Supporting Information

Tuning Radical Reactivity by Iodine in Oxidative C(sp^3)-H/C(sp)-H Cross-Coupling: An Easy Way toward Furans and Indolizines

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General information

The reactions were conducted in Schlenk tube under N_2 atmosphere. [D]-**2a** was synthesized according to a literature report.[1] Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates. Flash chromatography columns were packed with 200-300 mesh silica gel in petroleum (bp. 60-90 ^{o}C). Gas chromatographic analyses were performed on Varian GC 2000 gas chromatography instrument with a FID detector and naphthalene was added as internal standard. ^{1}H and ^{13}C NMR data were recorded with Bruker Advance III (400 MHz) spectrometers with tetramethylsilane as an internal standard. All chemical shifts (δ) are reported in ppm and coupling constants (J) in Hz. All chemical shifts are reported relative to tetramethylsilane and d-solvent peaks (77.00 ppm, chloroform), respectively.

General procedure

Method A: Oxidative cross-coupling/cyclization of β-keto esters with terminal alkynes

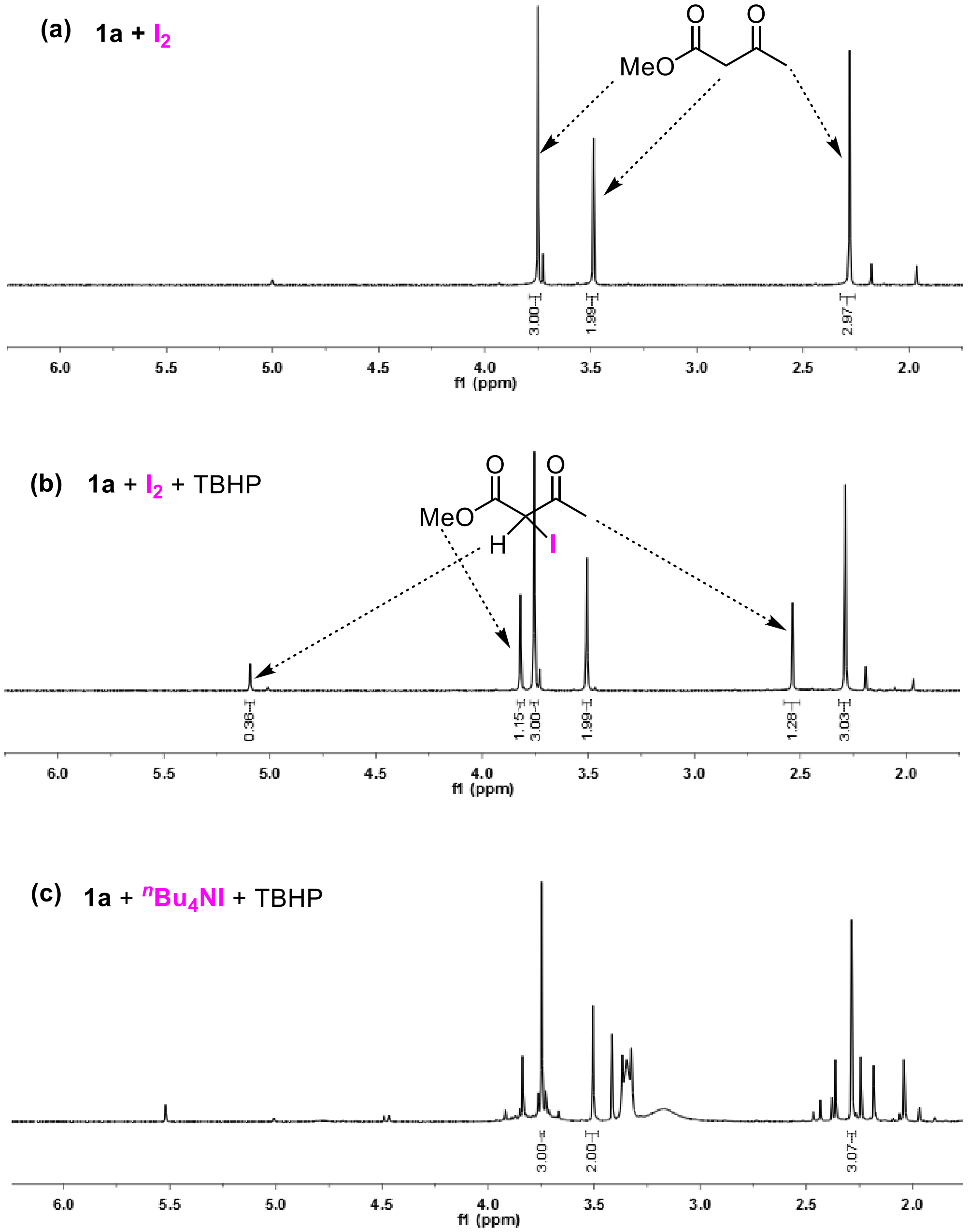
In a clean sealed Schlenk tube equipped with a stir bar, NaOAc (42.0 mg, 0.50 mmol), I_2 (50.8 mg, 0.20 mmol) were added under N_2 atmosphere. 1,2-Dichloroethane (DCE, 4.0 mL) was injected into the tube via syringe. After the dissolution of the I_2, β-ketone ester (1.5 mmol), alkyne (0.50 mmol) and CHP (70% in cumene, 217.1 mg, 1.0 mmol) was subsequently injected into the reaction tube. The reaction was then stirred at 90 ^{o}C for 10 h. After completion, the reaction was quenched with saturated $NaHSO_3$ solution. Then the reaction was extracted with ethyl ether (3 x 10 mL). The organic layers were combined and dried over anhydrous Na_2SO_4. The pure product was obtained by flash column chromatography on silica gel (petroleum: ethyl acetate = 100:1).

Method B: Oxidative cross-coupling/cyclization of 2-alkylazaarenes with terminal alkynes

In a clean sealed Schlenk tube equipped with a stir bar, NaOAc (42.0 mg, 0.50 mmol), I_2 (38.1 mg, 0.15 mmol) were added under N_2 atmosphere. 1,2-Dichloroethane (DCE, 4.0 mL) was injected into the tube via syringe. After the dissolution of the I_2, 2-alkylazaarenes (1.5 mmol), alkyne (0.50 mmol) and CHP (70% in cumene, 217.1 mg, 1.0 mmol) was subsequently injected into the reaction tube. The reaction was then stirred at 100 ^{o}C for 10 h. After completion, the reaction was quenched with saturated $NaHSO_3$ solution. Then the reaction was extracted with ethyl ether (3 x 10 mL). The organic layers were combined and dried over anhydrous Na_2SO_4. The pure product was obtained by flash column chromatography on silica gel (petroleum: ethyl acetate = 20:1).

Figure S1

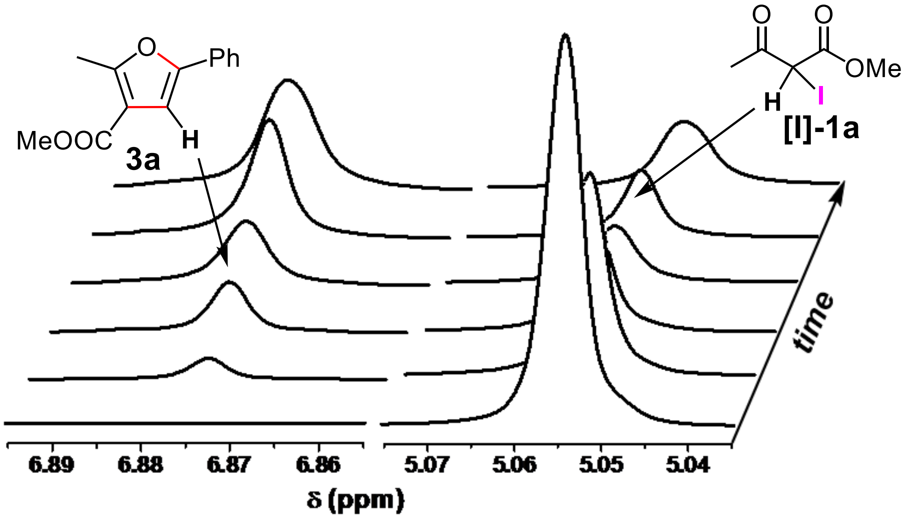
^{1}H NMR spectra study on the mixture of substrate **1a** with iodine and peroxides.



Reaction conditions: (a) **2b** (1.5 mmol) and I_2 (0.20 mmol) in $CDCl_3$ (2.0 mL), stirring at 90 ºC for 1 h; (b) **2b** (1.5 mmol), I_2 (0.20 mmol) and TBHP (1.5 mmol, 70% in aqueous solution) in $CDCl_3$ (2.0 mL), stirring at 90 ºC for 1 h; (c) **2b** (1.5 mmol) and ^{n}Bu$_4$NI (0.40 mmol) in $CDCl_3$ (2.0 mL), stirring at 90 ºC for 1 h.

Figure S2

^{1}H NMR spectra of the oxidative cross-coupling of **1a** with **2a**.



Reaction conditions: **1a** (1.5 mmol), **2a** (0.50 mmol), I_2 (0.20 mmol), TBHP (1.5 mmol, 70% in aqueous solution) with NaOAc (0.50 mmol), $CDCl_3$ (2.0 mL), 90 °C.

Isotope labeling experiment

Experiment procedure: In a clean sealed Schlenk tube equipped with a stir bar, ethyny-*d*-benzene (96%-d, 51.5 mg, 0.50 mmol), NaOAc (41.0 mg, 0.50 mmol), I$_2$ (50.8 mg, 0.20 mmol) were added under N$_2$ atmosphere. 1,2-Dichloroethane (DCE, 4.0 mL) was injected into the tube via syringe. After the dissolution of the I$_2$, ethyl acetoacetate (1.5 mmol) and TBHP (70% in water, 192.3 mg, 1.5 mmol) were dropped into the mixture under nitrogen. The reaction was then stirred at 90 ^{o}C for 12 h. The resulting reaction solution was purified by flash column chromatography with 39% yield of [D]-**3a** (*96%-D*).

[D]-3a

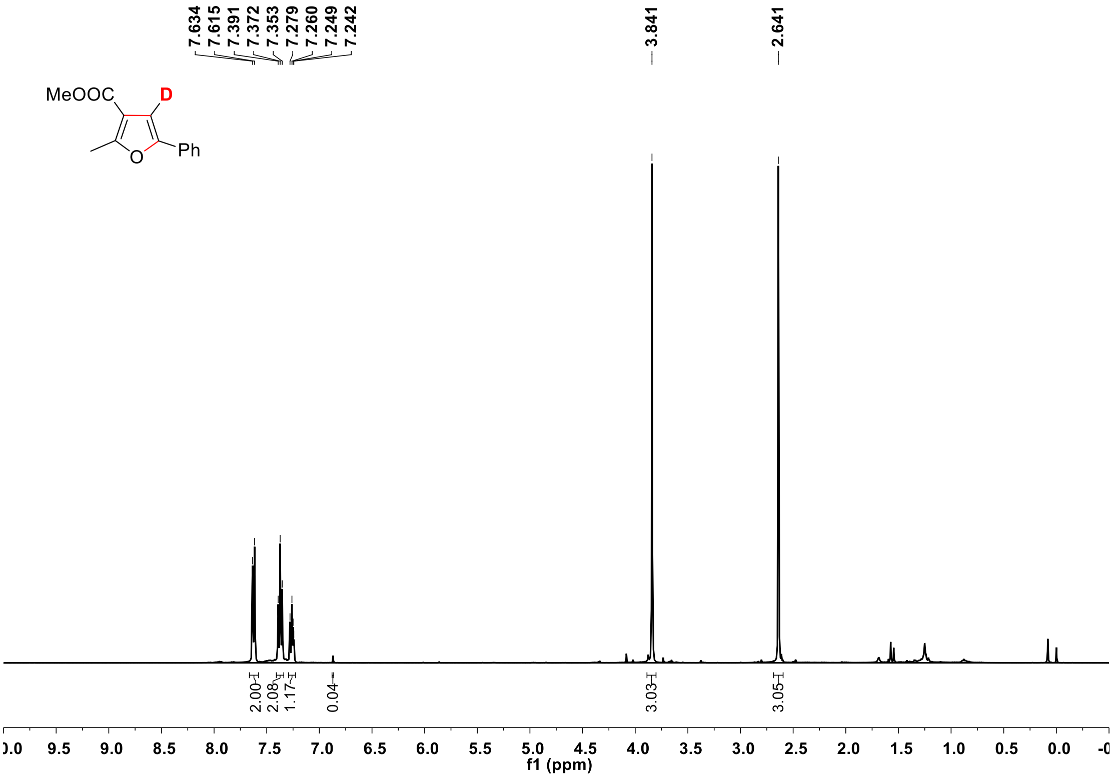


Figure S3

Free-energy profile and mechanism for oxidation of **R-3** with the help of iodine.

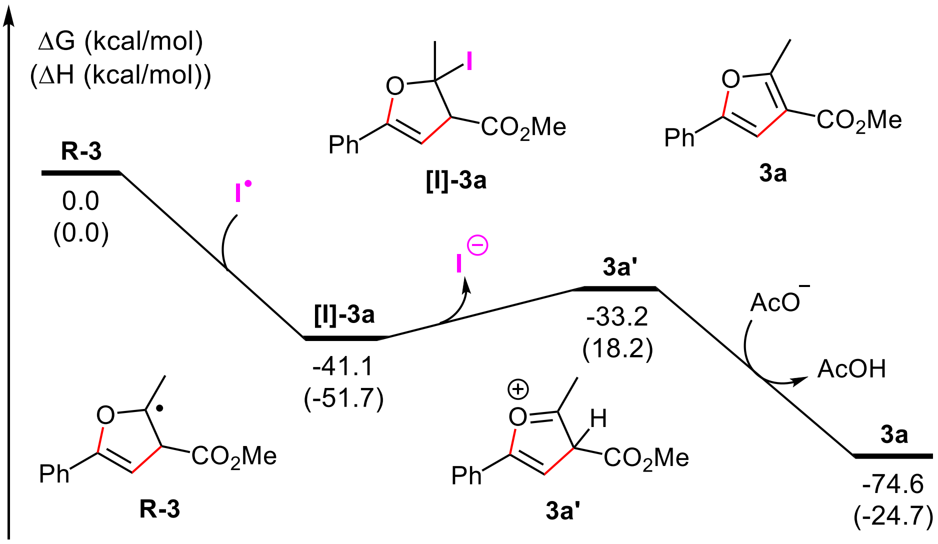
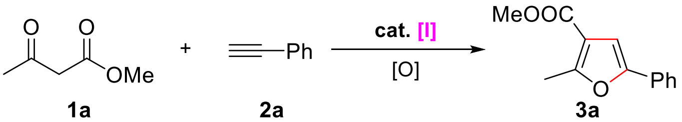


Table S1

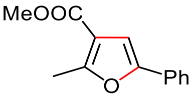
Screening of reaction conditions.



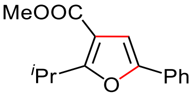
Entry	Catalyst	Oxidant	Solvent	Yield of **3a** (%)[b]
1	^{n}Bu$_4$NI	TBHP	DCE	trace
2	PhI	TBHP	DCE	n.d.
3	NIS	TBHP	DCE	trace
4	I_2	TBHP	DCE	**52**
5	none	TBHP	DCE	n.d.
6	I_2	TBHP	MeCN	n.d.
7	I_2	TBHP	EtOAc	n.d.
8	I_2	TBHP	Toluene	35
9	I_2	TBHP	DMSO	n.d.
10	I_2	DTBP	DCE	trace
11	I_2	TBPB	DCE	24
12	I_2	CHP	DCE	52
13	I_2	H_2O_2	DCE	n.d.
14[c]	I_2	TBHP	DCE	31

[a] The reaction was carried out in the presence of **1a** (1.5 mmol), **2a** (0.5 mmol), catalyst (0.20 mmol), oxidant (1.5 mmol, 70% in aqueous solution) with NaOAc (0.50 mmol), solvent (4.0 mL), 90 °C, 10 h. [b] Yield determined by GC analysis with biphenyl as the internal standard. [c] 20 mol% I_2 was used.

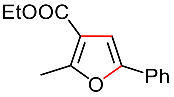
Detail descriptions for products



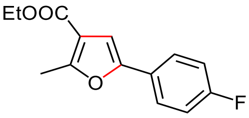
Methyl 2-methyl-5-phenylfuran-3-carboxylate (3a):[2] pale yellow liquid was obtained with 50% isolated yield following Method A. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 – 7.59 (m, 2H), 7.44-7.35 (m, 2H), 7.30 – 7.24 (m, 1H), 6.87 (s, 1H), 3.85 (s, 3H), 2.65 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.46, 158.73, 151.72, 129.97, 128.68, 127.61, 123.59, 115.05, 105.35, 51.38, 13.87.



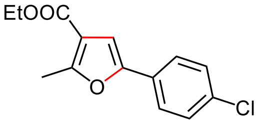
Methyl 2-isopropyl-5-phenylfuran-3-carboxylate (3b):[2] pale yellow liquid 51% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 7.6 Hz, 2H), 7.38 (t, J = 7.7 Hz, 2H), 7.27 (t, J = 6.5 Hz, 1H), 6.87 (s, 1H), 3.88 – 3.76 (m, 4H), 1.34 (d, J = 7.0 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.72, 164.34, 151.36, 130.13, 128.66, 127.57, 123.59, 113.10, 105.32, 51.33, 27.34, 20.84.



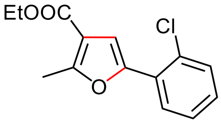
Ethyl 2-methyl-5-phenylfuran-3-carboxylate (3c):[3] pale yellow liquid was obtained with 60% isolated yield following Method A. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 – 7.60 (m, 2H), 7.37 (t, J = 7.7 Hz, 2H), 7.28 – 7.23 (m, 1H), 6.88 (s, 1H), 4.30 (q, J = 7.1 Hz, 2H), 2.64 (s, 3H), 1.36 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.05, 158.57, 151.63, 130.02, 128.67, 127.56, 123.57, 115.35, 105.44, 60.18, 14.35, 13.88.



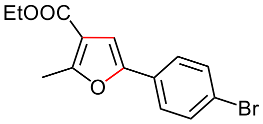
Ethyl 5-(4-fluorophenyl)-2-methylfuran-3-carboxylate (3d):[3] pale yellow liquid was obtained with 57% isolated yield following Method A. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (dd, J = 8.8, 5.3 Hz, 2H), 7.07 (t, J = 8.8 Hz, 2H), 6.81 (s, 1H), 4.31 (q, J = 7.1 Hz, 2H), 2.63 (s, 3H), 1.37 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.95, 162.18 (d, J_{C-F} = 248.3 Hz), 158.51, 150.77, 126.36 (d, J_{C-F} = 3.3 Hz), 125.35 (d, J_{C-F} = 4.1 Hz), 115.70 (d, J_{C-F} = 22.0 Hz), 115.37, 105.10 (d, J_{C-F} = 1.4 Hz), 60.21, 14.33, 13.84. ^{19}F NMR (377 MHz, $CDCl_3$) δ -113.77.



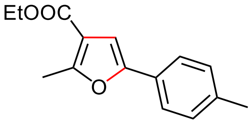
Ethyl 5-(4-chlorophenyl)-2-methylfuran-3-carboxylate (3e):[3] pale yellow liquid was obtained with 50% isolated yield following Method A. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.6 Hz, 2H), 7.33 (d, *J* = 8.5 Hz, 2H), 6.86 (s, 1H), 4.31 (q, *J* = 7.1 Hz, 2H), 2.63 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.83, 158.78, 150.53, 133.18, 128.85, 128.47, 124.76, 115.47, 105.90, 60.24, 14.32, 13.86.



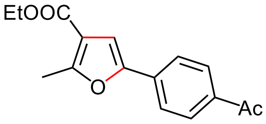
Ethyl 5-(2-chlorophenyl)-2-methylfuran-3-carboxylate (3f): pale yellow liquid was obtained with 53% isolated yield following Method A. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.42 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.35 (s, 1H), 7.30 (td, *J* = 7.8, 1.3 Hz, 1H), 7.19 (td, *J* = 7.8, 1.7 Hz, 1H), 4.32 (q, *J* = 7.1 Hz, 2H), 2.66 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.92, 158.61, 147.83, 130.68, 130.00, 128.32, 128.21, 127.48, 126.77, 115.41, 111.41, 60.22, 14.36, 13.82. HRMS (ESI) calcd for $C_{14}H_{13}ClO_3$ $[M+H]^+$: 265.0626; found: 265.0622.



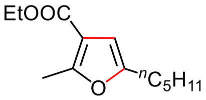
Ethyl 5-(4-bromophenyl)-2-methylfuran-3-carboxylate (3g):[3] pale yellow solid was obtained with 48% isolated yield following Method A. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 – 7.43 (m, 4H), 6.88 (s, 1H), 4.31 (q, *J* = 7.1 Hz, 2H), 2.63 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.79, 158.83, 150.53, 131.77, 128.87, 125.00, 121.30, 115.49, 106.02, 60.24, 14.32, 13.87.



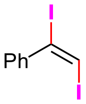
Ethyl 2-methyl-5-(p-tolyl)furan-3-carboxylate (3h):[3] pale yellow solid was obtained with 65% isolated yield following Method A. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.0 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 6.82 (s, 1H), 4.30 (q, *J* = 7.1 Hz, 2H), 2.64 (s, 3H), 2.34 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.13, 158.22, 151.84, 137.45, 129.34, 127.32, 123.53, 115.22, 104.64, 60.12, 21.24, 14.35, 13.87.



