Supporting Information for

A Highly Efficient Metal-Free Hydrocarbonylation of Alkynes with Propargylamines and Water

Yujuan Xie[a§], Liliang Huang[a§], Yayu Qi[a], Liangliang Song[b]* and Huangdi Feng[a,c]*

[a] College of Chemistry and Chemical Engineering, Shanghai University of Engineering Science, Shanghai, 201620, China

[b] International Innovation Center for Forest Chemicals and Materials, College of Chemical Engineering, Nanjing Forestry University, Nanjing 210037, Jiangsu, China

[c] Shanghai Frontiers Science Research Center for Druggability of Cardiovascular noncoding RNA, Institute for Frontier Medical Technology, Shanghai University of Engineering Science, Shanghai, 201620, China

[§]Y.X. and L.H. contributed equally to this paper

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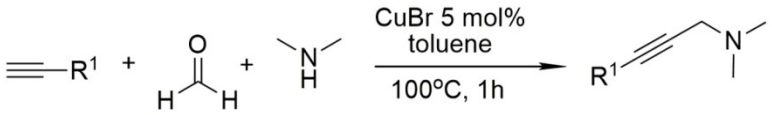
General Information

Unless otherwise noted, all commercial reagents (include part starting compounds 1 and 2) were used directly as purchased. All workup and purification procedures were carried out with reagent-grade solvents that had not been predried under an ambient atmosphere. Thin-layer chromatography (TLC) was performed, and visualization of the compounds was accomplished with UV light (254 nm) or iodine. Products were purified by flash chromatography on silica gel (100-200 mesh). The solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel and eluted with petroleum/ethyl acetate to afford the desired product .^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ operating at 400 MHz and 100 MHz, respectively. Proton chemical shifts are reported relative to the residual proton signals of the deuterated solvent $CDCl_3$ (7.29 ppm) or TMS. Carbon chemical shifts were internally referenced to the deuterated solvent signals in $CDCl_3$ (77.10 ppm). Chemical shifts are reported in δ (parts per million) values. Coupling constants *J* are reported in Hz. Proton coupling patterns were described as singlet (s), doublet (d), triplet (t), quartet (q), and multiple (m). High-resolution mass spectra were recorded on a liquid chromatograph mass spectrometer (LCMS-IT-TOF).

General Procedure for the Preparation of Propargylamine

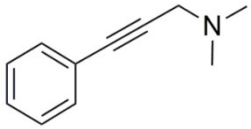


1a-1s

To a dried tube with a stirring bar were added CuBr (7.2 mg, 5 mol%), toluene (1.0 mL), alkyne (1.0 mmol), aldehyde (1.1 mmol), and secondary amine (1.2 mmol). Then the tube was sealed, and placed in a pre-heated oil bath at 100 ℃ stirring for 1 h. After cooling to room temperature, the solid was removed by filtration of the reaction mixture through a pad of celite. The filtrate was washed sequentially with DCM and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel and eluted with petroleum/ethyl

acetate (10/1) to afford the desired product **1a-1s**. The analytical data of propargylamines **1a-1s** are shown below.

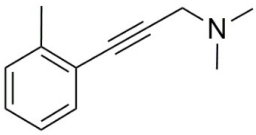
***N,N*-Dimethyl-3-phenylprop-2-yn-1-amine (1a)**



Purified by silica gel column chromatography (10−15% ethyl acetate in petroleum ether) afforded **1a** (147.3 mg, 93% yield) as yellow oil. *Known compound*.[1]

^{1}H NMR (400 MHz, Chloroform-d) δ 7.69–7.36 (m, 2H), 7.36–7.20 (m, 3H), 3.46 (s, 2H), 2.36 (s, 6H).

***N,N*-Dimethyl-3-o-tolylprop-2-yn-1-amine (1b)**



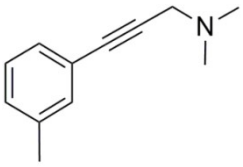
Purified by silica gel column chromatography (10−15% ethyl acetate in petroleum ether) afforded **1b** (175.9 mg, 93% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.48–7.39 (m, 1H), 7.24–7.17 (m, 2H), 7.17–7.08 (m, 1H), 3.56 (s, 2H), 2.44 (d, J = 23.1 Hz, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 140.0, 132.1, 129.4, 128.0, 125.5, 123.1, 84.2, 81.0, 48.6, 44.1, 20.9.

HRMS m/z (ESI^+): Calculated for $C_{12}H_{16}N$ ($[M+H]^+$): 174.1277, found 174.1269.

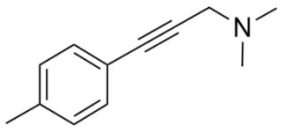
***N,N*-Dimethyl-3-m-tolylprop-2-yn-1-amine (1c)**



Purified by silica gel column chromatography (10−15% ethyl acetate in petroleum ether) afforded **1c** (161.9 mg, 94% yield) as yellow oil. *Known compound*.[2]

^{1}H NMR (400 MHz, Chloroform-d) δ 7.28–7.22 (m, 2H), 7.17 (t, J = 7.6 Hz, 1H), 7.09 (d, J = 7.6 Hz, 1H), 3.45 (s, 2H), 2.33 (d, J = 21.3 Hz, 9H).

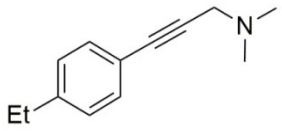
***N,N*-Dimethyl-3-p-tolylprop-2-yn-1-amine (1d)**



Purified by silica gel column chromatography (10−15% ethyl acetate in petroleum ether) afforded **1d** (161.0 mg, 93% yield) as yellow oil. *Known compound*.[3]

^{1}H NMR (400 MHz, Chloroform-d) δ 7.35 (d, *J* = 8.1 Hz, 2H), 7.11 (d, *J* = 7.8 Hz, 2H), 3.47 (s, 2H), 2.36 (d, *J* = 12.1 Hz, 9H).

3-(4-Ethylphenyl)-*N,N*-dimethylprop-2-yn-1-amine (1e)



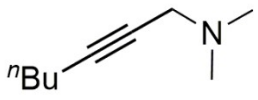
Purified by silica gel column chromatography (10−15% ethyl acetate in petroleum ether) afforded **1e** (168.1 mg, 90% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.35 (d, *J* = 8.2 Hz, 2H), 7.09 (d, *J* = 8.1 Hz, 2H), 3.42 (s, 2H), 2.59 (q, *J* = 7.6 Hz, 2H), 2.33 (s, 6H), 1.19 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.2, 131.7, 127.7, 120.5, 85.4, 83.8, 48.6, 44.1, 28.7, 15.3.

HRMS m/z (ESI^+): Calculated for $C_{13}H_{18}N$ ($[M+H]^+$): 188.1434, found 188.1426.

3-(4-Butylphenyl)-*N,N*-dimethylprop-2-yn-1-amine (1f)



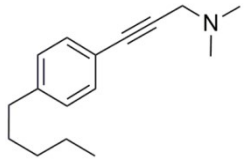
Purified by silica gel column chromatography (10−15% ethyl acetate in petroleum ether) afforded **1f** (189.2 mg, 88% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.36 (d, *J* = 8.2 Hz, 2H), 7.11 (d, *J* = 7.9 Hz, 2H), 3.47 (s, 2H), 2.60 (t, *J* = 7.7 Hz, 2H), 2.37 (s, 6H), 1.75–1.51 (m, 2H), 1.45–1.21 (m, 2H), 0.93 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 143.0, 131.6, 128.3, 120.4, 85.4, 83.8, 48.6, 44.1, 35.5, 33.4, 22.3, 13.9.

HRMS m/z (ESI$^+$): Calculated for $C_{15}H_{22}N$ ([M+H]$^+$): 216.1747, found 216.1747.

***N,N*-Dimethyl-3-(4-pentylphenyl)prop-2-yn-1-amine (1g)**



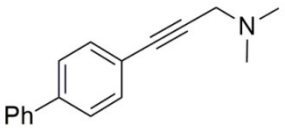
Purified by silica gel column chromatography (10−15% ethyl acetate in petroleum ether) afforded **1g** (190.1 mg, 83% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.31 (d, *J* = 7.8 Hz, 2H), 7.03 (d, *J* = 7.9 Hz 2H), 3.39 (s, 2H), 2.51 (t, *J* = 7.8 Hz, 2H), 2.30 (s, 6H), 1.70–1.42 (m, 2H), 1.37–1.09 (m, 4H), 0.85 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 142.8, 131.5, 128.2, 120.5, 85.4, 83.8, 48.5, 44.0, 35.7, 31.4, 30.9, 22.5, 13.9.

HRMS m/z (ESI$^+$): Calculated for $C_{16}H_{24}N$ ([M+H]$^+$): 230.1903, found 164.1432.

3-(Biphenyl-4-yl)-*N,N*-dimethylprop-2-yn-1-amine (1h)



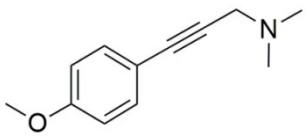
Purified by silica gel column chromatography (10−15% ethyl acetate in petroleum ether) afforded **1h** (187.8 mg, 80% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.66–7.52 (m, 6H), 7.49–7.41 (m, 2H), 7.41–7.32 (m, 1H), 3.54 (s, 2H), 2.44 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 140.8, 140.4, 132.2, 128.9, 127.6, 127.0, 127.0, 122.3, 85.5, 85.3, 48.7, 44.3.

HRMS m/z (ESI$^+$): Calculated for $C_{17}H_{18}N$ ([M+H]$^+$): 236.1434, found 236.1434.

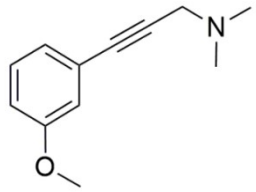
3-(4-Methoxyphenyl)-*N,N*-dimethylprop-2-yn-1-amine (1i)



Purified by silica gel column chromatography (10−15% ethyl acetate in petroleum ether) afforded **1i** (181.4 mg, 96% yield) as yellow oil. *Known compound*.[5]

^{1}H NMR (400 MHz, Chloroform-d) δ 7.33–7.27 (m, 2H), 6.77–6.68 (m, 2H), 3.65 (s, 3H), 3.36 (s, 2H), 2.27 (s, 6H).

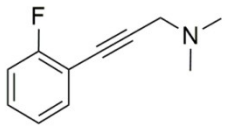
3-(3-Methoxyphenyl)-*N*,*N*-dimethylprop-2-yn-1-amine (1j)



Purified by silica gel column chromatography (10−15% ethyl acetate in petroleum ether) afforded **1j** (179.6 mg, 95% yield) as yellow oil. *Known compound*.[4]

^{1}H NMR (400 MHz, Chloroform-d) δ 7.20–7.12 (m, 1H), 7.06–7.00 (m, 1H), 6.97–6.91 (m, 1H), 6.84–6.79 (m, 1H), 3.74 (s, 3H), 3.43 (s, 2H), 2.33 (s, 6H).

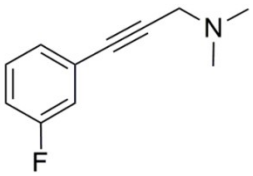
3-(2-Fluorophenyl)-*N*,*N*-dimethylprop-2-yn-1-amine (1k)



Purified by silica gel column chromatography (10−15% ethyl acetate in petroleum ether) afforded **1k** (154.1 mg, 87% yield) as yellow oil. *Known compound*.[6]

^{1}H NMR (400 MHz, Chloroform-d) δ 7.53–7.35 (m, 1H), 7.33–7.19 (m, 1H), 7.13–6.98 (m, 2H), 3.51 (s, 2H), 2.37 (s, 6H).

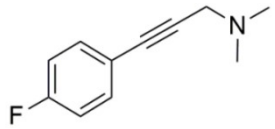
3-(3-Fluorophenyl)-*N*,*N*-dimethylprop-2-yn-1-amine (1l)



Purified by silica gel column chromatography (10−15% ethyl acetate in petroleum ether) afforded **1l** (150.9 mg, 85% yield) as yellow oil. *Known compound*.[7]

^{1}H NMR (400 MHz, Chloroform-d) δ 7.29–7.18 (m, 2H), 7.15–7.09 (m, 1H), 7.04–6.92 (m, 1H), 3.45 (s, 2H), 2.35 (s, 6H).

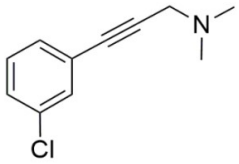
3-(4-Fluorophenyl)-*N,N*-dimethylprop-2-yn-1-amine (1m)



Purified by silica gel column chromatography (10−15% ethyl acetate in petroleum ether) afforded **1m** (152.4 mg, 86% yield) as yellow oil. *Known compound*.[3]

^{1}H NMR (400 MHz, Chloroform-d) δ 7.48–7.26 (m, 2H), 7.05–6.78 (m, 2H), 3.40 (s, 2H), 2.31 (s, 6H).

