Supporting Information

An In Situ Masking Strategy Enables Radical Monodecarboxylative C–C Bond Coupling of Malonic Acid Derivatives

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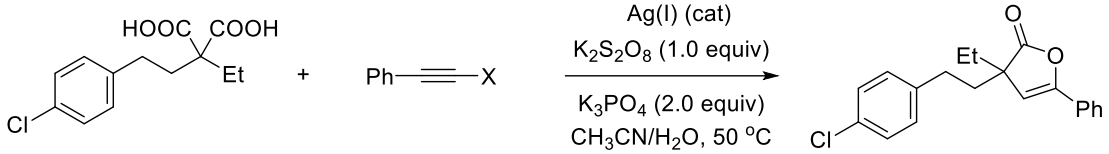
Contents

1. General Information

All reagents and organic solvents were purchased from TCI, Sigma-Aldrich, Adamas-beta and Energy Chemical of the highest purity grade and used without further purification unless otherwise noted. Distilled water needs to be degassed before use. ^{1}H, ^{19}F, and ^{13}C NMR spectra were recorded in $CDCl_3$ on Joel 400 MHz spectrometers. The chemical shifts (δ) are reported in ppm and coupling constants (*J*) in Hz. HRMS-ESI spectra were recorded on Xevo G2-XS QTof and Waters Micromass GCT Premier. The malonic acid substrates were prepared according to the conventional literature methods.[1,2] The ethynylbenziodoxolones (EBX) reagents were prepared according to the methods reported by Waser.[3]

2. Screening of conditions

Table S1. Optimization of the reaction conditions: effects of silver catalysts and alkynylating reagents[a]



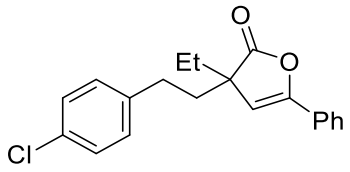
1a **2** **3a**

entry	Ag(I) cat	**2** (X)	solvent (v/v)	yield of **3a** (%)[b]
1	Ag_2O (5 mol%)	BI[c]	MeCN:H_2O=1:1 (4 mL)	33
2	$AgClO_4$ (10 mol%)	BI[c]	MeCN:H_2O=1:1 (4 mL)	32
3	Ag_2CO_3 (5 mol%)	BI[c]	MeCN:H_2O=1:1 (4 mL)	40
4	AgF (10 mol%)	BI[c]	MeCN:H_2O=1:1 (4 mL)	40
5	$AgNO_3$ (10 mol%)	Cl	MeCN:H_2O=1:1 (4 mL)	< 5%
6	$AgNO_3$ (10 mol%)	Br	MeCN:H_2O=1:1 (4 mL)	< 5%
7	$AgNO_3$ (10 mol%)	SO_2Ph	MeCN:H_2O=1:1 (4 mL)	5%

[a]Reaction conditions: **1a** (0.2 mmol), **2** (0.2 mmol), Ag(I) (10 mol%), $K_2S_2O_8$ (0.2 mmol), K_3PO_4 (0.4 mmol), CH_3CN (2.0 mL), H_2O (2.0 mL), under N_2 at 50 °C for 12 h. [b]Isolated yield. [c]BI = benziodoxolone.

3. General Procedure for An In Situ Masking Strategy Enables Radical Monodecarboxylative C-C Bond Coupling of Malonic Acid Derivatives

gem-Dicarboxylic acid (0.20 mmol, 1.0 equiv.), Ph-EBX (0.30 mmol, 1.5 equiv.), K_3PO_4 (0.40 mmol, 2.0 equiv.), $AgNO_3$ (0.02 mmol, 0.1 equiv.), and $K_2S_2O_8$ (0.20 mmol, 1.0 equiv.) were placed in a Schlenk tube. The tube was evacuated and filled with nitrogen three times. Then solvent acetonitrile/water/hexane (8 mL, 1/3/4 v/v/v) was added, the resulting reaction mixture was stirred at 65 °C for 12 h. The reaction was quenched with 3M HCl (2 mL), extracted with EtOAc (3 mL × 5), the combined organic phase was washed with brine and concentrated in vacuo, the residue was purified by column chromatography on silica gel or preparative TLC to give the desired product.



(3a)

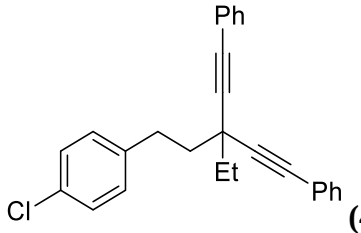
3-(4-chlorophenethyl)-3-ethyl-5-phenylfuran-2(3H)-one:

According to the general procedure, a mixture of **1a** (54.1 mg, 0.2 mmol, 1.0 equiv.), Ph-EBX (104.4 mg, 0.3 mmol, 1.5 equiv.), $AgNO_3$ (3.4 mg, 0.02 mmol, 0.1 equiv.), K_3PO_4 (84.9 mg, 0.4 mmol, 2.0 equiv.) and $K_2S_2O_8$ (54.0 mg, 0.2 mmol, 1.0 equiv.) in acetonitrile/water/*n*-hexane (8 mL, 1/3/4 v/v/v) was stirred at 65 °C for 12 h. The product **3a** was isolated by preparative TLC (petroleum ether/ethyl acetate = 20/1) as a yellow solid (47.1 mg, 72%), and product **4a** was isolated as a byproduct, but in a very low yield (less than 5%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 – 7.57 (m, 2H), 7.49 – 7.34 (m, 3H), 7.24 – 7.15 (m, 2H), 7.07 (t, *J* = 5.3 Hz, 2H), 5.69 (s, 1H), 2.64 – 2.41 (m, 2H), 2.15 – 2.03 (m, 1H), 2.00 – 1.92 (m, 1H), 1.90 – 1.83 (m, 1H), 1.81 – 1.72 (m, 1H), 0.90 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 180.7, 152.5, 139.7, 131.9, 129.8, 128.8, 128.6, 128.3, 125.0, 105.6, 55.0, 38.8, 30.9, 30.8, 9.2.

HRMS-ESI (m/z) calcd for $C_{20}H_{19}ClO_2Na$ [(M + Na) $^+$] 349.0966, found 349.0967.

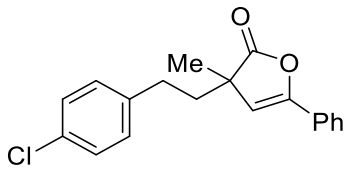


(4a)

(3-(4-chlorophenethyl)-3-ethylpenta-1,4-diyne-1,5-diyl)-dibenzene:

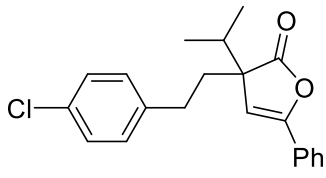
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 – 7.45 (m, 4H), 7.32 – 7.31 (m, 6H), 7.26 – 7.25 (m, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 3.10 – 3.01 (m, 2H), 2.06 (t, *J* = 16.0 Hz, 2H), 1.90 (q, *J* = 7.3 Hz, 2H), 1.27 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 140.7, 131.9, 131.7, 130.1, 128.6, 128.4, 128.2, 123.3, 90.7, 82.4, 43.7, 37.6, 35.6, 32.0, 10.2.
HRMS-ESI (m/z) calcd for $C_{27}H_{24}Cl$ [(M + H) $^+$] 383.1561, found 383.1564.



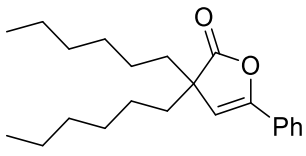
(3b)

3-(4-chlorophenethyl)-3-methyl-5-phenylfuran-2(3H)-one:
According to the general procedure, the product **3b** was isolated by preparative TLC (petroleum ether/ethyl acetate = 20/1) as a yellow solid (31.3 mg, 50%).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (dd, *J* = 7.9, 1.6 Hz, 2H), 7.46 – 7.36 (m, 3H), 7.24 – 7.15 (m, 2H), 7.06 (d, *J* = 8.4 Hz, 2H), 5.76 (s, 1H), 2.64 – 2.56 (m, 1H), 2.54 – 2.42 (m, 1H), 2.15 – 2.07 (m, 1H), 1.98 – 1.90 (m, 1H), 1.43 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 181.2, 151.9, 139.5, 132.0, 129.8, 128.9, 128.7, 128.3, 125.0, 107.6, 49.6, 40.0, 31.1, 23.9.
HRMS-ESI (m/z) calcd for $C_{19}H_{18}ClO_2$ [(M + H) $^+$] 313.0990, found 313.0995.



(3c)

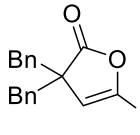
3-(4-chlorophenethyl)-3-isopropyl-5-phenylfuran-2(3H)-one:
According to the general procedure, the product **3c** was isolated by preparative TLC (petroleum ether/ethyl acetate = 20/1) as a yellow solid (42.3 mg, 62%).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 – 7.55 (m, 2H), 7.51 – 7.35 (m, 3H), 7.21 (d, *J* = 8.2 Hz, 2H), 7.06 (d, *J* = 8.3 Hz, 2H), 5.68 (s, 1H), 2.69 – 2.35 (m, 2H), 2.20 – 1.83 (m, 3H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.92 (d, *J* = 6.7 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 180.6, 152.8, 139.8, 131.9, 129.8, 128.9, 128.7, 128.3, 125.0, 103.6, 58.6, 37.2, 35.1, 30.9, 18.4, 17.9.
HRMS-ESI (m/z) calcd for $C_{21}H_{21}ClO_2Na$ [(M + Na) $^+$] 363.1122, found 363.1125.



(3d)

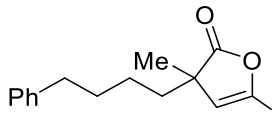
3,3-dihexyl-5-phenylfuran-2(3H)-one:
According to the general procedure, the product **3d** was isolated by preparative TLC (petroleum ether/ethyl acetate = 20/1) as a colorless oil (40.7 mg, 62%).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 – 7.58 (m, 2H), 7.46 – 7.32 (m, 3H), 5.69 (s, 1H), 1.94 – 1.55 (m, 4H), 1.40 – 1.13 (m, 16H), 0.84 (t, *J* = 6.8 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 181.5, 151.8, 129.6, 128.8, 128.6, 124.9, 106.8, 54.6, 37.8, 31.7, 29.5, 25.0, 22.7, 14.2.
HRMS-ESI (m/z) calcd for $C_{22}H_{33}O_2$ [(M + H) $^+$] 329.2475, found 329.2486.



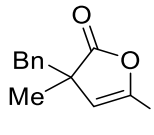
(3e)

3,3-dibenzyl-5-phenylfuran-2(3H)-one:
According to the general procedure, the product **3e** was isolated by preparative TLC (petroleum ether/ethyl acetate = 20/1) as a yellow solid (36.1 mg, 53%).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 – 7.31 (m, 2H), 7.30 – 7.26 (m, 3H), 7.25 – 7.20 (m, 4H), 7.20 – 7.12 (m, 6H), 5.67 (s, 1H), 3.20 (d, *J* = 13.2 Hz, 2H), 3.04 (d, *J* = 13.2 Hz, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 180.0, 151.6, 135.8, 130.1, 129.6, 128.6, 128.4, 127.2, 125.0, 105.3, 57.1, 43.5.
HRMS-ESI (m/z) calcd for $C_{24}H_{21}O_2$ [(M + H) $^+$] 341.1536, found 341.1544.



(3f)

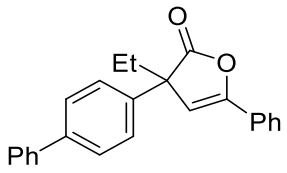
3-methyl-5-phenyl-3-(4-phenylbutyl)-furan-2(3H)-one:
According to the general procedure, the product **3f** was isolated by preparative TLC (petroleum ether/ethyl acetate = 20/1) as a yellow solid (39.2 mg, 64%).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (dd, *J* = 7.8, 1.4 Hz, 2H), 7.41 (dt, *J* = 15.2, 5.1 Hz, 3H), 7.24 (t, *J* = 7.4 Hz, 2H), 7.19 – 7.08 (m, 3H), 5.73 (s, 1H), 2.56 (t, *J* = 7.8 Hz, 2H), 1.89 – 1.77 (m, 1H), 1.73 – 1.66 (m, 1H), 1.67 – 1.52 (m, 2H), 1.38 (s, 3H), 1.35 – 1.20 (m, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 181.7, 151.5, 142.4, 129.6, 128.8, 128.5, 128.4, 125.8, 124.9, 108.1, 49.6, 38.2, 35.7, 31.7, 25.0, 23.7.
HRMS-ESI (m/z) calcd for $C_{21}H_{23}O_2$ [(M + H) $^+$] 307.1693, found 307.1700.



(3g)

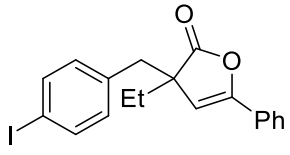
3-benzyl-3-methyl-5-phenylfuran-2(3H)-one:
According to the general procedure, the product **3g** was isolated by preparative TLC (petroleum ether/ethyl acetate = 20/1) as a yellow solid (39.1 mg, 74%).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 – 7.47 (m, 2H), 7.35 (d, *J* = 5.8 Hz, 3H), 7.25 – 7.20 (m, 3H), 7.16 (d, *J* = 7.0 Hz, 2H), 5.73 (s, 1H), 3.07 (d, *J* = 13.2 Hz, 1H), 2.95 (d, *J* = 13.2 Hz, 1H), 1.43 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 181.2, 151.3, 136.1, 130.1, 129.6, 128.7, 128.4, 127.1, 124.9, 107.5, 50.8, 44.3, 23.1.
HRMS-ESI (m/z) calcd for $C_{18}H_{17}O_2$ [(M + H) $^+$] 265.1223, found 265.1232.



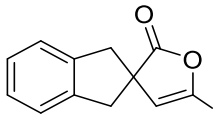
(3h)

3-([1,1'-biphenyl]-4-yl)-3-ethyl-5-phenylfuran-2(3H)-one:
According to the general procedure, the product **3h** was isolated by preparative TLC (petroleum ether/ethyl acetate = 20/1) as a yellow solid (43.6 mg, 64%).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (dd, *J* = 8.0, 1.6 Hz, 2H), 7.60 – 7.56 (m, 6H), 7.46 – 7.40 (m, 5H), 7.36 – 7.33 (m, 1H), 6.15 (s, 1H), 2.32 – 2.23 (m, 1H), 2.23 – 2.14 (m, 1H), 0.98 (t, *J* = 7.4 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 179.0, 152.5, 140.8, 140.6, 138.1, 130.0, 128.9, 128.9, 128.3, 127.6, 127.6, 127.2, 127.1, 125.1, 105.7, 57.7, 32.7, 9.7.
HRMS-ESI (m/z) calcd for $C_{24}H_{21}O_2$ [(M + H) $^+$] 341.1536, found 341.1537.



(3i)

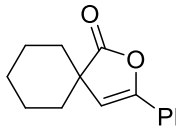
3-ethyl-3-(4-iodobenzyl)-5-phenylfuran-2(3H)-one:
According to the general procedure, the product **3i** was isolated by preparative TLC (petroleum ether/ethyl acetate = 20/1) as a yellow solid (56.1 mg, 70%).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (d, *J* = 8.2 Hz, 2H), 7.53 – 7.49 (m, 2H), 7.41 – 7.33 (m, 3H), 6.89 (d, *J* = 8.3 Hz, 2H), 5.63 (s, 1H), 3.01 (d, *J* = 13.3 Hz, 1H), 2.91 (d, *J* = 13.3 Hz, 1H), 1.93 (dq, *J* = 14.8, 7.4 Hz, 1H), 1.75 (dq, *J* = 14.9, 7.5 Hz, 1H), 0.88 (t, *J* = 7.5 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 180.1, 152.2, 137.4, 135.7, 132.0, 129.9, 128.7, 128.1, 125.0, 104.9, 92.7, 56.2, 43.0, 30.3, 9.3.
HRMS-ESI (m/z) calcd for $C_{19}H_{17}O_2NaI$ [(M + Na) $^+$] 427.0165, found 427.0166.



(3j)

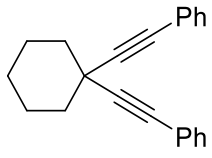
5-phenyl-1',3'-dihydro-2H-spiro[furan-3,2'-inden]-2-one:
According to the general procedure, the product **3j** was isolated by preparative TLC (petroleum ether/ethyl acetate = 20/1) as a yellow solid (30.4 mg, 58%).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (dd, *J* = 7.7, 1.8 Hz, 2H), 7.46 – 7.34 (m, 3H), 7.23 (d, *J* = 9.3 Hz, 4H), 5.98 (s, 1H), 3.56 (d, *J* = 15.6 Hz, 2H), 3.15 (d, *J* = 15.6 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 181.3, 152.0, 140.2, 129.8, 128.8, 128.4, 127.4, 124.9, 124.6, 108.4, 55.1, 43.9.
HRMS-ESI (m/z) calcd for $C_{18}H_{15}O_2$ [(M + H) $^+$] 263.1067, found 263.1078.



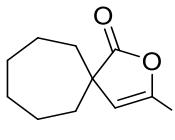
(3k)

3-phenyl-2-oxaspiro [4.5] dec-3-en-1-one:
According to the general procedure, a mixture of **1k** (34.4 mg, 0.2 mmol, 1.0 equiv.), Ph-EBX (104.4 mg, 0.3 mmol, 1.5 equiv.), AgF (7.6 mg, 0.06 mmol, 0.3 equiv.), K_3PO_4 (84.9 mg, 0.4 mmol, 2.0 equiv.) and $K_2S_2O_8$ (54.0 mg, 0.2 mmol, 1.0 equiv.) in acetonitrile/water/*n*-hexane (8 mL, 1/3/4 v/v/v) was stirred at 65 ^{o}C for 12 h. The product **3k** was isolated by preparative TLC (petroleum ether/ethyl acetate = 20/1) as a yellow solid (20.5 mg, 45%), and **3k'** was isolated as a byproduct (5.7 mg, 10%).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 – 7.58 (m, 2H), 7.46 – 7.33 (m, 3H), 6.10 (s, 1H), 1.91 – 1.82 (m, 4H), 1.78 – 1.61 (m, 3H), 1.57 – 1.40 (m, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 181.4, 151.5, 129.6, 128.8, 128.7, 124.9, 107.1, 50.0, 33.9, 25.4, 22.4.
HRMS-ESI (m/z) calcd for $C_{15}H_{17}O_2$ [(M + H) $^+$] 229.1223, found 229.1234.



(3k')

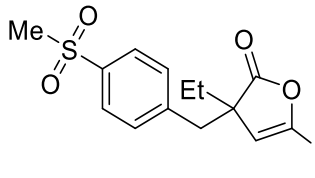
(cyclohexane-1,1-diylbis(ethyne-2,1-diyl))dibenzene:
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 – 7.36 (m, 4H), 7.26 – 7.19 (m, 6H), 1.96 – 1.89 (m, 4H), 1.70 – 1.60 (m, 4H), 1.41 (d, *J* = 4.9 Hz, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 131.9, 128.3, 128.0, 123.6, 92.2, 81.5, 39.2, 32.4, 25.5, 22.7.
HRMS-ESI (m/z) calcd for $C_{22}H_{21}$ [(M + H) $^+$] 285.1638, found 285.1646.



(3l)

3-phenyl-2-oxaspiro [4.6] undec-3-en-1-one:
According to the general procedure, the product **3l** was isolated by preparative TLC (petroleum ether/ethyl acetate = 20/1) as a yellow solid (27.6 mg, 57%).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 – 7.56 (m, 2H), 7.45 – 7.29 (m, 3H), 5.96 (s, 1H), 2.01 – 1.94 (m, 2H), 1.93 – 1.83 (m, 2H), 1.81 – 1.75 (m, 2H), 1.73 – 1.63 (m, 4H), 1.62 – 1.51 (m, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 182.4, 151.1, 129.5, 128.8, 128.7, 124.9, 108.9, 52.2, 36.7, 29.5, 24.0.

HRMS-ESI (m/z) calcd for $C_{16}H_{19}O_2$ [(M + H) $^+$] 243.1380, found 243.1391.



(3m)

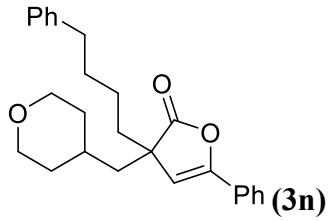
3-ethyl-3-(4-(methylsulfonyl)-benzyl)-5-phenylfuran-2(3H)-one:

According to the general procedure, the product **3m** was isolated by preparative TLC (petroleum ether/ethyl acetate = 2/1) as a yellow solid (29.1 mg, 41%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, *J* = 8.2 Hz, 2H), 7.49 – 7.47 (m, 2H), 7.39 – 7.31 (m, 5H), 5.66 (s, 1H), 3.18 (d, *J* = 13.1 Hz, 1H), 3.07 (d, *J* = 13.1 Hz, 1H), 2.96 (s, 3H), 1.98 (dq, *J* = 14.7, 7.4 Hz, 1H), 1.80 (td, *J* = 14.8, 7.4 Hz, 1H), 0.92 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 179.8, 152.4, 142.6, 139.1, 131.0, 129.9, 128.8, 127.8, 127.4, 124.9, 104.4, 56.3, 44.5, 43.1, 30.6, 9.3.

HRMS-ESI (m/z) calcd for $C_{20}H_{21}O_4S$ [(M + H) $^+$] 357.1155, found 357.1158.



(3n)

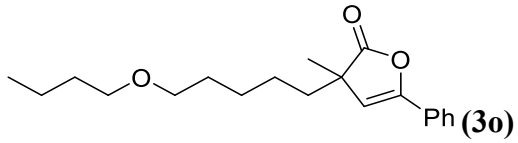
5-phenyl-3-(4-phenylbutyl)-3-((tetrahydro-2H-pyran-4-yl)-methyl)-furan-2(3H)-one:

According to the general procedure, the product **3n** was isolated by preparative TLC (petroleum ether/ethyl acetate = 20/1) as a white solid (44.5 mg, 57%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (dd, *J* = 7.9, 1.6 Hz, 2H), 7.47 – 7.38 (m, 3H), 7.23 (d, *J* = 7.5 Hz, 2H), 7.18 – 7.09 (m, 3H), 5.71 (s, 1H), 3.85 (dd, *J* = 11.4, 3.5 Hz, 2H), 3.33 – 3.20 (m, 2H), 2.55 (t, *J* = 7.8 Hz, 2H), 1.86 – 1.77 (m, 2H), 1.74 – 1.65 (m, 2H), 1.60 – 1.44 (m, 5H), 1.38 – 1.25 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 181.4, 151.7, 142.3, 129.8, 128.9, 128.4, 128.3, 125.9, 125.0, 106.5, 67.8, 67.8, 53.4, 44.6, 39.0, 35.7, 34.4, 33.5, 32.7, 31.6, 24.3.

HRMS-ESI (m/z) calcd for $C_{26}H_{31}O_3$ [(M + H) $^+$] 391.2268, found 391.2268.

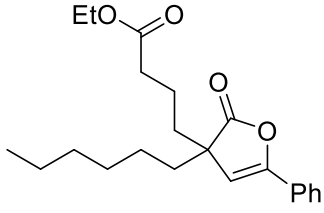


(3o)

3-(5-butoxypentyl)-3-methyl-5-phenylfuran-2(3H)-one:

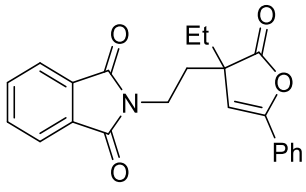
According to the general procedure, the product **3o** was isolated by preparative TLC (petroleum ether/ethyl acetate = 20/1) as a yellow oil (37.3 mg, 59%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 – 7.57 (m, 2H), 7.43 – 7.32 (m, 3H), 5.75 (s, 1H), 3.38 – 3.34 (m, 4H), 1.83 – 1.72 (m, 1H), 1.70 – 1.61 (m, 1H), 1.60 – 1.46 (m, 4H), 1.46 – 1.29 (m, 8H), 1.23 – 1.17 (m, 1H), 0.90 (t, *J* = 7.4 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 181.7, 151.4, 129.6, 128.8, 128.5, 124.9, 108.1, 70.7, 70.7, 49.6, 38.4, 31.9, 29.6, 26.4, 25.1, 23.7, 19.5, 14.0.
HRMS-ESI (m/z) calcd for $C_{20}H_{29}O_3$ [(M + H) $^+$] 317.2111, found 317.2116.



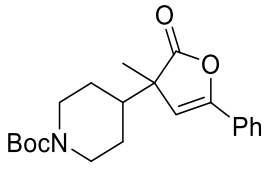
(3p)

ethyl 4-(3-hexyl-2-oxo-5-phenyl-2,3-dihydrofuran-3-yl)-butanoate:
According to the general procedure, the product **3p** was isolated by preparative TLC (petroleum ether/ethyl acetate = 10/1) as a colorless oil (53.1 mg, 74%).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63 (d, *J* = 7.2 Hz, 2H), 7.48 – 7.34 (m, 3H), 5.72 (s, 1H), 4.10 (q, *J* = 7.2 Hz, 2H), 2.36 – 2.18 (m, 2H), 1.83 – 1.61 (m, 5H), 1.55 – 1.46 (m, 1H), 1.26 – 1.22 (m, 11H), 0.84 (t, *J* = 6.5 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 181.0, 173.1, 152.1, 129.6, 128.8, 128.4, 124.9, 106.1, 60.5, 54.3, 37.6, 36.9, 34.2, 31.6, 29.4, 24.8, 22.6, 20.5, 14.3, 14.1.
HRMS-ESI (m/z) calcd for $C_{22}H_{30}O_4Na$ [(M + Na) $^+$] 381.2036, found 381.2047.



(3q)

2-(2-(3-ethyl-2-oxo-5-phenyl-2,3-dihydrofuran-3-yl)-ethyl)-isoindoline-1,3-dione:
According to the general procedure, the product **3q** was isolated by preparative TLC (petroleum ether/ethyl acetate = 5/1) as a yellow solid (49.1 mg, 68%).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 – 7.74 (m, 2H), 7.69 (dt, *J* = 4.9, 3.1 Hz, 2H), 7.58 (dd, *J* = 6.0, 2.2 Hz, 2H), 7.44 – 7.35 (m, 3H), 5.74 (s, 1H), 3.78 – 3.65 (m, 2H), 2.29 – 2.08 (m, 2H), 1.94 – 1.84 (m, 1H), 1.81 – 1.74 (dq, *J* = 14.4, 7.4 Hz, 1H), 0.90 (t, *J* = 7.4 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 179.9, 168.0, 152.8, 134.1, 132.1, 129.8, 128.7, 128.2, 125.0, 123.3, 104.8, 53.2, 34.7, 34.3, 30.8, 9.0.
HRMS-ESI (m/z) calcd for $C_{22}H_{20}NO_4$ [(M + H) $^+$] 362.1387, found 362.1392.



(3r)

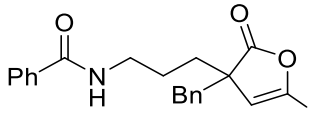
tert-butyl-4-(3-methyl-2-oxo-5-phenyl-2,3-dihydrofuran-3-yl)piperidine-1-carboxylate：

According to the general procedure, the product **3r** was isolated by preparative TLC (petroleum ether/ethyl acetate = 5/1) as a yellow solid (35.7 mg, 50%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (dd, *J* = 7.8, 1.6 Hz, 2H), 7.45 – 7.37 (m, 3H), 5.73 (s, 1H), 4.25 – 4.09 (m, 2H), 2.67 (s, 2H), 1.94 – 1.77 (m, 2H), 1.57 – 1.48 (m, 1H), 1.43 (s, 9H), 1.40 (s, 3H), 1.28 – 1.19 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 181.1, 154.7, 152.2, 129.8, 128.8, 128.2, 124.9, 105.6, 79.7, 52.8, 43.2, 28.5, 27.7, 26.9, 21.3.

HRMS-ESI (m/z) calcd for $C_{21}H_{27}NO_4Na$ [(M + Na) $^+$] 380.1832, found 380.1824.



(3s)

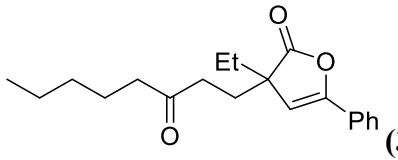
N-(3-(3-benzyl-2-oxo-5-phenyl-2,3-dihydrofuran-3-yl)-propyl)-benzamide:

According to the general procedure, the product **3s** was isolated by preparative TLC (petroleum ether/ethyl acetate = 5/1) as a yellow oil (53.4 mg, 65%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 – 7.66 (m, 2H), 7.53 – 7.41 (m, 3H), 7.41 – 7.30 (m, 5H), 7.24 – 7.16 (m, 3H), 7.13 (dd, *J* = 7.8, 6.2 Hz, 2H), 6.39 (s, 1H), 5.60 (s, 1H), 3.39 (dd, *J* = 13.2, 6.8 Hz, 2H), 3.06 (d, *J* = 13.2 Hz, 1H), 2.96 (d, *J* = 13.2 Hz, 1H), 2.01 – 1.91 (m, 1H), 1.86 – 1.75 (m, 1H), 1.65 (qd, *J* = 11.9, 6.9 Hz, 1H), 1.45 (qd, *J* = 12.1, 7.1 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 180.6, 167.7, 152.0, 135.6, 134.5, 131.6, 130.0, 129.8, 128.7, 128.7, 128.4, 128.1, 127.2, 127.0, 125.0, 105.4, 55.5, 44.0, 39.7, 34.0, 25.6.

HRMS-ESI (m/z) calcd for $C_{27}H_{26}NO_3$ [(M + H) $^+$] 412.1907, found 412.1909.



(3t)

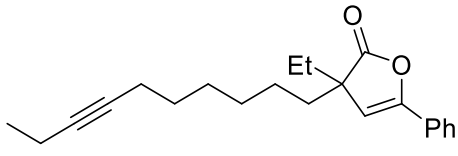
3-ethyl-3-(3-oxooctyl)-5-phenylfuran-2(3H)-one:

According to the general procedure, the product **3t** was isolated by preparative TLC (petroleum ether/ethyl acetate = 10/1) as a colorless oil (50.9 mg, 81%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 – 7.49 (m, 2H), 7.47 – 7.31 (m, 3H), 5.61 (s, 1H), 2.38 – 2.23 (m, 4H), 2.19 – 2.07 (m, 1H), 1.97 (dt, *J* = 14.3, 7.3 Hz, 1H), 1.84 (dq, *J* = 14.8, 7.4 Hz, 1H), 1.73 (td, *J* = 14.9, 7.5 Hz, 1H), 1.50 – 1.39 (m, 2H), 1.22 – 1.09 (m, 4H), 0.89 (t, *J* = 7.5 Hz, 3H), 0.82 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 210.0, 180.7, 152.3, 129.8, 128.9, 128.2, 124.9, 105.8, 54.5, 43.2, 38.0, 31.4, 30.7, 30.5, 23.6, 22.5, 14.0, 9.3.

HRMS-ESI (m/z) calcd for $C_{20}H_{26}O_3Na$ [(M + Na) $^+$] 337.1774, found 337.1779.



(3u)

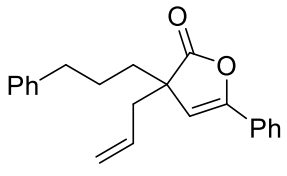
3-(dec-7-yn-1-yl)-3-ethyl-5-phenylfuran-2(3H)-one:

According to the general procedure, the product **3u** was isolated by preparative TLC (petroleum ether/ethyl acetate = 20/1) as a yellow oil (28.6 mg, 44%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63 (dd, *J* = 7.9, 1.4 Hz, 2H), 7.48 – 7.32 (m, 3H), 5.68 (s, 1H), 2.22 – 2.05 (m, 4H), 1.92 – 1.59 (m, 4H), 1.49 – 1.39 (m, 2H), 1.38 – 1.23 (m, 6H), 1.09 (t, *J* = 7.4 Hz, 3H), 0.88 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 181.3, 152.0, 129.6, 128.8, 128.5, 124.9, 106.2, 81.8, 79.5, 55.1, 37.3, 30.7, 29.4, 29.1, 28.7, 25.0, 18.8, 14.5, 12.5, 9.3.

HRMS-ESI (m/z) calcd for $C_{22}H_{29}O_2$ [(M + H) $^+$] 325.2162, found 325.2168.



(3v)

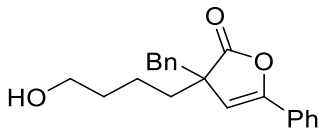
3-allyl-5-phenyl-3-(3-phenylpropyl)-furan-2(3H)-one:

According to the general procedure, the product **3v** was isolated by preparative TLC (petroleum ether/ethyl acetate = 20/1) as a yellow oil (38.2 mg, 60%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 – 7.53 (m, 2H), 7.41 – 7.36 (m, 3H), 7.26 – 7.21 (m, 2H), 7.15 (dd, *J* = 20.3, 7.2 Hz, 3H), 5.80 – 5.45 (m, 2H), 5.09 (dd, *J* = 17.8, 13.9 Hz, 2H), 2.68 – 2.50 (m, 2H), 2.49 – 2.44 (m, 2H), 1.91 – 1.80 (m, 1H), 1.80 – 1.69 (m, 1H), 1.70 – 1.49 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 180.4, 152.0, 141.7, 132.1, 129.7, 128.8, 128.5, 128.3, 126.0, 125.0, 119.5, 105.8, 54.3, 41.9, 36.5, 36.0, 26.9.

HRMS-ESI (m/z) calcd for $C_{22}H_{23}O_2$ [(M + H) $^+$] 319.1693, found 319.1700.



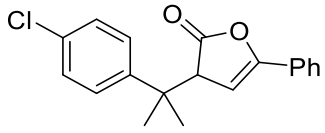
(3w)

3-benzyl-3-(4-hydroxybutyl)-5-phenylfuran-2(3H)-one:

According to the general procedure, a mixture of **1w** (53.3 mg, 0.2 mmol, 1.0 equiv.), Ph-EBX (104.4 mg, 0.3 mmol, 1.5 equiv.), $AgNO_3$ (3.4 mg, 0.02 mmol, 0.1 equiv.), K_3PO_4 (84.9 mg, 0.4 mmol, 2.0 equiv.) and $K_2S_2O_8$ (27.0 mg, 0.1 mmol, 0.5 equiv.) in acetonitrile/water/*n*-hexane (8 mL, 1/3/4 v/v/v) was stirred at 65 ^{o}C for 6 h. The product **3w** was isolated by preparative TLC (petroleum ether/ethyl acetate = 5/1) as a white solid (33.5 mg, 52%).

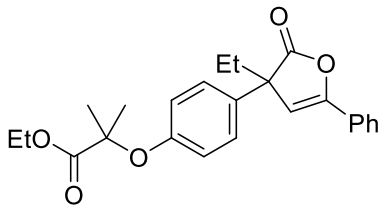
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 – 7.45 (m, 2H), 7.37 – 7.35 (m, 3H), 7.25 – 7.17 (m, 3H), 7.13 (d, *J* = 7.4 Hz, 2H), 5.68 (s, 1H), 3.58 (dt, *J* = 6.4, 3.0 Hz, 2H), 3.07 (d,

J = 13.2 Hz, 1H), 2.97 (d, *J* = 13.2 Hz, 1H), 1.92 (td, *J* = 12.7, 4.8 Hz, 1H), 1.75 (td, *J* = 12.8, 4.6 Hz, 1H), 1.59 – 1.47 (m, 2H), 1.44 – 1.36 (m, 1H), 1.33 – 1.17 (m, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 180.7, 151.8, 135.9, 130.1, 129.7, 128.7, 128.4, 128.3, 127.1, 125.0, 105.7, 62.6, 55.8, 44.0, 36.8, 32.8, 21.5.
HRMS-ESI (m/z) calcd for $C_{21}H_{23}O_3$ [(M + H) $^+$] 323.1642, found 323.1654.



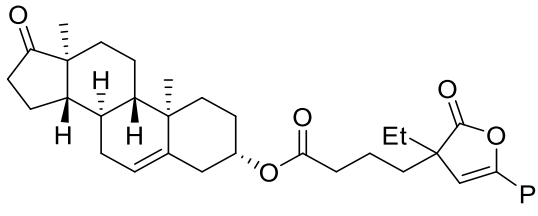
(3x)

3-(2-(4-chlorophenyl)-propan-2-yl)-5-phenylfuran-2(3H)-one:
According to the general procedure, the product **3x** was isolated by preparative TLC (petroleum ether/ethyl acetate = 20/1) as a yellow solid (16.3 mg, 26%).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 – 7.58 (m, 2H), 7.36 (dd, *J* = 8.2, 6.3 Hz, 4H), 7.25 – 7.20 (m, 1H), 7.15 – 7.12 (m, 2H), 5.62 (s, 1H), 3.75 (s, 1H), 1.46 (s, 3H), 0.98 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 173.4, 156.2, 134.3, 133.7, 131.0, 130.9, 129.1, 128.7, 128.7, 127.2, 103.3, 56.8, 45.2, 26.4, 24.6.
HRMS-ESI (m/z) calcd for $C_{19}H_{18}ClO_2$ [(M + H) $^+$] 313.0990, found 313.0997.



(3y)

ethyl2-(4-(3-ethyl-2-oxo-5-phenyl-2,3-dihydrofuran-3-yl)-phenoxy)-2-methyl-propanoate:
According to the general procedure, the product **3y** was isolated by preparative TLC (petroleum ether/ethyl acetate = 10/1) as a colorless oil (51.3 mg, 65%).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (dd, *J* = 7.9, 1.5 Hz, 2H), 7.46 – 7.39 (m, 3H), 7.37 (d, *J* = 8.8 Hz, 2H), 6.82 (d, *J* = 8.8 Hz, 2H), 6.08 (s, 1H), 4.22 (q, *J* = 7.2 Hz, 2H), 2.22 – 2.14 (m, 1H), 2.13 – 2.04 (m, 1H), 1.58 (s, 6H), 1.24 (t, *J* = 7.1 Hz, 3H), 0.92 (t, *J* = 7.4 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 179.2, 174.3, 155.1, 152.2, 132.4, 129.9, 128.9, 128.3, 127.5, 125.1, 119.2, 105.9, 79.2, 61.6, 57.2, 32.7, 25.5, 14.2, 9.6.
HRMS-ESI (m/z) calcd for $C_{24}H_{27}O_5$ [(M + H) $^+$] 395.1853, found 395.1855.



(3z)

10,13-dimethyl-17-oxo-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl-4-(3-ethyl-2-oxo-5-phenyl-2,3-dihydrofuran-3-yl) butanoate:

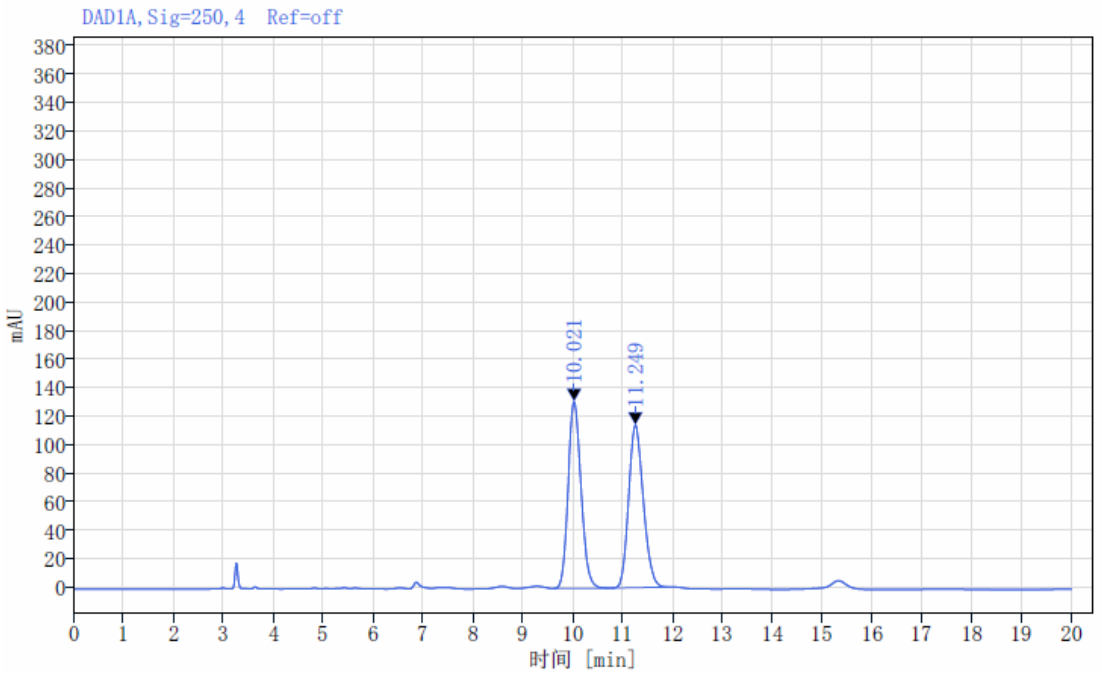
According to the general procedure, the product **3z** was isolated by preparative TLC (petroleum ether/ethyl acetate = 5/1) as a yellow solid (45.7 mg, 42%), and the dr ratio of product **3z** was determined to be 1/1 by chiral HPLC analysis.

^{1}H NMR (400 MHz, $CDCl_3$) (taken as a mixture of diastereomers): δ 7.63 (dd, *J* = 7.9, 1.6 Hz, 2H), 7.45 – 7.36 (m, 3H), 5.70 (s, 1H), 5.39 (d, *J* = 3.1 Hz, 1H), 4.64 – 4.54 (m, 1H), 2.46 (dd, *J* = 19.3, 8.7 Hz, 1H), 2.36 – 2.21 (m, 4H), 2.15 – 2.03 (m, 2H), 2.00 – 1.90 (m, 1H), 1.90 – 1.82 (m, 4H), 1.80 – 1.74 (m, 2H), 1.73 – 1.59 (m, 6H), 1.59 – 1.42 (m, 4H), 1.34 – 1.24 (m, 2H), 1.18 – 1.09 (m, 1H), 1.04 (s, 3H), 0.92 – 0.84 (m, 6H).

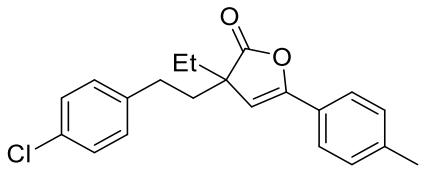
^{13}C NMR (100 MHz, $CDCl_3$) (taken as a mixture of diastereomers): δ 221.1, 180.8, 172.4, 152.2, 139.9, 129.6, 128.7, 128.3, 124.9, 121.9, 105.7, 73.8, 54.8, 51.7, 50.1, 47.6, 38.1, 36.9, 36.7, 36.4, 35.9, 34.4, 31.5, 31.4, 30.8, 30.5, 27.7, 21.9, 20.5, 20.3, 19.4, 13.6, 9.2.

HRMS-ESI (m/z) calcd for $C_{35}H_{45}O_5$ $[(M + H)^+]$ 545.3262, found 545.3267.

HPLC (CHIRALPAK AD-H, Daicel, 4.6 x 250 mm, hexane/IPA=80:20, 1.0 mL/ min, 250 nm), t_1 = 10.02, t_2 = 11.25.



Retention Time min	Peak width	Peak Area	Peak Hight	Relative Area %
10.021	1.12	2348.41	130.44	50.28
11.249	1.13	2322.02	113.50	49.72



(3aa)

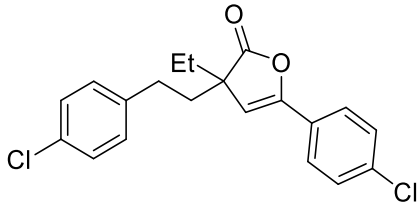
3-(4-chlorophenethyl)-3-ethyl-5-(p-tolyl)furan-2(3H)-one：

According to the general procedure, the product **3aa** was isolated by preparative TLC (petroleum ether/ethyl acetate = 20/1) as a yellow solid (40.9 mg, 60%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 (d, *J* = 8.1 Hz, 2H), 7.22 (dd, *J* = 10.9, 8.3 Hz, 4H), 7.06 (d, *J* = 8.3 Hz, 2H), 5.62 (s, 1H), 2.62 – 2.53 (m, 1H), 2.52 – 2.43 (m, 1H), 2.39 (s, 3H), 2.13 – 2.01 (m, 1H), 1.99 – 1.90 (m, 1H), 1.85 (dt, *J* = 14.8, 7.3 Hz, 1H), 1.75 (dq, *J* = 14.6, 7.4 Hz, 1H), 0.89 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 180.9, 152.5, 140.0, 139.7, 131.9, 129.8, 129.5, 128.6, 125.2, 124.9, 104.6, 55.0, 38.9, 30.9, 30.8, 21.6, 9.2.

HRMS-ESI (m/z) calcd for $C_{21}H_{22}ClO_2$ [(M + H) $^+$] 341.1303, found 341.1311.



(3ab)

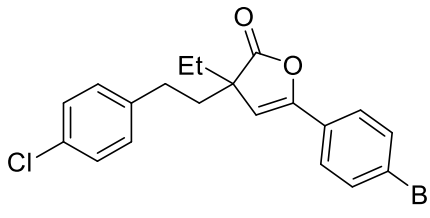
3-(4-chlorophenethyl)-5-(4-chlorophenyl)-3-ethylfuran-2(3H)-one：

According to the general procedure, the product **3ab** was isolated by preparative TLC (petroleum ether/ethyl acetate = 20/1) as a yellow solid (36.1 mg, 50%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 – 7.43 (m, 2H), 7.37 – 7.27 (m, 2H), 7.15 – 7.08 (m, 2H), 6.97 (d, *J* = 8.5 Hz, 2H), 5.60 (s, 1H), 2.56 – 2.33 (m, 2H), 2.05 – 1.97 (m, 1H), 1.95 – 1.83 (m, 1H), 1.78 (dt, *J* = 14.9, 7.4 Hz, 1H), 1.74 – 1.62 (m, 1H), 0.82 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 180.3, 151.5, 139.5, 135.7, 132.0, 129.8, 129.1, 128.7, 126.8, 126.3, 106.2, 55.1, 38.7, 30.9, 30.7, 9.2.

HRMS-ESI (m/z) calcd for $C_{20}H_{19}Cl_2O_2$ [(M + H) $^+$] 361.0757, found 361.0759.