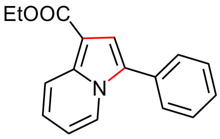
Ethyl 5-(4-acetylphenyl)-2-methylfuran-3-carboxylate (3i):[3] white solid was obtained with 48% isolated yield following Method A. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.97 (d, *J* = 8.6 Hz, 2H), 7.71 (d, *J* = 8.6 Hz, 2H), 7.04 (s, 1H), 4.32 (q, *J* = 7.1 Hz, 2H), 2.67 (s, 3H), 2.61 (s, 3H), 1.38 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 197.28, 163.68, 159.71, 150.43, 135.65, 134.01, 128.92, 123.32, 115.80, 107.98, 60.34, 26.54, 14.32, 13.96.



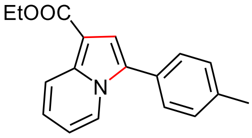
Ethyl 2-methyl-5-pentylfuran-3-carboxylate (3j):[2] pale yellow solid was obtained with 46% isolated yield following Method A. ^{1}H NMR (400 MHz, CDCl$_3$) δ 6.22 (s, 1H), 4.26 (q, *J* = 7.1 Hz, 2H), 2.57 – 2.49 (m, 5H), 1.67 – 1.55 (m, 2H), 1.38 – 1.27 (m, 7H), 0.90 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 164.47, 157.48, 154.39, 113.78, 105.36, 59.92, 31.27, 27.64, 27.47, 22.39, 14.39, 13.99, 13.73.



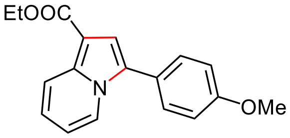
(1,2-diiodovinyl)benzene (4):[4] white solid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.37 – 7.28 (m, 5H), 7.25 (s, 1H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 142.95, 128.89, 128.43, 128.36, 96.19, 80.87.



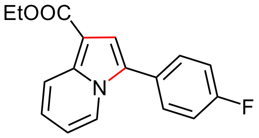
Ethyl 3-phenylindolizine-1-carboxylate (6a):[5] white solid was obtained with 90% isolated yield following Method B. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.35 – 8.18 (m, 2H), 7.55 – 7.41 (m, 4H), 7.40 – 7.33 (m, 1H), 7.30 (s, 1H), 7.07 – 6.99 (m, 1H), 6.65 (td, *J* = 6.7, 1.5 Hz, 1H), 4.39 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 164.78, 136.10, 130.96, 128.84, 128.29, 127.74, 126.17, 123.08, 122.02, 119.89, 115.87, 112.36, 104.01, 59.33, 14.49.



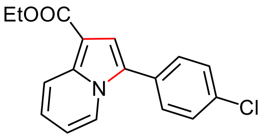
Ethyl 3-(p-tolyl)indolizine-1-carboxylate (6b):[5] white solid was obtained with 90% isolated yield following Method B. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.60 – 8.09 (m, 2H), 7.43 (d, *J* = 8.1 Hz, 2H), 7.36 – 7.26 (m,3H), 7.06 (ddd, *J* = 9.0, 6.6, 1.0 Hz, 1H), 6.68 (td, *J* = 6.9, 1.3 Hz, 1H), 4.44 (q, *J* = 7.1 Hz, 2H), 2.44 (s, 3H), 1.46 (t, *J* = 7.1 Hz, 3H).^{13}C NMR (101 MHz, CDCl$_3$) δ 164.83, 137.66, 136.00, 129.53, 128.27, 128.03, 126.27, 123.14, 121.86, 119.86, 115.58, 112.25, 103.87, 59.30, 21.08, 14.50.



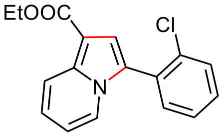
Ethyl 3-(4-methoxyphenyl)indolizine-1-carboxylate (6c):[5] white solid was obtained with 96% isolated yield following Method B. 1H NMR (400 MHz, CDCl3) δ 8.22 (dd, J = 18.9, 8.1 Hz, 2H), 7.44 (d, J = 8.7 Hz, 2H), 7.24 (s, 1H), 7.08 – 6.99 (m, 3H), 6.67 (t, J = 6.5 Hz, 1H), 4.39 (q, J = 7.1 Hz, 2H), 3.86 (s, 3H), 1.42 (t, J = 7.1 Hz, 3H). 13C NMR (101 MHz, CDCl3) δ 165.04, 159.33, 135.94, 130.04, 126.15, 123.43, 123.24, 121.93, 119.99, 115.49, 114.40, 112.36, 103.82, 59.45, 55.30, 14.62.



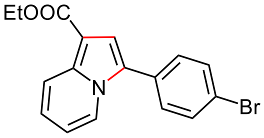
Ethyl 3-(4-fluorophenyl)indolizine-1-carboxylate (6d):[5] white solid was obtained with 80% isolated yield following Method B. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.25 (d, *J* = 9.1 Hz, 1H), 8.16 (d, *J* = 7.1 Hz, 1H), 7.56 – 7.41 (m, 2H), 7.25 (s, 1H), 7.21 – 7.11 (m, 2H), 7.05 (ddd, *J* = 8.9, 6.6, 0.9 Hz, 1H), 6.68 (td, *J* = 7.0, 1.2 Hz, 1H), 4.38 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H).^{13}C NMR (101 MHz, CDCl$_3$) δ 164.78, 162.22 (d, $J_{C\text{-}F}$ = 249.1 Hz), 136.07, 130.31 (d, $J_{C\text{-}F}$ = 8.1 Hz), 127.12 (d, $J_{C\text{-}F}$ = 3.3 Hz) 125.08, 122.92, 122.10, 119.99, 115.98 (d, $J_{C\text{-}F}$ = 21.7 Hz), 115.96, 112.56, 104.05,59.43, 14.51. ^{19}F NMR (377 MHz, CDCl$_3$) δ -112.97.



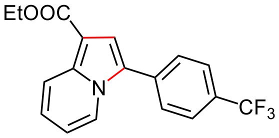
Ethyl 3-(4-chlorophenyl)indolizine-1-carboxylate (6e):[5] white solid was obtained with 94% isolated yield following Method B. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.21 (dd, *J* = 26.7, 8.1 Hz, 2H), 7.41 (s, 4H), 7.26 (s, 1H), 7.15 – 6.98 (m, 1H), 6.67 (td, *J* = 6.9, 1.2 Hz, 1H), 4.38 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H).^{13}C NMR (101 MHz, CDCl$_3$) δ 164.60, 136.23, 133.47, 129.41, 129.07, 124.79, 122.85, 122.18, 119.97, 116.13, 112.62, 104.22, 59.40, 14.47.



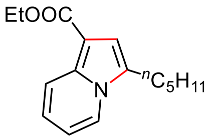
Ethyl 3-(2-chlorophenyl)indolizine-1-carboxylate (6f):[5] white solid was obtained with 84% isolated yield following Method B. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.29 (d, J = 9.1 Hz, 1H), 7.66 (d, J = 7.0 Hz, 1H), 7.56 – 7.47 (m, 1H), 7.46 – 7.29 (m, 4H), 7.09 (ddd, J = 8.9, 6.7, 0.8 Hz, 1H), 6.69 (td, J = 6.9, 1.1 Hz, 1H), 4.39 (q, J = 7.1 Hz, 2H), 1.41 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 164.80, 135.81, 134.71, 132.95, 130.02, 129.85, 129.82, 127.04, 124.15, 123.19, 122.29, 119.70, 117.00, 112.19, 103.69, 59.40, 14.53. HRMS (ESI) calcd for $C_{17}H_{14}ClNO_2$ [M+H]$^+$: 300.0786; found: 300.0780.



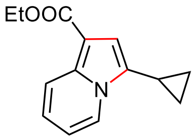
Ethyl 3-(4-bromophenyl)indolizine-1-carboxylate (6g):[5] white solid was obtained with 90% isolated yield following Method B. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.22 (dd, J = 21.9, 8.1 Hz, 2H), 7.64 – 7.53 (m, 2H), 7.41 – 7.33 (m, 2H), 7.27 (d, J = 3.4 Hz, 1H), 7.05 (ddd, J = 9.0, 6.6, 0.9 Hz, 1H), 6.68 (td, J = 6.9, 1.2 Hz, 1H), 4.38 (q, J = 7.1 Hz, 2H), 1.41 (t, J = 7.1 Hz, 3H).^{13}C NMR (101 MHz, CDCl$_3$) δ 164.69, 136.33, 132.10, 129.95, 129.76, 124.89, 122.92, 122.29, 121.68, 120.07, 116.20, 112.73, 104.31, 59.49, 14.54. HRMS (ESI) calcd for $C_{17}H_{14}BrNO_2$ [M+H]$^+$: 344.0281; found: 344.0274.



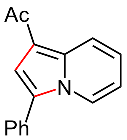
Ethyl 3-(4-(trifluoromethyl)phenyl)indolizine-1-carboxylate (6h):[5] white solid was obtained with 80% isolated yield following Method B. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.27 (d, J = 8.4 Hz, 2H), 7.67 (dd, J = 37.5, 8.1 Hz, 4H), 7.35 (s, 1H), 7.08 (dd, J = 9.1, 6.9 Hz, 1H), 6.72 (t, J = 7.0 Hz, 1H), 4.39 (q, J = 7.1 Hz, 2H), 1.42 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 164.62, 136.69, 134.71, 129.43 (q, $J_{C\text{-}F}$ = 32.7 Hz), 128.17, 125.94 (q, $J_{C\text{-}F}$ = 3.7 Hz), 124.60, 123.93 (q, $J_{C\text{-}F}$ = 273.0 Hz), 122.91, 122.64, 120.19, 116.92, 112.98, 104.70, 59.58, 14.48. ^{19}F NMR (377 MHz, CDCl$_3$) δ -62.53. HRMS (ESI) calcd for $C_{18}H_{14}F_3NO_2$ [M+H]$^+$: 334.1049; found: 334.1043.



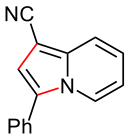
Ethyl 3-pentylindolizine-1-carboxylate (6i):[11] pale yellow oil. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.19 (d, J = 9.0 Hz, 1H), 7.84 (d, J = 7.0 Hz, 1H), 7.09 – 6.96 (m, 2H), 6.75 (t, J = 6.8 Hz, 1H), 4.36 (q, J = 7.1 Hz, 2H), 2.77 (t, J = 7.6 Hz, 2H), 1.84 – 1.71 (m, 2H), 1.46 – 1.34 (m, 7H), 0.93 (t, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 165.20, 135.58, 125.74, 122.66, 121.08, 119.96, 113.58, 112.07, 102.72, 59.36, 31.63, 26.53, 25.67, 22.48, 14.68, 14.00.



Ethyl 3-cyclopropylindolizine-1-carboxylate (6j):[5] pale yellow oil was obtained with 10% isolated yield following Method B. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.18 (t, J = 7.4 Hz, 2H), 7.07 (dd, J = 8.9, 7.0 Hz, 1H), 6.98 (s, 1H), 6.78 (t, J = 6.8 Hz, 1H), 4.35 (q, J = 7.1 Hz, 2H), 1.87 – 1.77 (m, 1H), 1.40 (t, J = 7.1 Hz, 3H), 1.08 – 0.97 (m, 2H), 0.74 – 0.64 (m, 2H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 165.10, 135.69, 127.36, 123.31, 121.76, 119.78, 113.64, 112.06, 102.31, 59.34, 14.66, 5.94, 5.36.



1-(3-Phenylindolizin-1-yl)ethanone (6k):[5] white solid was obtained with 92% isolated yield following Method B. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.53 (d, J = 9.0 Hz, 1H), 8.29 (d, J = 7.1 Hz, 1H), 7.58 – 7.47 (m, 4H), 7.42 (ddd, J = 8.5, 3.3, 1.6 Hz, 1H), 7.23 – 7.10 (m, 2H), 6.77 (td, J = 6.9, 1.2 Hz, 1H), 2.56 (s, 3H).^{13}C NMR (101 MHz, CDCl$_3$) δ 193.02, 135.83, 130.98, 129.10, 128.60, 128.12, 126.27, 123.84, 123.15, 120.99, 116.42, 113.55, 113.41, 27.96. HRMS (ESI) calcd for $C_{16}H_{13}NO$ [M+H]$^+$: 236.1073; found: 236.1066.



3-Phenylindolizine-1-carbonitrile (6l):[5] white solid was obtained with 46% isolated yield following Method B. ^{1}H NMR (400 MH/z, CDCl$_3$) δ 8.29 (d, J = 7.1 Hz, 1H), 7.69 (d, J = 9.0 Hz, 1H), 7.54 – 7.49 (m, 4H), 7.48 – 7.41 (m, 1H), 7.11 – 7.06 (m, 1H), 7.05 (s, 1H), 6.75 (td, J = 7.1, 1.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.35, 130.11, 129.21, 128.62, 128.56, 126.90, 123.68, 122.32, 118.17, 116.94, 116.20, 113.06, 82.10. HRMS (ESI) calcd for $C_{15}H_{10}N_2$ $[M+H]^+$: 219.0917; found: 219.0914.

General computational calculation details

Completes Reference for Gaussian 09

Gaussian 09, Revision A.2, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, N. J.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian, Inc., Wallingford CT, **2009**.

Absolute Calculation Energies, Enthalpies, and Free Energies

All the DFT calculations were carried out with the GAUSSIAN 09 series of programs.[6] Density functional theory B3LYP[7] with a standard 6-31+G(d) basis set (SDD basis set for I) was used for geometry optimizations. Harmonic frequency calculations were performed for all stationary points to confirm them as a local minima or transition structures and to derive the thermochemical corrections for the enthalpies and free energies. M11 functional,[8] recently proposed by Truhlar group, is used to calculate the single point energies, which could give more accuracy energetic information.[9] The solvent effects were considered by single point calculations on the gas-phase stationary points with a SMD continuum solvation model.[10] The larger basis set 6-311+G(d, p) (SDD basis set for I) is used in the solvation single point calculations. The energies given in this paper are the M11 calculated Gibbs free energies in DCE solvent.

Geometry	$E_{\text{(elec-B3LYP)}}{}^{a}$	$E_{\text{(solv, M11)}}{}^{b}$	$G_{\text{(corr-B3LYP)}}{}^{c}$	$H_{\text{(corr-B3LYP)}}{}^{d}$	IF^{e}
R-3	-728.839058	-728.659059	0.186288	0.247151	-
3a-I	-740.304939	-740.093721	0.187539	0.251343	-
3a′	-728.620062	-728.508646	0.187386	0.248345	-
3a	-728.3033841	-728.110082	0.178582	0.237468	-

[a]The electronic energy calculated by B3LYP in gas phase. [b]The electronic energy calculated by M11 in DCE solvent. [c]The thermal correction to Gibbs free energy calculated by B3LYP in gas phase. [d]The thermal correction to enthalpy calculated by B3LYP in gas phase. [e]The B3LYP calculated imaginary frequencies for the transition states.

B3LYP Geometries for All the Optimized Compounds and Transition States

R-3

C	-1.22473900	1.27933500	0.10463100
C	-1.60107700	-0.04264100	0.74188700
H	-2.00801500	0.10798200	1.76326600
C	-2.69322000	-0.78680600	-0.03759200
C	-1.90643200	2.58740200	0.28031200
H	-2.98875300	2.46780000	0.17312600
H	-1.71423400	3.02266600	1.27891800
H	-1.55934600	3.31294700	-0.46431200
O	0.15117300	1.32896600	-0.05585300
O	-2.54023700	-1.80811100	-0.67187300
O	-3.87961400	-0.14913900	0.08020900
C	-4.98519000	-0.73553900	-0.63526900
H	-4.77485400	-0.75306900	-1.70801900
H	-5.16529500	-1.75520400	-0.28467000
C	-0.27019300	-0.74663300	0.74734600
C	0.67802300	0.08991000	0.28774300
C	2.12068900	-0.06779000	0.08256700
C	2.76751200	-1.26713300	0.43488900
C	2.88303600	0.97542800	-0.47109300
C	4.13831400	-1.41768200	0.23677300
H	2.19594600	-2.08465700	0.86494700
C	4.25705800	0.82006600	-0.66822300
H	2.39409200	1.90358600	-0.74685600
C	4.89058400	-0.37425300	-0.31629300
H	4.62163700	-2.35107900	0.51371400
H	4.83211000	1.63583300	-1.09894000
H	-0.12863800	-1.77334300	1.05265600
H	5.95982800	-0.49376500	-0.47049300
H	-5.84124600	-0.09540600	-0.41927900

3a-I

C	0.64926600	-0.12735500	1.11675200
C	0.83840200	1.34650900	0.67870700
H	0.93366400	1.92264300	1.61913800
C	2.06390500	1.71627000	-0.14418000
C	1.32975300	-0.60098400	2.37979100
H	2.41384700	-0.51971400	2.28165000
H	0.99732600	0.02730300	3.21777700
H	1.06267200	-1.63803700	2.59512800
O	-0.72949500	-0.29541400	1.19553000
O	2.03391400	2.30076700	-1.20456500
O	3.19569900	1.37410600	0.50235000
C	4.42732100	1.63142300	-0.20239500
H	4.44793300	1.05801300	-1.13264100
H	4.52149000	2.69742300	-0.42416400
C	-0.49070100	1.63404200	0.03616500
C	-1.35391900	0.67388500	0.40241300
C	-2.77810900	0.45905400	0.14168600
C	-3.55058300	1.46654600	-0.46595500
C	-3.39407100	-0.75564000	0.48880500
C	-4.90223900	1.25777400	-0.72988100
H	-3.09256100	2.41621700	-0.72779900
C	-4.75059100	-0.95831400	0.22578300
H	-2.80527300	-1.53806600	0.95526500
C	-5.50886200	0.04391700	-0.38425800
H	-5.48557700	2.04428800	-1.20144700
H	-5.21330900	-1.90381900	0.49635100
H	-0.68463500	2.48294900	-0.60259800
I	1.37305400	-1.54706700	-0.60692200
H	-6.56428600	-0.11594700	-0.58860300
H	5.21845500	1.30286000	0.47169700

3a′

C	-1.16653300	1.24276700	0.32028500
C	-1.56226500	-0.11479600	0.79214800
H	-1.95545200	0.00059800	1.82012500
C	-2.73269300	-0.80898300	0.01756100
C	-1.96622200	2.46297500	0.11620700
H	-2.56436600	2.34423400	-0.79906700
H	-2.68549800	2.59373100	0.93147000
H	-1.32193500	3.33874600	0.01486500
O	0.09395400	1.27694000	0.08462400
O	-2.67487100	-1.96185100	-0.31619400
O	-3.75396700	0.02836300	-0.13896600
C	-4.95362300	-0.52662800	-0.76761100

H	-4.70962100	-0.87888300	-1.77115900
H	-5.33304800	-1.34838800	-0.15824800
C	-0.26010200	-0.84982500	0.75820800
C	0.70945500	-0.02225900	0.33899400
C	2.13668900	-0.08638600	0.08183200
C	2.79254300	-1.32986300	0.18524900
C	2.87365000	1.06274400	-0.26175300
C	4.16137500	-1.41567400	-0.04805500
H	2.23481500	-2.22659700	0.43962900
C	4.24534300	0.96490400	-0.49411900
H	2.38401500	2.02721200	-0.34516300
C	4.89130300	-0.26957700	-0.38782100
H	4.66015900	-2.37690300	0.03106600
H	4.80872200	1.85492200	-0.75780800
H	-0.15204500	-1.89228800	1.01967400
H	5.95951600	-0.34144000	-0.57016900
H	-5.65971100	0.30104400	-0.79765500

3a

C	-1.16445200	1.19819400	0.00005700
C	-1.51948100	-0.13484000	0.00012400
C	-2.84584400	-0.77036900	0.00024200
C	-1.90009700	2.49180000	0.00005200
H	-2.97516000	2.31372700	0.00015400
H	-1.63734600	3.08645300	0.88445500
H	-1.63750100	3.08635900	-0.88446000
O	0.19206200	1.29185400	-0.00003400
O	-3.01784100	-1.97705600	0.00027500
O	-3.87303300	0.11690300	0.00018700
C	-5.19206900	-0.45853400	0.00022400
H	-5.33986600	-1.07420700	-0.89101000
H	-5.33996900	-1.07383600	0.89170100
C	-0.29474700	-0.88636500	0.00008300
C	0.72822800	0.01715000	-0.00003300
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C	3.00024800	1.05218800	0.00010700
C	4.18661100	-1.47631800	-0.00053100
H	2.18556600	-2.25844500	-0.00067300
C	4.39071100	0.93049800	0.00002500
H	2.54171300	2.03577300	0.00035900
C	4.99182700	-0.33140200	-0.00029100
H	4.64211000	-2.46330800	-0.00079000
H	5.00592600	1.82680700	0.00021200