3-(3-Chlorophenyl)-*N,N*-dimethylprop-2-yn-1-amine (1n)



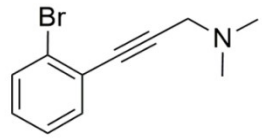
Purified by silica gel column chromatography (10−15% ethyl acetate in petroleum ether) afforded **1n** (146.5 mg, 76% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.60–7.02 (m, 4H), 3.37 (s, 2H), 2.27 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 134.0, 131.5, 129.7, 129.3, 128.2, 125.0, 86.1, 83.9, 48.4, 44.1.

HRMS m/z (ESI^+): Calculated for $C_{11}H_{13}ClN$ ($[M+H]^+$): 194.0731, found 194.0731.

3-(2-Bromophenyl)-*N,N*-dimethylprop-2-yn-1-amine (1o)



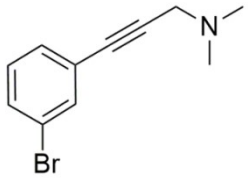
Purified by silica gel column chromatography (10−15% ethyl acetate in petroleum ether) afforded **1o** (191.7 mg, 81% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.68–7.51 (m, 1H), 7.51–7.41 (m, 1H), 7.33–7.18 (m, 1H), 7.17–7.03 (m, 1H), 3.54 (s, 2H), 2.40 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 133.5, 132.3, 129.1, 126.9, 125.4, 89.6, 83.9, 48.5, 44.1.

HRMS m/z (ESI^+): Calculated for $C_{11}H_{13}BrN$ ($[M+H]^+$): 238.0226, found 238.0226.

3-(3-Bromophenyl)-*N,N*-dimethylprop-2-yn-1-amine (1p)



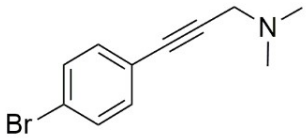
Purified by silica gel column chromatography (10−15% ethyl acetate in petroleum ether) afforded **1p** (189.4 mg, 80% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.50 (d, *J* = 1.9 Hz, 1H), 7.40–7.21 (m, 2H), 7.05 (t, *J* = 7.9 Hz, 1H), 3.38 (s, 2H), 2.27 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 134.4, 131.1, 130.2, 129.6, 125.2, 122.0, 86.2, 83.8, 48.4, 44.1.

HRMS m/z (ESI^+): Calculated for $C_{11}H_{13}BrN$ ($[M+H]^+$): 238.0226, found 238.0217.

3-(4-Bromophenyl)-*N,N*-dimethylprop-2-yn-1-amine (1q)



Purified by silica gel column chromatography (10−15% ethyl acetate in petroleum ether) afforded **1q** (179.7 mg, 76% yield) as yellow oil. *Known compound*.[5]

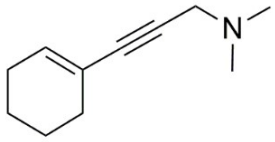
^{1}H NMR (400 MHz, Chloroform-d) δ 7.40 (dd, *J* = 8.5, 1.7 Hz, 2H), 7.27 (dd, *J* = 8.4, 1.6 Hz, 2H), 3.43 (s, 2H), 2.34 (d, *J* = 1.5 Hz, 6H).

***N,N*-Dimethylhept-2-yn-1-amine (1r)**

Purified by silica gel column chromatography (10−15% ethyl acetate in petroleum ether) afforded **1r** (90.4 mg, 65% yield) as yellow oil. *Known compound*.[8]

^{1}H NMR (400 MHz, Chloroform-d) δ 3.19 (s, 2H), 2.43–1.96 (m, 8H), 1.58–1.24 (m, 4H), 0.89 (t, *J* = 7.1 Hz, 3H).

3-Cyclohexenyl-*N,N*-dimethylprop-2-yn-1-amine (1s)



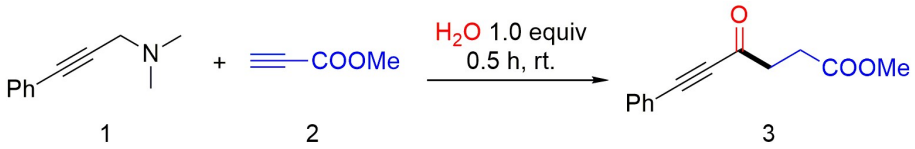
Purified by silica gel column chromatography (10−15% ethyl acetate in petroleum ether) afforded **1s** (120.1 mg, 74% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 6.23–5.94 (m, 1H), 3.31 (s, 2H), 2.26 (s, 6H), 2.18–1.95 (m, 4H), 1.74–1.39 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 134.0, 120.5, 87.0, 81.5, 48.5, 44.0, 29.4, 25.5, 22.3, 21.5.

HRMS m/z (ESI^+): Calculated for $C_{11}H_{18}N$ ($[M+H]^+$): 164.1434, found 164.1432.

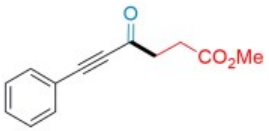
General Procedure for the Preparation of 3 and Its Characterization Data



1 2 3

General Procedure for Synthesis of Compounds 3: Under atmospheric stirring conditions, H_2O (0.5 equiv), amine **1** (0.5 mmol), and alkynyl ester **2** (1.2 mmol) were added in sequence, and then stirred at room temperature for 30 min. Subsequently, the reaction mixture was extracted and separated with a saturated NH_4Cl solution. The upper organic phase was washed with brine and dried with Na_2SO_4, then filtered, and the solvent was removed in a rotary evaporator. The residue was purified by flash chromatography (5−10% ethyl acetate in petroleum ether) to provide the desired product **3a-3w**.

Methyl 4-oxo-6-phenylhex-5-ynoate (3a)



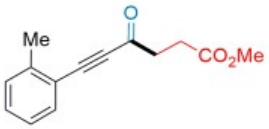
Purified by silica gel column chromatography (5−10% ethyl acetate in petroleum ether) afforded **3a** (188.8 mg, 87% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.55–7.46 (m, 2H), 7.45–7.36 (m, 1H), 7.36–7.27 (m, 2H), 3.63 (s, 3H), 2.96 (t, *J* = 6.8 Hz, 2H), 2.66 (t, *J* = 6.7 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 185.2, 172.4, 133.0, 130.8, 128.6, 119.7, 91.2, 87.4, 51.7, 40.0, 27.8.

HRMS m/z (ESI^+): Calculated for $C_{13}H_{13}O_3$ ($[M+H]^+$): 217.0859, found 217.0861.

Methyl 4-oxo-6-o-tolylhex-5-ynoate (3b)



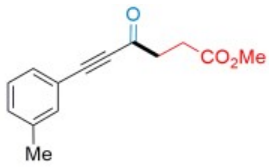
Purified by silica gel column chromatography (5−10% ethyl acetate in petroleum ether) afforded **3b** (64.5 mg, 56% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.57–7.47 (m, 1H), 7.38–7.29 (m, 1H), 7.27–7.22 (m, 1H), 7.22–7.16 (m, 1H), 3.69 (s, 3H), 3.18–2.94 (m, 2H), 2.81–2.61 (m, 2H), 2.48 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 185.2, 172.5, 142.2, 133.5, 130.9, 129.8, 125.9, 119.6, 91.2, 90.5, 51.8, 40.1, 27.9, 20.5.

HRMS m/z (ESI^+): Calculated for $C_{14}H_{15}O_3$ ($[M+H]^+$): 231.1016, found 231.1015.

Methyl 4-oxo-6-m-tolylhex-5-ynoate (3c)



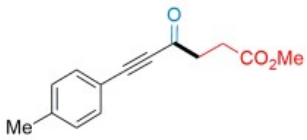
Purified by silica gel column chromatography (5−10% ethyl acetate in petroleum ether) afforded **3c** (87.8 mg, 76% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.48–7.31 (m, 2H), 7.31–7.16 (m, 2H), 3.69 (s, 3H), 3.00 (t, *J* = 6.8Hz, 2H), 2.70 (t, *J* = 6.7 Hz, 2H), 2.34 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 185.3, 172.5, 138.4, 133.5, 131.7, 130.2, 128.5, 119.6, 91.8, 87.2, 51.8, 40.0, 27.9, 21.1.

HRMS m/z (ESI$^+$): Calculated for $C_{14}H_{15}O_3$ ([M+H]$^+$): 231.1016, found 231.1016.

Methyl 4-oxo-6-p-tolylhex-5-ynoate (3d)



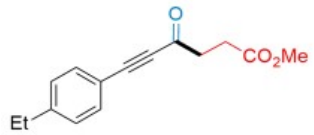
Purified by silica gel column chromatography (5−10% ethyl acetate in petroleum ether) afforded **3d** (80.5 mg, 69% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.72–7.39 (m, 2H), 7.31–7.02 (m, 2H), 3.69 (s, 3H), 3.00 (t, *J* = 6.8 Hz, 2H), 2.70 (t, *J* = 6.7 Hz, 2H), 2.37 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 185.3, 172.5, 141.5, 133.1, 129.4, 116.7, 92.1, 87.3, 51.8, 40.0, 27.9, 21.6.

HRMS m/z (ESI$^+$): Calculated for $C_{14}H_{15}O_3$ ([M+H]$^+$): 231.1016, found 231.1015.

Methyl 6-(4-ethylphenyl)-4-oxohex-5-ynoate (3e)



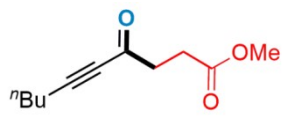
Purified by silica gel column chromatography (5−10% ethyl acetate in petroleum ether) afforded **3e** (as light yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 85.7 mg, 70% yield) 7.51 (d, *J* = 7.8 Hz, 2H), 7.23 (d, *J* = 7.8 Hz, 2H), 3.72 (s, 3H), 3.03 (t, *J* = 6.8 Hz, 2H), 2.81–2.46 (m, 4H), 1.26 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 185.3, 172.5, 147.7, 133.2, 128.2, 117.0, 92.1, 87.3, 51.8, 40.0, 29.0, 28.0, 15.0.

HRMS m/z (ESI$^+$): Calculated for $C_{15}H_{17}O_3$ ([M+H]$^+$): 245.1172, found 245.1171.

Methyl 6-(4-butylphenyl)-4-oxohex-5-ynoate (3f)



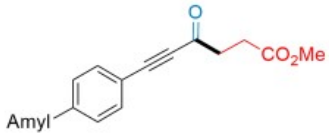
Purified by silica gel column chromatography (5−10% ethyl acetate in petroleum ether) afforded **3f** (114.4 mg, 84% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.49 (d, *J* = 8.0 Hz, 2H), 7.20 (d, *J* = 8.1 Hz, 2H), 3.70 (s, 3H), 3.02 (t, *J* = 6.8 Hz, 2H), 2.72 (t, *J* = 6.7 Hz, 2H), 2.64 (t, *J* = 7.7 Hz, 2H), 1.66–1.54 (m, 2H), 1.41–1.29 (m, 2H), 0.93 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 185.3, 172.5, 146.5, 133.1, 128.8, 116.9, 92.2, 87.3, 51.8, 40.0, 35.7, 33.1, 27.9, 22.2, 13.8.

HRMS m/z (ESI^+): Calculated for $C_{17}H_{21}O_3$ ($[M+H]^+$): 273.1485, found 273.1485.

Methyl 4-oxo-6-(4-pentylphenyl)hex-5-ynoate (3g)



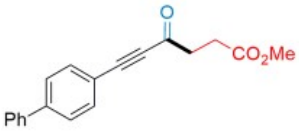
Purified by silica gel column chromatography (5−10% ethyl acetate in petroleum ether) afforded **3g** (113.1 mg, 79% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.51 (d, *J* = 8.3 Hz, 2H), 7.21 (d, *J* = 8.2 Hz, 2H), 3.72 (s, 3H), 3.03 (t, *J* = 6.8 Hz, 2H), 2.73 (t, *J* = 6.8 Hz, 2H), 2.64 (t, *J* = 6.7 Hz, 2H), 1.71–1.56 (m, 2H), 1.45–1.20 (m, 4H), 0.91 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 185.3, 172.5, 146.5, 133.1, 128.8, 116.9, 92.2, 87.3, 51.8, 40.0, 36.0, 31.4, 30.7, 28.0, 22.4, 13.9.

HRMS m/z (ESI^+): Calculated for $C_{18}H_{23}O_3$ ($[M+H]^+$): 287.1642, found 287.1643.

