Supplementary Information

Palladium-Catalyzed Site-Selective Arylation of Aliphatic Ketones Enabled by A Transient Ligand

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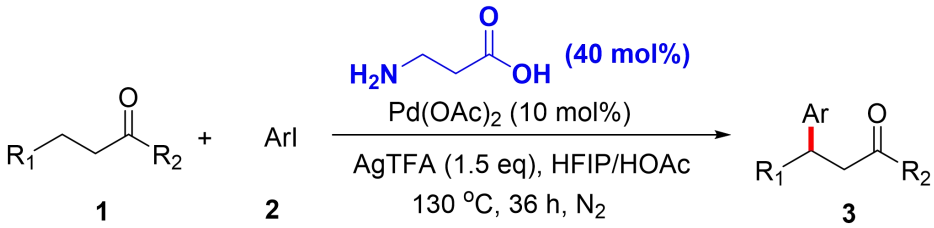
Supplementary Methods

General Information

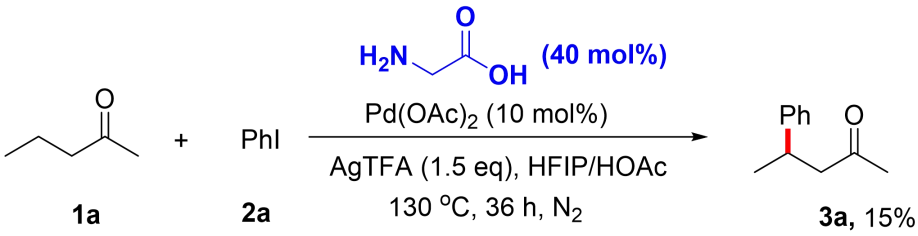
All the solvents and commercially available reagents were purchased from commercial sources (Adamas-beta®, TCI, J&K@, Sigma-Aldrich) and used directly. Thin layer chromatography (TLC) was performed on EMD precoated plates (silica gel 60 F254, Art 5715) and visualized by fluorescence quenching under UV light or phosphomolybdic acid solution (10 wt. % in ethanol). Column chromatography was performed on EMD Silica Gel 60 (200–300 Mesh) using a forced flow of 0.5–1.0 bar. The ^{1}H and ^{13}C NMR spectra were obtained on a Bruker AVANCE III-400 or 500 spectrometer. ^{1}H NMR data was reported as: chemical shift (δ ppm), multiplicity, coupling constant (Hz), and integration. ^{13}C NMR data was reported in terms of chemical shift (δ ppm), multiplicity, and coupling constant (Hz). Infrared (IR) spectra were recorded on a Nicolet 6700 spectrophotometer and are reported as wave number (cm^{-1}). Mass (MS) analysis was obtained using HP-6890 Series GC/MS system with Electronic Ionization (EI).

General procedure for the synthesis of 3



A 50 mL Schlenk tube was charged with β-alanine (7.13 mg, 0.08 mmol), $Pd(OAc)_2$ (4.49 mg, 0.02 mmol) and AgTFA (66.26 mg, 0.3 mmol). The tube was evacuated and filled with N_2 three times. Then, aliphatic ketone (**1**, 0.2 mmol), aryl iodide (**2**, 0.4 mmol) and the mixture of HFIP (1.5 mL) and HOAc (0.5 mL) were quickly added into the tube. The reaction mixture was stirred vigorously at room temperature for 60 min and then heated to 130 ˚C for 36 h. After cooling to room temperature, the reaction mixture was diluted with EtOAc (15 mL), filtered through a pad of Celite, and the filtrate was concentrated in vacuo. The residue was purified by flash chromatography on silica gel to yield the desired product **3**.

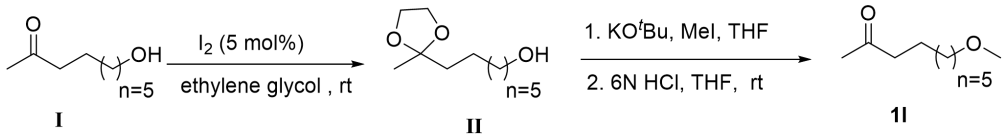
The procedure for glycine as the transient ligand



A 50 mL Schlenk tube was charged with glycine (6.00 mg, 0.08 mmol), $Pd(OAc)_2$(4.49 mg, 0.02 mmol) and AgTFA (66.26 mg, 0.3 mmol). The tube was evacuated and filled with N_2 with three times. Next, 2-pentanone (**1a**, 0.2 mmol), iodobenzene (**2a**, 0.4 mmol) and the mixture of HFIP (1. 5 mL) and HOAc (0. 5 mL) were added into the tube quickly. The reaction was then stirred vigorously at room temperature for 60 min before heated to 130 ˚C for 36 h. After cooling to room temperature, the reaction mixture was diluted with EtOAc (15 mL), filtered through a pad of Celite, and the filtrate was then concentrated in vacuo. The residue was purified by flash chromatography on silica gel to yield the desired product **3a** (15% yield).

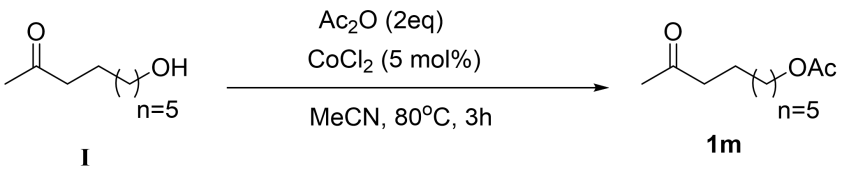
Procedure for preparation of starting materials

The procedure for the preparation of starting material 1l



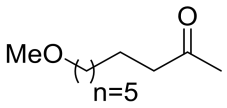
To a stirred solution of 9-hydroxynonan-2-one [4] **I** (5 mmol) in ethylene glycol (5 mL) was added iodine (0.25 mmol) and the mixture was stirred at room temperature overnight. The reaction was quenched with water (10 mL), and extracted with EtOAc (3 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered, and the solvent was evaporated to afford the crude oil, and it was purified by flash chromatography on silica gel to afford **II** as colorless oil (0.49 g, 48%). To a solution of **II** (2 mmol) in THF (10 mL) was added *t*-BuOK (4 mmol) in a few portions at room temperature, after 30 min, MeI (4 mmol) was added slowly to the mixture at 0 °C. Then, the reaction was warmed to 25 °C and stirred overnight. The reaction was quenched with water (10 mL), and extracted with EtOAc (3 x 10 mL). The combined organic layers were dried (Na_2SO_4), filtered, and the solvent was evaporated to afford the crude oil, then THF (5mL) and 6N HCl (5mL) were added and stirred overnight. The reaction was diluted with water (10 mL), and extracted with EtOAc (3 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered, and the solvent was evaporated to afford the crude oil. The crude oil was purified by flash chromatography on silica gel to afford **1l** as colorless oil (0.25 g, 73%).

The procedure for the preparation of starting material 1m



To a stirred solution of **I** (5 mmol) and $CoCl_2$ (0.25 mmol) in MeCN (10 mL) was added dropwise Ac_2O (10 mml) and the mixture was stirred at 80°C for 3 hours. The reaction was diluted with water (5 mL), and extracted with EtOAc (3 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered, and the solvent was evaporated to afford the crude oil. The crude oil was purified by flash chromatography on silica gel to afford **1m** as colorless oil (0.90 g, 90%).

Analytical Data of compounds



1l

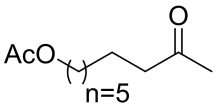
Colorless oil, yield: 72%

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.36 – 3.31 (m, 5H), 2.40 (t, *J* = 7.2 Hz, 2H), 2.11 (s, 3H), 1.59 – 1.53 (m, 4H), 1.35 – 1.24 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 209.22, 72.84, 58.51, 43.74, 29.82, 29.56, 29.21, 29.09, 25.95, 23.76.

IR (KBr) ν 2931, 2857, 1716, 1360, 1275, 1260, 1120, 764, 749 cm^{-1}.

Ms (EI): m/z = 172.0 [M^+].



1m

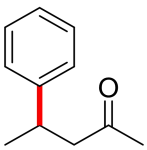
Colorless oil, yield: 90%

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.02 (t, *J* = 6.8 Hz, 2H), 2.40 (t, *J* = 7.2 Hz, 2H), 2.11 (s, 3H), 2.02 (s, 3H), 1.61 – 1.53 (m, 4H), 1.37 – 1.21 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 209.15, 171.19, 64.51, 43.67, 29.85, 28.99, 28.51, 25.72, 23.67, 20.98.

IR (KBr) ν 2934, 2858, 1738, 1716, 1366, 1242, 764, 750 cm^{-1}.

Ms (EI): m/z = 200.9 [M^+].

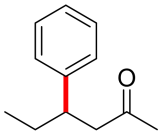


3a

Colorless oil, yield: 62%, [known compound[6]].

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 – 7.30 (m, 2H), 7.24 – 7.20 (m, 3H), 3.37 – 3.30 (m, 1H), 2.78 (dd, *J* = 16.5, 6.5 Hz, 1H), 2.68 (dd, *J* = 16.5, 8.0 Hz, 1H), 2.09 (s, 3H), 1.29 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 207.80, 146.18, 128.55, 126.77, 126.32, 52.01, 35.48, 30.55, 22.01.

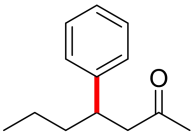


3b

Colorless oil, yield: 57%, [known compound[11]].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.26 (m, 2H), 7.21 – 7.15 (m, 3H), 3.06 – 2.99 (m, 1H), 2.72 (dd, *J* = 7.2, 0.8 Hz, 2H), 2.01 (s, 3H), 1.72 – 1.53 (m, 2H), 0.78 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 207.99, 144.32, 128.44, 127.55, 126.34, 50.57, 43.01, 30.61, 29.36, 11.96.

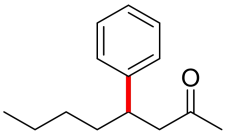


3c

Colorless oil, yield: 61%, [known compound[12]].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.26 (m, 2H), 7.20 – 7.16 (m, 3H), 3.16 – 3.09 (m, 1H), 2.73 (dd, *J* = 16.0, 7.6 Hz, 1H), 2.68 (dd, *J* = 16.0, 7.2 Hz, 1H), 2.01 (s, 3H), 1.62 – 1.52 (m, 2H), 1.20 – 1.10 (m, 2H), 0.84 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 207.98, 144.59, 128.45, 127.48, 126.31, 50.94, 41.09, 38.71, 30.64, 20.51, 13.95.

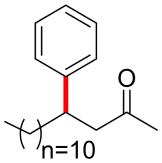


3d

Colorless oil, yield: 60%, [known compound[13]].

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.27 (m, 2H), 7.20 – 7.16 (m, 3H), 3.13 – 3.07 (m, 1H), 2.71 (dd, *J* = 7.5, 3.0 Hz, 2H), 2.01 (s, 3H), 1.63 – 1.54 (m, 2H), 1.29 – 1.09 (m, 4H), 0.82 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 208.05, 144.63, 128.45, 127.48, 126.30, 50.97, 41.31, 36.19, 30.64, 29.58, 22.59, 13.94.



3e

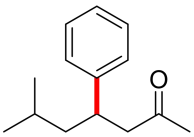
Colorless oil, yield: 50%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.26 (m, 2H), 7.20 – 7.16 (m, 3H), 3.14 – 3.07 (m, 1H), 2.70 (dd, *J* = 7.2, 2.4 Hz, 2H), 2.01 (s, 3H), 1.60 – 1.57 (m, 2H), 1.31 – 1.20 (m, 18H), 0.87 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 208.03, 144.64, 128.45, 127.48, 126.30, 50.98, 41.35, 36.50, 31.91, 30.64, 29.62, 29.61, 29.59, 29.54, 29.48, 29.34, 27.39, 22.69, 14.11.

IR (KBr) ν 3028, 2925, 2854, 1718, 1454, 1356, 1159, 757, 700, 547 cm^{-1}.

Ms (EI): m/z = 302.4 [M^+].



3f

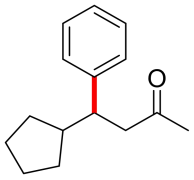
Colorless oil, yield: 55%

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.26 (m, 2H), 7.20 – 7.16 (m, 3H), 3.26 – 3.19 (m, 1H), 2.71 (dd, *J* = 16.0, 7.6 Hz, 1H), 2.64 (dd, *J* = 16.0, 6.8 Hz, 1H), 1.99 (s, 3H), 1.59 – 1.53 (m, 1H), 1.41 – 1.27 (m, 2H), 0.88 (d, *J* = 6.4 Hz, 3H), 0.81 (d, *J* = 6.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 207.95, 144.54, 128.48, 127.49, 126.32, 51.47, 45.65, 39.16, 30.68, 25.32, 23.46, 21.63.

IR (KBr) ν 3026, 2925, 2857, 1715, 1494, 1452, 1357, 1158, 755, 700, 539 cm^{-1}.

Ms (EI): m/z = 252.2 [M$^+$].



3g

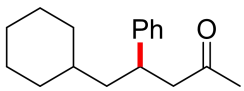
Colorless oil, yield: 50%

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 – 7.24 (m, 2H), 7.18 – 7.14 (m, 3H), 2.94 – 2.88 (m, 1H), 2.79 (d, *J* = 7.2 Hz, 2H), 2.06 – 1.97 (m, 1H), 1.93 (s, 3H), 1.88 – 1.80 (m, 1H), 1.66 – 1.32 (m, 5H), 1.26 – 1.19 (m, 1H), 1.04 – 0.99 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 208.26, 144.49, 128.29, 127.85, 126.23, 49.83, 47.33, 46.41, 31.40, 31.38, 30.72, 25.23, 24.93.

IR (KBr) ν 3027, 2952, 2867, 1716, 1452, 1357, 1166, 755, 701, 540 cm^{-1}.

Ms (EI): m/z = 216.2 [M$^+$].



3h

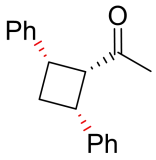
Colorless oil, yield: 51%

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.29 (m, 2H), 7.22 – 7.19 (m, 3H), 3.32 – 3.25 (m, 1H), 2.72 (dd, *J* = 16.0, 8.0 Hz, 1H), 2.66 (dd, *J* = 16.0, 6.8 Hz, 1H), 2.01 (s, 3H), 1.87 – 1.84 (m, 1H), 1.68 – 1.40 (m, 6H), 1.13 – 0.85 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 208.16, 144.69, 128.49, 127.47, 126.28, 51.47, 44.22, 38.29, 34.69, 34.04, 32.55, 30.73, 26.59, 26.18, 26.07.

IR (KBr) ν 3027, 2922, 2850, 1717, 1449, 1356, 1157, 758, 700 cm^{-1}.

Ms (EI): m/z = 244.8 [M$^+$].



3i

d.r. > 20:1:1

Colorless oil, yield: 50%.

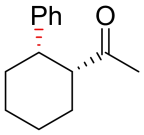
The relative stereochemistry was determined by NOSEY analysis and literature report [1].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.29 (m, 8H), 7.25 – 7.21 (m, 2H), 3.65 – 3.58 (dd, *J* = 18.0, 10.0 Hz, 2H), 3.38 (t, *J* = 9.6 Hz, 1H), 2.71 –2.64 (m, 1H), 2.31 (q, *J* = 10.4 Hz, 1H), 1.96 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 207.63, 143.13, 128.65, 126.91, 126.74, 61.55, 39.35, 32.72, 28.90.

IR (KBr) ν 3027, 2936, 1706, 1495, 1355, 1170, 744, 699 cm^{-1}.

Ms (EI): m/z = 250.1 [M^+].



3j

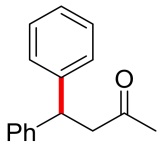
d.r. > 20:1

Colorless oil, yield: 37%, [known compound[14]].

The relative stereochemistry was determined by NOSEY analysis and literature report [1].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 – 7.25 (m, 2H), 7.18 – 7.15 (m, 3H), 2.77 – 2.74 (m, 2H), 1.93 – 1.83 (m, 4H), 1.80 (s, 3H), 1.48 – 1.42 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 212.12, 144.82, 128.51, 127.31, 126.40, 57.36, 46.49, 34.46, 29.88, 29.56, 26.26, 25.56.

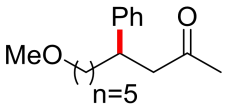


3k

Colorless oil, yield: 41%, [known compound[8]].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.15 (m, 10H), 4.59 (t, *J* = 7.6 Hz, 1H), 3.17 (d, *J* = 7.6 Hz, 2H), 2.07 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 206.81, 143.87, 128.60, 127.73, 126.47, 49.72, 46.09, 30.64.



3l

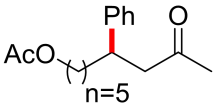
Colorless oil, yield: 43%

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (t, *J* = 7.6 Hz, 2H), 7.20 – 7.15 (m, 3H), 3.31 – 7.29 (m, 5H), 3.12 – 3.09 (m, 1H), 2.76 – 2.65 (m, 2H), 2.01 (s, 3H), 1.60 – 1.55 (m, 2H), 1.52 – 1.45 (m, 2H), 1.32 – 1.11 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 207.89, 144.48, 128.45, 127.45, 126.32, 72.74, 58.47, 50.94, 41.23, 36.36, 30.62, 29.42, 27.17, 26.00.

IR (KBr) ν 2930, 2857, 1715, 1275, 1260, 1119, 913, 748, 701 cm^{-1}.

Ms (EI): m/z = 248.2 [M$^+$].



3m

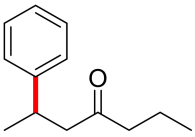
Colorless oil, yield: 41%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (t, *J* = 7.6 Hz, 2H), 7.23 – 7.18 (m, 3H), 4.01 (t, *J* = 6.8 Hz, 2H), 3.16 – 3.09 (m, 1H), 2.79 – 2.68 (m, 2H), 2.04 (s, 6H), 1.65 – 1.54 (m, 4H), 1.33 – 1.14 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 207.92, 171.21, 144.37, 128.51, 127.44, 126.41, 64.50, 50.92, 41.16, 36.25, 30.67, 28.42, 27.02, 25.83, 20.99.

IR (KBr) ν 2931, 2855, 1712, 1737, 1275, 1260, 764, 750 cm^{-1}.

Ms (EI): m/z = 276.9 [M$^+$].

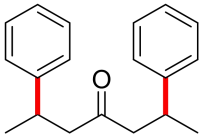


3na

Colorless oil, yield: 23%, [known compound[7]].

^{1}H NMR (400 MHz, $CDCl_3$) δ7.30 – 7.26 (m, 2H), 7.22 – 7.15 (m, 3H), 3.36 – 3.28 (m, 1H), 2.71 (dd, *J* = 16.0, 6.4 Hz, 1H), 2.62 (dd, *J* = 16.0, 8.0 Hz, 1H), 2.35 – 2.21 (m, 2H), 1.58 – 1.49 (m, 2H), 1.26 (d, *J* = 6.8 Hz, 3H), 0.84 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 209.99, 146.36, 128.50, 126.80, 126.25, 51.16, 45.46, 35.43, 21.95, 17.09, 13.67.



3nb (d.r. = 1:1)

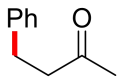
Colorless oil, yield: 20%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.24 (m, 4H), 7.20 – 7.13 (m, 6H), 3.29 – 3.23 (m, 2H), 2.68 – 2.46 (m, 4H), 1.19 (d, *J* = 6.8 Hz, 3H), 1.17 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 208.70, 208.58, 146.24, 146.21, 128.50, 126.78, 126.75, 126.26, 126.24, 51.87, 51.75, 35.30, 35.23, 21.87.

IR (KBr) ν3027, 2961, 2920, 2850, 1713, 1493, 1452, 1372, 760, 699, 534cm^{-1}.

Ms (EI): m/z = 266.2 [M^+].

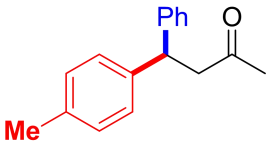


3oa

Colorless oil, yield: 30%, [known compound[15]].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (t, *J* = 7.2 Hz, 2H), 7.21 – 7.18 (m, 3H), 2.90 (t, *J* = 7.6 Hz, 2H), 2.76 (t, *J* = 7.6 Hz, 2H), 2.14 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 207.87, 141.01, 128.50, 128.29, 126.12, 45.18, 30.05, 29.77.



4

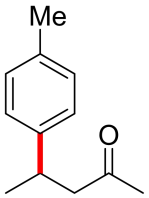
Colorless oil, yield: 41%

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 – 7.06 (m, 9H), 4.54 (t, *J* = 7.6 Hz, 1H), 3.15 (d, *J* = 7.6 Hz, 2H), 2.28 (s, 3H), 2.06 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 206.96, 144.12, 140.86, 135.99, 129.29, 128.58, 127.66, 127.57, 126.38, 49.81, 45.75, 30.63, 20.96.

IR (KBr) ν 3025, 2923, 1718, 1512, 1356, 1158, 699, 547 cm^{-1}.

Ms (EI): m/z = 238.1 [M^+].

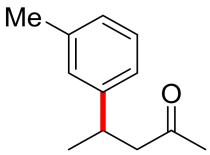


3p

Colorless oil, yield: 55%, [known compound[5]].

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13 (s, 4H), 3.33 – 3.26 (m, 1H), 2.76 (dd, *J* = 16.5, 6.5 Hz, 1H), 2.66 (dd, *J* = 16.5, 8.0 Hz, 1H), 2.34 (s, 3H), 2.08 (s, 3H), 1.27 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 207.92, 143.16, 135.79, 129.22, 126.62, 52.13, 35.12, 30.52, 22.11, 20.96.

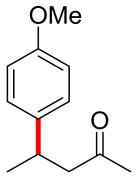


3q

Colorless oil, yield: 65%, [known compound[11]].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (t, *J* = 7.6 Hz, 1H), 7.01 – 7.00 (m, 3H), 3.31 – 3.22 (m, 1H), 2.74 (dd, *J* = 16.0, 6.4 Hz, 1H), 2.64 (dd, *J* = 16.0, 8.0 Hz, 1H), 2.33 (s, 3H), 2.06 (s, 3H), 1.25 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 207.88, 146.17, 138.09, 128.45, 127.60, 127.07, 123.71, 52.05, 35.42, 30.55, 22.03, 21.47.

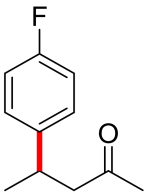


3r

Colorless oil, yield: 60%, [known compound[16]].

^{1}H NMR (400 MHz, CDCl3) δ 7.20 – 7.05 (m, 2H), 6.90 – 6.76 (m, 2H), 3.78 (s, 3H), 3.26 (dd, *J* = 14.2, 7.0 Hz, 1H), 2.72 (dd, *J* = 16.0, 6.8 Hz, 1H), 2.62 (dd, *J* = 16.0, 7.7 Hz, 1H), 2.05 (s, 3H), 1.24 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, CDCl3) δ 207.98 (s), 158.05, 138.26, 127.66, 113.93, 55.24, 52.28, 34.76, 30.56, 22.22.

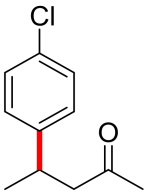


3s

Colorless oil, yield: 62%, [known compound[7]].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 – 7.14 (m, 2H), 7.00 – 6.94 (m, 2H), 3.34 – 3.26 (m, 1H), 2.72 (dd, *J* = 16.4, 6.8 Hz, 1H), 2.64 (dd, *J* = 16.4, 7.6 Hz, 1H), 2.06 (s, 3H), 1.24 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 207.49, 161.38 (d, *J* = 244.0 Hz), 141.83 (d, *J* = 3.2 Hz), 128.16 (d, *J* = 7.8 Hz), 115.26 (d, *J* = 21.1 Hz), 52.06, 34.70, 30.56, 22.15.

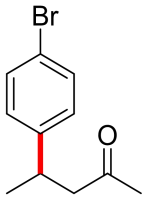


3t

Colorless oil, yield: 70%, [known compound[8]].

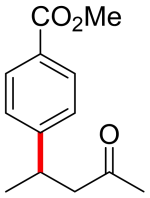
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.4 Hz, 2H), 7.14 (d, *J* = 8.4 Hz, 2H), 3.33 – 3.25 (m, 1H),

2.72 (dd, *J* = 16.4, 6.8 Hz, 1H), 2.64 (dd, *J* = 16.4, 7.6 Hz, 1H), 2.06 (s, 3H), 1.24 (d, *J* = 7.0 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 207.27, 144.68, 131.93, 128.64, 128.18, 51.79, 34.78, 30.56, 21.96.



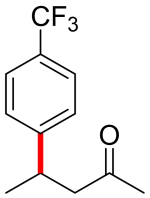
3u

Colorless oil, yield: 65%, [known compound[8]].
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.0 Hz, 2H), 7.11 (d, *J* = 8.5 Hz, 2H), 3.33 – 3.26 (m, 1H), 2.73 (dd, *J* = 16.5, 6.5 Hz, 1H), 2.66 (dd, *J* = 16.5, 7.5 Hz, 1H), 2.09 (s, 3H), 1.26 (d, *J* = 7.0 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 207.24, 145.20, 131.59, 128.59, 119.96, 51.72, 34.82, 30.56, 21.91.



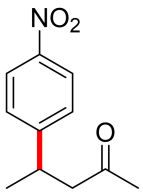
3v

Colorless oil, yield: 55%.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.5 Hz, 2H), 7.40 – 7.21 (d, *J* = 8.5 Hz, 2H), 3.91 (s, 3H), 3.43 – 3.35 (m, 1H), 2.78 (dd, *J* = 16.5, 6.5 Hz, 1H), 2.70 (dd, *J* = 16.5, 8.0 Hz, 1H), 2.09 (s, 3H), 1.29 (d, *J* = 7.0 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 207.11, 166.98, 151.61, 129.93, 128.33, 126.86, 51.99, 51.50, 35.33, 30.55, 21.75.
IR (KBr) ν 2957, 1720, 1611, 1436, 1280, 1114, 1019, 774, 708, 539 cm^{-1}.
Ms (EI): m/z = 220.1 [M^+].