H	-0.22711200	-1.96434900	0.00014600
H	6.07467800	-0.42348400	-0.00035300
H	-5.87638700	0.39066800	0.00001300

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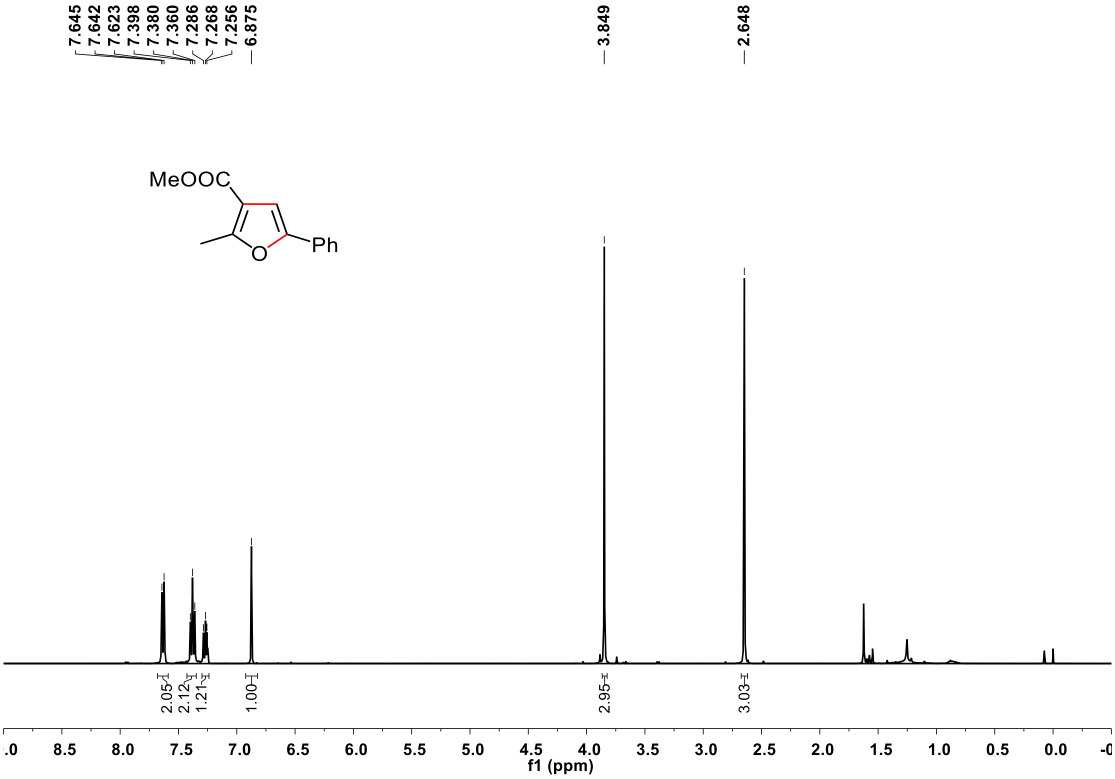
Copies of product NMR Spectra

3a

^{1}H NMR



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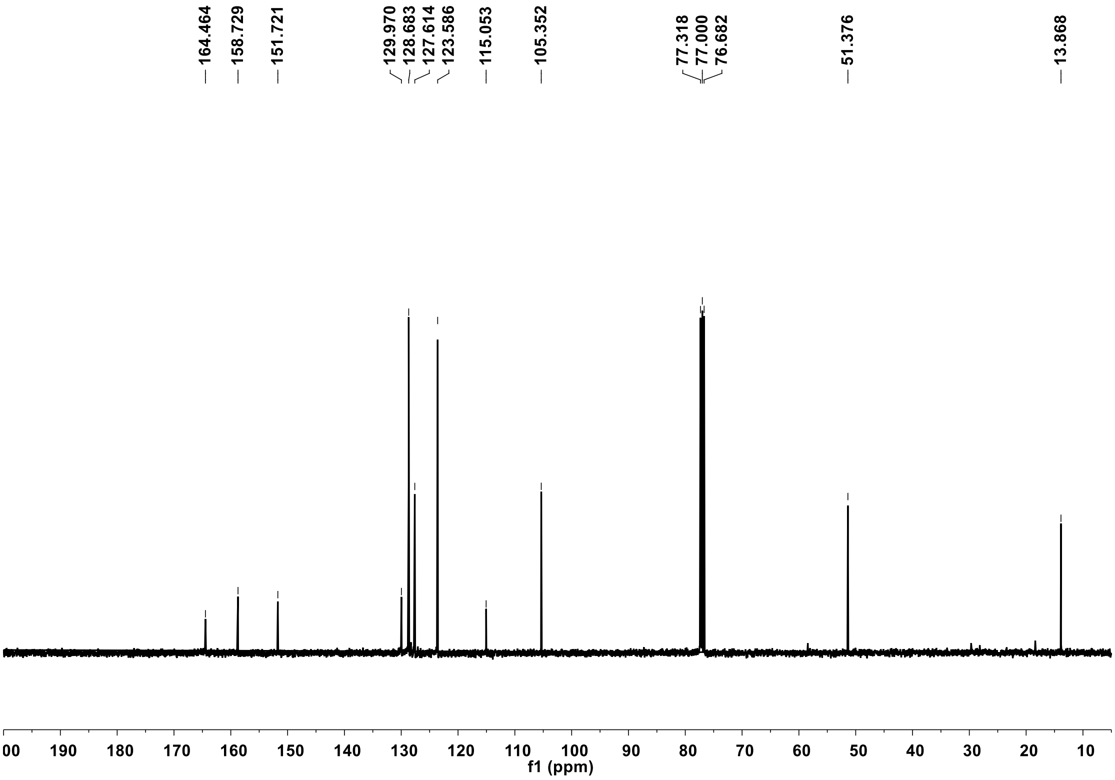
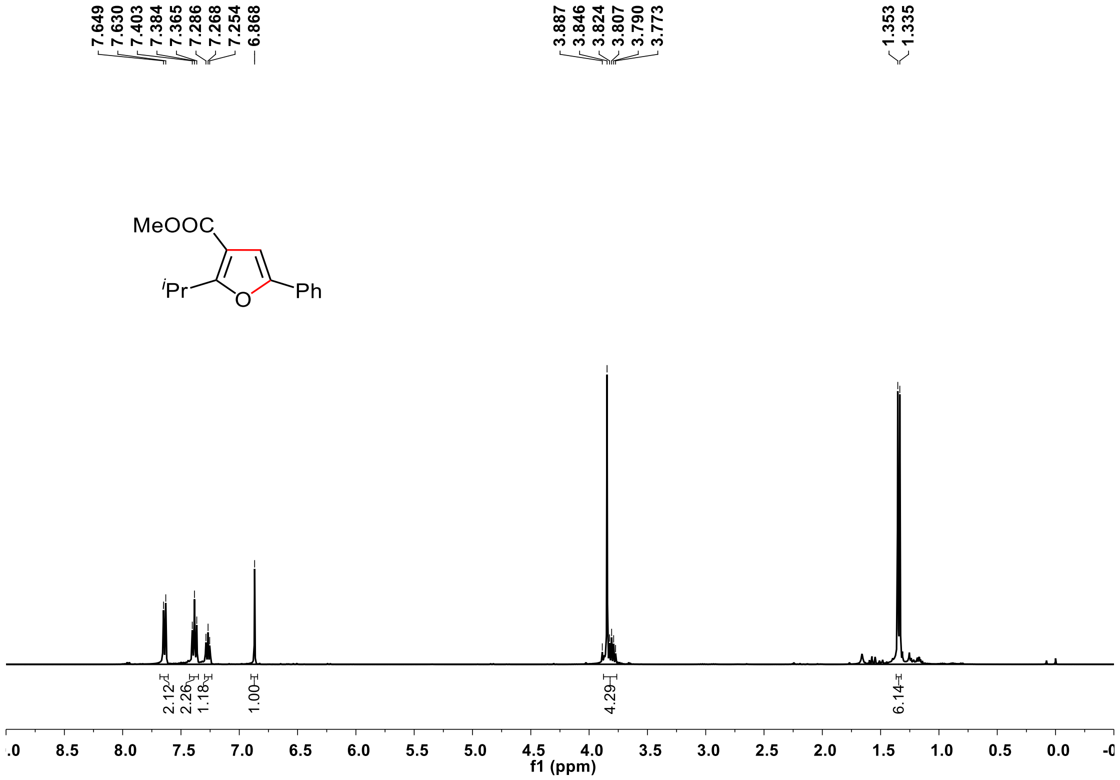
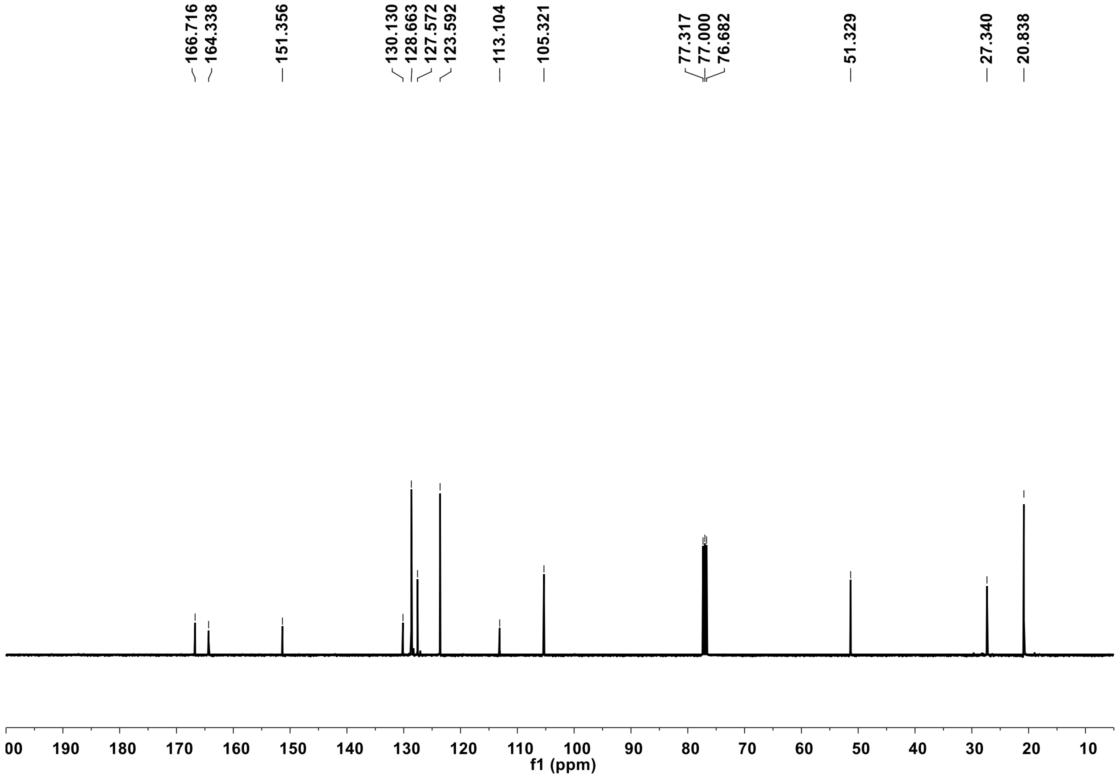