(3ac)

5-(4-bromophenyl)-3-(4-chlorophenethyl)-3-ethylfuran-2(3H)-one:

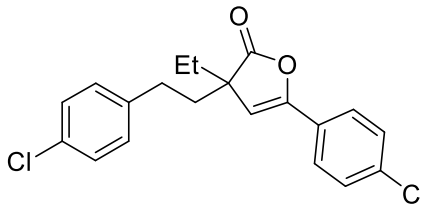
According to the general procedure, the product **3ac** was isolated by preparative TLC (petroleum ether/ethyl acetate = 20/1) as a yellow solid (49.5 mg, 61%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, *J* = 8.6 Hz, 2H), 7.51 – 7.45 (m, 2H), 7.20 (d, *J* = 8.3 Hz, 2H), 7.05 (d, *J* = 8.3 Hz, 2H), 5.69 (s, 1H), 2.64 – 2.43 (m, 2H), 2.13 – 2.05

(m, 1H), 2.00 – 1.91 (m, 1H), 1.86 (dt, *J* = 14.9, 7.4 Hz, 1H), 1.76 (dq, *J* = 14.8, 7.4 Hz, 1H), 0.89 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 180.3, 151.5, 139.5, 132.1, 132.0, 129.8, 128.7, 127.2, 126.5, 124.0, 106.3, 55.1, 38.7, 30.9, 30.7, 9.2.

HRMS-ESI (m/z) calcd for $C_{20}H_{18}BrClO_2Na$ [(M + Na) $^+$] 427.0071, found 427.0079.



(3ad)

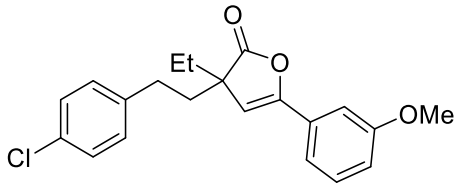
4-(4-(4-chlorophenethyl)-4-ethyl-5-oxo-4,5-dihydrofuran-2-yl)benzonitrile：

According to the general procedure, the product **3ad** was isolated by preparative TLC (petroleum ether/ethyl acetate = 5/1) as a colorless oil (35.2 mg, 50%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 – 7.61 (m, 4H), 7.24 – 7.13 (m, 2H), 6.99 – 6.96 (m, 2H), 5.79 (s, 1H), 2.65 – 2.44 (m, 2H), 2.08 – 2.00 (m, 1H), 1.96 – 1.86 (m, 1H), 1.85 – 1.79 (m, 1H), 1.77 – 1.69 (m, 1H), 0.91 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 179.7, 150.7, 139.2, 132.6, 132.2, 132.1, 129.7, 128.7, 125.4, 118.4, 113.0, 109.6, 55.2, 38.5, 30.9, 30.7, 9.2.

HRMS-ESI (m/z) calcd for $C_{21}H_{19}ClNO_2$ [(M + H) $^+$] 352.1099, found 352.1107.



(3ae)

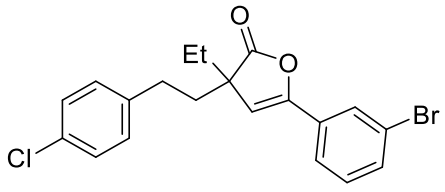
3-(4-chlorophenethyl)-3-ethyl-5-(3-methoxyphenyl)-furan-2(3H)-one:

According to the general procedure, the product **3ae** was isolated by preparative TLC (petroleum ether/ethyl acetate = 20/1) as a yellow solid (44.2 mg, 62%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (t, *J* = 7.9 Hz, 1H), 7.25 – 7.18 (m, 3H), 7.17 – 7.12 (m, 1H), 7.06 (d, *J* = 8.3 Hz, 2H), 6.94 (dd, *J* = 8.2, 2.4 Hz, 1H), 5.69 (s, 1H), 3.85 (s, 3H), 2.63 – 2.54 (m, 1H), 2.53 – 2.44 (m, 1H), 2.14 – 2.04 (m, 1H), 2.01 – 1.91 (m, 1H), 1.86 (dt, *J* = 14.8, 7.4 Hz, 1H), 1.76 (dq, *J* = 14.7, 7.5 Hz, 1H), 0.90 (t, *J* = 7.5 Hz, 3H).

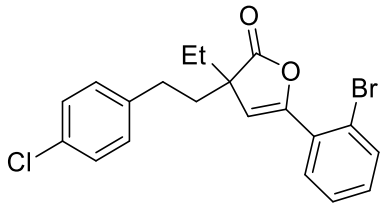
^{13}C NMR (100 MHz, $CDCl_3$): δ 180.7, 159.9, 152.3, 139.6, 131.9, 129.9, 129.8, 129.5, 128.6, 117.4, 115.9, 110.0, 106.0, 55.5, 55.1, 38.8, 30.9, 30.8, 9.3.

HRMS-ESI (m/z) calcd for $C_{21}H_{22}ClO_3$ [(M + H) $^+$] 357.1252, found 357.1252.



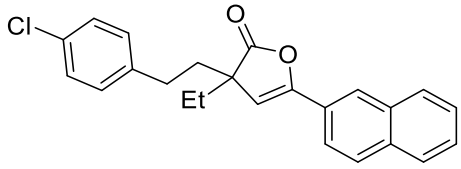
(3af)

5-(3-bromophenyl)-3-(4-chlorophenethyl)-3-ethylfuran-2(3H)-one:
According to the general procedure, the product **3af** was isolated by preparative TLC (petroleum ether/ethyl acetate = 20/1) as a colorless oil (45.4 mg, 56%).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (d, *J* = 1.3 Hz, 1H), 7.53 (dd, *J* = 13.0, 4.4 Hz, 2H), 7.30 (t, *J* = 7.9 Hz, 1H), 7.25 – 7.17 (m, 2H), 7.06 (d, *J* = 8.1 Hz, 2H), 5.72 (s, 1H), 2.63 – 2.44 (m, 2H), 2.16 – 2.04 (m, 1H), 2.02 – 1.92 (m, 1H), 1.87 (dq, *J* = 14.7, 7.4 Hz, 1H), 1.77 (dq, *J* = 14.6, 7.4 Hz, 1H), 0.90 (t, *J* = 7.4 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 180.2, 151.0, 139.5, 132.7, 132.0, 130.4, 130.2, 129.8, 128.7, 128.0, 123.5, 123.0, 107.1, 55.1, 38.8, 30.9, 30.7, 9.2.
HRMS-ESI (m/z) calcd for $C_{20}H_{19}BrClO_2$ [(M + H) $^+$] 405.0251, found 405.0252.



(3ag)

5-(2-bromophenyl)-3-(4-chlorophenethyl)-3-ethylfuran-2(3H)-one:
According to the general procedure, the product **3ag** was isolated by preparative TLC (petroleum ether/ethyl acetate = 20/1) as a colorless oil (43.8 mg, 54%).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 – 7.56 (m, 2H), 7.31 (dd, *J* = 11.8, 4.1 Hz, 1H), 7.20 – 7.10 (m, 3H), 7.01 (d, *J* = 8.3 Hz, 2H), 6.07 (s, 1H), 2.66 – 2.50 (m, 1H), 2.49 – 2.35 (m, 1H), 2.08 – 1.98 (m, 1H), 1.91 (dd, *J* = 12.2, 5.1 Hz, 1H), 1.85 – 1.78 (m, 1H), 1.75 – 1.66 (m, 1H), 0.87 (t, *J* = 7.5 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 180.2, 150.1, 139.6, 134.4, 132.0, 130.6, 129.8, 129.0, 128.7, 127.7, 121.2, 112.8, 55.4, 38.8, 31.0, 30.7, 9.3.
HRMS-ESI (m/z) calcd for $C_{20}H_{19}BrClO_2$ [(M + H) $^+$] 405.0251, found 405.0250.

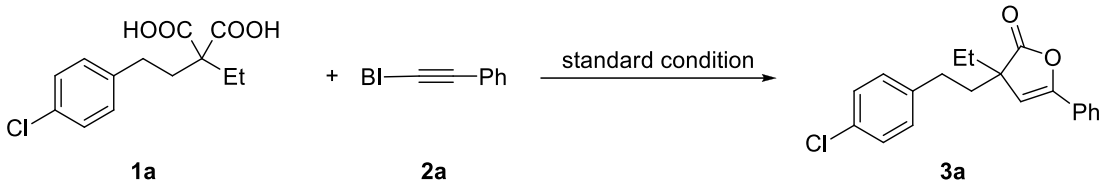


(3ah)

3-(4-chlorophenethyl)-3-ethyl-5-(naphthalen-2-yl)-furan-2(3H)-one:
According to the general procedure, the product **3ah** was isolated by preparative TLC (petroleum ether/ethyl acetate = 20/1) as a white solid (33.2 mg, 44%).
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13 (s, 1H), 7.90 – 7.84 (m, 3H), 7.66 (dd, *J* = 8.6, 1.3 Hz, 1H), 7.53 (dd, *J* = 6.2, 3.2 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 7.07 (d, *J* = 8.3 Hz, 2H), 5.80 (s, 1H), 2.65 – 2.49 (m, 2H), 2.20 – 2.08 (m, 1H), 2.05 – 1.95 (m, 1H), 1.90 (dt, *J* = 14.8, 7.3 Hz, 1H), 1.80 (dq, *J* = 14.7, 7.5 Hz, 1H), 0.93 (t, *J* = 7.4 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 180.7, 152.5, 139.7, 133.8, 133.2, 132.0, 129.8, 128.8, 128.7, 127.9, 127.2, 127.0, 125.3, 124.9, 121.9, 106.3, 55.2, 38.9, 31.0, 30.8, 9.3.
HRMS-ESI (m/z) calcd for $C_{24}H_{22}ClO_2$ [(M + H) $^+$] 377.1303, found 377.1312.

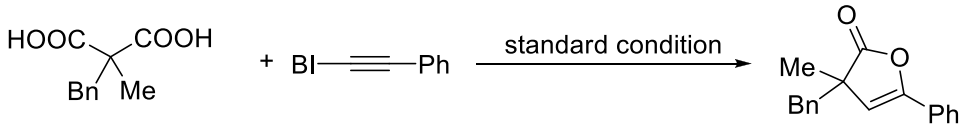
4. Synthetic Applications

4.1 Gram-Scale Synthesis



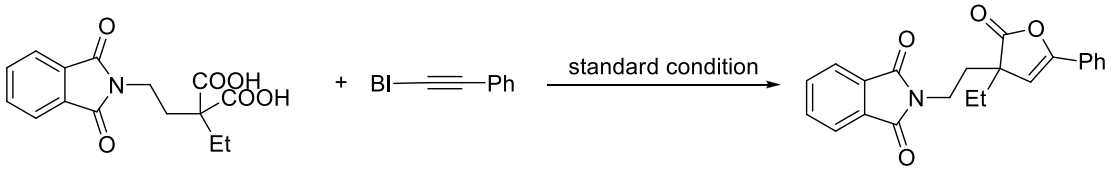
1a **2a** **3a**

1a (1.00 g, 3.70 mmol, 1.0 equiv.), **2a** (1.93 g, 5.54 mmol, 1.5 equiv.), K_3PO_4 (1.57 g, 7.40 mmol, 2 equiv.), $AgNO_3$ (62.8 mg, 0.37 mmol, 0.1 equiv.) and $K_2S_2O_8$ (1.00 g, 3.70 mmol, 1 equiv.) were placed in a 250 mL flask. The flask was evacuated and filled with nitrogen. Then acetonitrile (18 mL), water (54 mL) and *n*-hexane (72 mL) were added, the resulting reaction mixture was heated up to 65 °C and stirred for 12 h. The reaction was quenched with 3M HCl (pH = 2), extracted with EtOAc, the combined organic phase was dried over anhydrous Na_2SO_4 and concentrated in vacuo, the residue was purified by column chromatography on silica gel to give the desired product **3a** (944 mg, 78%).



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

1g (1.00 g, 4.80 mmol, 1.0 equiv.), **2a** (2.51 g, 7.20 mmol, 1.5 equiv.), K_3PO_4 (2.00 g, 9.60 mmol, 2 equiv.), $AgNO_3$ (81.5 mg, 0.48 mmol, 0.1 equiv.) and $K_2S_2O_8$ (1.30 g, 4.80 mmol, 1 equiv.) were placed in a 250 mL flask. The flask was evacuated and filled with nitrogen. Then acetonitrile (24 mL), water (72 mL) and *n*-hexane (96 mL) were added, the resulting reaction mixture was heated up to 65 °C and stirred for 12 h. The reaction was quenched with 3M HCl (pH = 2), extracted with EtOAc, the combined organic phase was dried over anhydrous Na_2SO_4 and concentrated in vacuo, the residue was purified by column chromatography on silica gel to give the desired product **3g** (888 mg, 70%).

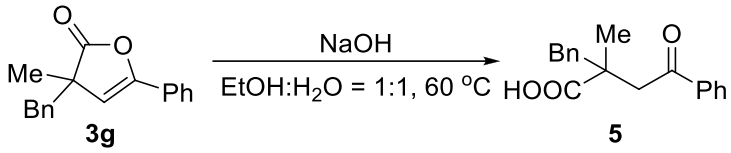


1q **2a** **3q**

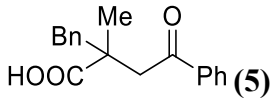
1q (1.00 g, 3.30 mmol, 1.0 equiv.), **2a** (1.70 g, 4.9 mmol, 1.5 equiv.), K_3PO_4 (1.40 g, 6.6 mmol, 2 equiv.), $AgNO_3$ (56.0 mg, 0.33 mmol, 0.1 equiv.) and $K_2S_2O_8$ (893 mg, 3.30 mmol, 1 equiv.) were placed in a 250 mL flask. The flask was evacuated and filled with nitrogen. Then acetonitrile (16 mL), water (48 mL) and *n*-hexane (64 mL) were

added, the resulting reaction mixture was heated up to 65 °C and stirred for 12 h. The reaction was quenched with 3M HCl (pH = 2), extracted with EtOAc, the combined organic phase was dried over anhydrous Na_2SO_4 and concentrated in vacuo, the residue was purified by column chromatography on silica gel to give the desired product **3q** (836 mg, 70%).

4.2 Transformations of Compound 3g



3g **5**



(5)

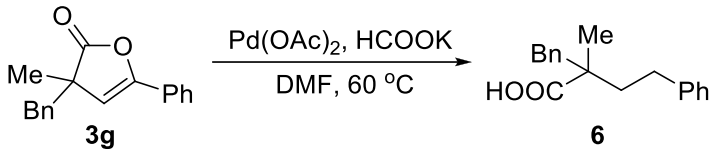
2-benzyl-2-methyl-4-oxo-4-phenylbutanoic-acid:

3g (528 mg, 2 mmol) was dissolved in ethanol (20 mL) and then 8M NaOH (20 mL) was added, the mixture was heated up to 60 °C and stirred for 12 h. Then the resulting mixture was cooled to room temperature, and HCl (3 M) was added until pH = 3. The solution was extracted with EtOAc. The organic layer was washed with brine and dried over Na_2SO_4. The organic solution was evaporated and the residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1 v/v) to give the desired product **5** as an orange solid (536 mg, 95%).

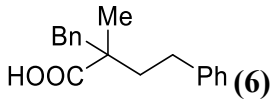
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 – 7.88 (m, 2H), 7.59 – 7.53 (m, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.30 – 7.20 (m, 3H), 7.16 – 7.10 (m, 2H), 3.33 (d, *J* = 18.2 Hz, 1H), 3.24 – 3.13 (m, 2H), 3.07 (d, *J* = 13.3 Hz, 1H), 1.32 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 197.7, 183.2, 136.9, 133.4, 130.6, 128.7, 128.3, 128.1, 126.9, 45.6, 44.4, 43.7, 22.5.

HRMS-ESI (m/z) calcd for $C_{18}H_{18}O_3Na$ [(M + Na) $^+$] 305.1148, found 305.1161.



3g **6**



(6)

2-benzyl-2-methyl-4-phenylbutanoic-acid:

$Pd(OAc)_2$ (2.2 mg, 0.01 mmol.) and HCO_2K (42.1 mg, 0.5 mmol.) were added to a stirred solution of **3g** (26.4 mg, 0.1 mmol) in DMF (0.2 mL). The reaction mixture was stirred at 60 °C for 24 h. Then EtOAc and a saturated $NaHCO_3$ solution were added to the cooled mixture, the organic layer was separated, washed with water, and dried over

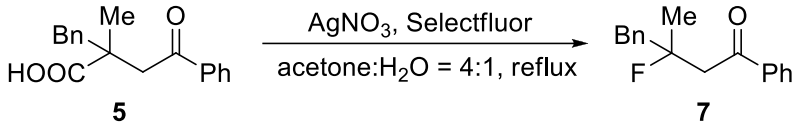
Na_2SO_4. Concentration and purification by preparative TLC (petroleum ether/ethyl acetate = 5/1 v/v) to give the product **6** as a yellow solid (16.1 mg, 60%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 – 7.25 (m, 4H), 7.24 – 7.22 (m, 1H), 7.21 – 7.18 (m, 5H), 3.10 (d, *J* = 13.3 Hz, 1H), 2.82 (d, *J* = 13.3 Hz, 1H), 2.74 – 2.57 (m, 2H), 2.10 (td, *J* = 12.8, 4.9 Hz, 1H), 1.75 (td, *J* = 12.7, 5.3 Hz, 1H), 1.22 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 183.3, 142.0, 137.2, 130.4, 128.6, 128.5, 128.3, 126.8, 126.07, 47.5, 45.4, 41.3, 31.4, 20.7.

HRMS-ESI (m/z) calcd for $C_{18}H_{21}O_2$ [(M + H) $^+$] 269.1536, found 269.1534.

4.3 Transformations of Compound 5



5 **7**

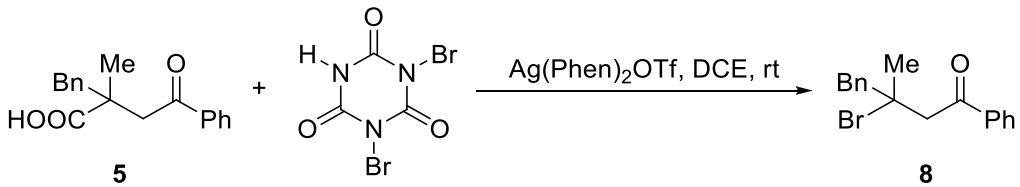
5 (28.2 mg, 0.1 mmol, 1.0 equiv.), $AgNO_3$ (5.1 mg, 0.03 mmol, 0.3 equiv.) and Selectfluor (141.7 mg, 0.4 mmol, 4 equiv.) were placed in a Schlenk-tube. The reaction vessel was evacuated and filled with nitrogen. Acetone (1.6 mL) and water (0.4 mL) were then added. The reaction mixture was then stirred at refluxing temperature for 12 h. Upon completion of the reaction, the resulting mixture was cooled down to room temperature and extracted with dichloromethane (5 mL × 3). The combined organic phase was dried over anhydrous Na_2SO_4. After the removal of solvent under reduced pressure, the crude product was purified by preparative TLC (petroleum ether/ethyl acetate = 50:1) to give the pure product **7** as a white solid (19.5 mg, 76%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 – 7.84 (m, 2H), 7.56 (ddd, *J* = 8.7, 2.6, 1.3 Hz, 1H), 7.47 – 7.39 (m, 2H), 7.31 – 7.18 (m, 5H), 3.32 (dd, *J* = 16.2, 12.2 Hz, 1H), 3.27 – 3.09 (m, 3H), 1.54 (d, *J* = 22.6 Hz, 3H).

^{19}F NMR (376 MHz, $CDCl_3$): δ -136.07 (s, 1F).

^{13}C NMR (100 MHz, $CDCl_3$): δ 197.4 (d, *J* = 11.4 Hz), 137.4, 136.6, 133.4, 130.6, 128.7, 128.3, 126.8, 96.2 (d, *J* = 170.7 Hz), 46.6 (d, *J* = 24.4 Hz), 45.5 (d, *J* = 21.1 Hz), 25.4 (d, *J* = 23.4 Hz).

HRMS-ESI (m/z) calcd for $C_{17}H_{17}FONa$ [(M + Na) $^+$] 279.1156, found 279.1157.



5 **8**

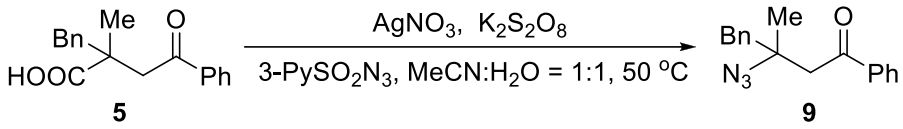
To a 10 mL flask were added **5** (28.2 mg, 0.1 mmol, 1.0 equiv.), $Ag(Phen)_2OTf$ (3.0 mg, 0.005 mmol, 0.05 equiv.) and dibromoisocyanuric acid (28.7 mg, 0.1 mmol, 1.0 equiv.) under N_2 atmosphere. 1, 2-Dichloroethane (4 mL) was then added. The mixture was stirred at room temperature for 12 h. The resulting mixture was filtered. The white precipitate was washed with CH_2Cl_2 (5 mL × 3). The combined organic phase was

concentrated under reduced pressure. The residue was purified by preparative TLC (petroleum ether/ ethyl acetate = 50:1) to afford the pure product **8** as a colorless oil (21.6 mg, 68%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 – 7.85 (m, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.31 – 7.22 (m, 5H), 3.16 – 3.01 (m, 4H), 1.52 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 197.6, 137.5, 136.4, 133.4, 130.7, 128.8, 128.4, 128.2, 127.1, 63.4, 45.6, 45.2, 23.7.

HRMS-ESI (m/z) calcd for $C_{17}H_{18}BrO$ [(M + H) $^+$] 317.0536, found 317.0540.



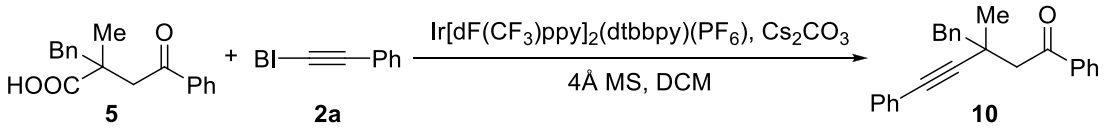
5 **9**

5 (28.2 mg, 0.1 mmol, 1.0 equiv.), $AgNO_3$ (5.1 mg, 0.03 mmol, 0.3 equiv.), $K_2S_2O_8$ (81.2 mg, 0.3 mmol, 3 equiv.) and 3-$PySO_2N_3$ (55.3 mg, 0.30 mmol, 3 equiv.) were placed in a Schlenk tube. Acetonitrile (0.5 mL) and water (0.5 mL) were then added under N_2 atmosphere. The reaction solution was stirred at 50 °C for 12 h. The resulting mixture was cooled down to room temperature and extracted with CH_2Cl_2 (5 mL × 4). The combined organic phase was dried over anhydrous Na_2SO_4. After the removal of solvent under reduced pressure, the crude product was purified by preparative TLC (petroleum ether/ ethyl acetate = 50:1) to give the product **9** as a colorless oil (24.5 mg, 88%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 – 7.91 (m, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.33 – 7.22 (m, 5H), 3.66 – 3.52 (m, 4H), 2.06 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 197.2, 137.3, 137.1, 133.5, 131.0, 128.8, 128.2, 128.1, 127.1, 67.2, 50.4, 49.7, 32.5.

HRMS-ESI (m/z) calcd for $C_{17}H_{18}N_3O$ [(M + H) $^+$] 280.1444, found 280.1455.



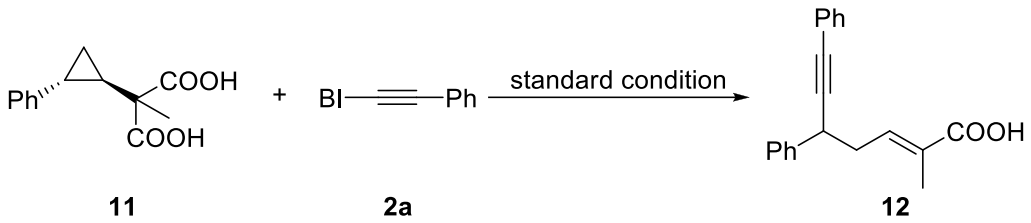
5 **2a** **10**

5 (28.2 mg, 0.1 mmol, 1.0 equiv.), **2a** (41.8 mg, 0.12 mmol, 1.2 equiv.), Cs_2CO_3 (97.7 mg, 0.3 mmol, 3.0 equiv.), 4 Å MS (10 mg), Ir[dF(CF_3)ppy]$_2$(dtbbpy)(PF_6) (3.4 mg, 0.003 mmol, 0.03 equiv.) and CH_2Cl_2 (2.0 mL) were added to a 10 mL Schlenk flask equipped with a magnetic stir bar. The reaction mixture was degassed and filled with nitrogen. The solution was then stirred at a distance of ca. 5 cm from a 12 W blue LED at 35 °C for 48 h. Then, the solvent was removed under vacuum and the crude reaction mixture was purified by preparative TLC (petroleum ether/ ethyl acetate = 50:1) to provide pure product **10** as a colorless oil (15.2 mg, 45%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 – 7.86 (m, 2H), 7.46 (dd, *J* = 11.5, 4.3 Hz, 1H), 7.36 (t, *J* = 7.3 Hz, 2H), 7.30 (d, *J* = 7.8 Hz, 2H), 7.25 – 7.20 (m, 2H), 7.20 – 7.14 (m, 4H), 7.10 – 7.05 (m, 2H), 3.24 (d, *J* = 15.1 Hz, 1H), 3.09 (d, *J* = 13.1 Hz, 1H), 2.95 (dd, *J* = 14.0, 5.2 Hz, 2H), 1.41 (s, 3H).

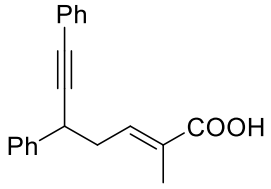
^{13}C NMR (100 MHz, $CDCl_3$): δ 198.7, 138.1, 137.7, 133.0, 131.5, 131.0, 128.6, 128.2, 128.0, 127.8, 126.8, 123.6, 95.0, 83.8, 47.1, 47.1, 35.7, 27.2.
HRMS-ESI (m/z) calcd for $C_{25}H_{22}ONa$ [$(M + Na)^+$] 361.1563, found 361.1572.

5. Mechanistic Experiments



11 **2a** **12**

11[4](46.8 mg, 0.20 mmol, 1.0 equiv.), **2a** (104.4 mg, 0.30 mmol, 1.5 equiv.), K_3PO_4 (84.9 mg, 0.40 mmol, 2.0 equiv.), $AgNO_3$ (3.4 mg, 0.02 mmol, 0.1 equiv.), and $K_2S_2O_8$ (54.0 mg, 0.20 mmol, 1.0 equiv.) were placed in a Schlenk tube. The tube was evacuated and filled with nitrogen. Then solvent acetonitrile/water/hexane (8 mL, 1/3/4 v/v/v) was added, the resulting reaction mixture was stirred at 65 °C for 12 h. The reaction was quenched with 3M HCl (2 mL), extracted with EtOAc (3 mL × 5), the combined organic phase was washed with brine and concentrated in vacuo, the product **12** was isolated by preparative TLC (dichloromethane/methanol = 20/1) as a white solid (11.6 mg, 20%), and 2-oxo-2-phenylethyl (*E*)-2-methyl-5,7-diphenylhept-2-en-6-ynoate was isolated as a byproduct (9.8 mg, 12%).



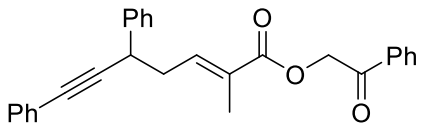
(12)

2-methyl-5,7-diphenylhept-2-en-6-ynoic acid:

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 – 7.41 (m, 4H), 7.36 (t, *J* = 7.5 Hz, 2H), 7.32 – 7.27 (m, 4H), 7.05 (t, *J* = 7.4 Hz, 1H), 4.03 (t, *J* = 7.0 Hz, 1H), 2.76 (t, *J* = 7.2 Hz, 2H), 1.78 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 173.4, 141.3, 140.9, 131.8, 129.2, 128.8, 128.4, 128.1, 127.6, 127.3, 123.4, 90.2, 84.1, 37.9, 37.8, 12.4.

HRMS-ESI (m/z) calcd for $C_{20}H_{19}O_2$ [(M + H) $^+$] 291.1380, found 291.1387.

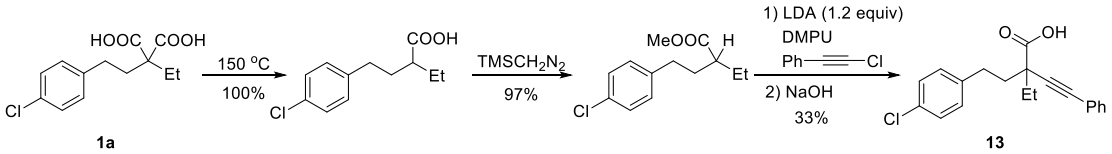


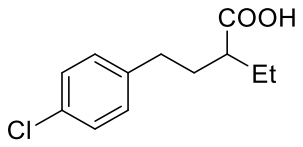
2-oxo-2-phenylethyl (*E*)-2-methyl-5,7-diphenylhept-2-en-6-ynoate:

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 – 7.92 (m, 2H), 7.62 – 7.58 (m, 1H), 7.50 – 7.44 (m, 6H), 7.38 – 7.34 (m, 2H), 7.30 – 7.27 (m, 4H), 7.09 (dt, *J* = 1.3, 7.4 Hz, 1H), 5.40 (d, *J* = 1.4 Hz, 2H), 4.03 (t, *J* = 7.1 Hz, 1H), 2.79 – 2.75 (m, 2H), 1.86 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 192.5, 167.2, 140.8, 140.0, 134.3, 133.8, 131.7, 128.9, 128.8, 128.6, 128.2, 127.9, 127.8, 127.4, 127.1, 123.3, 90.2, 83.9, 66.2, 37.8, 37.7, 12.7.

HRMS-ESI (m/z) calcd for $C_{28}H_{24}O_3$ [(M + H) $^+$] 409.1798, found 409.1799.





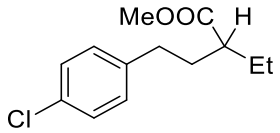
4-(4-chlorophenyl)-2-ethylbutanoic acid:

To a 25 mL flask was added **1a** (2.0 g, 7.30 mmol), the solid was heated at 150 °C under nitrogen atmosphere for 2h, then cooled to room temperature, the residue was used directly for the next step.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24 (d, *J* = 8.8 Hz, 2H), 7.12 (d, *J* = 8.3 Hz, 2H), 2.70 – 2.55 (m, 2H), 2.37 – 2.30 (m, 1H), 2.02 – 1.92 (m, 1H), 1.80 – 1.67 (m, 2H), 1.62 – 1.56 (m, 1H), 0.95 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 182.7, 139.9, 131.7, 129.8, 128.4, 46.3, 33.2, 32.9, 25.2, 11.6.

HRMS-ESI (m/z) calcd for $C_{12}H_{15}ClO_2$ [(M + H + CH_3CN) $^+$] 268.1099, found 268.1100.



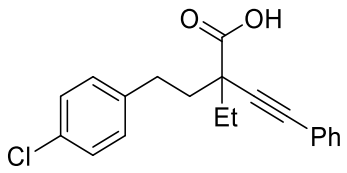
methyl-4-(4-chlorophenyl)-2-ethylbutanoate:

4-(4-Chlorophenyl)-2-ethylbutanoic acid (1.65 g, 7.30 mmol) was dissolved in DCM/MeOH (15 mL, 4/1 v/v), and then $TMSCH_2N_2$ (5.5 mL, 11.0 mmol, 2.0 M in hexanes) was added. The mixture was stirred at room temperature for 30 minutes. Then acetic acid was added to consume the remaining $TMSCH_2N_2$. This solution was evaporated and residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 20/1 v/v) to give the desired product methyl-4-(4-chlorophenyl)-2-ethylbutanoate as a colorless oil (1.7 g, 97%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25 (dd, *J* = 8.3, 4.8 Hz, 2H), 7.10 (d, *J* = 8.3 Hz, 2H), 3.69 (s, 3H), 2.62 – 2.48 (m, 2H), 2.37 – 2.25 (m, 1H), 1.98 – 1.89 (m, 1H), 1.78 – 1.62 (m, 2H), 1.60 – 1.47 (m, 1H), 0.88 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.6, 140.2, 131.7, 129.9, 128.6, 51.60, 46.7, 33.7, 33.2, 25.7, 11.9.

HRMS-ESI (m/z) calcd for $C_{13}H_{17}ClO_2Na$ [(M + Na) $^+$] 263.0809, found 263.0818.



(13)

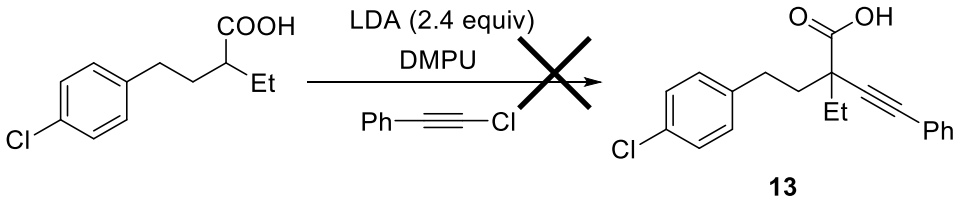
2-(4-chlorophenethyl)-2-ethyl-4-phenylbut-3-ynoic acid:

Diisopropylamine (DIPA) (506 mg, 5.0 mmol.) in dry THF (6 mL) was cooled to 0 °C. After the addition of *n*-BuLi (2.0 mL, 2.5 M in hexane.), the reaction mixture was stirred for 30 minutes at 0 °C. Then methyl 4-(4-chlorophenyl)-2-ethylbutanoate (1.0 g, 4.2 mmol.) and DMPU (538 mg, 4.2 mmol.) were added dropwise at -78 °C. The reaction mixture was stirred for 30 minutes at -78 °C before adding the chlorinated acetylene (1.4 g, 10.3 mmol.).[5] The reaction mixture was allowed to warm up to room temperature and stirred overnight, then water was added to quench the reaction. The aqueous phase was extracted with EtOAc (10 mL × 3). The combined organic layers were washed with water and brine before drying over Na_2SO_4 and concentrated under reduced pressure. Then the residue was stirred in a 1/1 mixture of THF and aqueous NaOH solution (15M) at 80 °C overnight. After cooling to room temperature, the aqueous phase was separated. Then HCl solution (3M) was added to the aqueous phase to adjust the pH to 3 and the resulting solution extracted with diethyl ether. The combined organic phases were washed with brine, dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by column chromatography to give the desired product **13** as a colorless oil (450 mg, 33%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (d, *J* = 3.3 Hz, 2H), 7.35 – 7.27 (m, 3H), 7.22 (d, *J* = 8.1 Hz, 2H), 7.13 (d, *J* = 8.2 Hz, 2H), 2.94 (td, *J* = 12.9, 4.4 Hz, 1H), 2.74 (td, *J* = 12.9, 4.8 Hz, 1H), 2.22 (td, *J* = 12.6, 4.9 Hz, 1H), 2.07 – 1.95 (m, 2H), 1.88 (dq, *J* = 14.3, 7.2 Hz, 1H), 1.13 (t, *J* = 7.3 Hz, 3H).

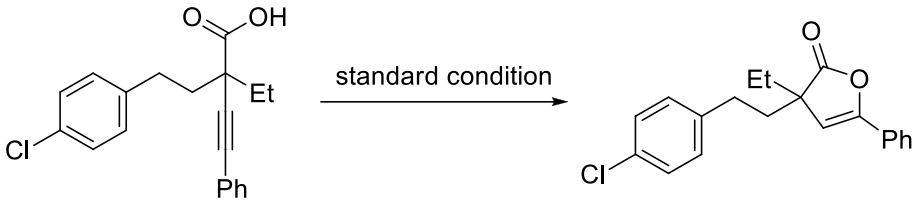
^{13}C NMR (100 MHz, $CDCl_3$): δ 179.6, 140.0, 131.9, 131.9, 130.0, 128.6, 128.4, 123.0, 88.1, 85.7, 49.8, 40.6, 32.9, 31.6, 9.9.

HRMS-ESI (m/z) calcd for $C_{20}H_{20}ClO_2$ [(M + H) $^+$] 327.1146, found 327.1151.



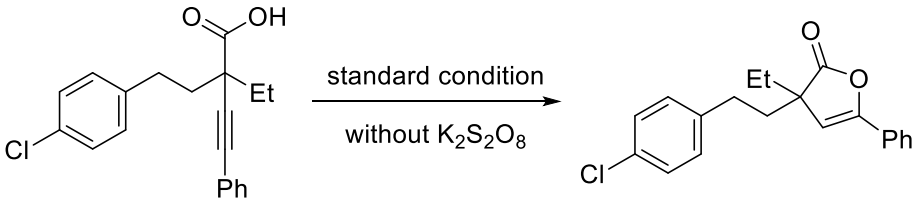
13

Note: The direct alkynylation of 4-(4-chlorophenyl)-2-ethylbutanoic acid with phenylethynyl chloride was attempted with 2.4 equivalents of base by following the procedure of preparation of **13** from methyl-4-(4-chlorophenyl)-2-ethylbutanoate above, but the alkynylation product **13** was not observed in the reaction and the monocarboxylic acid was fully recovered.



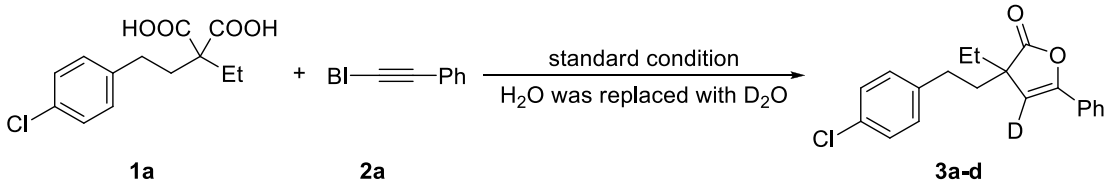
13 **3a**

13 (65.4 mg, 0.20 mmol, 1.0 equiv.), Ph-EBX (104.4 mg, 0.30 mmol, 1.5 equiv.), K_3PO_4 (84.9 mg, 0.40 mmol, 2.0 equiv.), $AgNO_3$ (3.4 mg, 0.02 mmol, 0.1 equiv.), and $K_2S_2O_8$ (54.0 mg, 0.20 mmol, 1.0 equiv.) were placed in a Schlenk tube. The tube was evacuated and filled with nitrogen. Then solvent acetonitrile/water/hexane (8 mL, 1/3/4 v/v/v) was added, the resulting reaction mixture was stirred at 65 °C for 12 h. The reaction was quenched with 3M HCl (2 mL), extracted with EtOAc (3 mL × 5), the combined organic phase was washed with brine and concentrated in vacuo, the product **3a** was isolated by preparative TLC (petroleum ether/ ethyl acetate = 20:1) as a colorless oil (47.7 mg, 73%).



13 **3a**

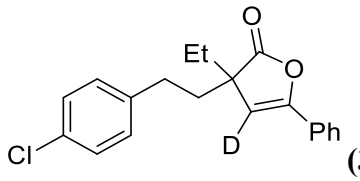
13 (65.4 mg, 0.20 mmol, 1.0 equiv.), Ph-EBX (104.4 mg, 0.30 mmol, 1.5 equiv.), K_3PO_4 (84.9 mg, 0.40 mmol, 2.0 equiv.), $AgNO_3$ (3.4 mg, 0.02 mmol, 0.1 equiv.) were placed in a Schlenk tube. The tube was evacuated and filled with nitrogen. Then solvent acetonitrile/water/hexane (8 mL, 1/3/4 v/v/v) was added, the resulting reaction mixture was stirred at 65 °C for 12 h. The reaction was quenched with 3M HCl (2 mL), extracted with EtOAc (3 mL × 5), the combined organic phase was washed with brine and concentrated in vacuo, the product **3a** was isolated by preparative TLC (petroleum ether/ ethyl acetate = 20:1) as a colorless oil (52.2 mg, 80%).



1a **2a** **3a-d**

1a (54.0 mg, 0.2 mmol, 1.0 equiv.), **2a** (104.4 mg, 0.30 mmol, 1.5 equiv.), K_3PO_4 (84.9 mg, 0.40 mmol, 2.0 equiv.), $AgNO_3$ (3.4 mg, 0.02 mmol, 0.1 equiv.), and $K_2S_2O_8$ (54.0 mg, 0.20 mmol, 1.0 equiv.) were placed in a Schlenk tube. The tube was evacuated and filled with nitrogen. Then solvent acetonitrile/deuterium oxide/*n*-hexane (8 mL, 1/3/4 v/v/v) was added, the resulting reaction mixture was stirred at 65 °C for 12 h. The reaction was quenched with 3M HCl (2 mL), extracted with EtOAc (3 mL × 5), the combined organic phase was washed with brine and concentrated in vacuo, the residue

was purified by preparative TLC (petroleum ether/ ethyl acetate = 20:1) to give the desired product (39.3 mg, 60%).



(3a-d)

3-(4-chlorophenethyl)-3-ethyl-5-phenylfuran-2(3H)-one-4-d:

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 – 7.60 (m, 2H), 7.46 – 7.39 (m, 3H), 7.23 – 7.17 (m, 2H), 7.06 (t, *J* = 5.4 Hz, 2H), 2.61 – 2.54 (m, 1H), 2.53 – 2.43 (m, 1H), 2.15 – 2.03 (m, 1H), 2.00 – 1.92 (m, 1H), 1.90 – 1.83 (m, 1H), 1.81 – 1.72 (m, 1H), 0.89 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 180.7, 152.4, 139.6, 131.9, 129.8, 128.9, 128.6, 128.3, 125.0, 105.3 (t, *J* = 27.0 Hz), 54.9, 38.8, 30.9, 30.8, 9.3.

HRMS-ESI (m/z) calcd for $C_{20}H_{19}DClO_2$ [(M + H) $^{+}$] 328.1209, found 328.1212.

6. Electrochemical Measurements

Cyclic Voltammetry was recorded on an electrochemical workstation CS150H (CorrTest®) using a glassy carbon working electrode, Ag/AgCl in 3 M KCl reference electrode, and a platinum counter electrode. Measurements were performed by dissolving 0.2 mmol of potassium carboxylate salts in approximately 8 mL of a 0.1 M tetrabutylammonium hexafluorophosphate ($TBAPF_6$) solution in acetonitrile. (Note: to have a good solubility of the corresponding potassium salt in acetonitrile, 0.3 mL of water was required.) The potential range scanned for background, potassium pivalate and potassium 2,2-dimethylmalonate was between 0.0 V and 3.0 V at a 100 mV/s. $E_{p/2}$ is given as the half-wave potential for irreversible oxidation, where the current is equal to one-half the peak current of the oxidation event. Potassium carboxylate salts were made by reactions of the corresponding acid with 1 equivalent or 2 equivalents of KOH in a solution of THF. Then solvent was evaporated in vacuo to give potassium pivalate or potassium 2,2-dimethylmalonate.

