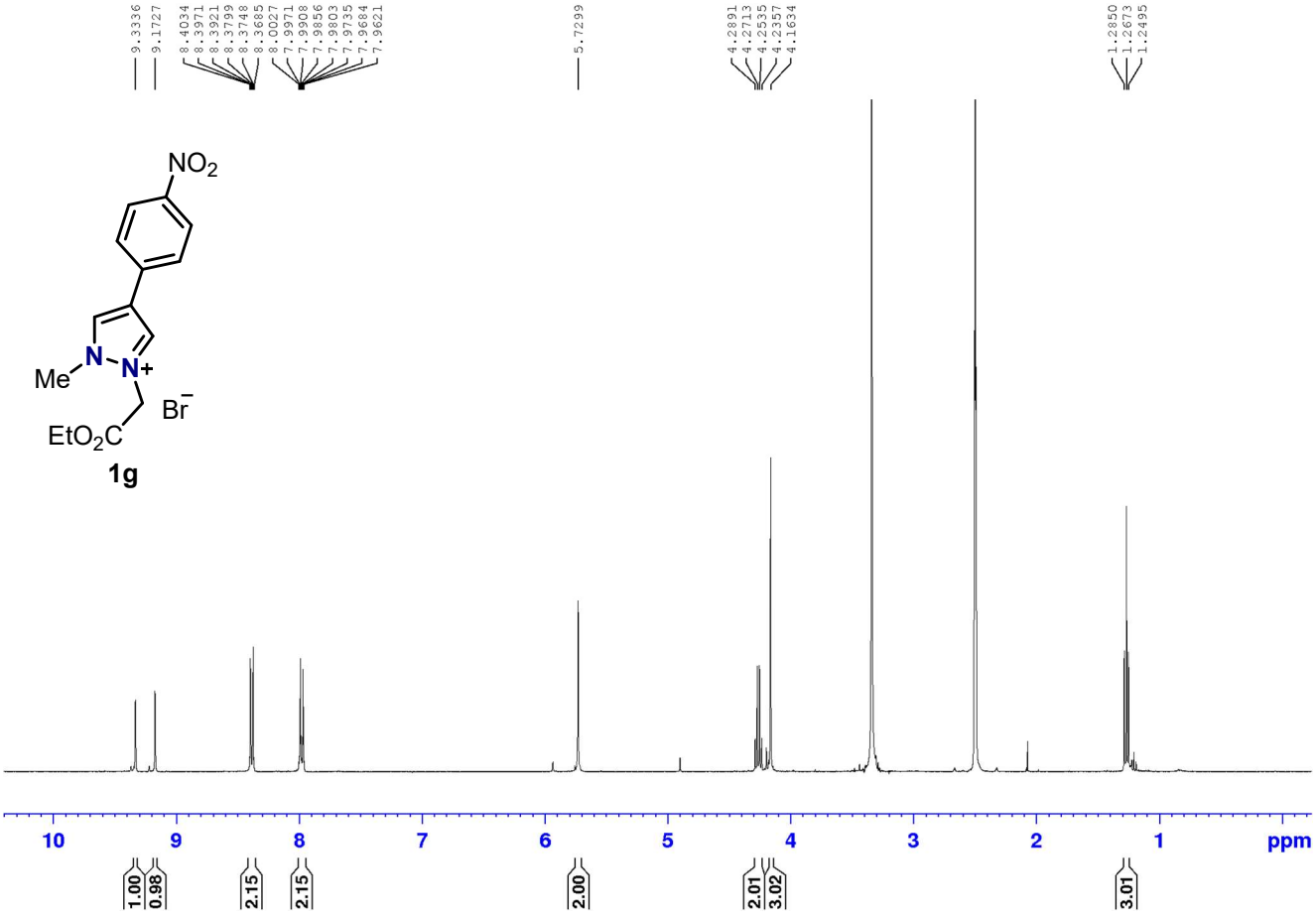


^{1}H NMR (400 MHz, DMSO-d6)



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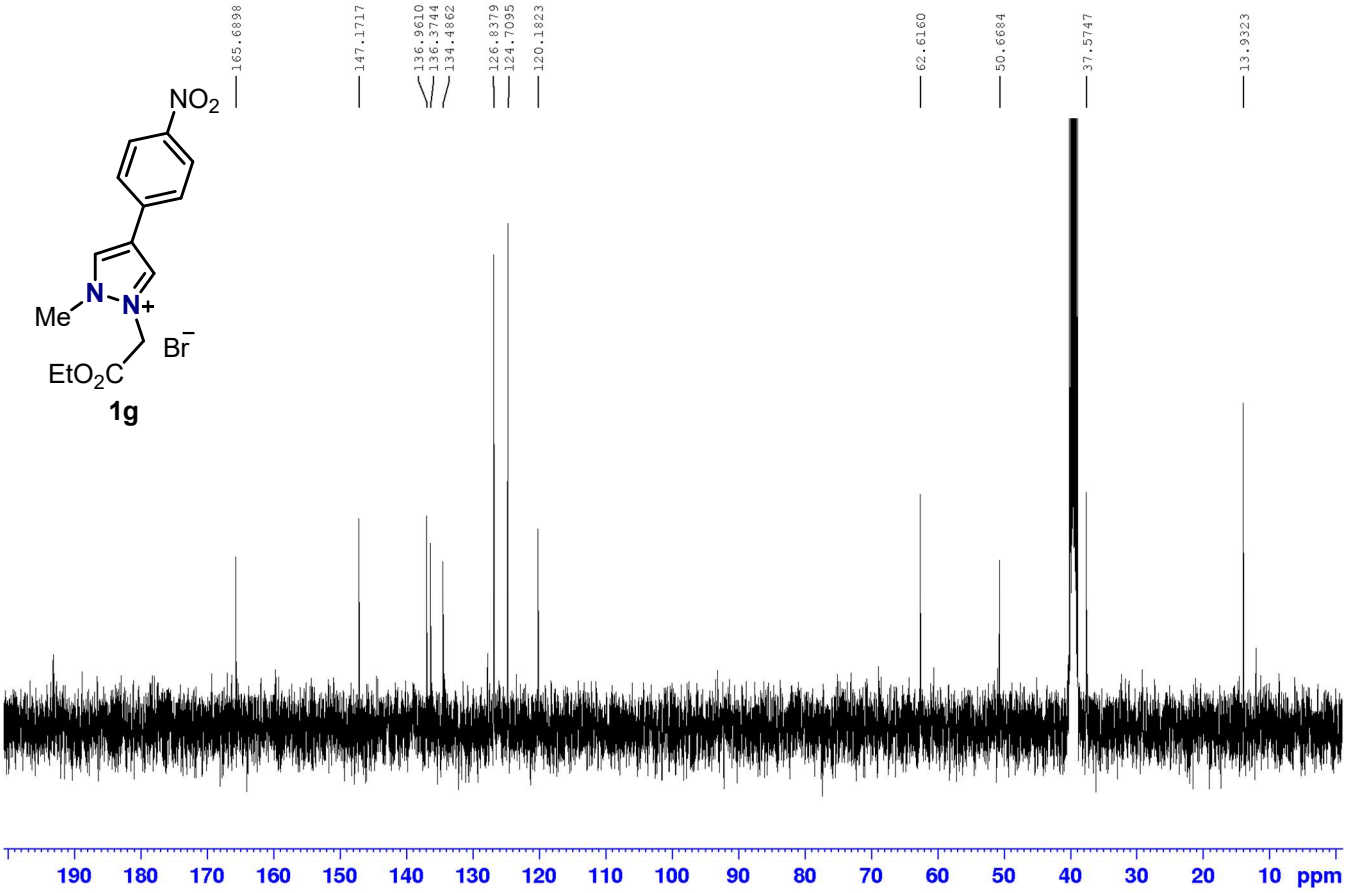

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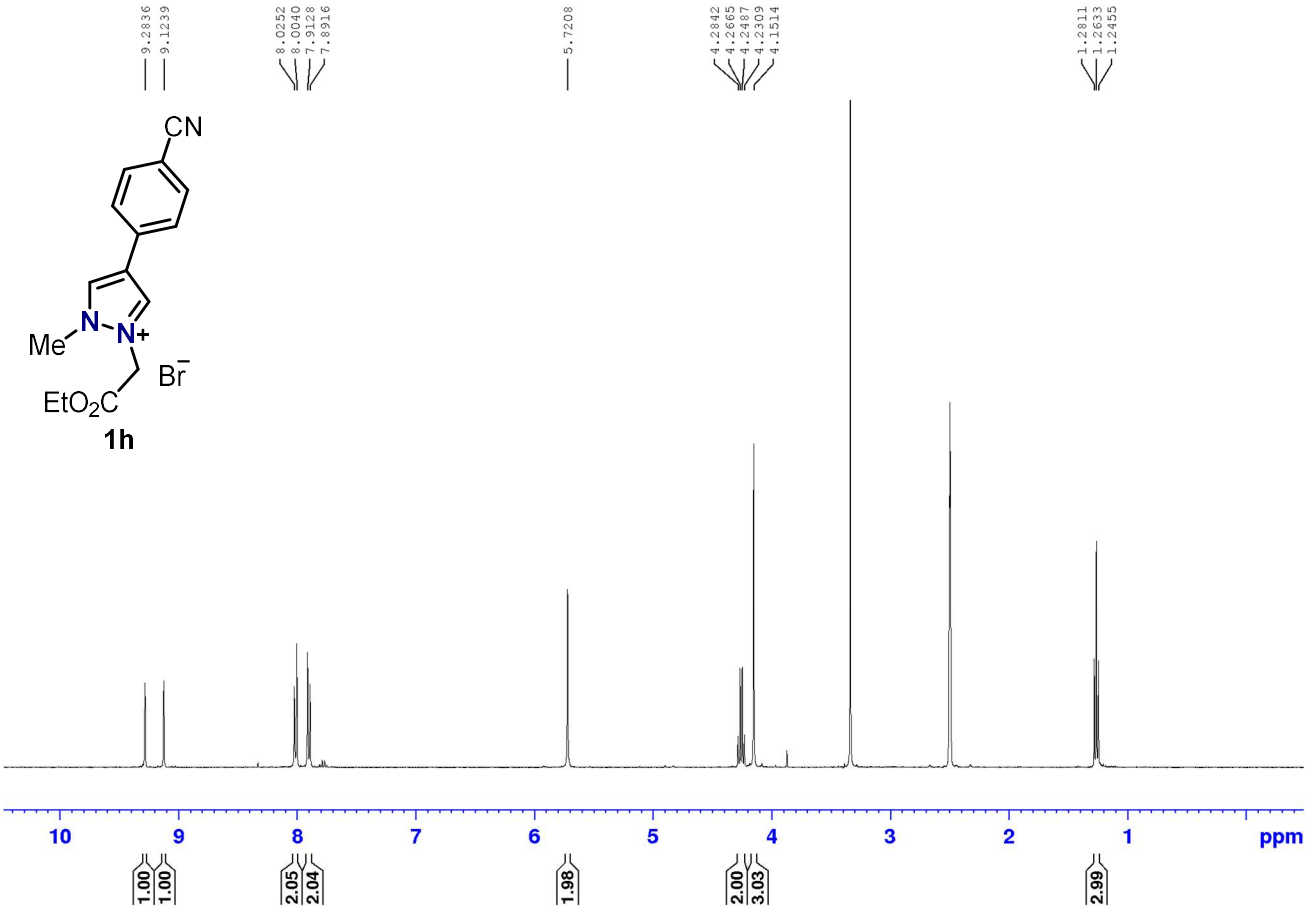

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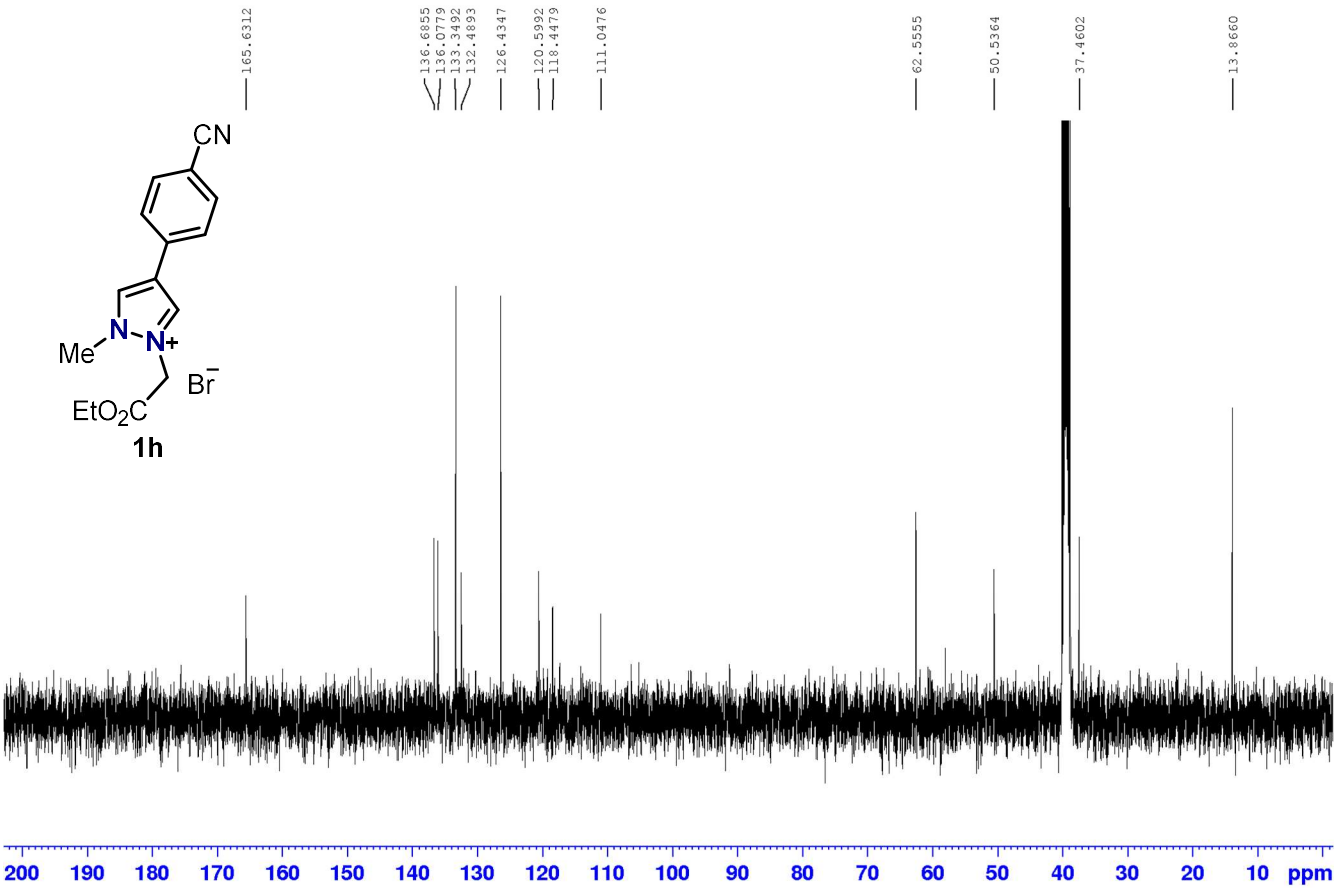
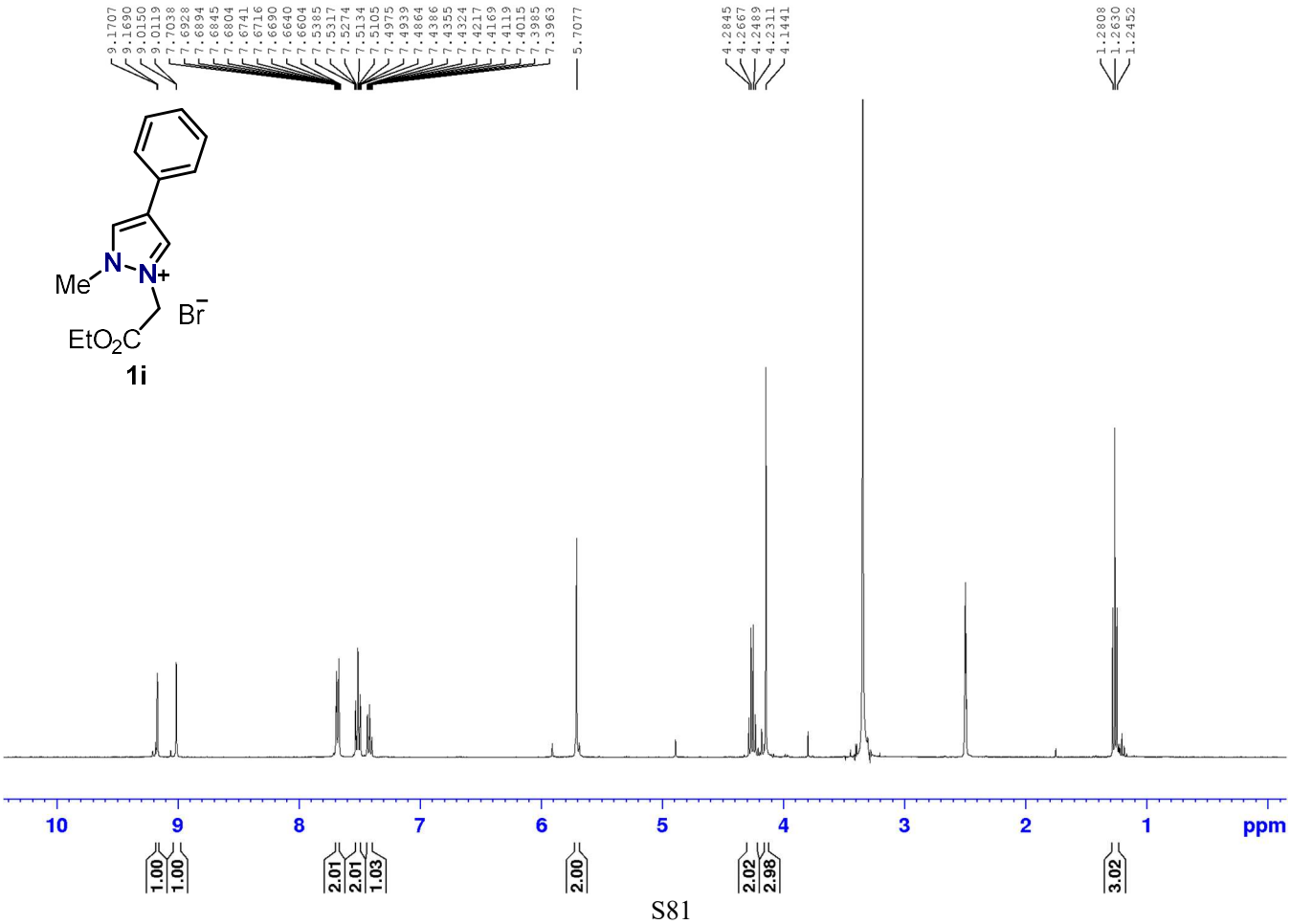
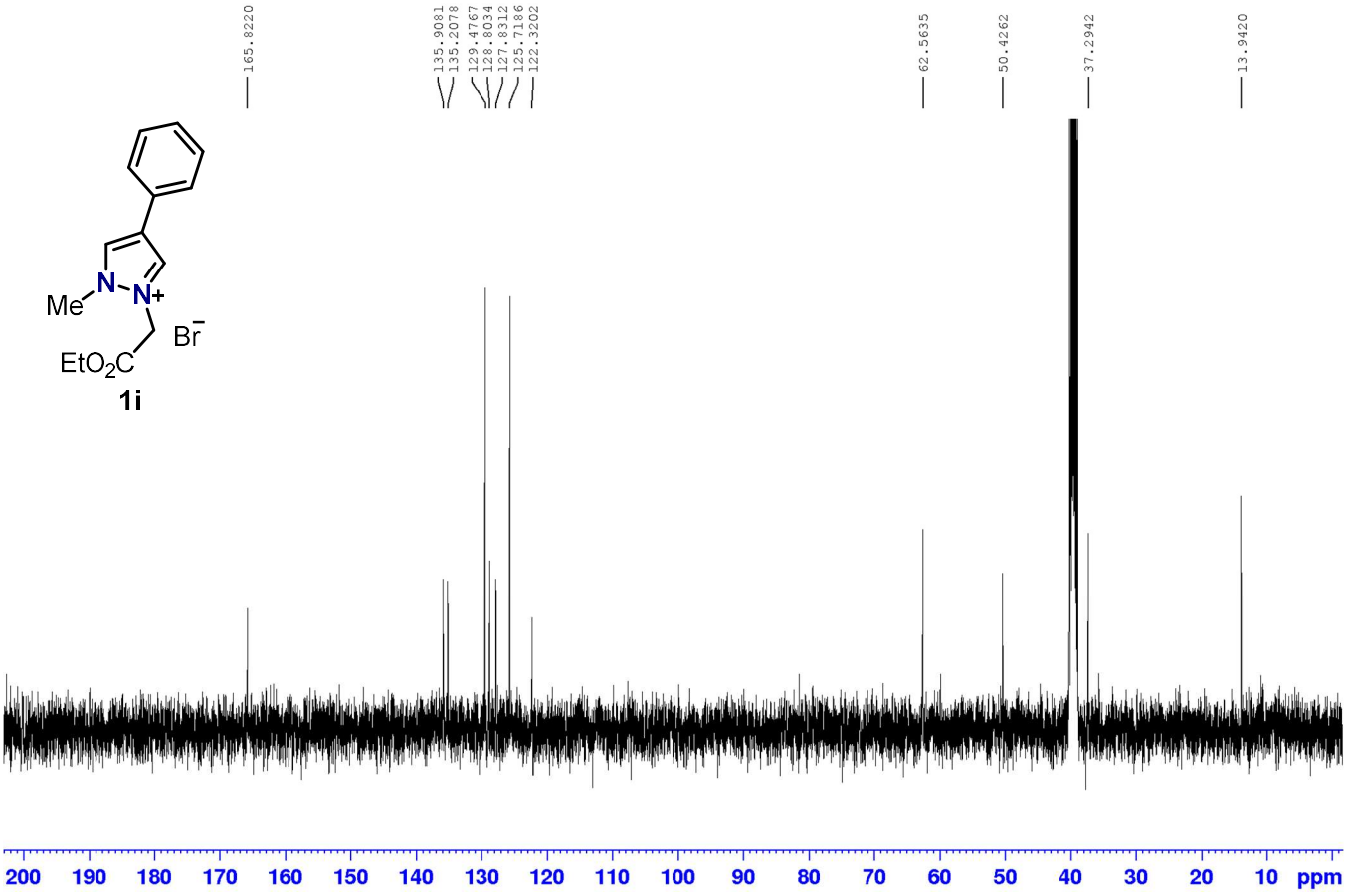


^{1}H NMR (400 MHz, DMSO-d6)



^{13}C NMR (100 MHz, DMSO-d6)



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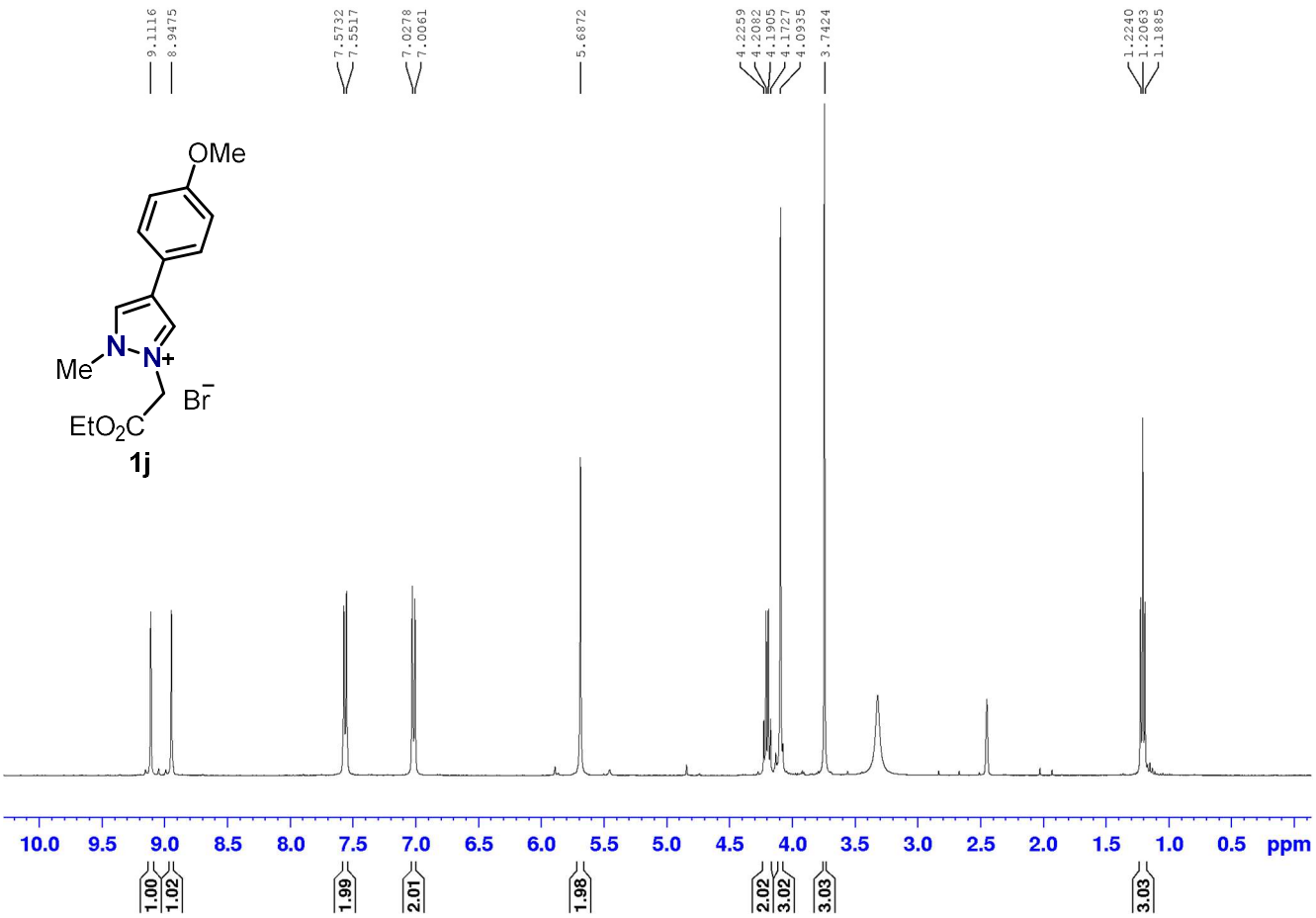

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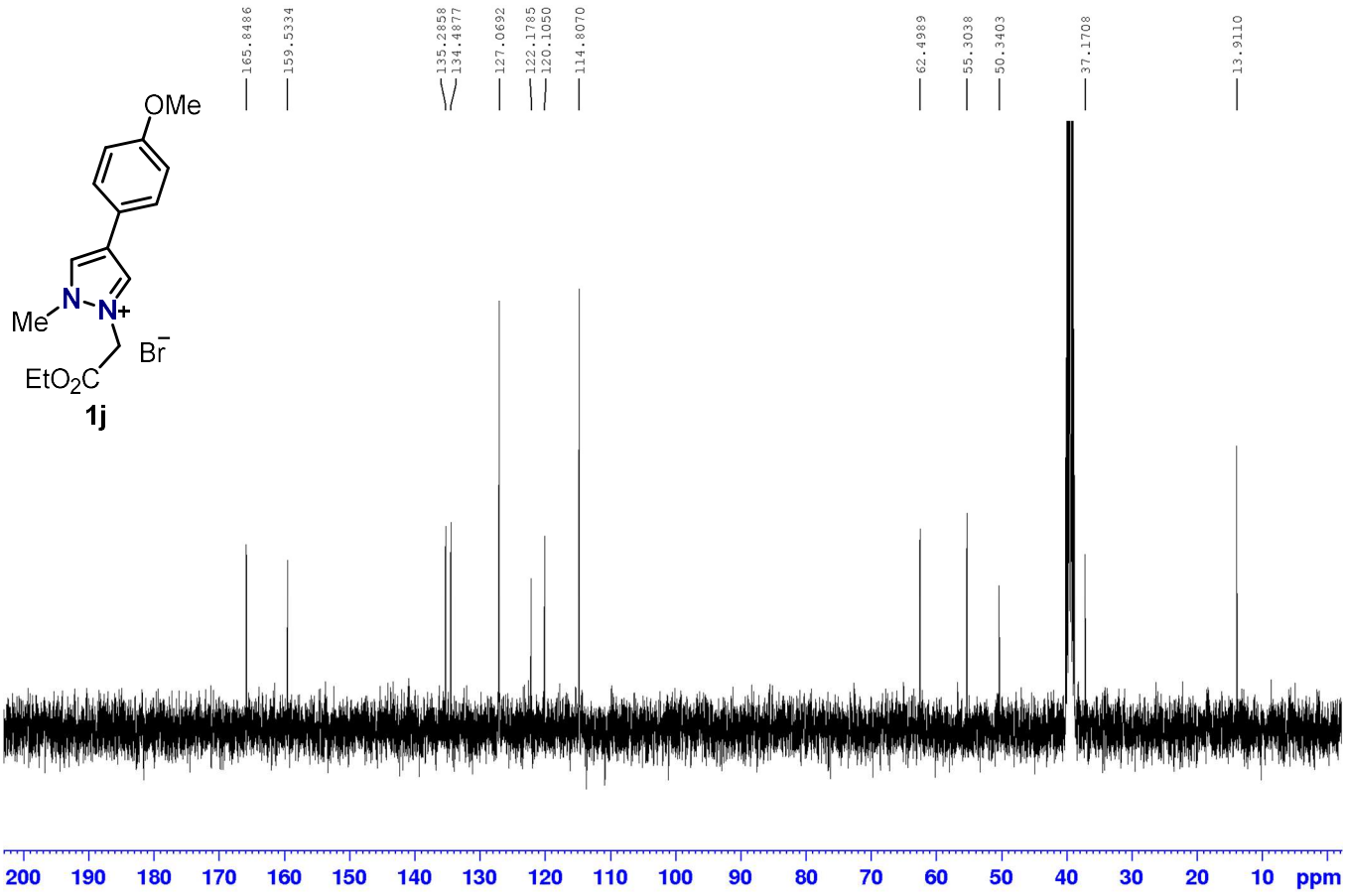

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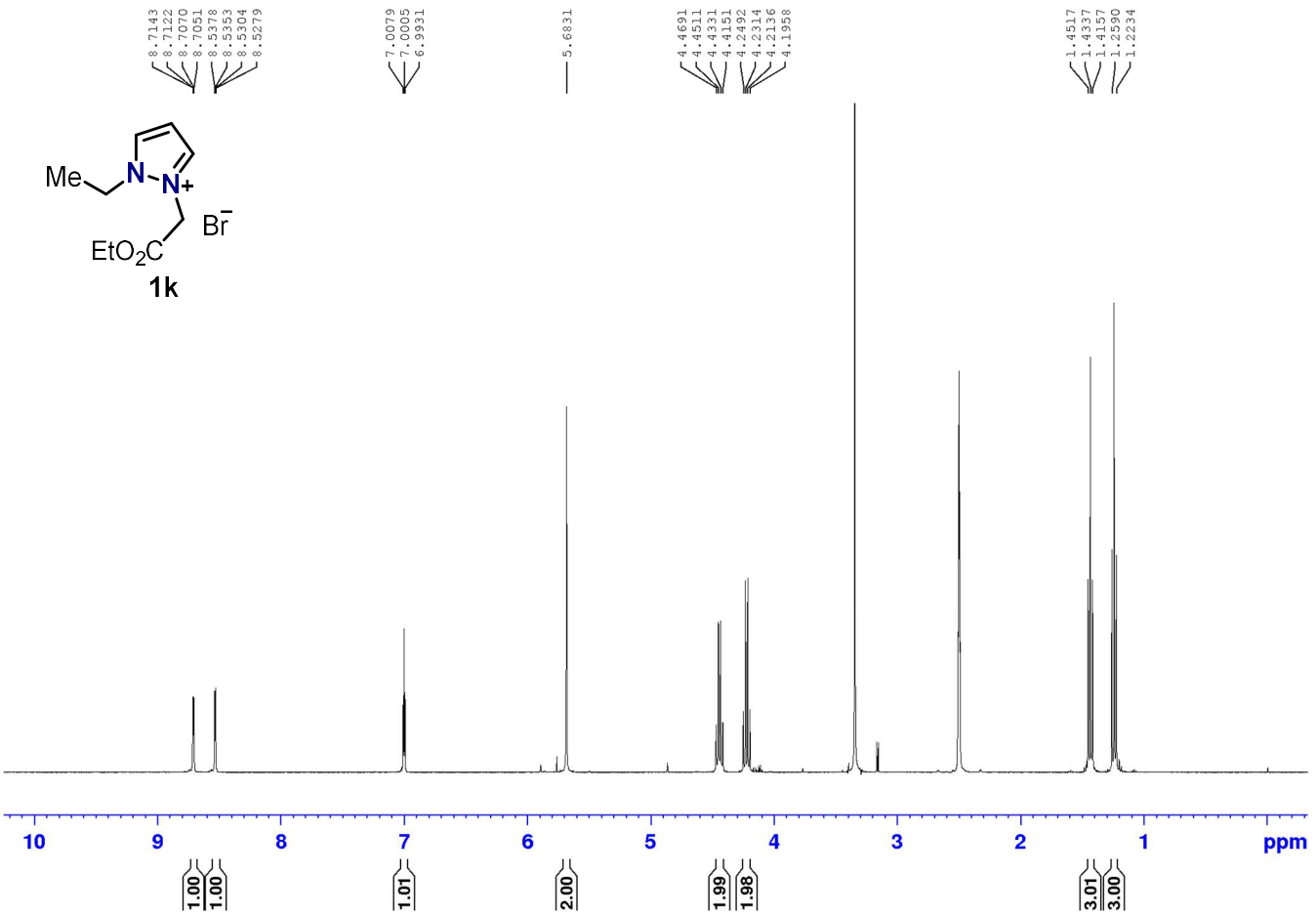