3b

^{1}H NMR

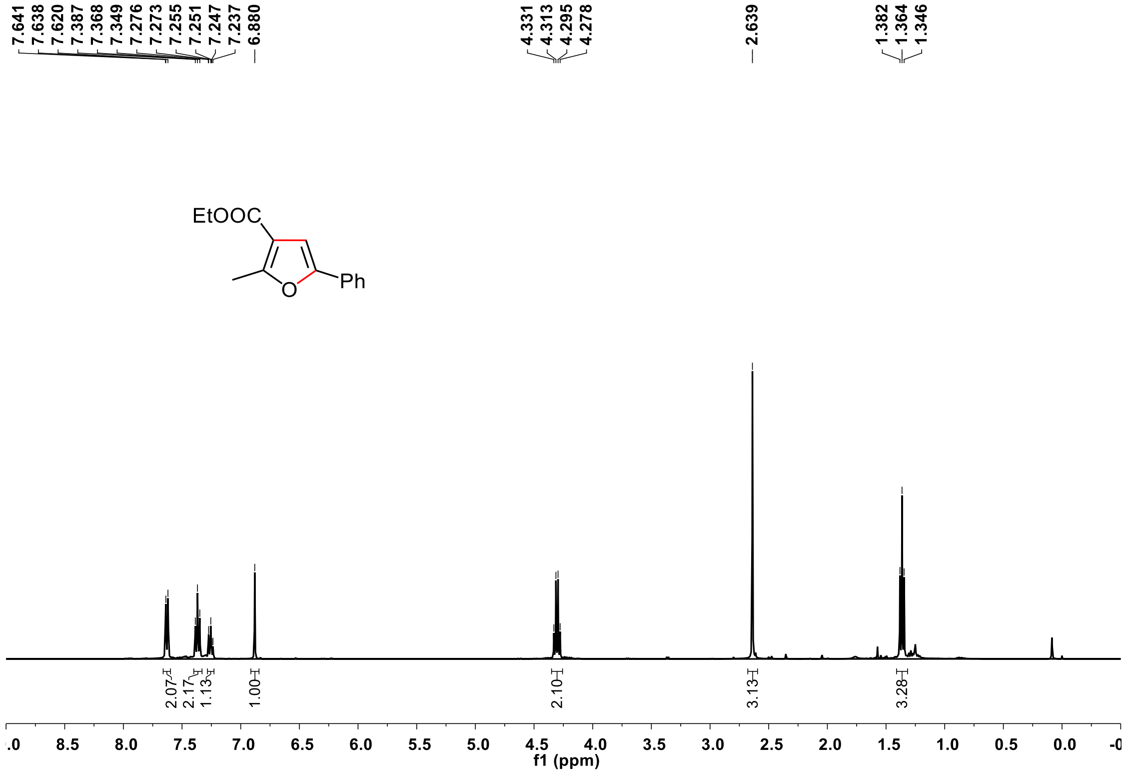


^{13}C NMR

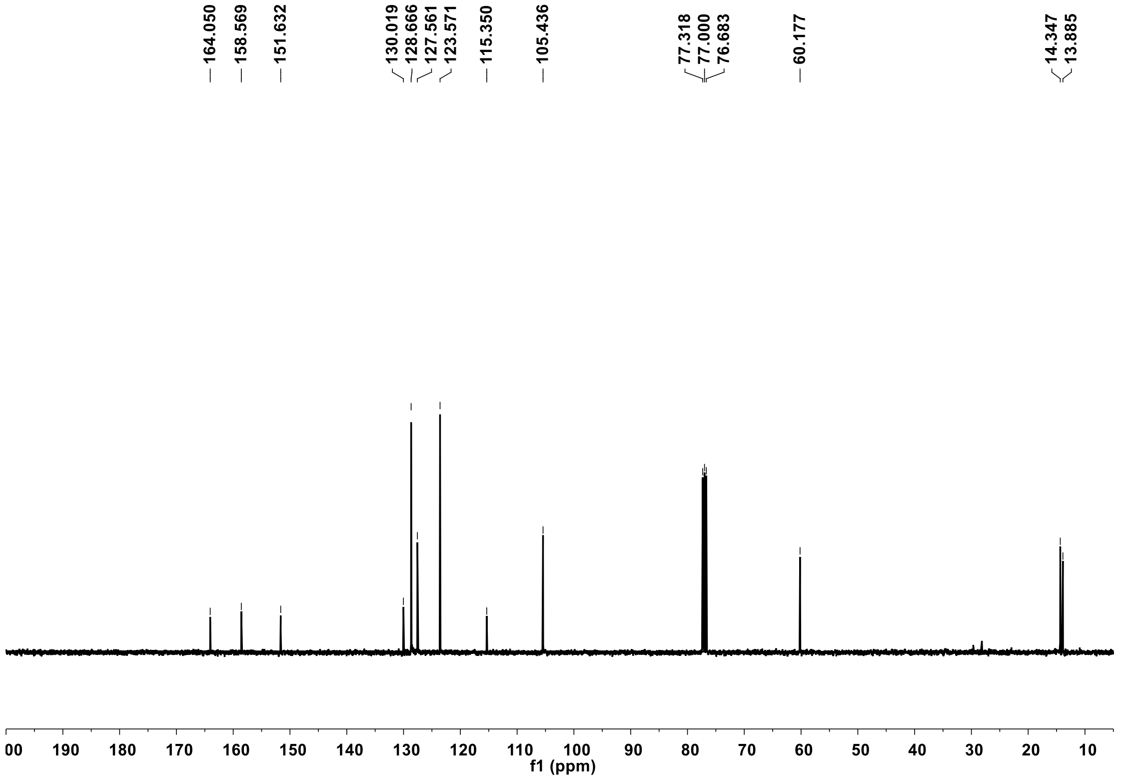


3c

^{1}H NMR

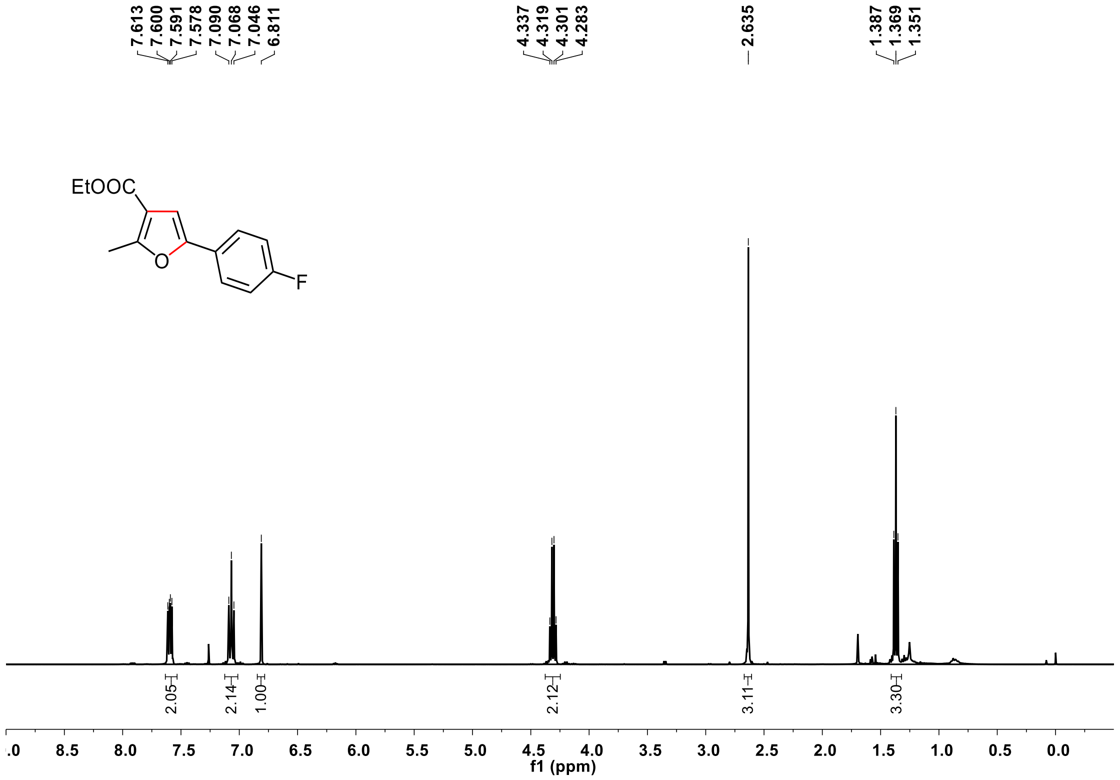


^{13}C NMR

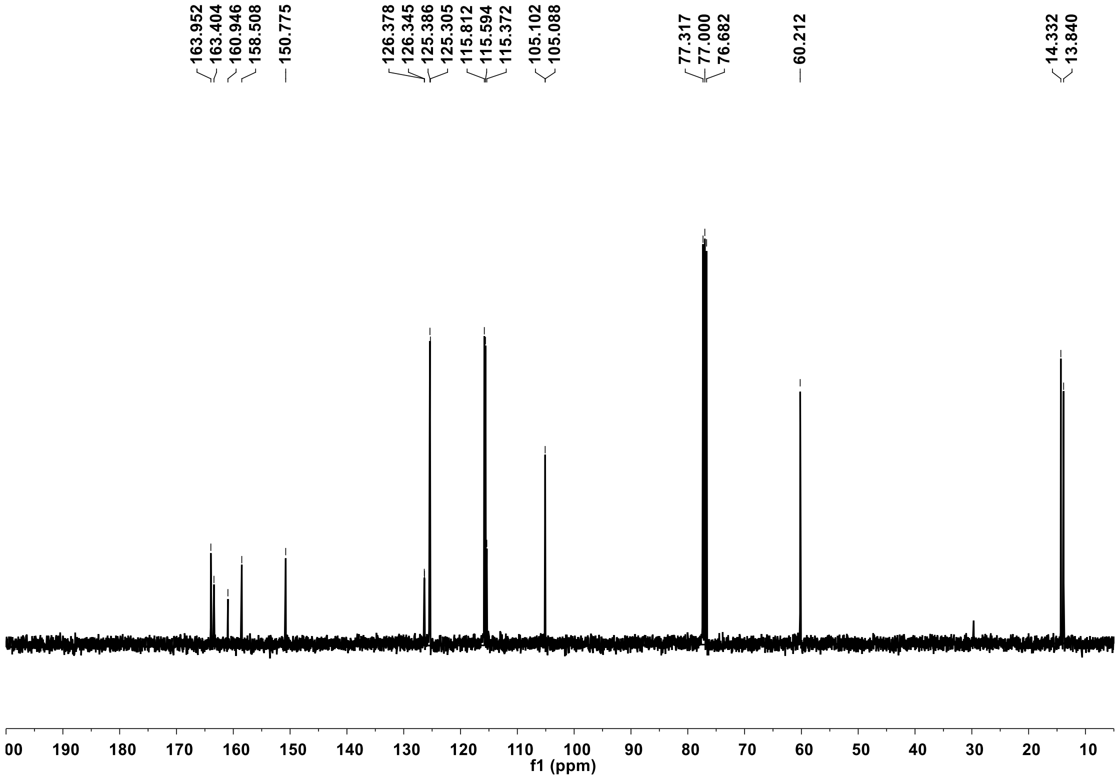


3d

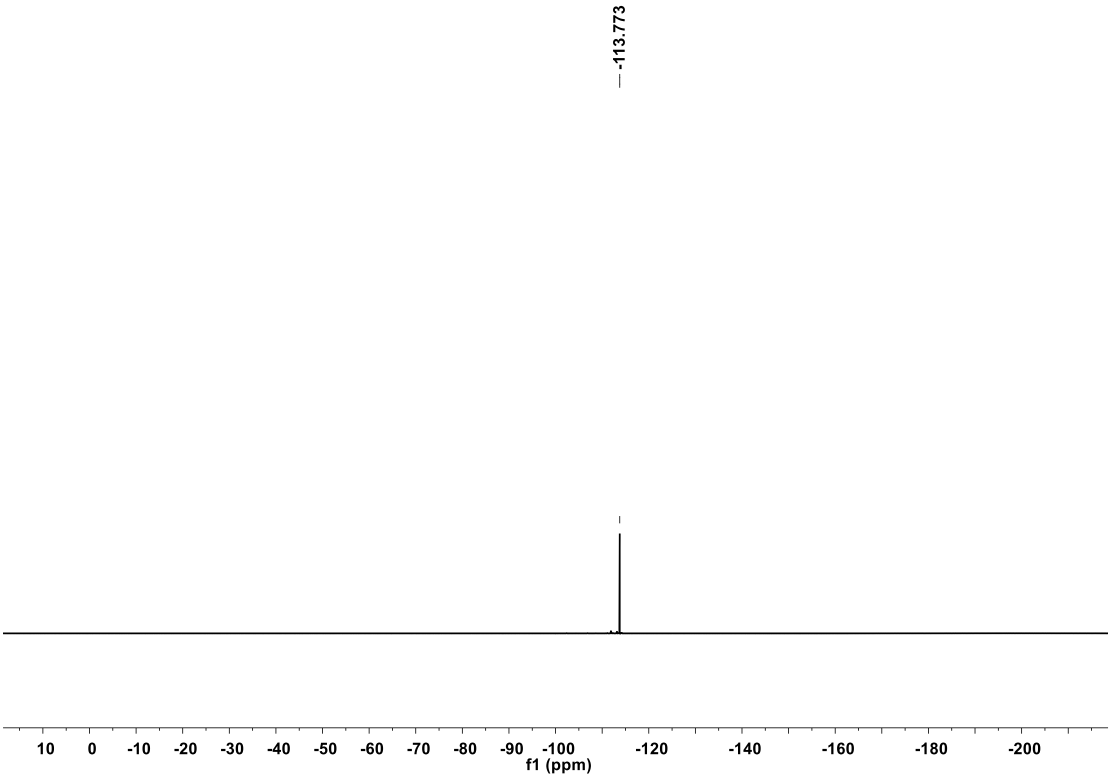
^{1}H NMR



^{13}C NMR



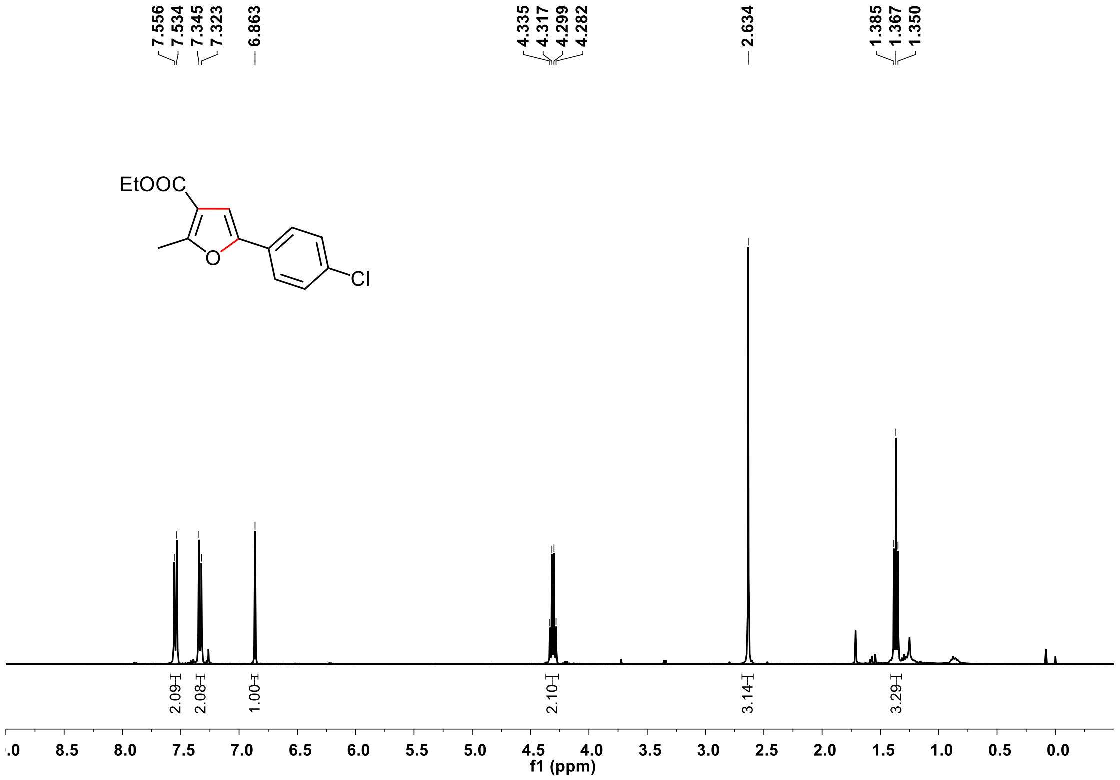
^{19}F NMR



-113.773
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-120
-140
-160
-180
-200
f1 (ppm)

3e

^{1}H NMR



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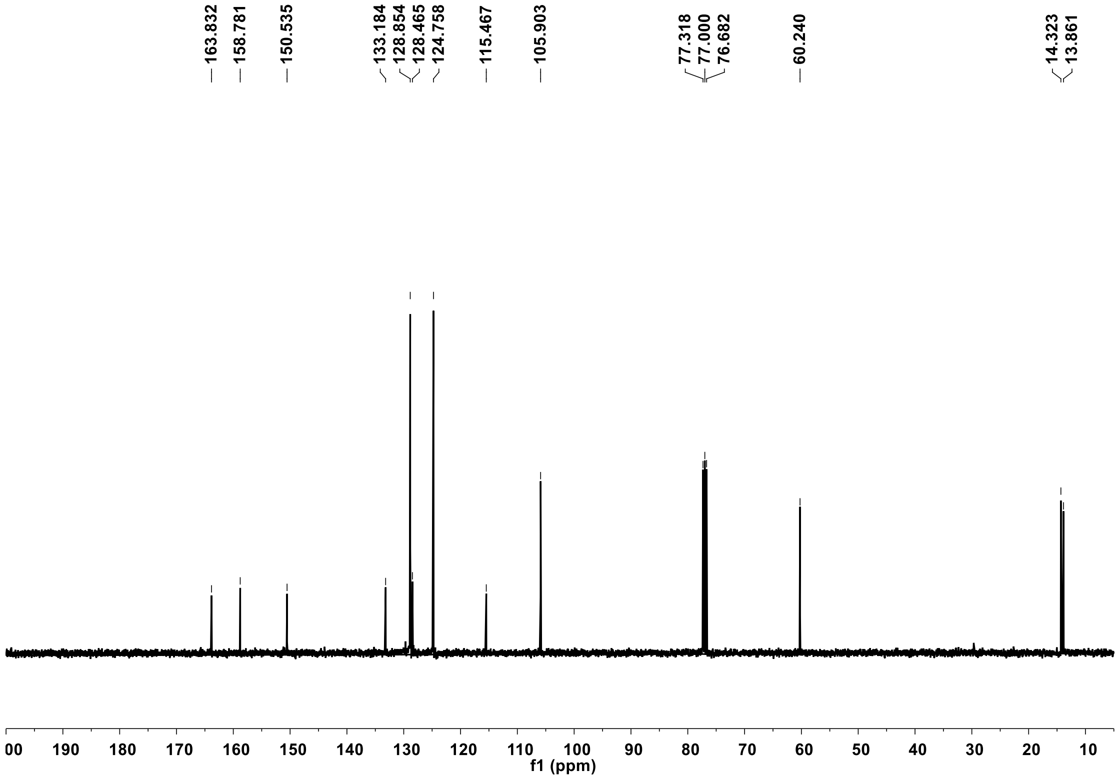
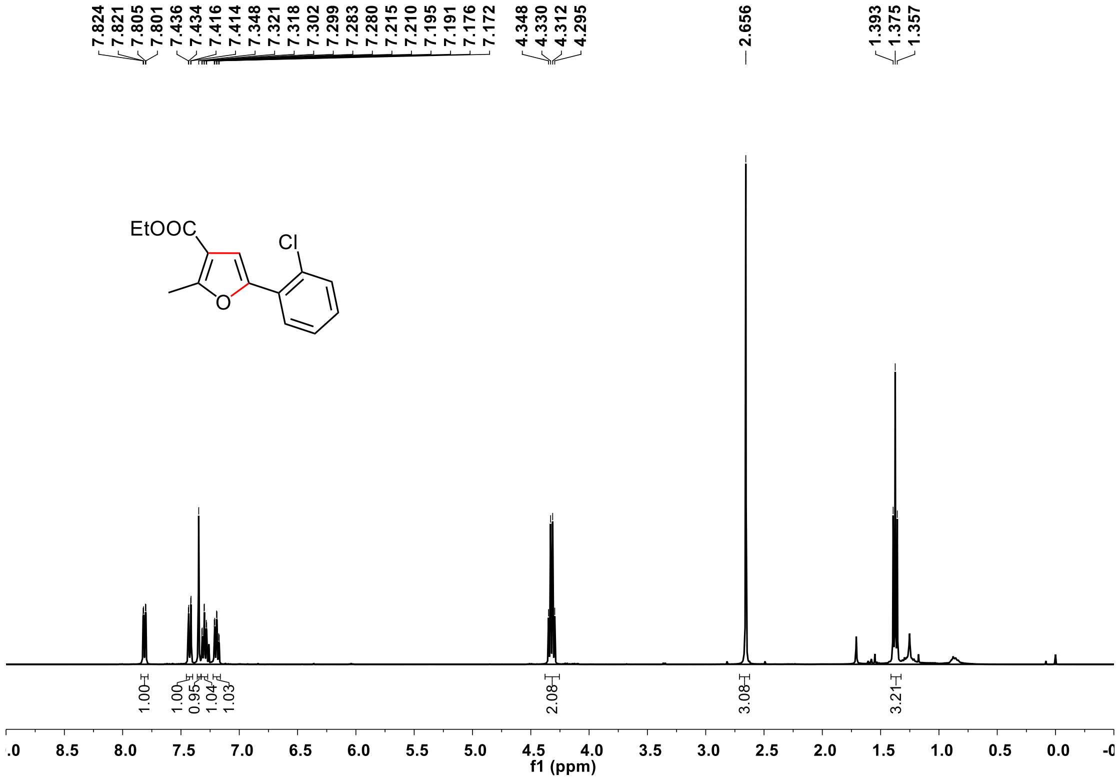


3f

^{1}H NMR



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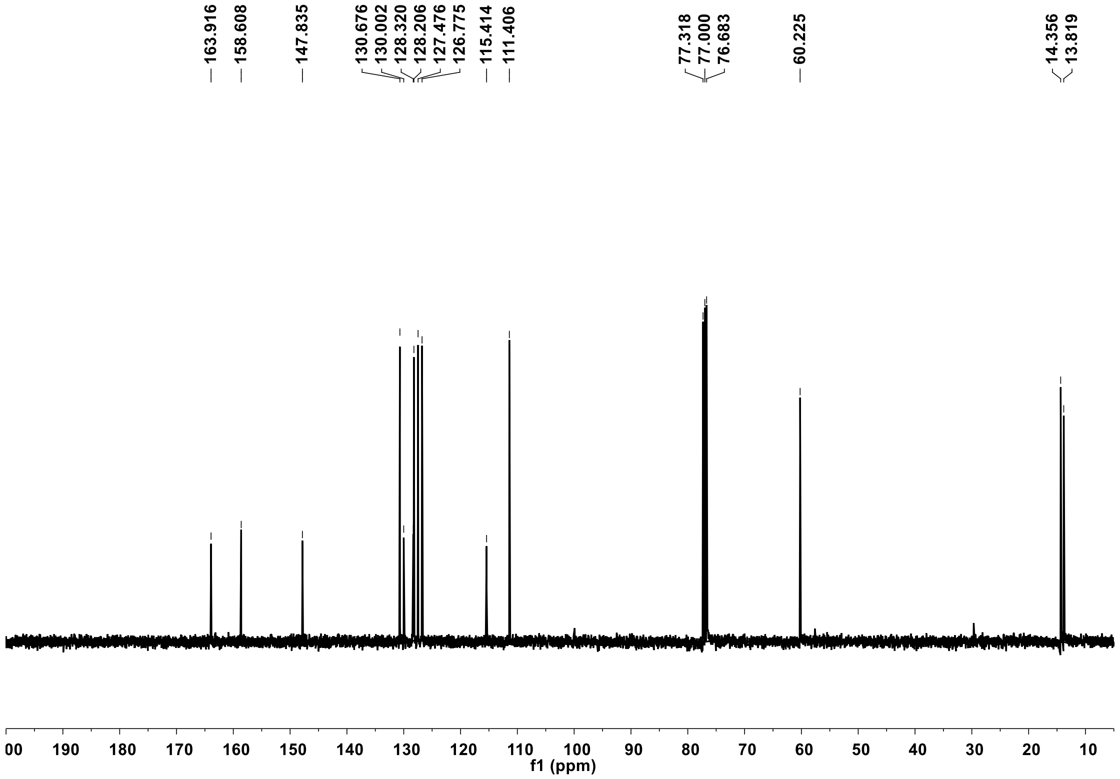
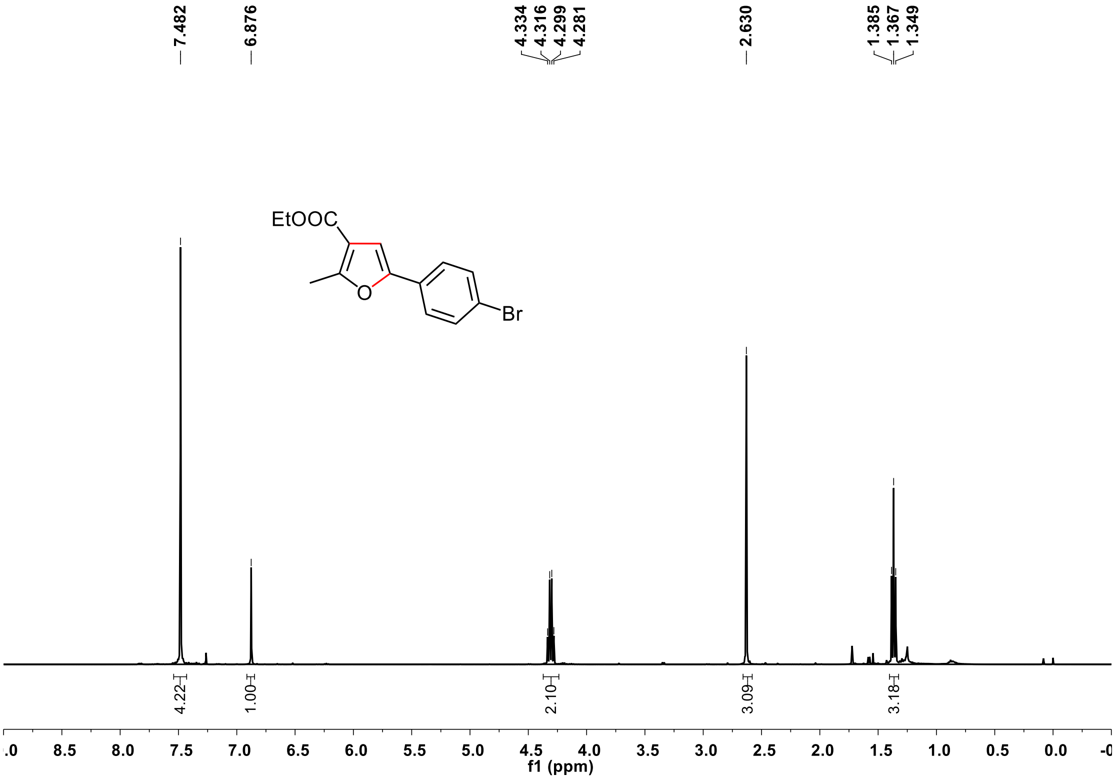


3g

^{1}H NMR



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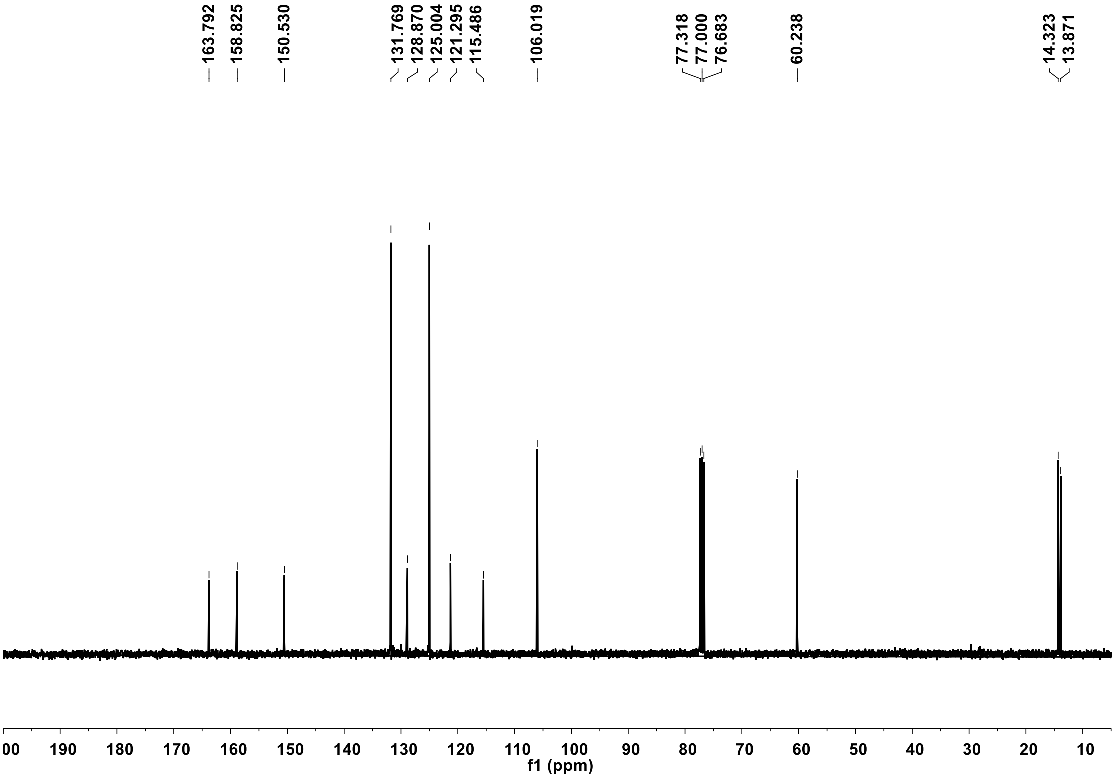
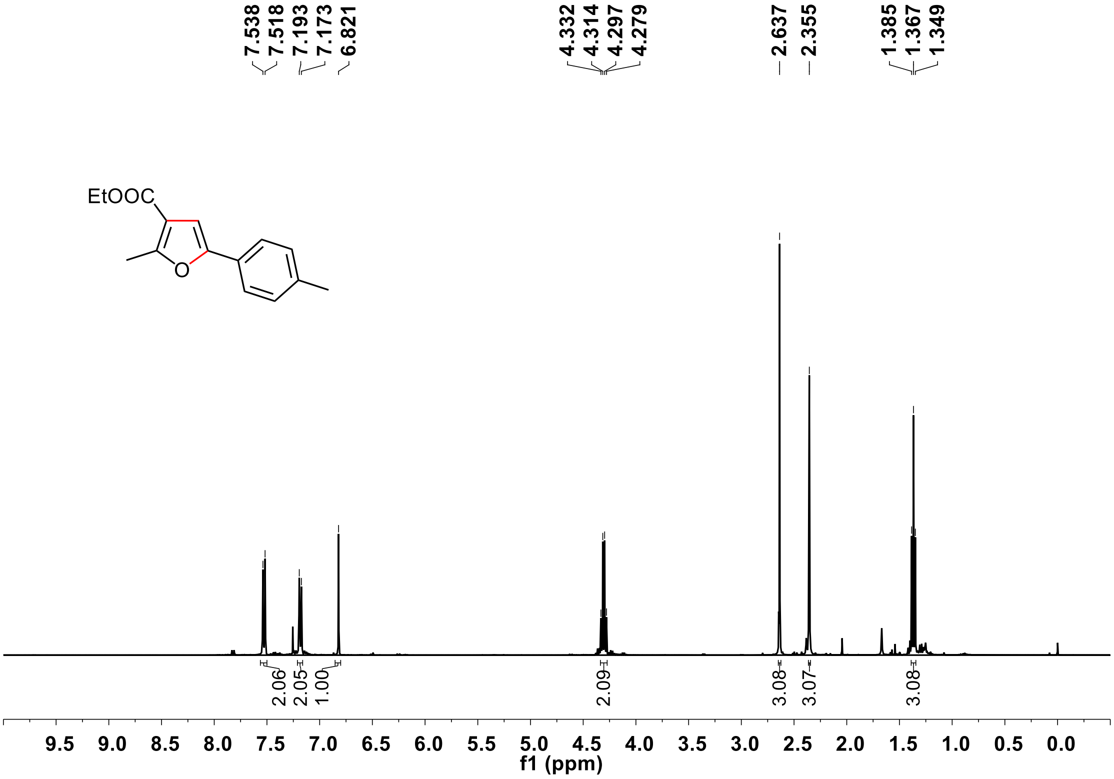