Methyl 6-(biphenyl-4-yl)-4-oxohex-5-ynoate (3h)



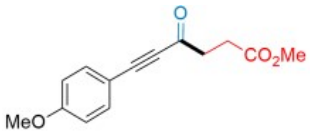
Purified by silica gel column chromatography (5−10% ethyl acetate in petroleum ether) afforded **3h** (126.3 mg, 86% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.65–7.61 (m, 2H), 7.61–7.56 (m, 4H), 7.49–7.42 (m, 2H), 7.41–7.35 (m, 1H), 3.71 (s, 3H), 3.04 (t, *J* = 6.7 Hz, 2H), 2.73 (t, *J* = 6.7 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 185.2, 172.5, 143.6, 139.7, 133.6, 129.0, 128.2, 127.2, 127.1, 118.5, 91.4, 88.1, 51.8, 40.0, 27.9.

HRMS m/z (ESI^+): Calculated for $C_{19}H_{17}O_3$ ($[M+H]^+$): 293.1172, found 293.1171.

Methyl 6-(4-methoxyphenyl)-4-oxohex-5-ynoate (3i)



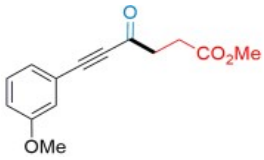
Purified by silica gel column chromatography (5−10% ethyl acetate in petroleum ether) afforded **3i** (55.2 mg, 45% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.52 (d, *J* = 8.9 Hz, 2H), 6.89 (d, *J* = 8.9 Hz, 2H), 3.83 (s, 3H), 3.69 (s, 3H), 2.99 (t, *J* = 6.7 Hz, 2H), 2.70 (t, *J* = 6.7 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 185.3, 172.6, 161.8, 135.1, 114.4, 111.5, 92.6, 87.3, 55.4, 51.8, 39.9, 28.0.

HRMS m/z (ESI^+): Calculated for $C_{14}H_{15}O_4$ ($[M+H]^+$): 247.0965, found 247.0964.

Methyl 6-(3-methoxyphenyl)-4-oxohex-5-ynoate (3j)



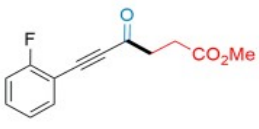
Purified by silica gel column chromatography (5−10% ethyl acetate in petroleum ether) afforded **3j** (45.9 mg, 37% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.40–7.24 (m, 1H), 7.22–7.13 (m, 1H), 7.13–7.05 (m, 1H), 7.05–6.96 (m, 1H), 3.80 (s, 3H), 3.70 (s, 3H), 3.02 (t, *J* = 6.7 Hz, 2H), 2.71 (t, *J* = 6.7 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 185.3, 172.5, 159.5, 129.7, 125.5, 120.7, 91.3, 87.1, 55.3, 51.8, 40.0, 27.9.

HRMS m/z (ESI^+): Calculated for $C_{14}H_{15}O_4$ ($[M+H]^+$): 247.0965, found 247.0964.

Methyl 6-(2-fluorophenyl)-4-oxohex-5-ynoate (3k)



Purified by silica gel column chromatography (5−10% ethyl acetate in petroleum ether) afforded **3k** (104.4 mg, 89% yield) as light yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.77–7.50 (m, 1H), 7.50–7.37 (m, 1H), 7.30–

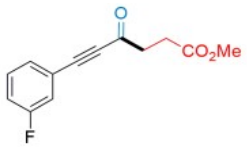
7.04 (m, 2H), 3.70 (s, 3H), 3.03 (t, J = 6.6 Hz, 2H), 2.72 (t, J = 6.7 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 185.0, 172.4, 163.6 (d, J = 255.8 Hz), 134.6, 132.8 (d, J = 8.1 Hz), 124.3 (d, J = 3.8 Hz), 115.9 (d, J = 20.4 Hz), 108.7 (d, J = 15.3 Hz), 91.7 (d, J = 3.2 Hz), 84.6, 51.8, 40.0, 27.8.

^{19}F NMR (376 MHz, Chloroform-d) δ -107.14.

HRMS m/z (ESI^+): Calculated for $C_{13}H_{12}FO_3$ ($[M+H]^+$): 235.0765, found 235.0765.

Methyl 6-(3-fluorophenyl)-4-oxohex-5-ynoate (3l)



Purified by silica gel column chromatography (5−10% ethyl acetate in petroleum ether) afforded **3l** (110.9 mg, 95% yield) as yellow oil.

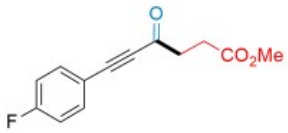
^{1}H NMR (400 MHz, Chloroform-d) δ 7.36–7.26 (m, 2H), 7.25–7.15 (m, 1H), 7.15–7.04 (m, 1H), 3.65 (s, 3H), 2.98 (t, J = 6.7 Hz, 2H), 2.67 (t, J = 6.6 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 185.0, 172.3, 162.2 (d, J = 248.2 Hz), 136.8, 124.5, 121.6 (d, J = 9.3 Hz), 118.8 (dd, J = 135.7, 22.2 Hz), 89.2 (d, J = 3.5 Hz), 87.6, 51.8, 40.0, 27.7.

^{19}F NMR (376 MHz, Chloroform-d) δ -111.71.

HRMS m/z (ESI^+): Calculated for $C_{13}H_{12}FO_3$ ($[M+H]^+$): 235.0765, found 235.0766.

Methyl 6-(4-fluorophenyl)-4-oxohex-5-ynoate (3m)



Purified by silica gel column chromatography (5−10% ethyl acetate in petroleum ether) afforded **3m** (106.5 mg, 91% yield) as yellow oil.

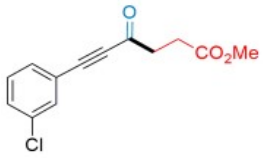
^{1}H NMR (400 MHz, Chloroform-d) δ 7.75–7.34 (m, 2H), 7.24–6.95 (m, 2H), 3.70 (s, 3H), 3.02 (t, J = 6.6 Hz, 2H), 2.71 (t, J = 6.7 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 185.2, 172.5, 165.3, 162.8, 135.3 (d, J = 8.9 Hz), 116.2 (d, J = 22.4 Hz), 90.2, 87.3 (d, J = 1.5 Hz), 51.9, 40.0, 27.8.

^{19}F NMR (376 MHz, Chloroform-d) δ -106.08.

HRMS m/z (ESI$^+$): Calculated for $C_{13}H_{12}FO_3$ ([M+H]$^+$): 235.0765, found 235.0766.

Methyl 6-(3-chlorophenyl)-4-oxohex-5-ynoate (3n)



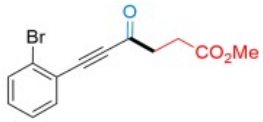
Purified by silica gel column chromatography (5−10% ethyl acetate in petroleum ether) afforded **3n** (113.1 mg, 90% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.49 (d, *J* = 1.8 Hz, 1H), 7.44–7.34 (m, 2H), 7.28 (t, *J* = 7.9 Hz, 1H), 3.66 (s, 3H), 2.98 (t, *J* = 6.7 Hz, 2H), 2.67 (t, *J* = 6.7 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 184.9, 172.3, 134.5, 132.5, 131.0, 131.0, 129.9, 121.5, 89.0, 87.8, 51.8, 40.0, 27.7.

HRMS m/z (ESI$^+$): Calculated for $C_{13}H_{12}ClO_3$ ([M+H]$^+$): 251.0469, found 251.0470.

Methyl 6-(2-bromophenyl)-4-oxohex-5-ynoate (3o)



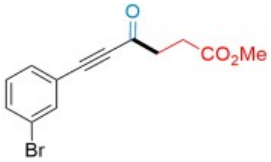
Purified by silica gel column chromatography (5−10% ethyl acetate in petroleum ether) afforded **3o** (112.2 mg, 76% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.64 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.61–7.58 (m, 1H), 7.35–7.30 (m, 2H), 3.72 (s, 3H), 3.07 (t, *J* = 6.7 Hz, 2H), 2.76 (t, *J* = 6.8 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 185.2, 172.4, 134.9, 132.8, 131.9, 127.3, 126.8, 122.3, 90.6, 89.3, 51.9, 40.2, 27.9.

HRMS m/z (ESI$^+$): Calculated for $C_{13}H_{12}BrO_3$ ([M+H]$^+$): 294.9964, found 294.9964.

Methyl 6-(3-bromophenyl)-4-oxohex-5-ynoate (3p)



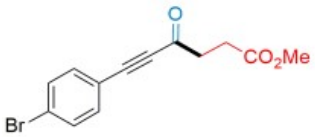
Purified by silica gel column chromatography (5−10% ethyl acetate in petroleum ether) afforded **3p** (125.1 mg, 85% yield) as light yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.69 (t, *J* = 1.8 Hz, 1H), 7.60–7.54 (m, 1H), 7.50–7.44 (m, 1H), 7.24 (t, *J* = 7.9 Hz, 1H), 3.68 (s, 3H), 3.00 (t, *J* = 6.7 Hz, 2H), 2.69 (t, *J* = 6.7 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 185.0, 172.4, 135.5, 133.9, 131.5, 130.1, 122.4, 121.8, 89.0, 87.9, 51.9, 40.0, 27.8.

HRMS m/z (ESI^+): Calculated for $C_{13}H_{12}BrO_3$ ($[M+H]^+$): 294.9964, found 294.9964.

Methyl 6-(4-bromophenyl)-4-oxohex-5-ynoate (3q)



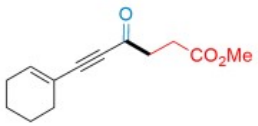
Purified by silica gel column chromatography (5−10% ethyl acetate in petroleum ether) afforded **3q** (121.4 mg, 82% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.50 (d, *J* = 8.5 Hz, 2H), 7.40 (d, *J* = 8.6 Hz, 2H), 3.67 (s, 3H), 2.99 (t, *J* = 6.7 Hz, 2H), 2.68 (t, *J* = 6.7 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 185.0, 172.4, 134.3, 132.0, 125.6, 118.7, 89.8, 88.2, 51.8, 40.0, 27.8.

HRMS m/z (ESI^+): Calculated for $C_{13}H_{12}BrO_3$ ($[M+H]^+$): 294.9964, found 294.9966.

Methyl 6-cyclohexenyl-4-oxohex-5-ynoate (3s)



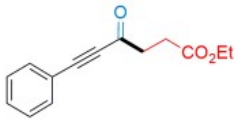
Purified by silica gel column chromatography (5−10% ethyl acetate in petroleum ether) afforded **3s** (29.4 mg, 27% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 6.47 (t, *J* = 2.1 Hz, 1H), 3.70 (s, 3H), 2.92 (t, *J* = 6.8 Hz, 2H), 2.67 (t, *J* = 6.8 Hz, 2H), 2.23–2.10 (m, 4H), 1.73–1.57 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 185.5, 172.6, 142.6, 118.9, 94.0, 85.7, 51.8, 39.9, 28.3, 28.0, 26.1, 21.9, 21.1.

HRMS m/z (ESI^+): Calculated for $C_{13}H_{17}O_3$ ($[M+H]^+$): 221.1172, found 221.1173.

Ethyl 4-oxo-6-phenylhex-5-ynoate (3t)



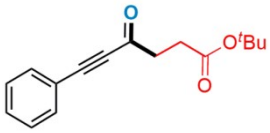
Purified by silica gel column chromatography (5−10% ethyl acetate in petroleum ether) afforded **3t** (76.8 mg, 67% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.61–7.47 (m, 2H), 7.47–7.41 (m, 1H), 7.39–7.32 (m, 2H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.00 (t, *J* = 6.7 Hz, 2H), 2.68 (t, *J* = 6.7 Hz, 2H), 1.24 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 185.3, 172.0, 133.0, 130.8, 128.6, 119.8, 91.2, 87.4, 60.7, 40.0, 28.2, 14.1.

HRMS m/z (ESI^+): Calculated for $C_{14}H_{15}O_3$ ($[M+H]^+$): 230.1016, found 230.1017.

Tert-butyl 4-oxo-6-phenylhex-5-ynoate (3u)



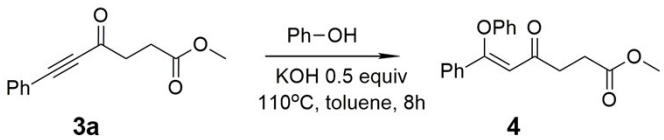
Purified by silica gel column chromatography (5−10% ethyl acetate in petroleum ether) afforded **3u** (39.7 mg, 31% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.62–7.55 (m, 2H), 7.51–7.44 (m, 1H), 7.42–7.35 (m, 2H), 2.97 (t, *J* = 6.8 Hz, 2H), 2.65 (t, *J* = 6.7 Hz, 2H), 1.47 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 185.7, 171.2, 133.0, 130.7, 128.6, 119.9, 91.2, 87.5, 80.9, 40.2, 29.5, 28.0.

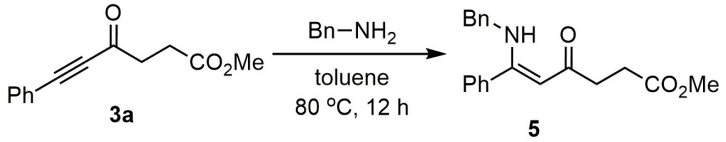
HRMS m/z (ESI^+): Calculated for $C_{16}H_{19}O_3$ ($[M+H]^+$): 259.1329, found 259.1325.