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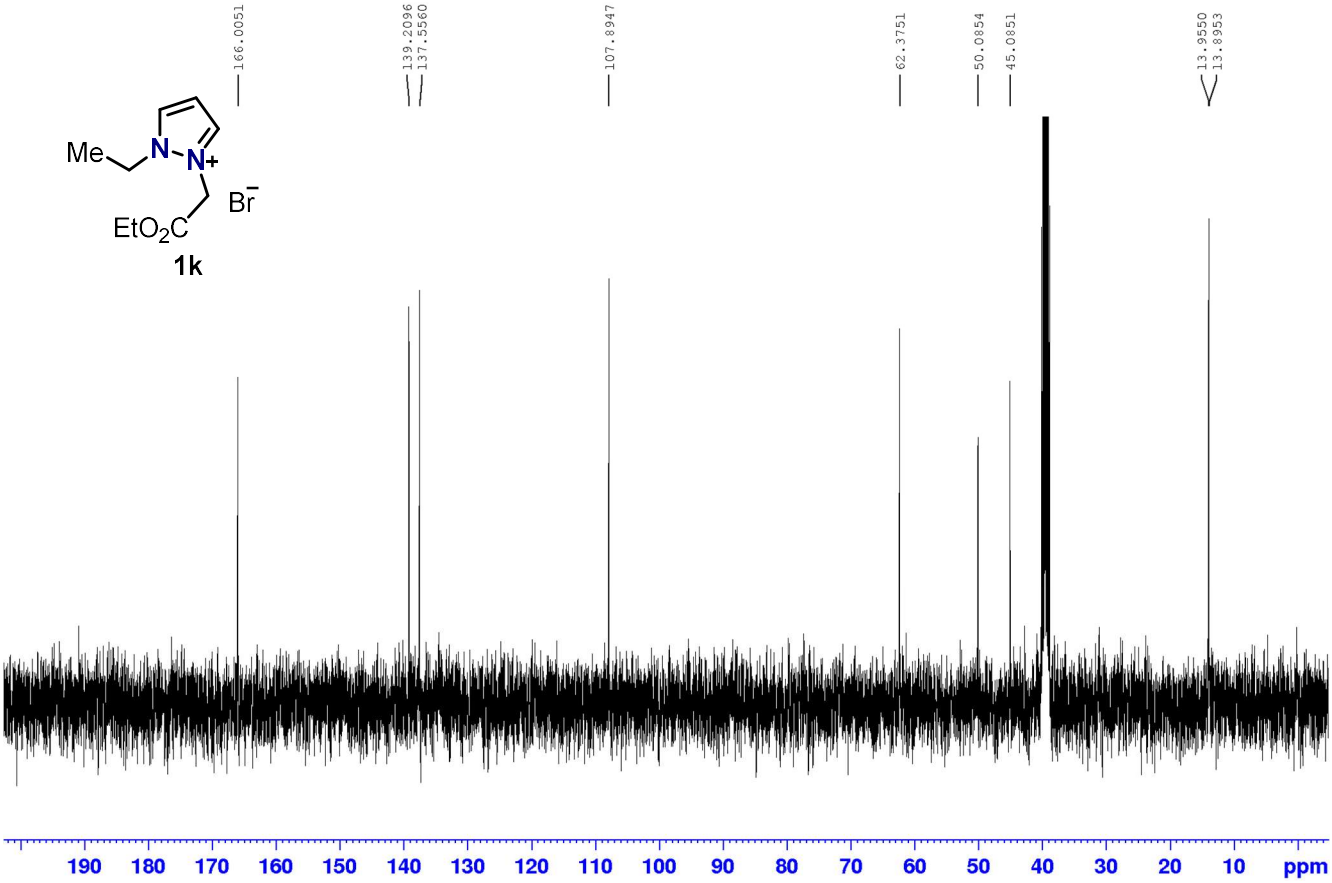

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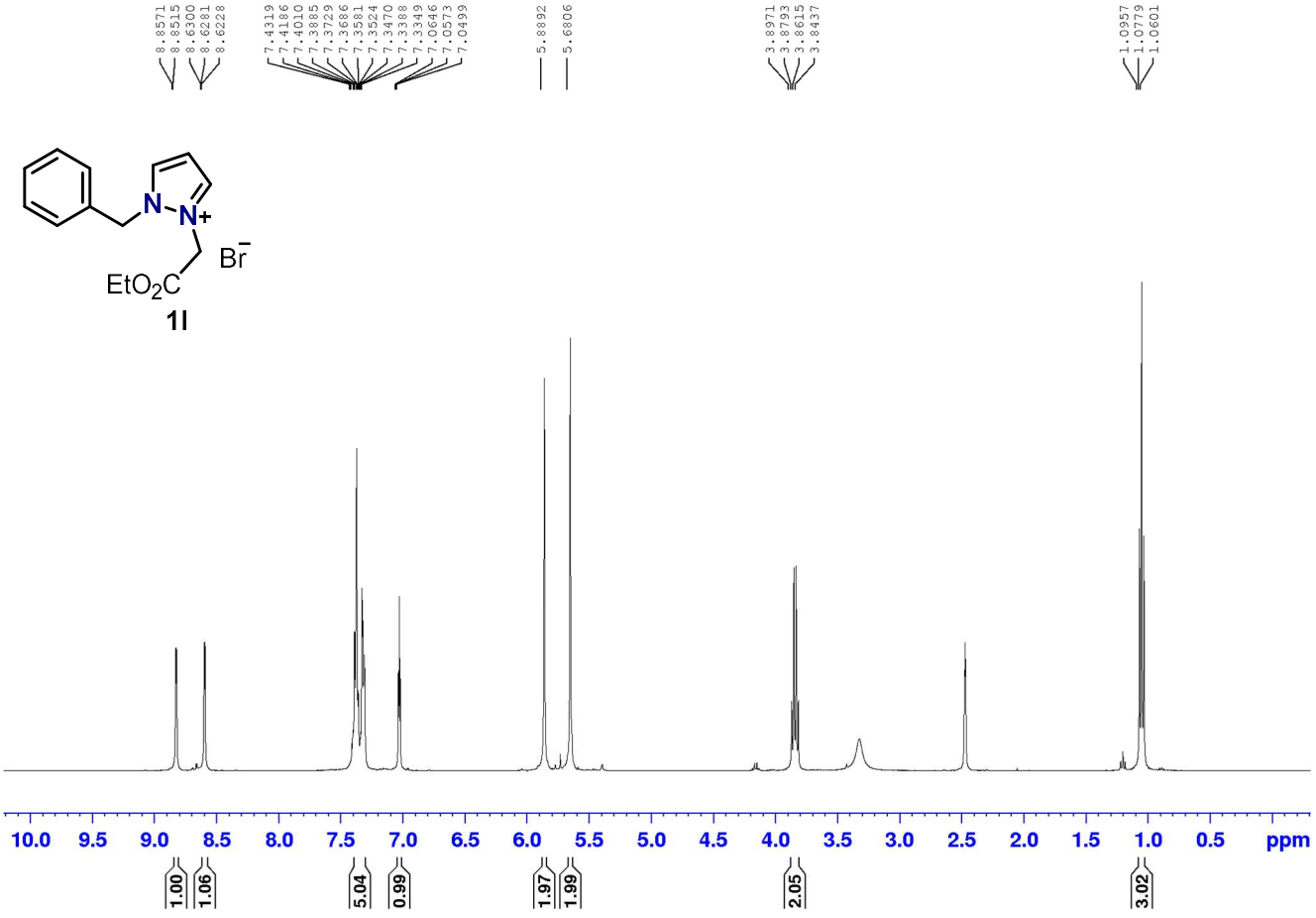

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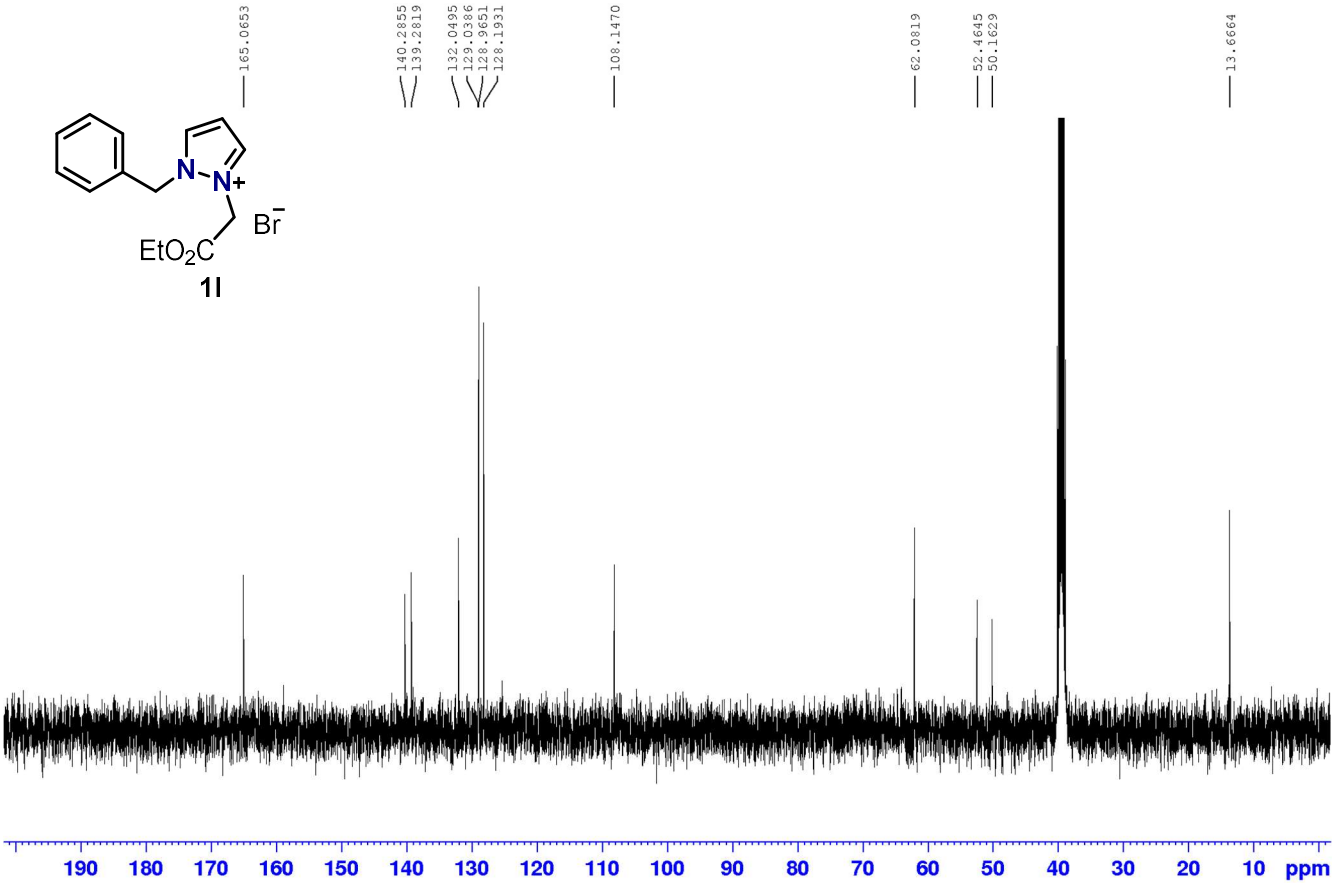

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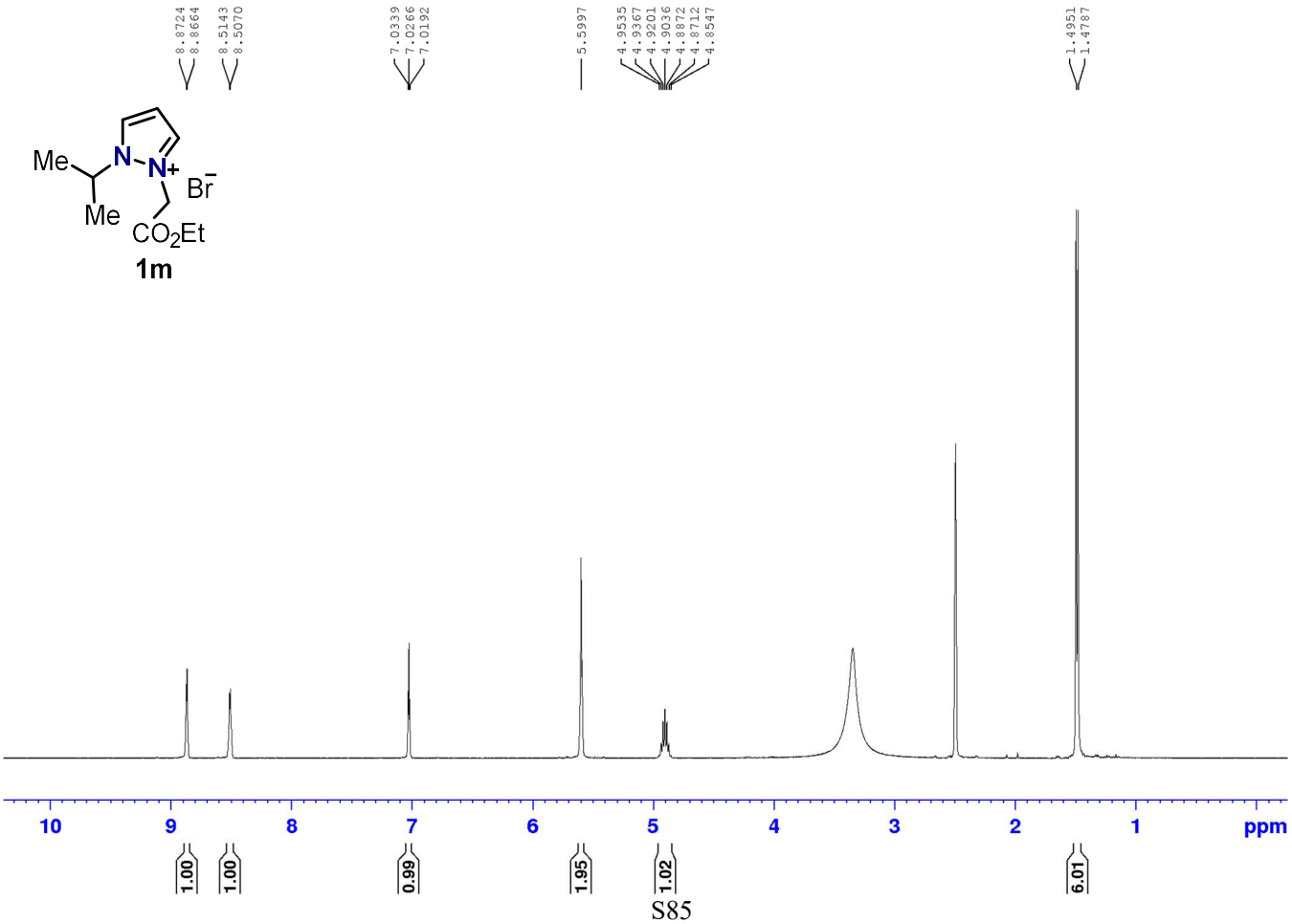

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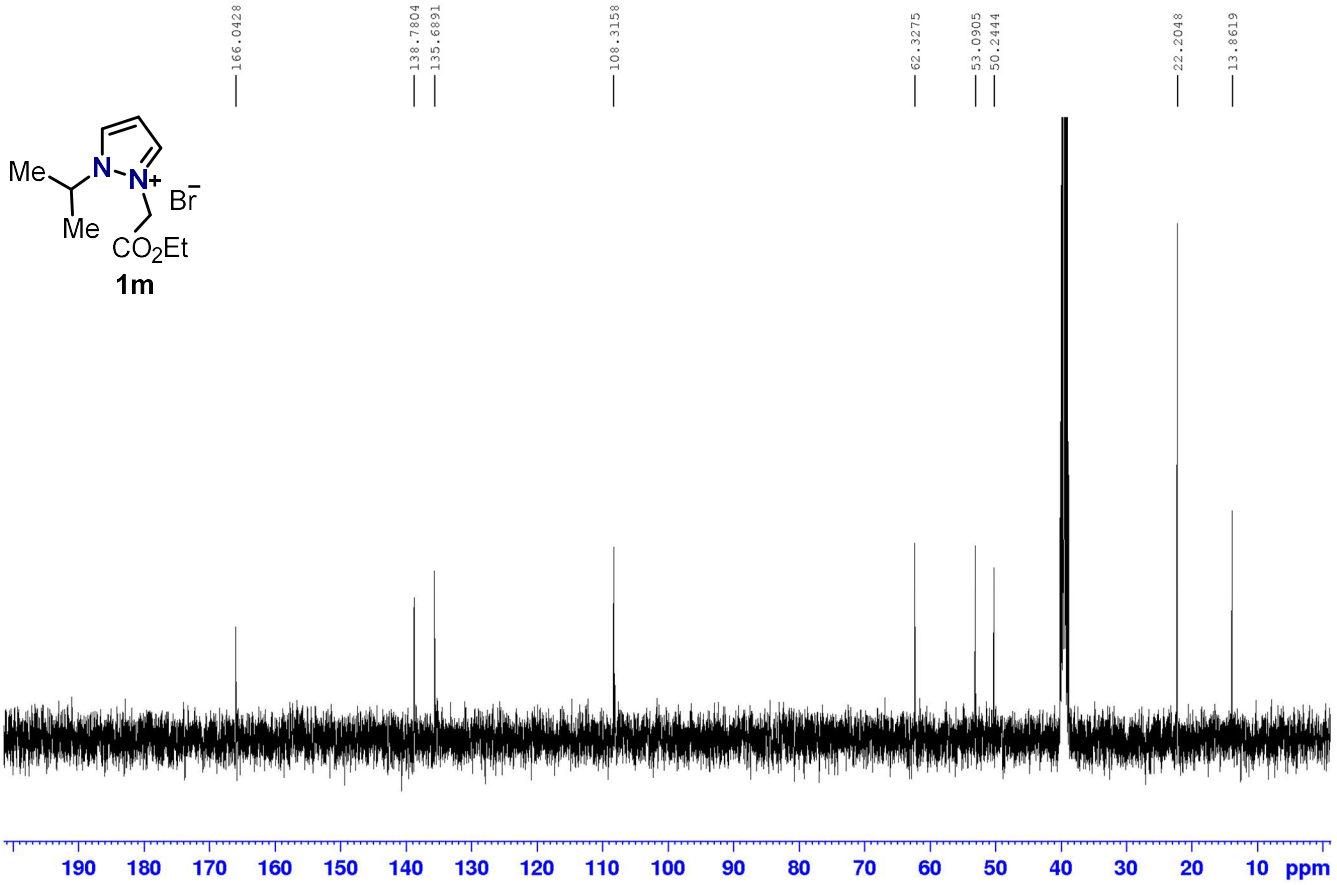

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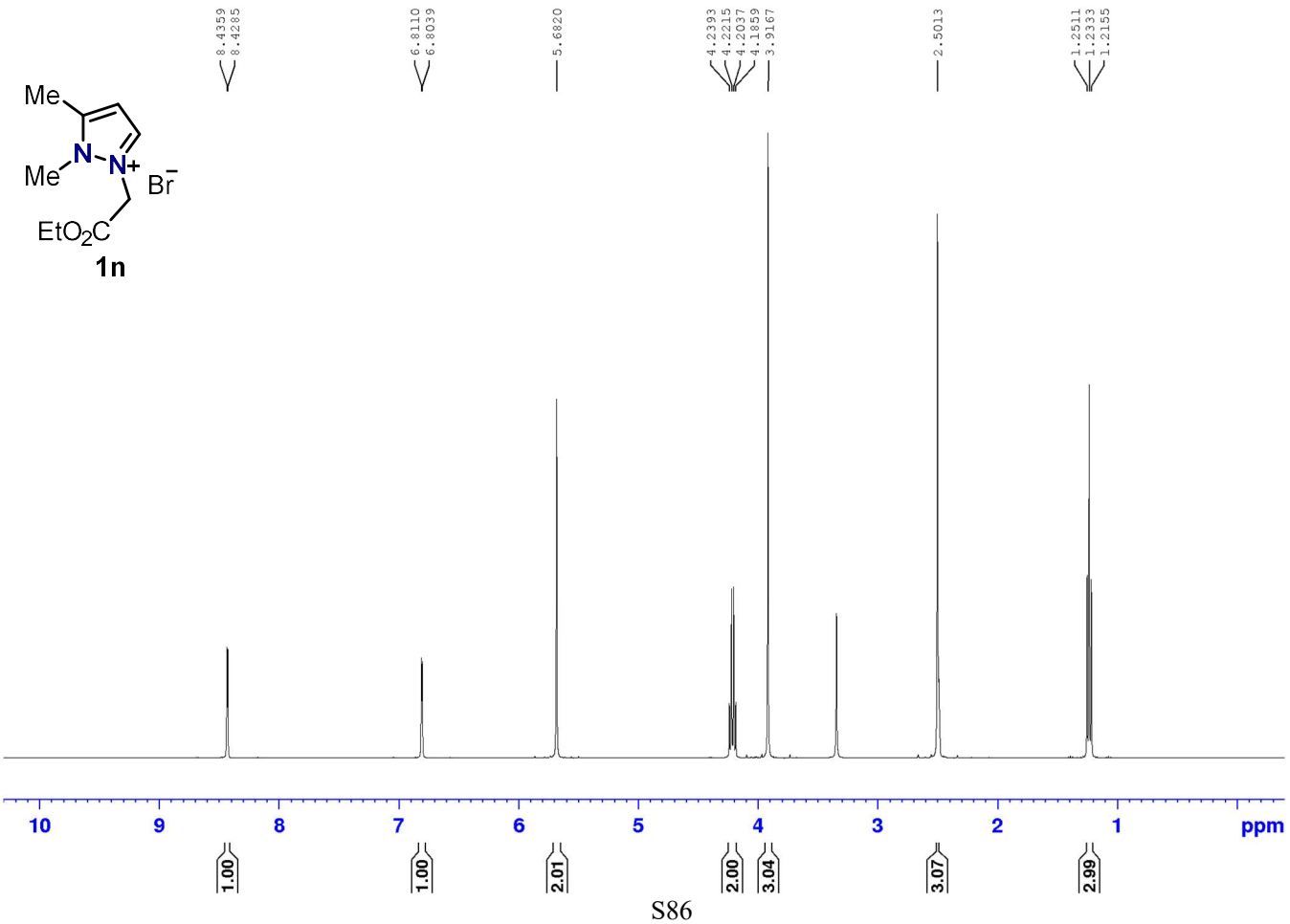

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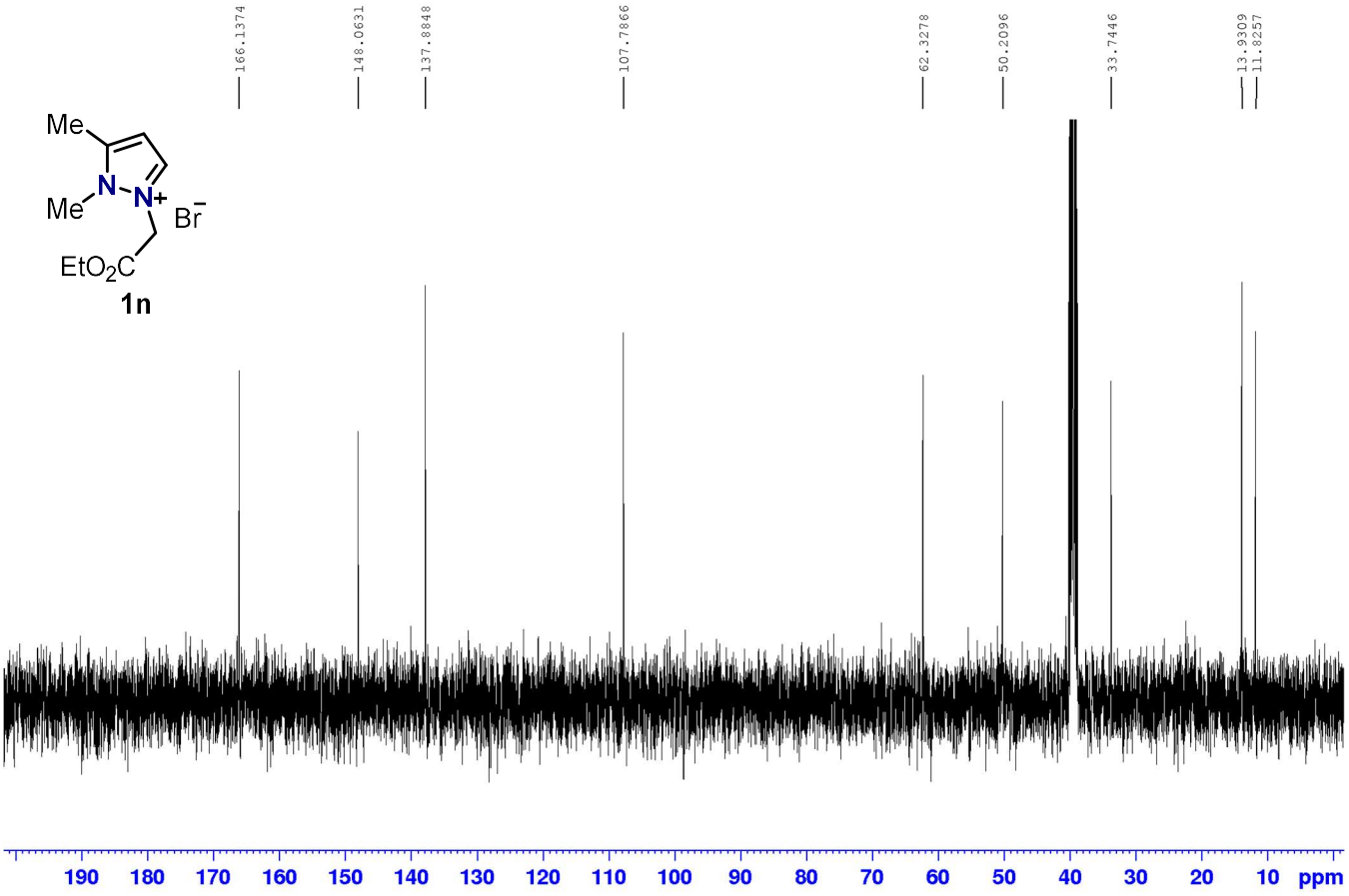

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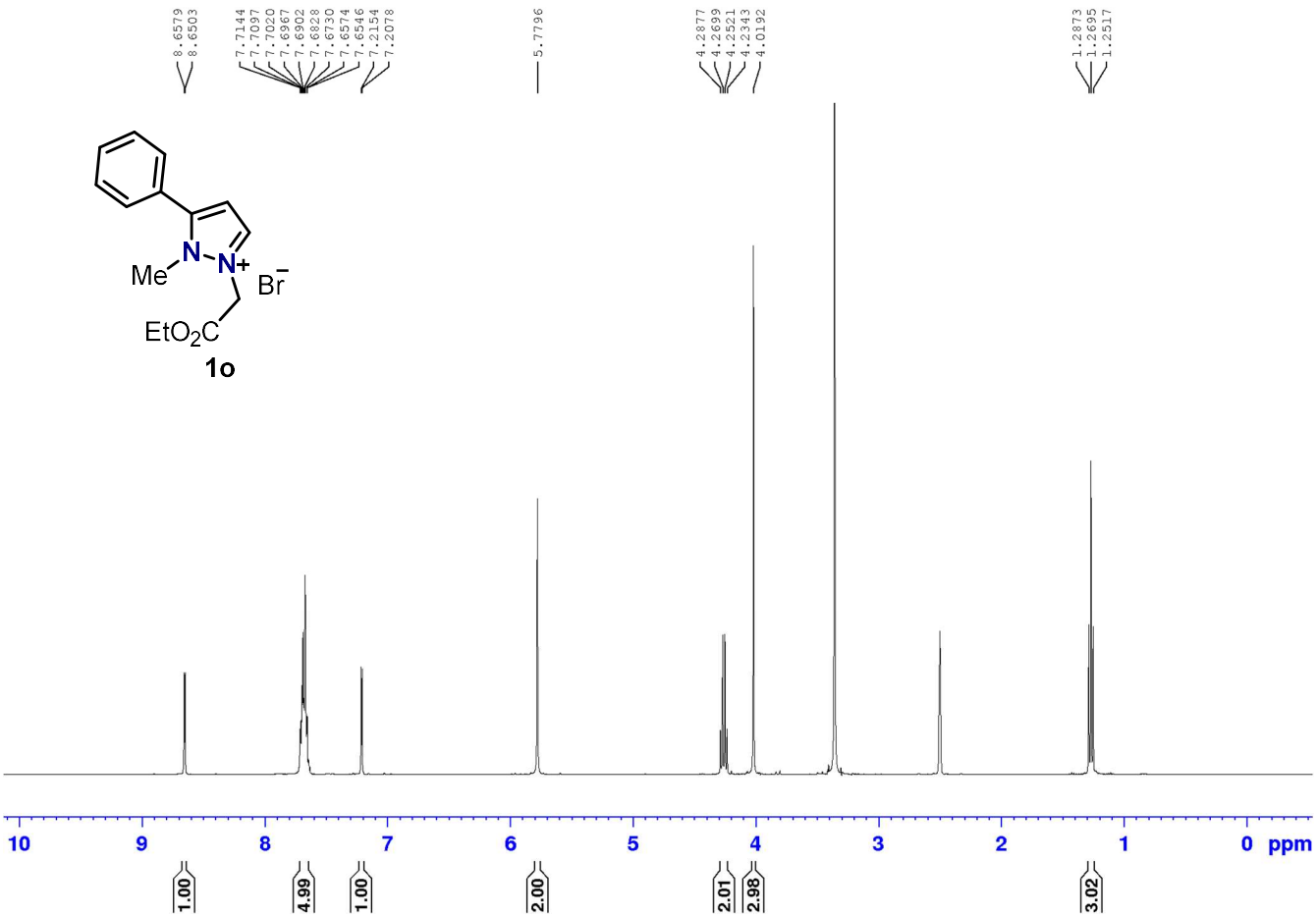

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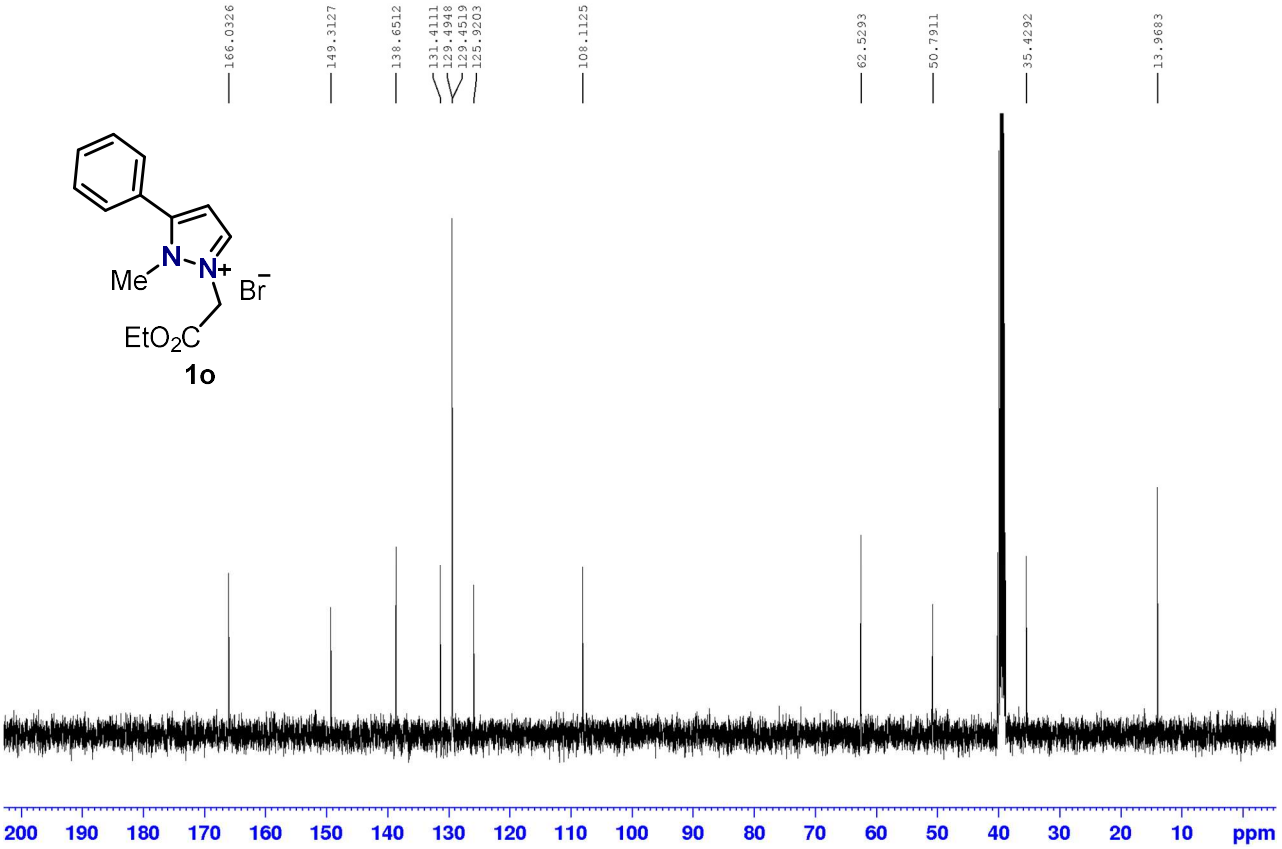

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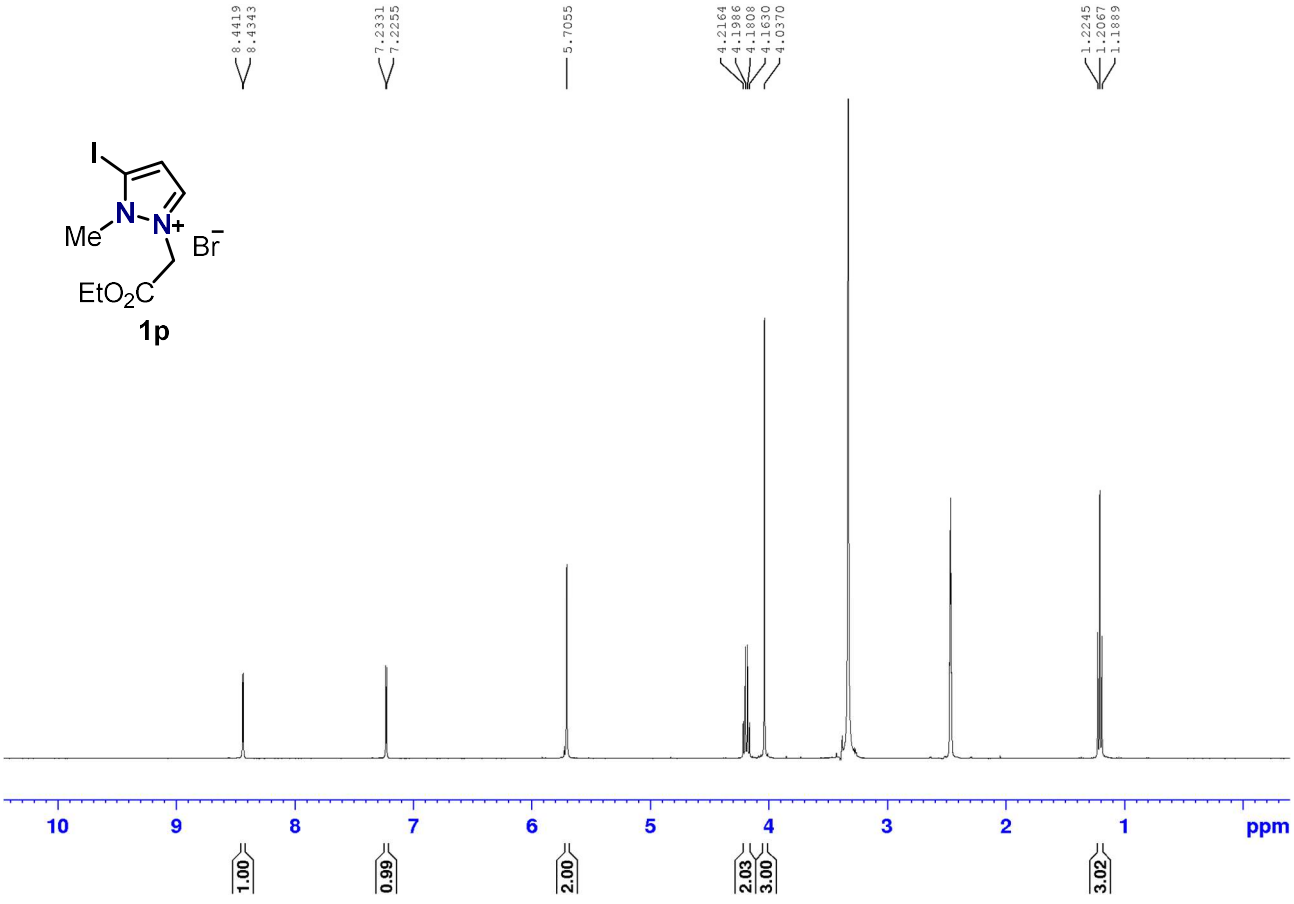

