Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supplementary Information

Photoredox Ni-catalyzed decarboxylative arylation of oxamic acids for amide synthesis

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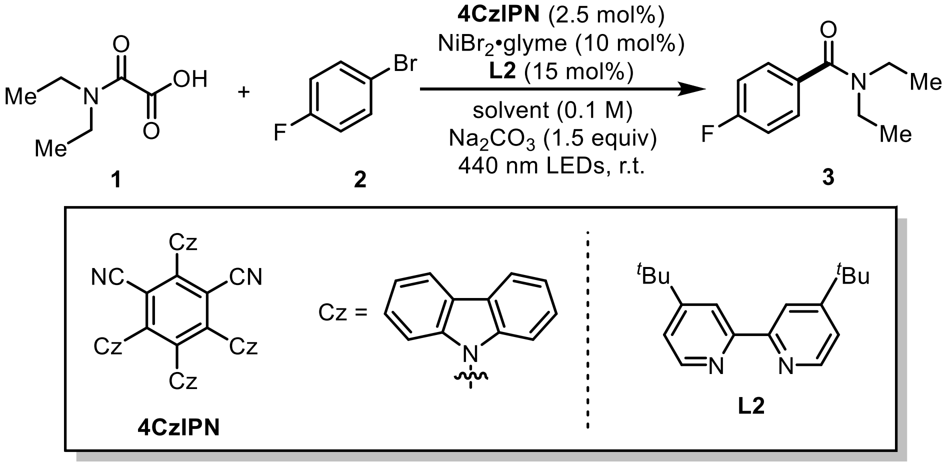
1. General Information

All reactions were performed in oven-dried Schlenk glass tubes unless otherwise noted. The tubes were fitted with a rubber septum. The reactions were conducted under nitrogen atmosphere. Flash chromatography was performed using silica gel 60 (200-400 mesh). Reagents obtained from commercial sources were used as supplied unless stated otherwise. 1,4-dioxane and acetonitrile (CH_3CN) was dried over activated molecular sieves for 24 hours prior to use. ^{1}H NMR spectra were recorded on a Bruker Avance (300, 400 or 500 MHz) spectrometer using $CDCl_3$ as solvent and referenced relative to TMS (δ = 0.00 ppm). Chemical shifts are reported in ppm and coupling constants (J) in Hertz. ^{13}C NMR spectra were recorded on the same instruments (101 or 126 MHz) with total proton decoupling referenced relative to $CDCl_3$ (δ = 77.16 ppm). Data are represented as follows: chemical shift, multiplicity (br. s = broad singlet, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants in Hertz (Hz), integration. Infrared (IR) spectra were obtained using a Thermo Fisher Nicolet 6700 spectrometer. The High-resolution mass spectral (HRMS) data were obtained on Thermo Fisher Scientific Exactive Orbitrap (APCI or ESI). Cyclic voltammetry (CV) data were measured with Shanghai Chenhua CHI660E.

2 Optimization of the Reaction Conditions

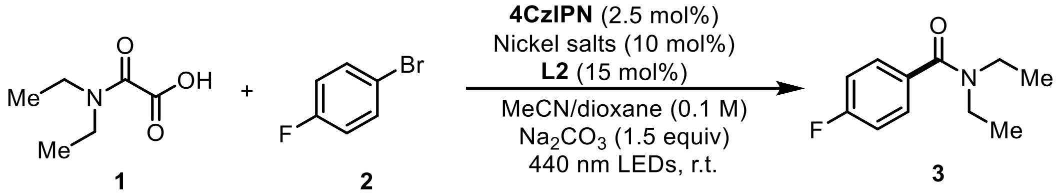
Table S1: Solvent screening[a)]



Entry	Solvent	Yield (%)[b)]
1	DME	20
2	DMSO	10
3	MeCN	14
4	dioxane	23
5	DCM	<5
6	EtOAc	18
7	THF	16
8	THF/dioxane (v:v = 1:3)	30
9	MeCN/dioxane (v:v = 1:3)	62
10	EtOAc/dioxane (v:v = 1:3)	29
11	DCM/dioxane (v:v = 1:3)	<5
12	DMF/dioxane (v:v = 1:3)	37
13	MeCN/dioxane (v:v = 1:9)	34
14	MeCN/dioxane (v:v = 3:1)	37
15	MeCN/dioxane (v:v = 1:1)	56

a) Reaction Conditions: Reactions performed on a 0.2 mmol scale at ambient temperature for 12 hours under illumination by blue LEDs (440 nm, 10 W) with **1** (0.3 mmol, 1.5 equiv), **2** (0.2 mmol, 1.0 equiv), and Na_2CO_3 (1.5 equiv) in 2.0 mL of solvent. b) Yield determined by ^{19}F NMR analysis of the crude mixture using 1-bromo-2-fluorobenzene as the internal standard.

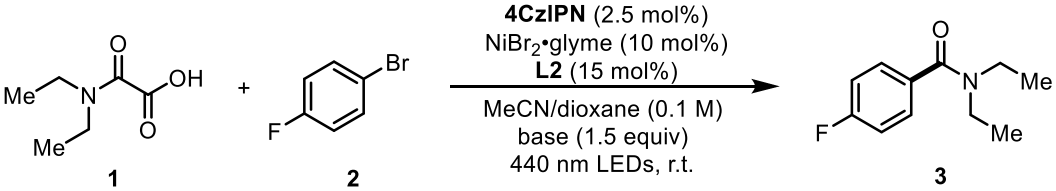
Table S2: Nickel salts effect in the reaction$^{a)}$



Entry	Nickel salts	Yield (%)$^{b)}$
1	$NiBr_2$•diglyme	55
2	$NiBr_2$•$3H_2O$	32
3	$Ni(OTf)_2$	<5
4	$NiCl_2$•glyme	2

a) Reaction Conditions: Reactions performed on a 0.2 mmol scale at ambient temperature for 12 hours under illumination by blue LEDs (440 nm, 10 W) with **1** (0.3 mmol, 1.5 equiv), **2** (0.2 mmol, 1.0 equiv), and Na_2CO_3 (1.5 equiv) in 2.0 mL of solvent. b) Yield determined by ^{19}F NMR analysis of the crude mixture using 1-bromo-2-fluorobenzene as the internal standard.

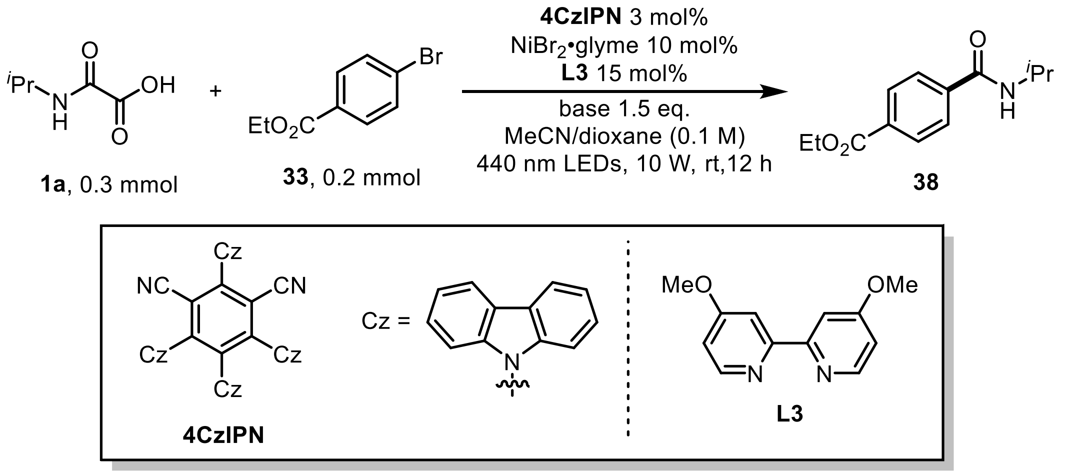
Table S3: Base effect in the reaction [a)]



Entry	Base additive	Yield (%)[b)]
1	Na_2CO_3	62
2	K_2CO_3	6
3	$NaHCO_3$	<5
4	Li_2CO_3	<5
5	Cs_2CO_3	<5
6	LiO*t*Bu	<5
7	NaO*t*Bu	39
8	NaOMe	60
9	NaOEt	<5
10	NaOAc	<5
11	Et_3N	<5
12	TMG	30
13	BTMG	11
14	2,6-lutidine	<5
15[c)]	Na_2CO_3	44
16[d)]	Na_2CO_3	43
17[e)]	Na_2CO_3	39

a) Reaction Conditions: Reactions performed on a 0.2 mmol scale at ambient temperature for 12 hours under illumination by blue LEDs (440 nm, 10 W) with **1** (0.3 mmol, 1.5 equiv), **2** (0.2 mmol, 1.0 equiv), and base (1.5 equiv) in 2.0 mL of solvent. b) Yield determined by ^{19}F NMR analysis of the crude mixture using 1-bromo-2-fluorobenzene as the internal standard. c) Na_2CO_3 loading was 1.0 equiv. d) Na_2CO_3 loading was 2.0 equiv. e) Na_2CO_3 loading was 3.0 equiv. TMG: 1,1,3,3-tetramethylguanidine; BTMG: 2-(tert-Butyl)-1,1,3,3-tetramethylguanidine.

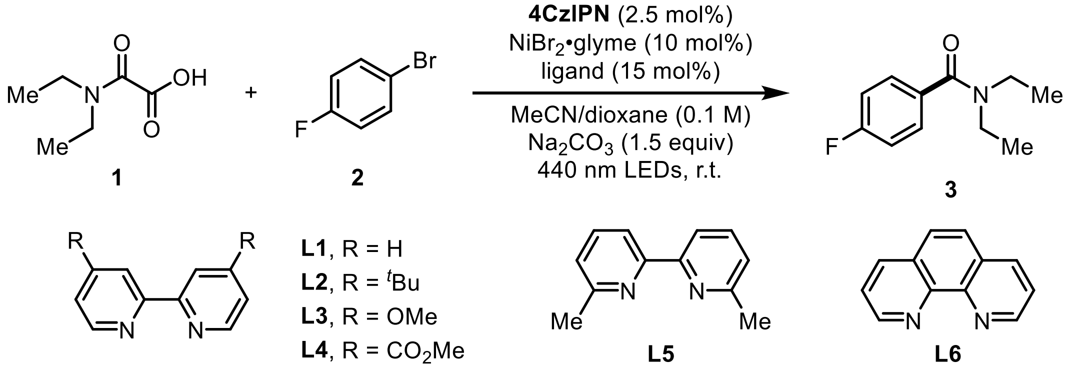
Table S4: Reaction conditions optimization for the synthesis of secondary amides[a)]



Entry	Base	Yield (%)[b)]
1	TMG	43
2	2,6-lutidine	<5
3	DIPA	<5
4	2,4,6-collidine	<5
5	Na_2CO_3	<5

a) Reaction Conditions: Reactions performed on a 0.2 mmol scale at ambient temperature for 12 hours under illumination by blue LEDs (440 nm, 10 W) with **1a** (0.3 mmol, 1.5 equiv), **33** (0.2 mmol, 1.0 equiv), and base (1.5 equiv) in 2.0 mL of solvent. b) Isolated yield. DIPA: 2,6-diisopropylaniline.

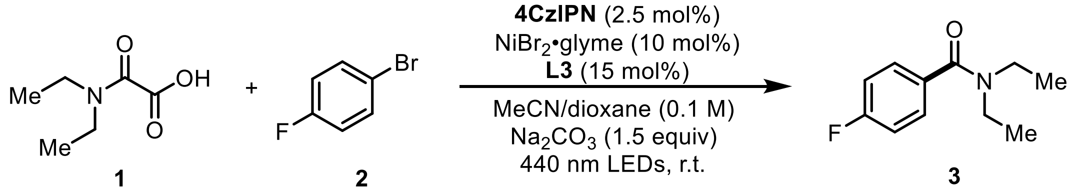
Table S5: Ligand effect in the reaction[a)]



Entry	Ligand	Yield (%)[b)]
1	**L1**	44
2	**L2**	62
3	**L3**	63
4	**L4**	<5
5	**L5**	<5
6	**L6**	19

a) Reaction Conditions: Reactions performed on a 0.2 mmol scale at ambient temperature for 12 hours under illumination by blue LEDs (440 nm, 10 W) with **1** (0.3 mmol, 1.5 equiv), **2** (0.2 mmol, 1.0 equiv), and Na_2CO_3 (1.5 equiv) in 2.0 mL of solvent. b) Yield determined by ^{19}F NMR analysis of the crude mixture using 1-bromo-2-fluorobenzene as the internal standard.

Table S6: Photocatalyst loading effect in the reaction[a)]

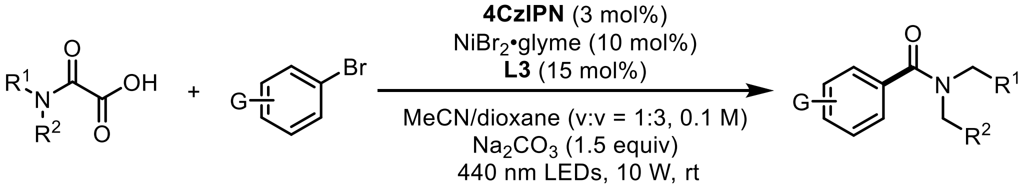


Entry	Ligand	Yield (%)[b)]
1	**L3**	63
2[c)]	**L3**	46
3[d)]	**L3**	**81(80)**[e)]

a) Reaction Conditions: Reactions performed on a 0.2 mmol scale at ambient temperature for 12 hours under illumination by blue LEDs (440 nm, 10 W) with **1** (0.3 mmol, 1.5 equiv), **2** (0.2 mmol, 1.0 equiv), and Na_2CO_3 (1.5 equiv) in 2.0 mL of solvent. b) Yield determined by ^{19}F NMR analysis of the crude mixture using 1-bromo-2-fluorobenzene as the internal standard. c) 4CzIPN loading was 1.0 mol%. d) 4CzIPN loading was 3.0 mol%. e) Yield of isolated product in parentheses.

3 General Procedure and Spectra Data for Products

3.1 General Procedure



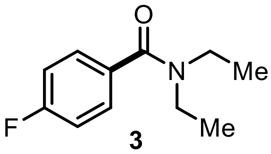
Method A

Under nitrogen atmosphere, $NiBr_2$•glyme (0.02 mmol) and 4,4'-dimethoxy-2,2'-bipyridine **L3** (0.03 mmol) were dissolved in 0.5 mL MeCN as the nickel catalyst solution and stirred for 30 min prior to use. To a 10 mL oven-dried Schlenk tube equipped with a stirring bar was added photocatalyst **4CzIPN** (3 mol%) and Na_2CO_3 (0.3 mmol, 1.5 equiv). The reaction tube was then flushed with nitrogen gas. After that, a solution of oxamic acids (0.3 mmol, 1.5 equiv) and aryl bromine (0.2 mmol, 1.0 equiv) in dioxane (1.5 mL) was added to the tube. Subsequently, the nickel catalyst solution was syringed into the reaction vessel. The vial was placed into photosyn-10 LEDs (λ = 440 nm, 10 W). Stirring was maintained for 12 hours, after this period the irradiation was stopped. The mixture was concentrated under vacuum and purified by flash chromatography (PE/EA = 4:1) to afford the corresponding product.

Method B

Under nitrogen atmosphere, $NiBr_2$•glyme (0.02 mmol) and 4,4'-dimethoxy-2,2'-bipyridine **L3** (0.03 mmol) were dissolved in 0.5 mL MeCN as the nickel catalyst solution and stirred for 30 min prior to use. To a 10 mL oven-dried Schlenk tube equipped with a stirring bar was added photocatalyst **4CzIPN** (3 mol%) and oxamic acids (0.3 mmol, 1.5 eqiv). The reaction tube was then flushed with nitrogen gas. After that, a solution of aryl bromine (0.2 mmol, 1.0 equiv) and TMG (0.3 mmol, 1.5 equiv) in dioxane (1.5 mL) was added to the tube. Subsequently, the nickel catalyst solution was syringed into the reaction vessel. The vial was placed into photosyn-10 LEDs (λ = 440 nm, 10 W). Stirring was maintained for 12 hours, after this period the irradiation was stopped. The mixture was concentrated under vacuum and purified by flash chromatography (PE/EA = 4:1) to afford the corresponding product.

3.2 Spectra Data for Products



3

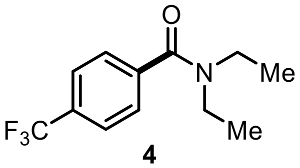
Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (4:1) as the eluent. Colorless oil (31.3 mg, 80% yield).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.42 – 7.33 (m, 2H), 7.07 (t, *J* = 8.5 Hz, 2H), 3.40 (d, *J* = 101.8 Hz, 4H), 1.17 (s, 6H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 170.21, 162.95 (d, *J* = 248.7 Hz), 133.34 (d, *J* = 3.6 Hz), 128.44 (d, *J* = 8.3 Hz), 115.29 (d, *J* = 21.7 Hz), 43.26, 39.42, 13.90, 12.90.

^{19}F NMR (377 MHz, Chloroform-*d*) δ-111.53.

Spectral data for this compound were consistent with those in the literature. [1]



4

Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (4:1) as the eluent. Colorless oil (35.5 mg, 72% yield).

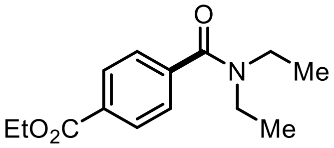
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.67 (d, *J* = 8.0 Hz, 2H), 7.49 (d, *J* = 8.0 Hz, 2H), 3.56 (q, *J* = 7.3 Hz, 2H), 3.22 (q, *J* = 7.3 Hz, 2H), 1.19 (dt, *J* = 59.3, 7.1 Hz, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 168.79, 139.83, 130.15 (q, *J* = 32.6 Hz), 125.69, 124.53 (q, *J* = 3.8 Hz), 122.81 (d, *J* = 272.4 Hz), 42.24, 38.37, 13.18, 11.85.

^{19}F NMR (377 MHz, Chloroform-*d*) δ -62.84.

HRMS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{12}H_{15}NOF_3$ 246.1100; Found 246.1096.

IR (KBr): 2965, 1636, 1434, 1325, 1263, 1104, 1066, 797 cm^{-1}.



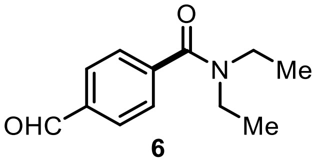
5

Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (5:1) as the eluent. Colorless oil (43.0 mg, 86% yield).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.04 – 7.97 (m, 2H), 7.39 – 7.33 (m, 2H), 4.32 (q, *J* = 7.2 Hz, 2H), 3.48 (d, *J* = 7.4 Hz, 2H), 3.14 (q, *J* = 7.3 Hz, 2H), 1.33 (t, *J* = 7.2 Hz, 3H), 1.18 (d, *J* = 7.4 Hz, 3H), 1.02 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 169.28, 164.96, 140.47, 129.98, 128.72, 125.23, 60.18, 42.21, 38.31, 13.29, 13.18, 11.88.

Spectral data for this compound were consistent with those in the literature. [2]



6

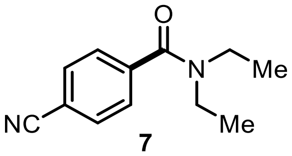
Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (2:1) as the eluent. Colorless oil (28.2 mg, 69% yield).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 10.05 (s, 1H), 7.93 (d, *J* = 8.1 Hz, 2H), 7.53 (d, *J* = 8.1 Hz, 2H), 3.57 (q, *J* = 7.2 Hz, 2H), 3.22 (q, *J* = 7.2 Hz, 2H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.11 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 191.59, 169.90, 142.98, 136.54, 129.92, 126.93, 43.24, 39.37, 14.21, 12.89.

HRMS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{12}H_{16}NO_2$ 206.1176; Found 206.1174.

IR (KBr): 2976, 2931, 1703, 1627, 1434, 1289, 1208, 1096, 827 cm^{-1}.



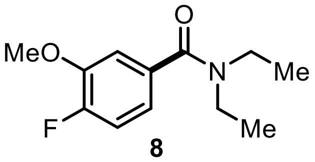
7

Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (4:1) as the eluent. Colorless oil (29.8 mg, 74% yield).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.71 (d, *J* = 8.3 Hz, 2H), 7.51 – 7.37 (m, 2H), 3.56 (q, *J* = 7.6 Hz, 2H), 3.21 (d, *J* = 8.2 Hz, 2H), 1.18 (dt, *J* = 71.6, 7.0 Hz, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 169.19, 141.60, 132.41, 127.07, 118.22, 113.01, 43.27, 39.46, 14.21, 12.85.

Spectral data for this compound were consistent with those in the literature. [3]



8

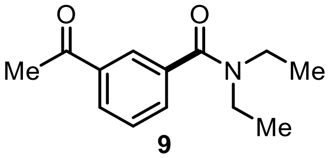
Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (4:1) as the eluent. Colorless oil (32.8 mg, 73% yield).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.12 – 6.95 (m, 2H), 6.94 – 6.79 (m, 1H), 3.90 (d, *J* = 6.3 Hz, 3H), 3.51 (s, 2H), 3.28 (s, 2H), 1.21 (d, *J* = 40.1 Hz, 6H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 170.31, 152.76 (d, *J* = 248.4 Hz), 147.76 (d, *J* = 10.9 Hz), 133.55 (d, *J* = 4.3 Hz), 118.81 (d, *J* = 7.2 Hz), 115.84 (d, *J* = 18.8 Hz), 112.14 (d, *J* = 2.3 Hz), 56.27, 43.32, 39.44, 14.26, 12.87.

^{19}F NMR (377 MHz, Chloroform-*d*) δ -133.72.

Spectral data for this compound were consistent with those in the literature. [4]



9

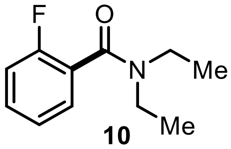
Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (2:1) as the eluent. Yellow oil (33.5 mg, 76% yield).

^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.99 (dd, *J* = 9.4, 1.7 Hz, 2H), 7.64 – 7.46 (m, 2H), 3.72 – 3.10 (m, 4H), 2.62 (s, 3H), 1.44 – 1.02 (m, 6H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 197.43, 170.26, 137.71, 137.19, 130.82, 128.92, 128.86, 126.28, 43.40, 39.44, 26.69, 14.24, 12.89.

HRMS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{13}H_{18}NO_2$ 220.1332; Found 220.1329.

IR (KBr): 2978, 2936, 1685, 1627, 1429, 1257, 1100, 797 cm^{-1}.



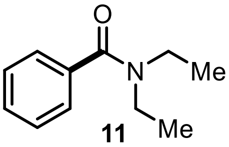
10

Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (6:1) as the eluent. Colorless oil (16.4 mg, 42% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.29 (m, 2H), 7.18 (td, *J* = 7.5, 1.1 Hz, 1H), 7.09 (ddd, *J* = 9.4, 8.3, 1.1 Hz, 1H), 3.58 (q, *J* = 7.1 Hz, 2H), 3.21 (q, *J* = 7.1 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.08 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.14, 158.05 (d, *J* = 246.9 Hz), 130.65 (d, *J* = 7.9 Hz), 128.42 (d, *J* = 4.0 Hz), 125.41 (d, *J* = 18.7 Hz), 124.47 (d, *J* = 3.5 Hz), 115.81 (d, *J* = 21.3 Hz)., 43.02, 39.18, 13.98, 12.89.

^{19}F NMR (377 MHz, Chloroform-*d*) δ -115.96, -115.98, -115.99, -115.99, -116.00.
Spectral data for this compound were consistent with those in the literature. [5]



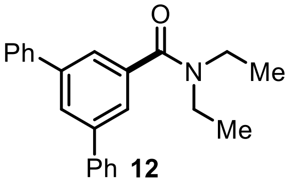
11

Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (4:1) as the eluent. Colorless oil (29.1 mg, 82% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.24 (m, 5H), 3.48 (s, 2H), 3.18 (s, 2H), 1.26 – 1.11 (m, 3H), 1.04 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.27, 136.32, 128.05, 127.37, 125.27, 42.25, 38.21, 13.19, 11.92.

Spectral data for this compound were consistent with those in the literature. [1]



12

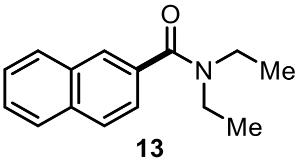
Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (4:1) as the eluent. Colorless oil (54.6 mg, 83% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.82 (t, *J* = 1.8 Hz, 1H), 7.68 – 7.61 (m, 4H), 7.56 (d, *J* = 1.7 Hz, 2H), 7.46 (dd, *J* = 8.3, 6.7 Hz, 4H), 7.41 – 7.34 (m, 2H), 3.70 – 3.50 (m, 2H), 3.35 (s, 2H), 1.22 (d, *J* = 51.6 Hz, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.13, 142.09, 140.49, 138.40, 128.93, 127.79, 127.28, 126.77, 123.90, 43.43, 39.34, 14.42, 13.00.

HRMS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{23}H_{24}NO$ 330.1852; Found 330.1844.

IR (KBr): 3038, 2974, 2933, 1631, 1472, 1430, 1273, 1108, 755 cm^{-1}.



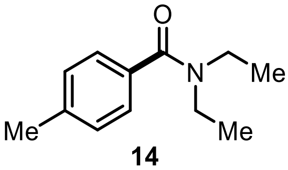
13

Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (4:1) as the eluent. Colorless oil (35.0 mg, 77% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.78 (q, *J* = 6.0 Hz, 4H), 7.42 (ddd, *J* = 18.7, 7.2, 2.4 Hz, 3H), 3.52 (s, 2H), 3.23 (s, 2H), 1.32 – 0.98 (m, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.26, 133.62, 132.36, 131.76, 127.27, 127.22, 126.76, 125.72, 125.55, 124.72, 122.92, 42.34, 38.31, 13.24, 11.97.

Spectral data for this compound were consistent with those in the literature. [1]



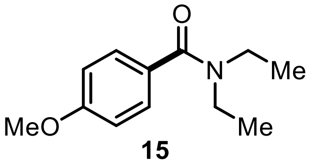
14

Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V$_{PE}$/V$_{EA}$ (5:1) as the eluent. White solid (26.4 mg, 69% yield).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.29 – 7.24 (m, 2H), 7.18 (d, *J* = 7.8 Hz, 2H), 3.40 (d, *J* = 122.3 Hz, 4H), 2.37 (s, 3H), 1.38 – 1.00 (m, 6H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 171.45, 139.02, 134.47, 128.94, 126.37, 43.31, 39.17, 21.29, 14.09, 13.04.

Spectral data for this compound were consistent with those in the literature. [1]



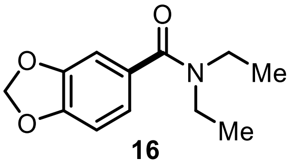
15

Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V$_{PE}$/V$_{EA}$ (3:1) as the eluent. Colorless oil (34.3 mg, 83% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33 – 7.24 (m, 2H), 6.88 – 6.77 (m, 2H), 3.75 (s, 3H), 3.55 – 3.10 (m, 4H), 1.21 – 1.02 (m, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.19, 159.24, 128.53, 127.17, 112.61, 54.29, 42.30, 38.52, 13.20, 12.44.

Spectral data for this compound were consistent with those in the literature. [3]



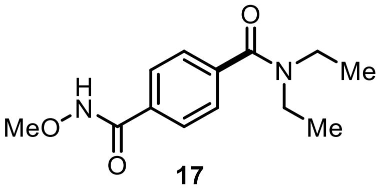
16

Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (4:1) as the eluent. Colorless oil (33.6 mg, 76% yield).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 6.87 (dd, *J* = 7.6, 1.1 Hz, 2H), 6.80 (dt, *J* = 7.4, 1.0 Hz, 1H), 5.98 (d, *J* = 1.0 Hz, 2H), 3.60 – 3.22 (m, 4H), 1.17 (s, 6H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 170.67, 148.29, 147.53, 131.08, 120.51, 108.15, 107.42, 101.24, 40.32, 13.52.

Spectral data for this compound were consistent with those in the literature. [6]



17

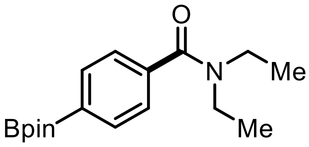
Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (4:1) as the eluent. Colorless oil (17.7 mg, 35% yield).

^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.07 (d, *J* = 8.4 Hz, 2H), 7.43 (d, *J* = 8.3 Hz, 2H), 3.93 (s, 3H), 3.67 – 3.43 (m, 2H), 3.33 – 3.13 (m, 2H), 1.18 (d, *J* = 45.8 Hz, 6H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 170.24, 166.44, 141.64, 130.71, 129.78, 126.31, 52.22, 43.21, 39.34, 14.17, 12.88.

HRMS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{13}H_{19}N_2O_3$ 251.1390; Found 251.1390.

IR (KBr): 2926, 1724, 1630, 1432, 1278, 1107, 1018, 784 cm^{-1}.



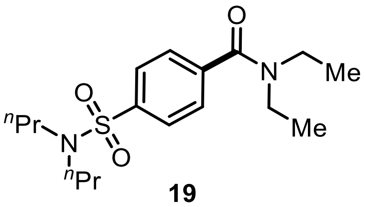
18

Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (4:1) as the eluent. White solid (35.4 mg, 58% yield, 72 h).

^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.83 (d, *J* = 7.9 Hz, 2H), 7.39 – 7.32 (m, 2H), 3.54 (s, 2H), 3.21 (s, 2H), 1.35 (s, 12H), 1.24 (d, *J* = 7.1 Hz, 3H), 1.08 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.19, 139.89, 134.78, 125.45, 83.99, 43.20, 39.21, 24.89, 14.20, 12.93.

Spectral data for this compound were consistent with those in the literature. [7]



19

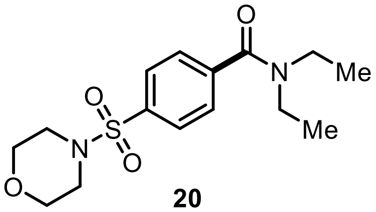
Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (4:1) as the eluent. White solid (55.1 mg, 81% yield).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.84 (d, *J* = 8.4 Hz, 2H), 7.53 – 7.45 (m, 2H), 3.68 – 3.45 (m, 2H), 3.28 – 3.14 (m, 2H), 3.11 – 3.05 (m, 4H), 1.62 – 1.50 (m, 4H), 1.26 (d, *J* = 6.7 Hz, 3H), 1.11 (d, *J* = 7.4 Hz, 3H), 0.88 (t, *J* = 7.4 Hz, 6H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 169.64, 141.06, 140.90, 127.29, 126.89, 50.09, 43.27, 39.43, 22.03, 14.14, 12.85, 11.11.

HRMS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{17}H_{29}N_2O_3S$ 341.1893; Found 341.1886.

IR (KBr): 2970, 2936, 2877, 1634, 1462, 1432, 1340, 1158, 1093, 993, 594 cm^{-1}.



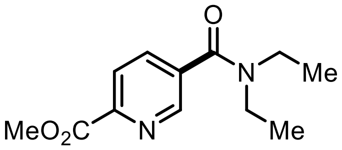
20

Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (2:1) as the eluent. Yellow oil (45.5 mg, 70% yield).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.83 – 7.78 (m, 2H), 7.58 – 7.53 (m, 2H), 3.80 – 3.71 (m, 4H), 3.57 (q, *J* = 7.2 Hz, 2H), 3.21 (q, *J* = 7.1 Hz, 2H), 3.07 – 2.98 (m, 4H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.12 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 169.36, 141.87, 135.87, 128.11, 127.08, 66.05, 45.94, 43.29, 39.44, 14.21, 12.86.

Spectral data for this compound were consistent with those in the literature. [6]



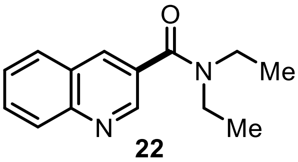
21

Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (2:1) as the eluent. Colorless oil (44.4 mg, 94% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.68 (d, *J* = 2.2 Hz, 1H), 8.12 (d, *J* = 7.9 Hz, 1H), 7.81 (dd, *J* = 8.0, 2.1 Hz, 1H), 3.96 (s, 3H), 3.51 (q, *J* = 7.2 Hz, 2H), 3.17 (q, *J* = 7.3 Hz, 2H), 1.14 (dt, *J* = 53.6, 7.0 Hz, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.58, 164.05, 147.12, 146.18, 134.99, 134.40, 123.93, 52.07, 42.41, 38.70, 13.29, 11.85.

Spectral data for this compound were consistent with those in the literature. [6]



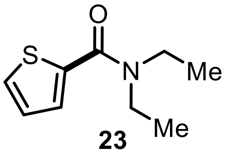
22

Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (2:1) as the eluent. Colorless oil (34.7 mg, 76% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.87 (d, *J* = 2.2 Hz, 1H), 8.13 (d, *J* = 2.3 Hz, 1H), 8.06 (d, *J* = 8.5 Hz, 1H), 7.78 (d, *J* = 8.2 Hz, 1H), 7.75 – 7.66 (m, 1H), 7.52 (t, *J* = 7.6 Hz, 1H), 3.40 (d, *J* = 111.6 Hz, 4H), 1.32 – 0.96 (m, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.69, 147.06, 146.99, 133.04, 129.41, 129.14, 128.39, 127.17, 126.36, 126.09, 42.53, 38.65, 13.36, 11.94.

Spectral data for this compound were consistent with those in the literature. [8]



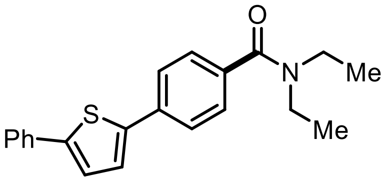
23

Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (12:1) as the eluent. Colorless oil (28.1 mg, 77% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 (dd, *J* = 5.0, 1.1 Hz, 1H), 7.32 (dd, *J* = 3.7, 1.1 Hz, 1H), 7.04 (dd, *J* = 5.1, 3.6 Hz, 1H), 3.54 (q, *J* = 7.1 Hz, 4H), 1.25 (t, *J* = 7.1 Hz, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 163.85, 138.35, 128.22, 127.98, 126.69, 42.10, 13.69.

Spectral data for this compound were consistent with those in the literature. [1]



24

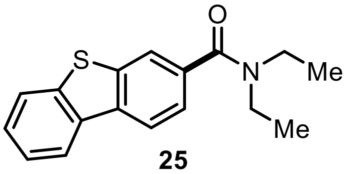
Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (4:1) as the eluent. Yellow solid (35.8 mg, 53% yield, 36 h).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.63 (t, *J* = 7.6 Hz, 4H), 7.42 – 7.35 (m, 4H), 7.33 – 7.26 (m, 3H), 3.43 (d, *J* = 105.4 Hz, 4H), 1.22 (d, *J* = 33.3 Hz, 6H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 170.83, 144.34, 142.64, 136.21, 135.16, 134.19, 128.95, 127.69, 127.16, 125.70, 125.45, 124.58, 124.11, 43.42, 39.46, 14.13, 12.98.

HRMS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{21}H_{22}NOS$ 336.1417; Found 336.1407.

IR (KBr): 3055, 2979, 2935, 1711, 1629, 1428, 1286, 1221, 1095, 755 cm^{-1}.



25

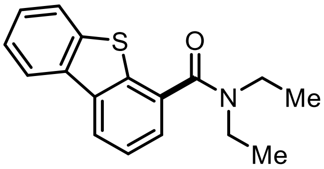
Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (4:1) as the eluent. White solid (33.8 mg, 60% yield).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.15 (t, *J* = 8.1 Hz, 2H), 7.86 (dt, *J* = 13.9, 4.3 Hz, 2H), 7.47 (dd, *J* = 9.9, 5.4 Hz, 3H), 3.44 (d, *J* = 133.3 Hz, 4H), 1.20 (d, *J* = 58.2 Hz, 6H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 170.87, 139.98, 139.53, 136.09, 135.69, 134.97, 127.16, 124.60, 122.88, 122.72, 121.84, 121.48, 120.95, 43.41, 39.47, 14.16, 13.04.

HRMS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{17}H_{18}NOS$ 284.1104; Found 284.1097.

IR (KBr): 3056, 2973, 2932, 1627, 1428, 1288, 1099, 754 cm^{-1}.



26

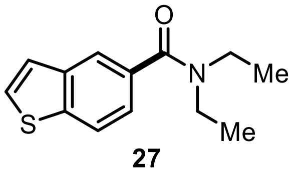
Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (4:1) as the eluent. White solid (47.1 mg, 83% yield).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.21 – 8.12 (m, 2H), 7.88 – 7.82 (m, 1H), 7.53 – 7.40 (m, 4H), 3.47 (d, *J* = 129.5 Hz, 4H), 1.22 (t, *J* = 47.0 Hz, 6H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 169.39, 139.74, 137.27, 136.41, 135.11, 131.79, 127.16, 124.54, 124.42, 124.33, 122.81, 122.07, 121.73, 43.19, 39.44, 14.27, 13.24.

HRMS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{17}H_{18}NOS$ 284.1104; Found 284.1098.

IR (KBr): 3076, 2979, 2935, 1624, 1433, 1386, 1284, 1130, 756 cm^{-1}.



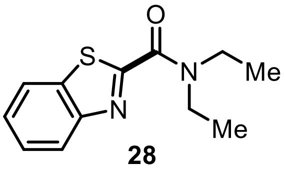
27

Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (4:1) as the eluent. Colorless oil (42.4 mg, 91% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.89 (d, *J* = 8.2 Hz, 1H), 7.84 (d, *J* = 1.6 Hz, 1H), 7.49 (d, *J* = 5.5 Hz, 1H), 7.41 – 7.30 (m, 2H), 3.76 – 3.14 (m, 4H), 1.38 – 1.02 (m, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.40, 140.35, 139.30, 133.50, 127.52, 123.99, 122.55, 122.45, 121.60, 43.41, 39.31, 14.28, 12.99.

Spectral data for this compound were consistent with those in the literature. [6]



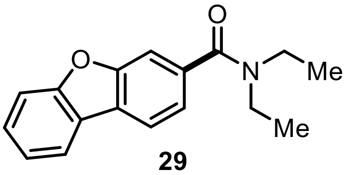
28

Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (4:1) as the eluent. Colorless oil (24.4 mg, 52% yield).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.07 (d, *J* = 8.1 Hz, 1H), 7.94 (d, *J* = 7.9 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 1H), 7.45 (t, *J* = 7.5 Hz, 1H), 4.07 (q, *J* = 7.0 Hz, 2H), 3.60 (q, *J* = 7.1 Hz, 2H), 1.31 (dt, *J* = 16.4, 7.1 Hz, 6H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 165.22, 160.62, 153.41, 136.27, 126.43, 126.31, 124.62, 121.76, 43.17, 42.33, 14.58, 12.72.

Spectral data for this compound were consistent with those in the literature. [9]



29

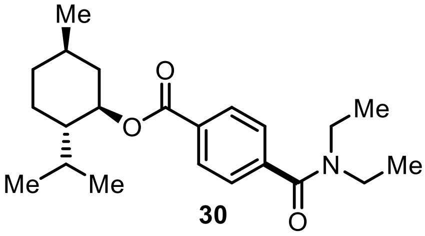
Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (4:1) as the eluent. White solid (36.0 mg, 69% yield).

^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.96 (dd, *J* = 8.0, 2.1 Hz, 2H), 7.64 – 7.55 (m, 2H), 7.53 – 7.42 (m, 1H), 7.36 (td, *J* = 7.1, 6.3, 1.2 Hz, 2H), 3.45 (d, *J* = 72.9 Hz, 4H), 1.38 – 1.01 (m, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.85, 156.76, 155.71, 136.15, 127.71, 125.01, 123.65, 123.01, 121.16, 120.90, 120.74, 111.83, 109.98, 43.41, 39.46, 14.25, 12.95.

HRMS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{17}H_{18}NO_2$ 268.1332; Found 268.1328.

IR (KBr): 2974, 2932, 1628, 1427, 1291, 1201, 1081, 845 cm^{-1}.