Further application and transformations



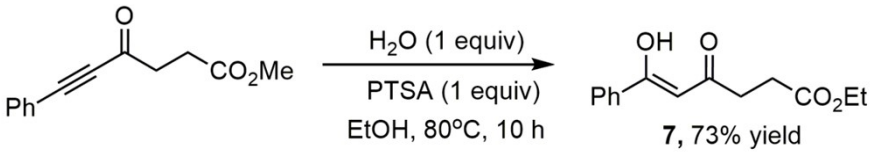
Synthesis of Compounds 4: Under atmospheric stirring conditions, KOH (0.25 mmol, 0.5 equiv), compounds **3a** (0.5 mmol, 1.0 equiv), phenol (0.5mmol, 1.0 equiv), and toluene (2.0 mL) were added in sequence, and then stirred at 100 °C for 8 h. Subsequently, the reaction mixture was extracted and separated with a saturated

NH_4Cl solution. The upper organic phase was washed with brine and dried with Na_2SO_4, then filtered, and the solvent was removed in a rotary evaporator. The residue was purified by flash chromatography (5−10% ethyl acetate in petroleum ether) to provide the desired product **4** (145.9 mg, 94% yield).

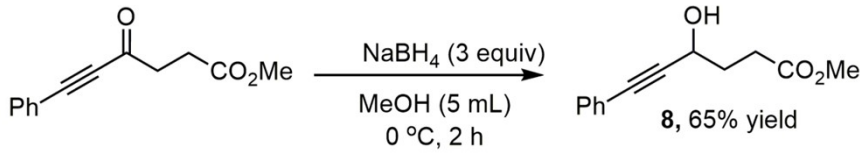


Synthesis of Compounds 5: Under atmospheric stirring conditions, compounds **3a** (0.5 mmol, 1.0 equiv), benzylamine (0.5 mmol, 1.0 equiv), and toluene (2.0 mL) were measured in sequence, and then stirred at 80 °C for 12 h. Subsequently, the reaction mixture was extracted and separated with a saturated NH_4Cl solution. The upper organic phase was washed with brine and dried with Na_2SO_4, then filtered, and the solvent was removed in a rotary evaporator. The residue was purified by flash chromatography (5−10% ethyl acetate in petroleum ether) to provide the desired product **5** (119.9 mg, 78% yield).

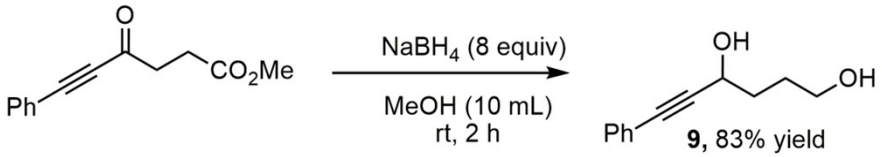
Synthesis of Compounds 6: Under atmospheric stirring conditions, CuI (0.05 mmol, 10 mol%), compounds **3a** (0.5 mmol, 1.0 equiv), DBU (0.5 mmol, 1.0 equiv), and toluene (2.0 mL) were added in sequence, and then stirred at 110 °C for 12 h. Subsequently, the reaction mixture was extracted and separated with a saturated NH_4Cl solution. The upper organic phase was washed with brine and dried with Na_2SO_4, then filtered, and the solvent was removed in a rotary evaporator. The residue was purified by flash chromatography (5−10% ethyl acetate in petroleum ether) to provide the desired product **6** (168.2 mg, 87% yield).



Synthesis of Compounds 7: Under atmospheric stirring conditions, PTSA (0.5 mmol, 1.0 equiv), H_2O (0.5 mmol, 1.0 equiv), compounds **3a** (0.5 mmol, 1.0 equiv), and EtOH (2.0 mL) were added in sequence, and then stirred at 80 °C for 10 h. Subsequently, the reaction mixture was extracted and separated with a saturated NH_4Cl solution. The upper organic phase was washed with brine and dried with Na_2SO_4, then filtered, and the solvent was removed in a rotary evaporator. The residue was purified by flash chromatography (20–25% ethyl acetate in petroleum ether) to provide the desired product **7** (91.2 mg, 73% yield).



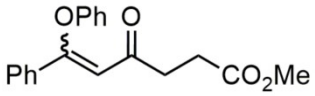
Synthesis of Compounds 8: Under atmospheric stirring conditions, $NaBH_4$ (1.5 mmol, 3.0 equiv), compounds **3a** (0.5 mmol, 1.0 equiv), and MeOH (5 mL) were added in sequence, and then stirred at 0 °C for 2 h. Subsequently, the reaction mixture was extracted and separated with a saturated NH_4Cl solution. The upper organic phase was washed with brine and dried with Na_2SO_4, then filtered, and the solvent was removed in a rotary evaporator. The residue was purified by flash chromatography (30–40% ethyl acetate in petroleum ether) to provide the desired product **8** (71.1 mg, 65% yield).



Synthesis of Compounds 9: Under atmospheric stirring conditions, $NaBH_4$ (4.0 mmol, 8.0 equiv), compounds **3a** (0.5 mmol, 1.0 equiv), and MeOH (10 mL) were added in sequence, and then stirred at rt for 2 h. Subsequently, the reaction mixture was extracted and separated with a saturated NH_4Cl solution. The upper organic phase

was washed with brine and dried with Na_2SO_4, then filtered, and the solvent was removed in a rotary evaporator. The residue was purified by flash chromatography (70−80% ethyl acetate in petroleum ether) to provide the desired product **9** (79.0 mg, 83% yield).

(Z) -Methyl 4-oxo-6-phenoxy-6-phenylhex-5-enoate (4)



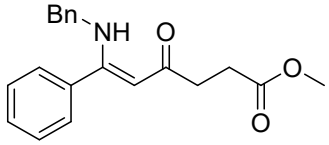
Purified by silica gel column chromatography (5−10% ethyl acetate in petroleum ether) afforded **4** (145.9 mg, 94% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.60 (m, 2H), 7.50–7.41 (m, 2H), 7.39–7.12 (m, 4H), 7.06–6.92 (m, 2H), 6.29 (d, *J* = 1.4 Hz, 0.65H), 5.57 (s, 0.35H), 3.65 (d, *J* = 14.0 Hz, 3H), 3.14 (t, *J* = 6.5 Hz, 1.3H), 2.61 (q, *J* = 7.0 Hz, 2H), 2.52 (d, *J* = 6.5 Hz, 0.7H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 197.5, 196.5, 173.4, 173.3, 169.1, 160.9, 156.0, 154.0, 134.0, 133.8, 130.6, 130.5, 130.1, 129.8, 129.4, 128.8, 128.1, 127.6, 125.6, 123.0, 121.3, 117.0, 116.3, 106.4, 51.6, 38.2, 37.7, 28.1, 28.0.

HRMS m/z (ESI^+): Calculated for $C_{19}H_{19}O_4$ ($[M+H]^+$): 311.1278, found 311.1273.

***(Z)*-Methyl 4-oxo-6-phenyl-6-(phenylamino)hex-5-enoate (5)**



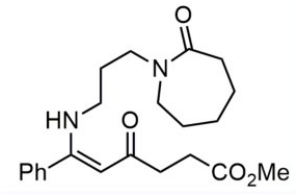
Purified by silica gel column chromatography (5−10% ethyl acetate in petroleum ether) afforded **5** (119.9 mg, 78% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 10.96 (t, *J* = 6.7 Hz, 1H), 7.47–6.89 (m, 10H), 5.16 (s, 1H), 4.33 (d, *J* = 6.6 Hz, 2H), 3.70 (s, 3H), 2.70 (dd, *J* = 24.8, 6.6 Hz, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 196.0, 173.9, 165.1, 138.5, 135.2, 129.5, 128.7, 128.5, 127.7, 127.3, 126.9, 96.5, 51.6, 48.3, 36.3, 29.1.

HRMS m/z (ESI^+): Calculated for $C_{20}H_{22}NO_3$ ($[M+H]^+$): 324.1594, found 324.1599.

***(Z)*-Methyl 4-oxo-6-(3-(2-oxoazepan-1-yl)propylamino)-6-phenylhex-5-enoate (6)**



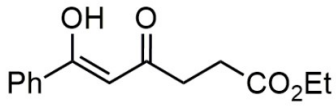
Purified by silica gel column chromatography (5−10% ethyl acetate in petroleum ether) afforded **6** (168.2 mg, 87% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 10.56 (t, *J* = 6.2 Hz, 1H), 7.45–7.26 (m, 3H), 7.23 (d, *J* = 5.0 Hz, 2H), 4.95 (s, 1H), 3.59 (s, 3H), 3.24 (t, *J* = 6.9 Hz, 2H), 3.19–3.10 (m, 2H), 3.05 (d, *J* = 7.0 Hz, 2H), 2.65–2.48 (m, 4H), 2.42–2.27 (m, 2H), 1.67–1.53 (m, 4H), 1.50–1.37 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 195.4, 175.6, 173.7, 165.1, 135.2, 129.3, 128.4, 127.6, 95.8, 51.5, 49.5, 45.6, 42.2, 37.0, 36.1, 29.8, 29.5, 29.1, 28.6, 23.2.

HRMS m/z (ESI^+): Calculated for $C_{22}H_{31}N_2O_4$ ($[M+H]^+$): 387.2278, found 387.2278.

***(Z)*-Ethyl 6-hydroxy-4-oxo-6-phenylhex-5-enoate (7)**



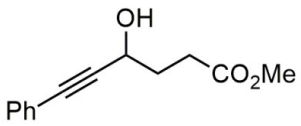
Purified by silica gel column chromatography (20−25% ethyl acetate in petroleum ether) afforded **7** (91.2 mg, 73% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 15.84 (s, 1H), 7.97–7.83 (m, 2H), 7.56–7.38 (m, 3H), 6.21 (s, 1H), 4.17 (q, *J* = 7.4 Hz, 2H), 2.82 (t, *J* = 6.9 Hz, 2H), 2.70 (t, *J* = 6.9 Hz, 2H), 1.27 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 197.0, 180.6, 172.5, 134.3, 132.2, 128.6, 126.9, 96.2, 60.7, 34.5, 29.1, 14.2.

HRMS m/z (ESI^+): Calculated for $C_{14}H_{17}O_4$ ($[M+H]^+$): 249.1121, found 249.1122.

Methyl 4-hydroxy-6-phenylhex-5-ynoate (8)

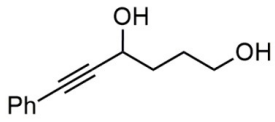


Purified by silica gel column chromatography (30−40% ethyl acetate in petroleum ether) afforded **8** (71.1 mg, 65% yield) as yellow oil. *Known compound*.[9]

^{1}H NMR (400 MHz, Chloroform-d) δ 7.48–7.41 (m, 2H), 7.36–7.26 (m, 3H), 4.73 (d, *J* = 5.6 Hz, 1H), 3.71 (s, 3H), 2.70–2.56 (m, 3H), 2.16 (q, *J* = 6.7 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 174.1, 131.7, 128.5, 128.3, 122.4, 89.1, 85.4, 62.0, 51.8, 32.5, 29.8.

6-Phenylhex-5-yne-1,4-diol (9)



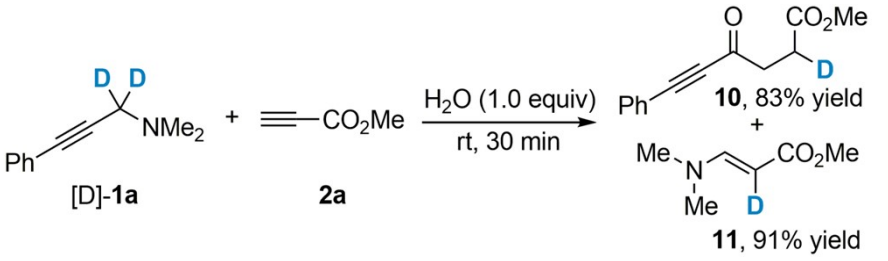
Purified by silica gel column chromatography (70−80% ethyl acetate in petroleum ether) afforded **9** (79.0 mg, 83% yield) as yellow oil. *Known compound*.[10]

^{1}H NMR (400 MHz, Chloroform-d) δ 7.56–7.39 (m, 2H), 7.30 (d, *J* = 5.4 Hz, 3H), 4.67 (s, 1H), 3.71 (q, *J* = 5.7 Hz, 4H), 2.04–1.49 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 131.7, 128.4, 128.3, 122.7, 90.1, 84.8, 62.4, 34.9, 28.4.