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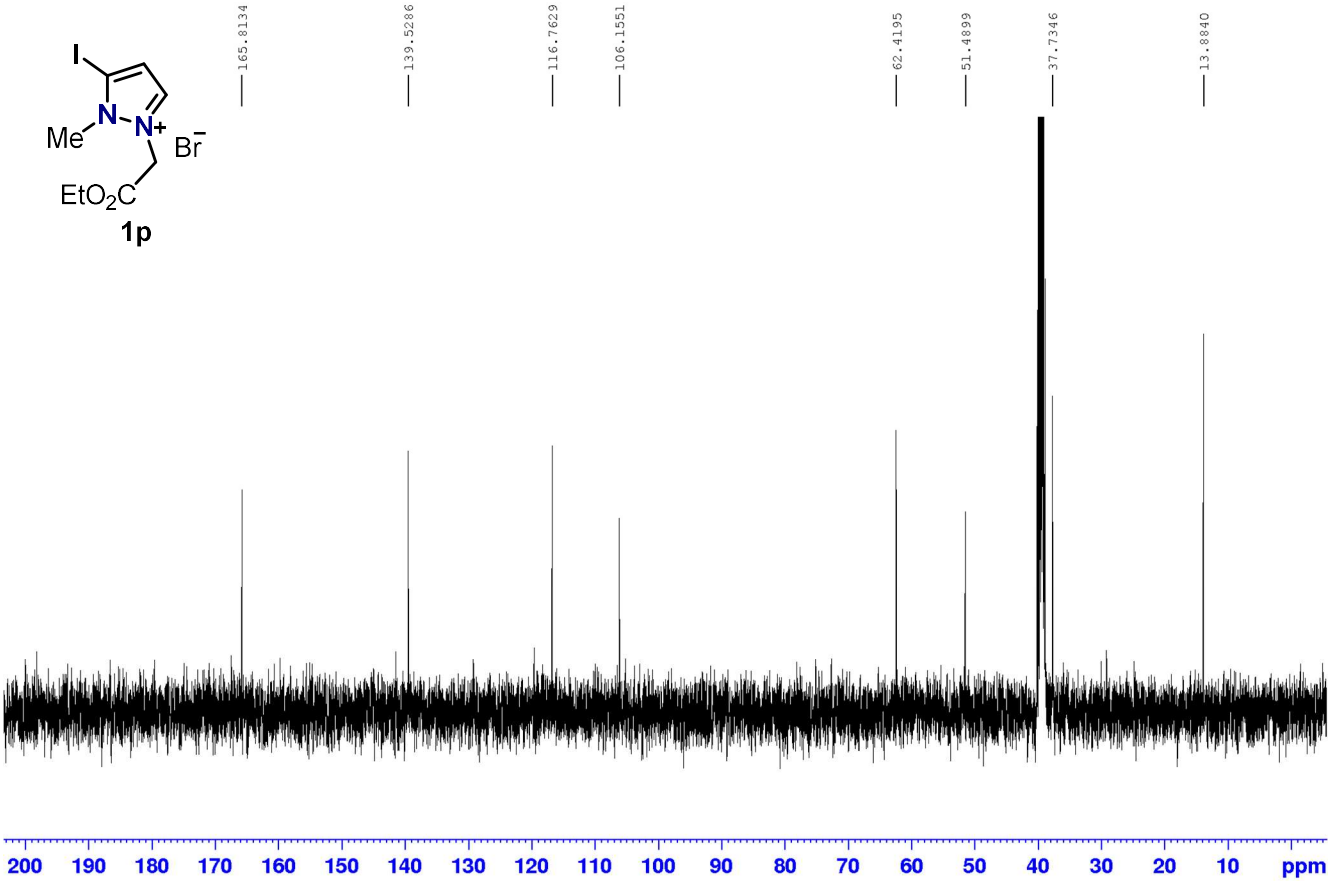

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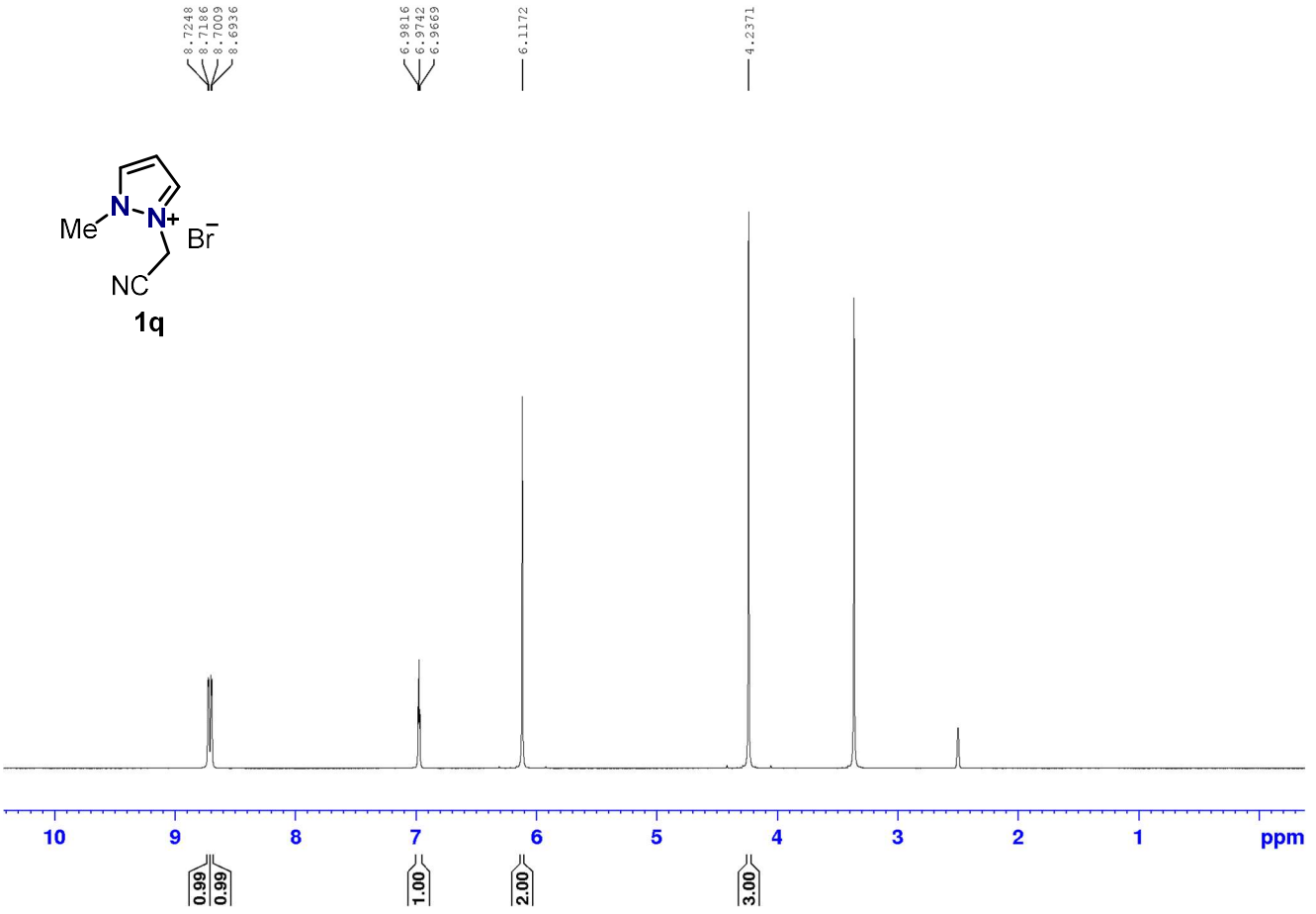
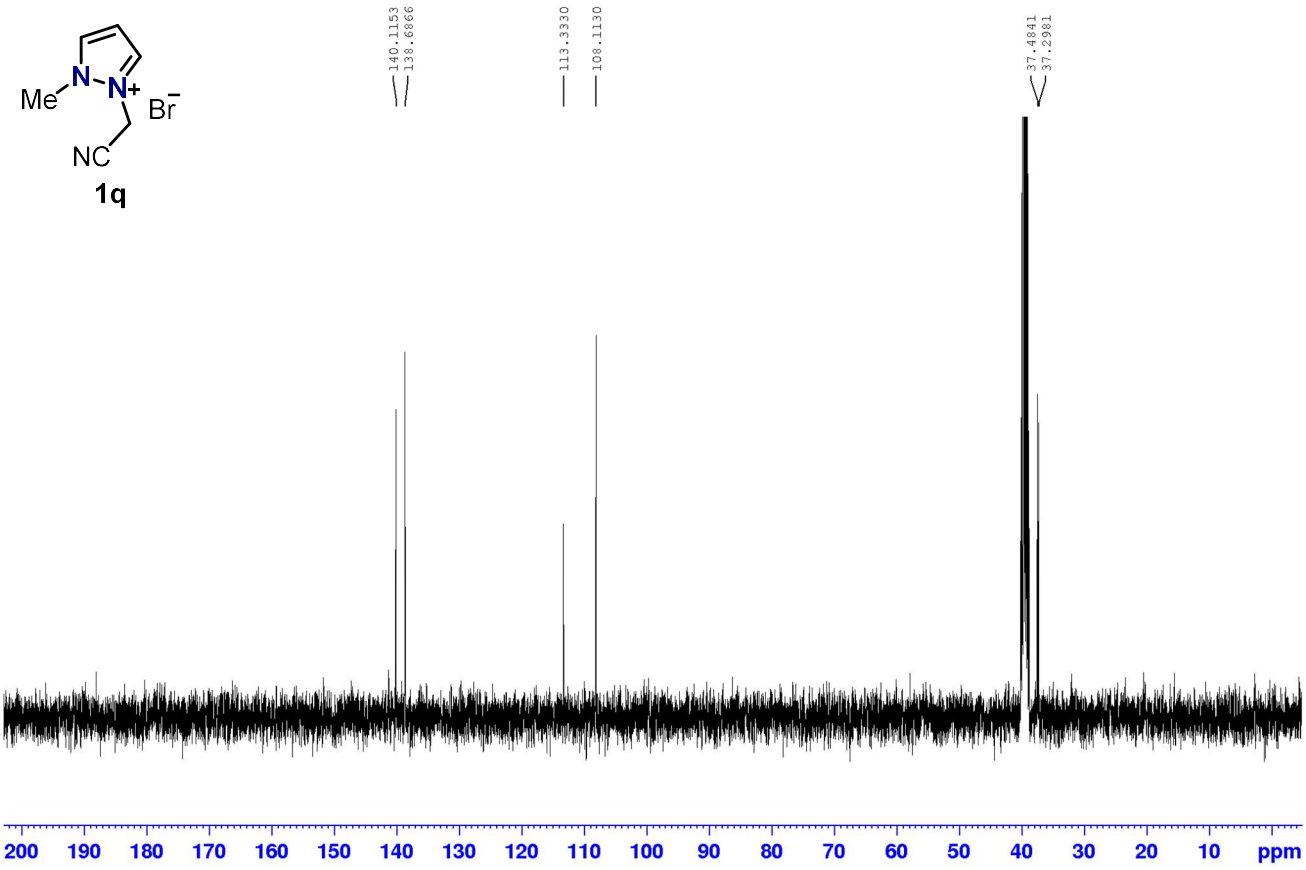
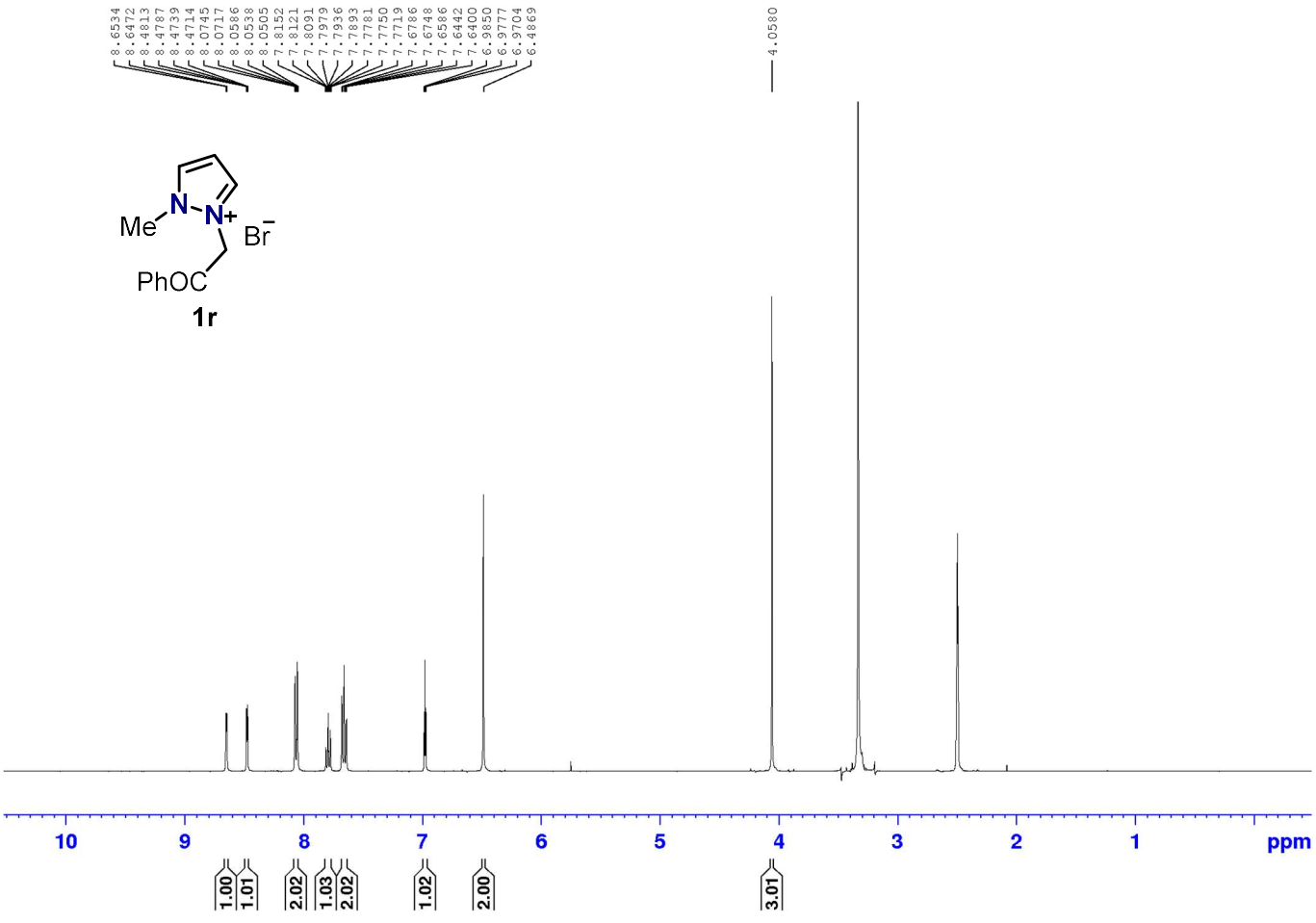


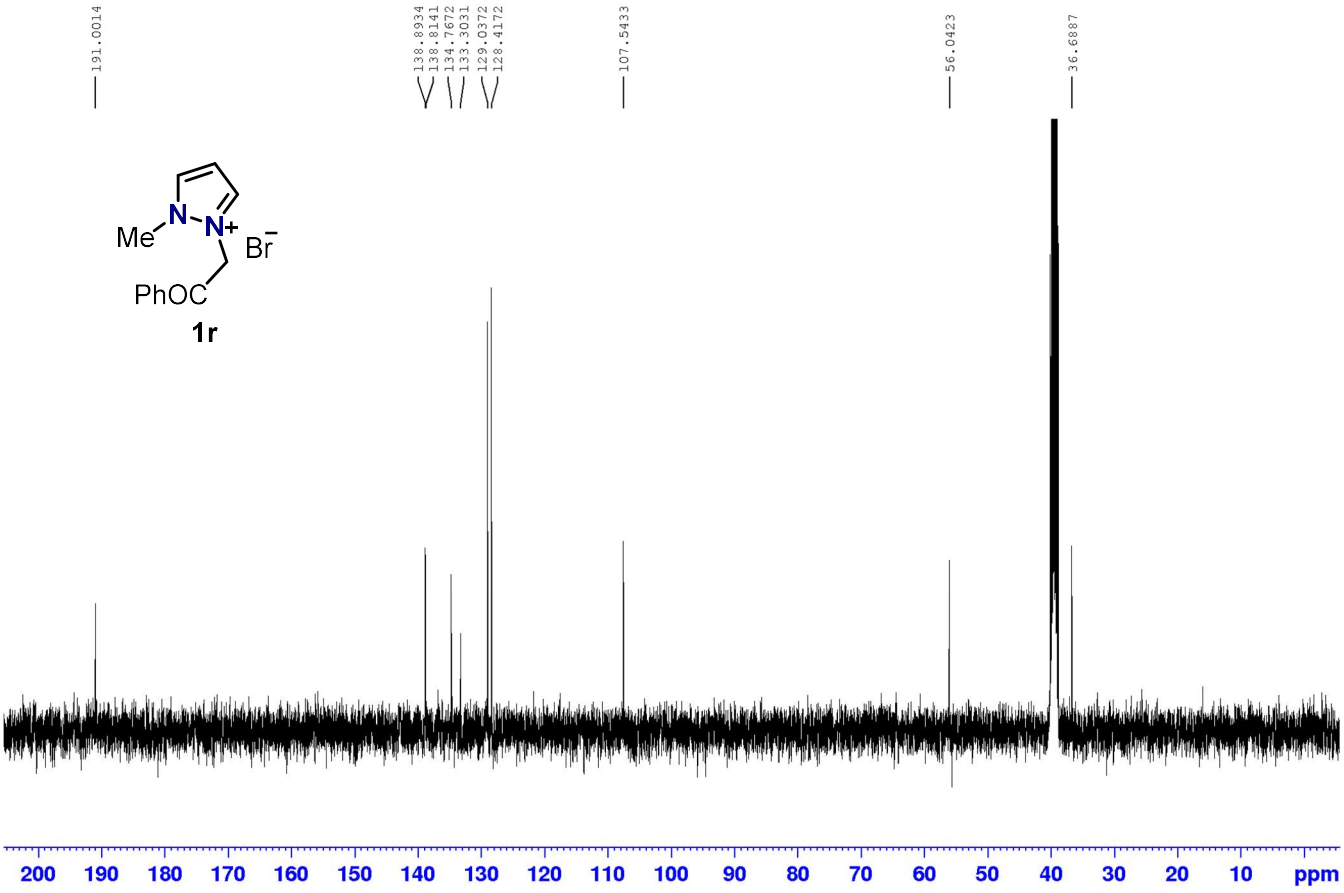
^{13}C NMR (100 MHz, DMSO-d6)



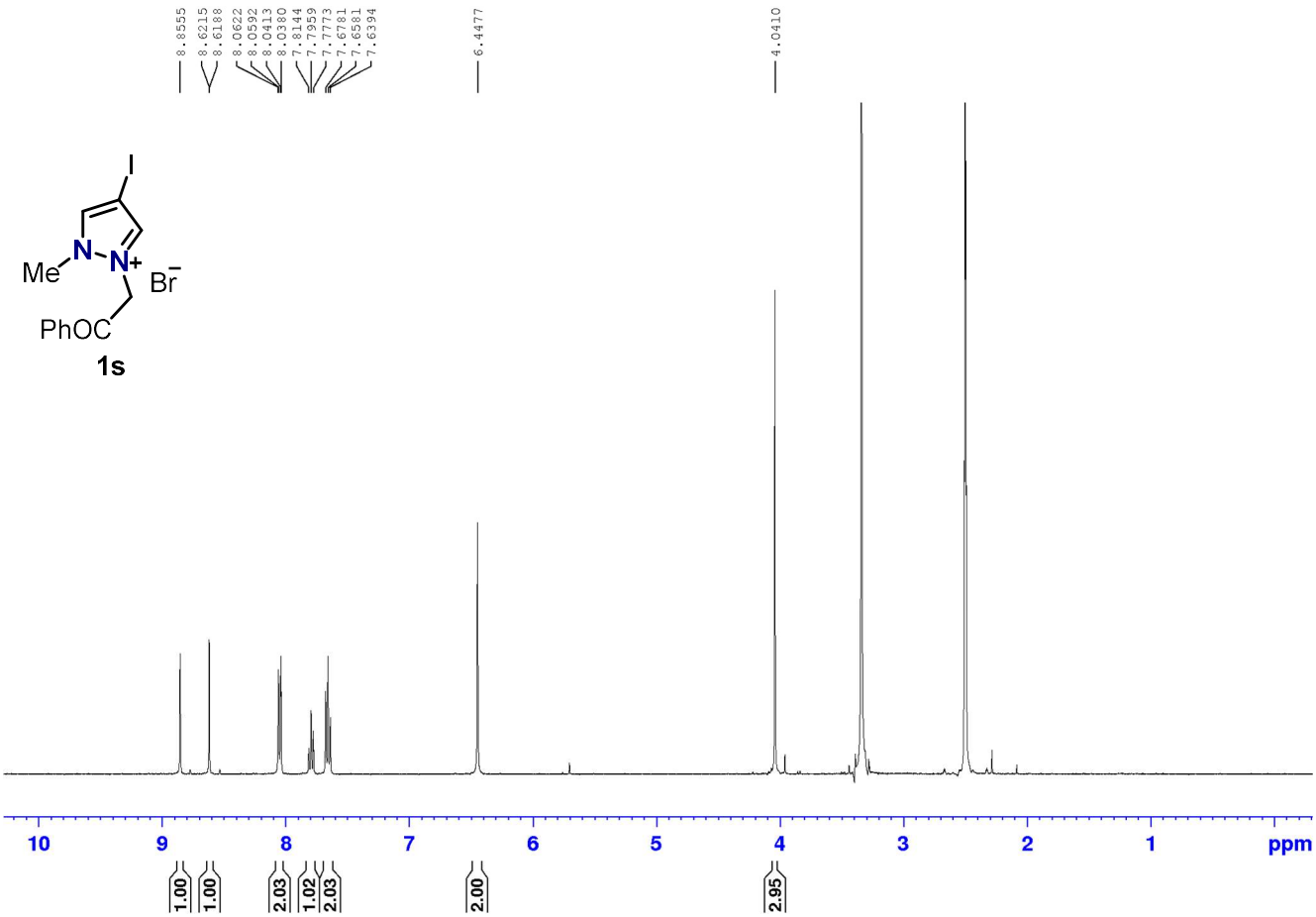
^{1}H NMR (400 MHz, DMSO-d6)



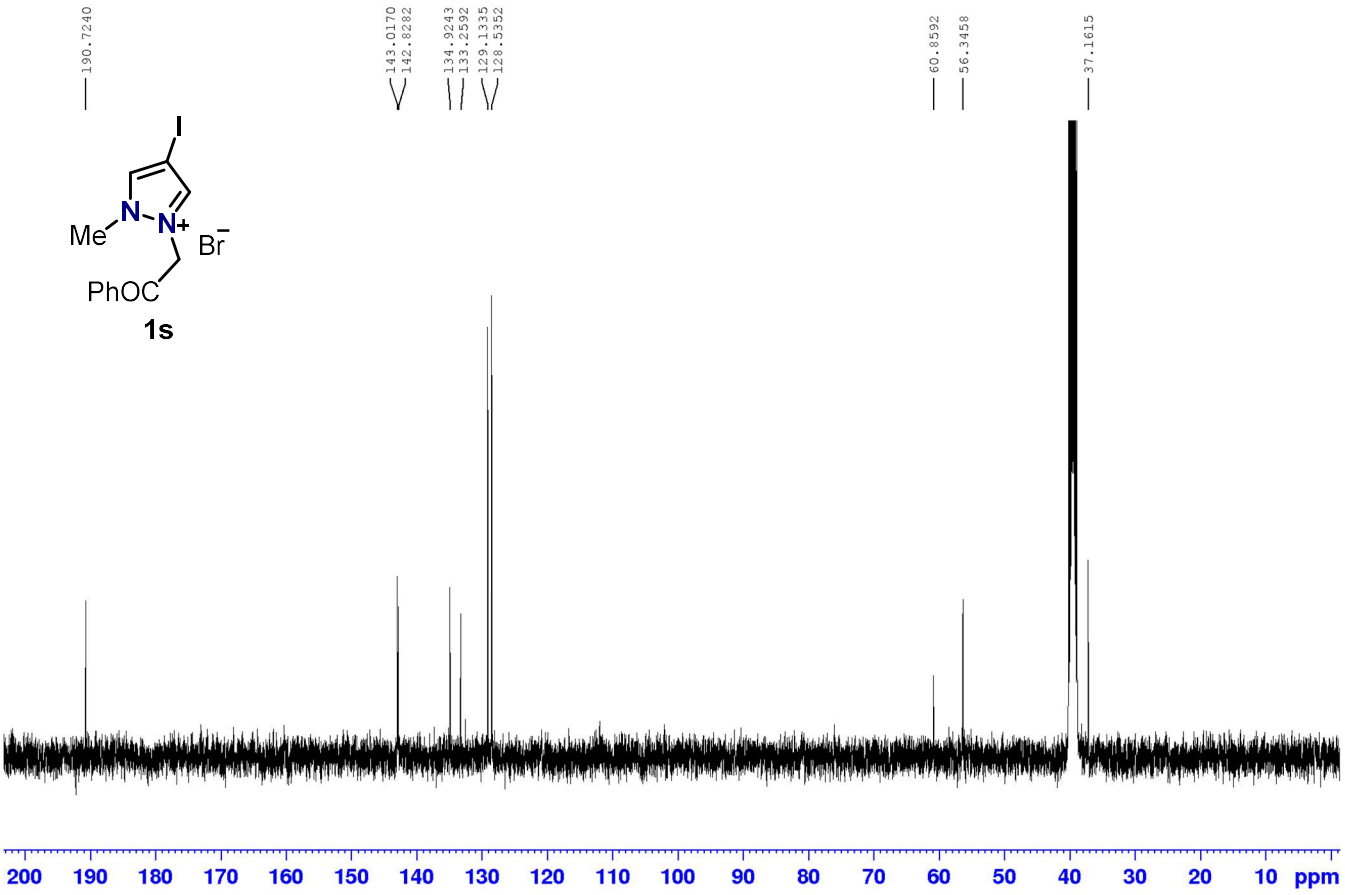
^{13}C NMR (100 MHz, DMSO-d6)



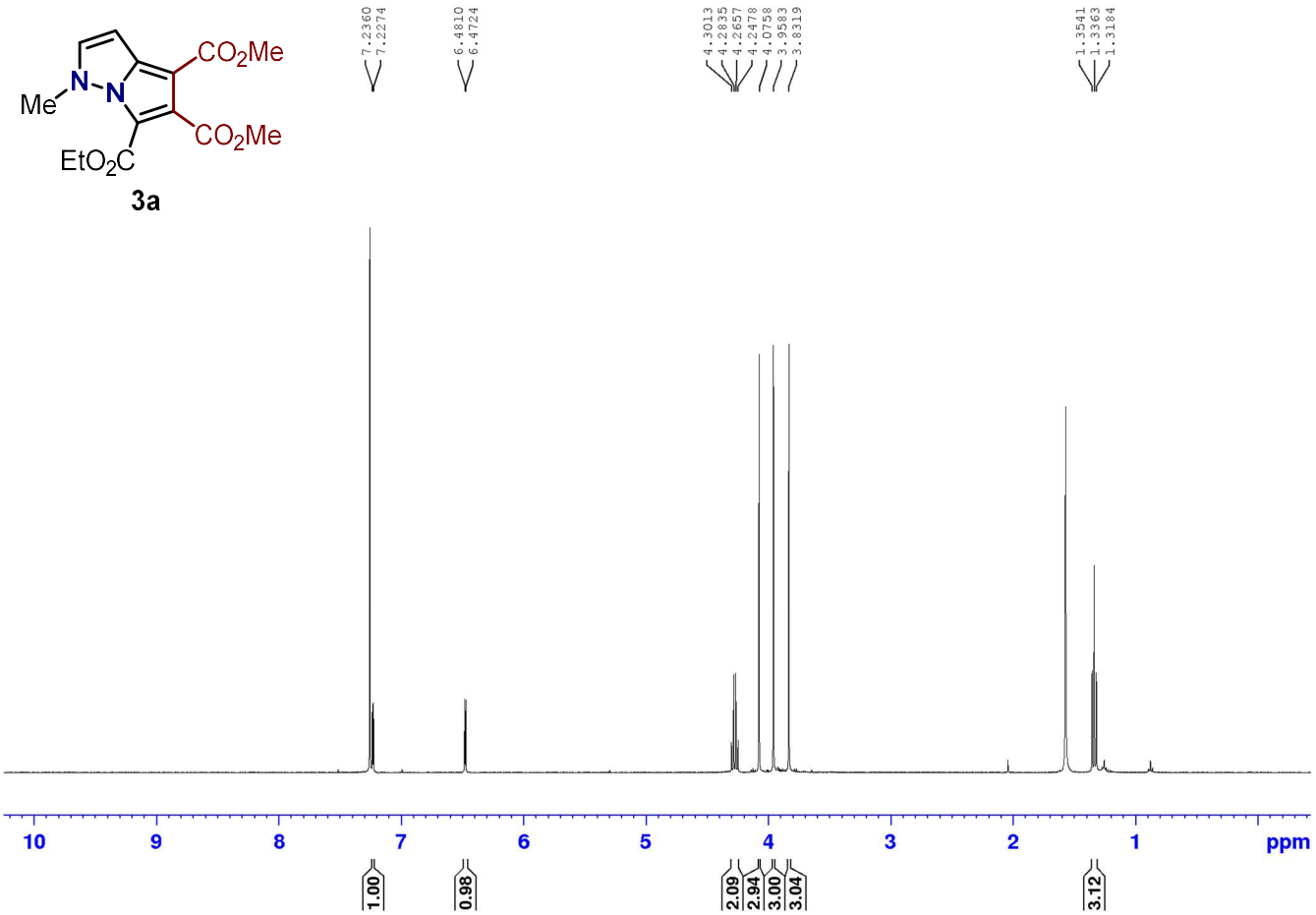
^{1}H NMR (400 MHz, DMSO-d6)



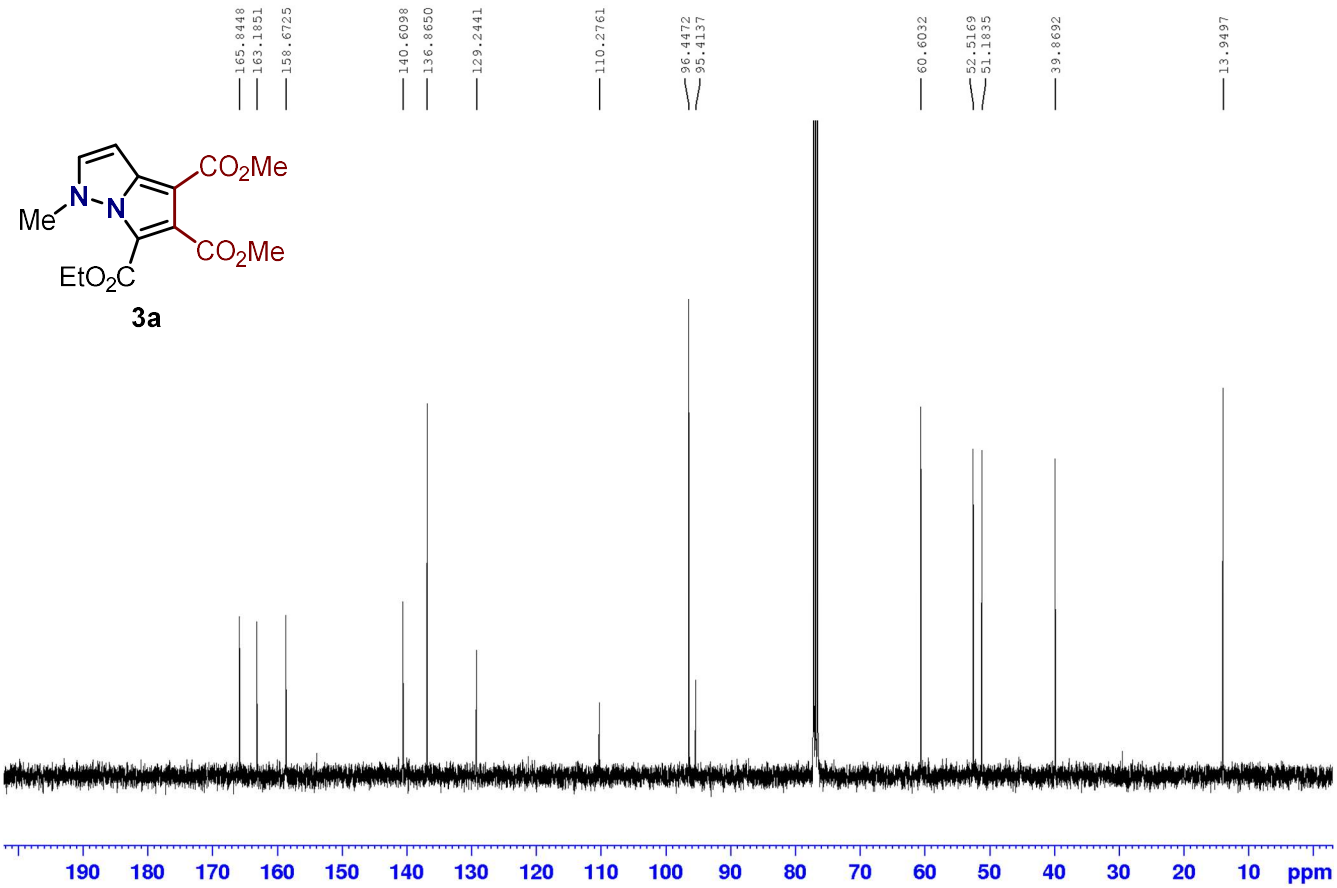
^{13}C NMR (100 MHz, DMSO-d6)