30

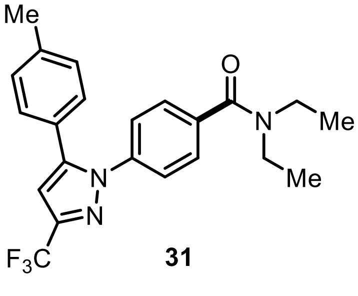
Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (4:1) as the eluent. Colorless oil (47.5 mg, 66% yield).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.10 – 8.03 (m, 2H), 7.43 (d, *J* = 8.2 Hz, 2H), 4.95 (td, *J* = 10.9, 4.4 Hz, 1H), 3.56 (d, *J* = 9.1 Hz, 2H), 3.22 (d, *J* = 9.9 Hz, 2H), 2.17 – 2.09 (m, 1H), 1.95 (pd, *J* = 7.0, 2.7 Hz, 1H), 1.74 (dt, *J* = 11.6, 2.9 Hz, 2H), 1.57 (dddt, *J* = 13.8, 10.6, 6.4, 3.2 Hz, 2H), 1.26 (s, 4H), 1.17 – 1.03 (m, 5H), 0.93 (dd, *J* = 6.8, 5.1 Hz, 6H), 0.80 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 170.32, 165.46, 141.45, 131.41, 129.72, 126.24, 75.19, 47.31, 43.20, 40.98, 39.32, 34.33, 31.46, 26.59, 23.73, 22.00, 20.73, 16.57, 14.18, 12.90.

HRMS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{22}H_{34}NO_3$ 360.2533; Found 360.2525.

IR (KBr): 2955, 2870, 1713, 1637, 1456, 1273, 1109, 1018, 785cm^{-1}.



31

Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (4:1) as the eluent. White solid (59.8 mg, 74% yield).

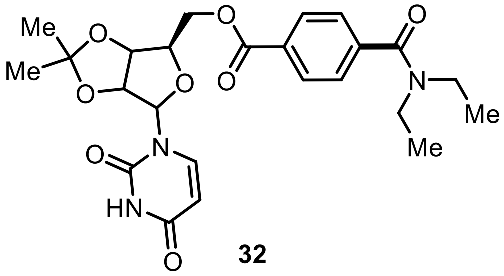
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 (d, *J* = 1.3 Hz, 4H), 7.17 – 7.09 (m, 4H), 6.73 (s, 1H), 3.54 (d, *J* = 9.0 Hz, 2H), 3.21 (d, *J* = 9.2 Hz, 2H), 2.36 (s, 3H), 1.31 – 1.04 (m, 6H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 170.15, 145.00, 143.49 (q, *J* = 38.3 Hz), 139.81, 139.40, 137.13, 129.59, 128.71, 127.27, 125.92, 125.34, 121.23 (q, *J* = 268.9 Hz), 105.66 (q, *J* = 2.0 Hz), 43.34, 39.46, 21.29, 14.20, 12.89.

^{19}F NMR (377 MHz, Chloroform-*d*) δ -62.28.

HRMS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{22}H_{23}N_3OF_3$ 402.1788; Found 402.1780.

IR (KBr): 3124, 2978, 2934, 1632, 1468, 1430, 1276, 1236, 1133, 857 cm^{-1}.



32

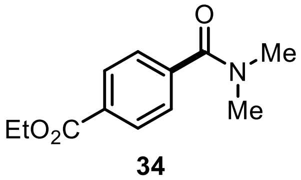
Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (2:1) as the eluent. White solid (87.7 mg, 90% yield).

^{1}H NMR (300 MHz, Chloroform-*d*) δ 9.68 (s, 1H), 8.15 – 7.98 (m, 2H), 7.53 – 7.39 (m, 2H), 7.29 (d, *J* = 1.1 Hz, 1H), 5.72 – 5.58 (m, 2H), 5.09 (dd, *J* = 6.4, 1.8 Hz, 1H), 4.95 (dd, *J* = 6.4, 4.0 Hz, 1H), 4.67 – 4.42 (m, 3H), 3.55 (d, *J* = 9.3 Hz, 2H), 3.35 – 3.07 (m, 2H), 1.58 (s, 3H), 1.37 (s, 3H), 1.24 (d, *J* = 9.0 Hz, 3H), 1.11 (d, *J* = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.15, 165.51, 163.59, 150.06, 142.63, 141.86, 130.14, 129.90, 126.40, 114.58, 102.55, 95.54, 85.76, 84.61, 81.32, 64.86, 43.25, 39.37, 27.15, 25.31, 14.20, 12.89.

HRMS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{24}H_{30}N_3O_8$ 488.2027; Found 488.2014.

IR (KBr): 3062, 2984, 2936, 1698, 1626, 1456, 1380, 1274, 1092, 861 cm^{-1}.



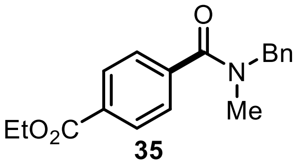
34

Prepared according to the the method **B** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (2:1) as the eluent. Colorless oil (29.1 mg, 67% yield, 36 h).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.09 (d, *J* = 8.4 Hz, 2H), 7.51 – 7.43 (m, 2H), 4.40 (q, *J* = 7.1 Hz, 2H), 3.13 (s, 3H), 2.95 (s, 3H), 1.41 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.66, 165.96, 140.55, 131.36, 129.68, 126.98, 61.25, 39.39, 35.30, 14.31.

Spectral data for this compound were consistent with those in the literature. [6]



35

Prepared according to the the method **A** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (6:1) as the eluent. Colorless oil (31.1 mg, 52% yield).

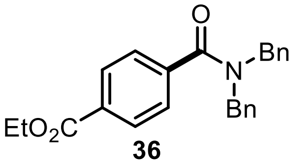
Prepared according to the the method **B** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (6:1) as the eluent. Colorless oil (31.1 mg, 52% yield).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.07 (dd, *J* = 21.7, 7.9 Hz, 2H), 7.55 – 7.49 (m, 2H), 7.41 – 7.28 (m, 4H), 7.15 (d, *J* = 7.4 Hz, 1H), 4.76 (s, 1H), 4.47 (s, 1H), 4.38 (dq, *J* = 14.1, 7.4 Hz, 2H), 3.06 (s, 1H), 2.84 (s, 2H), 1.46 – 1.33 (m, 3H).

^{13}C NMR (101 MHz, CDCl3) δ 171.37, 170.67, 165.90, 140.49, 140.36, 136.74, 136.18, 131.46, 129.77, 128.95, 128.80, 128.26, 127.80, 127.68, 126.93, 126.76, 126.65, 61.27, 55.03, 50.81, 36.83, 33.24, 14.30.

HRMS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{18}H_{20}NO_3$ 298.1438; Found 298.1431.

IR (KBr): 2980, 1718, 1637, 1450, 1274, 1106, 1020, 733 cm^{-1}.



36

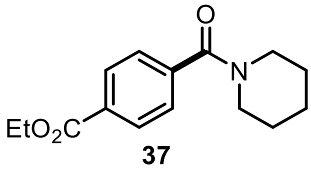
Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (6:1) as the eluent. Colorless oil (65.7 mg, 88% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.06 (d, *J* = 8.4 Hz, 2H), 7.55 (d, *J* = 8.3 Hz, 2H), 7.33 (dt, *J* = 22.0, 7.5 Hz, 8H), 7.12 (d, *J* = 7.3 Hz, 2H), 4.72 (s, 2H), 4.41 – 4.31 (m, 4H), 1.38 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.34, 165.84, 140.39, 136.70, 136.04, 131.49, 129.86, 128.97, 128.81, 128.50, 127.84, 127.70, 126.94, 126.66, 61.27, 51.42, 47.02, 14.30.

HRMS (ESI) m/z: [M+H]$^+$ Calcd. for $C_{24}H_{24}NO_3$ 374.1751; Found 374.1742.

IR (KBr): 3030, 2981, 2931, 1717, 1638, 1423, 1273, 1104, 740 cm^{-1}.



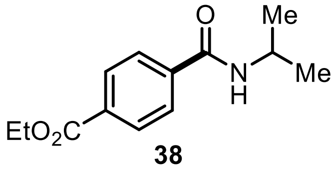
37

Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (4:1) as the eluent. Colorless oil (19.6 mg, 38% yield).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.08 (d, *J* = 7.9 Hz, 2H), 7.45 (d, *J* = 8.0 Hz, 2H), 4.39 (q, *J* = 7.2 Hz, 2H), 3.72 (s, 2H), 3.29 (s, 2H), 1.68 (s, 4H), 1.51 (s, 2H), 1.40 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 169.28, 165.96, 140.77, 131.21, 129.74, 126.71, 61.21, 48.65, 43.10, 26.52, 25.59, 24.52, 14.31.

Spectral data for this compound were consistent with those in the literature. [10]



38

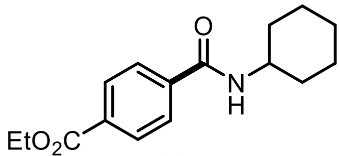
Prepared according to the method **B** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (6:1) as the eluent. White solid (19.7 mg, 42% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.13 – 8.05 (m, 2H), 7.80 (d, *J* = 8.4 Hz, 2H), 6.08 (d, *J* = 7.9 Hz, 1H), 4.40 (q, *J* = 7.2 Hz, 2H), 4.29 (dp, *J* = 7.8, 6.5 Hz, 1H), 1.41 (t, *J* = 7.2 Hz, 3H), 1.28 (d, *J* = 6.6 Hz, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.88, 138.80, 132.87, 129.74, 126.87, 61.35, 42.15, 22.79, 14.29.

HRMS (ESI) m/z: [M+H]$^+$ Calcd. for $C_{13}H_{18}NO_3$ 236.1281; Found 236.1277.

IR (KBr): 2975, 2931, 1717, 1632, 1537, 1457, 1277, 1110, 1021, 701cm^{-1}.



39

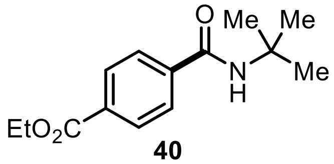
Prepared according to the the method **B** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (6:1) as the eluent. White solid (21.1 mg, 38% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.12 – 8.04 (m, 2H), 7.80 (d, *J* = 8.4 Hz, 2H), 6.10 (d, *J* = 8.1 Hz, 1H), 4.40 (q, *J* = 7.1 Hz, 2H), 4.04 – 3.91 (m, 1H), 2.04 (dd, *J* = 12.4, 4.0 Hz, 2H), 1.82 – 1.71 (m, 2H), 1.66 (dt, *J* = 12.9, 3.7 Hz, 1H), 1.42 (q, *J* = 7.2 Hz, 5H), 1.24 (dtd, *J* = 22.6, 11.5, 11.1, 3.6 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.88, 165.81, 138.92, 132.85, 129.74, 126.88, 61.34, 48.95, 33.17, 25.54, 24.92, 14.29.

HRMS (ESI) m/z: [M+H]$^+$ Calcd. for $C_{16}H_{22}NO_3$ 276.1594; Found 276.1590.

IR (KBr): 2936, 2854, 1715, 1632, 1546, 1275, 1105, 737 cm^{-1}.



40

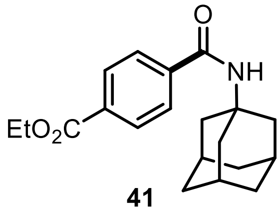
Prepared according to the the method **B** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (8:1) as the eluent. Yellow solid (26.8 mg, 54% yield).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.11 – 8.02 (m, 2H), 7.77 (d, *J* = 8.4 Hz, 2H), 6.03 (s, 1H), 4.39 (q, *J* = 7.1 Hz, 2H), 1.48 (s, 9H), 1.41 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 166.07, 165.90, 139.74, 132.68, 129.71, 126.75, 61.32, 51.92, 28.82, 14.29.

HRMS (ESI) m/z: [M+H]$^+$ Calcd. for $C_{14}H_{19}NO_3$ 250.1438; Found 250.1434.

IR (KBr): 2972, 1721, 1647, 1536, 1455, 1277, 1107, 1021, 873, 733 cm^{-1}.



41

Prepared according to the the method **B** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (25:1) as the eluent. Yellow solid (47.8 mg, 73% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.11 – 8.02 (m, 2H), 7.81 – 7.73 (m, 2H), 5.84 (s, 1H), 4.39 (q, *J* = 7.2 Hz, 2H), 2.14 (s, 9H), 1.73 (d, *J* = 2.8 Hz, 6H), 1.41 (t, *J* = 7.1 Hz, 3H).

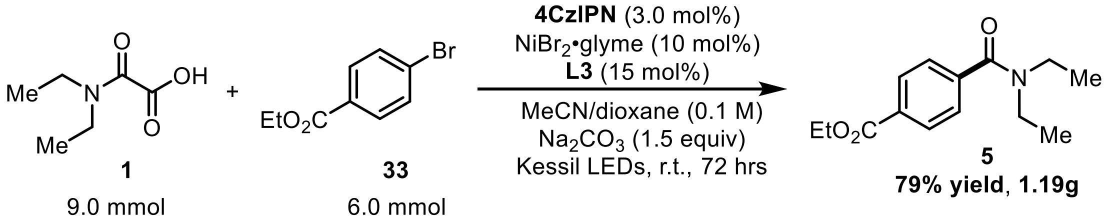
^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.91, 165.78, 139.88, 132.66, 129.71, 126.74, 61.31, 52.62, 41.63, 36.35, 29.50, 14.29.

HRMS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{20}H_{26}NO_3$ 228.1907; Found 328.1900.

IR (KBr): 2909, 2854, 1720, 1647, 1534, 1276, 1106, 1021, 733 cm^{-1}.

4 Gram-scale Synthesis and Strategy Expansion

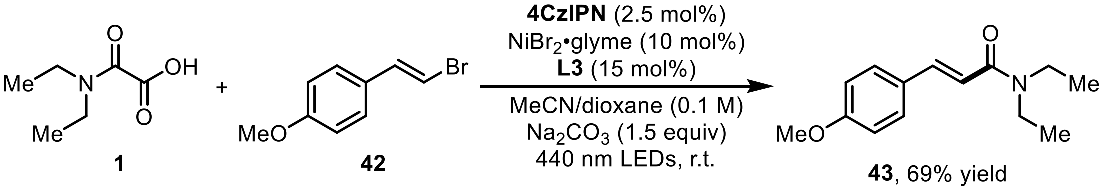
4.1 Gram-scale synthesis



Under nitrogen atmosphere, $NiBr_2$•glyme (0.6 mmol) and 4,4'-dimethoxy-2,2'-bipyridine **L3** (0.9 mmol) were dissolved in 15.0 mL MeCN as the nickel catalyst solution and stirred for 30 min prior to use. To a 100 mL oven-dried Schlenk tube equipped with a stirring bar was added photocatalyst 4CzIPN (3 mol%) and Na_2CO_3 (9.0 mmol, 1.5 equiv). The reaction tube was then flushed with nitrogen gas. After that, a solution of *N*,*N*-diethyloxamic acid **1** (9.0 mmol, 1.5 equiv) and ethyl 4-bromobenzoate **33** (9.0 mmol, 1.0 equiv) in dioxane (45 mL) was added to the tube. Subsequently, the nickel catalyst solution was syringed into the reaction vessel. The vial was placed into Kessil LEDs (λ = 440 nm, 10 W). Stirring was maintained for 72 hours, after this period the irradiation was stopped. The mixture was concentrated under vacuum and purified by flash chromatography (hexanes/ethyl acetate = 4:1) to afford the corresponding product **5**.

Figure S1: Reaction setup/appearance for gram-scale synthesis

4.2 Strategy expansion to the synthesis of unsaturated amide



Prepared according to the method **A** described above, and the pure product was isolated by flash chromatography column with V_{PE}/V_{EA} (4:1) as the eluent. Colorless oil (32.3 mg, 69% yield). *E*/*Z* = 3:1.

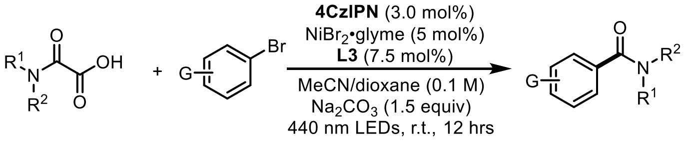
^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.60 (d, *J* = 15.3 Hz, 0.3H), 7.40 (d, *J* = 8.7 Hz, 0.6H), 7.33 – 7.25 (m, 2H), 6.82 (d, *J* = 8.7 Hz, 0.6H), 6.79 – 6.71 (m, 2H), 6.63 (d, *J* = 15.6 Hz, 0.3H), 6.45 (d, *J* = 12.6 Hz, 1H), 5.87 (d, *J* = 12.6 Hz, 1H), 3.76 (s, 0.8H), 3.72 (s, 3H), 3.40 (q, *J* = 7.1 Hz, 3H), 3.21 (q, *J* = 7.2 Hz, 2H), 1.11 (t, *J* = 7.1 Hz, 4H), 0.92 (t, *J* = 7.2 Hz, 3H).

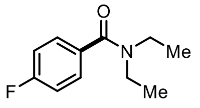
^{13}C NMR (126 MHz, Chloroform-*d*) δ 168.47, 165.99, 160.76, 159.71, 141.87, 132.40, 130.02, 129.23, 128.36, 121.63, 115.52, 114.22, 113.79, 55.22, 42.56, 38.97, 14.05, 12.55.

HRMS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{14}H_{20}NO_2$ 234.1489; Found 234.1485.

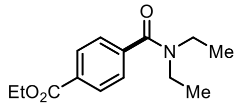
IR (KBr): 3054, 2977, 2927, 2849, 1712, 1611, 1512, 1261, 737 cm^{-1}.

4.3 Reaction using 5 mol% nickel catalyst loading

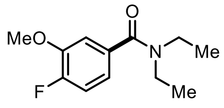




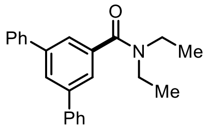
3, 72% yield



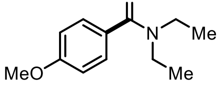
5, 74% yield



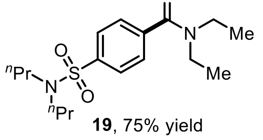
8, 71% yield



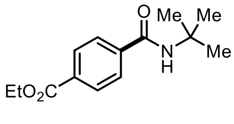
12, 76% yield



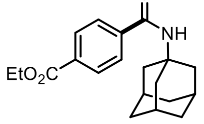
15, 53% yield



19, 75% yield



40, 64% yield[a]

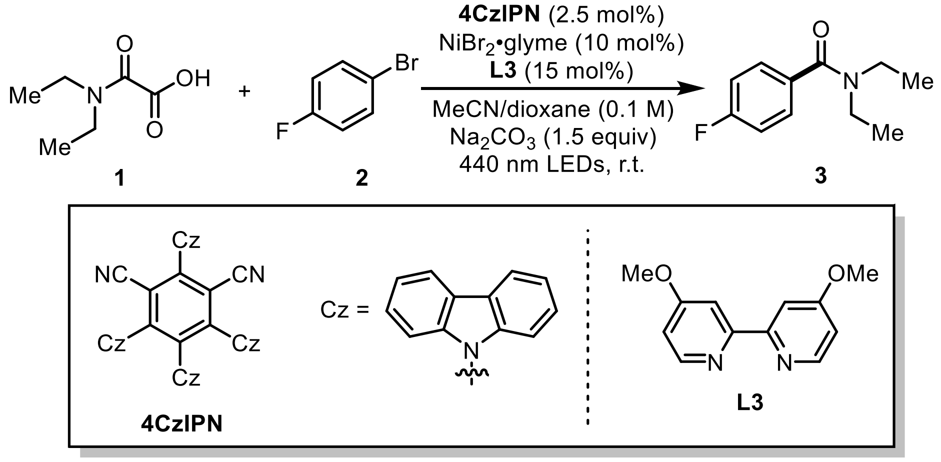


41, 62% yield[a]

[a] TMG (1,1,3,3-tetramethylguanidine) was used instead of Na_2CO_3 as the base additive

5 Mechanistic Studies

5.1 Table S7: Control Experiments[a)]



Entry	Variation	Yield (%)[b)]
1	none	80
2	w/o Na_2CO_3	0
3	w/o 4CzIPN	0
4	w/o Light	0
5	w/o Ni $NiBr_2$ glyme /**L3**	0
6	w/o $NiBr_2$ glyme	0
7	w/o **L3**	0

a) Reaction Conditions: Reactions performed on a 0.2 mmol scale at ambient temperature for 12 hours under illumination by blue LED (440 nm, 10 W) with **1** (0.3 mmol, 1.5 equiv), **2** (0.2 mmol, 1.0 equiv), and Na_2CO_3 (1.5 equiv) in 2.0 mL of solvent. b) Isolated yield. w/o: without.

5.2 Cyclic voltammetry studies

General information: Cyclic voltammetry (CV) experiments were conducted in a 10 mL glass vial fitted with a glassy carbon working electrode (3 mm in diameter), an $Ag/AgNO_3$ reference electrode, and a platinum wire counter electrode. The solution of interest was sparged with nitrogen for 3-5 minutes before data collection. Potentials were reported in against the SCE redox couple.

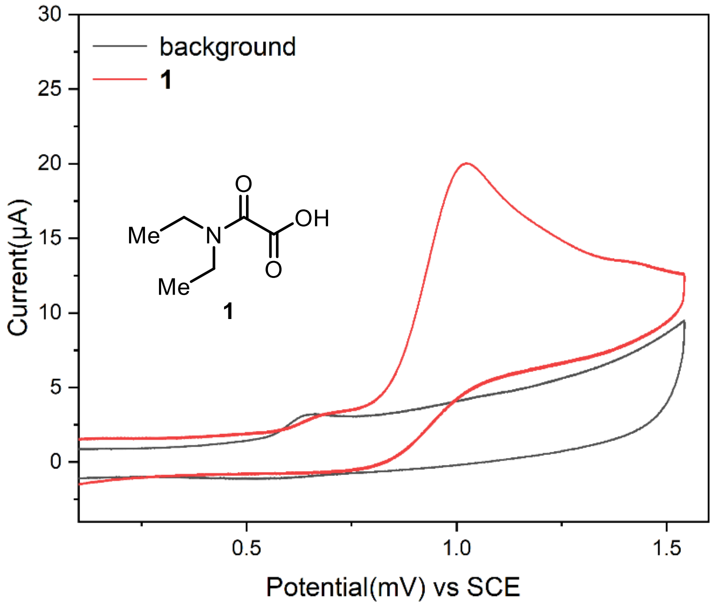


Figure S2: Cyclic voltammogram of 2-(diethylamino)-2-oxoacetic acid **1** and Na_2CO_3 in MeCN/dioxane (1:3). Conditions: $TBABF_4$ (0.10 M), **1** (10 mM), Na_2CO_3 (10 mM). Scan rate: 100 mV/s. ($E_{1/2}$ = 0.92 V vs SCE; E_p = 1.01 V vs SCE).

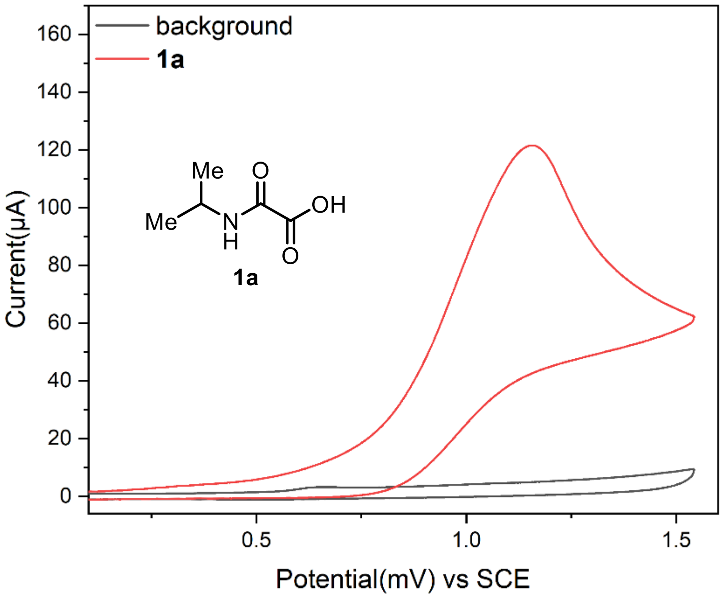


Figure S3: Cyclic voltammogram of 2-(isopropylamino)-2-oxoacetic acid **1a** and TMG in MeCN/dioxane (1:3). Conditions: $TBABF_4$ (0.10 M), **1a** (10 mM), TMG (10 mM). Scan rate: 100 mV/s. ($E_{1/2}$ = 0.97 V vs SCE; E_p = 1.14 V vs SCE).

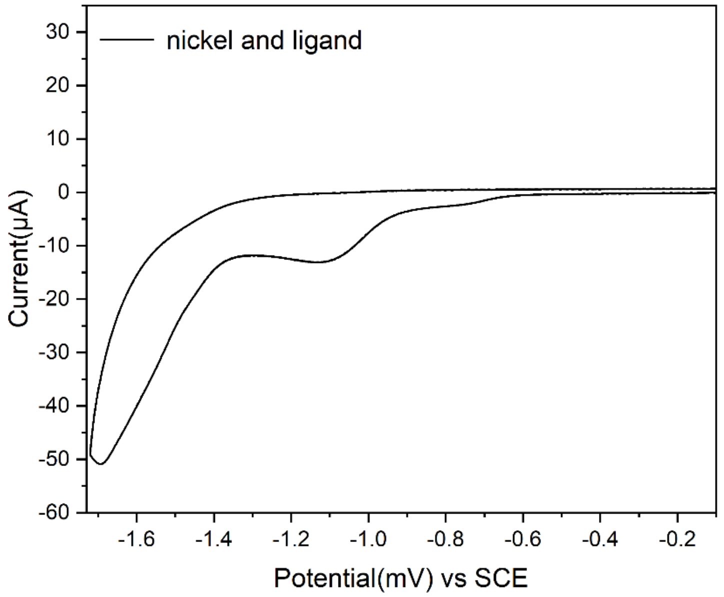


Figure S4: Cyclic voltammogram of $NiBr_2$•glyme and 4,4’-dOMebpy in MeCN/dioxane (1:3). Conditions: $TBABF_4$ (0.10 M), $NiBr_2$•glyme (1 mM), 4,4’-dOMebpy (1 mM). Scan rate: 100 mV/s. (E_p = -1.13 V vs SCE).

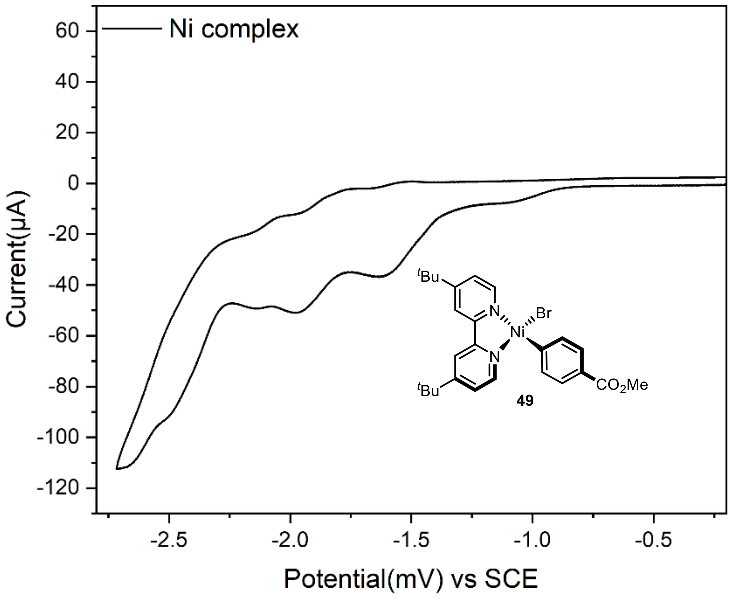
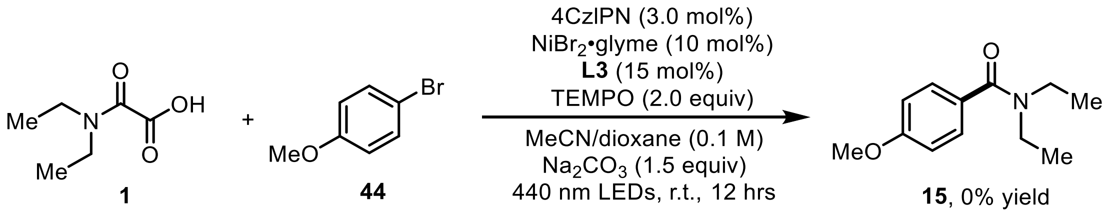
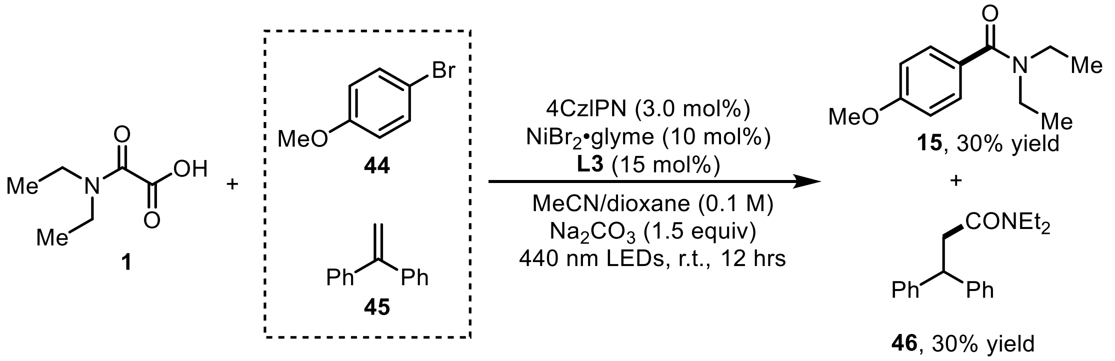


Figure S5: Cyclic voltammogram of arylnickel(II) complex **49** in MeCN/dioxane (1:3). Conditions: $TBABF_4$ (0.10 M), **49** (1.8 mM). Scan rate: 100 mV/s.

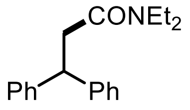
5.3 Radical trapping experiment



TEMPO (2.0 equiv) was subjected to the standard conditions and reacted for 12 hours. The reaction was fully inhibited and no desired product could be detected.



1,1-diphenylethylene (2.0 equiv) was subjected to the standard conditions and reacted for 12 hours. Besides the desired product **15**, the radical addition product **46** was isolated in 30% yield as well.

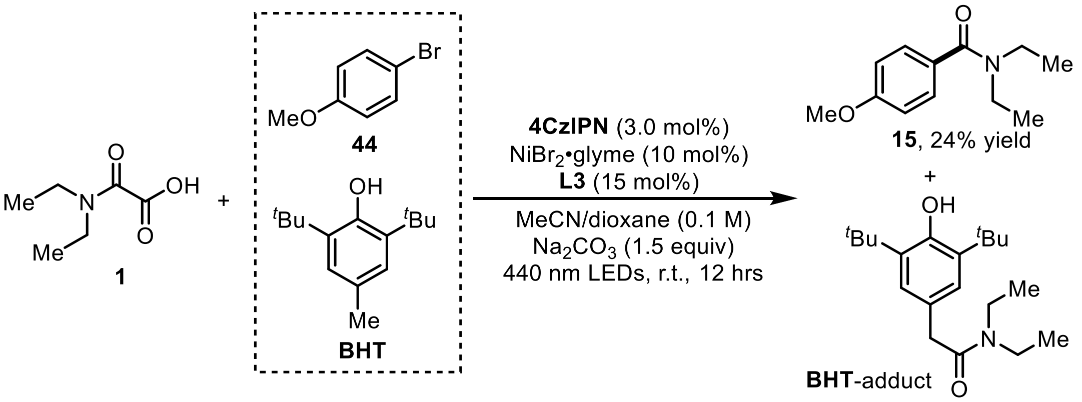


46

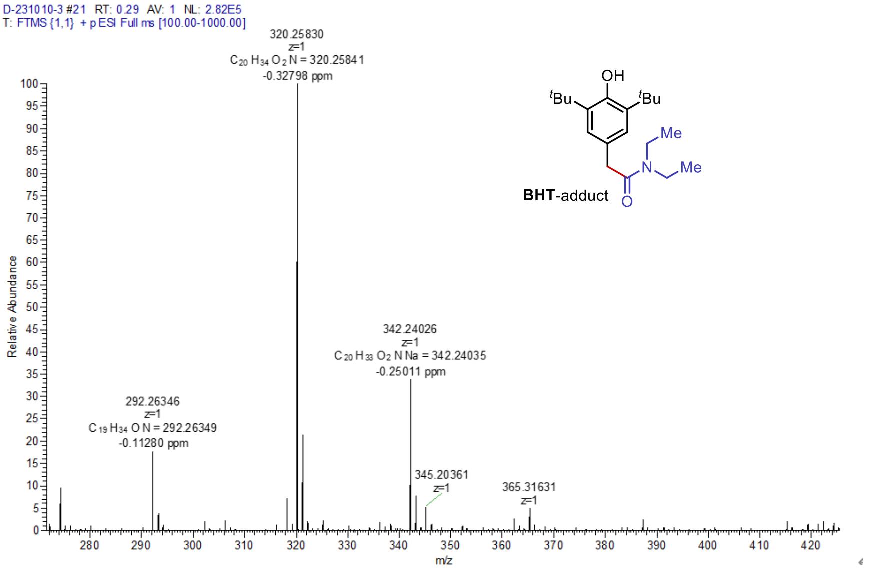
^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.30 – 7.20 (m, 8H), 7.16 (ddd, *J* = 8.7, 3.9, 2.3 Hz, 2H), 4.73 (t, *J* = 7.5 Hz, 1H), 3.28 (q, *J* = 7.1 Hz, 2H), 3.14 (q, *J* = 7.2 Hz, 2H), 3.00 (d, *J* = 7.5 Hz, 2H), 1.01 (dt, *J* = 18.7, 7.1 Hz, 6H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 170.21, 144.32, 128.43, 127.97, 126.31, 47.21, 41.93, 40.36, 39.07, 14.38, 12.94.

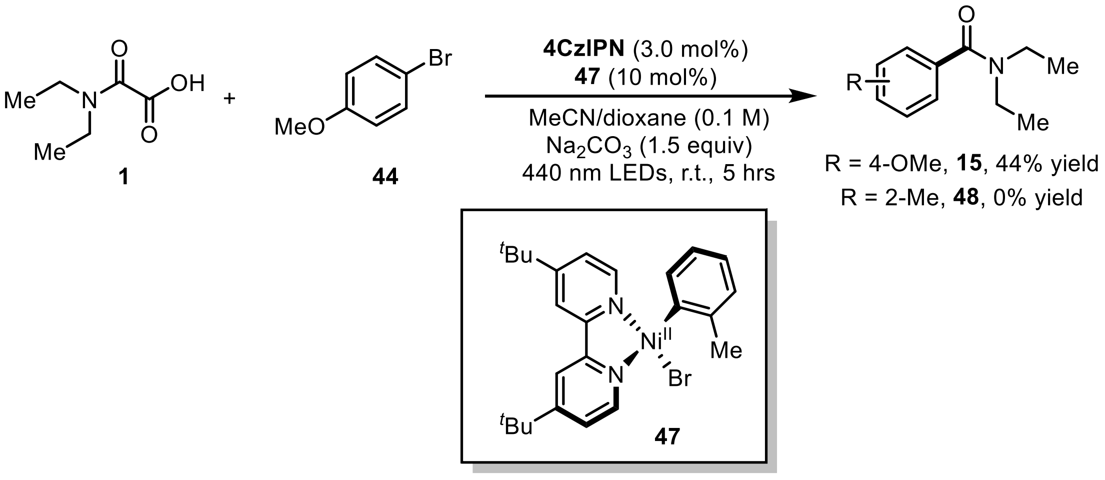
Spectral data for this compound were consistent with those in the literature.[11]



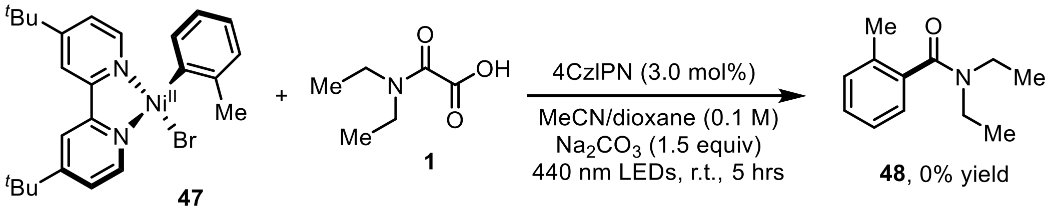
BHT (1.5 equiv) was added to the standard conditions and reacted for 12 hours. The BHT-adduct could be detected by HRMS analysis of the reaction system (see below).



5.4 Experiments with nickel complex 47

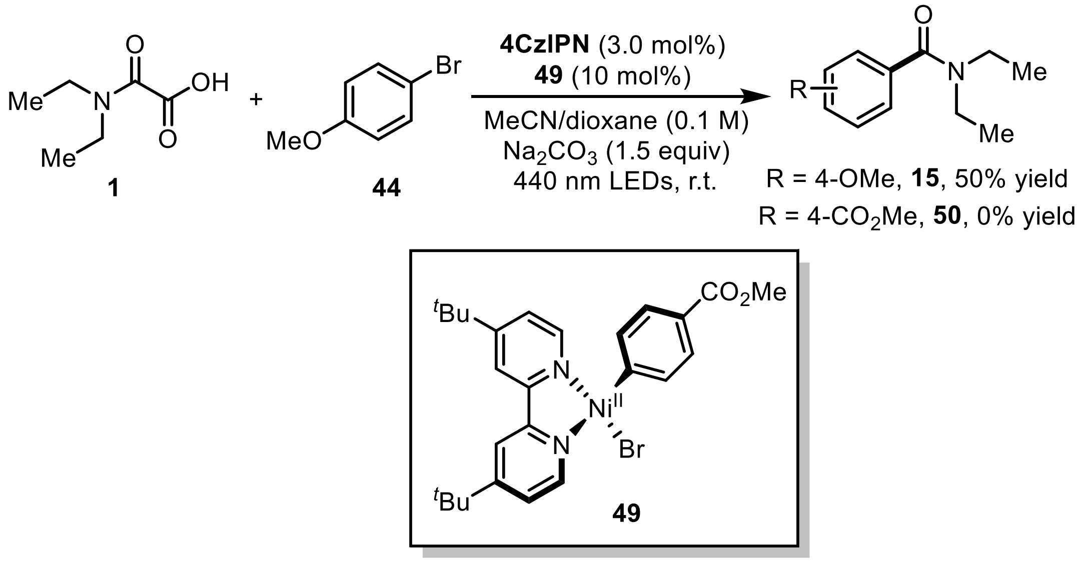


In an argon-filled glovebox, an oven-dried 10 mL Schlenk tube was charged with **4CzIPN** (3 mol%), nickel complex **47**[12] (10 mol%), Na_2CO_3 (0.075 mmol, 1.5 equiv) and a solution of *N,N*-diethyloxamic acid **1** (0.075 mmol, 1.5 equiv) and 4-bromomethoxybenzene **44** (0.05 mmol, 1.0 equiv) in MeCN/dioxane (v:v = 1:3, 0.1 M). The vial was placed into photosyn-10 LEDs (λ = 440 nm, 10 W). Stirring was maintained for 5 hours, after this period the irradiation was stopped. The mixture was concentrated under vacuum. Yield was determined by ^{1}H NMR analysis of the crude mixture using 1,1,2,2-tetrachloroethaneas the internal standard.