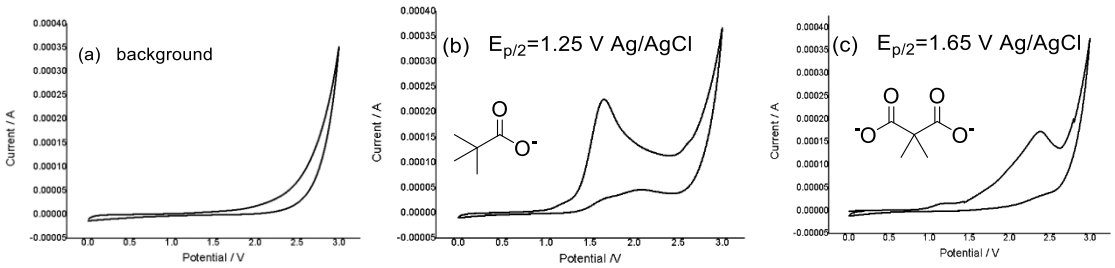


Figure 1: Cyclic voltammograms for (a) background (b) potassium pivalate and (c) potassium 2,2-dimethylmalonate

7. References

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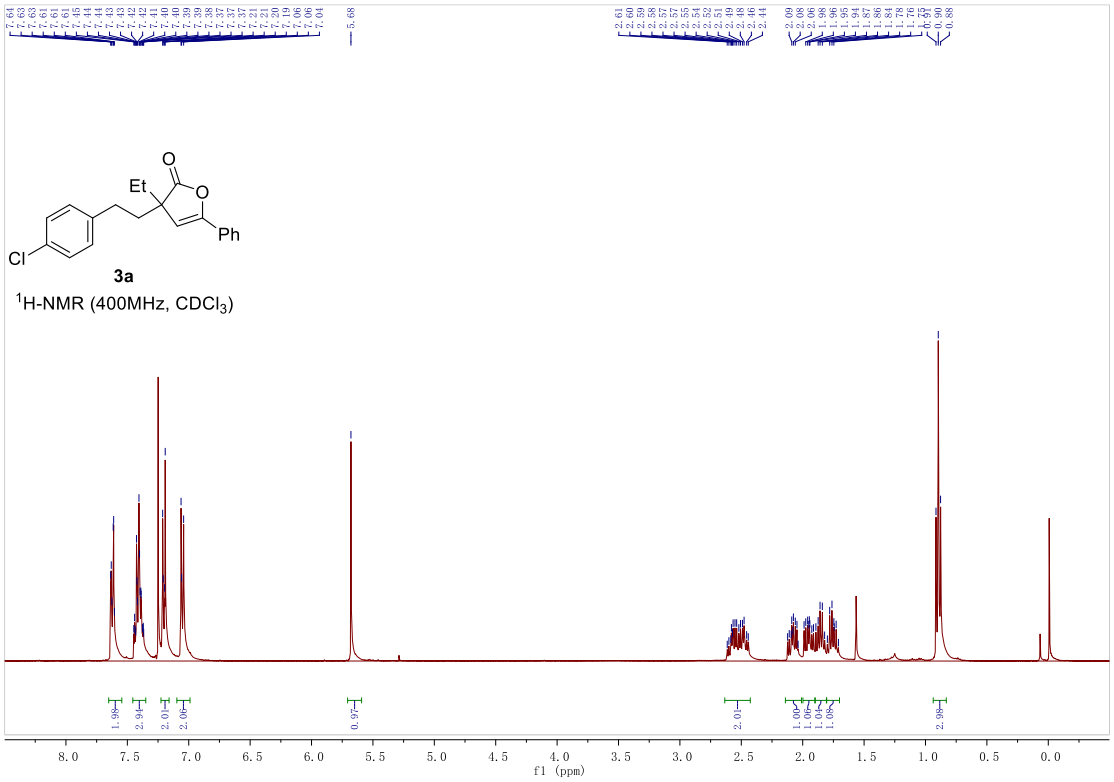
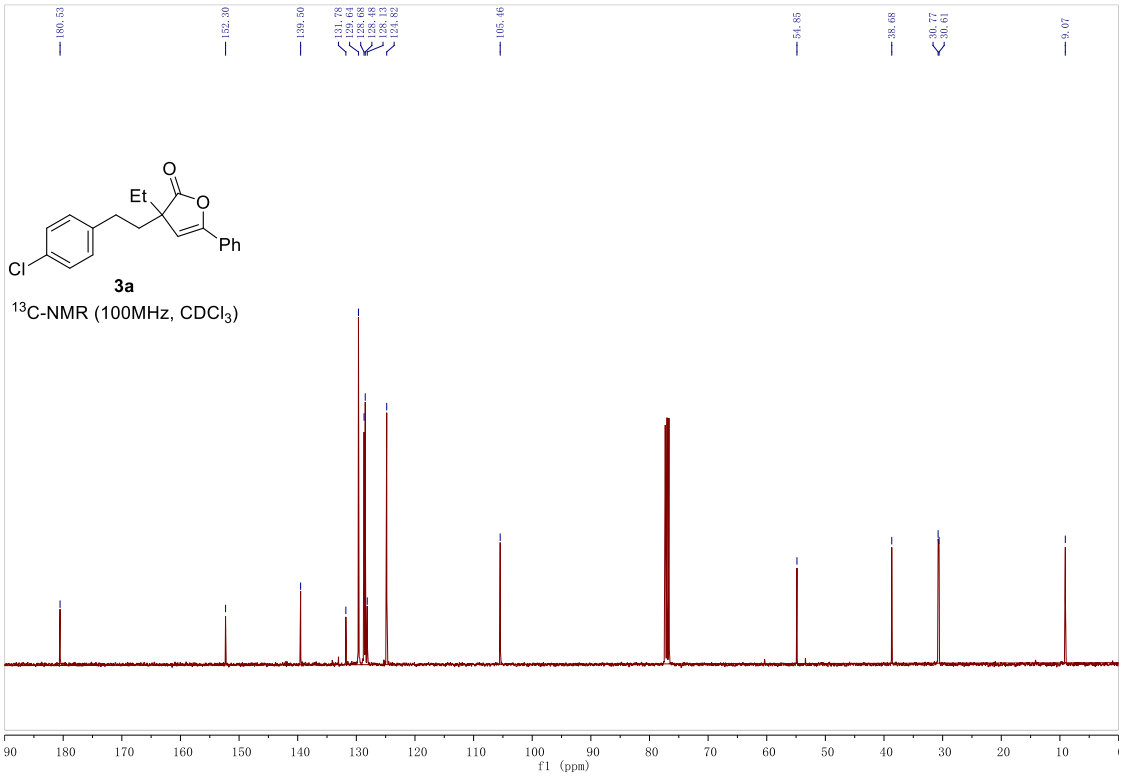
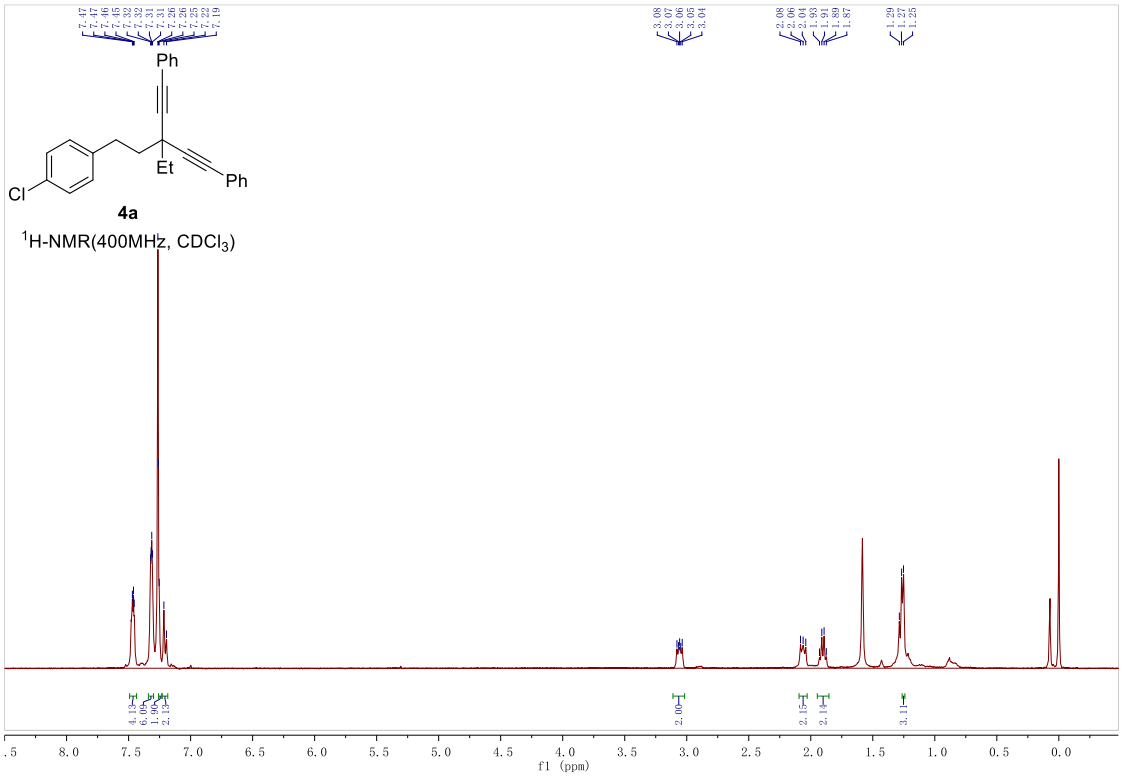
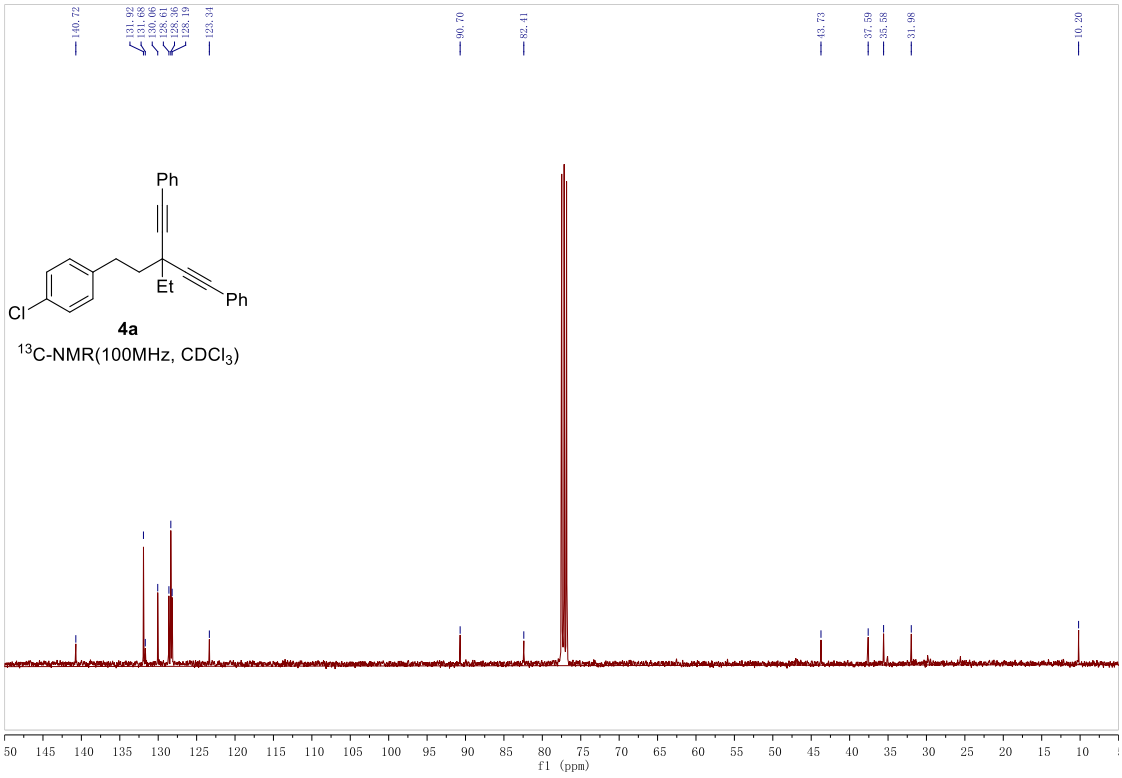
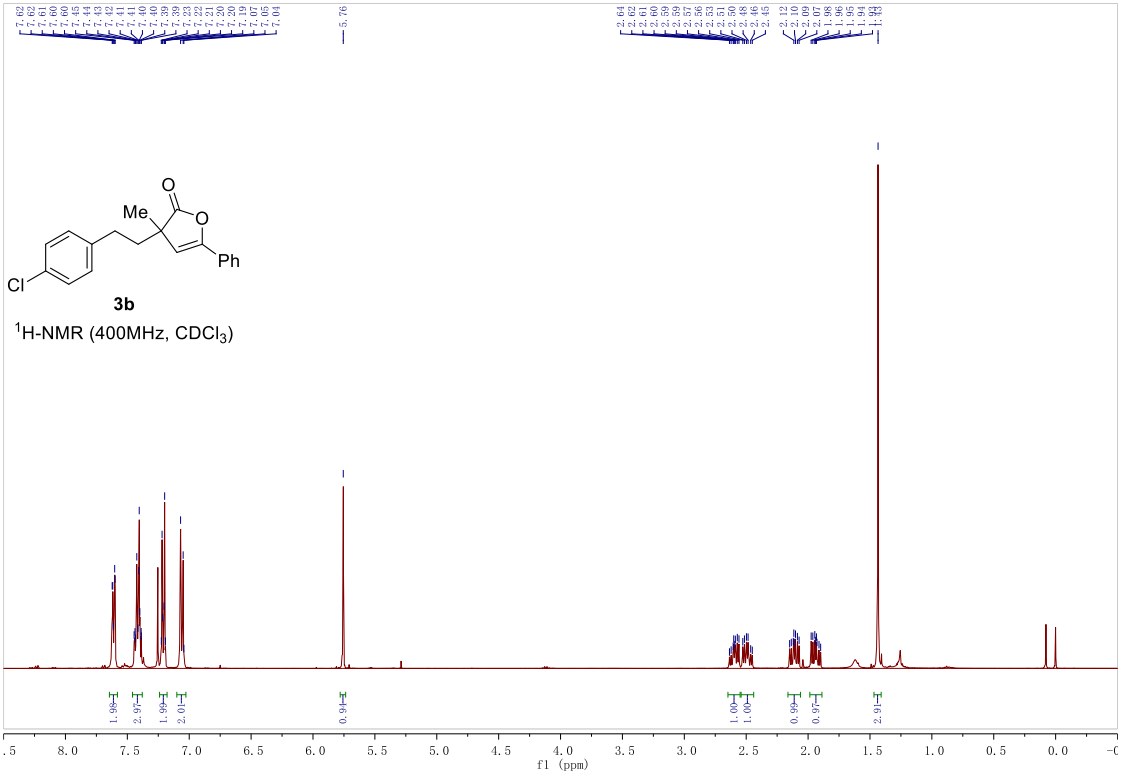
8. ^{1}H NMR, ^{19}F NMR and ^{13}C NMR Spectra Data

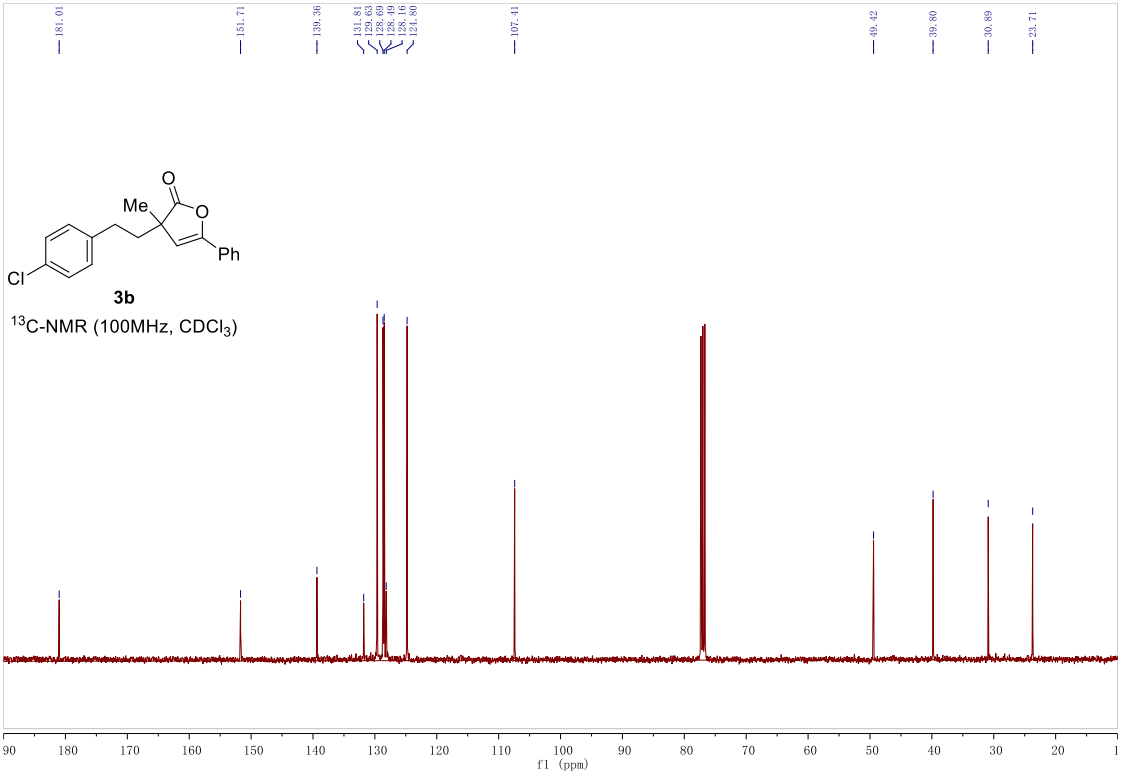





Ph
Et
Ph
Cl
4a
1H-NMR(400MHz, CDCl3)
f1 (ppm)


Ph
Et
Ph
Cl
4a
13C-NMR(100MHz, CDCl3)
f1 (ppm)


Me
O
O
Ph
Cl
3b
1H-NMR (400MHz, CDCl3)
f1 (ppm)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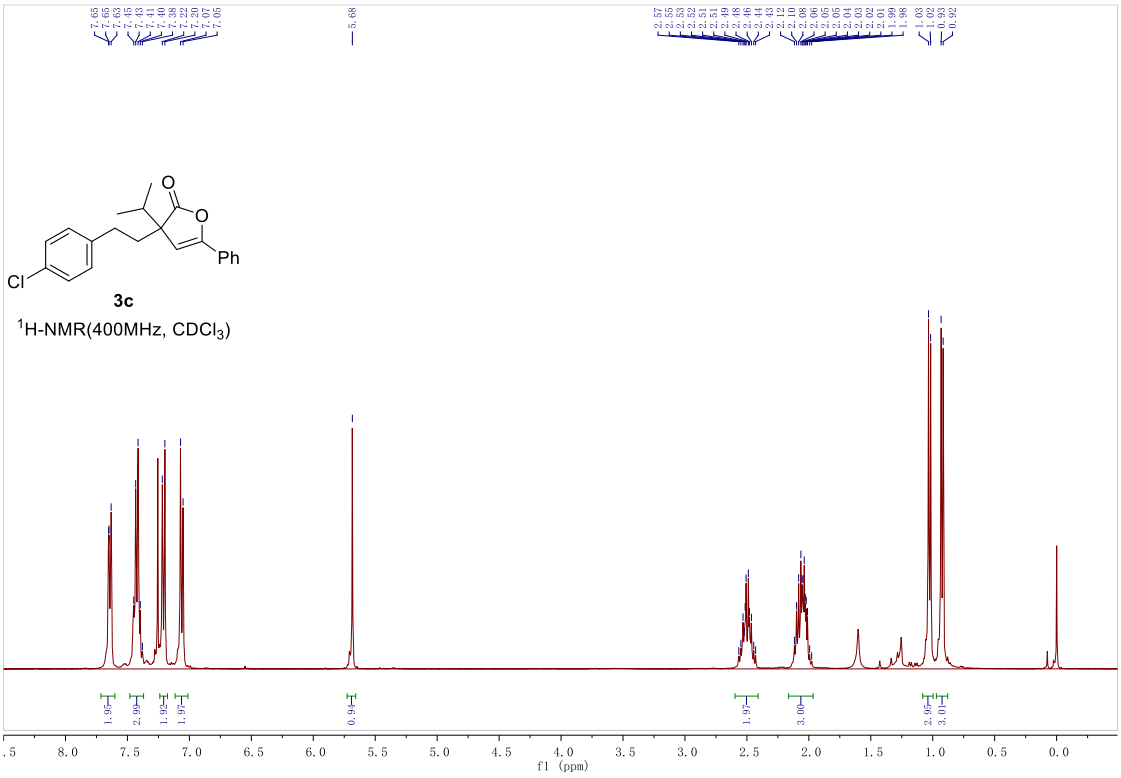
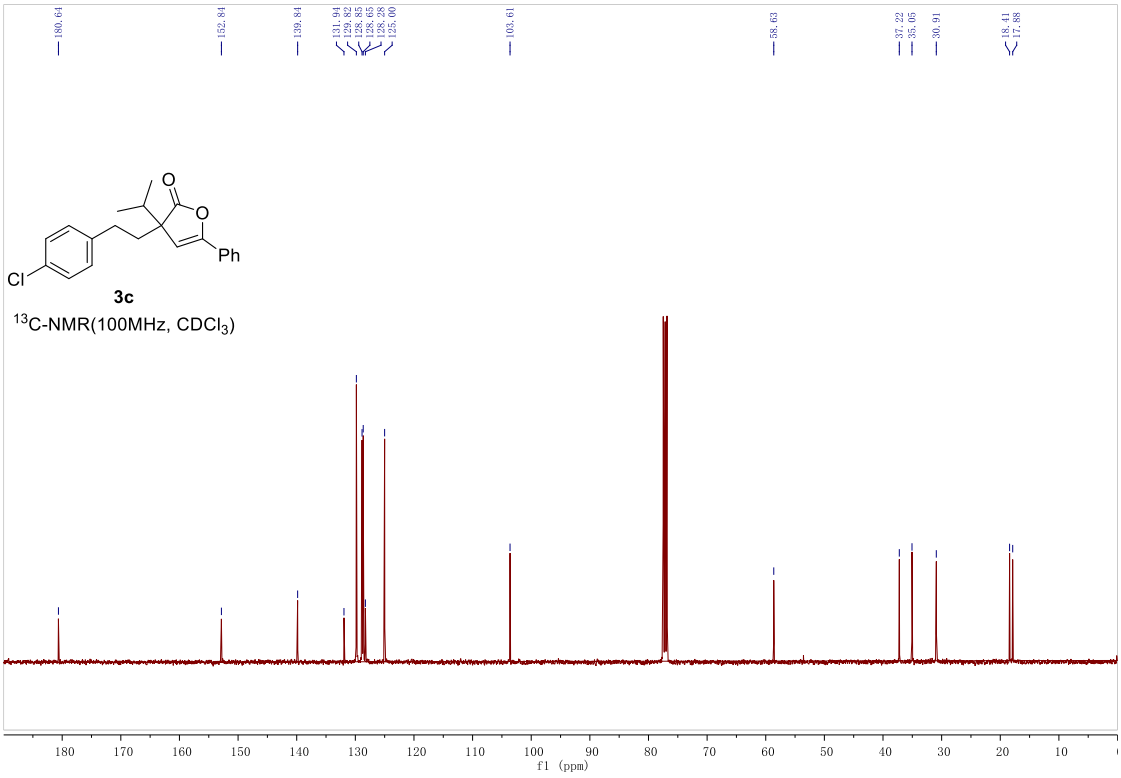
O
O
Ph
Cl
3b
13C-NMR (100MHz, CDCl3)
f1 (ppm)


Cl
O
O
Ph
3c
^{1}H-NMR(400MHz, CDCl$_3$)
f1 (ppm)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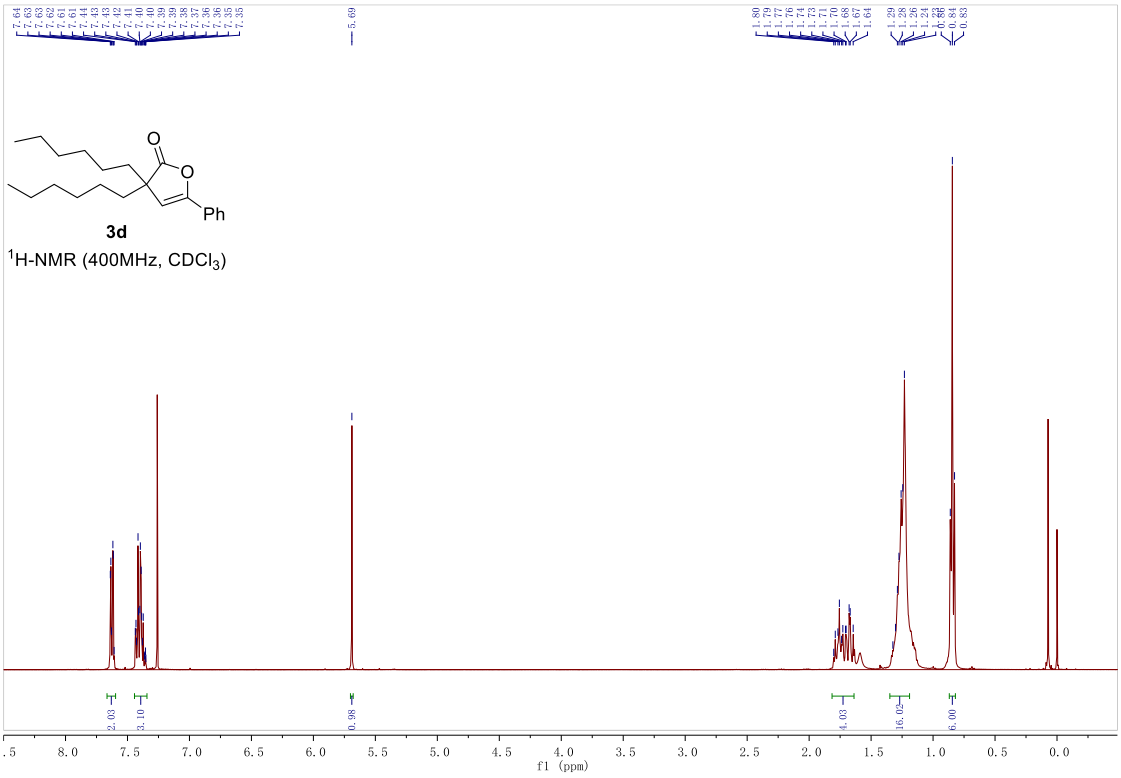
O
O
Ph
3c
^{13}C-NMR(100MHz, CDCl$_3$)
f1 (ppm)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7.43
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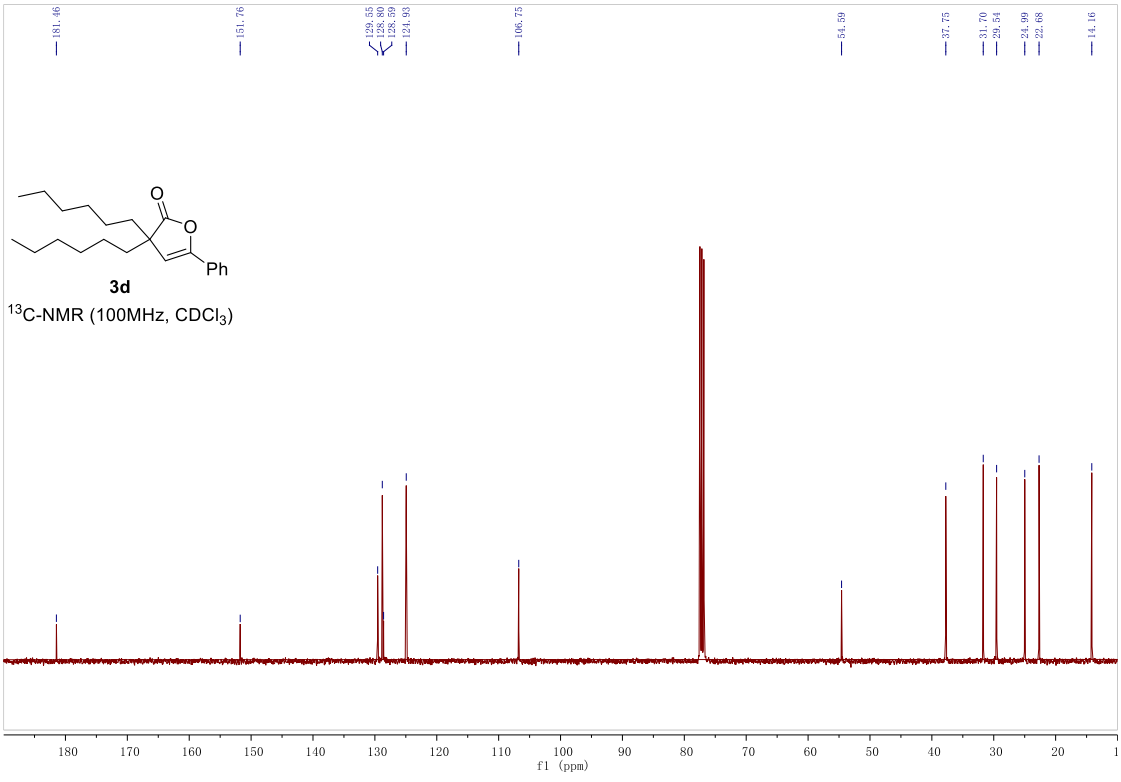
7.40
7.40
7.39
7.39
7.38
7.37
7.36
7.36
7.35
7.35
5.69
1.80
1.79
1.77
1.76
1.74
1.73
1.71
1.70
1.68
1.67
1.64
1.29
1.28
1.26
1.24
1.23
0.86
0.84
0.83
O
O
Ph
3d
1H-NMR (400MHz, CDCl3)
2.03
3.10
0.98
4.03
16.02
6.00
f1 (ppm)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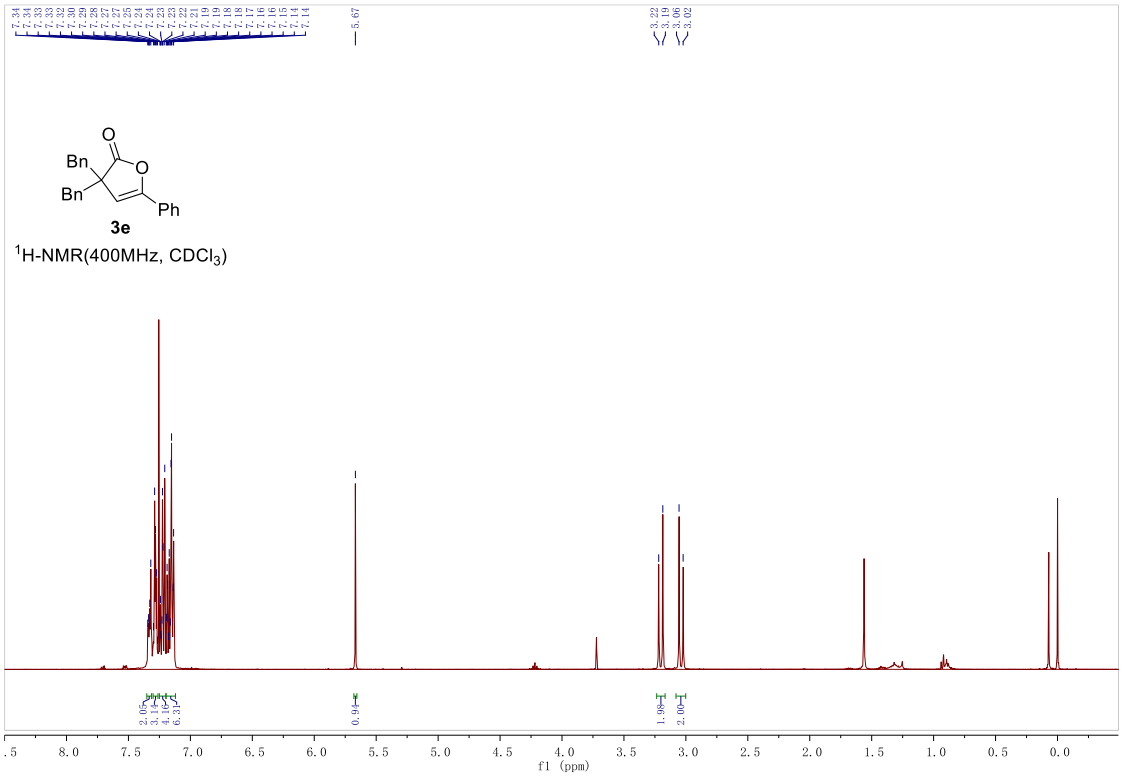
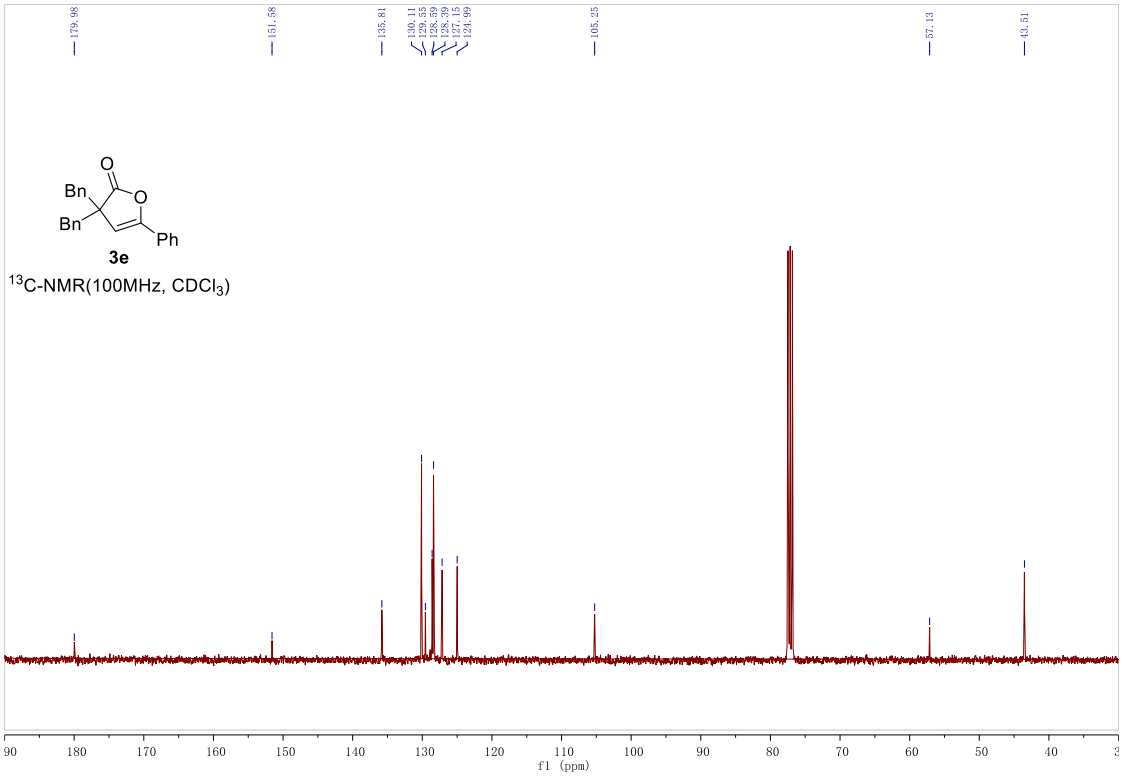
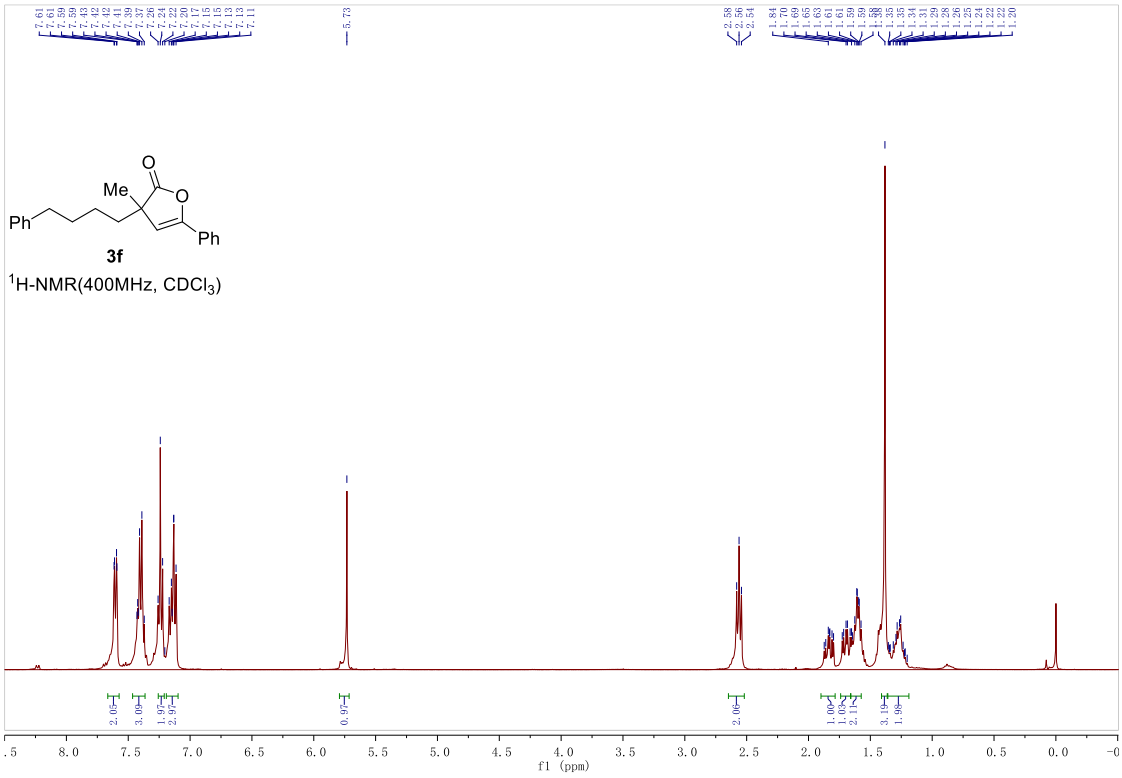
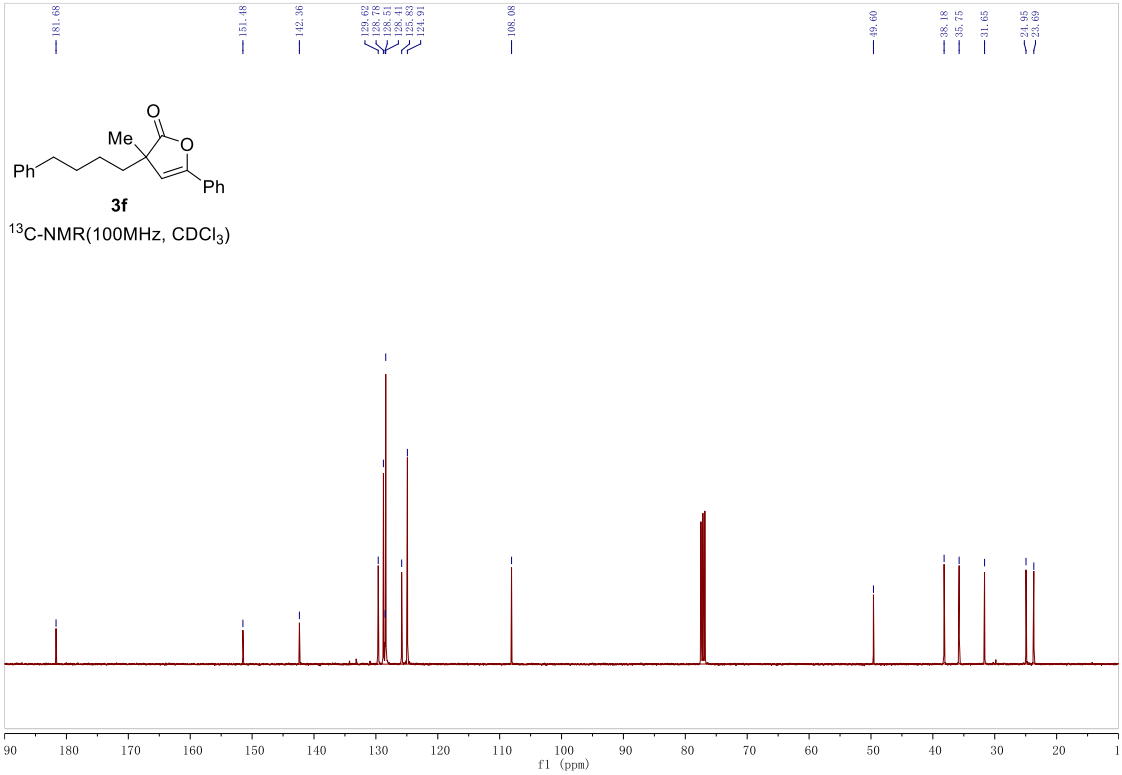
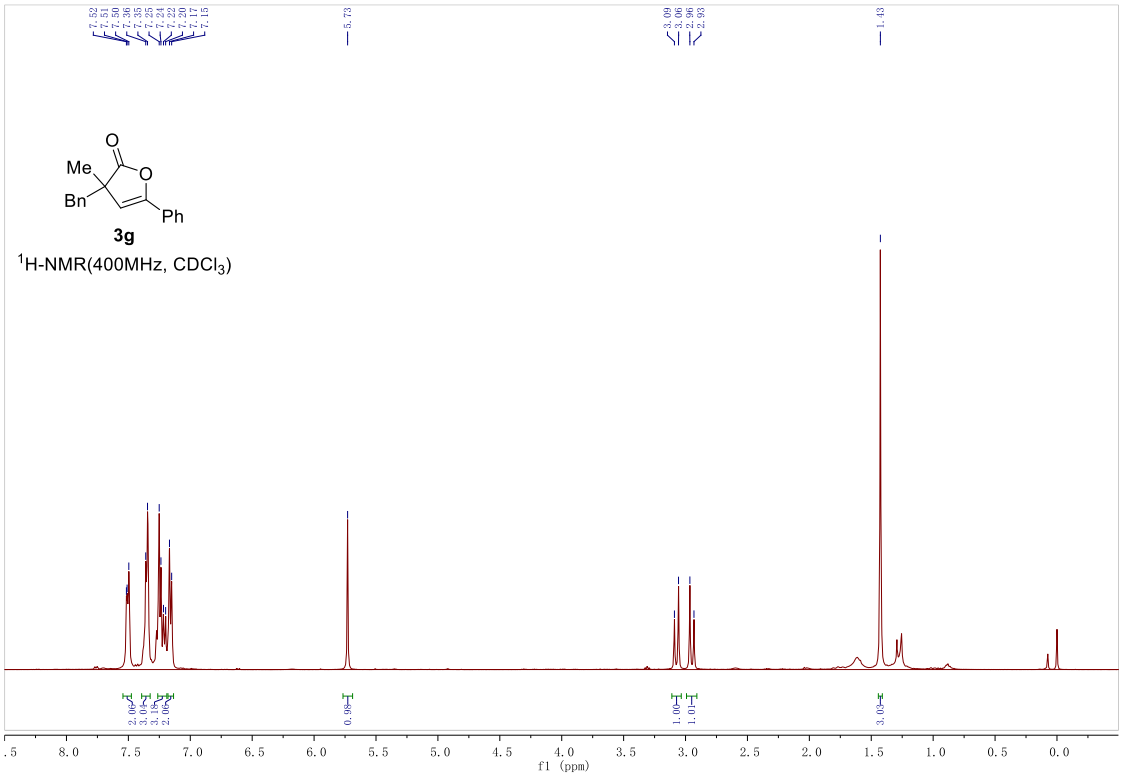
O
O
Ph
3d
13C-NMR (100MHz, CDCl3)
f1 (ppm)


Bn
Bn
O
O
Ph
3e
1H-NMR(400MHz, CDCl3)
f1 (ppm)


Bn
Bn
O
O
Ph
3e
13C-NMR(100MHz, CDCl3)
f1 (ppm)


Me
O
O
Ph
Ph
3f
1H-NMR(400MHz, CDCl3)
f1 (ppm)