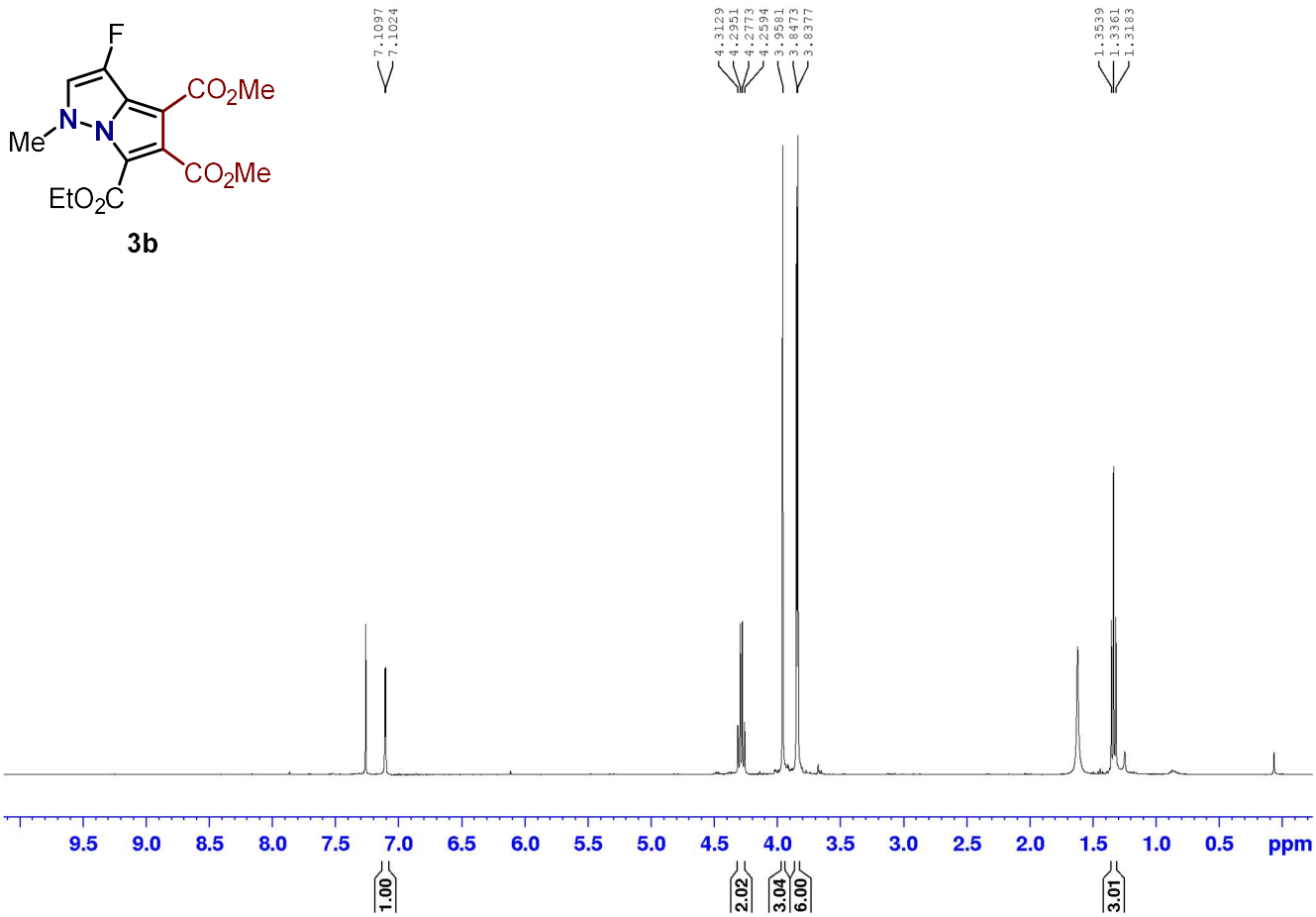
^{1}H NMR (400 MHz, $CDCl_3$)



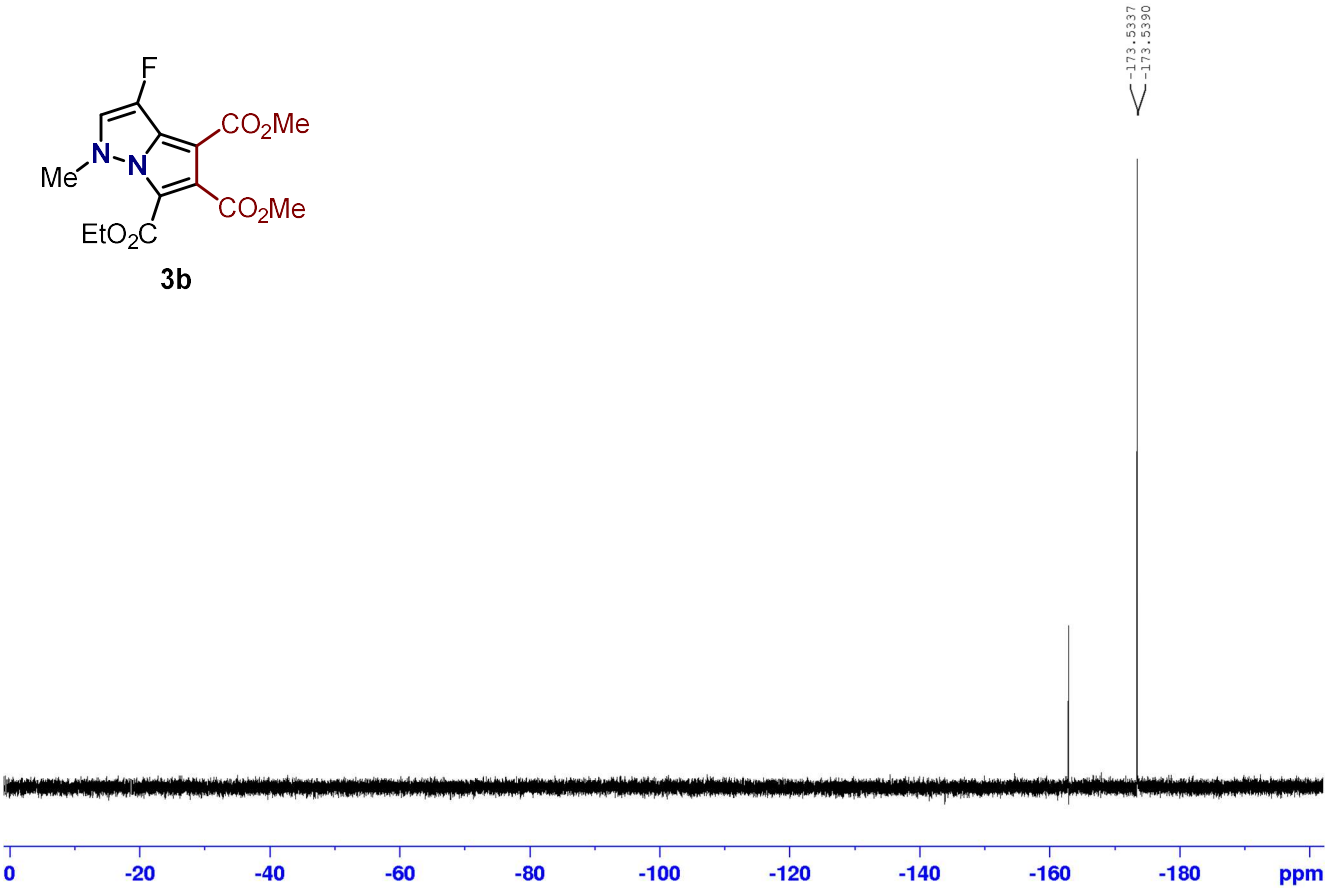
^{13}C NMR (100 MHz, $CDCl_3$)



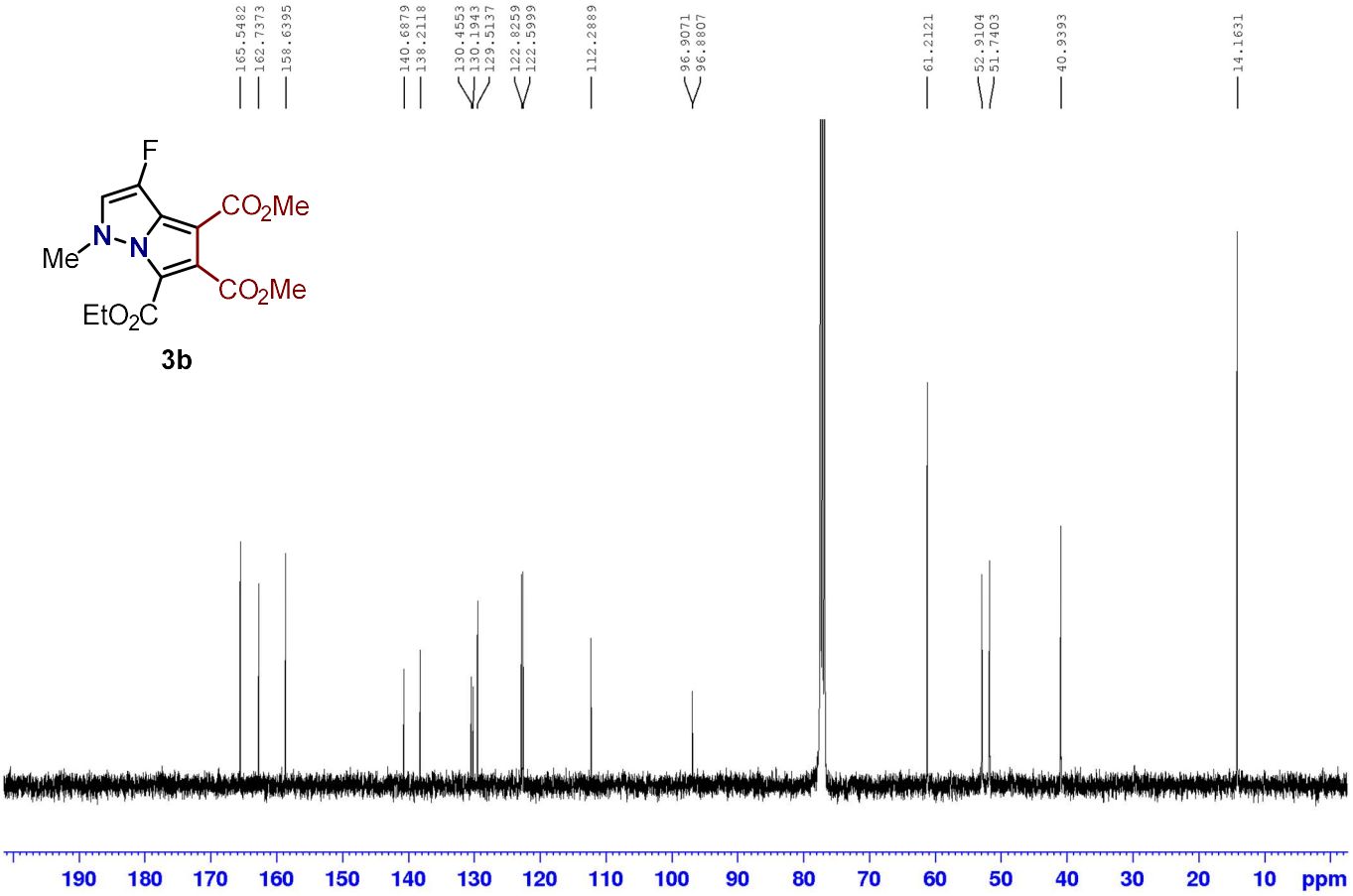
^{1}H NMR (400 MHz, $CDCl_3$)



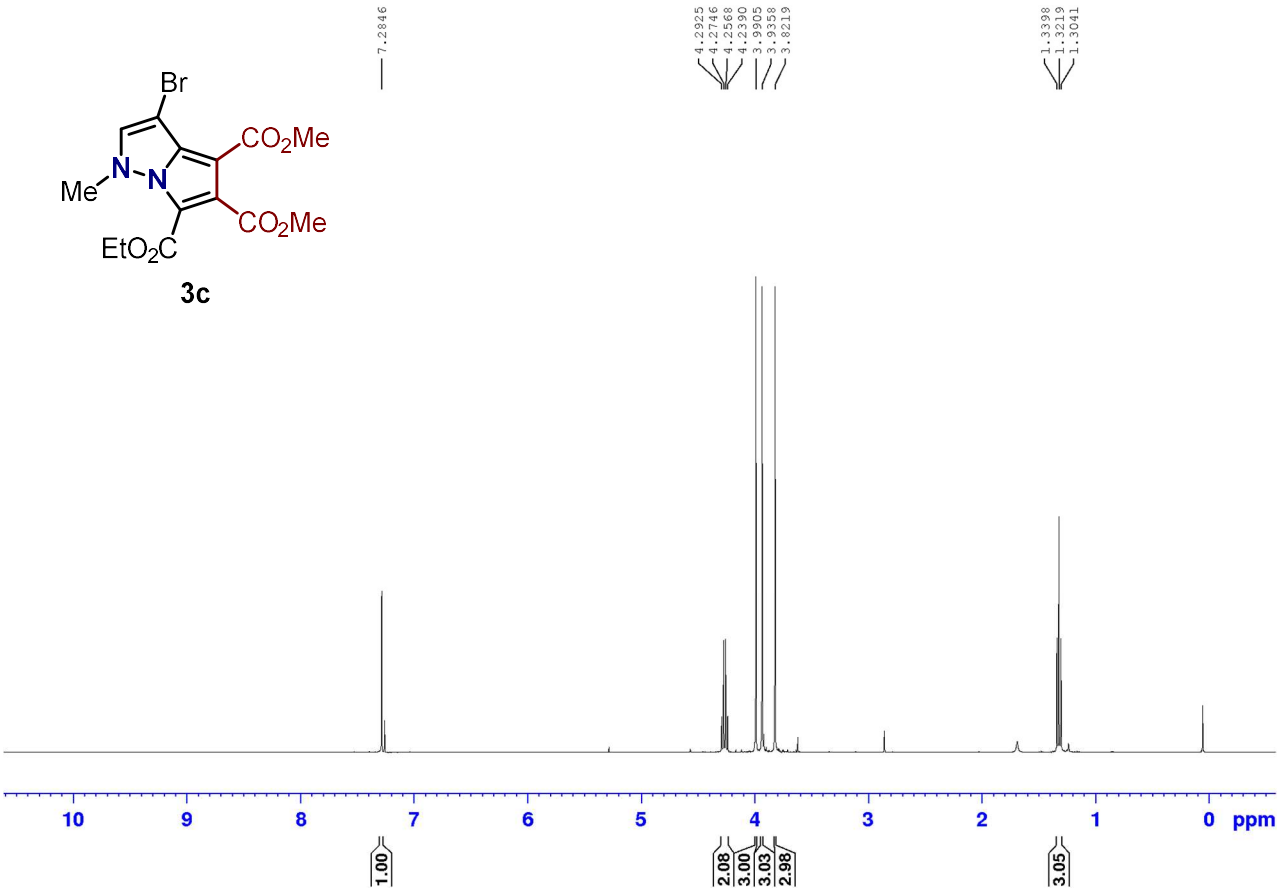
^{19}F NMR (376 MHz, $CDCl_3$, C_6F_6)



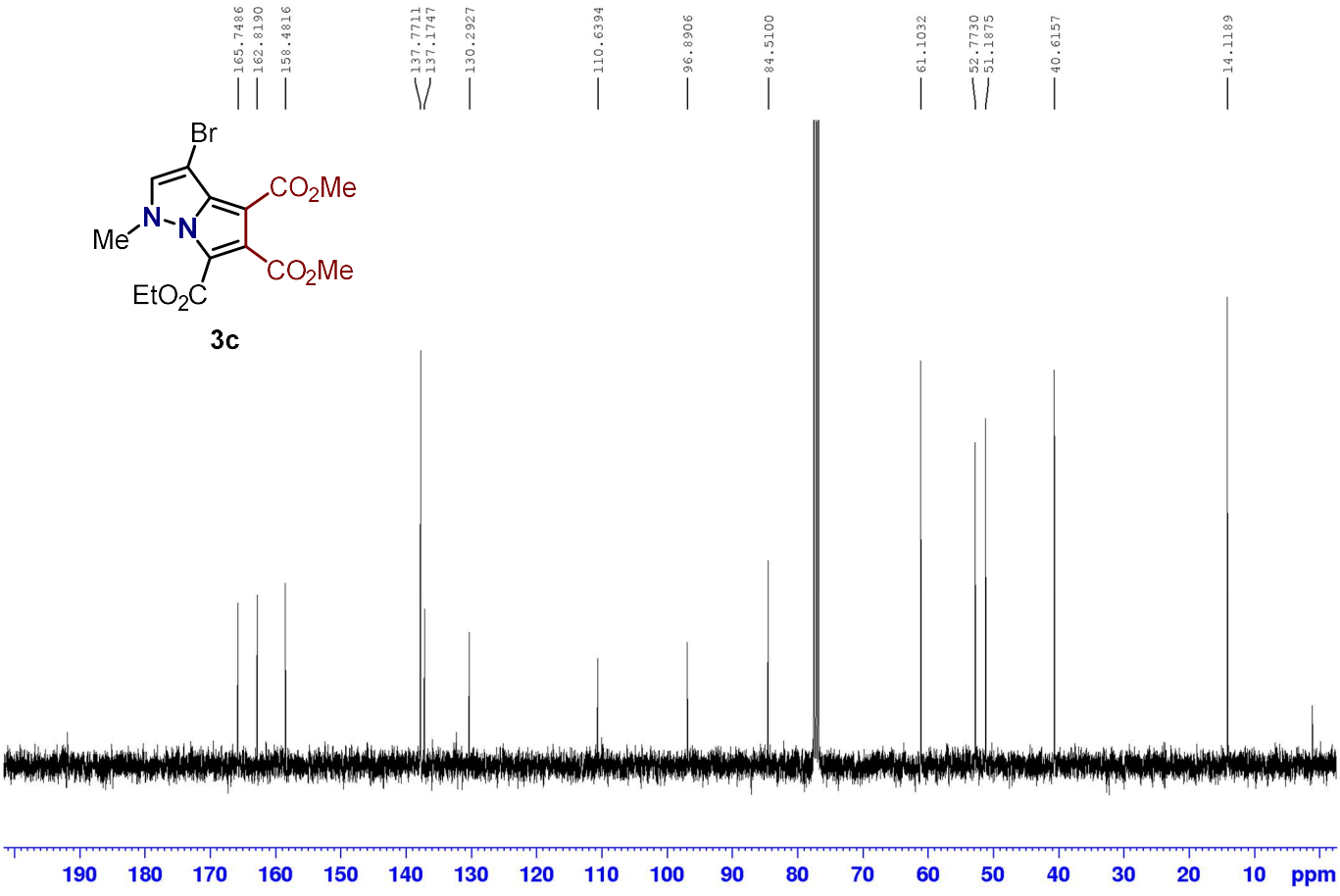
^{13}C NMR (100 MHz, $CDCl_3$)



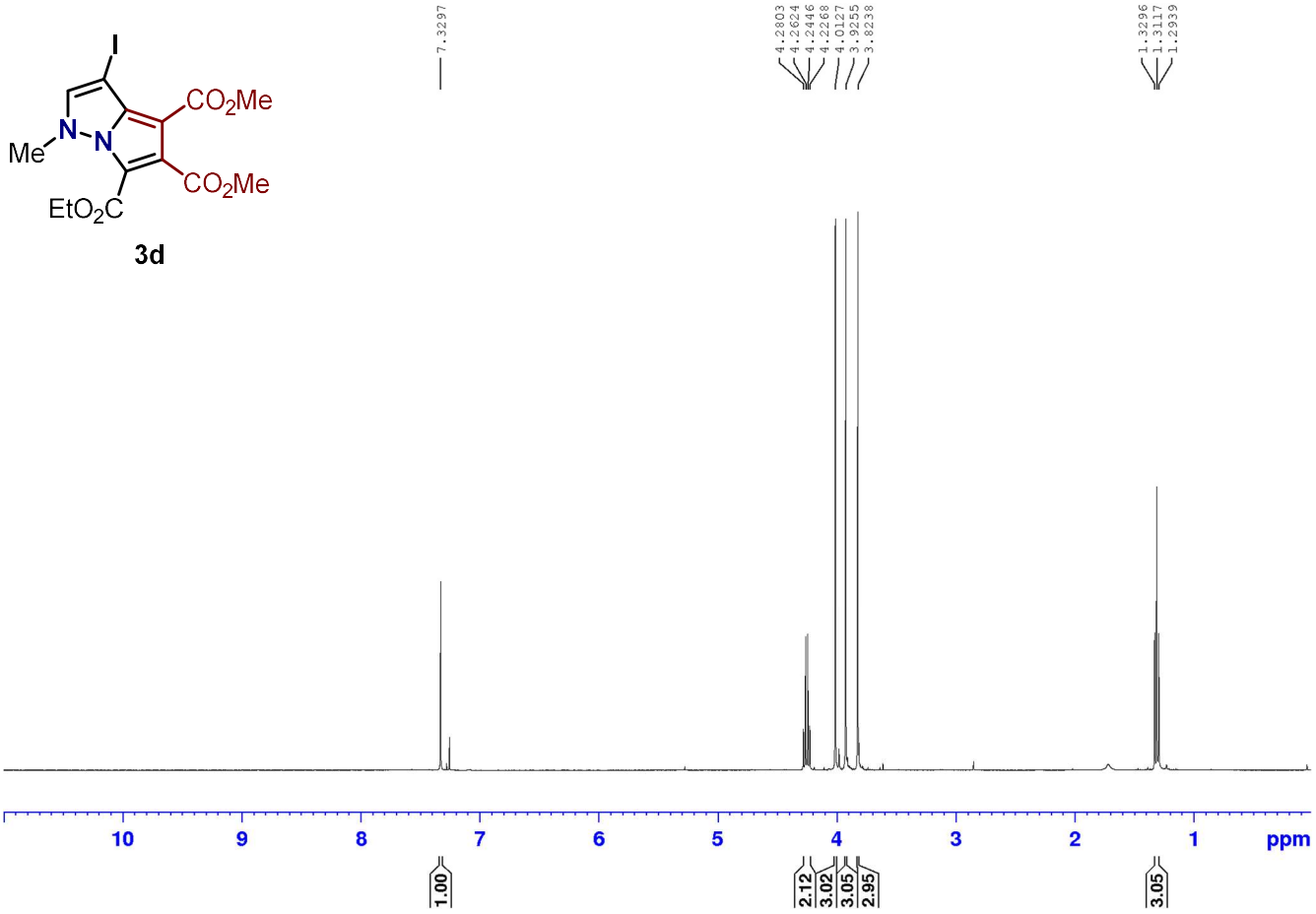
^{1}H NMR (400 MHz, $CDCl_3$)



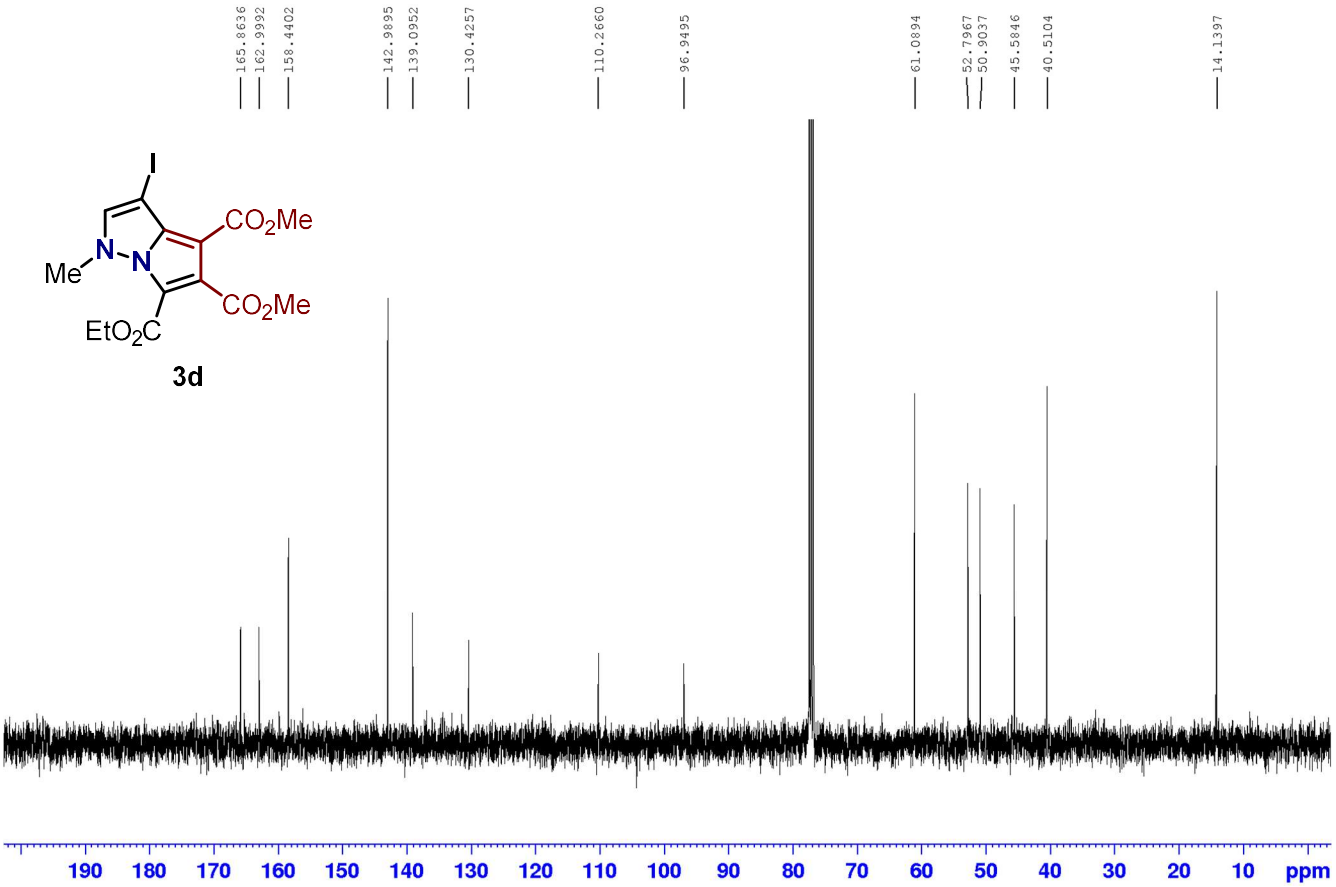
^{13}C NMR (100 MHz, $CDCl_3$)



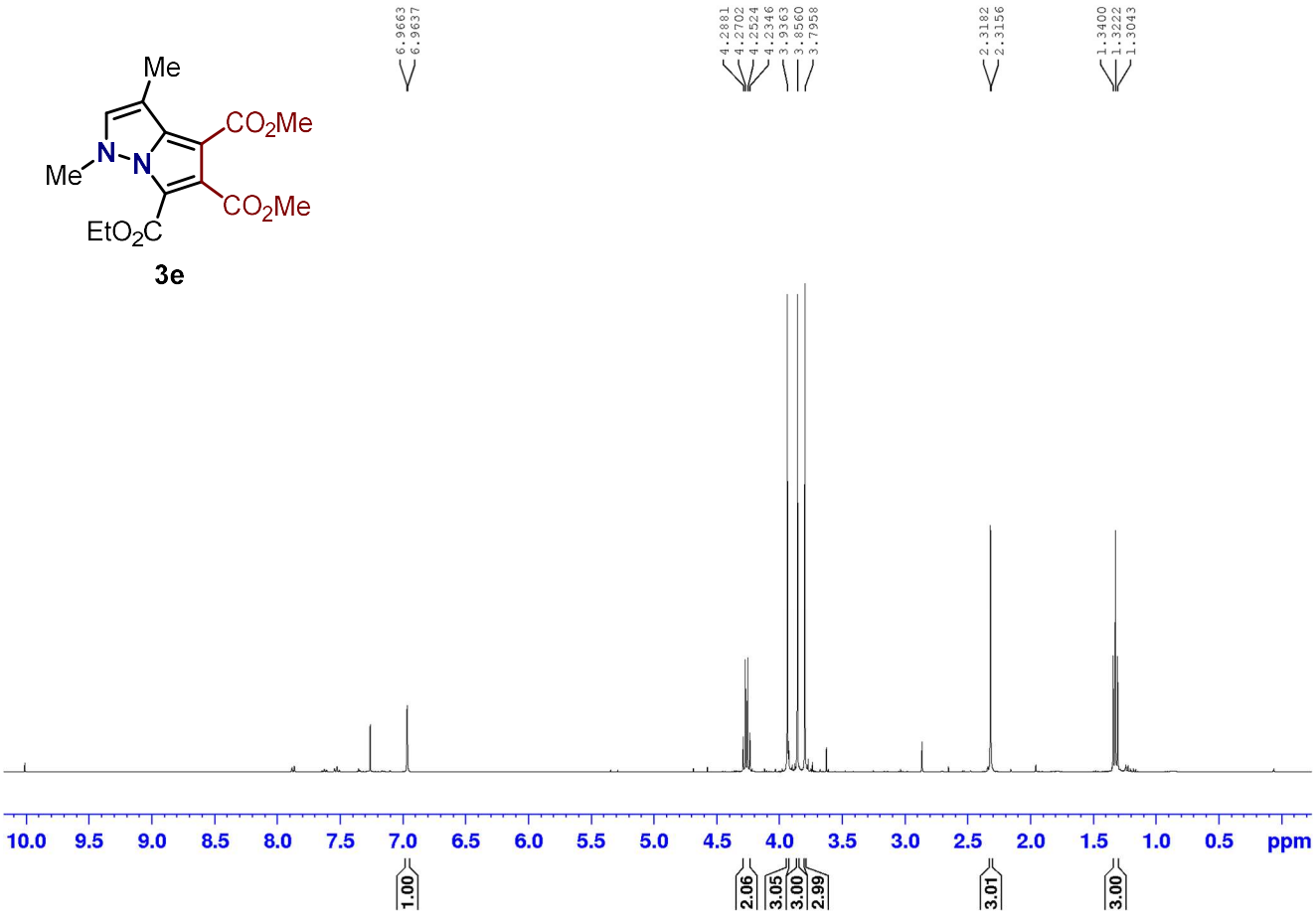
^{1}H NMR (400 MHz, $CDCl_3$)



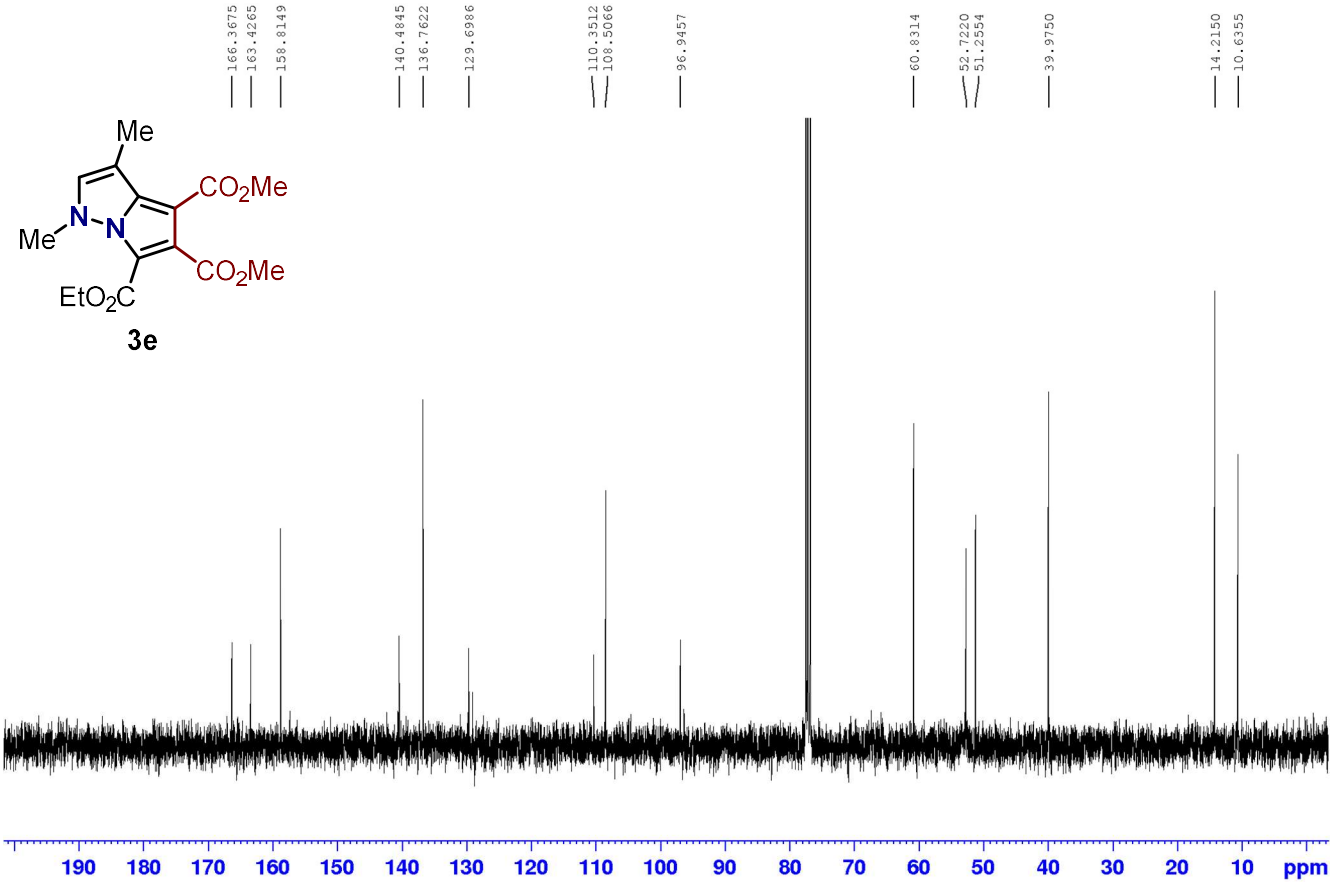
^{13}C NMR (100 MHz, $CDCl_3$)



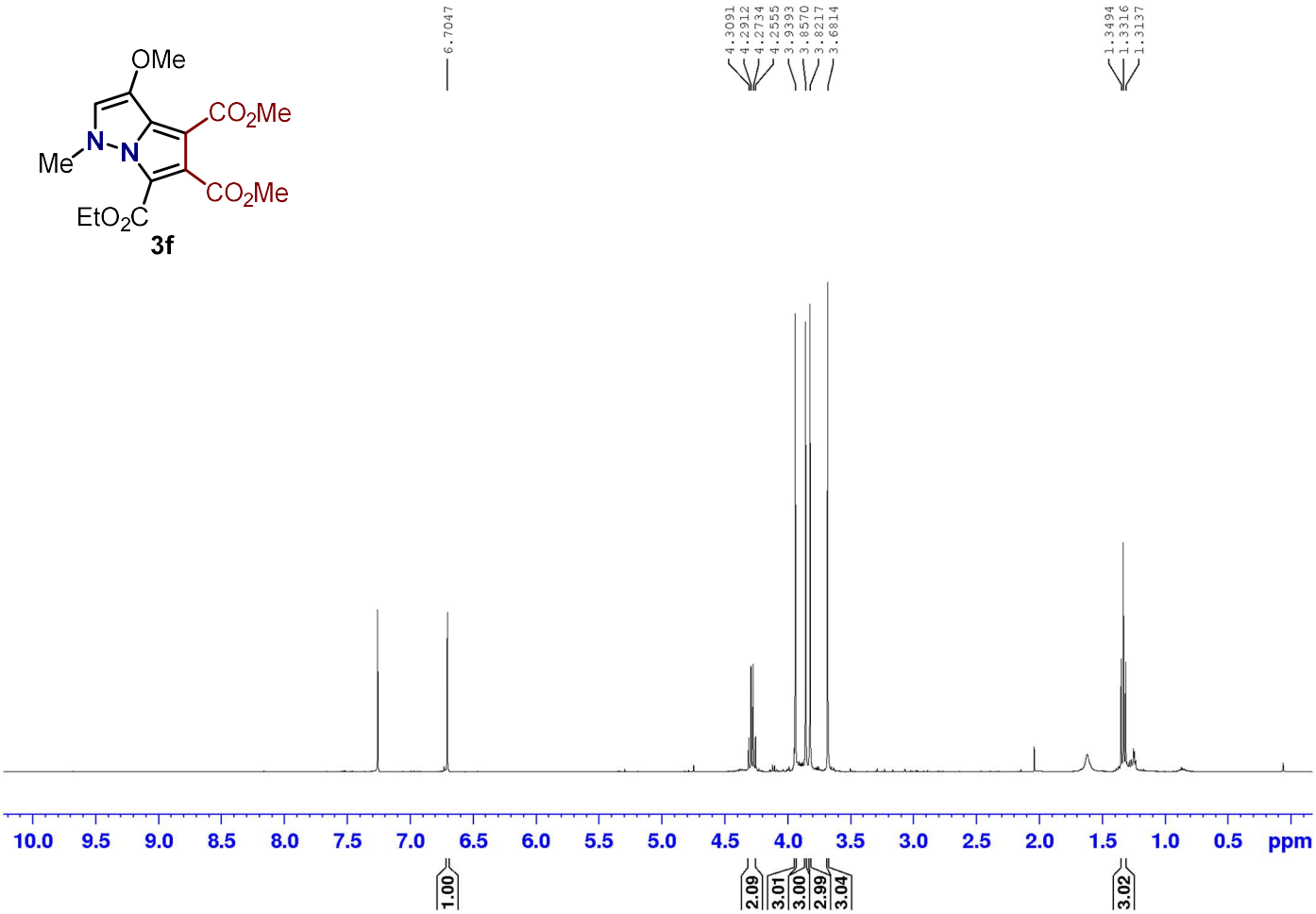
^{1}H NMR (400 MHz, $CDCl_3$)