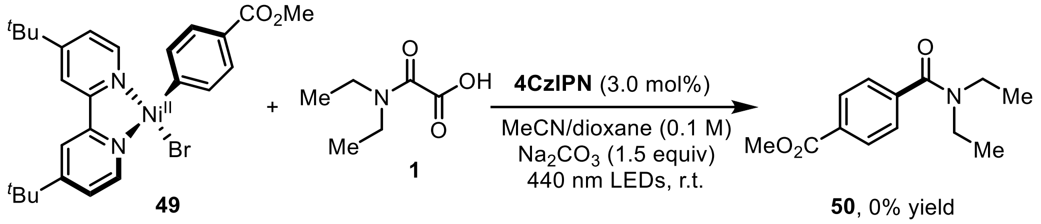
In an argon-filled glovebox, an oven-dried 10 mL Schlenk tube was charged with **4CzIPN** (3 mol%), nickel complex **47** (0.05 mmol, 1.0 equiv), Na_2CO_3 (0.075 mmol, 1.5 equiv) and a solution of *N,N*-diethyloxamic acid **1** (0.075 mmol, 1.5 equiv) in MeCN/dioxane (v:v = 1:3, 0.1 M). The vial was placed into photosyn-10 LEDs (λ = 440 nm, 10 W). Stirring was maintained for 5 hours, after this period the irradiation was stopped. Yield was determined by ^{1}H NMR analysis of the crude mixture using 1,1,2,2-tetrachloroethane as the internal standard.

5.5 Experiments with nickel complex 49

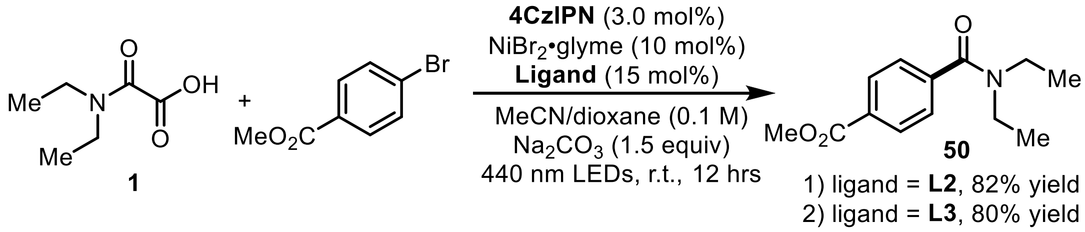


In an argon-filled glovebox, an oven-dried 10 mL Schlenk tube was charged with **4CzIPN** (3 mol%), nickel complex **49**[13,14] (10 mol%), Na_2CO_3 (0.15 mmol, 1.5 equiv) and a solution of *N,N*-diethyloxamic acid **1** (0.15 mmol, 1.5 equiv) and 4-bromomethoxybenzene **44** (0.10 mmol, 1.0 equiv) in MeCN/dioxane (v:v = 1:3, 0.1 M).

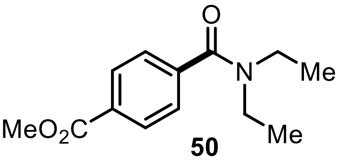
The vial was placed into photosyn-10 LEDs (λ = 440 nm, 10 W). Stirring was maintained for 12 hours, after this period the irradiation was stopped. The mixture was concentrated under vacuum. Yield was determined by ^{1}H NMR analysis of the crude mixture using 1,1,2,2-tetrachloroethaneas the internal standard.



In an argon-filled glovebox, an oven-dried 10 mL Schlenk tube was charged with **4CzIPN** (3 mol%), nickel complex **49** (0.10 mmol, 1.0 equiv), Na_2CO_3 (0.15 mmol, 1.5 equiv) and a solution of *N*,*N*-diethyloxamic acid **1** (0.15 mmol, 1.5 equiv) in MeCN/dioxane (v:v = 1:3, 0.1 M). The vial was placed into photosyn-10 LEDs (λ = 440 nm, 10 W). Stirring was maintained for 12 hours, after this period the irradiation was stopped. Yield was determined by ^{1}H NMR analysis of the crude mixture using 1,1,2,2-tetrachloroethane as the internal standard.



The desired coupling product **50** can be smoothly obtained under our standard conditions in good yield by using either ligand **L2** or **L3**.



50

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.12 – 8.04 (m, 2H), 7.47 – 7.41 (m, 2H), 3.93 (s, 3H), 3.56 (d, *J* = 7.3 Hz, 2H), 3.21 (d, *J* = 7.3 Hz, 2H), 1.25 (d, *J* = 7.2 Hz, 3H), 1.10 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 170.25, 166.46, 141.58, 130.65, 129.79, 126.29, 52.28, 43.23, 39.33, 14.19, 12.88.

Spectral data for this compound were consistent with those in the literature.[15]

6 References

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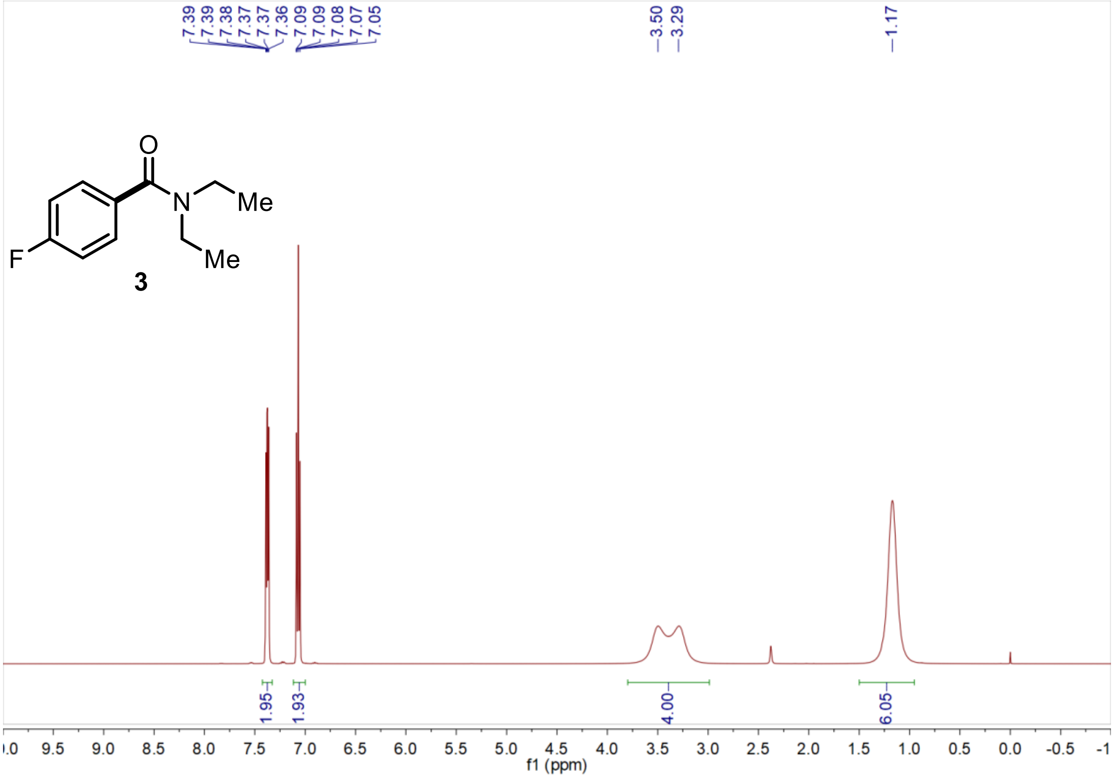
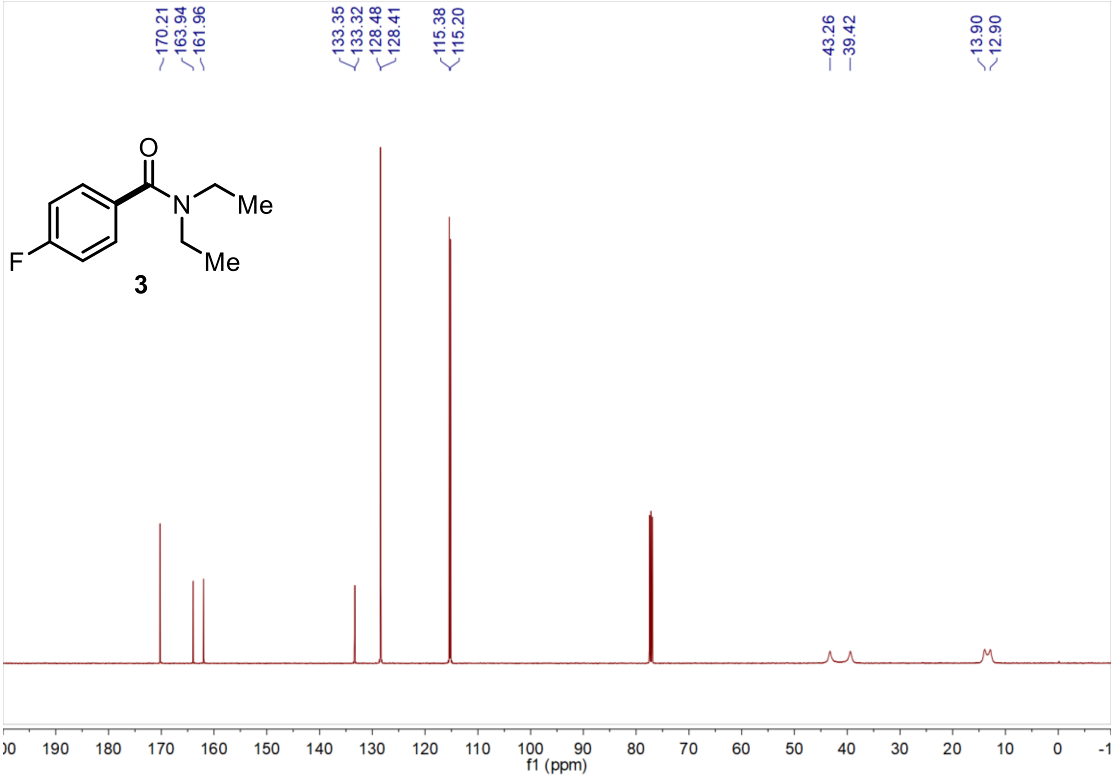
7 NMR Spectra Data

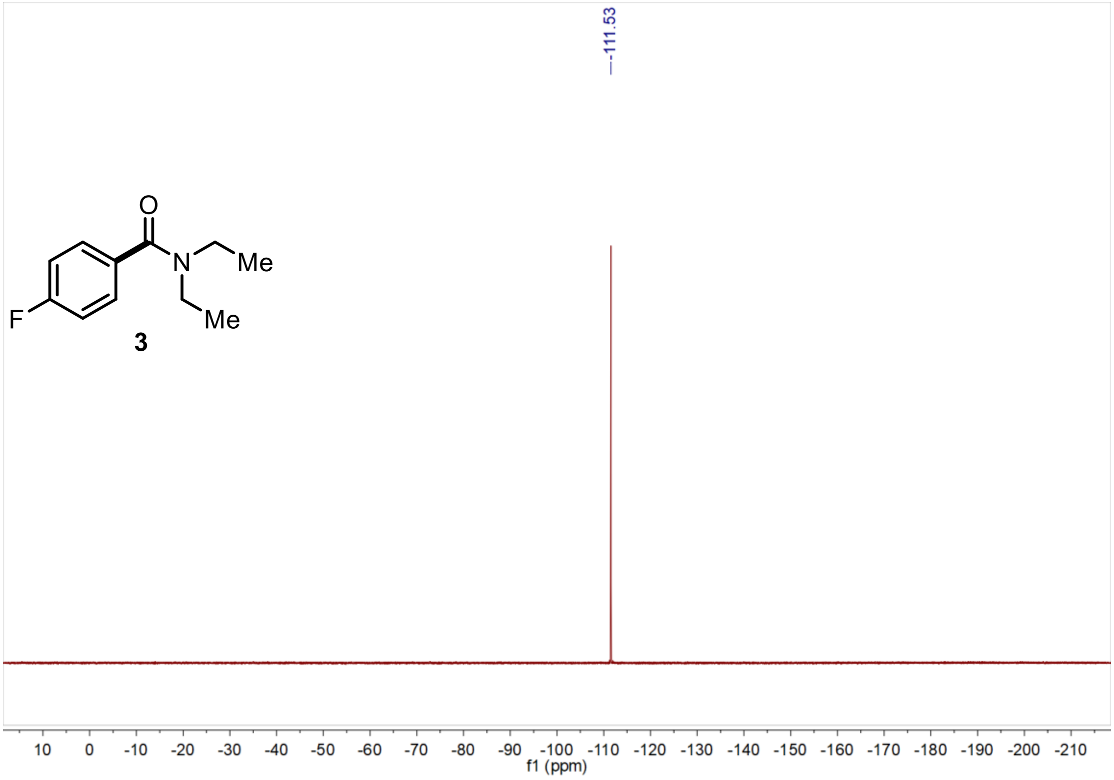
^{1}H NMR (500 MHz, Chloroform-*d*)



^{13}C NMR (126 MHz, Chloroform-*d*)



^{19}F NMR (337 MHz, Chloroform-*d*)



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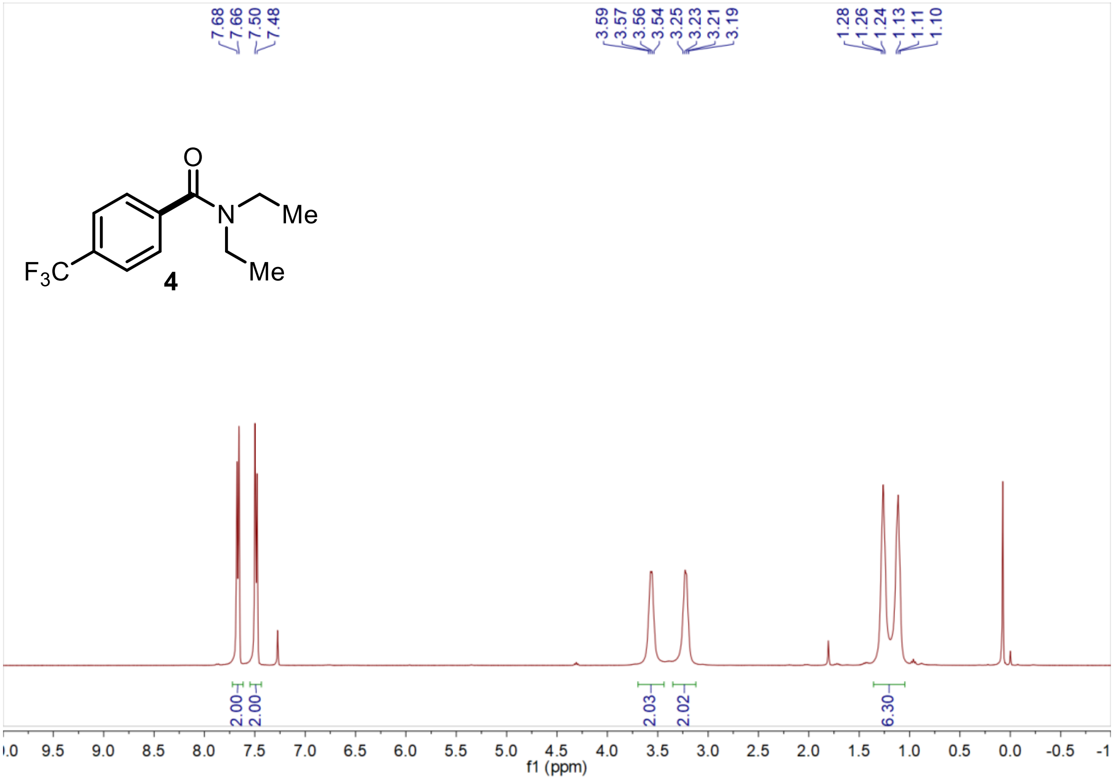
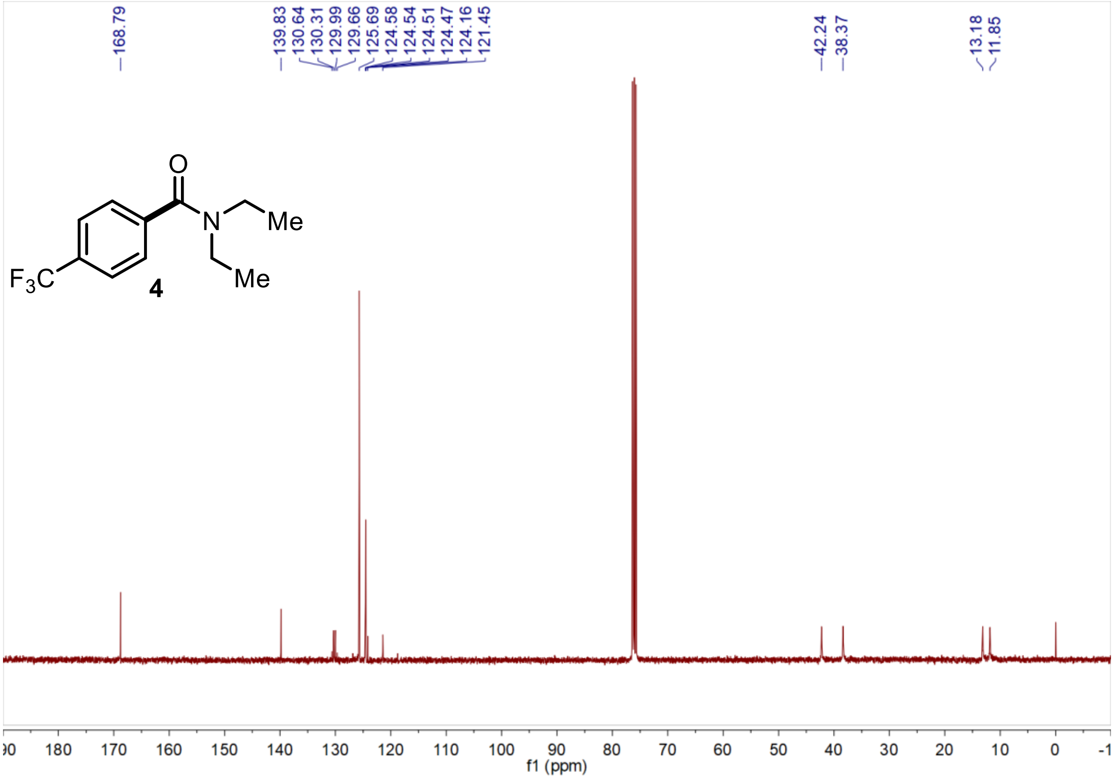


^{13}C NMR (101 MHz, Chloroform-*d*)



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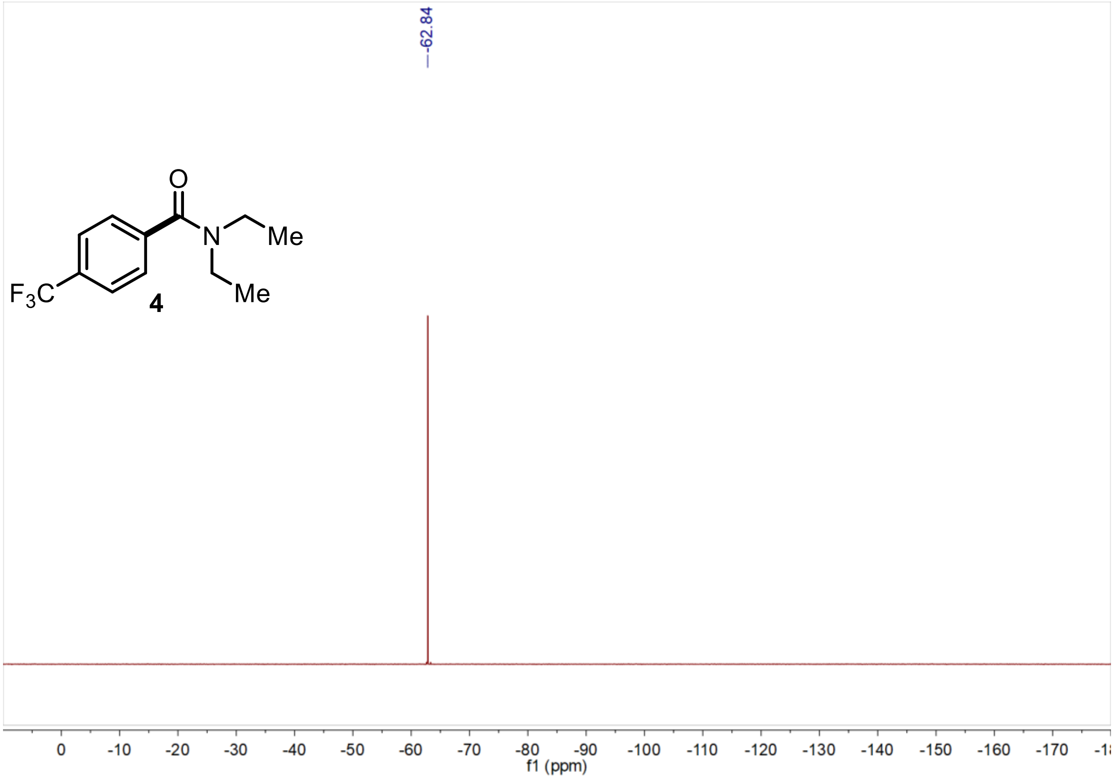

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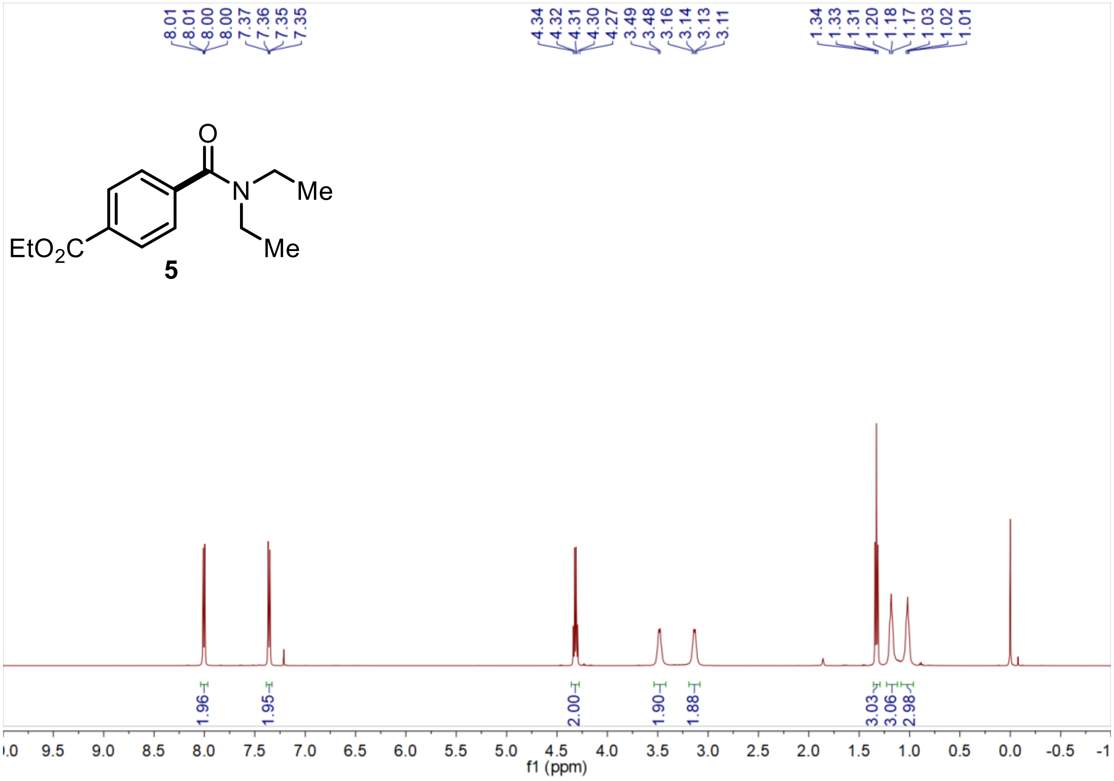

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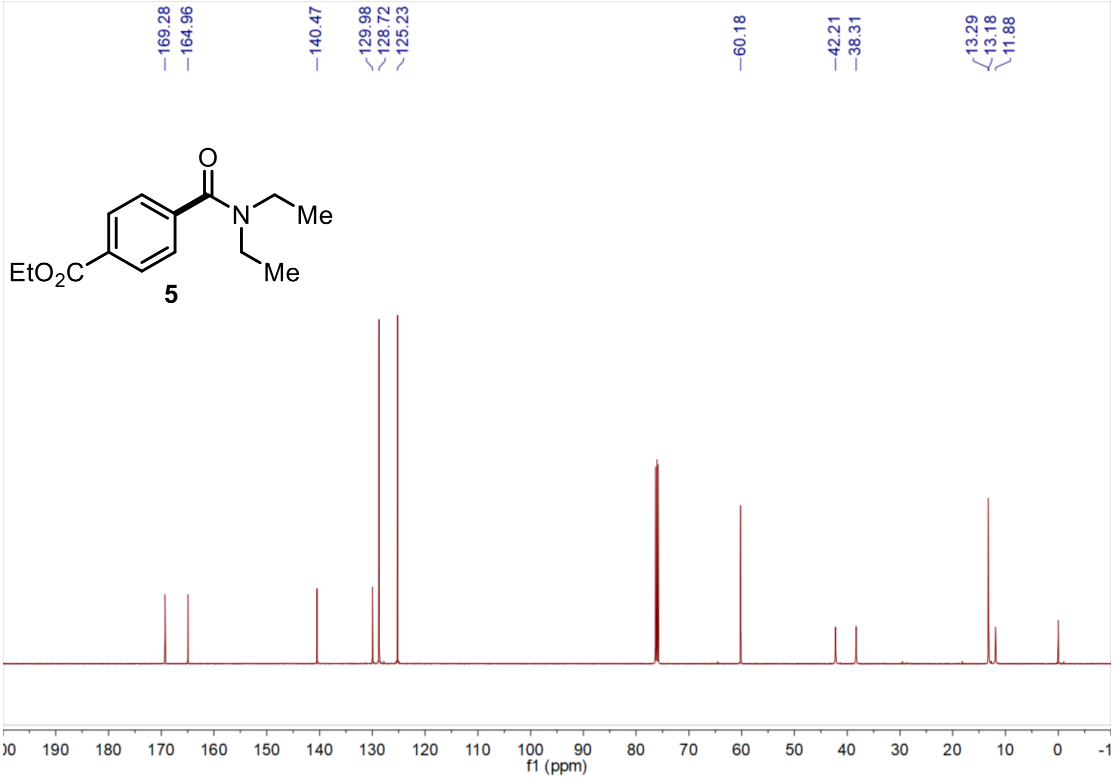

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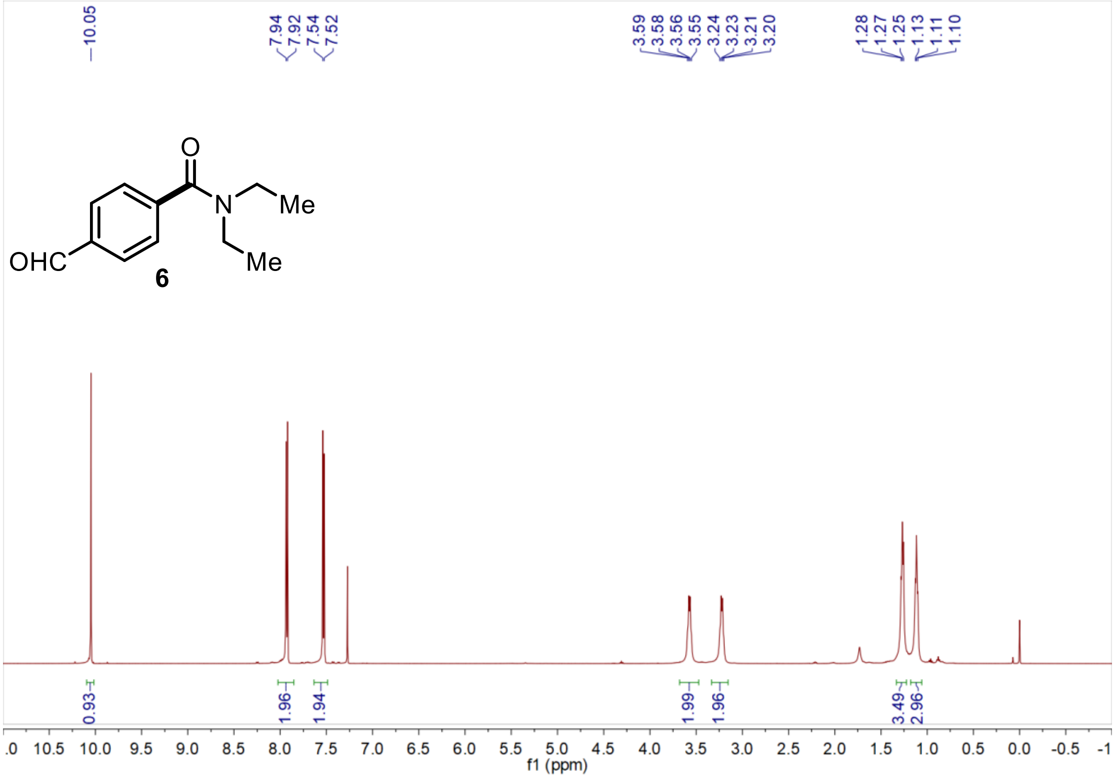

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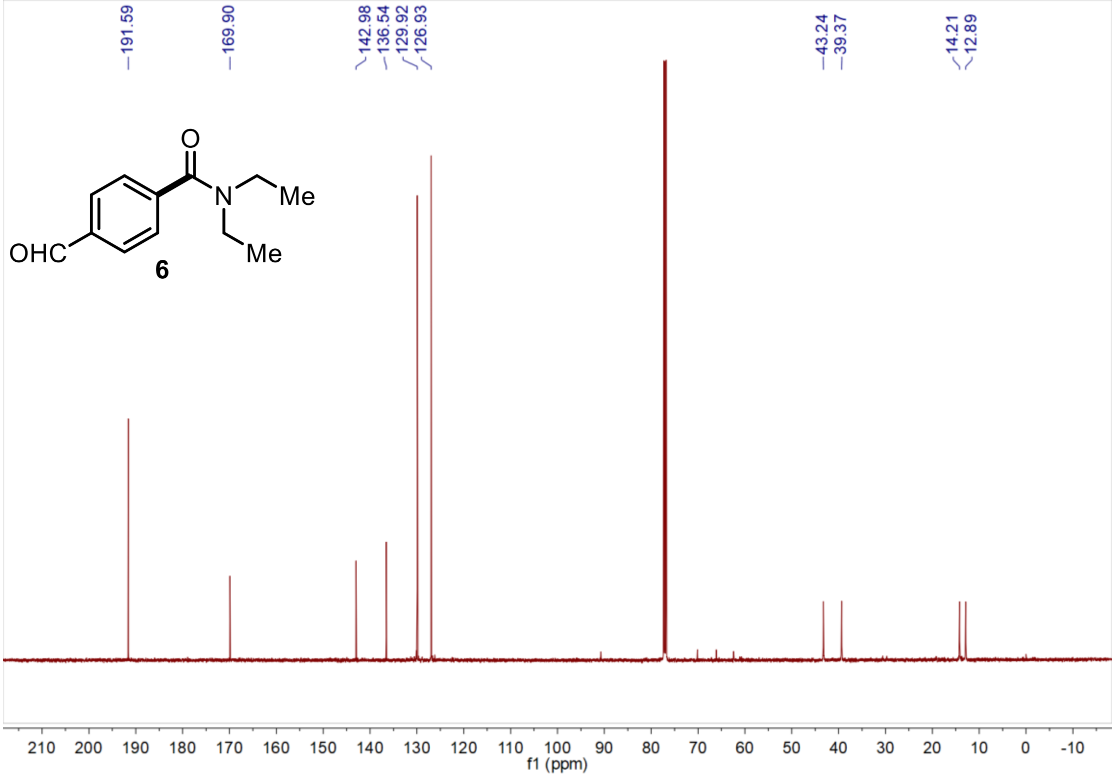
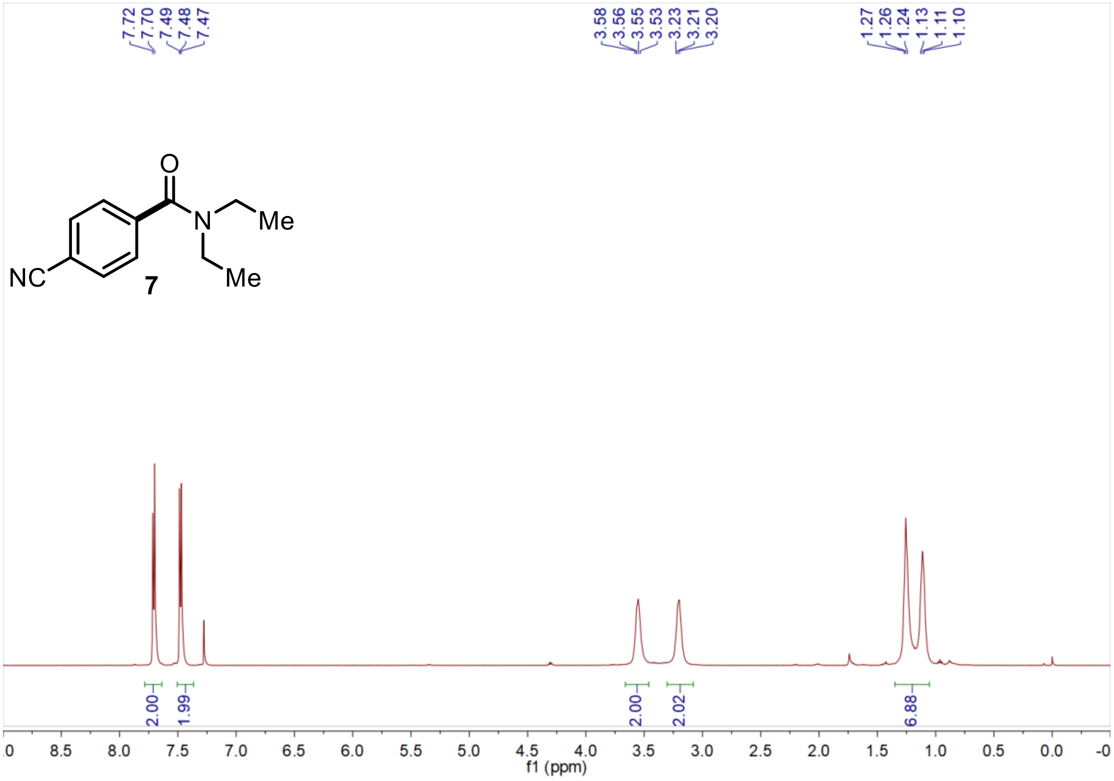


^{1}H NMR (400 MHz, Chloroform-*d*)



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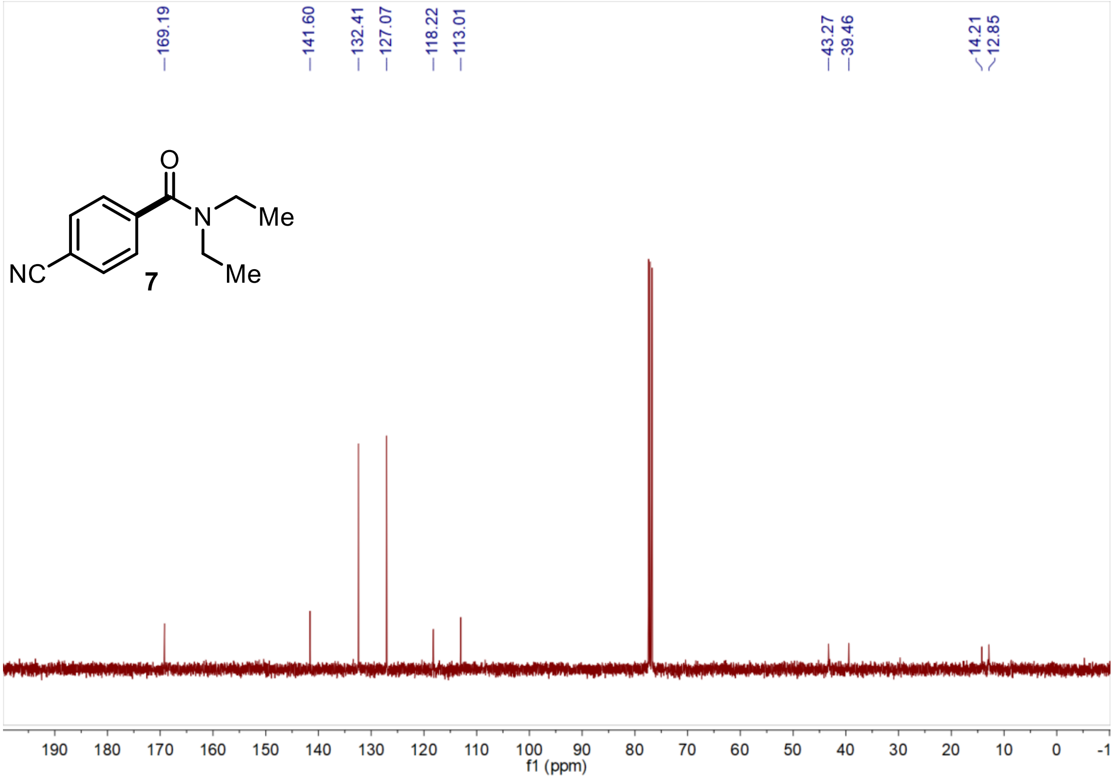

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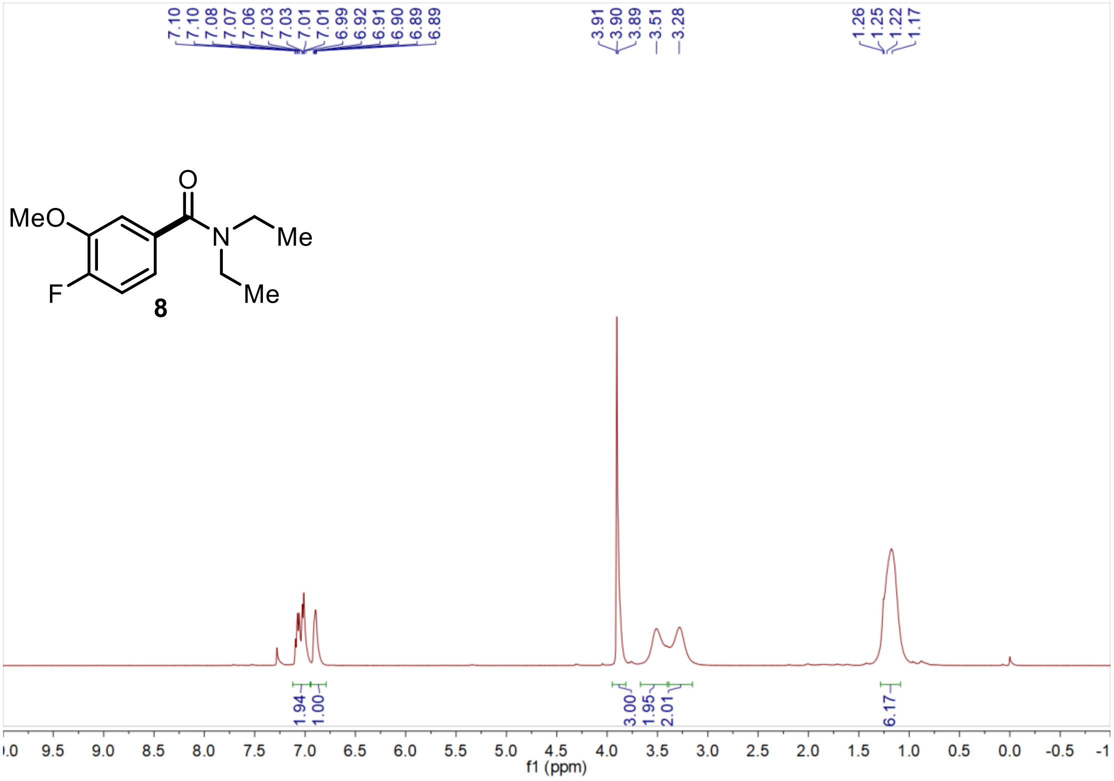

