Supporting Information

Nickel-Catalyzed Acylation of Vinylpyridine with Alkylzincs under 1 atm CO

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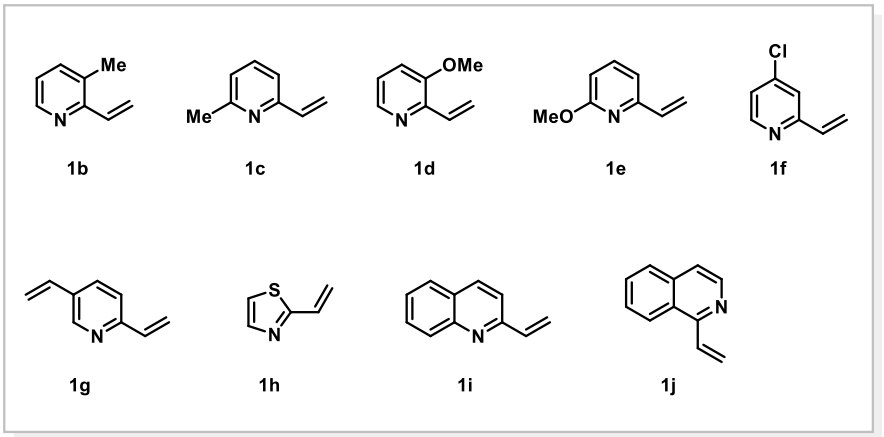
General Information

All reaction with CO gas was carried out in fume hood with the CO detector. All catalytic reactions were carried out under 1 atm of CO and anhydrous conditions running in dried glassware unless otherwise indicated. All raw materials synthesis were carried out under nitrogen atmosphere and anhydrous conditions unless otherwise indicated. THF was distilled from sodium/benzophenone. DMA (CAS 121-69-7) was purchased from Adamas (99.8%, SafeDry, Water ≤ 50 ppm (by K.F.), SafeSeal). $NiBr_2$·DME (CAS 28923-39-9) was purchased from Sinocompound. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.20 mm Huanghai silica gel plates (HSGF 254) using UV light as the visualizing agent and an acidic solution of phosphomolybdic acid (PMA) with heat as the stains. All new compounds were characterized by means of ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HRMS. NMR spectra were recorded using a Bruker AVANCE III 400 MHz NMR spectrometer and can be found at the end of the paper. High-resolution mass spectra (HRMS) were recorded on a Q Exactive plus 4G mass spectrometer using ESI-Quadrupole-Orbitrap LC-MS. All ^{1}H NMR data are reported in δ units, parts per million (ppm), and were calibrated relative to the signals for residual chloroform (7.26 ppm) in deuterochloroform ($CDCl_3$). All ^{13}C NMR data are reported in ppm relative to $CDCl_3$ (77.16 ppm) and were obtained with ^{1}H decoupling. The following abbreviations or combinations thereof were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, sext = sextet, bs = broad singlet, m = multiplet.

Experimental Procedures and Characterization Data for Substrates



Compounds **1b**[1], **1c**[2], **1d**[3], **1d**[4], **1e**[5], **1f**[6], **1g**[7], **1h**[8], **1i**[9], **1j**[10] were synthesized according to the published procedures.

a) Preparation of $ZnCl_2$ Solution (1.0 M in THF).

Zinc chloride (1.0 M in THF): Finely powdered anhydrous $ZnCl_2$ was weighed into a flame-dried Schlenk tube in the glove box in an inert atmosphere. The tube was heated with a heat gun for 2 min under vacuum and then backfilled with nitrogen (This process was repeated three times.). After cooling, the flask was backfilled with N_2, and THF (anhydrous, 1.0 M) was added. The suspension was vigorously stirred for 30 min before it was used.

b) General procedure A for preparation of ^{n}BuZnCl from transmetallation of nBuLi to $ZnCl_2$.

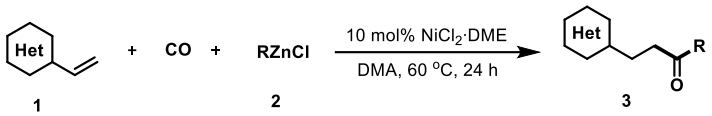
To a solution of $ZnCl_2$ (1.0 M) in THF was added ^{n}BuLi (2.4 M, 1.0 equiv) dropwise at 0 °C. The mixture was vigorously stirred at the same temperature for 30 min.

c) General procedure B for the preparation of organozinc reagents *via* direct insertion of zinc.

Anhydrous LiCl (2.0 equiv) was placed in an N_2-flushed sealed tube and dried for 10 min under the vacuum with heat gun. Zinc powder (2.0 equiv) was added under N_2 and the heterogeneous mixture of Zn and LiCl was dried again for 10 min under the vacuum with heat gun. The sealed tube was backfilled with N_2 (This process was repeated for three times). THF (1.0 M) was added and the Zn was activated with $BrCH_2CH_2Br$ (5 mol%) at 85 °C for 30 min. After cooling to room-temperature, Me_3SiCl (1 mol%) and I_2 (0.5 mol%) was added under N_2, then the mixture was refluxed for another 20 min. Alkyl bromide (1.0 equiv) was then added at room-temperature and the reaction mixture was stirred at a 65 °C oil bath for 12-48 h.

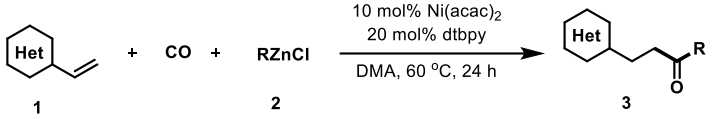
Experimental Procedures and Characterization Data for Products

a) General procedure C



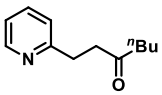
A 10 mL oven-dried tube charged with $NiCl_2$·DME (10 mol%) was evacuated and backfilled with N_2 three times. The reaction mixture was evacuated again and backfilled with CO (1 atm, balloon), followed by addition of DMA (0.2 M), vinylpyridine (1.0 equiv) and alkylzinc reagent (1.5 equiv) at r.t. The tube was screw-capped and the reaction mixture was allowed to stir at 60 °C oil bath for 24 h. The mixture was quenched with saturated aqueous $NaHCO_3$ and extracted with EtOAc. The separated organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to yield the crude product, which was purified by silica gel flash column chromatography.

b) General procedure D



A 10 mL oven-dried tube charged with $Ni(acac)_2$ (10 mol%) and dtbpy (20 mol%) was evacuated and backfilled with N_2 three times. The reaction mixture was evacuated again and backfilled with CO (1 atm, balloon), followed by addition of DMA (0.2 M), vinylpyridine (1.0 equiv) and alkylzinc reagent (1.5 equiv) at r.t. The tube was screw-capped and the reaction mixture was allowed to stir at 60 °C oil bath for 24 h. The mixture was quenched with saturated aqueous $NaHCO_3$ and extracted with EtOAc. The separated organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to yield the crude product, which was purified by silica gel flash column chromatography.

1-(Pyridin-2-yl)heptan-3-one (3a)



General procedure C was followed with **1a** on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 5/1-3/1) to afford **3a** as a colorless oil (25.6 mg, 67%).

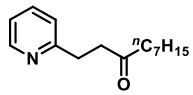
R_f = 0.31 (PE/EtOAc = 5/1);

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.49 (d, *J* = 4.4 Hz, 1H), 7.57 (td, *J* = 7.6, 1.6 Hz, 1H), 7.18 (d, *J* = 8.0 Hz, 1H), 7.10 (dd, *J* = 6.8, 5.6 Hz, 1H), 3.06 (t, *J* = 7.2 Hz, 2H), 2.91 (t, *J* = 7.2 Hz, 2H), 2.42 (t, *J* = 7.2 Hz, 2H), 1.54 (quin, *J* = 7.2 Hz, 2H), 1.31–1.23 (m, 2H), 0.88 (t, *J* = 7.2 Hz, 3H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 210.5, 160.7, 149.2, 136.5, 123.3, 121.3, 42.8, 41.6, 31.8, 26.0, 22.4, 13.9;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{12}H_{18}NO$: 192.1383; found: 192.1374.

1-(Pyridin-2-yl)decan-3-one (3b)



General procedure D was followed with **1a** on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 4/1) to afford **3b** as a colorless oil (25.6 mg, 55%).

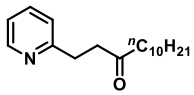
$\mathbf{R}_f$ = 0.42 (PE/EtOAc = 3/1);

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.49 (d, *J* = 4.0 Hz, 1H), 7.57 (td, *J* = 7.6, 1.6 Hz, 1H), 7.18 (d, *J* = 8.0 Hz, 1H), 7.09 (dd, *J* = 6.8, 5.2 Hz, 1H), 3.05 (t, *J* = 7.2 Hz, 2H), 2.91 (t, *J* = 7.2 Hz, 2H), 2.41 (t, *J* = 7.2 Hz, 2H), 1.55 (quin, *J* = 7.2 Hz, 2H), 1.29–1.24 (m, 8H), 0.86 (t, *J* = 7.2 Hz, 3H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 210.6, 160.8, 149.3, 136.5, 123.4, 121.3, 43.1, 41.7, 31.9, 31.8, 29.3, 29.2, 24.0, 22.7, 14.2;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{15}H_{24}NO$: 234.1852; found: 234.1846.

1-(Pyridin-2-yl)tridecan-3-one (3c)



General procedure D was followed with **1a** on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 3/1–2/1) to afford **3c** as a colorlessoil (25.2 mg, 46%).

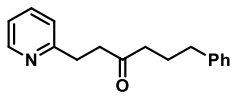
$\mathbf{R}_f$ = 0.30 (PE/EtOAc = 3/1);

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.49 (d, *J* = 4.0 Hz, 1H), 7.57 (td, *J* = 7.6, 1.6 Hz, 1H), 7.18 (d, *J* = 7.6 Hz, 1H), 7.10 (dd, *J* = 6.8, 5.2 Hz, 1H), 3.06 (t, *J* = 7.2 Hz, 2H), 2.91 (t, *J* = 7.2 Hz, 2H), 2.42 (t, *J* = 7.2 Hz, 2H), 1.55 (quin, *J* = 7.2 Hz, 2H), 1.31–1.24 (m, 14H). 0.87 (t, *J* = 6.8 Hz, 3H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 210.6, 160.8, 149.2, 136.5, 123.4, 121.3, 43.1, 41.7, 32.0, 31.9, 29.7, 29.6, 29.5, 29.4, 29.4, 24.0, 22.8, 14.2;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{18}H_{30}NO$: 276.2322; found: 276.2316.

6-Phenyl-1-(pyridin-2-yl)hexan-3-one (3d)



General procedure C was followed with **1a** on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 3/1–2/1) to afford **3d** as a colorless oil (25.8 mg, 51%).

$\mathbf{R}_f$ = 0.26 (PE/EtOAc = 3/1);

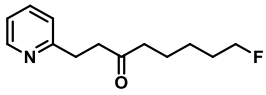
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.48 (d, *J* = 4.8 Hz, 1H), 7.56 (td, *J* = 8.0, 1.6 Hz, 1H), 7.29–7.25 (m, 2H), 7.20–7.14 (m, 4H), 7.09 (dd, *J* = 7.2, 4.8 Hz, 1H), 3.05 (t, *J* = 7.2

Hz, 2H), 2.89 (t, *J* = 7.2 Hz, 2H), 2.59 (t, *J* = 7.2 Hz, 2H), 2.45 (t, *J* = 7.2 Hz, 2H), 1.90 (quin, *J* = 7.2 Hz, 2H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 210.1, 160.6, 149.3, 141.8, 136.5, 128.6, 128.5, 126.0, 123.4, 121.3, 42.2, 41.7, 35.2, 31.8, 25.4;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{17}H_{20}NO$: 254.1539; found: 254.1535.

8-Fluoro-1-(pyridin-2-yl)octan-3-one (3e)



General procedure C was followed with **1a** on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 3/1–2/1) to afford **3e** as a colorless oil (20.5 mg, 46%).

R*f* = 0.33 (PE/EtOAc = 3/1);

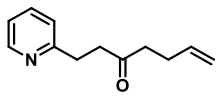
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.49 (d, *J* = 4.0 Hz, 1H), 7.57 (td, *J* = 7.6, 2.0 Hz, 1H), 7.17 (d, *J* = 7.6 Hz, 1H), 7.09 (dd, *J* = 7.6, 5.2 Hz, 1H), 4.47 (t, *J* = 6.0 Hz, 1H), 4.35 (t, *J* = 6.0 Hz, 1H), 3.06 (t, *J* = 7.2 Hz, 2H), 2.91 (t, *J* = 7.2 Hz, 2H), 2.45 (t, *J* = 7.2 Hz, 2H), 1.74–1.57 (m, 4H), 1.41–1.33 (m, 2H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 210.1, 160.6, 149.3, 136.5, 123.4, 121.3, 84.0 (d, $J_{C\text{-}F}$ = 163.3 Hz), 42.8, 41.7, 31.8, 30.3 (d, $J_{C\text{-}F}$ = 19.5 Hz), 24.9 (d, $J_{C\text{-}F}$ = 5.4 Hz), 23.4;

^{19}F NMR (376 MHz, $CDCl_3$): δ -218.4;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{13}H_{19}FNO$: 224.1445; found: 224.1441.

1-(Pyridin-2-yl)hept-6-en-3-one (3f)



General procedure C was followed with **1a** on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 3/1–2/1) to afford **3f** as a colorless oil (13.6 mg, 36%).

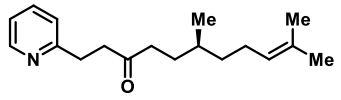
R*f* = 0.28 (PE/EtOAc = 3/1);

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.49 (d, *J* = 4.0 Hz, 1H), 7.57 (td, *J* = 7.6, 1.6 Hz, 1H), 7.18 (d, *J* = 7.6 Hz, 1H), 7.10 (dd, *J* = 7.2, 4.8 Hz, 1H), 5.78 (ddt, *J* = 16.8, 10.4, 6.8 Hz, 1H), 5.00 (dd, *J* = 17.2, 1.2 Hz, 1H), 4.95 (d, *J* = 11.2 Hz, 1H), 3.07 (t, *J* = 7.2 Hz, 2H), 2.93 (t, *J* = 7.2 Hz, 2H), 2.54 (t, *J* = 7.2 Hz, 2H), 2.32 (q, *J* = 6.8 Hz, 2H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 209.5, 160.6, 149.3, 137.3, 136.6, 123.4, 121.4, 115.3, 42.1, 41.8, 31.8, 27.9;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{12}H_{16}NO$: 190.1226; found: 190.1223.

6,10-Dimethyl-1-(pyridin-2-yl)undec-9-en-3-one (3g)



General procedure D was followed with **1a** on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 3/1) to afford **3g** as a colorlessoil (19.7 mg, 36%).

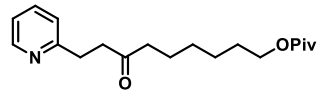
R_f = 0.41 (PE/EtOAc = 3/1);

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.49 (d, *J* = 4.4 Hz, 1H), 7.57 (td, *J* = 7.6, 2.0 Hz, 1H), 7.18 (d, *J* = 7.6 Hz, 1H), 7.09 (dd, *J* = 6.8, 5.6 Hz, 1H), 5.07 (tt, *J* = 6.8, 1.6 Hz, 1H), 3.06 (t, *J* = 7.2 Hz, 2H), 2.92 (t, *J* = 7.2 Hz, 2H), 2.49–2.35 (m, 2H), 2.01–1.88 (m, 2H), 1.67 (s, 3H), 1.58 (s, 3H), 1.42–1.25 (m, 4H), 1.17–1.08 (m, 1H), 0.84 (d, *J* = 6.4 Hz, 3H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 210.7, 160.7, 149.2, 136.5, 131.4, 124.8, 123.4, 121.3, 41.7, 40.8, 37.0, 32.2, 31.9, 30.8, 25.8, 25.6, 19.4, 17.8;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{18}H_{28}NO$: 274.2165; found: 274.2160.

7-Oxo-9-(pyridin-2-yl)nonyl pivalate (3h)



General procedure C was followed with **1a** on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 3/1–2/1) to afford **3h** as a colorless oil (26.1 mg, 41%).

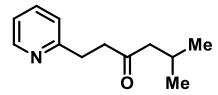
R_f = 0.19 (PE/EtOAc = 3/1);

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.48 (d, *J* = 4.0 Hz, 1H), 7.57 (td, *J* = 7.6, 2.0 Hz, 1H), 7.17 (d, *J* = 7.6 Hz, 1H), 7.08 (dd, *J* = 7.2, 5.2 Hz, 1H), 4.01 (t, *J* = 6.8 Hz, 2H), 3.05 (t, *J* = 7.2 Hz, 2H), 2.90 (t, *J* = 7.2 Hz, 2H), 2.42 (t, *J* = 7.2 Hz, 2H), 1.63–1.53 (m, 4H), 1.35–1.27 (m, 4H), 1.17 (s, 9H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 210.3, 178.8, 160.7, 149.2, 136.5, 123.4, 121.4, 64.4, 42.9, 41.7, 38.8, 31.8, 28.9, 28.6, 27.3, 25.9, 23.8;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{19}H_{30}NO_3$: 320.2220; found: 320.2213.

5-Methyl-1-(pyridin-2-yl)hexan-3-one (3i)



General procedure C was followed with **1a** on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 3/1–2/1) to afford **3i** as a colorless oil (17.6 mg, 46%).

R_f = 0.20 (PE/EtOAc = 5/1);

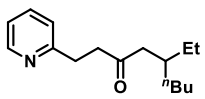
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.48 (d, *J* = 4.4 Hz, 1H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.18 (d, *J* = 7.6 Hz, 1H), 7.08 (dd, *J* = 7.2, 4.8 Hz, 1H), 3.05 (t, *J* = 7.2 Hz, 2H), 2.89 (t, *J* = 7.2 Hz, 2H), 2.30 (d, *J* = 7.2 Hz, 2H), 2.13 (quin, *J* = 6.8 Hz, 1H), 0.87 (d, *J* = 6.8 Hz,

6H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 210.1, 160.7, 149.2, 136.5, 123.4, 121.3, 52.1, 42.2, 31.8, 24.8, 22.7;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{12}H_{18}NO$: 192.1383; found: 192.1378.

5-Ethyl-1-(pyridin-2-yl)nonan-3-one (3j)



General procedure C was followed with **1a** on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 3/1–2/1) to afford **3j** as a colorless oil (18.3 mg, 37%).

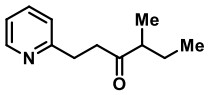
R_f = 0.34 (PE/EtOAc = 3/1);

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.49 (d, *J* = 4.4 Hz, 1H), 7.57 (td, *J* = 7.6, 1.6 Hz, 1H), 7.18 (d, *J* = 7.6 Hz, 1H), 7.09 (dd, *J* = 6.8, 5.2 Hz, 1H), 3.05 (t, *J* = 7.2 Hz, 2H), 2.90 (t, *J* = 7.2 Hz, 2H), 2.33 (d, *J* = 6.4 Hz, 2H), 1.85 (quin, *J* = 6.4 Hz, 1H), 1.32–1.17 (m, 8H), 0.85 (t, *J* = 7.2 Hz, 3H), 0.81 (t, *J* = 7.2 Hz, 3H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 210.6, 160.8, 149.2, 136.5, 123.5, 121.3, 47.7, 42.3, 35.4, 33.3, 31.9, 29.0, 26.5, 23.1, 14.2, 10.9;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{16}H_{26}NO$: 248.2009; found: 248.2003.

4-Methyl-1-(pyridin-2-yl)hexan-3-one (3k)



General procedure C was followed with **1a** on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 3/1–2/1) to afford **3k** as a colorless oil (11.9 mg, 31%).

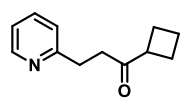
R_f = 0.31 (PE/EtOAc = 3/1);

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.49 (d, *J* = 4.4 Hz, 1H), 7.57 (td, *J* = 7.6, 2.0 Hz, 1H), 7.19 (d, *J* = 8.0 Hz, 1H), 7.09 (dd, *J* = 7.2, 5.2 Hz, 1H), 3.07–3.04 (m, 2H), 2.97–2.92 (m, 2H), 2.48 (sext, *J* = 6.8 Hz, 1H), 1.67 (quin, *J* = 7.2 Hz, 1H), 1.37 (quin, *J* = 7.2 Hz, 1H), 1.04 (d, *J* = 7.2 Hz, 3H), 0.83 (t, *J* = 7.6 Hz, 3H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 214.0, 160.9, 149.3, 136.5, 123.5, 121.3, 48.1, 40.3, 31.9, 26.0, 16.0, 11.7;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{12}H_{18}NO$: 192.1383; found: 192.1378.