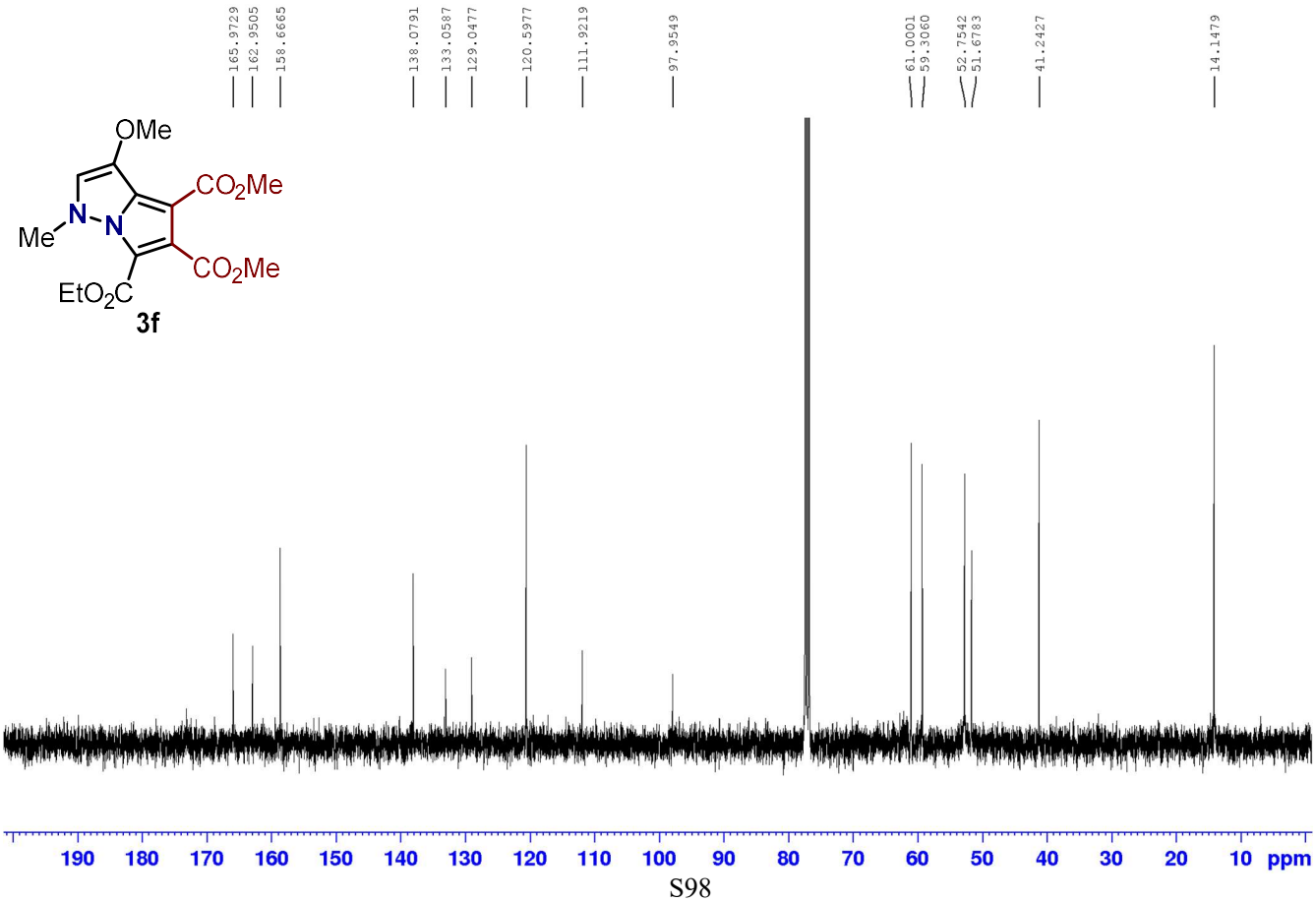
^{13}C NMR (100 MHz, $CDCl_3$)



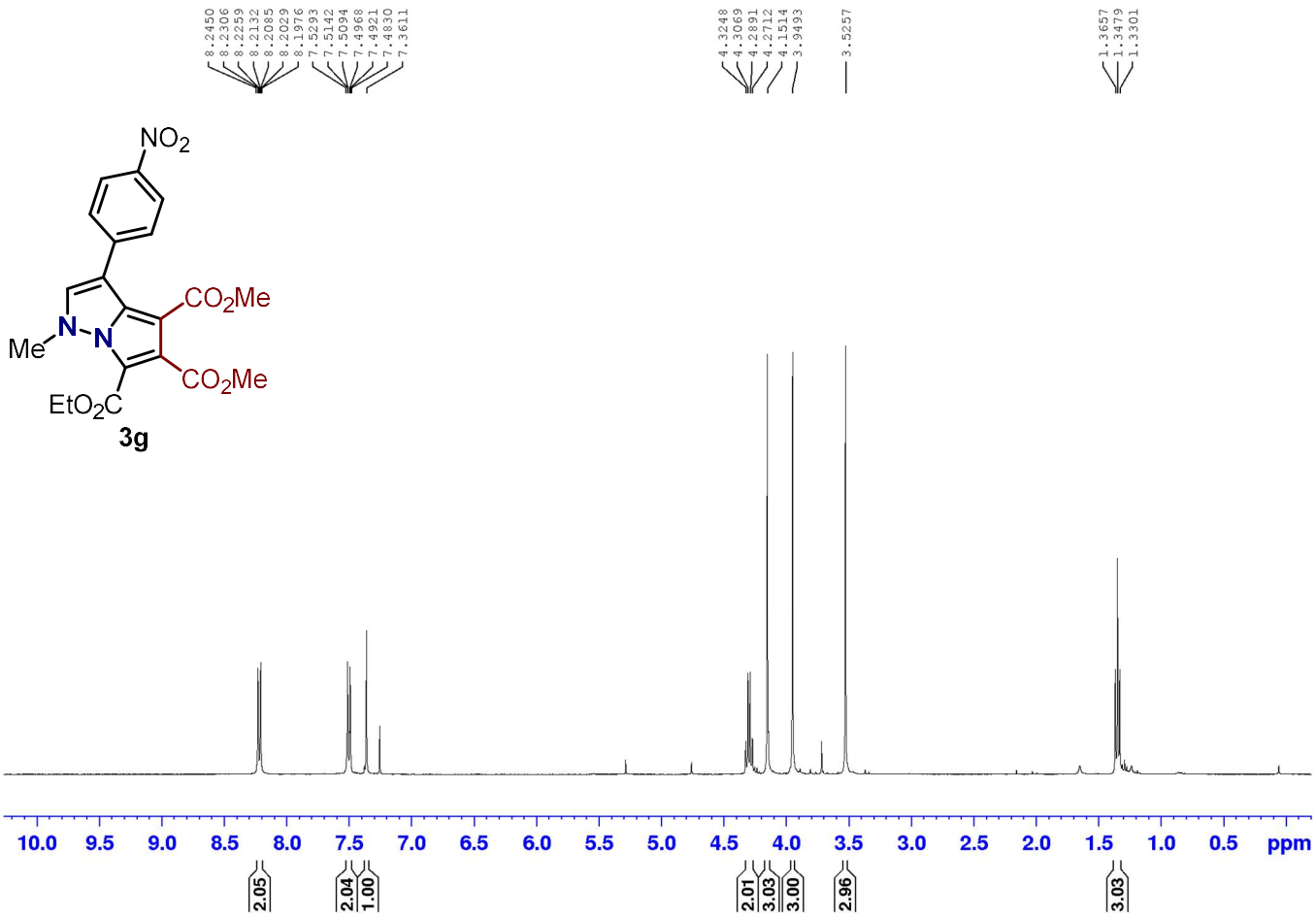
^{1}H NMR (400 MHz, $CDCl_3$)



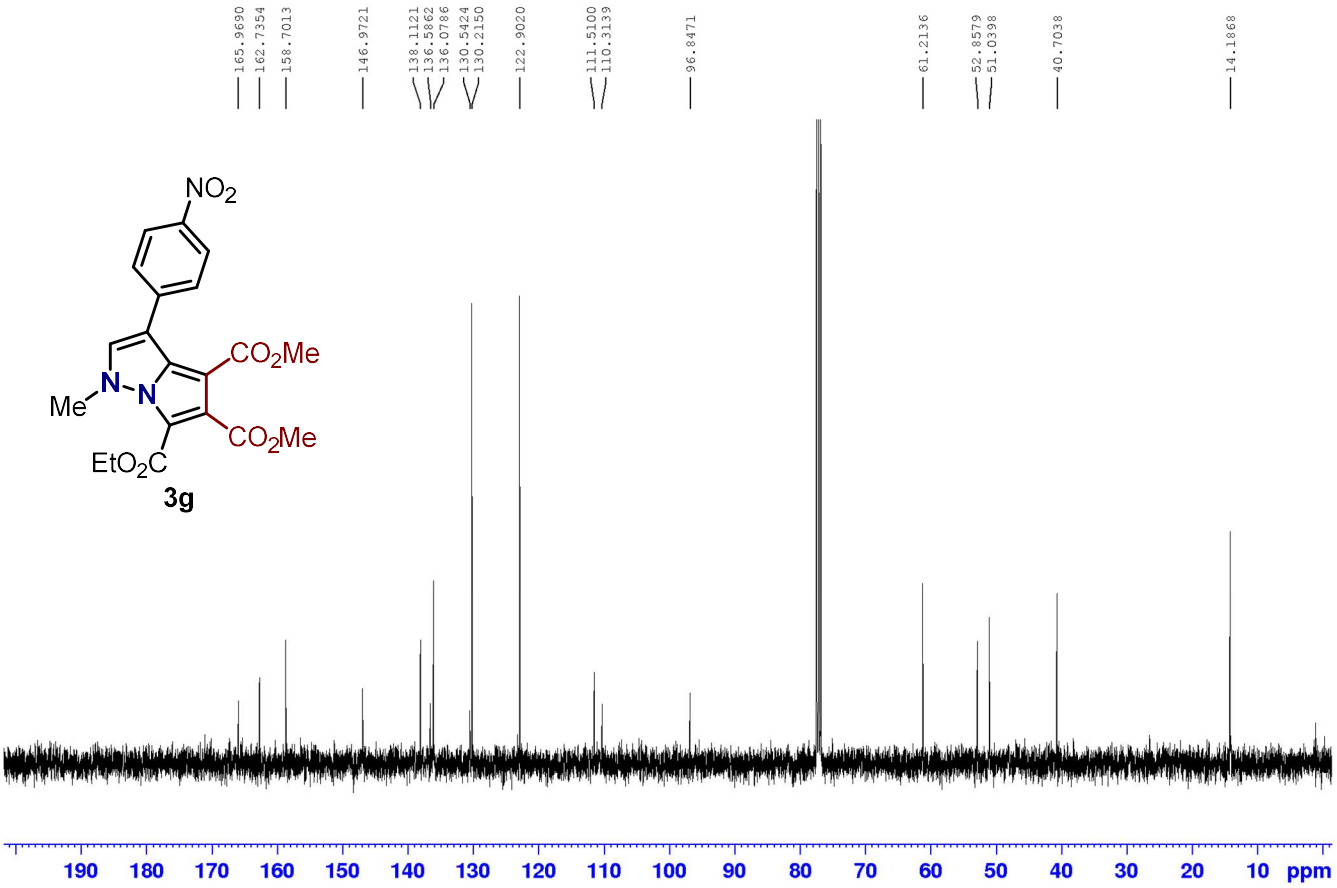
^{13}C NMR (100 MHz, $CDCl_3$)



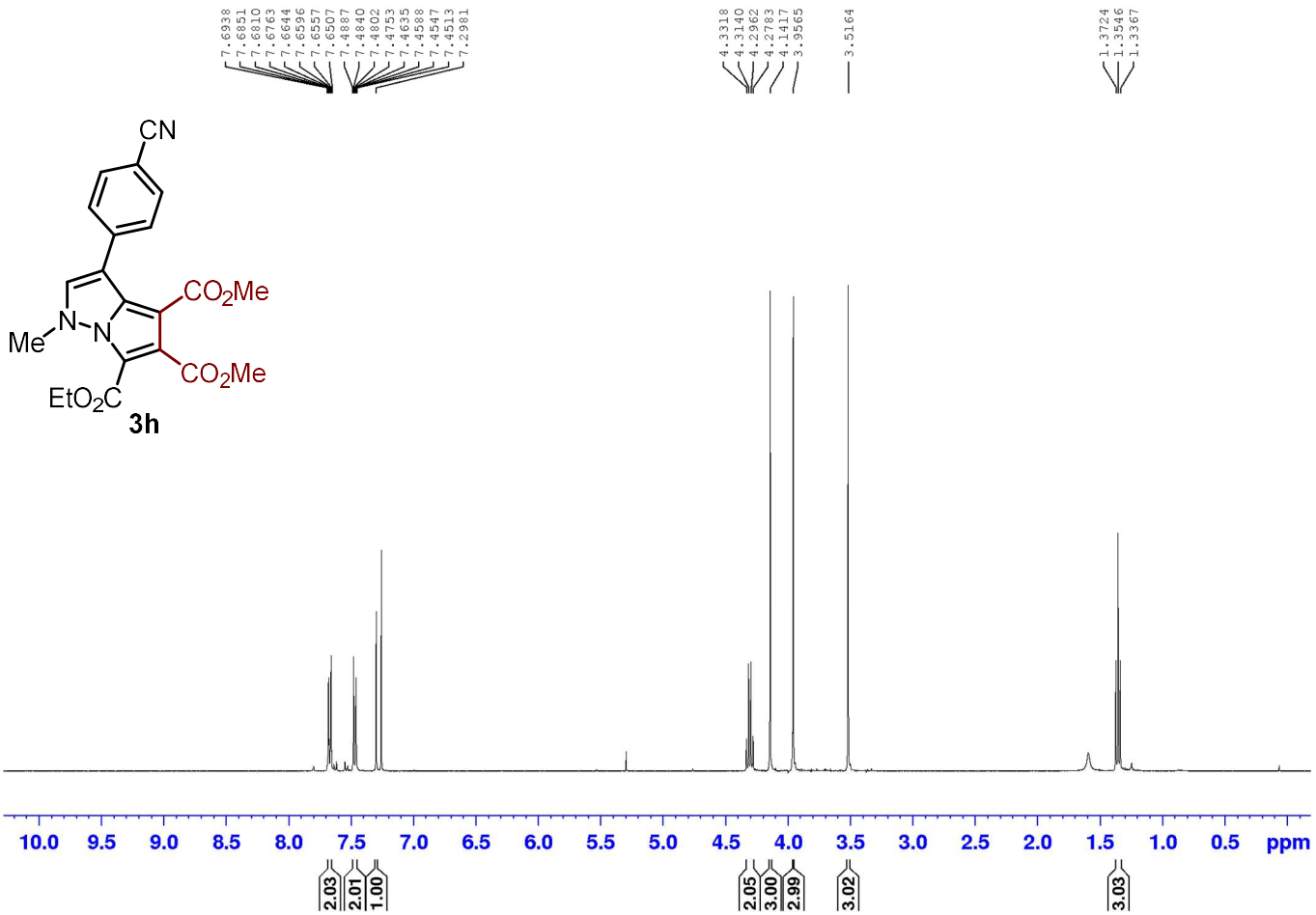
^{1}H NMR (400 MHz, $CDCl_3$)



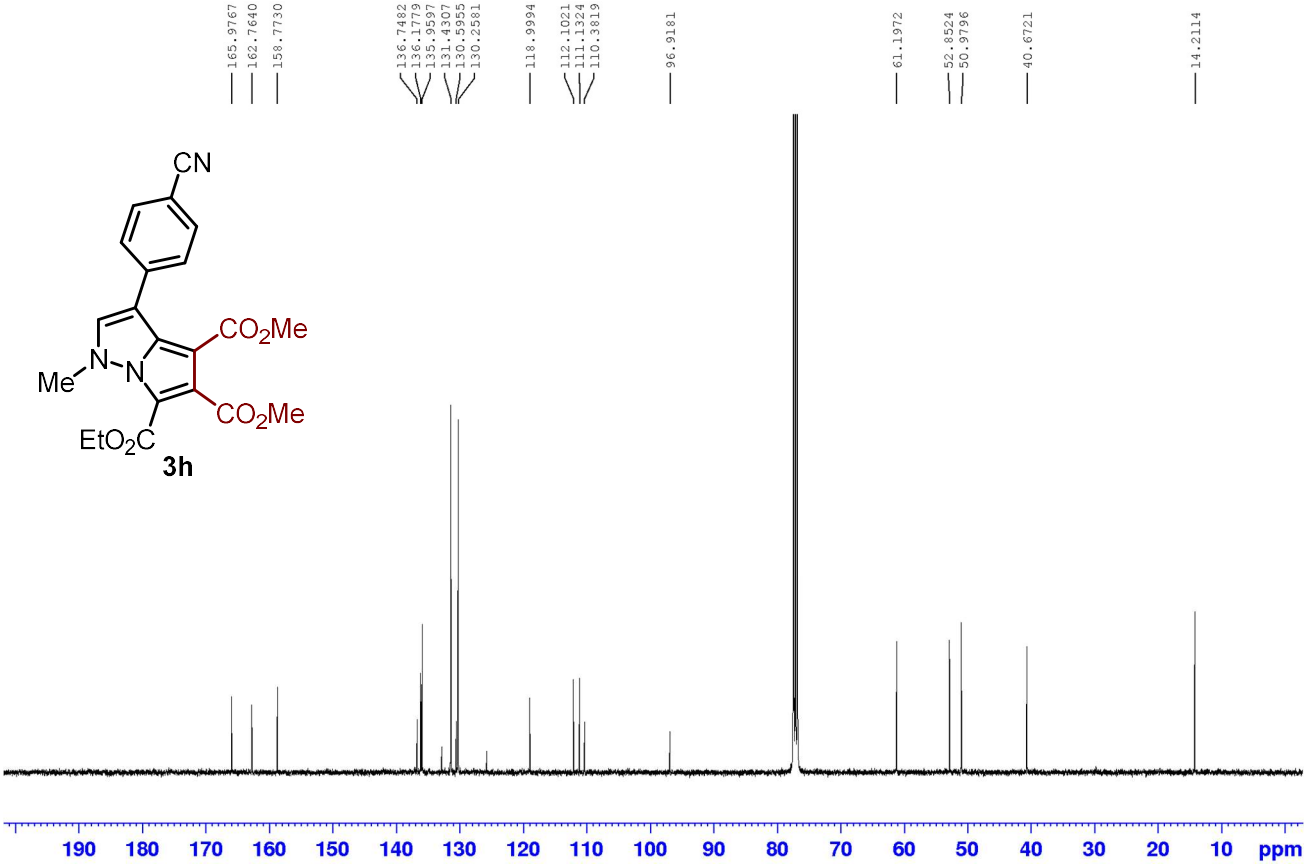
^{13}C NMR (100 MHz, $CDCl_3$)



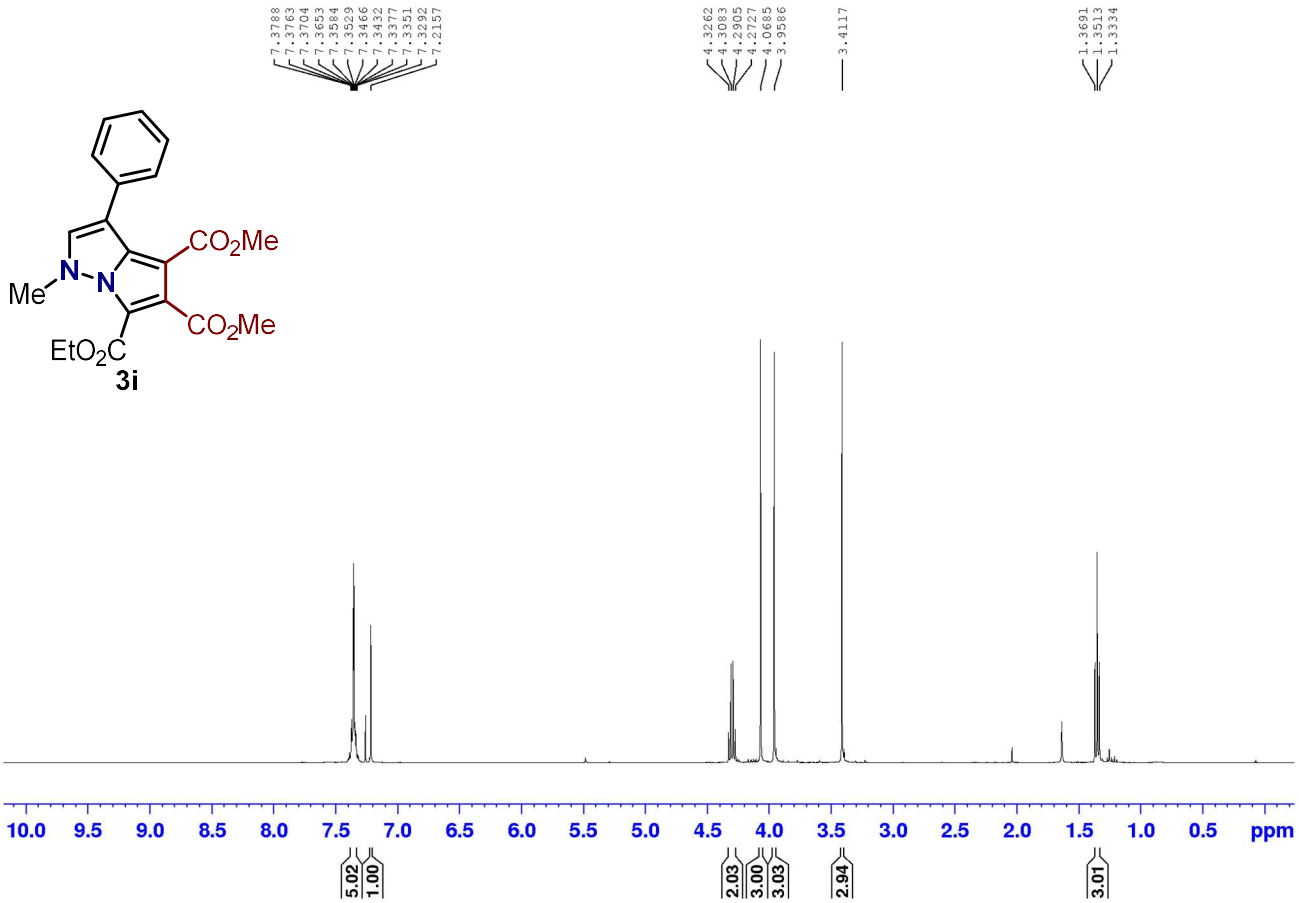
^{1}H NMR (400 MHz, $CDCl_3$)



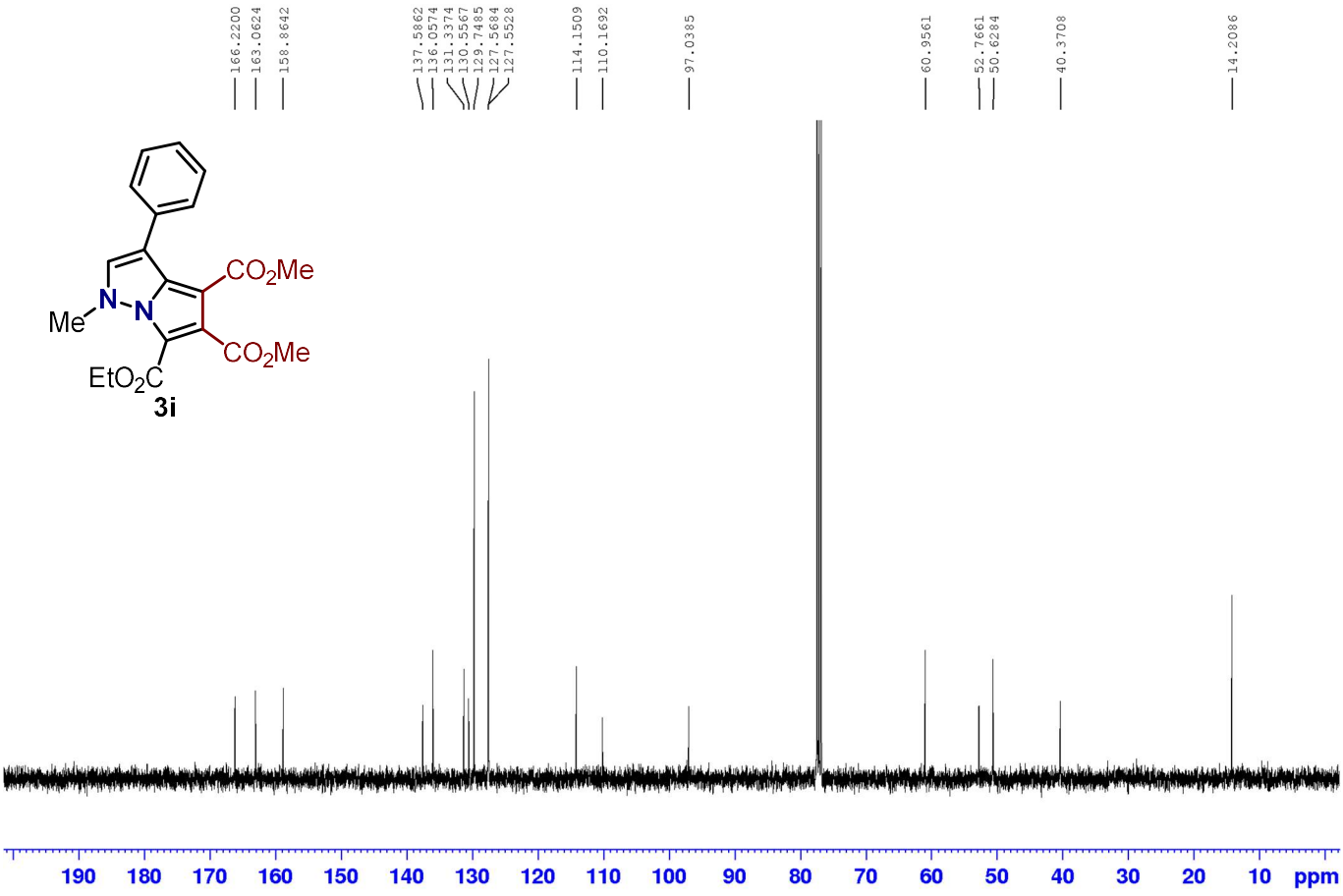
^{13}C NMR (100 MHz, $CDCl_3$)



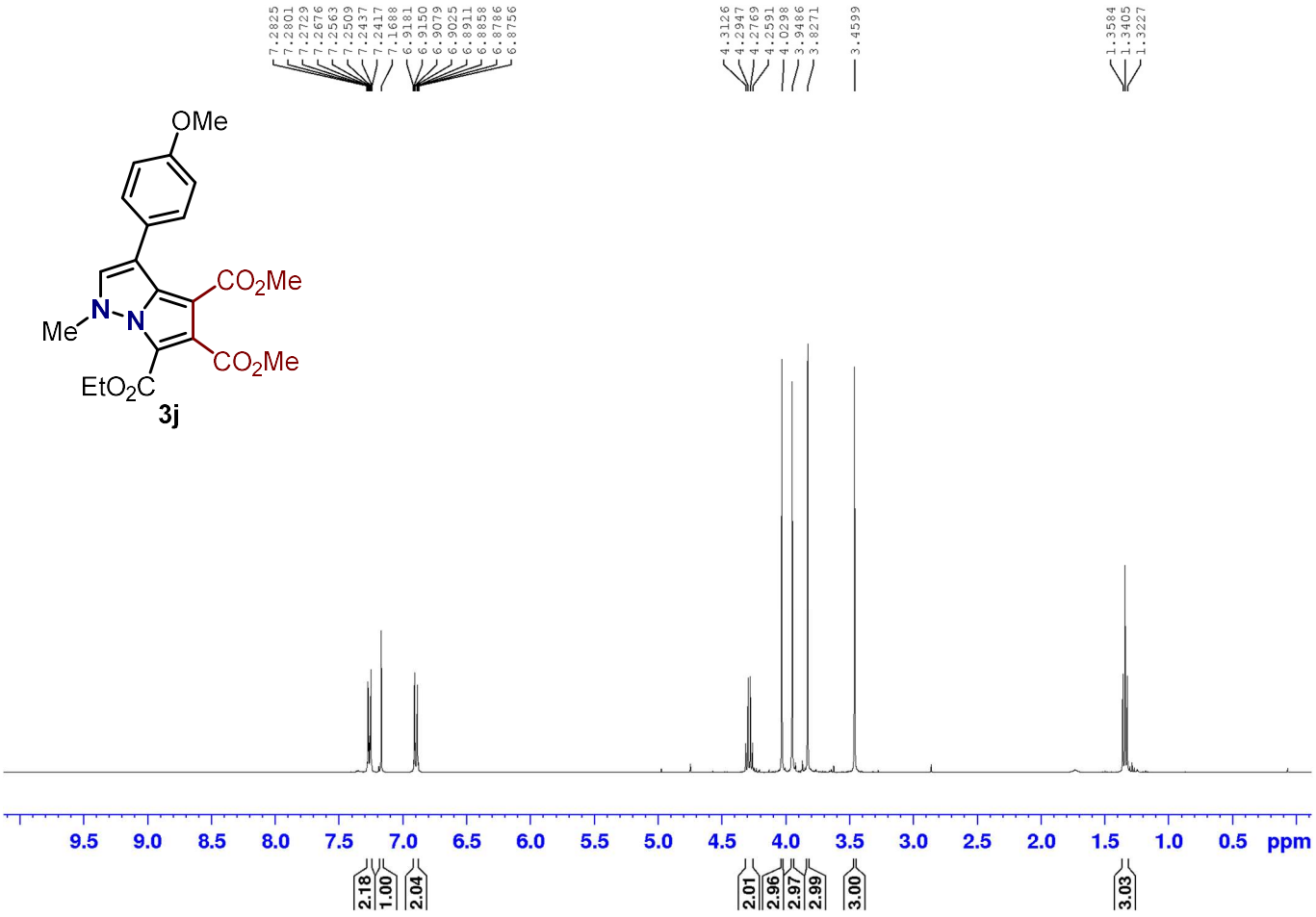
^{1}H NMR (400 MHz, $CDCl_3$)



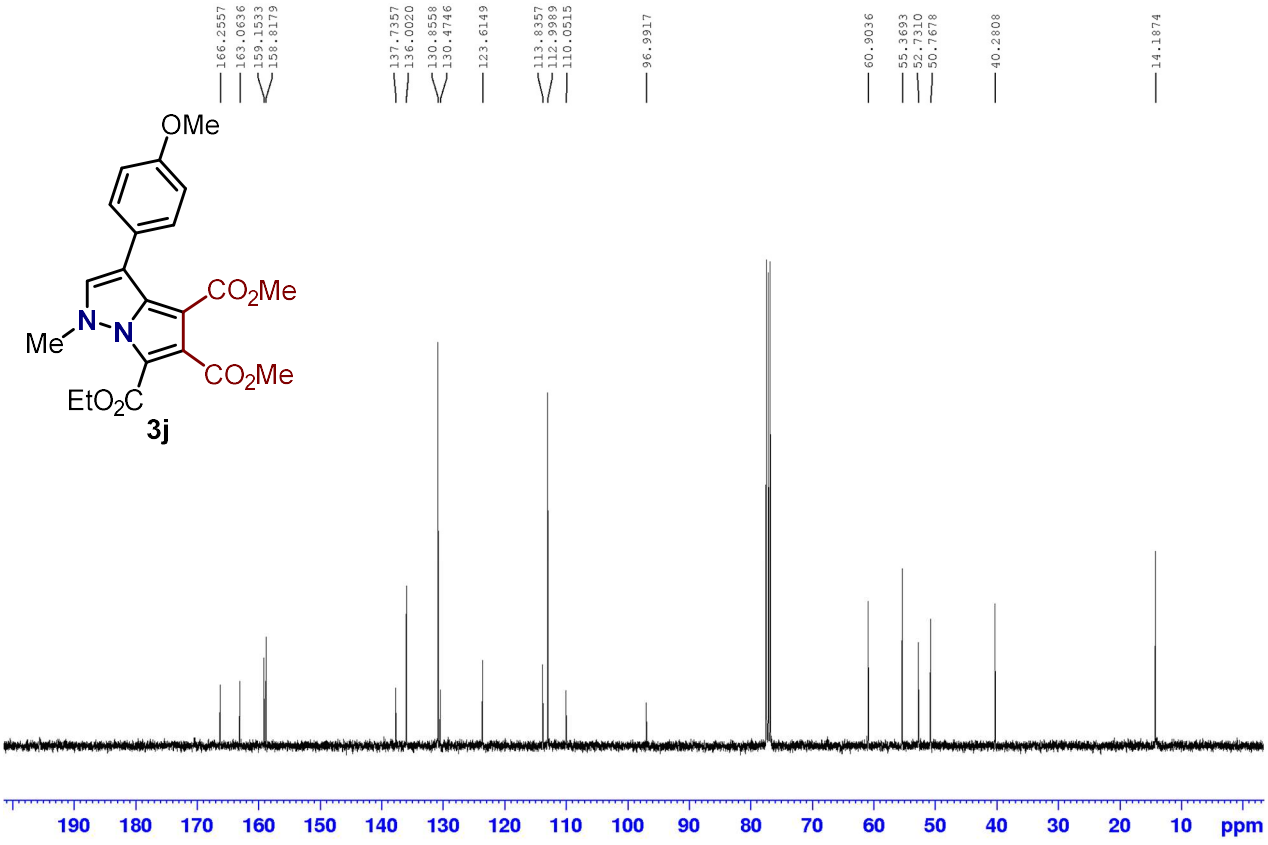
^{13}C NMR (100 MHz, $CDCl_3$)