3w

Colorless oil, yield: 73%, [known compound[9]].
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 3.44 – 3.37 (m, 1H), 2.79 (dd, *J* = 16.5, 6.5 Hz, 1H), 2.71 (dd, *J* = 16.5, 7.5 Hz, 1H), 2.10 (s, 3H), 1.29 (d, *J* = 7.0 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 206.94, 150.31, 128.65 (q, *J* = 32.4 Hz), 127.19, 125.48 (q, *J* = 3.7 Hz), 124.24 (q, *J* = 271.8 Hz), 51.49, 35.08, 30.51, 21.80.

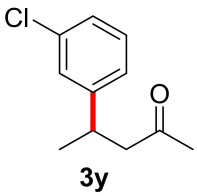


3x

Colorless oil, yield: 57%, [known compound[10]].

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.8 Hz, 2H), 7.38 (d, *J* = 8.8 Hz, 2H), 3.49 – 3.41 (m, 1H), 2.80 (dd, *J* = 17.2, 7.2 Hz, 1H), 2.74 (dd, *J* = 17.2, 7.2 Hz, 1H), 2.10 (s, 3H), 1.30 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 206.43, 153.99, 146.57, 127.76, 123.84, 51.20, 35.05, 30.49, 21.69.

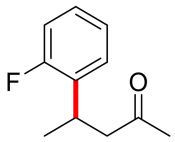


3y

Colorless oil, yield: 64%, [known compound[5]].

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 – 7.16 (m, 3H), 7.09 (d, *J* = 7.5 Hz, 1H), 3.33 – 3.26 (m, 1H), 2.74 (dd, *J* = 16.5, 6.5 Hz, 1H), 2.65 (dd, *J* = 16.5, 7.5 Hz, 1H), 2.08 (s, 3H), 1.25 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 207.13, 148.34, 134.29, 129.81, 126.95, 126.49, 125.15, 51.62, 35.04, 30.55, 21.83.

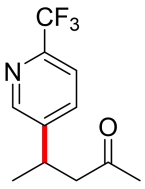


3z

Colorless oil, yield: 52%, [known compound[9]].

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 – 7.15 (m, 2H), 7.09 – 7.06 (m, 1H), 7.02 – 6.98 (m, 1H), 3.61 – 3.54 (m, 1H), 2.81 (dd, *J* = 16.5, 6.0 Hz, 1H), 2.70 (dd, *J* = 16.5, 8.0 Hz, 1H), 2.10 (s, 3H), 1.28 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 207.39, 160.68 (d, *J* = 245.2 Hz), 132.63 (d, *J* = 14.1 Hz), 128.26 (d, *J* = 5.2 Hz), 127.76 (d, *J* = 8.4 Hz), 124.18 (d, *J* = 3.4 Hz), 115.59 (d, *J* = 22.6 Hz),50.37, 30.23, 29.48, 20.48.



3za

Colorless oil, yield: 52%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, *J* = 1.6 Hz, 1H), 7.72 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.61 (d, *J* = 8.0 Hz, 1H), 3.49 – 3.40 (m, *J* = 7.0 Hz, 1H), 2.87 – 2.73 (m, 2H), 2.11 (s, 3H), 1.31 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 206.18, 149.08, 146.20 (q, *J* = 34.7 Hz), 144.91 (q, *J* = 1.1 Hz), 135.73, 121.61 (q, *J* = 273.8 Hz), 120.28 (q, *J* = 2.7 Hz), 50.87, 32.48, 30.37, 21.49.
IR (KBr) ν 2969, 2933, 1717, 1408, 1340, 1172, 1136, 1087, 1024, 853, 605 cm^{-1}.
Ms (EI): m/z = 230.9 [M^+].

Supplementary References

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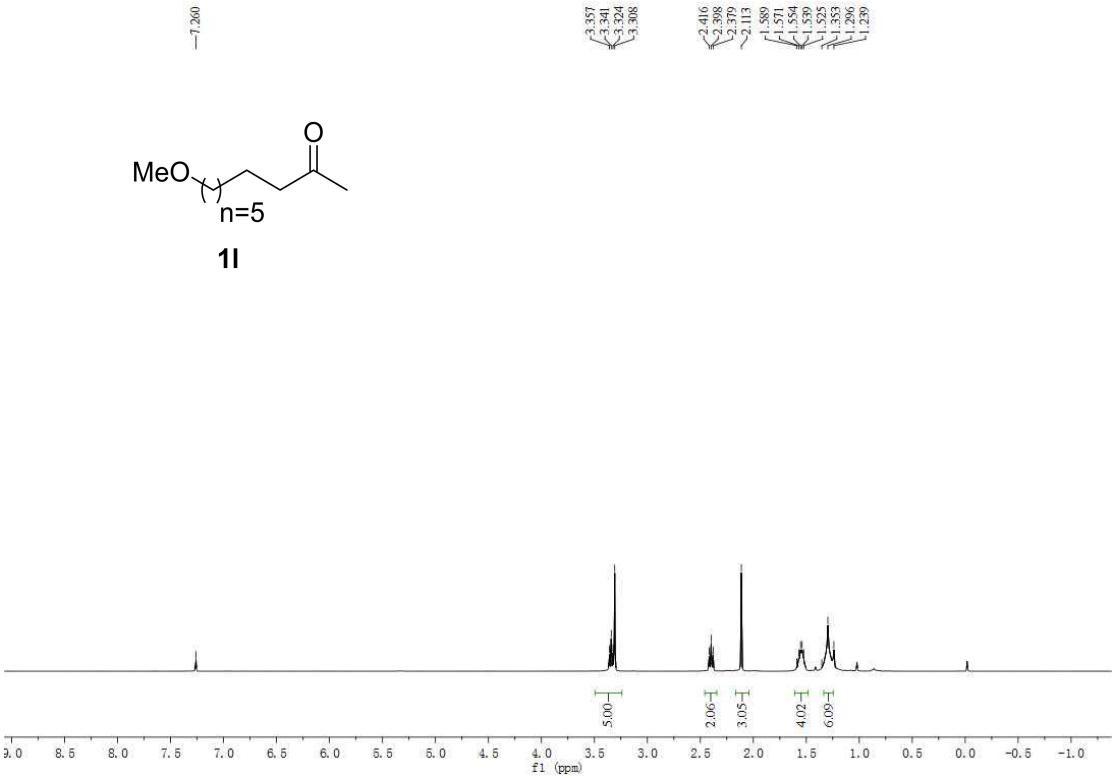
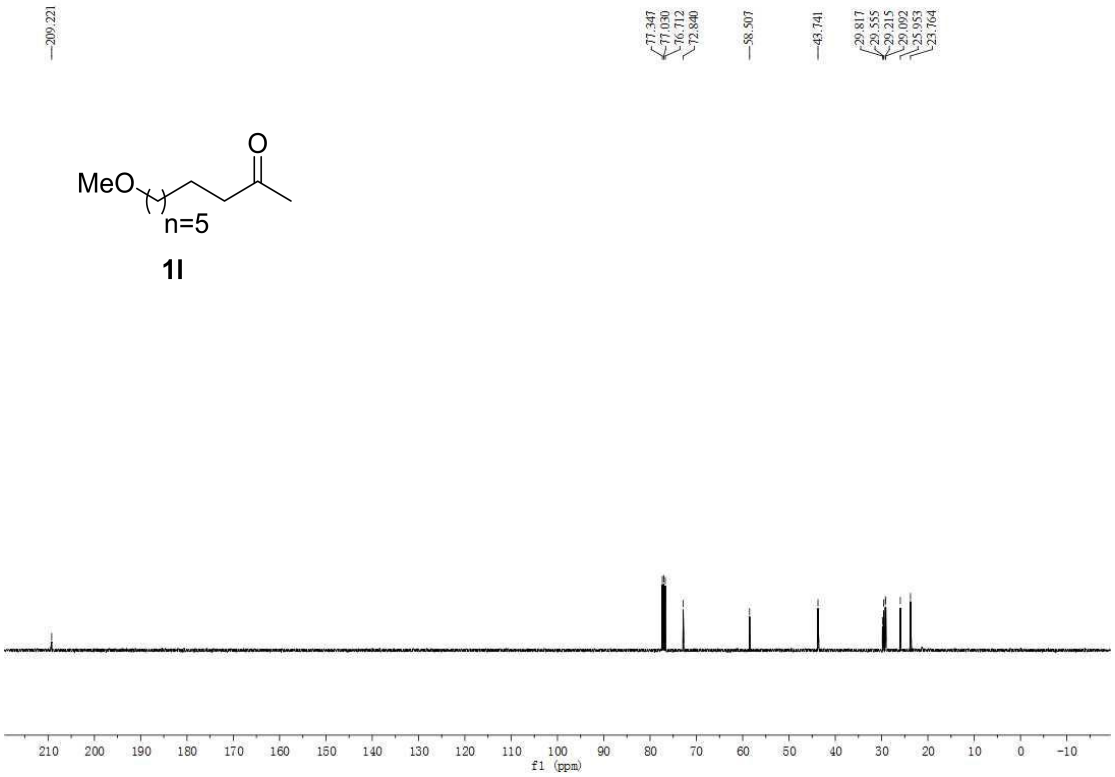
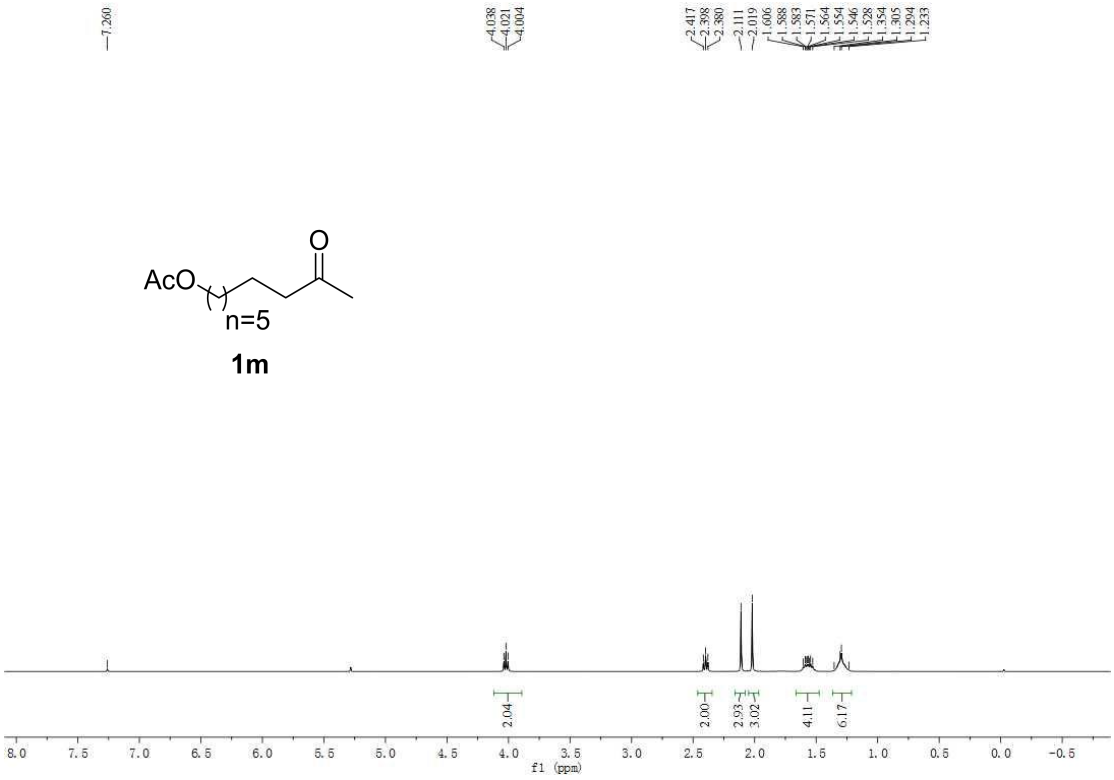
^{1}H and ^{13}C NMR Spectra



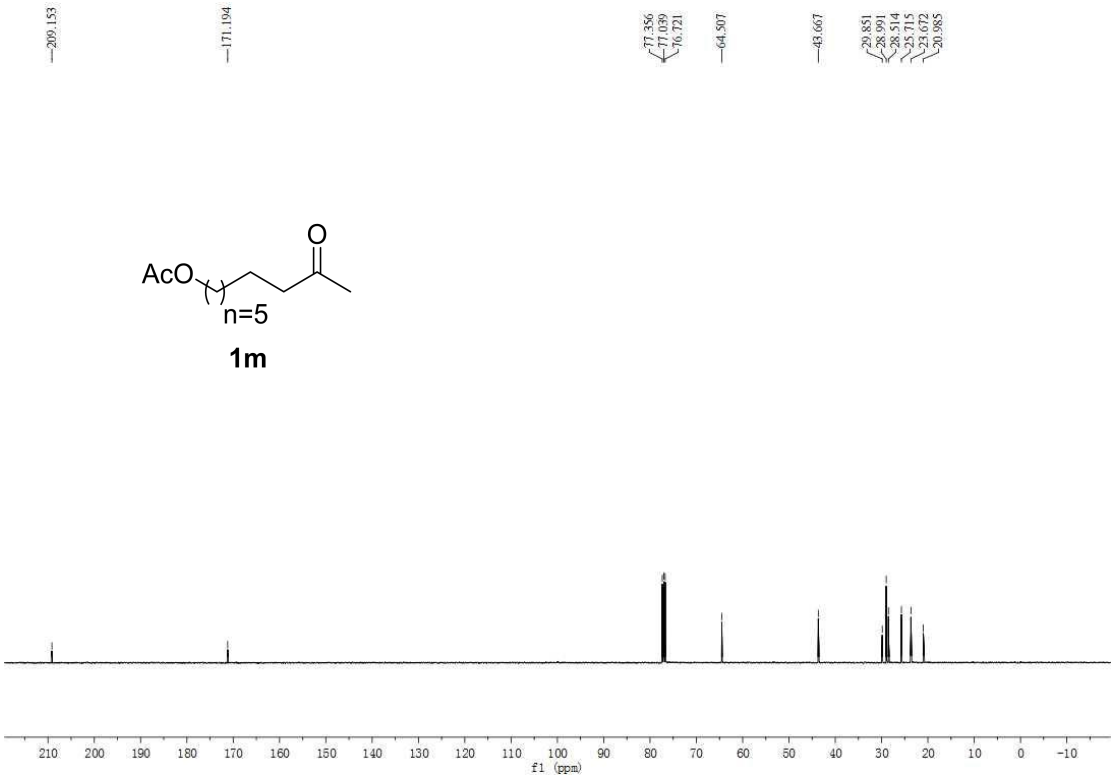
Supplementary Figure 1. ^{1}H NMR (400 MHz, $CDCl_3$)spectrum for 1l.



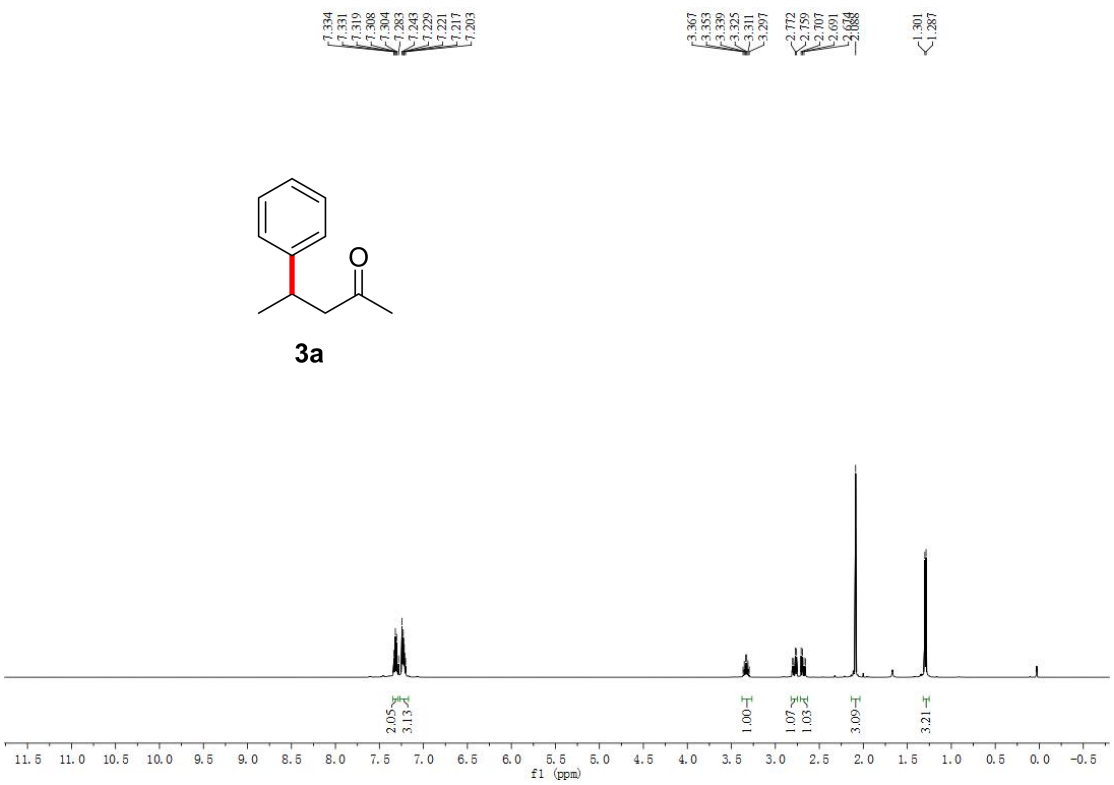
Supplementary Figure 2. ^{13}CNMR(126 MHz, $CDCl_3$) spectrum for 1l.



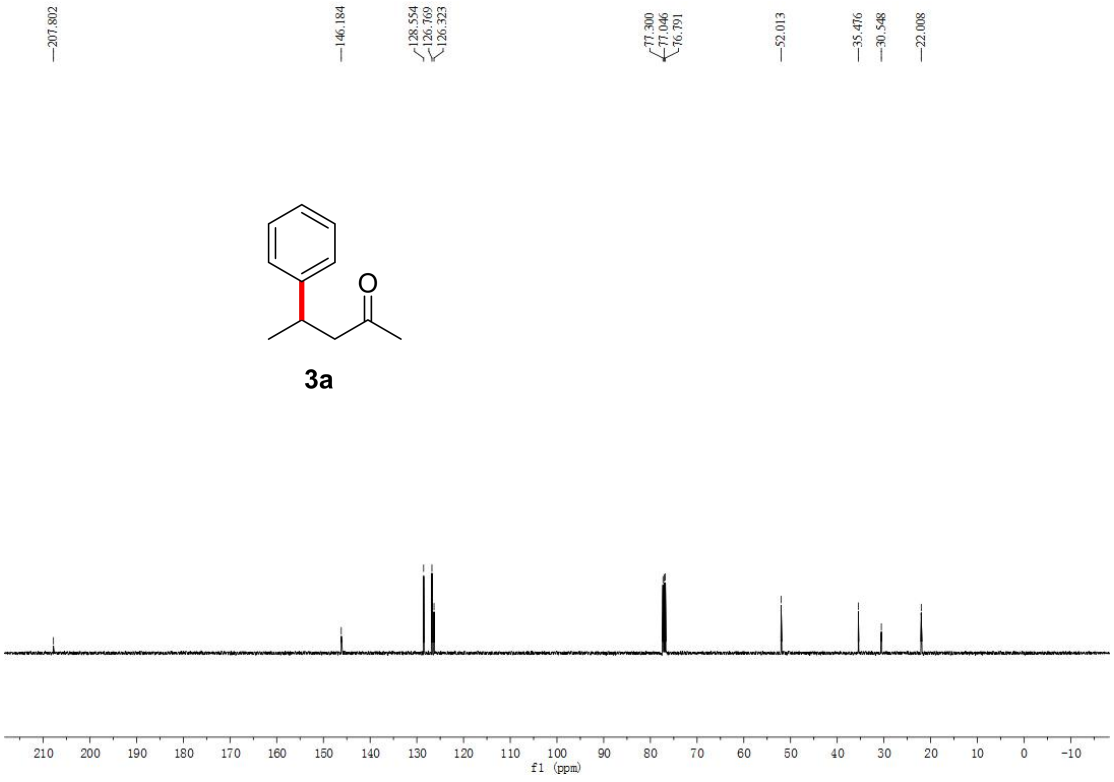
Supplementary Figure 3. ^{1}H NMR (400 MHz, $CDCl_3$)spectrum for 1m.



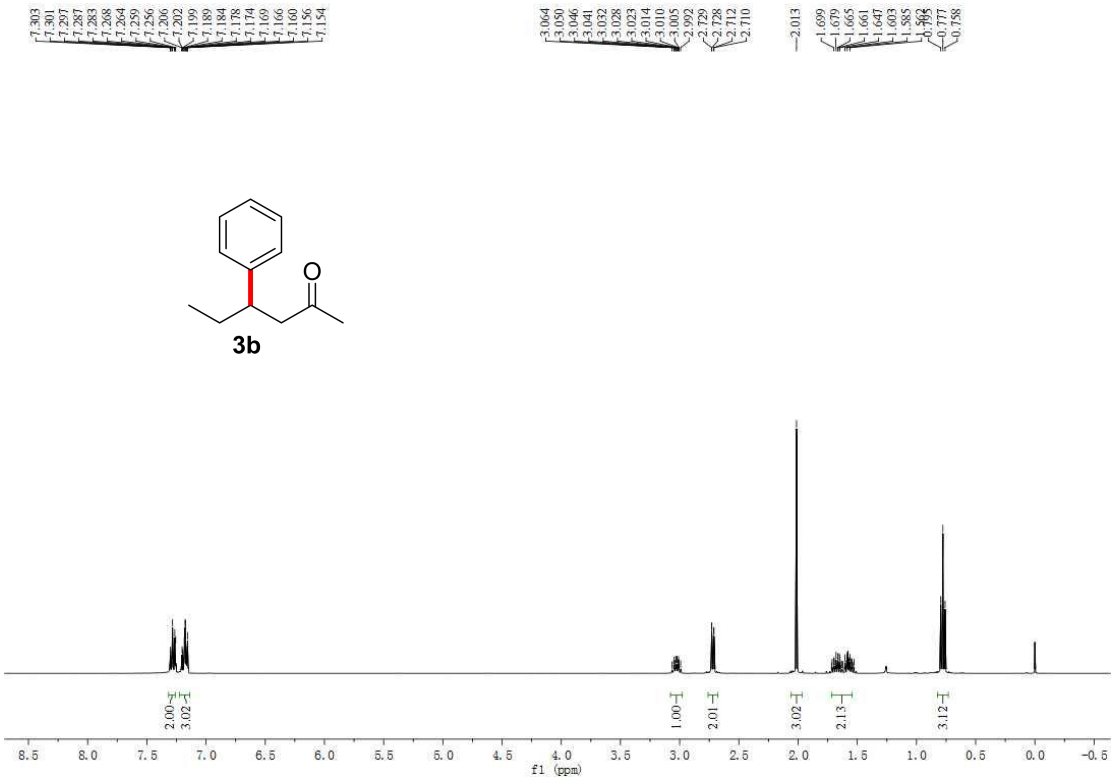
Supplementary Figure 4. ^{13}CNMR(101 MHz, $CDCl_3$) spectrum for 1m.



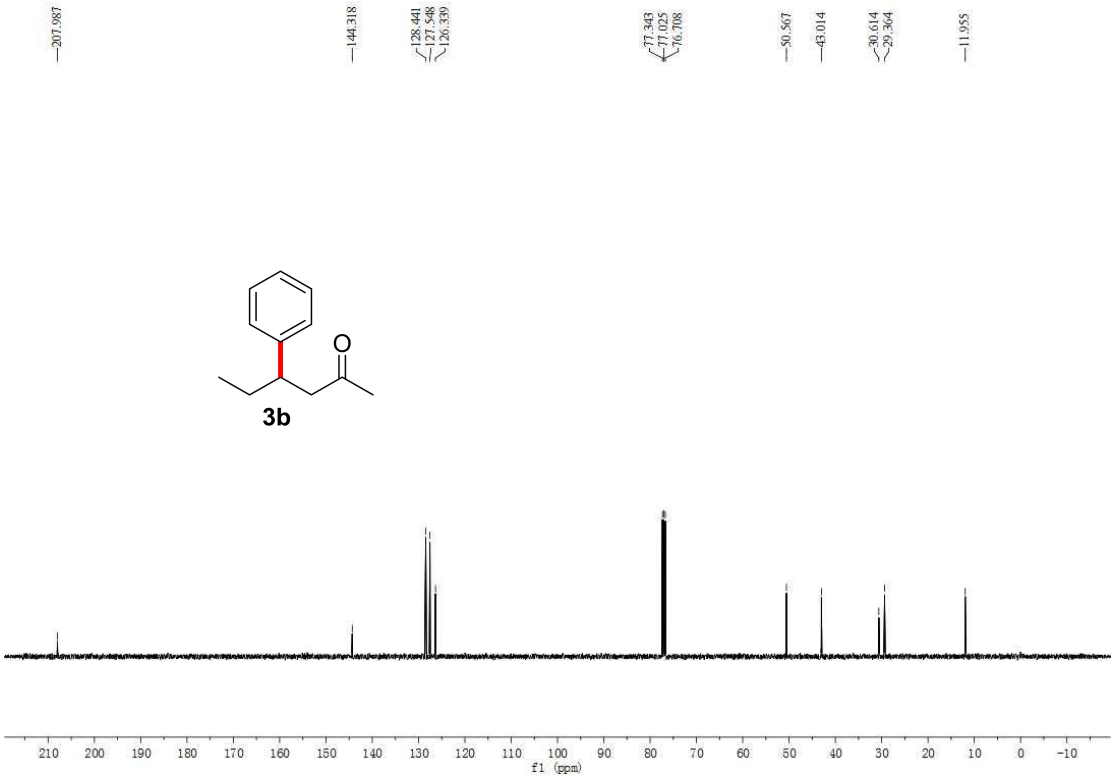
Supplementary Figure 5. ^{1}H NMR (500 MHz, $CDCl_3$) spectrum for 3a.