1-Cyclobutyl-3-(pyridin-2-yl)propan-1-one (3l)



General procedure D was followed with **1a** on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 3/1–2/1) to afford **3l** as a colorless oil (21.5 mg, 57%).

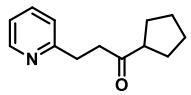
R_f = 0.25 (PE/EtOAc = 3/1);

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.48 (d, *J* = 4.0 Hz, 1H), 7.56 (td, *J* = 7.6, 2.0 Hz, 1H), 7.17 (d, *J* = 8.0 Hz, 1H), 7.08 (dd, *J* = 7.2, 4.8 Hz, 1H), 3.27 (quin, *J* = 8.4 Hz, 1H), 3.05 (t, *J* = 7.2 Hz, 2H), 2.85 (t, *J* = 7.2 Hz, 2H), 2.24–2.07 (m, 4H), 1.99–1.87 (m, 1H), 1.82–1.74 (m, 1H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 211.2, 160.8, 149.3, 136.5, 123.4, 121.3, 45.6, 39.0, 31.8, 24.4, 17.9;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{12}H_{16}NO$: 190.1226; found: 190.1223.

5-Methyl-1-(pyridin-2-yl)hexan-3-one (3m)



General procedure C was followed with **1a** on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 3/1–2/1) to afford **3m** as a colorless oil (18.3 mg, 45%).

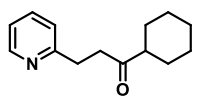
R$_f$ = 0.32 (PE/EtOAc = 3/1);

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.47 (d, *J* = 4.4 Hz, 1H), 7.54 (td, *J* = 7.6, 1.6 Hz, 1H), 7.16 (d, *J* = 7.6 Hz, 1H), 7.09 (ddd, *J* = 7.2, 4.8, 0.8 Hz, 1H), 3.06–3.02 (m, 2H), 2.96–2.92 (m, 2H), 2.87 (quin, *J* = 8.0 Hz, 1H), 1.81–1.67 (m, 4H), 1.65–1.50 (m, 4H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 212.6, 161.0, 149.3, 136.5, 123.4, 121.3, 51.7, 40.9, 32.0, 29.0, 26.1;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{13}H_{18}NO$: 204.1383; found: 204.1380.

1-Cyclohexyl-3-(pyridin-2-yl)propan-1-one (3n)



General procedure C was followed with **1a** on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 3/1) to afford **3n** as a colorless oil (26.5 mg, 61%).

R$_f$ = 0.35 (PE/EtOAc = 3/1);

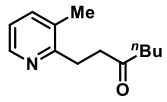
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.48 (d, *J* = 4.0 Hz, 1H), 7.55 (td, *J* = 7.6, 1.6 Hz, 1H), 7.16 (d, *J* = 7.6 Hz, 1H), 7.08 (dd, *J* = 6.8, 5.6 Hz, 1H), 3.03 (t, *J* = 6.8 Hz, 2H), 2.93 (t, *J* = 6.8 Hz, 2H), 2.35 (tt, *J* = 11.2, 3.2 Hz, 1H), 1.82–1.79 (m, 2H), 1.75–1.72 (m, 2H), 1.65–1.62 (m, 1H), 1.34–1.14 (m, 5H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 213.4, 160.9, 149.2, 136.5, 123.4, 121.3, 51.0, 39.8, 31.9, 28.6, 26.0, 25.8;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{14}H_{20}NO$: 218.1539; found: 218.1534.

1-(3-Methylpyridin-2-yl)heptan-3-one (3o)

General procedure C was followed with **1b** on 0.2 mmol scale. The reaction mixture



was purified by flash column chromatography (PE/EtOAc = 3/1) to afford **3o** as a colorless oil (18.8 mg, 46%).

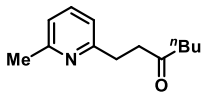
$\mathbf{R}_f$ = 0.31 (PE/EtOAc = 3/1);

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 (d, *J* = 4.0 Hz, 1H), 7.38 (d, *J* = 7.2 Hz, 1H), 7.01 (dd, *J* = 7.6, 4.8 Hz, 1H), 3.05–3.01 (m, 2H), 2.96–2.92 (m, 2H), 2.49 (t, *J* = 7.2 Hz, 2H), 2.32 (s, 3H), 1.58 (quin, *J* = 7.6 Hz, 2H), 1.31 (sext, *J* = 7.6 Hz, 2H), 0.90 (t, *J* = 7.2 Hz, 3H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 211.1, 158.6, 146.5, 137.4, 131.4, 121.3, 42.9, 40.2, 28.6, 26.2, 22.5, 18.9, 14.0;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{13}H_{20}NO$: 206.1539; found: 206.1530.

1-(6-Methylpyridin-2-yl)heptan-3-one (3p)



General procedure C was followed with **1c** on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 3/1) to afford **3p** as a colorless oil (20.4 mg, 50%).

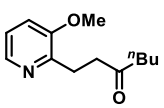
$\mathbf{R}_f$ = 0.30 (PE/EtOAc = 5/1);

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 (t, *J* = 7.6 Hz, 1H), 6.94 (t, *J* = 7.2 Hz, 2H), 3.01 (t, *J* = 7.2 Hz, 2H), 2.85 (t, *J* = 7.2 Hz, 2H), 2.49 (s, 3H), 2.41 (t, *J* = 7.2 Hz, 2H), 1.54 (quin, *J* = 7.6 Hz, 2H), 1.27 (sext, *J* = 7.6 Hz, 2H), 0.87 (t, *J* = 7.2 Hz, 3H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 210.6, 160.1, 157.9, 136.7, 120.8, 120.1, 42.8, 42.1, 32.1, 26.0, 24.6, 22.4, 14.0;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{13}H_{20}NO$: 206.1539; found: 206.1534.

1-(3-Methoxypyridin-2-yl)heptan-3-one (3q)



General procedure C was followed with **1d** on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 3/1) to afford **3q** as a colorless oil (19.5 mg, 44%).

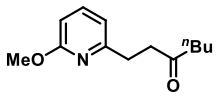
$\mathbf{R}_f$ = 0.46 (PE/EtOAc = 3/1);

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (dd, *J* = 4.0, 1.6 Hz, 1H), 7.10–7.05 (m, 2H), 3.82 (s, 3H), 3.08 (t, *J* = 7.2 Hz, 2H), 2.86 (t, *J* = 7.2 Hz, 2H), 2.47 (t, *J* = 7.6 Hz, 2H), 1.57 (quin, *J* = 7.6 Hz, 2H), 1.30 (sext, *J* = 7.6 Hz, 2H), 0.89 (t, *J* = 7.2 Hz, 3H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 211.1, 153.7, 150.6, 140.4, 122.0, 116.5, 55.3, 42.8, 40.0, 26.3, 26.2, 22.5, 14.0;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{13}H_{20}NO_2$: 222.1489; found: 222.1478.

1-(6-Methoxypyridin-2-yl)heptan-3-one (3r)



General procedure C was followed with **1e** on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 20/1) to afford **3r** as a colorless oil (14.6 mg, 33%).

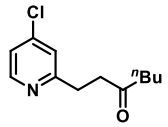
$\mathbf{R}_f$ = 0.41 (PE/EtOAc = 20/1);

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (dd, *J* = 7.2, 8.0 Hz, 1H), 6.73 (d, *J* = 7.2 Hz, 1H), 6.53 (d, *J* = 8.4 Hz, 1H), 3.89 (s, 3H), 2.98 (t, *J* = 6.8 Hz, 2H), 2.88 (t, *J* = 6.8 Hz, 2H), 2.45 (t, *J* = 7.2 Hz, 2H), 1.60–1.52 (m, 2H), 1.33–1.25 (m, 2H), 0.89 (t, *J* = 7.2 Hz, 3H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 210.8, 163.8, 158.4, 138.9, 115.6, 107.7, 53.3, 42.8, 41.4, 31.5, 26.1, 22.5, 14.0;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{13}H_{20}NO_2$: 222.1489; found: 222.1483.

1-(4-Chloropyridin-2-yl)heptan-3-one (3s)



General procedure C was followed with **1f** on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 3/1) to afford **3s** as a colorless oil (14.1 mg, 31%).

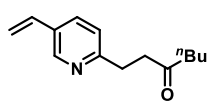
$\mathbf{R}_f$ = 0.49 (PE/EtOAc = 3/1);

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.38 (d, *J* = 5.2 Hz, 1H), 7.21 (d, *J* = 1.6 Hz, 1H), 7.11 (dd, *J* = 5.2, 2.0 Hz, 1H), 3.04 (t, *J* = 7.2 Hz, 2H), 2.91 (t, *J* = 7.2 Hz, 2H), 2.43 (t, *J* = 7.2 Hz, 2H), 1.55 (quin, *J* = 7.2 Hz, 2H), 1.29 (sext, *J* = 7.6 Hz, 2H), 0.88 (t, *J* = 7.2 Hz, 3H);

^{13}C NMR (100 MHz, $CDCl_3$) δ 210.1, 162.5, 150.1, 144.3, 123.7, 121.8, 42.8, 41.2, 31.6, 26.1, 22.5, 14.0;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{12}H_{17}ClNO$: 226.0993; found: 226.0984.

1-(5-Vinylpyridin-2-yl)heptan-3-one (3t)



General procedure C was followed with **1g** on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 5/1) to afford **3t** as a colorless oil (17.9 mg, 41%).

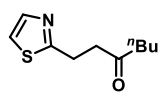
$\mathbf{R}_f$ = 0.39 (PE/EtOAc = 5/1);

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.47 (d, *J* = 1.6 Hz, 1H), 7.63 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.14 (d, *J* = 8.0 Hz, 1H), 6.66 (dd, *J* = 17.6, 10.8 Hz, 1H), 5.76 (d, *J* = 17.6 Hz, 1H), 5.31 (d, *J* = 11.2 Hz, 1H), 3.04 (t, *J* = 7.2 Hz, 2H), 2.90 (t, *J* = 7.2 Hz, 2H), 2.42 (t, *J* = 7.6 Hz, 2H), 1.54 (quin, *J* = 7.2 Hz, 2H), 1.28 (sext, *J* = 7.6 Hz, 2H), 0.88 (t, *J* = 7.2 Hz, 3H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 210.5, 160.1, 147.8, 133.5, 133.1, 130.8, 123.2, 115.4, 42.8, 41.6, 31.6, 26.1, 22.5, 14.0;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{14}H_{20}NO$: 218.1539; found: 218.1532.

1-(Thiazol-2-yl)heptan-3-one (3u)



General procedure C was followed with **1h** on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 3/1) to afford **3u** as a colorless oil (18.5 mg, 47%).

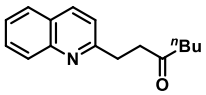
R_f = 0.47 (PE/EtOAc = 3/1);

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (d, *J* = 3.6 Hz, 1H), 7.18 (d, *J* = 3.2 Hz, 1H), 3.29 (t, *J* = 7.2 Hz, 2H), 2.97 (t, *J* = 7.2 Hz, 2H), 2.45 (t, *J* = 7.6 Hz, 2H), 1.57 (quin, *J* = 7.6 Hz, 2H), 1.33–1.27 (m, 2H). 0.89 (t, *J* = 7.2 Hz, 3H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 209.3, 169.6, 142.3, 118.5, 42.8, 41.7, 27.1, 26.1, 22.5, 14.0;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{10}H_{16}NOS$: 198.0947; found: 198.0939.

1-(Quinolin-2-yl)heptan-3-one (3v)



General procedure C was followed with **1i** on 0.1 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 10/1) to afford **3v** as a colorless oil (14.9 mg, 62%).

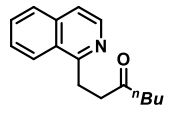
R_f = 0.51 (PE/EtOAc = 5/1);

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (d, *J* = 8.4 Hz, 1H), 7.99 (d, *J* = 8.4 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.67 (t, *J* = 7.6 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 1H), 7.31 (d, *J* = 8.4 Hz, 1H), 3.26 (t, *J* = 7.2 Hz, 2H), 3.03 (t, *J* = 7.2 Hz, 2H), 2.50 (t, *J* = 7.2 Hz, 2H), 1.58 (quin, *J* = 7.2 Hz, 2H), 1.31 (sext, *J* = 7.2 Hz, 2H). 0.89 (t, *J* = 7.2 Hz, 3H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 210.6, 161.2, 147.9, 136.3, 129.5, 128.8, 127.7, 126.9, 125.9, 121.9, 42.9, 41.3, 32.6, 26.1, 22.5, 14.0;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{16}H_{20}NO$: 242.1539; found: 242.1529.

1-(Isoquinolin-1-yl)heptan-3-one (3w)



General procedure D was followed with **1j** on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 5/1) to afford **3w** as a colorless oil (21.3 mg, 44%).

R_f = 0.42 (PE/EtOAc = 5/1);

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.38 (d, *J* = 6.0 Hz, 1H), 8.19 (d, *J* = 8.4 Hz, 1H), 7.79

(d, J = 8.0 Hz, 1H), 7.66 (t, J = 7.6 Hz, 1H), 7.59 (t, J = 7.6 Hz, 1H), 7.49 (d, J = 5.6 Hz, 1H), 3.59 (t, J = 7.2 Hz, 2H), 3.08 (t, J = 7.2 Hz, 2H), 2.54 (t, J = 7.6 Hz, 2H), 1.60 (quin, J = 7.6 Hz, 2H), 1.33 (sext, J = 7.6 Hz, 2H), 0.91 (t, J = 7.2 Hz, 3H);
^{13}C NMR (100 MHz, $CDCl_3$): δ 210.9, 160.0, 141.7, 136.1, 130.0, 127.4, 127.3, 127.1, 125.0, 119.5, 43.0, 40.2, 28.4, 26.1, 22.5, 14.0;
HRMS (ESI): $[M+H]^+$ Calcd for $C_{16}H_{20}NO$: 242.1539; found: 242.1534.

References

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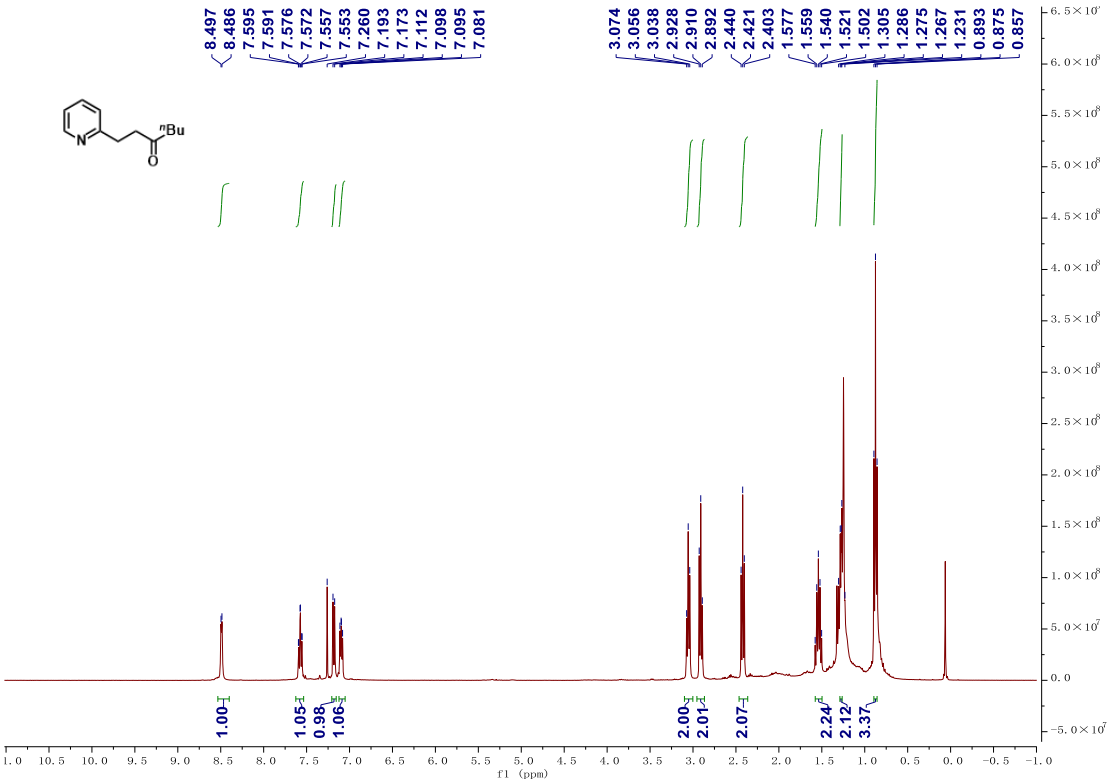
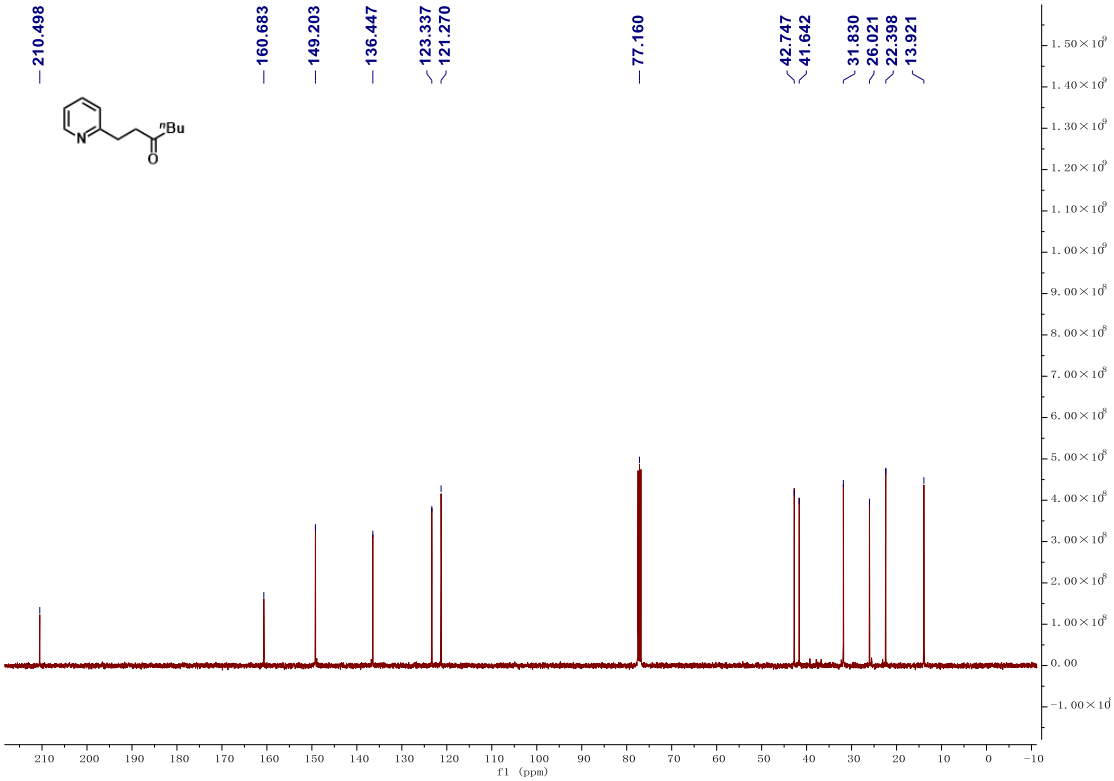
NMR Spectra

