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Supplementary Material

HFIP-assisted Brønsted acid catalysed synthesis of furan derivatives

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HFIP-Assisted Brønsted Acid Catalyzed Synthesis of Furan Derivatives

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Supporting Information

General Methods

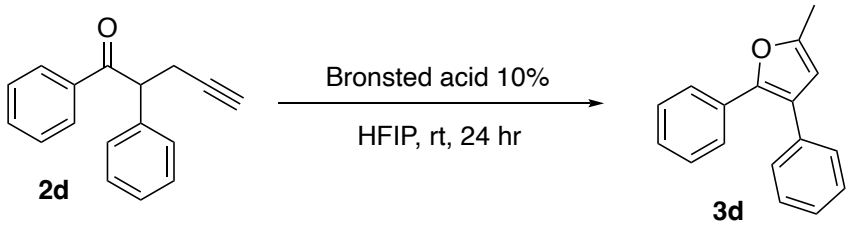
All reactions were conducted under ambient air using either oven dried glassware or disposable 20 mL glass vials. Solvents acetonitrile, tetrahydrofuran (THF), and 1,1,1,3,3,3-hexafluoro isopropanol (HFIP) were stored under molecular sieves. Commercially available reagents were used as purchased unless otherwise noted. Analytical thin layer chromatography (TLC) was performed using aluminium plates precoated with silica gel 60 F_{254} (0.2 mm). Flash chromatography employed 40-60 mesh silica gel. Solvent systems used for chromatography are quoted as volume percentages.

NMR spectroscopy was performed at 298 K using an Avance III HD 400 (400.1 MHz, ^{1}H; 100.6 MHz, ^{13}C) at the Mark Wainwright Analytical Centre at the University of New South Wales Sydney. ^{1}H NMR data are expressed in parts per million (ppm) downfield shift from tetramethylsilane with residual solvent as an internal reference (δ 7.26 ppm for chloroform) and is reported as position (δ in ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constant (J in Hz) and integration (number of protons). ^{13}C NMR spectra were recorded at 298 K with complete proton decoupling. ^{13}C NMR data are expressed in parts per million (ppm) downfield shift relative to the internal reference (δ 77.16 ppm for the central peak of deuterated chloroform).[1]

HRMS were performed at the Bioanalytical Mass Spectrometry Facility within the Mark Wainwright Analytical Centre on an Orbitrap LTQ XL (Thermo Fisher Scientific, San Jose, CA, USA) ion trap mass spectrometer.

Optimization Studies

Table S1. Optimization of reaction conditions (catalytic system).[a]

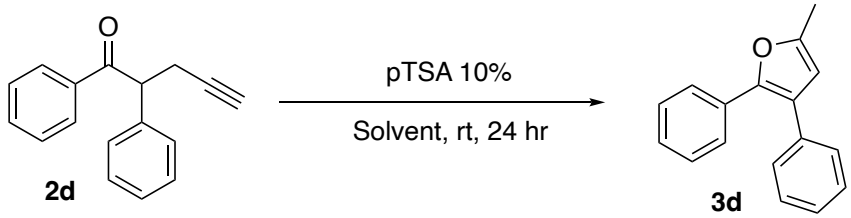


Entry	Bronsted acid	Temp. (°C)	Yield of 3a, %[b]
1	**pTSA**	**25**	**63**
2	HCl	25	49
3	TfOH	25	42
4	HBF_4	25	53
5	TFA	25	none
6	none	25	none

[a]1,2-diphenylpent-4-yn-1-one (0.2 mmol) **2d**, with Brønsted acid (0.02 mmol, 10 mol%) in 1,1,1,3,3,3-Hexafluoro-2-propanol (HFIP) (0.5 mL) catalyst, 24 h. [b]Yields of **3d** were calculated from ^{1}H NMR of the crude product mixture with mesitylene as an internal standard. pTSA = p-Toluenesulfonic acid, HCl = 4.0 M hydrogen chloride solution in dioxane, TfOH = triflic acid, HBF_4 = 50% tetrafluoro boronic acid in ether, TFA = trifluoroacetic acid. None = none detected on NMR

General optimization procedure for Table S1: 1,2-diphenylpent-4-yn-1-one (0.2 mmol) was added to a 4 mL vial equipped with a stirrer bar along with a Brønsted acid (0.02 mmol) and HFIP (0.5 mL). The mixture was stirred for 24 hours at room temperature and solvent was evaporated under reduced pressure. A known amount of mesitylene (0.2 mmol) was added to the residue and the sample was analysed using ^{1}H NMR to determine substrate conversion and product yield.

Table S2. Optimization of reaction conditions (solvent).[a]

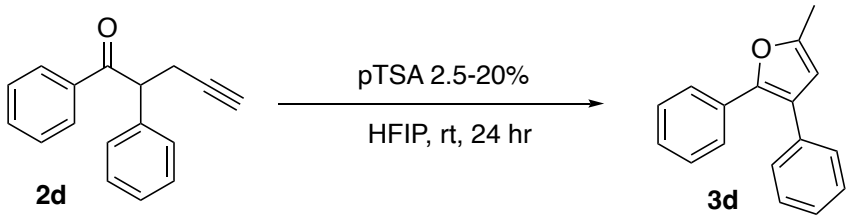


Entry	Bronsted acid	Temp. (°C)	Yield of 3a, %[b]
1	DCE	25	none
2	Toluene	25	none
3	THF	25	none
4	MeCN	25	none
5	Neat	25	none

[a]1,2-diphenylpent-4-yn-1-one (0.2 mmol) **2d**, with pTSA (0.02 mmol, 10 mol%) in solvent (0.5 mL), 24 h. [b]Yields of **3d** were calculated from ^{1}H NMR of the crude product mixture with mesitylene as an internal standard. DCE = 1,2-dichloroethane; DCM = dichloromethane; MeCN = acetonitrile; THF = tetrahydrofuran.

General optimization procedure for Table S2: 1,2-diphenylpent-4-yn-1-one (0.2 mmol) was added to a 4 mL vial equipped with a stirrer bar along with pTSA (0.02 mmol) and solvent (0.5 mL). The mixture was stirred for 24 hours at room temperature and solvent was evaporated under reduced pressure. A known amount of mesitylene (0.2 mmol) was added to the residue and the sample was analysed using ^{1}H NMR to determine substrate conversion and product yield.

Table S3. Optimization of reaction conditions (catalyst loading).[a]

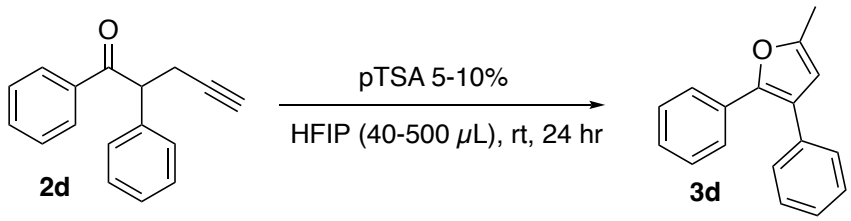


Entry	Cat. (mol%)	Temp. (°C)	Yield of **3a**, %[b]
1	20	25	88
2	**15**	**25**	**92**
3	10	25	63
4	5	25	48
5	2.5	25	16

[a]1,2-diphenylpent-4-yn-1-one (0.2 mmol) **2d**, with pTSA (2.5-20 mol%) in HFIP (0.5 mL) catalyst, 24 h. [b]Yields of **3d** were calculated from ^{1}H NMR of the crude product mixture with mesitylene as an internal standard.

General optimization procedure for Table S3: 1,2-diphenylpent-4-yn-1-one (0.2 mmol) was added to a 4 mL vial equipped with a stirrer bar along with pTSA (2.5-20 mol%) and solvent (0.5 mL). The mixture was stirred for 24 hours at room temperature and solvent was evaporated under reduced pressure. A known amount of mesitylene (0.2 mmol) was added to the residue and the sample was analysed using ^{1}H NMR to determine substrate conversion and product yield.

Table S4. Optimization of reaction conditions (solvent concentration and catalytic loading)[a]

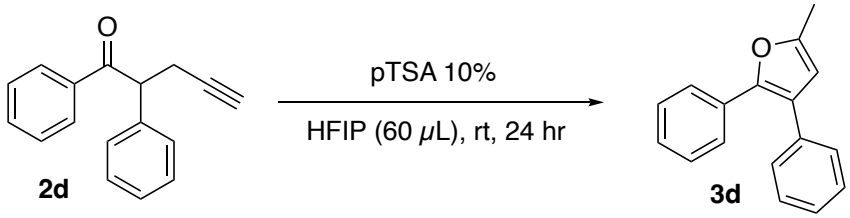


Entry	Cat. (mol%)	Solvent (μL)	Yield of **3a**, %[b]
1	10	500	77
2	10	200	95
3	10	80	100
4	**10**	**60**	**100**
5	10	40	96
6	5	80	87
7	5	60	97

[a]1,2-diphenylpent-4-yn-1-one (0.2 mmol) **2d**, with pTSA (2.5-20 mol%) in HFIP (0.5 mL) catalyst, 24 h. [b]Yields of **3d** were calculated from ^{1}H NMR of the crude product mixture with mesitylene as an internal standard.

General optimization procedure for Table S4: 1,2-diphenylpent-4-yn-1-one (0.2 mmol) was added to a 4 mL vial equipped with a stirrer bar along with pTSA (5-10 mol%) and solvent (40-500 μL). The mixture was stirred for 24 hours at room temperature and solvent was evaporated under reduced pressure. A known amount of mesitylene (0.2 mmol) was added to the residue and the sample was analysed using ^{1}H NMR to determine substrate conversion and product yield.

Table S5. Optimization of reaction conditions (time).[a]



Entry	Time (h)	Yield of **4a**, %[b]
1	**0.5**	47
2	**1**	61
3	**2**	**83**
4	**4**	**92**
5	**6**	**95**
6	**24**	**100**

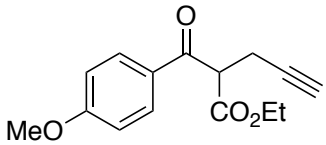
[a]1,2-diphenylpent-4-yn-1-one (0.2 mmol) **2a**, with pTSA (10 mol%) in HFIP (60 μL) catalyst, 24 h. [b] Yields of **3a** were calculated from ^{1}H NMR of the crude product mixture with mesitylene as an internal standard.

General optimization procedure for Table S5: 1,2-diphenylpent-4-yn-1-one (0.2 mmol) was added to a 4 mL vial equipped with a stirrer bar along with pTSA (0.02 mmol, 10 mol%) and solvent (60 μL). The mixture was stirred for 24 hours at room temperature and solvent was evaporated under reduced pressure. A known amount of mesitylene (0.2 mmol) was added to the residue and the sample was analysed using ^{1}H NMR to determine substrate conversion and product yield.

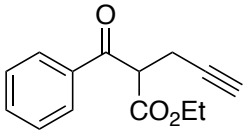
Substrate synthesis

General procedure for the synthesis of α-carboxyloxy ynone substrates (2a-c,e-f): To a reaction mixture of α-carboxyloxy ynone starting material (1 equiv.), potassium carbonate (1.2 equiv.) and potassium iodide (0.2 equiv.) in THF (5 mL per mmol of starting material), propargyl bromide (1.2 equiv.) was added dropwise and the reaction mixture was stirred at room temperature for 24-48 hours. The reaction was then quenched with water (~ 10 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic phase was washed with brine (20 mL), dried over anhydrous sodium sulfate and concentrated under reduced pressure and the residues were purified using column chromatography (silica-gel, EtOAc/hexanes).

General procedure for α-aryl ynone substrates (2d, g-j): To a reaction mixture of α-aryl ynone starting material (1 equiv.) and potassium tert-butoxide (1.5 equiv.) in THF (5 mL per mmol of starting material), propargyl bromide (1.2 equiv.) was added dropwise and the reaction mixture was heated at reflux for 2 hours. The reaction mixture was then quenched with saturated ammonium chloride solution (10 mL), then extracted with ethyl acetate (3 x 20 mL). The combined organic phase was washed with brine (20 mL), dried over anhydrous sodium sulfate and concentrated under reduced pressure and the residues were purified using column chromatography (silica-gel, EtOAc/hexanes).



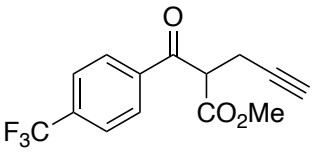
Ethyl 4-methoxy-β-oxo-α-2-propyn-1-ylbenzenepropanoate (2a): The alkylation reaction was performed according to the standard procedure on a 5.0 mmol scale. Purification by column chromatography (10% ethyl acetate in hexanes) yielded the title compound as a pale yellow oil (1.14 g, 4.36 mmol, 86% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.05 – 7.97 (m, 2H), 6.98 – 6.88 (m, 2H), 4.51 (t, J = 7.4 Hz, 1H), 4.14 (qd, *J* = 7.1, 1.8 Hz, 2H), 3.86 (s, 3H), 2.91 (ddd, *J* = 17.0, 7.8, 2.6 Hz, 1H), 2.81 (ddd, *J* = 17.0, 7.0, 2.7 Hz, 1H), 1.97 (t, *J* = 2.7 Hz, 1H), 1.17 (t, *J* = 7.1 Hz, 3H) ppm; **^{13}C NMR (101 MHz, $CDCl_3$)** δ 191.6, 168.6, 164.2, 131.4, 128.9, 114.0, 80.9, 70.4, 61.8, 55.6, 53.0, 18.5, 14.1 ppm. The NMR data are consistent with literature.[1]



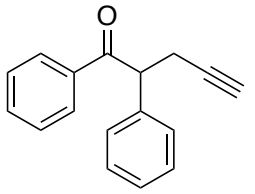
Ethyl β-oxo-α-2-propyn-1-ylbenzenepropanoate (2b): The alkylation reaction was performed according to the standard procedure on a 23 mmol scale. Purification by column chromatography (10% ethyl acetate in hexanes) yielded

the title compound as a pale yellow oil (1.68g, 7.28 mmol, 31% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.06 – 7.98 (m, 2H), 7.63 – 7.54 (m, 1H), 7.47 (ddd, *J* = 8.8, 7.0, 1.5 Hz, 2H), 4.56 (t, *J* = 7.4 Hz, 1H), 4.14 (qd, *J* = 7.1, 1.3 Hz, 2H), 2.88 (qdd, *J* = 17.0, 7.4, 2.6 Hz, 2H), 1.97 (t, *J* = 2.7 Hz, 1H), 1.15 (t, *J* = 7.1 Hz, 3H) ppm; **^{13}C NMR (101 MHz, $CDCl_3$)** δ 193.4, 168.4, 136.0, 133.9, 129.0, 128.9, 80.7, 70.5, 62.0, 53.3, 18.5, 14.0 ppm. The NMR data are consistent with literature.[1]

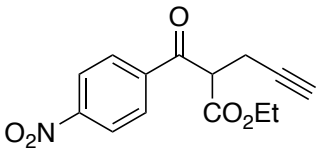
Benzenepropanoic acid, β-oxo-α-2-propyn-1-yl-4-(trifluoromethyl)-, methyl ester (2c): The alkylation reaction was performed according to the standard procedure on a 4.0 mmol scale. Purification by column chromatography (15% ethyl acetate in hexanes) yielded the title compound as a pale yellow oil (89.9 mg, 0.316 mmol, 8% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.17 – 8.10 (m, 2H), 7.77 (d, *J* = 8.4 Hz, 2H), 4.60 (t, *J* = 7.4 Hz, 1H), 3.71 (s, 3H), 3.00 – 2.84 (m, 2H), 1.99 (t, *J* = 2.7 Hz, 1H) ppm; **^{13}C NMR (101 MHz, $CDCl_3$)** δ 192.7, 168.4, 138.7, 135.4 (q, *J* =32.9 Hz), 129.3, 126.3 (q, *J* =3.7 Hz), 123.6 (q, *J* = 272.7 Hz), 80.2, 70.8, 53.3, 53.2, 18.5 ppm; **^{19}F NMR (376 MHz, $CDCl_3$)** δ -63.26 ppm. The NMR data are consistent with literature.[1]



1,2-Diphenyl-4-pentyn-1-one (2d): The alkylation reaction was performed twice according to the standard procedure on a 10 mmol scale. Purification by column chromatography (15% ethyl acetate in hexanes) yielded the product as a pale yellow solid (1.92 g, 8.19 mmol, 82% yield). Alternatively, purification by hot recrystallisation in hexane to yield the product as an off-white spiky crystals (1.10 g, 4.01 mmol, 40% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.99 – 7.92 (m, 2H), 7.51 – 7.45 (m, 1H), 7.42 – 7.35 (m, 2H), 7.33 – 7.27 (m, 4H), 7.26 – 7.21 (m, 1H), 4.78 (t, *J* = 7.3 Hz, 1H), 3.03 (ddd, *J* = 16.8, 7.3, 2.6 Hz, 1H), 2.70 (ddd, *J* = 16.8, 7.3, 2.6 Hz, 1H), 1.93 (t, *J* = 2.6 Hz, 1H) ppm; **^{13}C NMR (101 MHz, $CDCl_3$)** δ 198.1, 138.2, 136.3, 133.2, 129.2, 129.0, 128.7, 128.3, 127.8, 82.4, 69.9, 53.1, 23.5 ppm. The NMR data are consistent with literature.[2]