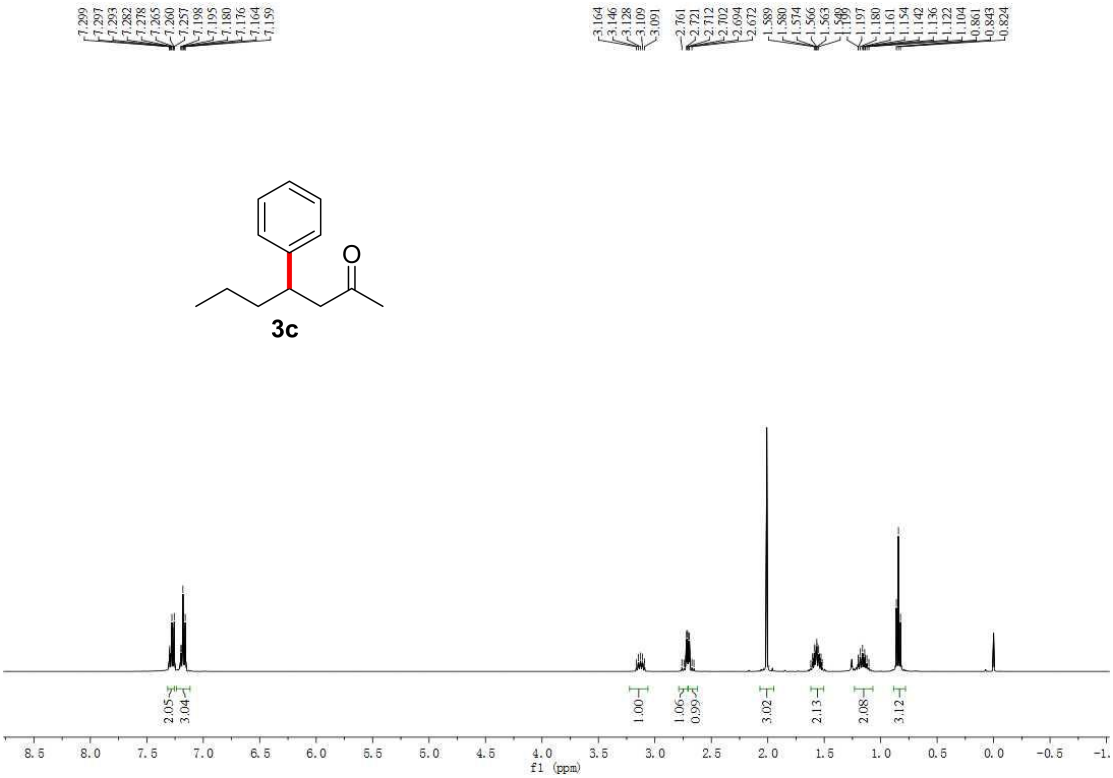
Supplementary Figure 6. ^{13}C NMR (126 MHz, $CDCl_3$) spectrum for 3a.



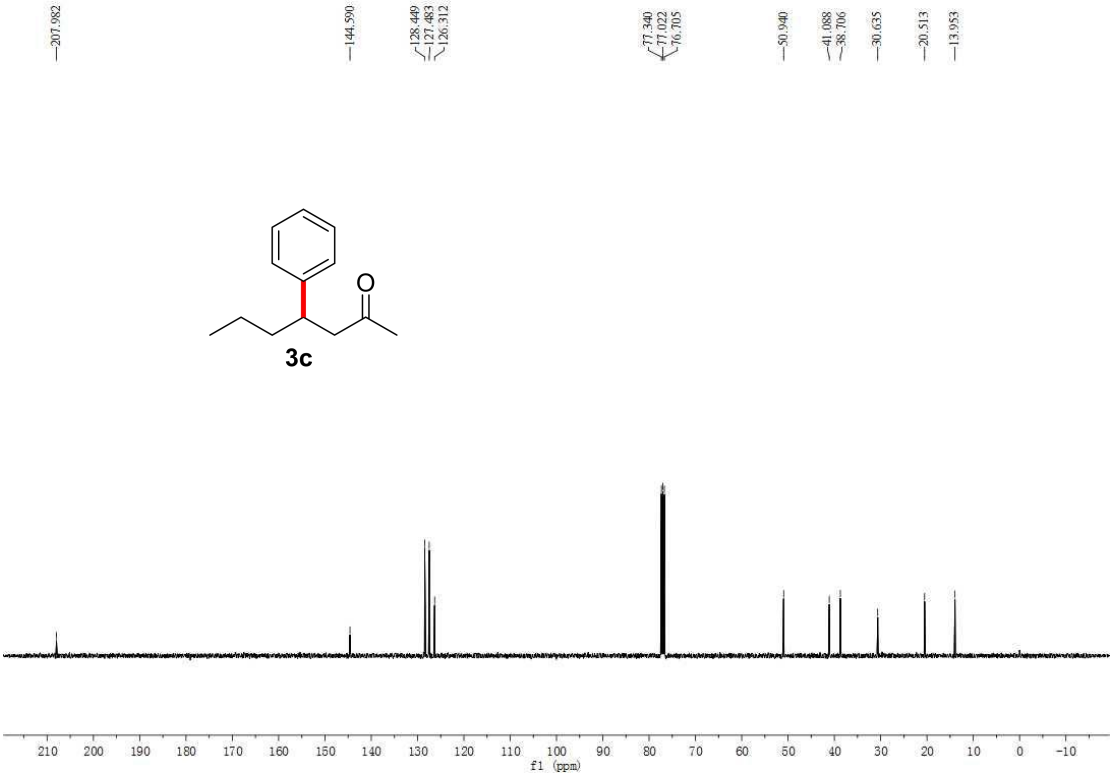
Supplementary Figure 7. ^{1}**H NMR (400 MHz, CDCl$_3$) spectrum for 3b.**



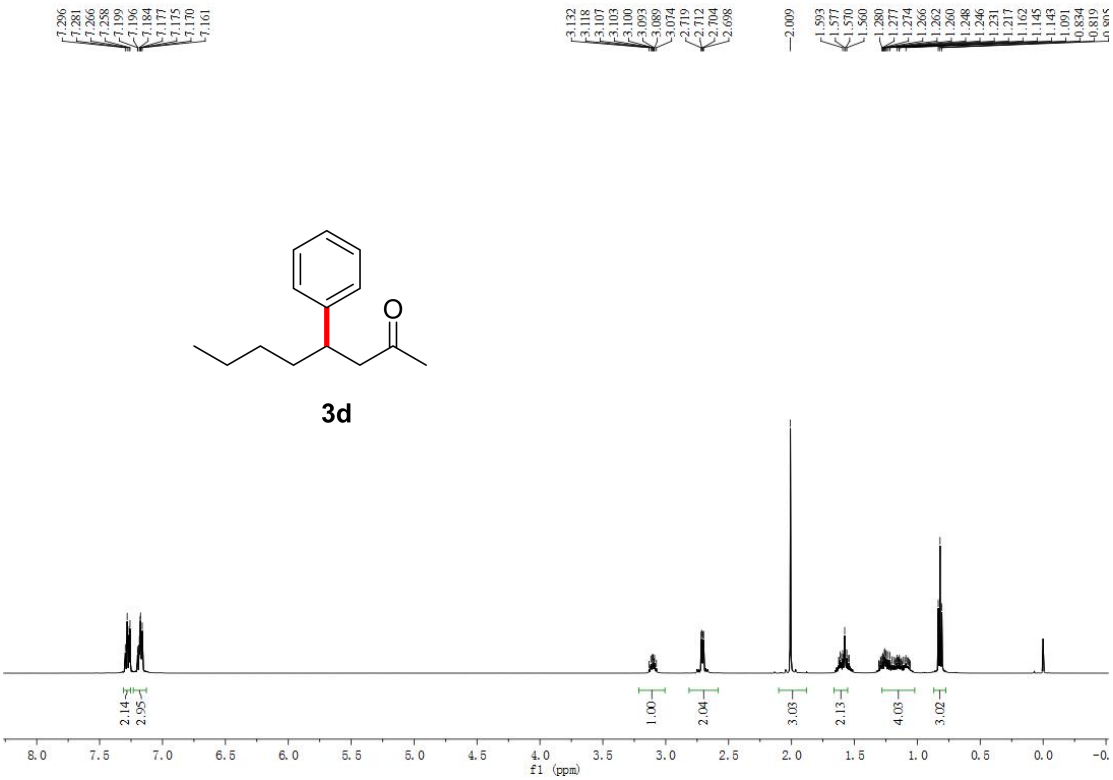
Supplementary Figure 8. ^{13}**C NMR (101 MHz, CDCl$_3$) spectrum for 3b.**



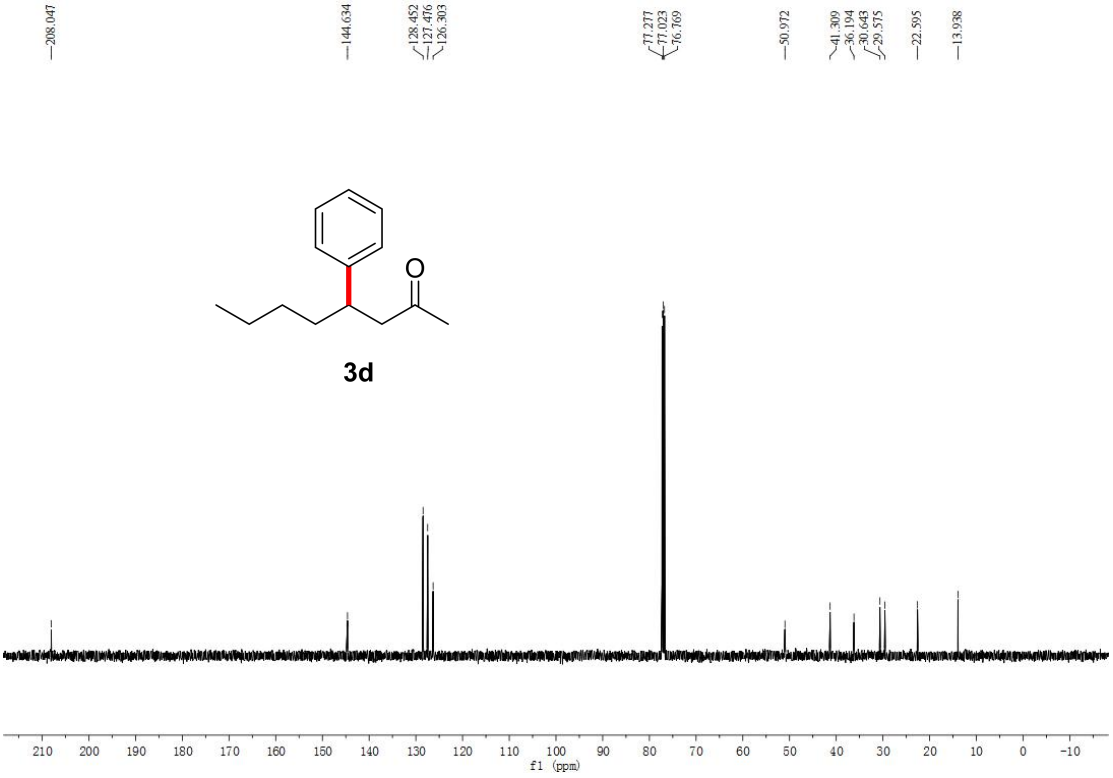
Supplementary Figure 9. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 3c.



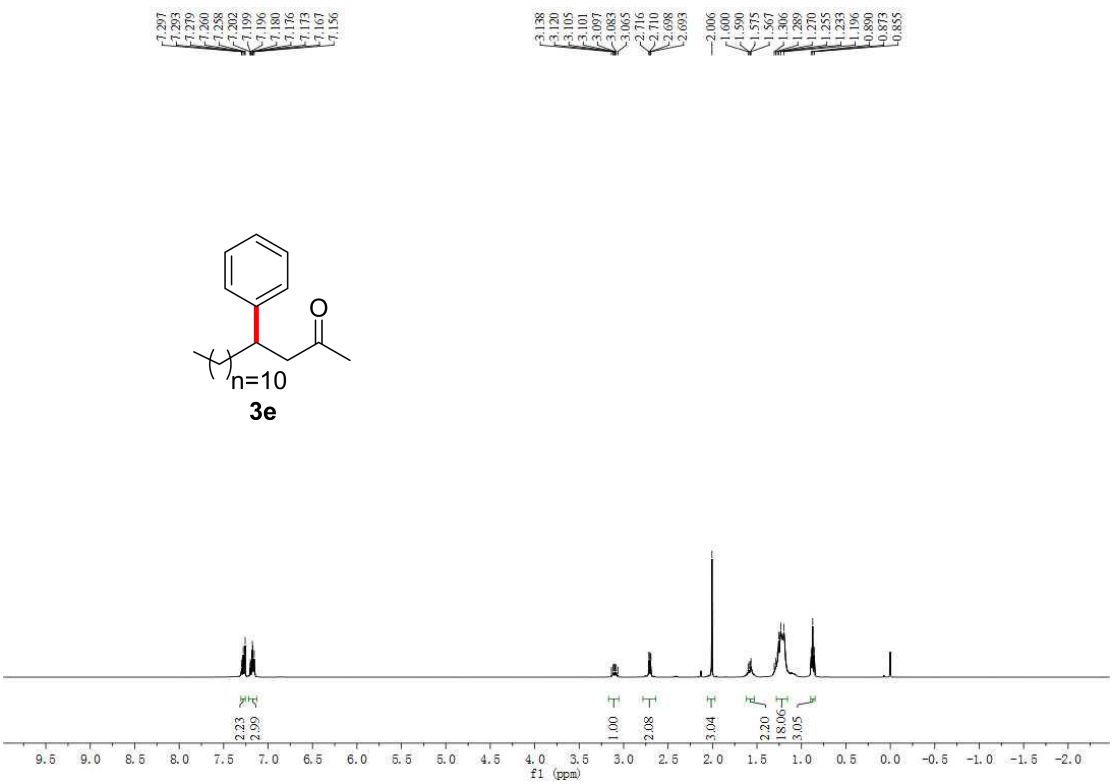
Supplementary Figure 10. ^{13}CNMR(101 MHz, $CDCl_3$) spectrum for 3c.



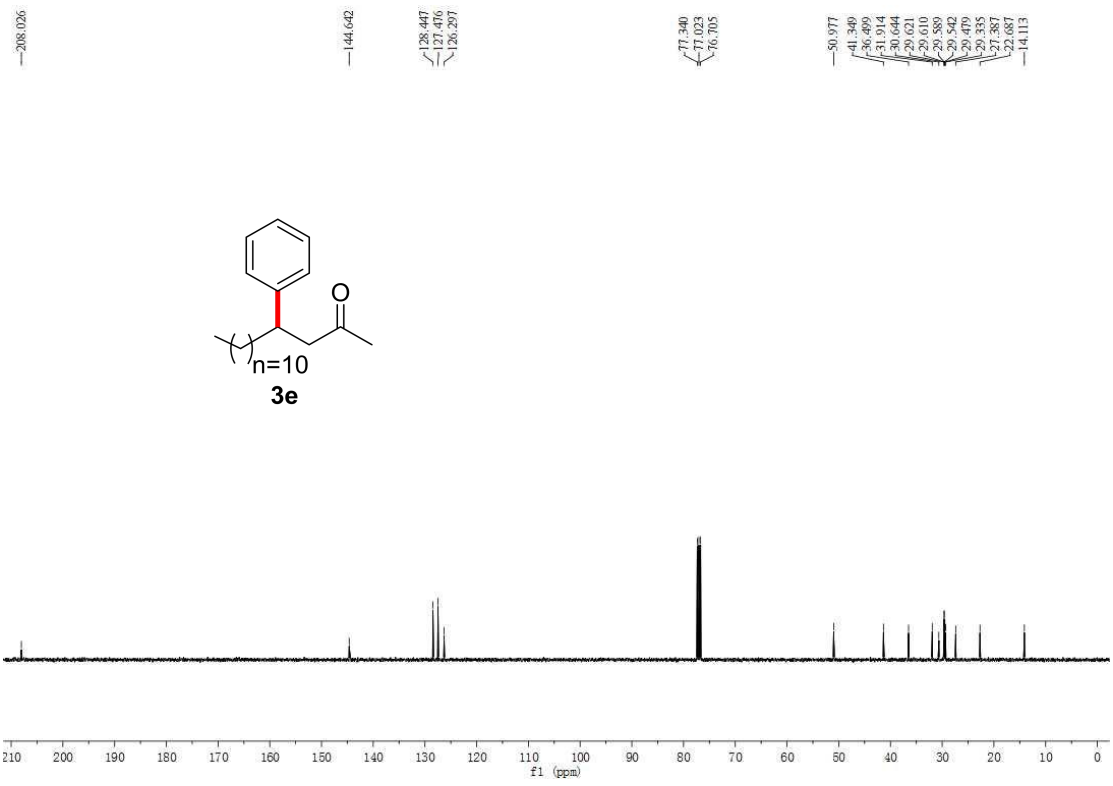
Supplementary Figure 11. ^{1}H NMR (500 MHz, $CDCl_3$) spectrum for 3d.



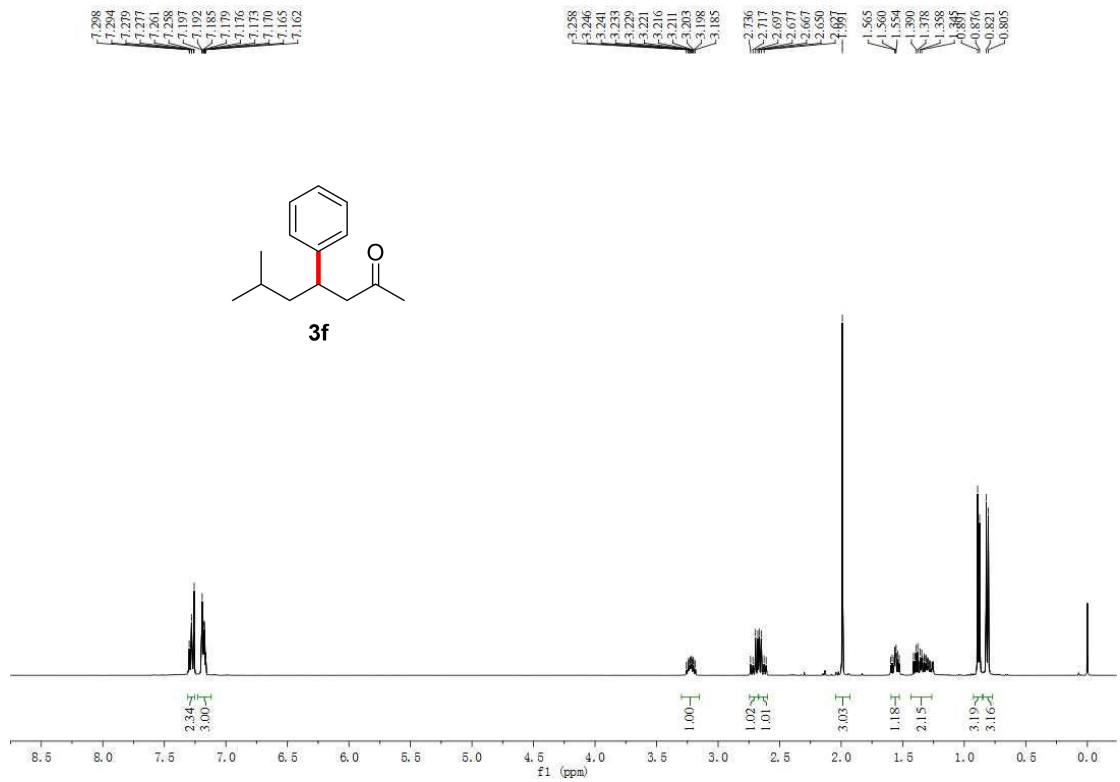
Supplementary Figure 12. ^{13}CNMR(126 MHz, $CDCl_3$) spectrum for 3d.



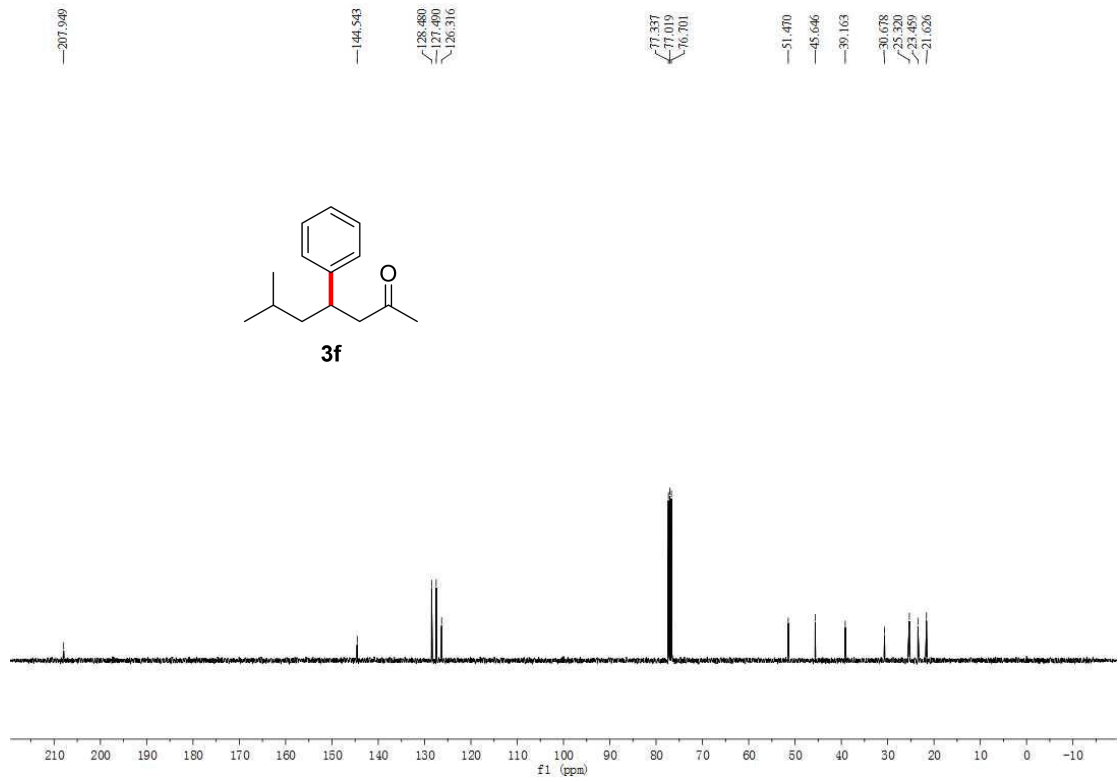
Supplementary Figure 13. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 3e.



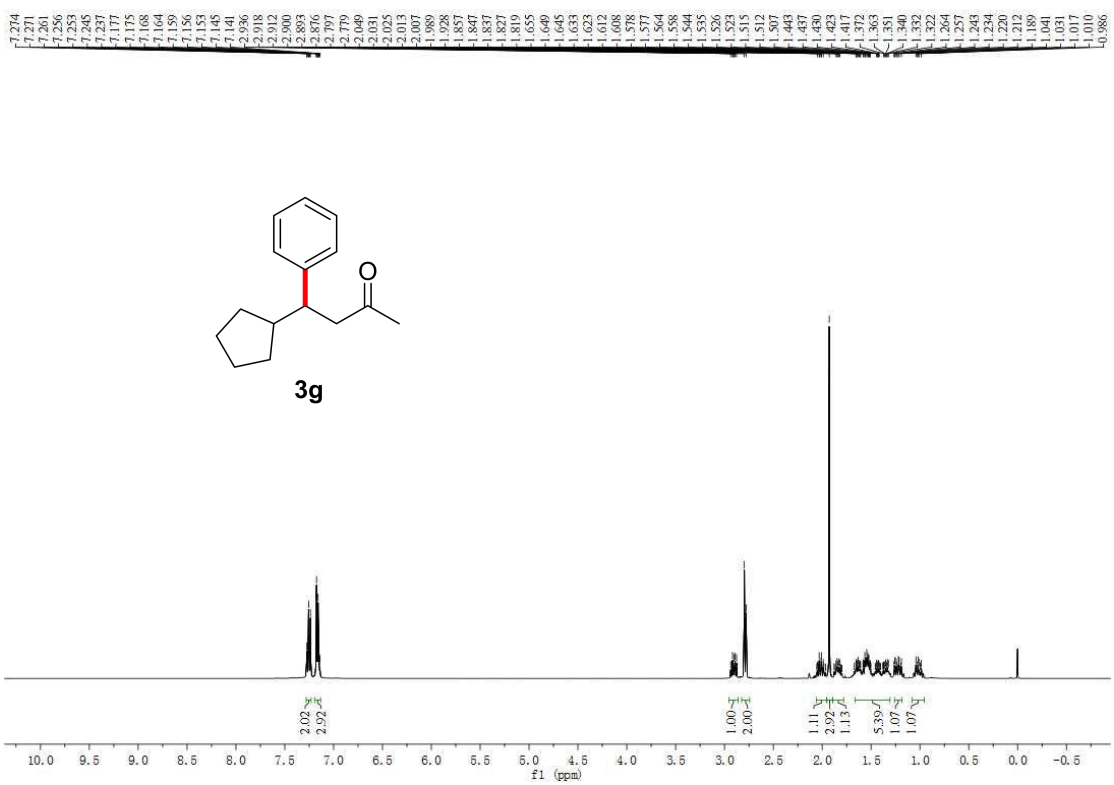
Supplementary Figure 14. ^{13}CNMR(101 MHz, $CDCl_3$) spectrum for 3e.