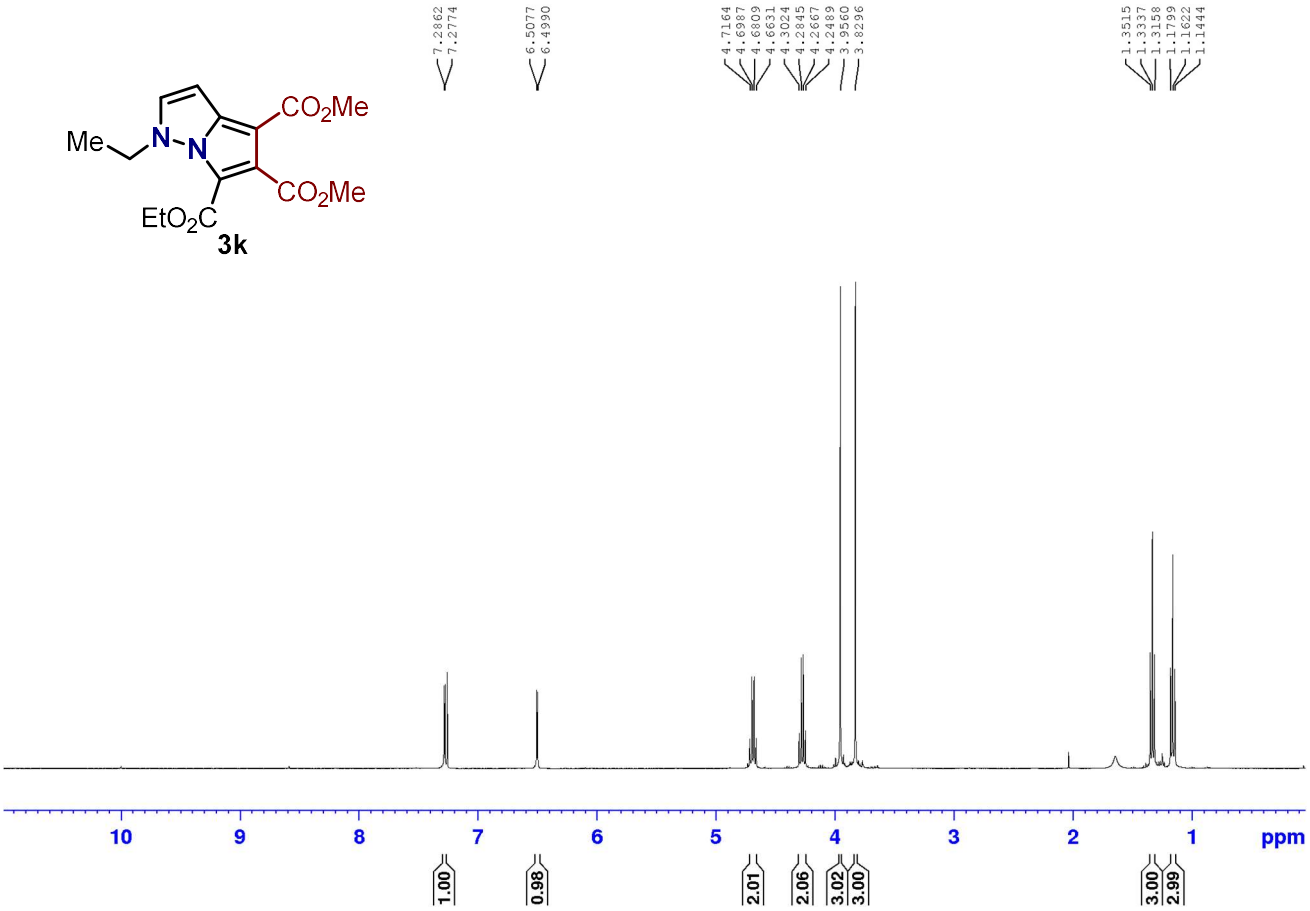
^{1}H NMR (400 MHz, $CDCl_3$)



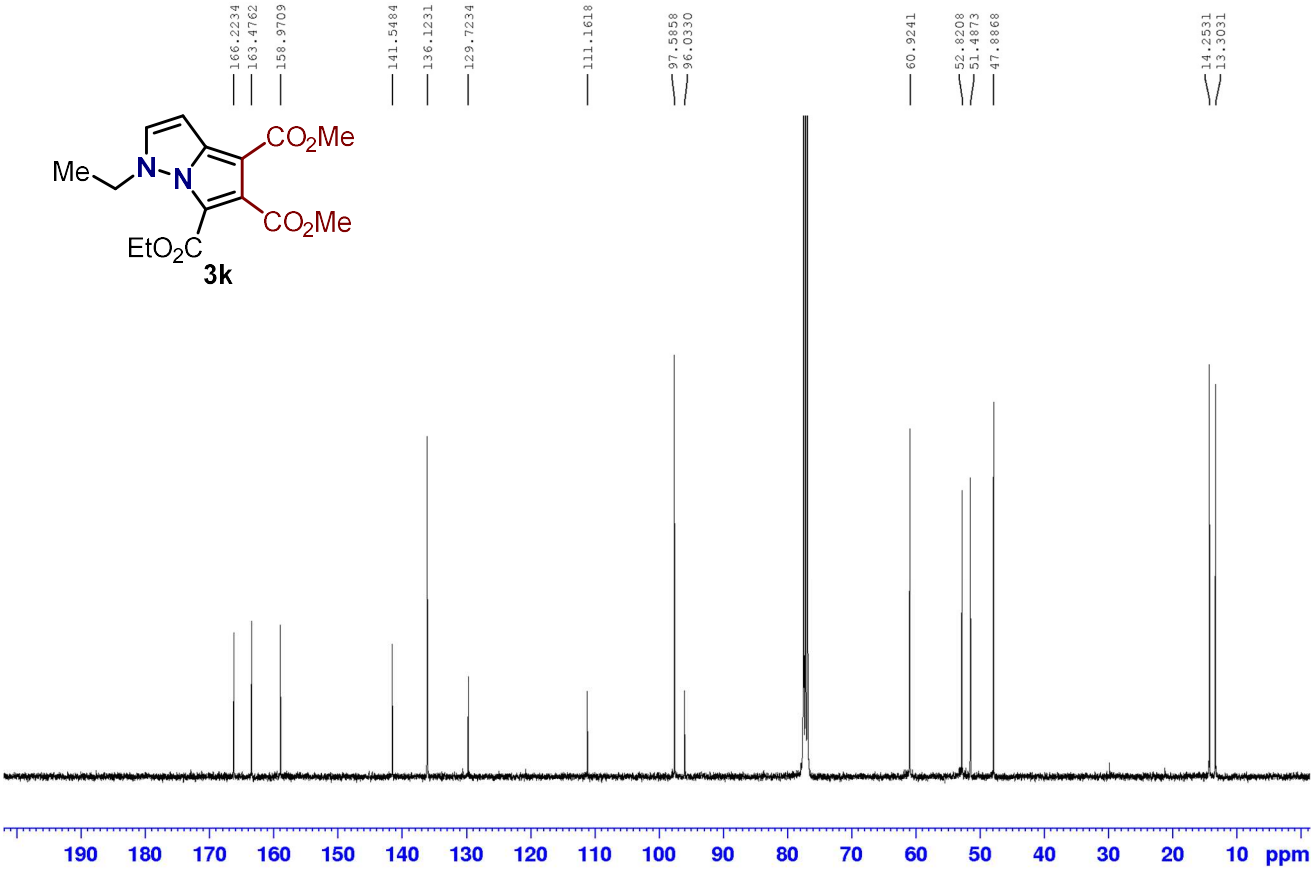
^{13}C NMR (100 MHz, $CDCl_3$)



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



^{13}C NMR (100 MHz, $CDCl_3$)



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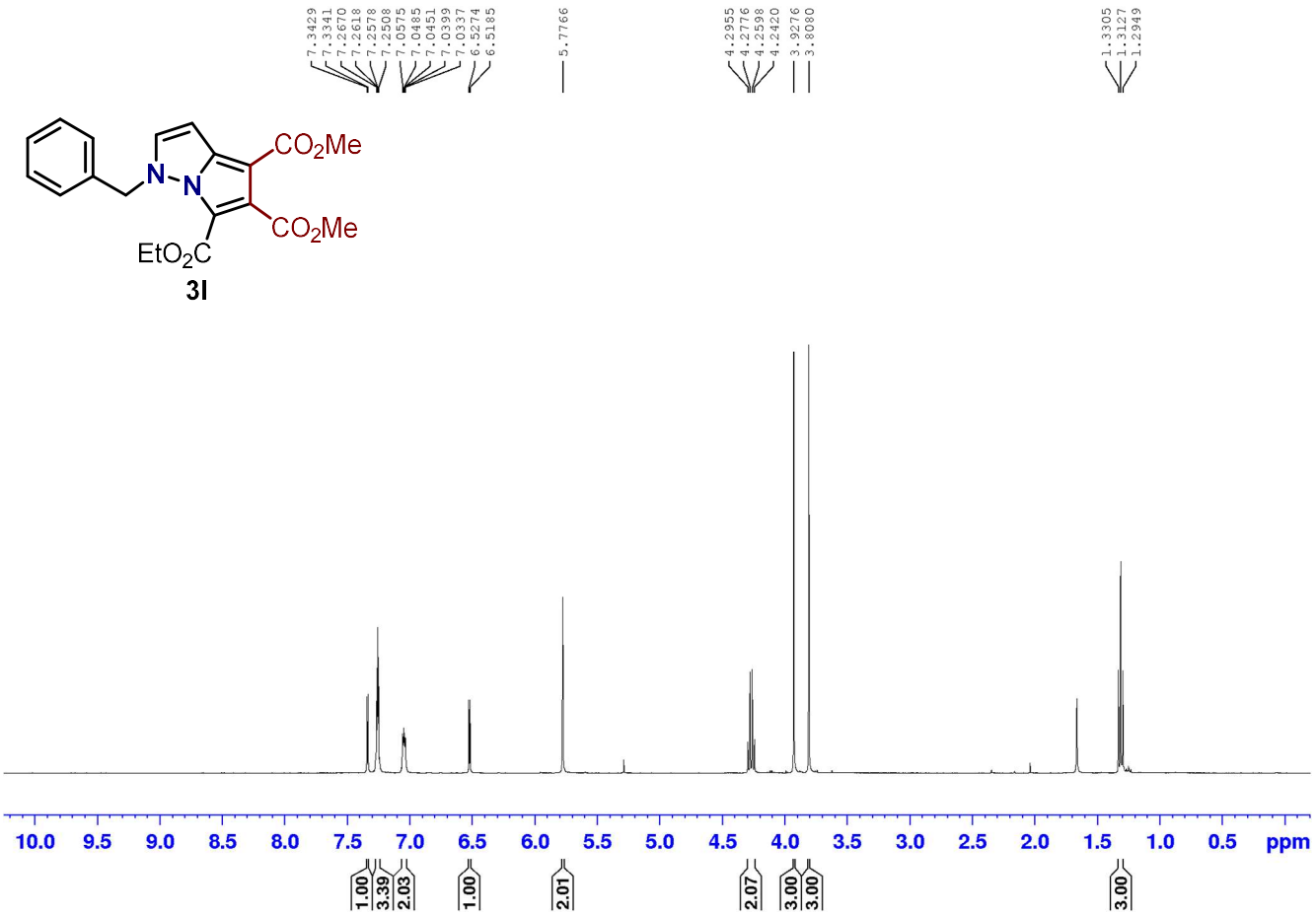

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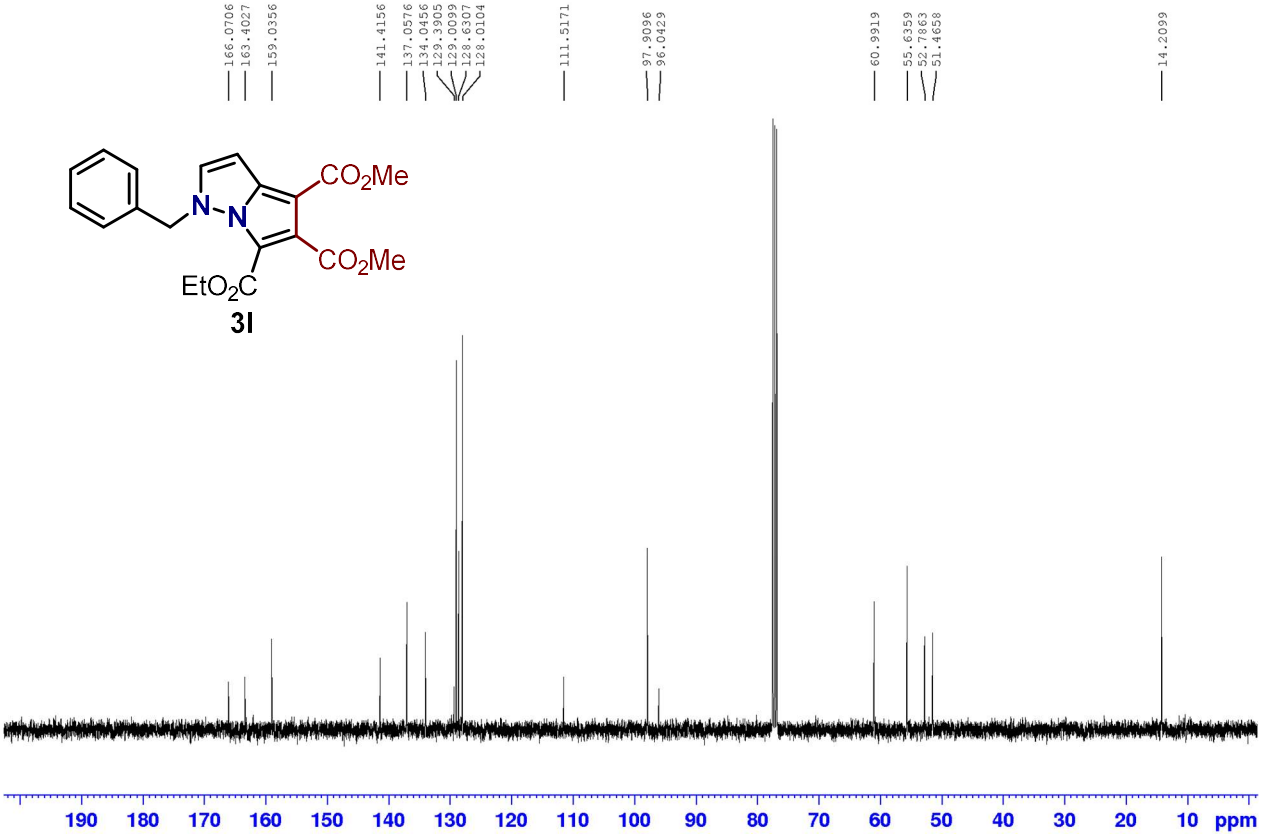
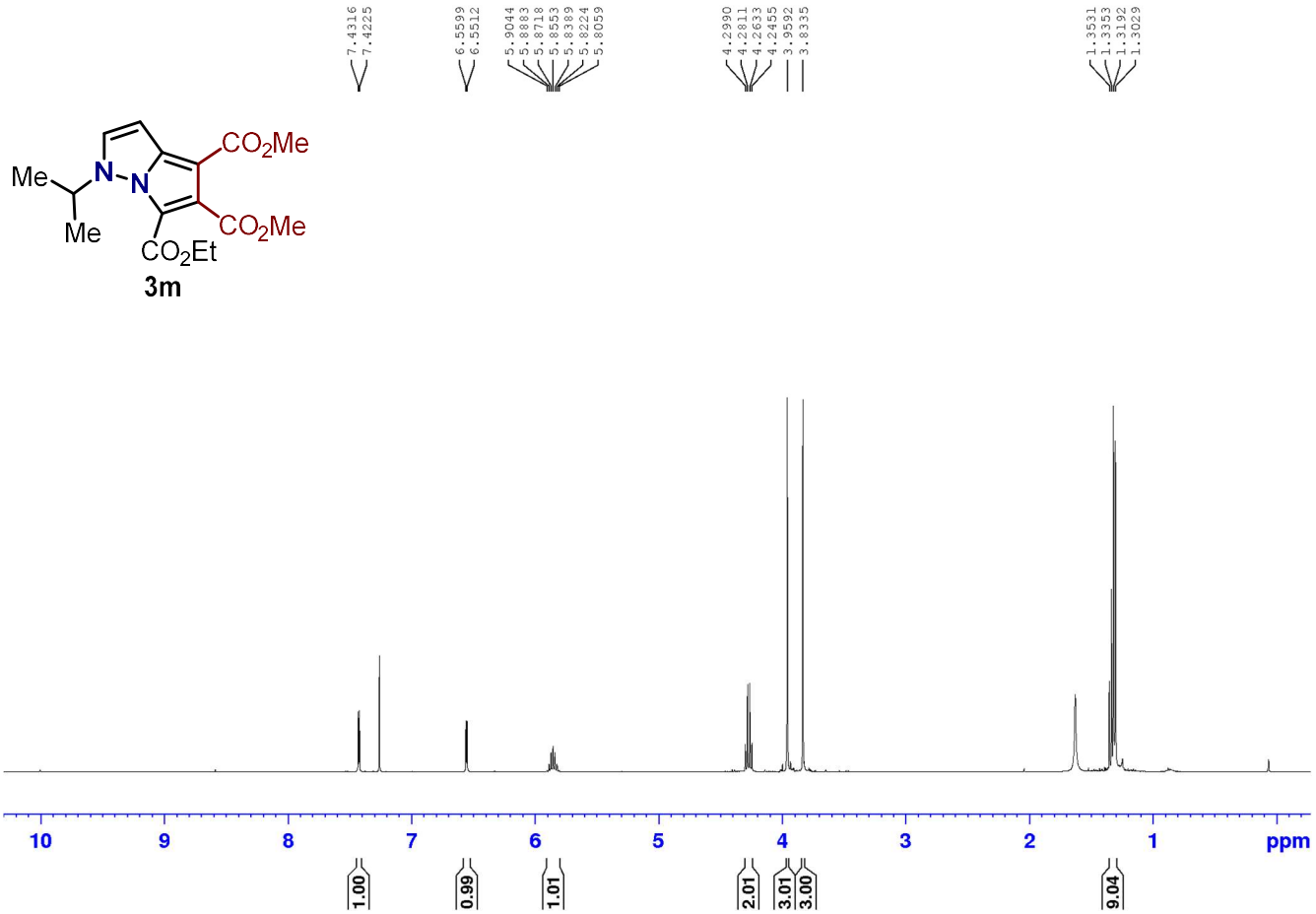
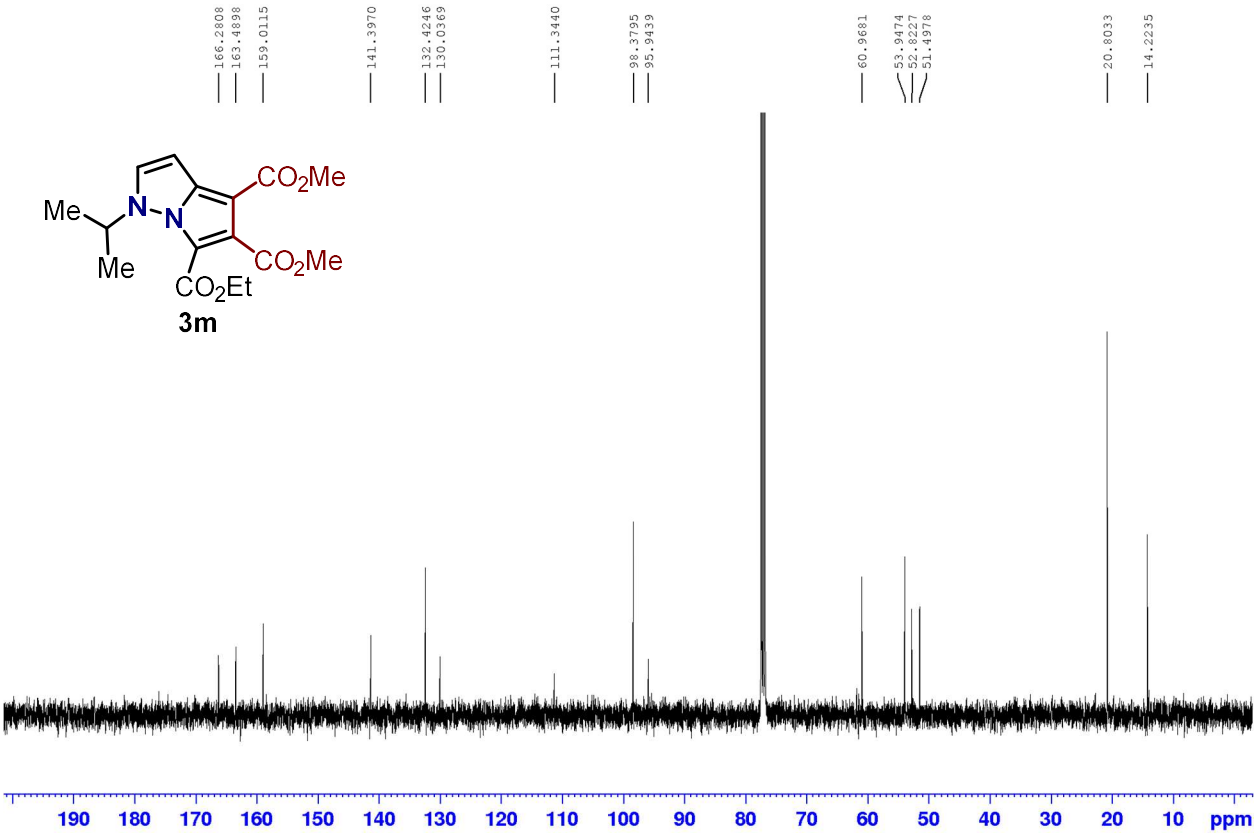


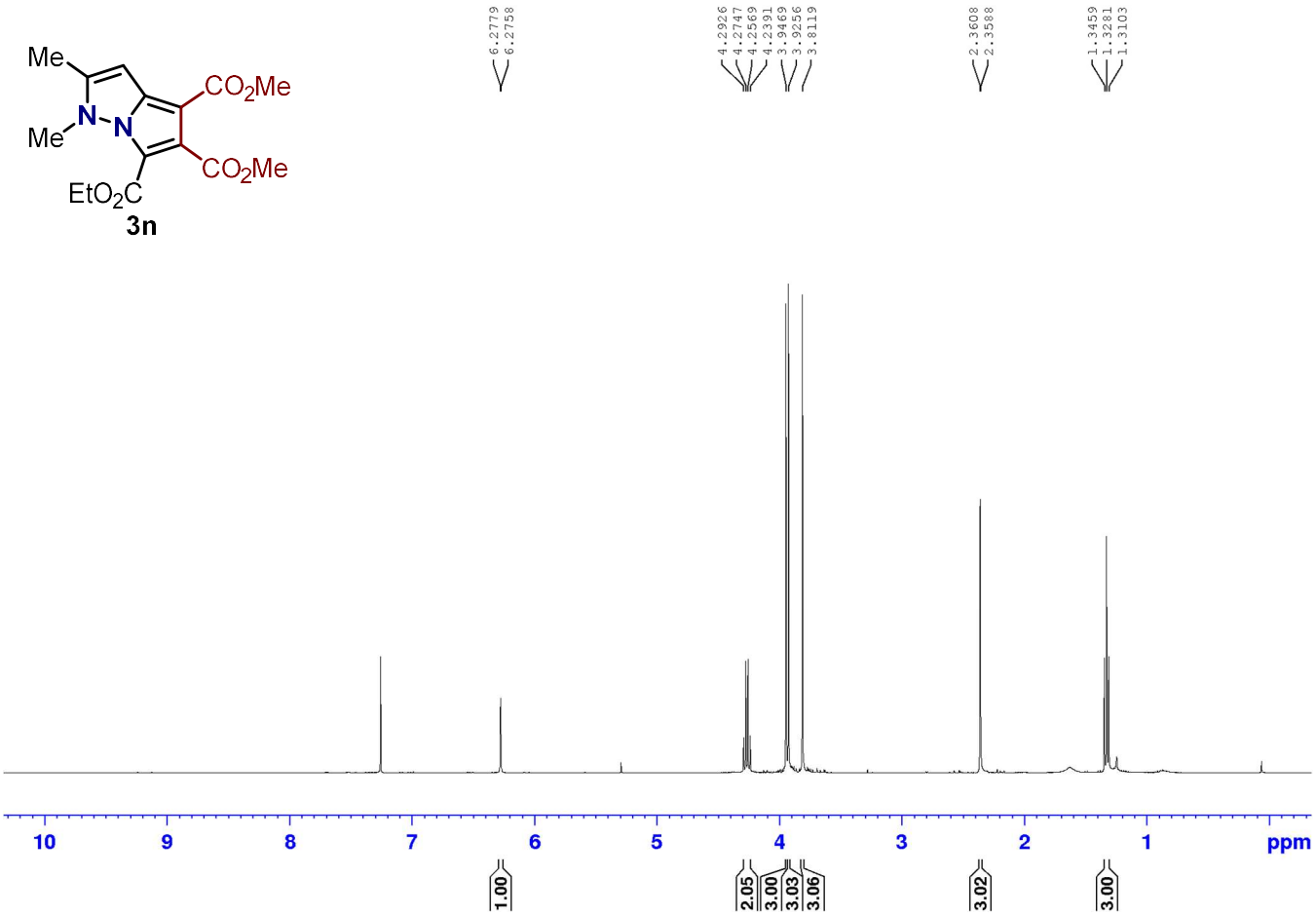
^{1}H NMR (400 MHz, $CDCl_3$)



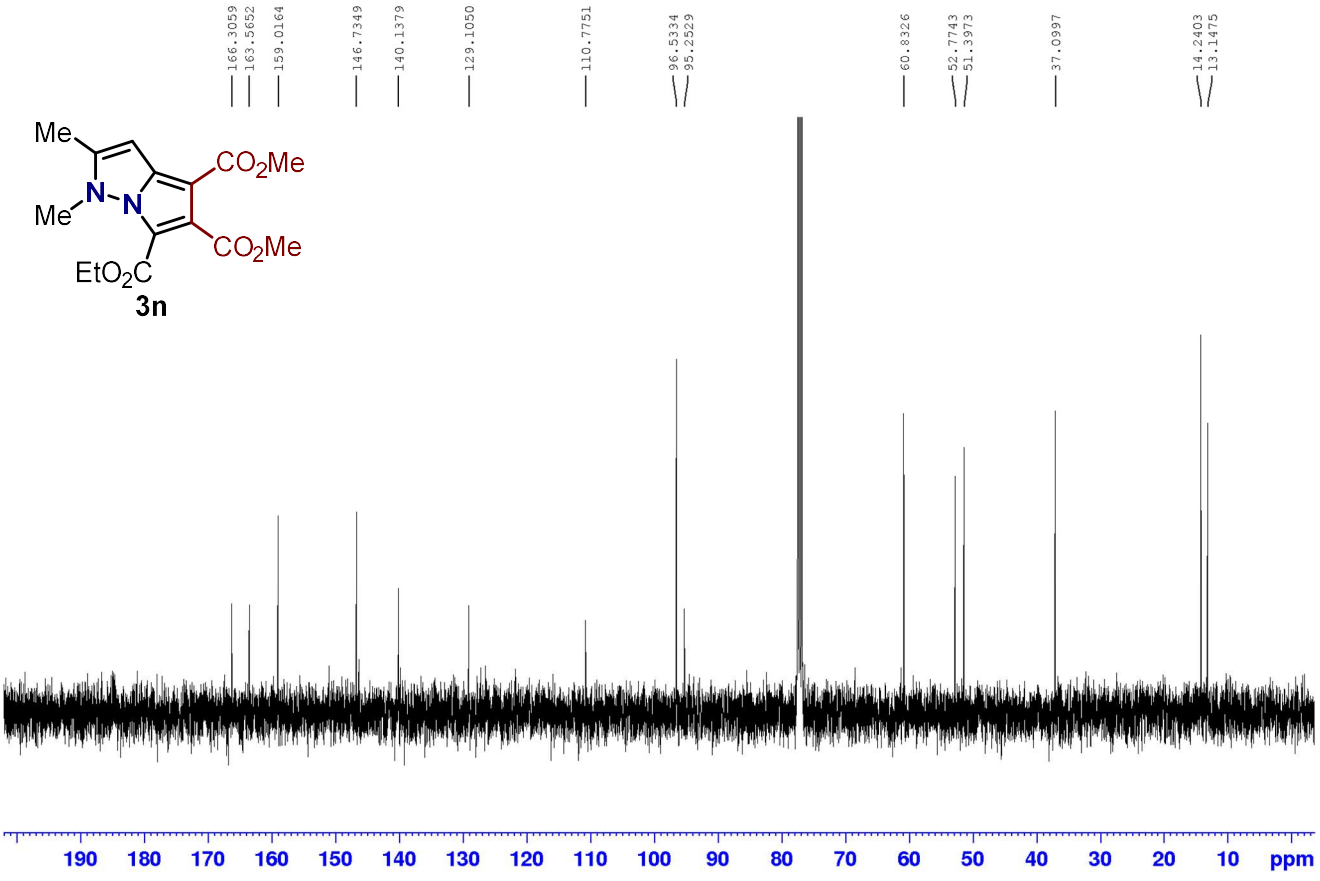
^{13}C NMR (100 MHz, $CDCl_3$)



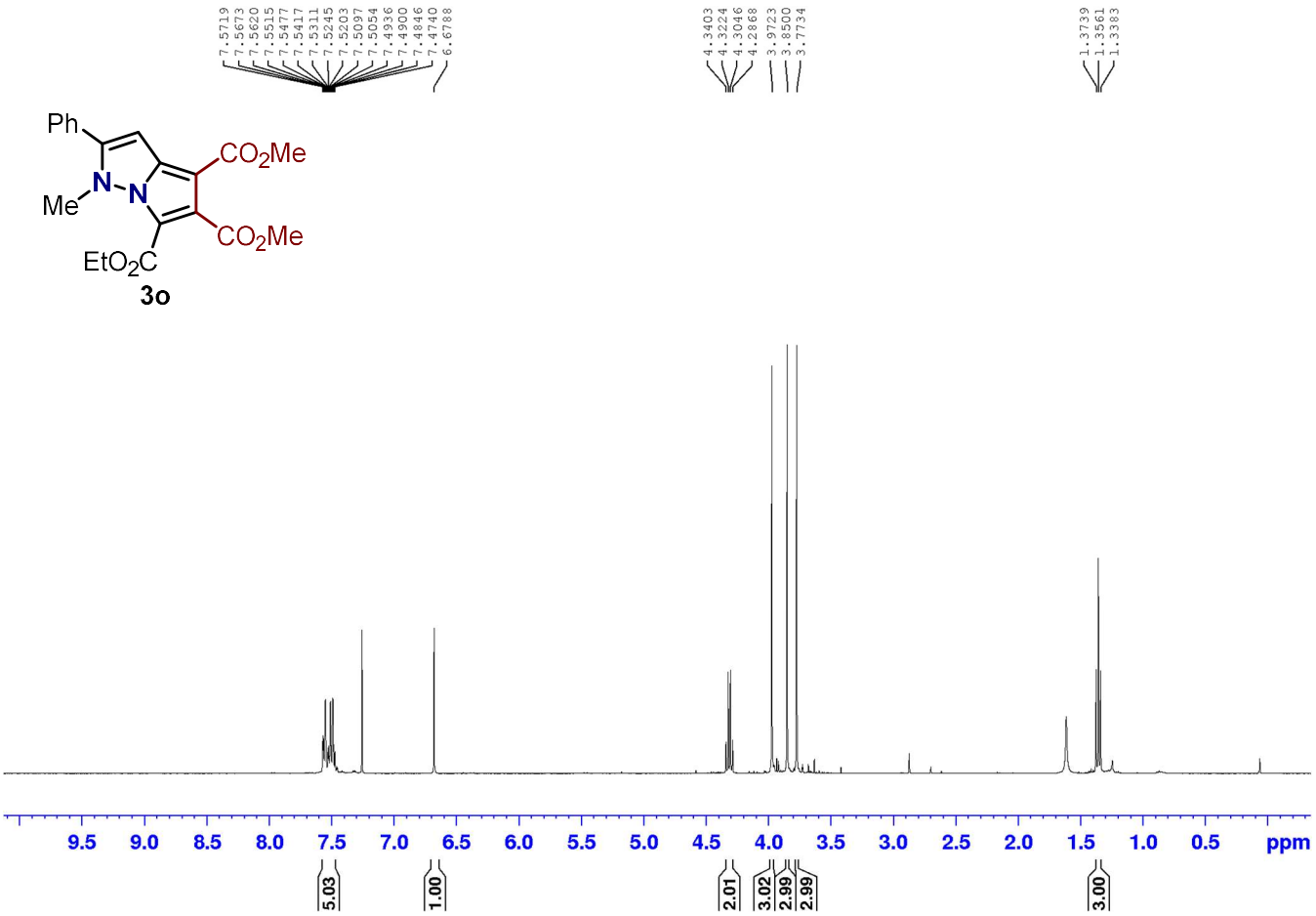
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (100 MHz, $CDCl_3$)



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



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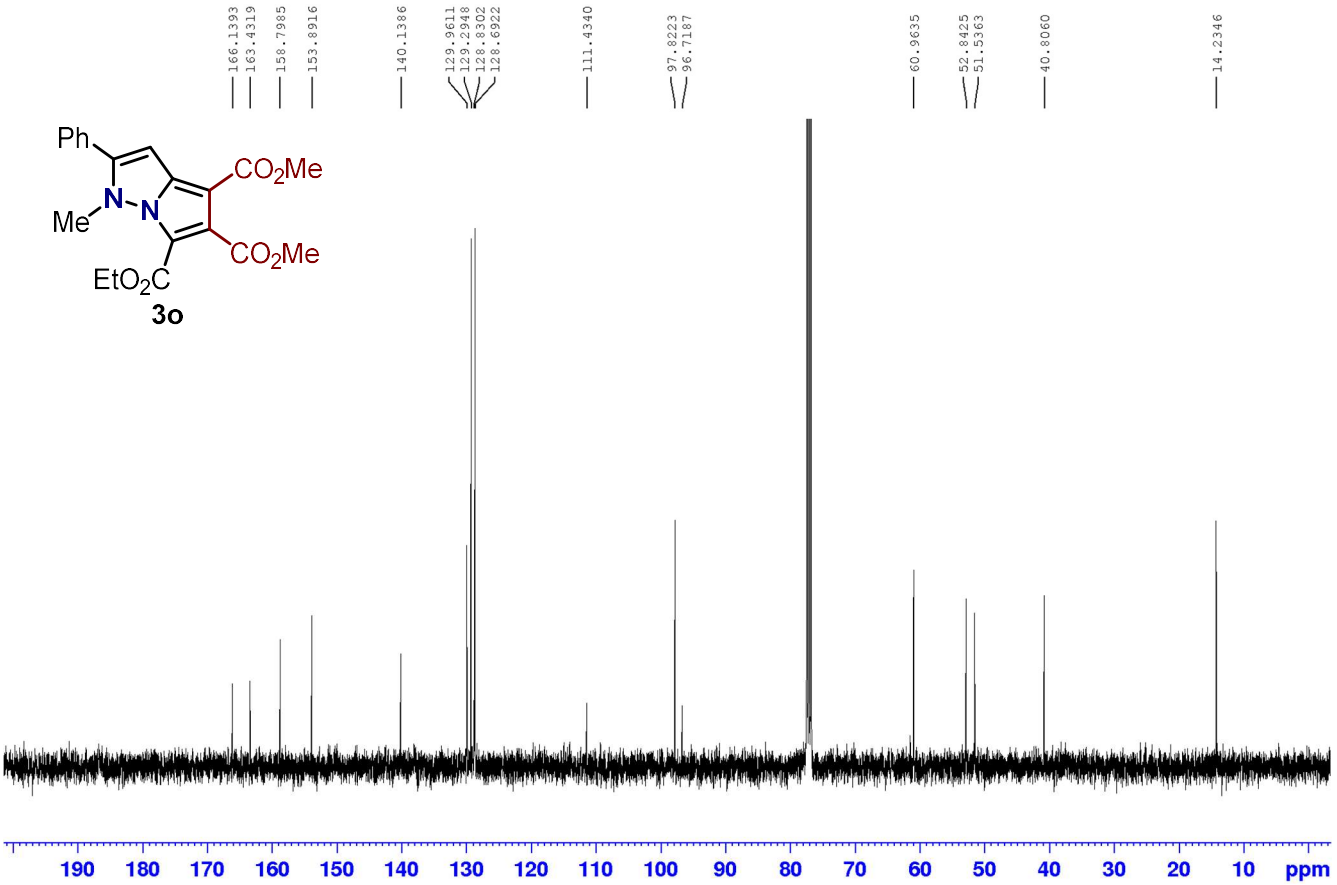