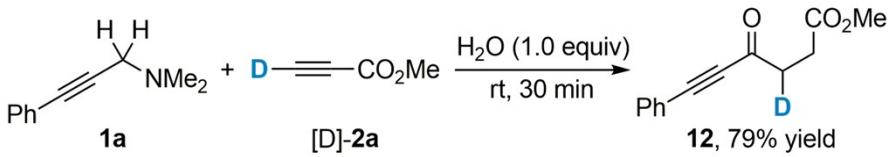
Control Experiments and Characterization Data

Scheme 3a



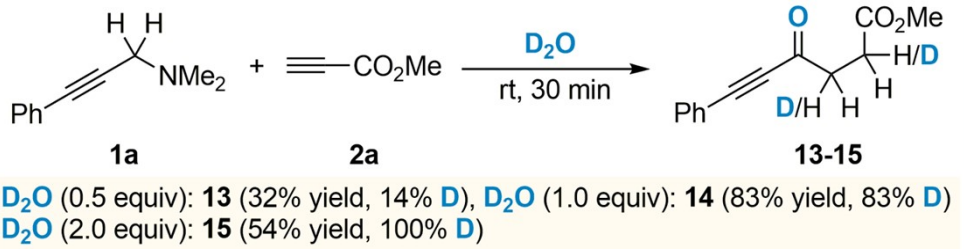
Synthesis of Compounds 10 and 11: Under atmospheric stirring conditions, H_2O (0.5 equiv), amine [D]-**1a** (0.5 mmol), and alkynyl ester **2a** (1.2 mmol) were added in sequence, and then stirred at room temperature for 30 min. Subsequently, the reaction mixture was extracted and separated with a saturated NH_4Cl solution. The upper organic phase was washed with brine and dried with Na_2SO_4, then filtered, and the solvent was removed in a rotary evaporator. The residue was purified by flash chromatography (5−10% ethyl acetate in petroleum ether) to provide the desired product **10** (179.9 mg, 83% yield) and **11** (58.8 mg, 91% yield).

Scheme 3b



Synthesis of Compounds 12: Under atmospheric stirring conditions, H_2O (0.5 equiv), amine **1a** (0.5 mmol), and alkynyl ester [D]-**2a** (1.2 mmol) were added in sequence, and then stirred at room temperature for 30 min. Subsequently, the reaction mixture was extracted and separated with a saturated NH_4Cl solution. The upper organic phase was washed with brine and dried with Na_2SO_4, then filtered, and the solvent was removed in a rotary evaporator. The residue was purified by flash chromatography (5−10% ethyl acetate in petroleum ether) to provide the desired product **12** (171.3 mg, 79% yield).

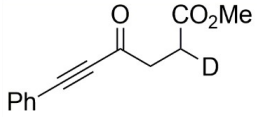
Scheme 3c



Synthesis of Compounds 13–15: Under atmospheric stirring conditions, D_2O (0.5equiv/ 1.0 equiv/2.0 equiv), amine **1a** (0.5 mmol), and alkynyl ester **2a** (1.2 mmol) were added in sequence, and then stirred at room temperature for 30 min. Subsequently, the reaction mixture was extracted and separated with a saturated

NH_4Cl solution. The upper organic phase was washed with brine and dried with Na_2SO_4, then filtered, and the solvent was removed in a rotary evaporator. The residue was purified by flash chromatography (5−10% ethyl acetate in petroleum ether) to provide the desired product **13**−**15**.

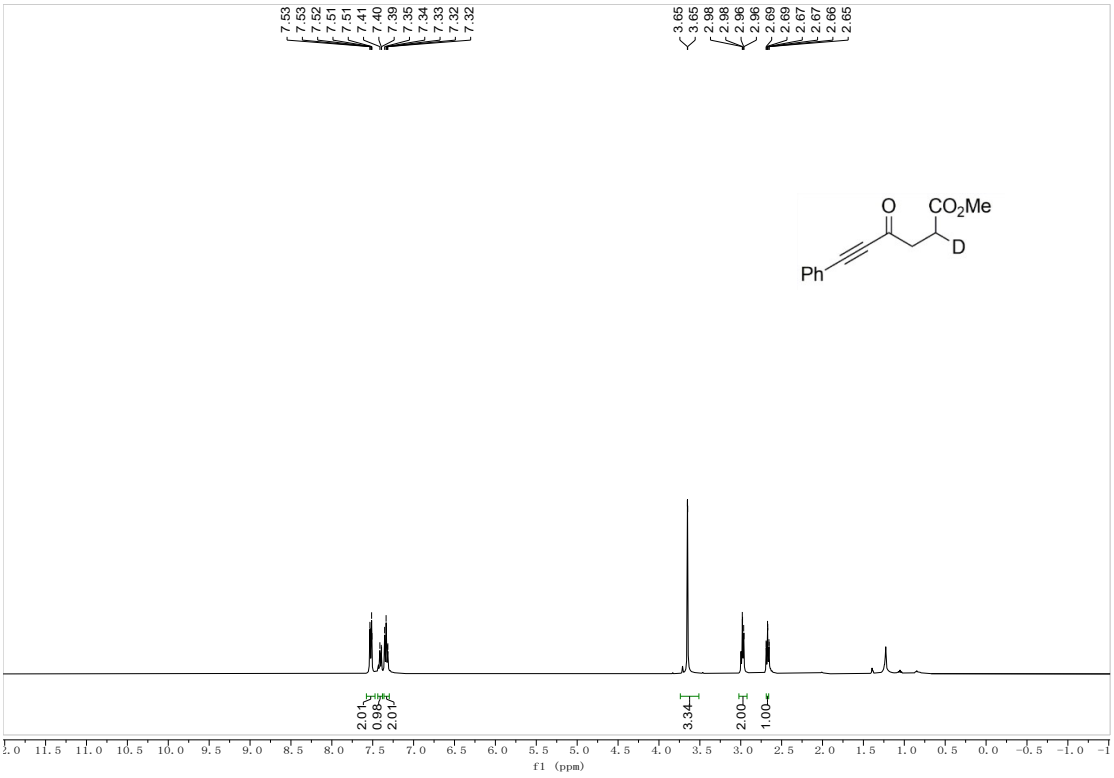
Characterization Data

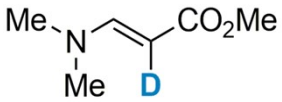


Purified by silica gel column chromatography (5−10% ethyl acetate in petroleum ether) afforded **10** (179.9 mg, 83% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.61–7.46 (m, 2H), 7.45–7.39 (m, 1H), 7.38–7.26 (m, 2H), 3.65 (s, 3H), 3.11–2.84 (m, 2H), 2.76–2.56 (m, 1H).

^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **10**

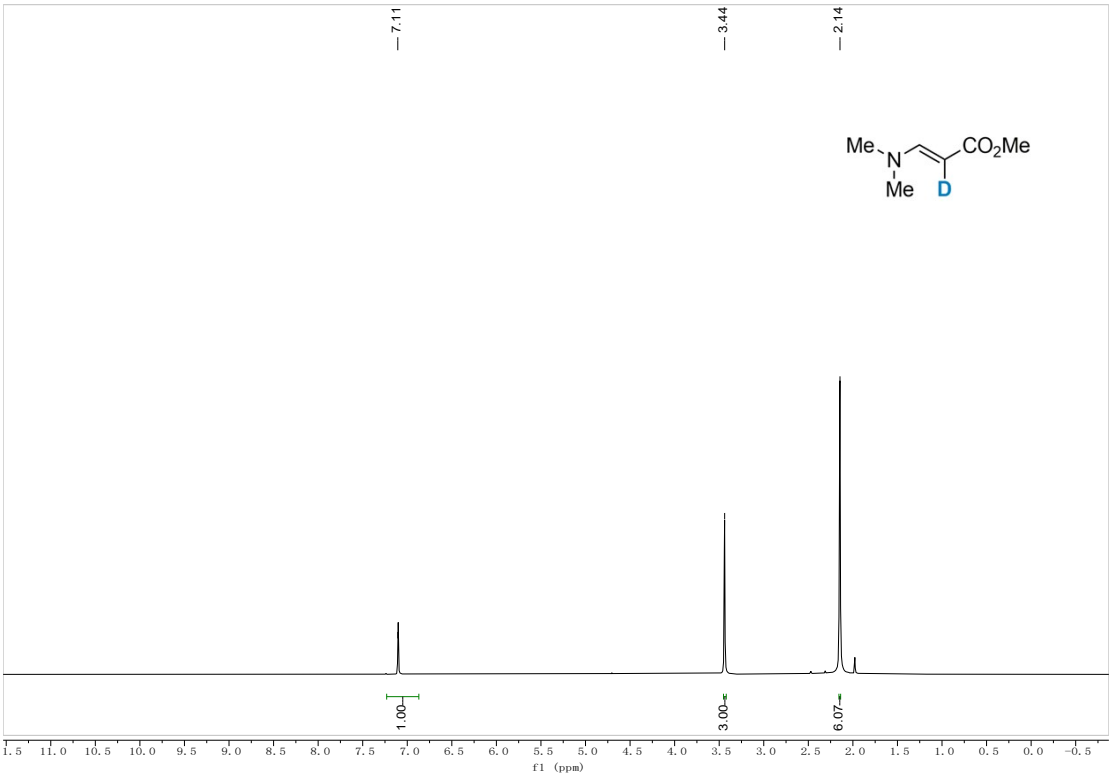


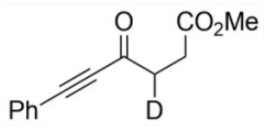


Purified by silica gel column chromatography (5−10% ethyl acetate in petroleum ether) afforded **11** (58.8 mg, 91% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.11 (s, 1H), 3.44 (s, 3H), 2.14 (s, 6H).

^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **11**

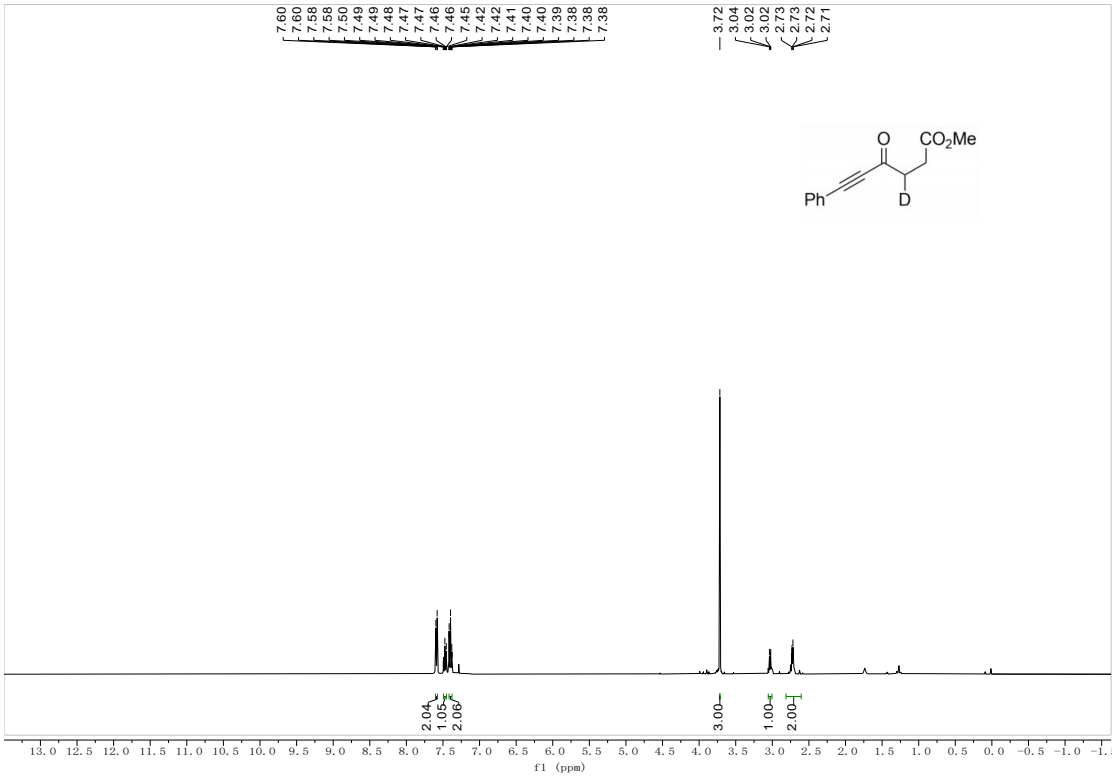


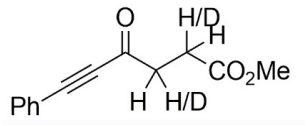


Purified by silica gel column chromatography (5−10% ethyl acetate in petroleum ether) afforded **12** (171.3 mg, 79% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.61–7.54 (m, 2H), 7.50–7.44 (m, 1H), 7.43–7.35 (m, 2H), 3.72 (s, 3H), 3.22–2.92 (m, 1H), 2.83–2.59 (m, 2H).