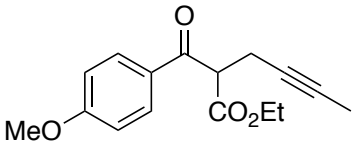


Ethyl 4-nitro-β-oxo-α-2-propyn-1-ylbenzenepropanoate (2e): The alkylation reaction was performed according to the standard procedure on a 5.0 mmol scale. Purification by column chromatography (15% ethyl acetate in hexanes) yielded the title compound as an orange-yellow oil (472 mg, 1.71 mmol, 34% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.36 – 8.29 (m, 2H), 8.22 – 8.14 (m, 2H), 4.57 (t, *J* = 7.4 Hz,

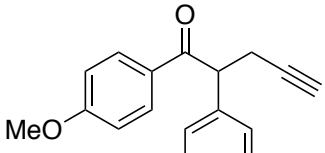


1H), 4.21 – 4.11 (m, 2H), 2.90 (dt, *J* = 7.7, 2.7 Hz, 2H), 1.98 (t, *J* = 2.7 Hz, 1H), 1.16 (t, *J* = 7.2 Hz, 3H) ppm; **^{13}C NMR (101 MHz, $CDCl_3$)** δ 192.4, 167.6, 150.7, 140.6, 130.0, 124.0, 80.1, 70.9, 62.4, 53.7, 18.3, 14.0 ppm. The NMR data are consistent with literature.[1]

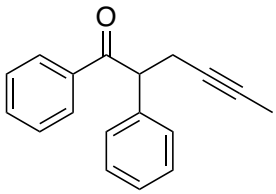
Ethyl α-2-butyn-1-yl-4-methoxy-β-oxobenzenepropanoate (2f): The alkylation reaction was performed according to the standard procedure on a 5.2 mmol scale. Purification by column chromatography (10% ethyl acetate in hexanes) yielded the title compound as a bright yellow oil (1.13g, 4.12 mmol, 79% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.03 – 7.95 (m, 2H), 6.96 – 6.88 (m, 2H), 4.44 (dd, *J* = 7.8, 7.0 Hz, 1H), 4.12 (qd, *J* = 7.2, 1.0 Hz, 2H), 3.84 (s, 3H), 2.88 – 2.65 (m, 2H), 1.66 (t, *J* = 2.6 Hz, 3H), 1.15 (t, *J* = 7.1 Hz, 3H) ppm; **^{13}C NMR (101 MHz, $CDCl_3$)** δ 192.2, 168.9, 164.0, 131.3, 129.0, 113.9, 77.7, 75.5, 61.6, 55.5, 53.5, 18.8, 14.0, 3.5 ppm; **IR (neat)** 2978, 2920, 2841, 1733, 1674, 1597, 1510, 1460, 1421 cm^{-1}; **HRMS (ESI^+)(m/z)** Anal. calcd. for $[M + H]^+$ $C_{16}H_{19}O_4^+$ 275.1278; found 275.1275.



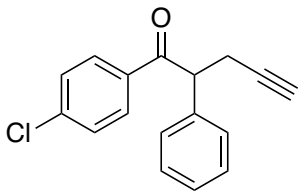
1-(4-Methoxyphenyl)-2-phenyl-4-pentyn-1-one (2g): The alkylation reaction was performed according to the standard procedure on a 5.5 mmol scale. Purification by column chromatography (15% ethyl acetate in hexanes) yielded the title compound as an off-white solid (1.32 g, 4.98 mmol, 91% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.89 (d, *J* = 9.0 Hz, 2H), 7.30 – 7.13 (m, 5H), 6.81 (d, *J* = 9.0 Hz, 2H), 4.67 (t, *J* = 7.3 Hz, 1H), 3.76 (s, 3H), 2.97 (ddd, *J* = 16.8, 7.2, 2.6 Hz, 1H), 2.64 (ddd, *J* = 16.8, 7.4, 2.6 Hz, 1H), 1.87 (t, *J* = 2.6 Hz, 1H) ppm; **^{13}C NMR (101 MHz, $CDCl_3$)** δ 196.4, 163.5, 138.5, 131.2, 129.2, 129.0, 128.1, 127.5, 113.8, 82.4, 69.7, 55.4, 52.6, 23.4 ppm. The NMR data are consistent with literature.[2]



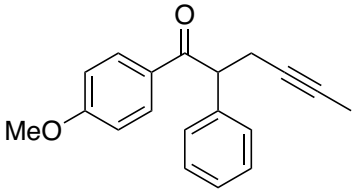
1,2-diphenylhex-4-yn-1-one one (2h): The alkylation reaction was performed according to the standard procedure on a 5.0 mmol scale. Purification by column chromatography (15% ethyl acetate in hexanes) yielded the title compound as an off-white solid (1.15 g, 4.63 mmol, 93% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.99 – 7.92 (m, 2H), 7.48 (td, *J* = 7.2, 1.4 Hz, 1H), 7.38 (ddd, *J* = 8.2, 6.6, 1.2 Hz, 2H), 7.30 (d, *J* = 4.4 Hz, 4H), 7.25 – 7.19 (m, 1H), 4.78 – 4.70 (m, 1H), 3.05 – 2.93 (ddd, 1H), 2.60 (ddd, *J* = 16.5, 7.7, 2.5 Hz, 1H), 1.70 (t, *J* = 2.5 Hz, 3H), 1.56 (s, 1H) ppm; **^{13}C NMR (101 MHz, $CDCl_3$)** δ 198.6, 138.7, 136.6, 133.1, 129.1, 129.0, 128.6, 128.2, 127.5, 53.6, 23.9,



3.6 ppm; **IR (neat)** 3058, 3025, 2908, 2850, 1677, 1595, 1493, 1446, 1419 cm^{-1}; **HRMS (ESI^+)(m/z)** Anal. calcd. for $[M + Na]^+$ $C_{18}H_{16}ONa^+$ 271.1093; found 271.1092.



1-(4-chlorophenyl)-2-phenylpent-4-yn-1-one (2i): The alkylation reaction was performed according to the standard procedure on a 2.0 mmol scale. Purification by column chromatography (5% ethyl acetate in hexanes) yielded the title compound as a white solid (420 mg, 1.56 mmol, 78% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.98 – 7.84 (m, 2H), 7.38 – 7.19 (m, 7H), 4.71 (t, *J* = 7.3 Hz, 1H), 3.03 (ddd, *J* = 16.8, 7.3, 2.6 Hz, 1H), 2.68 (ddd, *J* = 16.8, 7.2, 2.6 Hz, 1H), 1.94 (t, *J* = 2.6 Hz, 1H) ppm; **^{13}C NMR (101 MHz, $CDCl_3$)** δ 196.9, 139.7, 137.9, 134.6, 130.4, 129.3, 129.0, 128.2, 127.9, 82.2, 77.5, 77.2, 76.8, 70.0, 53.2, 23.5 ppm; **IR (neat)** 3286, 3064, 3032, 2952, 2115, 1673, 1585, 1488, 1452, 1426 cm^{-1}; **HRMS (ESI^+)(m/z)** Anal. calcd. for $[M + H]^+$ $C_{17}H_{14}ClO^+$ 269.0728; found 269.0725.

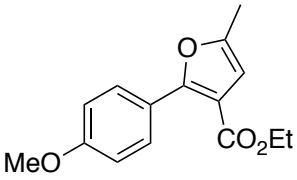


1-(4-methoxyphenyl)-2-phenylhex-4-yn-1-one (2j): The alkylation reaction was performed according to the standard procedure on a 3.0 mmol scale. Purification by column chromatography (2% ethyl acetate in hexanes) yielded the title compound as white crystals (0.393 g, 1.41 mmol, 47% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.97 – 7.88 (m, 2H), 7.32 – 7.13 (m, 5H), 6.87 – 6.79 (m, 2H), 4.66 (dd, *J* = 7.6, 6.9 Hz, 1H), 3.79 (s, 3H), 2.95 (ddq, *J* = 16.5, 7.6, 2.5 Hz, 1H), 2.57 (ddq, *J* = 16.5, 6.9, 2.5 Hz, 1H), 1.67 (t, *J* = 2.5 Hz, 3H) ppm; **^{13}C NMR (101 MHz, $CDCl_3$)** δ 197.1, 163.5, 139.2, 131.3, 129.6, 129.0, 128.2, 127.4, 113.8, 55.6, 53.2, 23.9, 3.7 ppm; **IR (neat)** 3060, 3029, 2959, 2918, 2834, 1663, 1601, 1574, 1509, 1451 cm^{-1}; **HRMS (ESI^+)(m/z)** Anal. calcd. for $[M + H]^+$ $C_{19}H_{19}O_2^+$ 279.1380; found 279.1374.

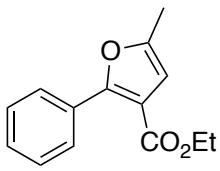
Substrate Scope – Formation of Furan Products

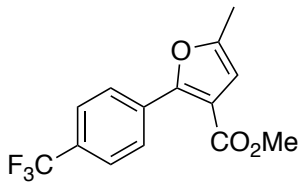
General procedure for the synthesis of furans 3a-j: The reaction substrate (0.5 or 1.0 mmol) was dissolved in 1,1,1,3,3,3-hexafluoro isopropanol (300 μL per mmol of substrate) with *p*-toluenesulfonic acid catalyst (10 mol%) in a reaction vial equipped with a stirrer bar. The reaction mixture was left to stir at room temperature for 24 hrs, or heated using a sand bath at 50 °C. Upon completion, the solvent was removed under reduced pressure and mesitylene (0.2 mmol) was added to the mixture as an internal standard. ^{1}H NMR specta were then obtained to estimate reaction yield before the reaction mixture was purified by flash column chromatography (silica-gel, ethyl acetate/hexanes).

Ethyl 2-(4-methoxyphenyl)-5-methyl-3-furancarboxylate (3a): Prepared according to the standard procedure from ethyl 4-methoxy-β-oxo-α-2-propyn-1-ylbenzenepropanoate (**2a**) on a 1.0 mmol scale. Purification by column chromatography (8% ethyl acetate in hexanes) yielded the titled compound as a colorless solid (172 mg, 0.66 mmol, 66% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.98 – 7.89 (m, 2H), 6.98 – 6.90 (m, 2H), 6.40 (q, *J* = 1.1 Hz, 1H), 4.27 (q, *J* = 7.1 Hz, 2H), 3.85 (s, 3H), 2.33 (d, *J* = 1.2 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H) ppm; **^{13}C NMR (101 MHz, $CDCl_3$)** δ 164.1, 160.2, 156.4, 150.5, 129.8, 123.0, 113.6, 113.4, 108.7, 60.4, 55.4, 14.4, 13.4 ppm. The NMR is consistent with literature data.[1]

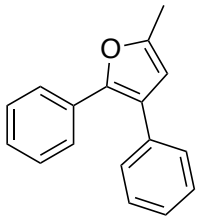


Ethyl 5-methyl-2-phenyl-3-furancarboxylate (3b): Prepared according to the standard procedure from ethyl β-oxo-α-2-propyn-1-ylbenzenepropanoate (**2b**) on a 1.0 mmol scale. Purification by column chromatography (8-15% ethyl acetate in hexanes) yielded the titled compound as a pale yellow oil (156 mg, 0.68 mmol, 68% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.01 – 7.94 (m, 2H), 7.47 – 7.32 (m, 3H), 6.45 (q, *J* = 1.1 Hz, 1H), 4.29 (q, *J* = 7.2 Hz, 2H), 2.35 (d, *J* = 1.1 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H) ppm; **^{13}C NMR (101 MHz, $CDCl_3$)** δ 163.9, 156.0, 151.2, 130.2, 129.0, 128.2, 128.1, 114.6, 108.9, 60.4, 14.3, 13.4 ppm. The NMR is consistent with literature data.[1]

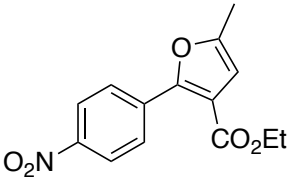




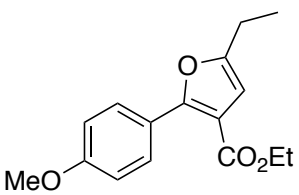
3-Furancarboxylic acid, 5-methyl-2-[4-(trifluoromethyl)phenyl]-, methyl ester (3c): Prepared according to the standard procedure from benzenepropanoic acid, β-oxo-α-2-propyn-1-yl-4-(trifluoromethyl)-, methyl ester (**2c**) on a 0.5 mmol scale. Purification by column chromatography (8% ethyl acetate in hexanes) yielded the titled compound as a yellow oil (55.4 mg, 0.19 mmol, 39% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.12 (d, *J* = 8.4 Hz, 2H), 7.66 (d, *J* = 8.3 Hz, 2H), 6.46 (q, *J* = 1.1 Hz, 1H), 3.83 (s, 3H), 2.37 (d, *J* = 1.1 Hz, 3H) ppm; **^{13}C NMR (101 MHz, $CDCl_3$)** δ 164.1, 154.2, 152.3, 133.3, 130.5 (q, *J* = 32.5 Hz), 128.2, 125.2 (q, *J* = 3.9 Hz), 124.2 (q, *J* = 272.7 Hz), 115.8, 109.3, 51.8, 13.5 ppm; **^{19}F NMR (376 MHz, $CDCl_3$)** δ -62.78 ppm. The NMR is consistent with literature data.[1]



5-Methyl-2,3-diphenylfuran (3d): Prepared according to the standard procedure from 1,2-diphenyl-4-pentyn-1-one (**2d**) on a 1.0 mmol scale. Purification by column chromatography (3-5% ethyl acetate in hexanes) yielded the titled compound as a pale yellow oil (215 mg, 0.92 mmol, 92% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.57 – 7.49 (m, 2H), 7.47 – 7.17 (m, 8H), 6.22 – 6.15 (m, 1H), 2.41 (dd, *J* = 4.3, 1.6 Hz, 3H) ppm; **^{13}C NMR (101 MHz, $CDCl_3$)** δ151.1, 146.6, 134.5, 131.3, 128.4, 128.4, 128.1, 126.9, 126.8, 125.7, 123.0, 110.0, 13.4 ppm. The NMR is consistent with literature data.[2]



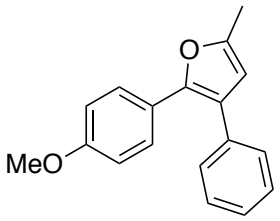
Methyl 5-methyl-2-(4-nitrophenyl)-3-furancarboxylate (3e): Prepared according to the standard procedure from ethyl 4-nitro-β-oxo-α-2-propyn-1-ylbenzenepropanoate (**2e**) on a 0.5 mmol scale. Purification by column chromatography (5% ethyl acetate in hexanes) yielded the titled compound as a bright yellow solid (37.4 mg, 0.14 mmol, 27% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.23 (d, *J* = 1.7 Hz, 4H), 6.51 (q, *J* = 1.0 Hz, 1H), 4.31 (q, *J* = 7.1 Hz, 2H), 2.39 (d, *J* = 1.1 Hz, 3H), 1.35 (t, *J* = 7.1 Hz, 3H) ppm; **^{13}C NMR (101 MHz, $CDCl_3$)** δ 163.4, 153.0, 152.8, 147.4, 135.8, 128.5, 123.5, 117.7, 110.0, 61.0, 14.3, 13.6 ppm. The NMR is consistent with literature data.[1]



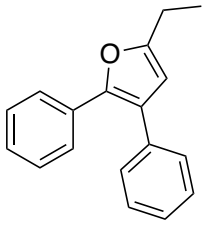
Ethyl 5-ethyl-2-(4-methoxyphenyl)furan-3-carboxylate (3f): Prepared according to the standard procedure from ethyl α-2-butyn-1-yl-4-methoxy-β-oxobenzenepropanoate (**2f**) on a 0.5 mmol scale. Purification by column chromatography (5% ethyl acetate in hexanes) yielded the titled compound

as a clear oil (47.1 mg, 0.17 mmol, 35% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.99 – 7.90 (m, 2H), 6.98 – 6.90 (m, 2H), 6.41 (t, *J* = 1.1 Hz, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 3.84 (s, 3H), 2.68 (qd, *J* = 7.6, 1.1 Hz, 2H), 1.31 (dt, *J* = 21.2, 7.3 Hz, 6H) ppm; **^{13}C NMR (101 MHz, $CDCl_3$)** δ 164.1, 160.2, 156.2, 156.1, 129.8, 123.0, 113.5, 113.2, 107.1, 77.5, 77.2, 76.8, 60.3, 55.4, 21.2, 14.4, 12.0 ppm; **IR (neat)** 3089, 3061, 2981, 2912, 2836, 1701, 1603, 1576, 1554, 1504, 1478 cm^{-1}; **HRMS (ESI^+)(m/z)** Anal. calcd. for $[M + H]^+$ $C_{16}H_{19}O_4^+$ 275.1278; found 275.1274.