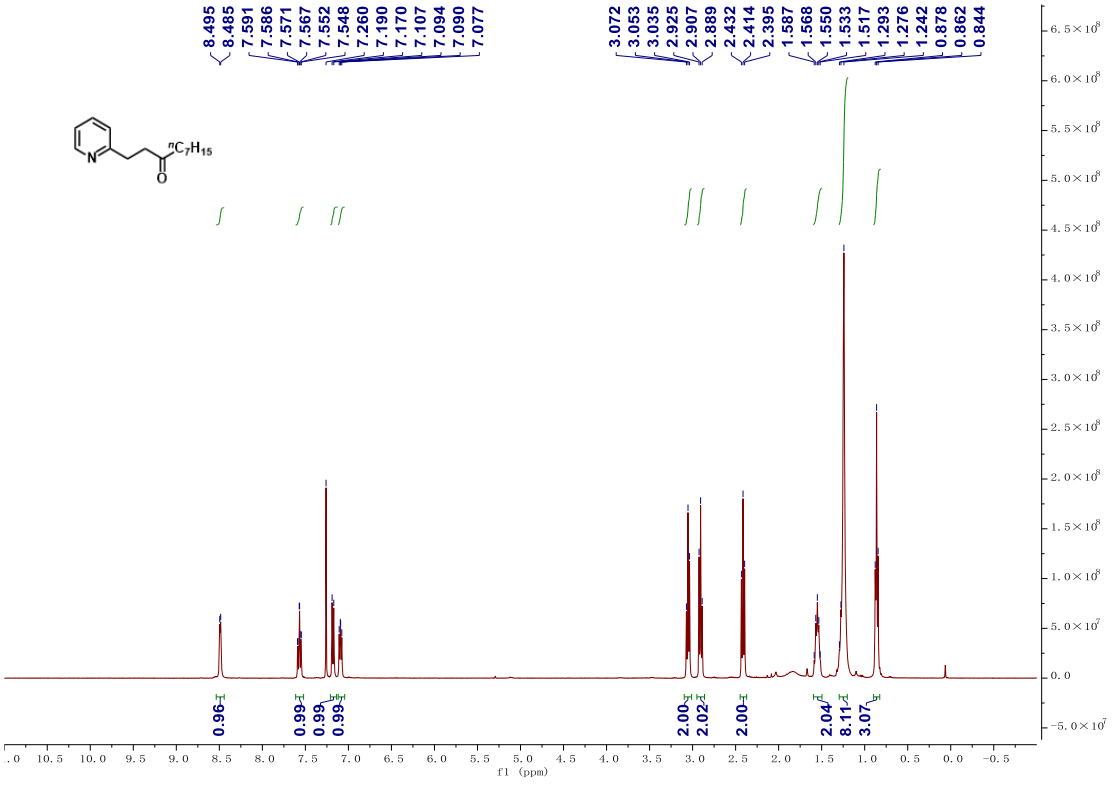
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3a**



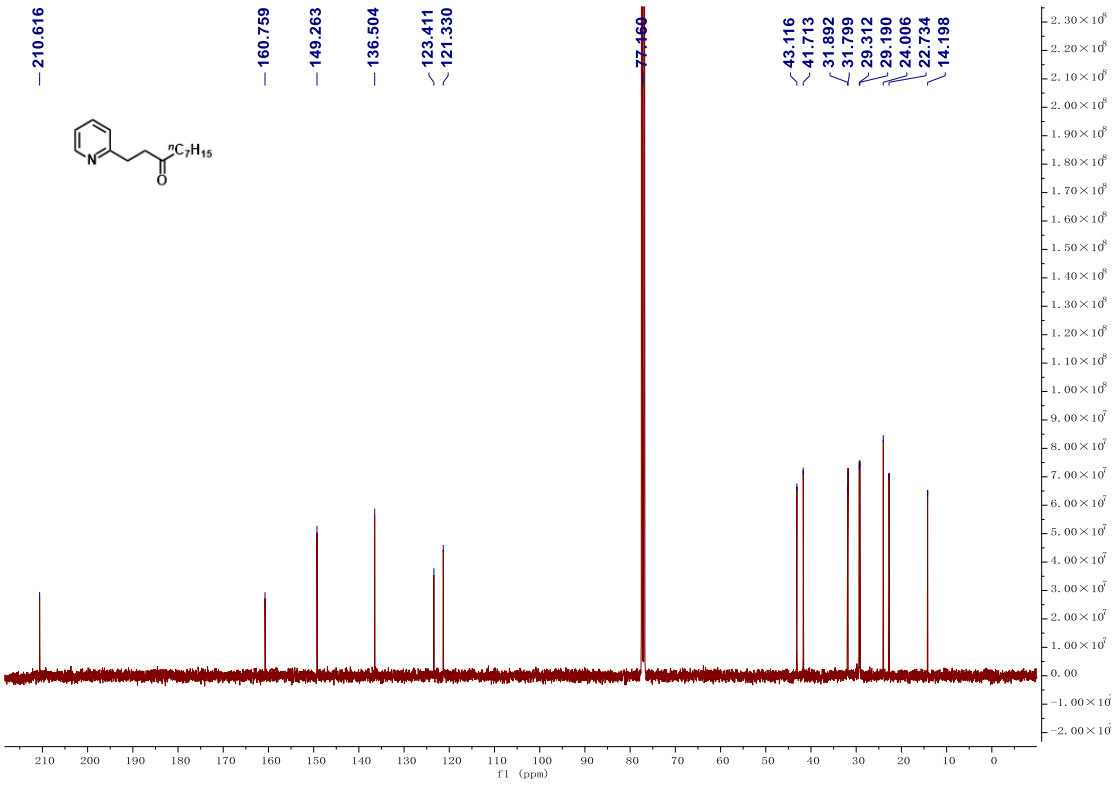
^{13}C NMR-spectrum (400 MHz, $CDCl_3$) of **3a**



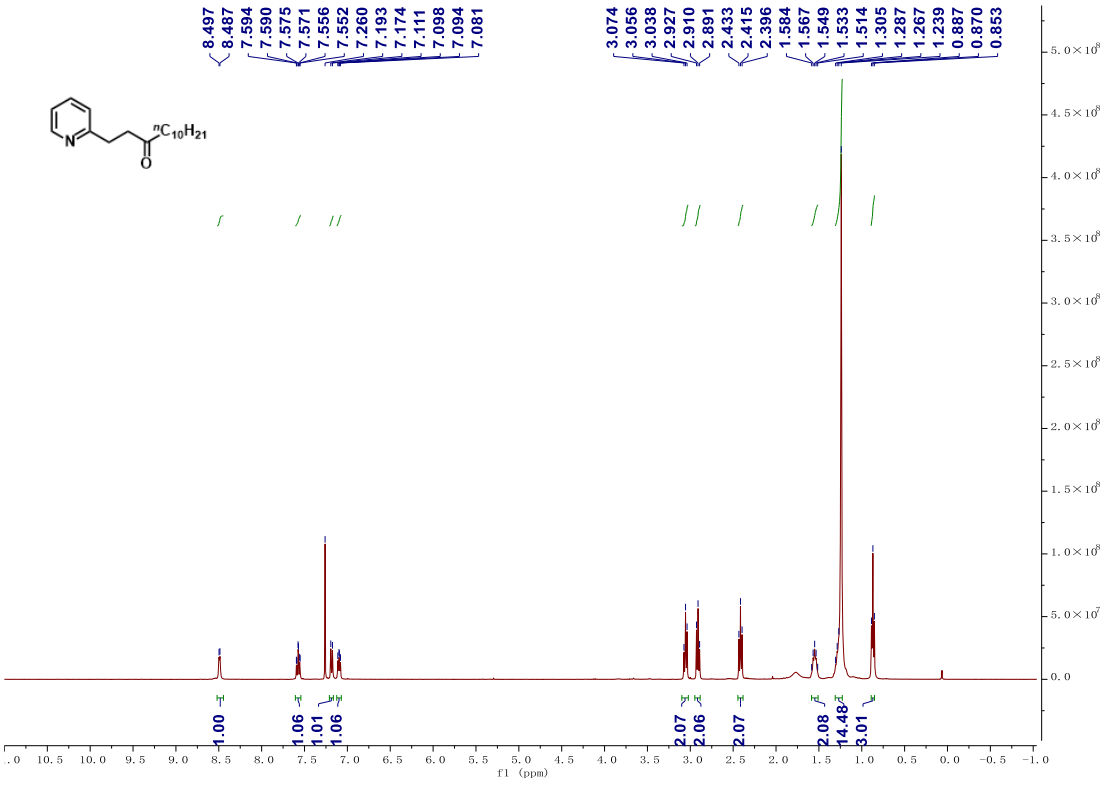
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3b**



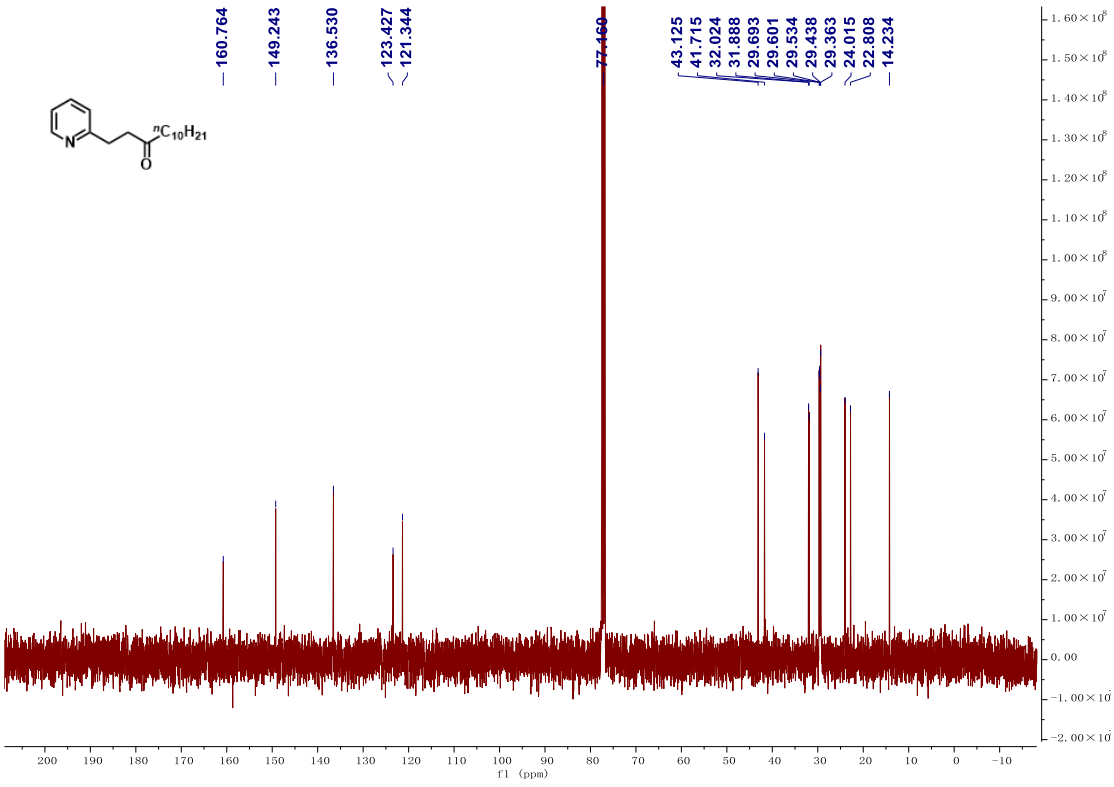
^{13}C NMR-spectrum (400 MHz, $CDCl_3$) of **3b**



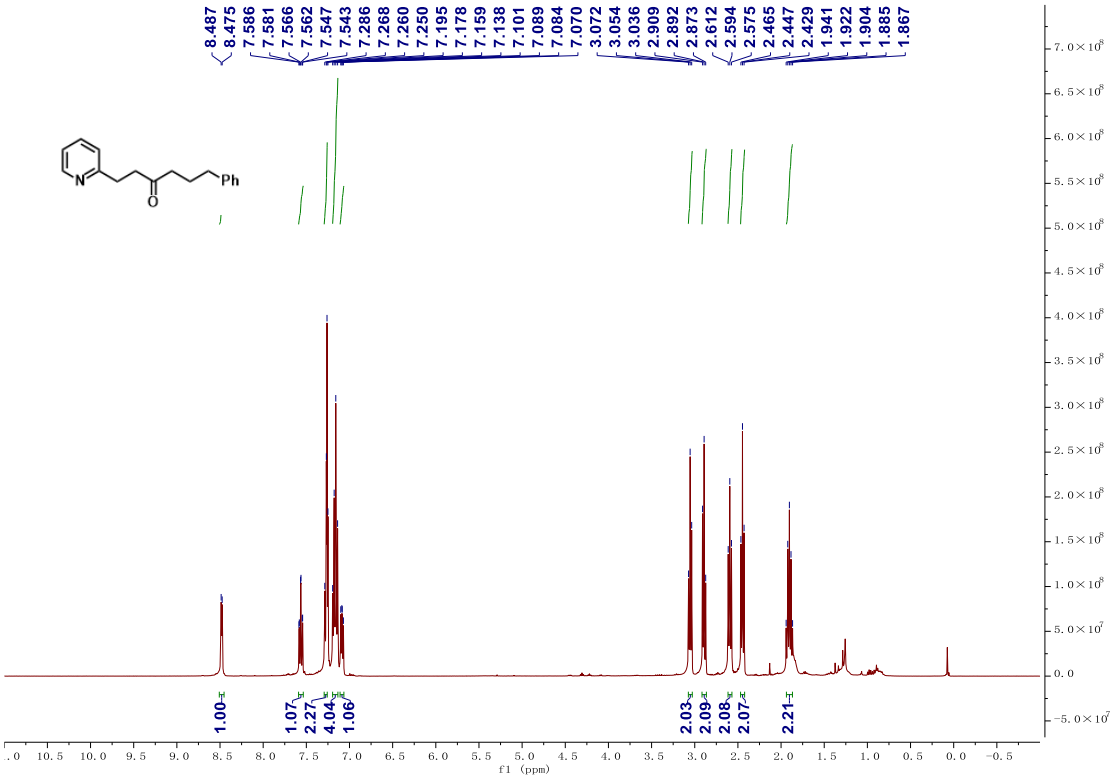
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3c**



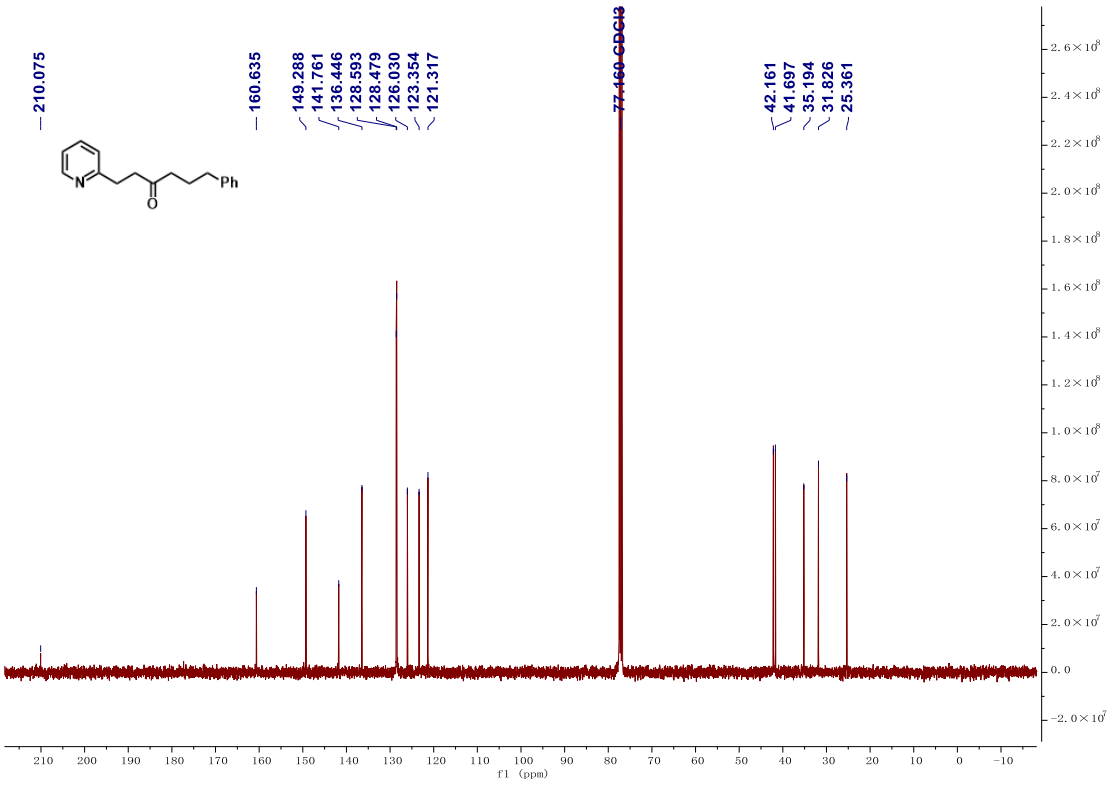
^{13}C NMR-spectrum (400 MHz, $CDCl_3$) of **3c**



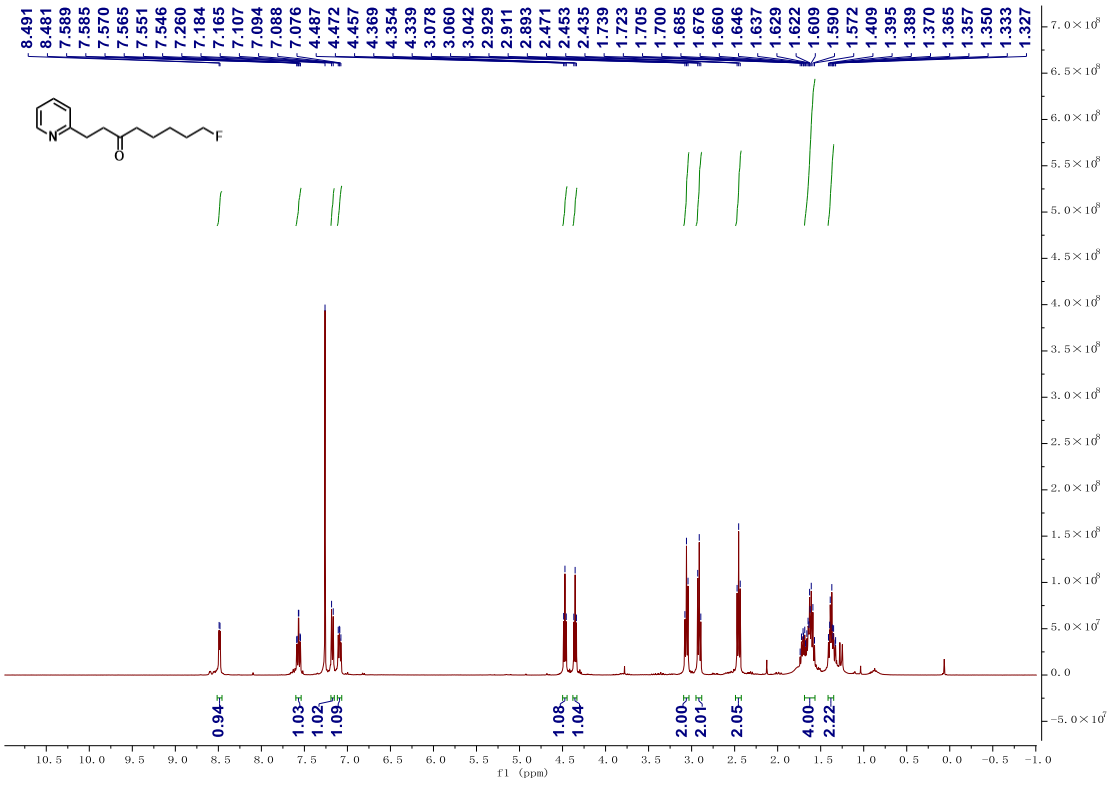
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3d**



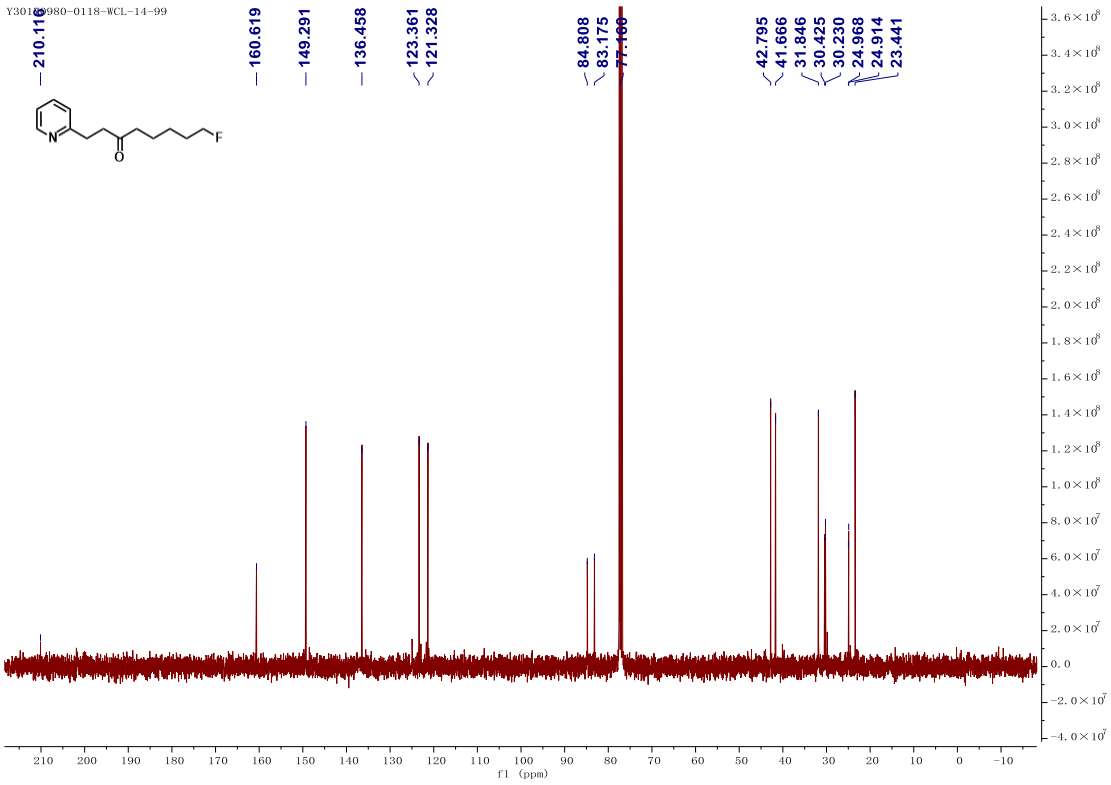
^{13}C NMR-spectrum (400 MHz, $CDCl_3$) of **3d**