^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **12**

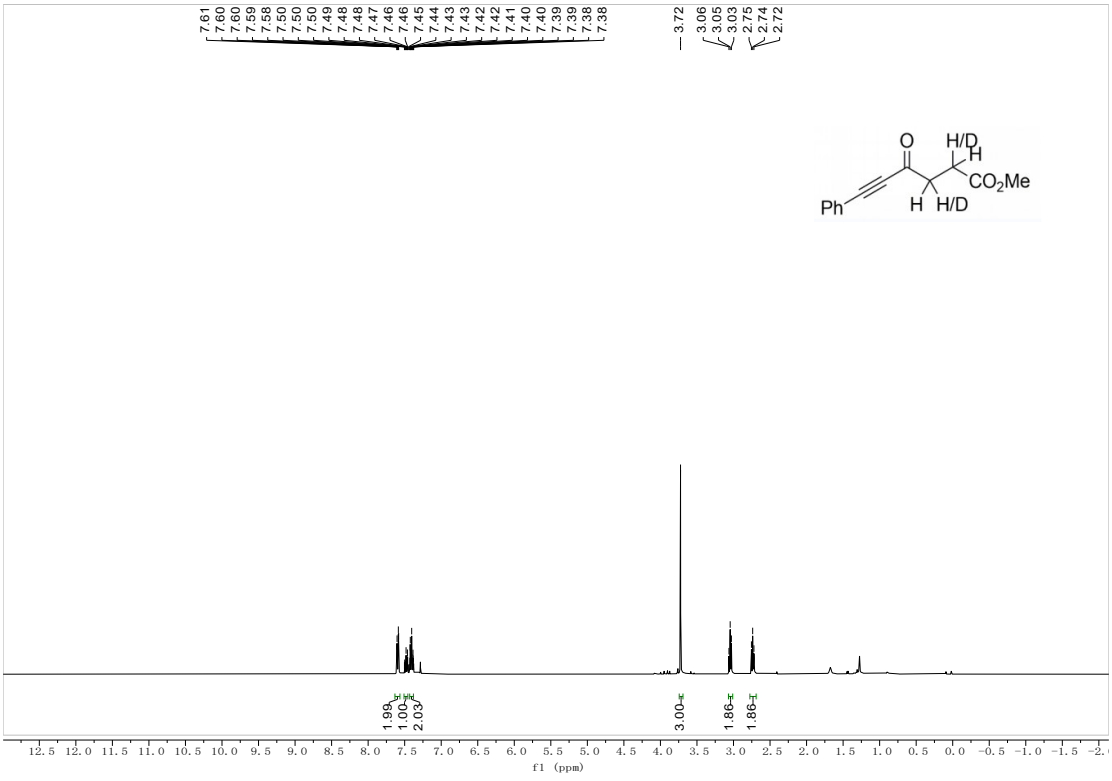




Purified by silica gel column chromatography (5−10% ethyl acetate in petroleum ether) afforded **13** (69.5 mg, 32% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.63–7.56 (m, 2H), 7.51–7.45 (m, 1H), 7.44–7.37 (m, 2H), 3.72 (s, 3H), 3.05 (t, *J* = 6.7 Hz, 1.86 H), 2.74 (t, *J* = 6.8 Hz, 1.86 H).

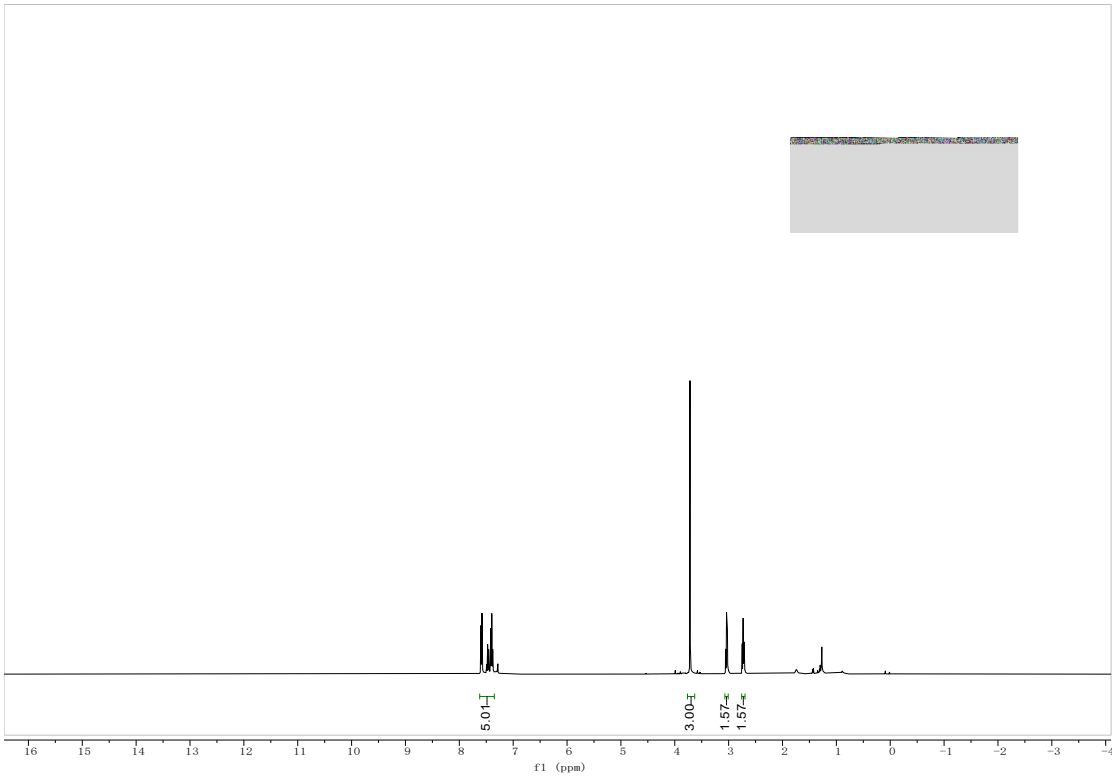
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **13**



Purified by silica gel column chromatography (5−10% ethyl acetate in petroleum ether) afforded **14** (180.1 mg, 83% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.64–7.34 (m, 5H), 3.72 (s, 3H), 3.04 (t, *J* = 6.6 Hz, 1.57 H), 2.73 (t, *J* = 6.7 Hz, 1.57 H).

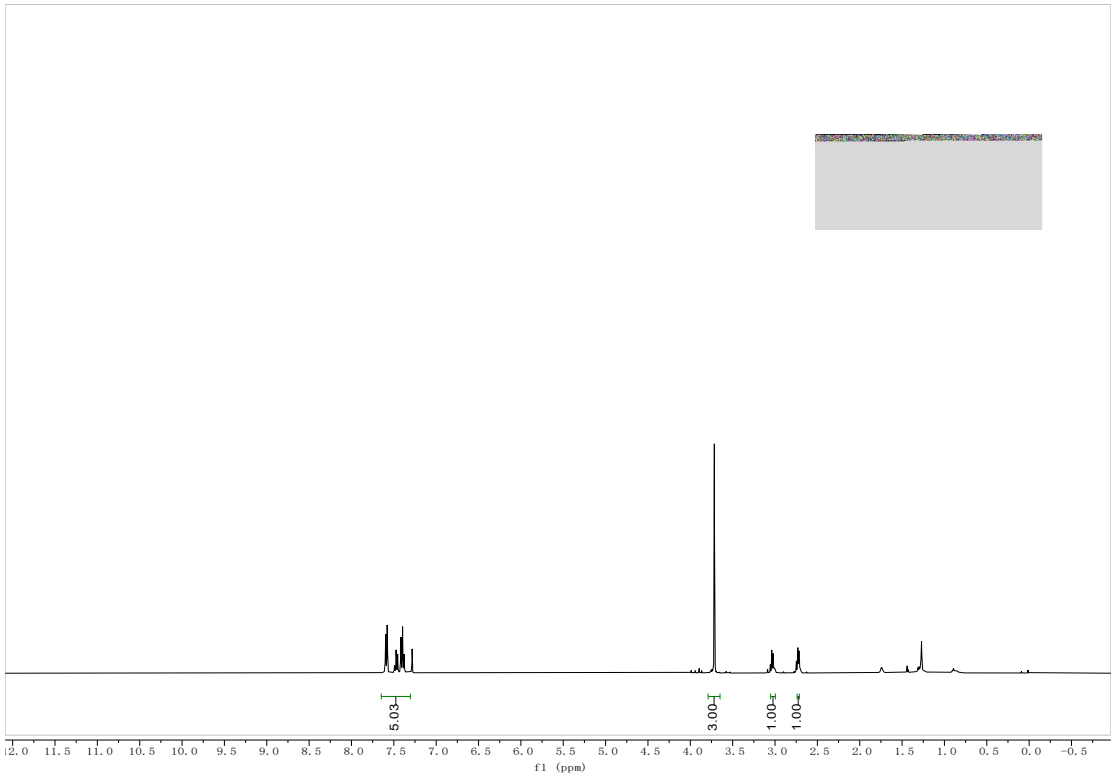
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **14**



Purified by silica gel column chromatography (5−10% ethyl acetate in petroleum ether) afforded **15** (117.2 mg, 54% yield) as yellow oil.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.95–6.77 (m, 5H), 3.72 (s, 3H), 3.14–2.93 (m, 1H), 2.80–2.59 (m, 1H).

^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **15**



References

[1] N. Parvin, N. Sen, S. Tothadi, S. Muhammed, P. Parameswaran, and S. Khan, *Organometal.,* 2020, **40**, 1626–1632.

[2] Q. Shen, L. Zhang, Y. R. Zhou and J. X. Li, *Tetrahedron Lett.,* 2013, **54**, 6725–6728.

[3] Z. W. Xu, X. Q. Yu, X. J. Feng and M. Bao, *J. Org. Chem.,* 2011, **76**, 6901–6905.

[4] I. Fish, A. Stößel, K. Eitel, C. Valant, S. Albold, H. Huebner, D. Möller, M. J. Clark, R. K. Sunahara, A. Christopoulos, B. K. S. Orcid and P. Gmeiner, *J. Med. Chem.,* 2017, **60**, 9239–9250.

[5] H. Helbert, P. Visser, J. G. H. Hermens, J. Buter and B. L. Feringa, *Nat. Catal.,* 2020, **3**, 664–671.

[6]M. Lemhadri, H. Doucet and M. Santelli, *Synthesis*, 2005, **8**, 1359–1367.

[7] V. S. Rawat, T. Bathini, S. Govardan and B. Sreedhar, *Org. Biomol. Chem.,* 2014, **12**, 6725–6729.

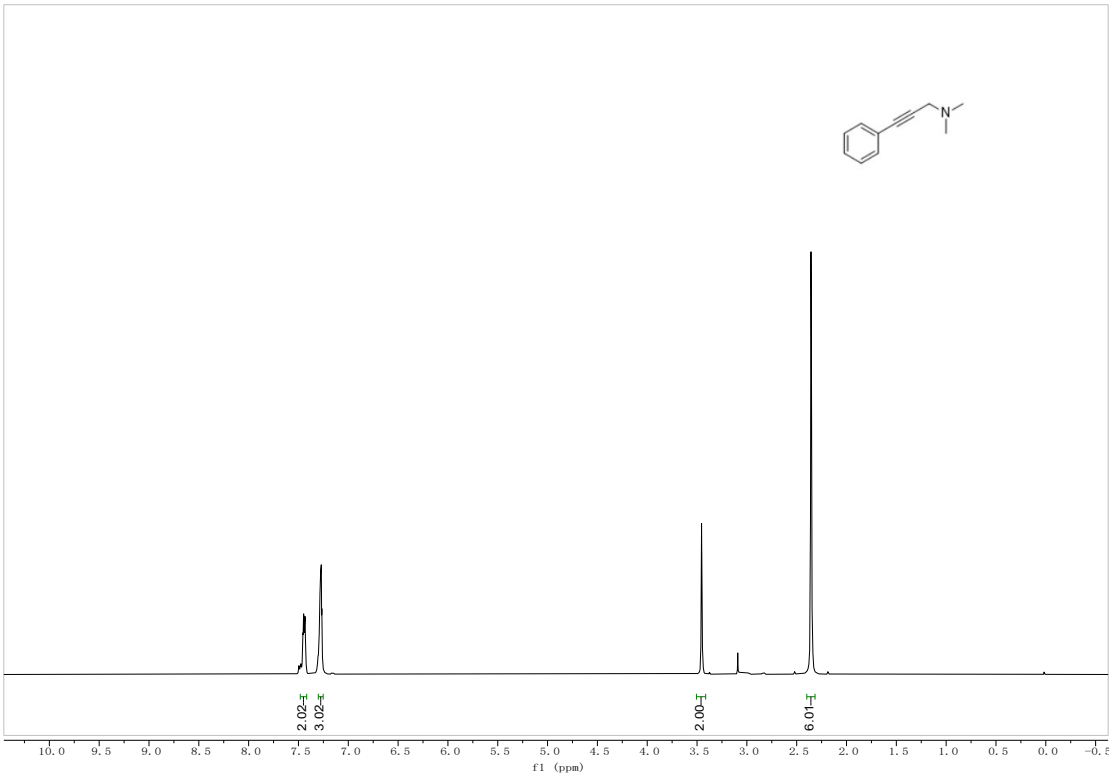
[8] L. W. Bieber and M. F. Silva, *Tetrahedron Lett.,* 2004, **45**, 8281–8283.