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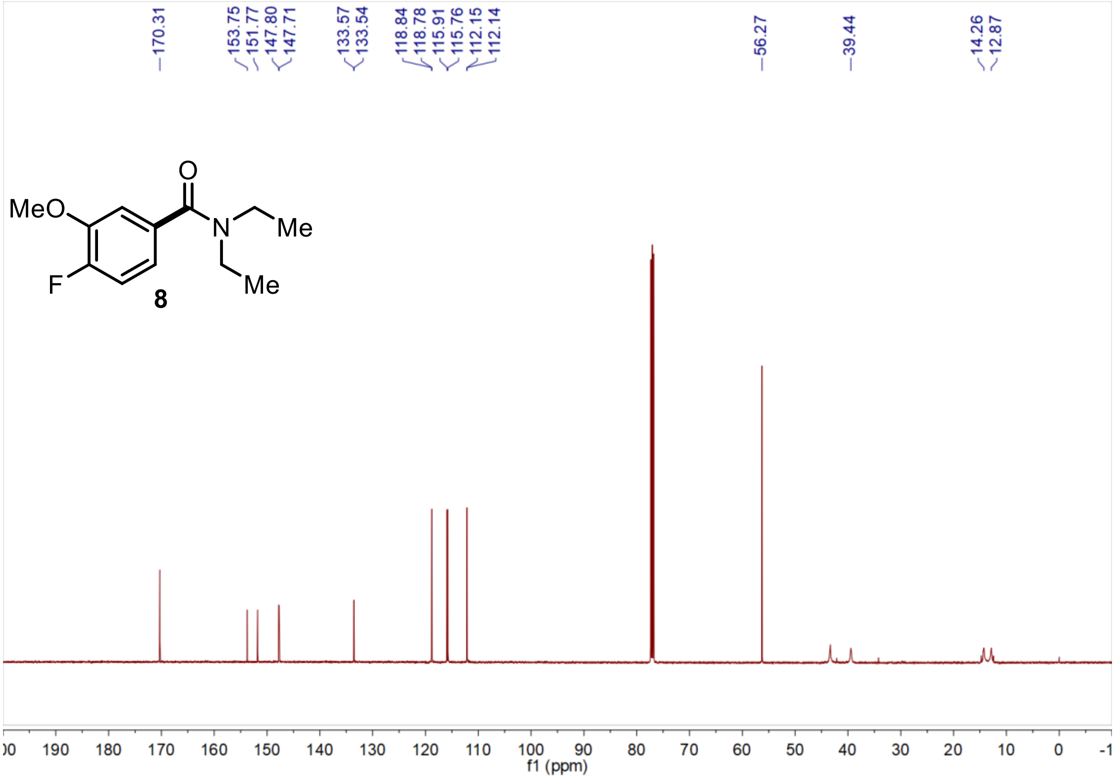
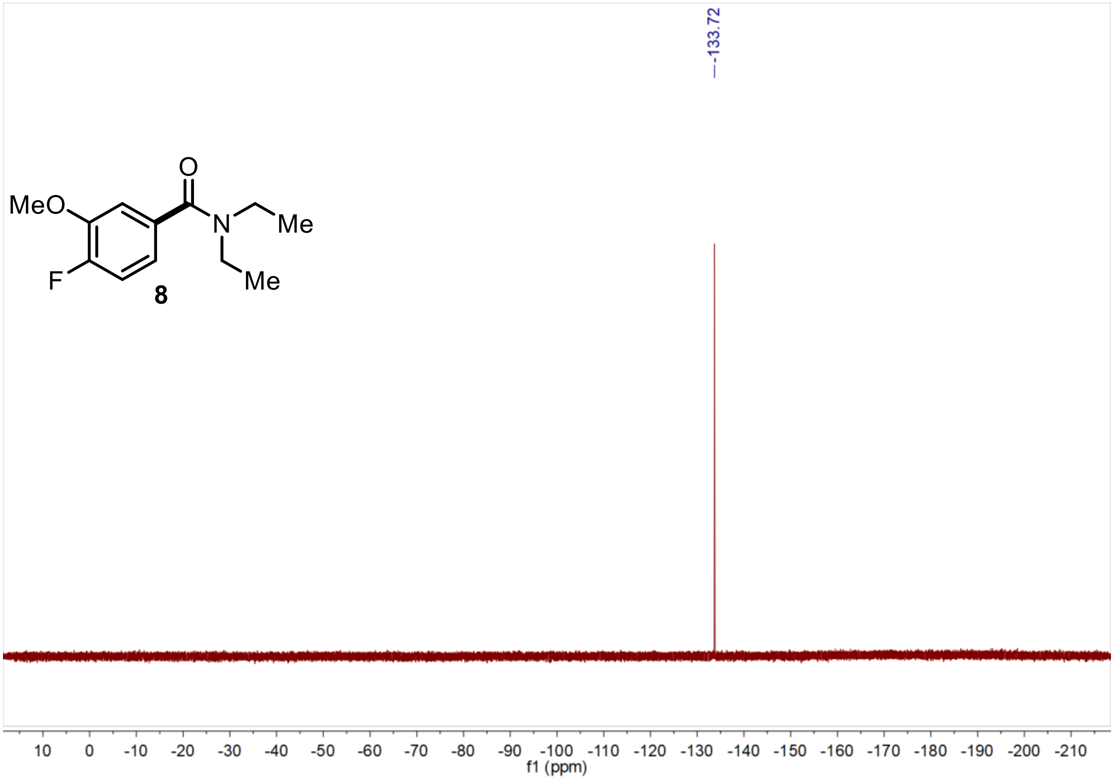


^{19}F NMR (377 MHz, Chloroform-*d*)



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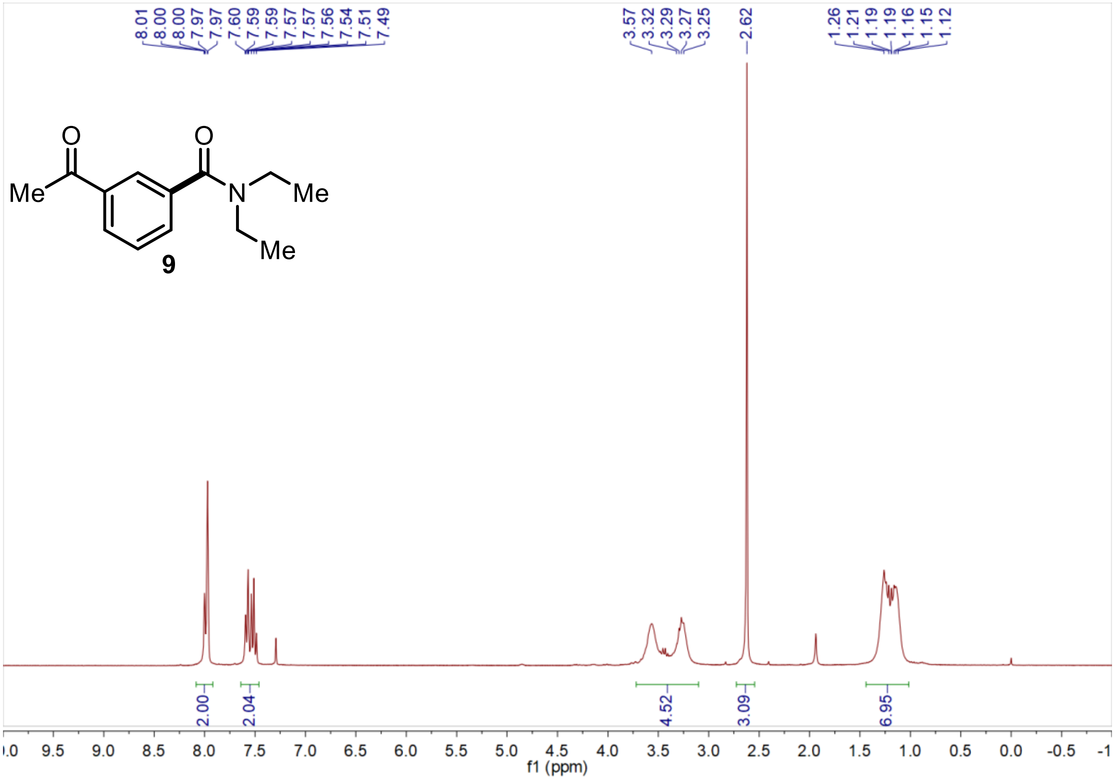

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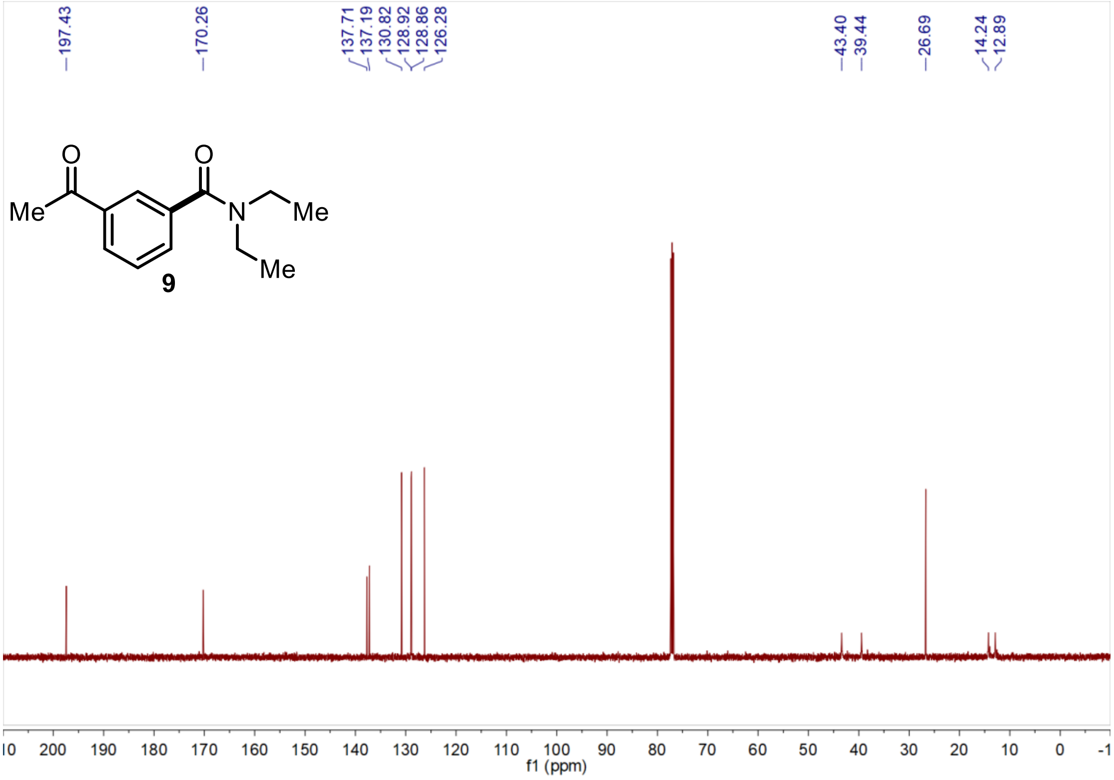

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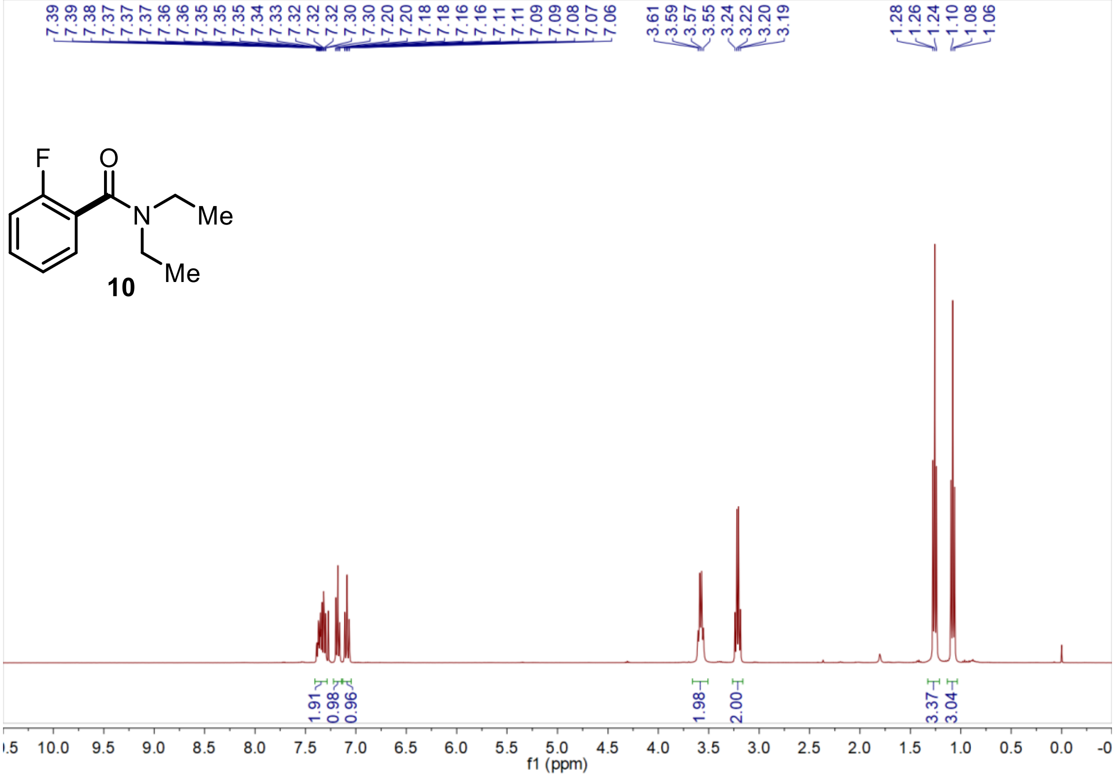

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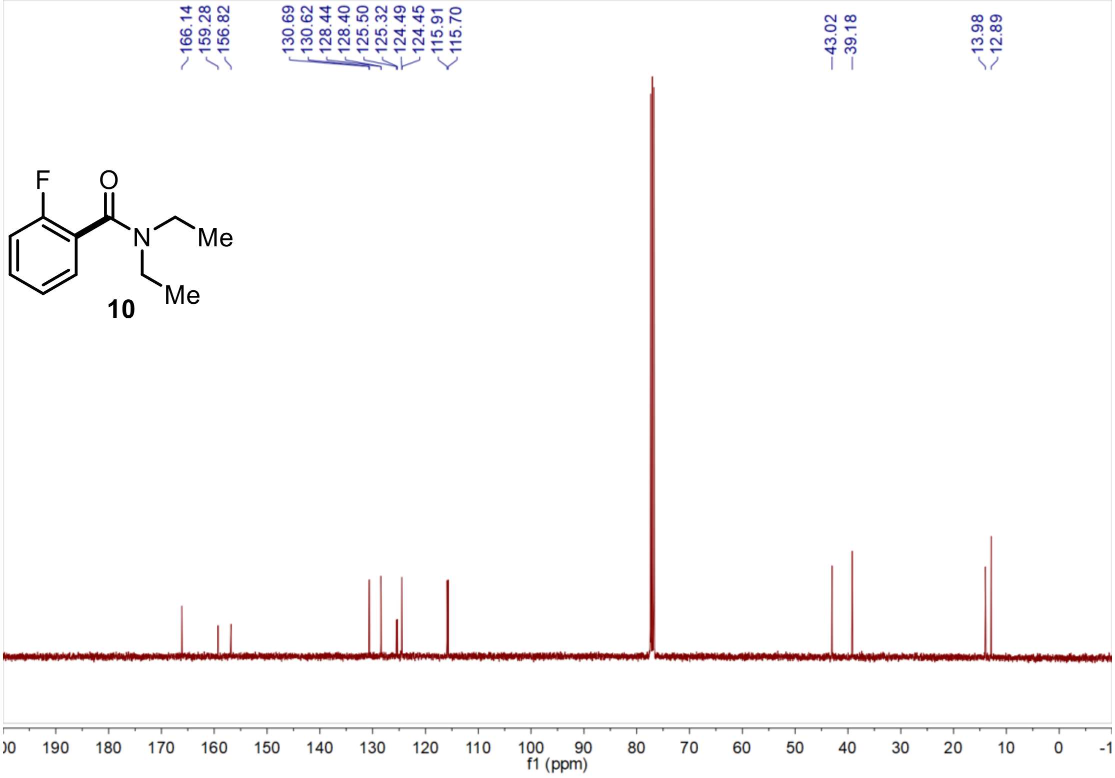

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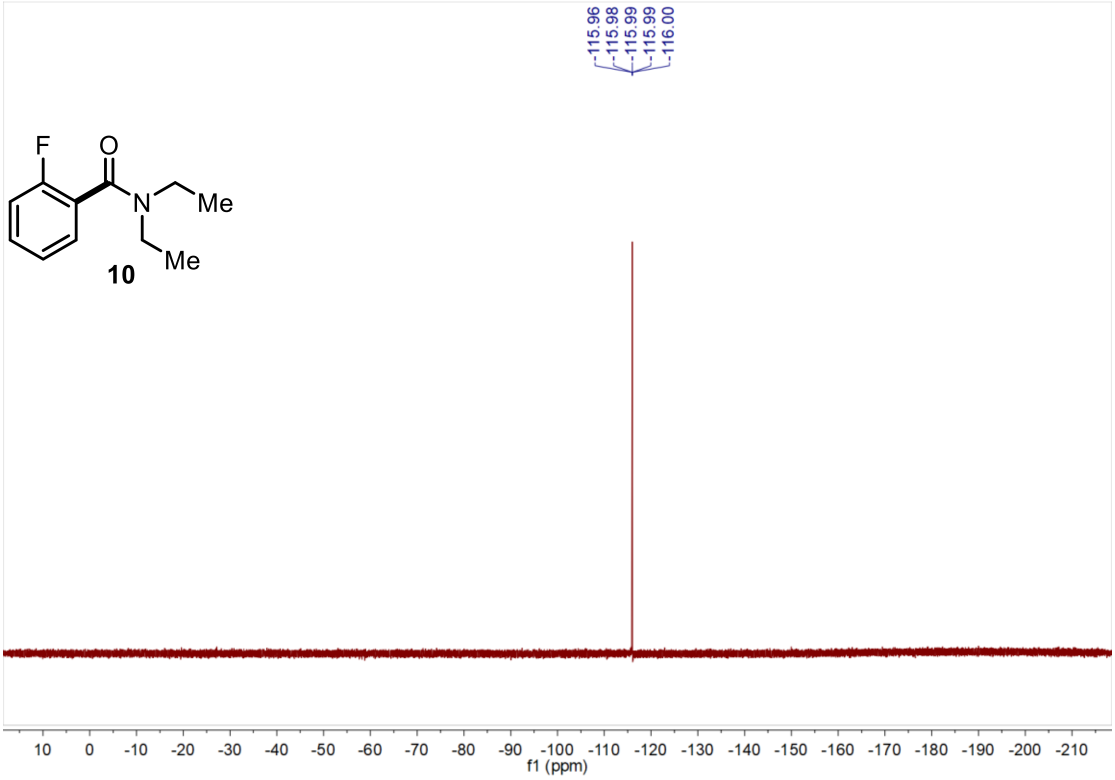

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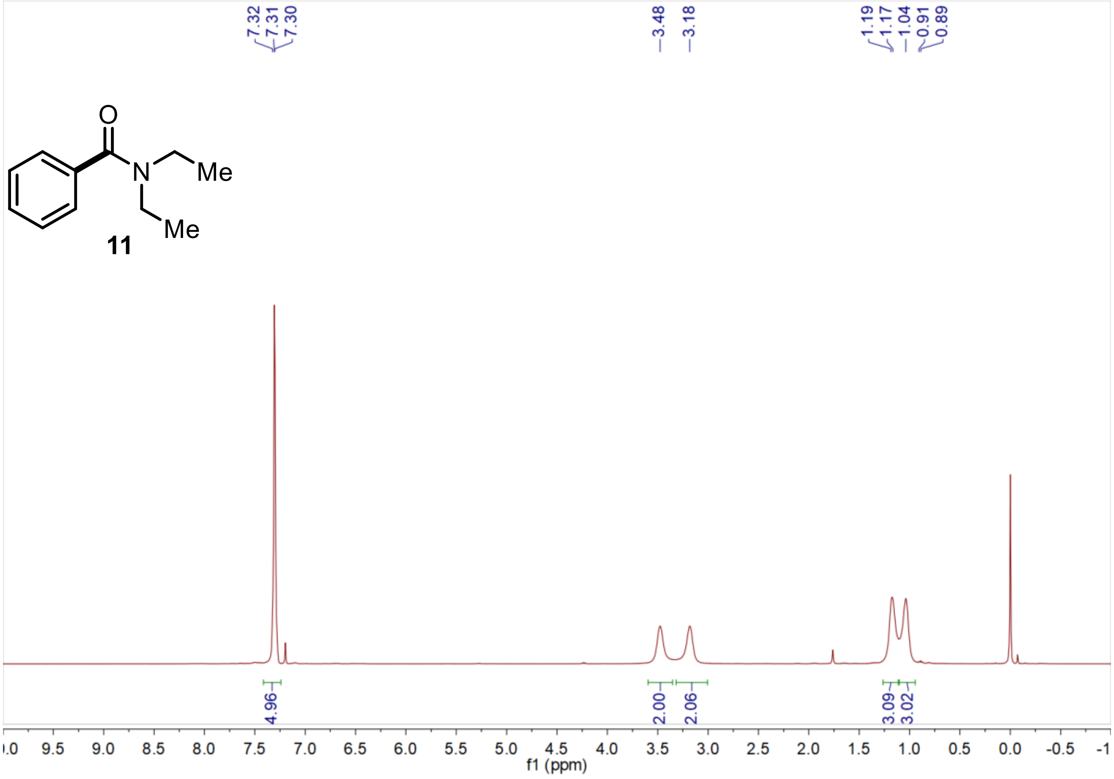

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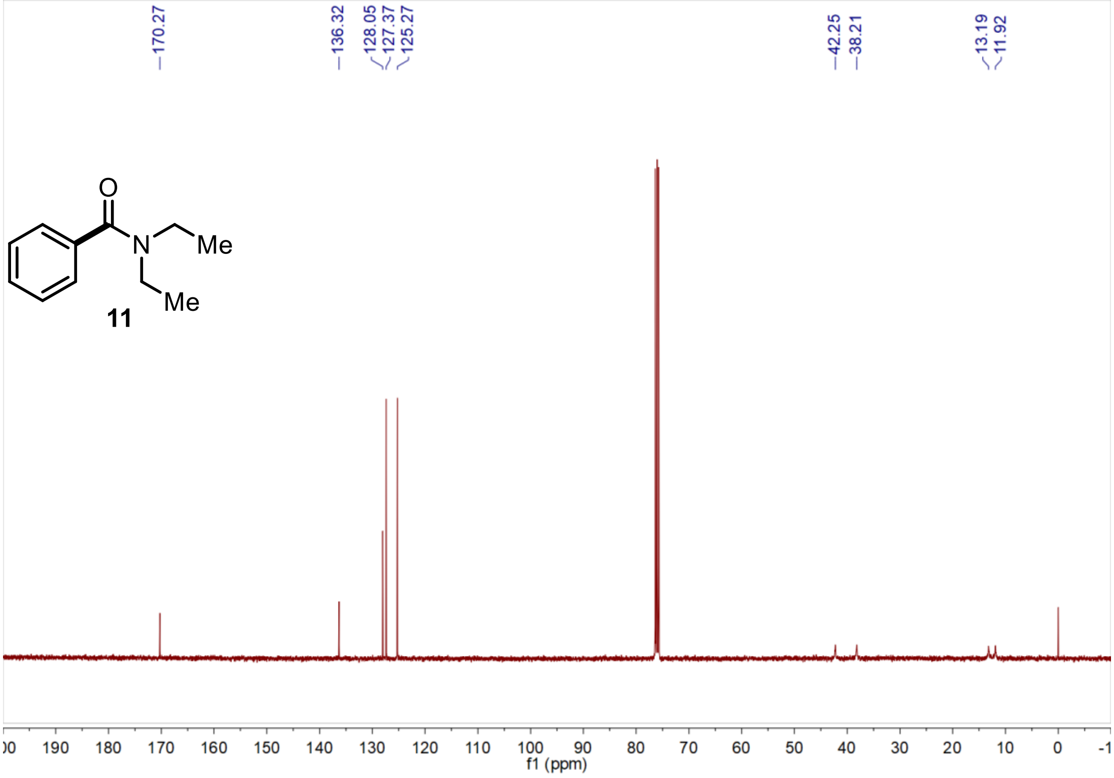

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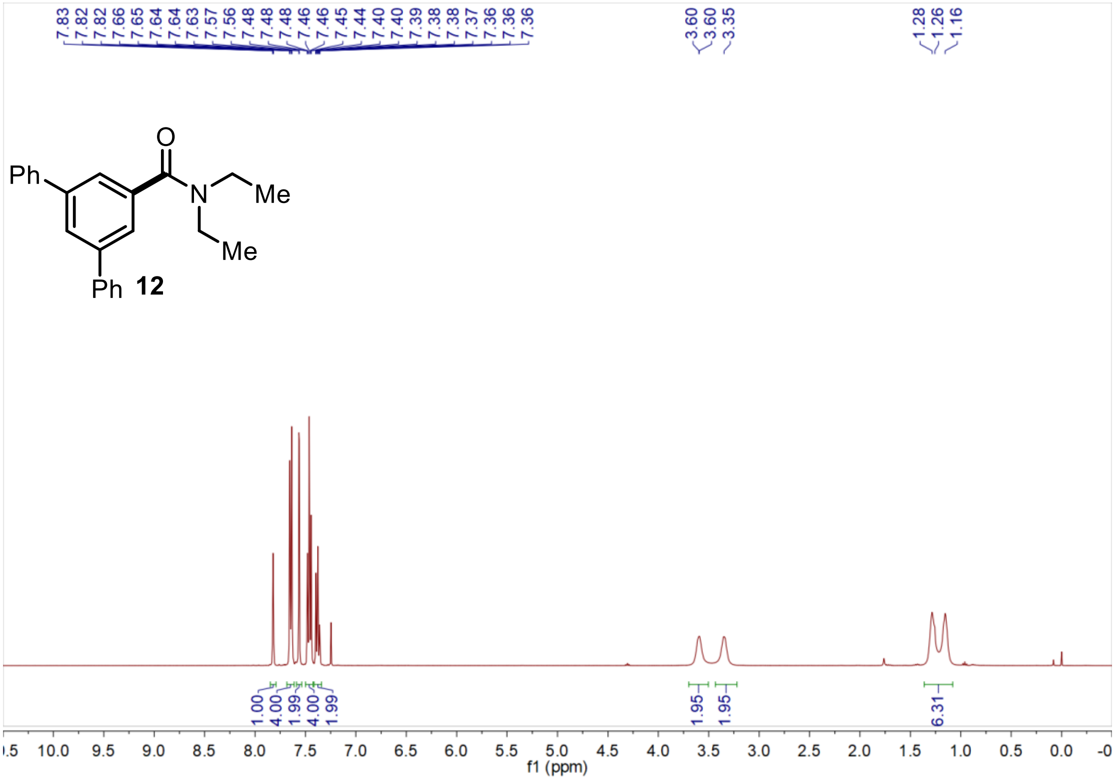

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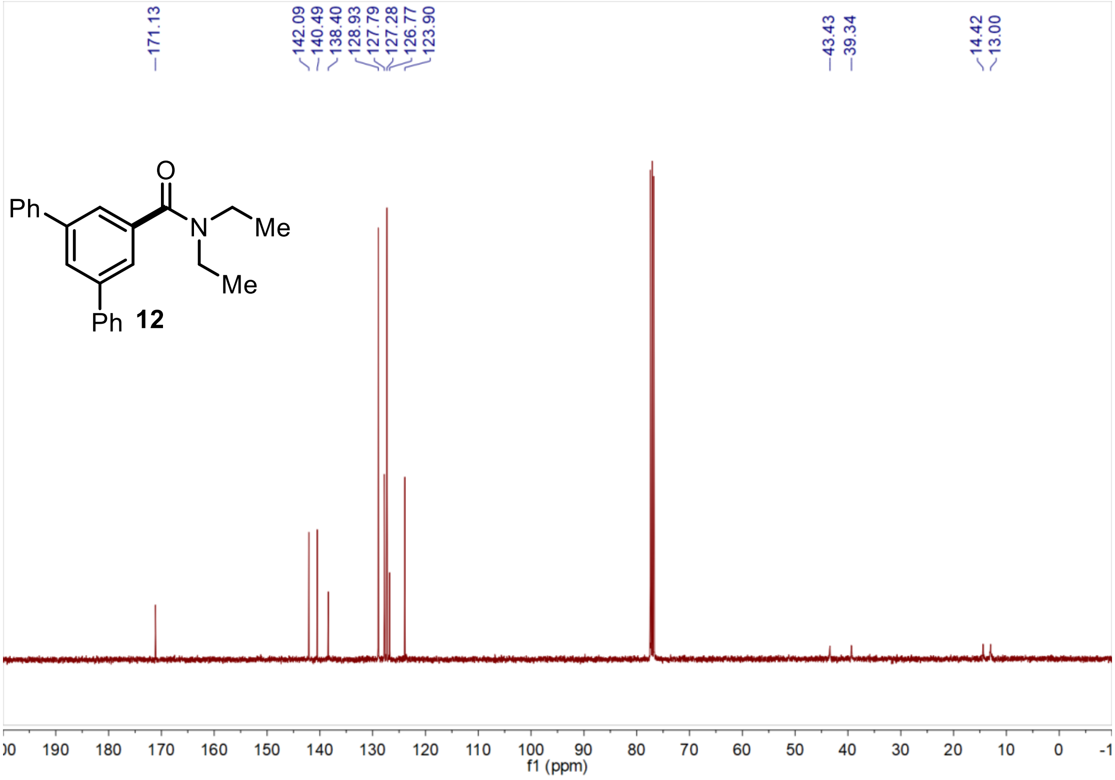

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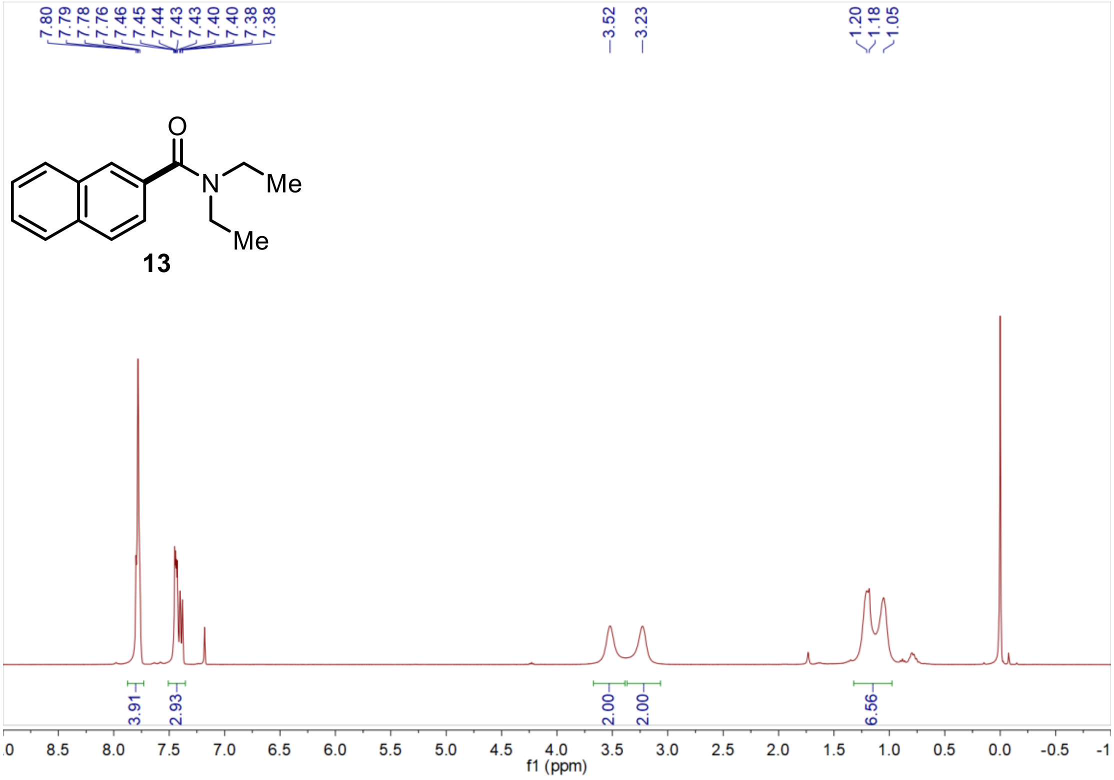

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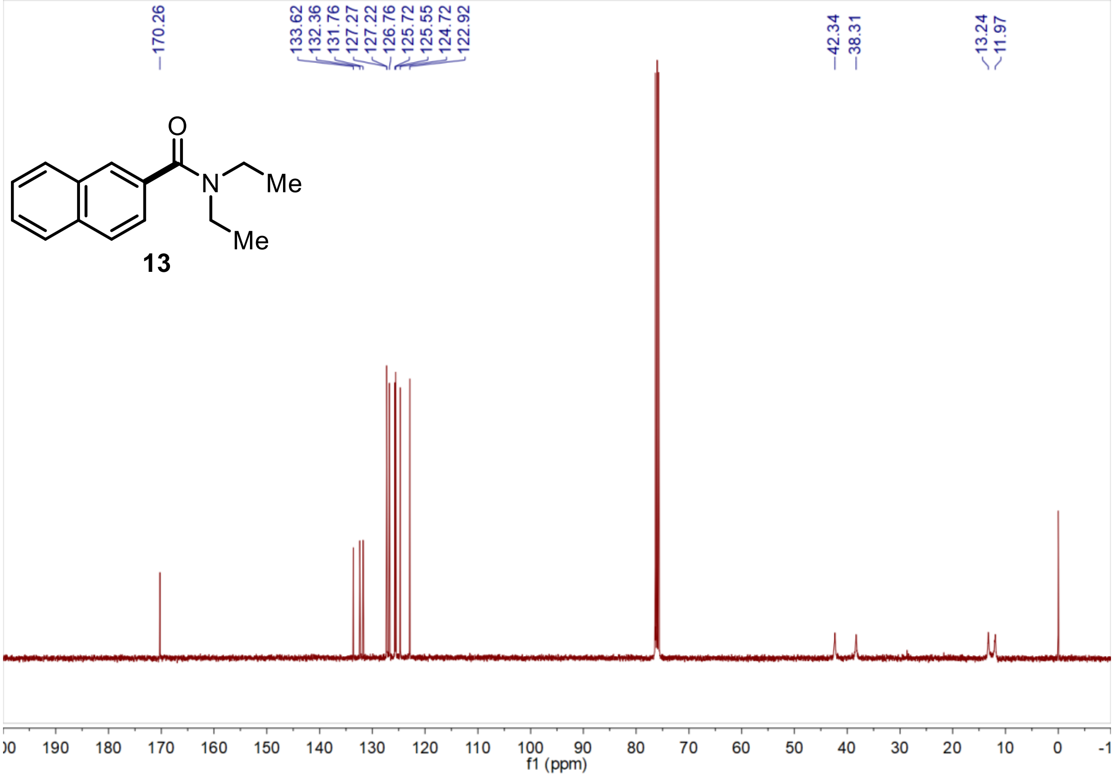

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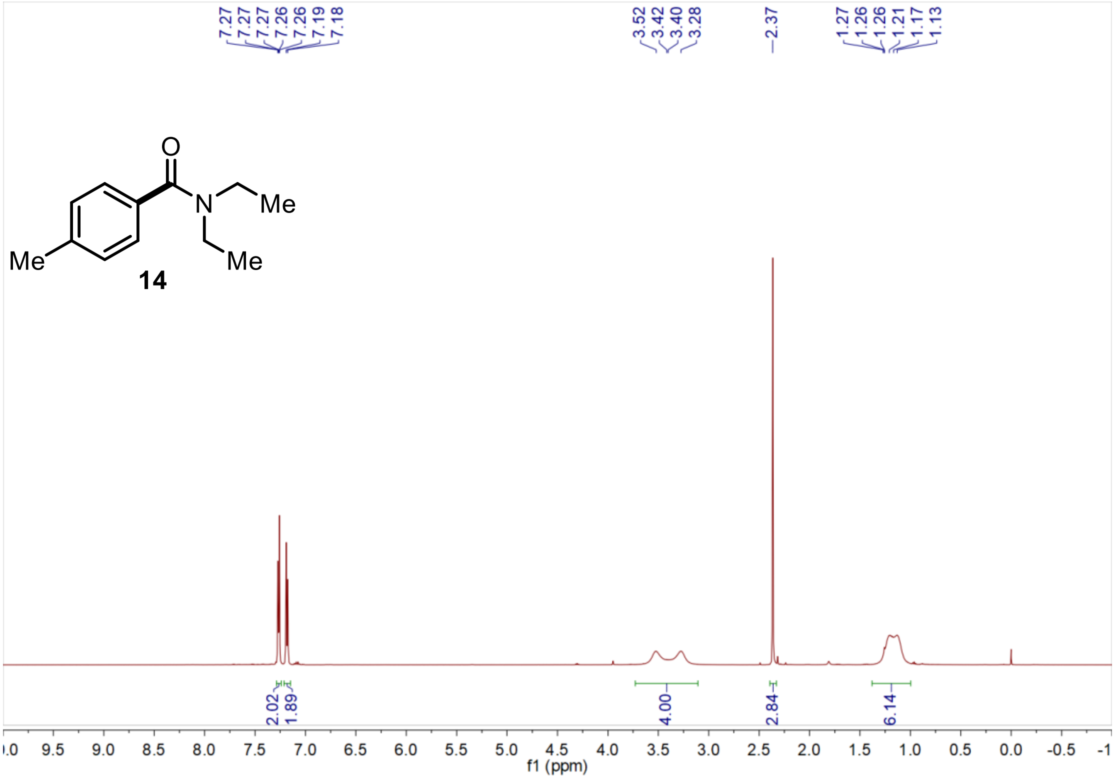
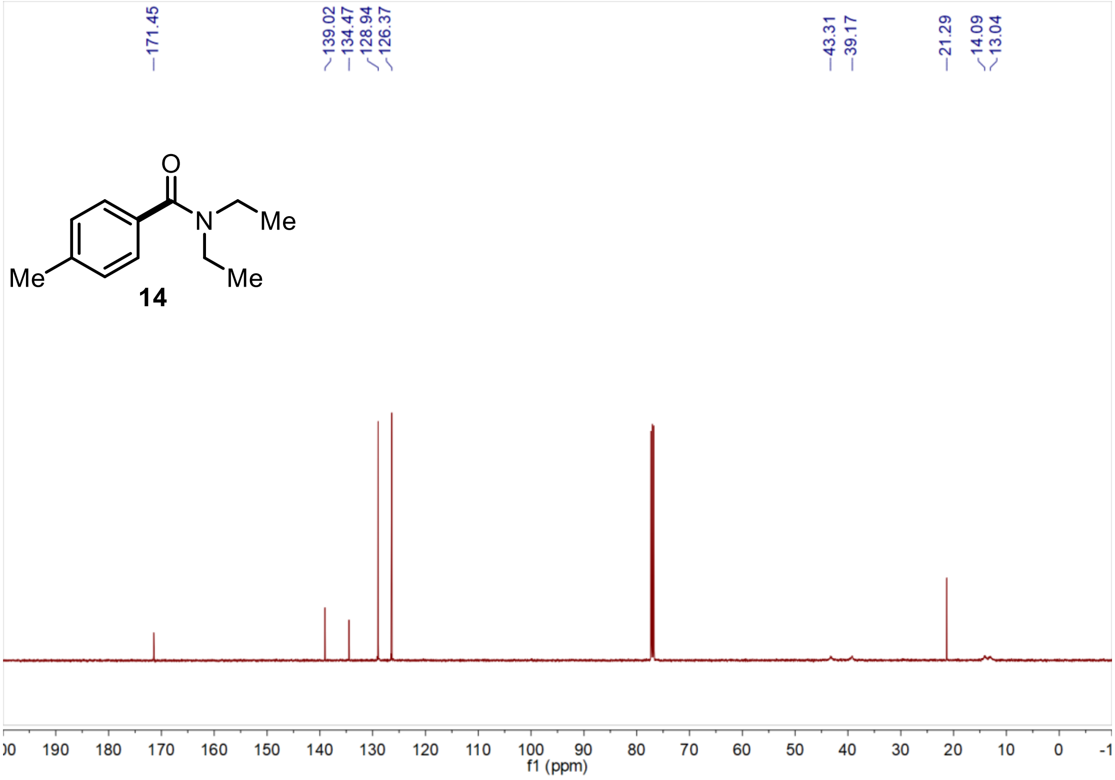