3h

^{1}H NMR



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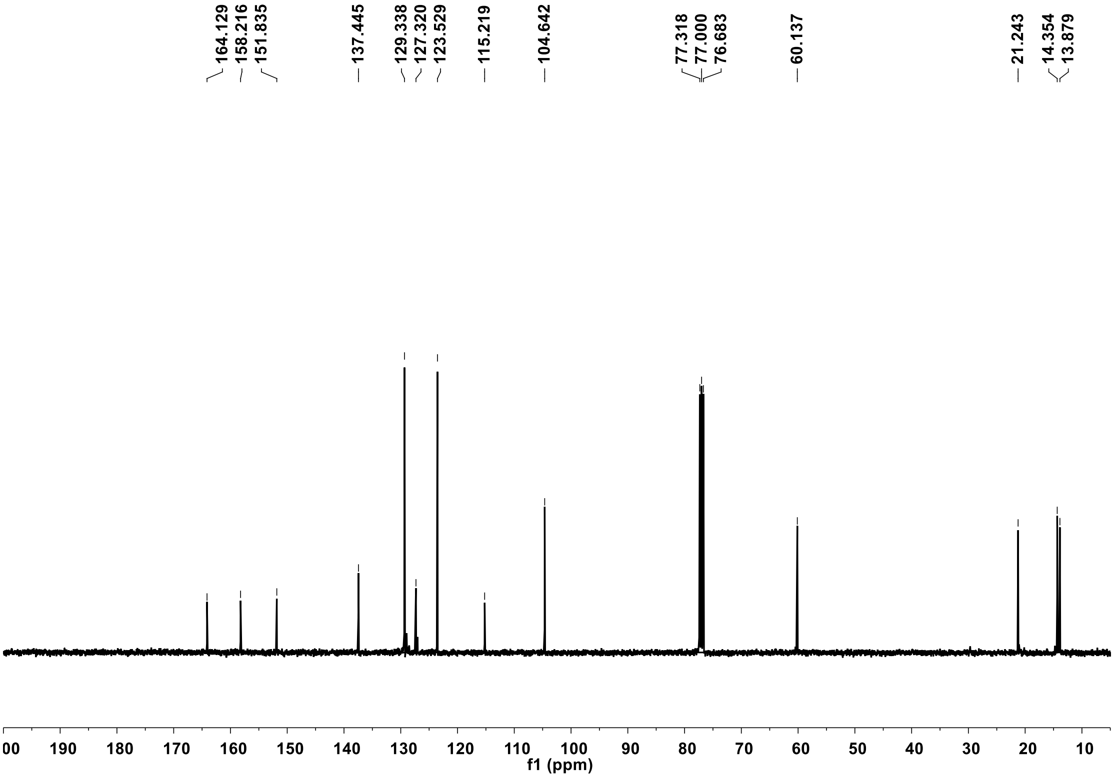
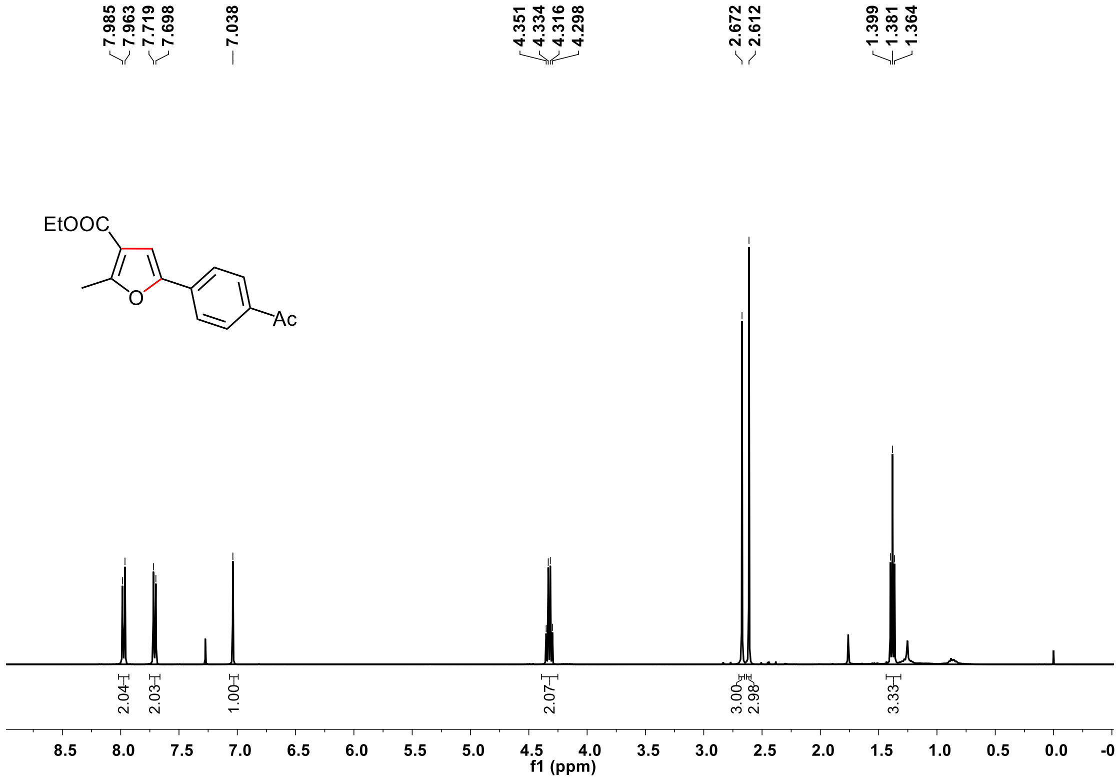


3i

^{1}H NMR



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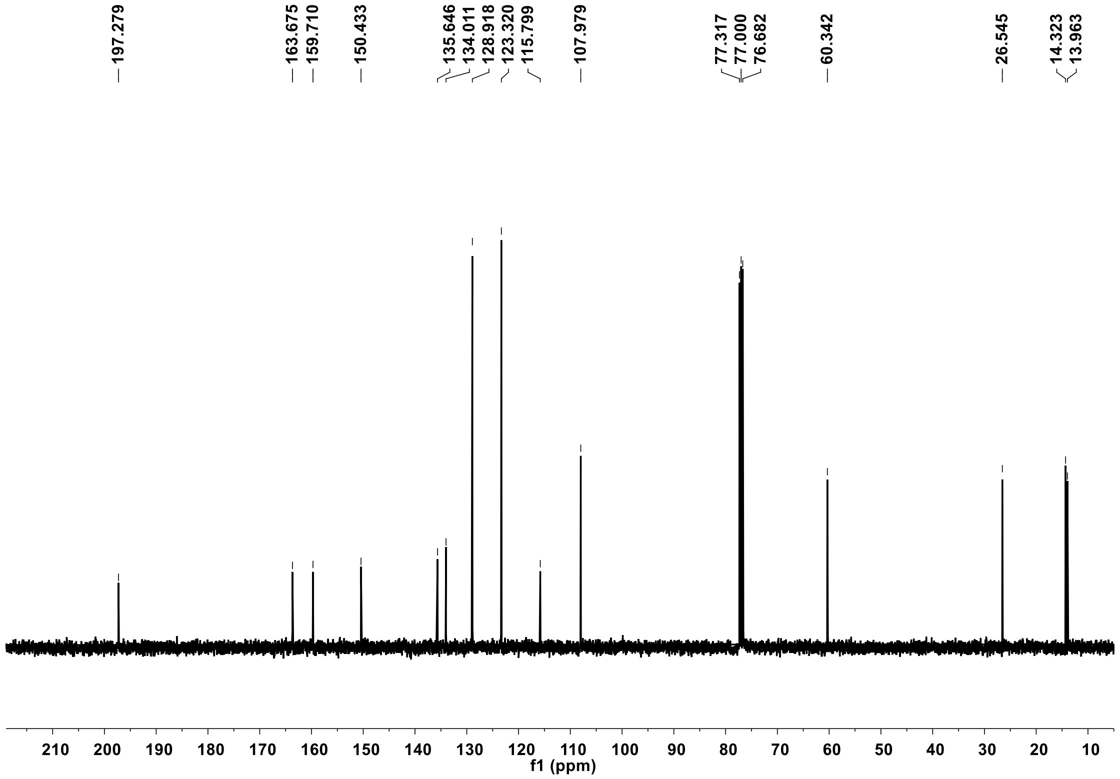
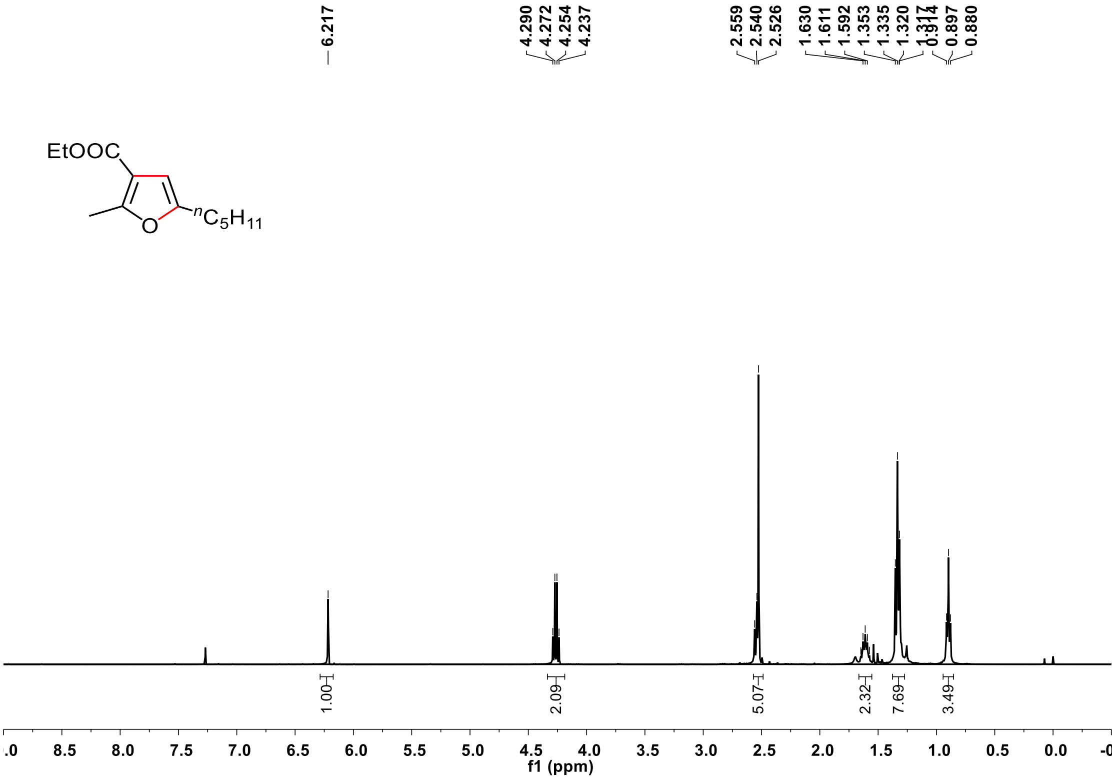


3j

^{1}H NMR



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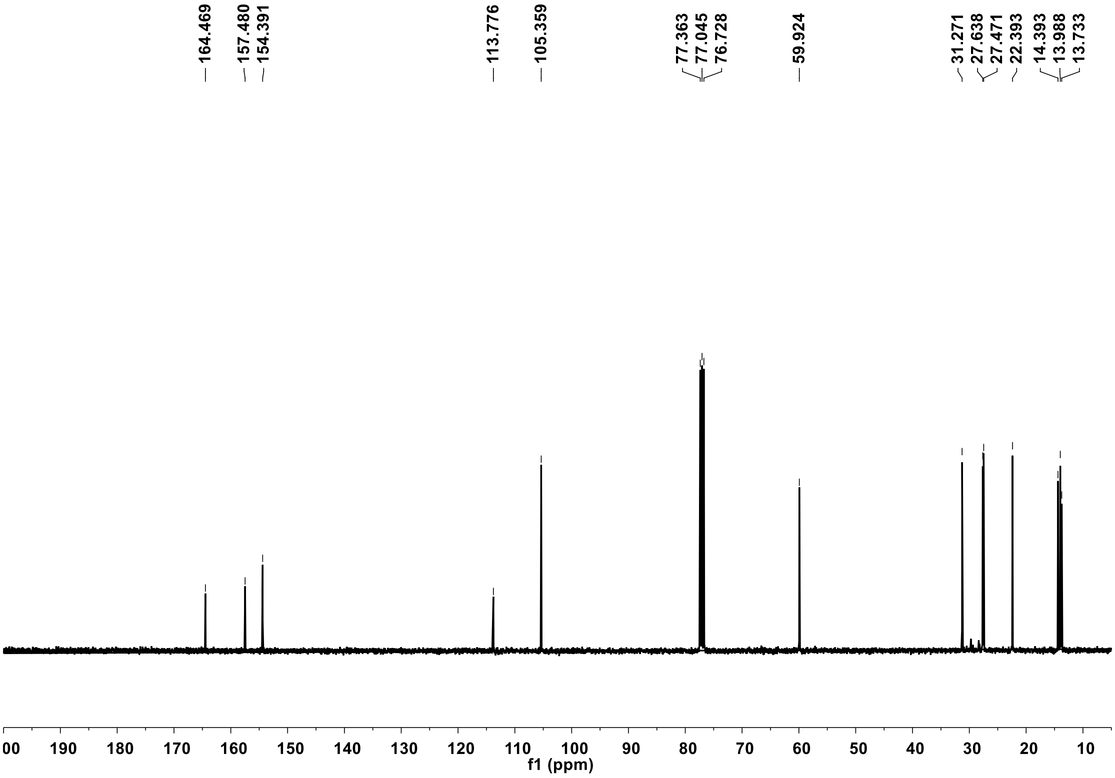
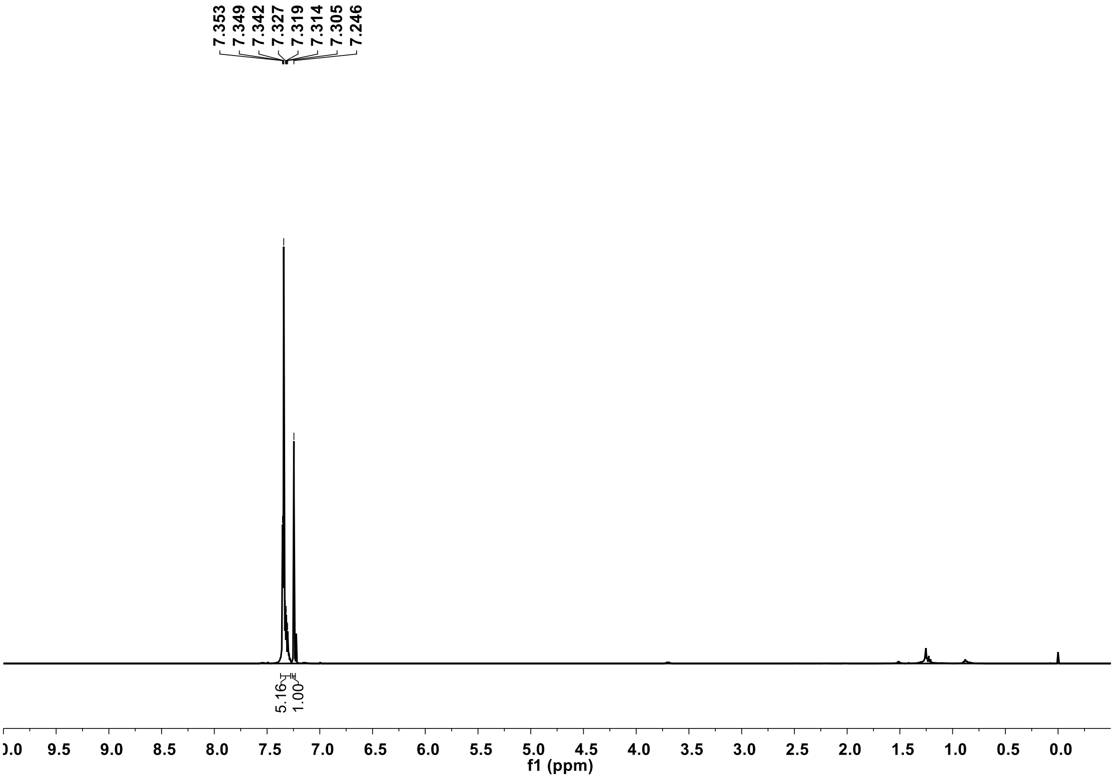
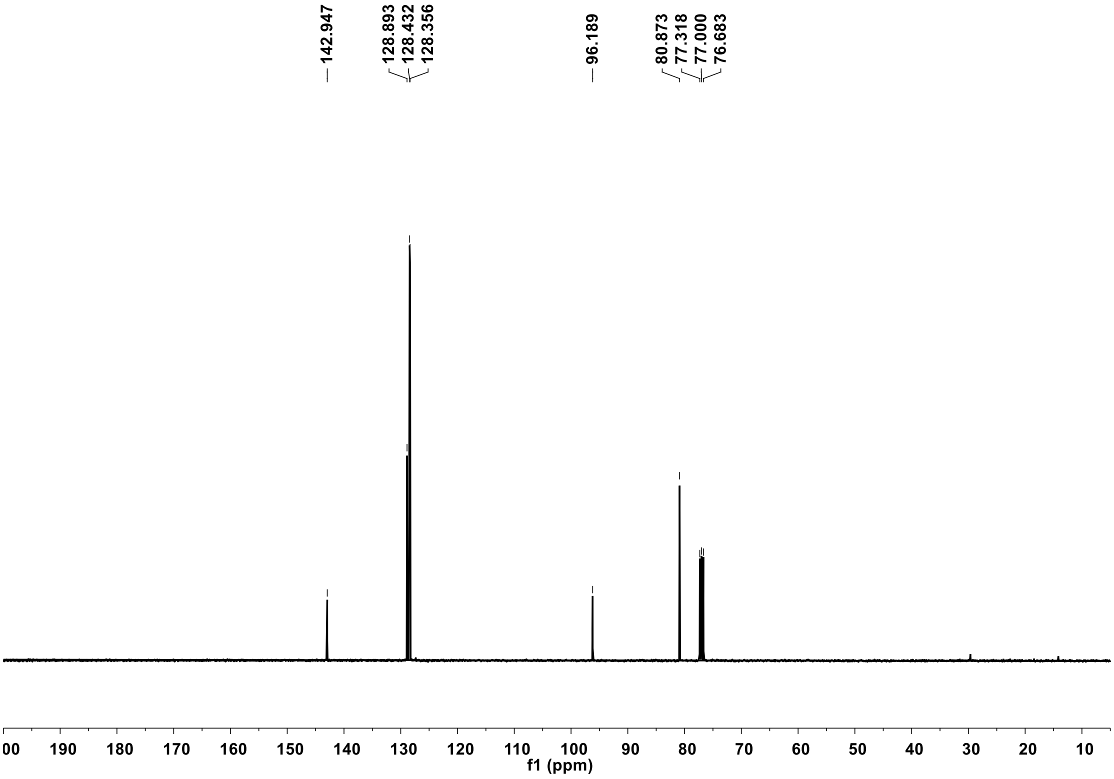