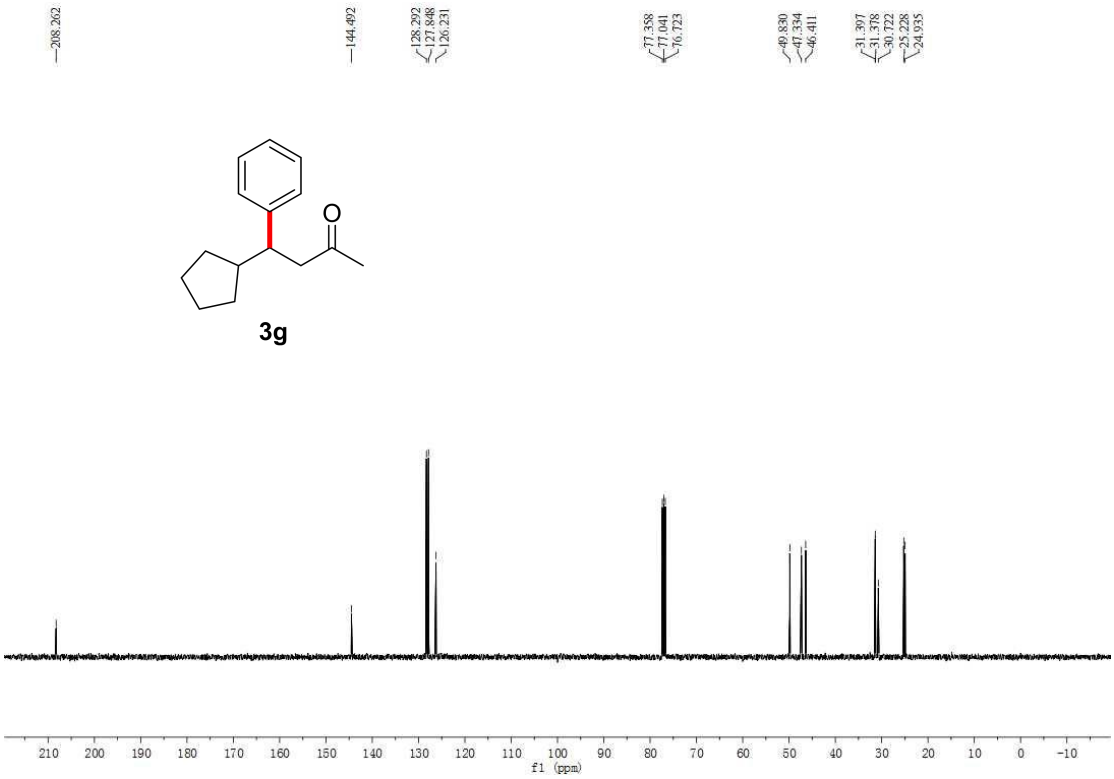
Supplementary Figure 15. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 3f.



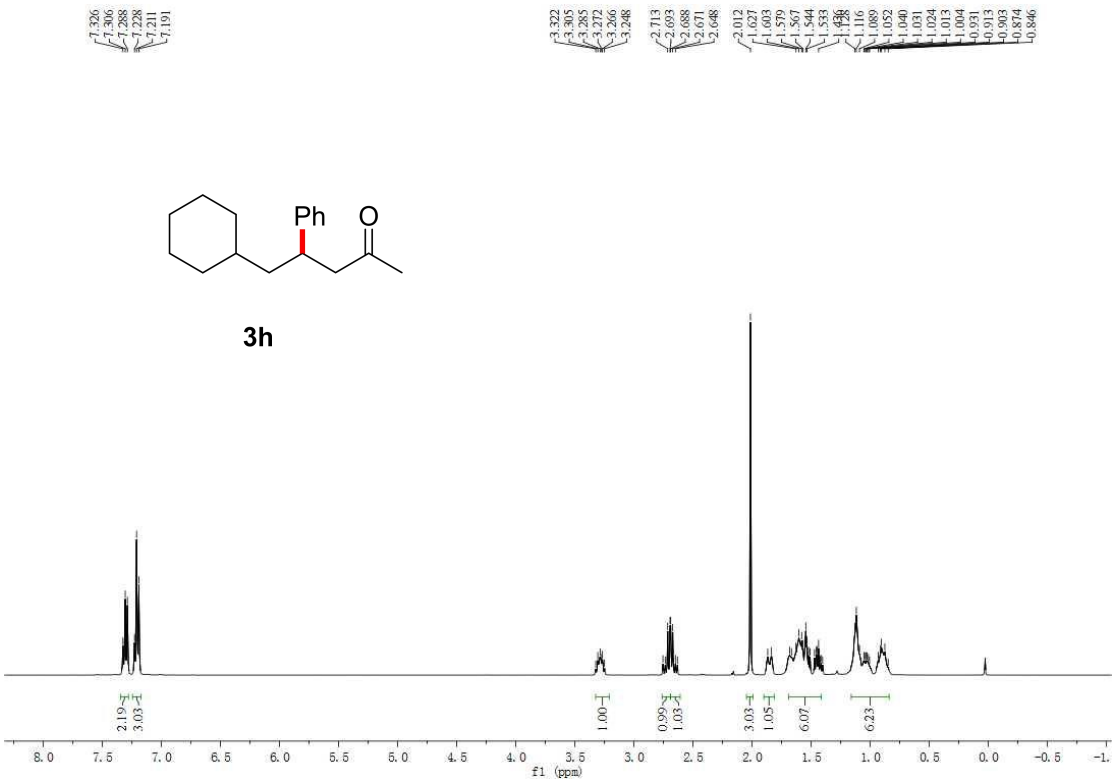
Supplementary Figure 16. ^{13}CNMR(101 MHz, $CDCl_3$) spectrum for 3f.



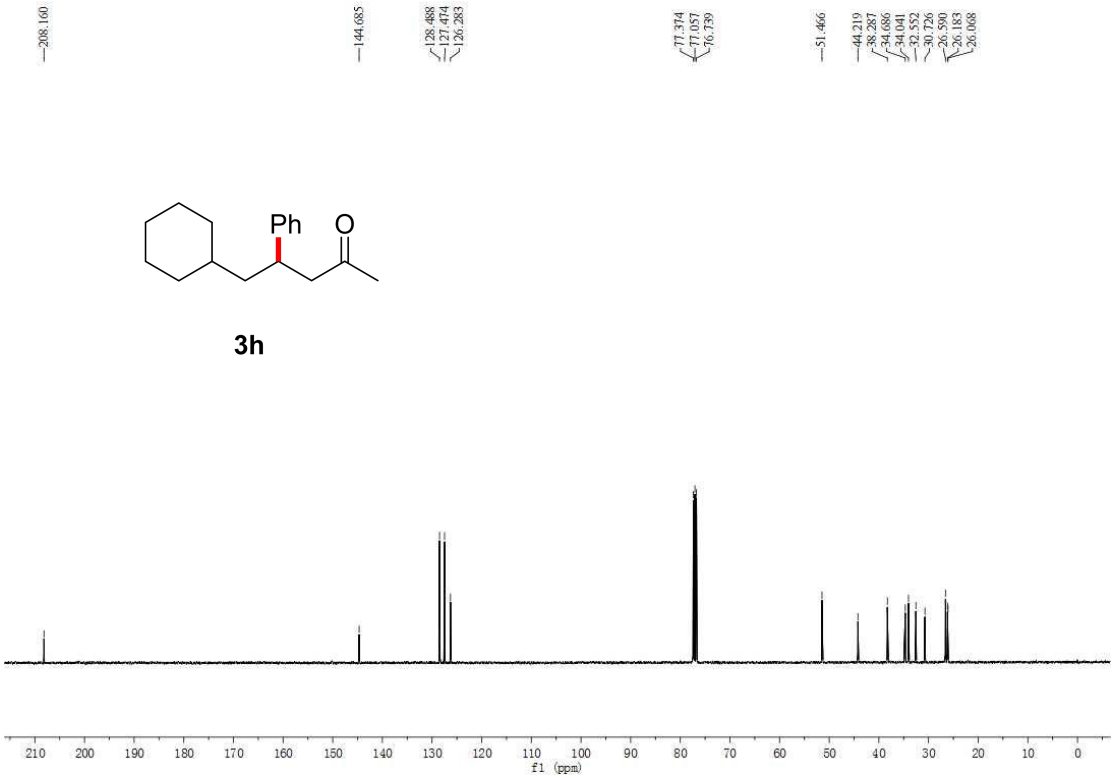
Supplementary Figure 17. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 3g.



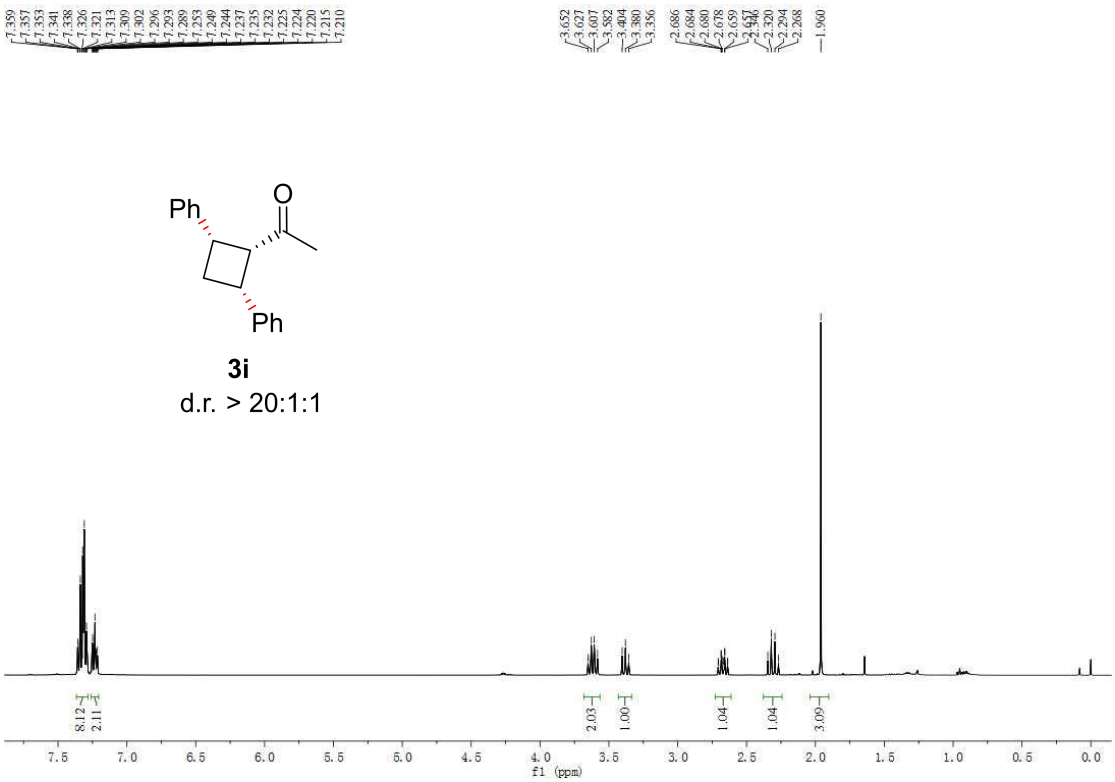
Supplementary Figure 18. ^{13}CNMR(101 MHz, $CDCl_3$) spectrum for 3g.



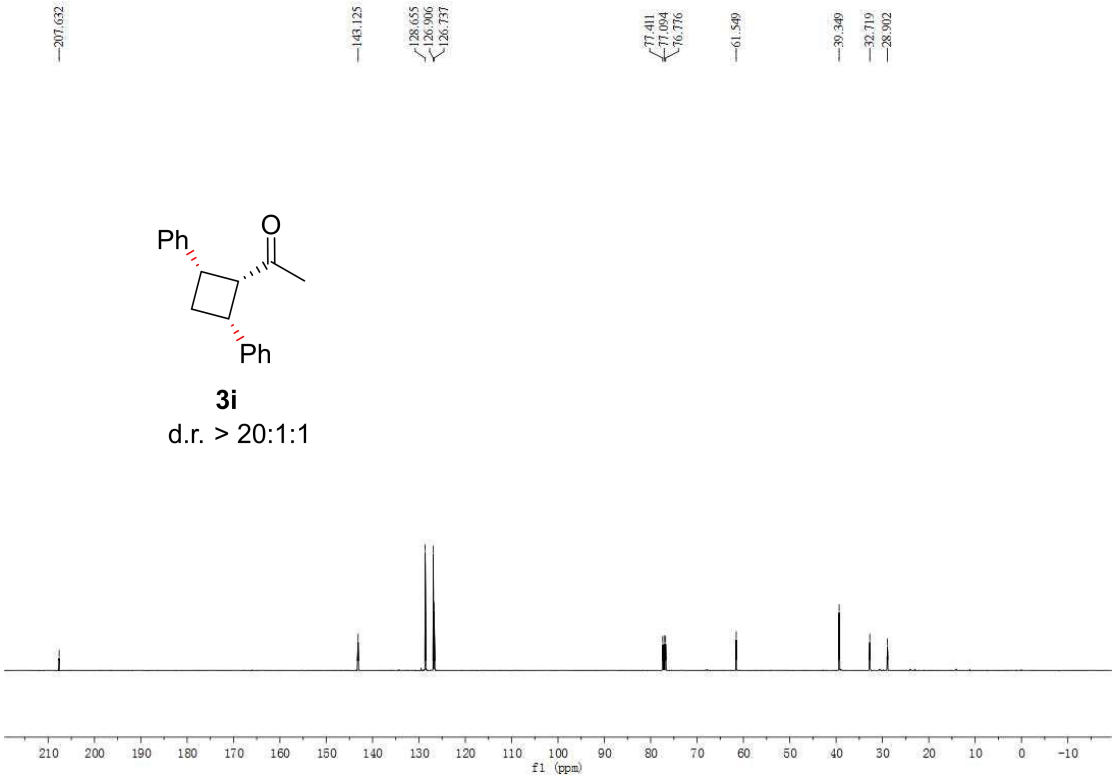
Supplementary Figure 19. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 3h.



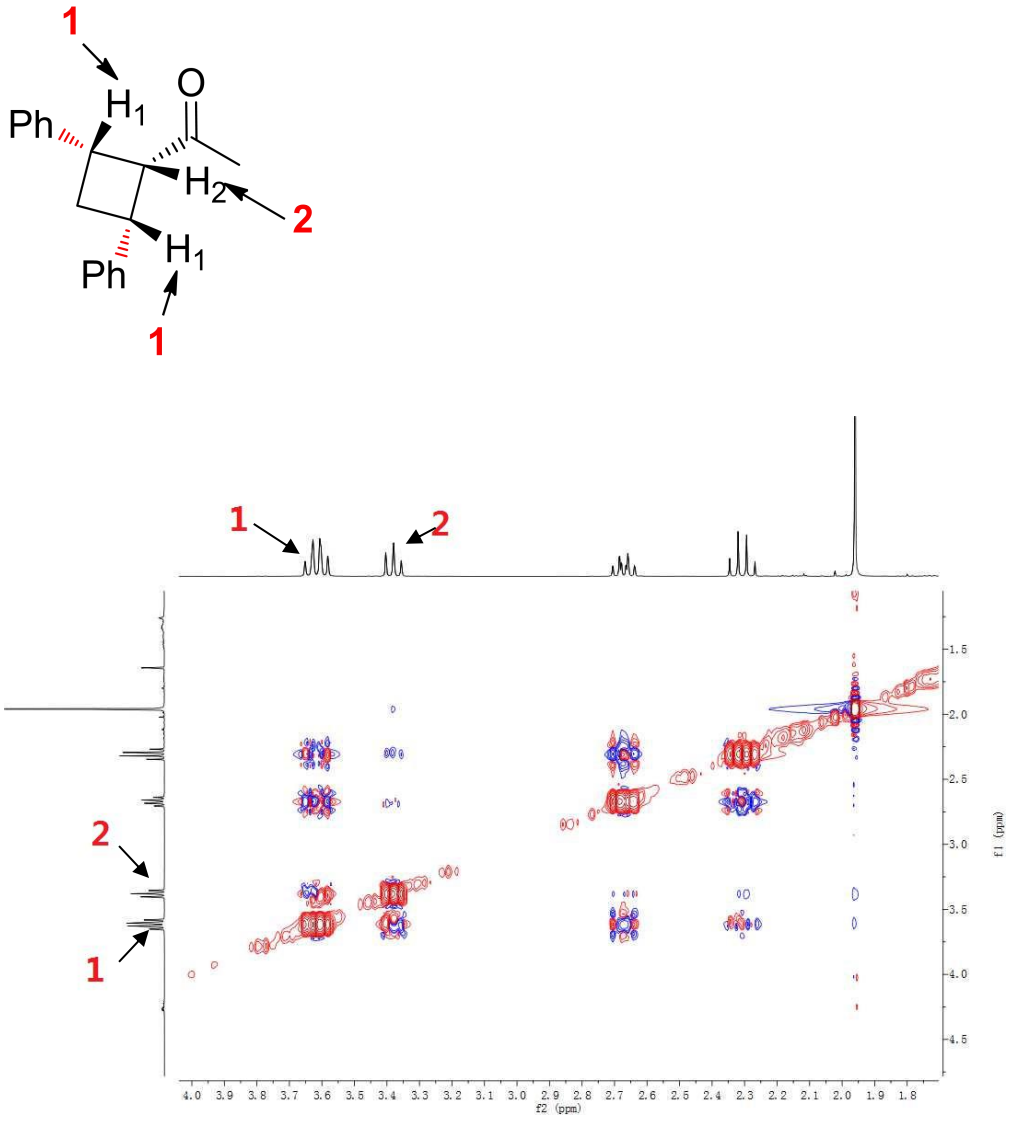
Supplementary Figure 20. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 3h.



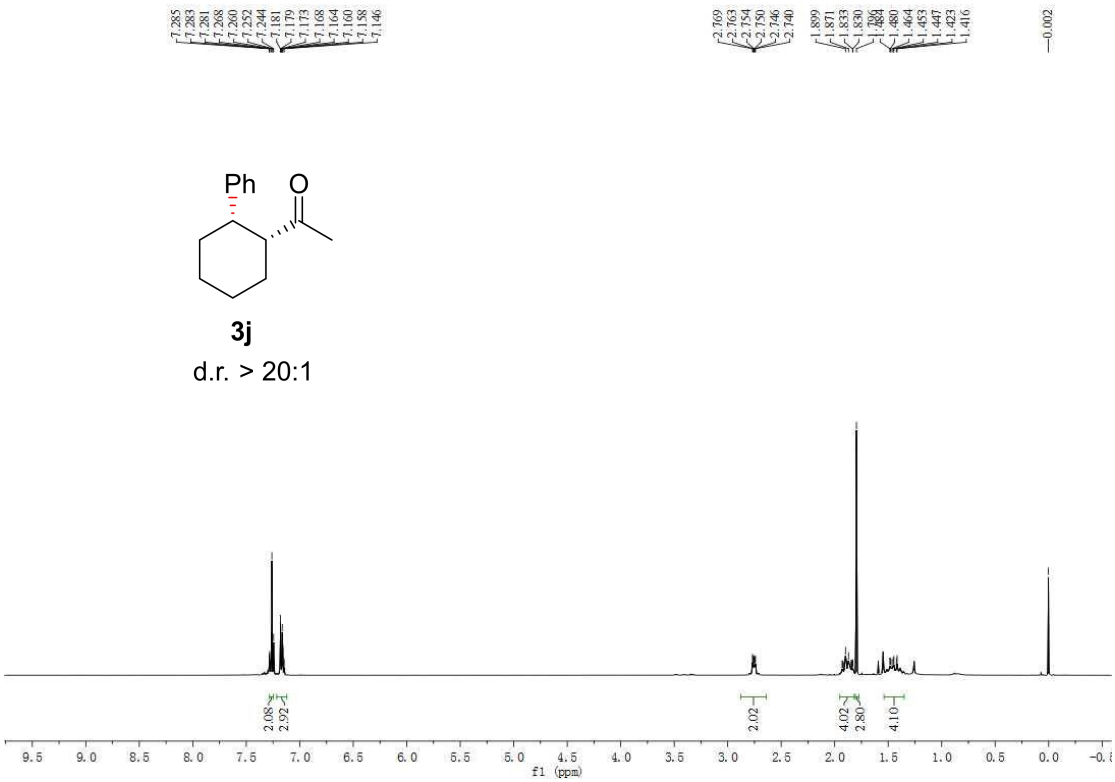
Supplementary Figure 21. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 3i.



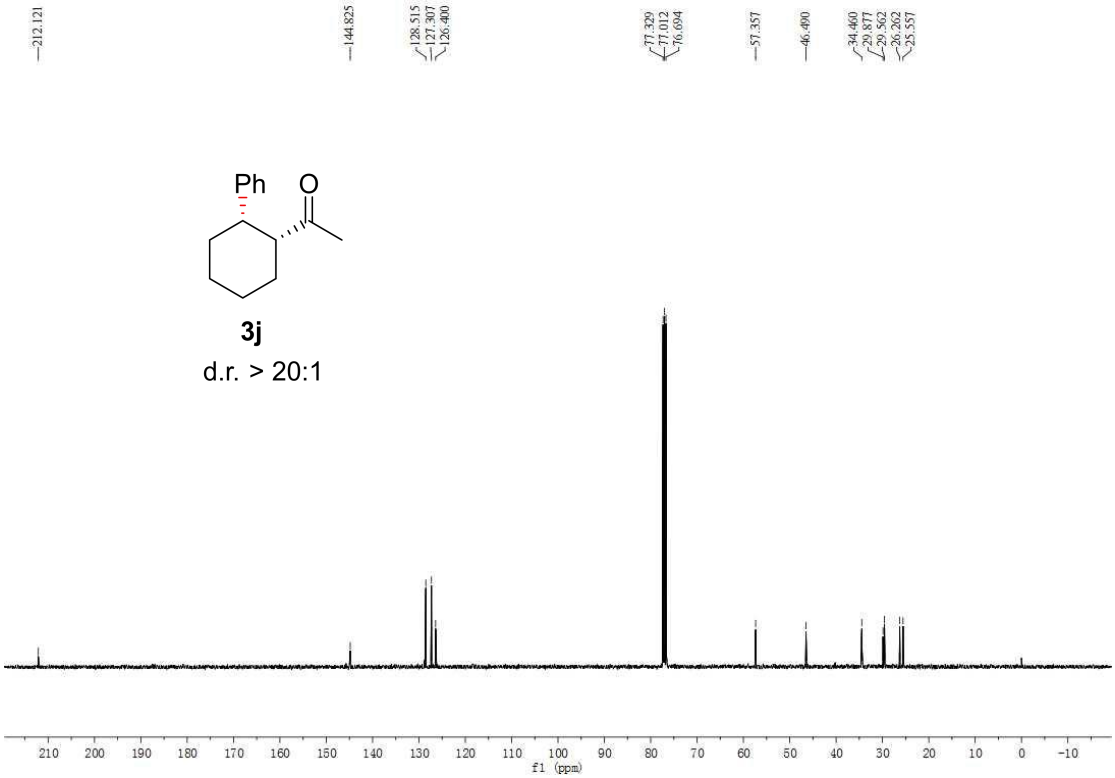
Supplementary Figure 22. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 3i.



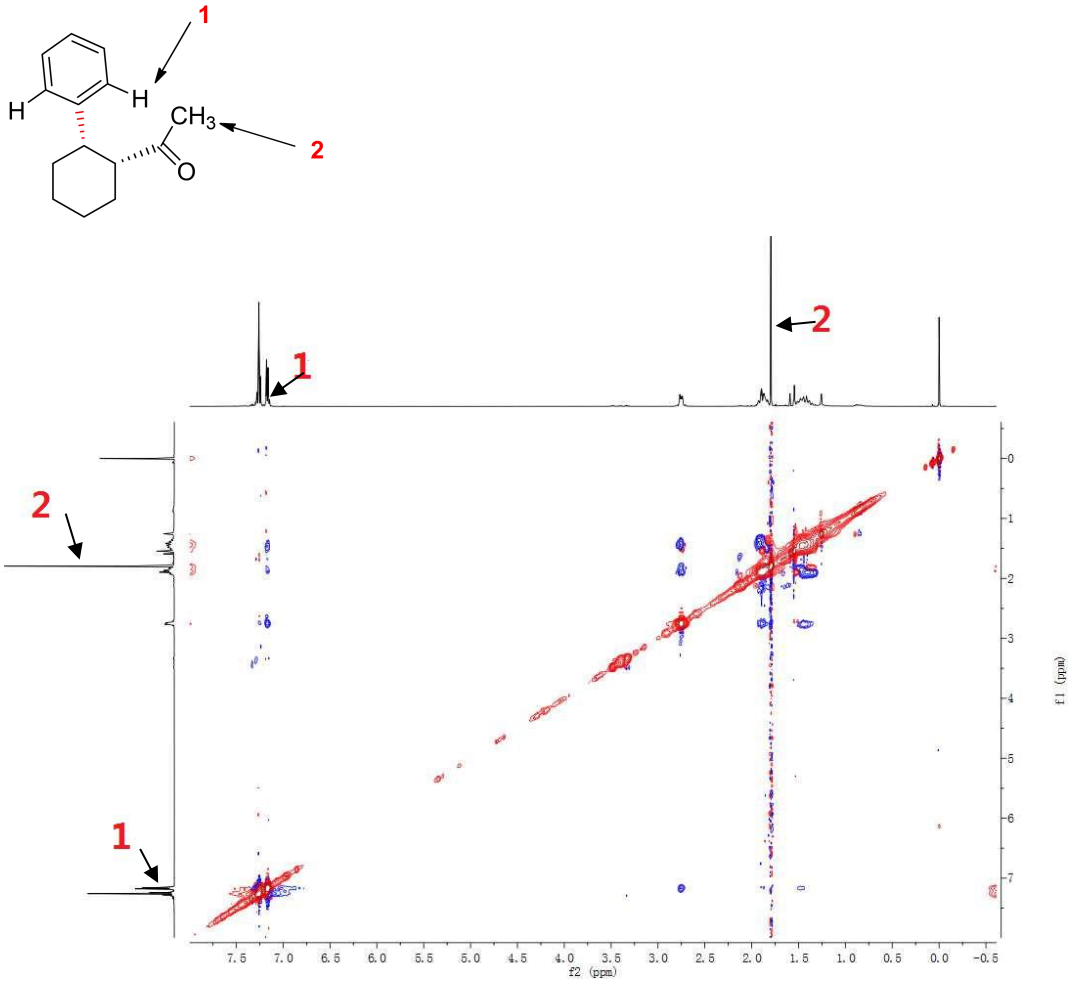
Supplementary Figure 23. NOE 2D spectrum for 3i.