^{13}C NMR (126 MHz, Chloroform-*d*)



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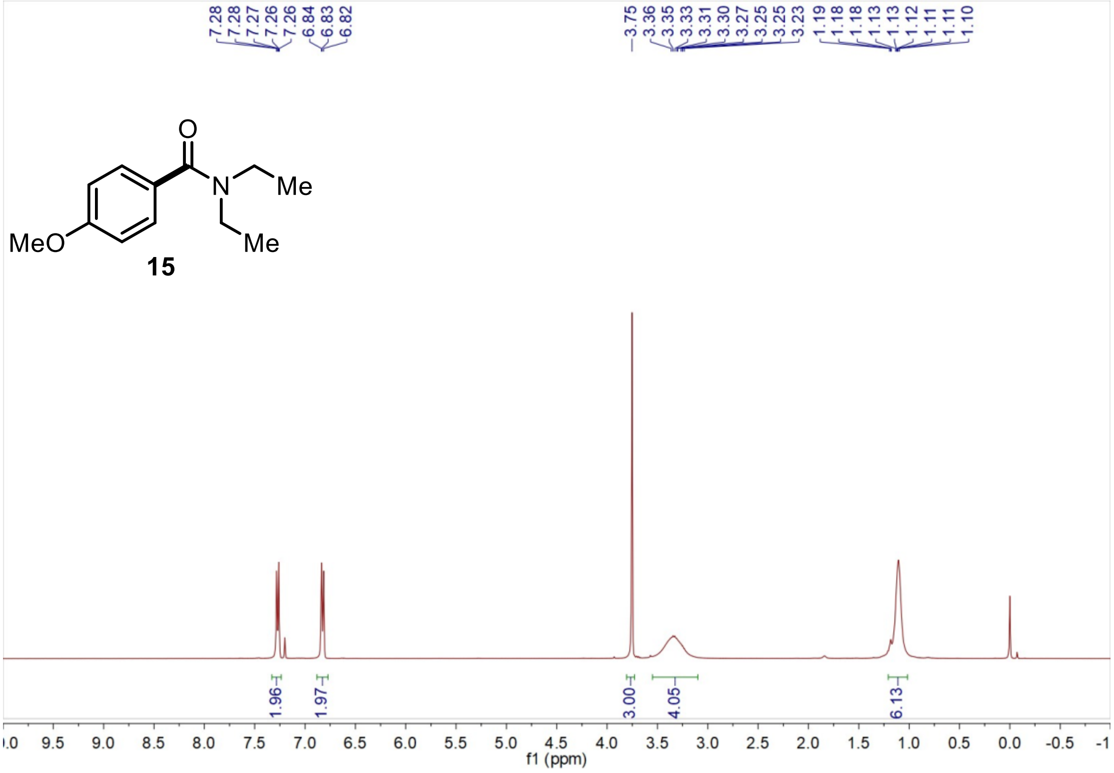

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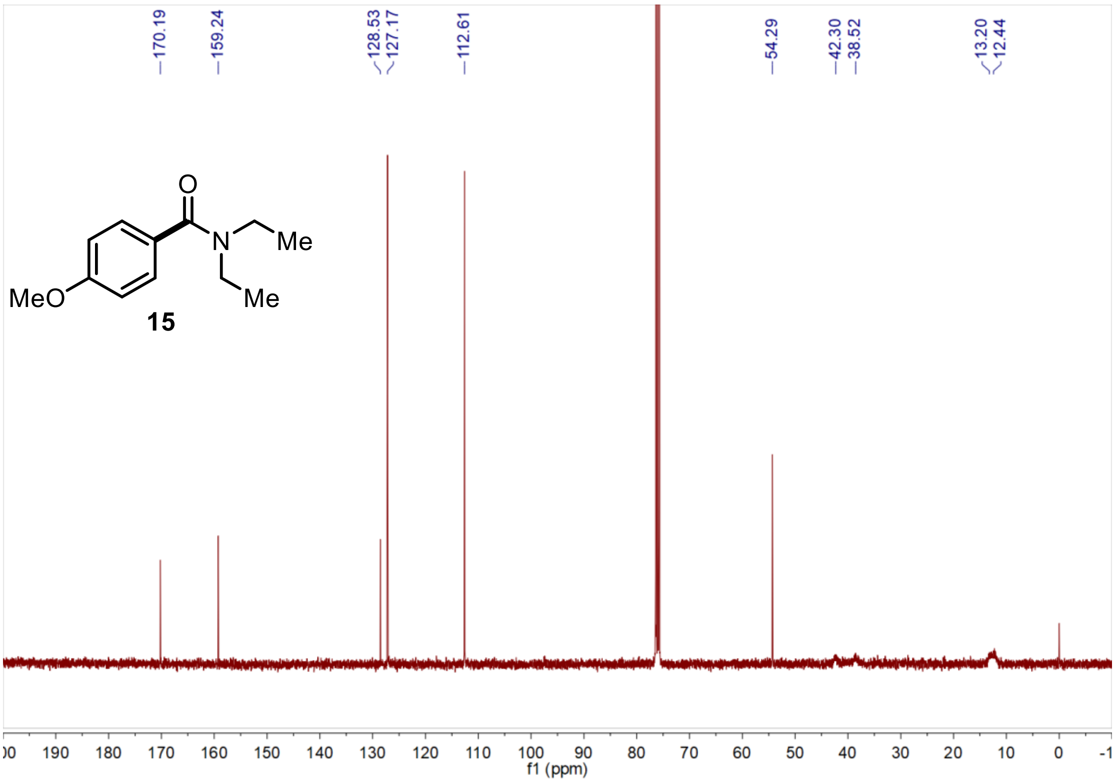

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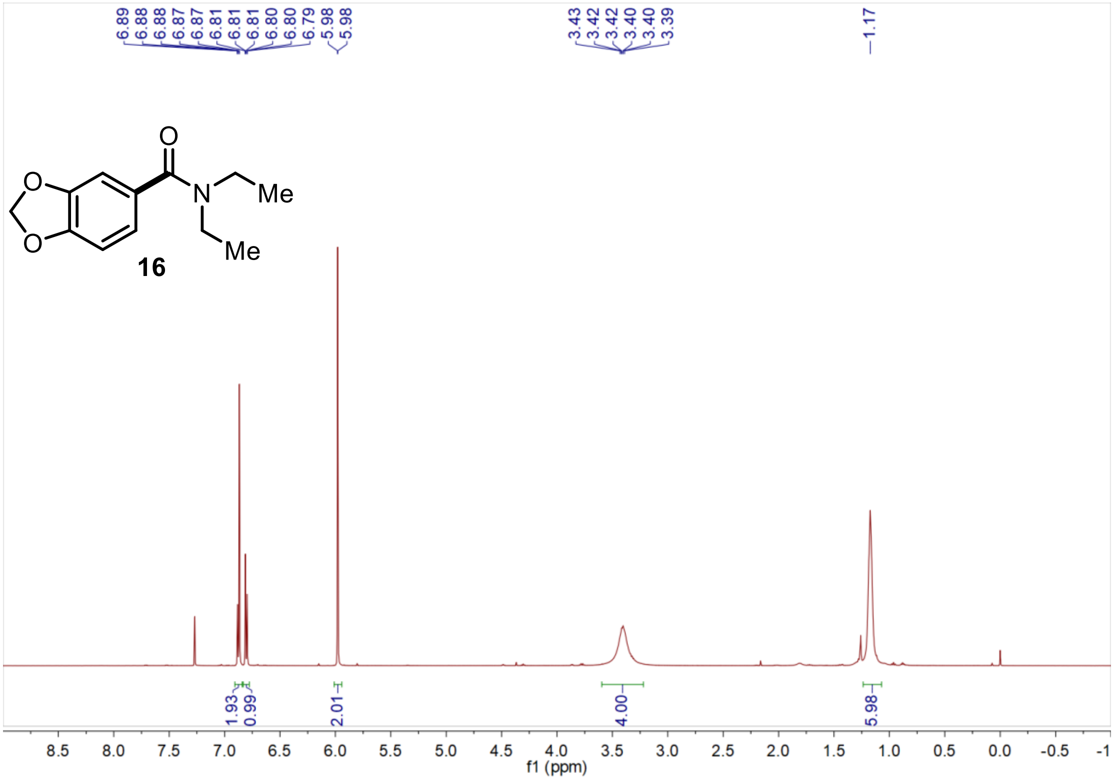

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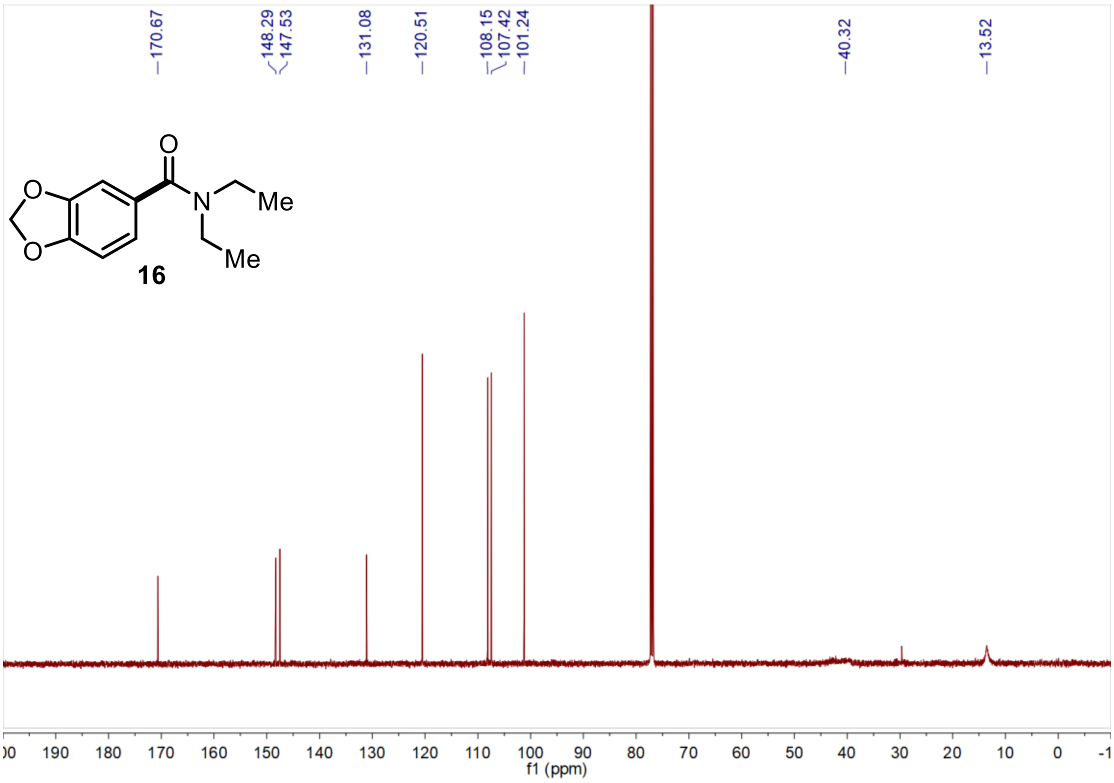

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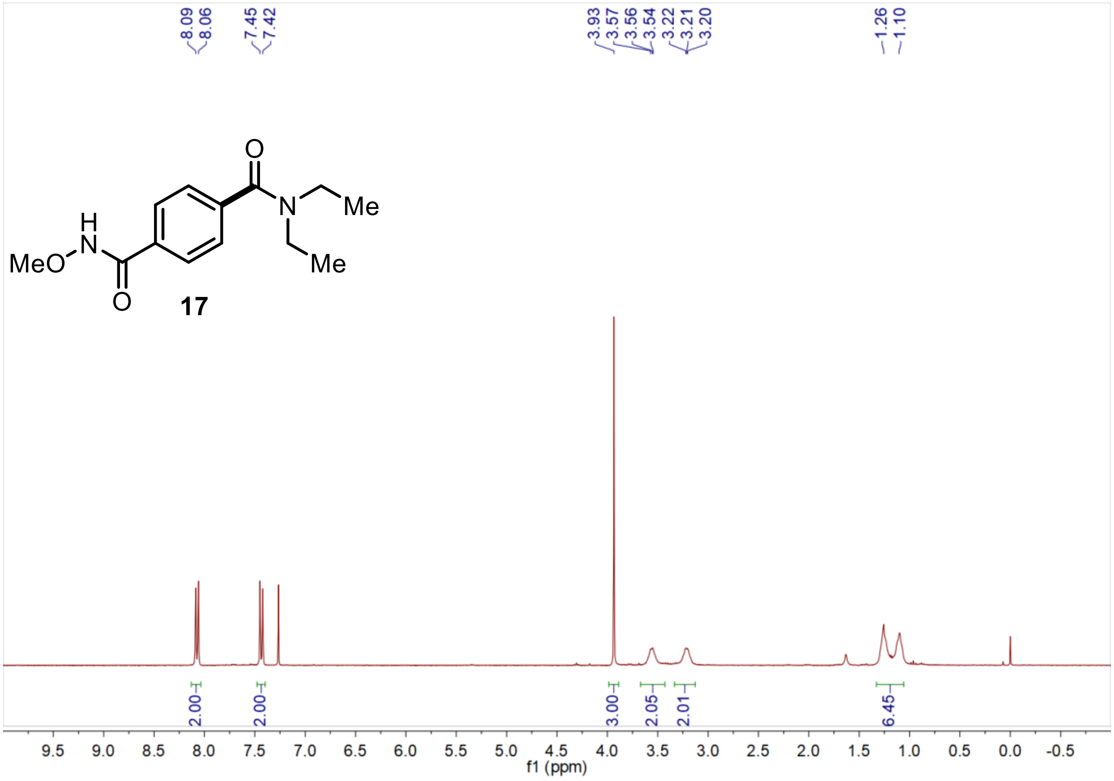

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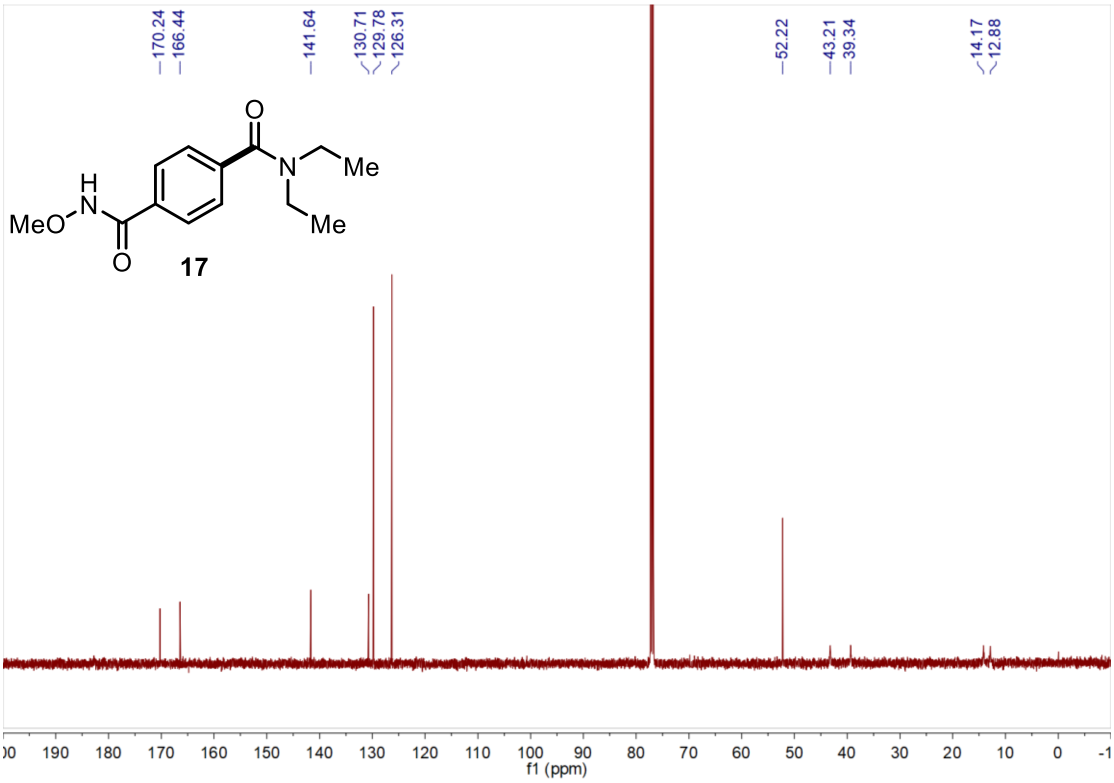

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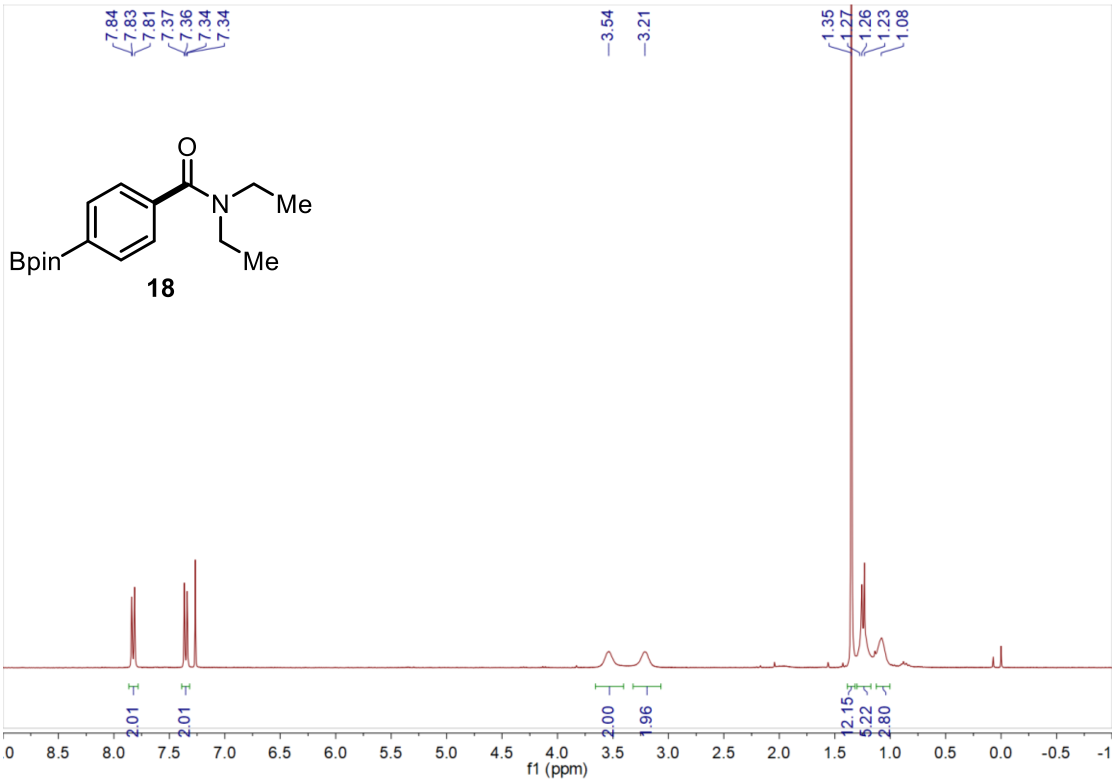

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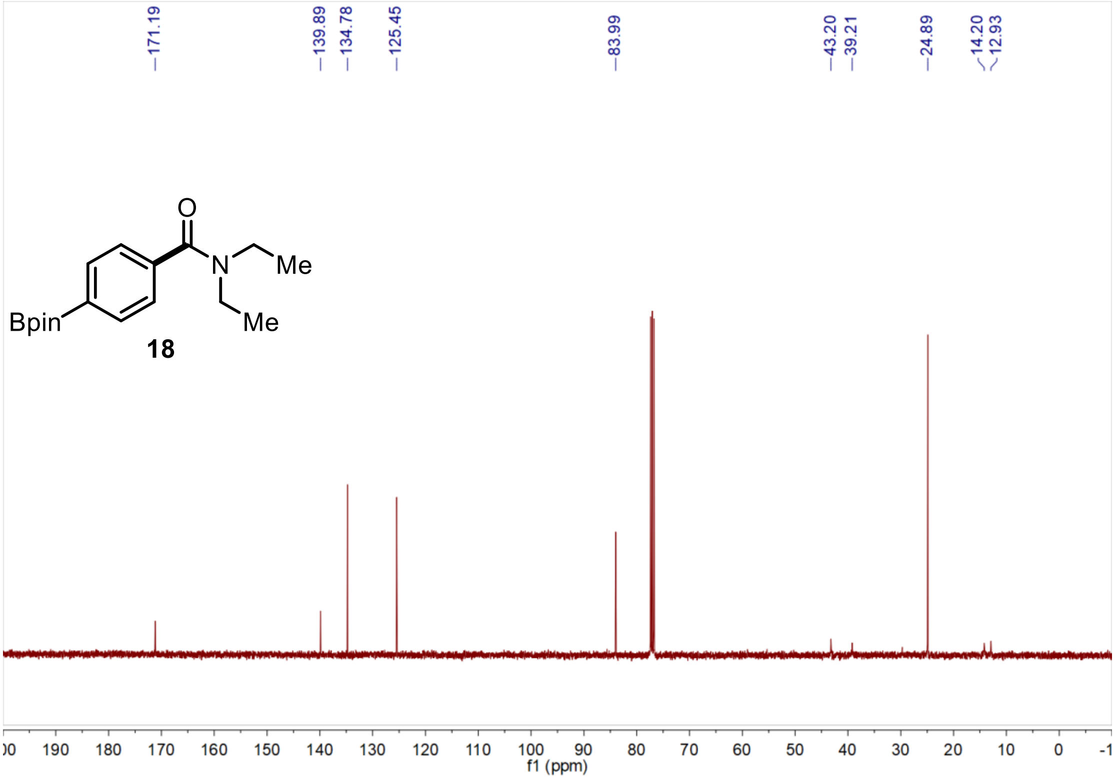

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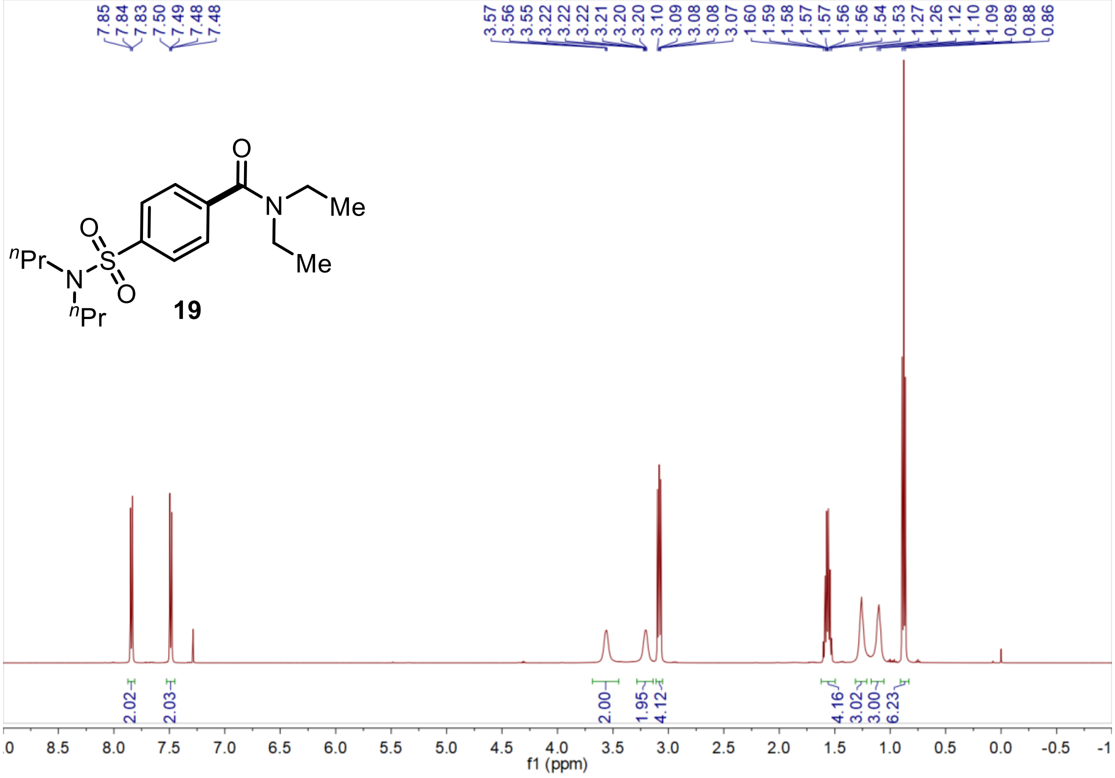

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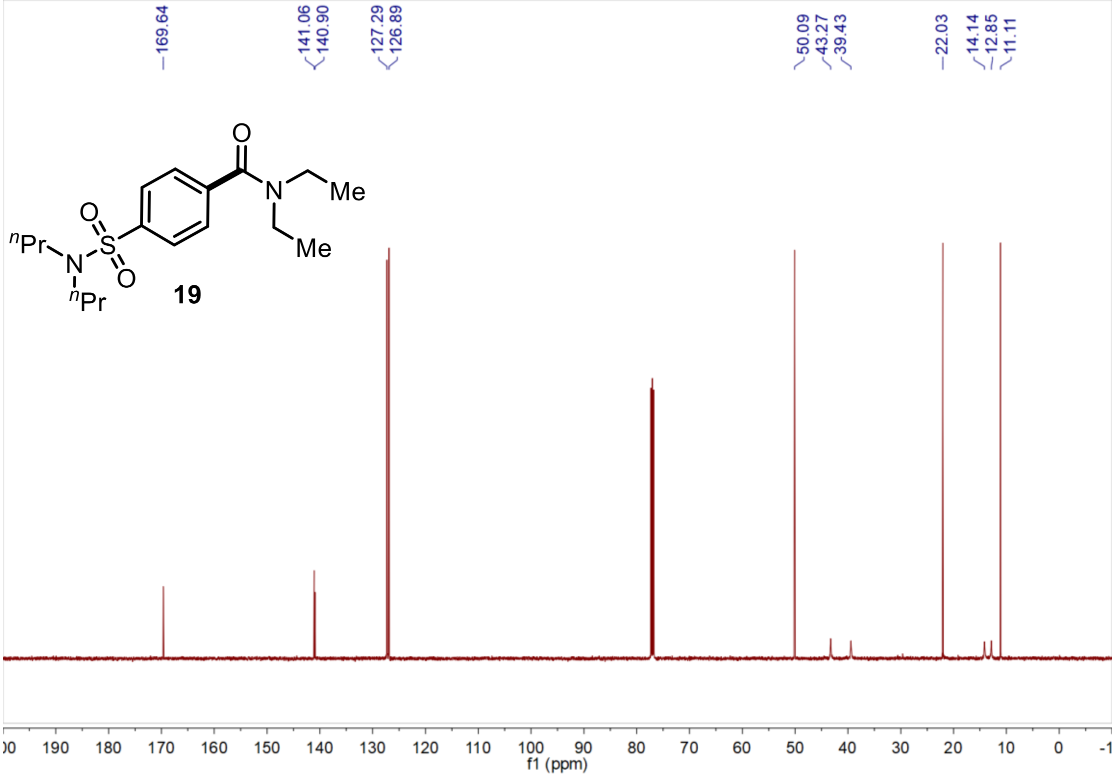

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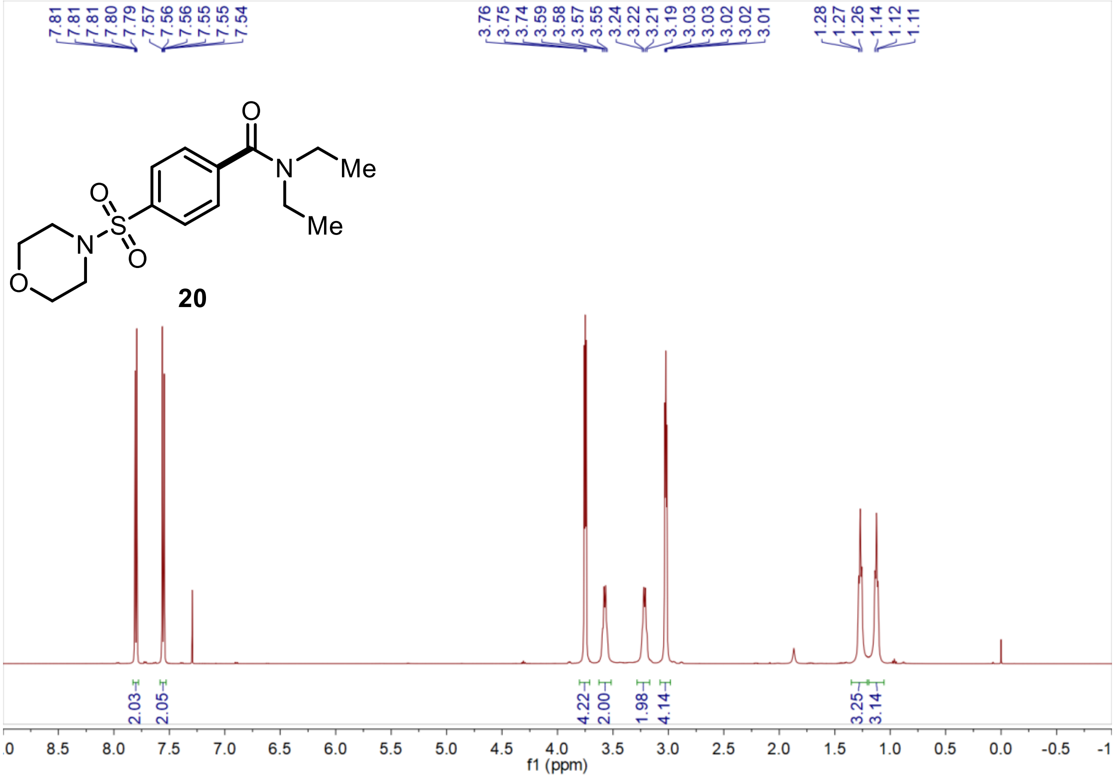

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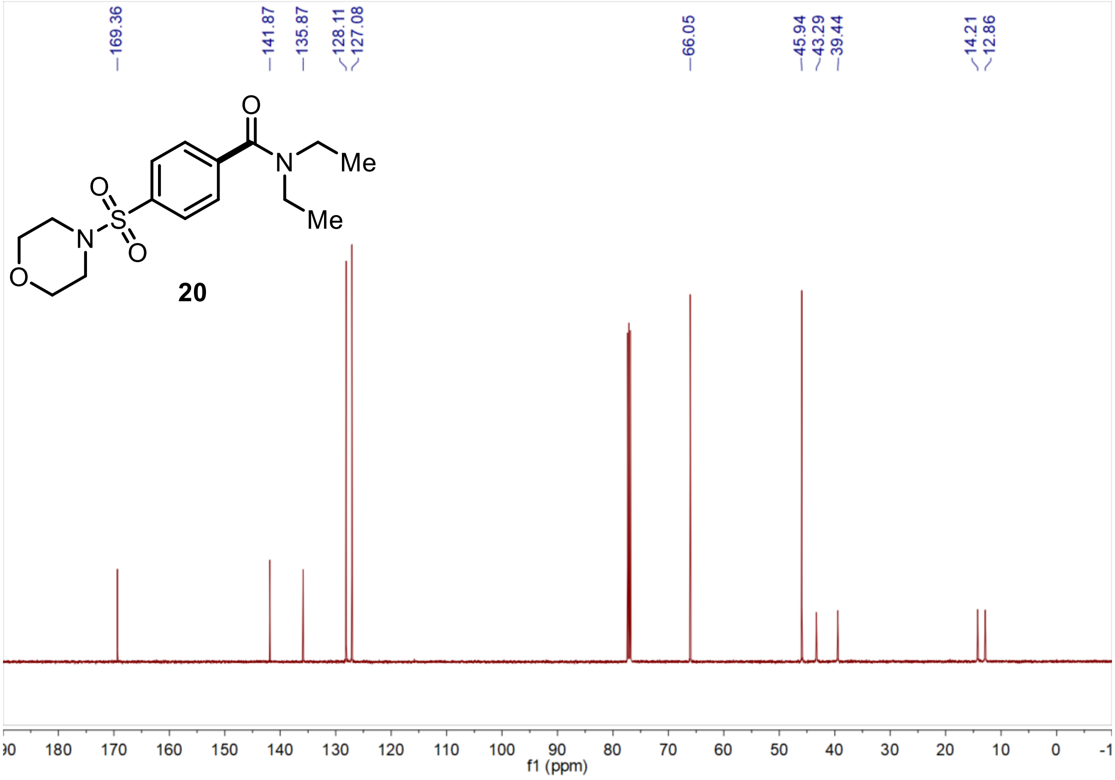

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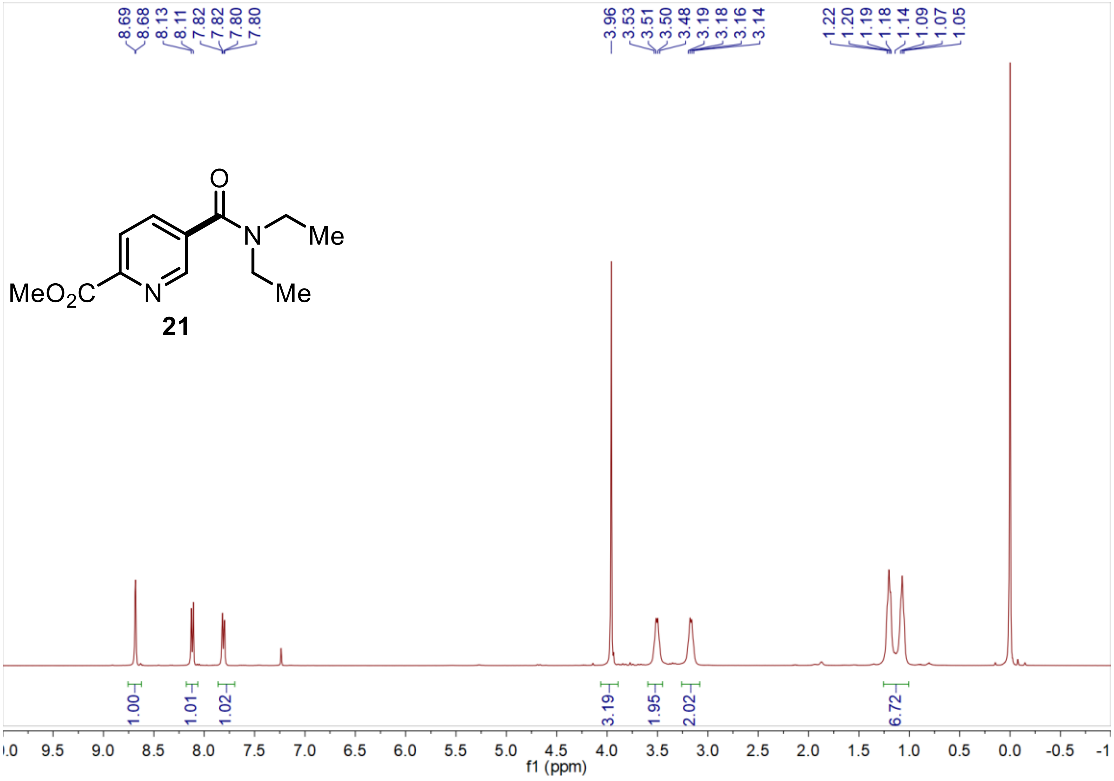

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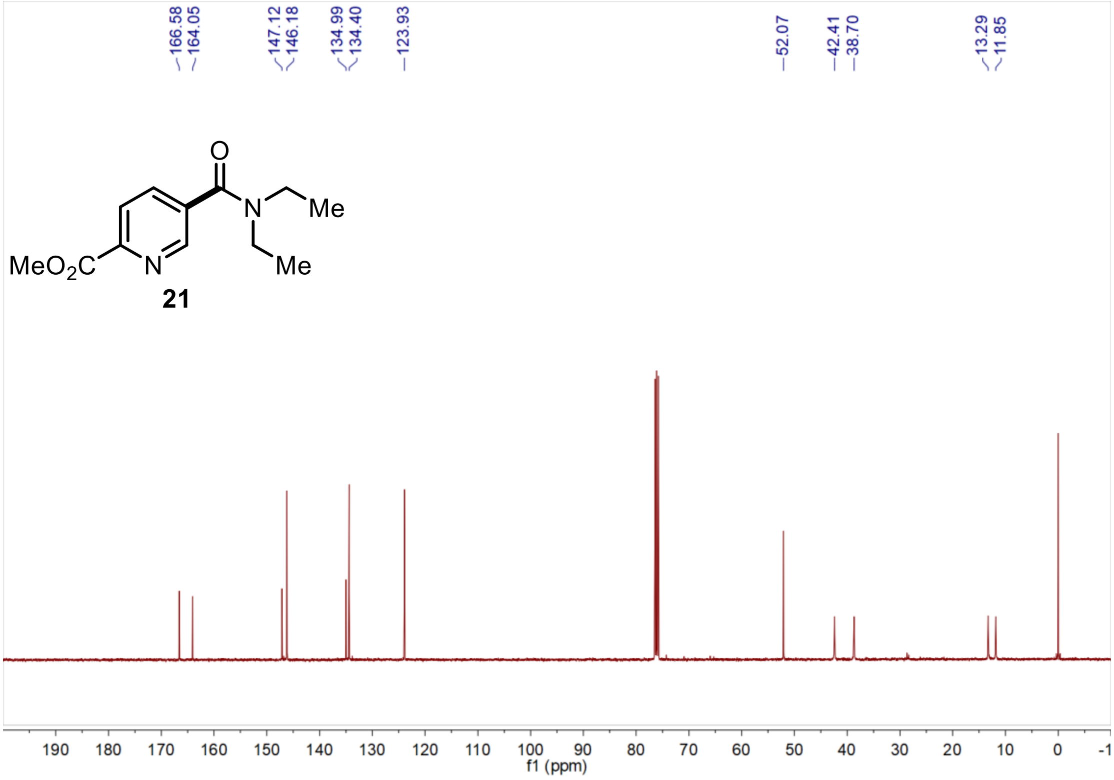

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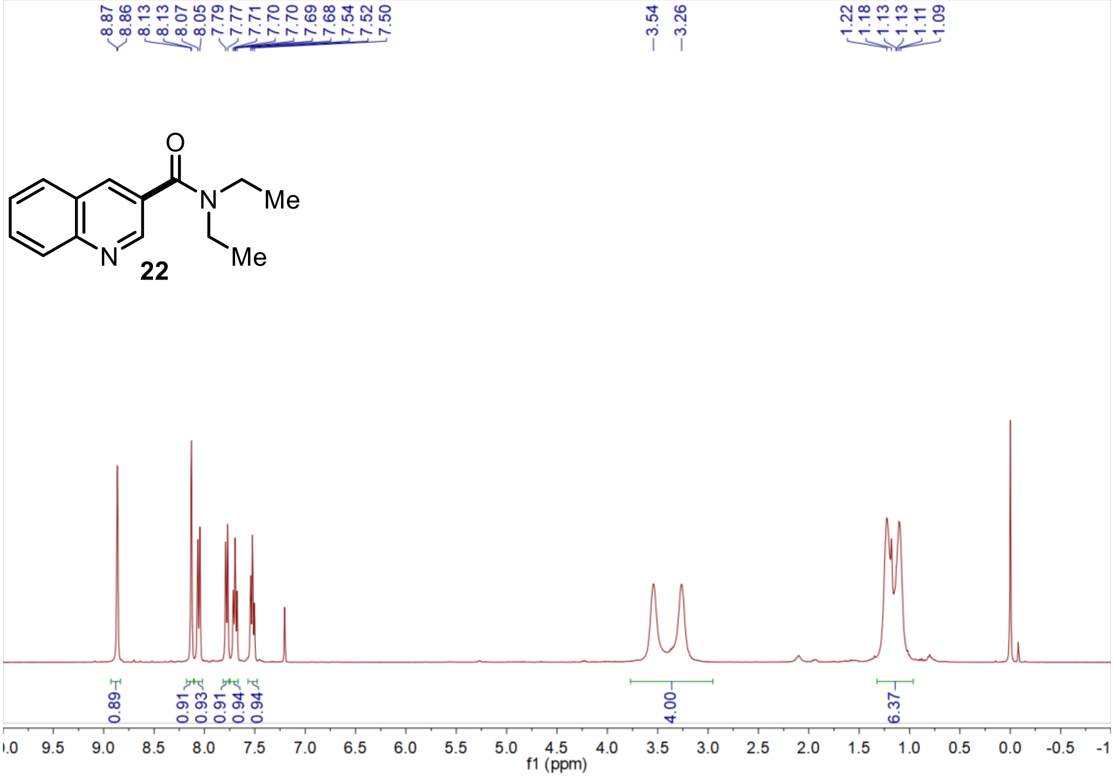