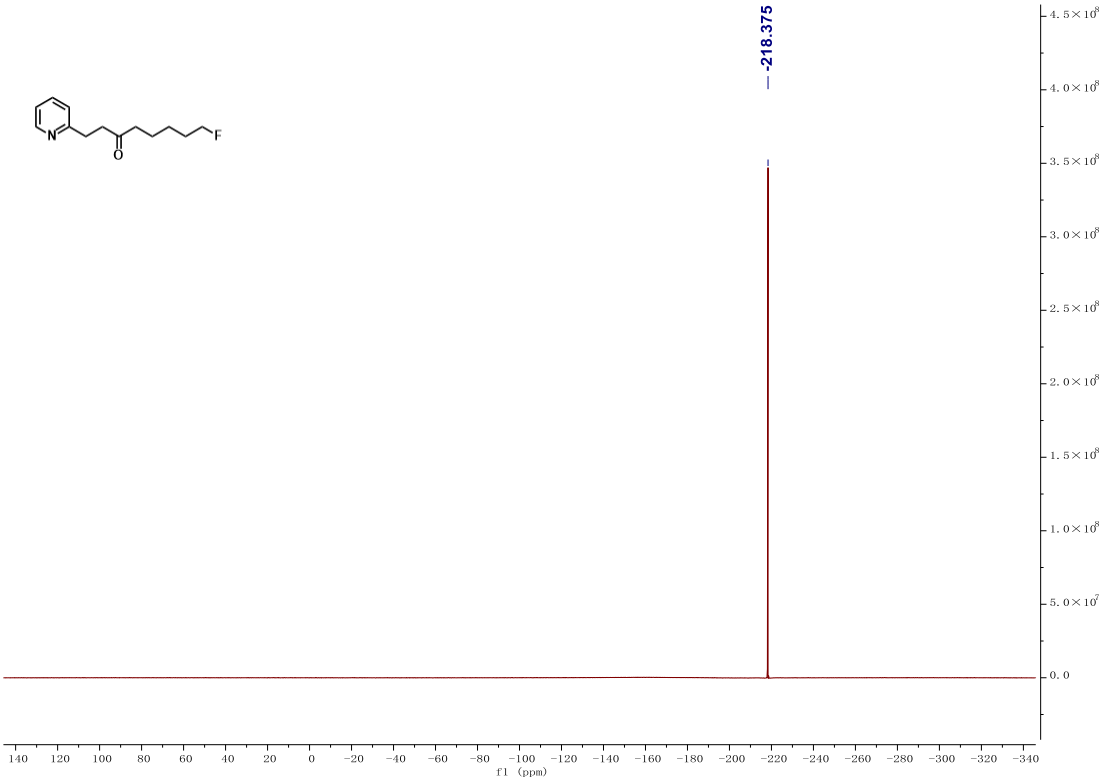
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3e**



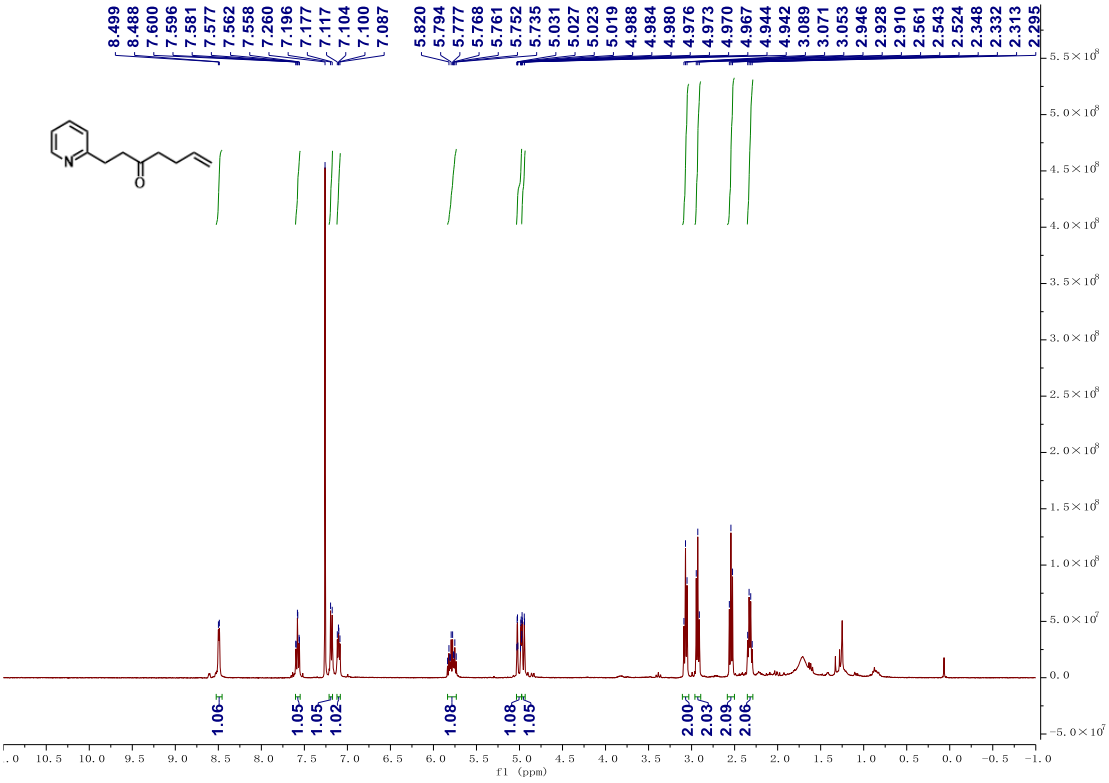
^{13}C NMR-spectrum (400 MHz, $CDCl_3$) of **3e**



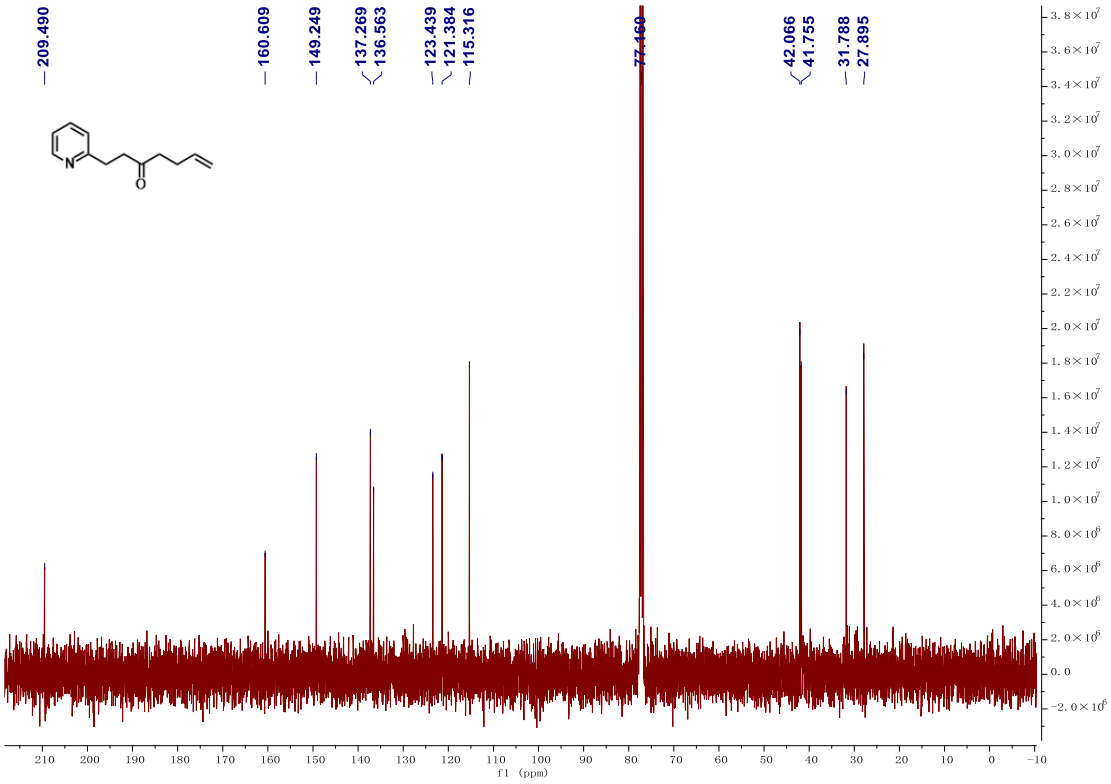
^{19}F NMR-spectrum (376 MHz, $CDCl_3$) of **3e**



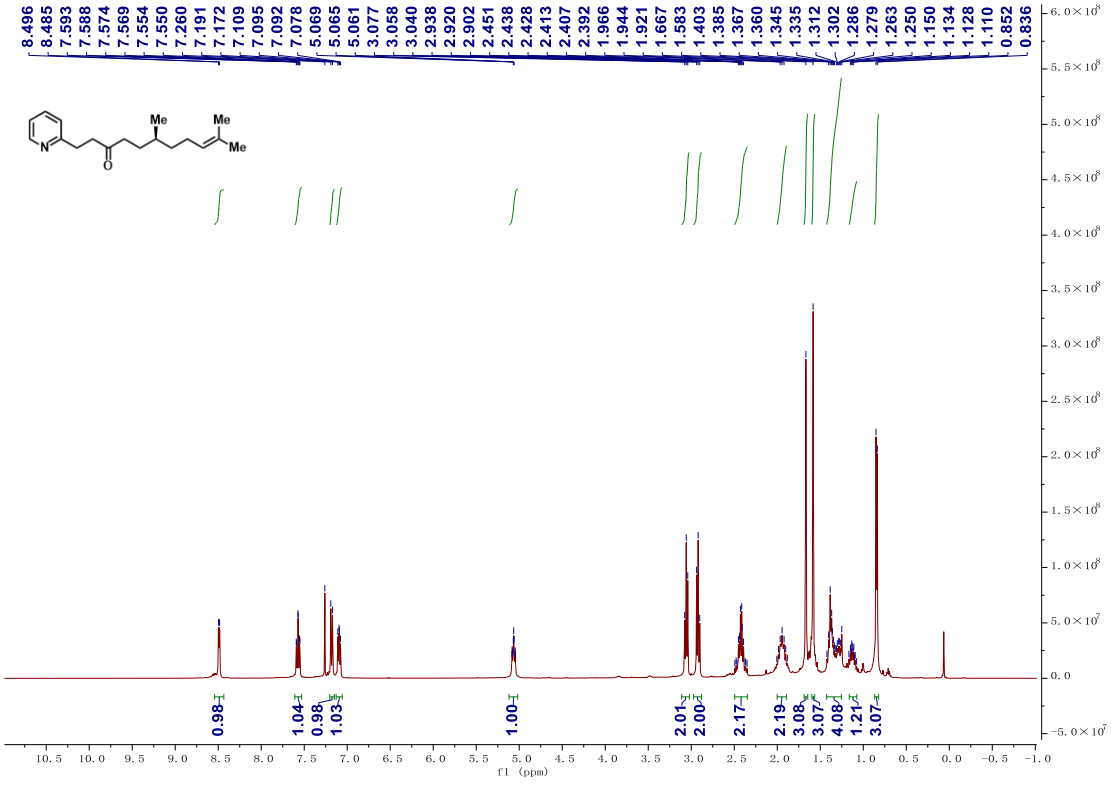
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3f**



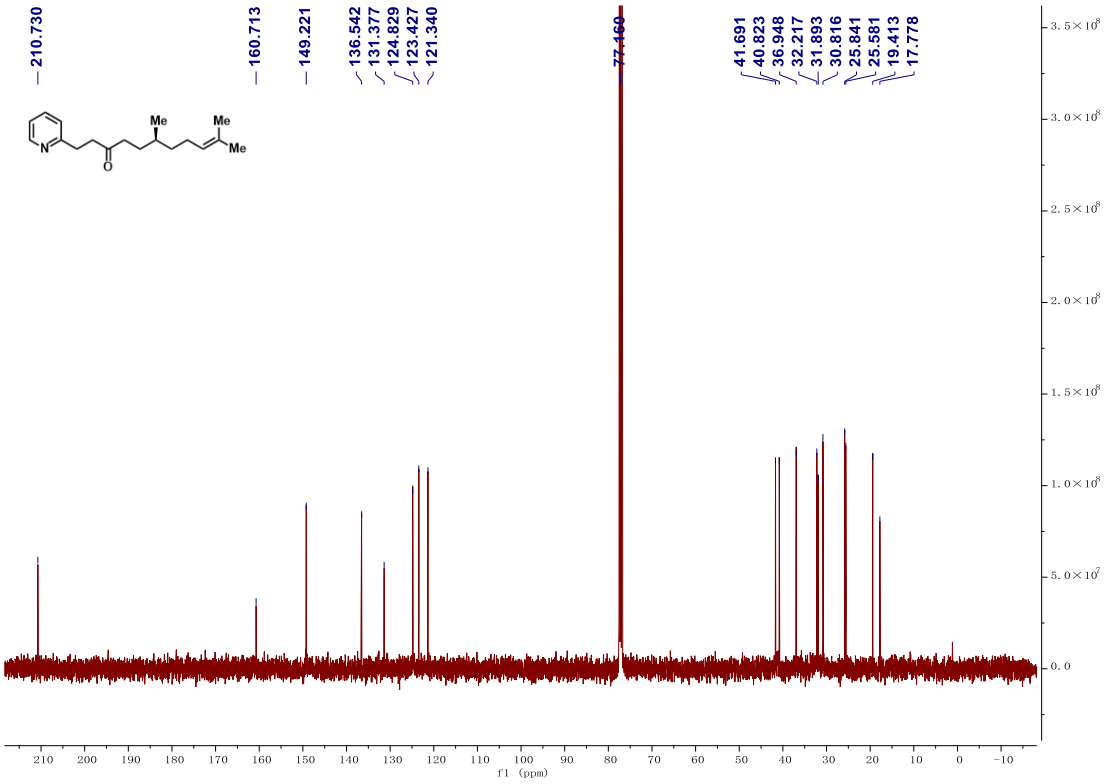
^{13}C NMR-spectrum (400 MHz, $CDCl_3$) of **3f**



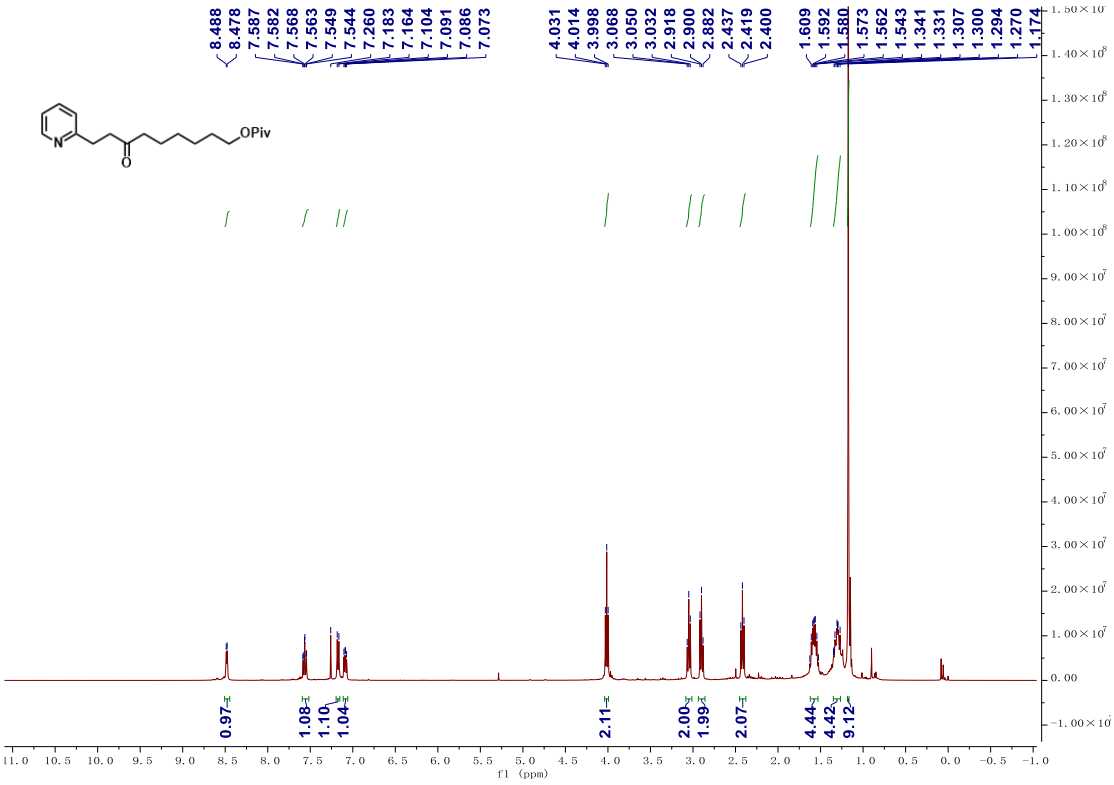
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3g**



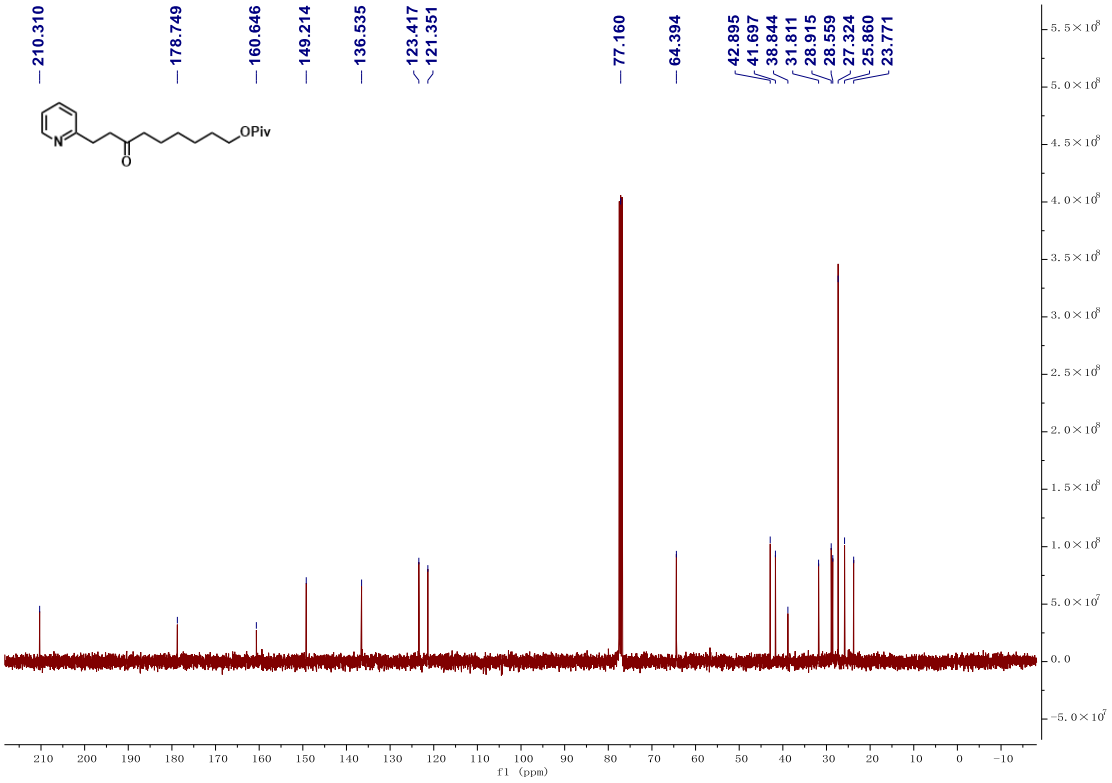
^{13}C NMR-spectrum (400 MHz, $CDCl_3$) of **3g**