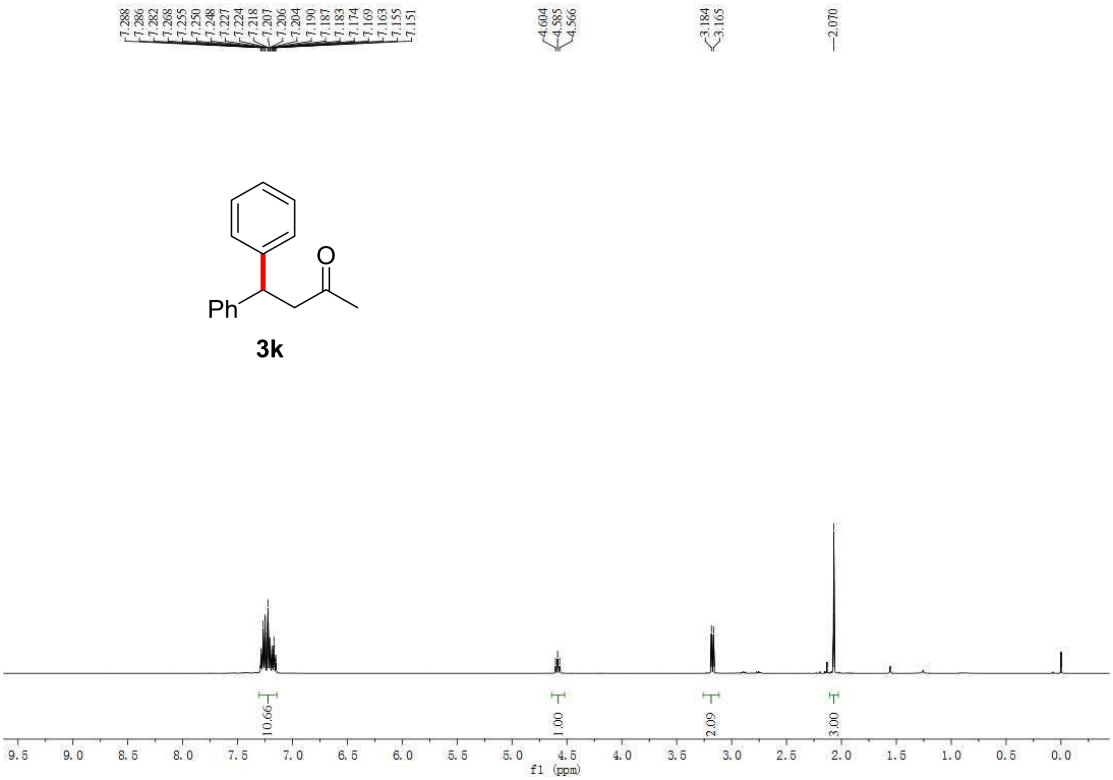
Supplementary Figure 24. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 3j.



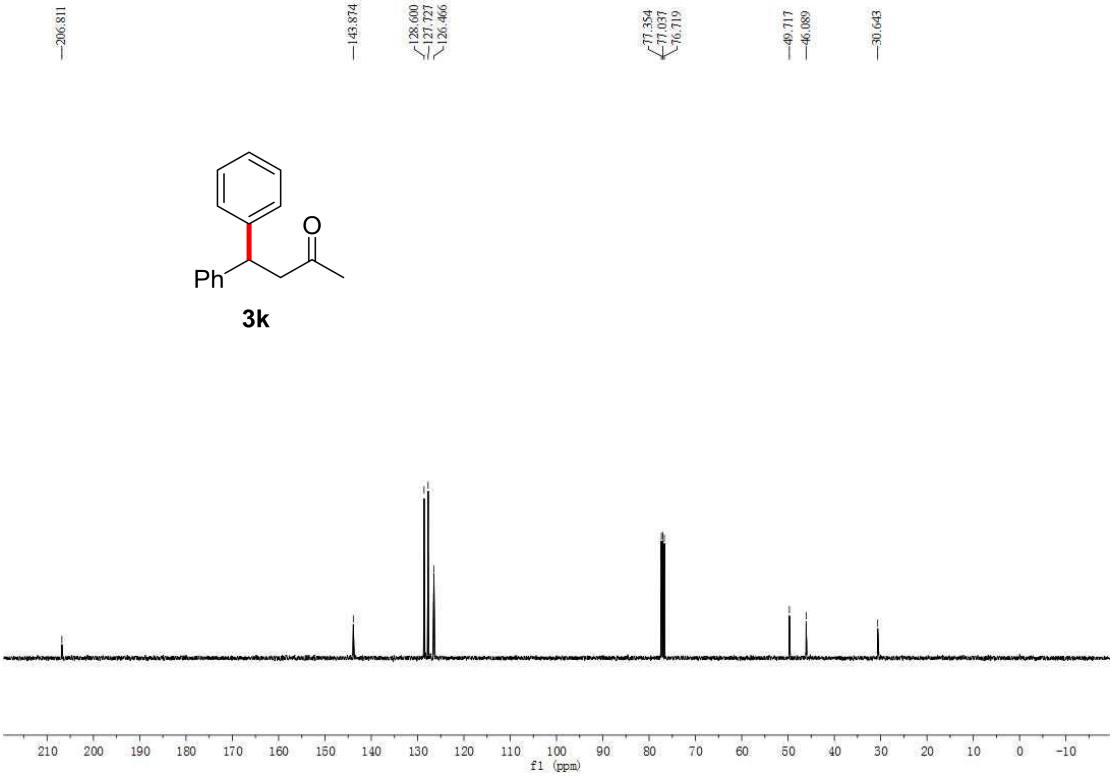
Supplementary Figure 25. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 3j.



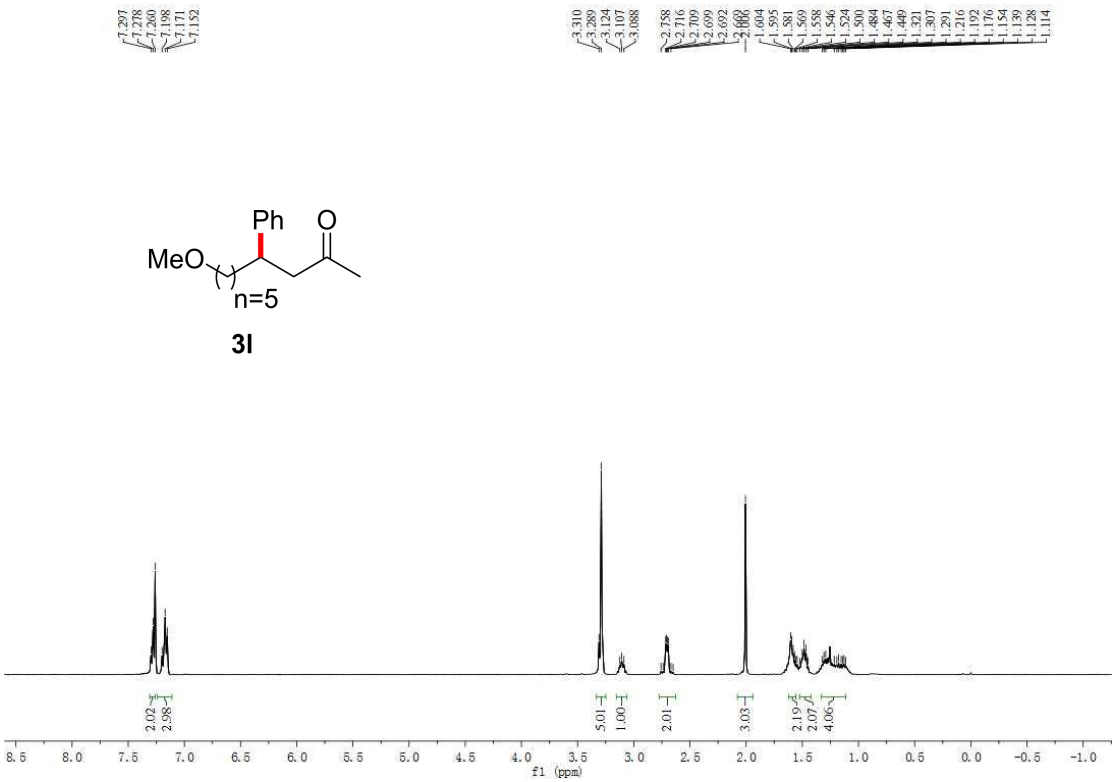
Supplementary Figure 26. NOE 2D spectrum for 3j.



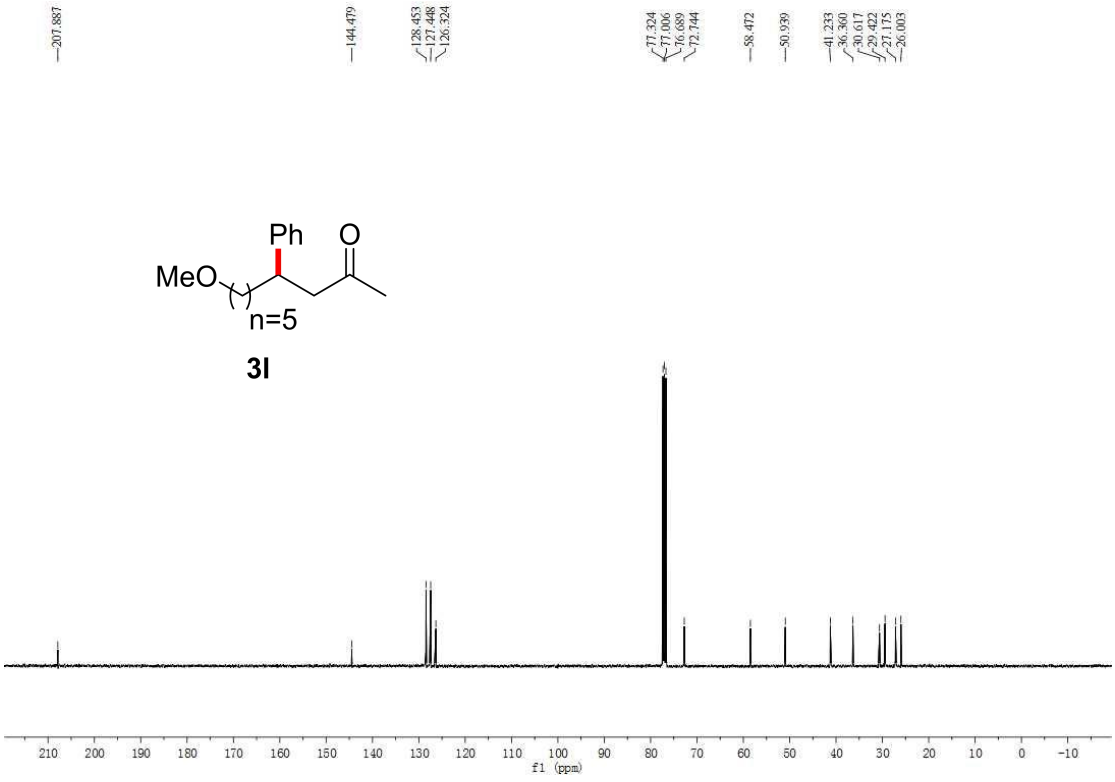
Supplementary Figure 27. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 3k.



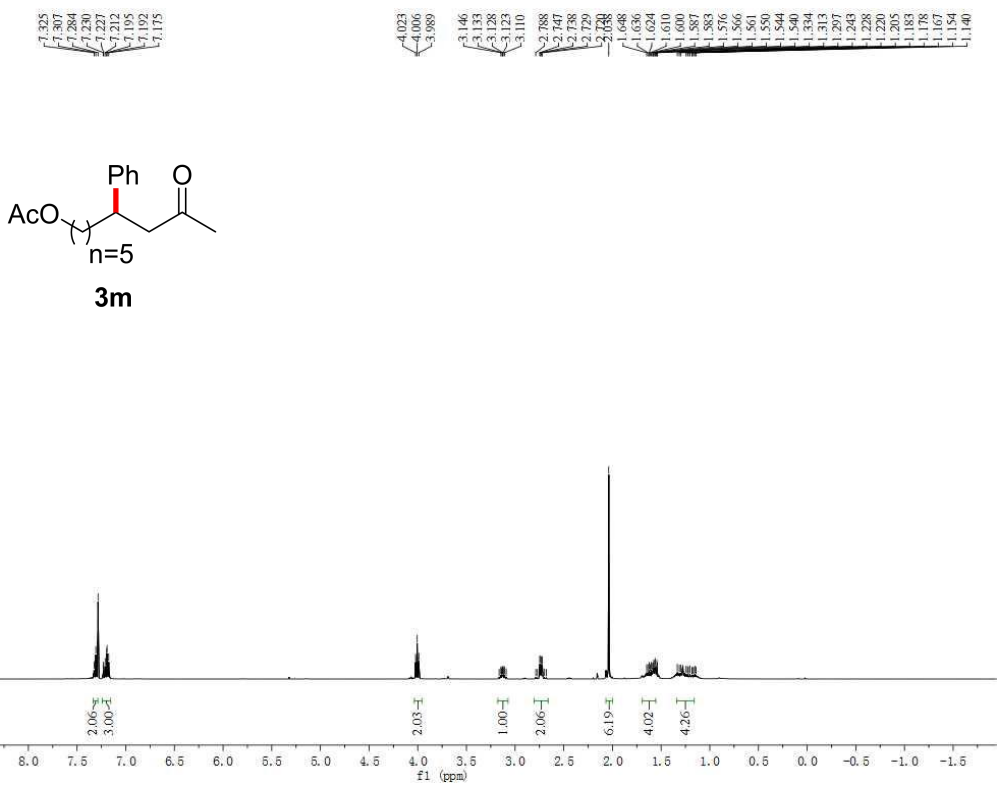
Supplementary Figure 28. ^{13}CNMR(101 MHz, $CDCl_3$) spectrum for 3k.



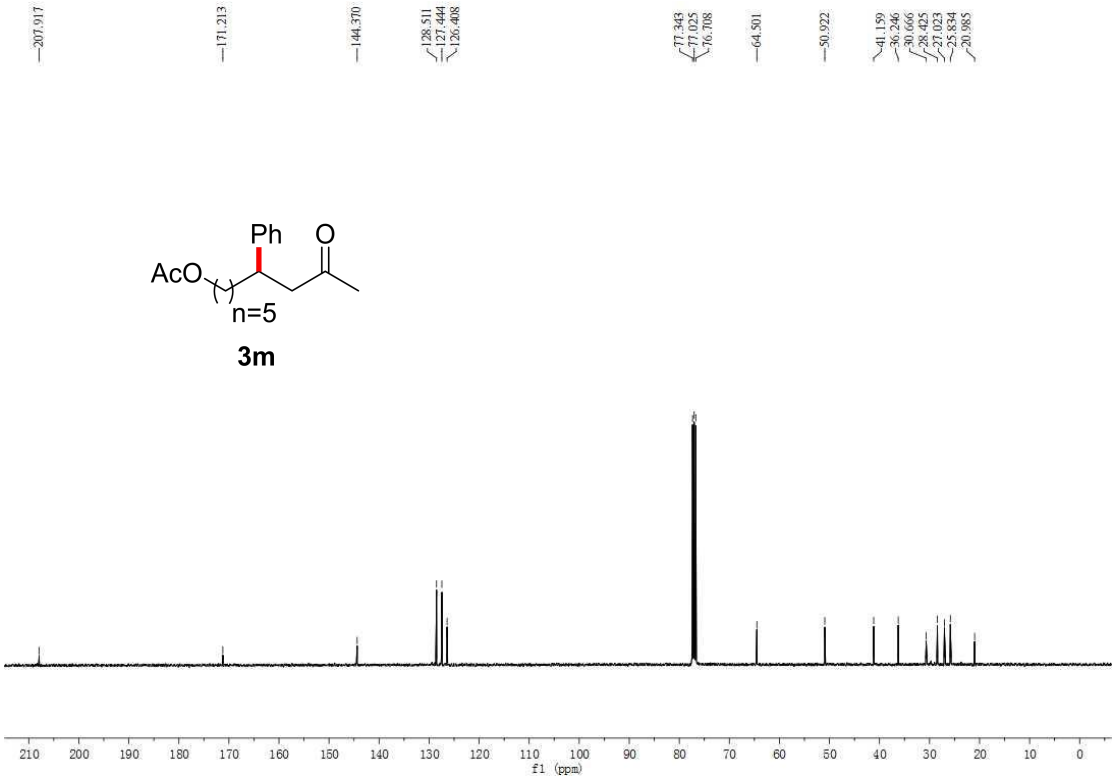
Supplementary Figure 29. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 3l.



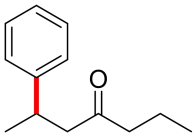
Supplementary Figure 30. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 3l.



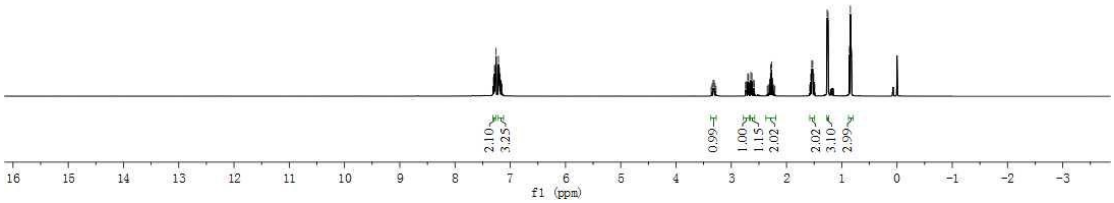
Supplementary Figure 31. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 3m.



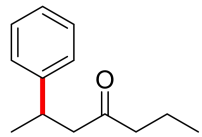
Supplementary Figure 32. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 3m.



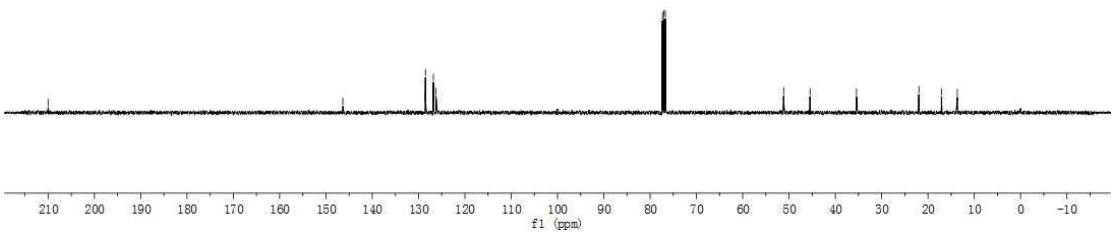
3na



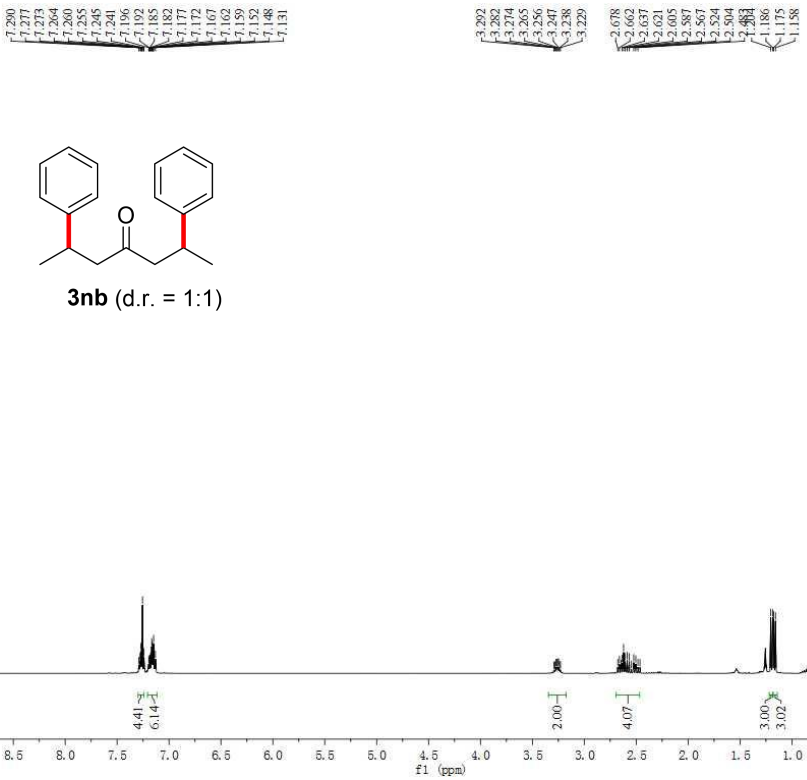
Supplementary Figure 33. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 3na.



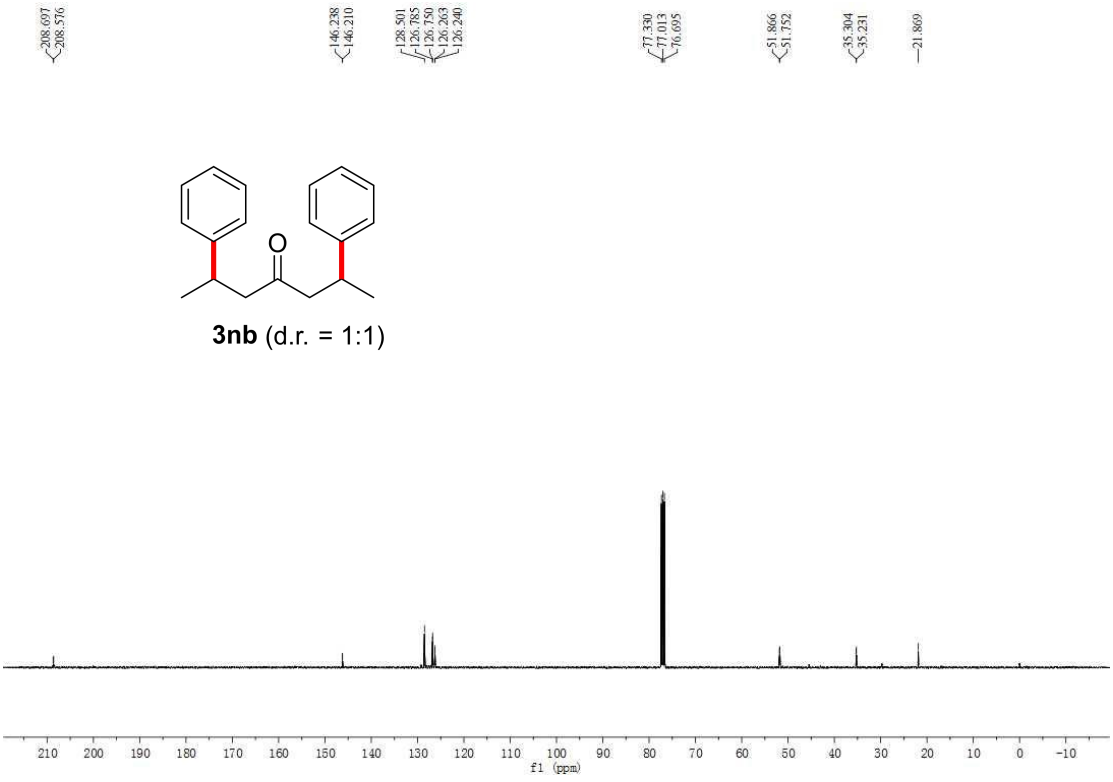
3na



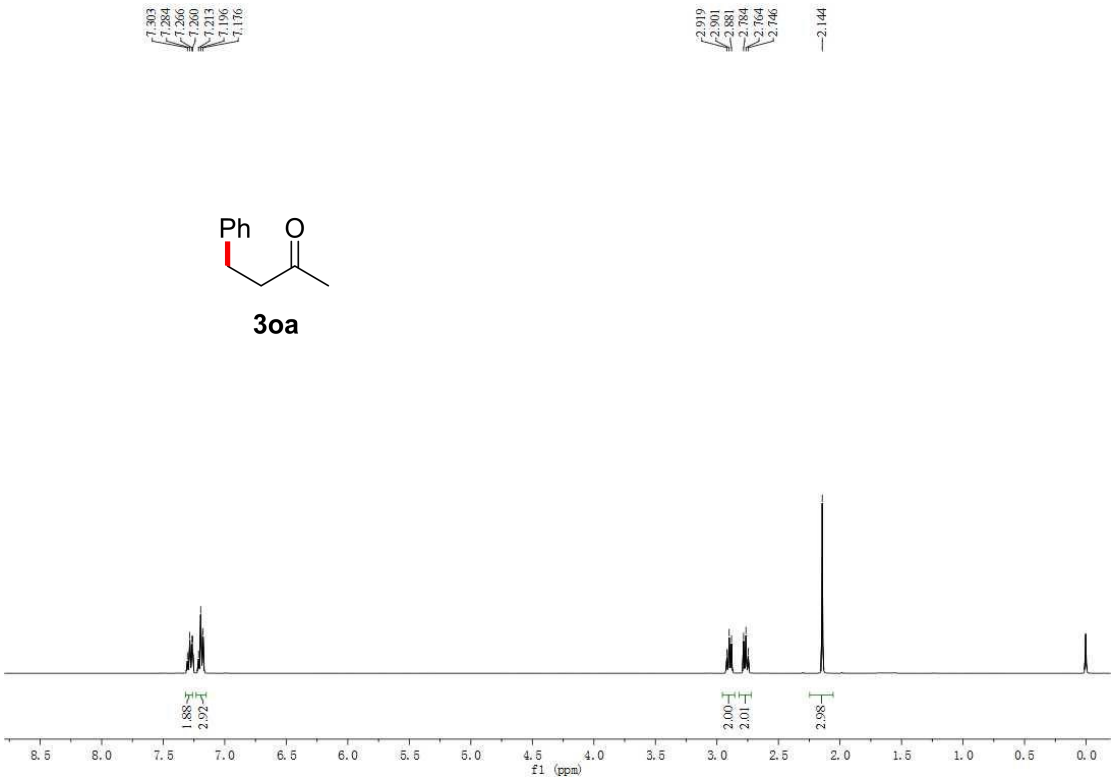
Supplementary Figure 34. ^{13}CNMR(101 MHz, $CDCl_3$) spectrum for 3na.