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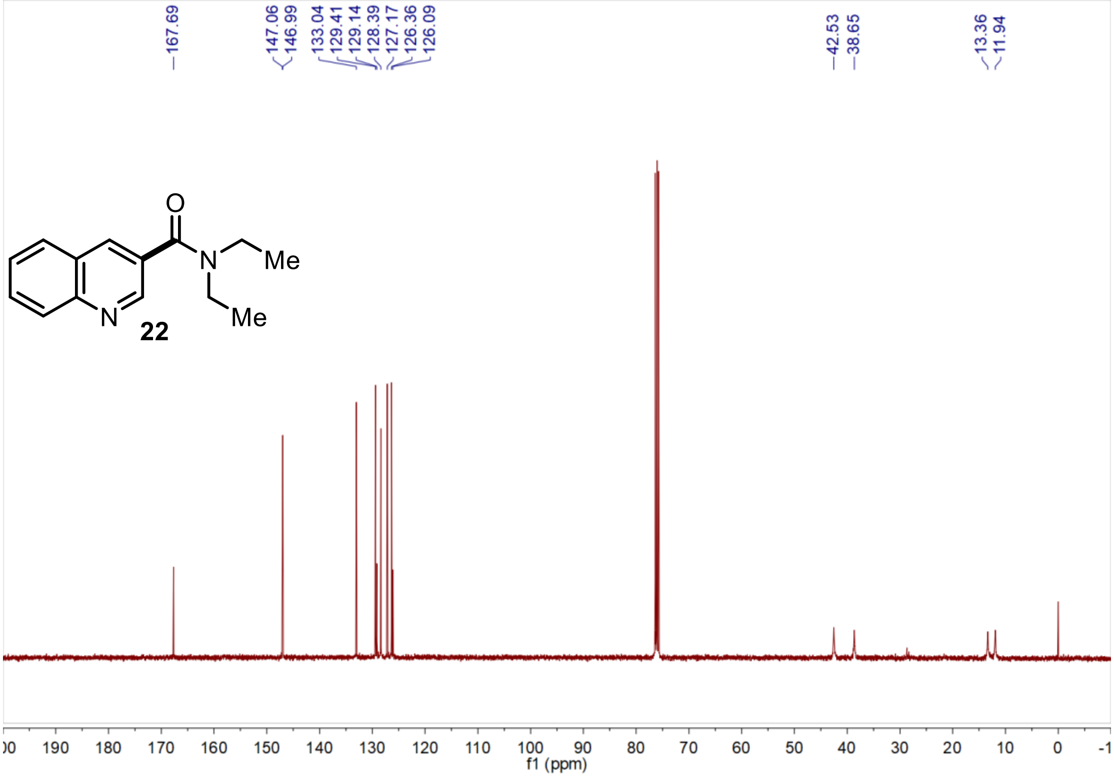

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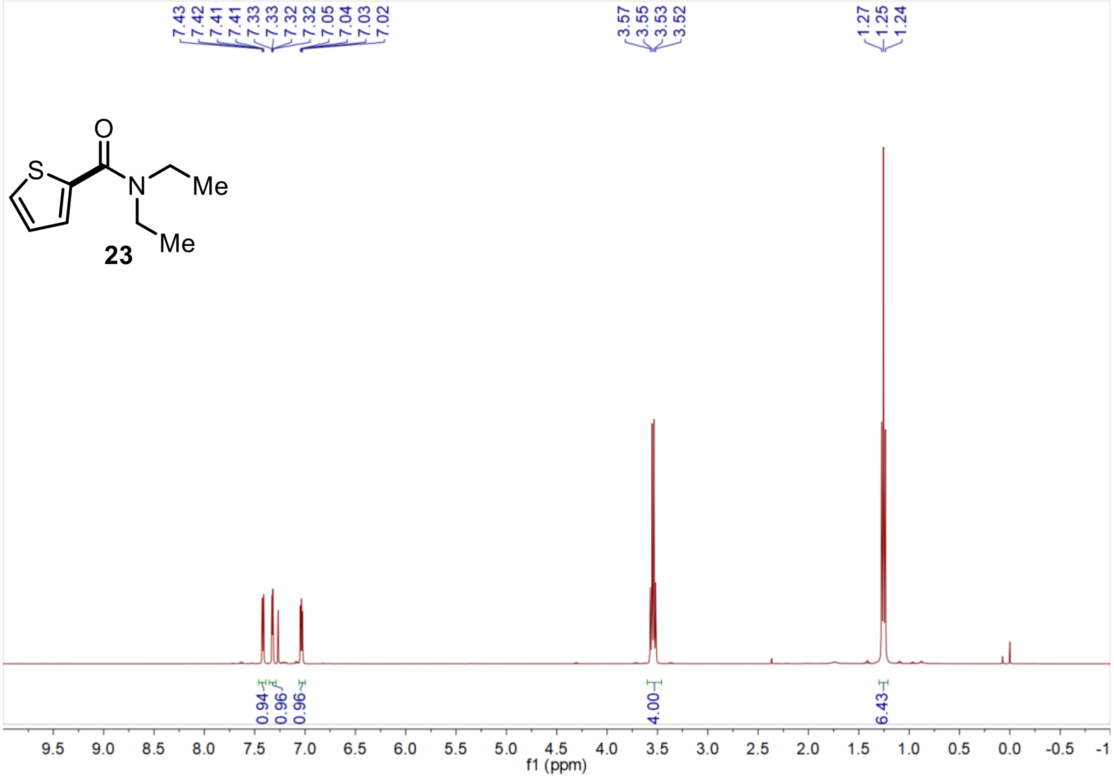

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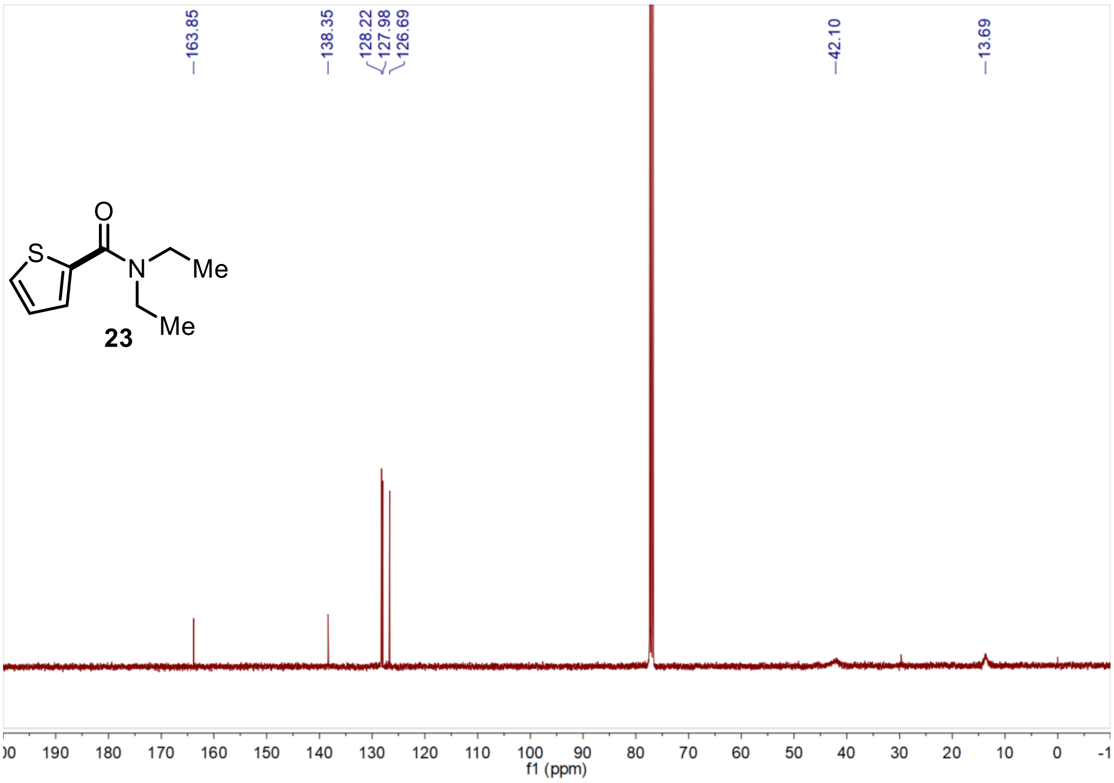

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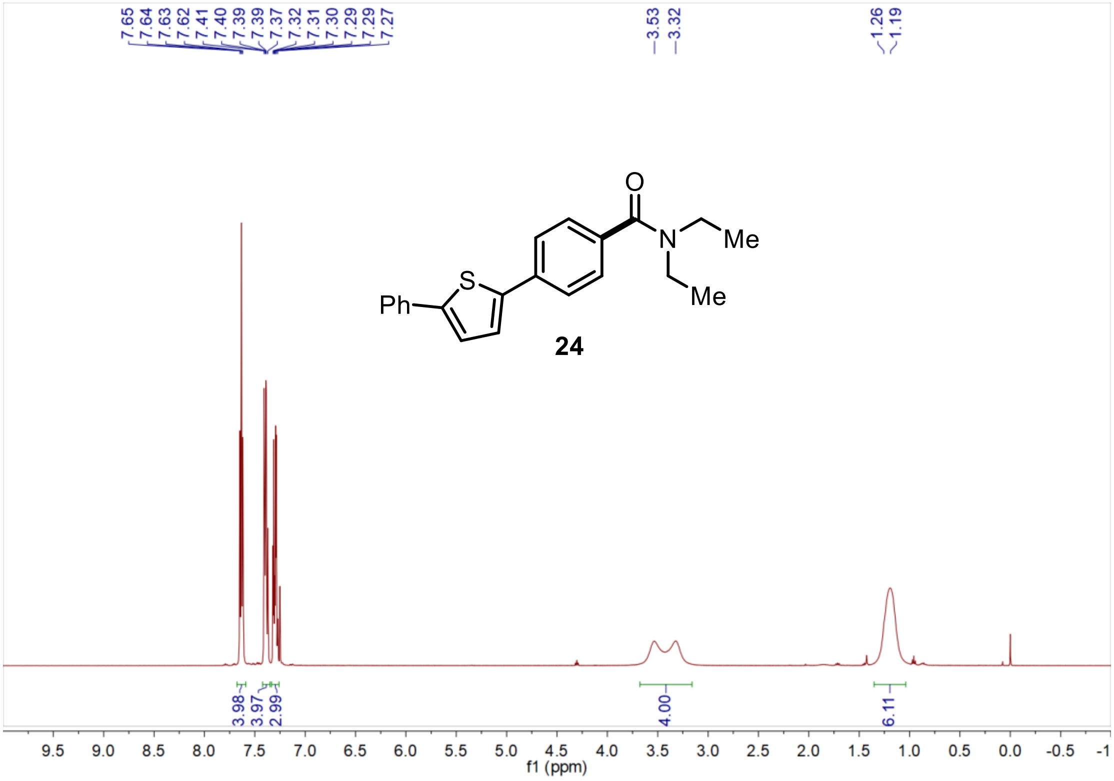
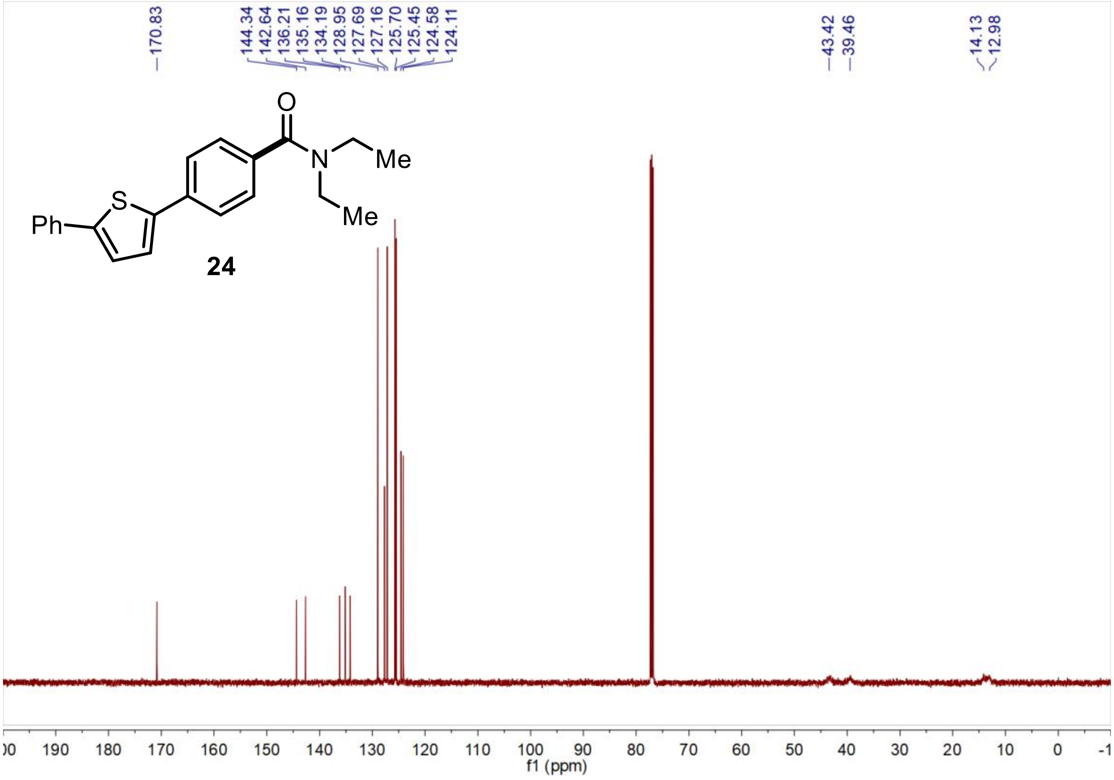
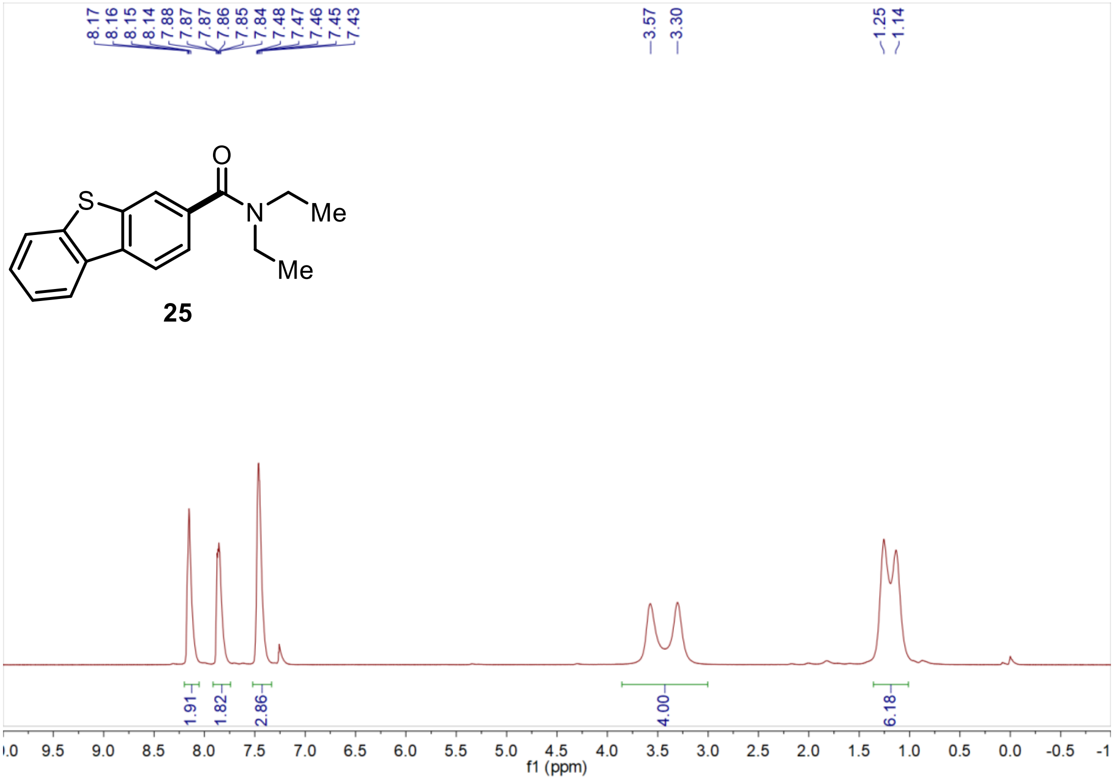


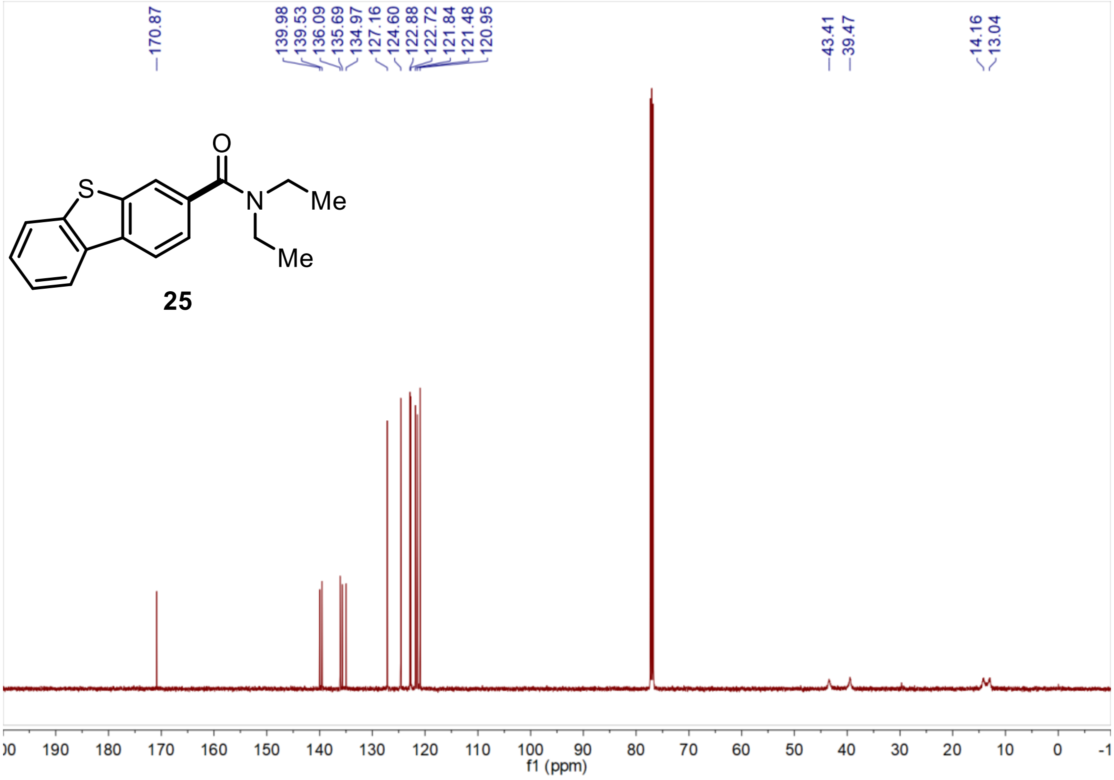
^{13}C NMR (126 MHz, Chloroform-*d*)



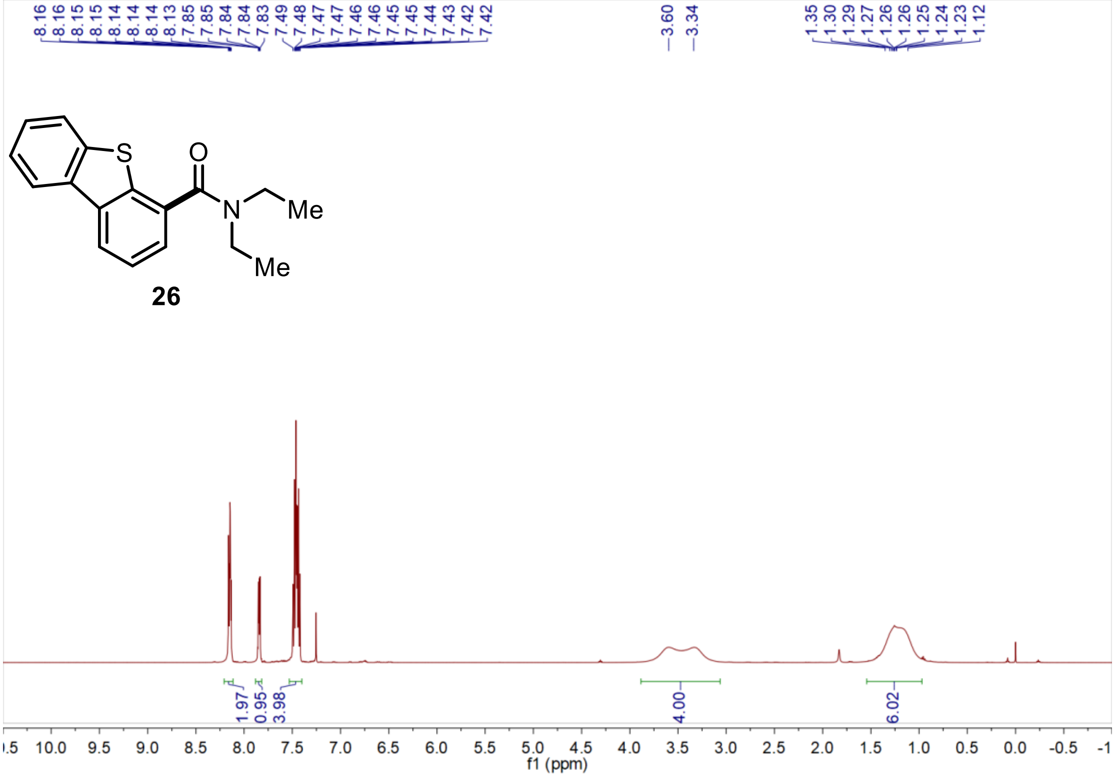
^{1}H NMR (500 MHz, Chloroform-*d*)



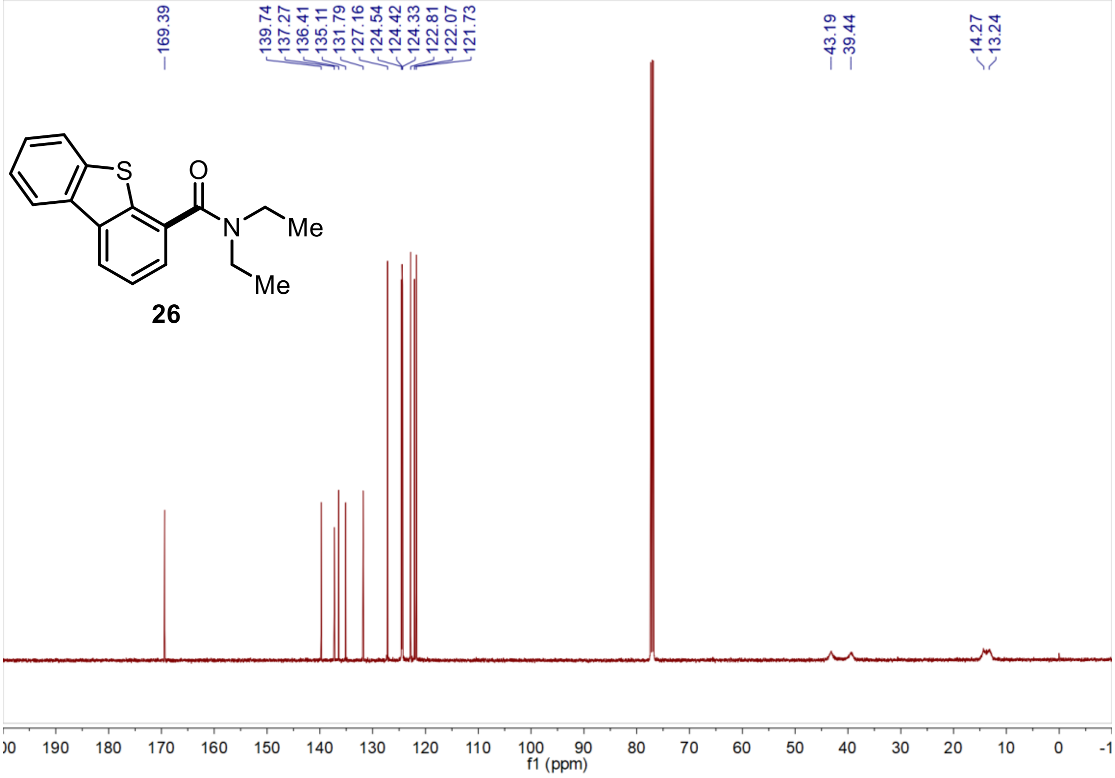
^{13}C NMR (126 MHz, Chloroform-*d*)



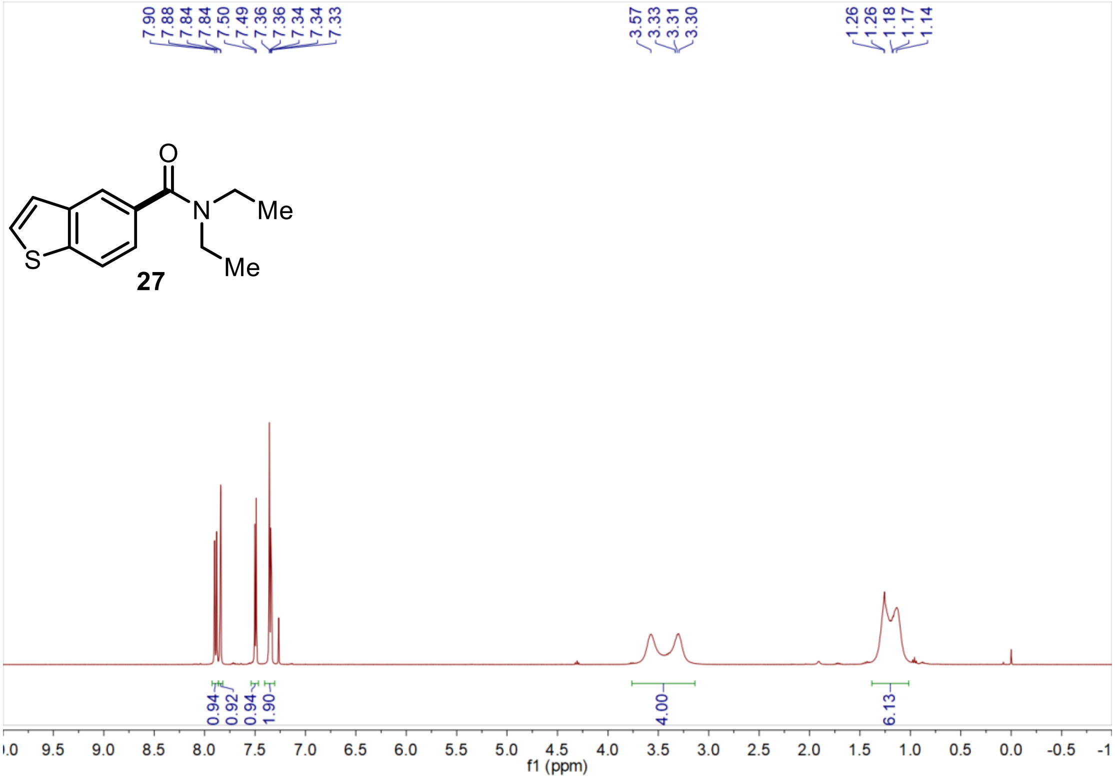
^{1}H NMR (500 MHz, Chloroform-*d*)



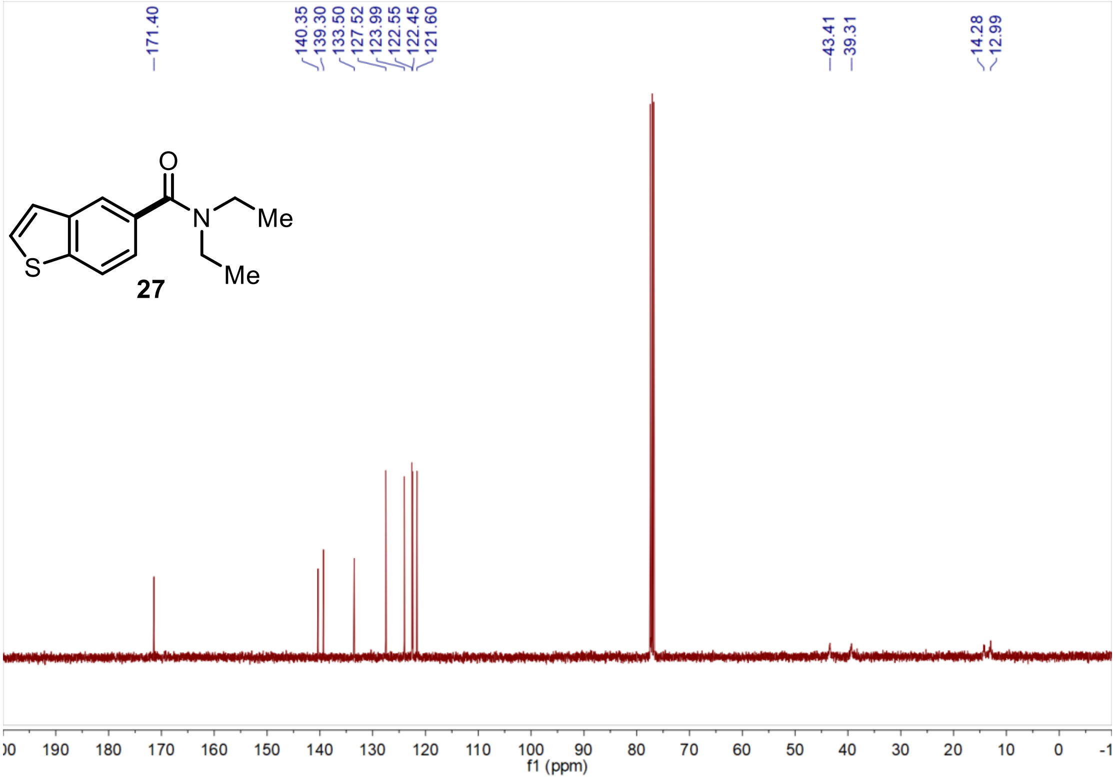
^{13}C NMR (126 MHz, Chloroform-*d*)



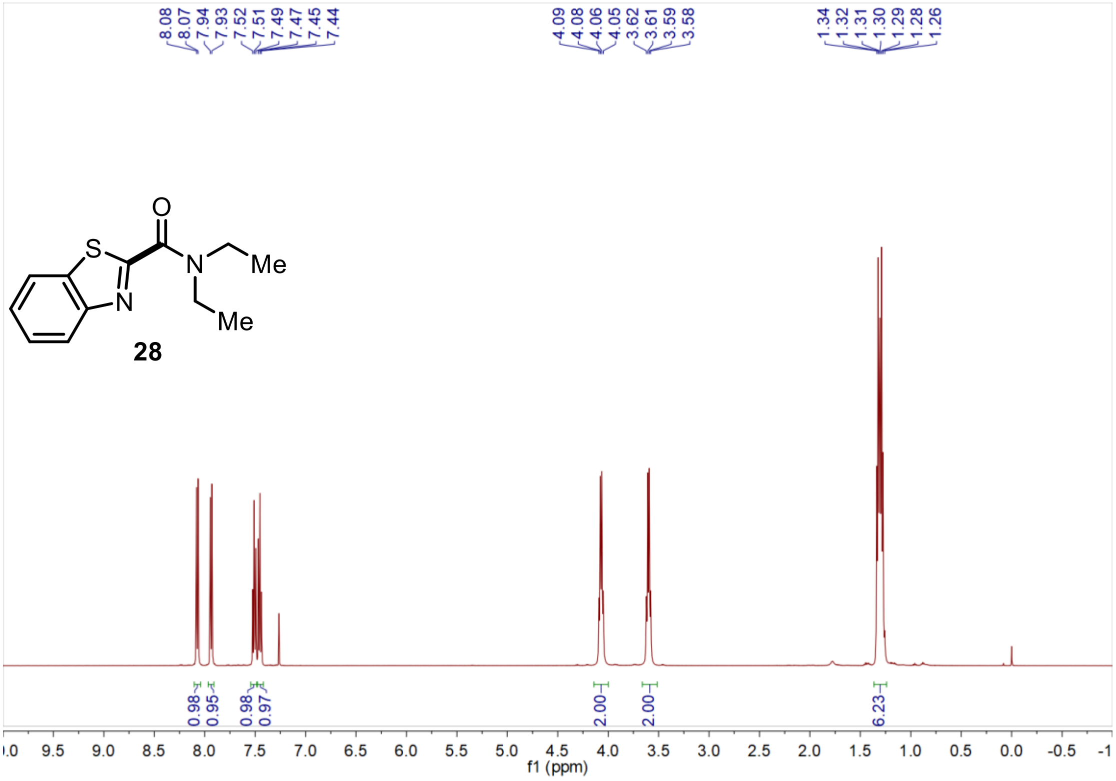
^{1}H NMR (400 MHz, Chloroform-*d*)



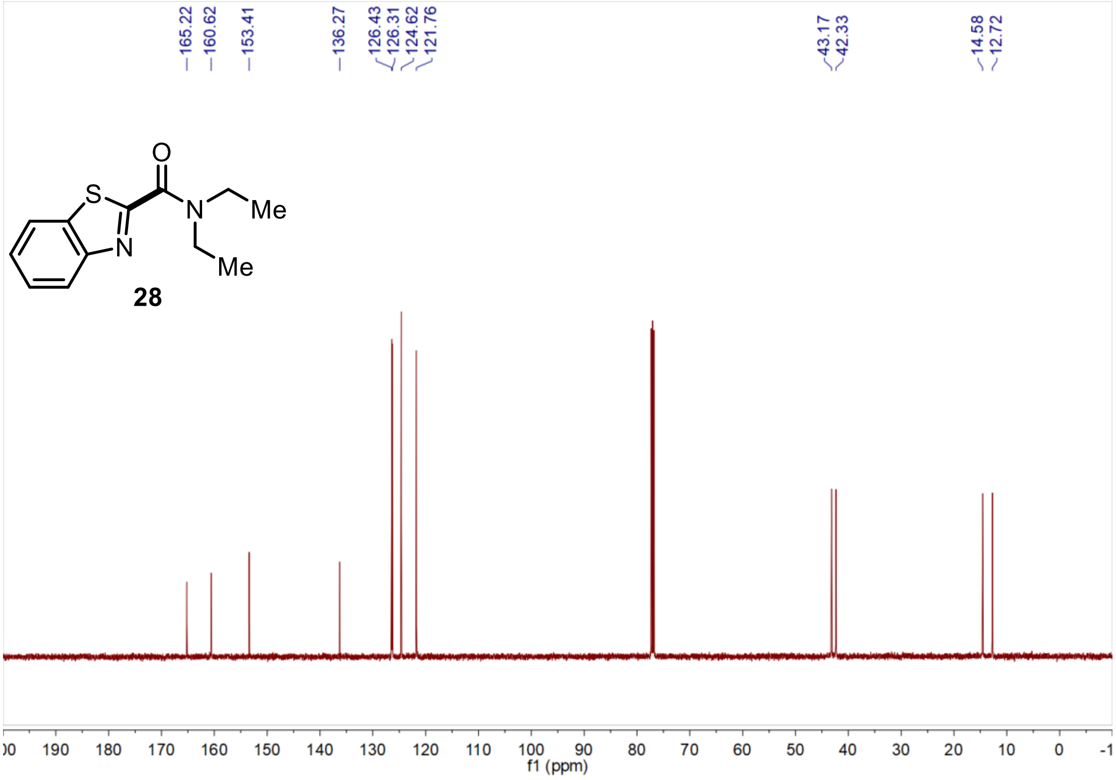
^{13}C NMR (101 MHz, Chloroform-*d*)



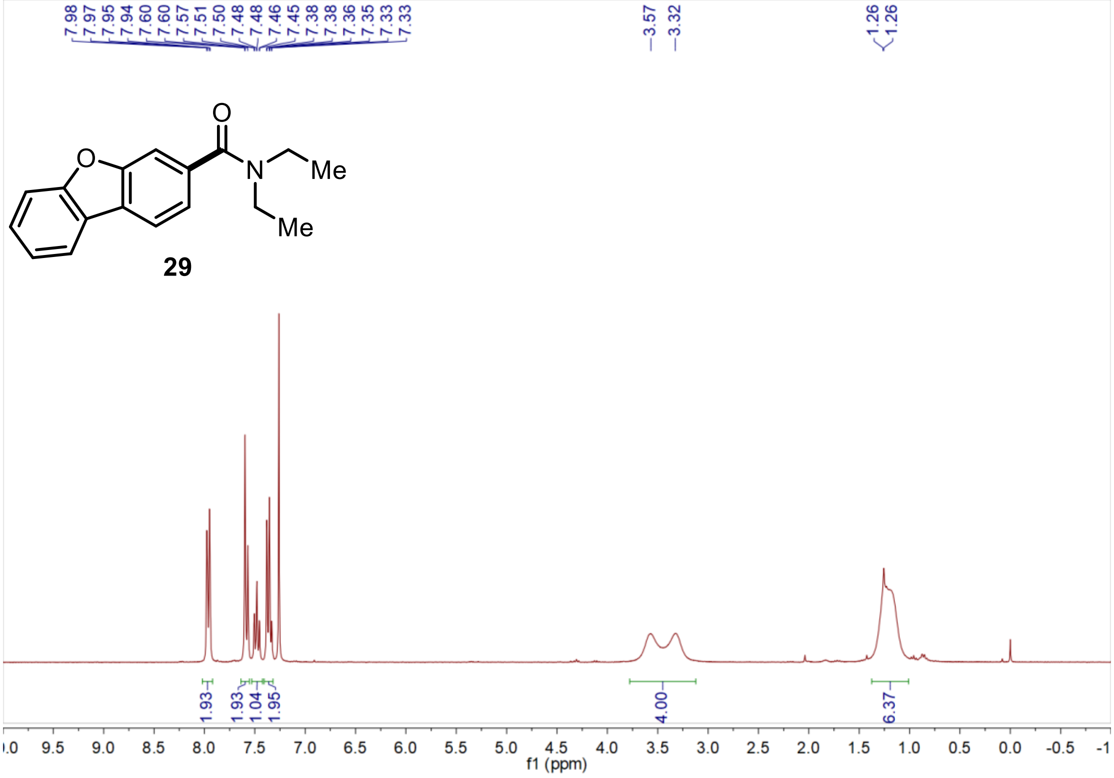
^{1}H NMR (500 MHz, Chloroform-*d*)