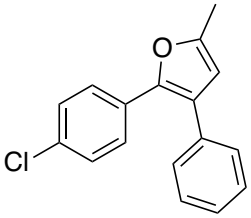
2-(4-Methoxyphenyl)-5-methyl-3-phenylfuran (3g): Prepared according to the standard procedure from 1-(4-methoxyphenyl)-2-phenyl-4-pentyn-1-one (**2g**) on a 0.5 mmol scale. Purification by column chromatography (4% ethyl acetate in hexanes) yielded the titled compound as a clear oil (106 mg, 0.40 mmol, 80% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.54 – 7.48 (m, 2H), 7.46 (dd, *J* = 8.2, 1.5 Hz, 2H), 7.39 (tt, *J* = 6.7, 1.0 Hz, 2H), 7.34 – 7.28 (m, 1H), 6.92 – 6.84 (m, 2H), 6.21 (t, *J* = 1.0 Hz, 1H), 3.84 (s, 3H), 2.43 (d, *J* = 1.1 Hz, 3H) ppm; **^{13}C NMR (101 MHz, $CDCl_3$)** δ 158.8, 150.8, 147.0, 134.9, 128.6, 128.5, 127.6, 126.8, 124.4, 121.8, 113.9, 109.8, 55.2, 13.6 ppm. The NMR is consistent with literature data.[2]



5-ethyl-2,3-diphenylfuran (3h): Prepared according to the standard procedure from 1,2-diphenylhex-4-yn-1-one (**2h**) on a 0.5 mmol scale. Purification by column chromatography (2% ethyl acetate in hexanes) yielded the titled compound as a yellow oil (116 mg, 0.47 mmol, 94% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.61 – 7.19 (m, 10H), 6.22 (m, 1H), 2.85 – 2.73 (m, 2H), 1.42 – 1.32 (m, 3H) ppm;**^{13}C NMR (101 MHz, $CDCl_3$)** δ 157.1, 146.8, 135.0, 131.7, 128.7, 128.4, 128.4, 127.2, 127.1, 126.1, 123.1, 108.7, 21.6, 12.2 ppm. The NMR is consistent with literature data.[3]

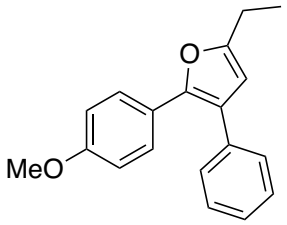


2-(4-chlorophenyl)-5-methyl-3-phenylfuran (3i): Prepared according to the standard procedure from 1-(4-chlorophenyl)-2-phenylpent-4-yn-1-one (**2i**) on a 0.5 mmol scale. Purification by column chromatography (2% ethyl acetate in hexanes) yielded the titled compound as a pale yellow oil (28.8 mg, 0.11 mmol, 21% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.46 – 7.41 (m, 2H), 7.41 – 7.28 (m, 5H), 7.28 – 7.19 (m, 2H), 6.17 (q, *J* = 1.0 Hz, 1H), 2.39 (d, *J* = 1.1 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 151.7, 145.8, 134.6, 132.8, 130.0, 128.8, 128.7, 128.7, 127.3, 127.2, 123.9, 110.5, 13.7 ppm;



IR (neat) 3057, 3028, 2917, 1897, 1674, 1599, 1570, 1553, 1498, 1479, 1443, 1400 cm^{-1}; **HRMS (ESI$^+$)(m/z)** Anal. calcd. for $[M]^+$ $C_{17}H_{13}ClO^+$ 268.0606; found 268.0606.

5-ethyl-2-(4-methoxyphenyl)-3-phenylfuran (3j): Prepared according to the standard procedure from 1-(4-methoxyphenyl)-2-phenylhex-4-yn-1-one (**2j**) on a 0.5 mmol scale. Purification by column chromatography (2% ethyl acetate in hexanes) yielded the titled compound as clear oil (94.7 mg, 0.34 mmol, 68% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.52 – 7.25 (m, 7H), 6.91 – 6.76 (m, 2H), 6.19 (t, J = 1.0 Hz, 1H), 3.83 (s, 3H), 2.76 (qd, J = 7.5, 1.0 Hz, 2H), 1.34 (t, J = 7.6 Hz, 3H) ppm; **^{13}C NMR (101 MHz, $CDCl_3$)** δ 196.9, 139.7, 137.9, 134.6, 130.4, 130.2, 129.3, 129.1, 129.0, 128.2, 127.9, 82.2, 70.0, 53.2, 23.5 ppm; **IR (neat)** 2969, 2934, 2905, 2834, 1600, 1559, 1509, 1460 cm^{-1}; **HRMS (ESI$^+$)(m/z)** Anal. calcd. for $[M + H]^+$ $C_{19}H_{19}O_2^+$ 279.1380; found 279.1377.



References

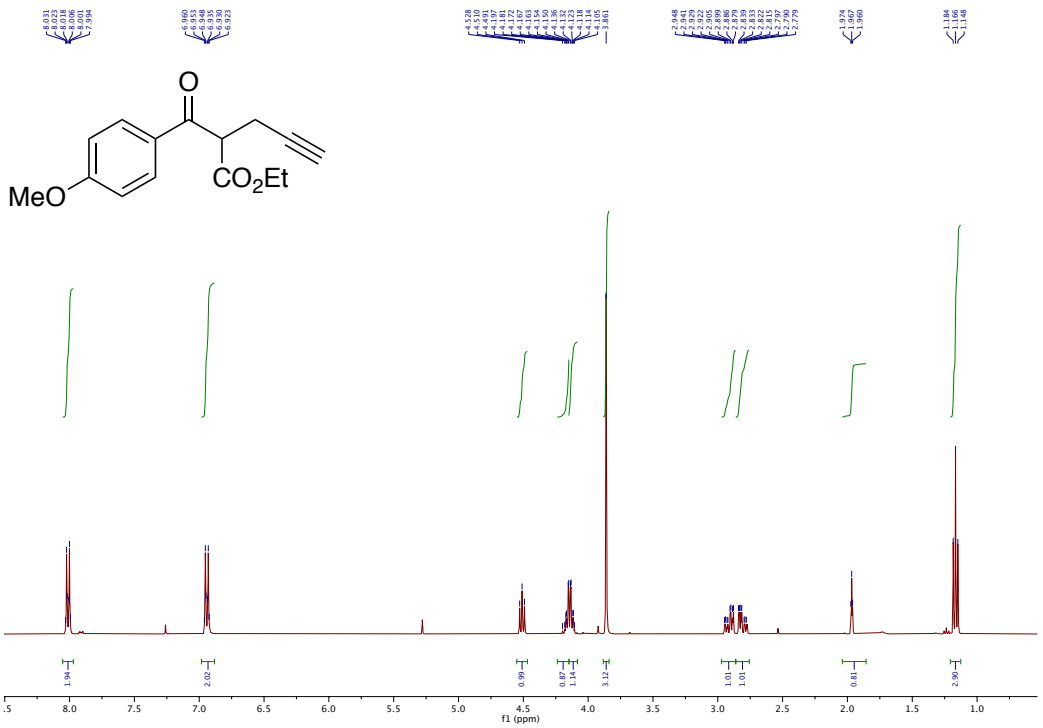
[1] Pace, D. P.; Robidas, R.; Tran, U. P. N.; Legault, C. Y.; Nguyen, T. V., Iodine-Catalyzed Synthesis of Substituted Furans and Pyrans: Reaction Scope and Mechanistic Insights. *J. Org. Chem.* **2021,** *86*, 8154.

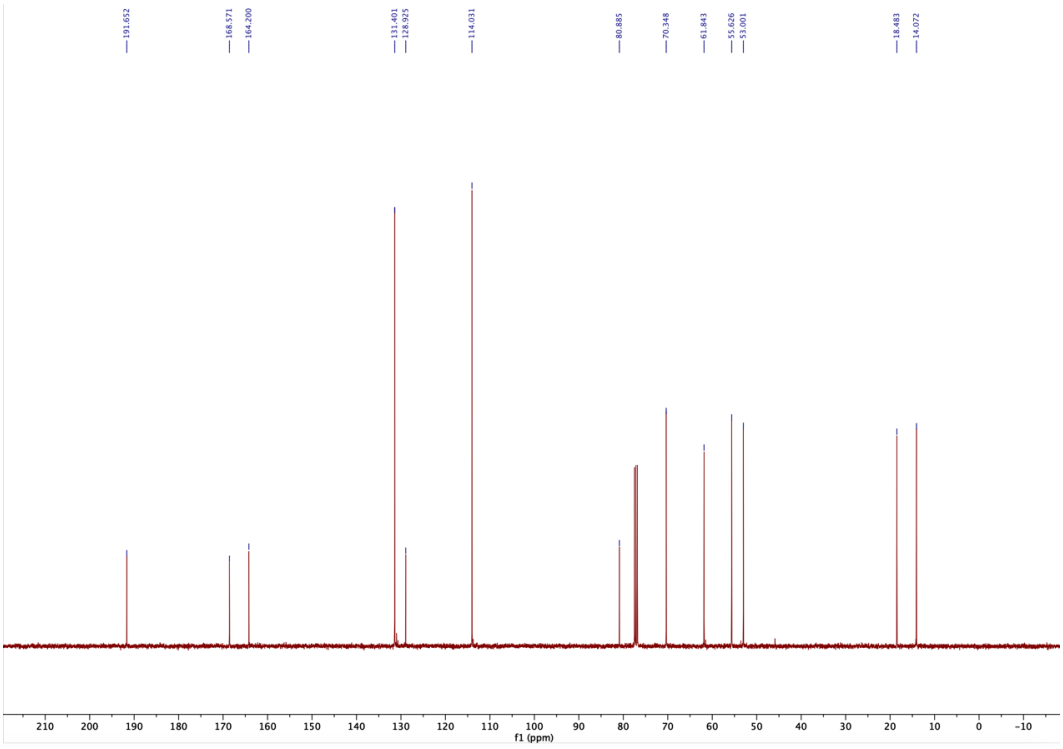
[2] Chan, C.-K.; Chen, Y.-C.; Chen, Y.-L.; Chang, M.-Y., Synthesis of substituted phenanthrofurans. *Tetrahedron* **2015,** *71*, 9187.

[3] Chen, L.; Du, Y.; Zeng, X.-P.; Shi, T.-D.; Zhou, F.; Zhou, J., Successively Recycle Waste as Catalyst: A One-Pot Wittig/1,4-Reduction/Paal–Knorr Sequence for Modular Synthesis of Substituted Furans. *Org. Lett.* **2015,** *17*, 1557.

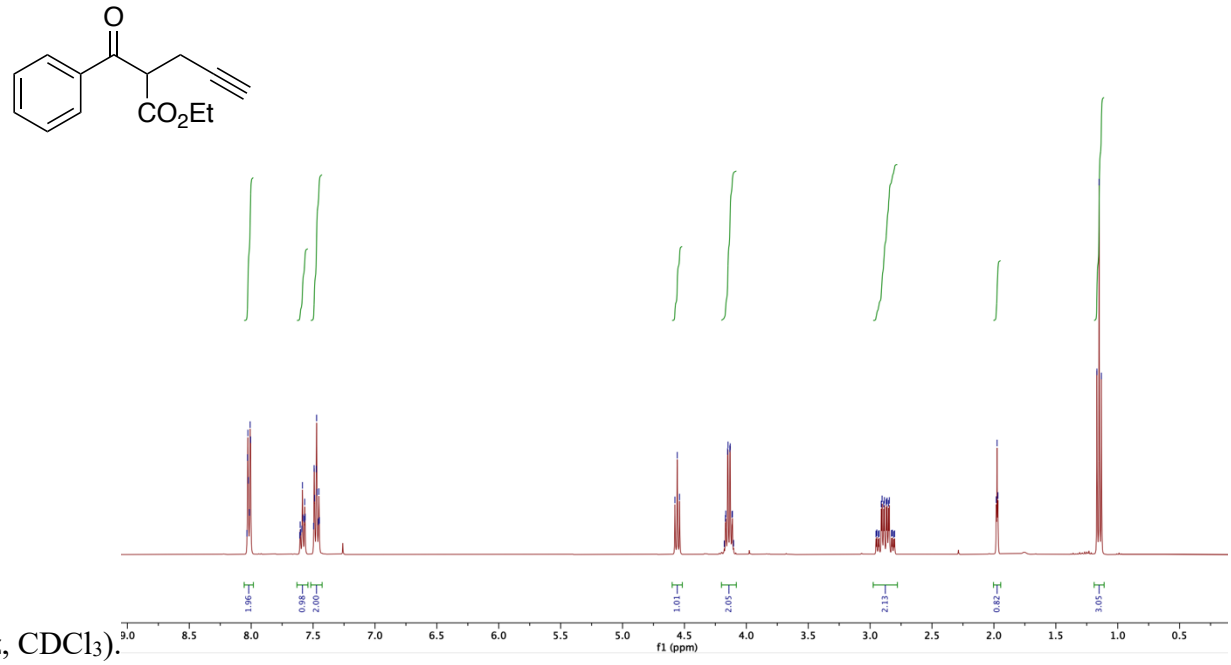
NMR Spectra for Starting Materials

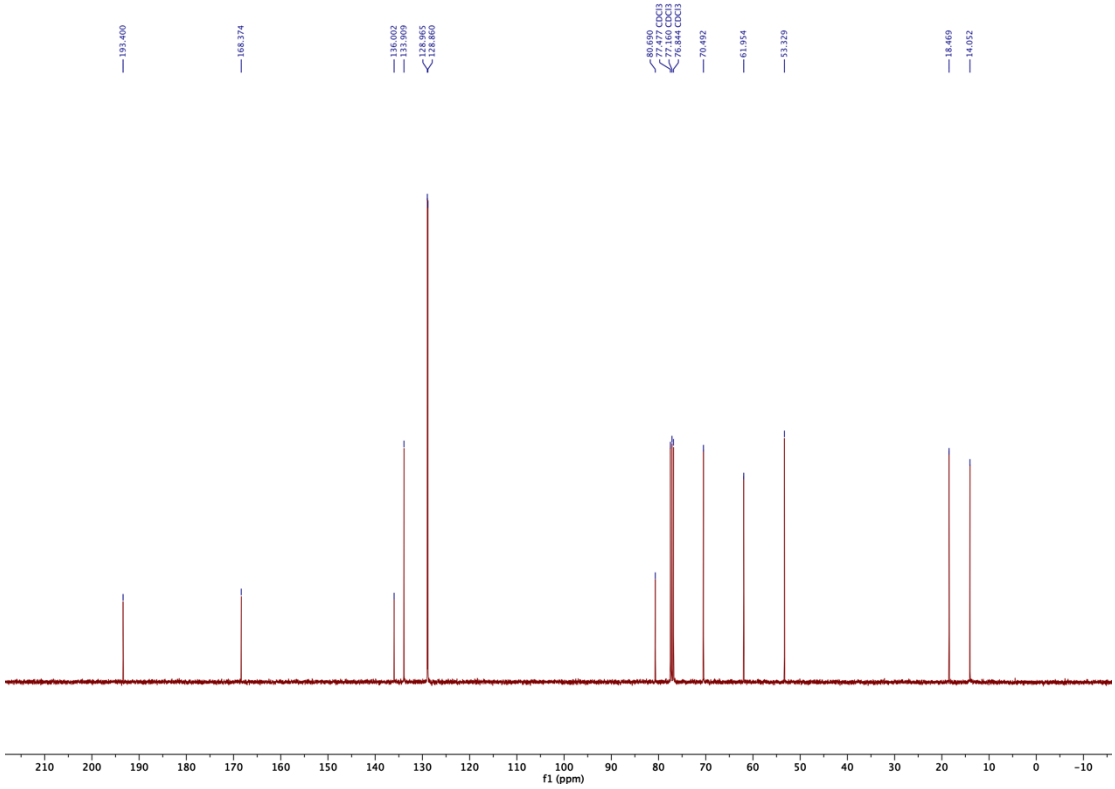
Ethyl 4-methoxy-β-oxo-α-2-propyn-1-ylbenzenepropanoate (2a): ^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (101 MHz, $CDCl_3$).