[9] Z. J. Fang and M. Wills, *J. Org. Chem.,* 2013, **78**, 8594–8605.

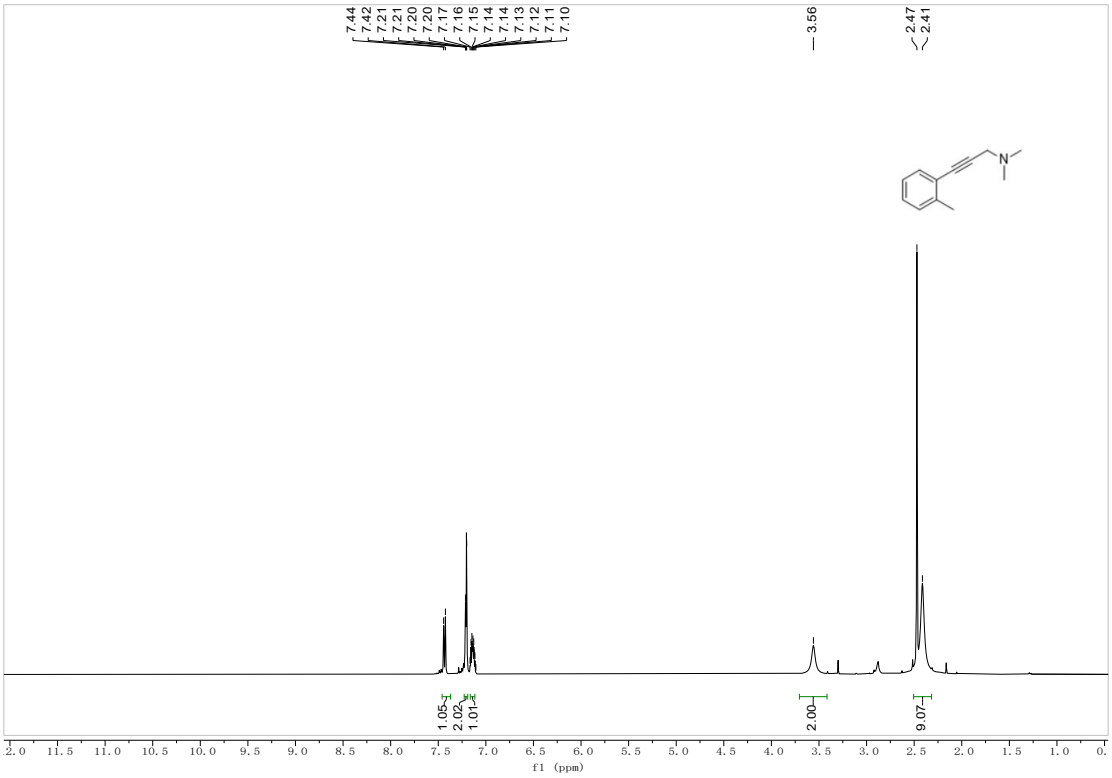
[10] X. B. Chen, Y. N. Zhang, H. X. Wan, W. Wang and S. L. Zhang, *Chem. Commun.*, 2016, **52**, 3532-3535

^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra

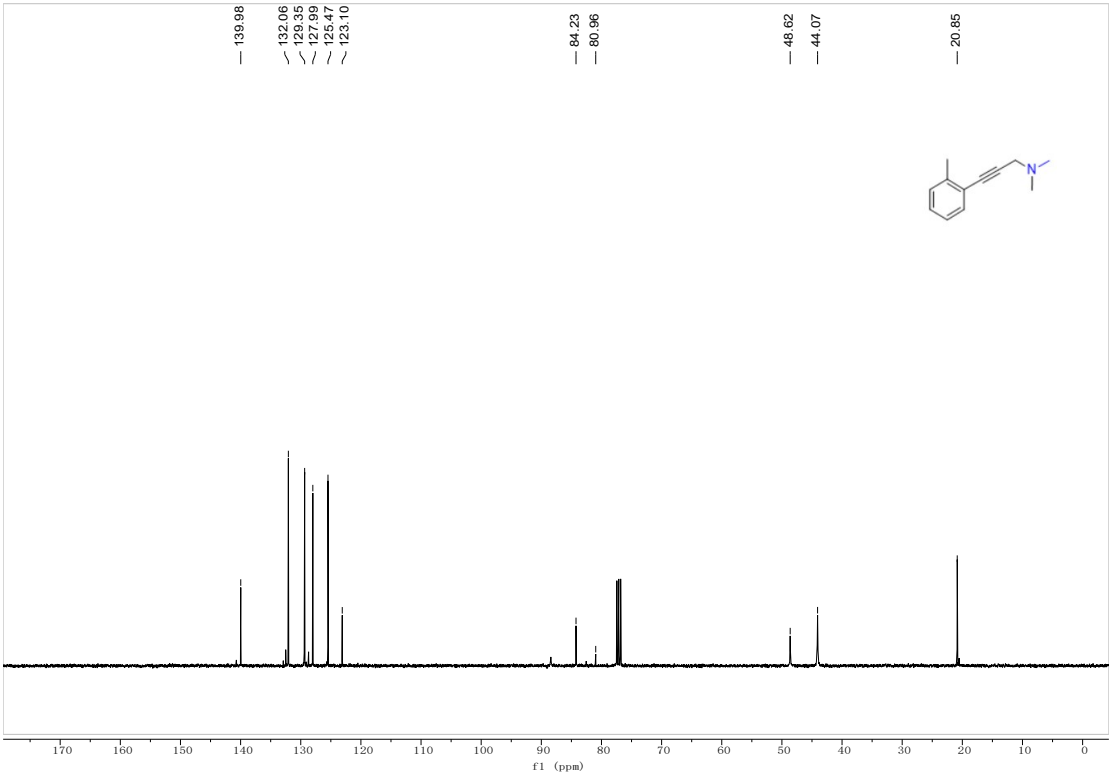
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **1a**



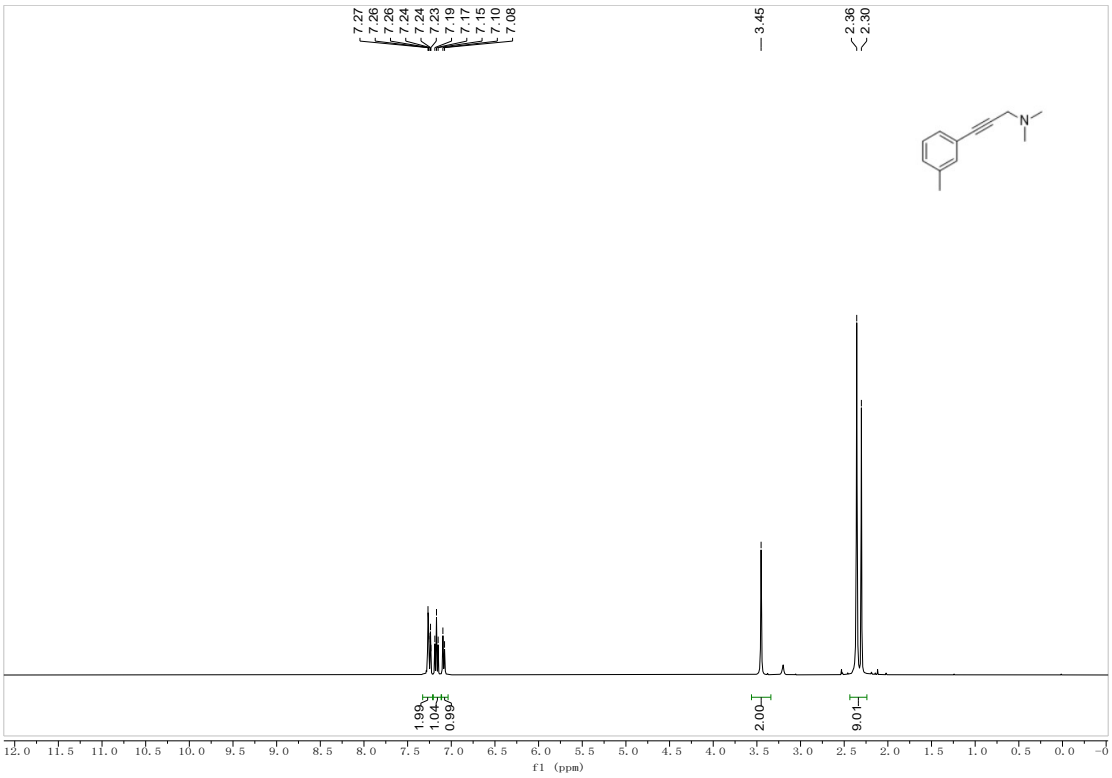
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **1b**



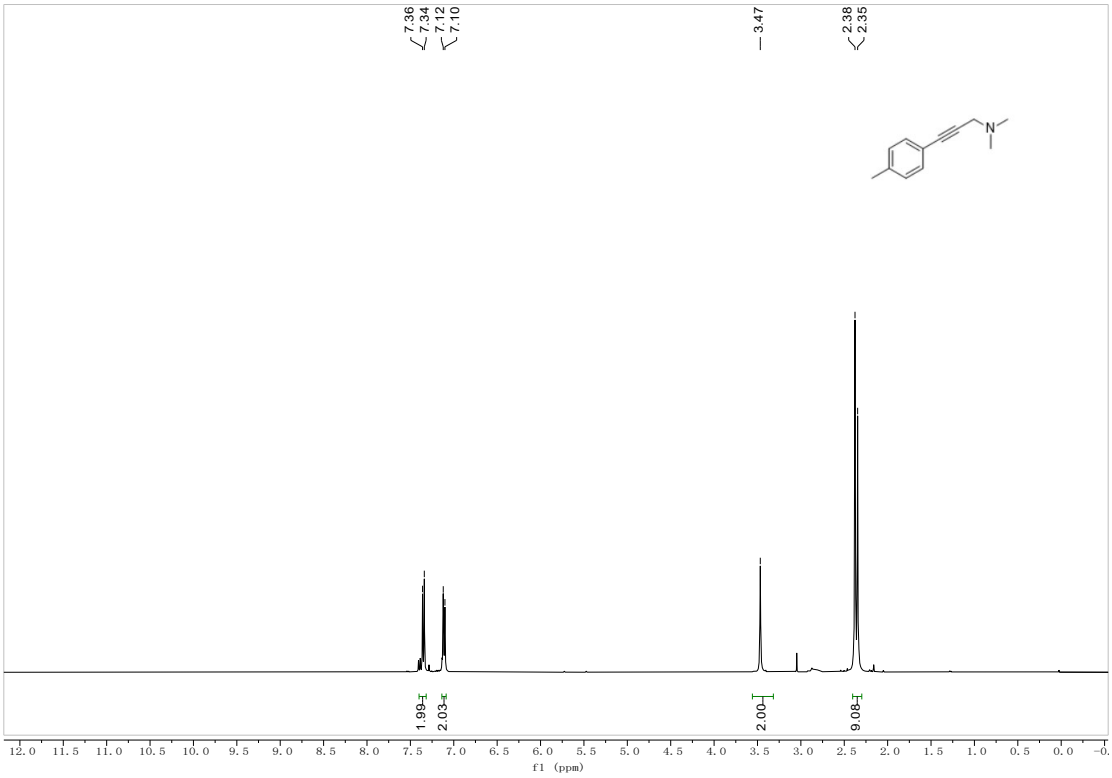
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **1b**