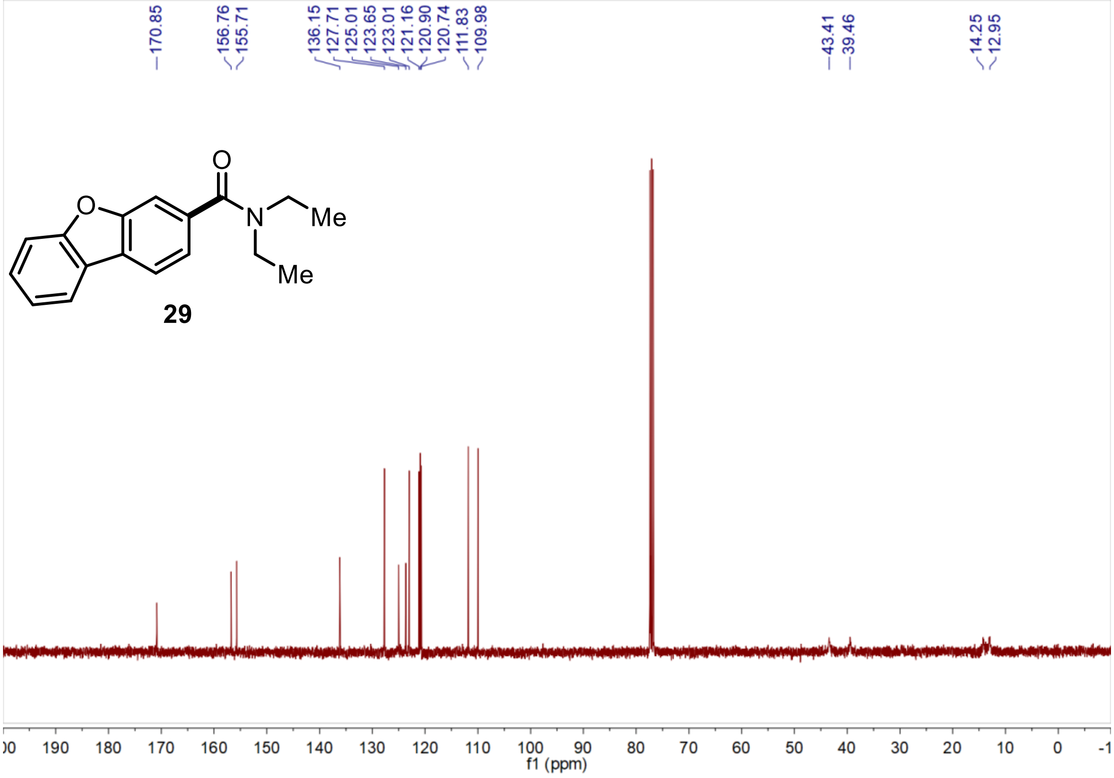
^{13}C NMR (126 MHz, Chloroform-*d*)



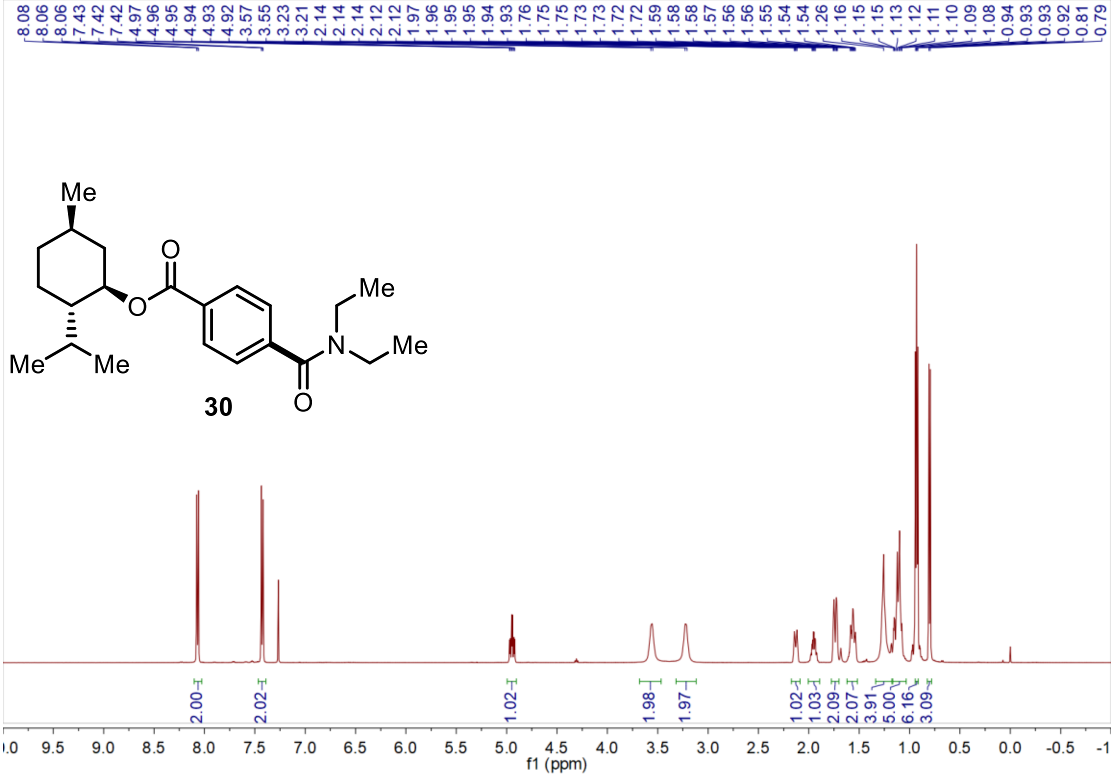
^{1}H NMR (300 MHz, Chloroform-*d*)



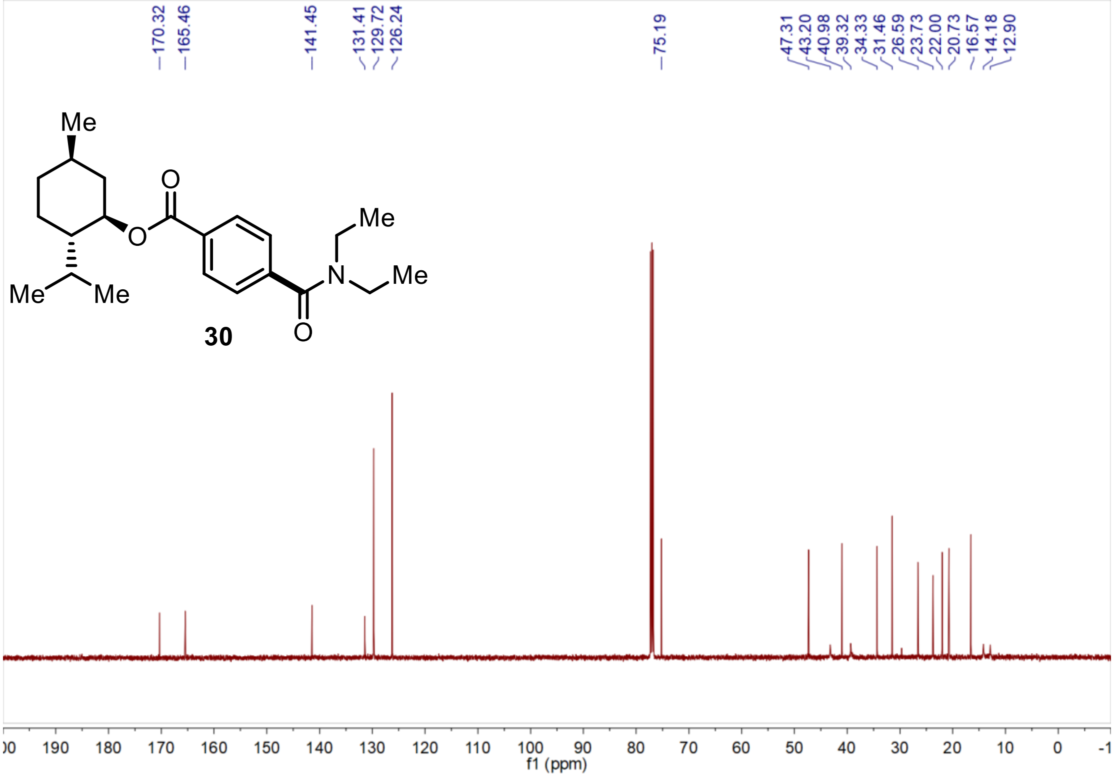
^{13}C NMR (101 MHz, Chloroform-*d*)



^{1}H NMR (400 MHz, Chloroform-*d*)



^{13}C NMR (101 MHz, Chloroform-*d*)



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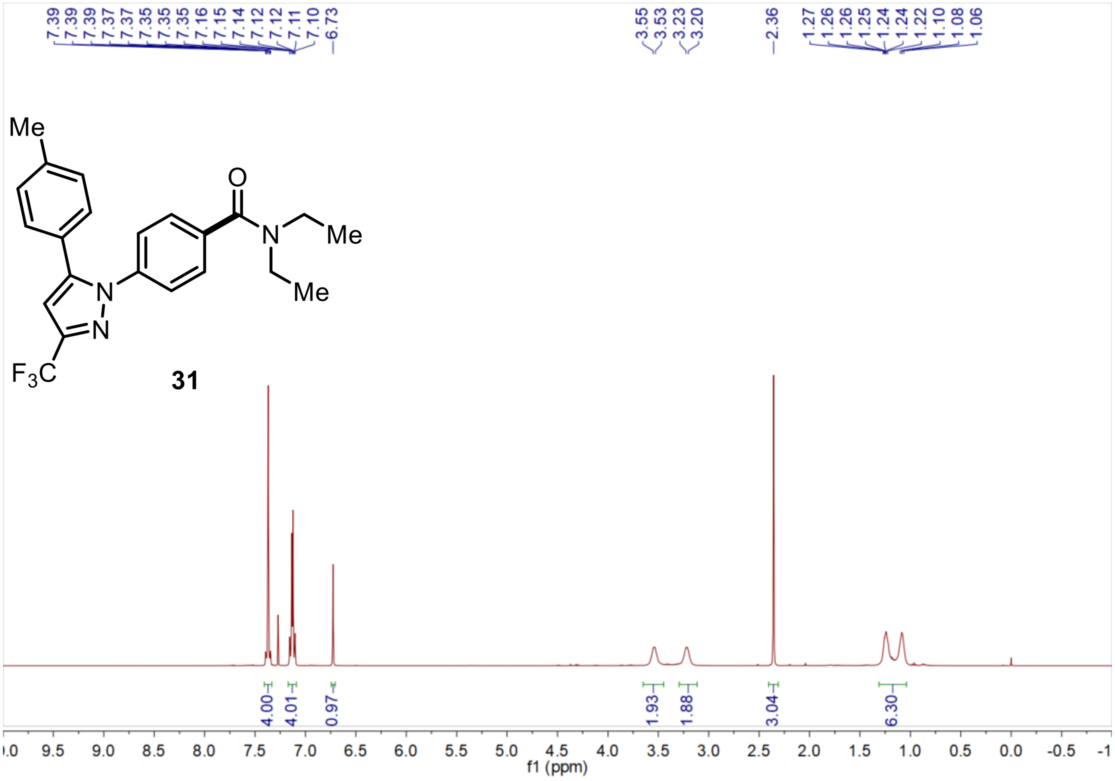
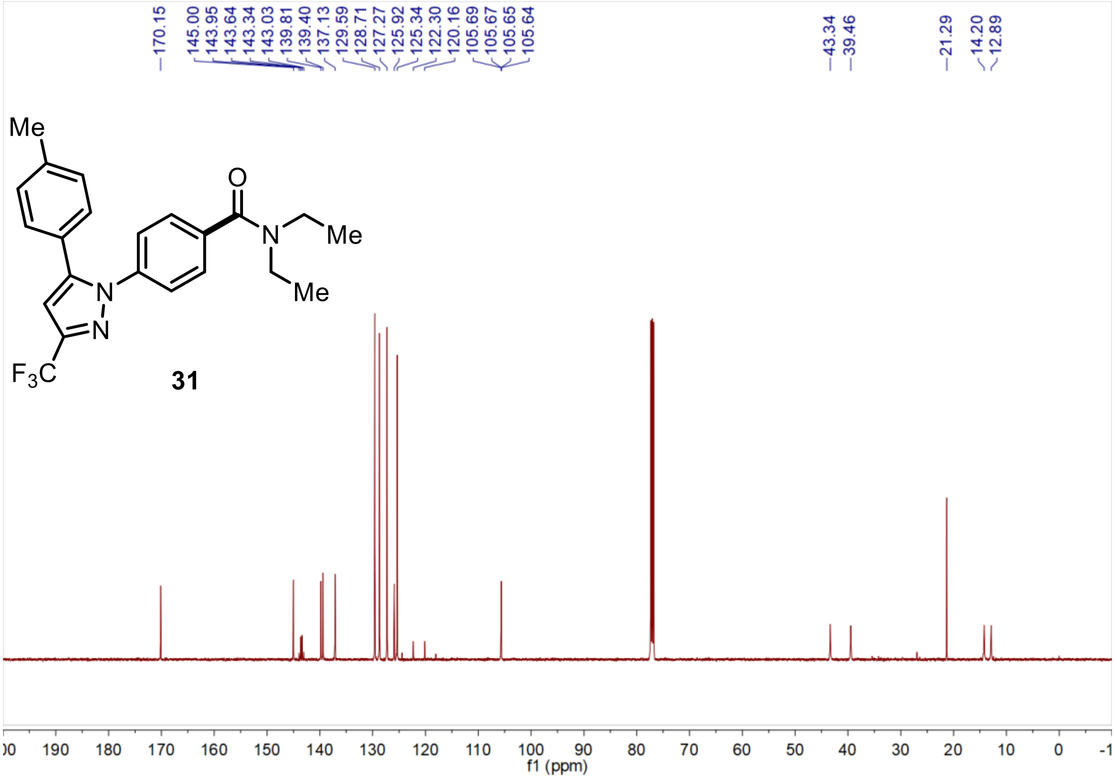
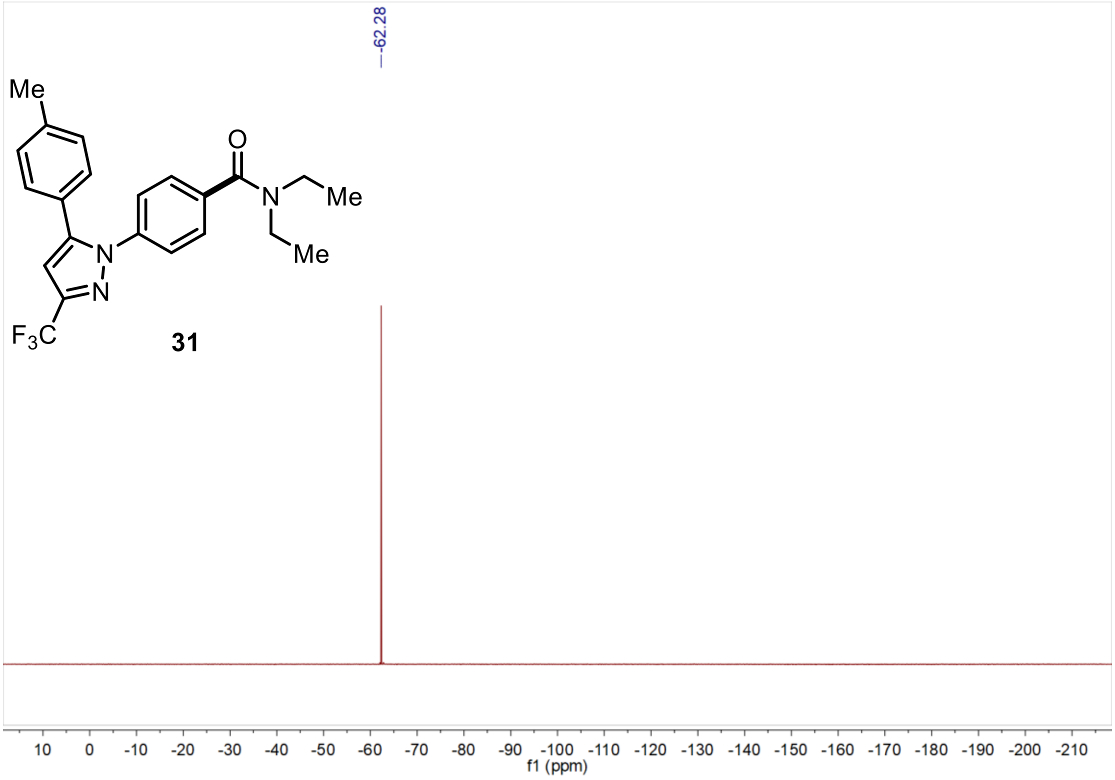


^{13}C NMR (126 MHz, Chloroform-*d*)



^{19}F NMR (377 MHz, Chloroform-*d*)



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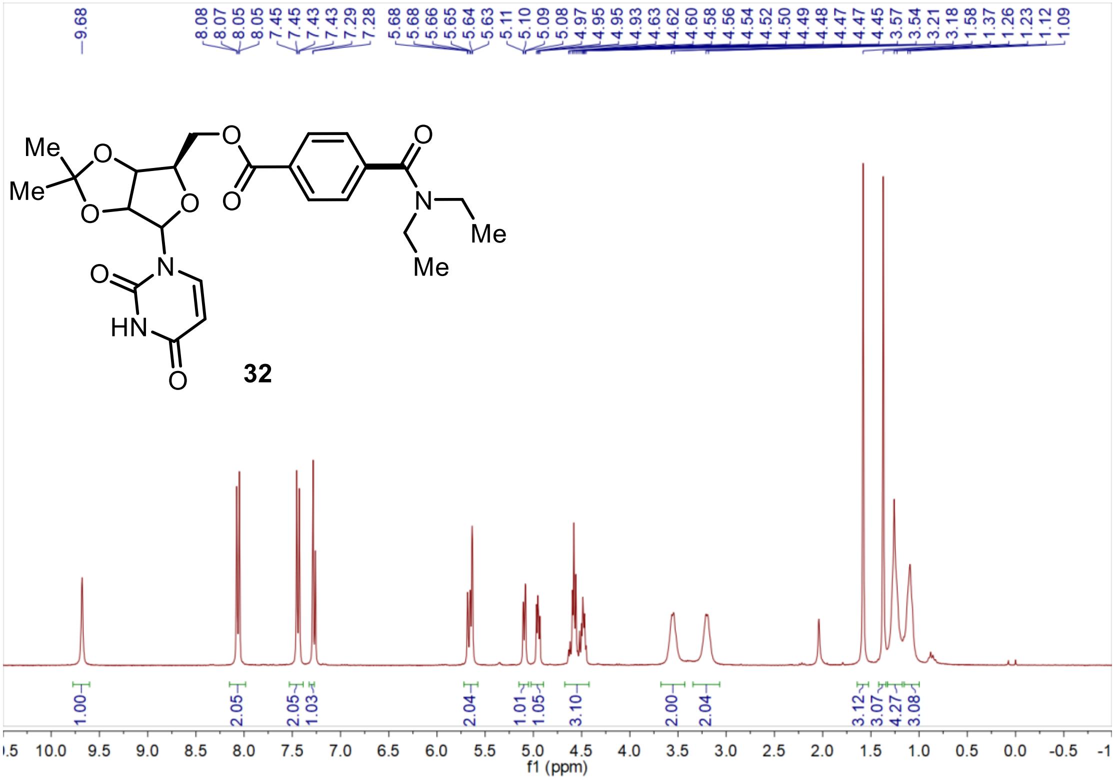
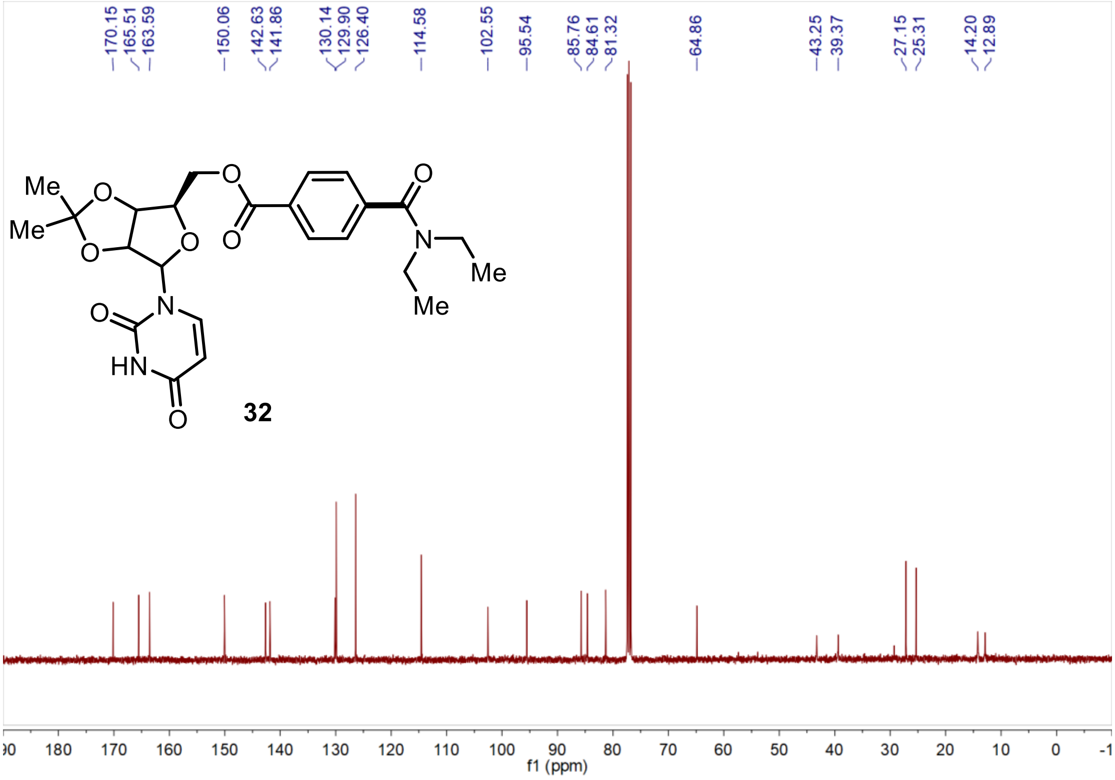
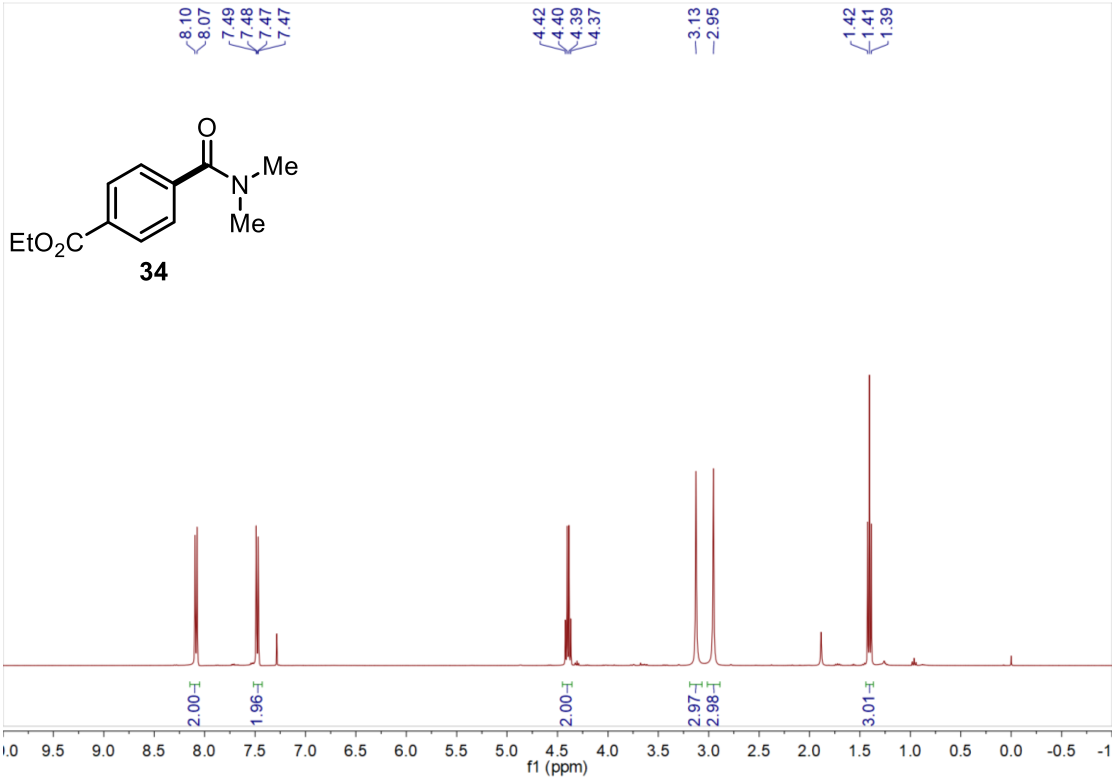
^{1}H NMR (300 MHz, Chloroform-*d*)



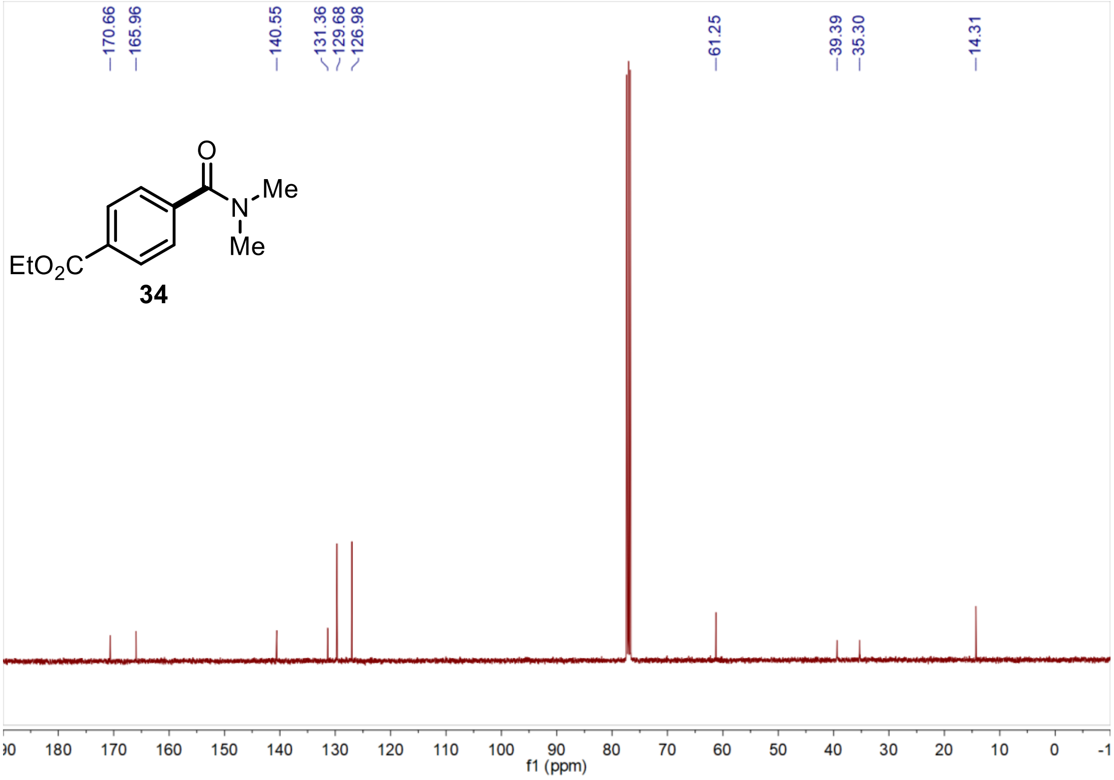
^{13}C NMR (101 MHz, Chloroform-*d*)



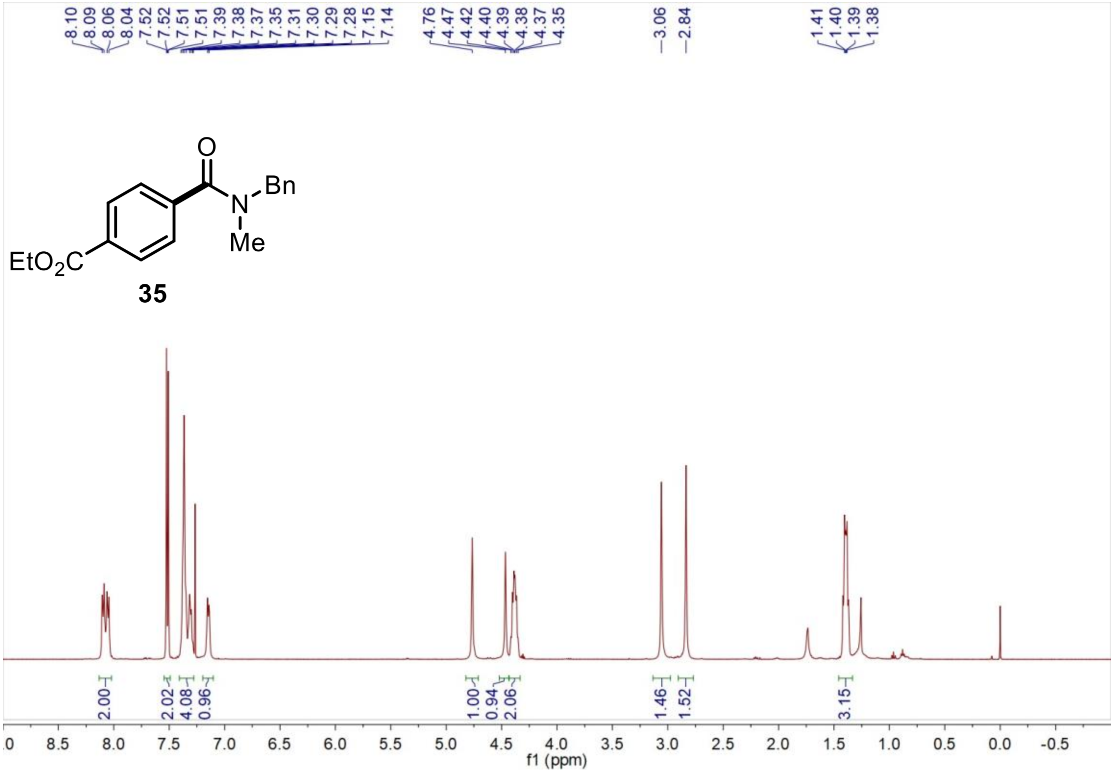
^{1}H NMR (300 MHz, Chloroform-*d*)



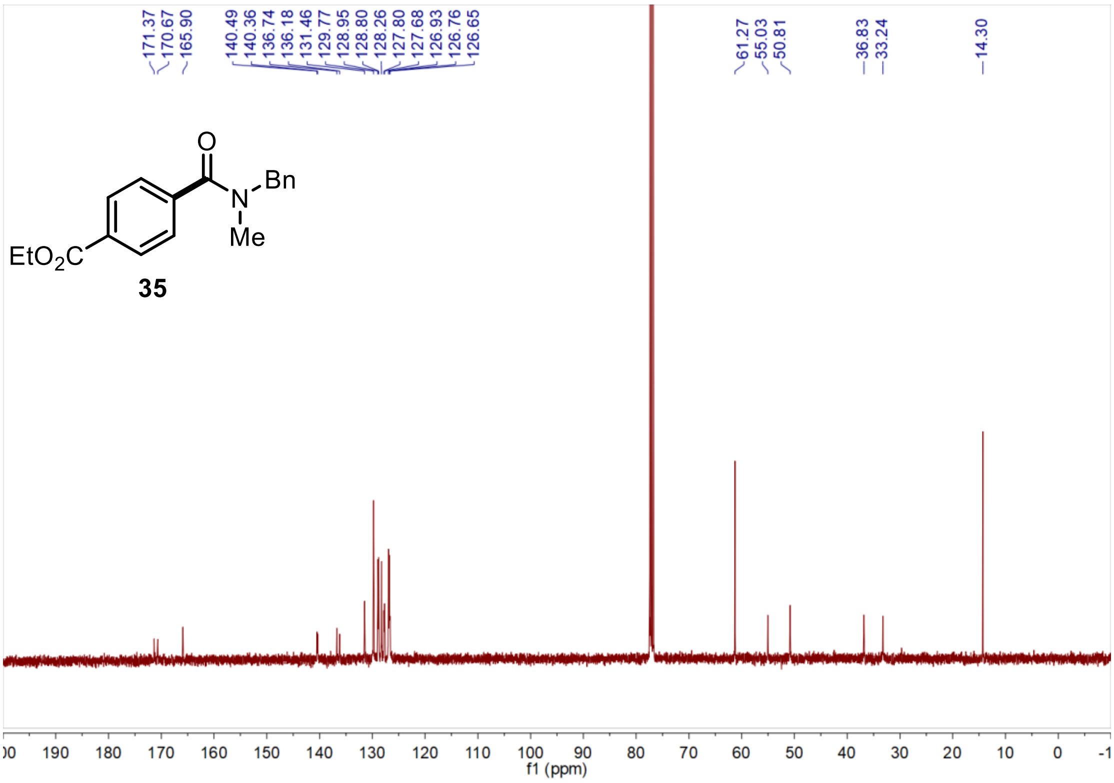
^{13}C NMR (101 MHz, Chloroform-*d*)



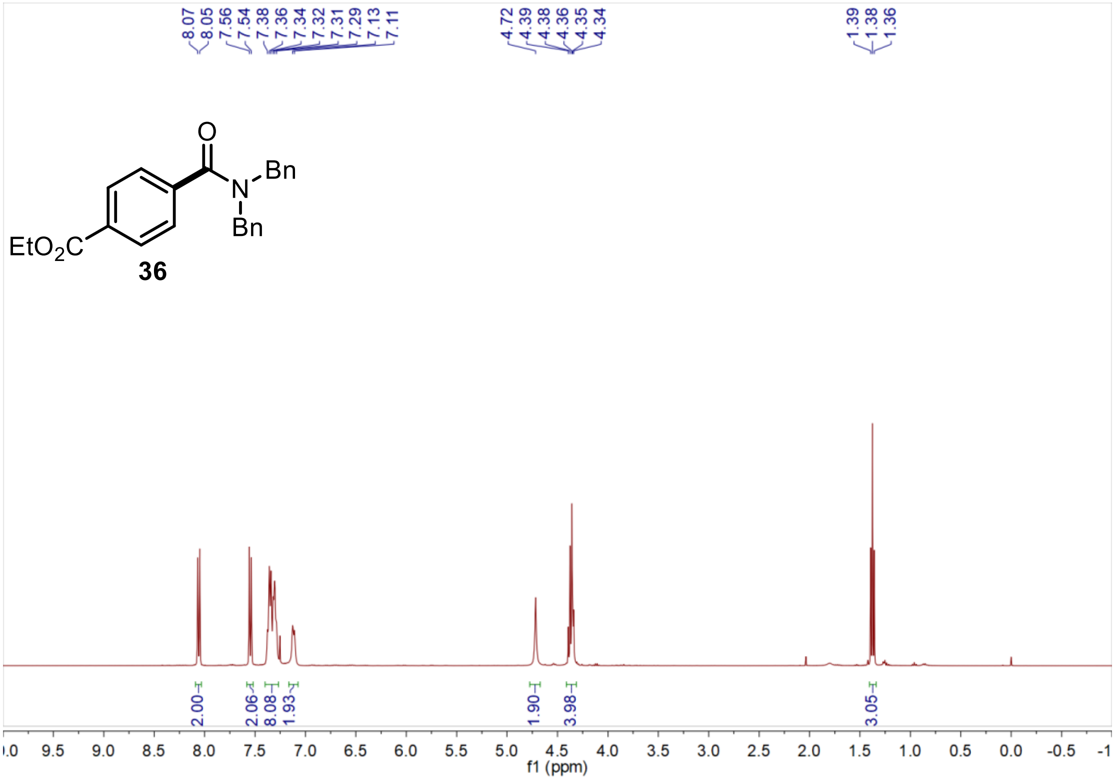
^{1}H NMR (400 MHz, Chloroform-*d*)



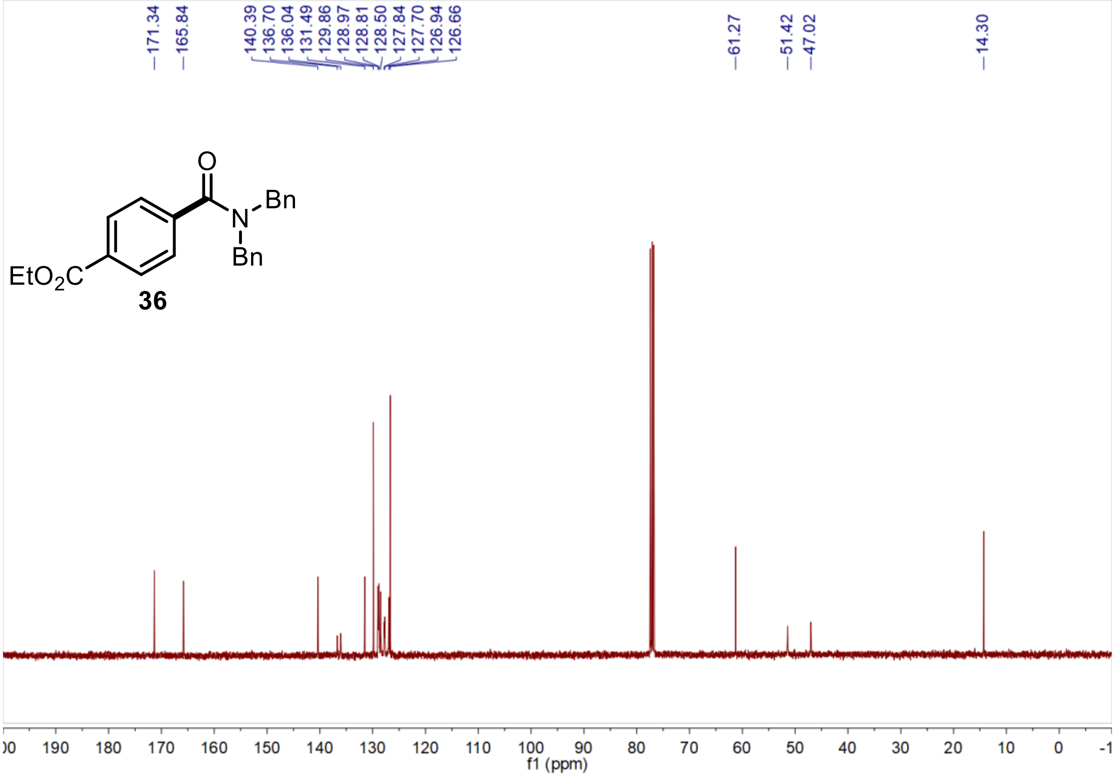
^{13}C NMR (101 MHz, Chloroform-*d*)



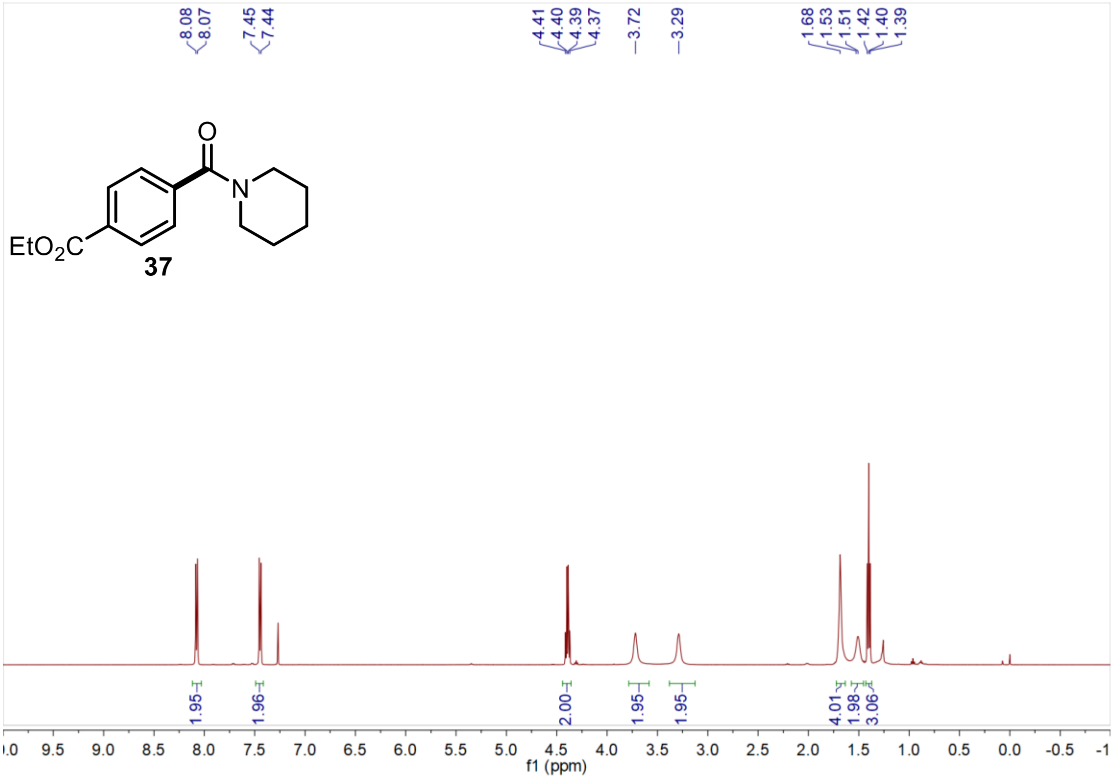
^{1}H NMR (400 MHz, Chloroform-*d*)