Me
O
O
Ph
Ph
3f
13C-NMR(100MHz, CDCl3)
f1 (ppm)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7.22
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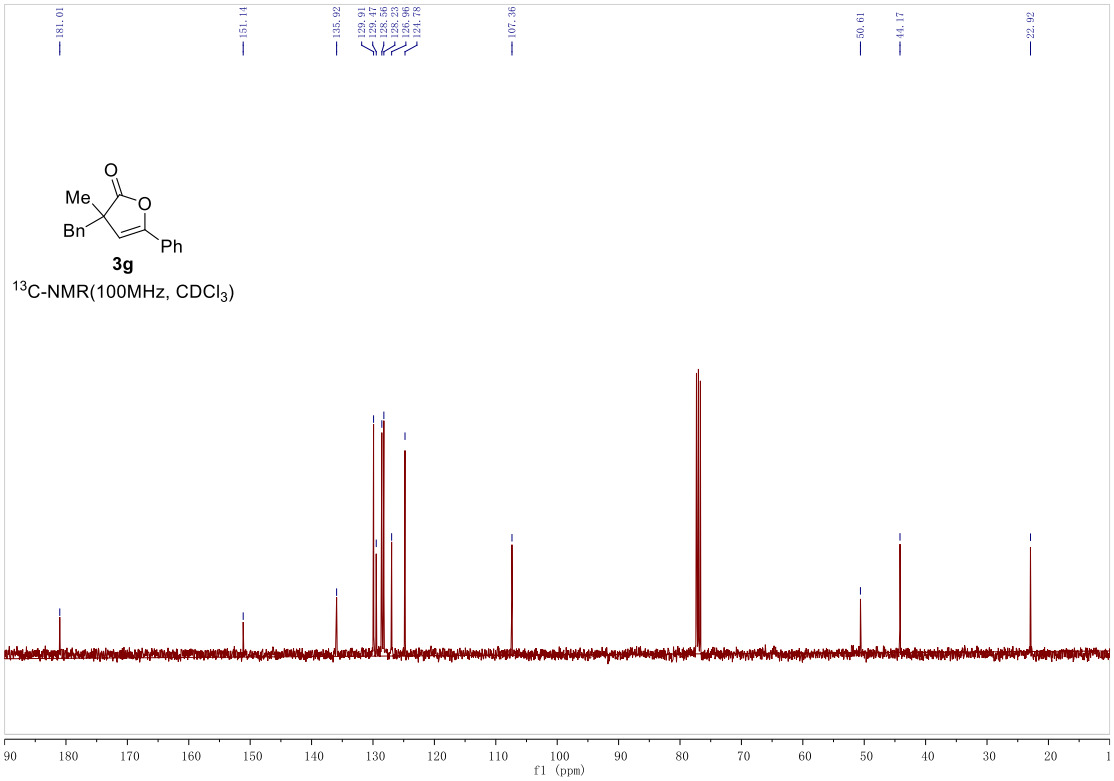
7.15
5.73
3.09
3.06
2.96
2.93
1.43
O
Me
O
Bn
Ph
3g
1H-NMR(400MHz, CDCl3)
2.00
3.04
3.10
2.06
0.98
1.00
1.01
3.03
f1 (ppm)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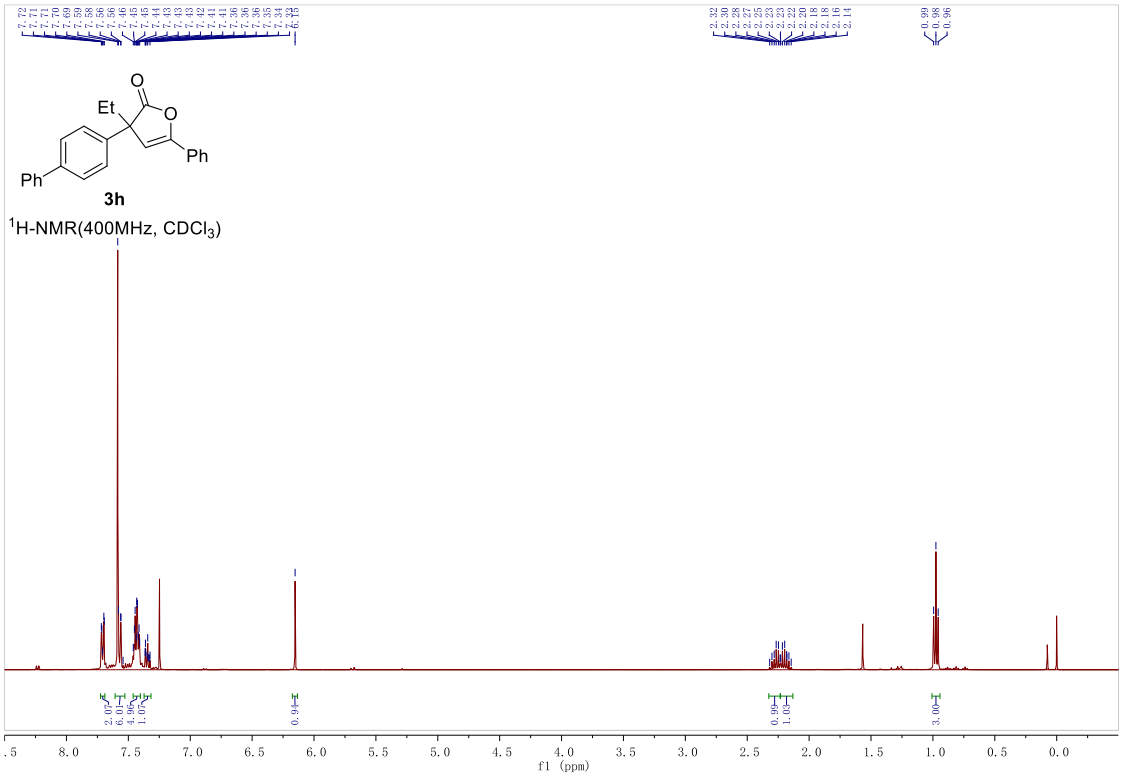
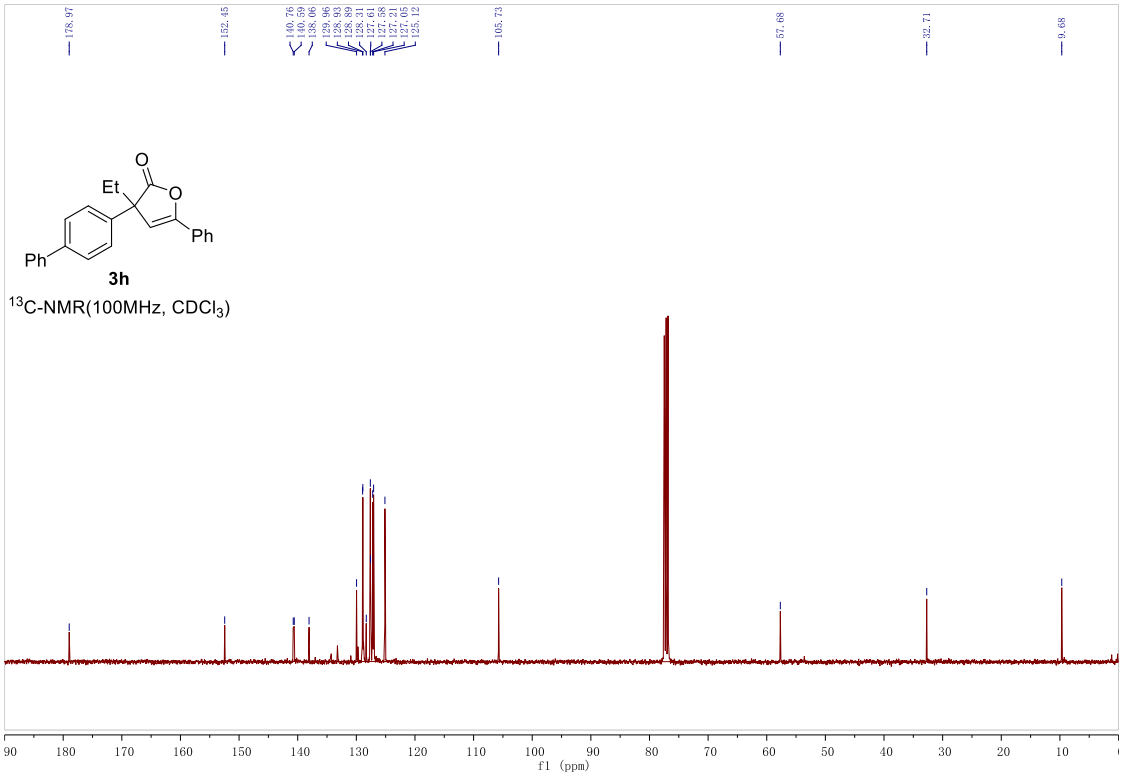
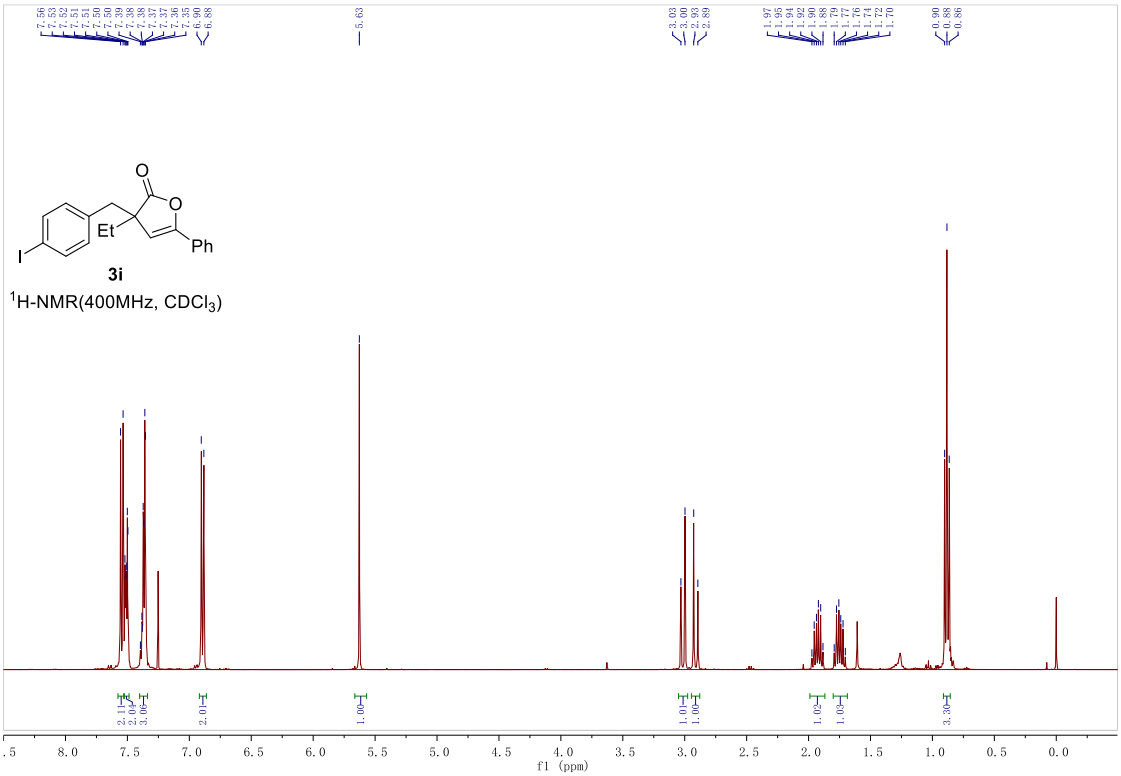
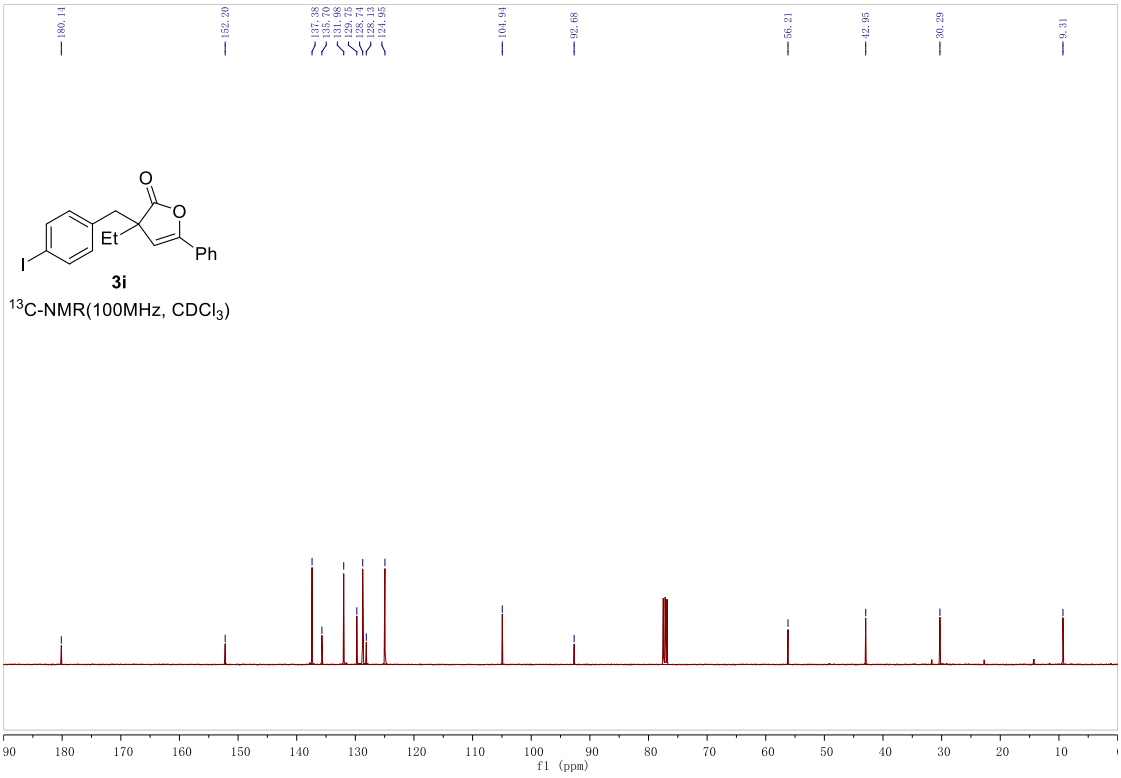
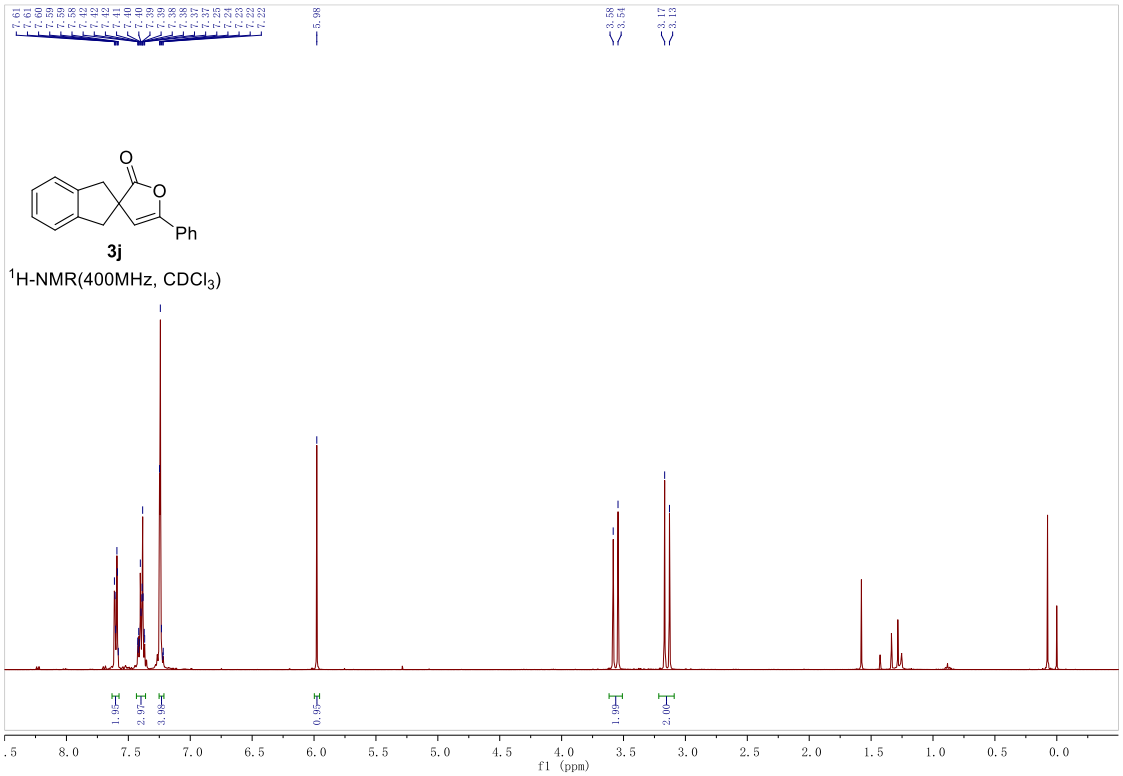
135.92
129.91
129.47
128.56
128.23
126.96
124.78
107.36
50.61
44.17
22.92
O
Me
O
Bn
Ph
3g
13C-NMR(100MHz, CDCl3)
f1 (ppm)


Et
O
O
Ph
Ph
3h
1H-NMR(400MHz, CDCl3)
f1 (ppm)


Et
O
O
Ph
Ph
3h
13C-NMR(100MHz, CDCl3)
f1 (ppm)


O
O
Et
Ph
I
3i
^{1}H-NMR(400MHz, CDCl$_3$)
f1 (ppm)


O
O
Et
Ph
I
3i
^{13}C-NMR(100MHz, CDCl$_3$)
f1 (ppm)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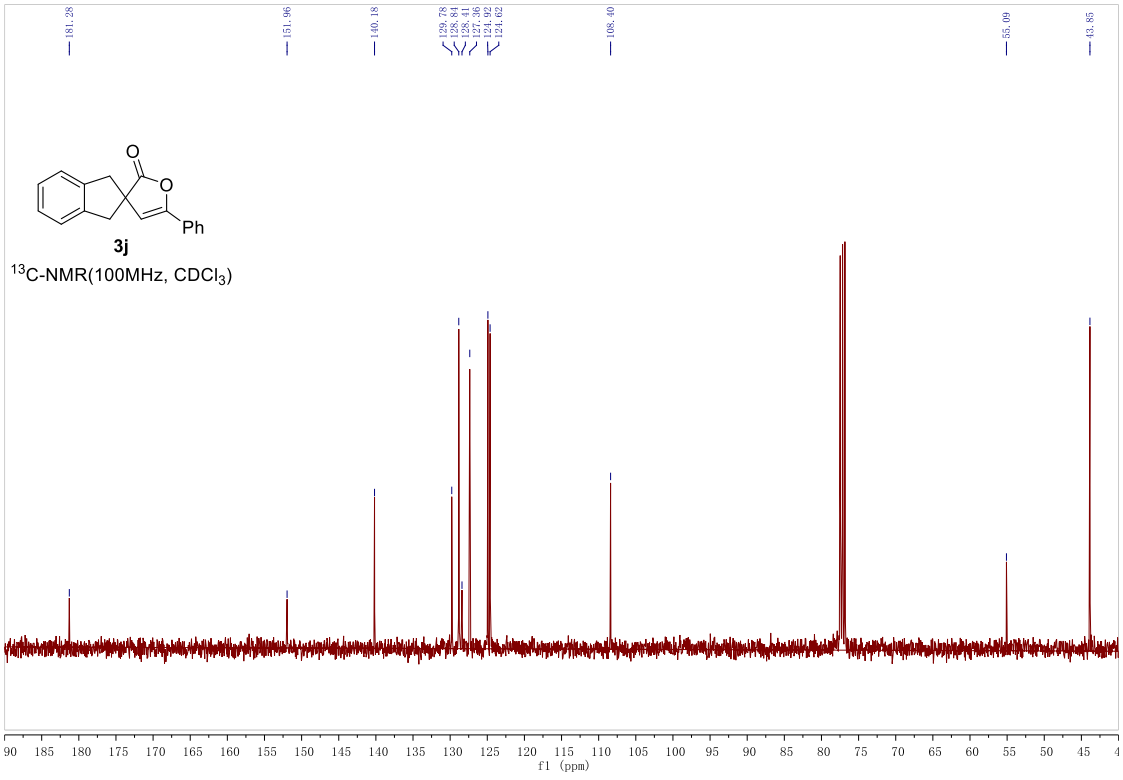
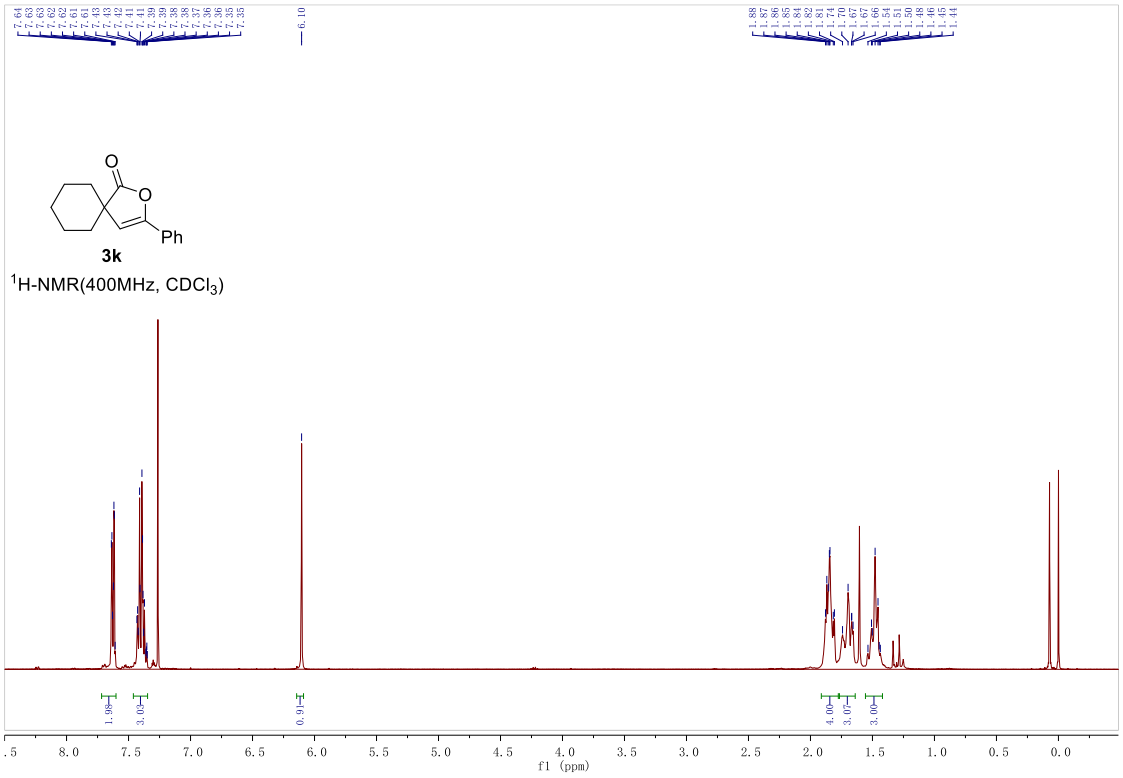
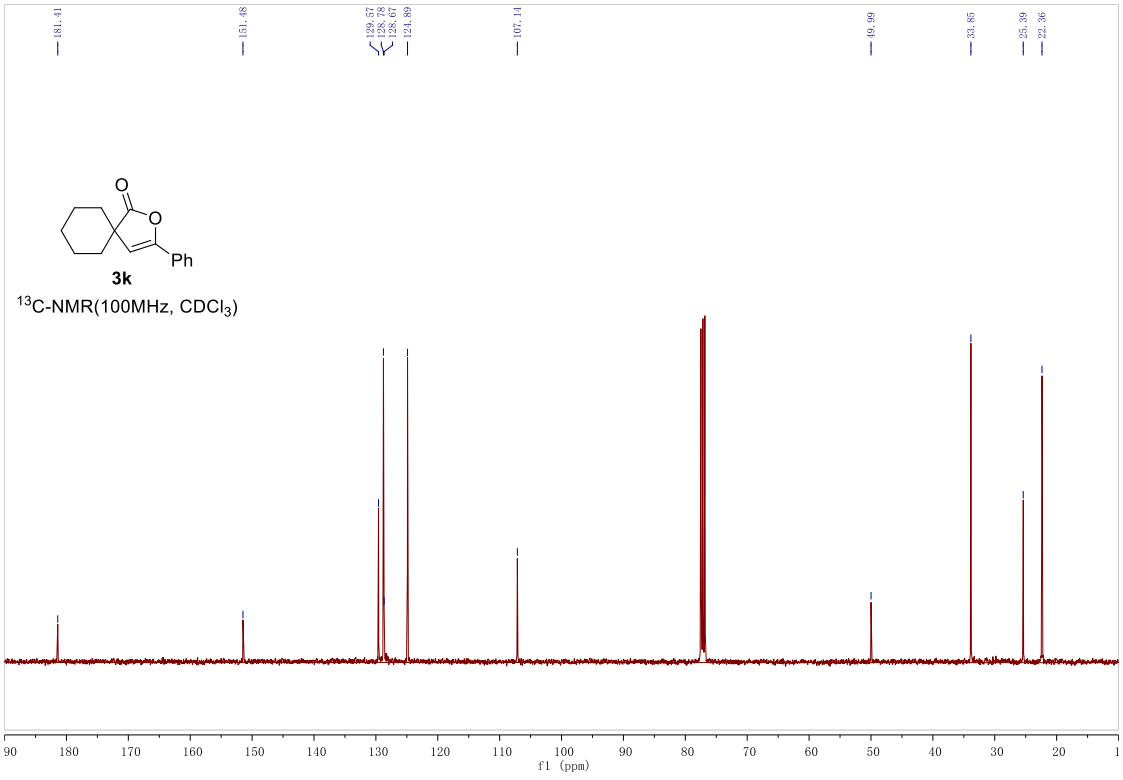
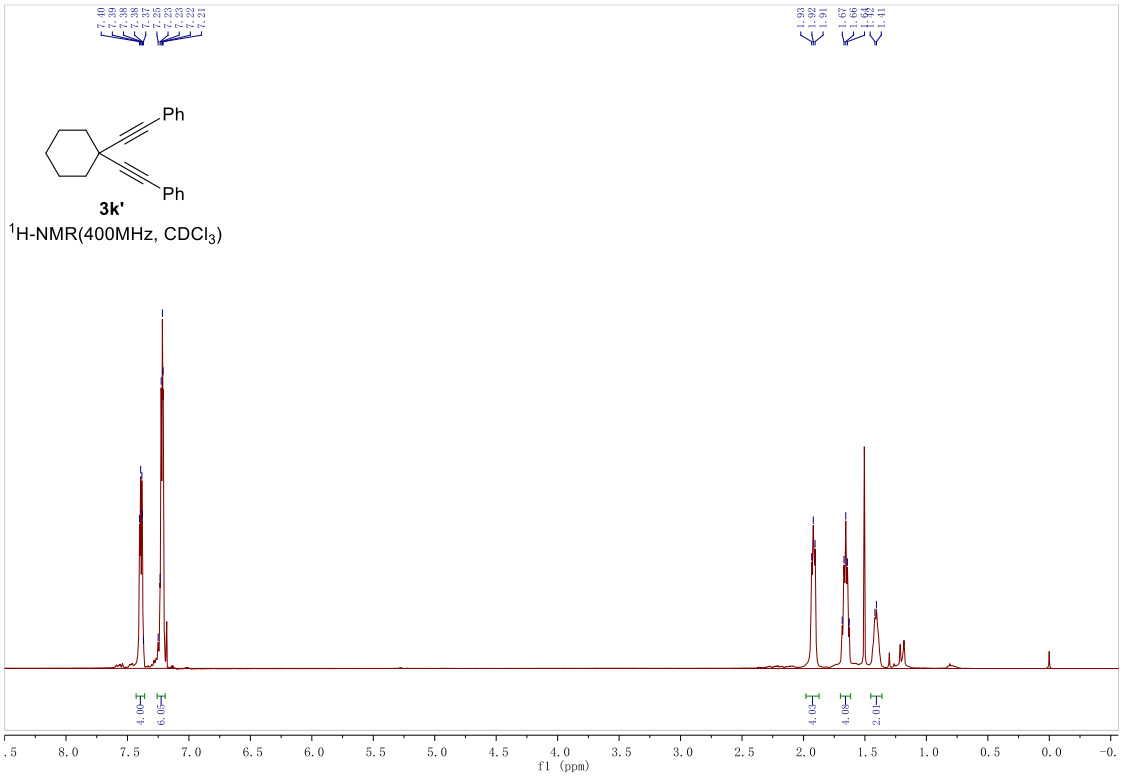
1H-NMR(400MHz, CDCl3)
f1 (ppm)


3j
13C-NMR(100MHz, CDCl3)
f1 (ppm)


O
O
Ph
3k
1H-NMR(400MHz, CDCl3)
f1 (ppm)


O
O
Ph
3k
13C-NMR(100MHz, CDCl3)
f1 (ppm)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Ph
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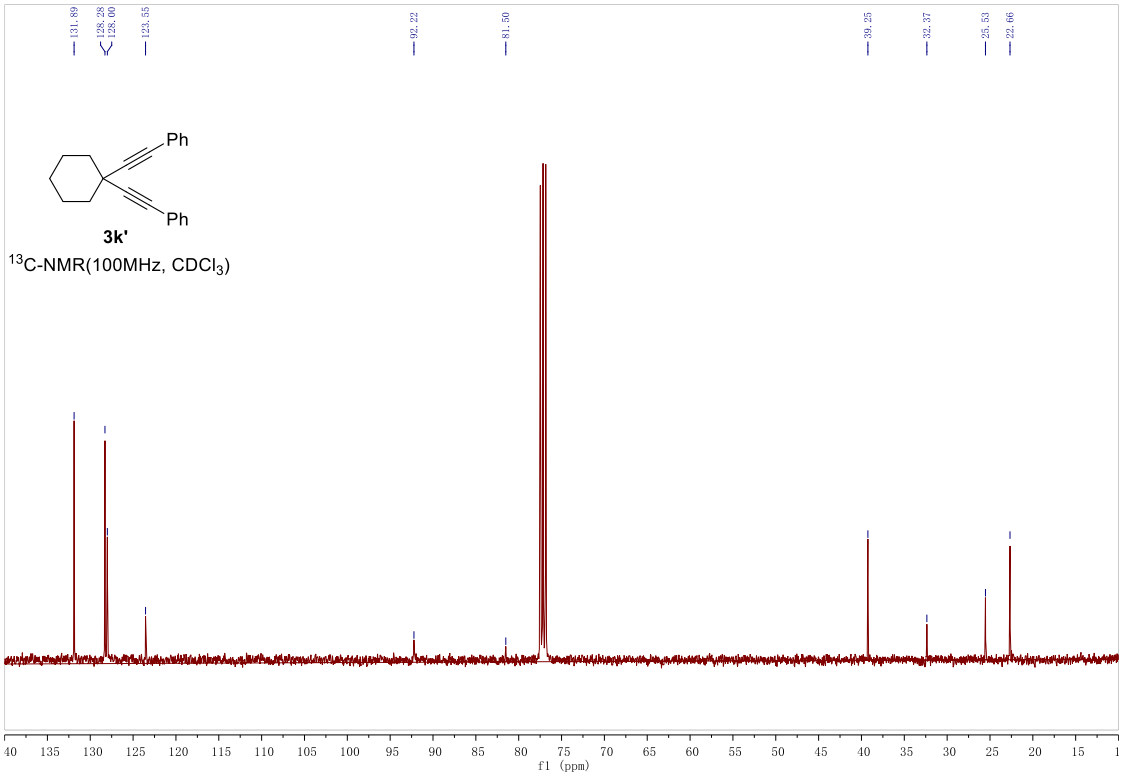
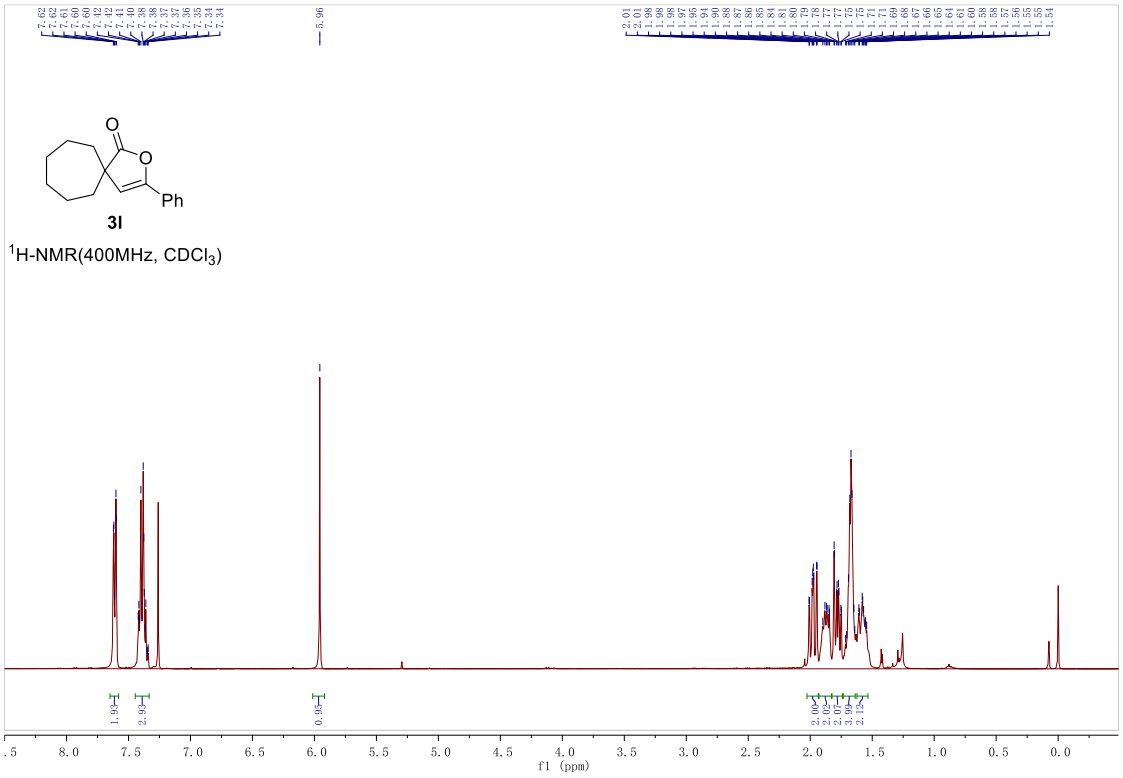
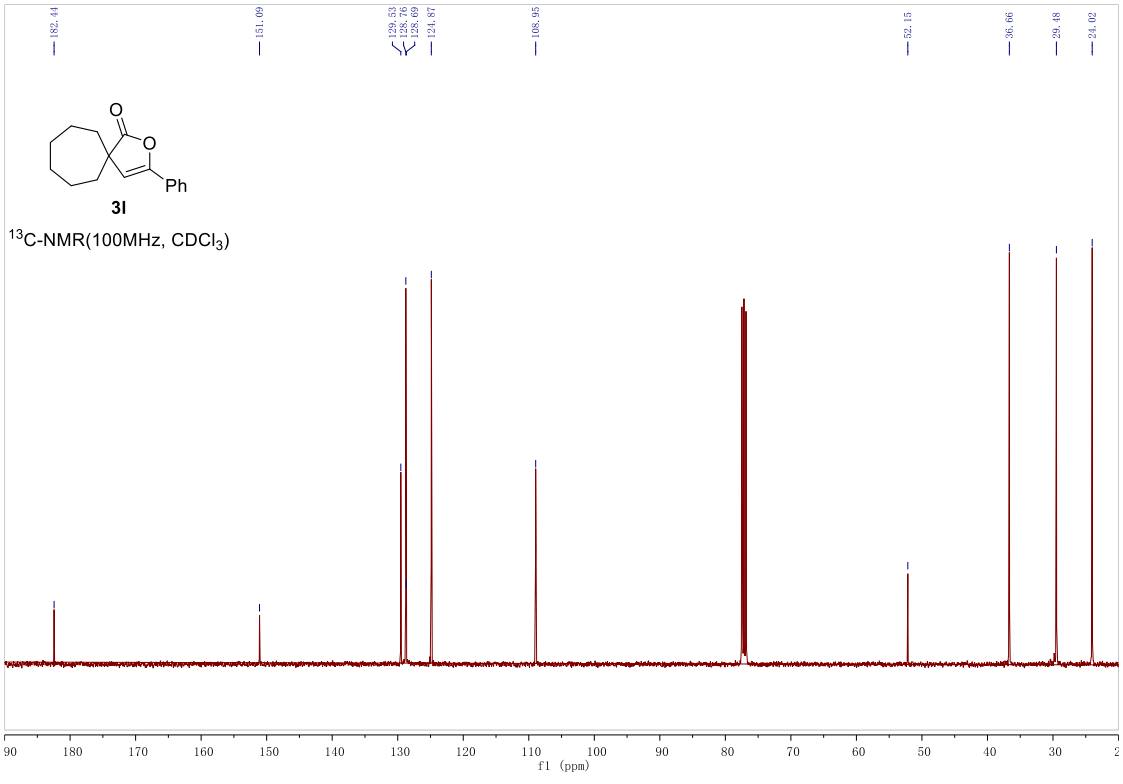
f1 (ppm)


Ph
Ph
3k'
13C-NMR(100MHz, CDCl3)
f1 (ppm)



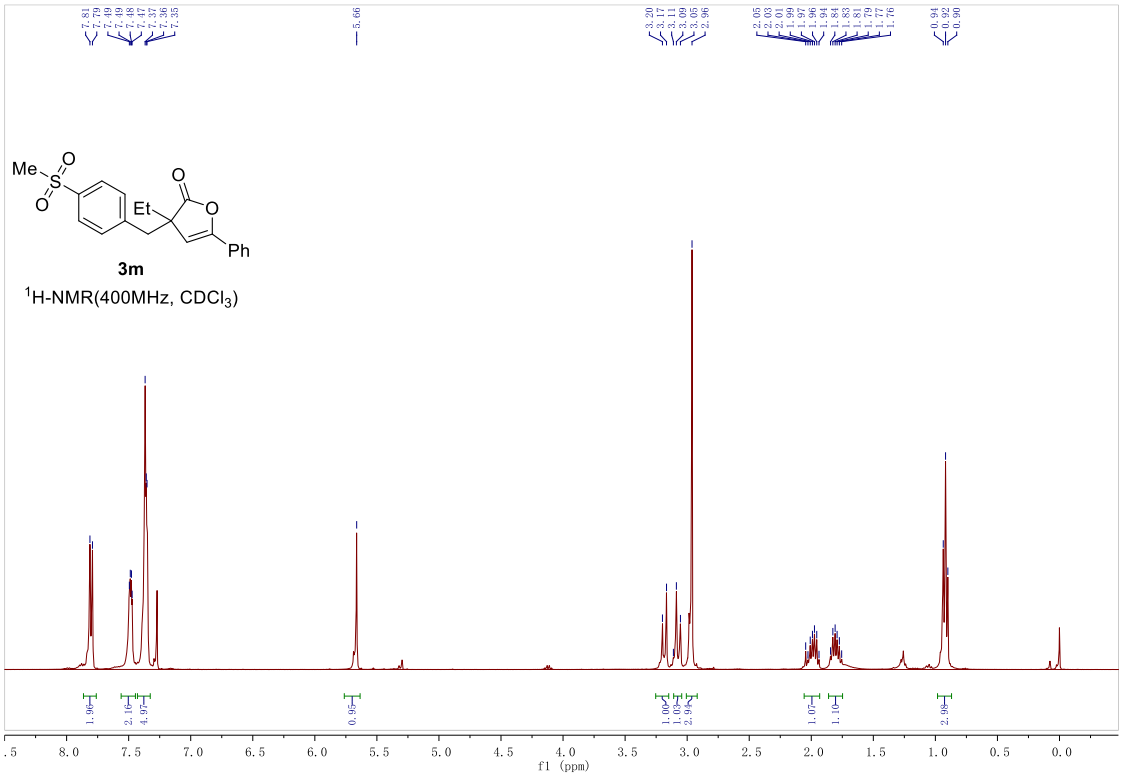
3l

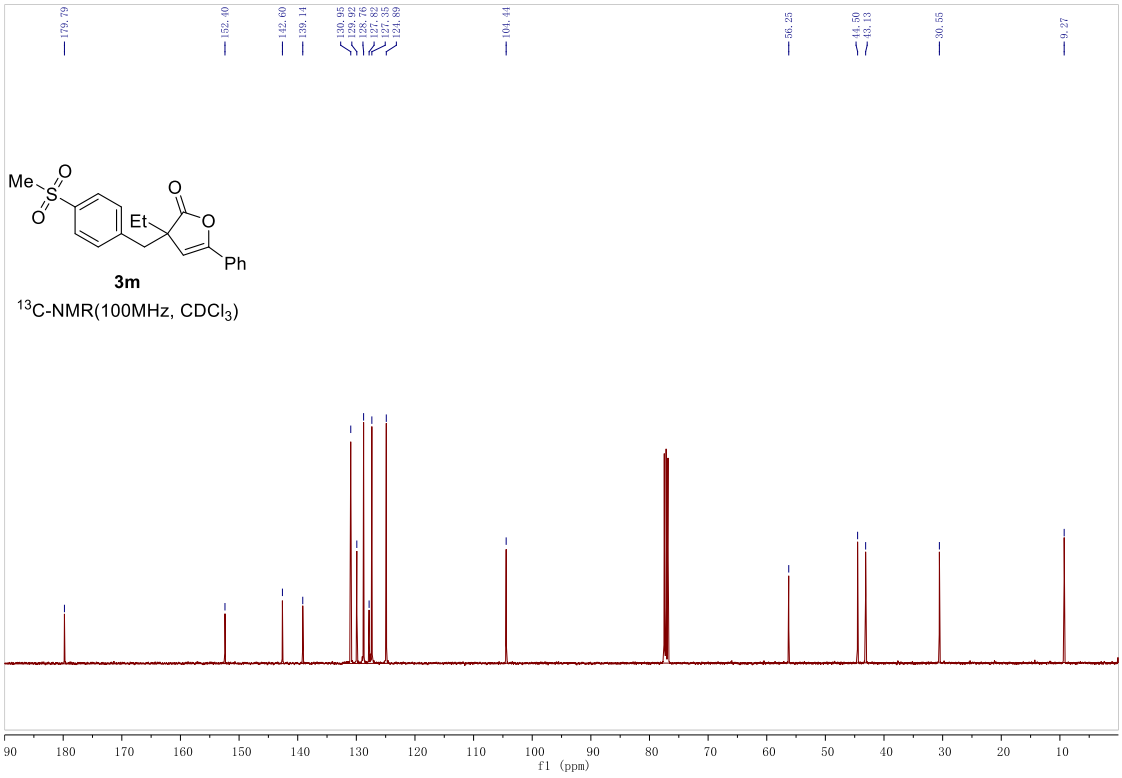
^{1}H-NMR(400MHz, $CDCl_3$)

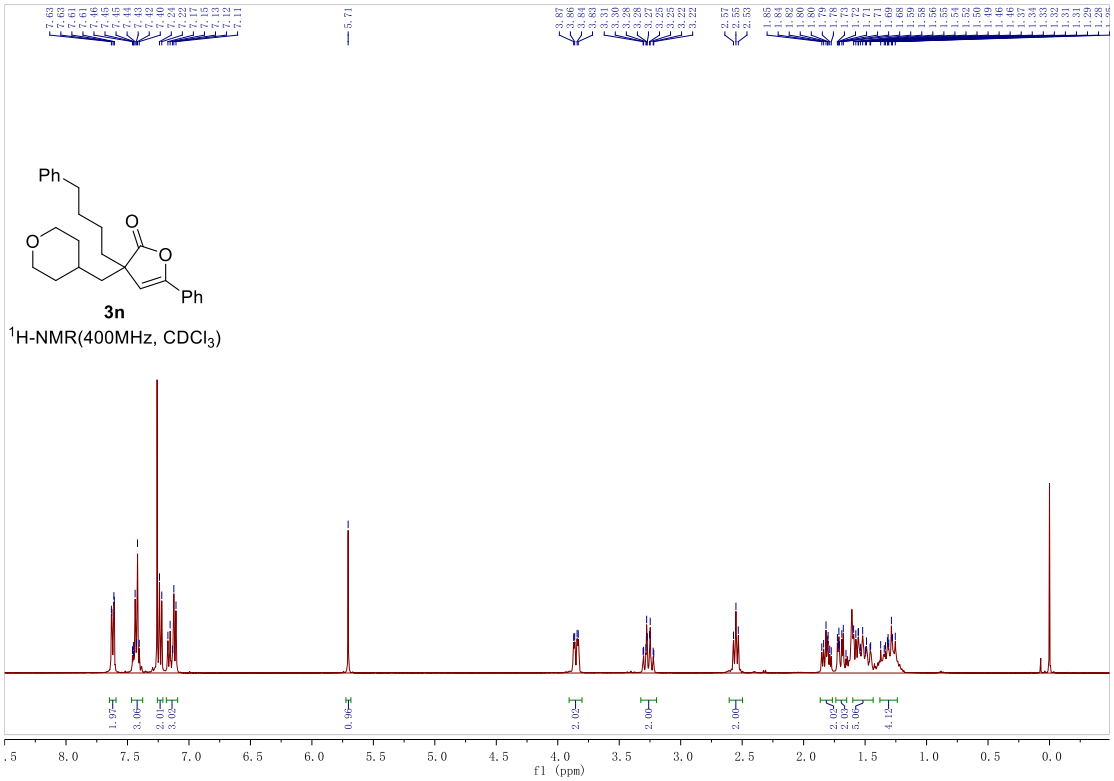


3l

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


Me
S
O
O
Et
O
O
Ph
3m
1H-NMR(400MHz, CDCl3)
f1 (ppm)


Me
S
O
O
Et
O
O
Ph
3m
13C-NMR(100MHz, CDCl3)
f1 (ppm)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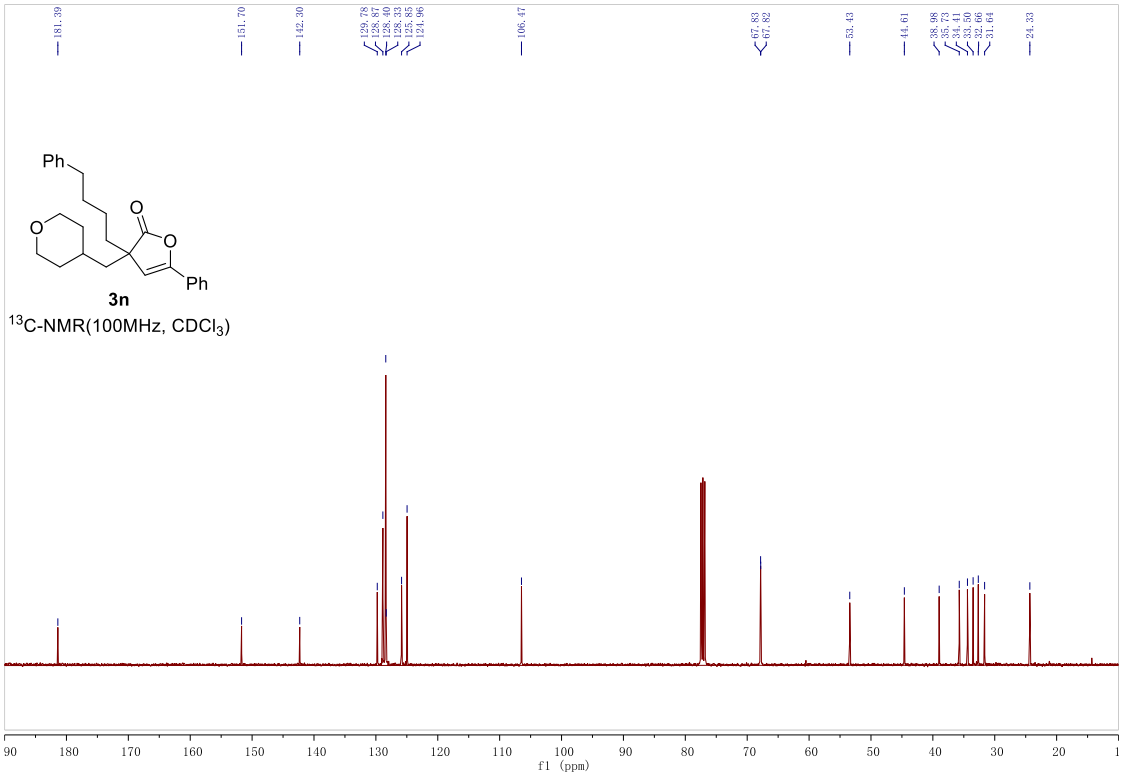
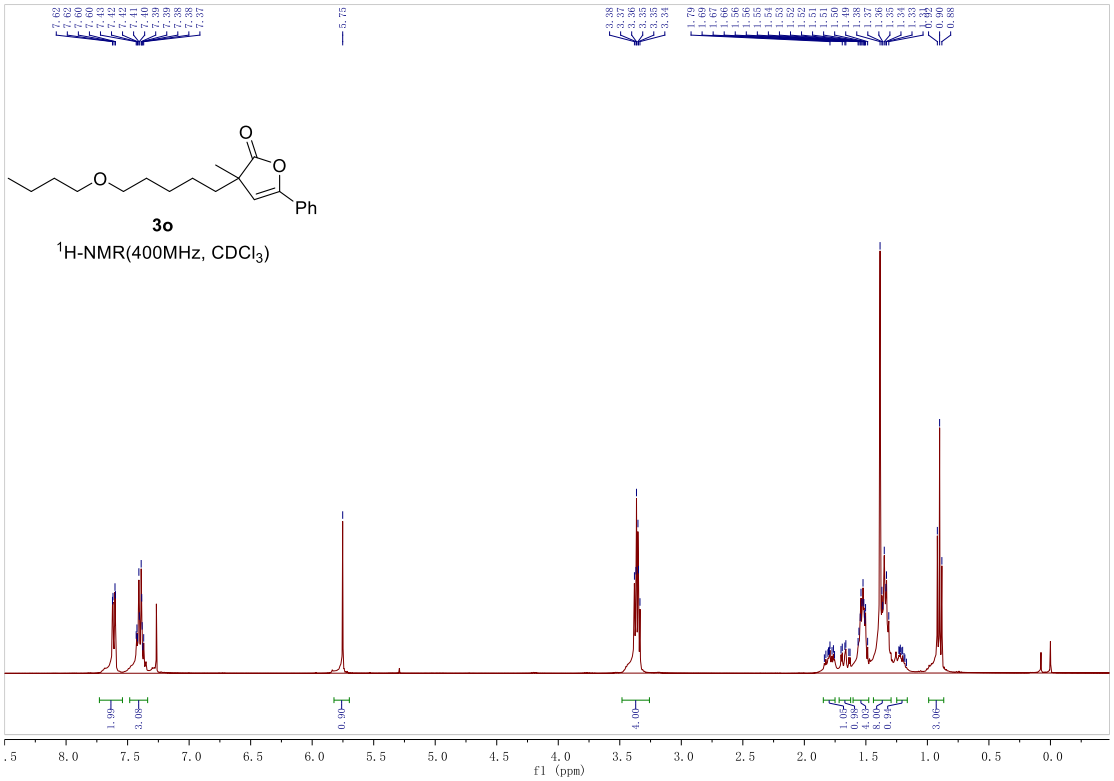
O
O
O
Ph
3n
1H-NMR(400MHz, CDCl3)
f1 (ppm)