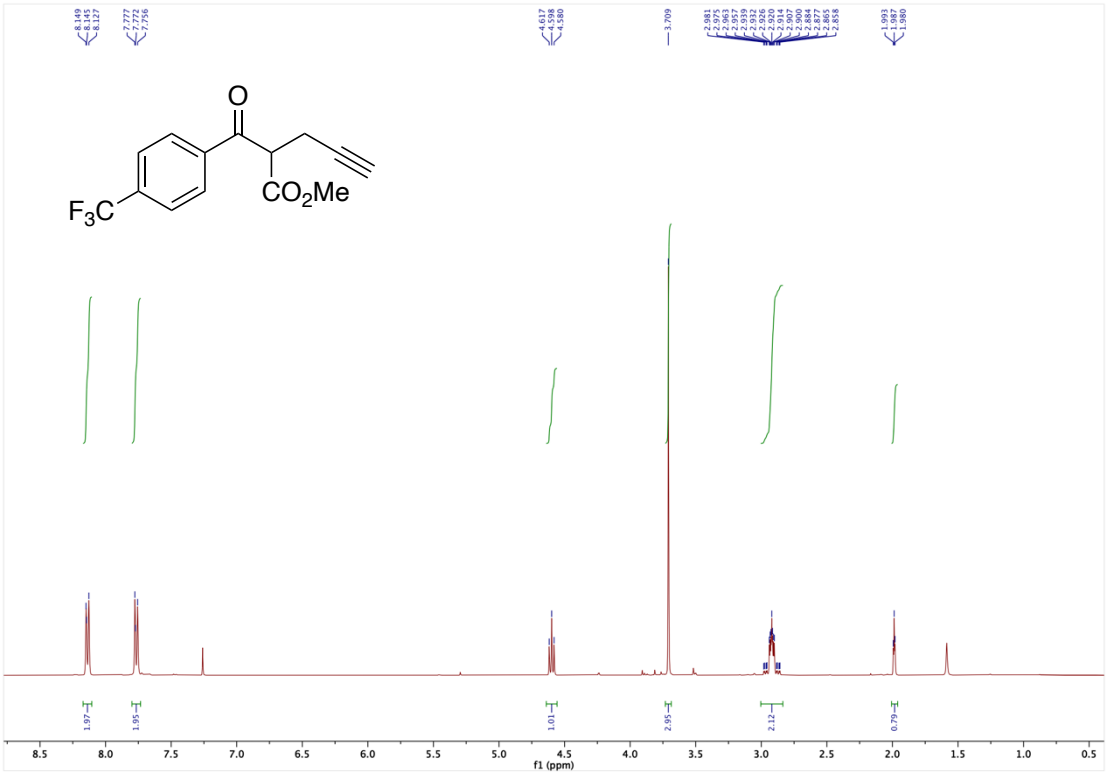


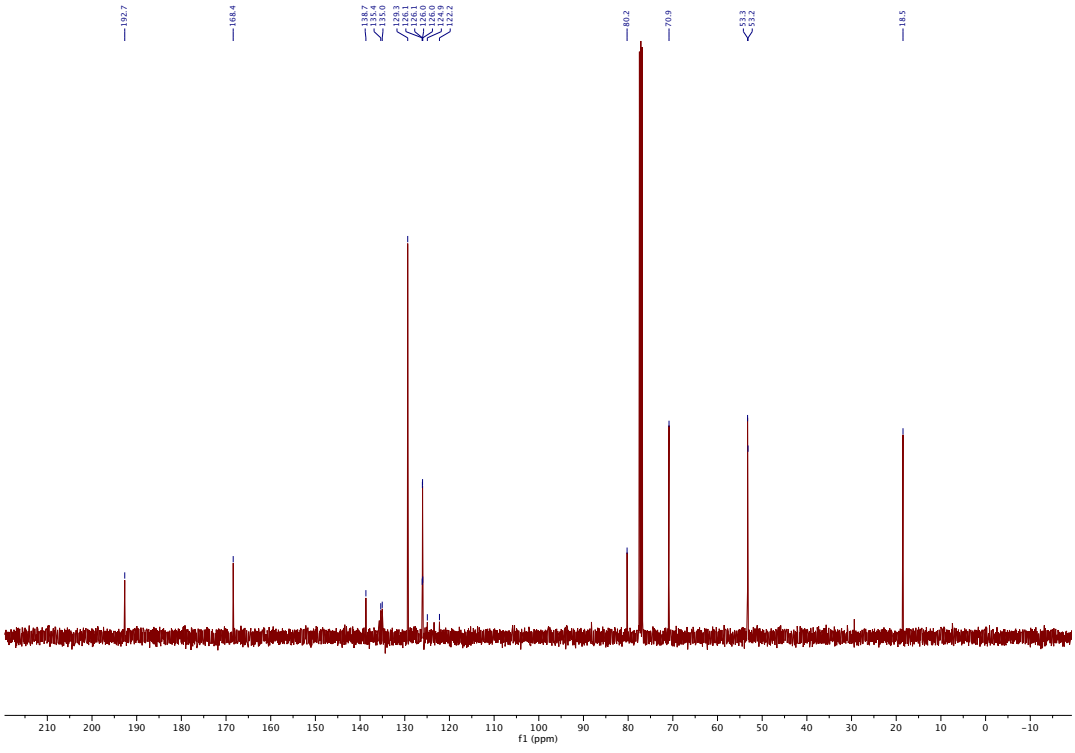
Ethyl β-oxo-α-2-propyn-1-ylbenzenepropanoate (2b): ^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (101 MHz, $CDCl_3$).



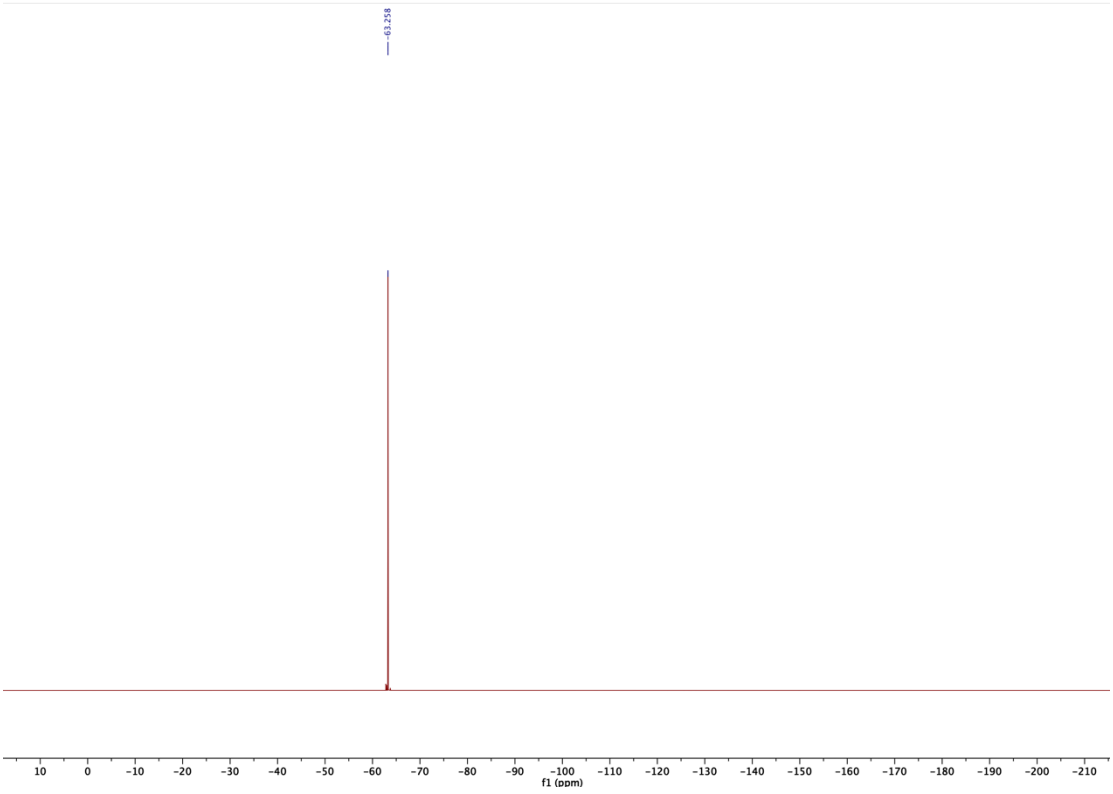


Benzenepropanoic acid, β-oxo-α-2-propyn-1-yl-4-(trifluoromethyl)-, methyl ester (2c): ^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (101 MHz, $CDCl_3$), ^{19}F NMR (376 MHz, CDCl3).

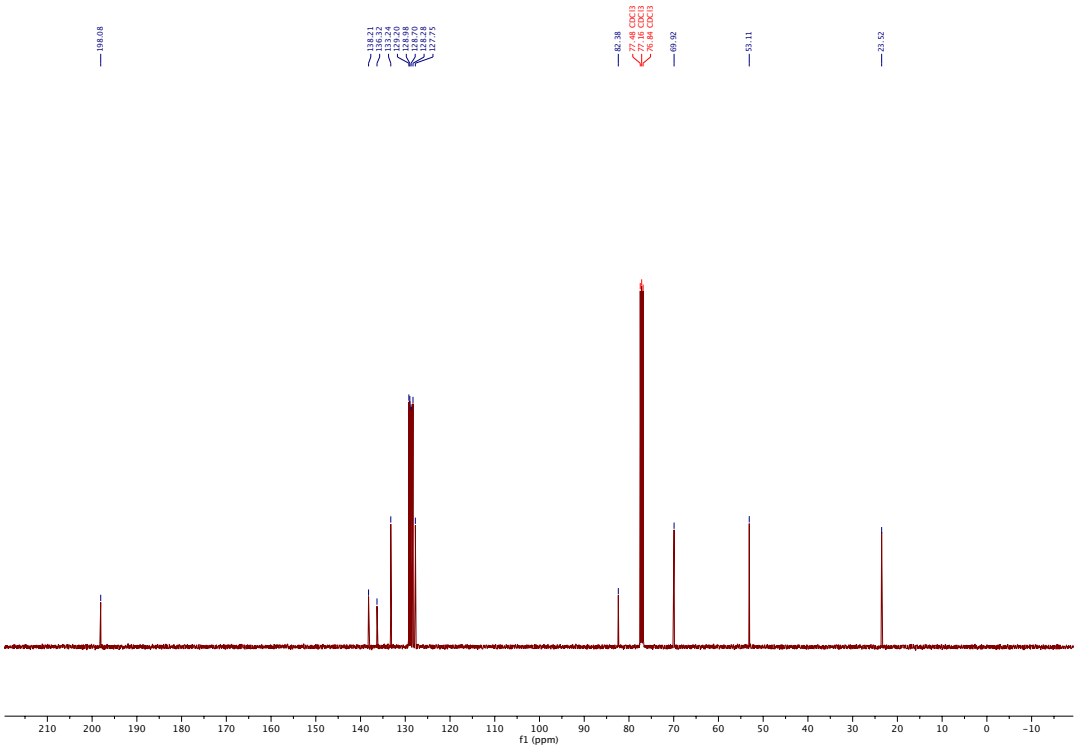




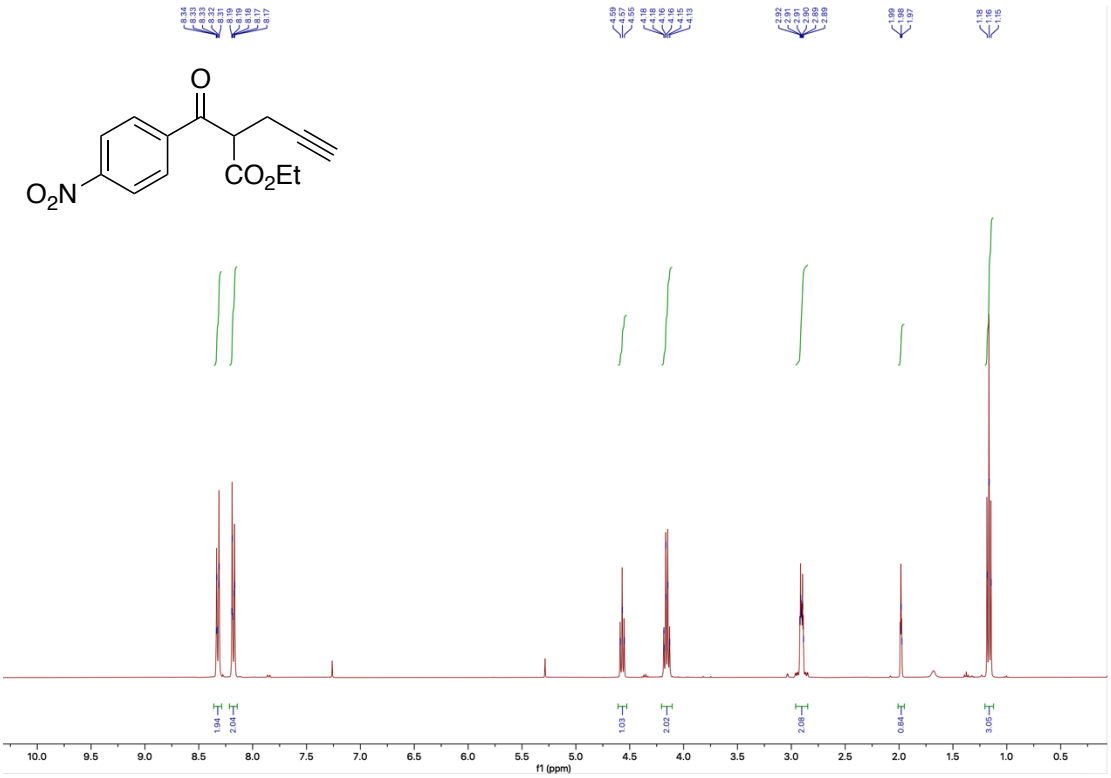
(Note: the quartet for CF_3 was very small so part of this signal was under the noises)

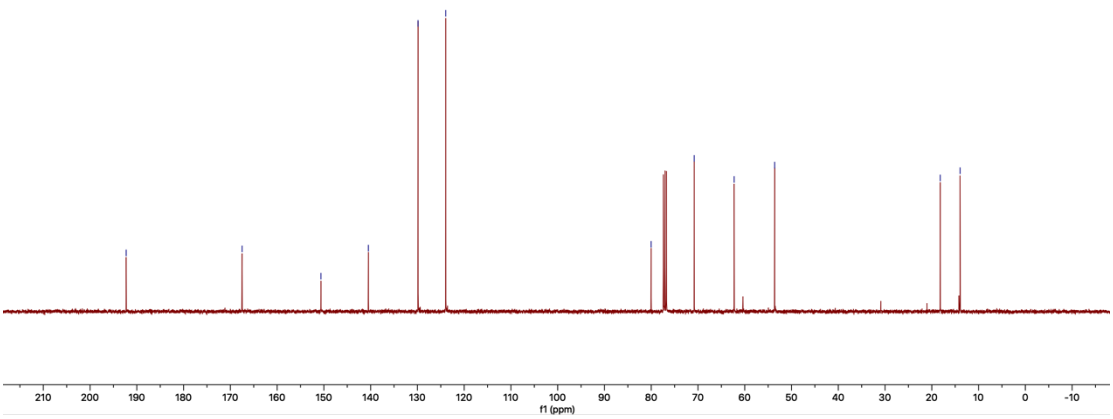

-63.258
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

1,2-Diphenyl-4-pentyn-1-one (2d): ^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (101 MHz, $CDCl_3$).