4

^{1}H NMR

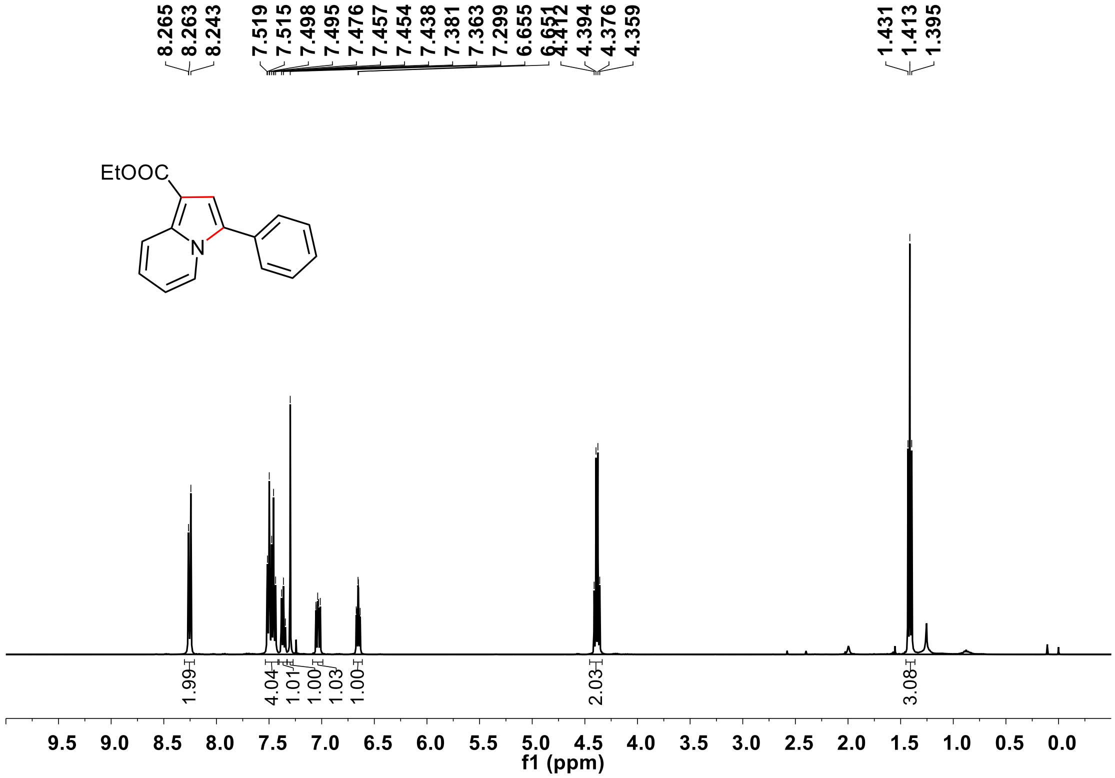


^{13}C NMR

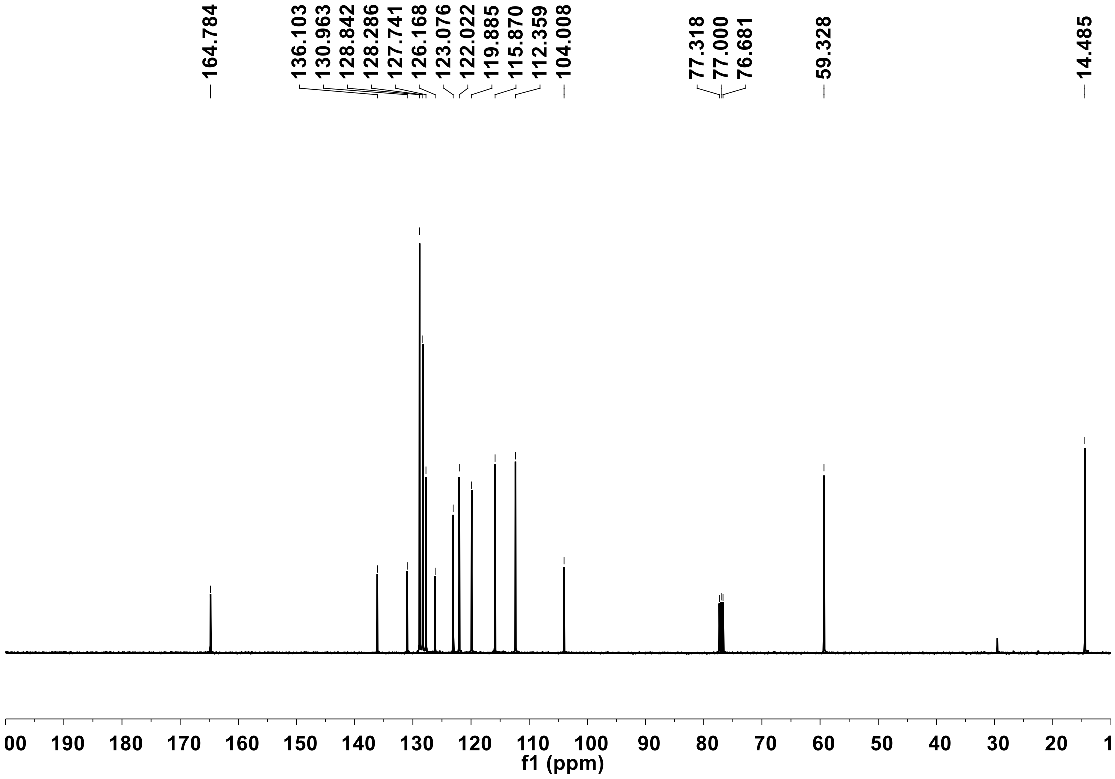


6a

^{1}H NMR

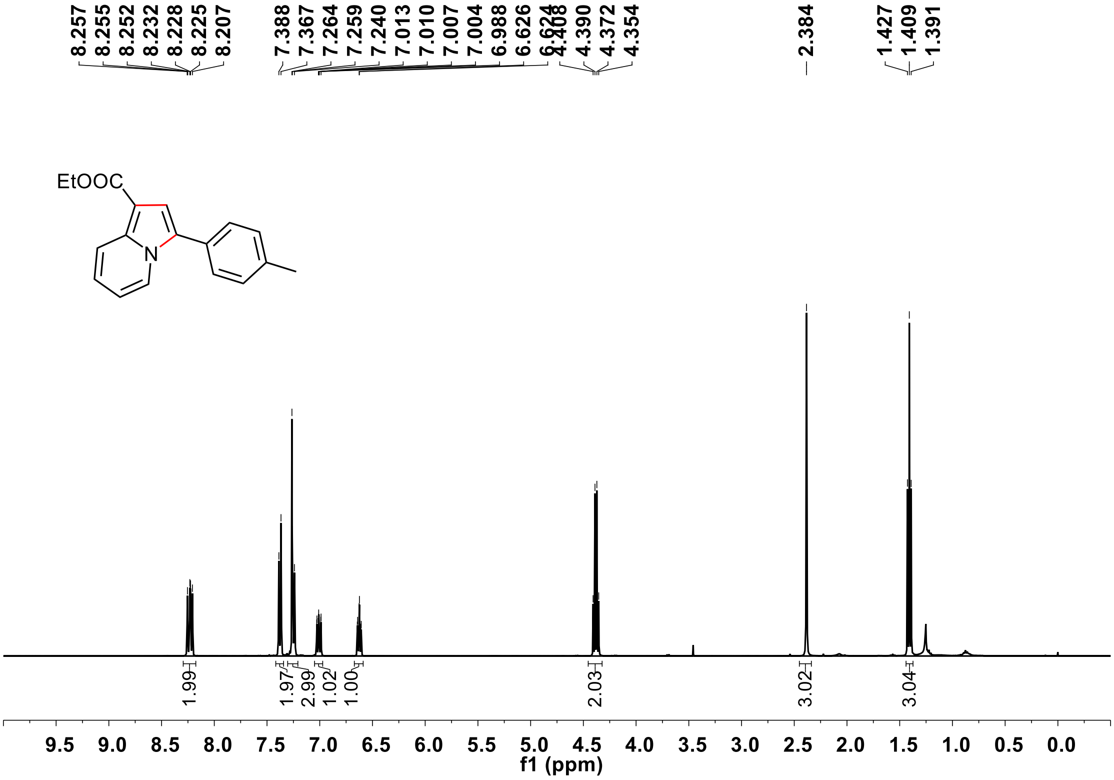


^{13}C NMR

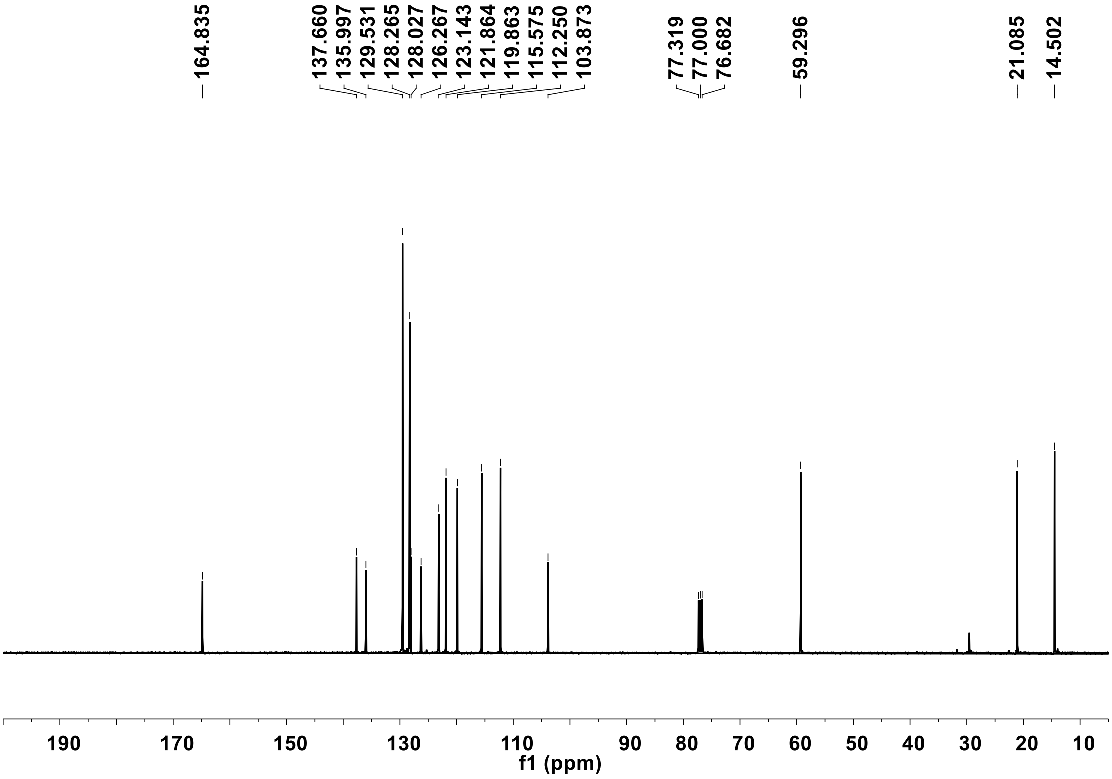


6b

^{1}H NMR

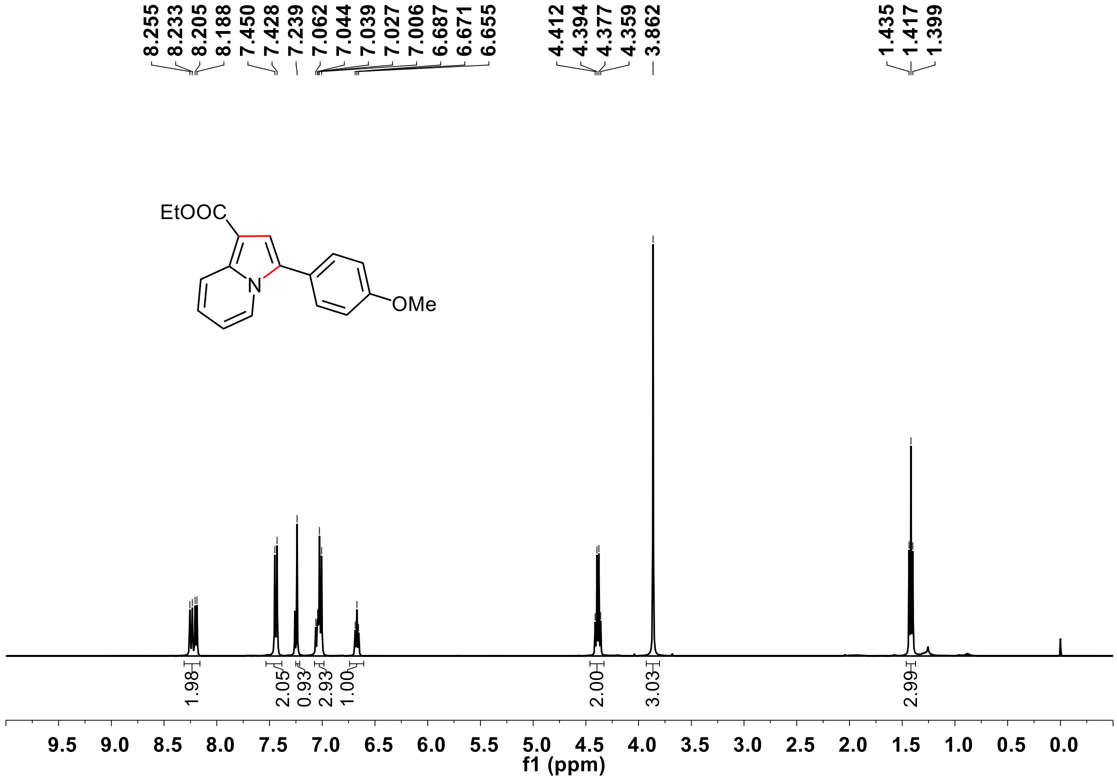


^{13}C NMR

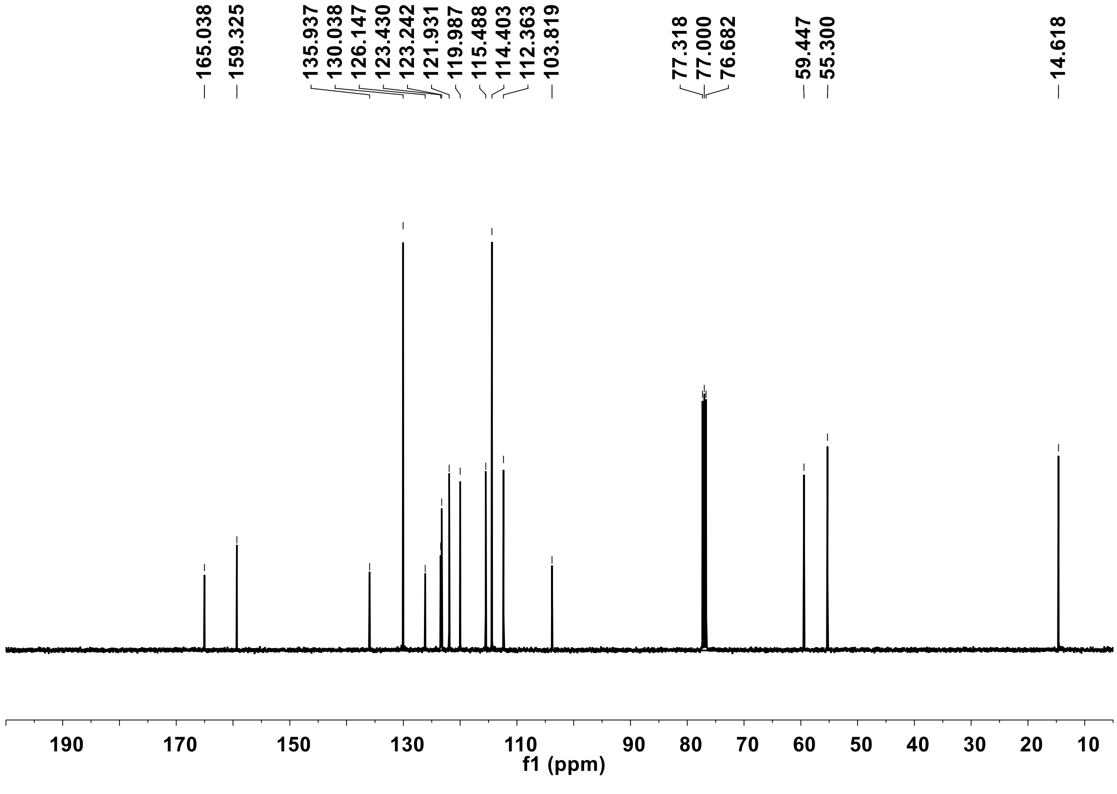


6c

^{1}H NMR

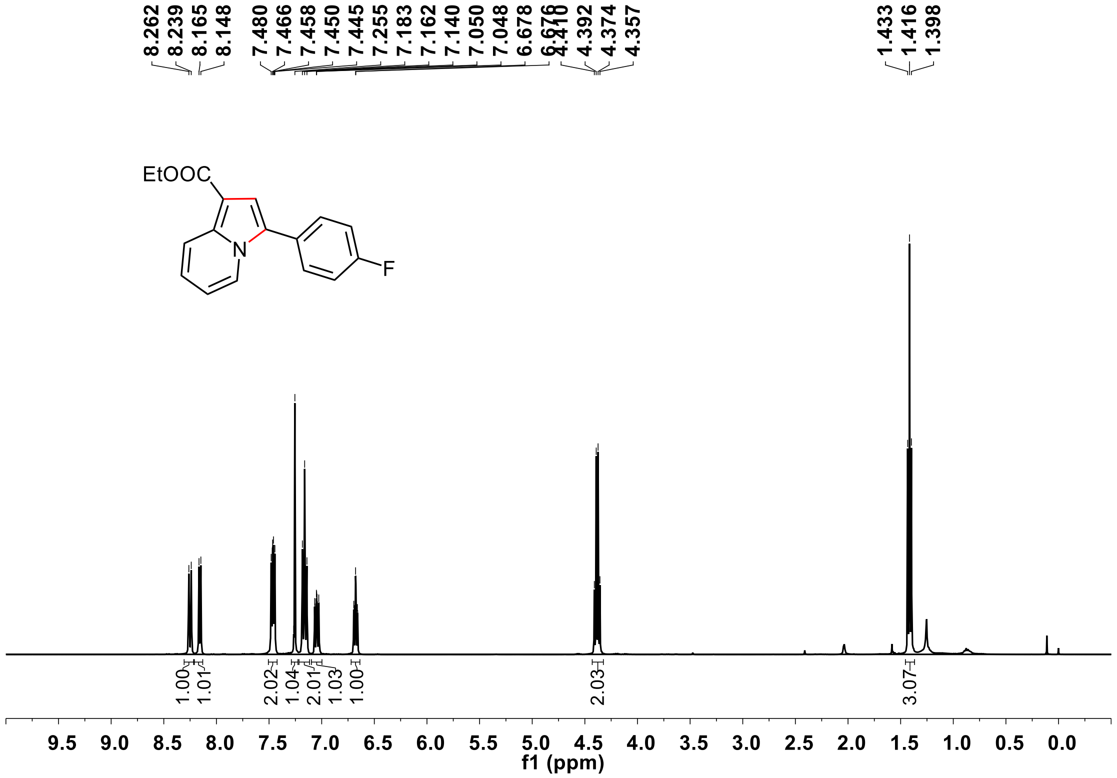


^{13}C NMR

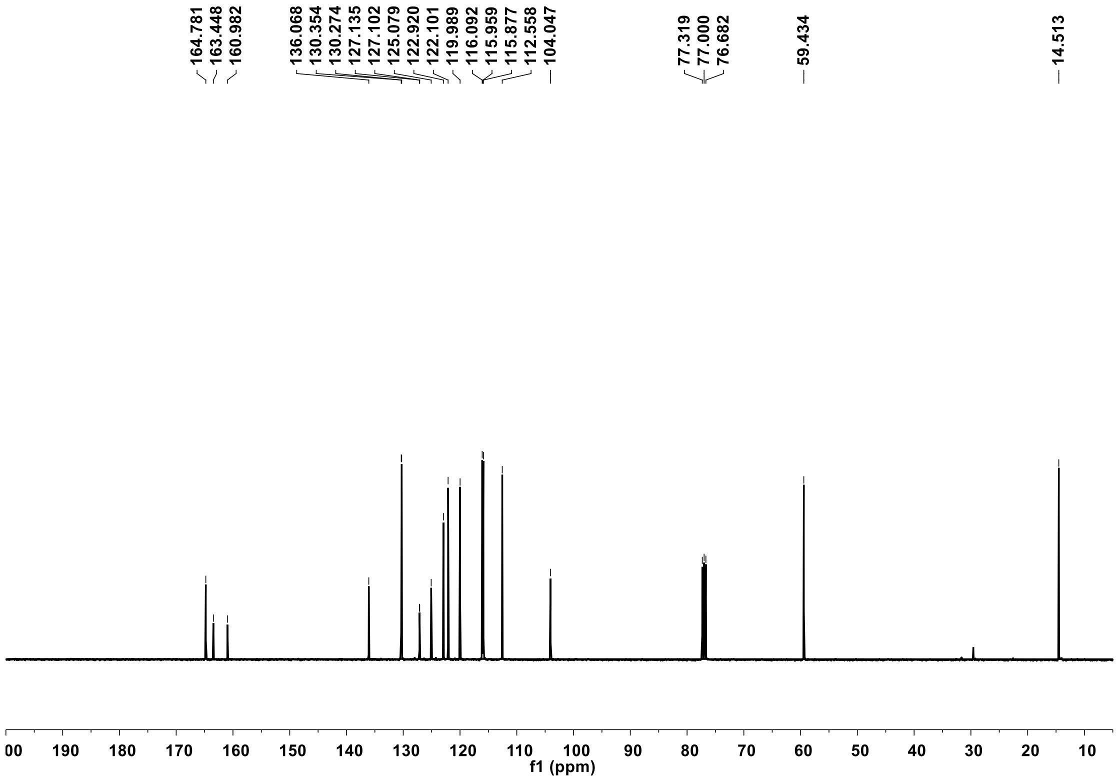


6d

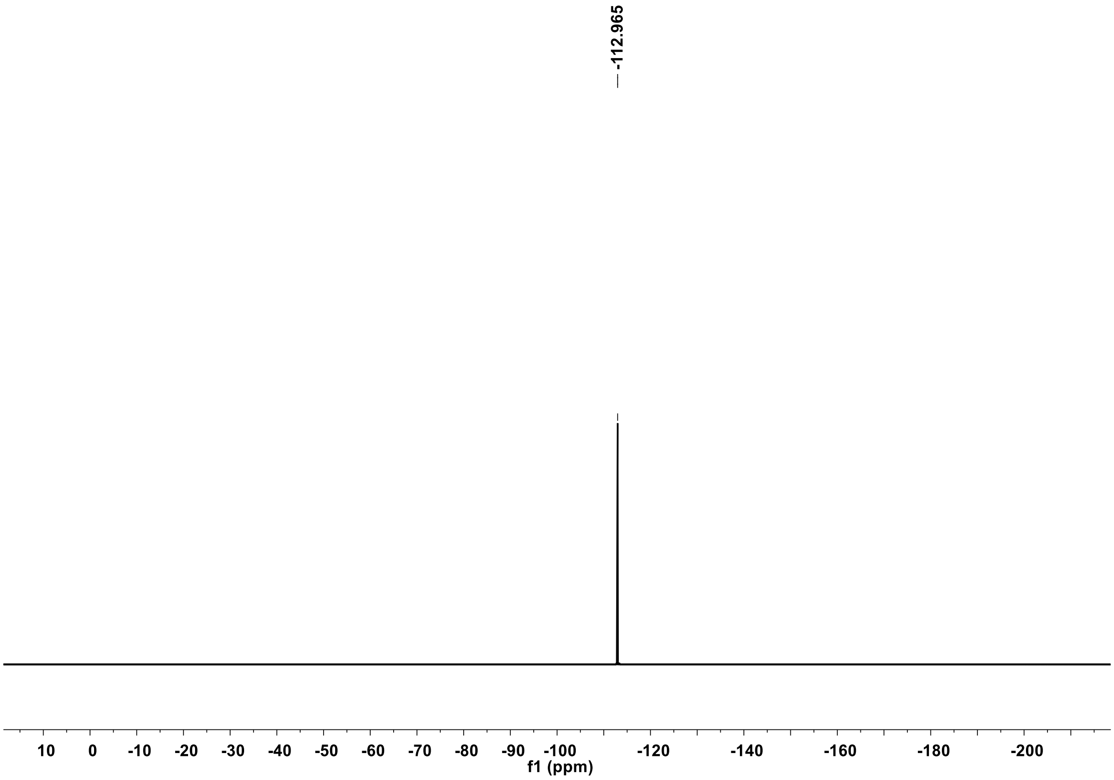
^{1}H NMR



^{13}C NMR



^{19}F NMR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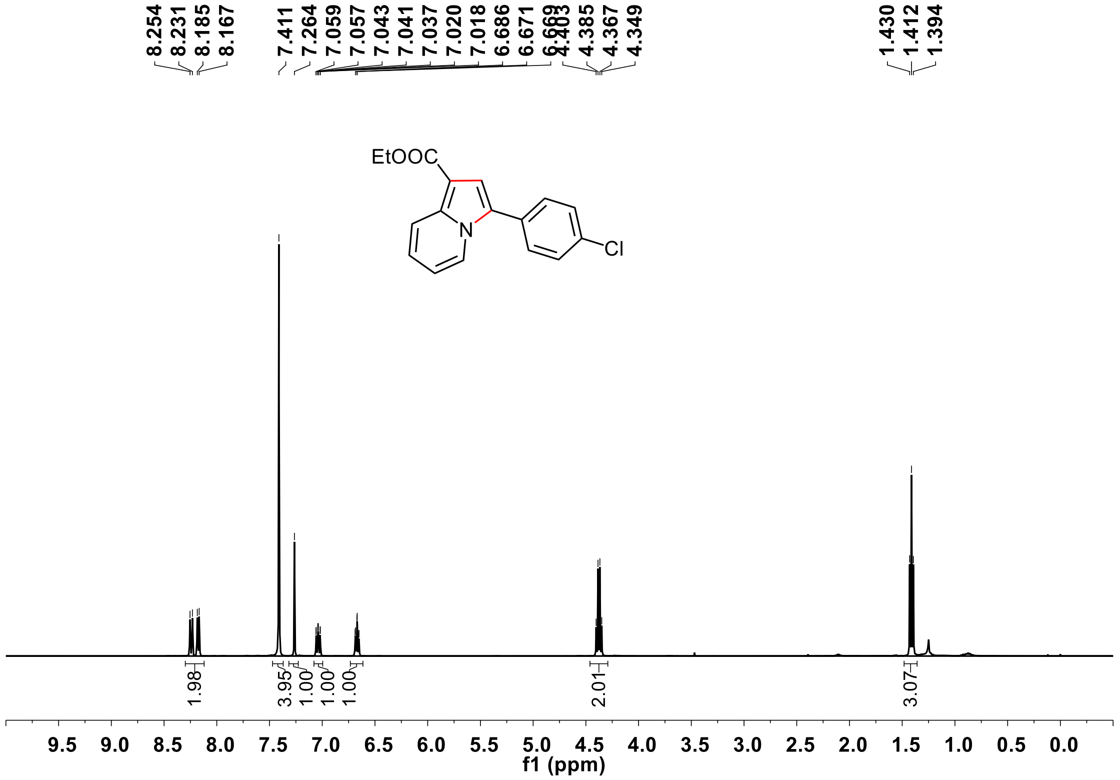
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-120
-140
-160
-180
-200
f1 (ppm)