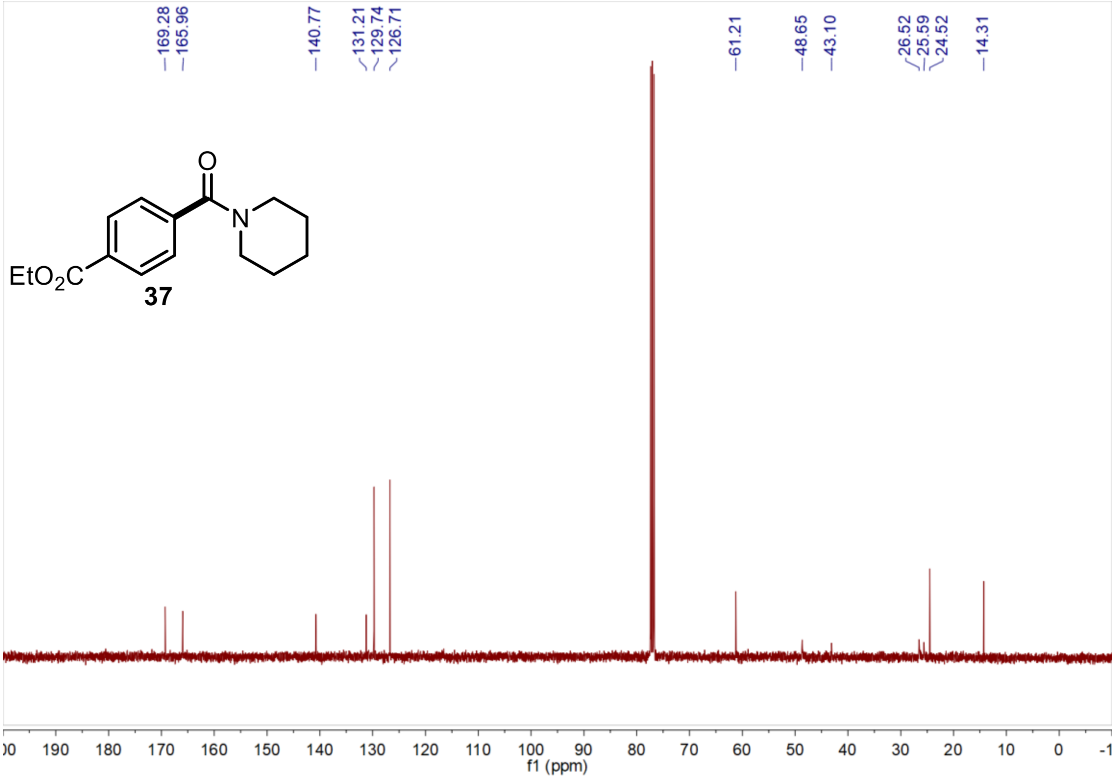
^{13}C NMR (101 MHz, Chloroform-*d*)



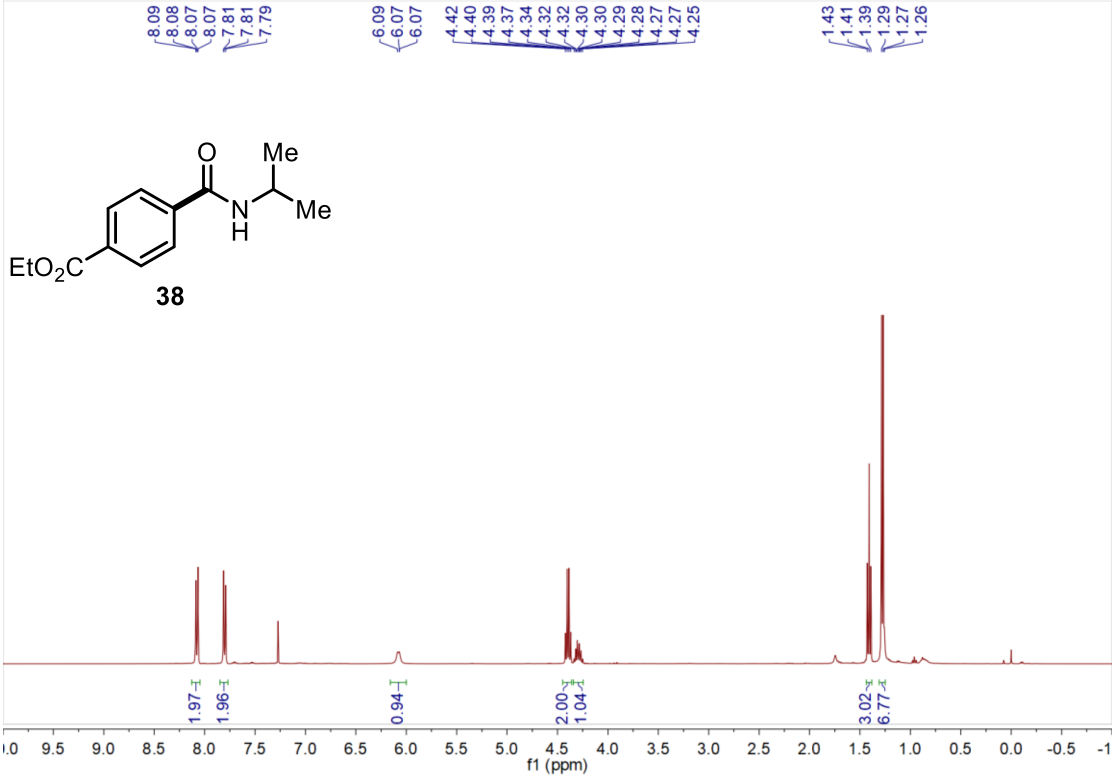
^{1}H NMR (500 MHz, Chloroform-*d*)



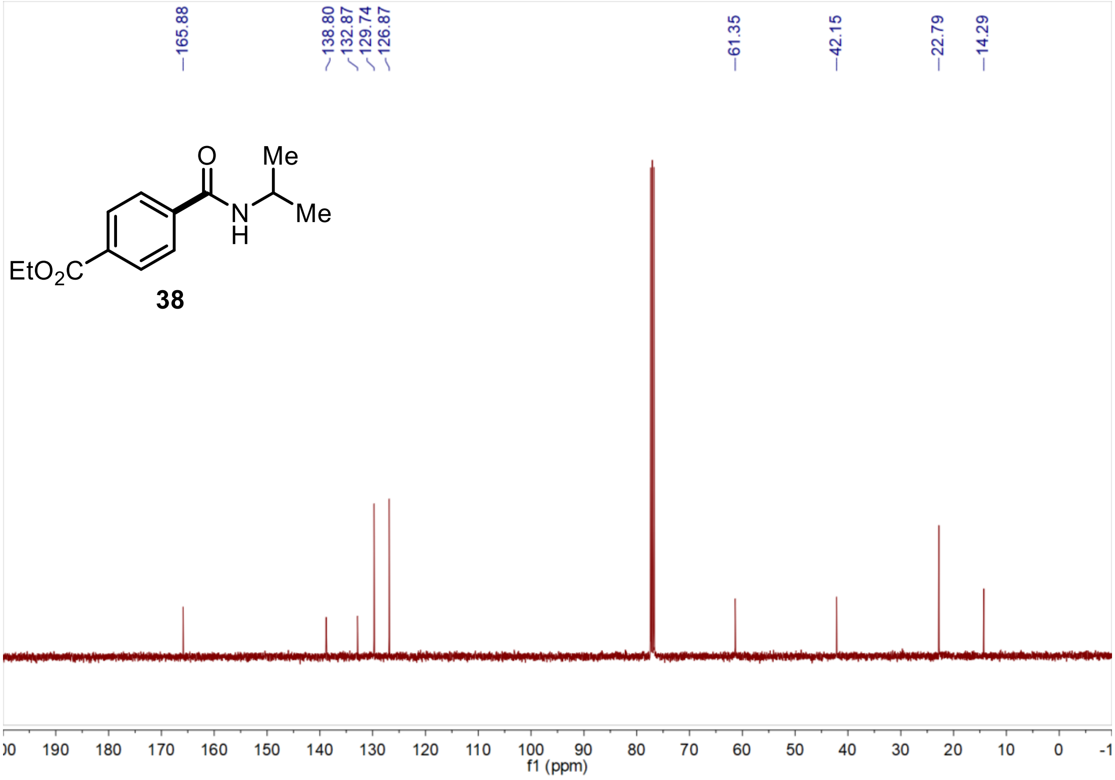
^{13}C NMR (101 MHz, Chloroform-*d*)



^{1}H NMR (400 MHz, Chloroform-*d*)



^{13}C NMR (101 MHz, Chloroform-*d*)



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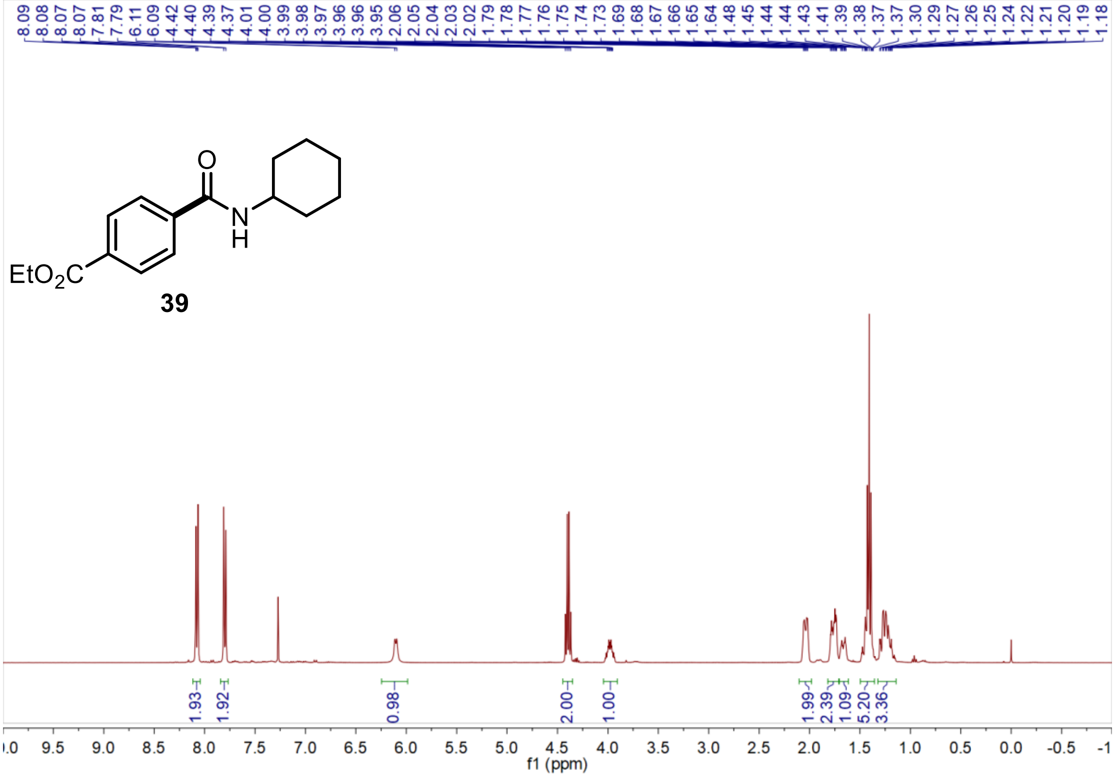

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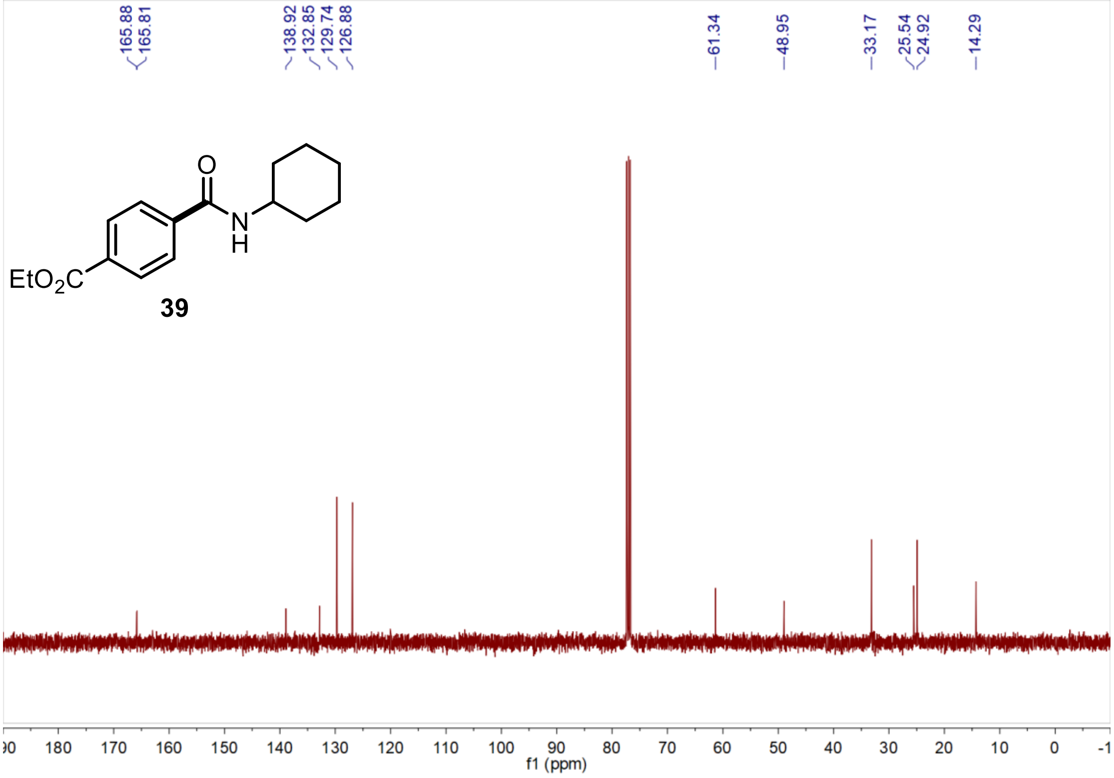

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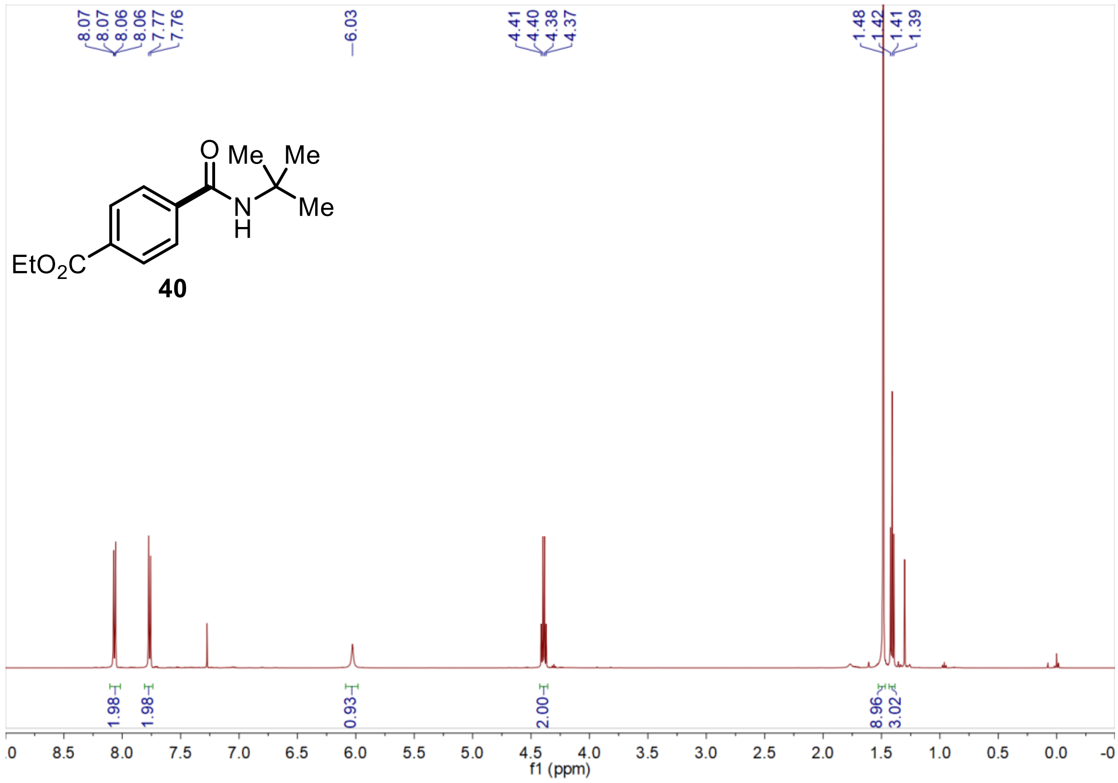
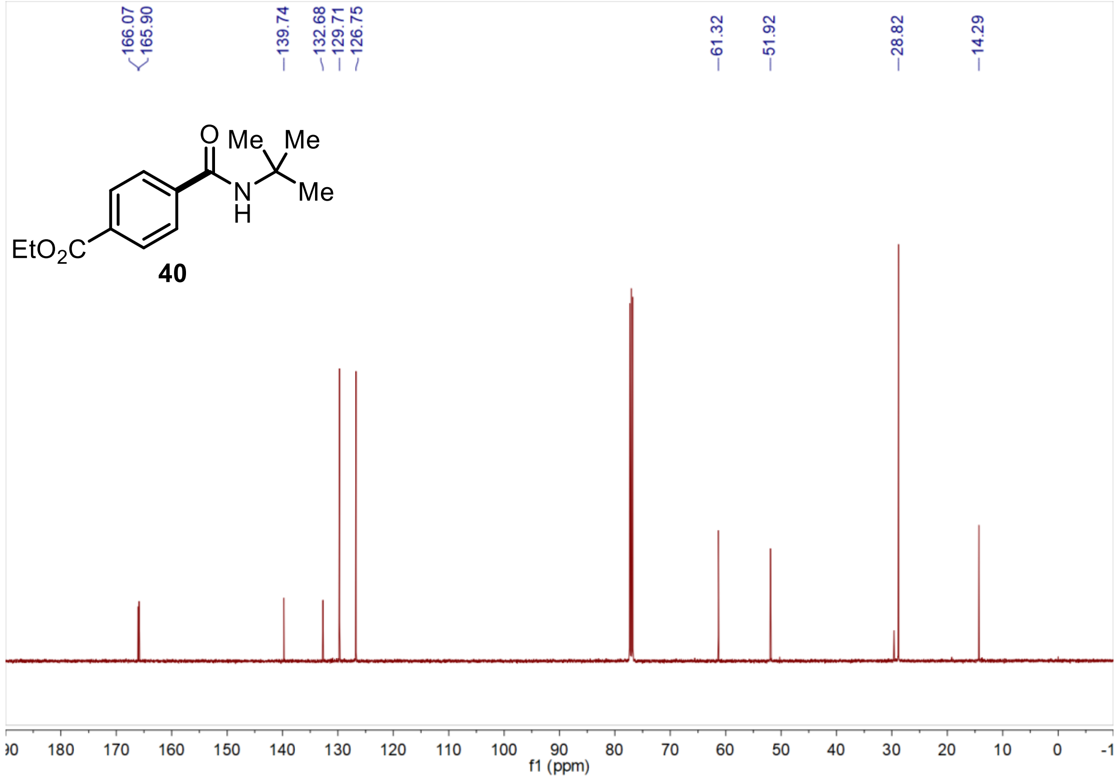
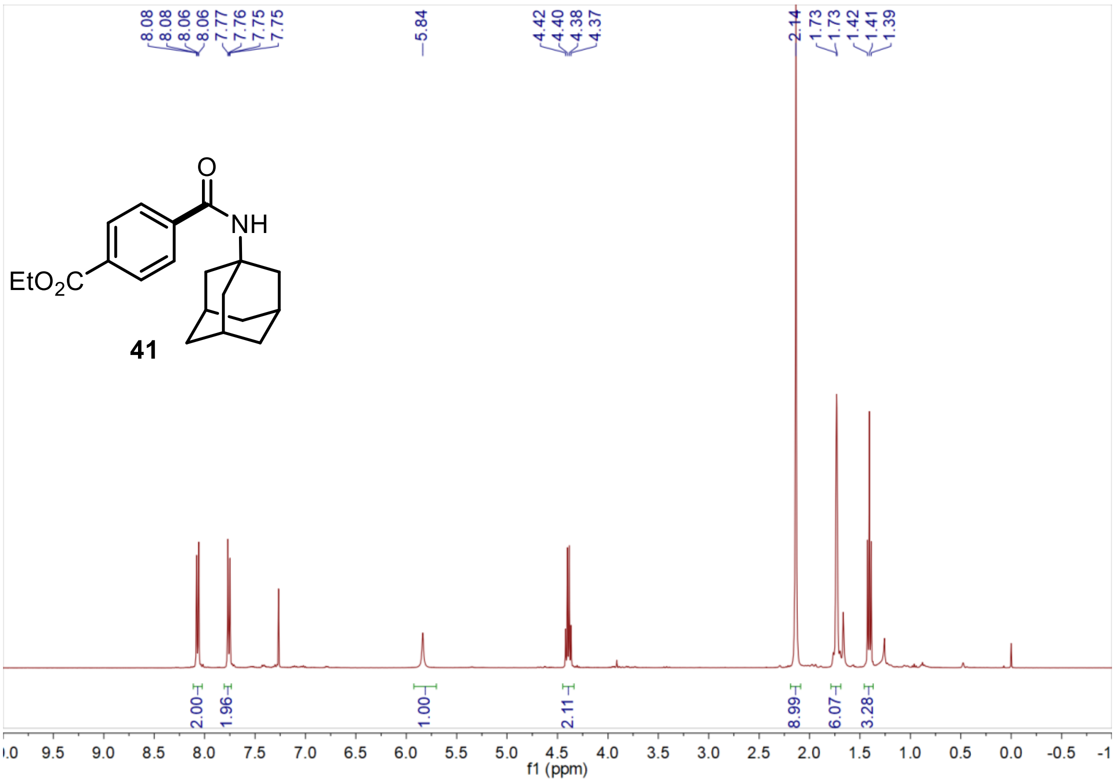


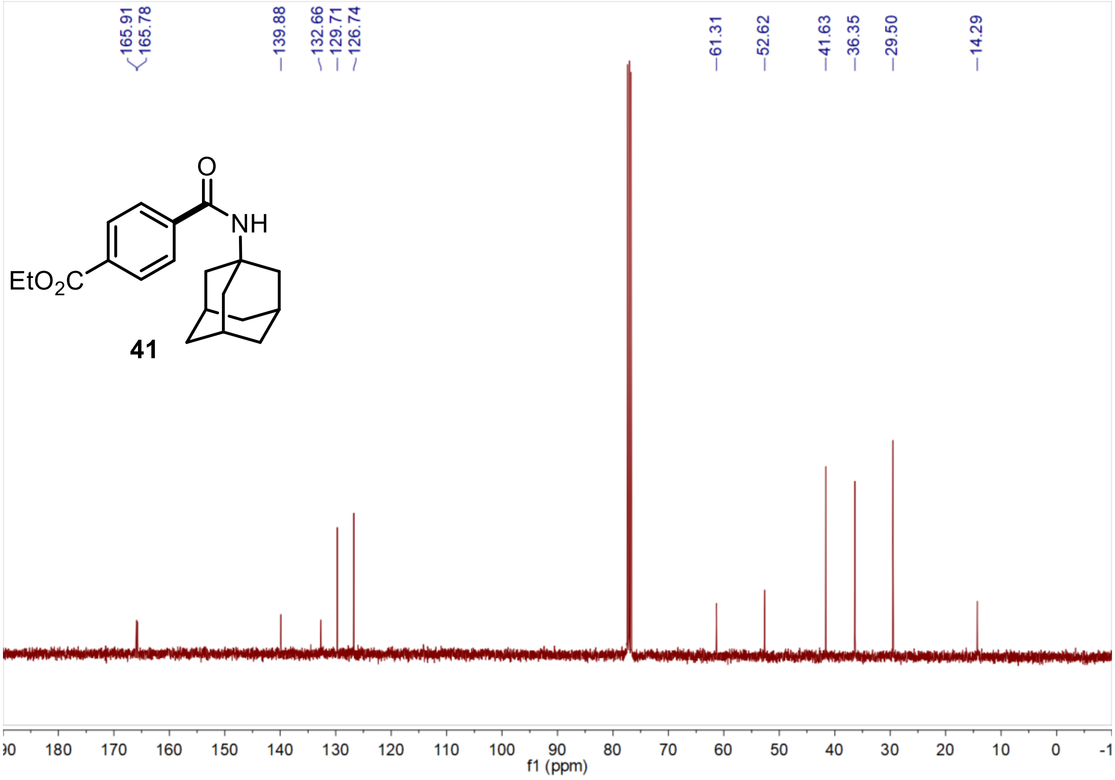
^{13}C NMR (126 MHz, Chloroform-*d*)



^{1}H NMR (400 MHz, Chloroform-*d*)



^{13}C NMR (101 MHz, Chloroform-*d*)



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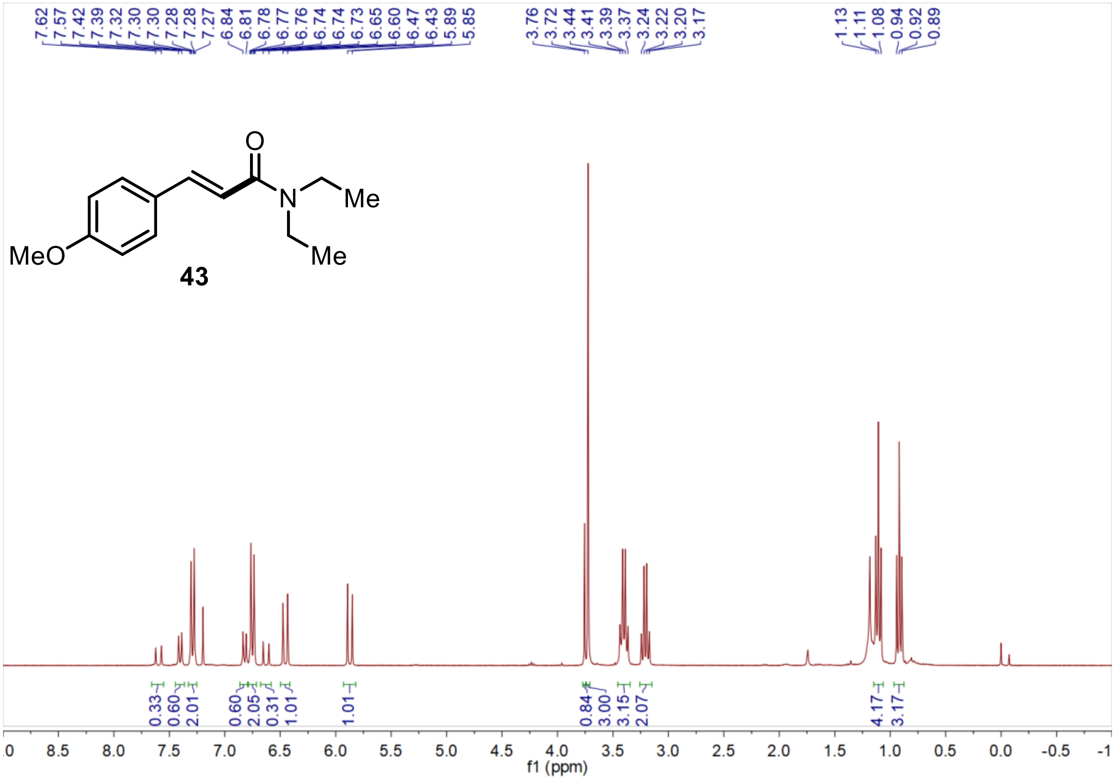
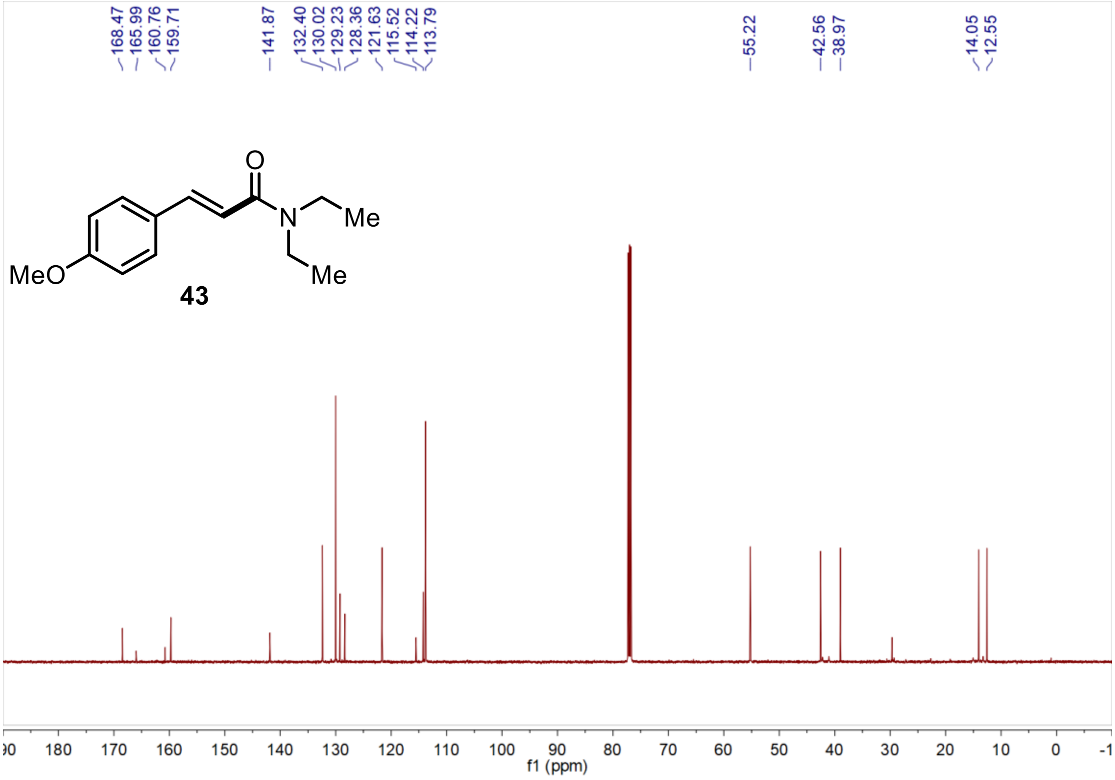
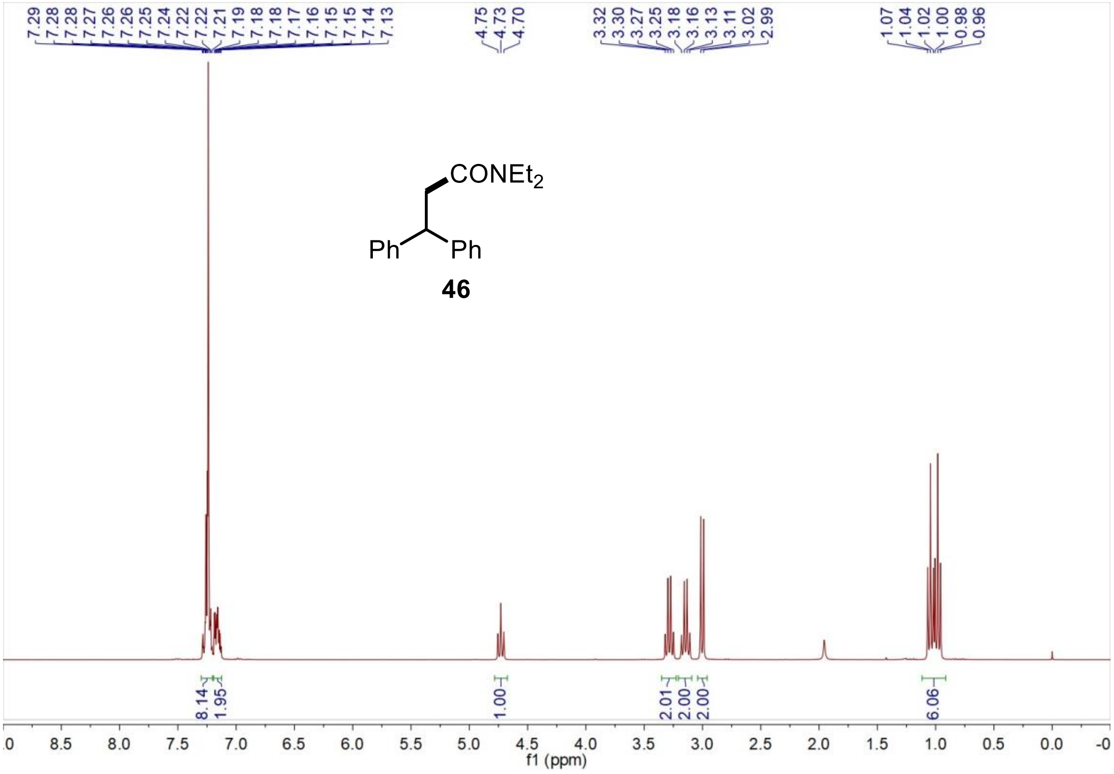


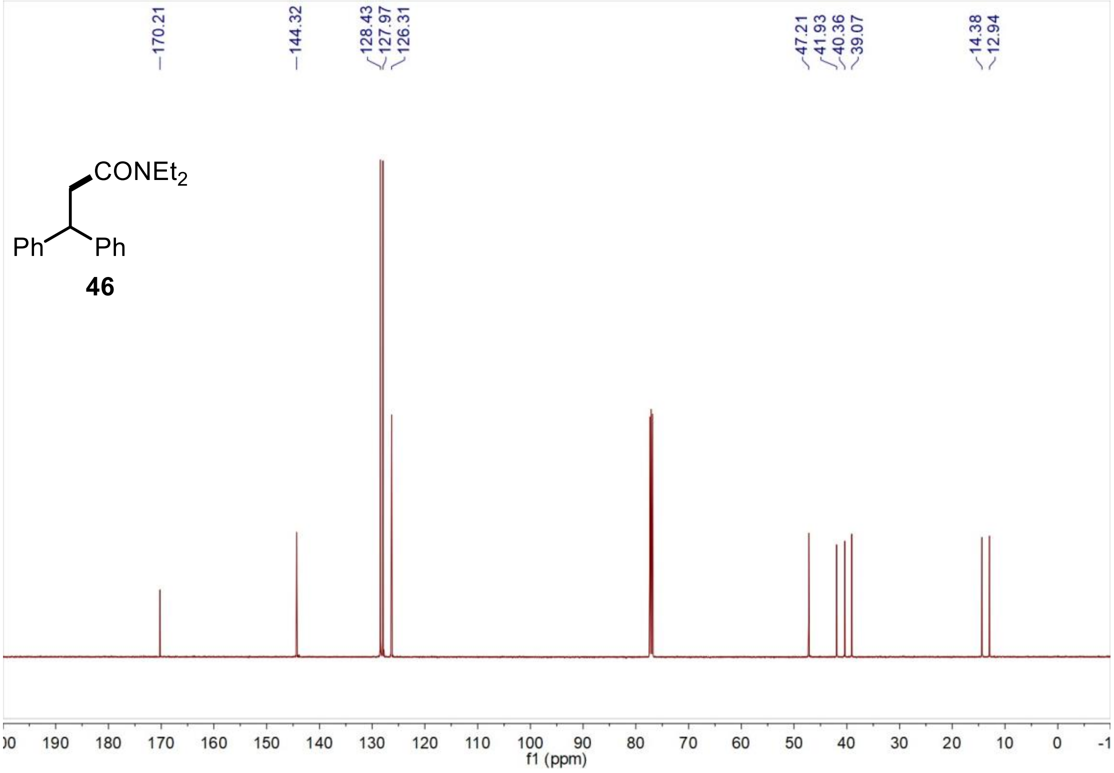
^{13}C NMR (101 MHz, Chloroform-*d*)



^{1}H NMR (300 MHz, Chloroform-*d*)



^{13}C NMR (126 MHz, Chloroform-*d*)



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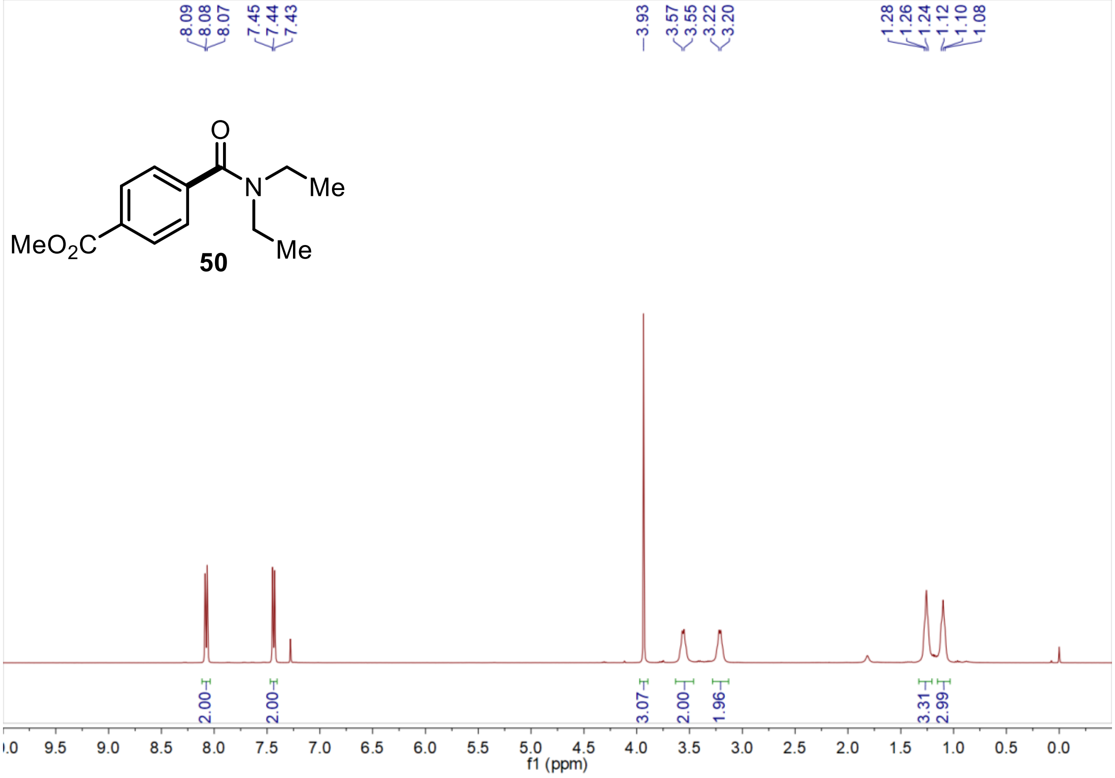

^{13}C NMR (126 MHz, Chloroform-*d*)