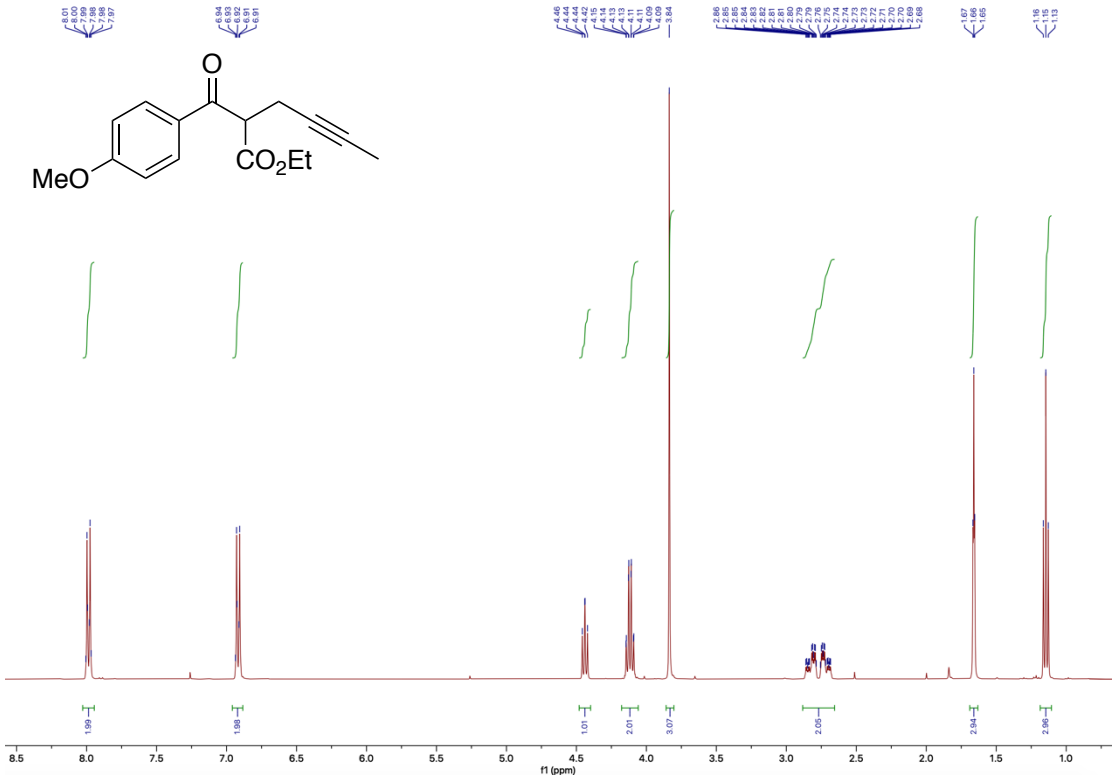


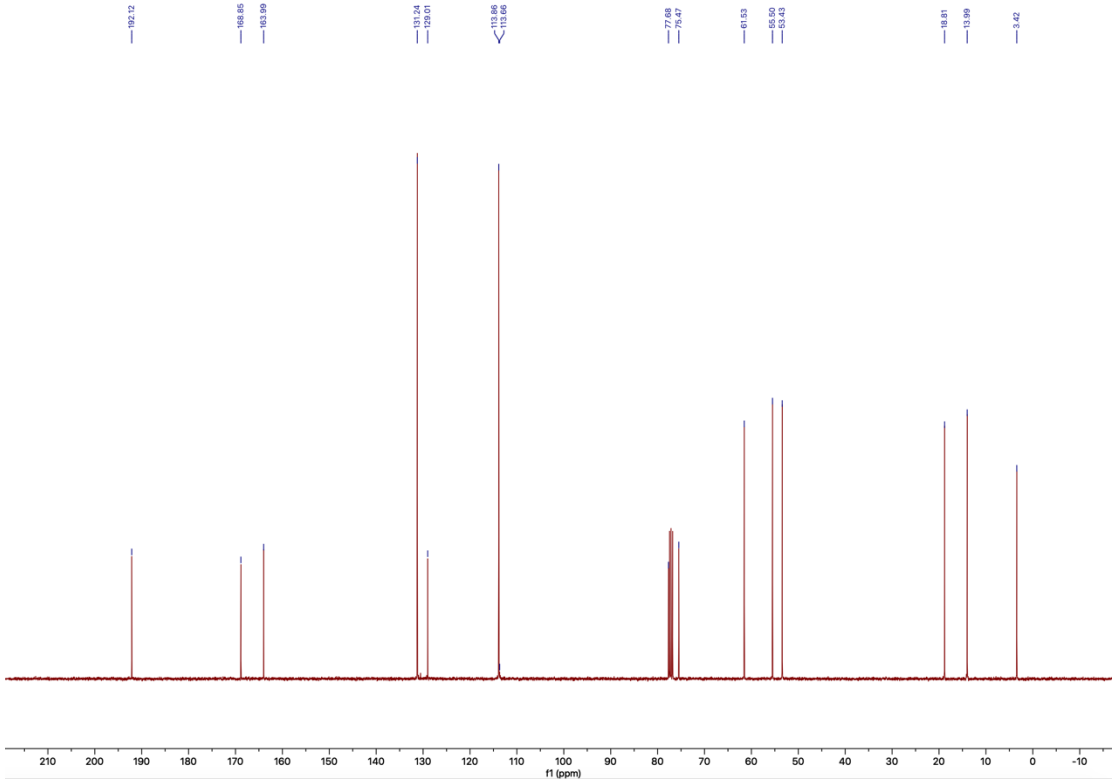
Ethyl 4-nitro-β-oxo-α-2-propyn-1-ylbenzenepropanoate (2e): ^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (101 MHz, $CDCl_3$).



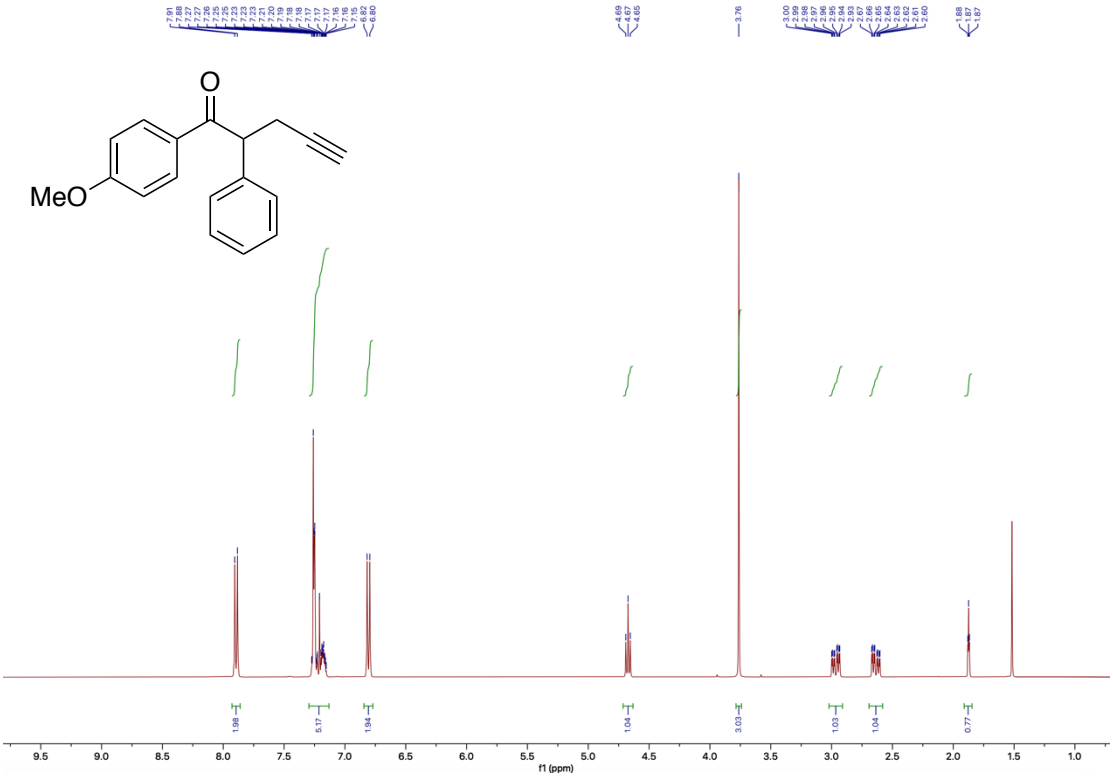


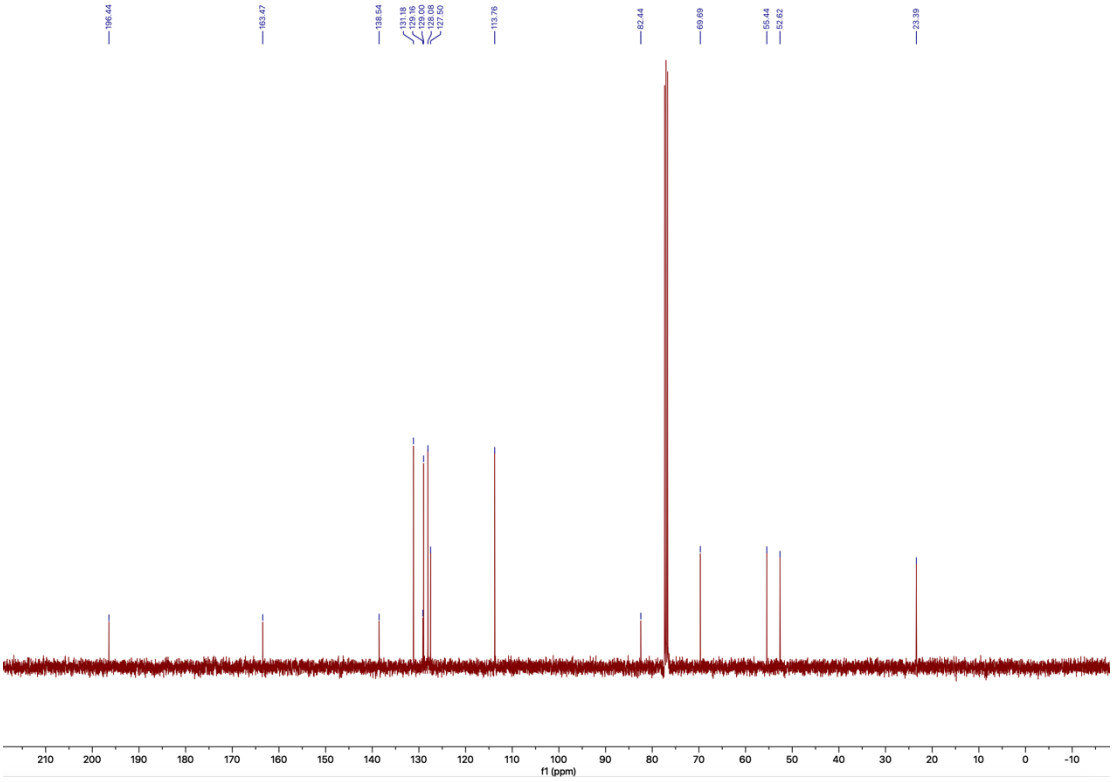
Ethyl α-2-butyn-1-yl-4-methoxy-β-oxobenzenepropanoate (2f): ^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (101 MHz, $CDCl_3$).



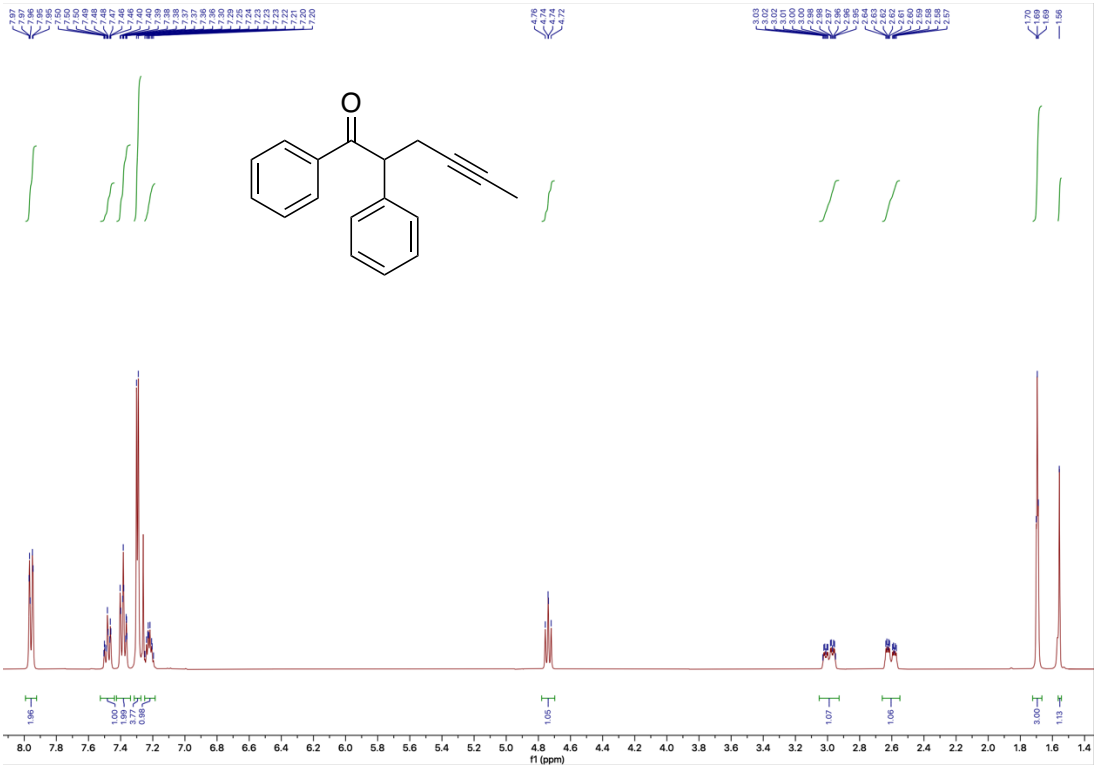


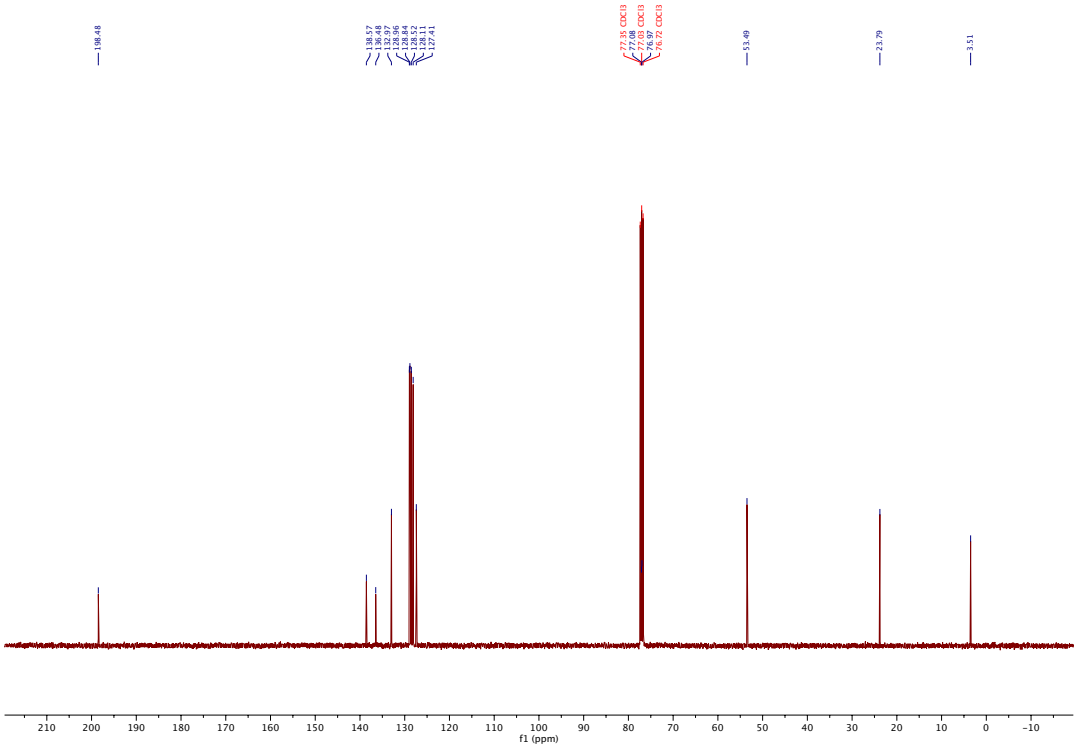
1-(4-Methoxyphenyl)-2-phenyl-4-pentyn-1-one (2g): ^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (101 MHz, $CDCl_3$).





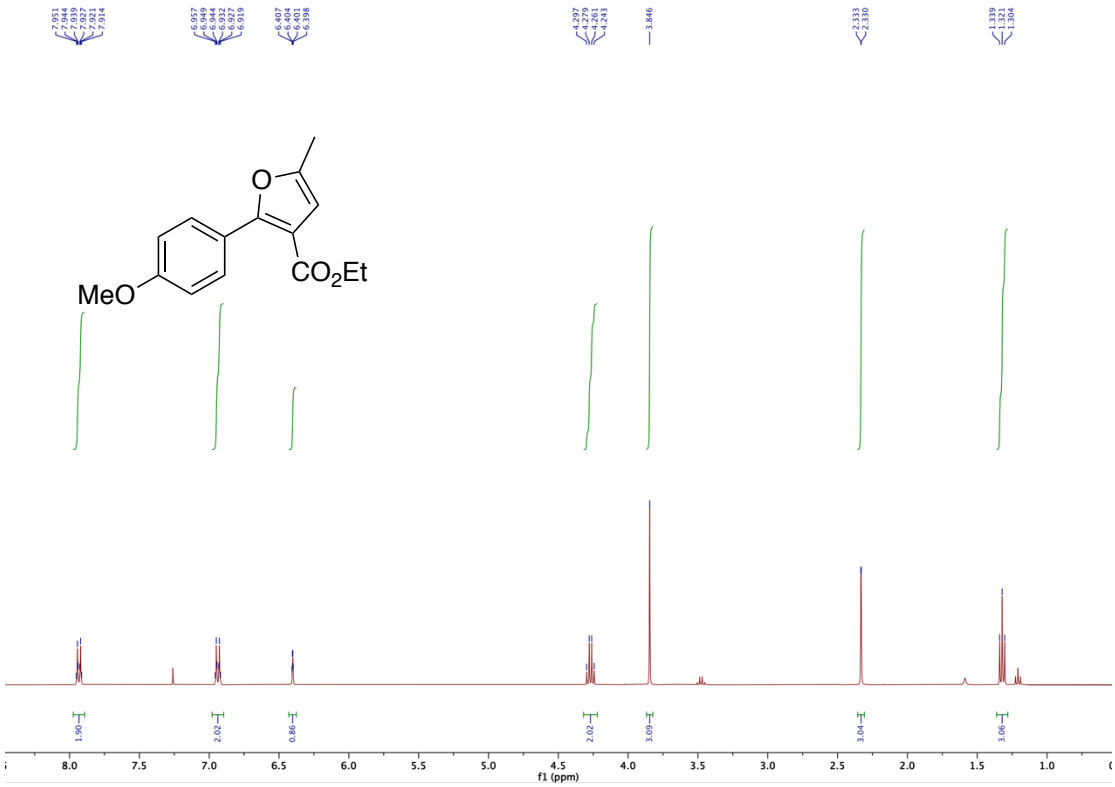
1,2-diphenylhex-4-yn-1-one one (2h): ^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (101 MHz, $CDCl_3$).