6e

^{1}H NMR



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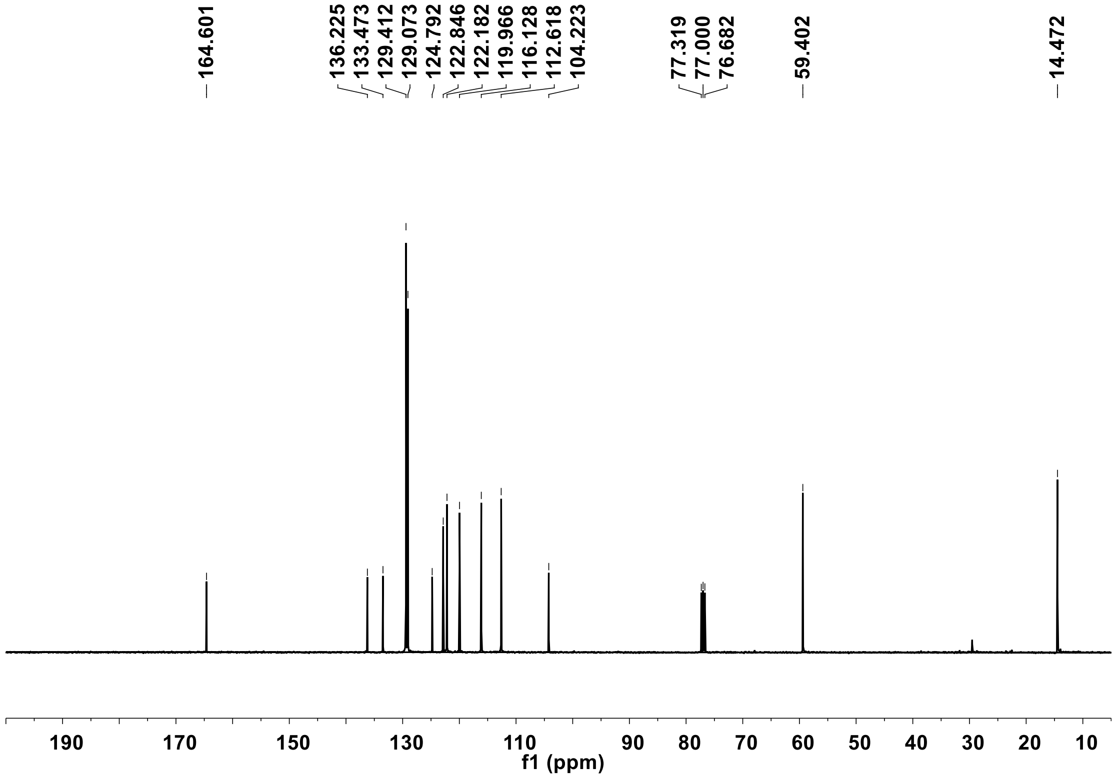
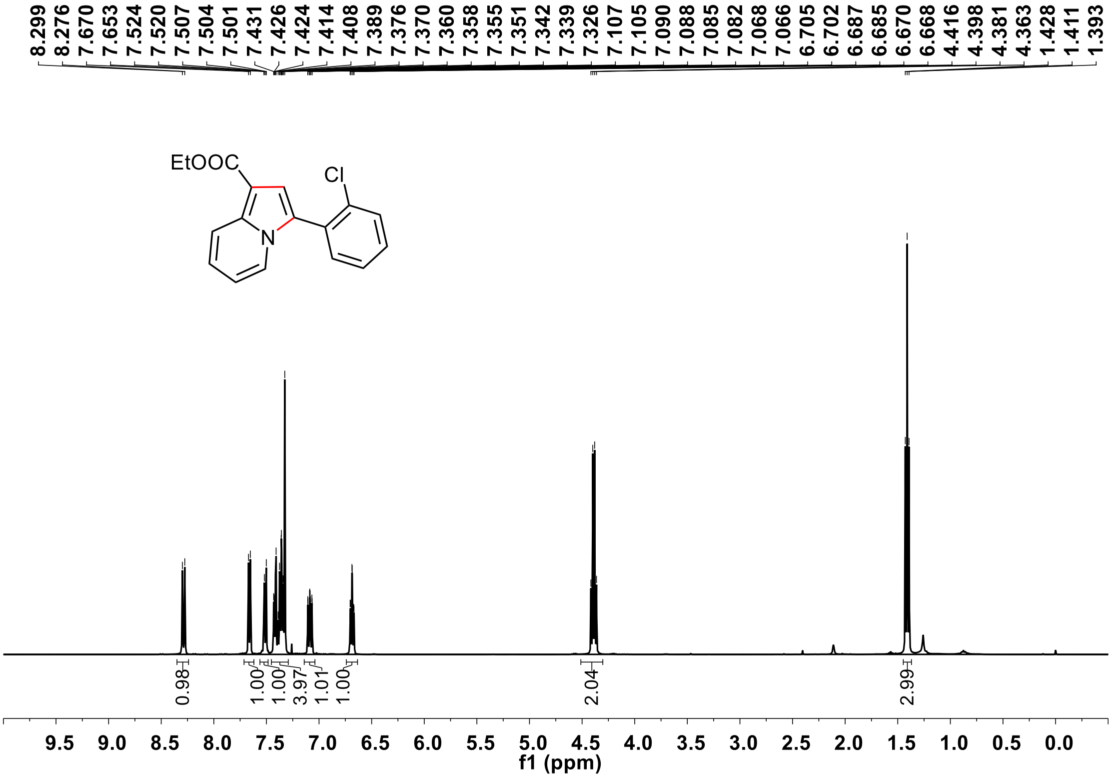
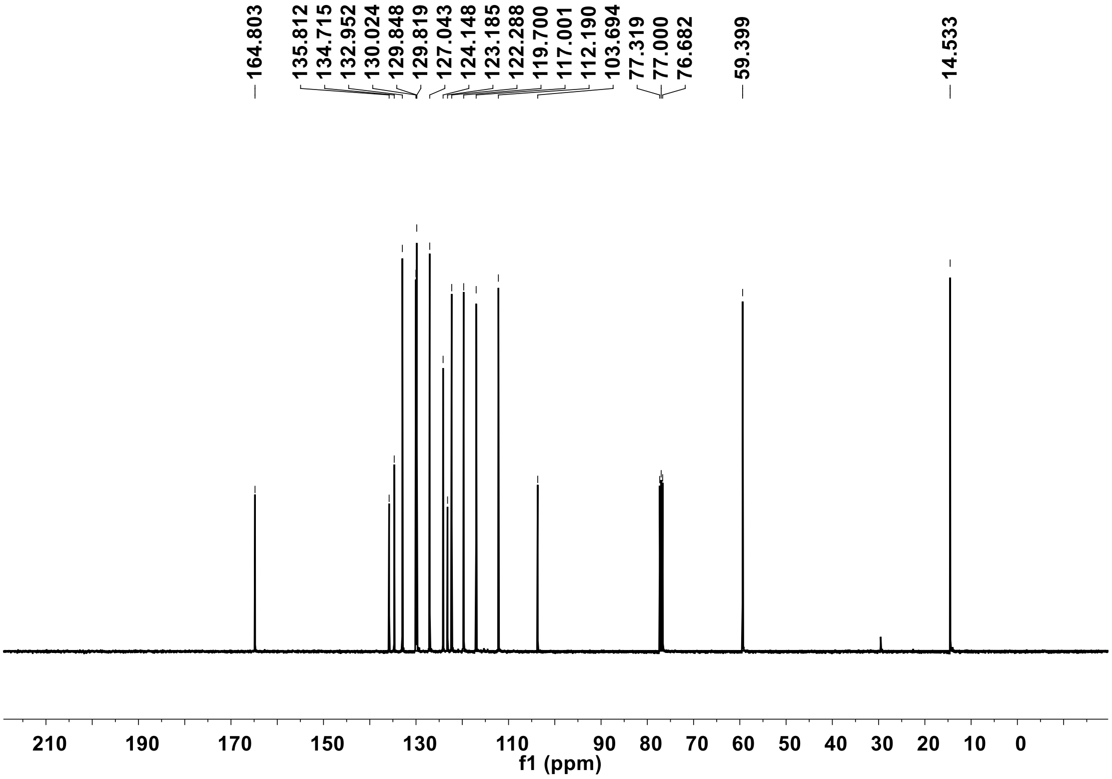


6f

^{1}H NMR

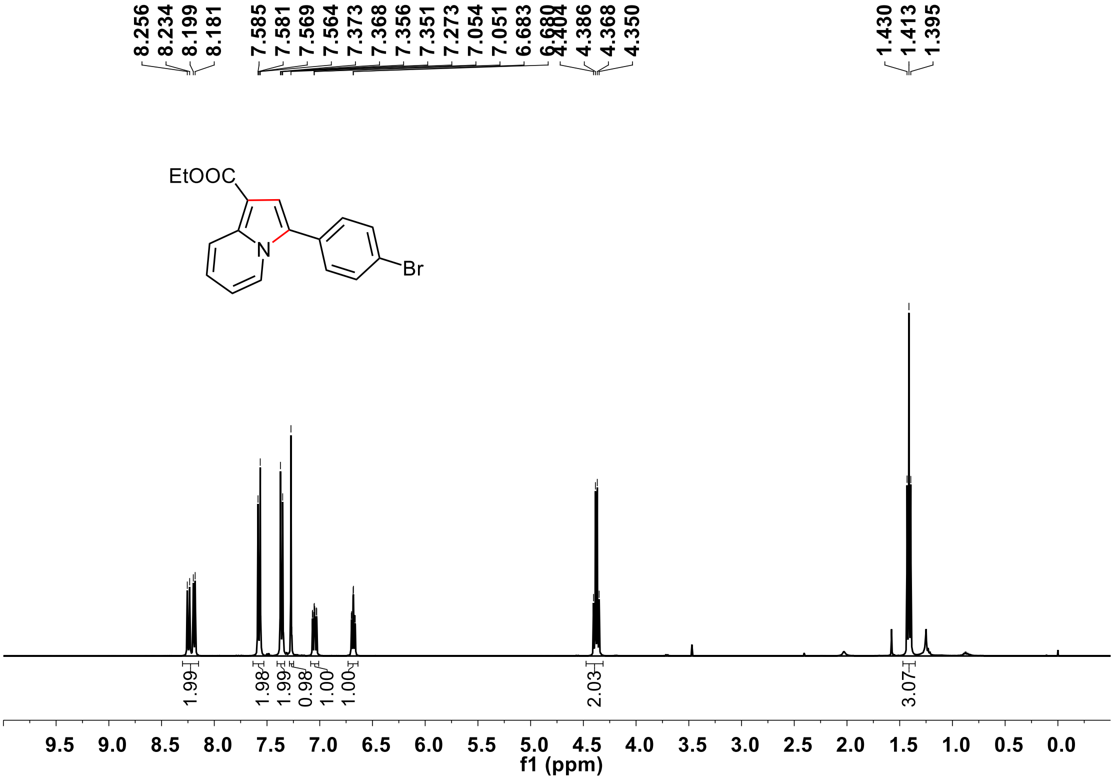


^{13}C NMR



6g

^{1}H NMR



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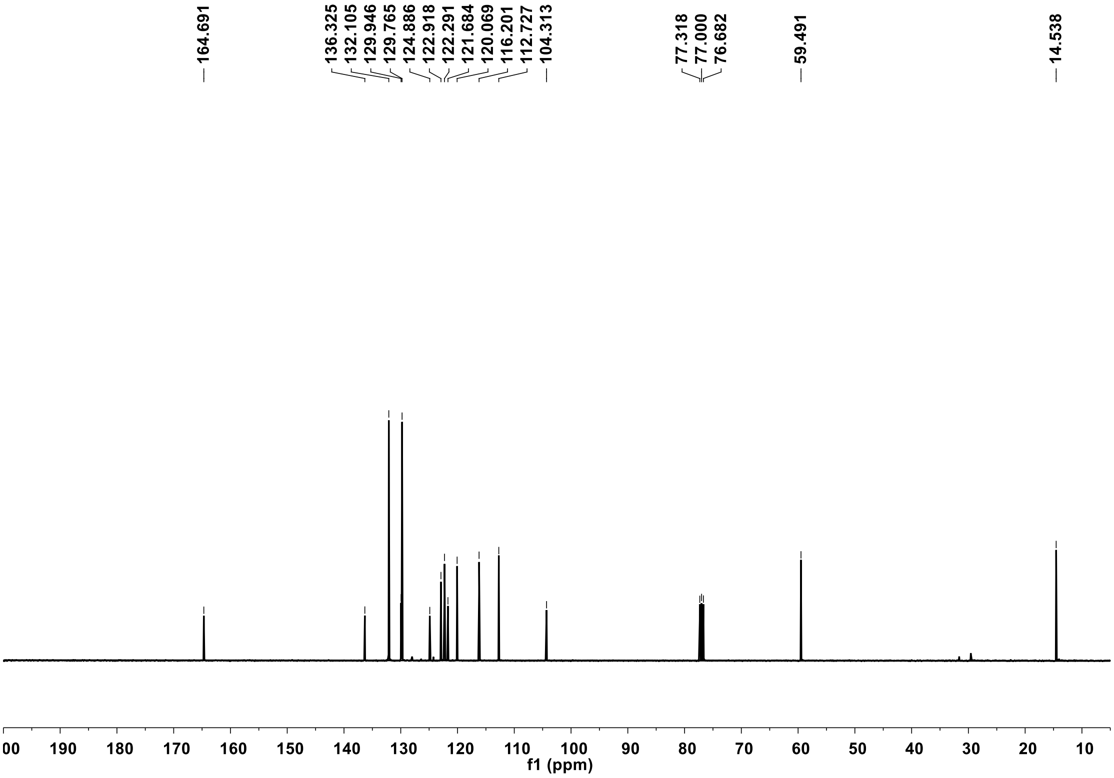
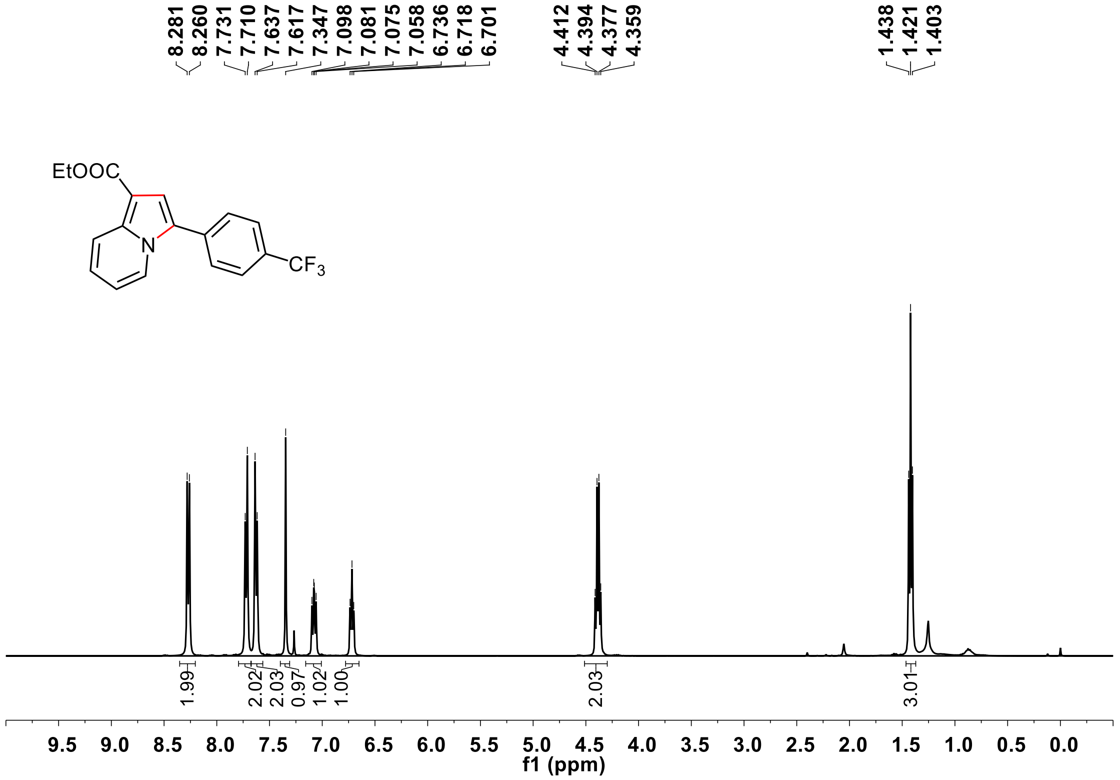


6h

^{1}H NMR



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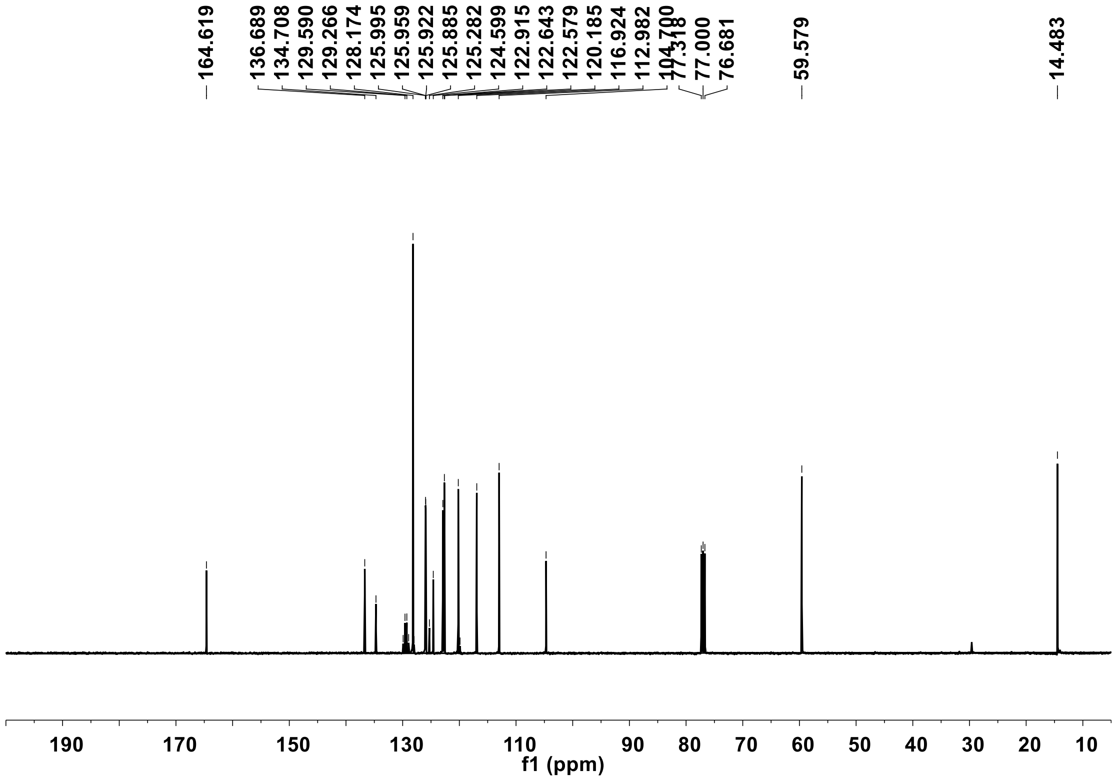