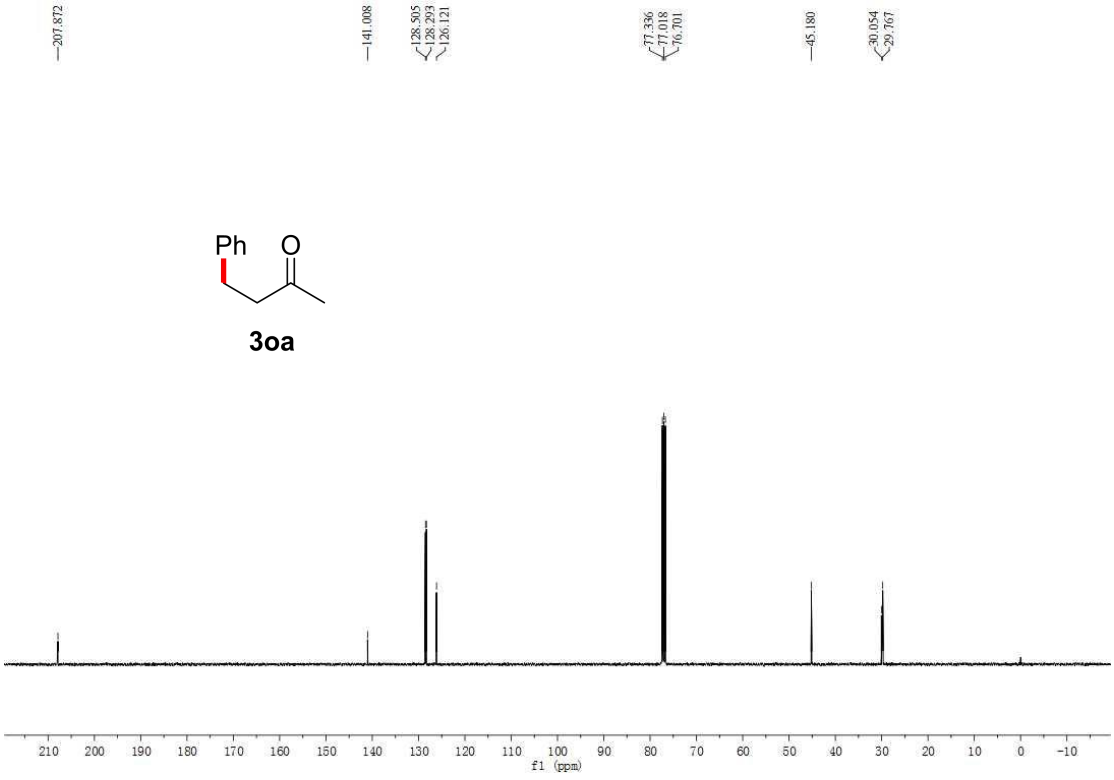
Supplementary Figure 35. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 3nb.



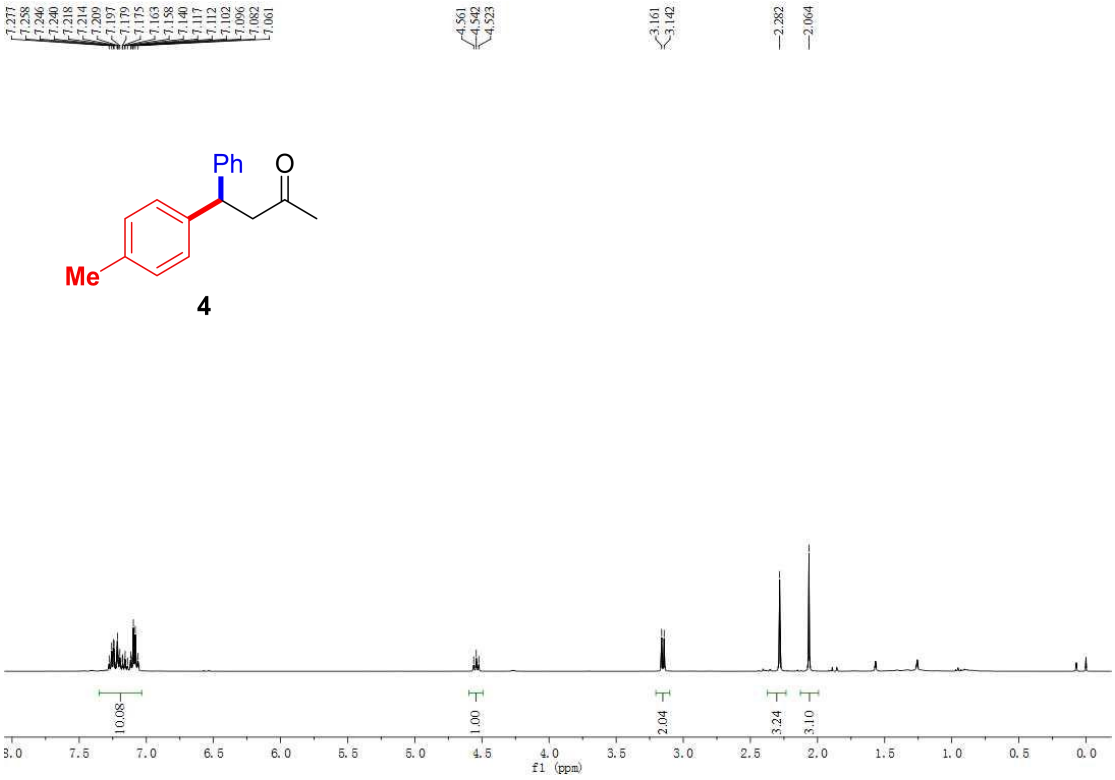
Supplementary Figure 36. ^{13}CNMR(101 MHz, $CDCl_3$) spectrum for 3nb.



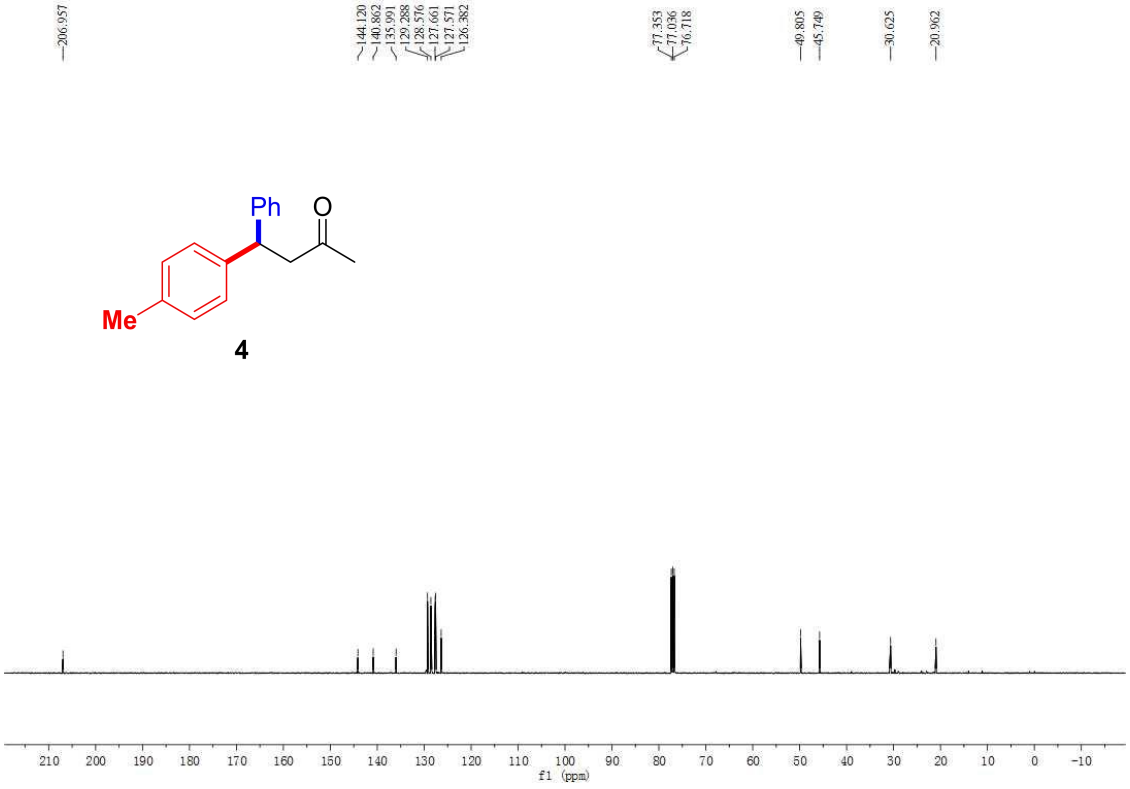
Supplementary Figure 37. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 3oa.



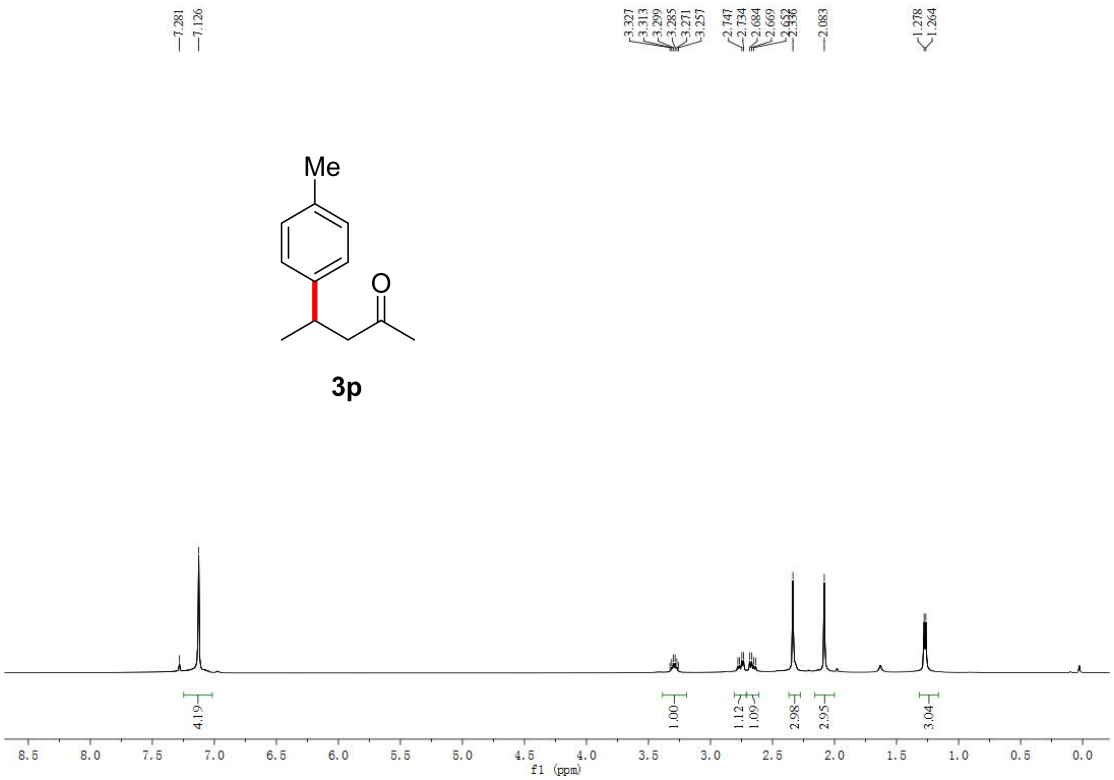
Supplementary Figure 38. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 3oa.



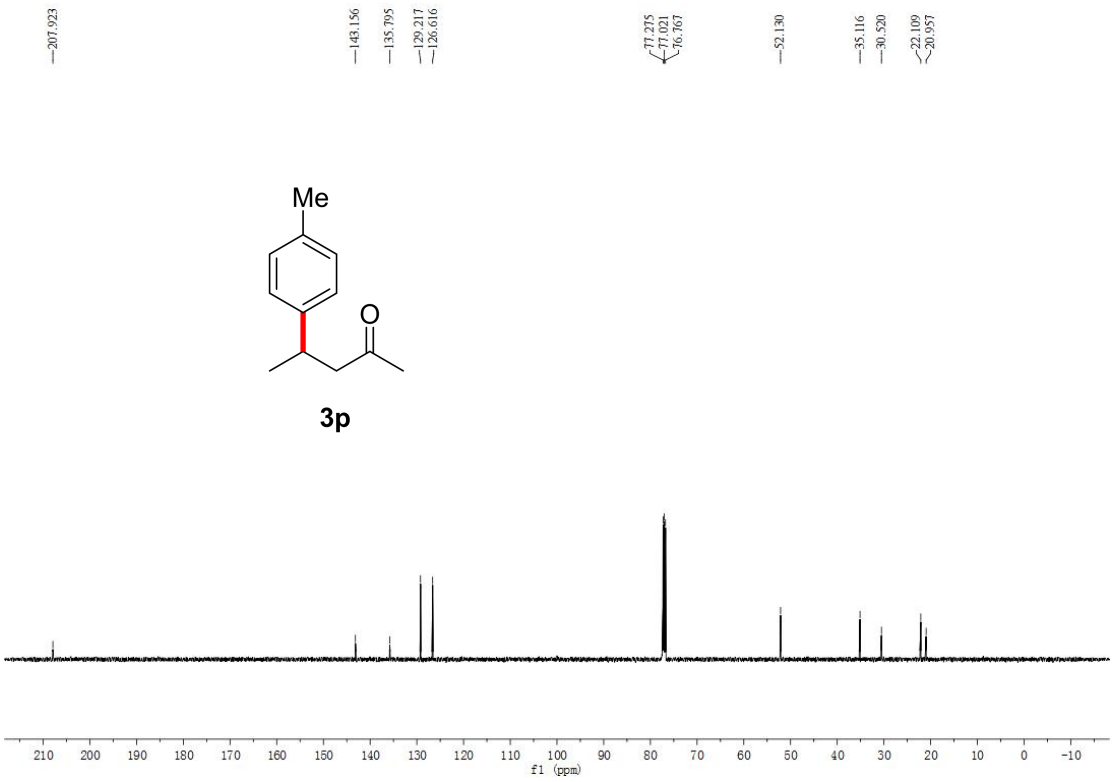
Supplementary Figure 39. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 4.



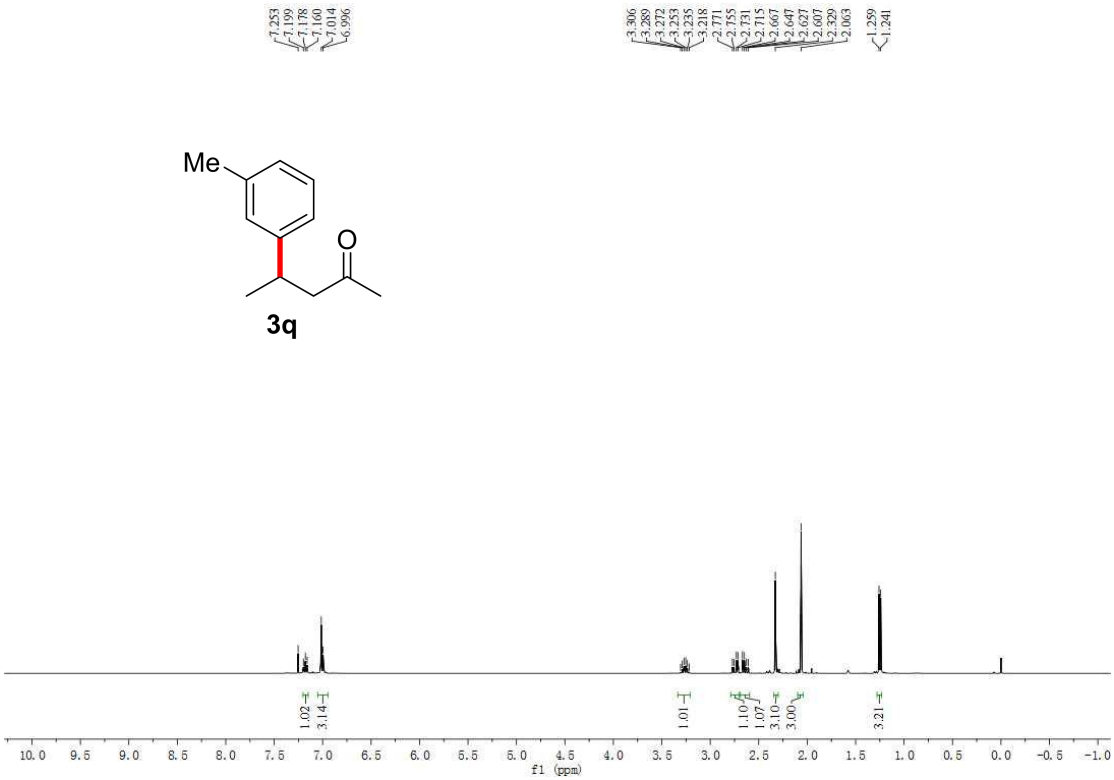
Supplementary Figure 40. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 4.



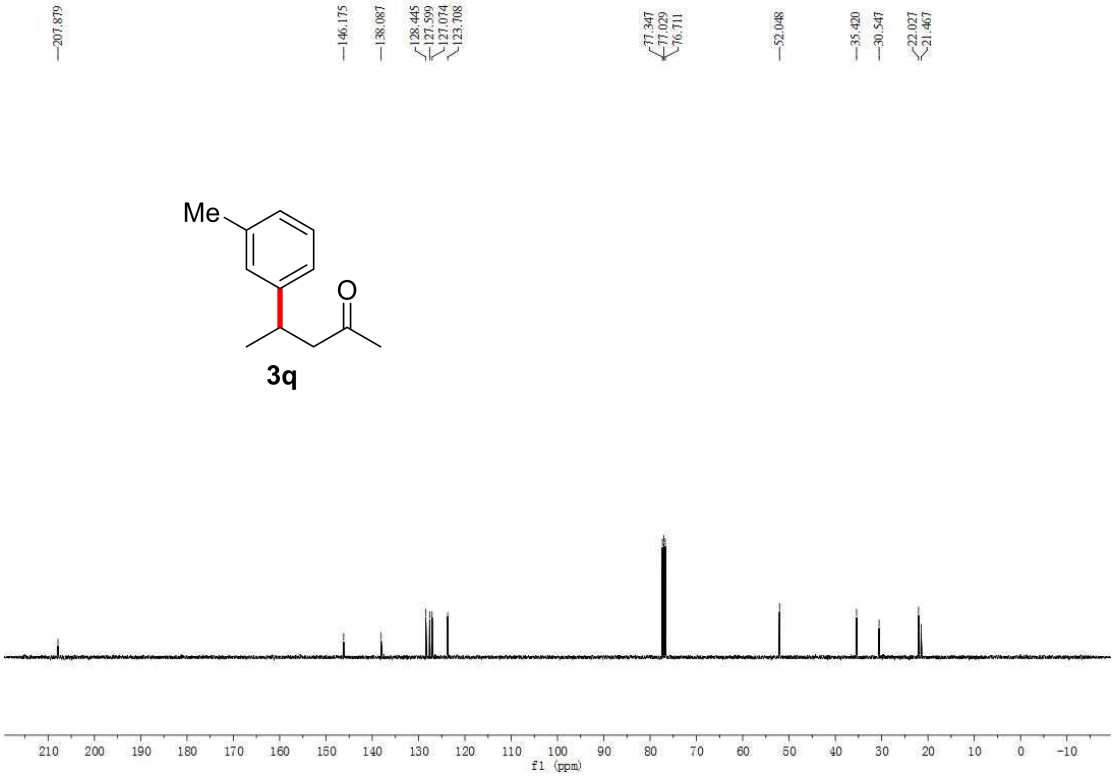
Supplementary Figure 41. ^{1}H NMR (500 MHz, $CDCl_3$) spectrum for 3p



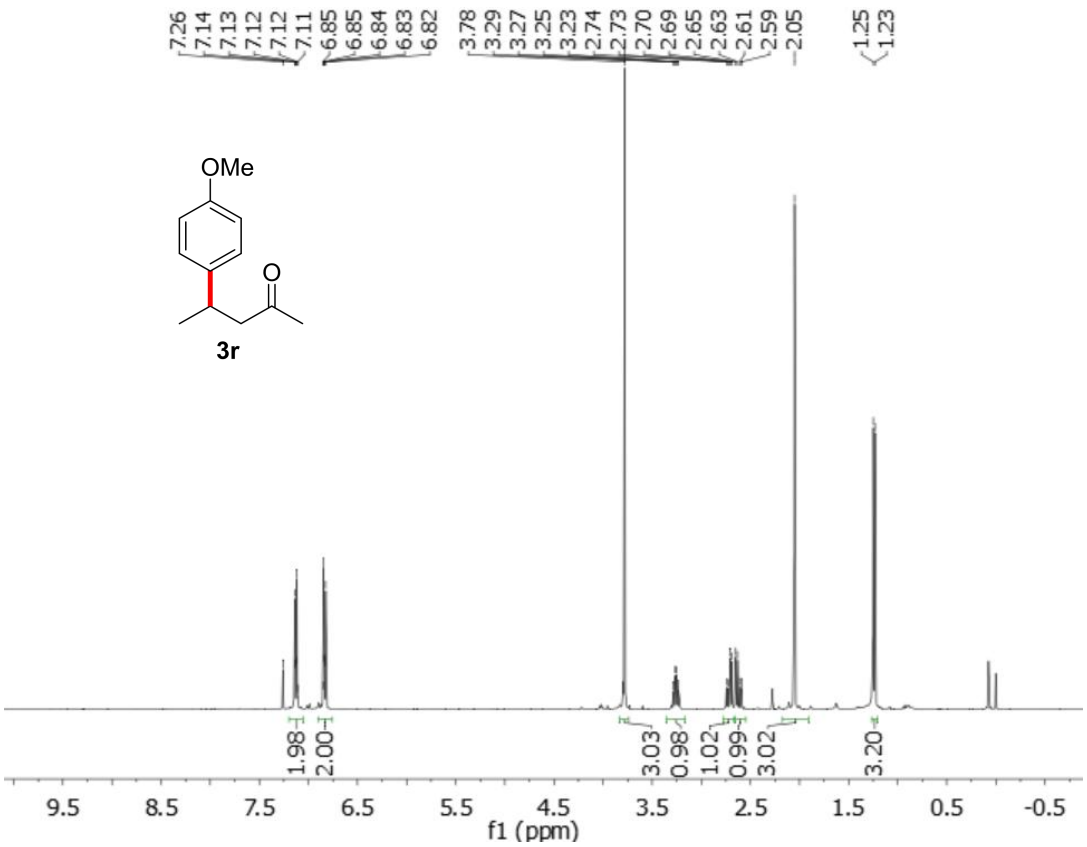
Supplementary Figure 42. ^{13}C NMR (126 MHz, $CDCl_3$) spectrum for 3p.



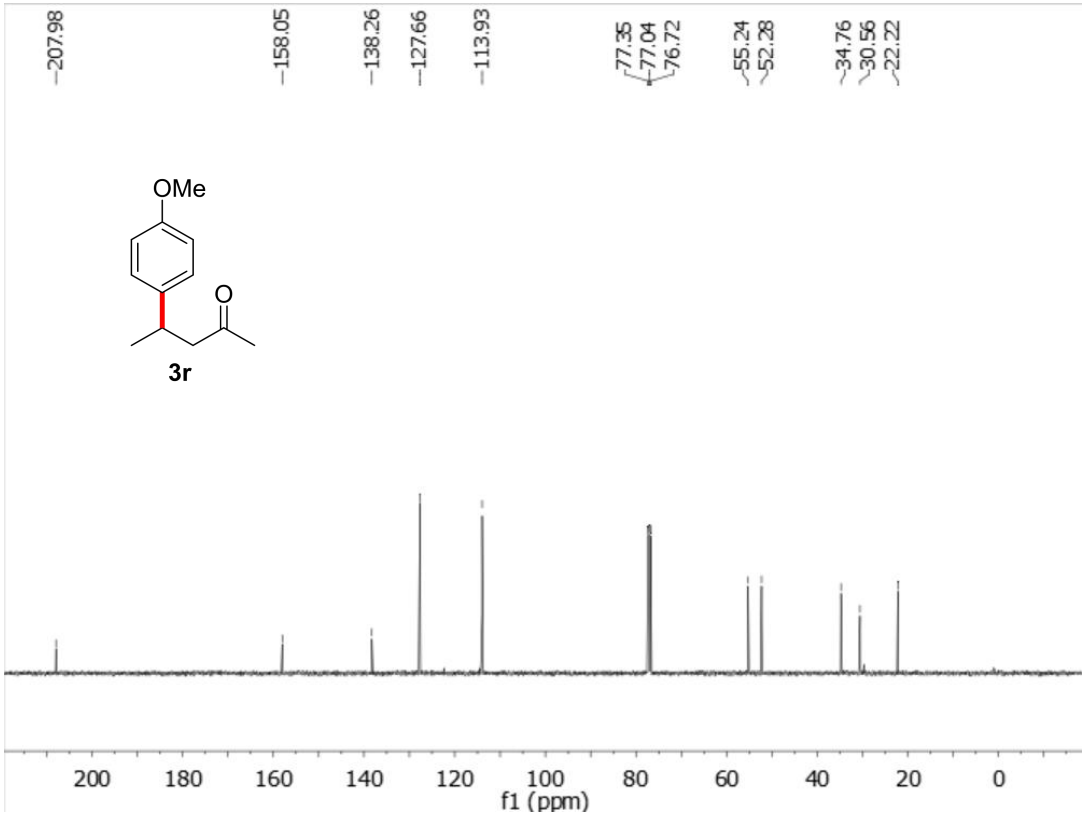
Supplementary Figure 43. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 3q.