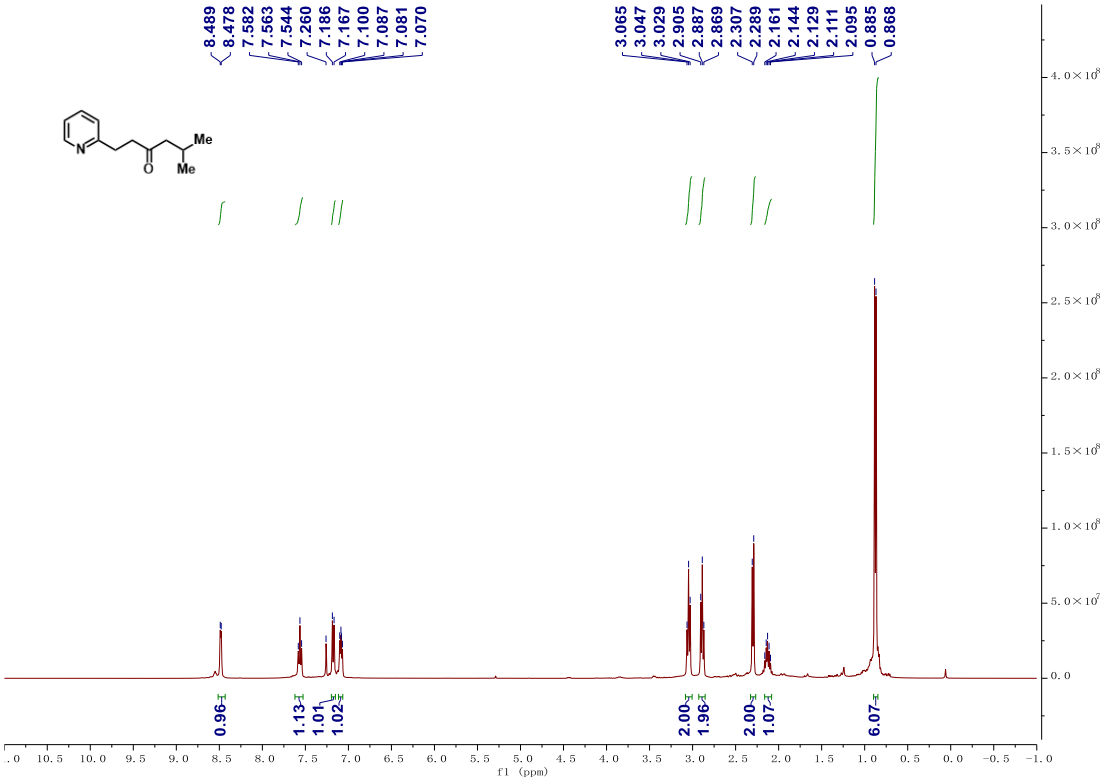
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3h**



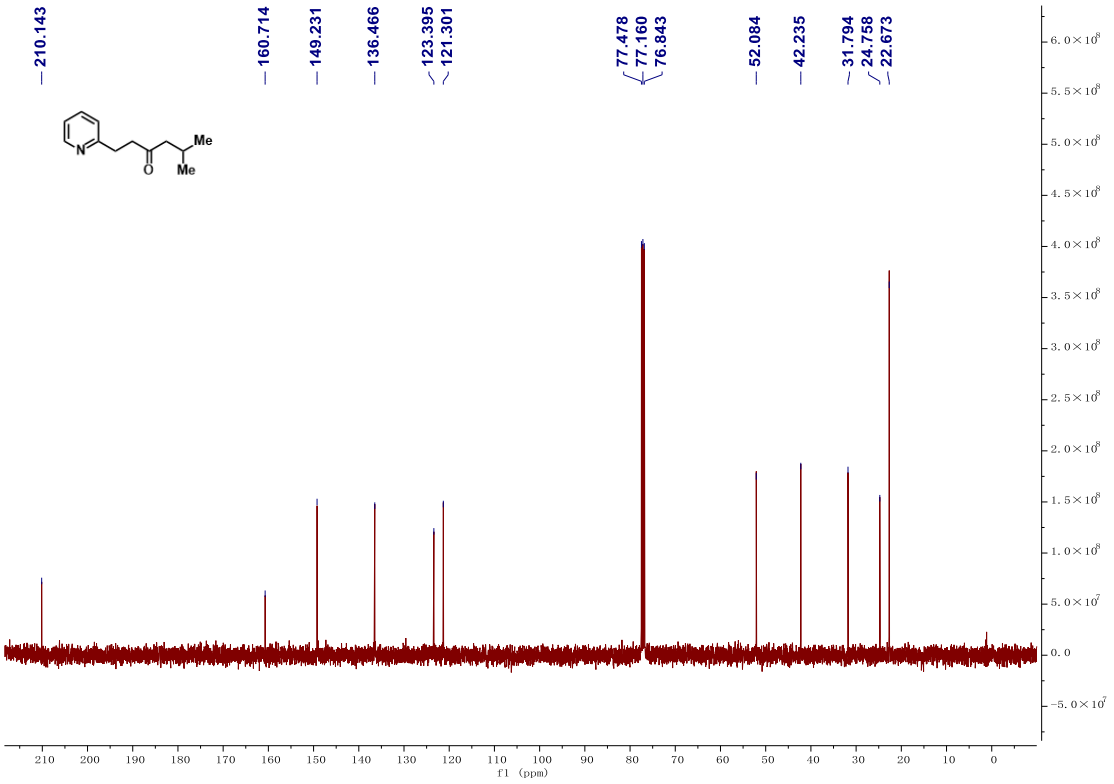
^{13}C NMR-spectrum (400 MHz, $CDCl_3$) of **3h**



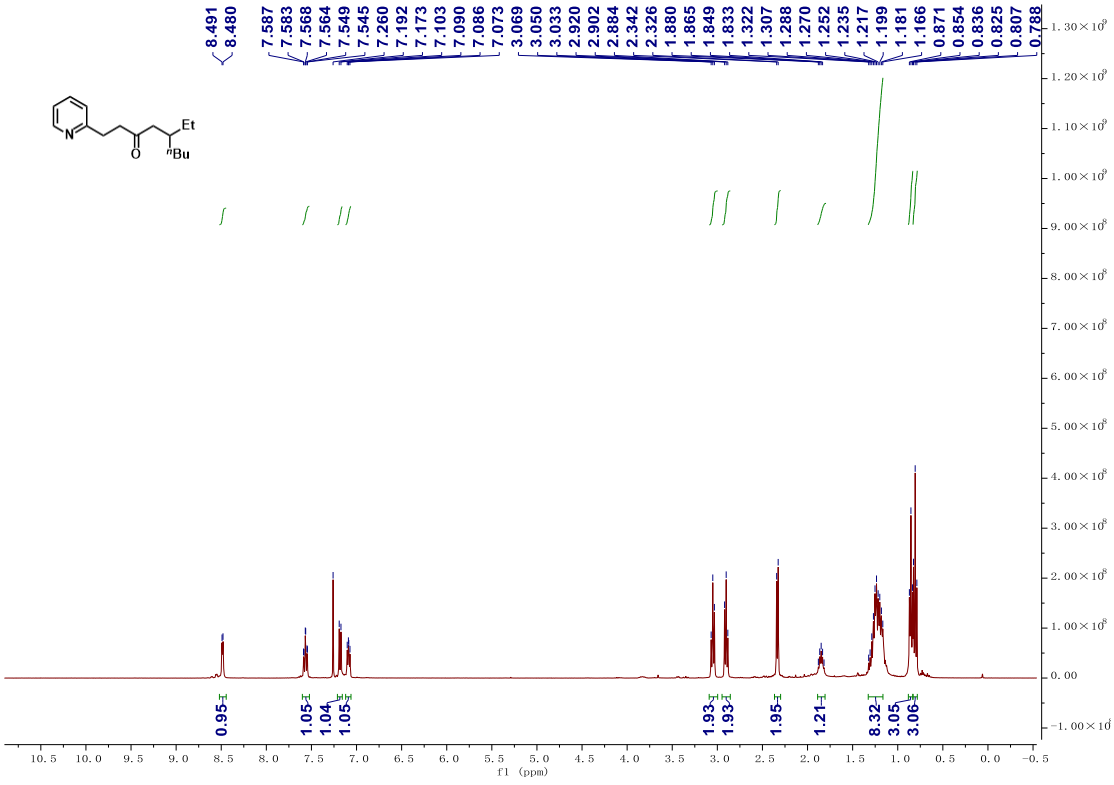
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3i**



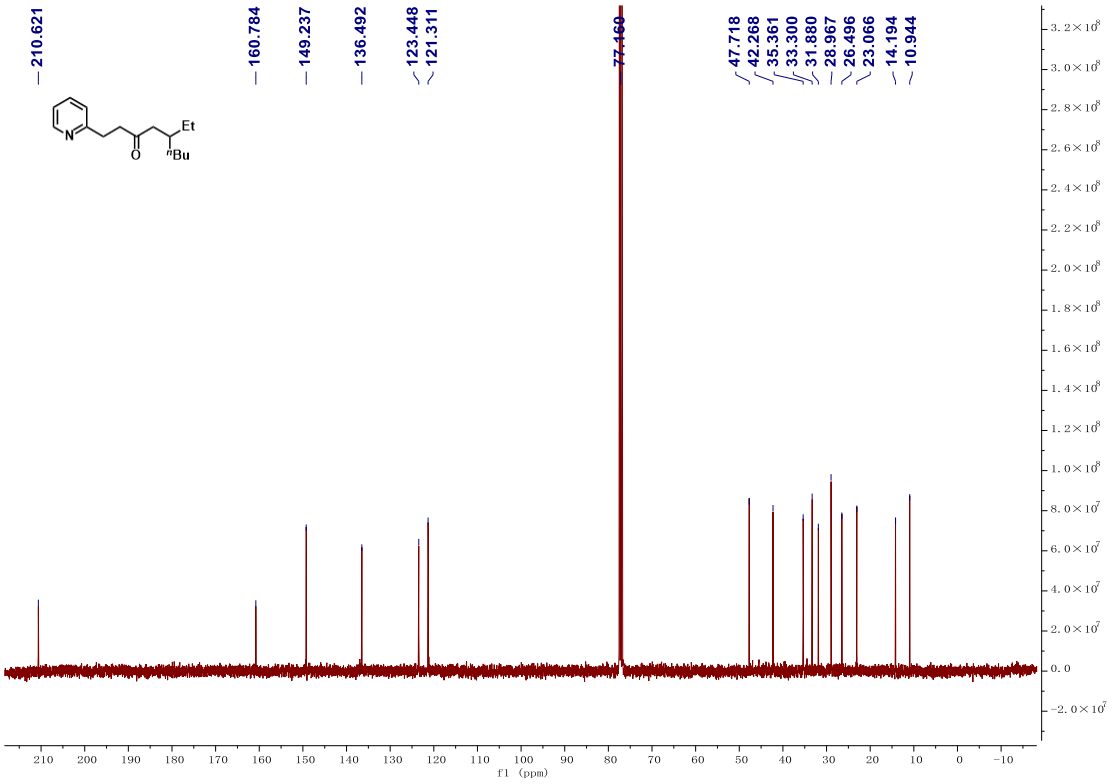
^{13}C NMR-spectrum (400 MHz, $CDCl_3$) of **3i**



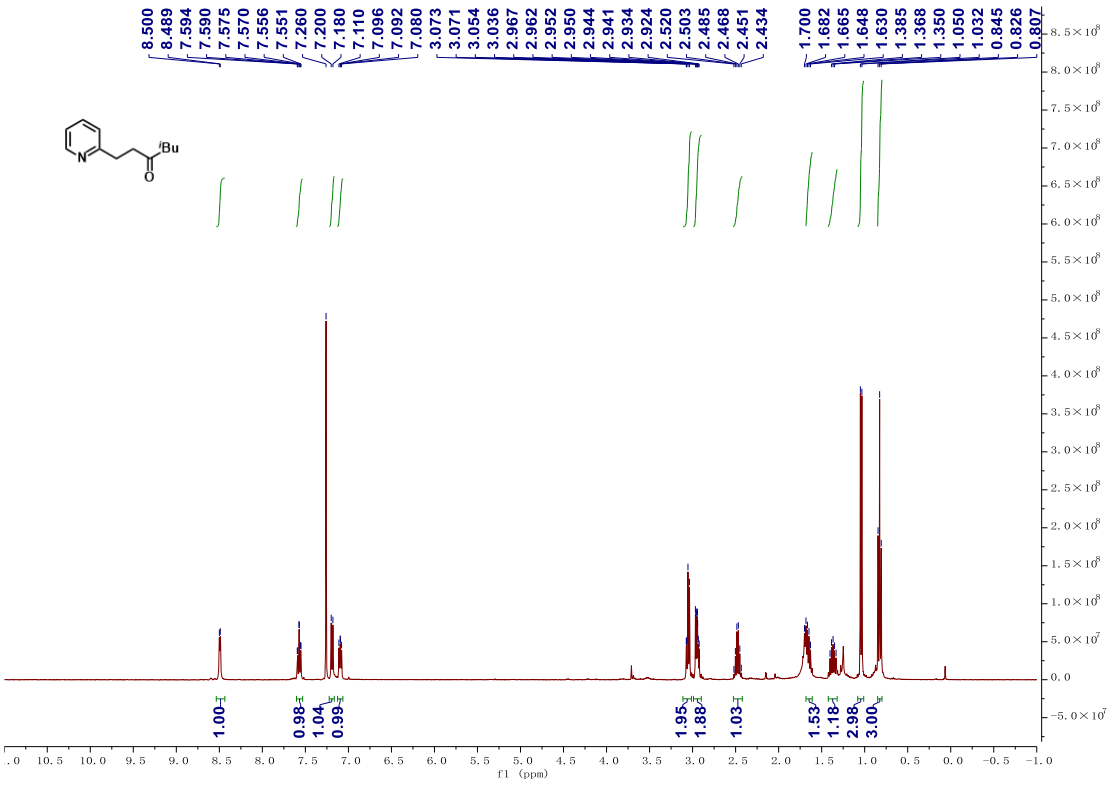
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3j**



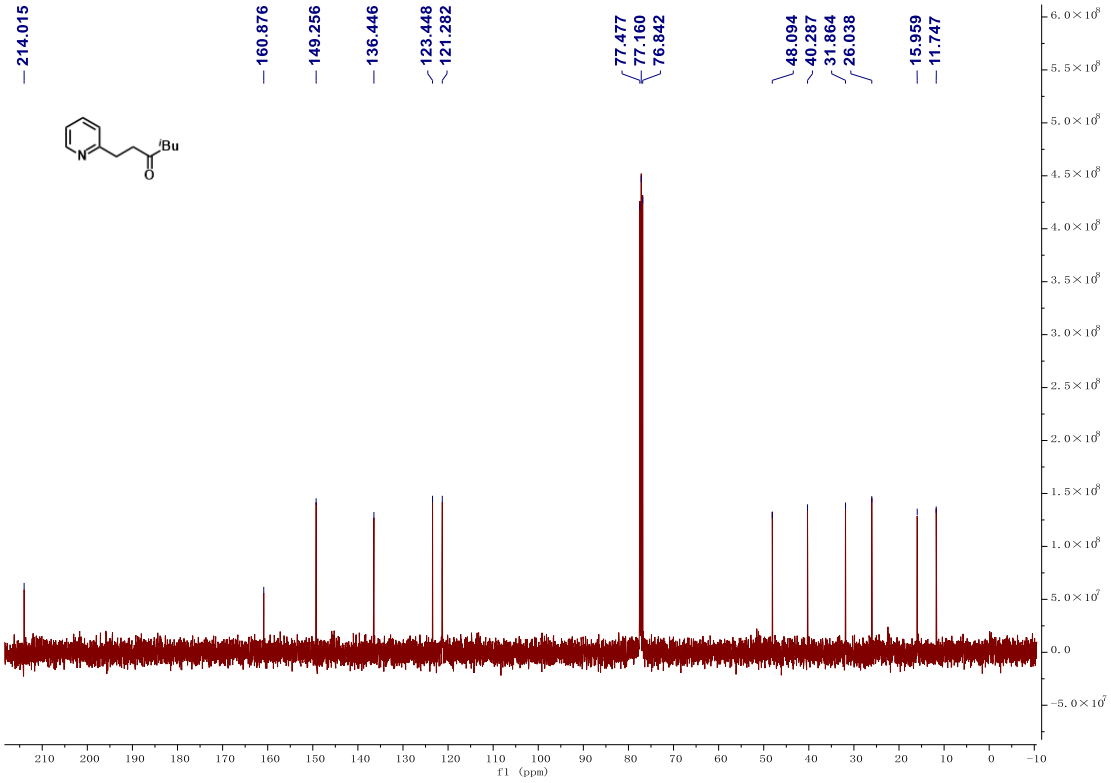
^{13}C NMR-spectrum (400 MHz, $CDCl_3$) of **3j**



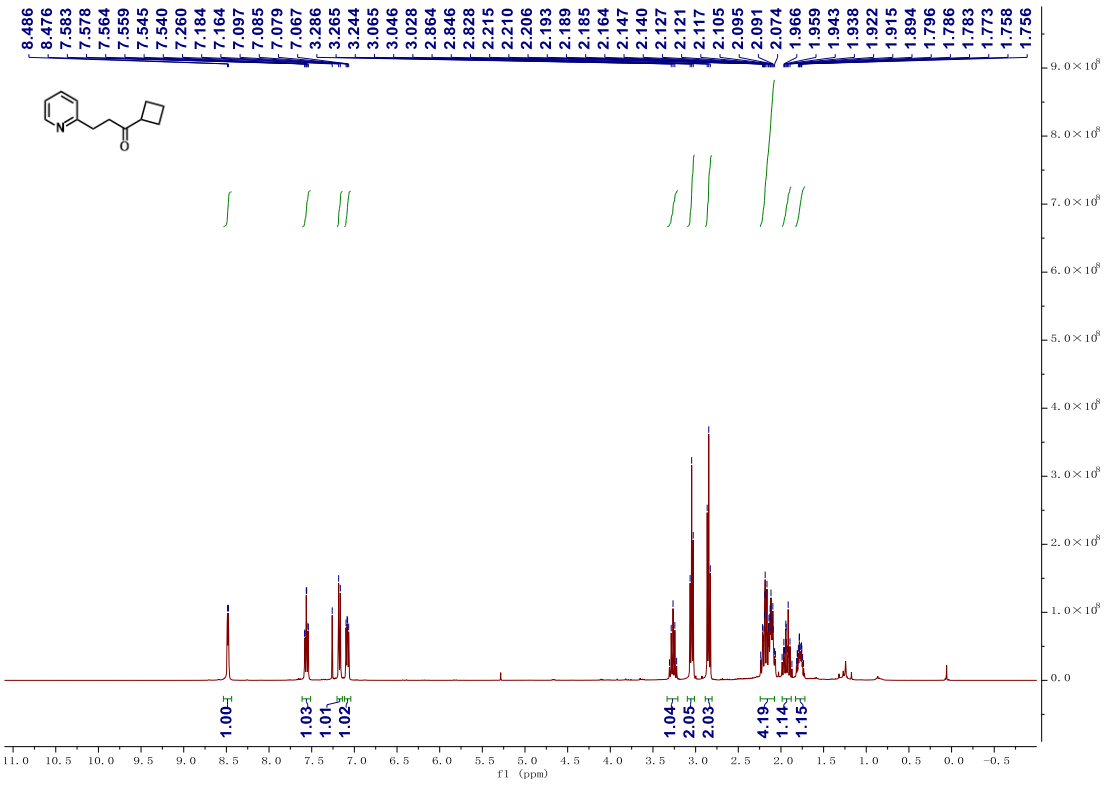
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3k**