Ph
O
O
O
Ph
3n
13C-NMR(100MHz, CDCl3)
f1 (ppm)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3.34
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1.54
1.53
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1.52
1.51
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1.50
1.49
1.38
1.37
1.36
1.35
1.34
1.33
0.92
0.90
0.88
O
O
O
Ph
3o
1H-NMR(400MHz, CDCl3)
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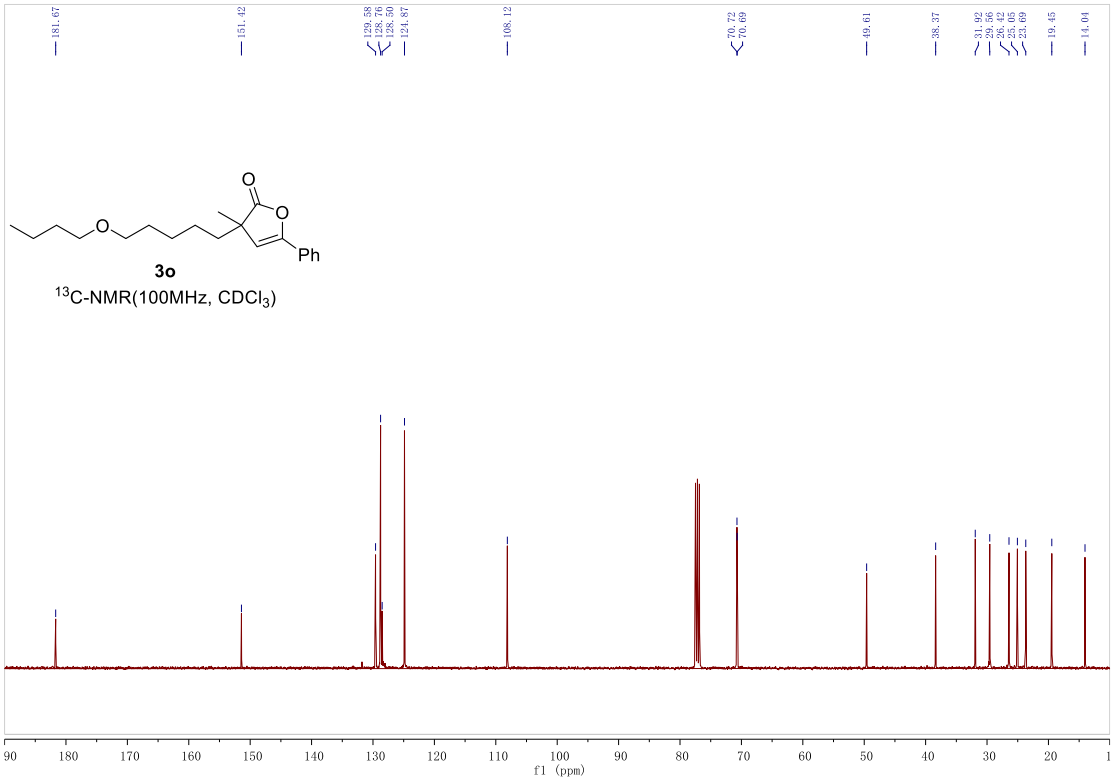
0.90
4.00
1.07
0.94
4.07
8.06
0.95
3.00
f1 (ppm)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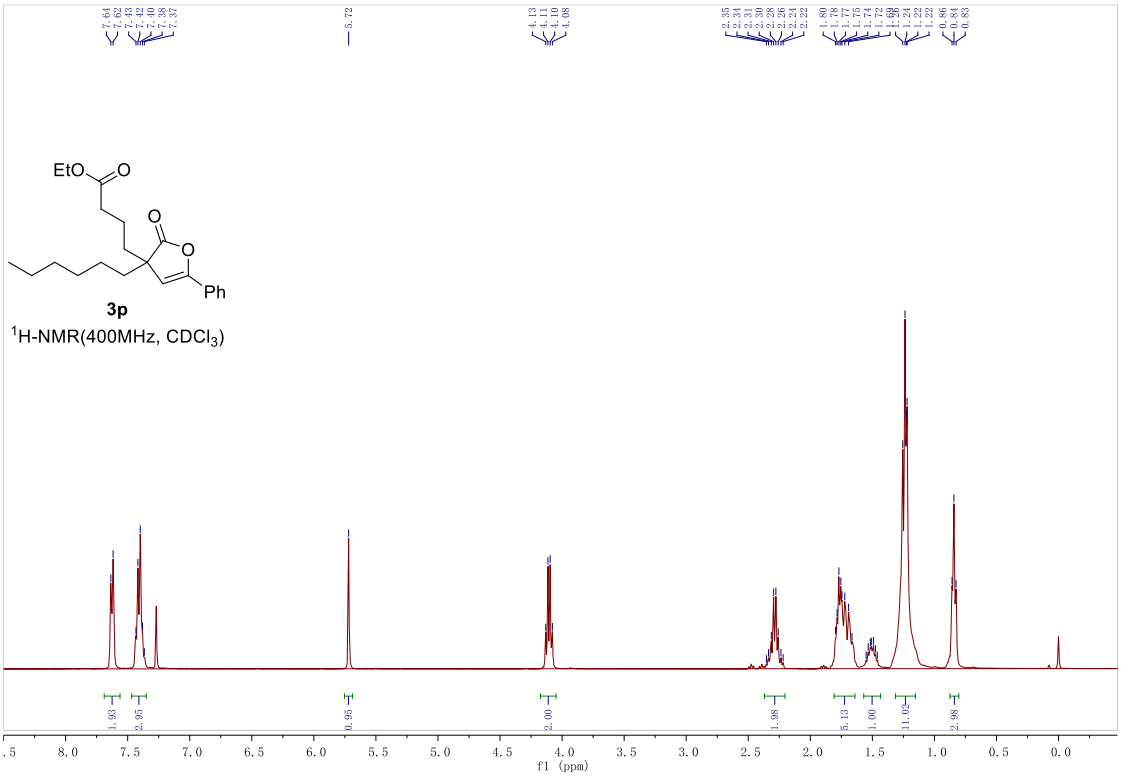
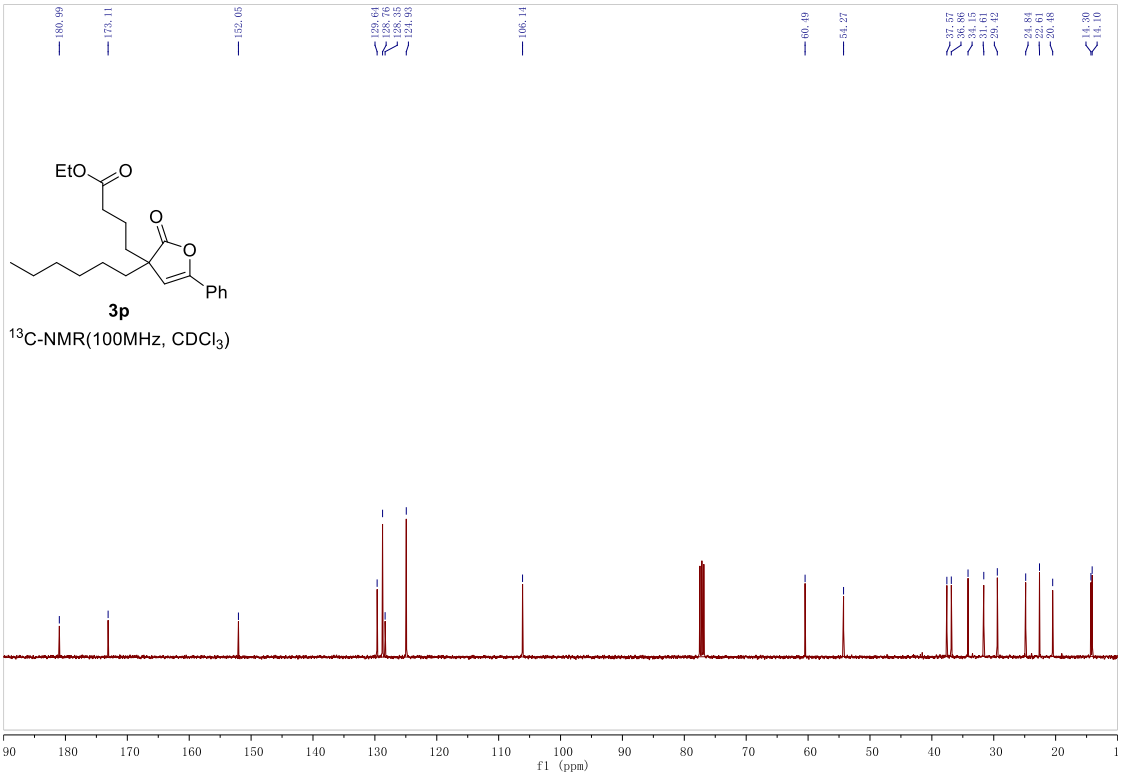
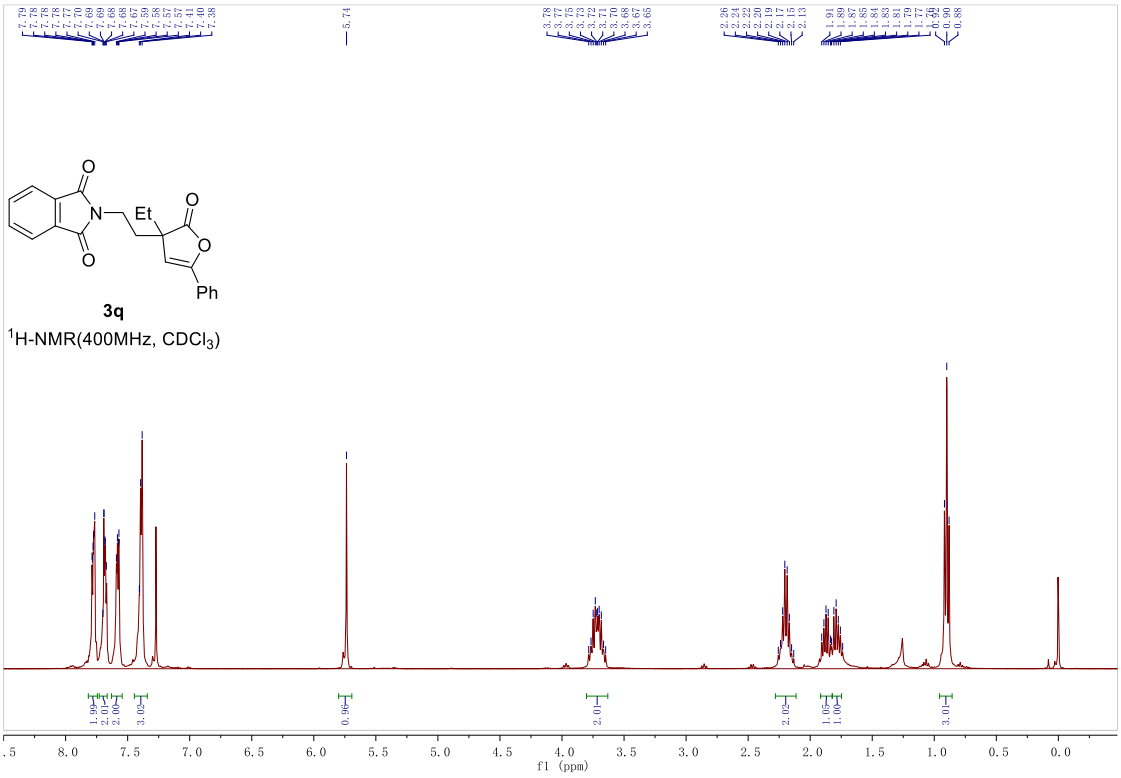
49.61
38.37
31.92
29.56
26.42
25.65
23.69
19.45
14.04
O
O
O
Ph
3o
13C-NMR(100MHz, CDCl3)
f1 (ppm)

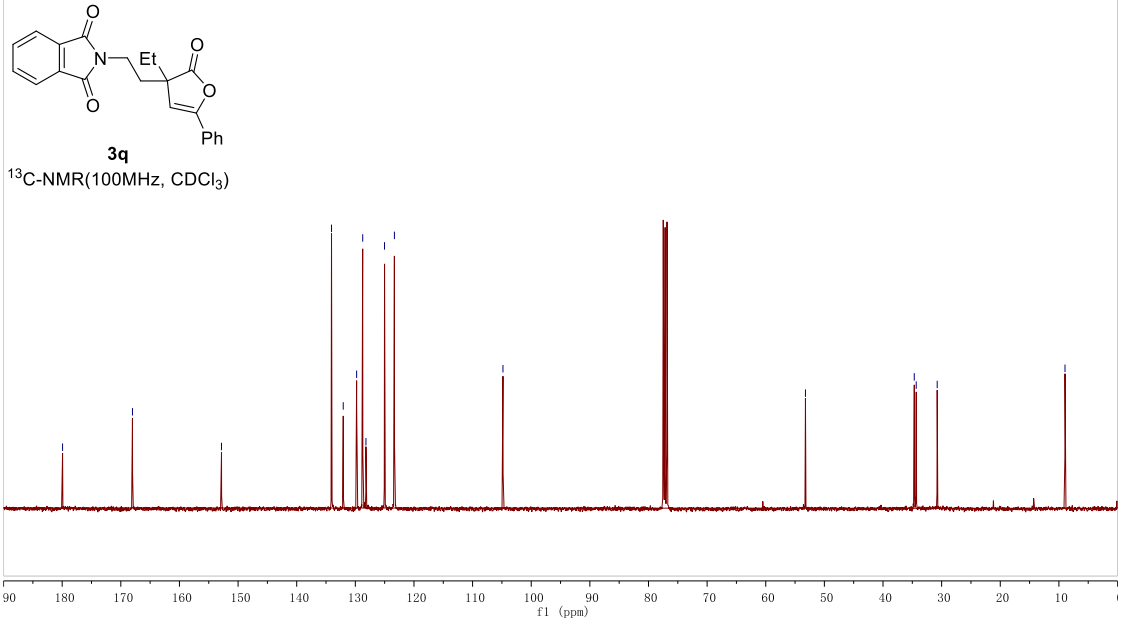

EtO
O
O
O
Ph
3p
1H-NMR(400MHz, CDCl3)
f1 (ppm)


EtO
O
O
O
Ph
3p
13C-NMR(100MHz, CDCl3)
f1 (ppm)



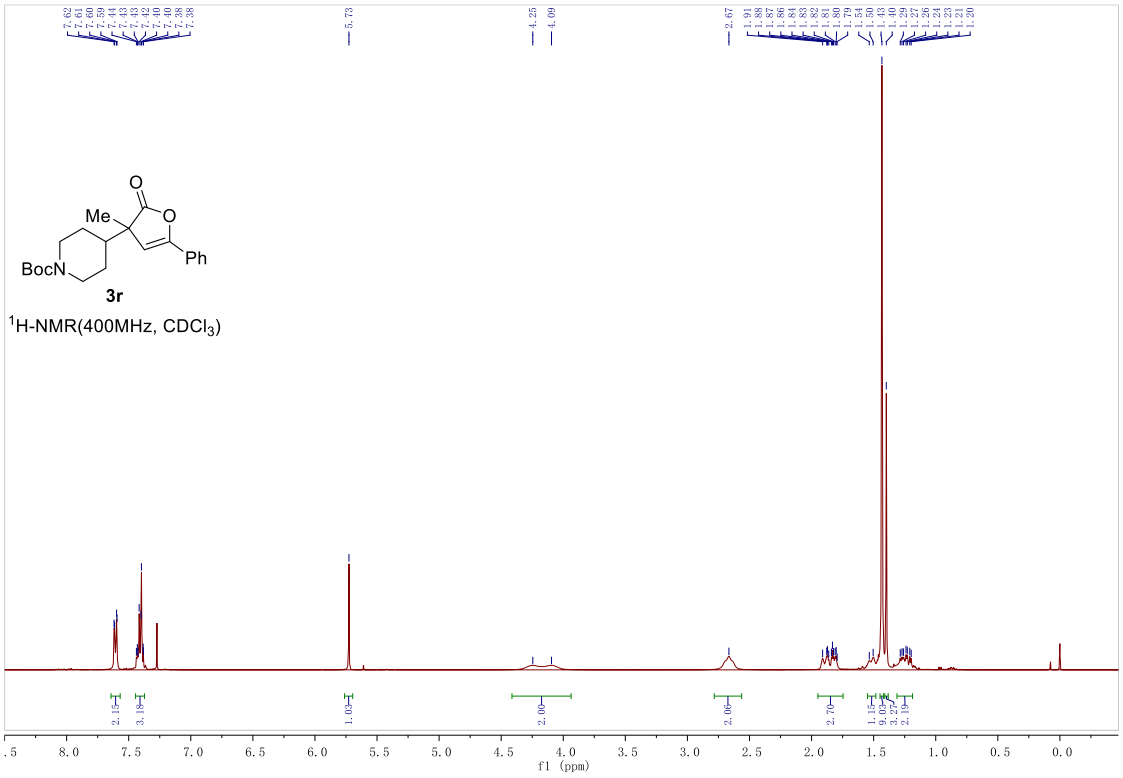
3q

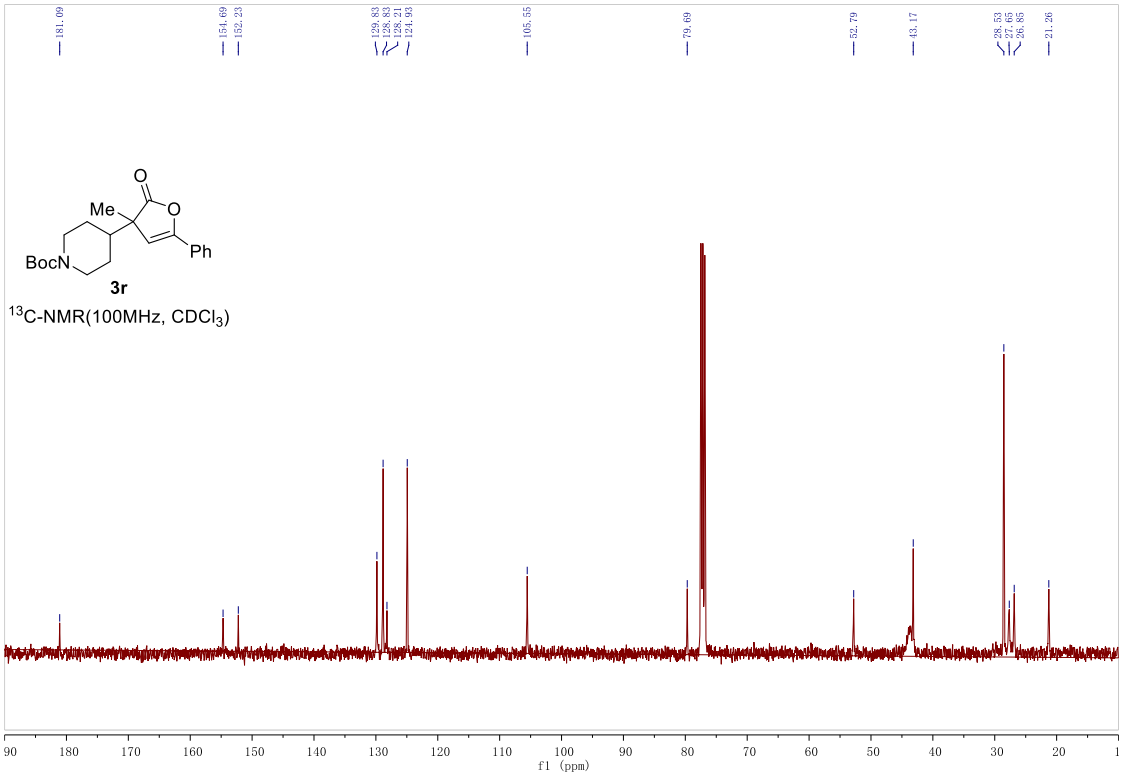
^{1}H-NMR(400MHz, $CDCl_3$)

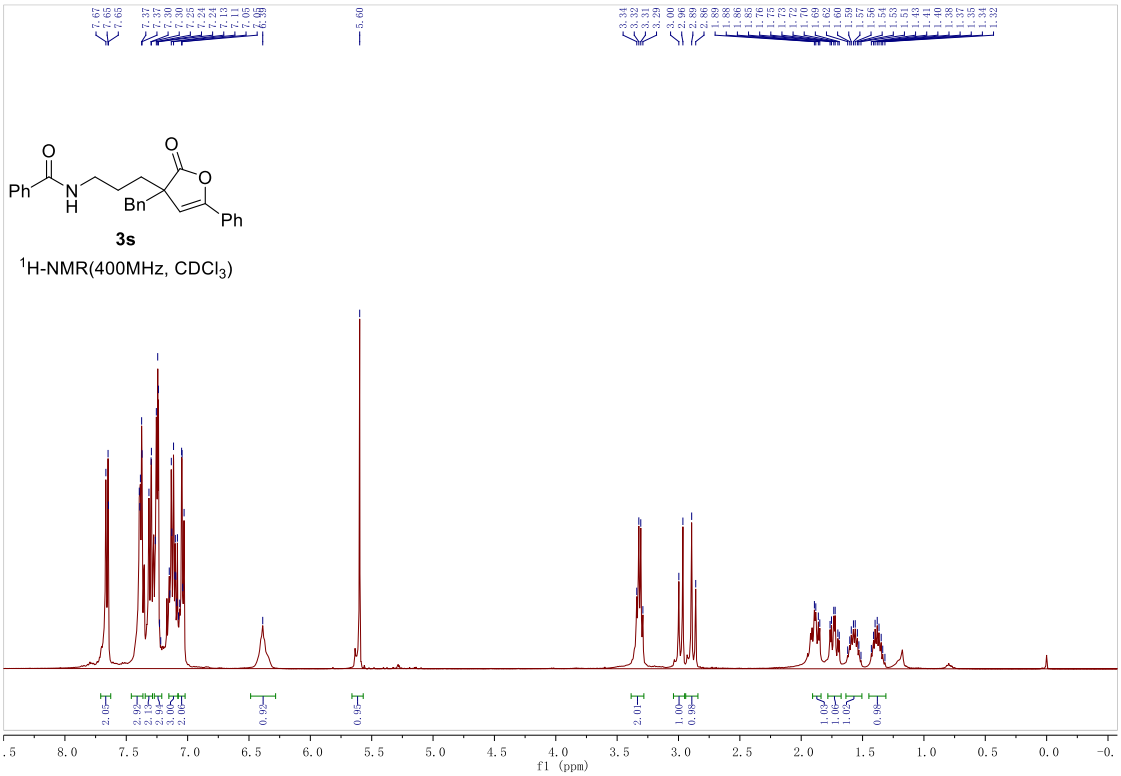


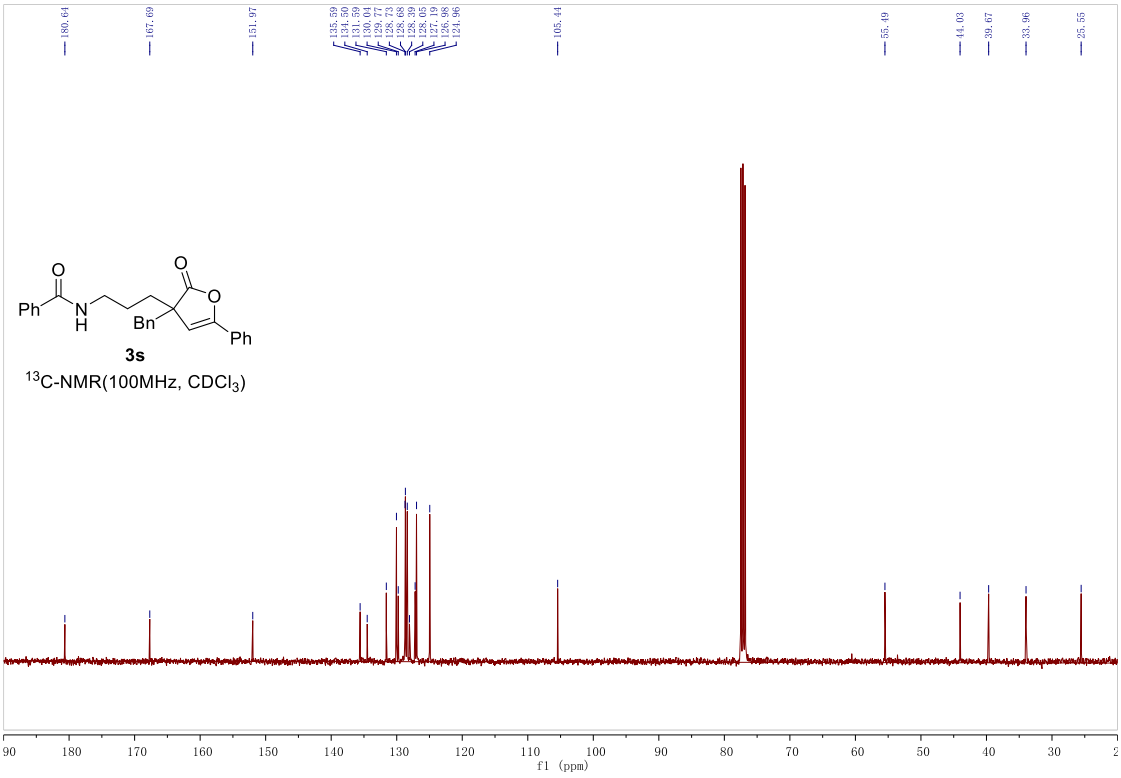
3q

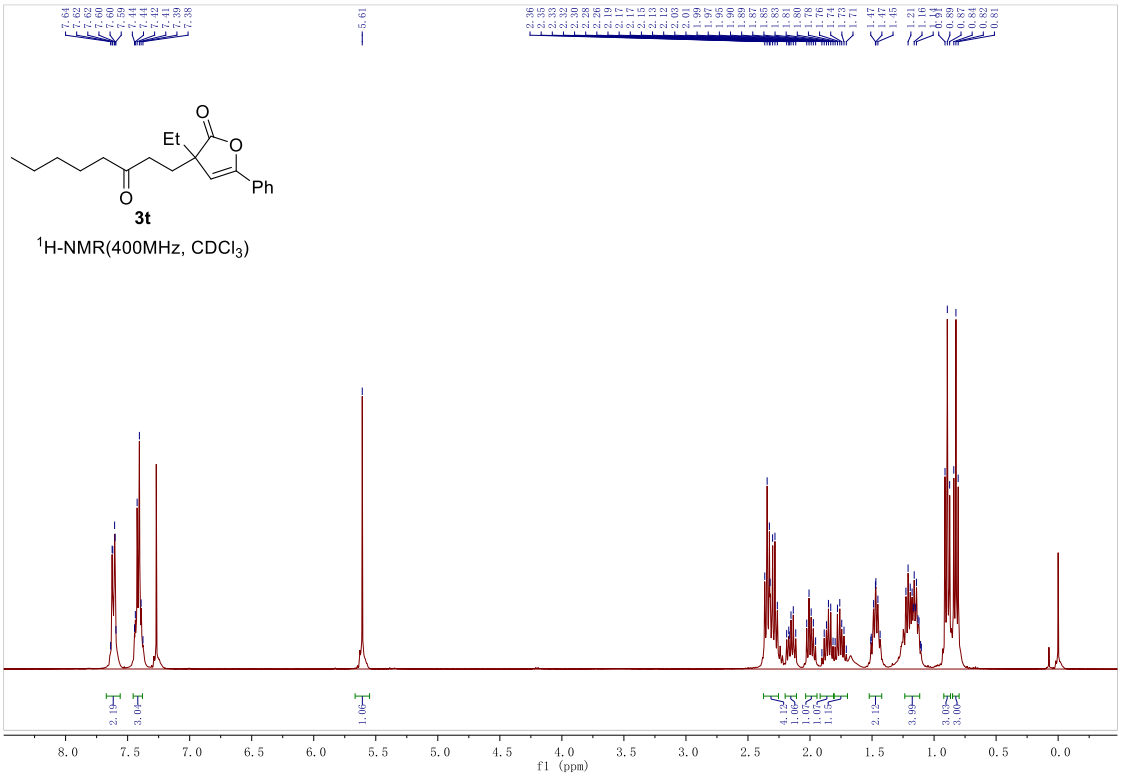
^{13}C-NMR(100MHz, $CDCl_3$)

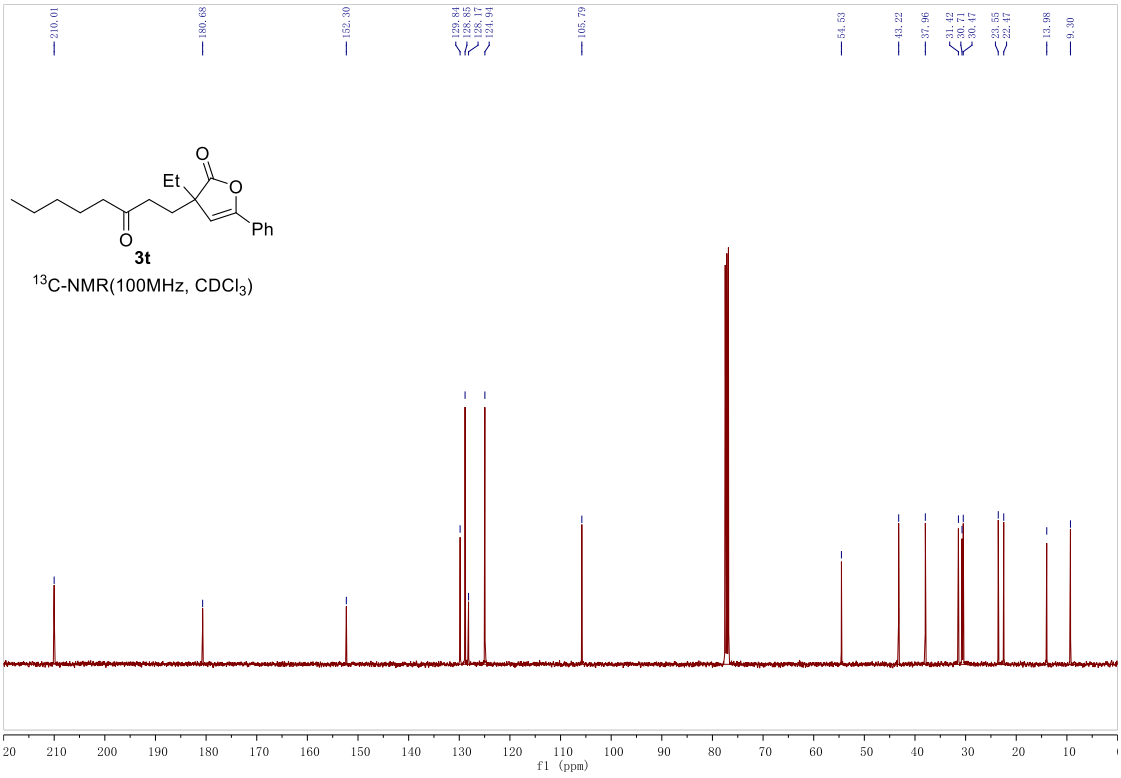

Me
O
O
Ph
BocN
3r
1H-NMR(400MHz, CDCl3)
f1 (ppm)

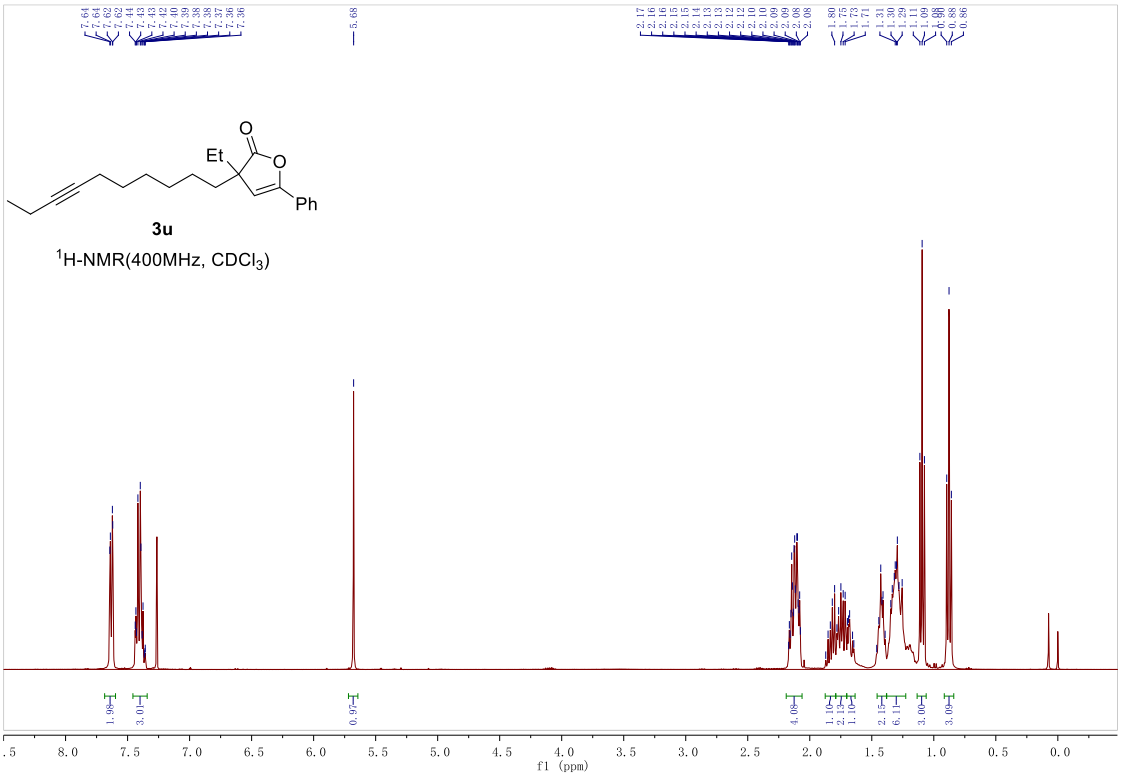

Me
O
O
Ph
BocN
3r
13C-NMR(100MHz, CDCl3)
f1 (ppm)

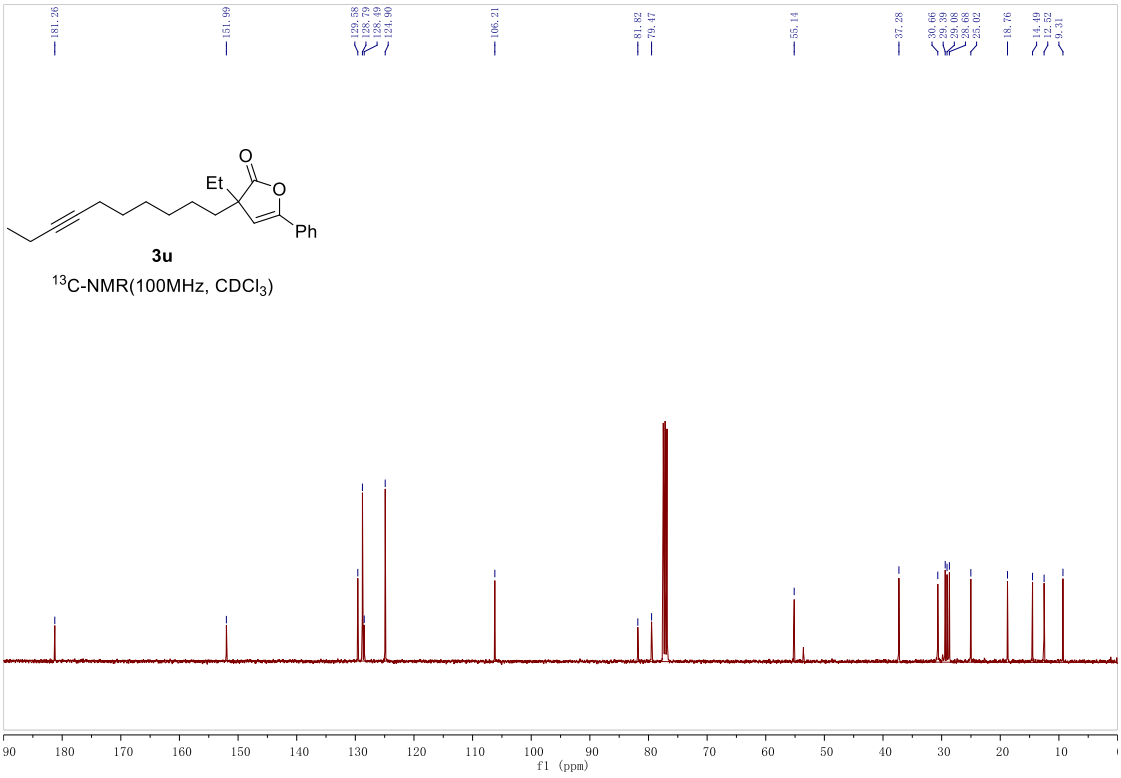

3s
1H-NMR(400MHz, CDCl3)
f1 (ppm)

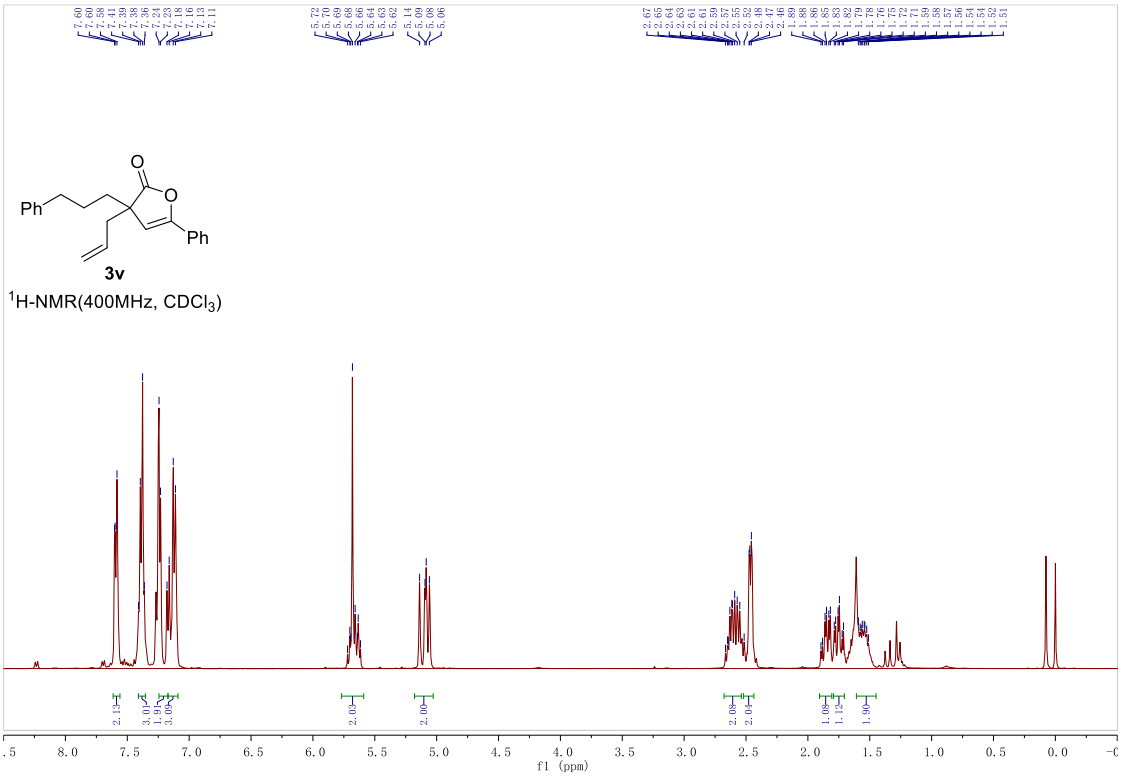

3s
13C-NMR(100MHz, CDCl3)
f1 (ppm)

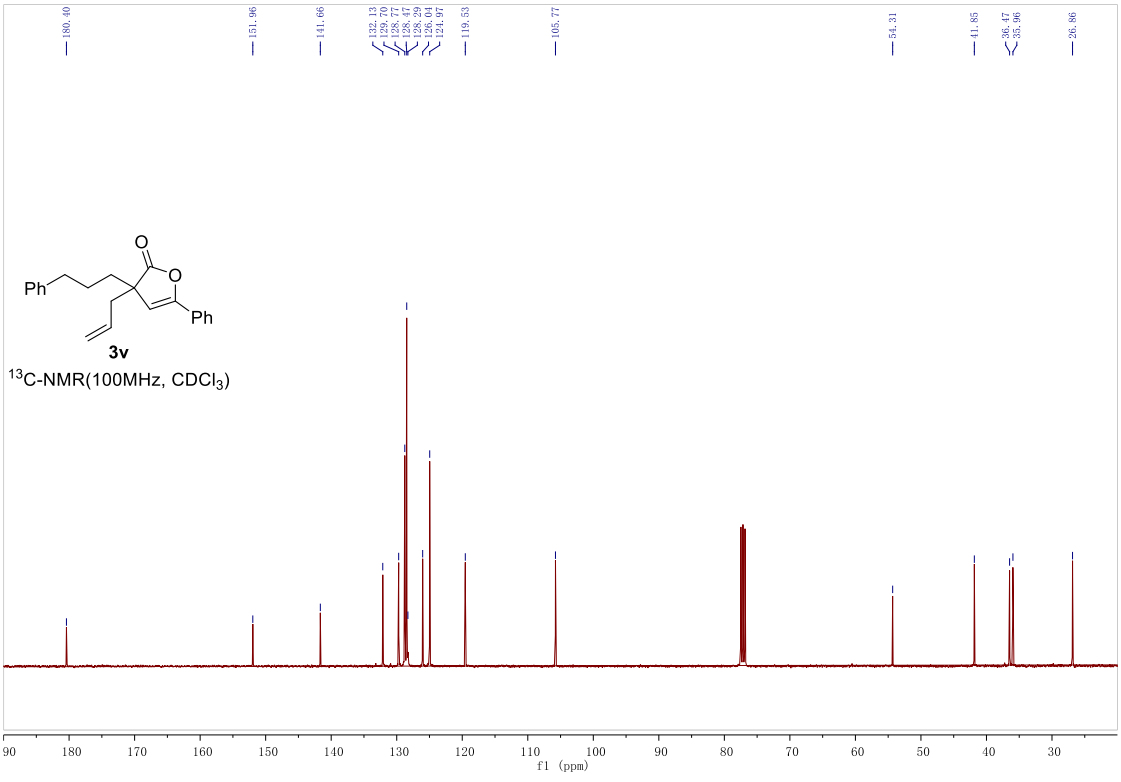

Et
O
O
O
Ph
3t
1H-NMR(400MHz, CDCl3)
f1 (ppm)

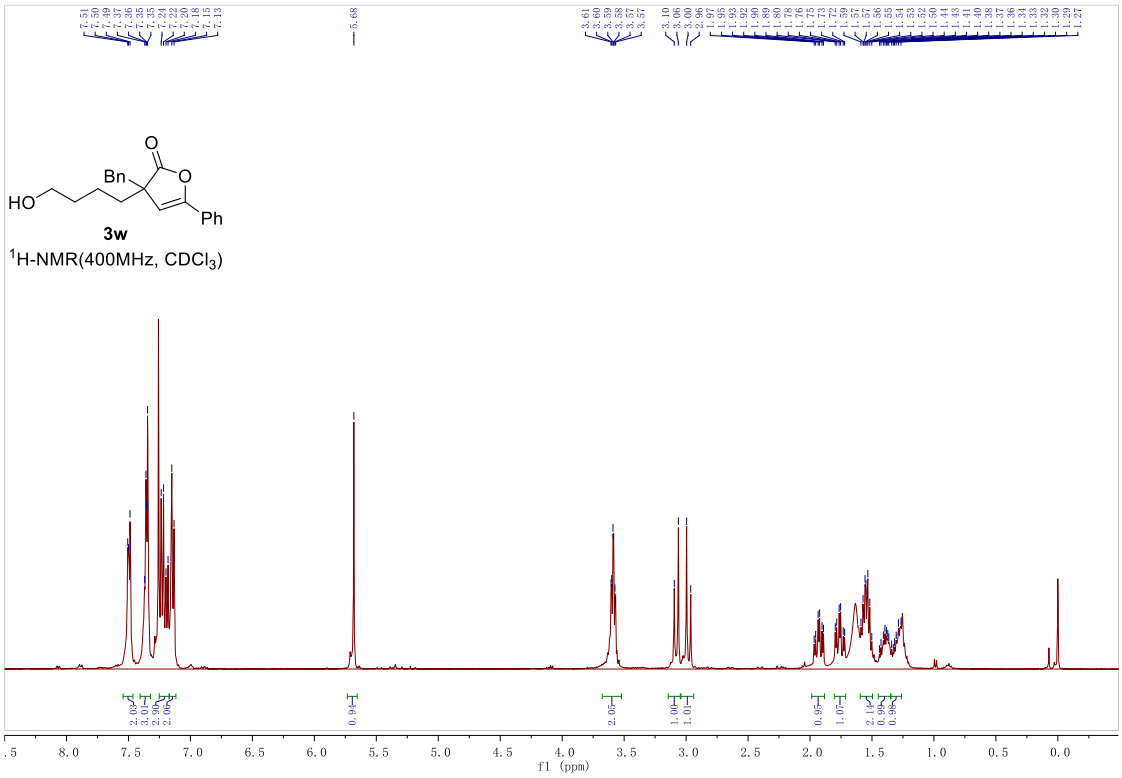

Et
O
O
O
Ph
3t
13C-NMR(100MHz, CDCl3)
f1 (ppm)