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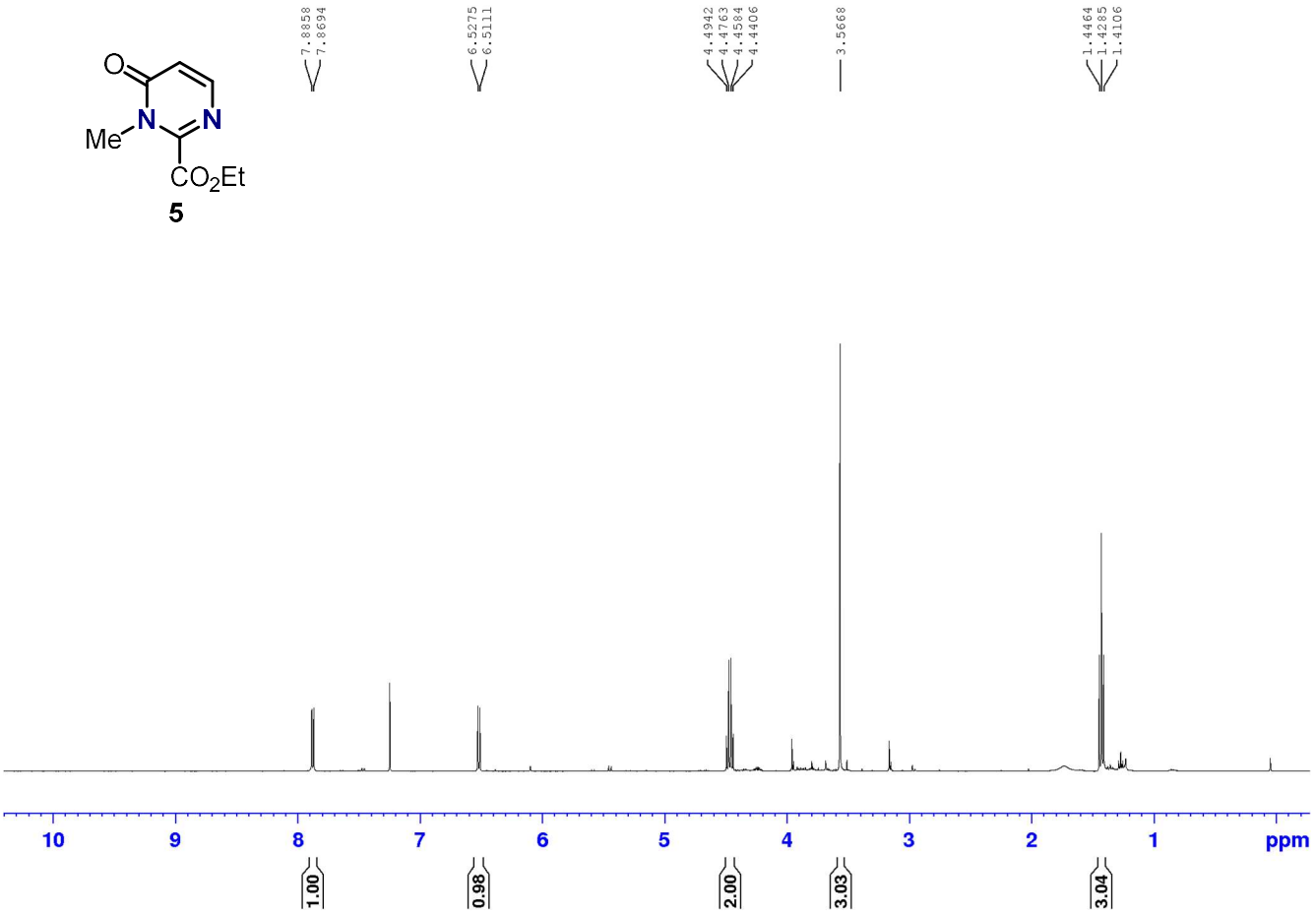
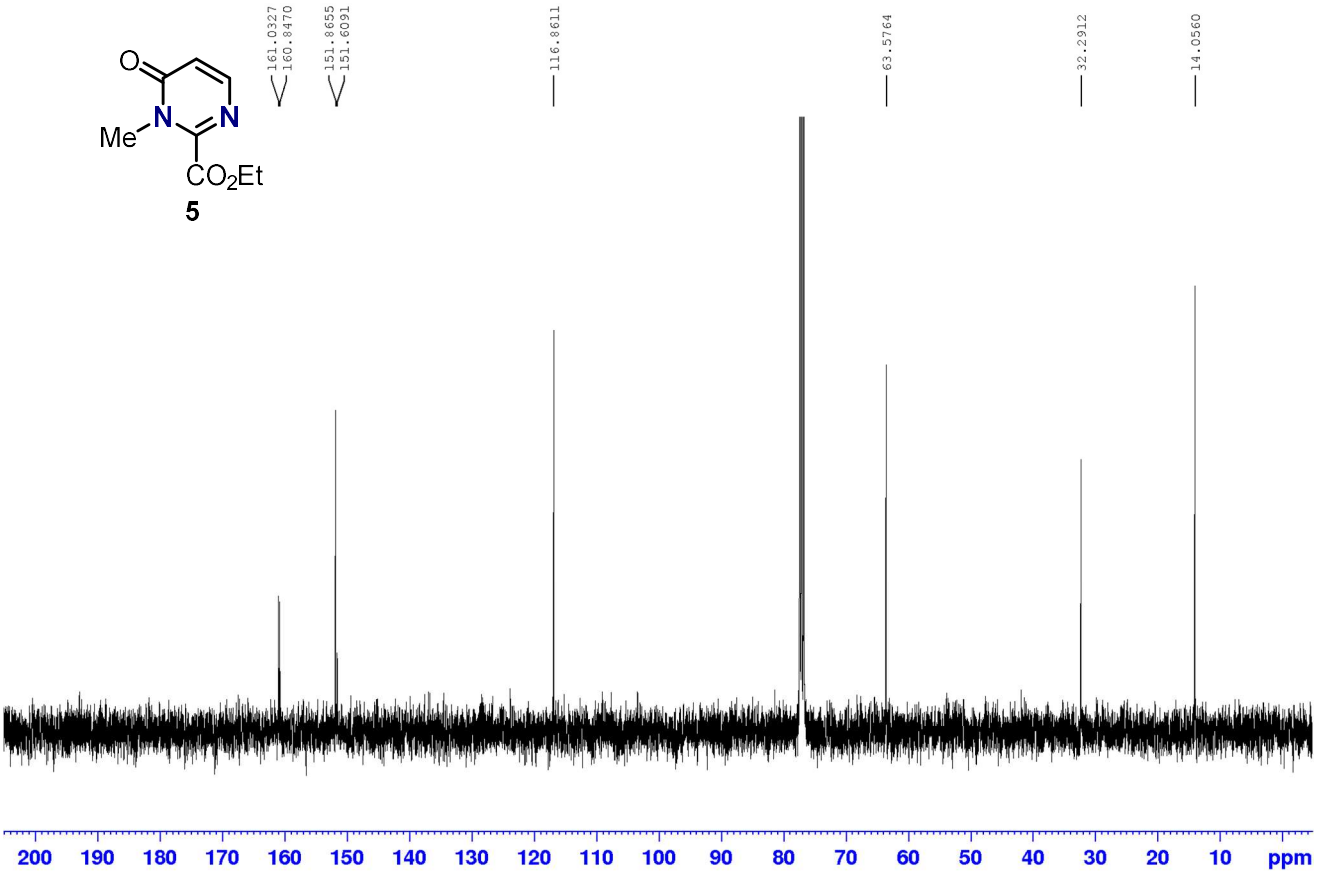
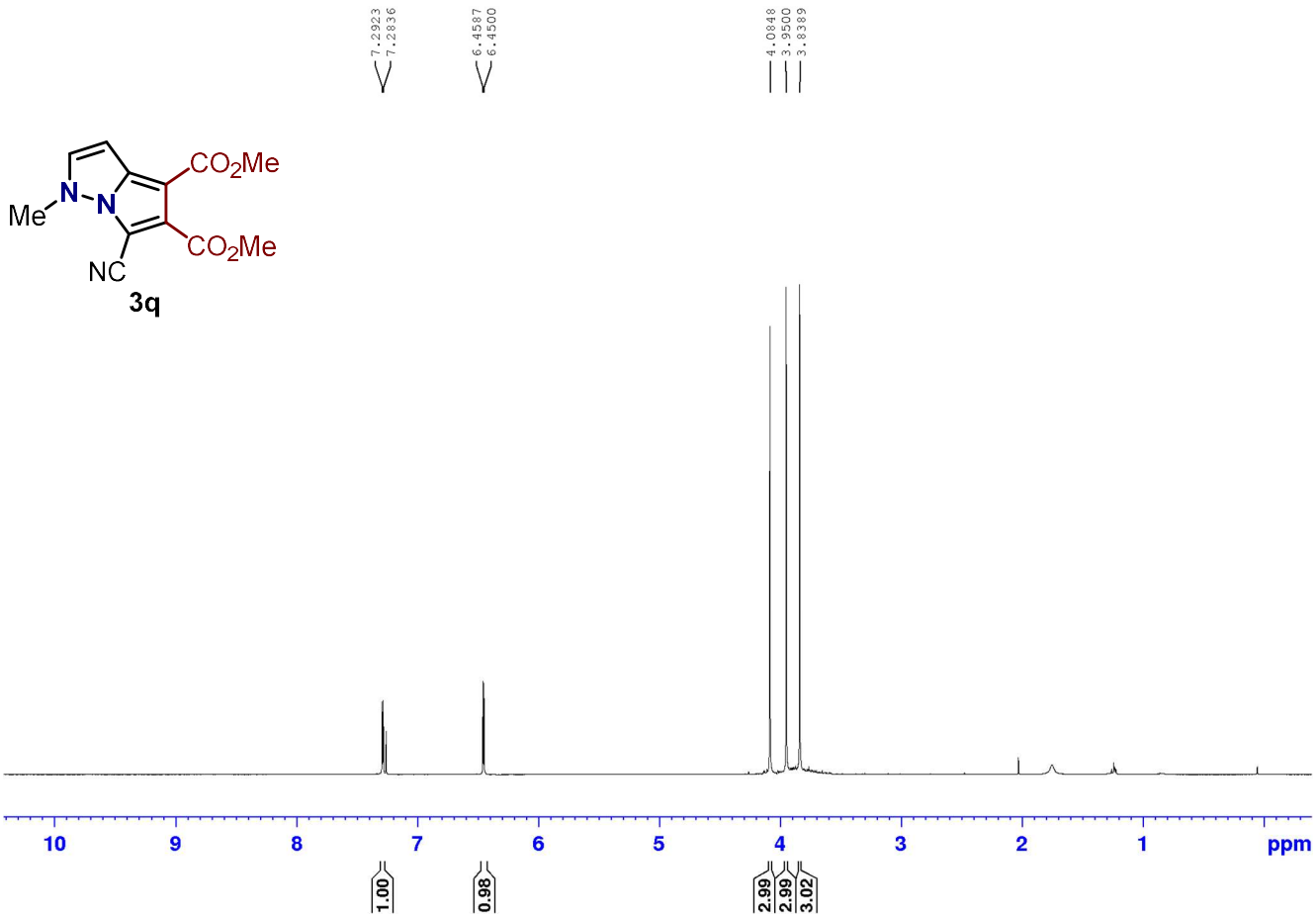


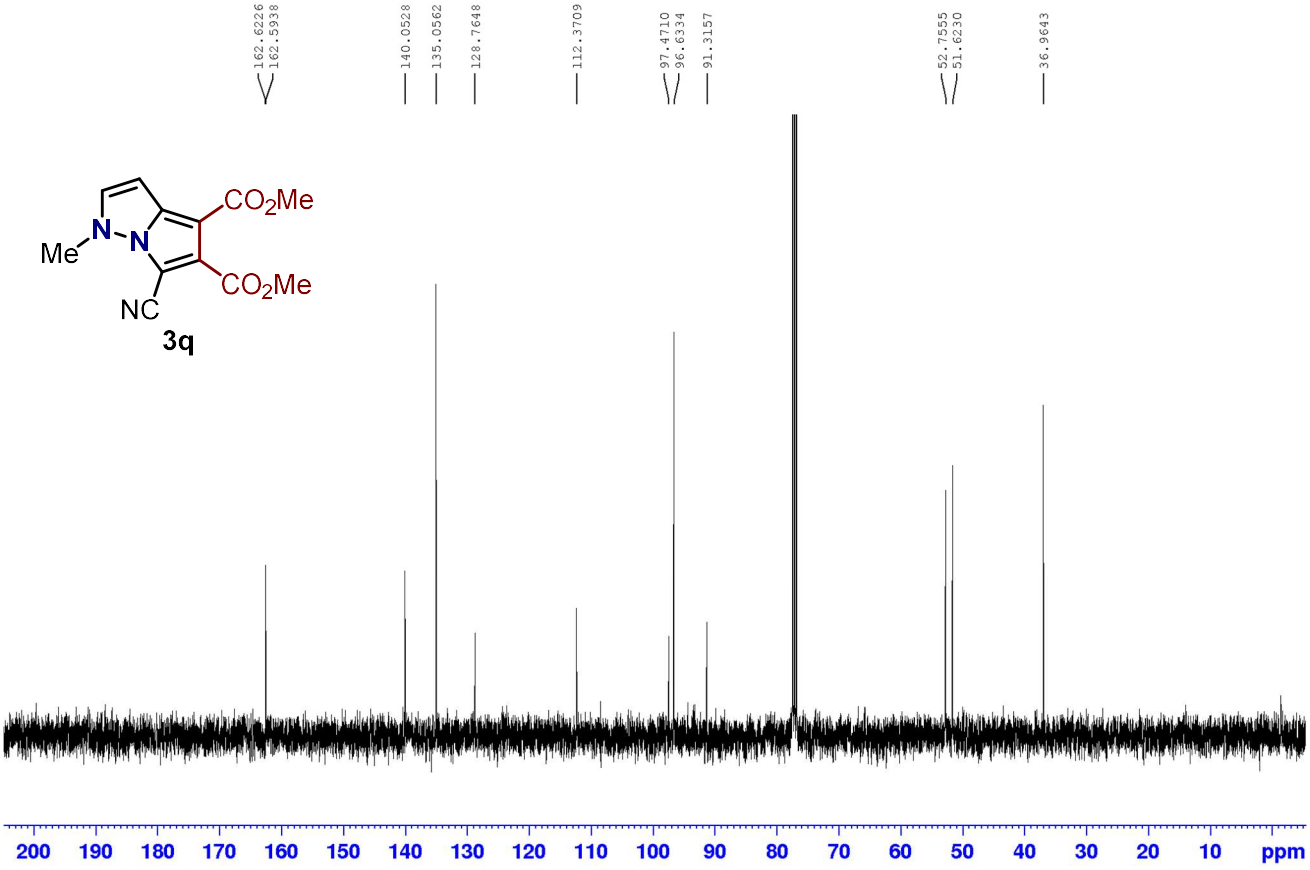
^{13}C NMR (100 MHz, $CDCl_3$)



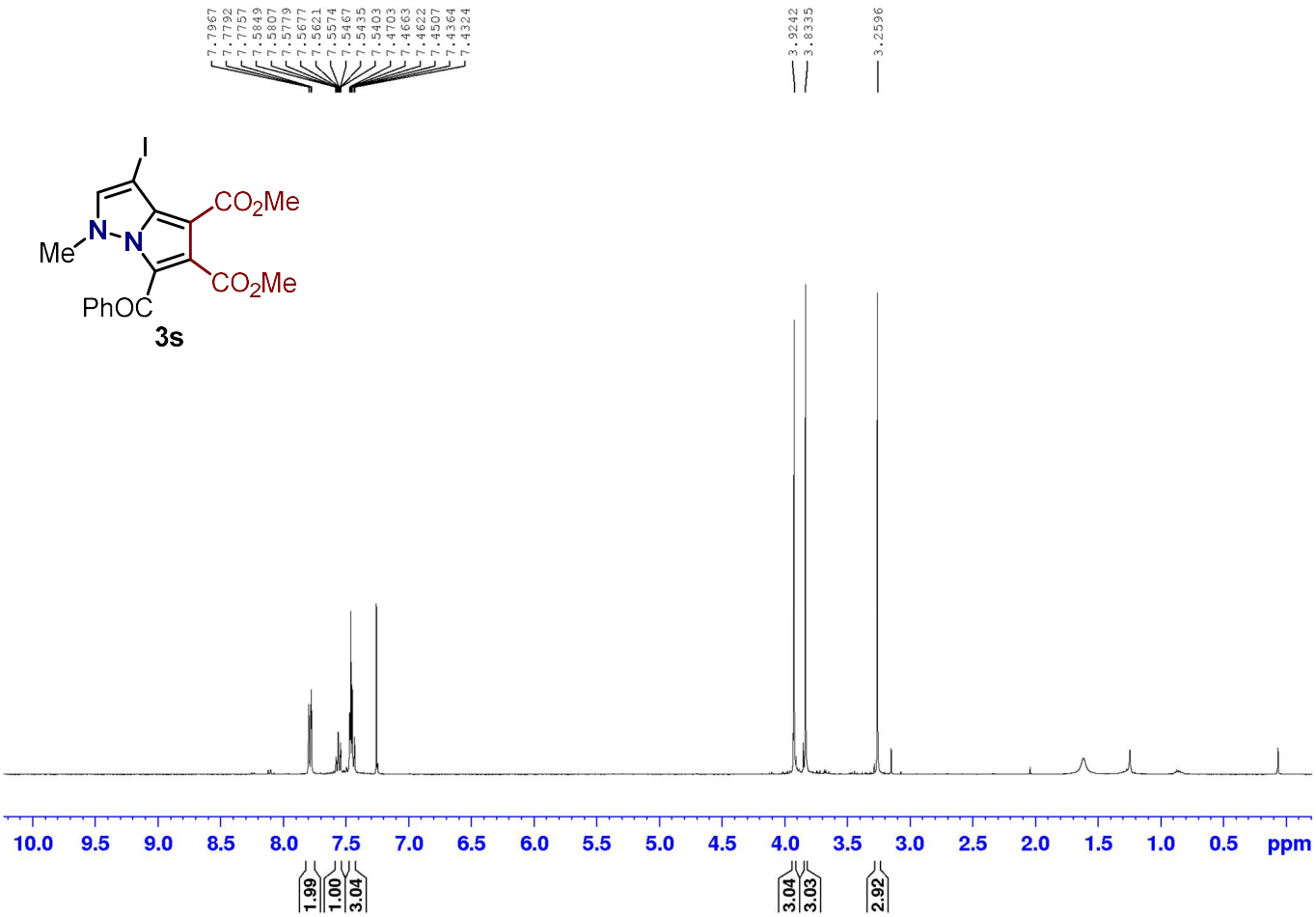
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (100 MHz, $CDCl_3$)



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



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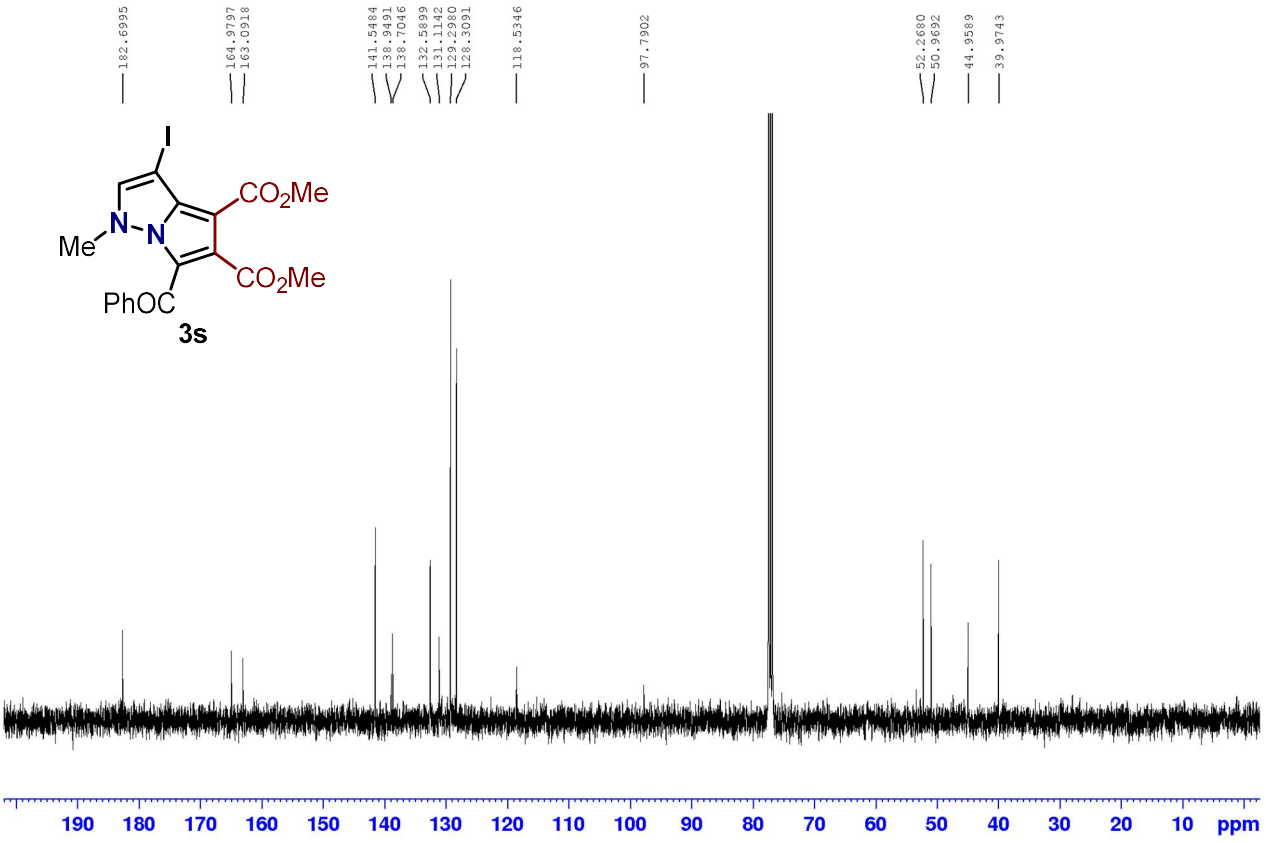
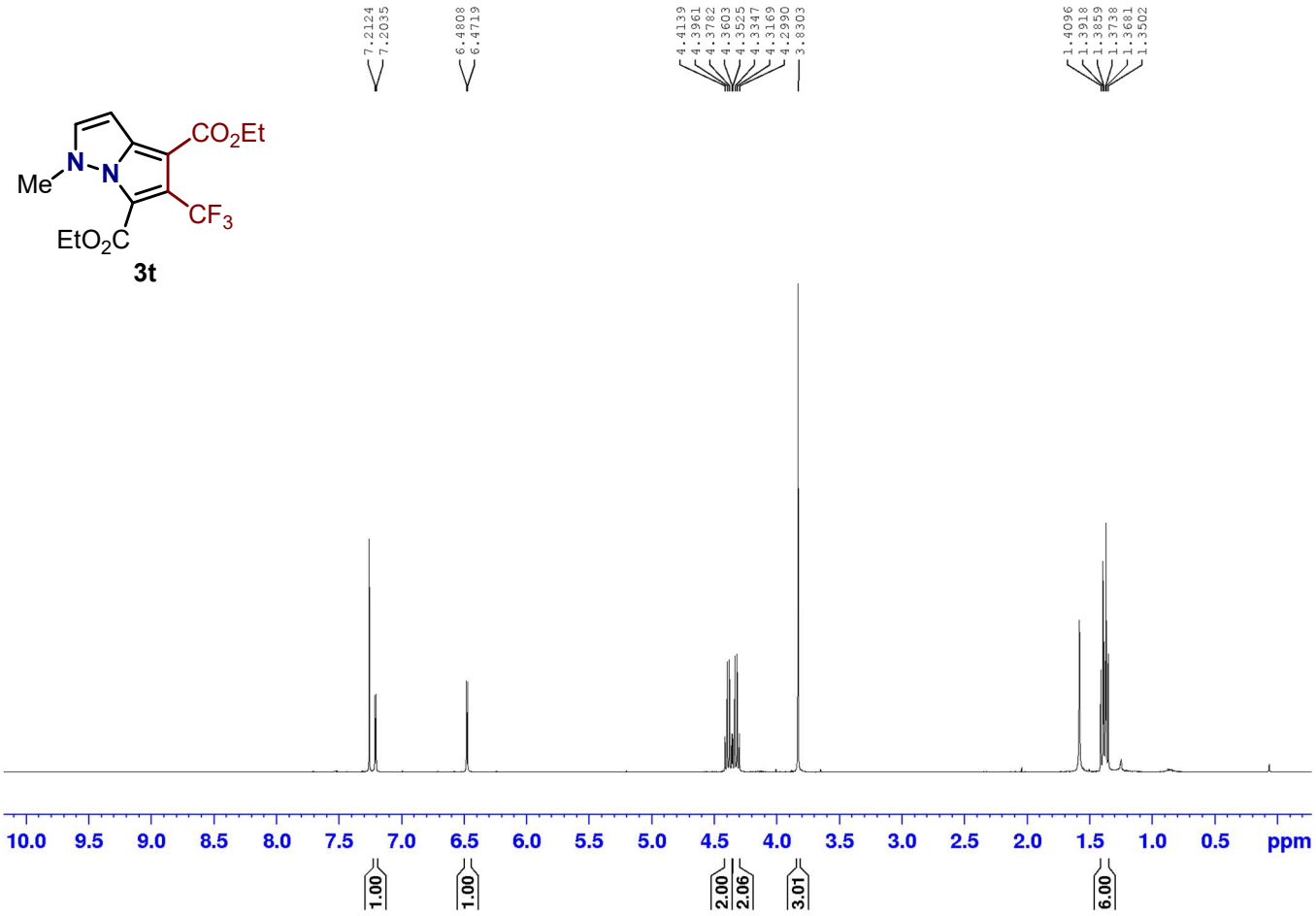
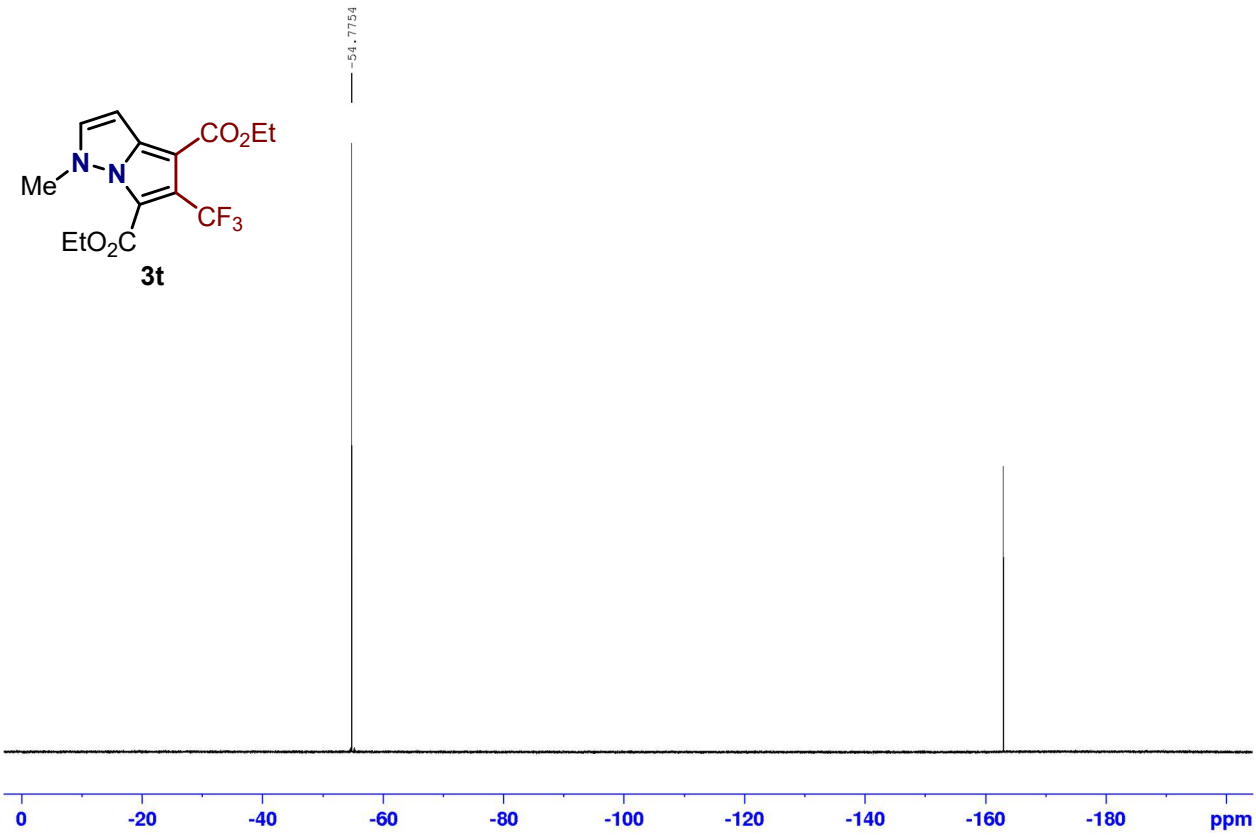


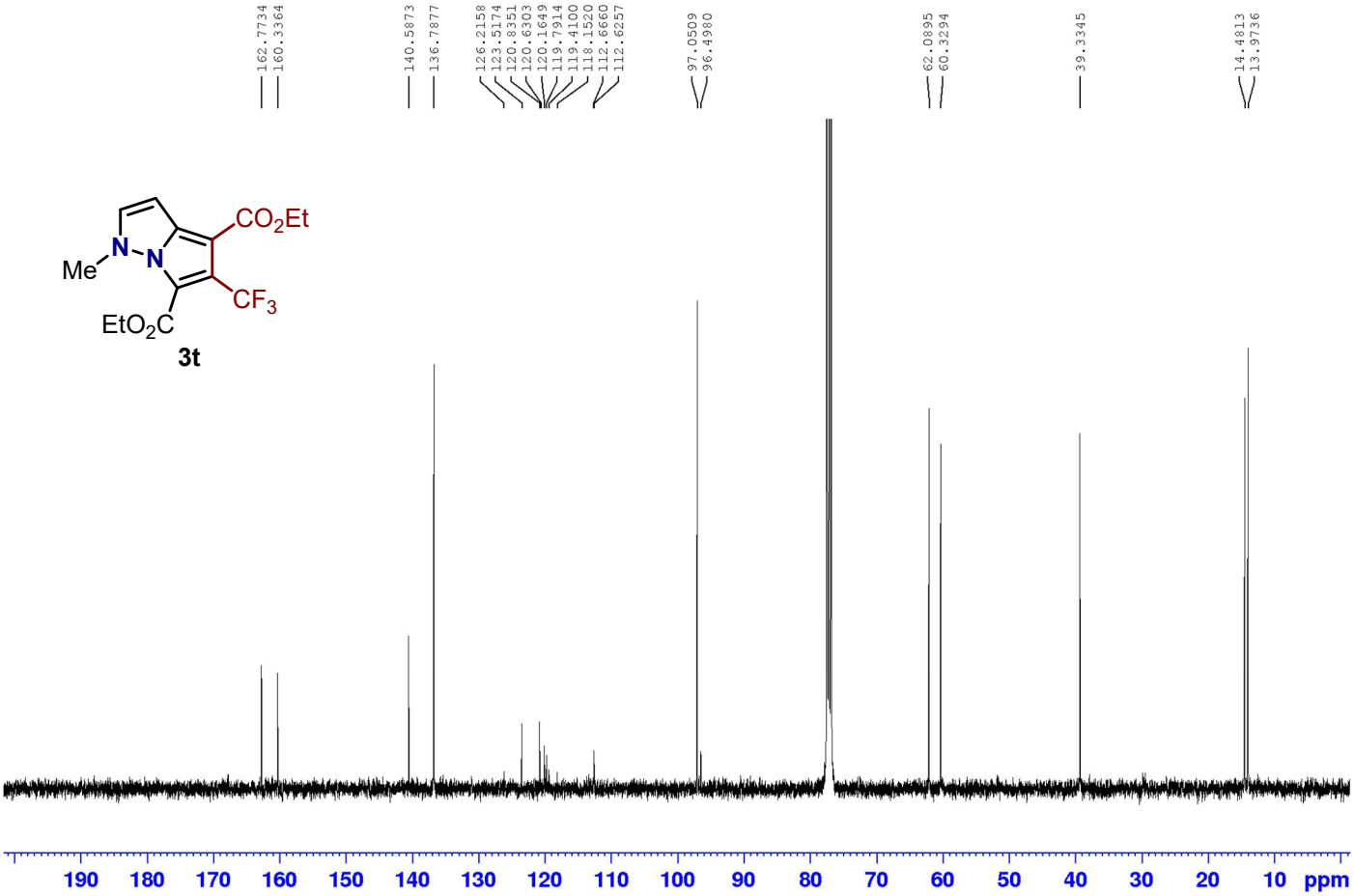
^{1}H NMR (400 MHz, $CDCl_3$)