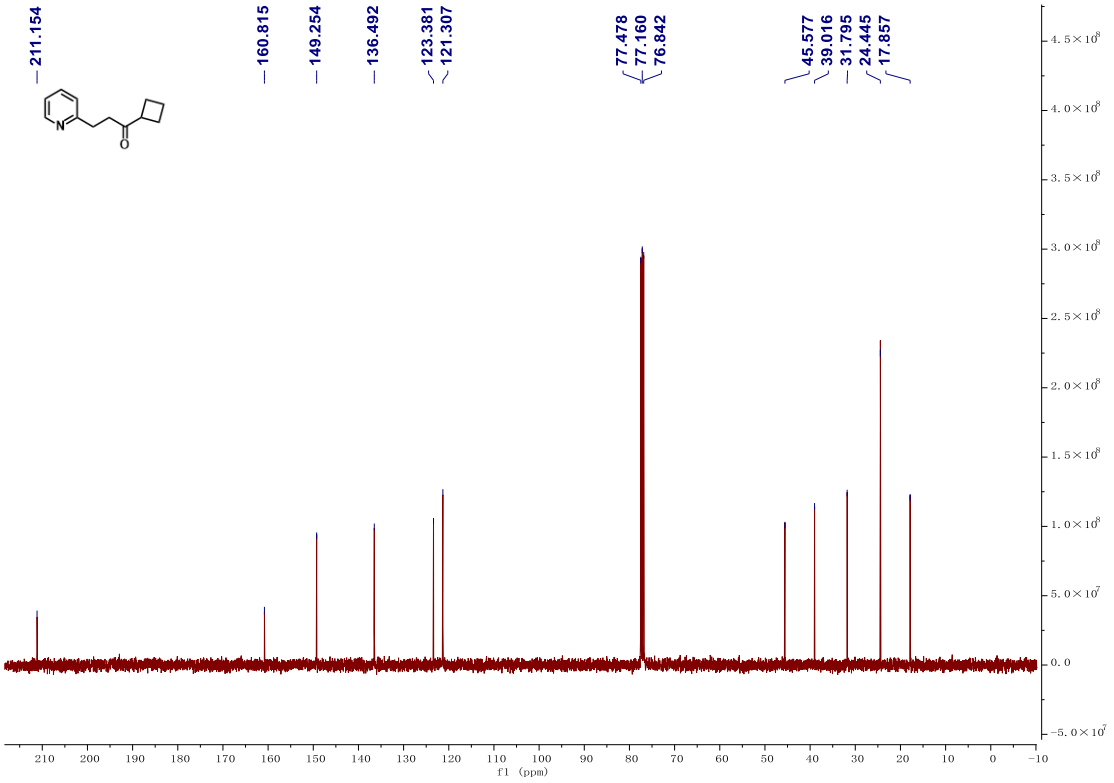
^{13}C NMR-spectrum (400 MHz, $CDCl_3$) of **3k**



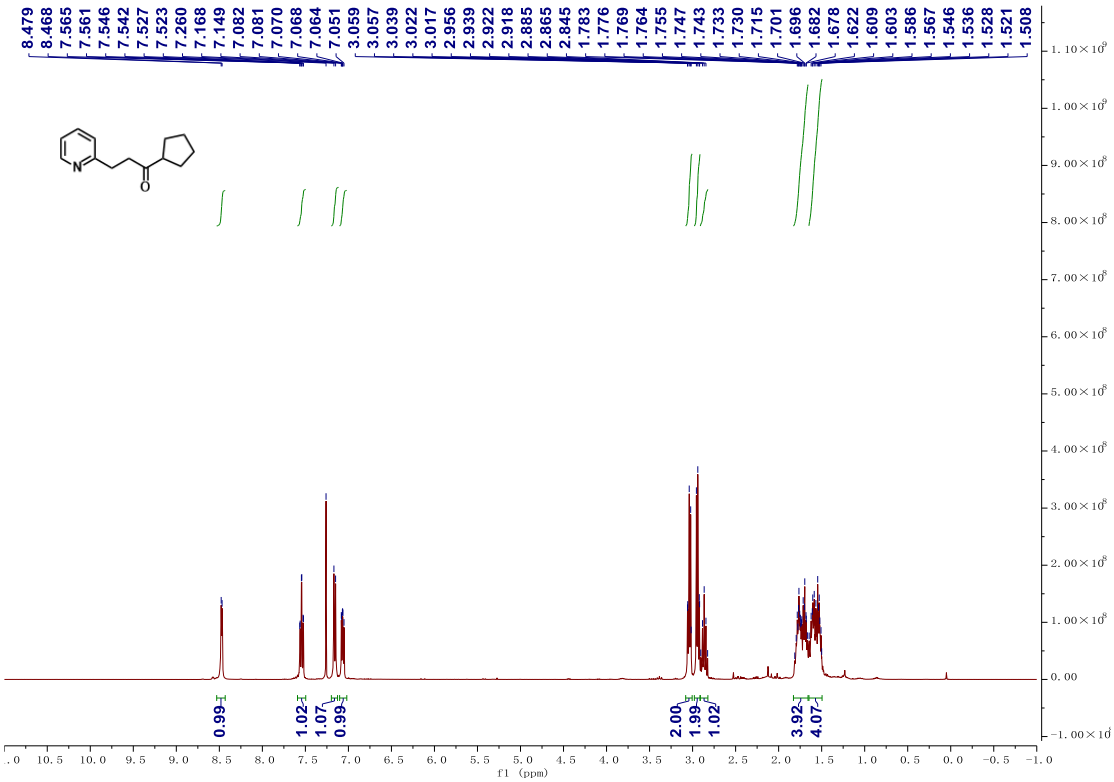
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3l**



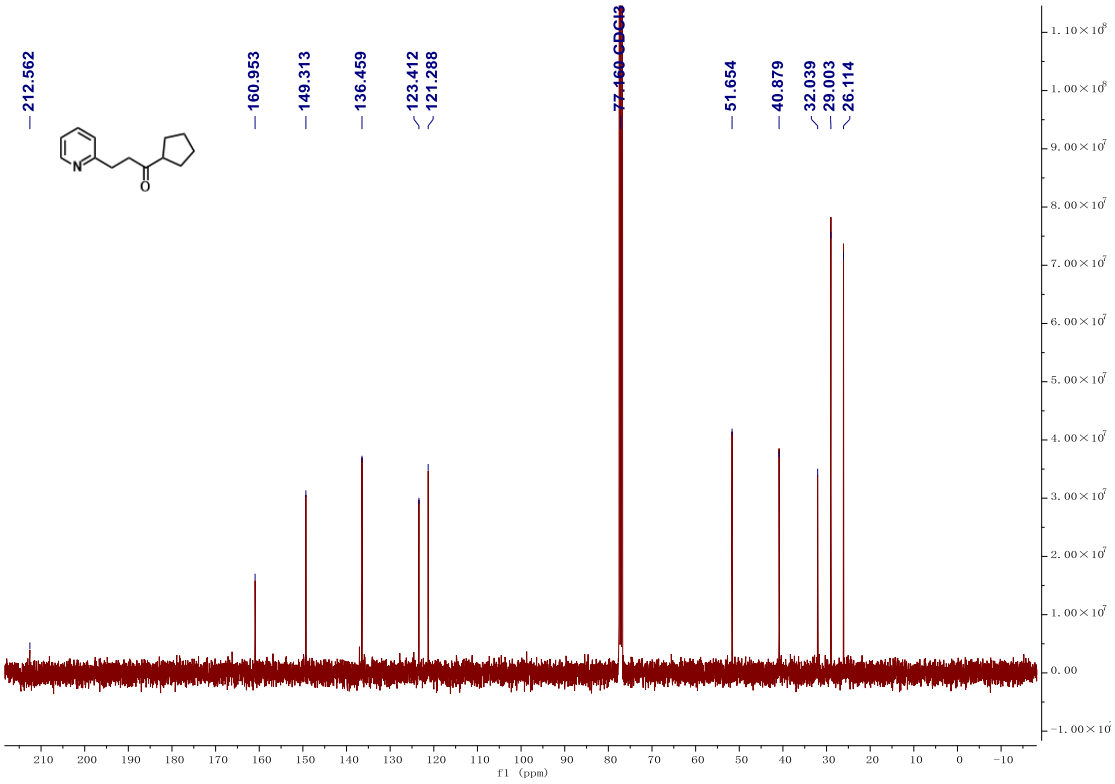
^{13}C NMR-spectrum (400 MHz, $CDCl_3$) of **3l**



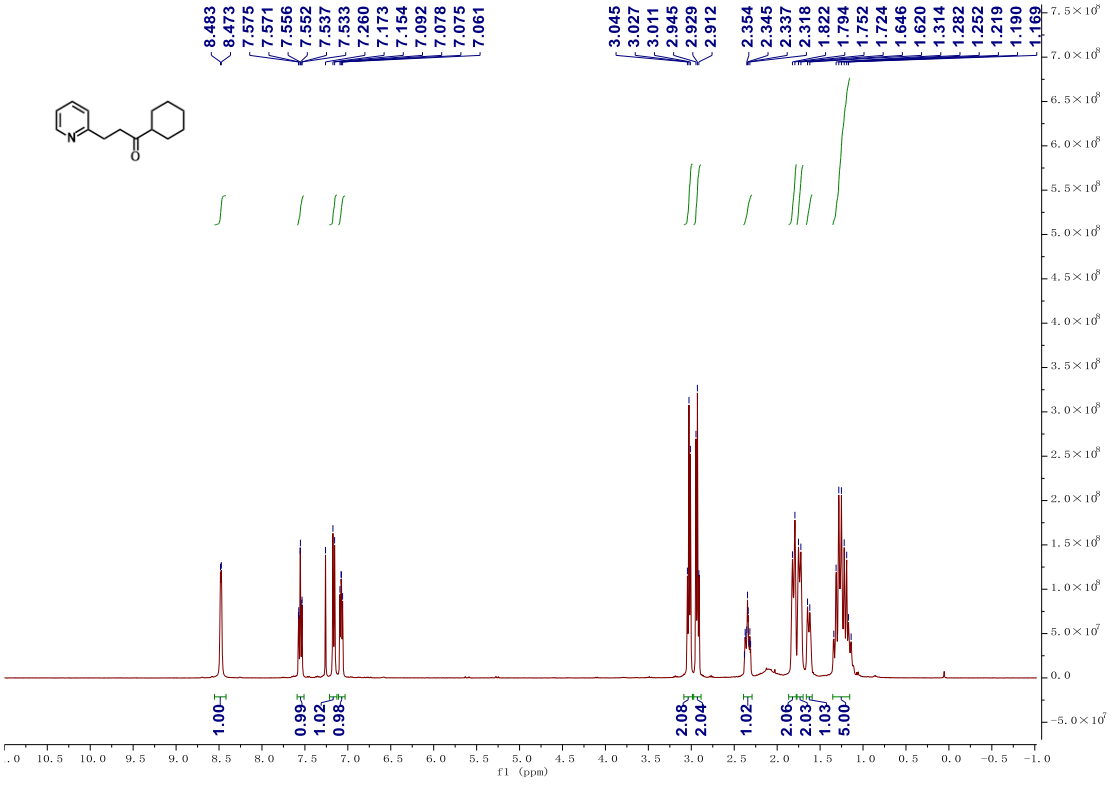
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3m**



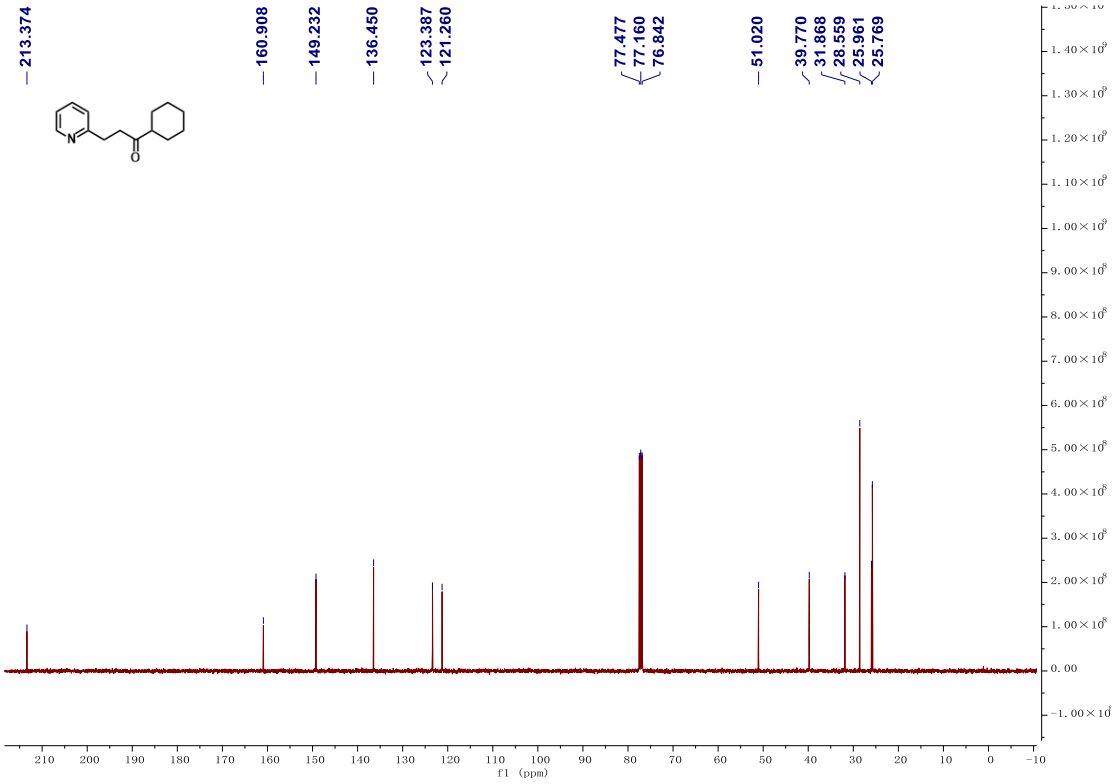
^{13}C NMR-spectrum (400 MHz, $CDCl_3$) of **3m**



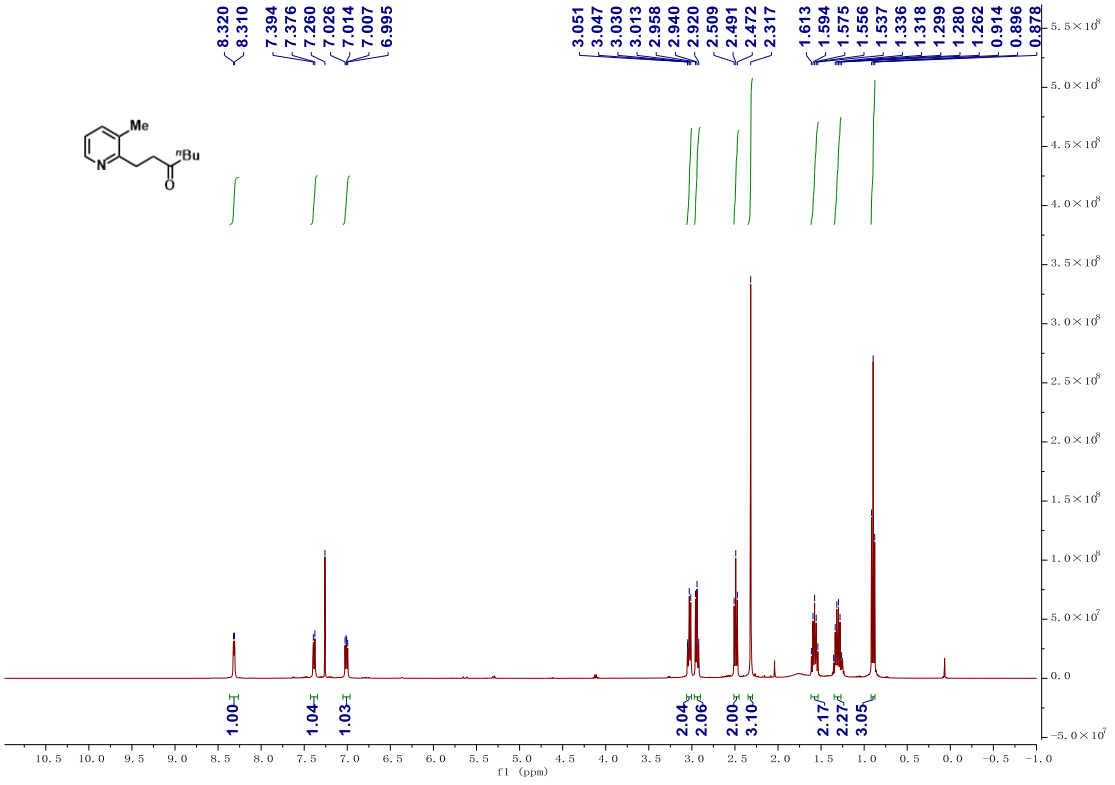
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3n**



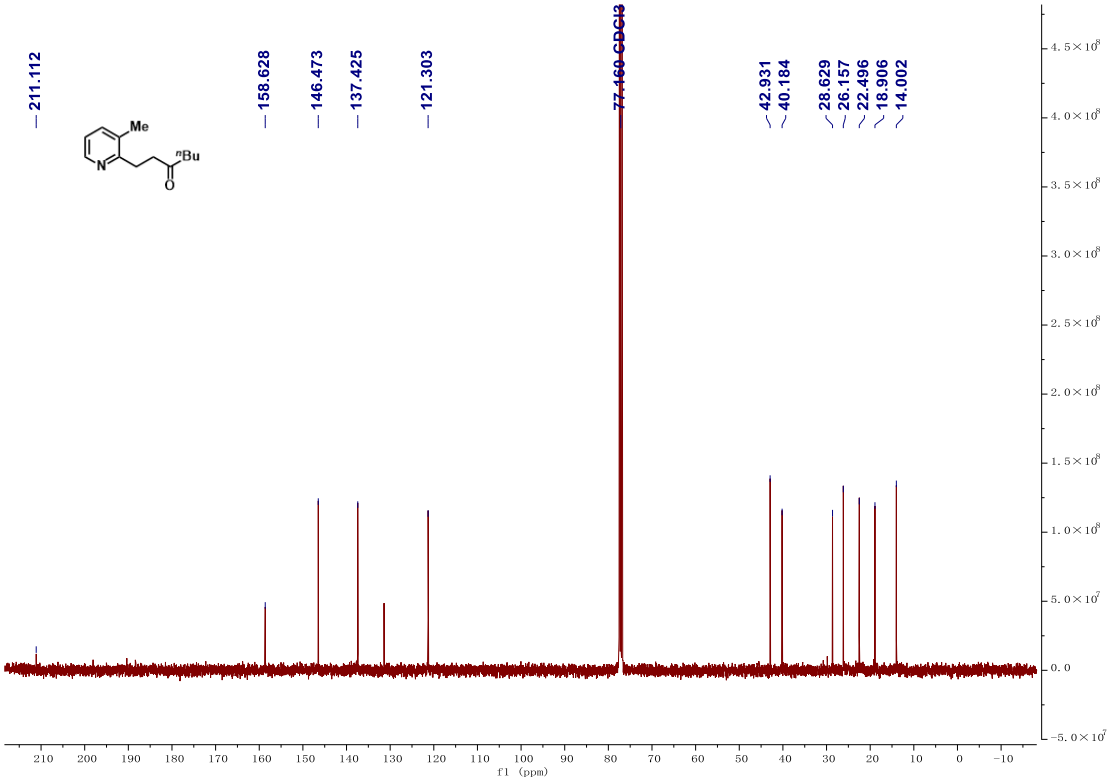
^{13}C NMR-spectrum (400 MHz, $CDCl_3$) of **3n**