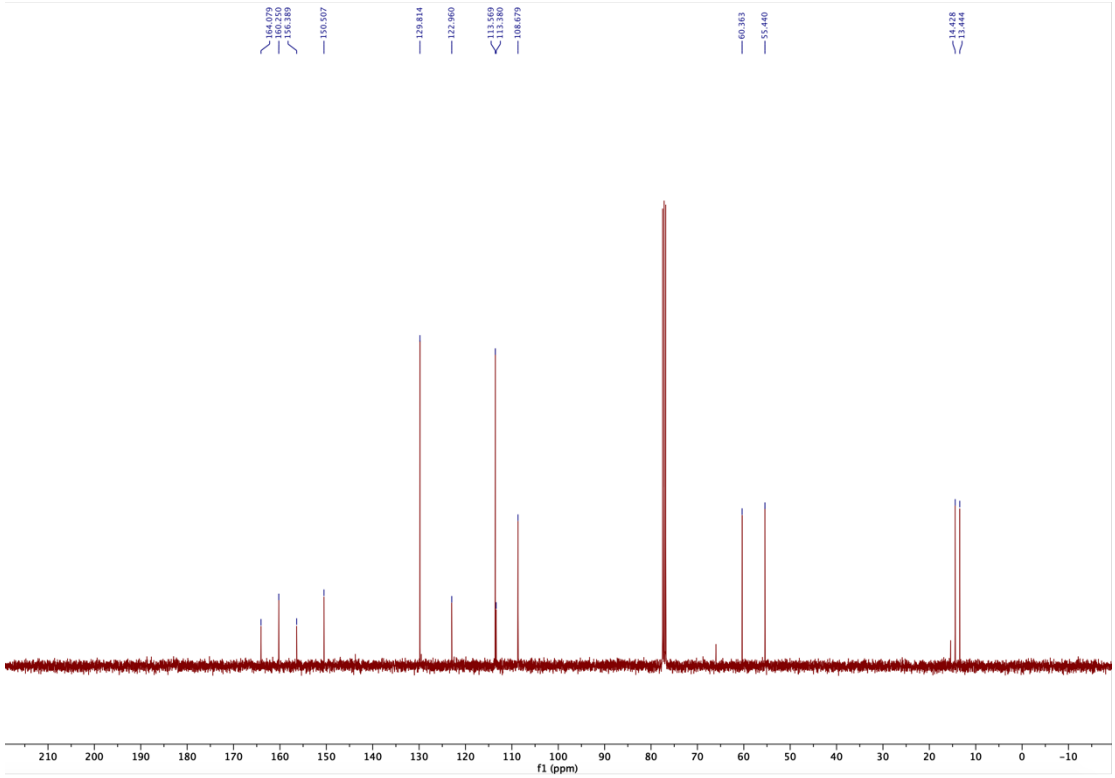




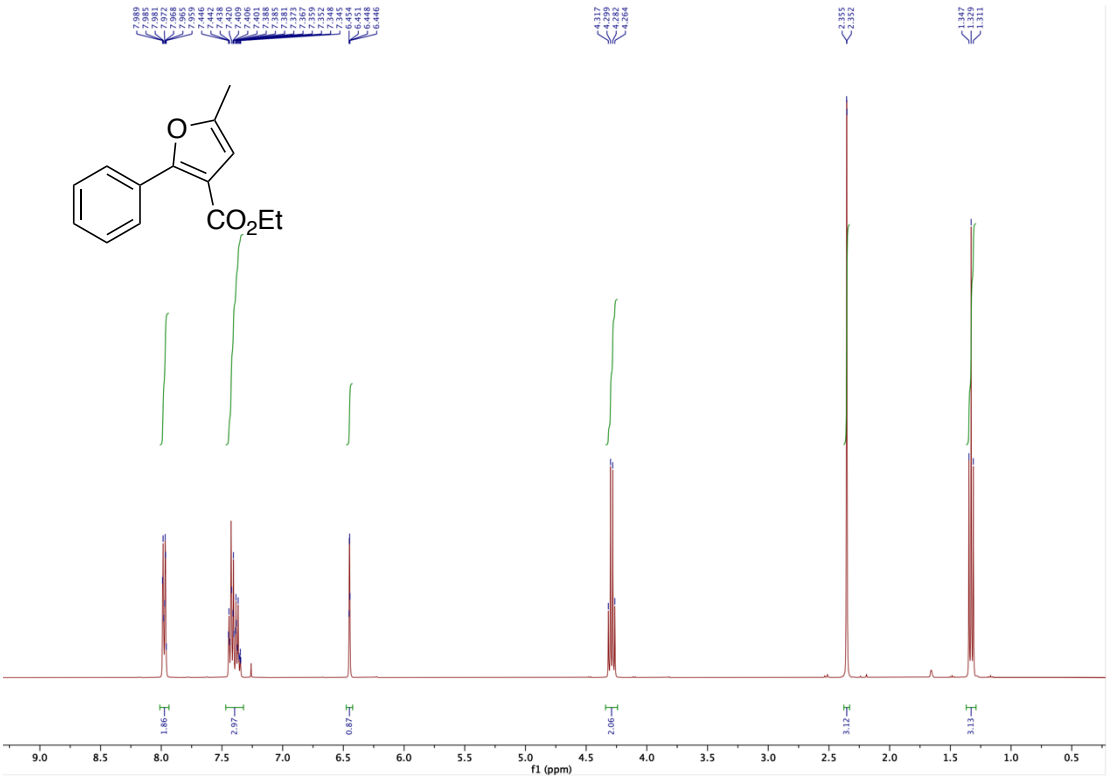
NMR Spectra of Products

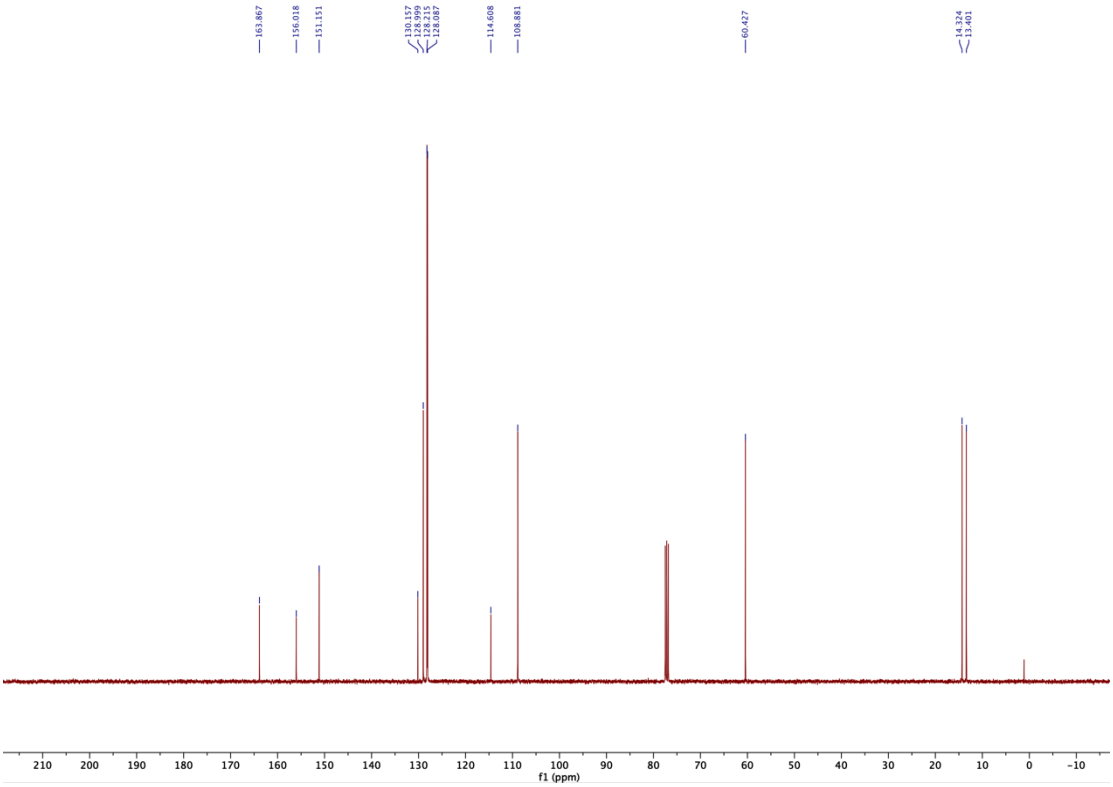
Ethyl 2-(4-methoxyphenyl)-5-methyl-3-furancarboxylate (3a): ^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (101 MHz, $CDCl_3$).



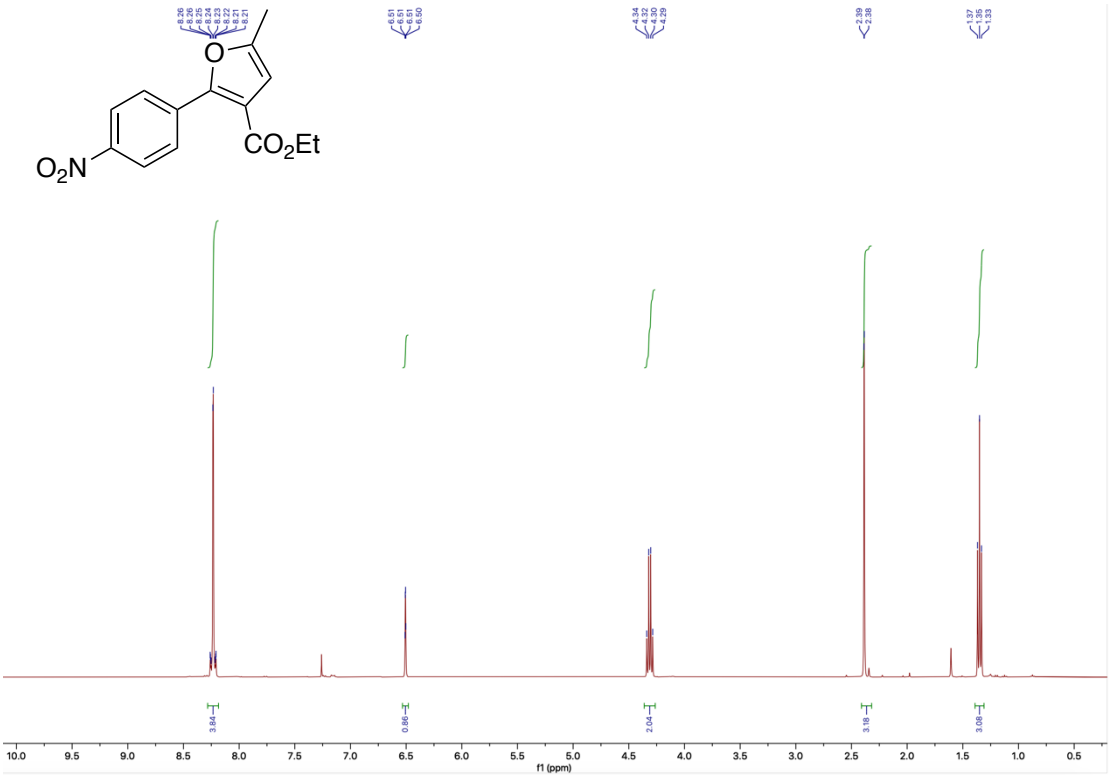


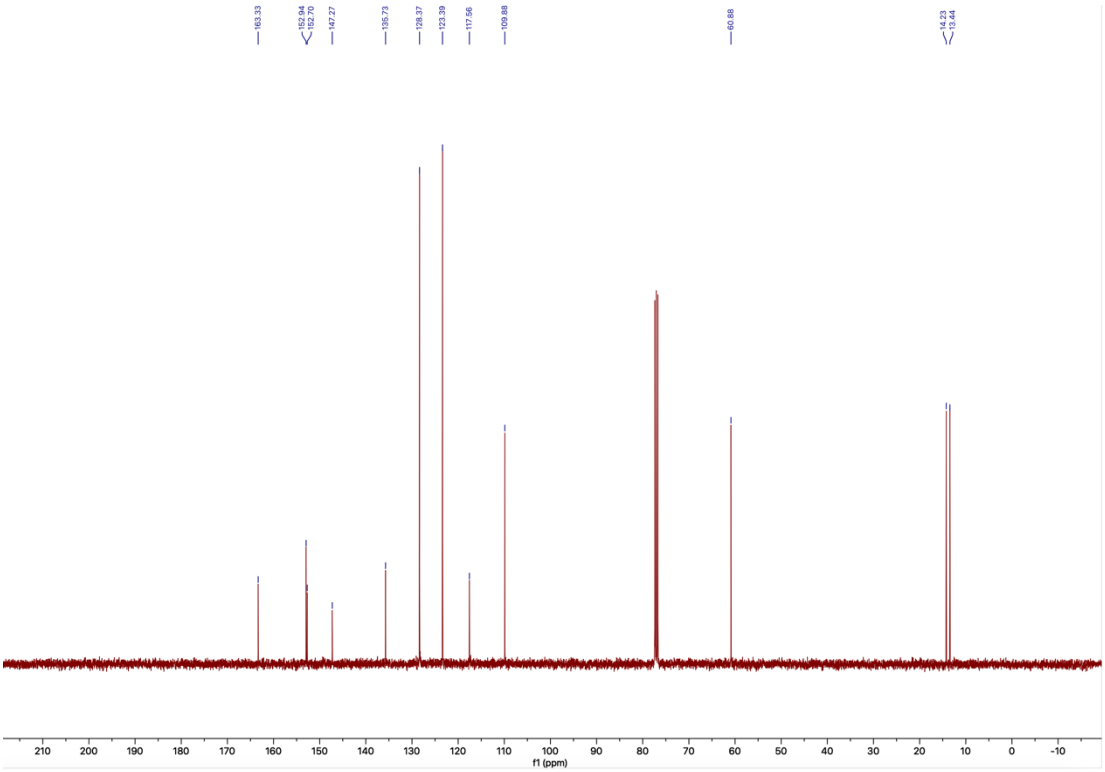
Ethyl 5-methyl-2-phenyl-3-furancarboxylate (3b): ^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (101 MHz, $CDCl_3$).