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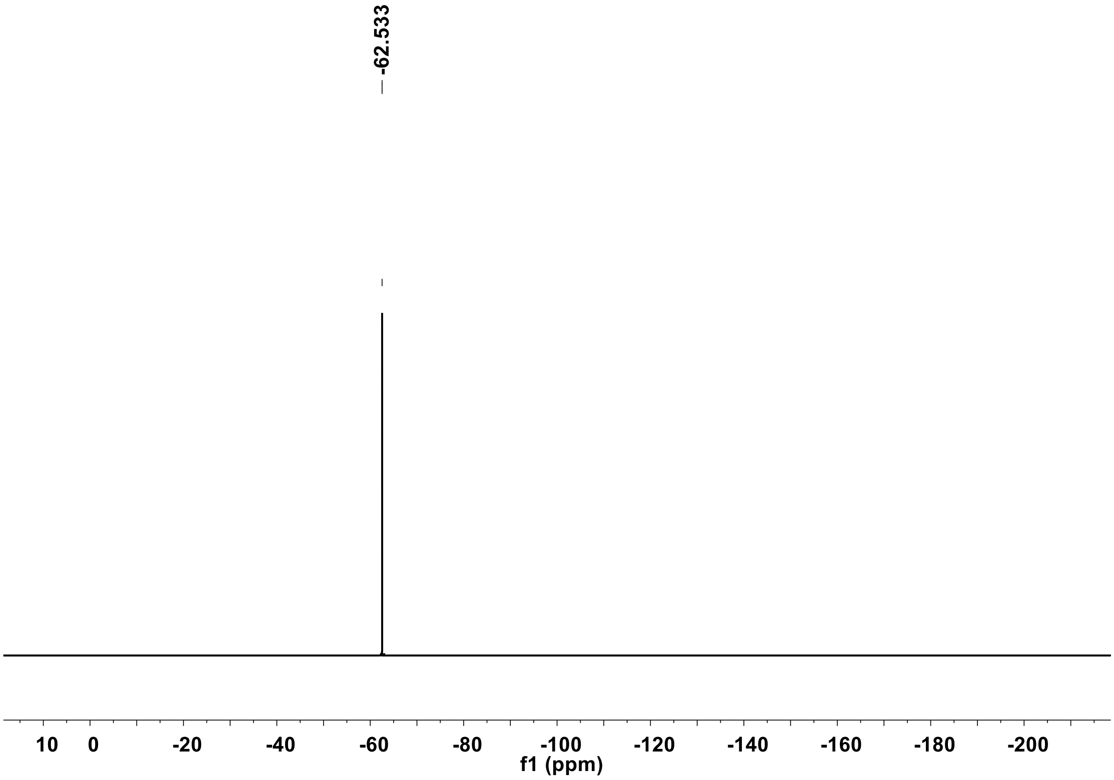
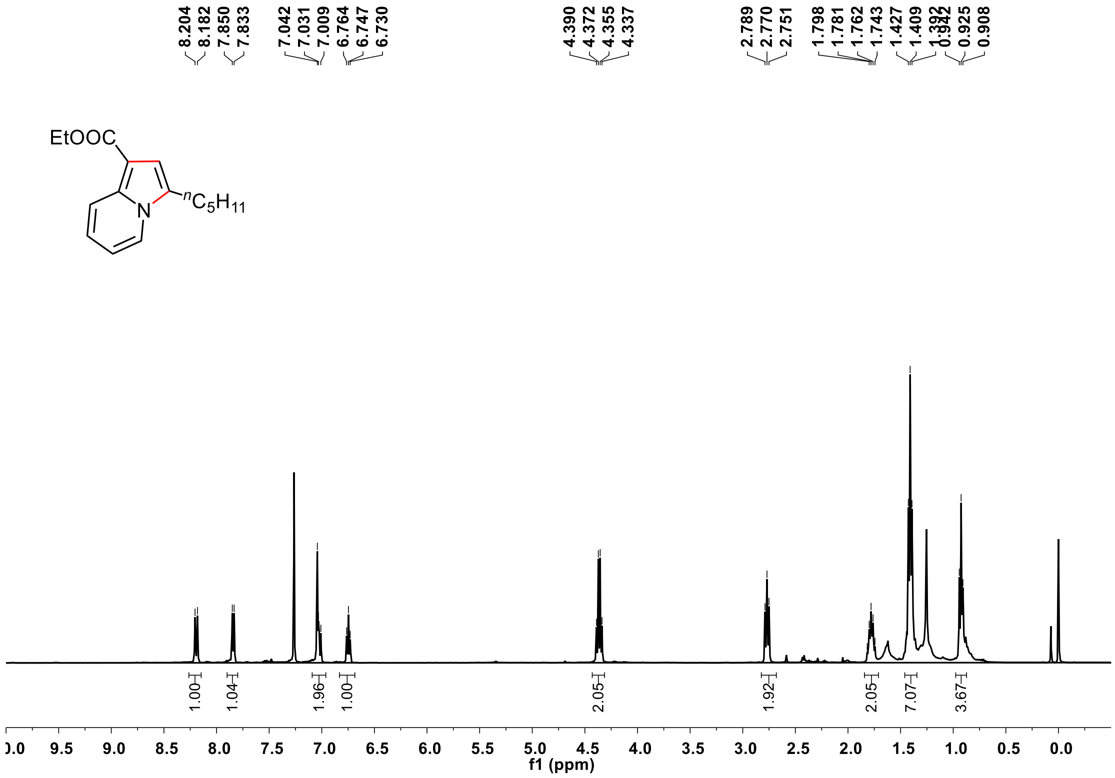
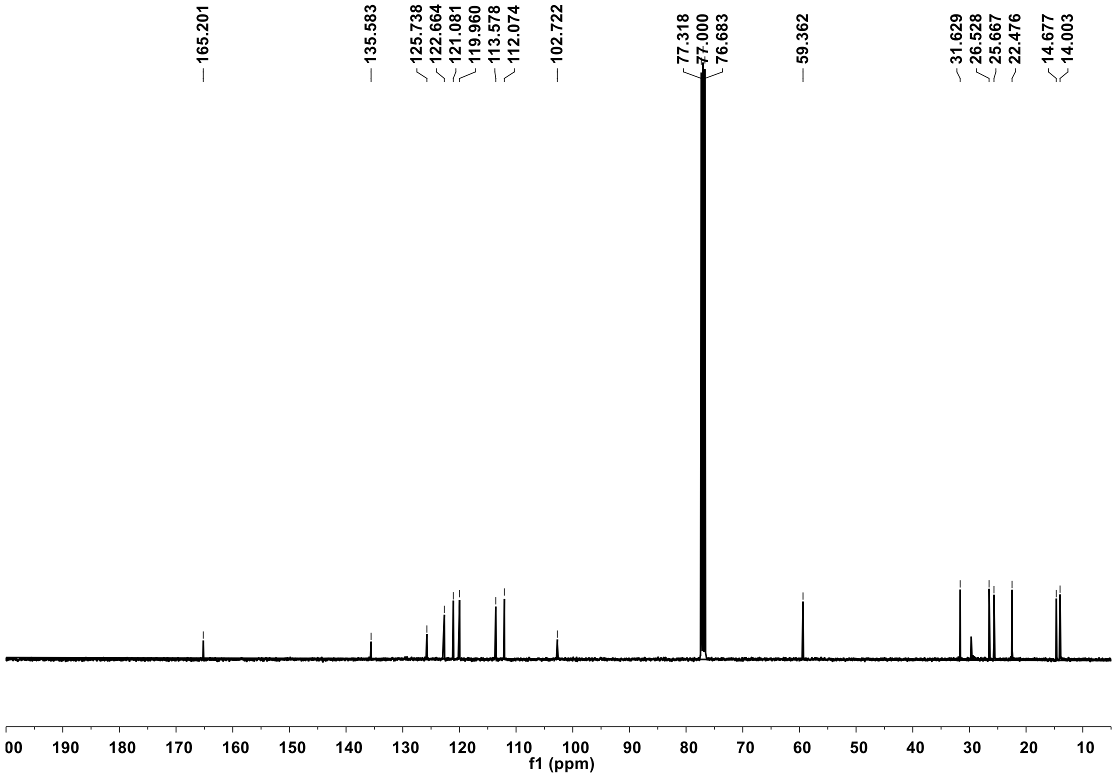


6i

^{1}H NMR

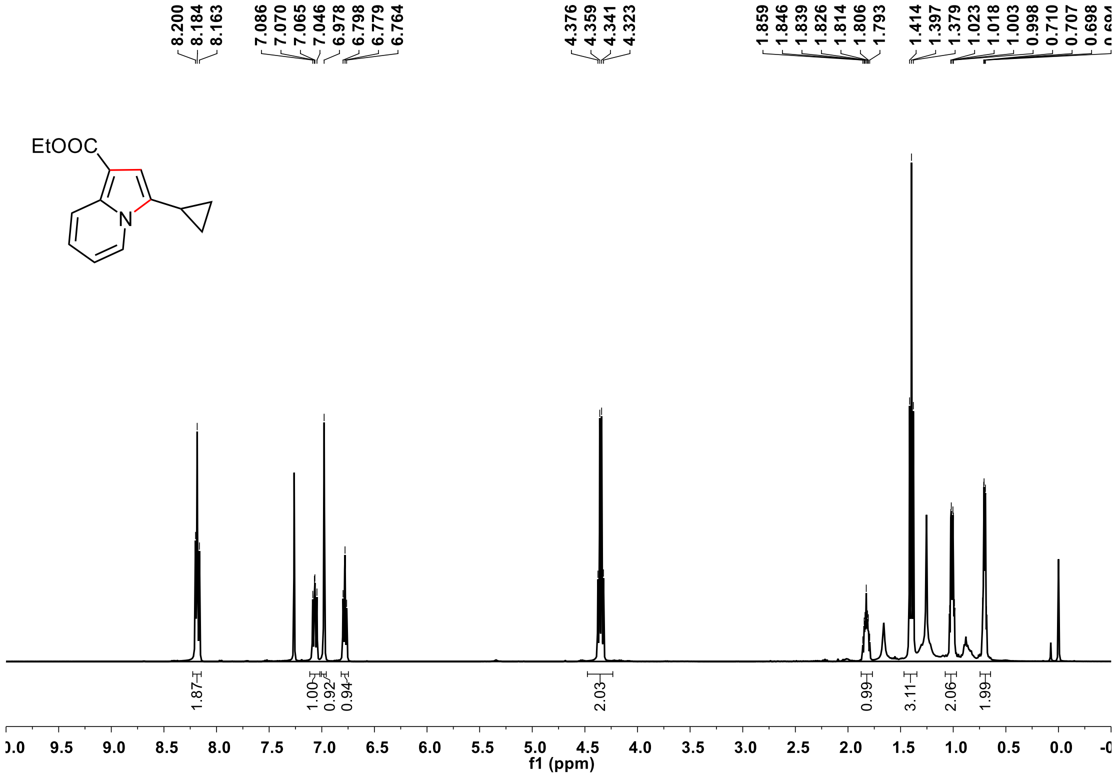


^{13}C NMR

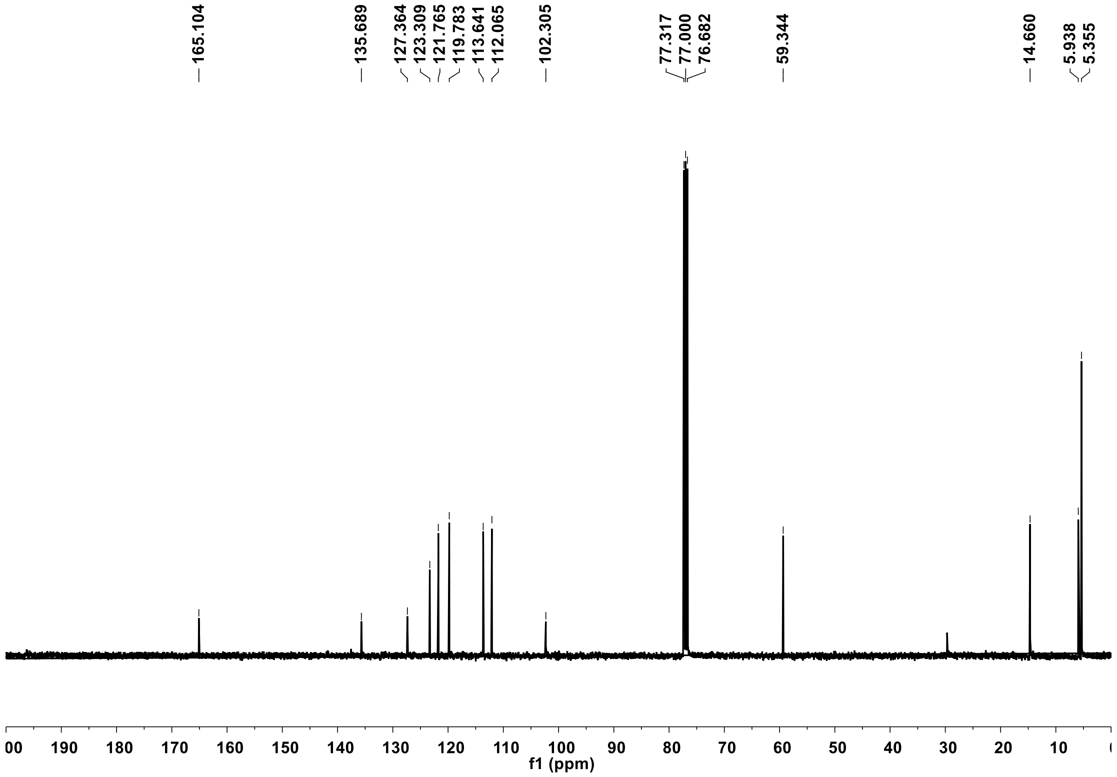


6j

^{1}H NMR

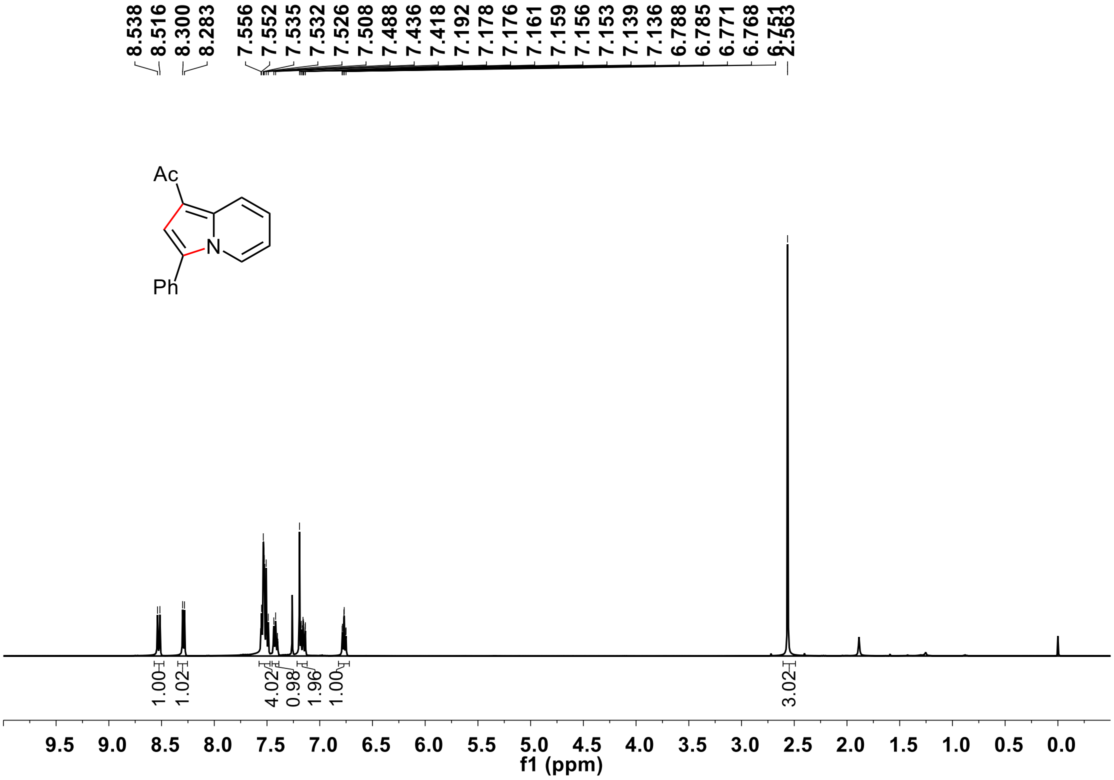


^{13}C NMR

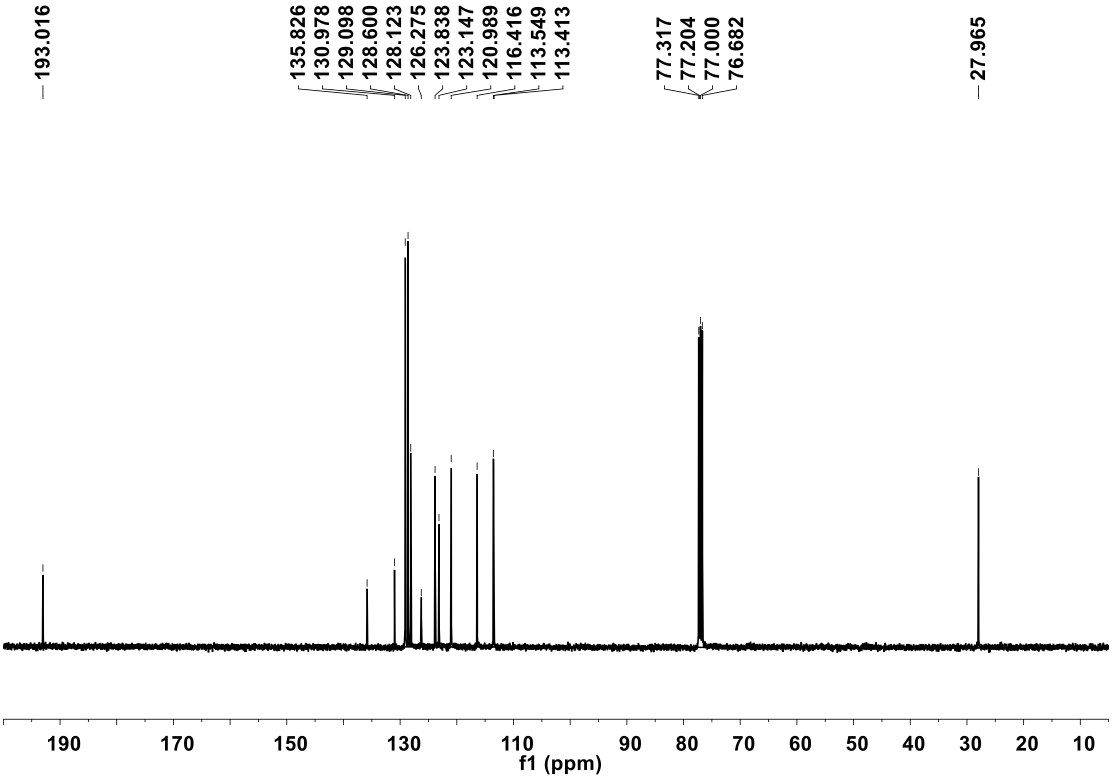


6k

^{1}H NMR

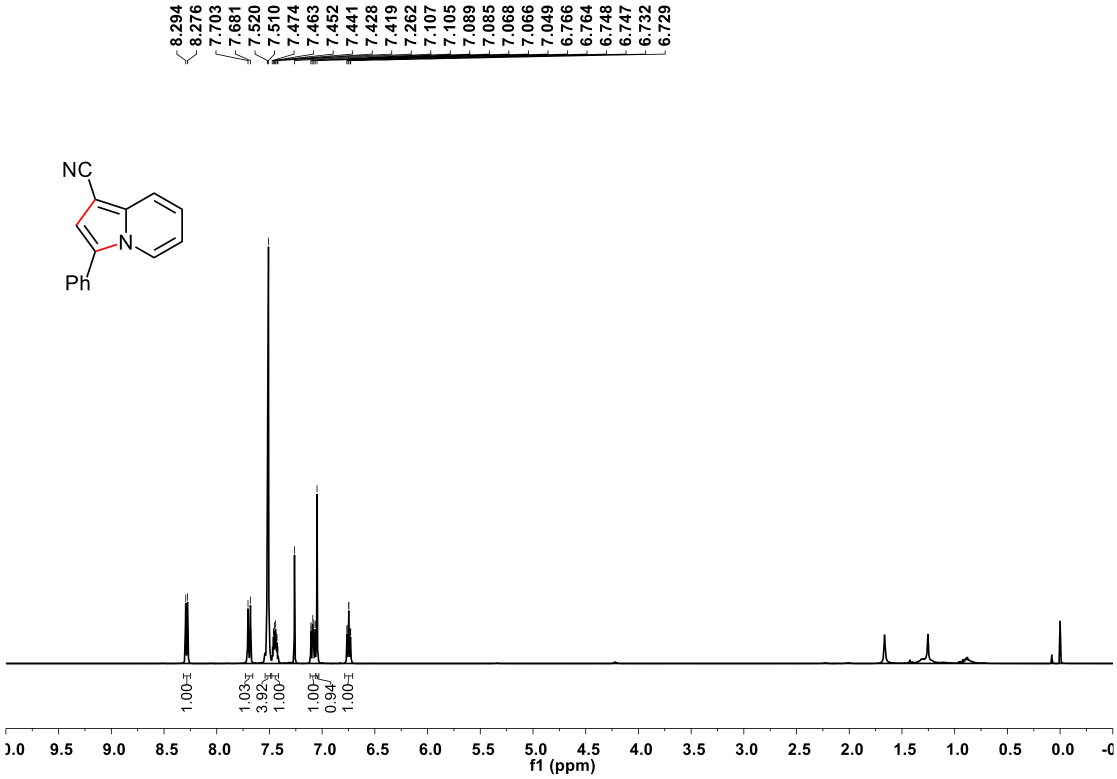


^{13}C NMR



6l

^{1}H NMR



^{13}C NMR