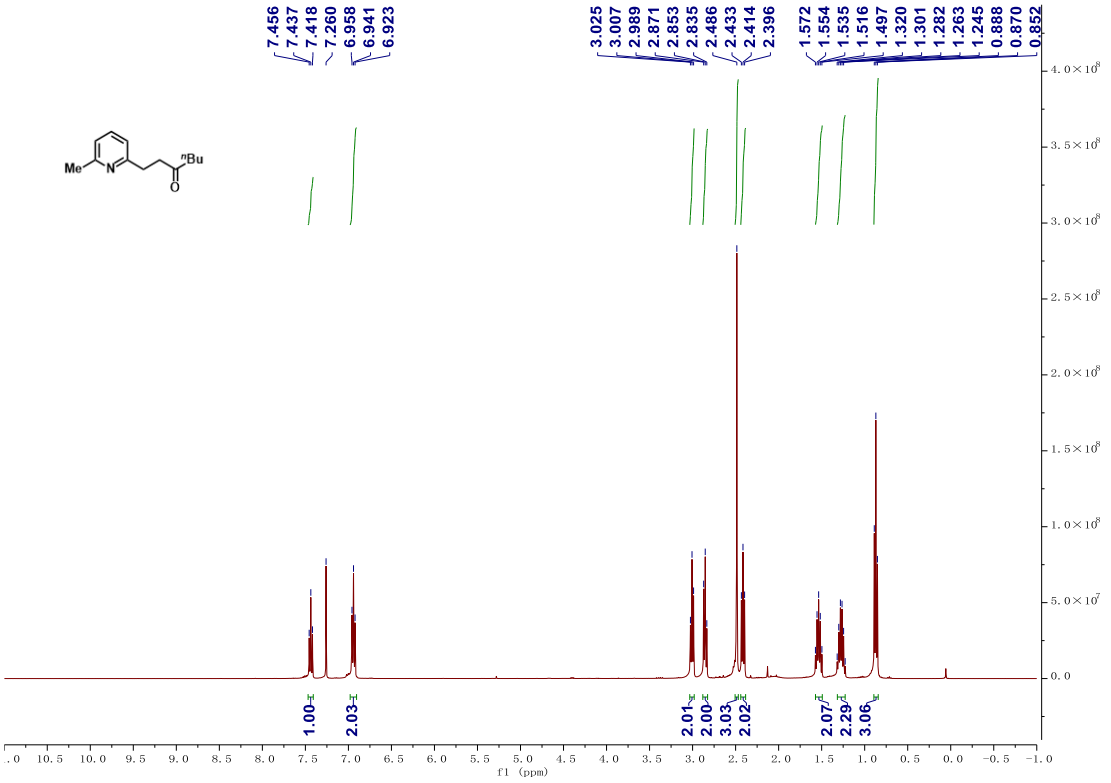
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3o**



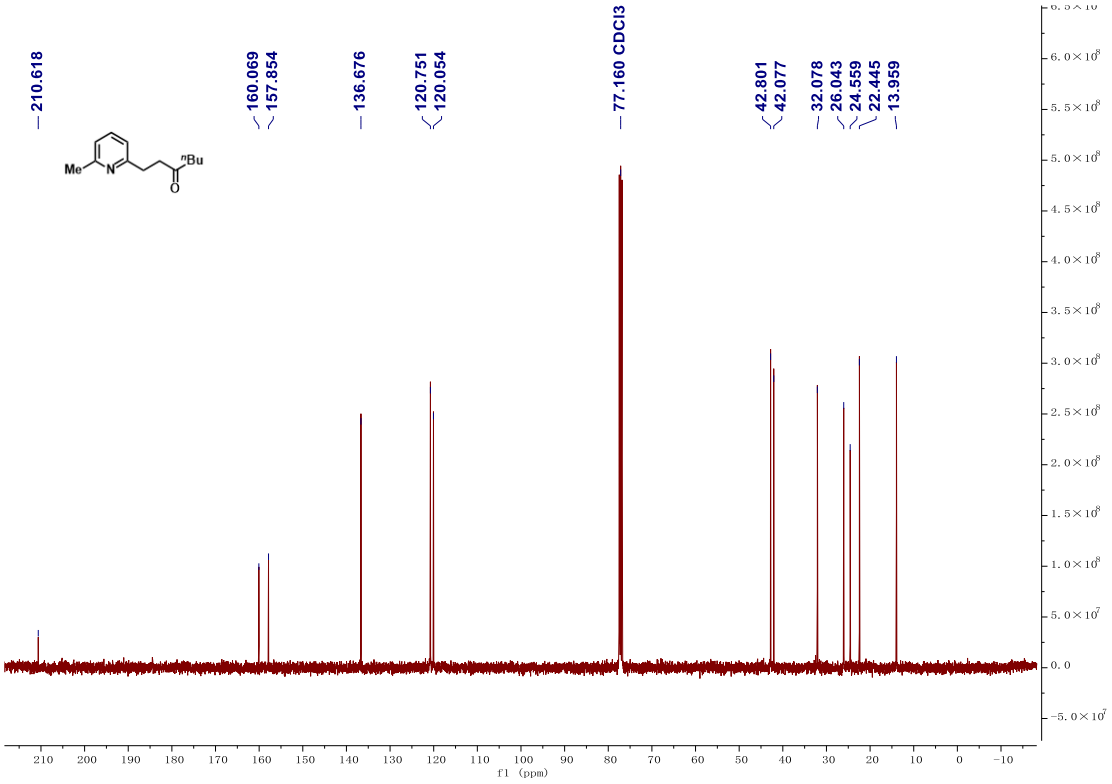
^{13}C NMR-spectrum (400 MHz, $CDCl_3$) of **3o**



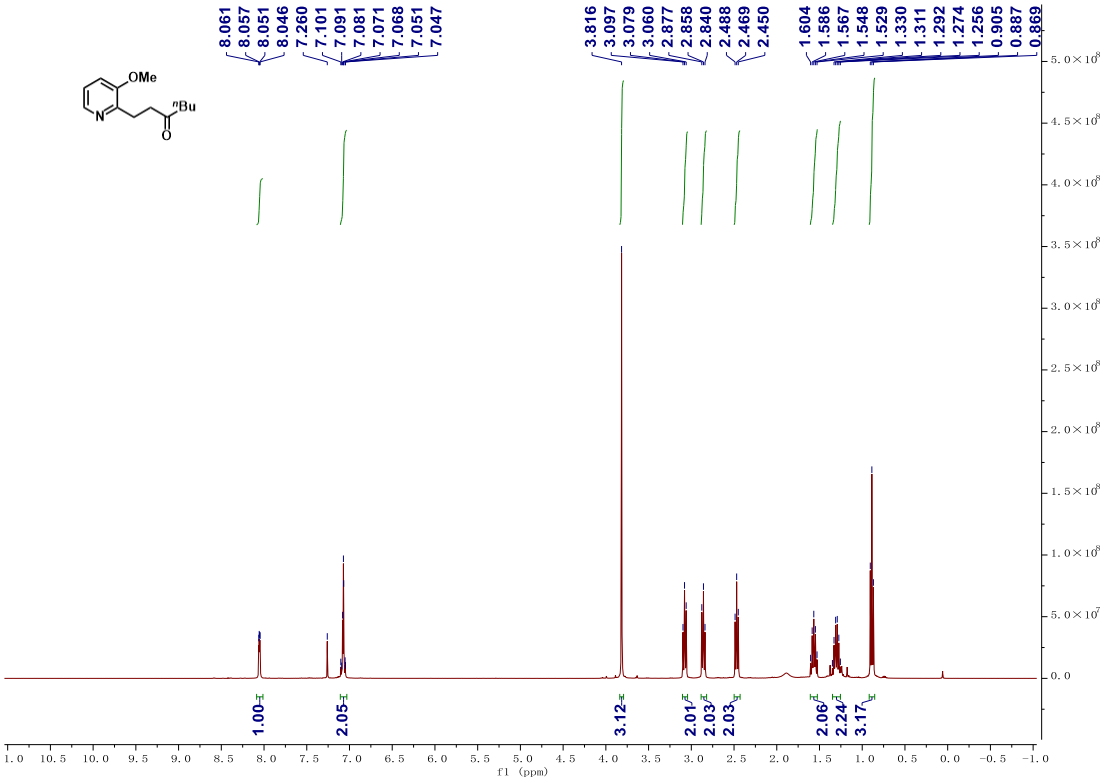
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3p**



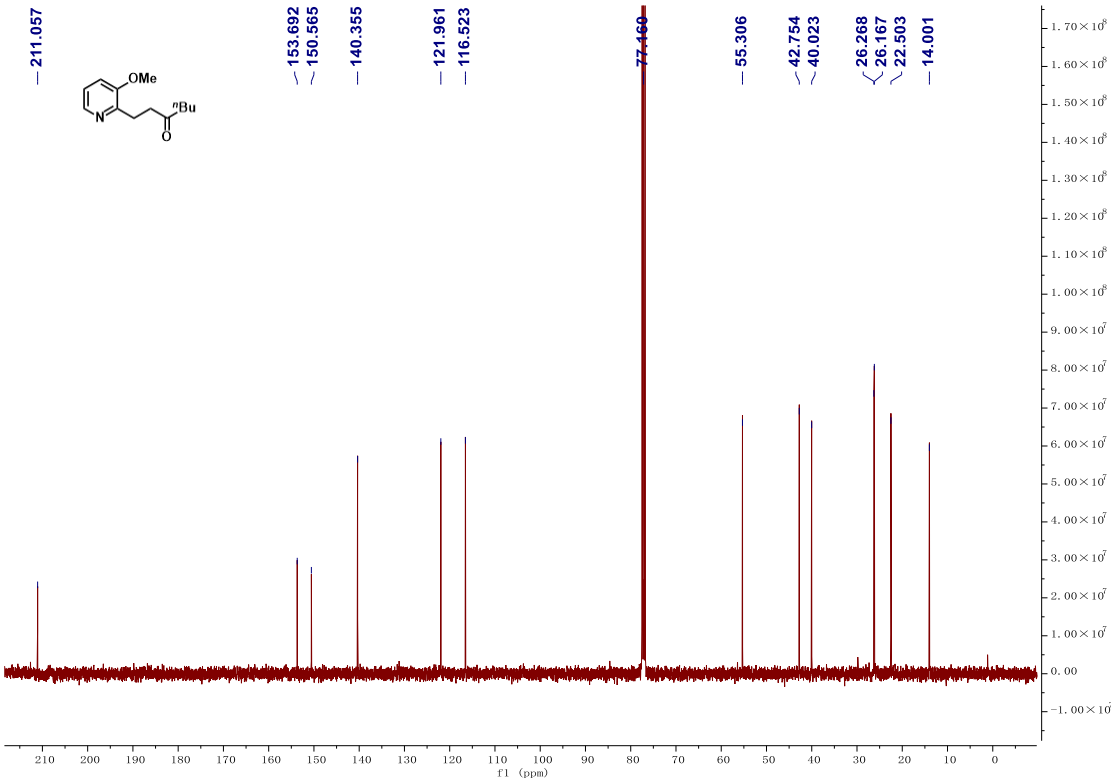
^{13}C NMR-spectrum (400 MHz, $CDCl_3$) of **3p**



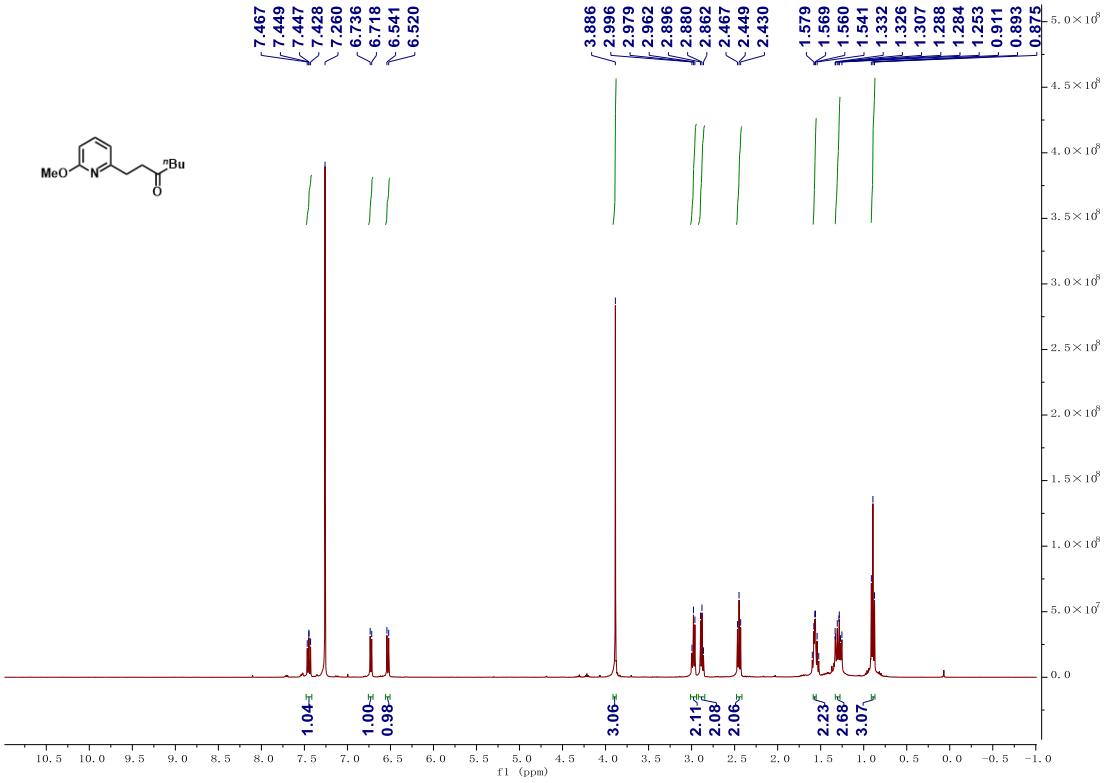
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3q**



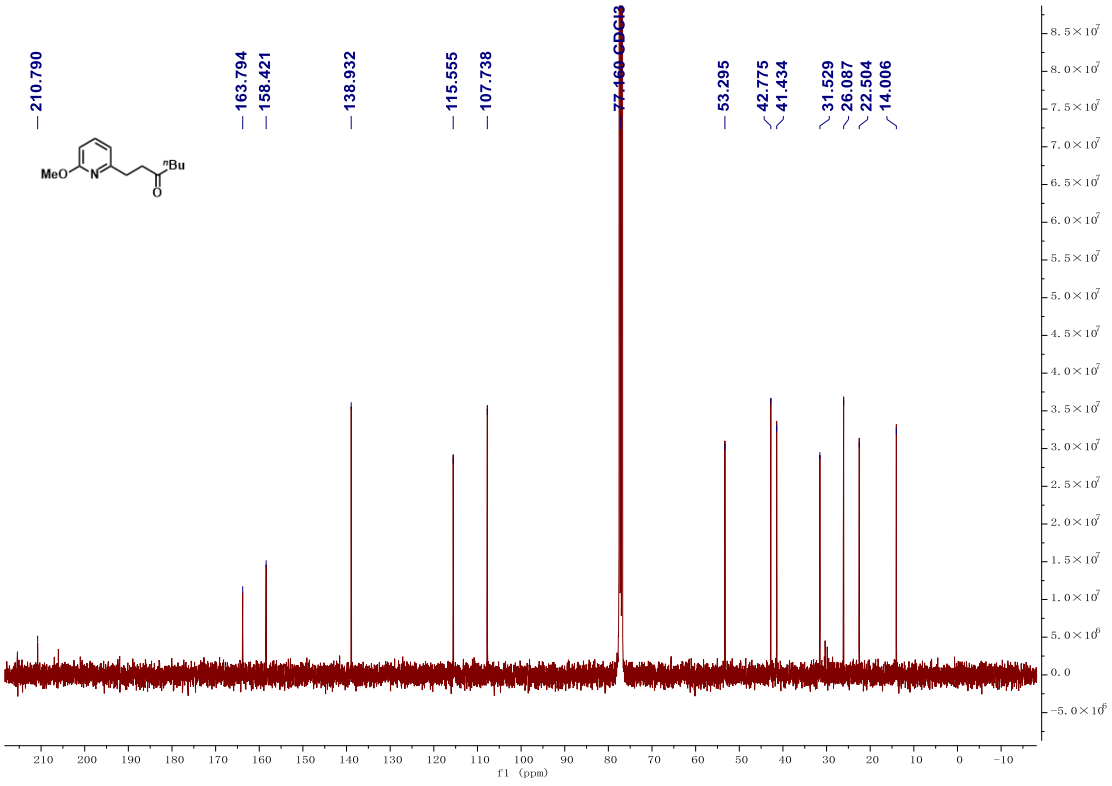
^{13}C NMR-spectrum (400 MHz, $CDCl_3$) of **3q**



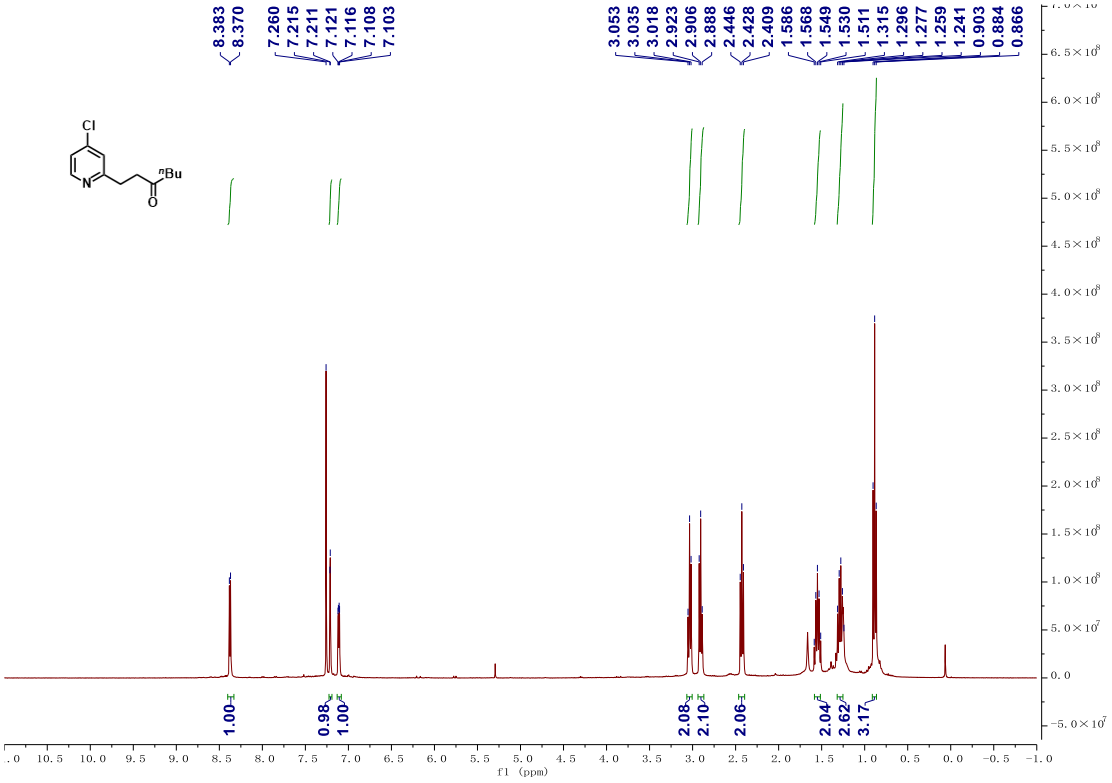
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3r**



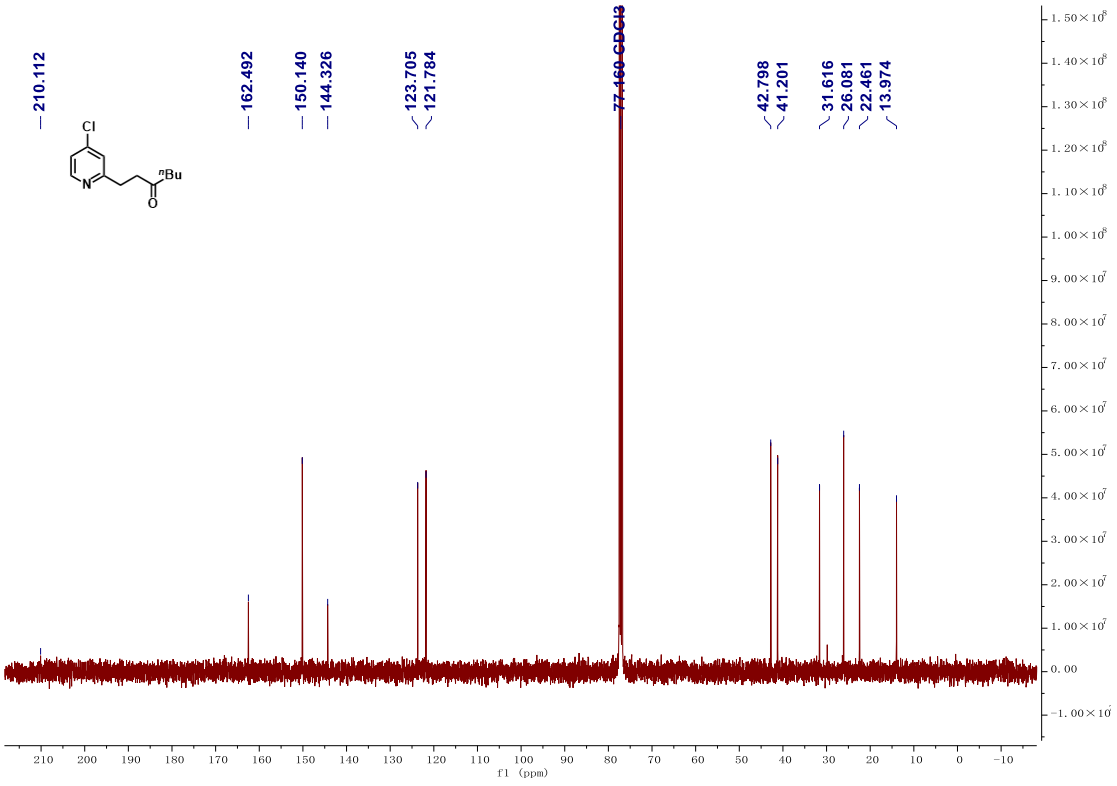
^{13}C NMR-spectrum (400 MHz, $CDCl_3$) of **3r**