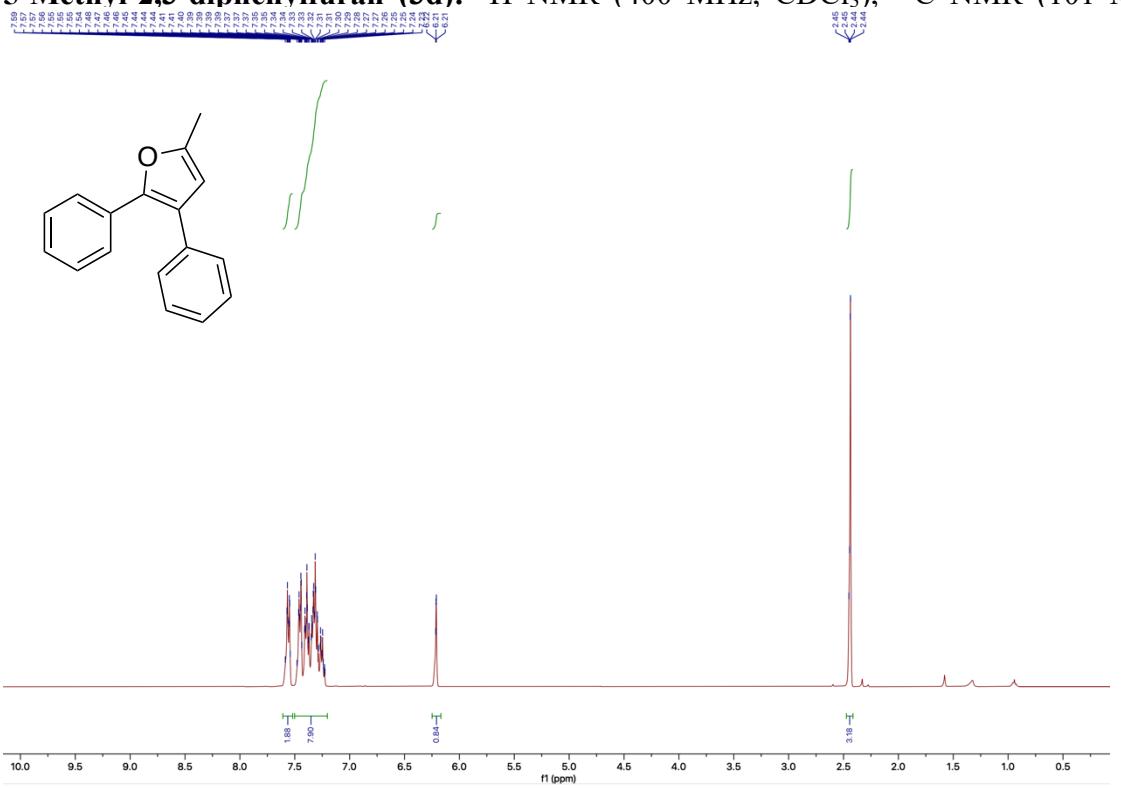


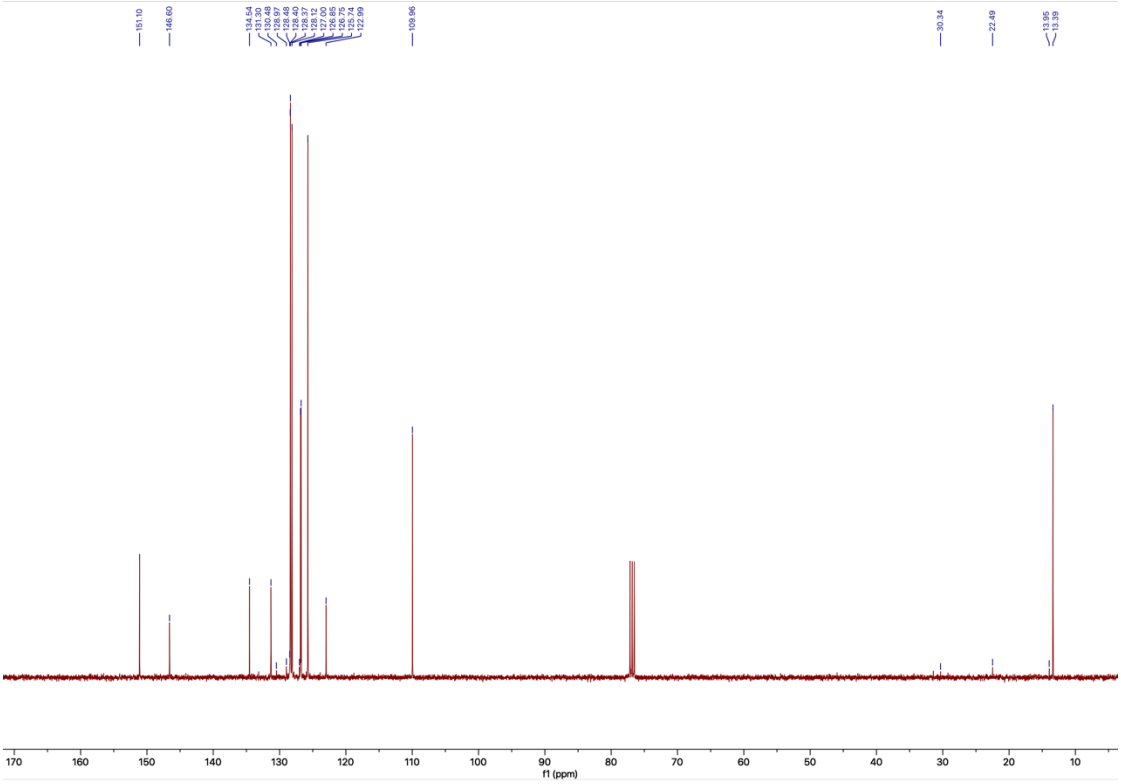
Methyl 5-methyl-2-(4-nitrophenyl)-3-furancarboxylate (3c): ^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (101 MHz, $CDCl_3$).



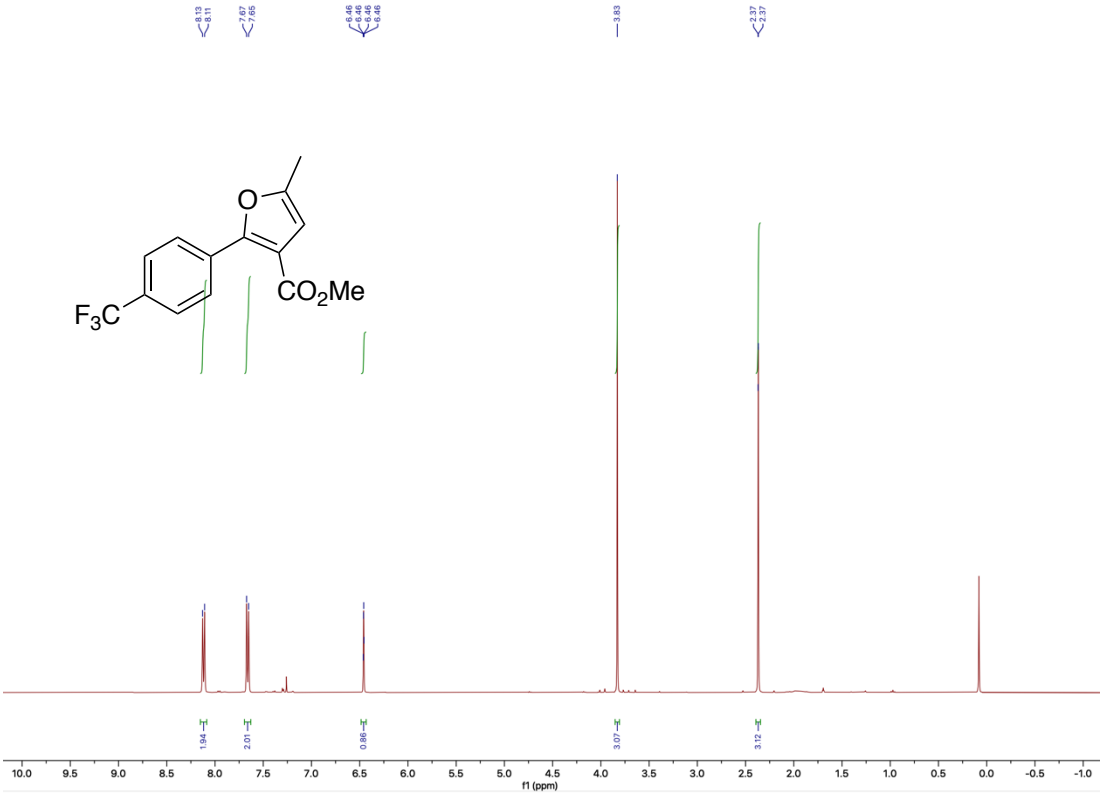


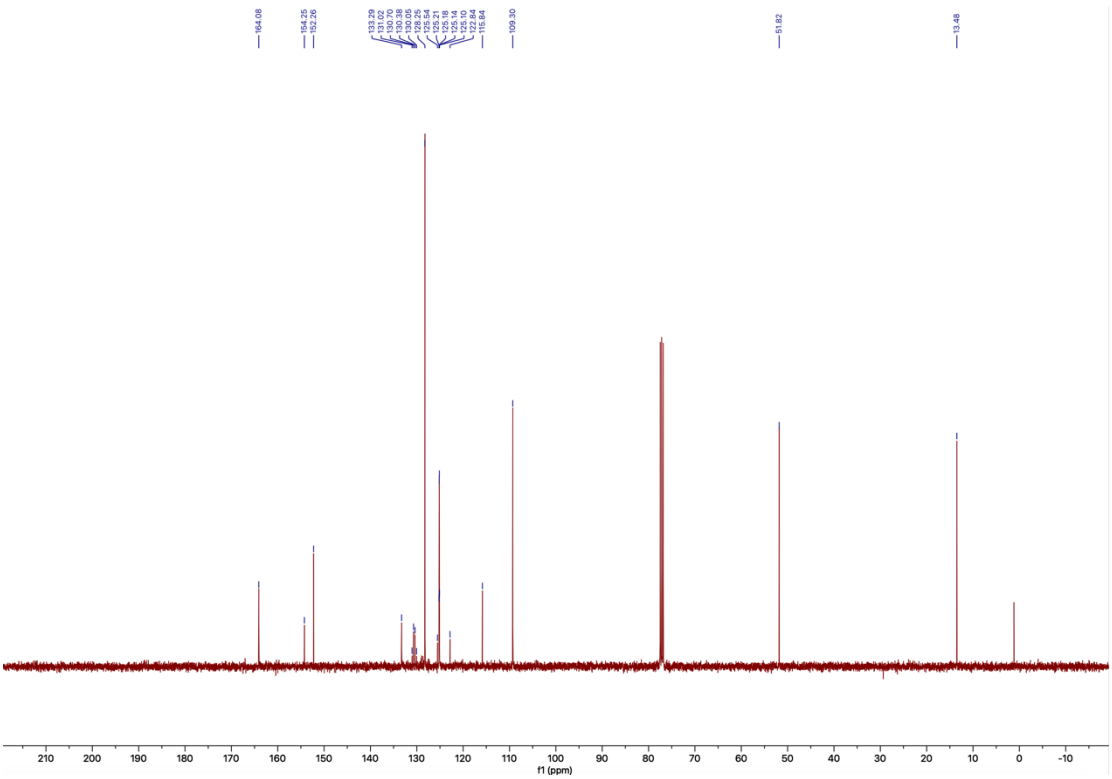
5-Methyl-2,3-diphenylfuran (3d): ^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (101 MHz, $CDCl_3$).

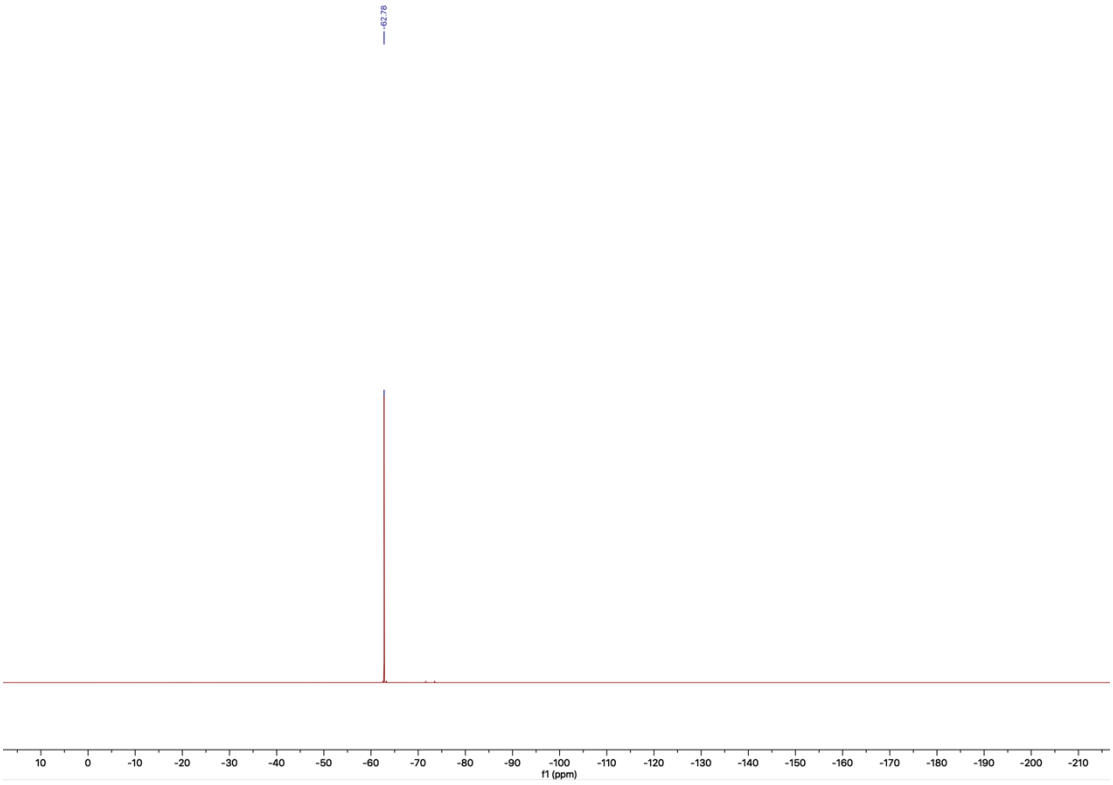




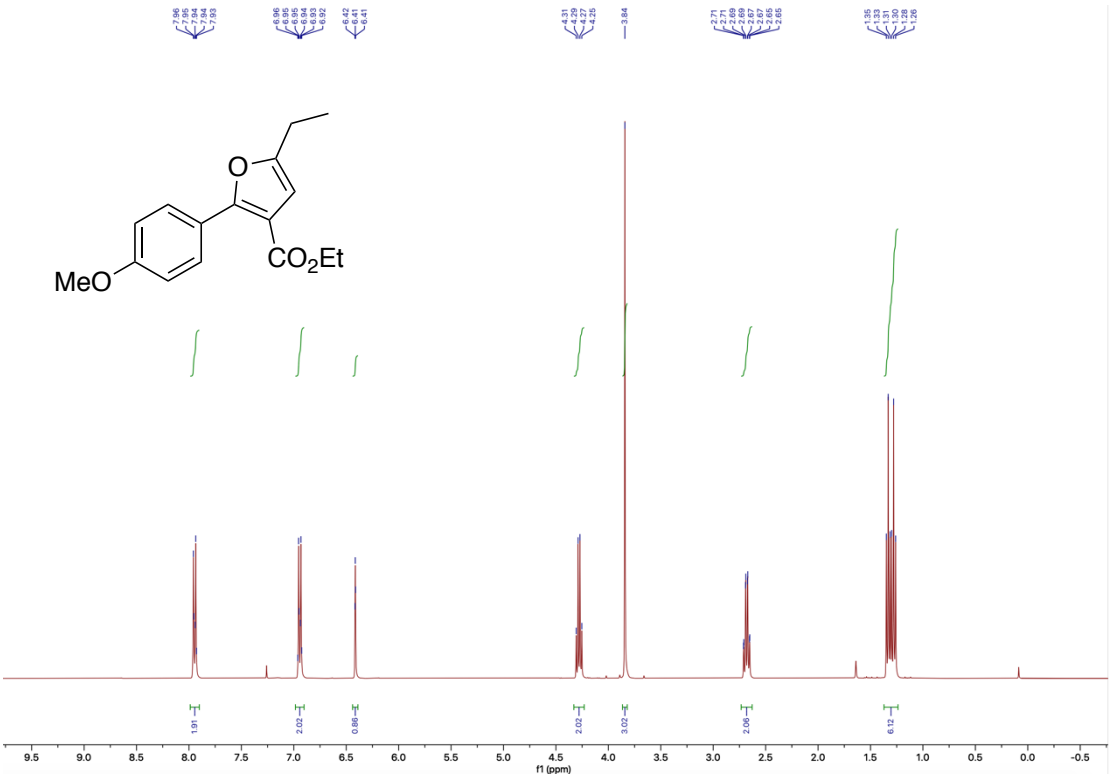
3-Furancarboxylic acid, 5-methyl-2-[4-(trifluoromethyl)phenyl]-, methyl ester (3e): ^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (101 MHz, $CDCl_3$), ^{19}F NMR (376 MHz, CDCl3)