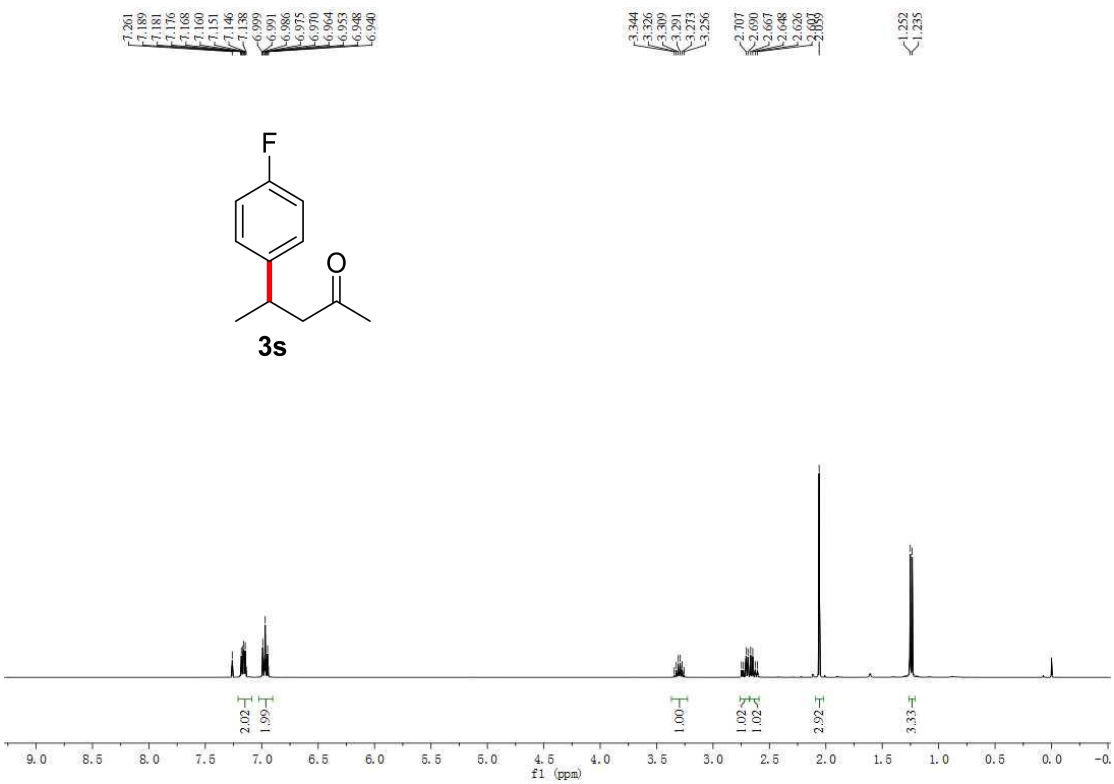
Supplementary Figure 44. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 3q.



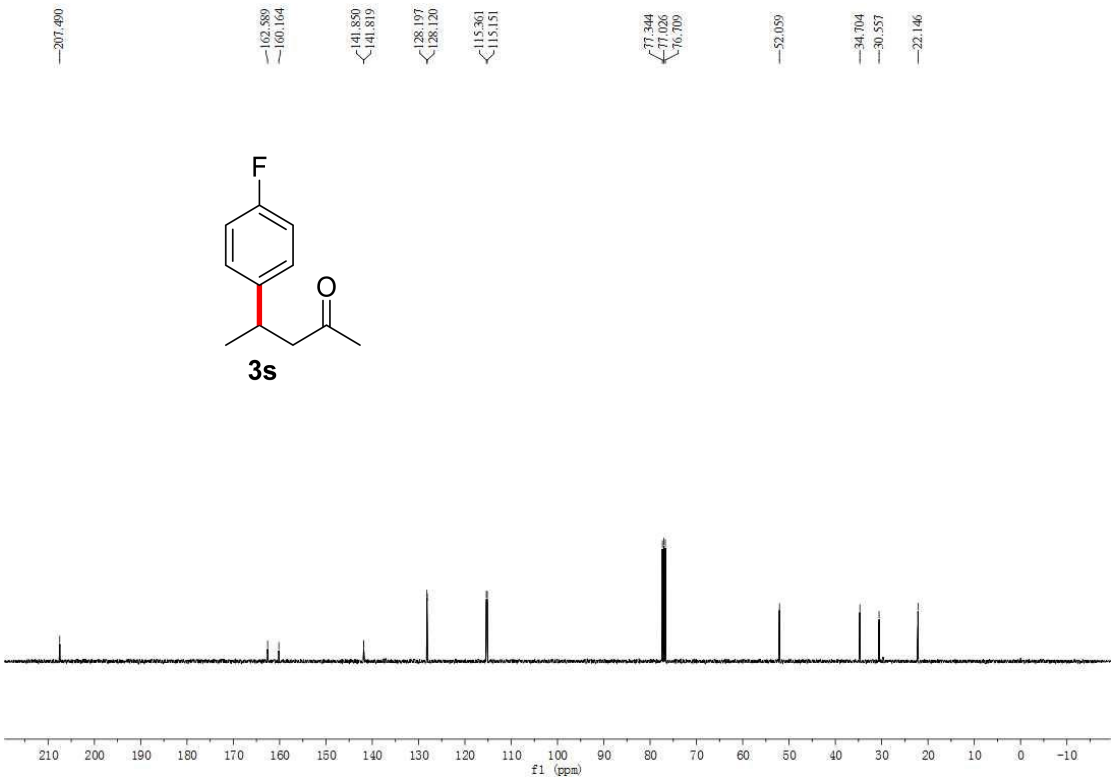
Supplementary Figure 45. ^{1}**H NMR (400 MHz, CDCl$_3$) spectrum for 3r.**



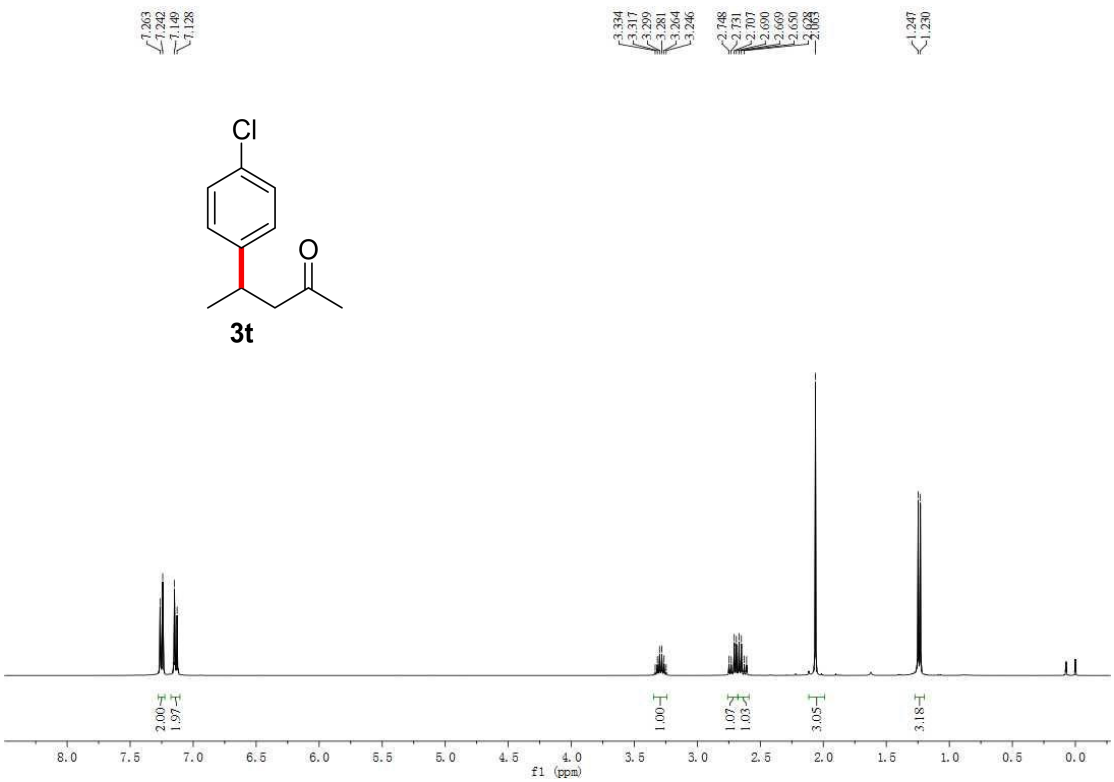
Supplementary Figure 46. ^{13}**C NMR (101 MHz, CDCl$_3$) spectrum for 3r.**



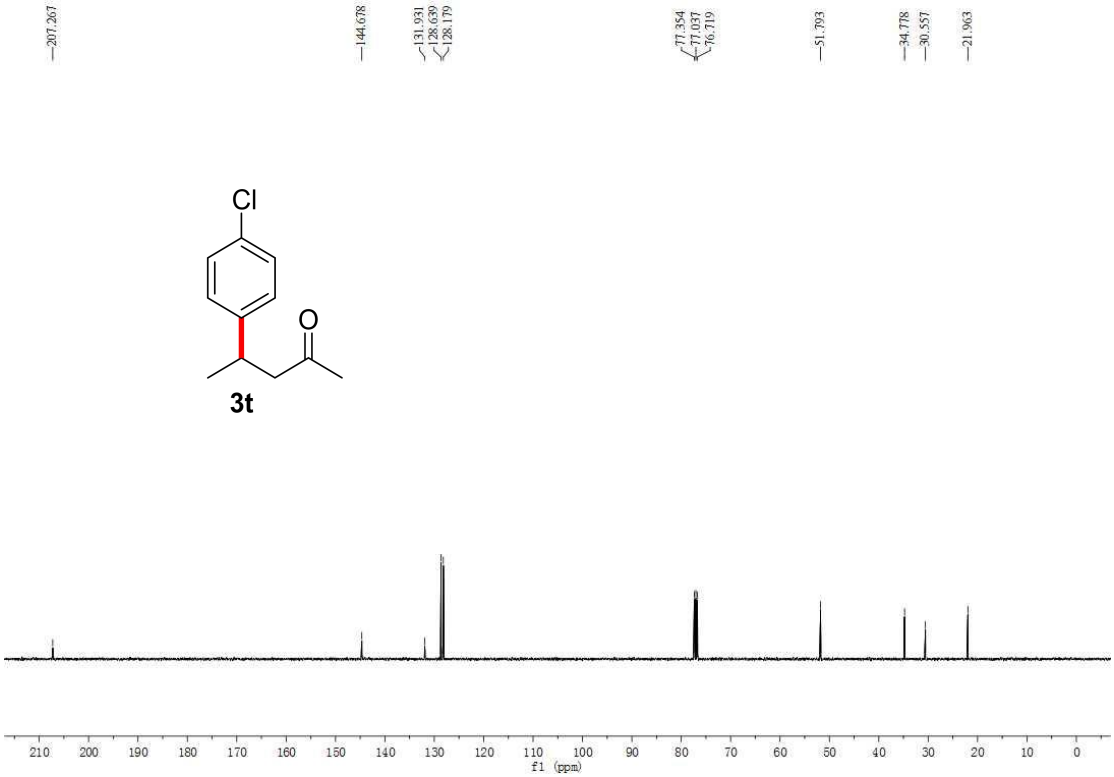
Supplementary Figure 47. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 3s.



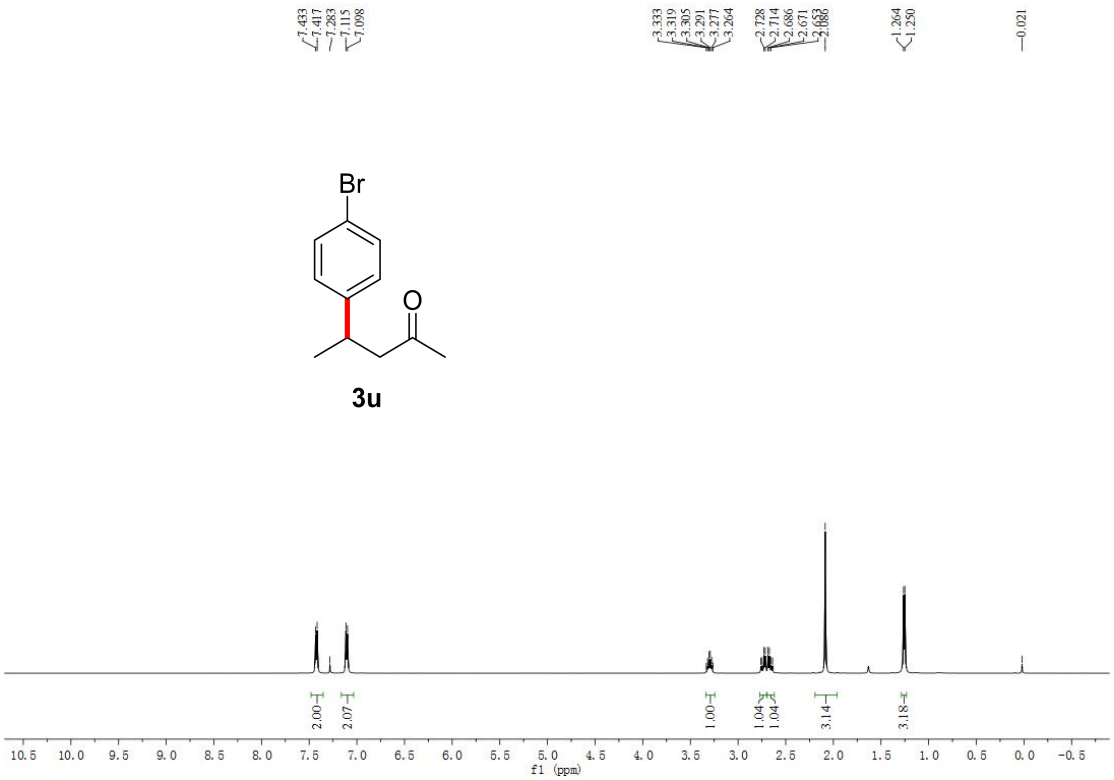
Supplementary Figure 48. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 3s.



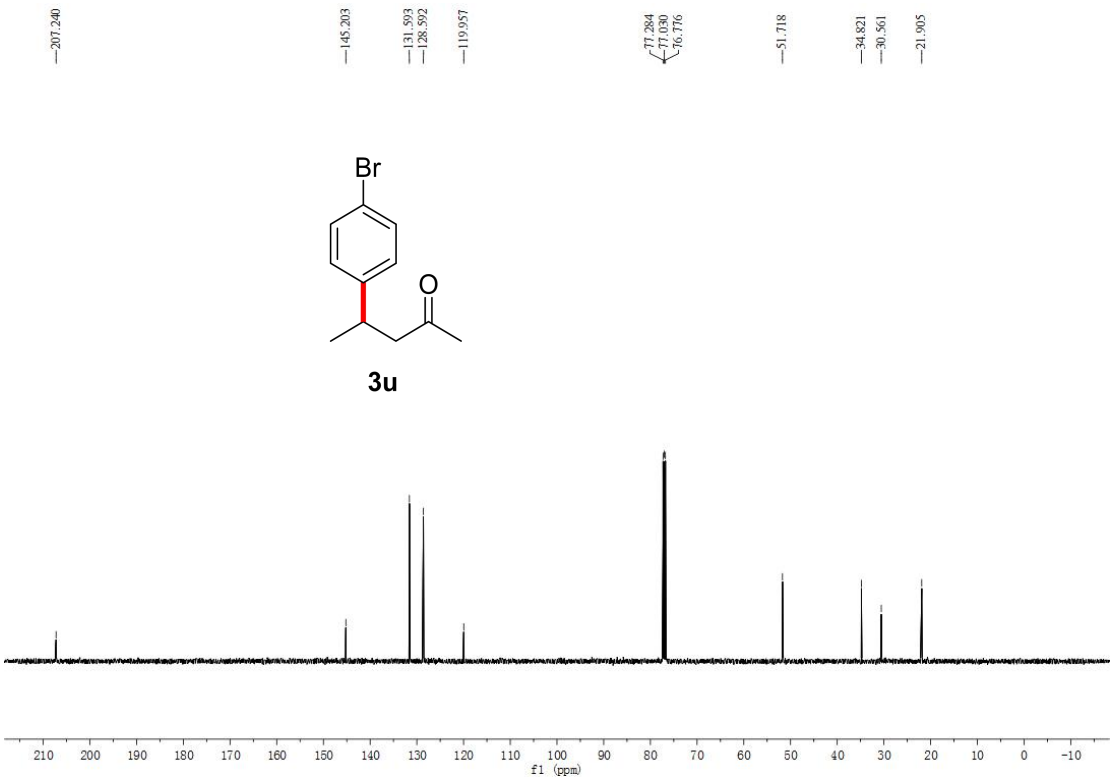
Supplementary Figure 49. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 3t.



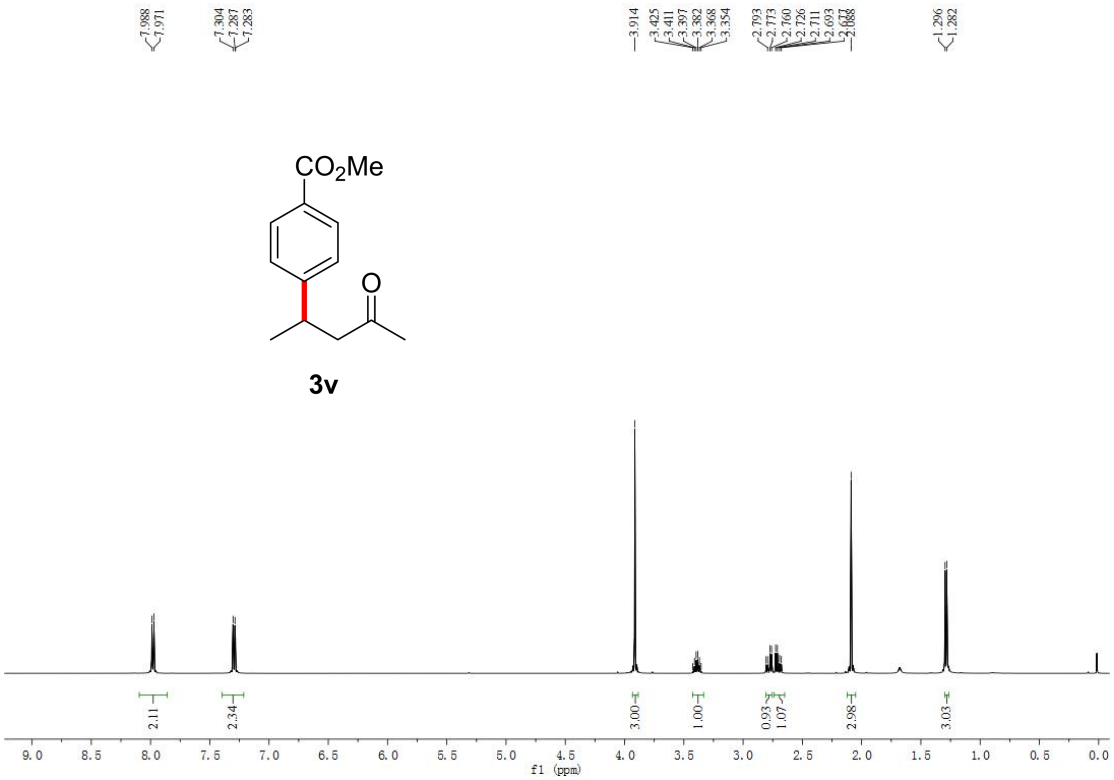
Supplementary Figure 50. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 3t.



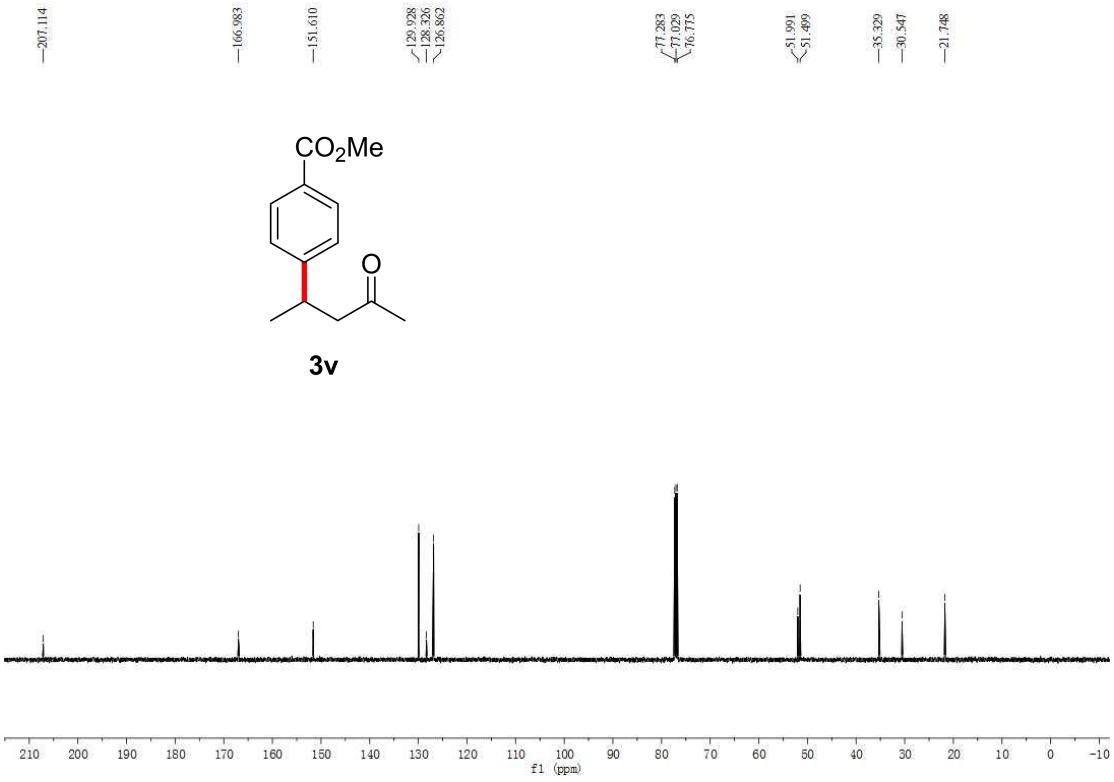
Supplementary Figure 51. ^{1}H NMR (500 MHz, $CDCl_3$) spectrum for 3u.



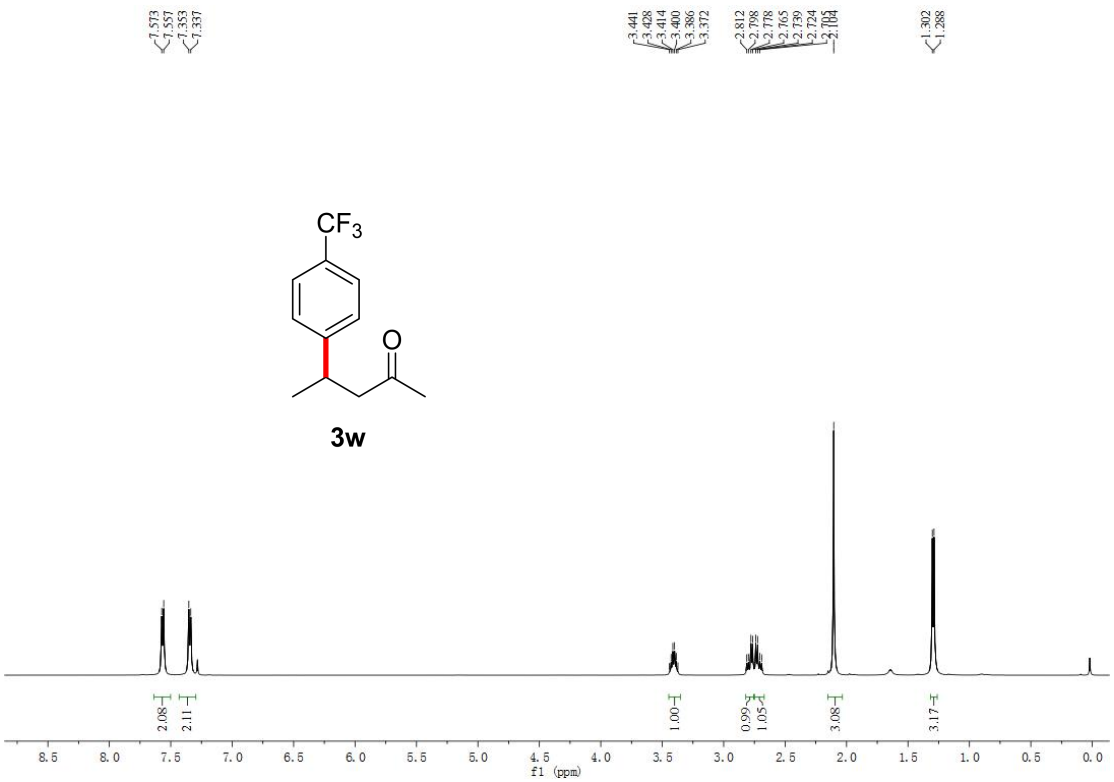
Supplementary Figure 52. ^{13}C NMR (126 MHz, $CDCl_3$) spectrum for 3u.