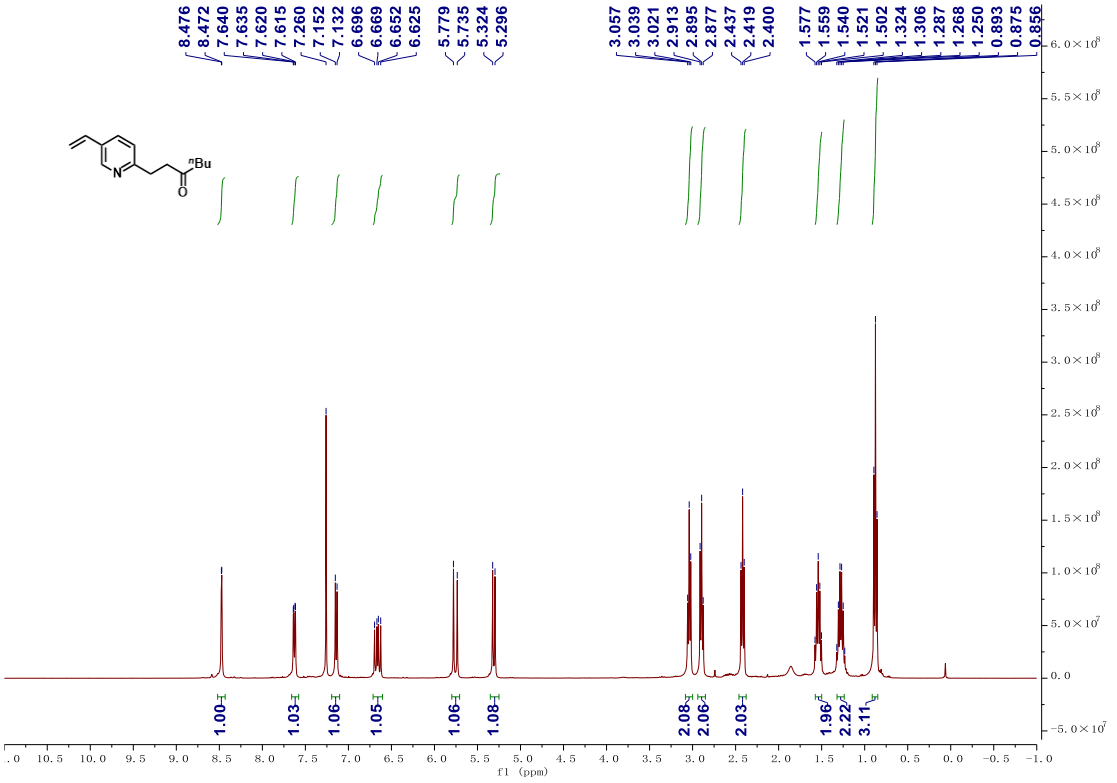
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3s**



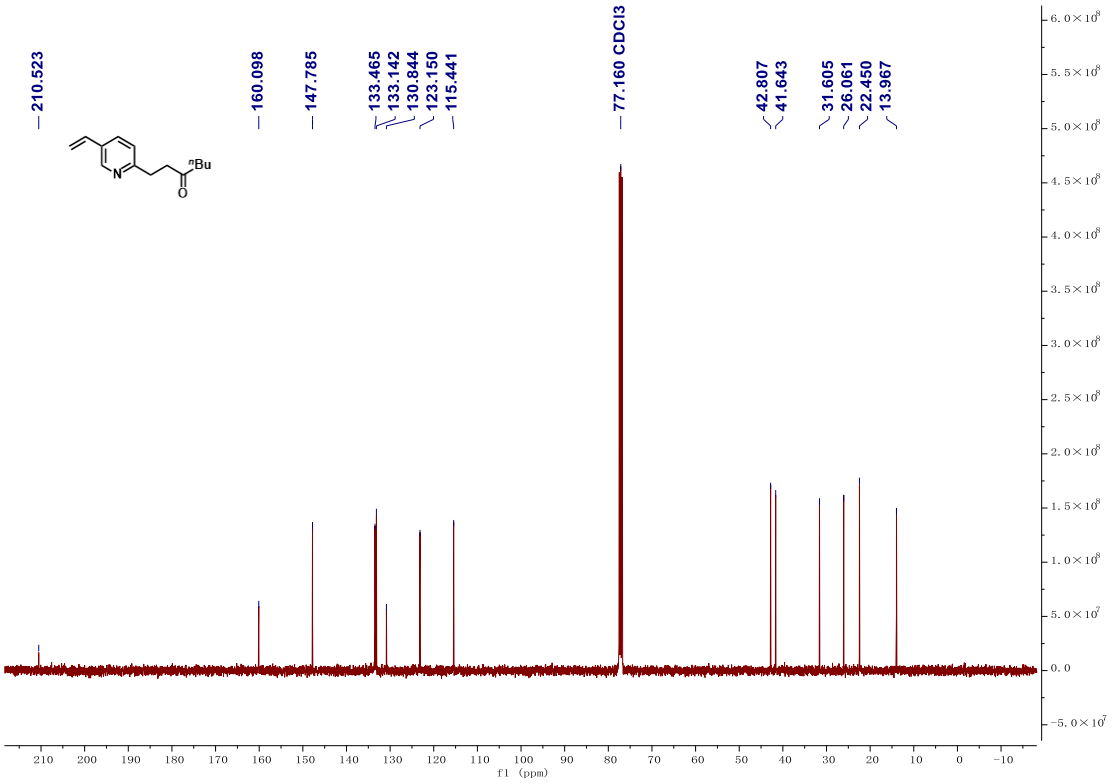
^{13}C NMR-spectrum (400 MHz, $CDCl_3$) of **3s**



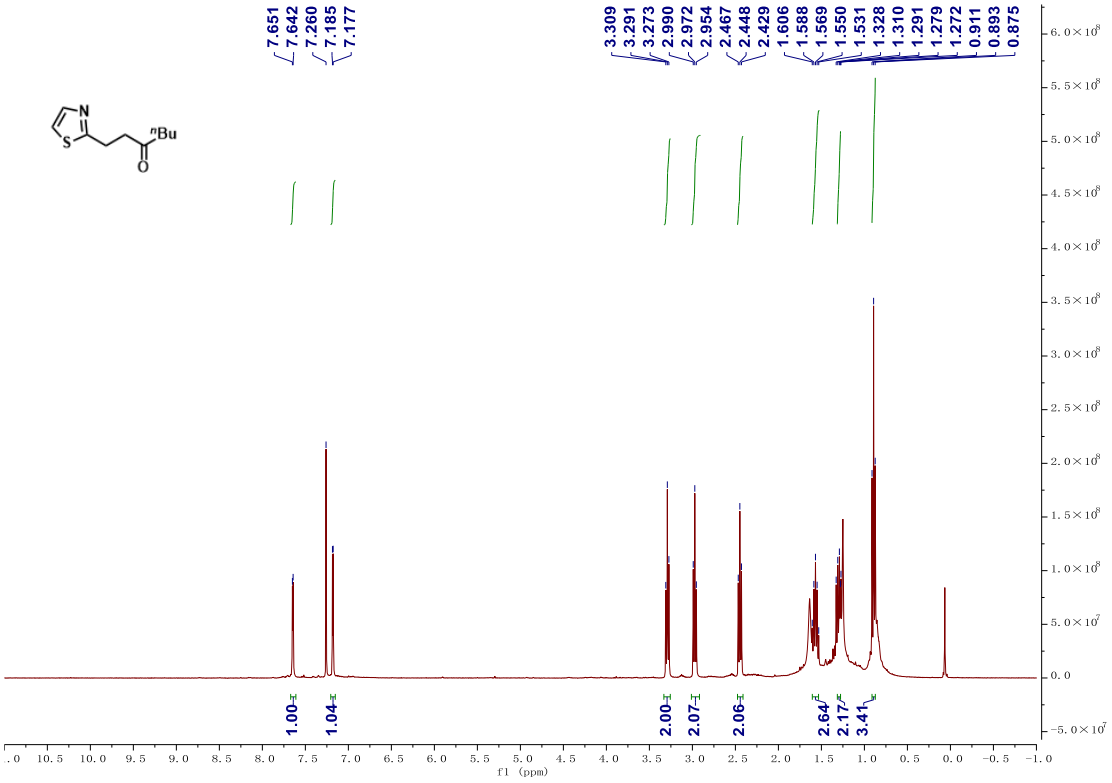
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3t**



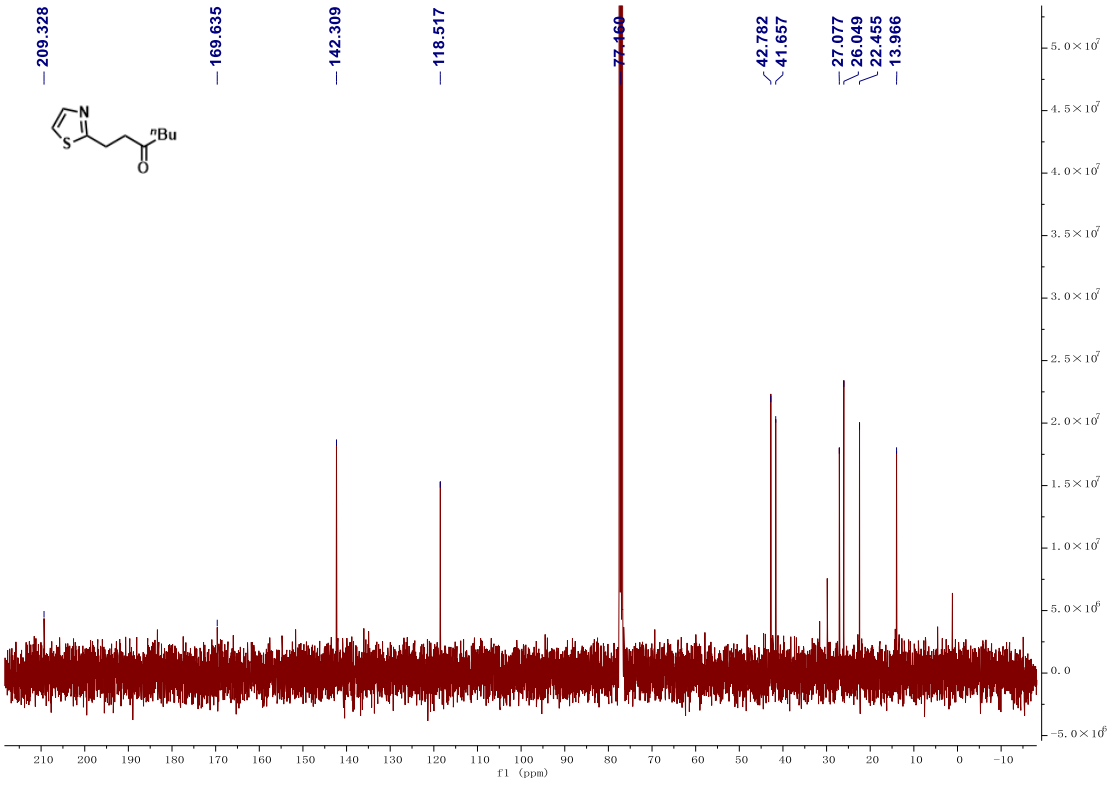
^{13}C NMR-spectrum (400 MHz, $CDCl_3$) of **3t**



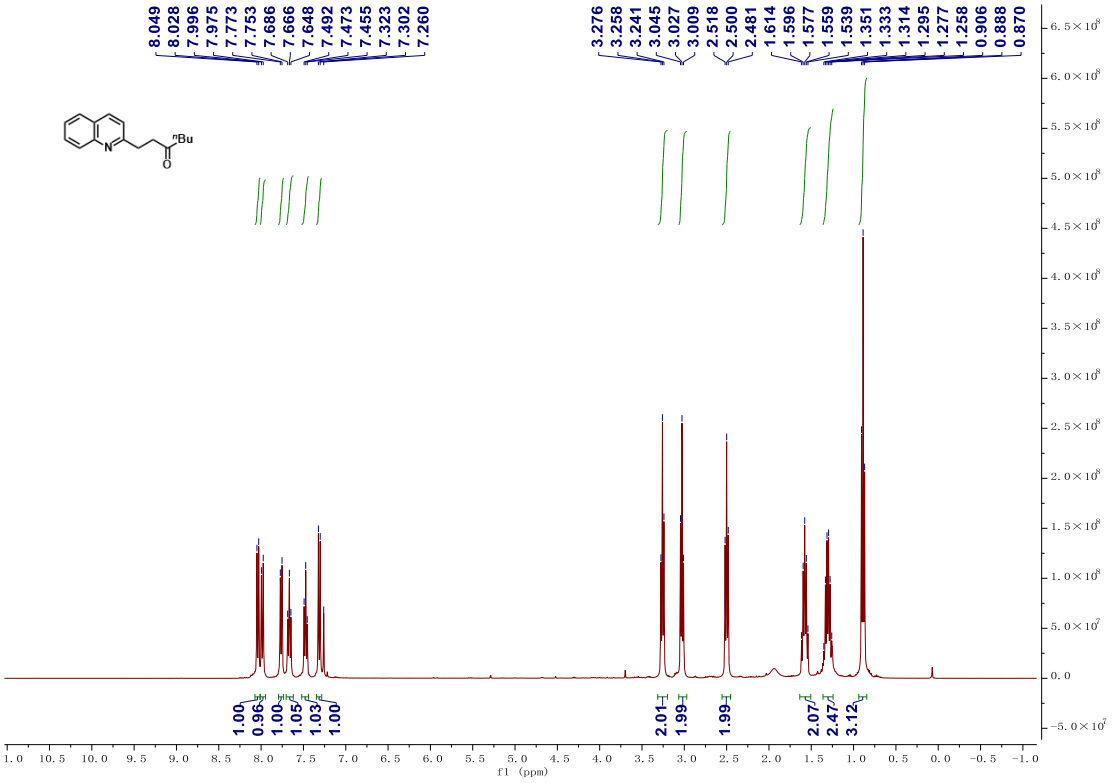
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3u**



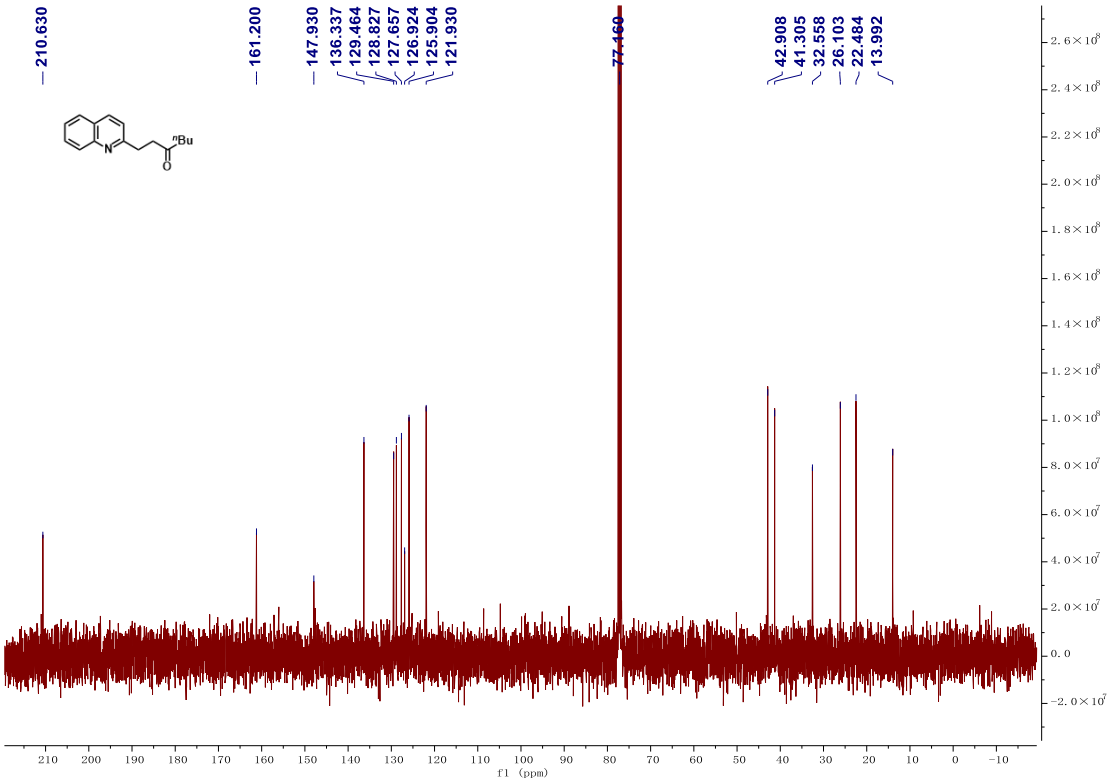
^{13}C NMR-spectrum (400 MHz, $CDCl_3$) of **3u**



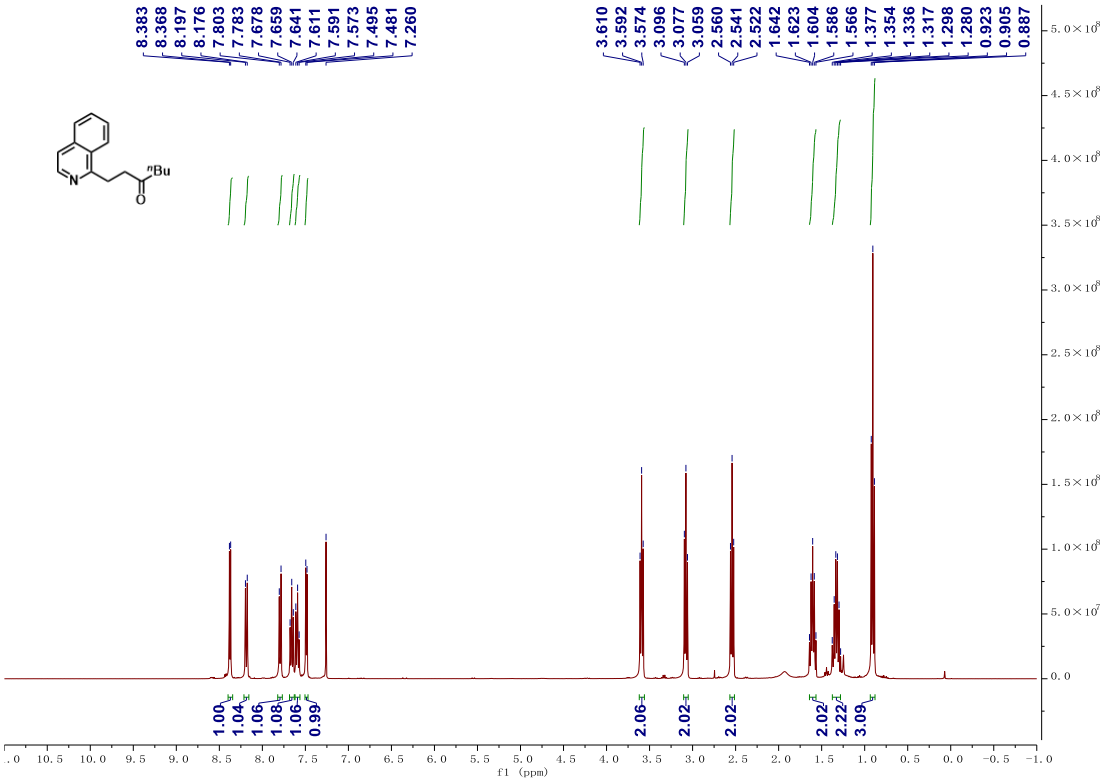
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3v**



^{13}C NMR-spectrum (400 MHz, $CDCl_3$) of **3v**



^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3w**



^{13}C NMR-spectrum (400 MHz, $CDCl_3$) of **3w**