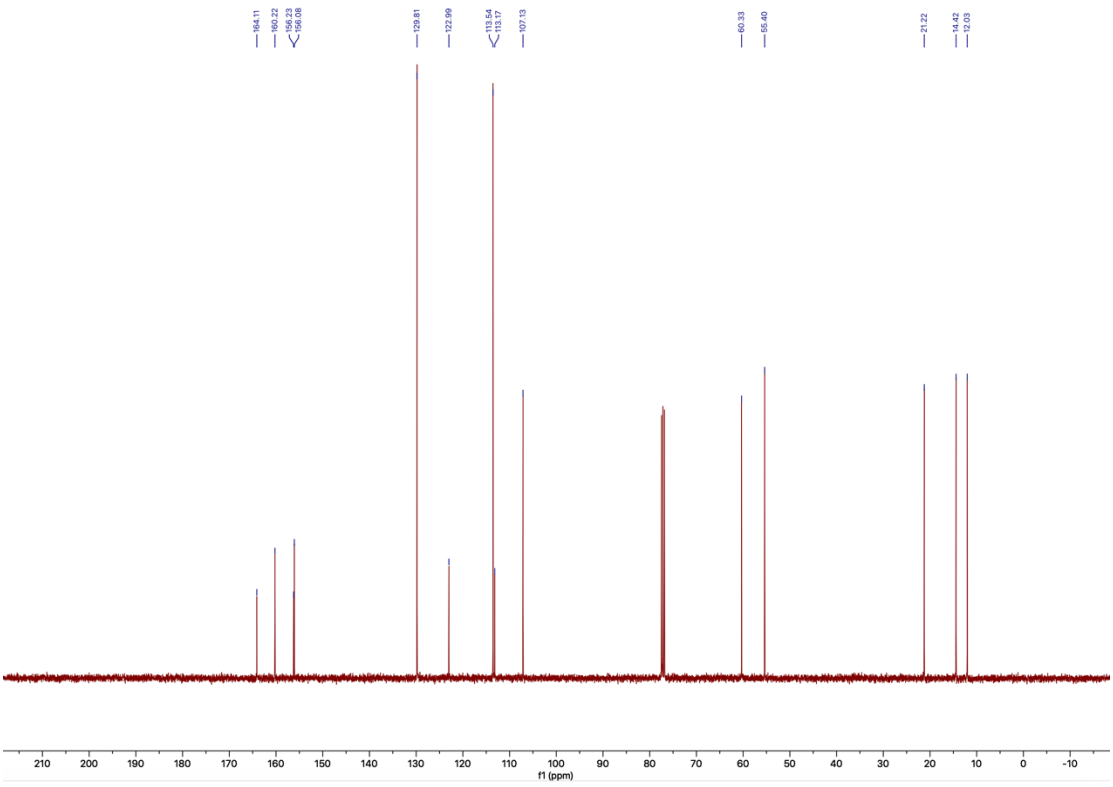




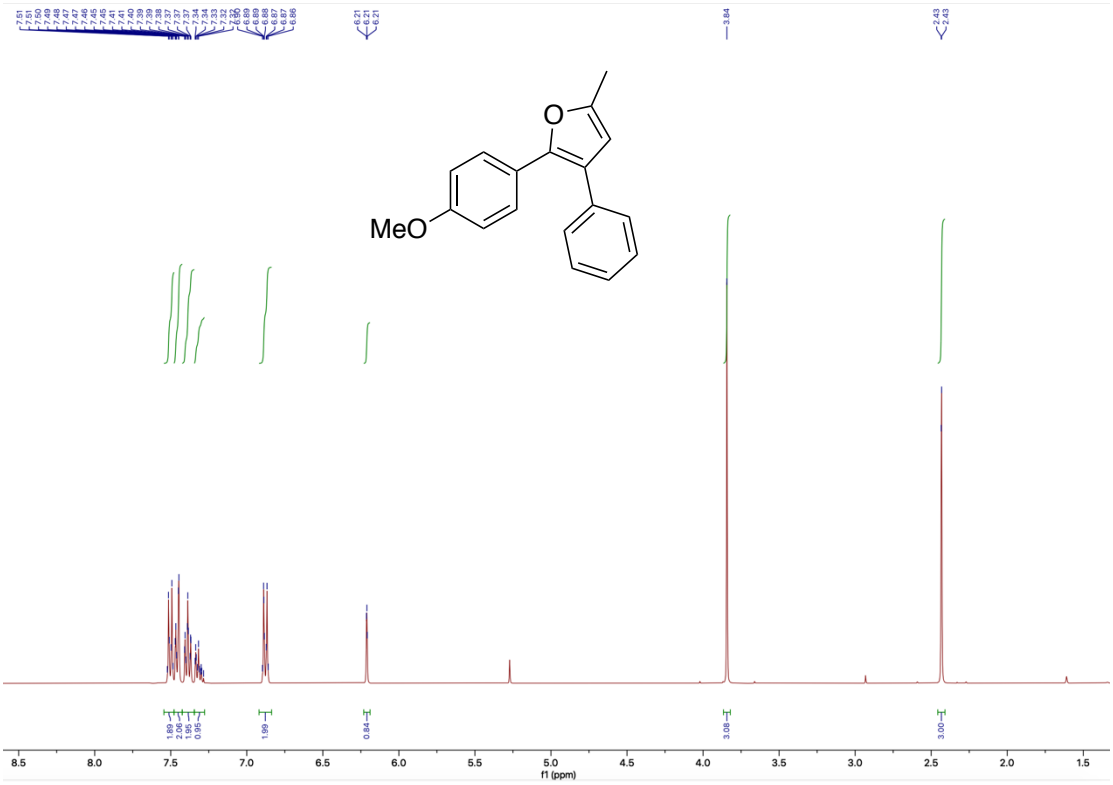

-62.78
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

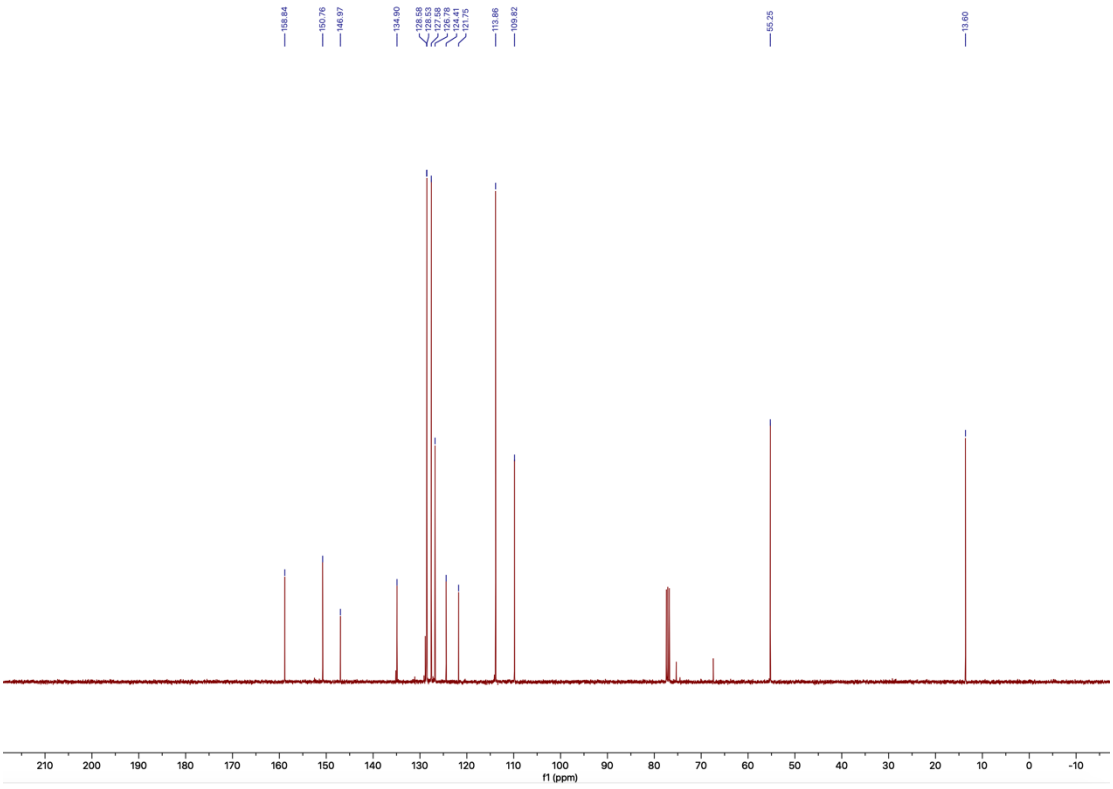
Ethyl 5-ethyl-2-(4-methoxyphenyl)furan-3-carboxylate (3f): ^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (101 MHz, $CDCl_3$).



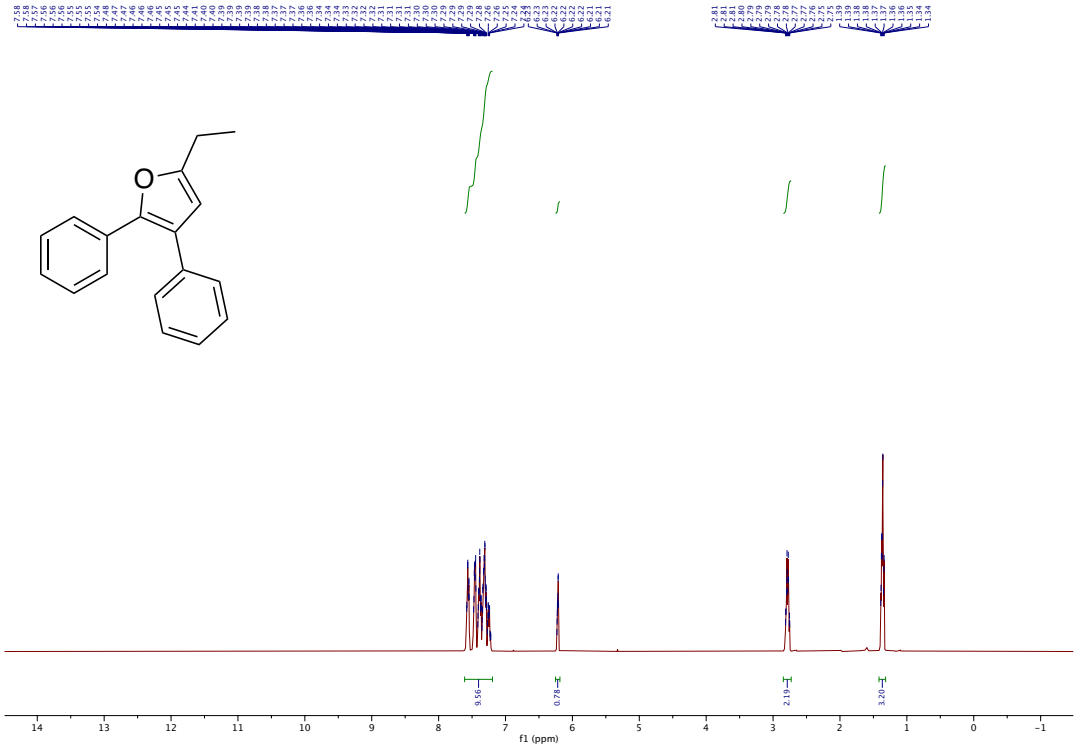


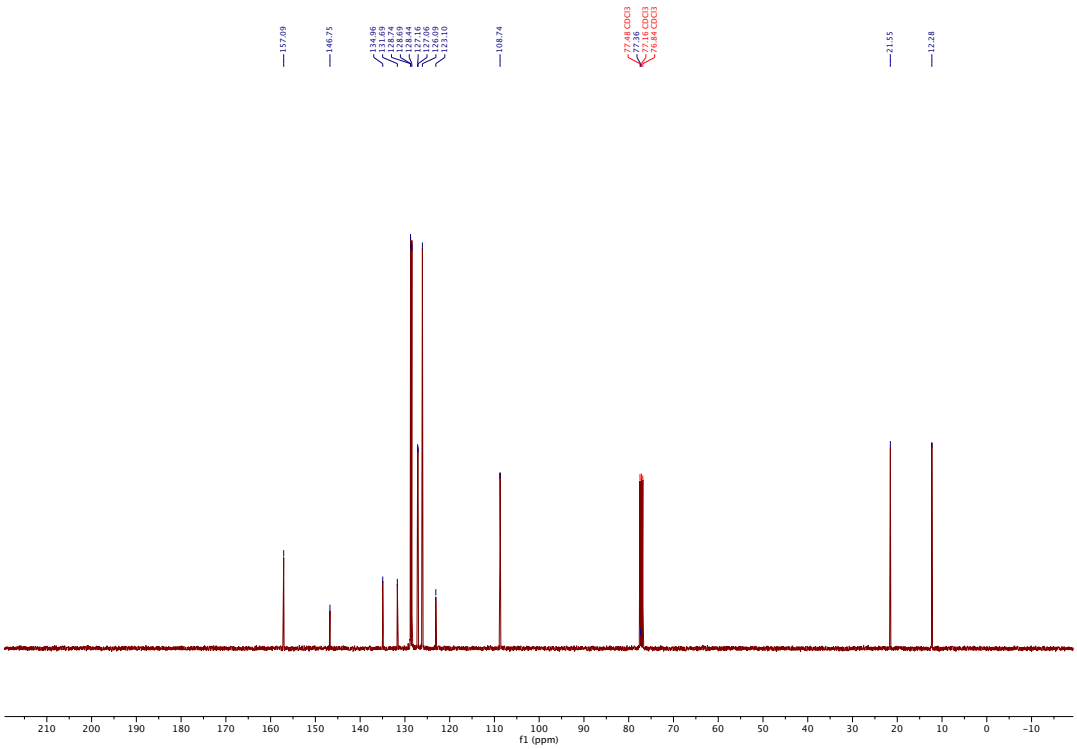
2-(4-Methoxyphenyl)-5-methyl-3-phenylfuran (3g): ^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (101 MHz, $CDCl_3$).



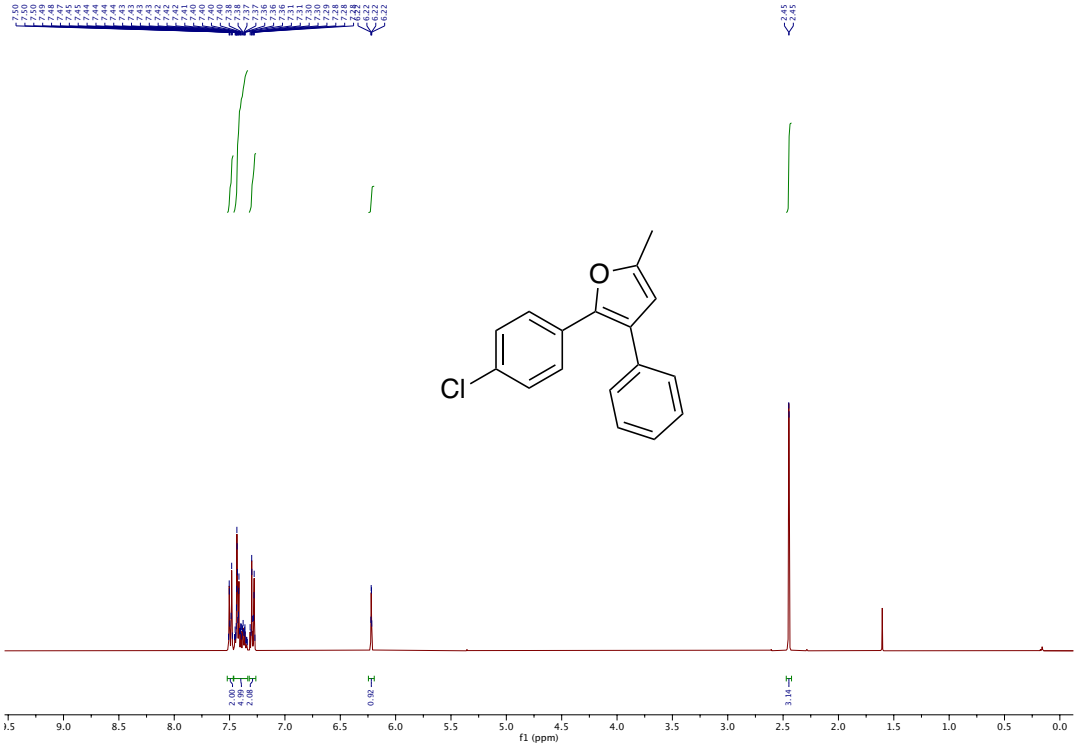


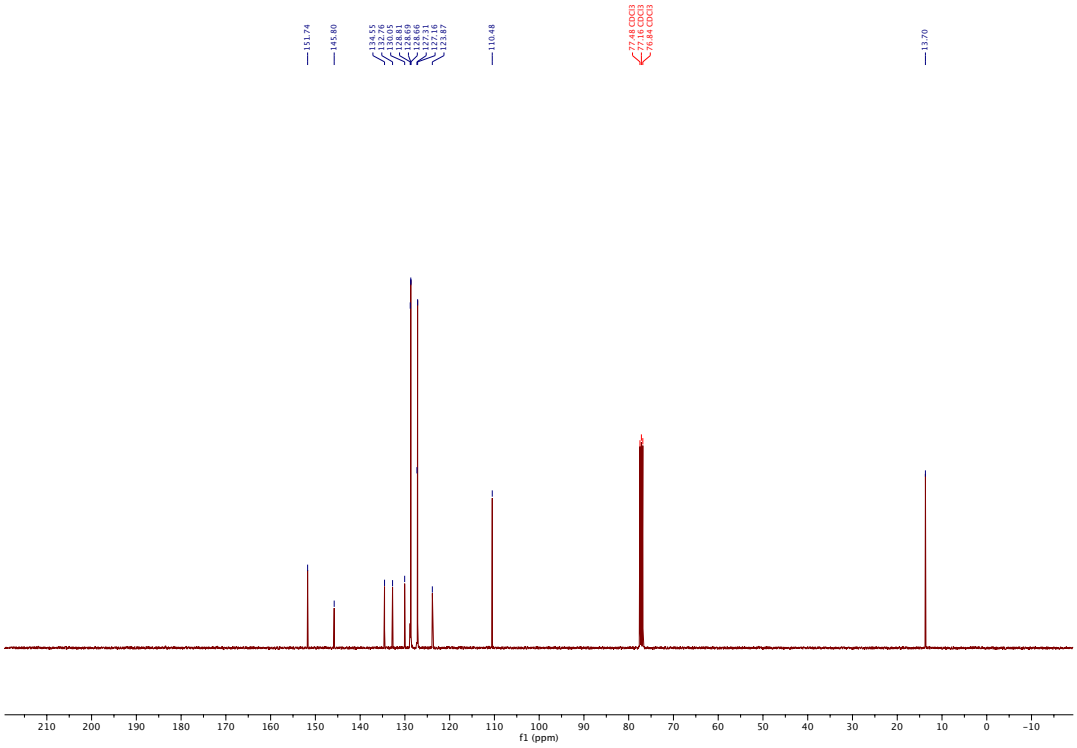
5-ethyl-2,3-diphenylfuran (3h): ^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (101 MHz, $CDCl_3$).





2-(4-chlorophenyl)-5-methyl-3-phenylfuran (3i): ^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (101 MHz, $CDCl_3$).





5-ethyl-2-(4-methoxyphenyl)-3-phenylfuran (3j): ^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (101 MHz, $CDCl_3$).