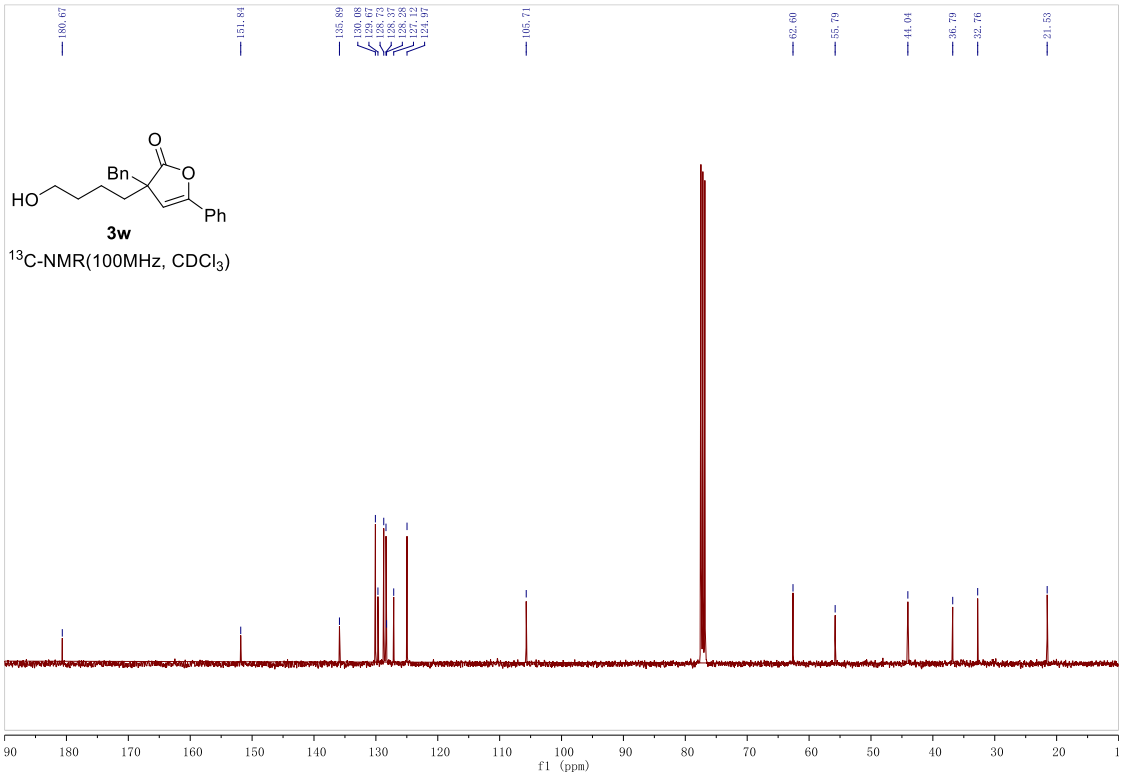

Et
O
O
Ph
3u
1H-NMR(400MHz, CDCl3)
f1 (ppm)

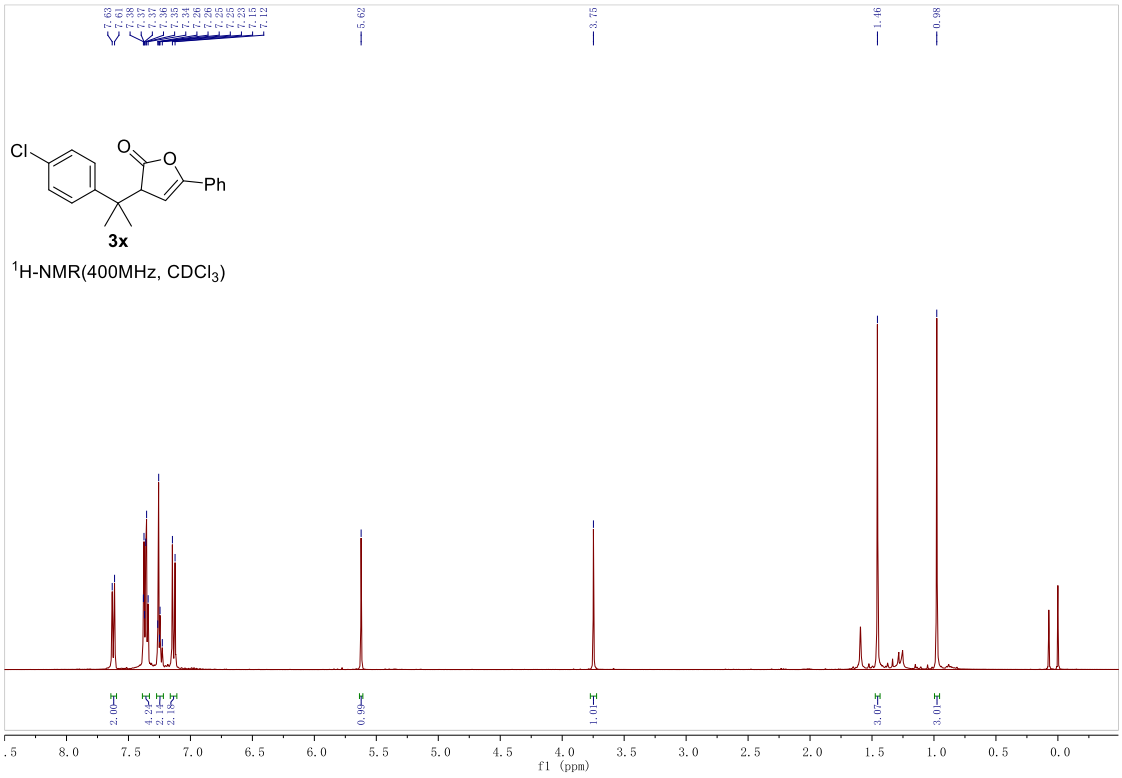

Et
O
O
Ph
3u
13C-NMR(100MHz, CDCl3)
f1 (ppm)

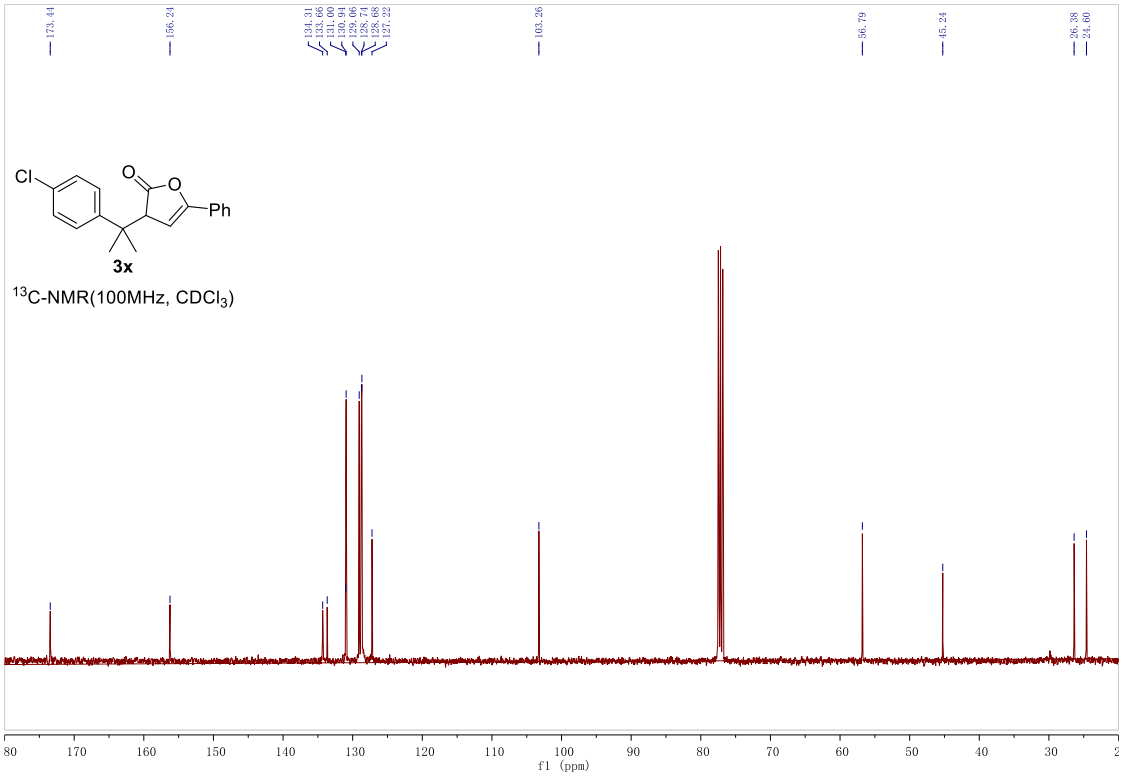

Ph
O
O
Ph
3v
1H-NMR(400MHz, CDCl3)
f1 (ppm)


Ph
O
O
Ph
3v
13C-NMR(100MHz, CDCl3)
f1 (ppm)

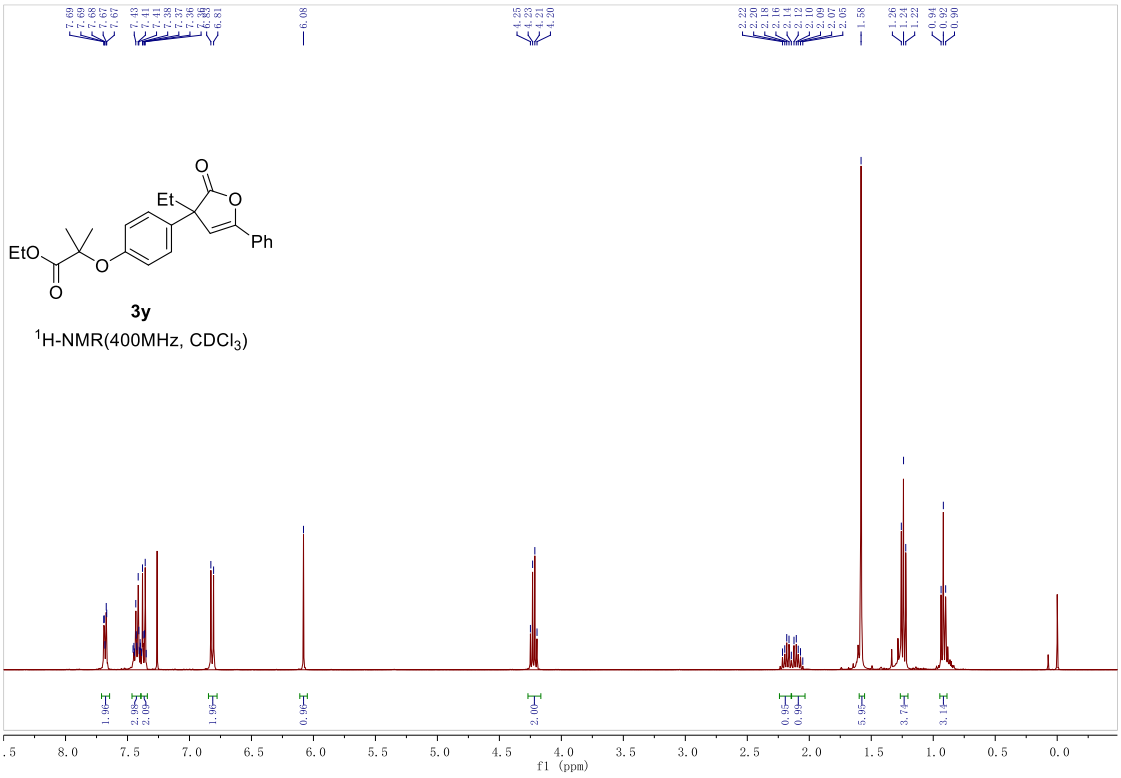

Bn
HO
O
O
Ph
3w
1H-NMR(400MHz, CDCl3)
f1 (ppm)

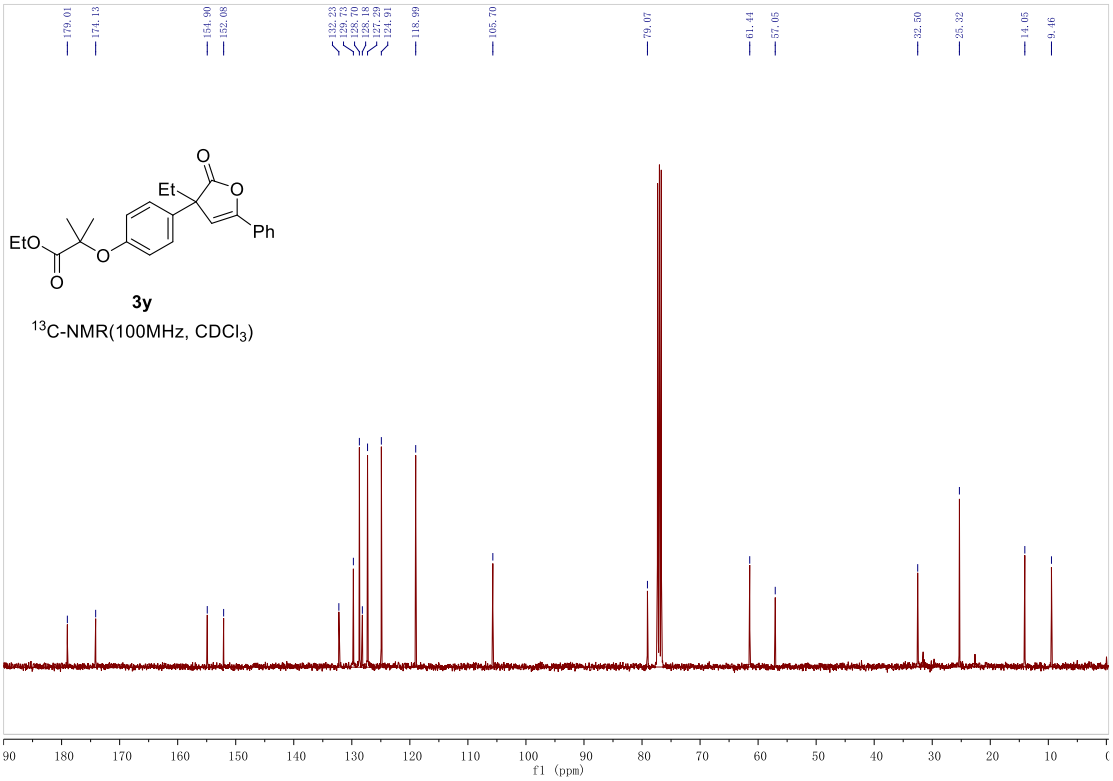

Bn
HO
O
O
Ph
3w
13C-NMR(100MHz, CDCl3)
f1 (ppm)

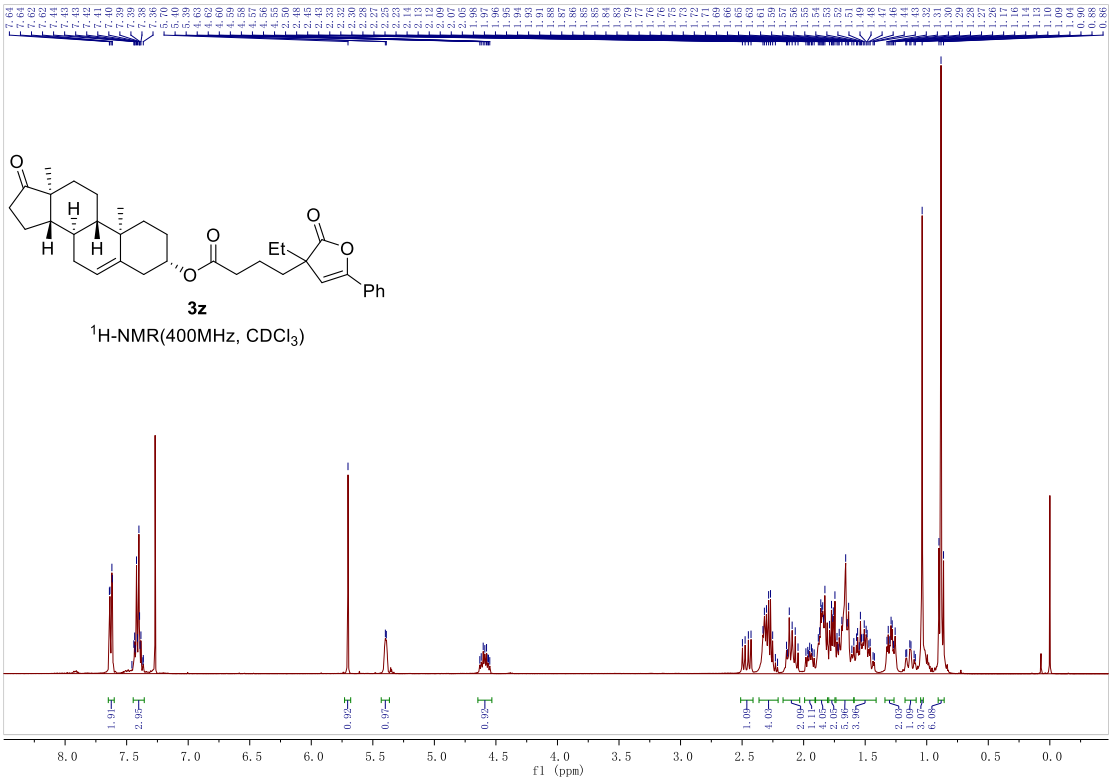

Cl
O
O
Ph
3x
1H-NMR(400MHz, CDCl3)
f1 (ppm)


Cl
O
O
Ph
3x
13C-NMR(100MHz, CDCl3)
f1 (ppm)

..

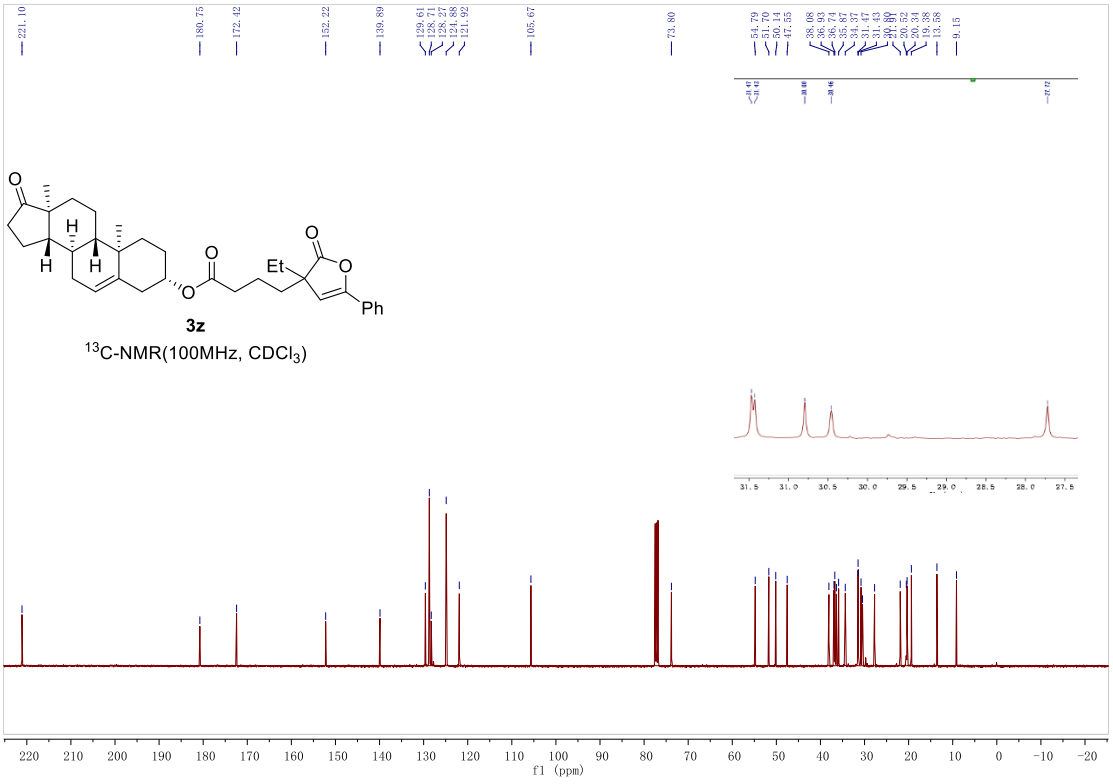

Et
O
O
Ph
EtO
O
O
3y
1H-NMR(400MHz, CDCl3)
f1 (ppm)


Et
O
O
Ph
EtO
O
O
3y
13C-NMR(100MHz, CDCl3)
f1 (ppm)



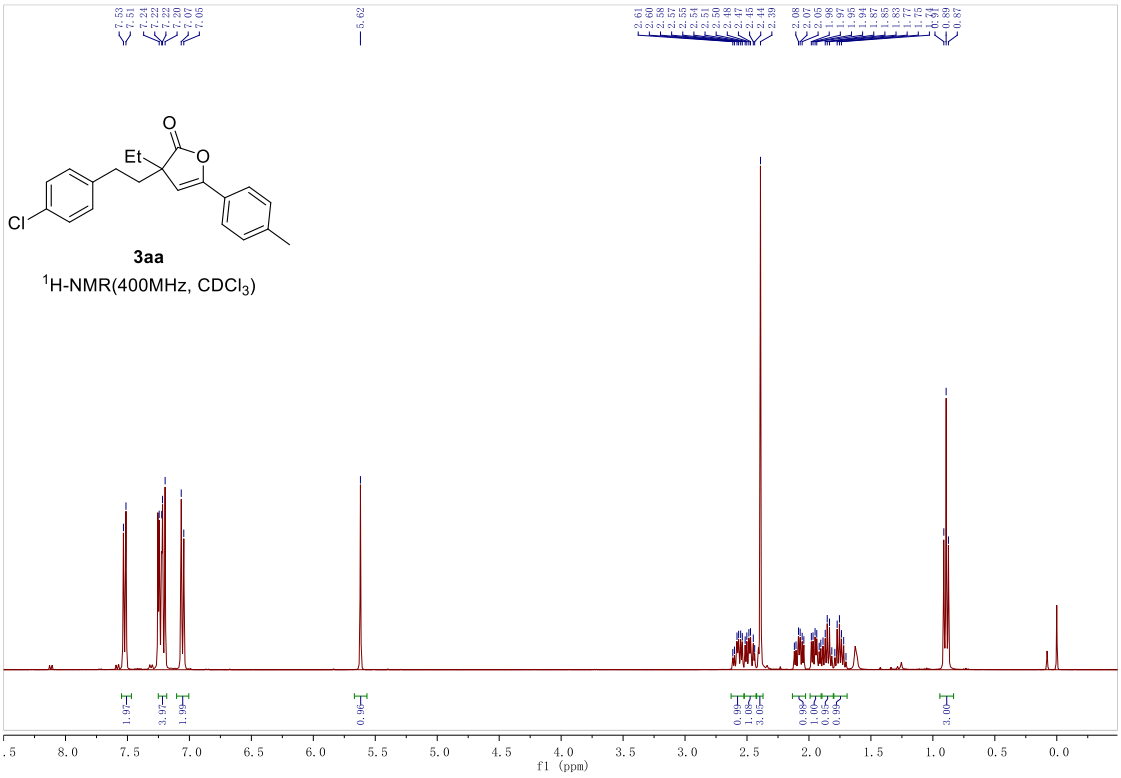
3z

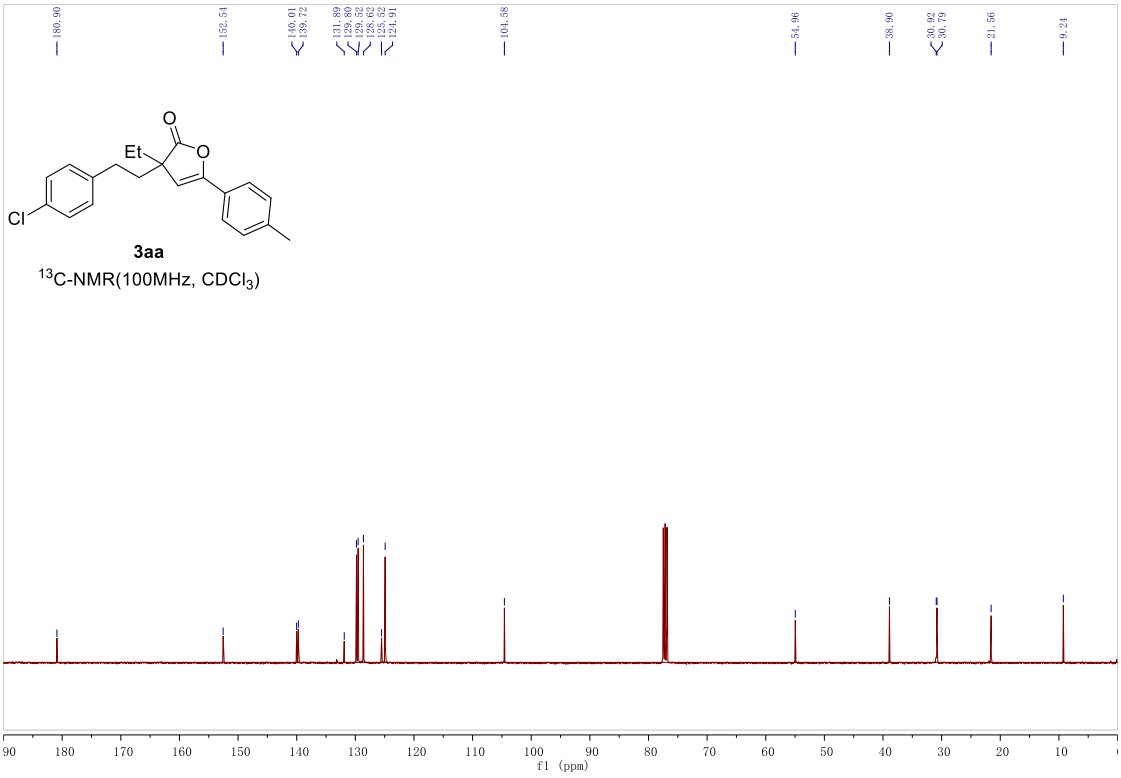
^{1}H-NMR(400MHz, $CDCl_3$)

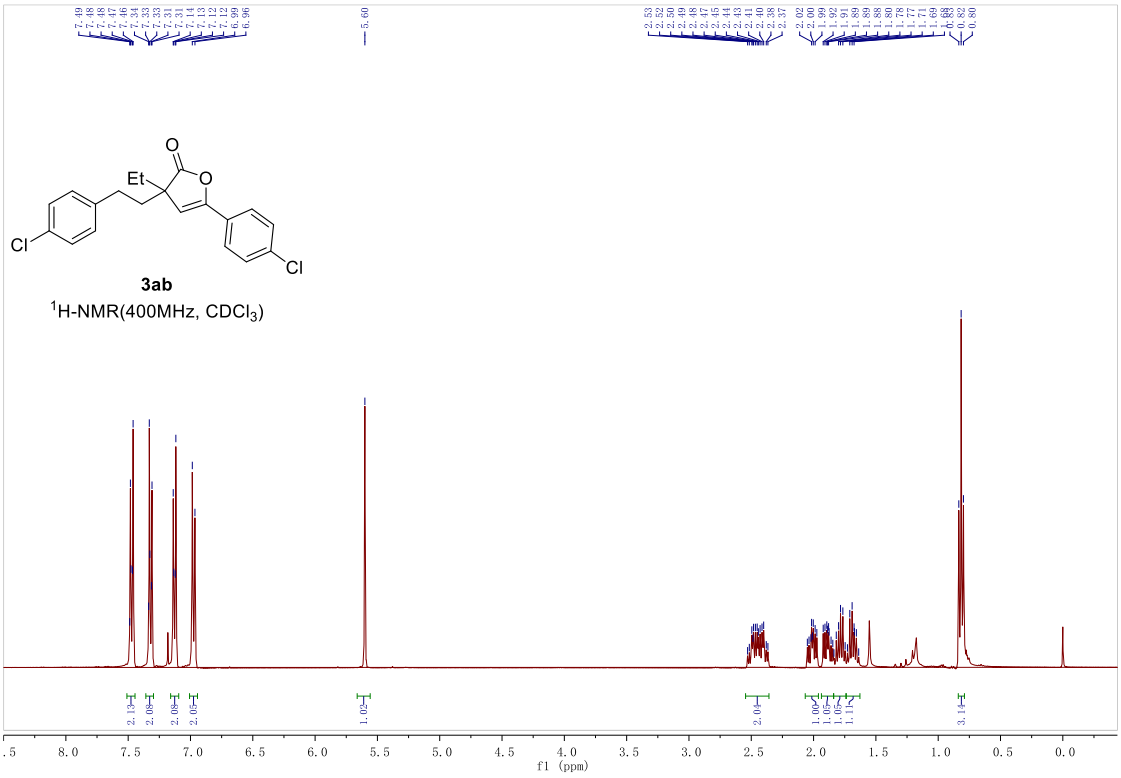


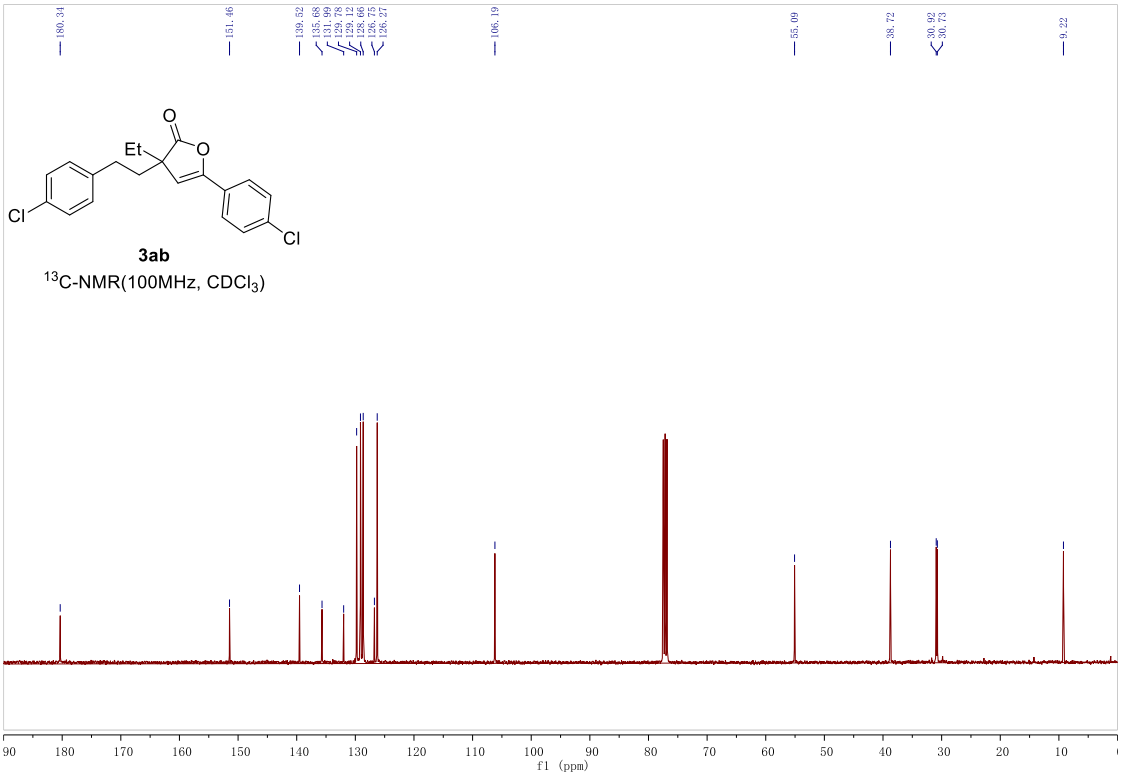
3z

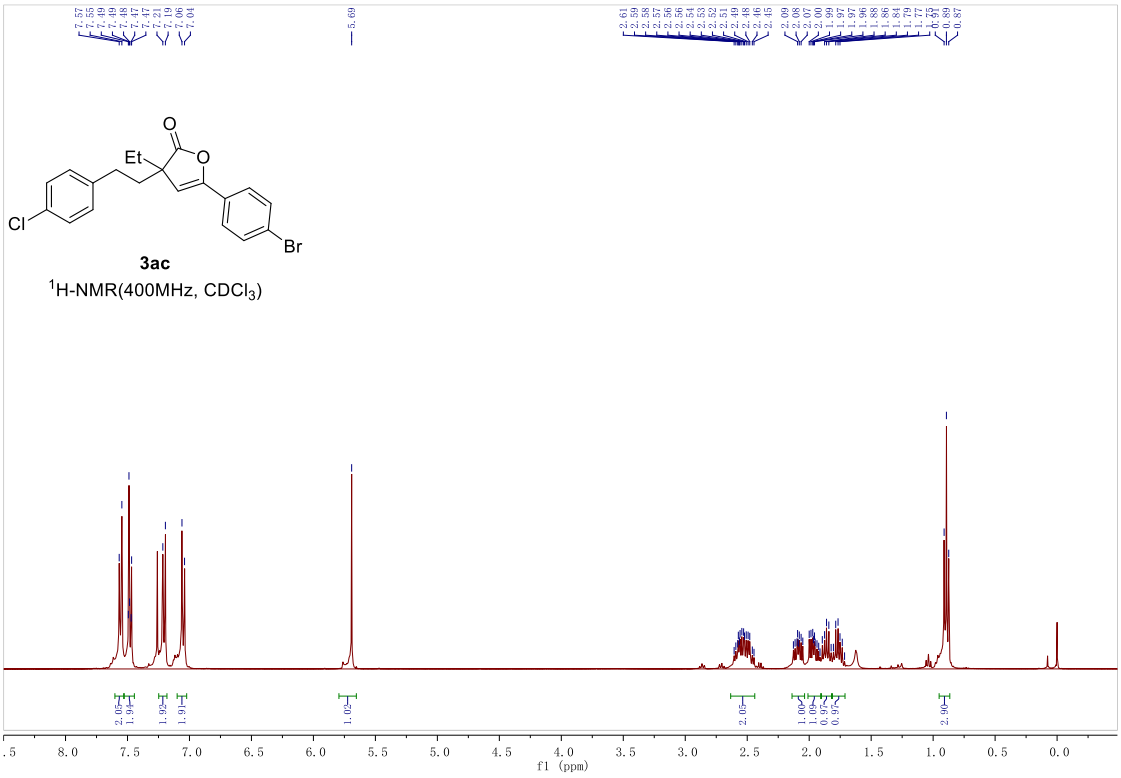
^{13}C-NMR(100MHz, $CDCl_3$)

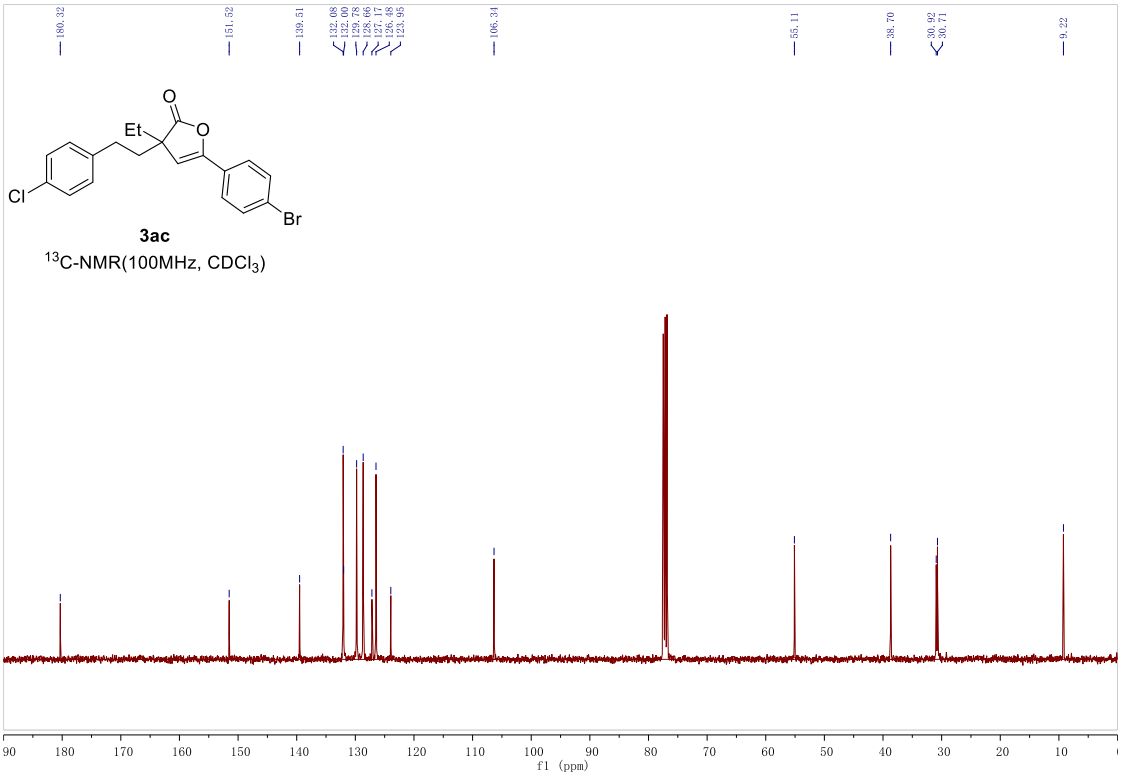

Et
O
O
Cl
3aa
1H-NMR(400MHz, CDCl3)
f1 (ppm)

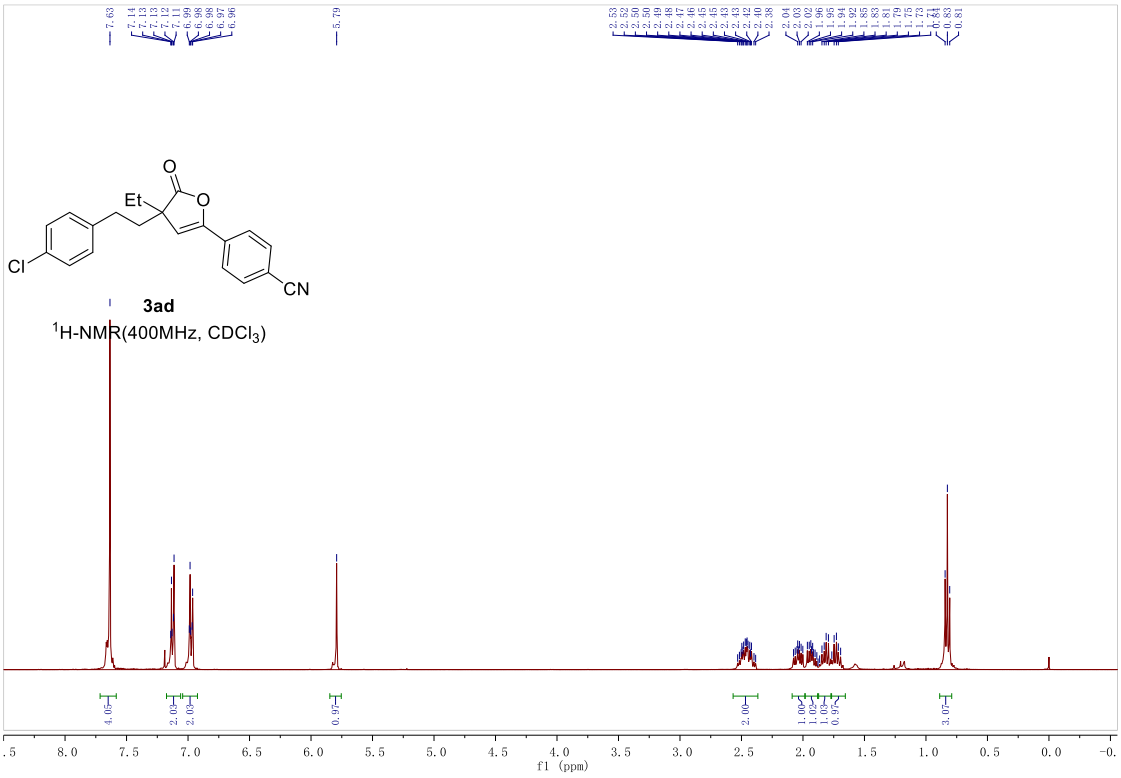

Et
O
O
Cl
3aa
13C-NMR(100MHz, CDCl3)
f1 (ppm)

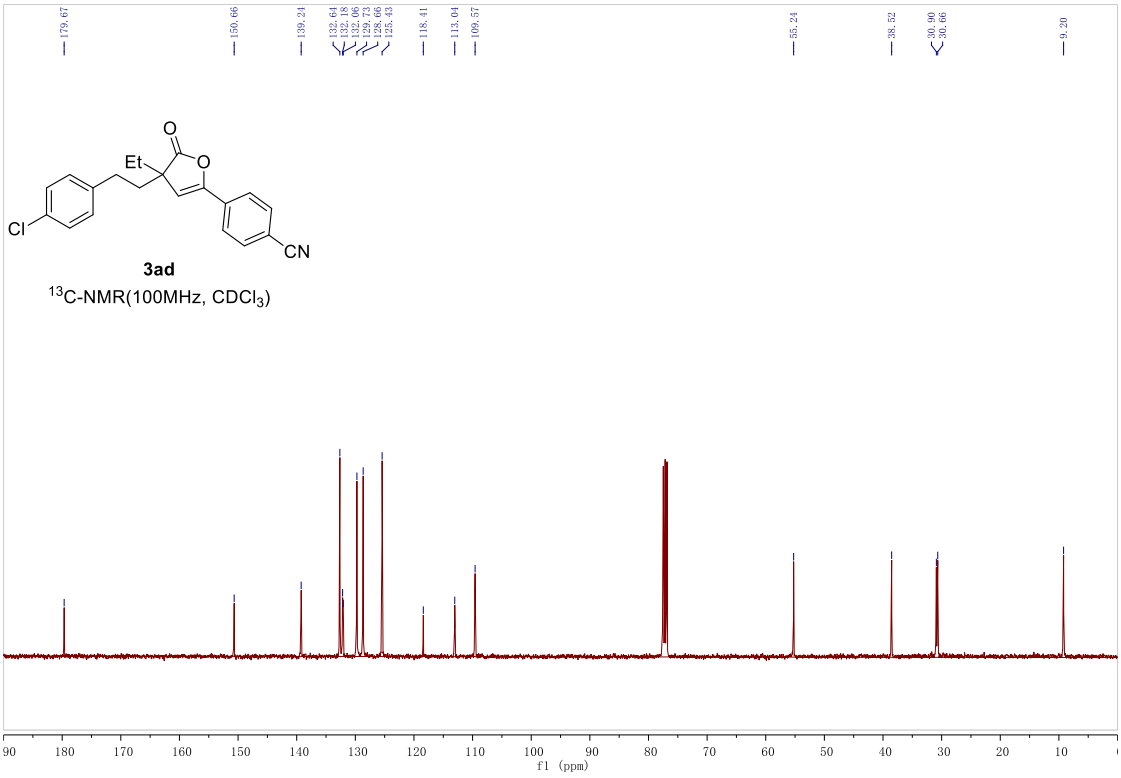

Et
O
O
Cl
Cl
3ab
1H-NMR(400MHz, CDCl3)
f1 (ppm)


Et
O
O
Cl
Cl
3ab
13C-NMR(100MHz, CDCl3)
f1 (ppm)


O
Et
O
Cl
Br
3ac
1H-NMR(400MHz, CDCl3)
f1 (ppm)


O
Et
O
Cl
Br
3ac
13C-NMR(100MHz, CDCl3)
f1 (ppm)


Et
O
O
Cl
CN
3ad
1H-NMR(400MHz, CDCl3)
f1 (ppm)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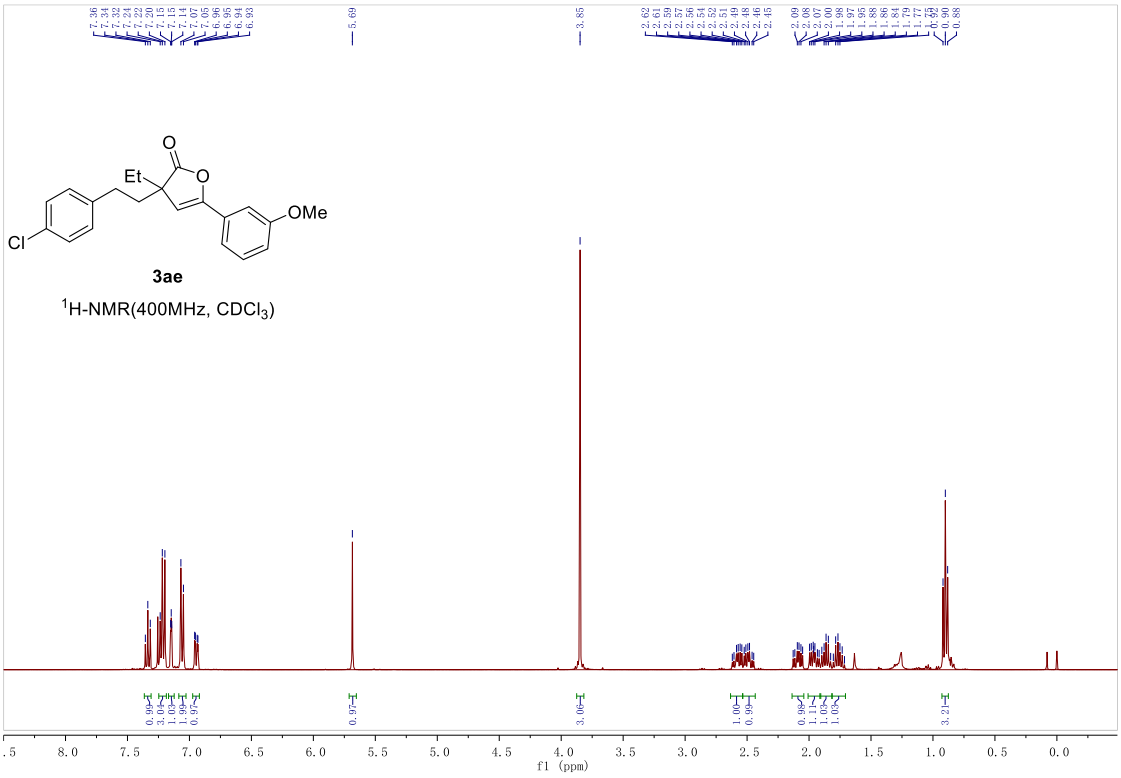
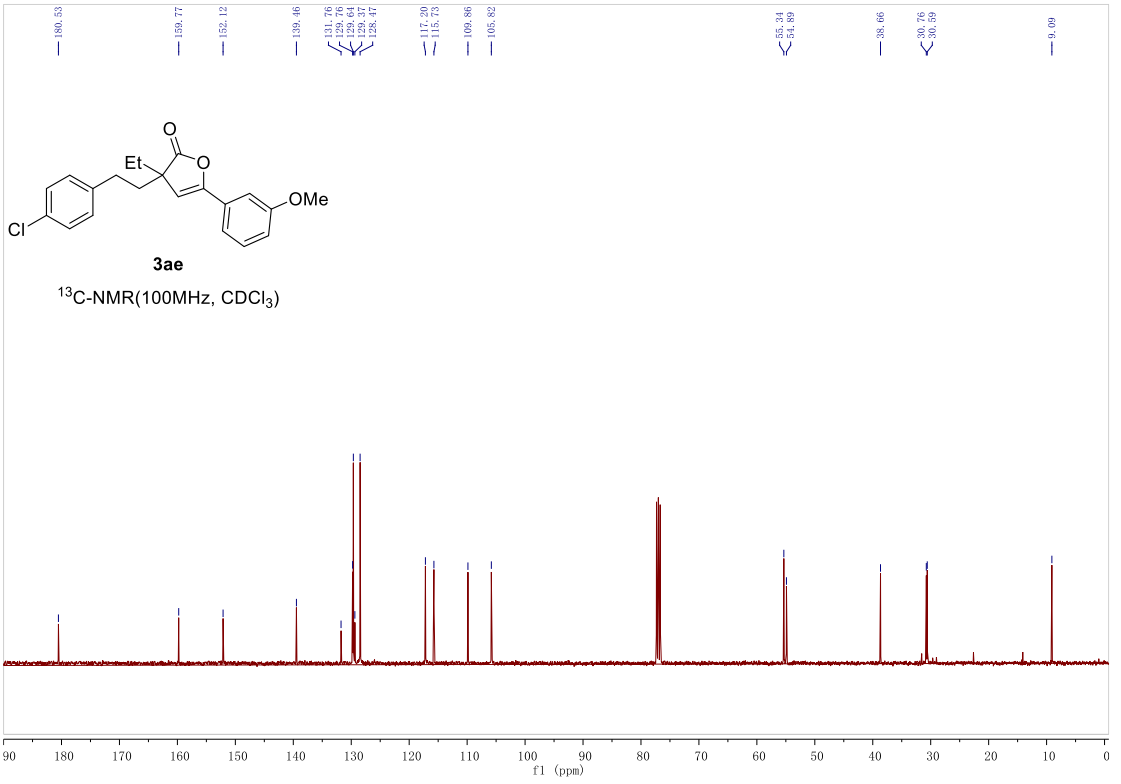
O
O
Cl
CN
3ad
13C-NMR(100MHz, CDCl3)
f1 (ppm)