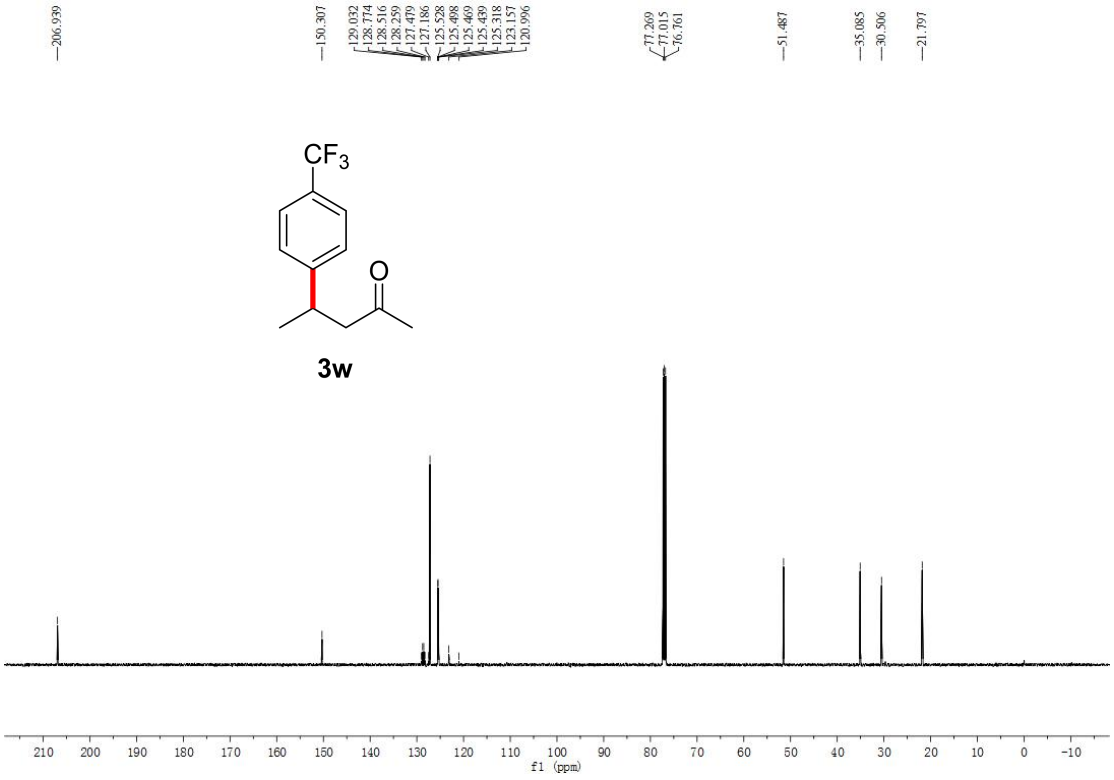
Supplementary Figure 53. ^{1}H NMR (500 MHz, $CDCl_3$) spectrum for 3v.



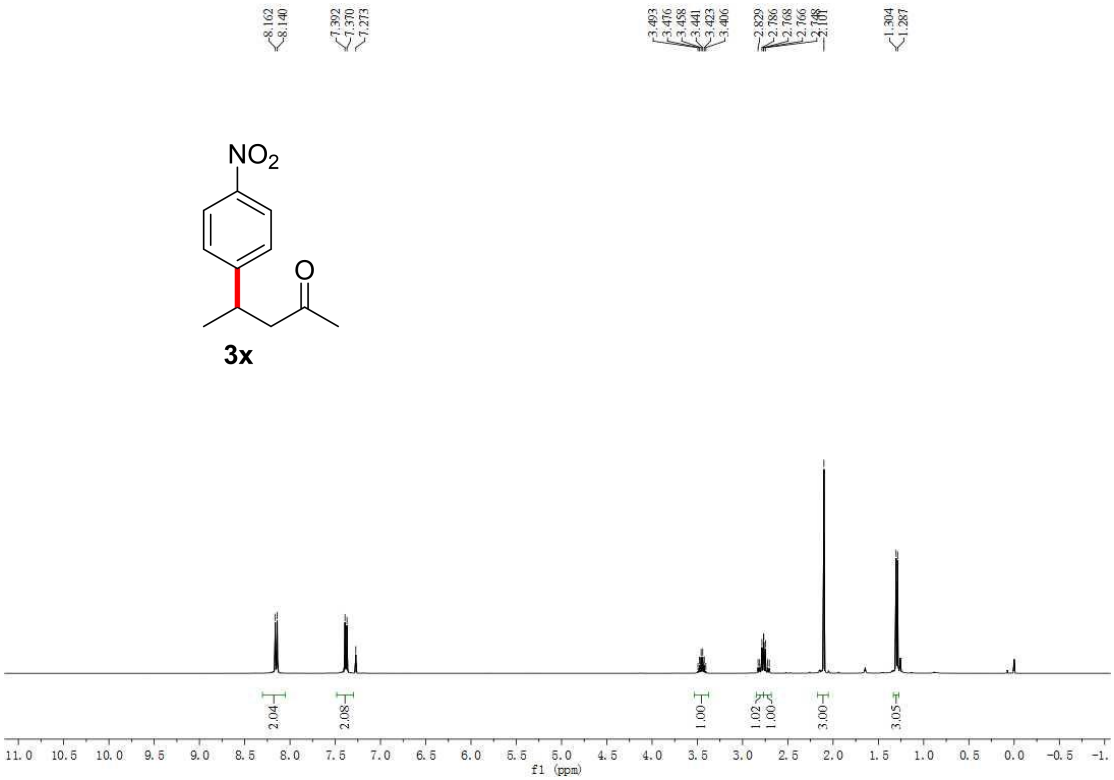
Supplementary Figure 54. ^{13}C NMR (126 MHz, $CDCl_3$) spectrum for 3v.



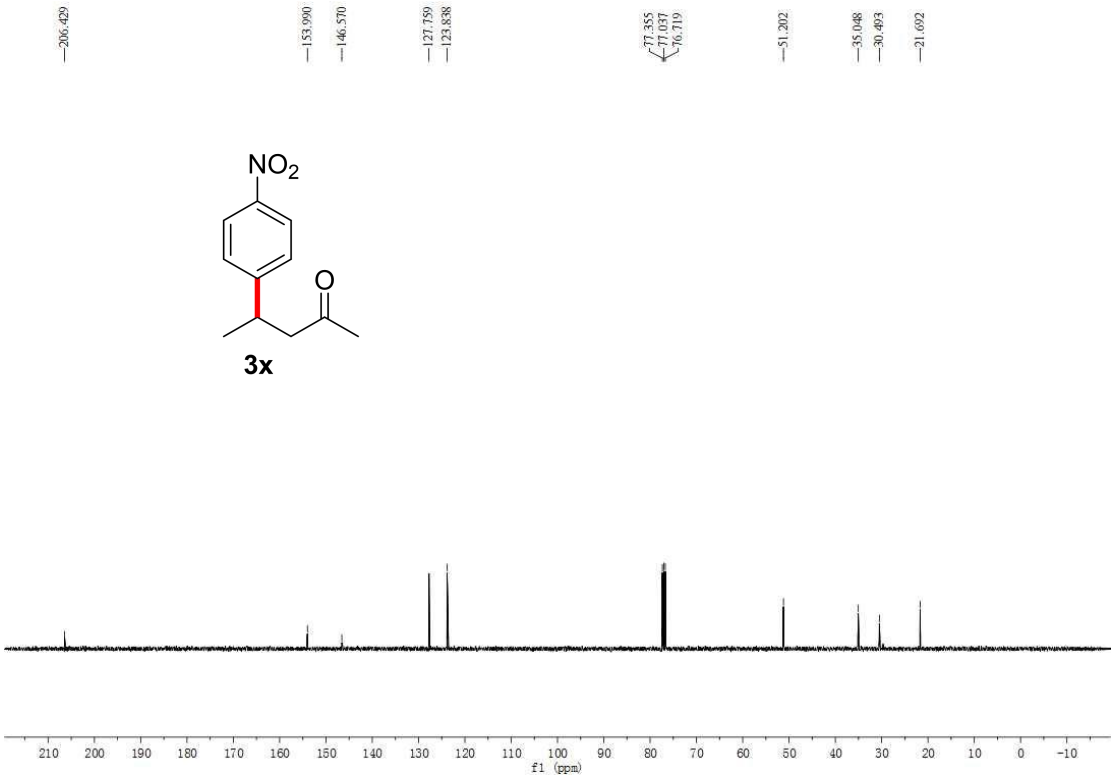
Supplementary Figure 55. ^{1}H NMR (500 MHz, $CDCl_3$) spectrum for 3w.



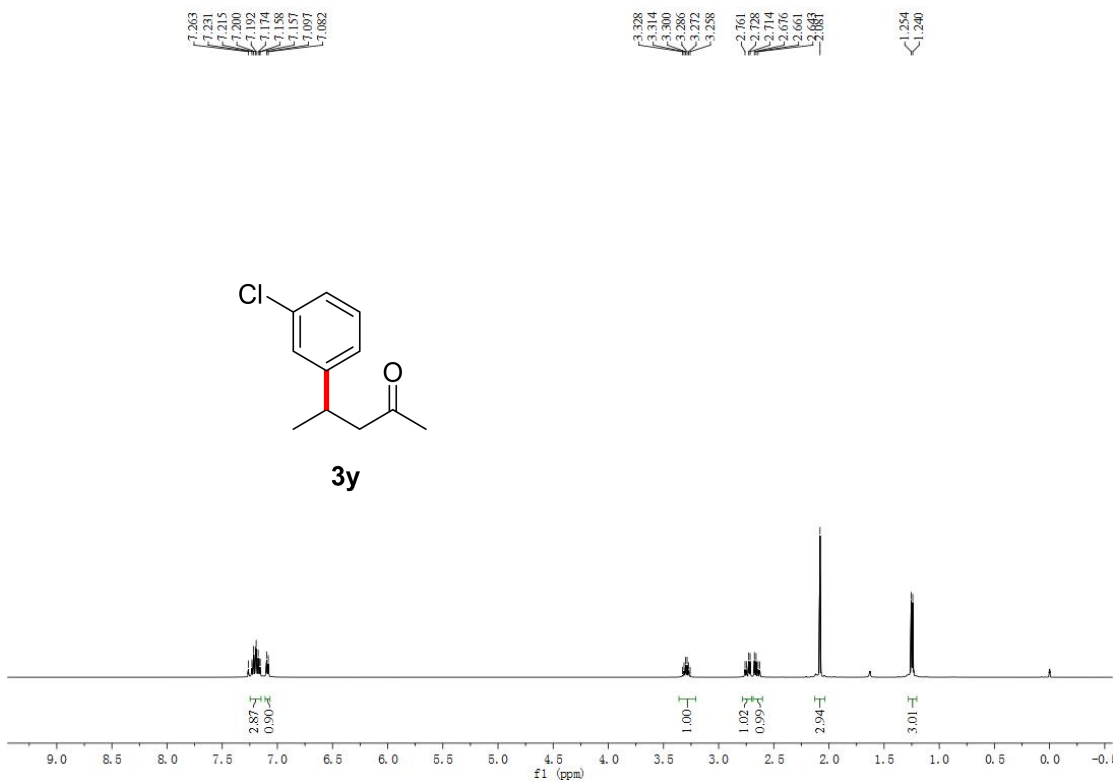
Supplementary Figure 56. ^{13}C NMR (126 MHz, $CDCl_3$) spectrum for 3w.



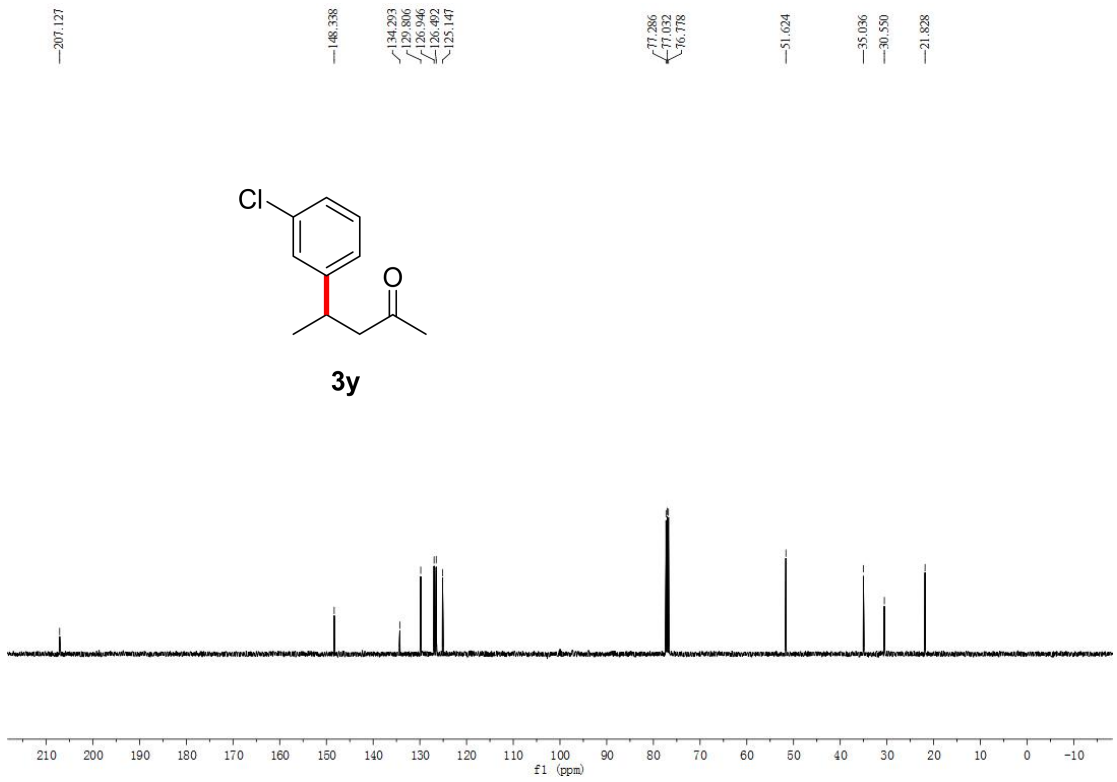
Supplementary Figure 57. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 3x.



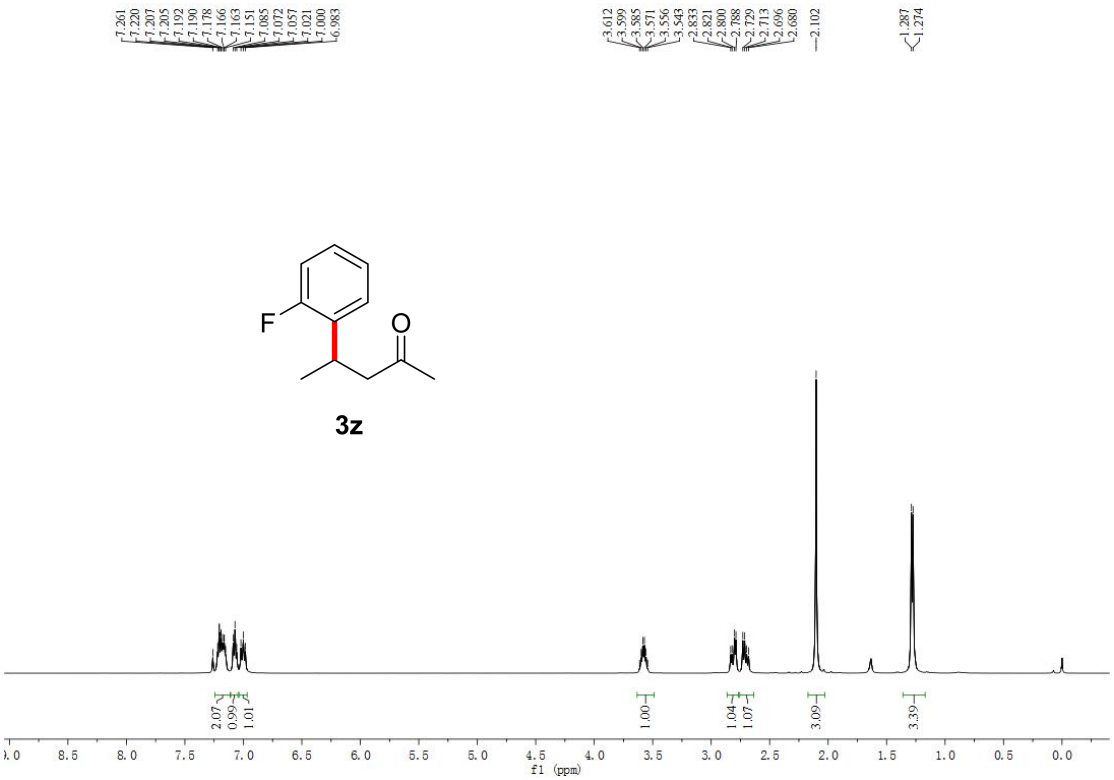
Supplementary Figure 58. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 3x.



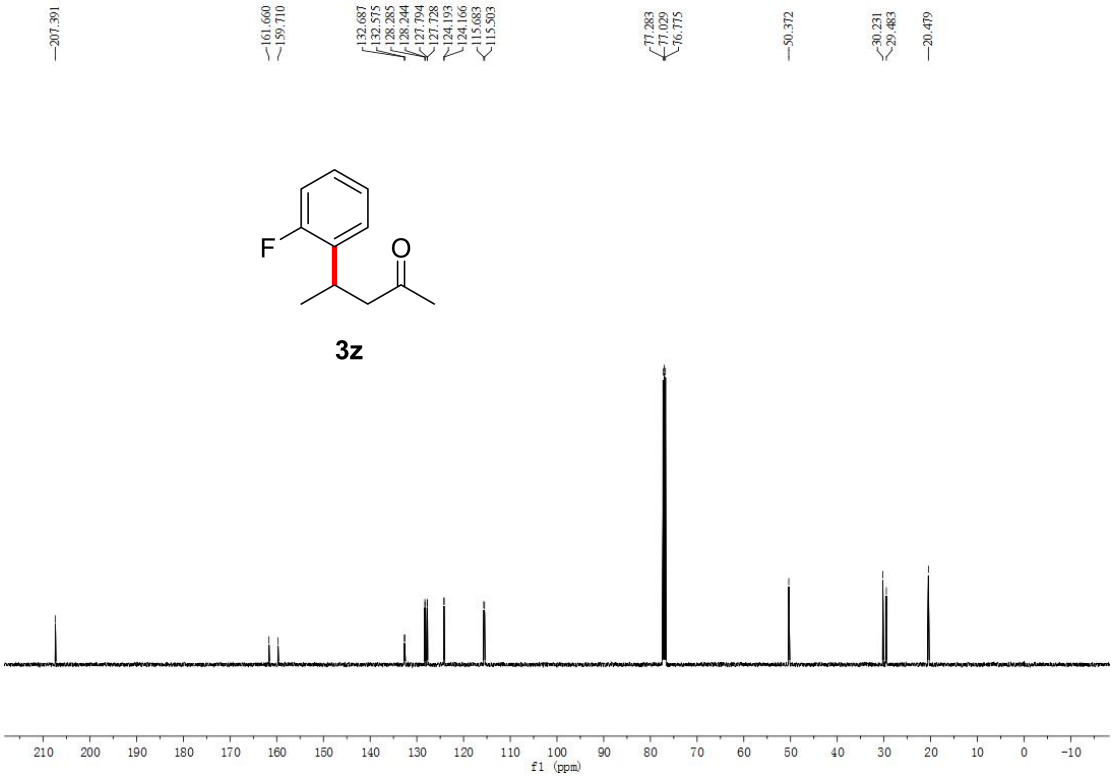
Supplementary Figure 59. ^{1}H NMR (500 MHz, $CDCl_3$) spectrum for 3y.



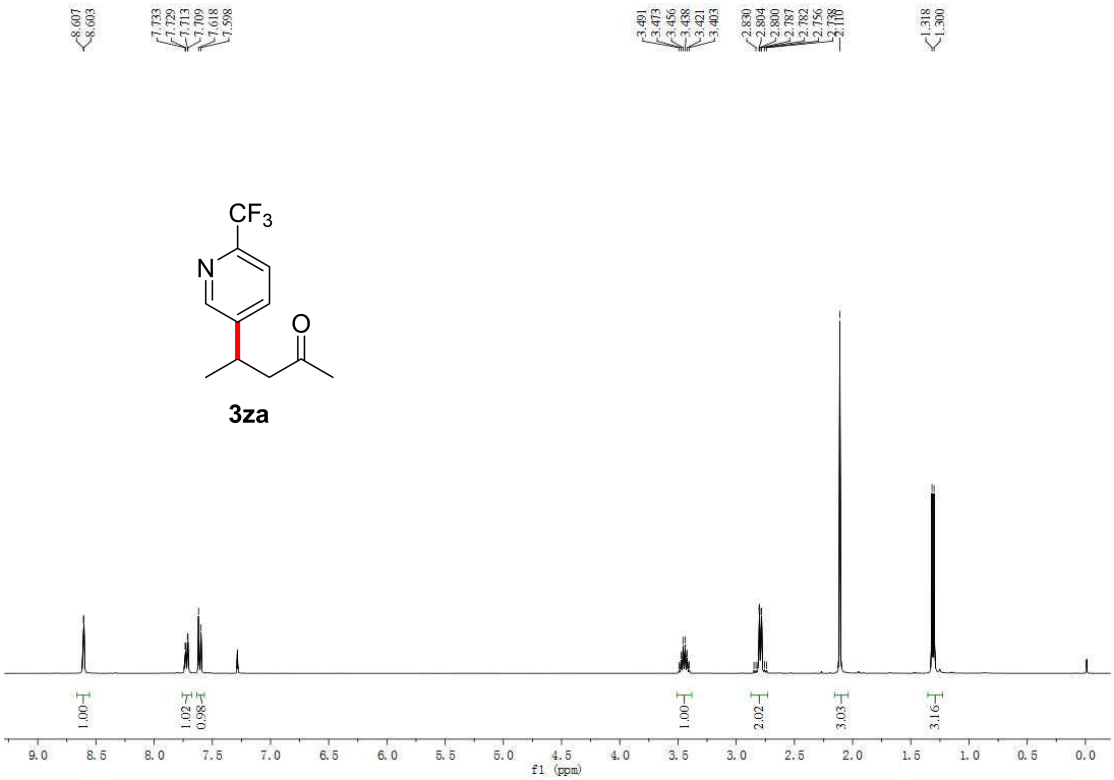
Supplementary Figure 60. ^{13}C NMR (126 MHz, $CDCl_3$) spectrum for 3y.



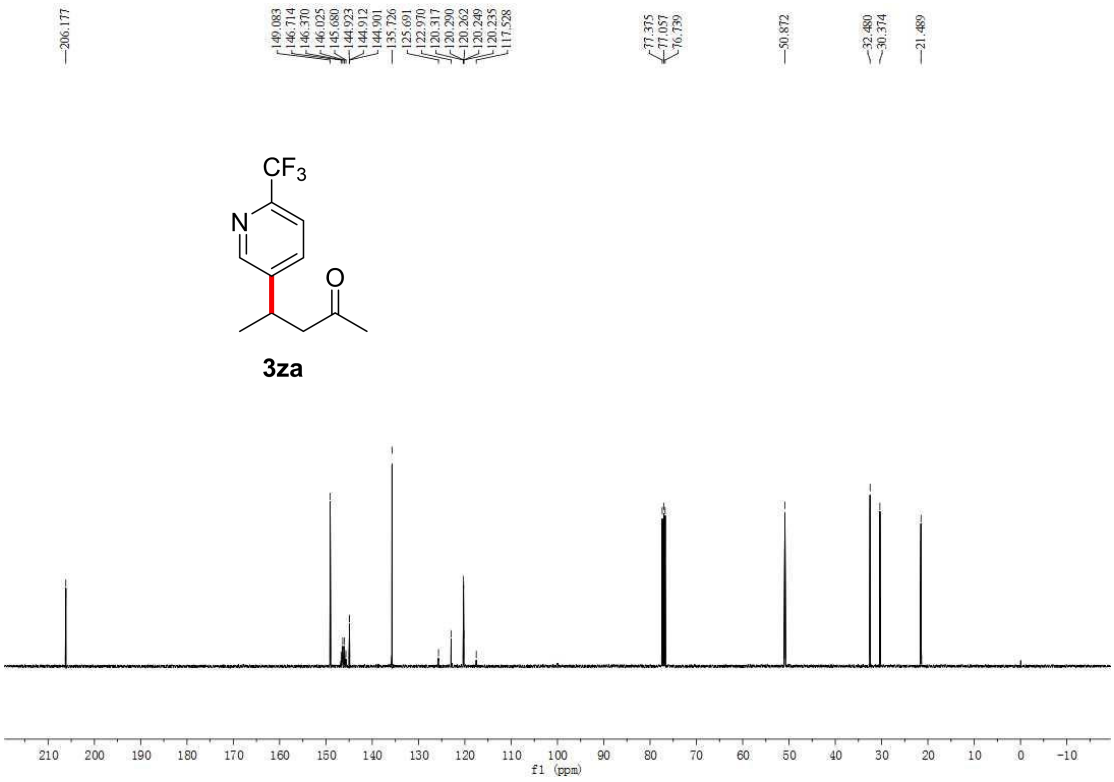
Supplementary Figure 61. ^{1}H NMR (500 MHz, $CDCl_3$) spectrum for 3z.



Supplementary Figure 62. ^{13}C NMR (126 MHz, $CDCl_3$) spectrum for 3z.



Supplementary Figure 63. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum for 3za.



Supplementary Figure 64. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum for 3za.