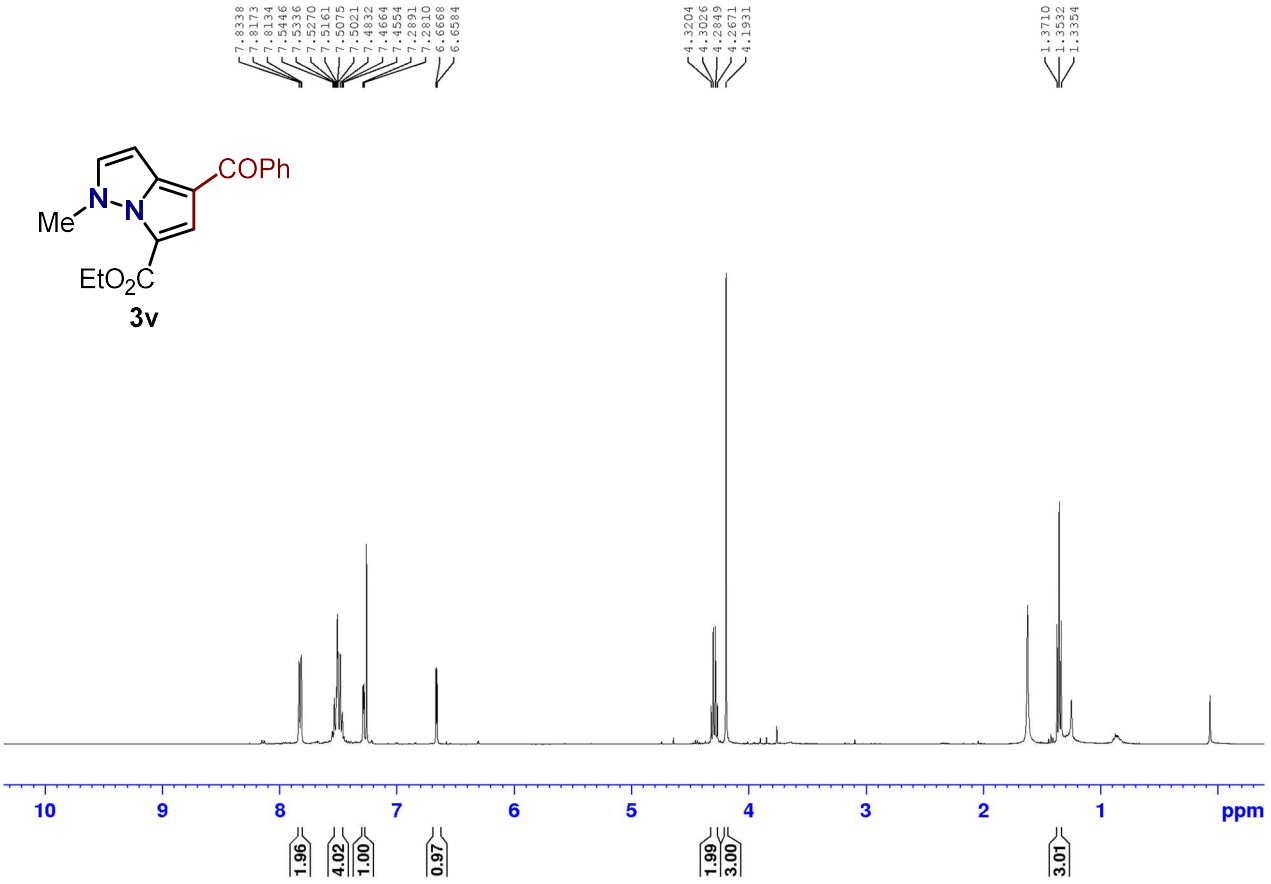
^{19}F NMR (376 MHz, $CDCl_3$, C_6F_6)



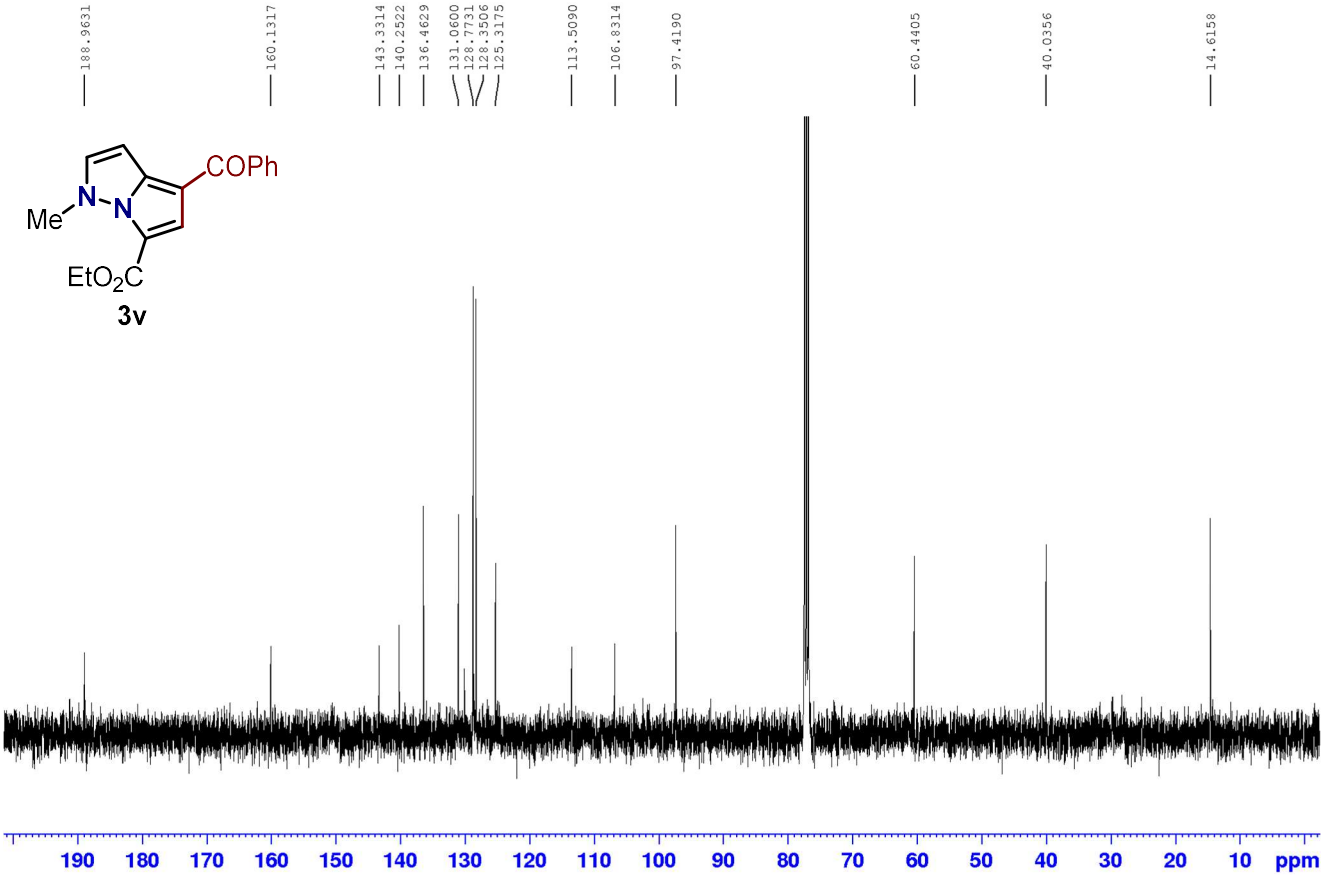
^{13}C NMR (100 MHz, $CDCl_3$)



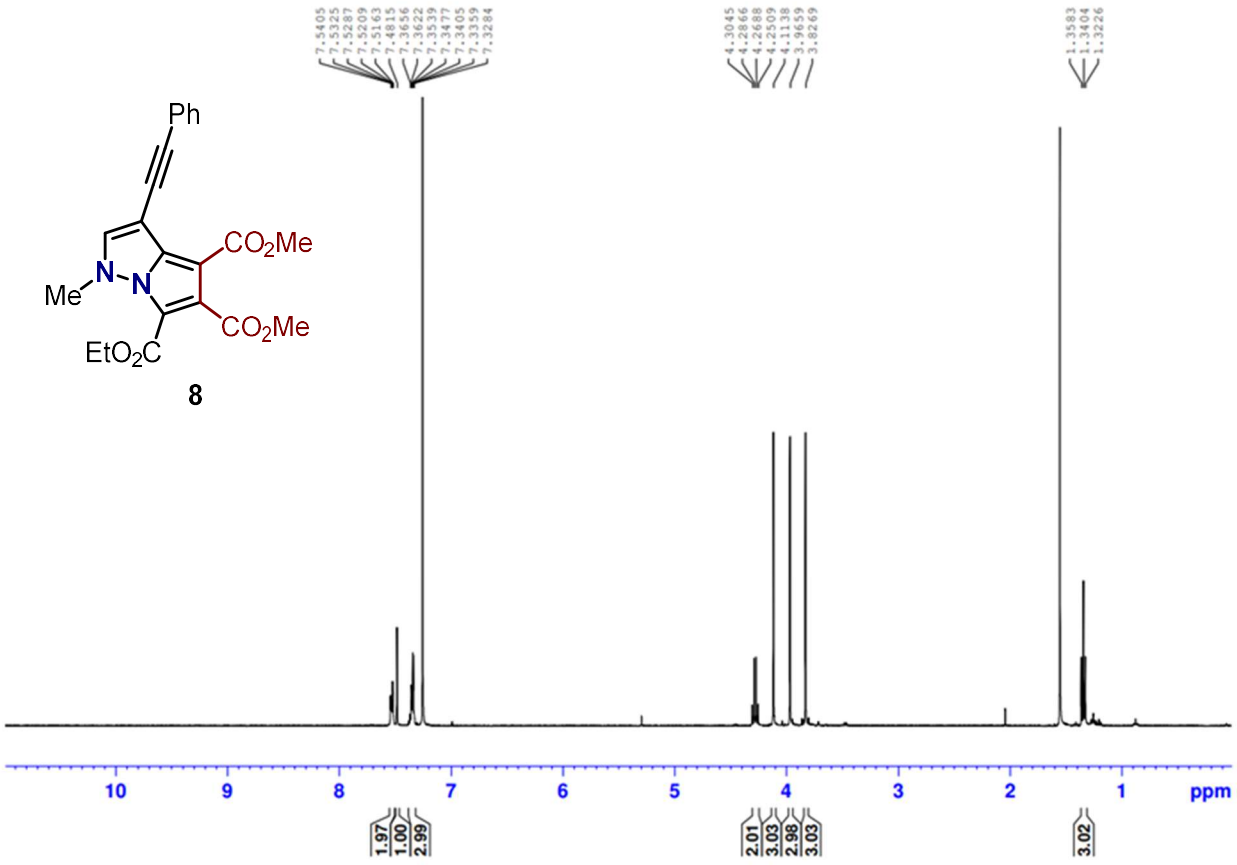
^{1}H NMR (400 MHz, $CDCl_3$)



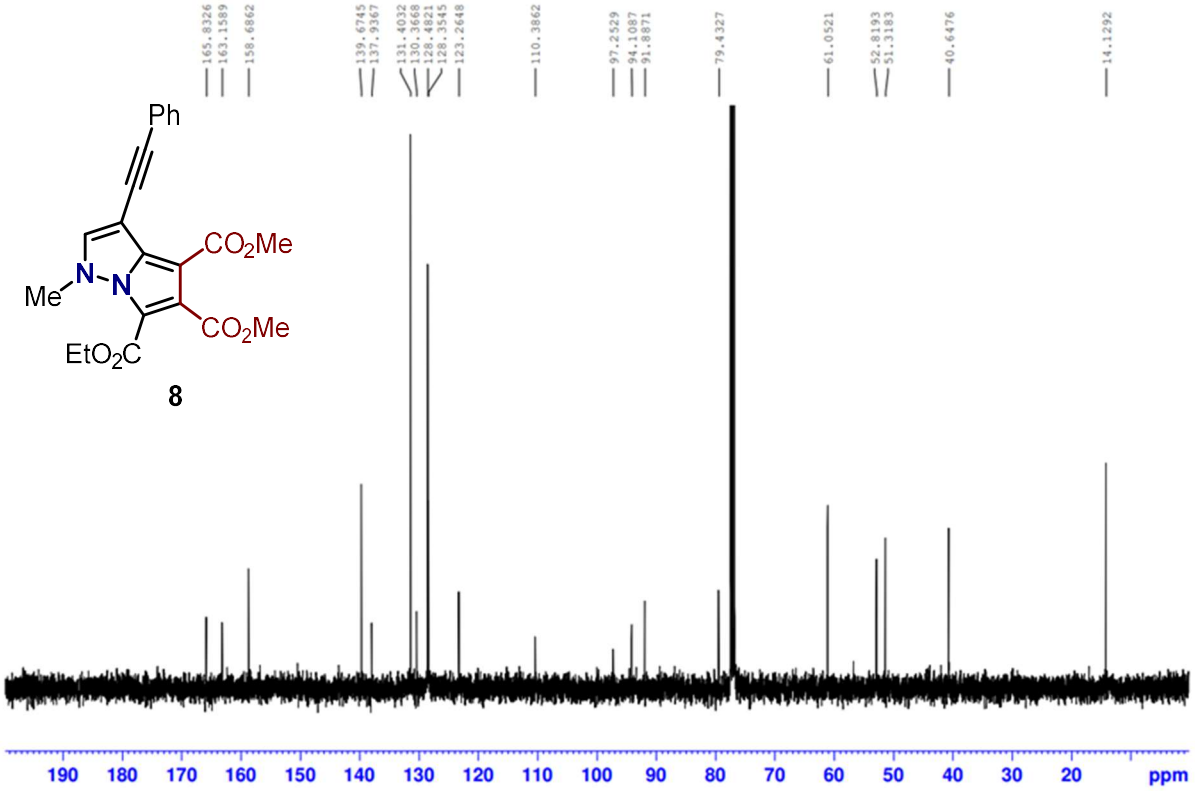
^{13}C NMR (100 MHz, $CDCl_3$)



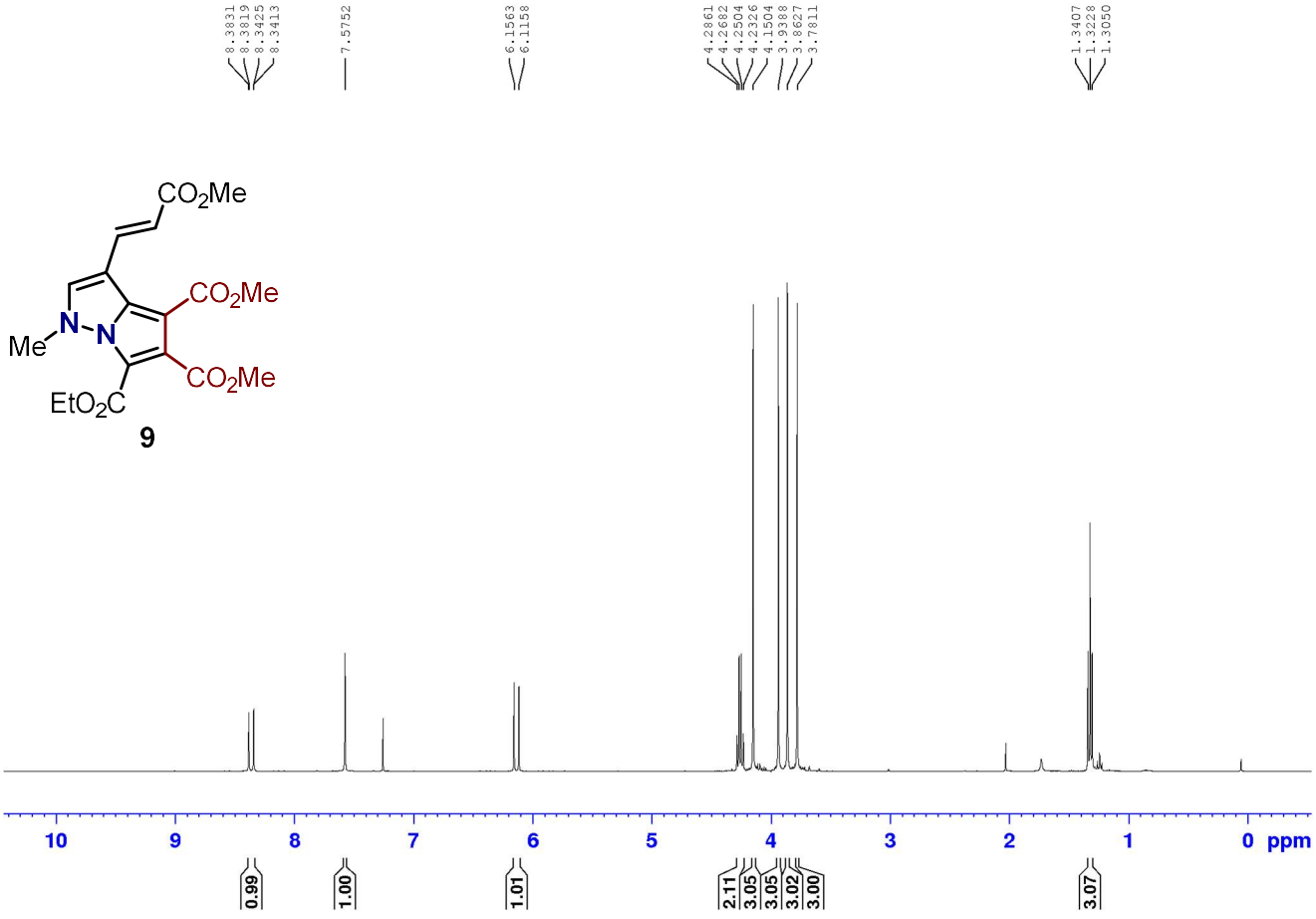
^{1}H NMR (400 MHz, $CDCl_3$)



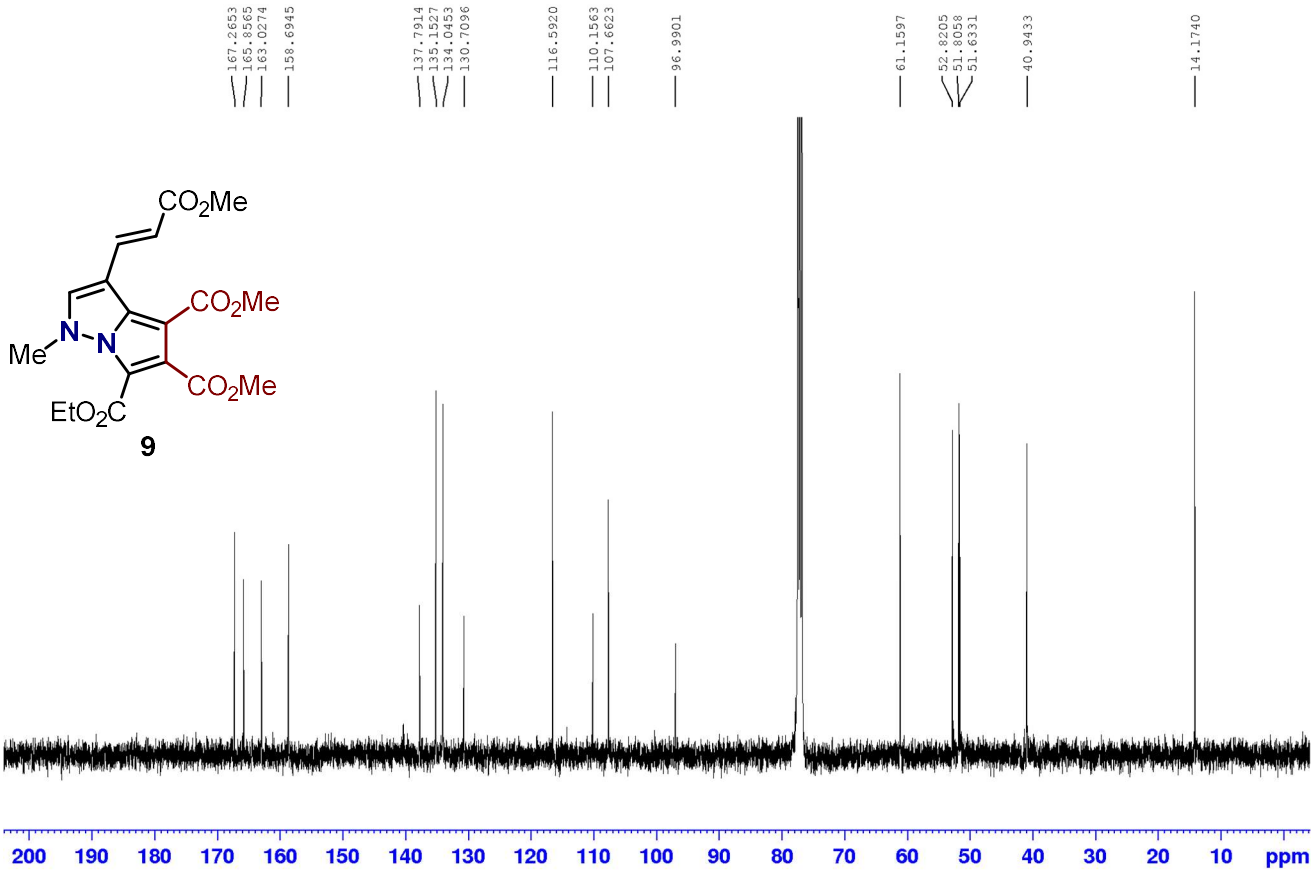
^{13}C NMR (100 MHz, $CDCl_3$)



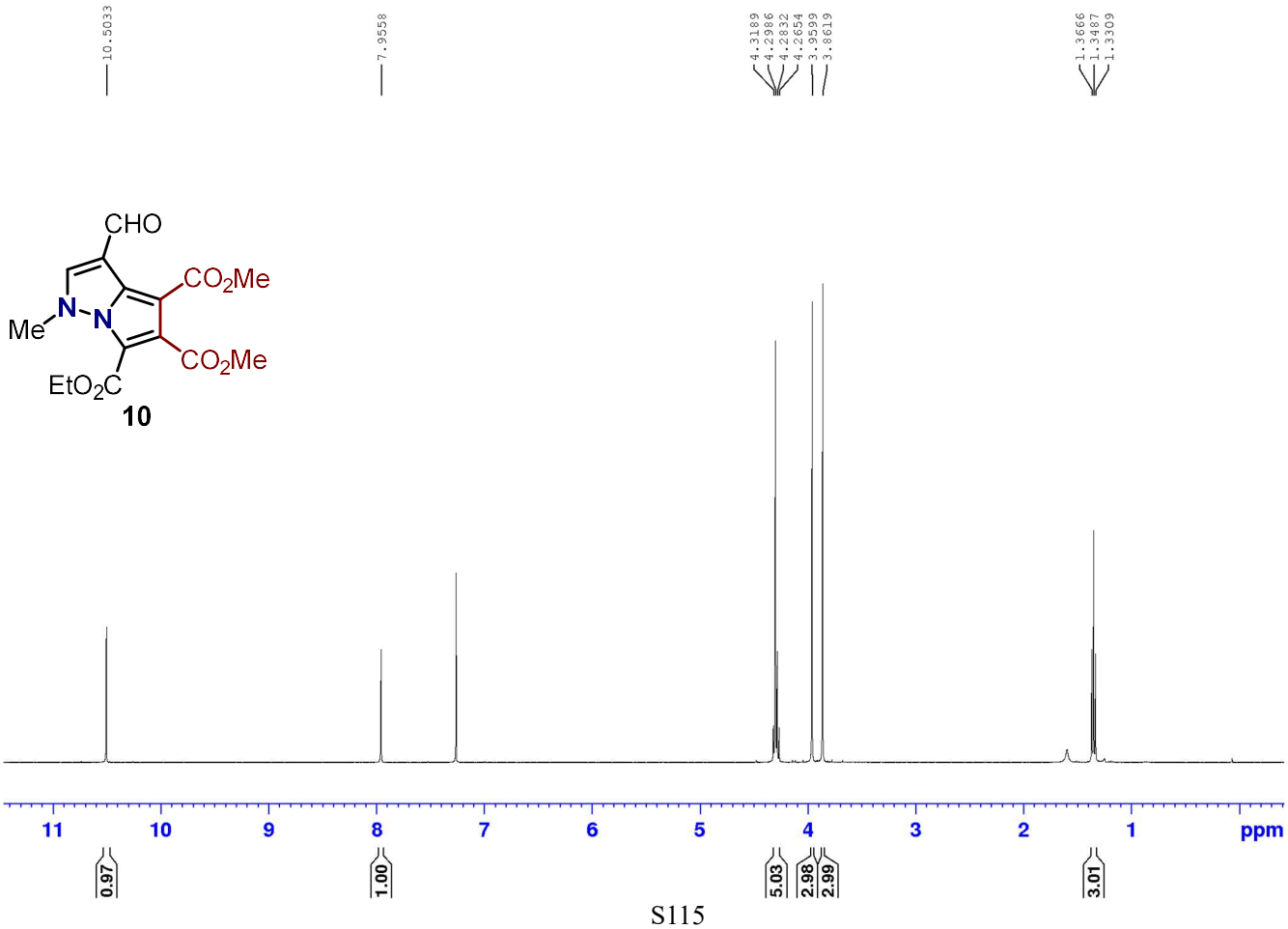
^{1}H NMR (400 MHz, $CDCl_3$)



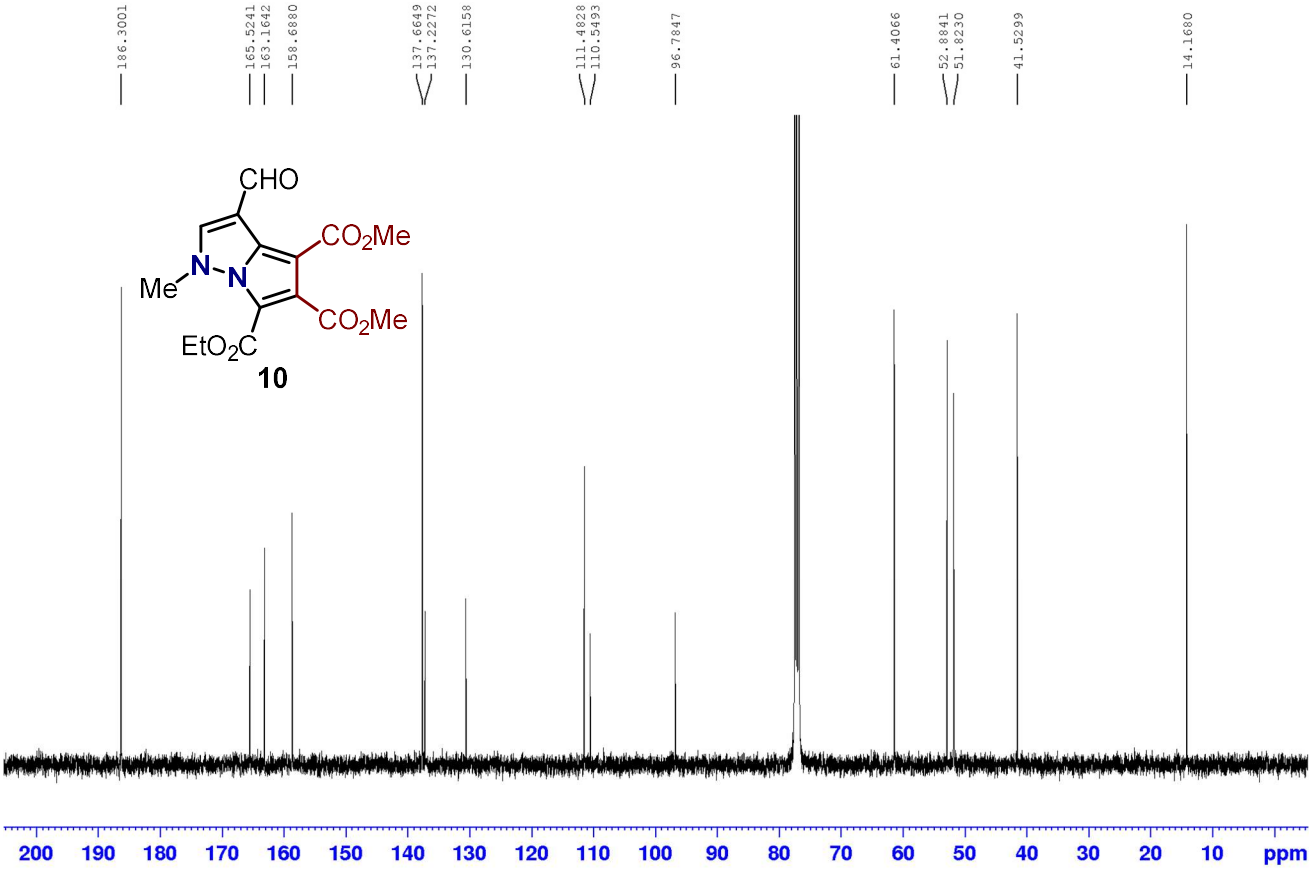
^{13}C NMR (100 MHz, $CDCl_3$)



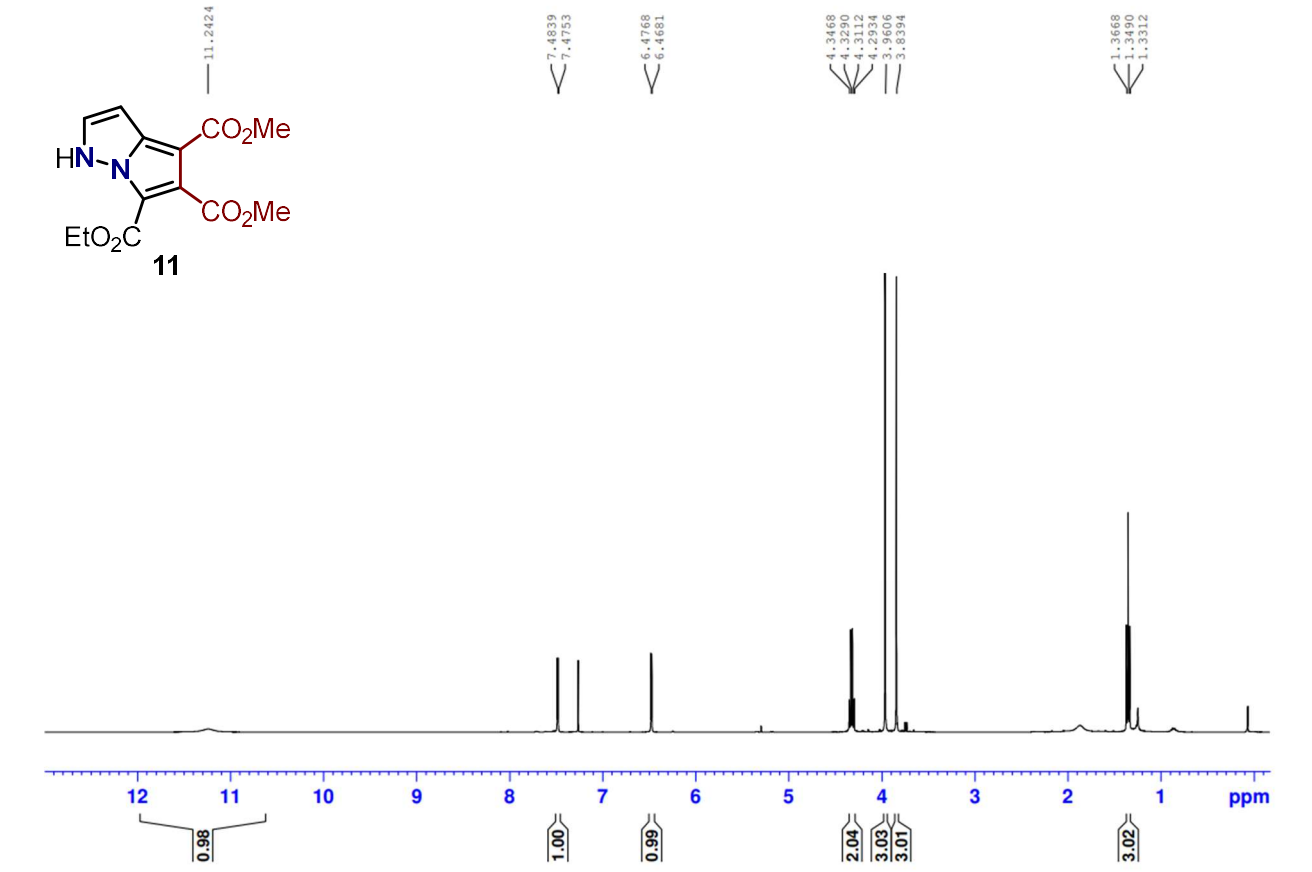
^{1}H NMR (400 MHz, $CDCl_3$)



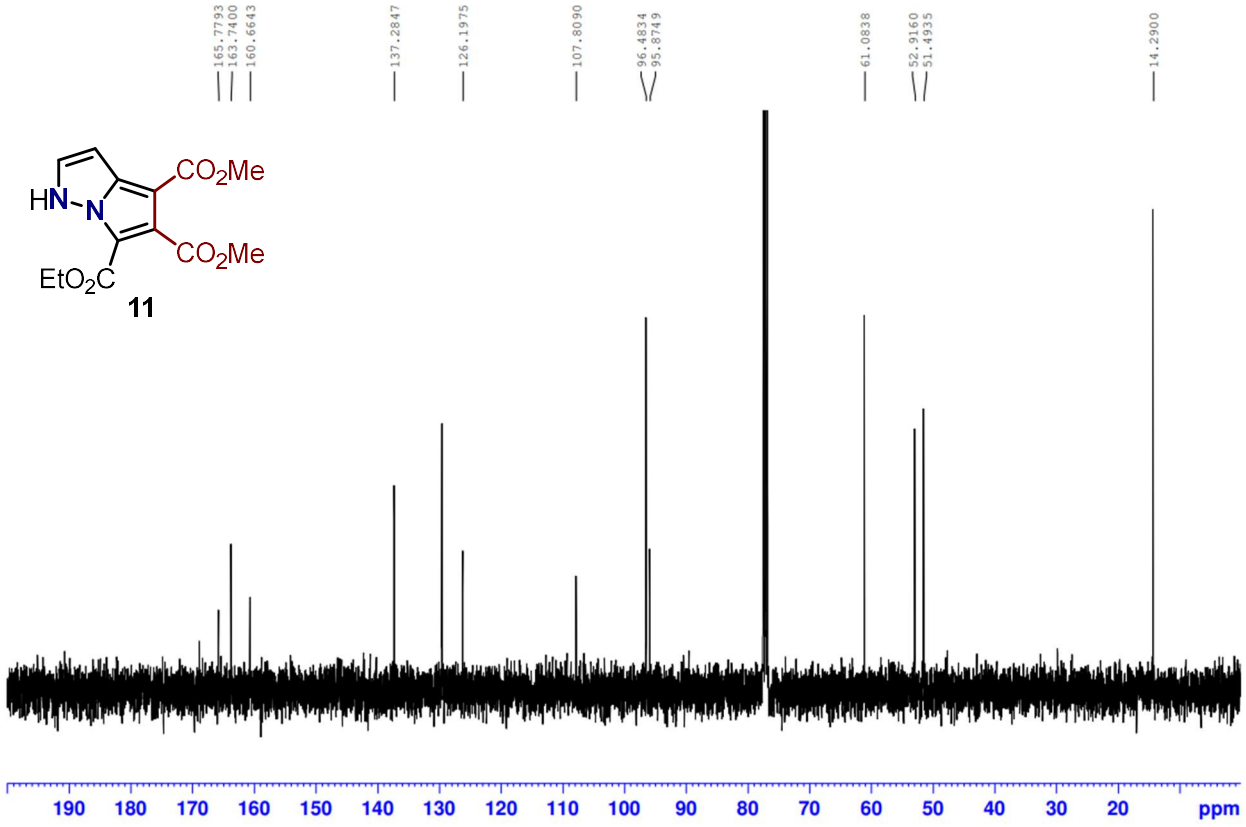
^{13}C NMR (100 MHz, $CDCl_3$)



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



^{13}C NMR (100 MHz, $CDCl_3$)



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