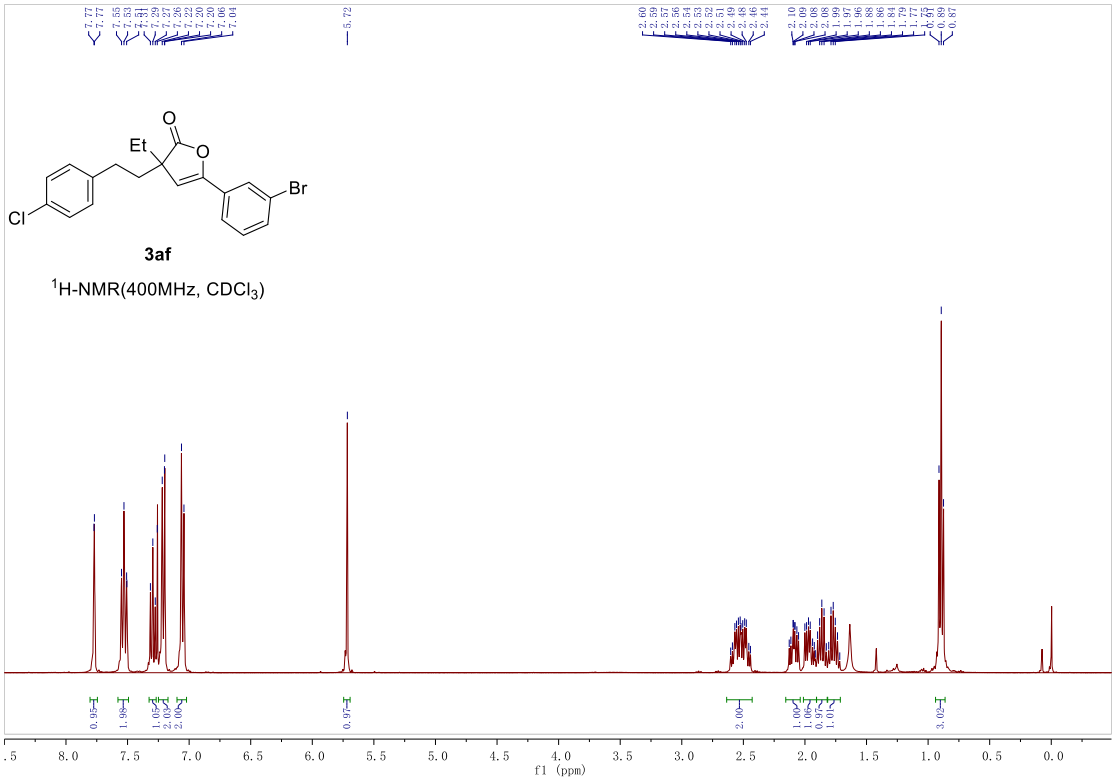
3ae

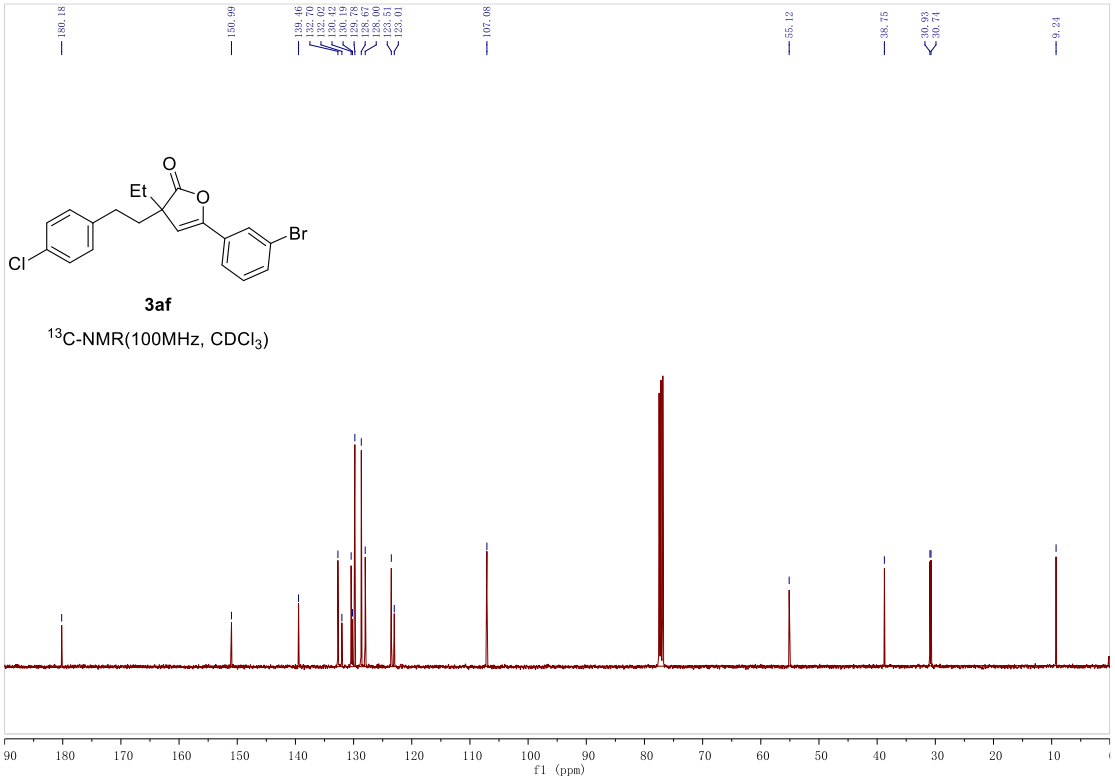
^{1}H-NMR(400MHz, $CDCl_3$)

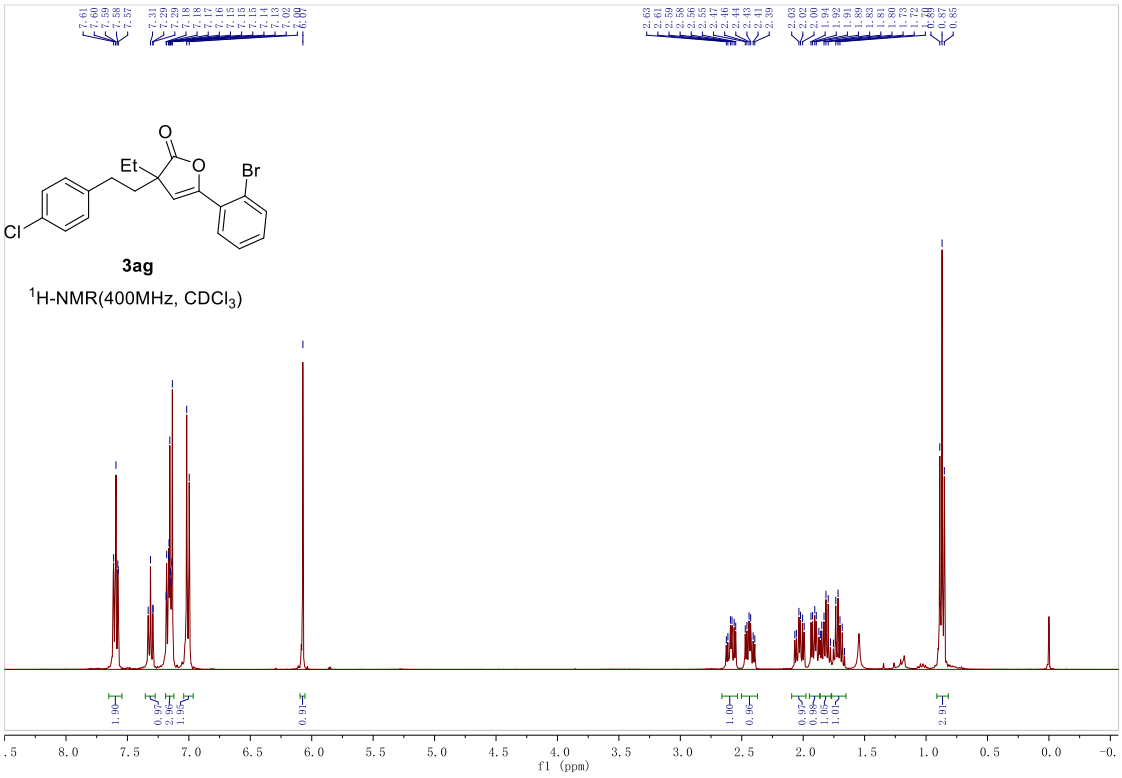


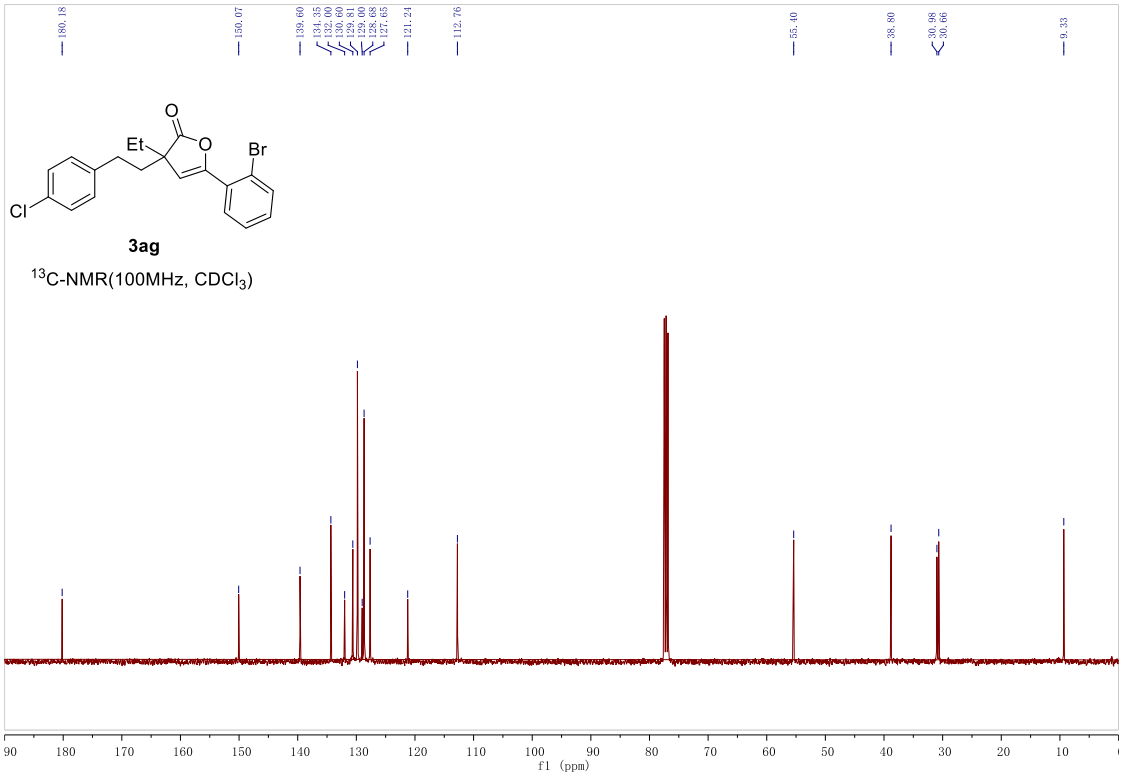
3ae

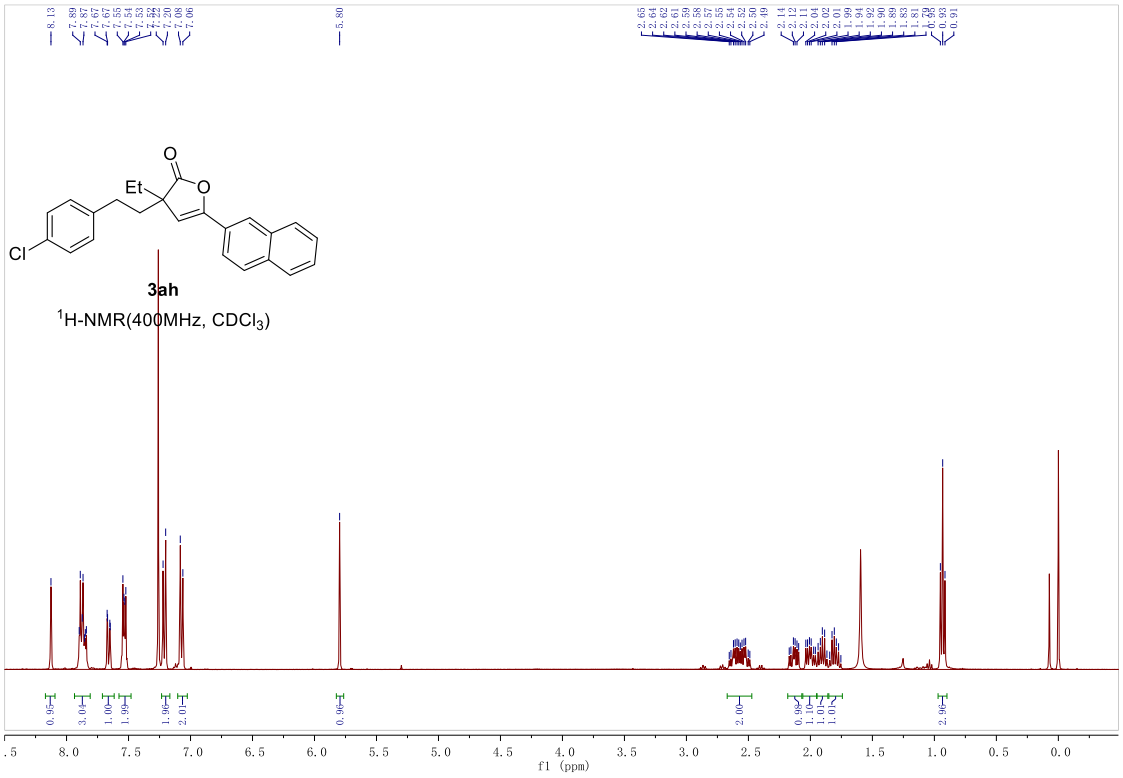
^{13}C-NMR(100MHz, $CDCl_3$)

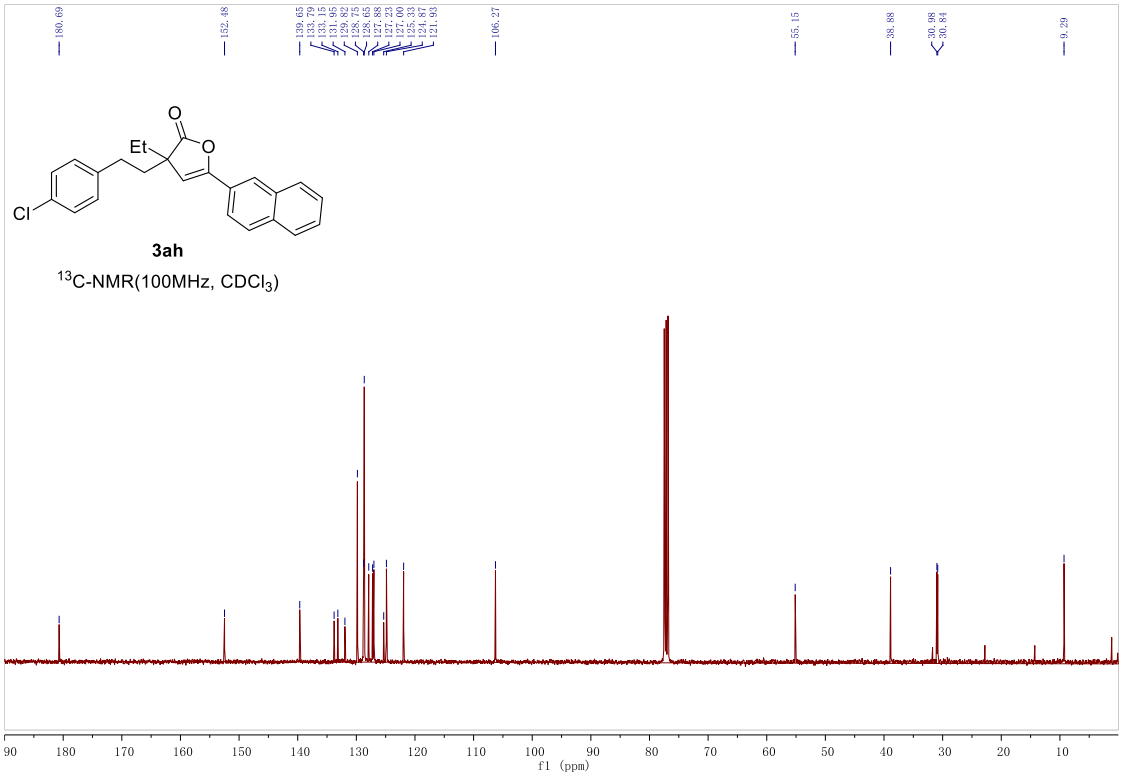

Et
O
O
Br
Cl
3af
1H-NMR(400MHz, CDCl3)
f1 (ppm)

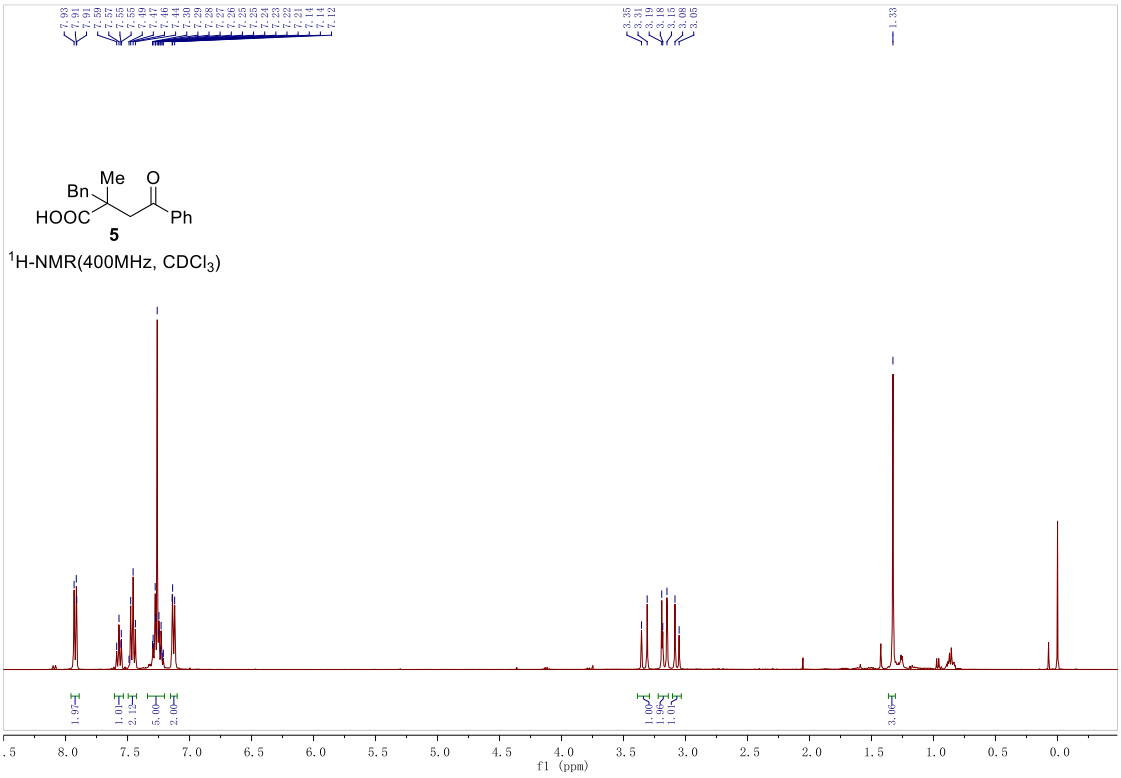

Et
O
O
Br
Cl
3af
13C-NMR(100MHz, CDCl3)
f1 (ppm)

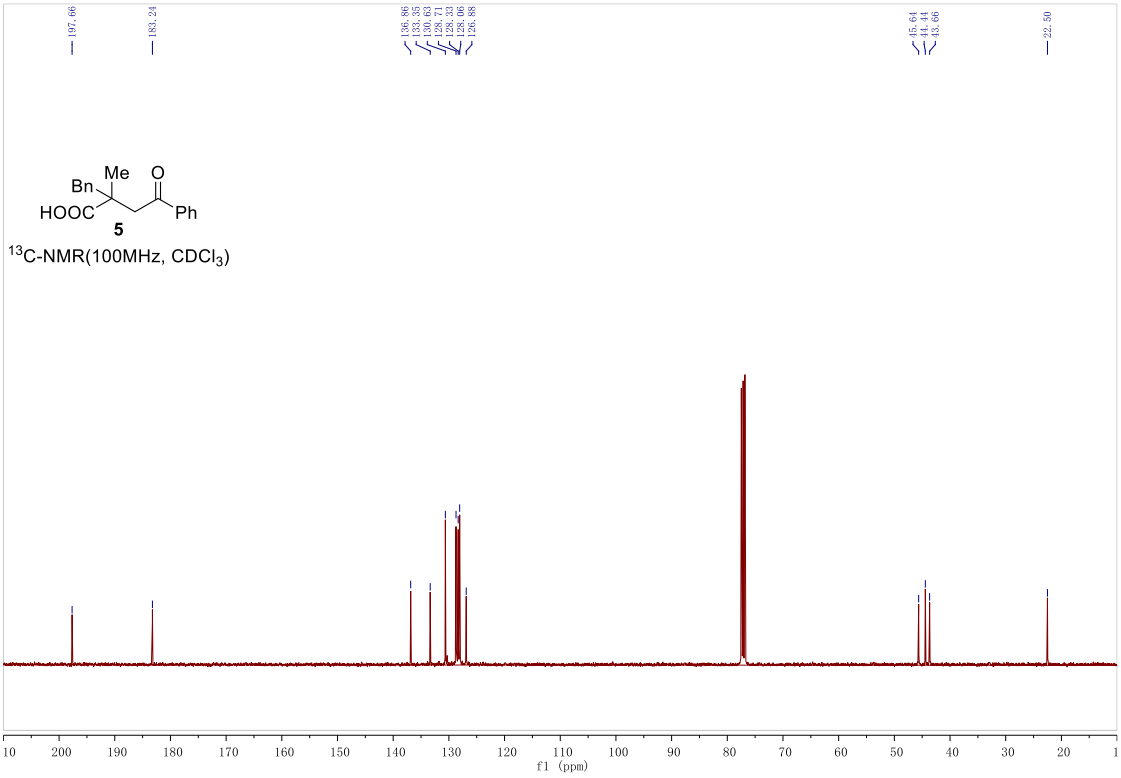

Et
O
O
Br
Cl
3ag
1H-NMR(400MHz, CDCl3)
f1 (ppm)

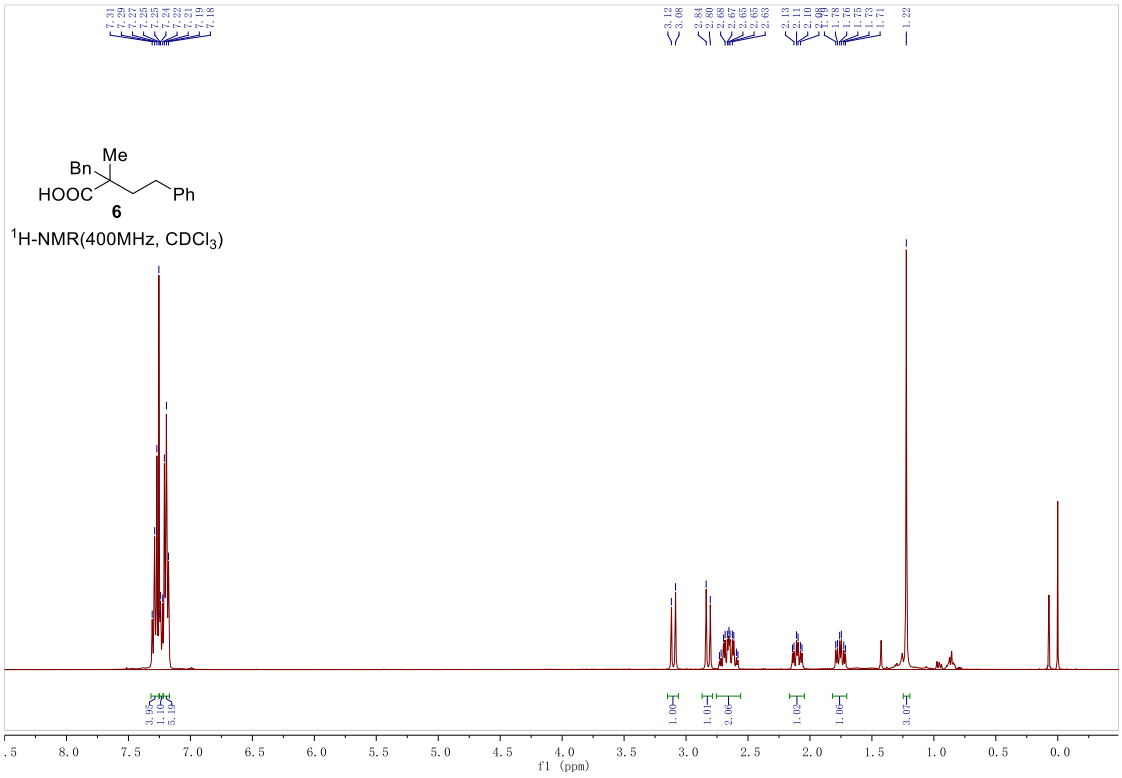

Et
O
O
Br
Cl
3ag
13C-NMR(100MHz, CDCl3)
f1 (ppm)

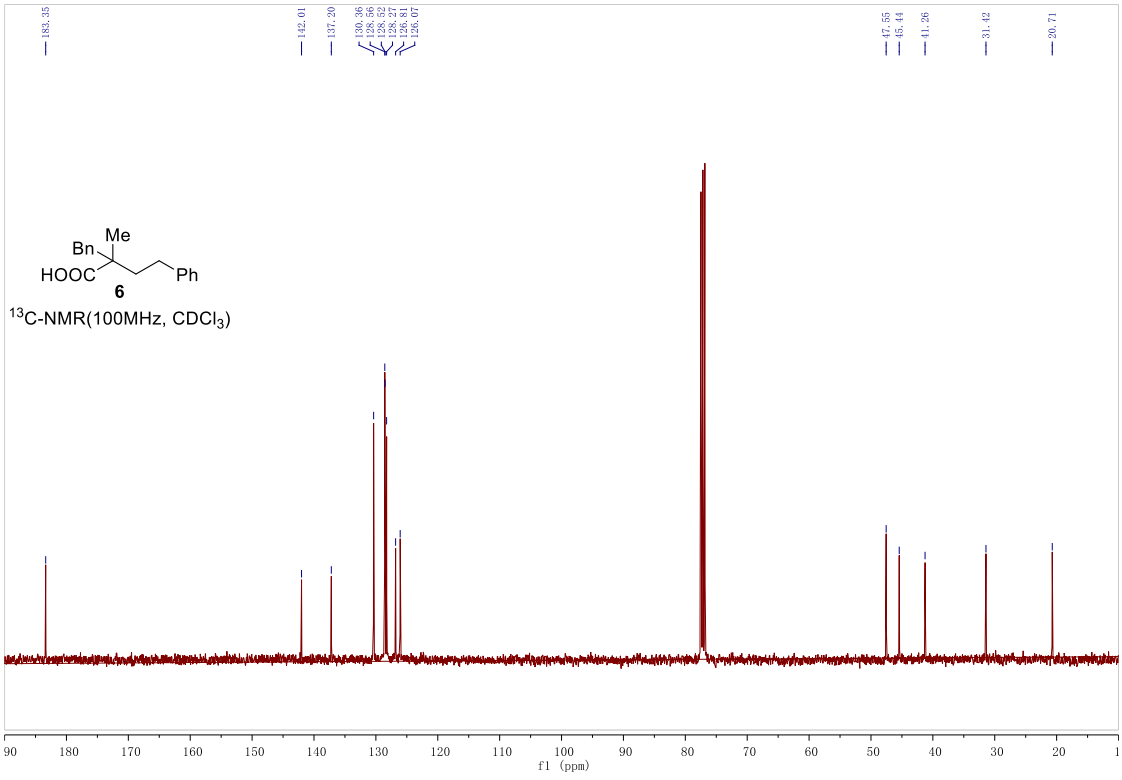

Et
O
O
Cl
3ah
1H-NMR(400MHz, CDCl3)
f1 (ppm)

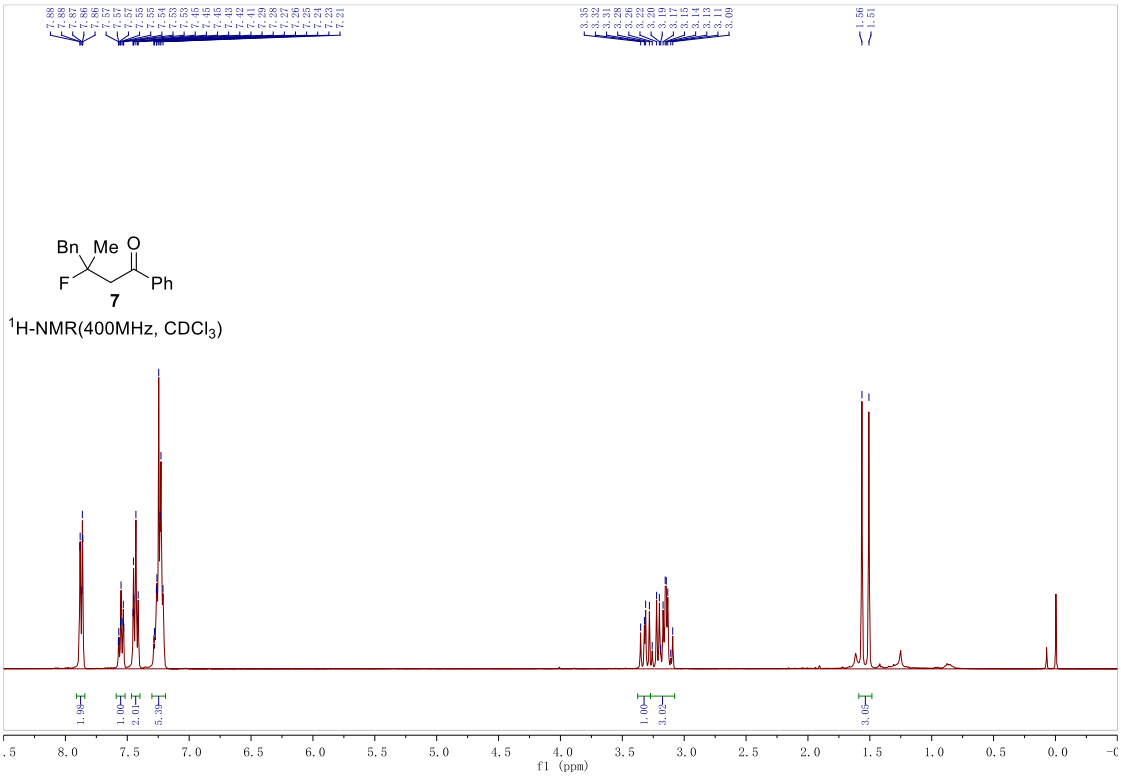

Et
O
O
Cl
3ah
13C-NMR(100MHz, CDCl3)
f1 (ppm)

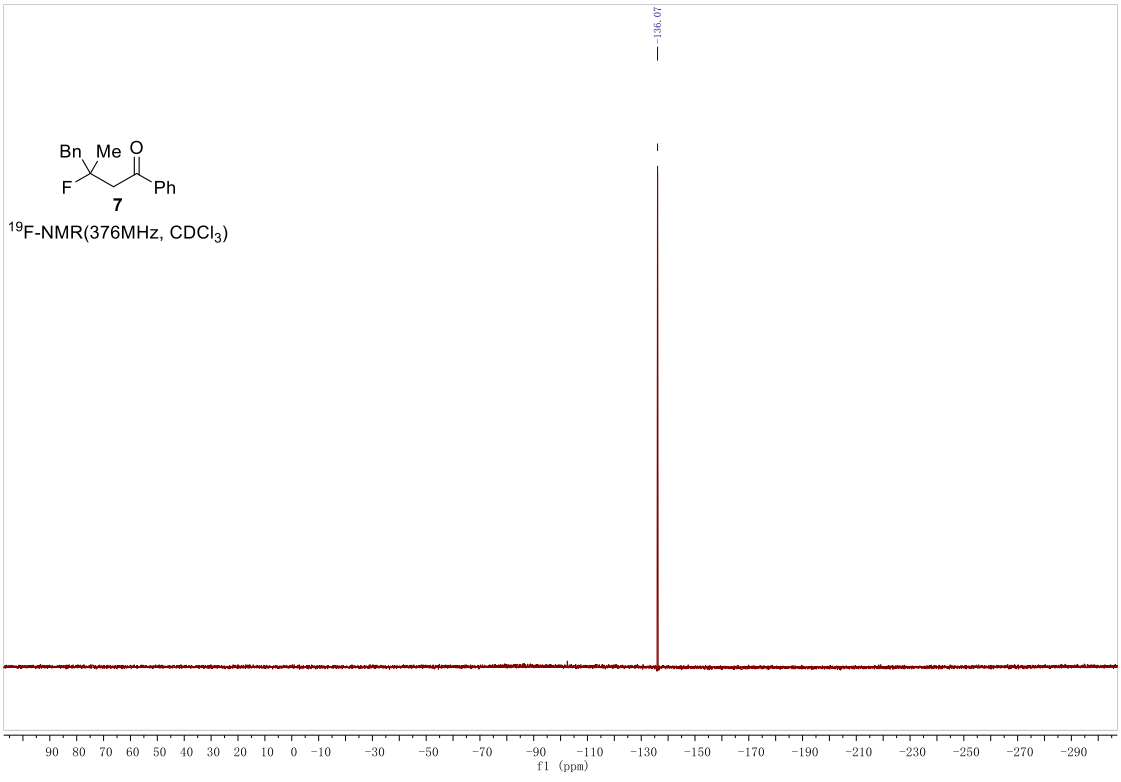

Me
O
Bn
HOOC
Ph
5
1H-NMR(400MHz, CDCl3)
f1 (ppm)

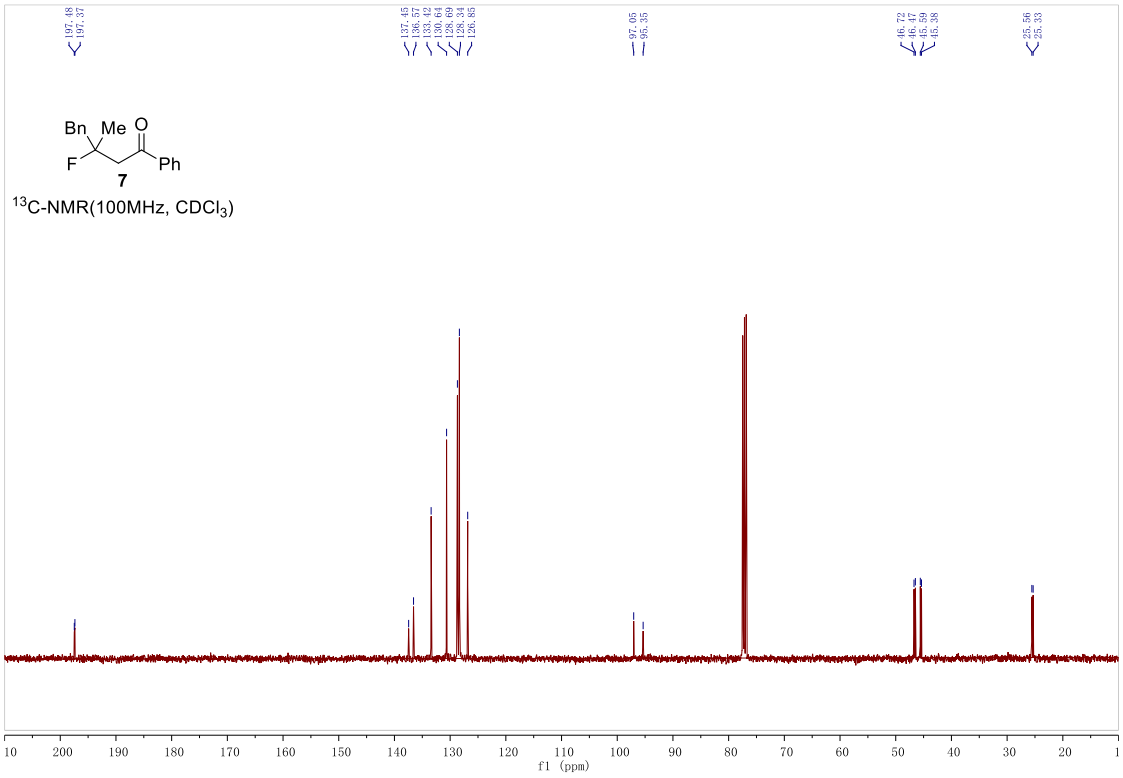

Me
O
Bn
HOOC
Ph
5
13C-NMR(100MHz, CDCl3)
f1 (ppm)

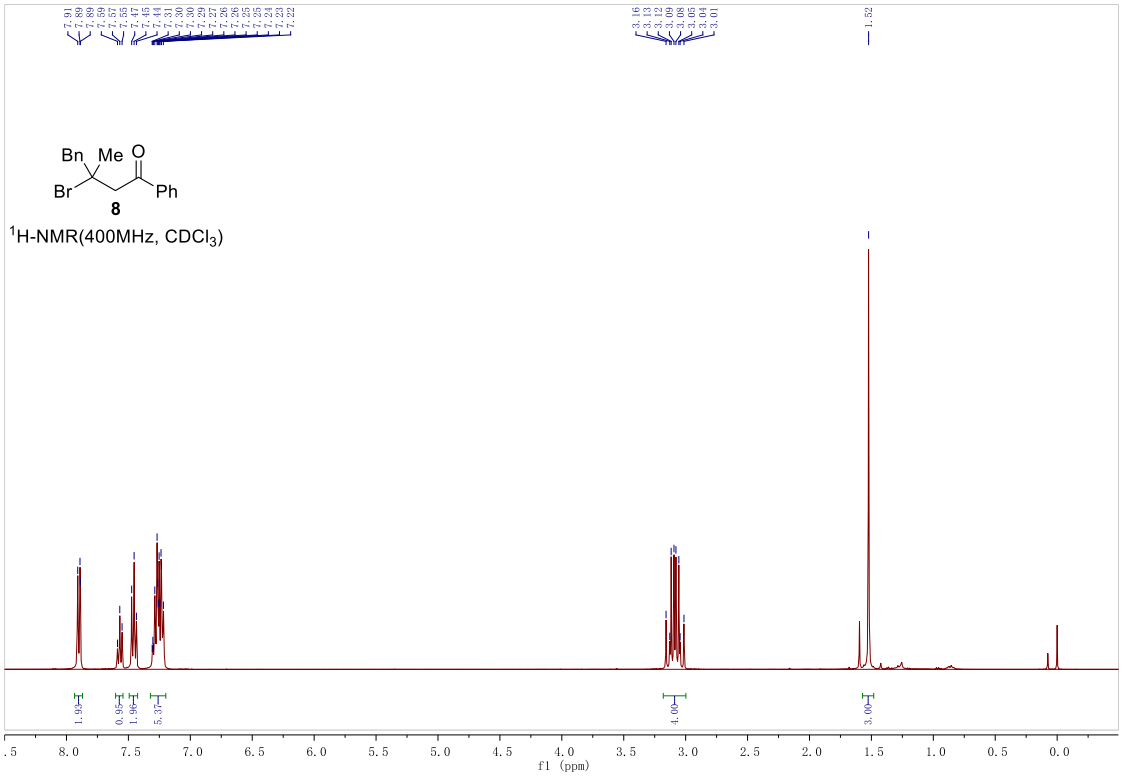

Me
Bn
HOOC
Ph
6
1H-NMR(400MHz, CDCl3)
f1 (ppm)

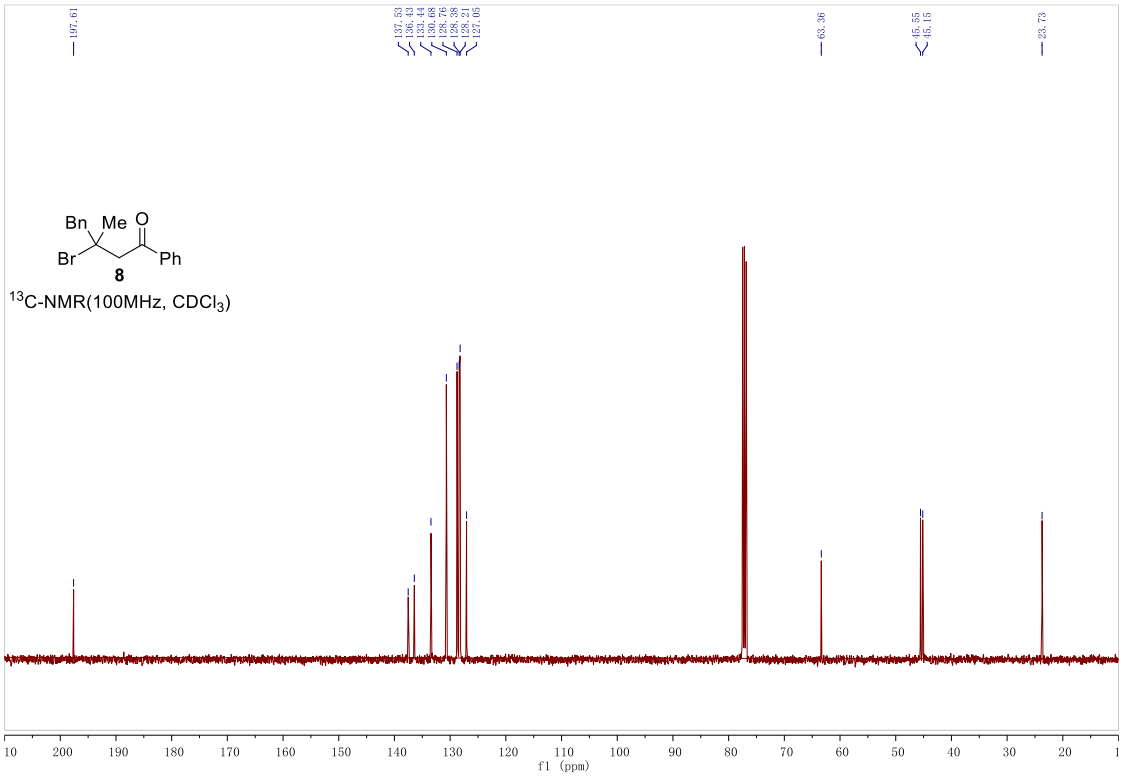

Me
Bn
HOOC
Ph
6
13C-NMR(100MHz, CDCl3)
f1 (ppm)

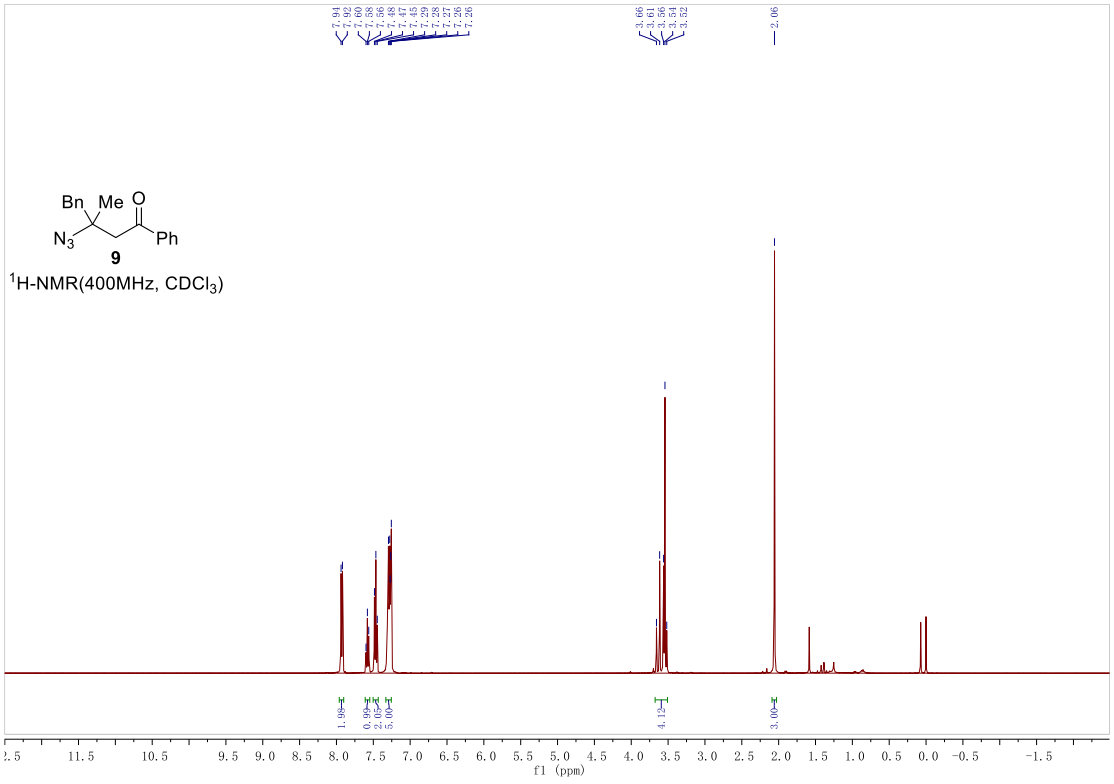

Bn Me O
F Ph
7
1H-NMR(400MHz, CDCl3)
f1 (ppm)

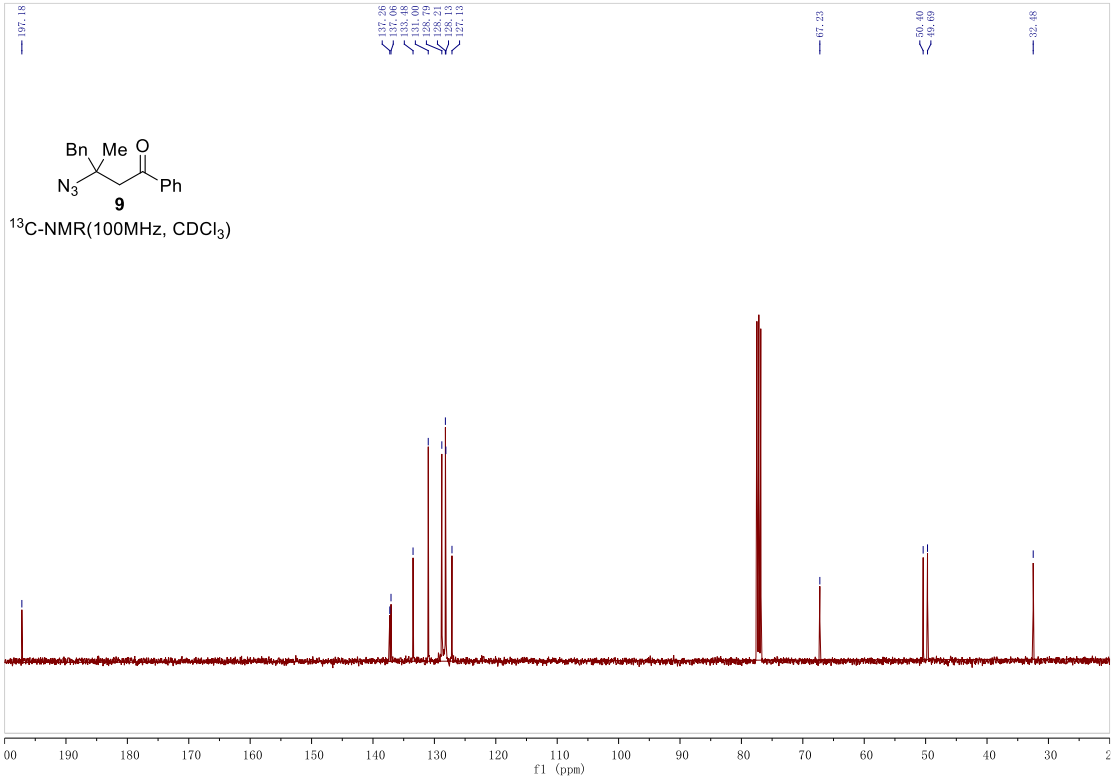

-136.07
Bn Me O
F Ph
7
19F-NMR(376MHz, CDCl3)
f1 (ppm)


Bn
Me
O
F
Ph
7
13C-NMR(100MHz, CDCl3)
f1 (ppm)


Bn
Me
O
Br
Ph
8
1H-NMR(400MHz, CDCl3)
f1 (ppm)


197.61
137.53
136.43
133.44
130.68
128.76
128.38
126.21
121.05
63.36
45.55
45.15
23.73
Bn Me O
Br Ph
8
13C-NMR(100MHz, CDCl3)
f1 (ppm)


7.94
7.92
7.60
7.58
7.56
7.48
7.47
7.45
7.29
7.28
7.27
7.26
7.26
3.66
3.61
3.56
3.54
3.52
2.06
Bn Me O
N3 Ph
9
1H-NMR(400MHz, CDCl3)
1.00
0.69
0.65
5.00
4.12
3.00
f1 (ppm)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137.26
133.66
133.48
131.00
128.79
128.21
128.13
127.13
67.23
50.40
49.69
32.48
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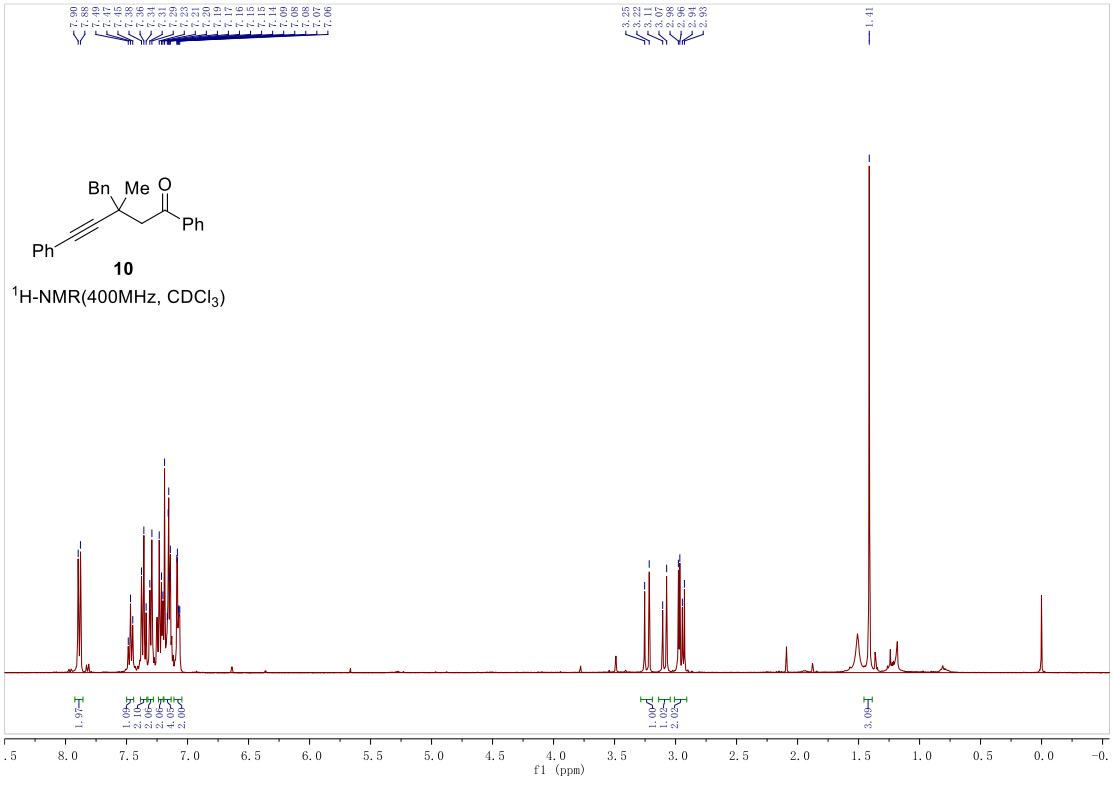
N3
Ph
9
13C-NMR(100MHz, CDCl3)
f1 (ppm)


7.90
7.88
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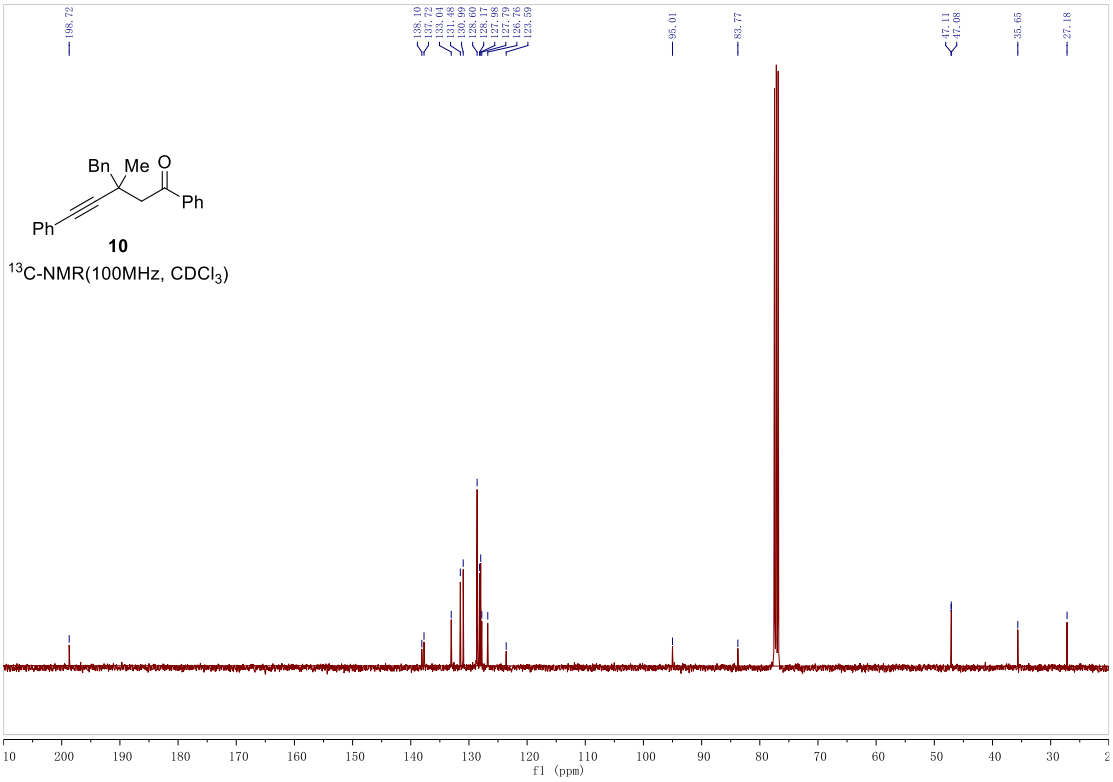
7.47
7.45
7.38
7.36
7.34
7.31
7.29
7.23
7.21
7.20
7.19
7.17
7.16
7.15
7.14
7.09
7.08
7.07
7.06
3.25
3.22
3.11
3.07
2.98
2.96
2.94
2.93
1.41
Bn Me O
Ph
Ph
10
1H-NMR(400MHz, CDCl3)
1.97
1.09
2.10
2.09
2.09
4.05
2.06
1.04
1.02
2.02
3.09
f1 (ppm)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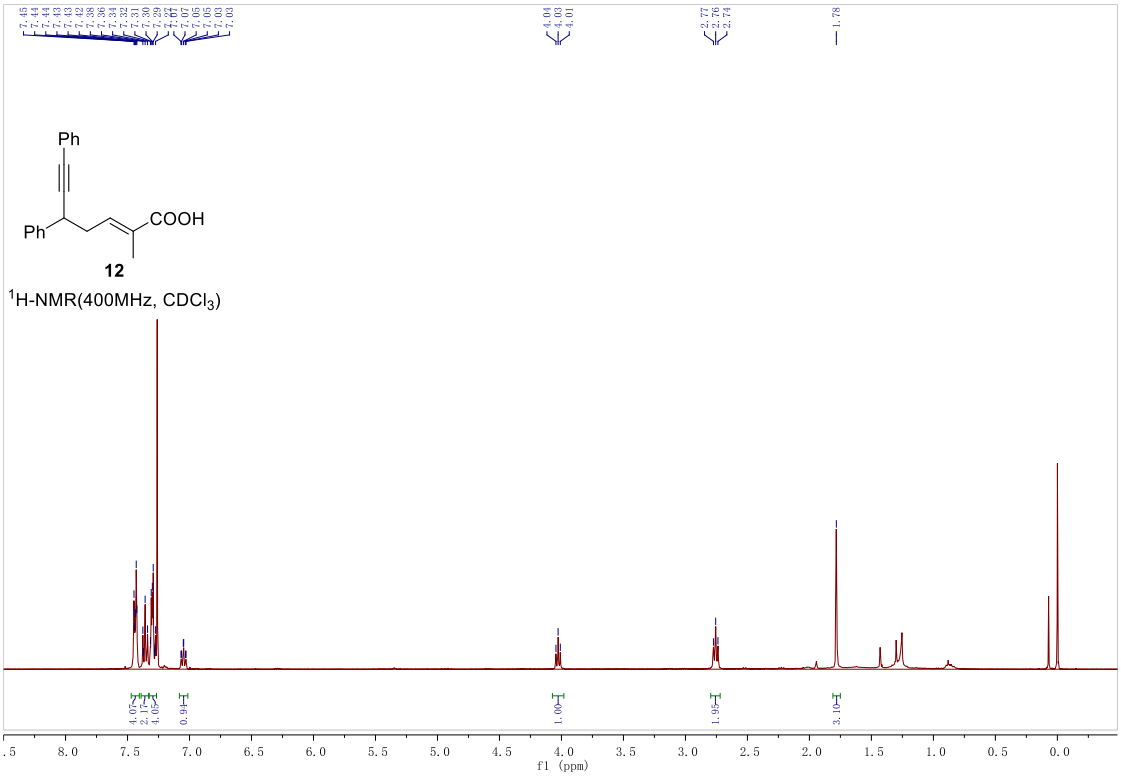
138.10
137.72
133.04
131.48
130.96
128.60
128.17
127.98
127.79
126.76
123.59
95.01
83.77
47.11
47.08
35.65
27.18
Bn
Me
O
Ph
Ph
10
13C-NMR(100MHz, CDCl3)
f1 (ppm)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7.44
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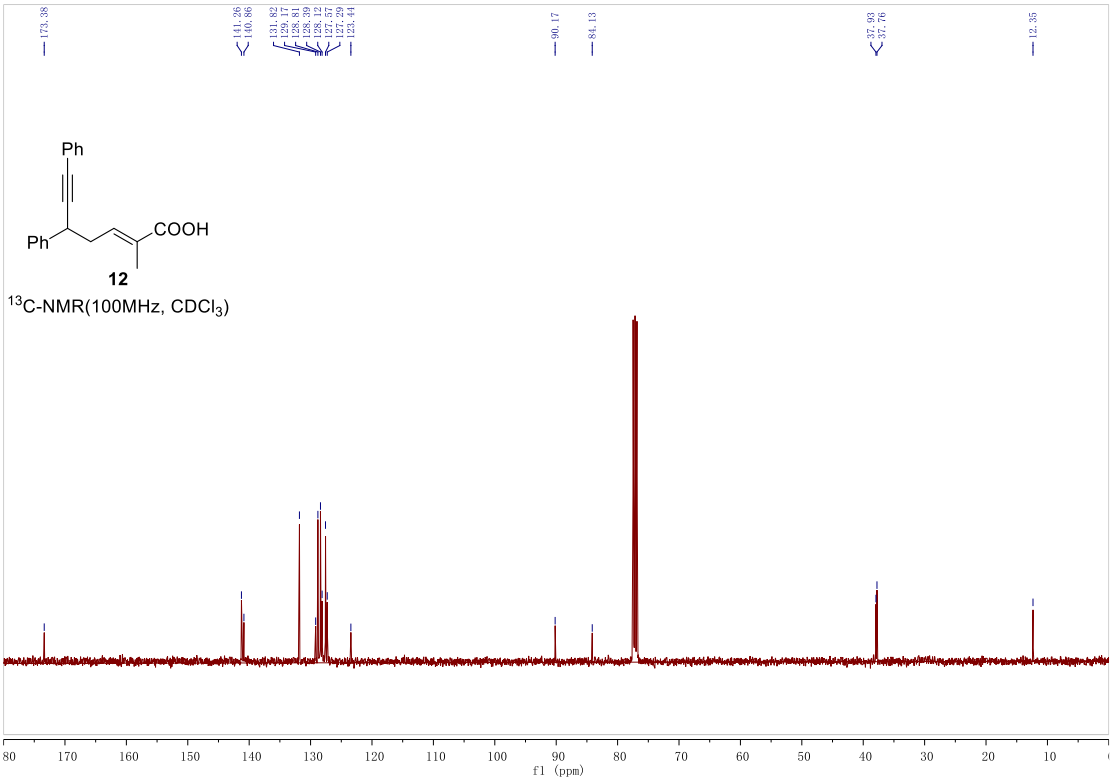
7.43
7.43
7.42
7.38
7.36
7.34
7.32
7.31
7.30
7.29
7.27
7.07
7.05
7.03
4.04
4.03
4.01
2.77
2.76
2.74
1.78
Ph
Ph
COOH
12
1H-NMR(400MHz, CDCl3)
4.07
2.17
4.05
0.94
1.00
1.95
3.10
f1 (ppm)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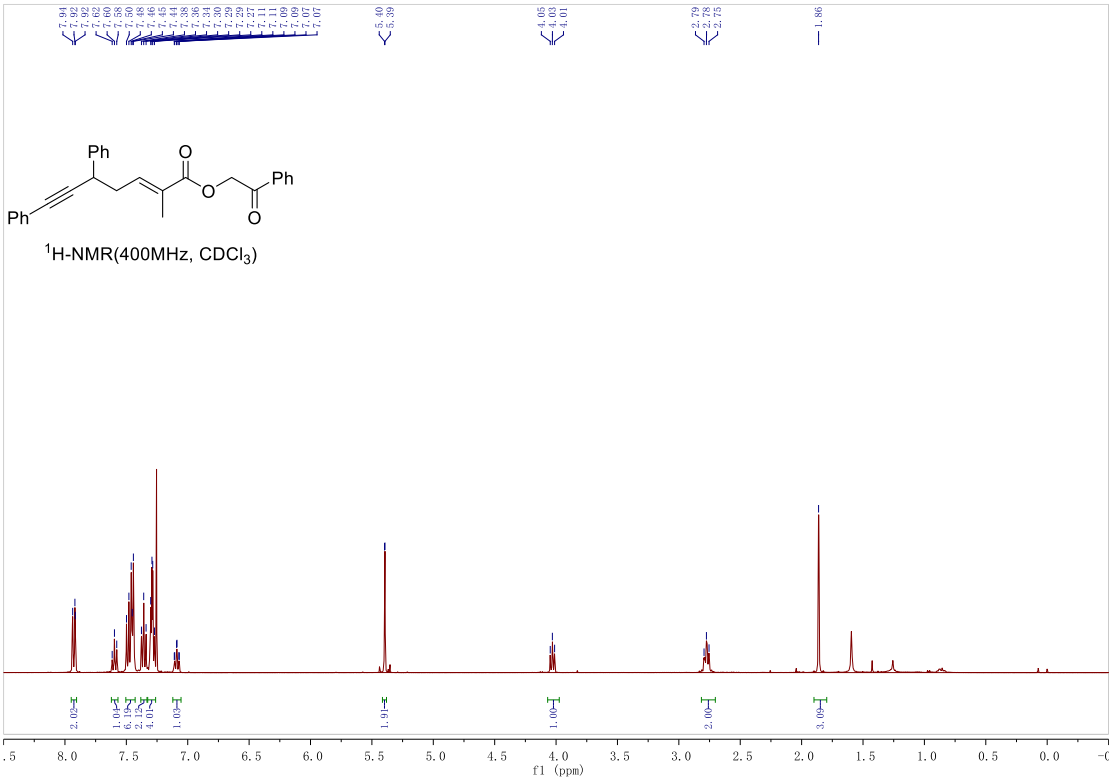
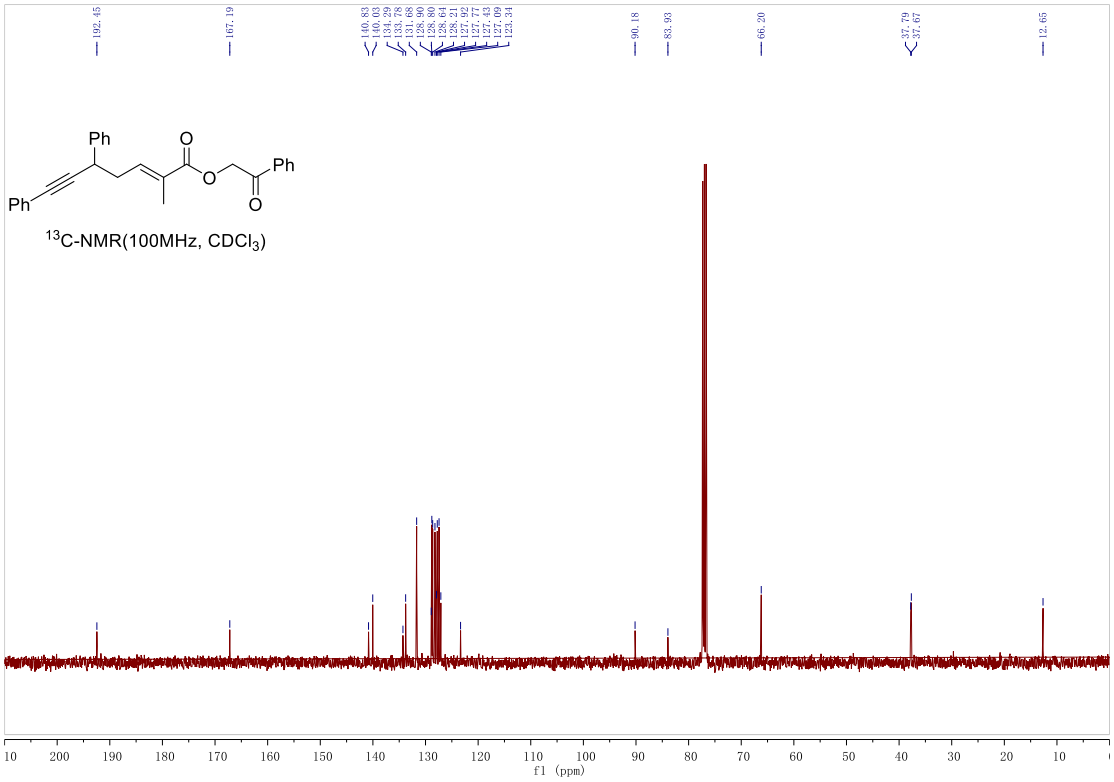
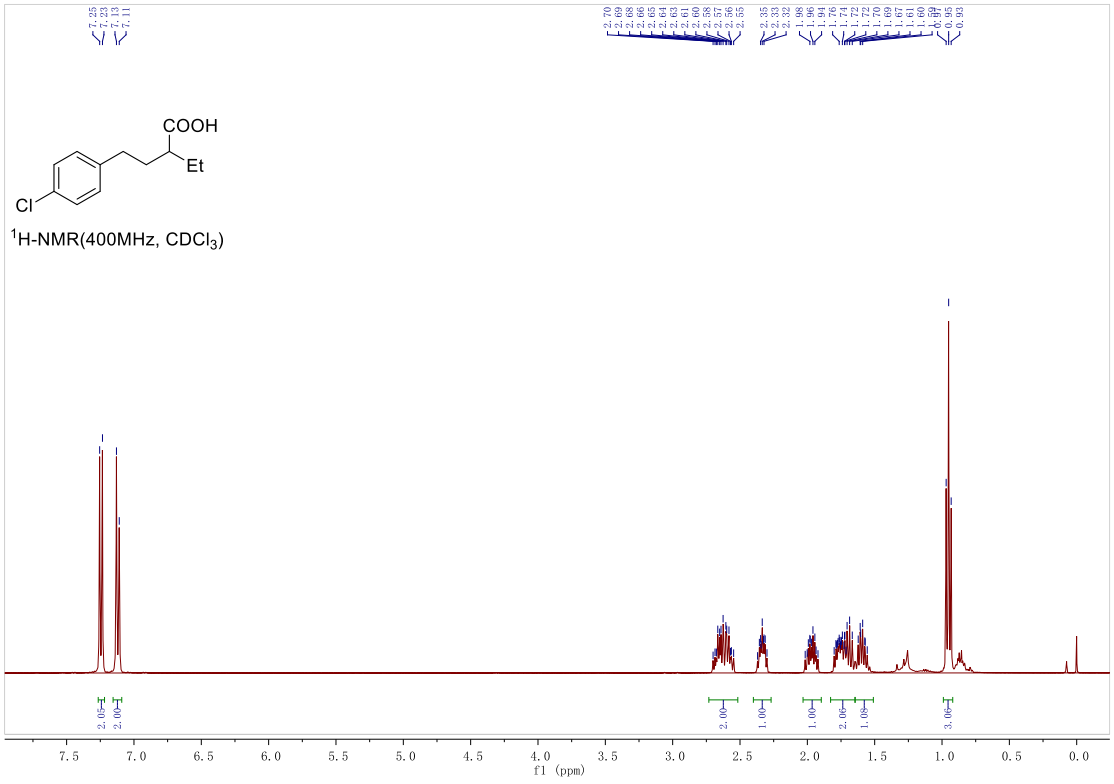
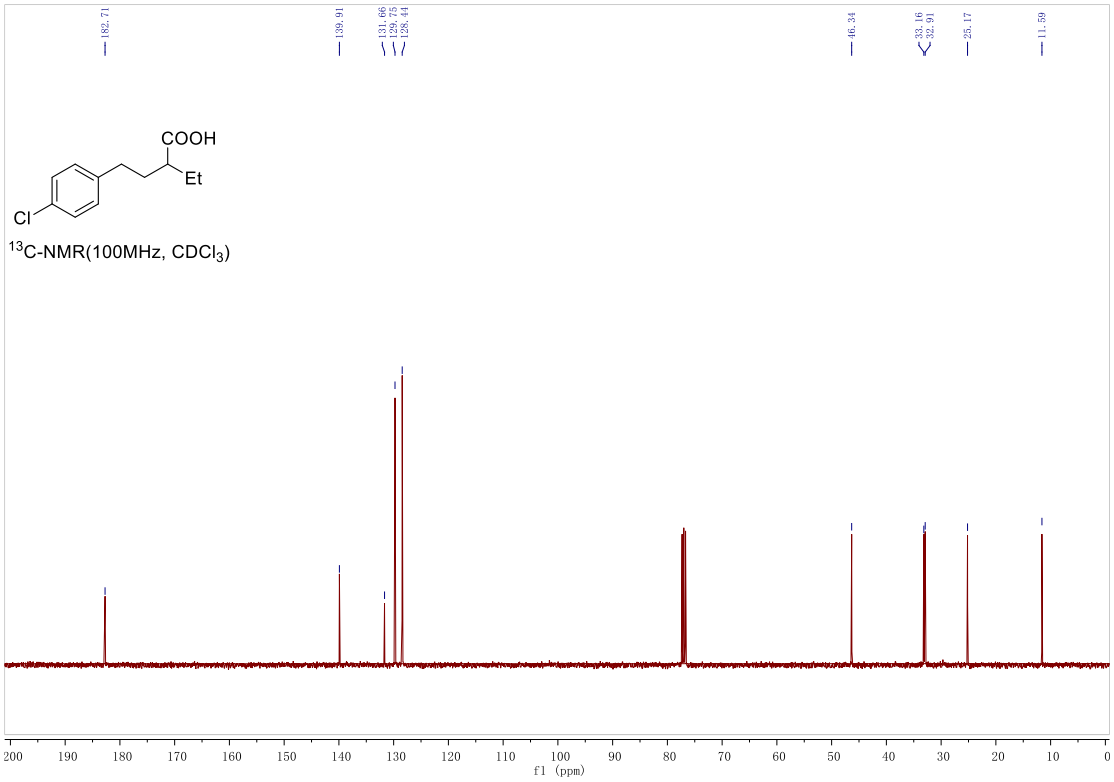
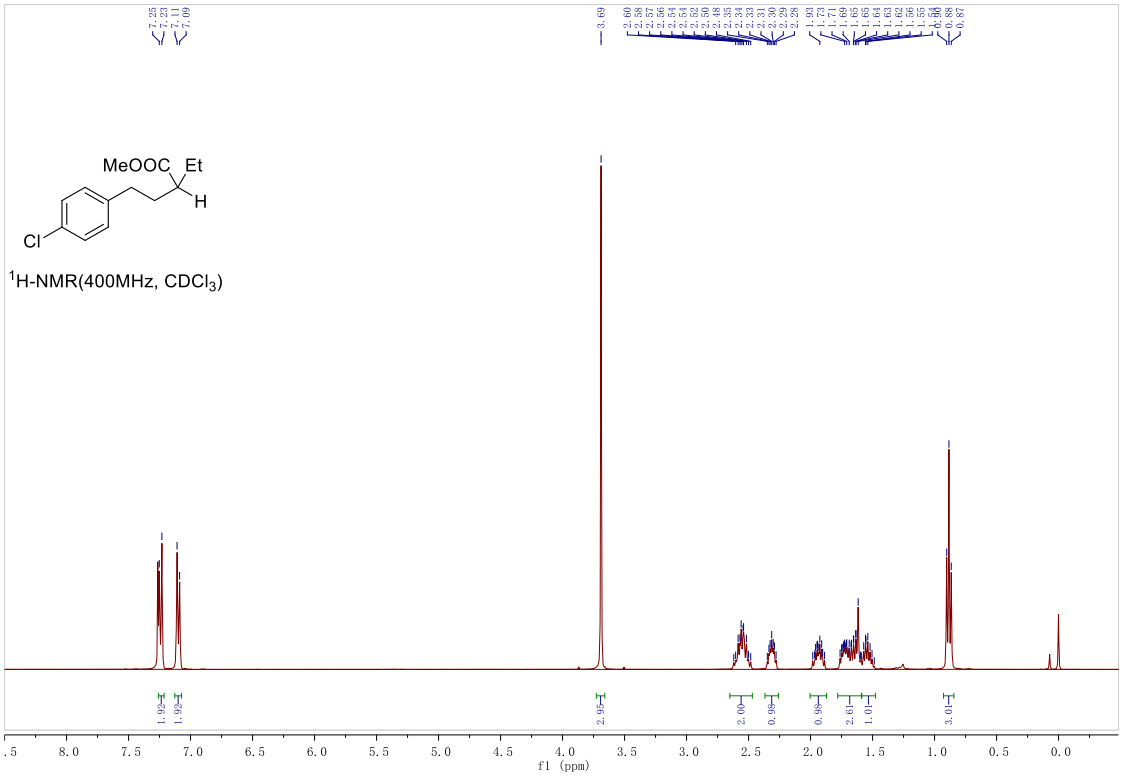
141.26
140.86
131.82
129.17
128.81
128.39
128.12
127.57
127.29
123.44
90.17
84.13
37.93
37.76
12.35
Ph
Ph
COOH
12
13C-NMR(100MHz, CDCl3)
f1 (ppm)

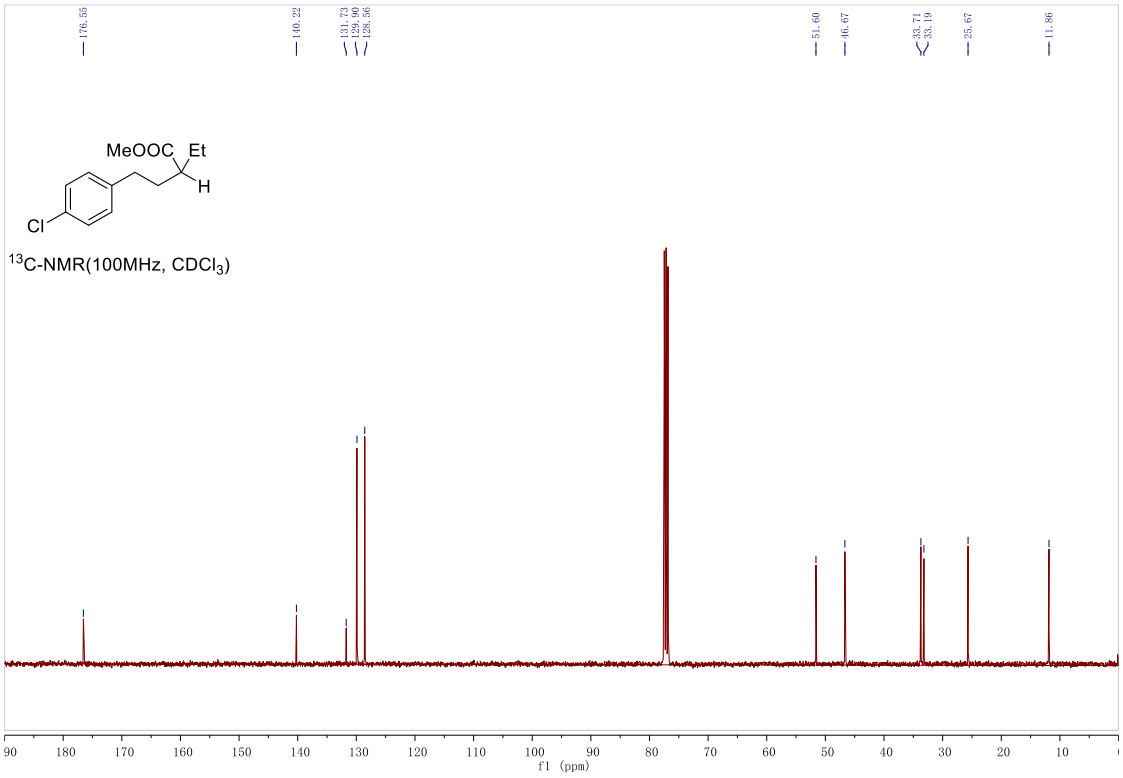

7.94
7.92
7.92
7.62
7.60
7.58
7.50
7.48
7.46
7.45
7.44
7.38
7.36
7.34
7.30
7.29
7.27
7.11
7.09
7.09
7.07
7.07
5.40
5.39
4.05
4.03
4.01
2.79
2.78
2.75
1.86
Ph
O
Ph
O
O
Ph
1H-NMR(400MHz, CDCl3)
2.02
1.04
6.15
2.15
4.01
1.03
1.91
1.00
2.00
3.09
f1 (ppm)

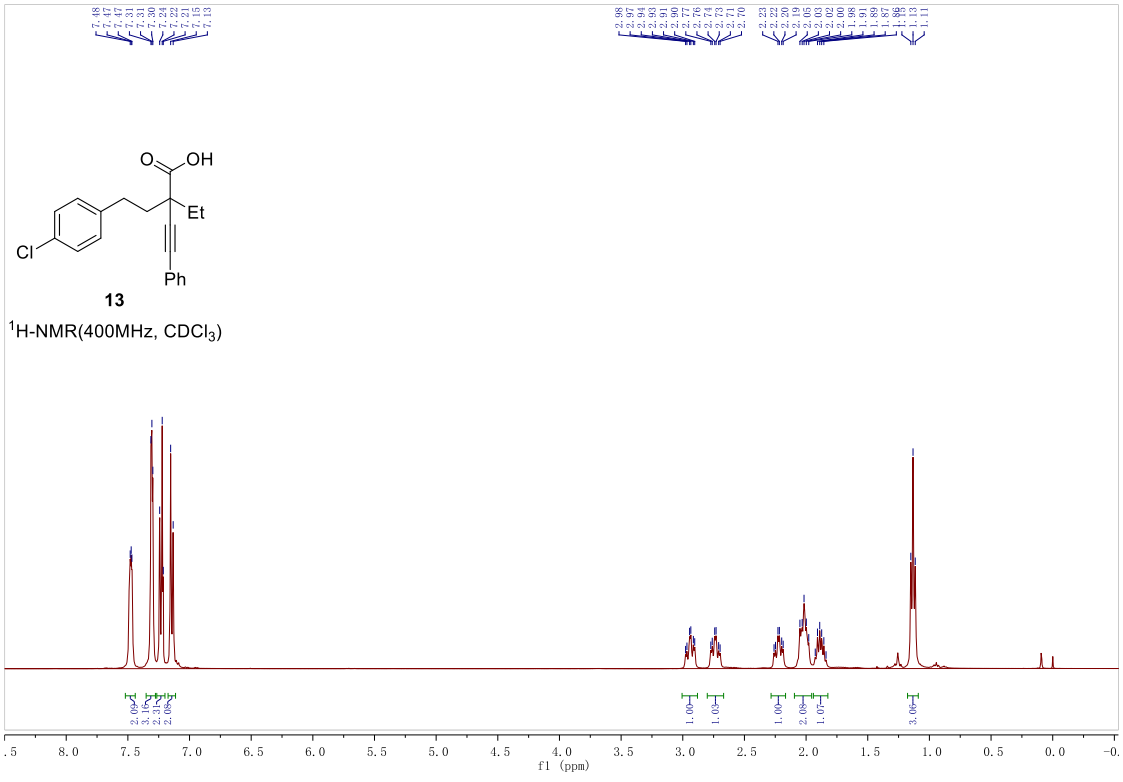

Ph
O
O
Ph
Ph
O
13C-NMR(100MHz, CDCl3)
f1 (ppm)

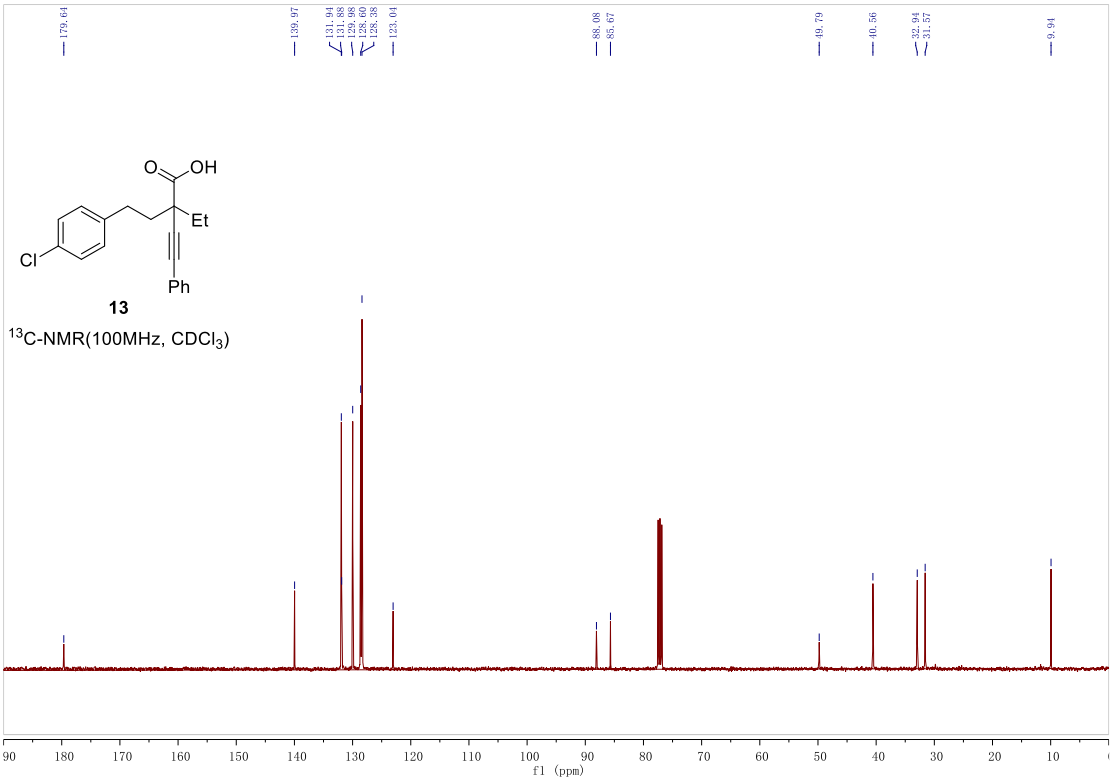

COOH
Et
Cl
1H-NMR(400MHz, CDCl3)
f1 (ppm)

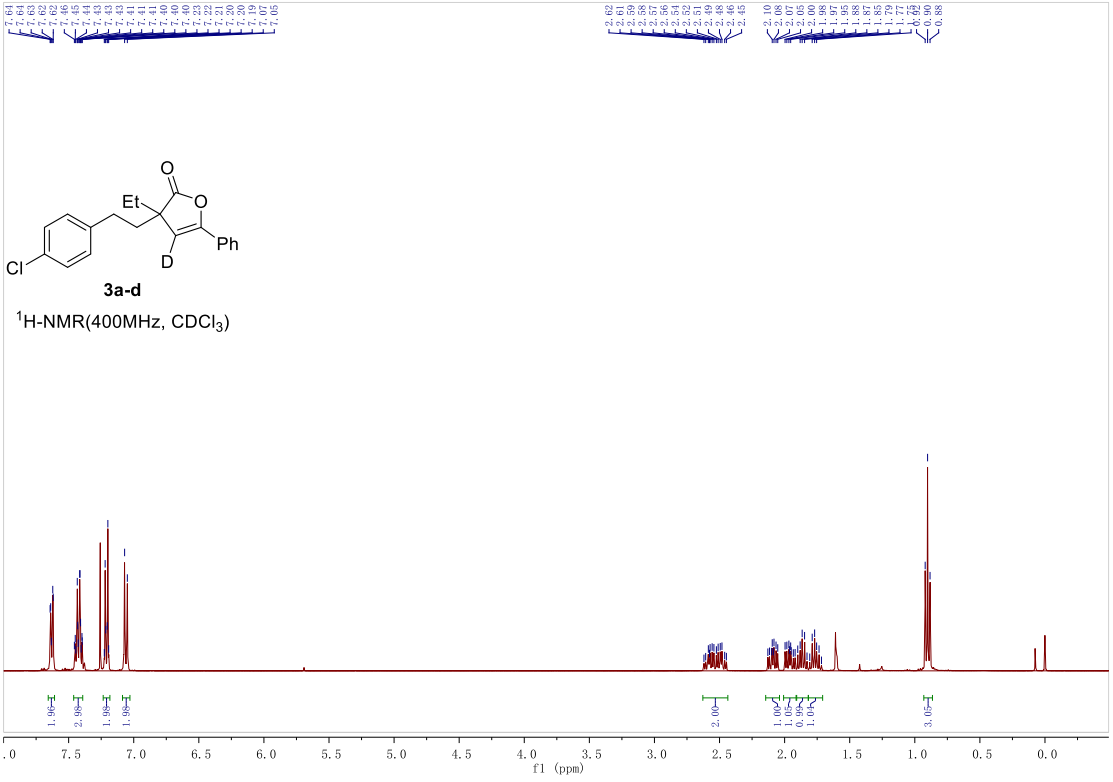

182.71
139.91
131.66
129.75
128.44
46.34
33.16
32.91
25.17
11.59
COOH
Et
Cl
13C-NMR(100MHz, CDCl3)
f1 (ppm)

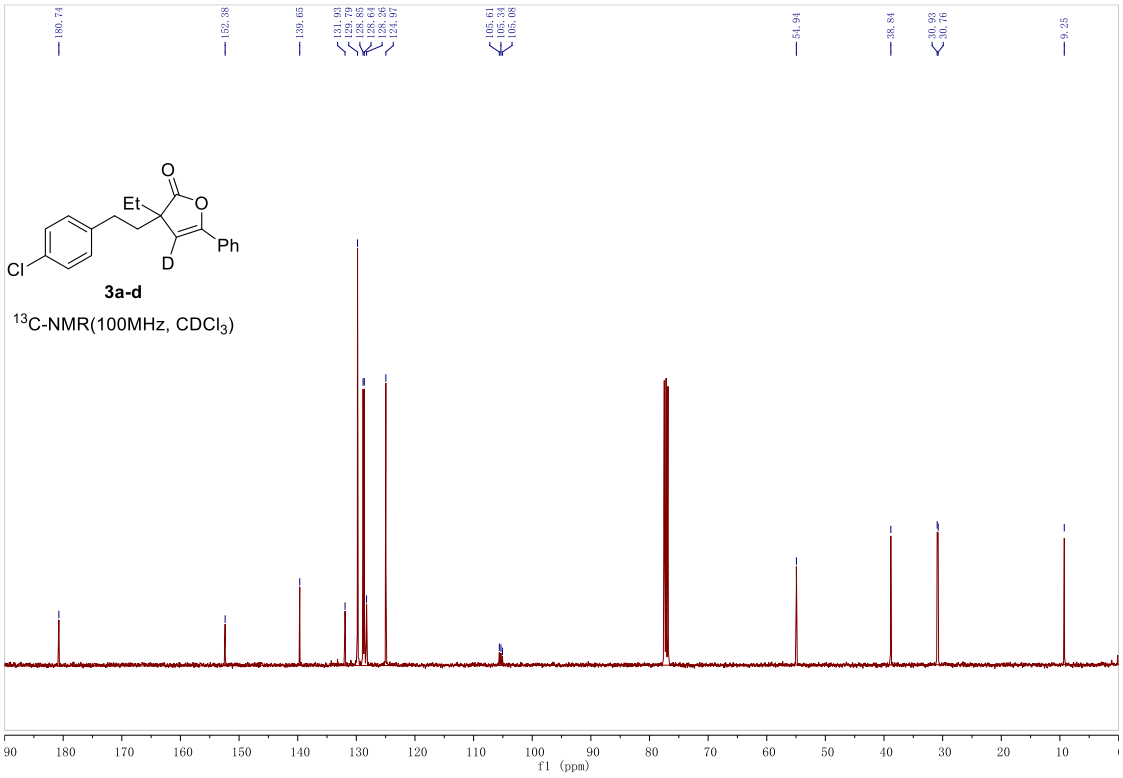

7.25
7.23
7.11
7.09
3.69
MeOOC
Et
H
Cl
1H-NMR(400MHz, CDCl3)
1.92
1.92
2.95
2.00
0.98
0.98
2.61
1.01
3.01
f1 (ppm)


MeOOC
Et
H
Cl
13C-NMR(100MHz, CDCl3)
f1 (ppm)


O
OH
Et
Cl
Ph
13
1H-NMR(400MHz, CDCl3)
f1 (ppm)


179.64
139.97
131.94
131.88
128.98
128.80
128.38
123.04
88.08
85.67
49.79
40.56
32.94
31.57
9.94
O
OH
Et
Cl
Ph
13
13C-NMR(100MHz, CDCl3)
f1 (ppm)


O
Et
O
Ph
Cl
D
3a-d
1H-NMR(400MHz, CDCl3)
f1 (ppm)


180.74
152.38
139.65
131.93
129.79
128.85
128.64
126.26
124.97
105.61
105.34
105.08
54.94
38.84
30.93
30.76
9.25
O
Et
O
Ph
D
Cl
3a-d
13C-NMR(100MHz, CDCl3)
90 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)