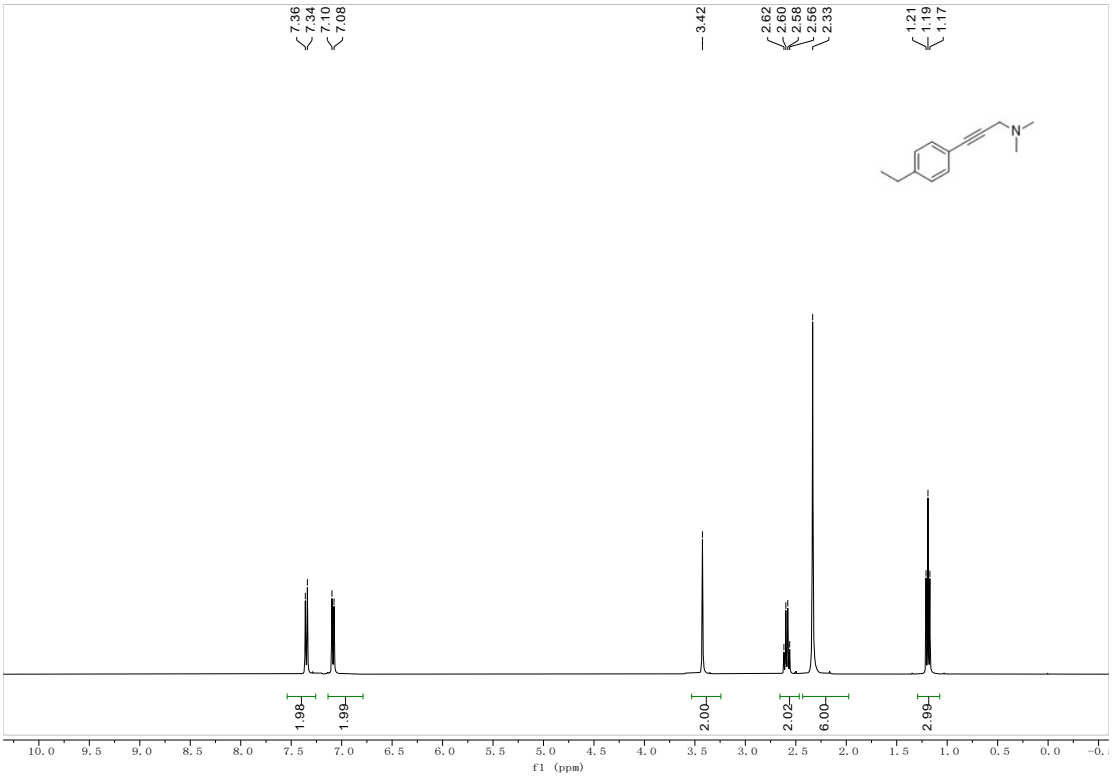
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **1c**



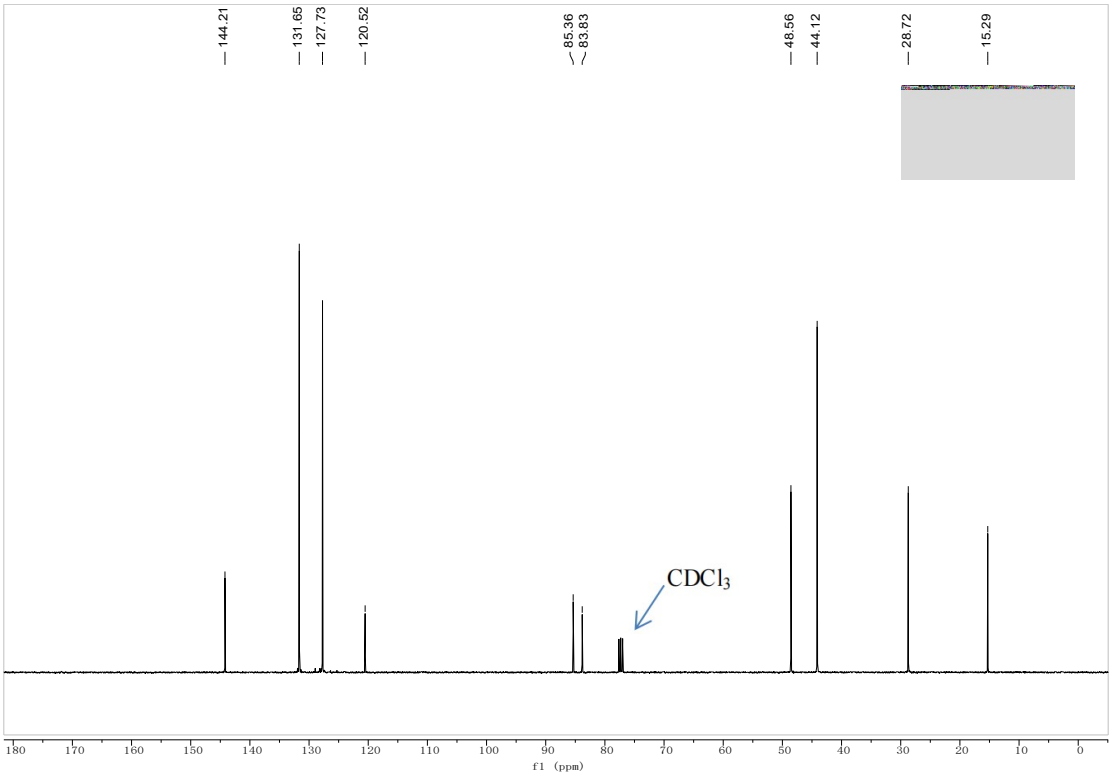
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **1d**



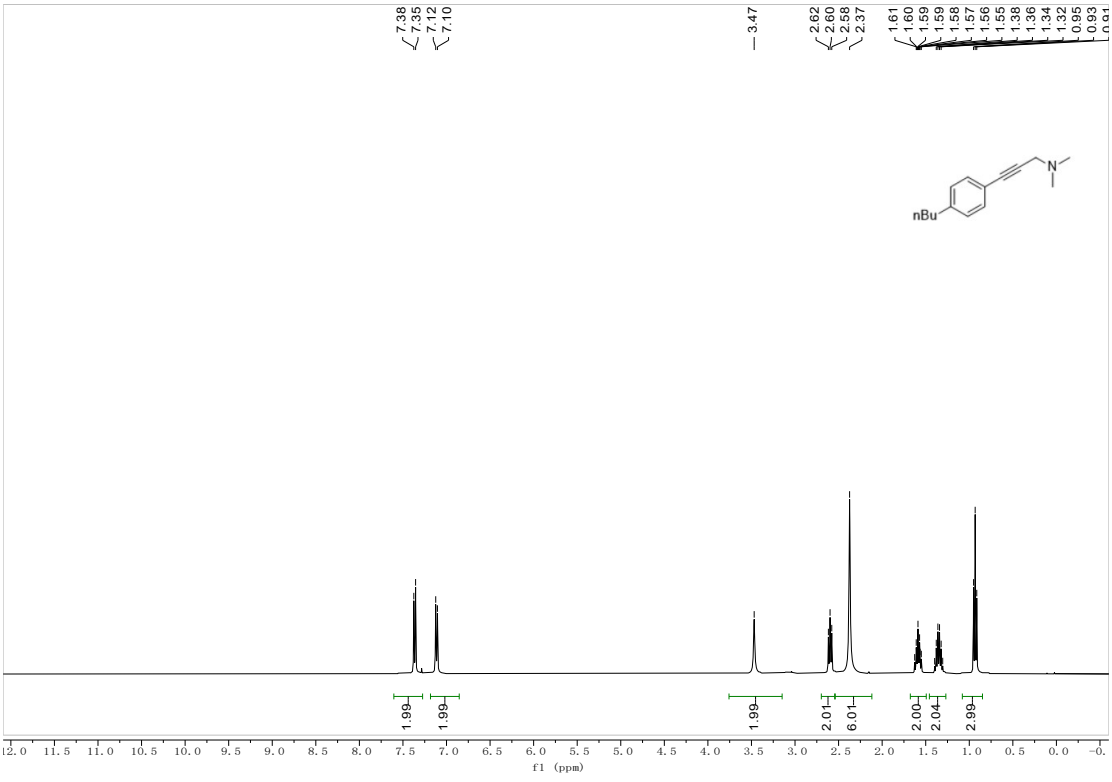
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **1e**



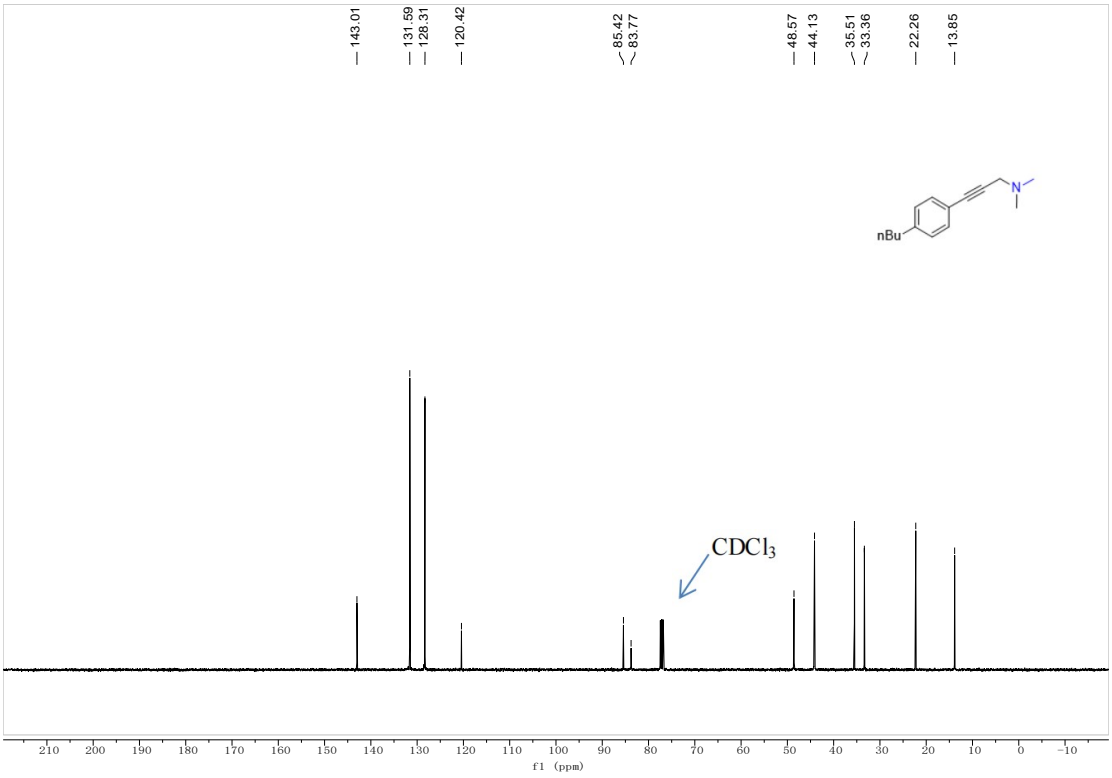
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **1e**



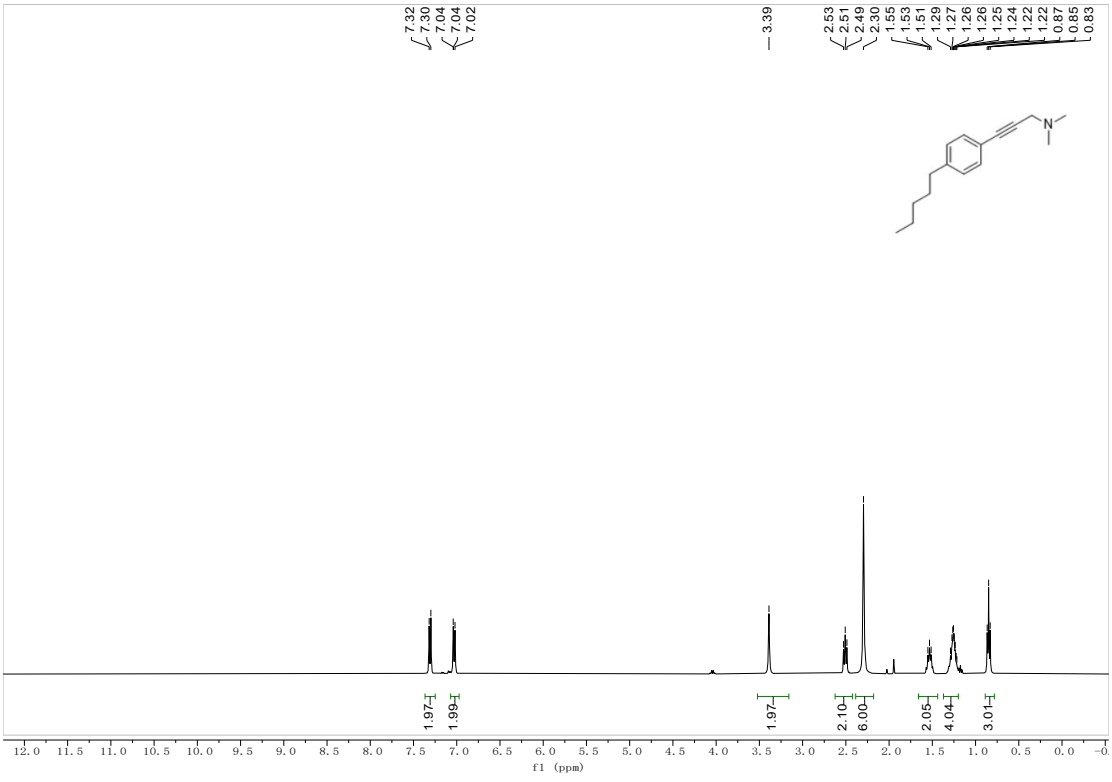
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **1f**



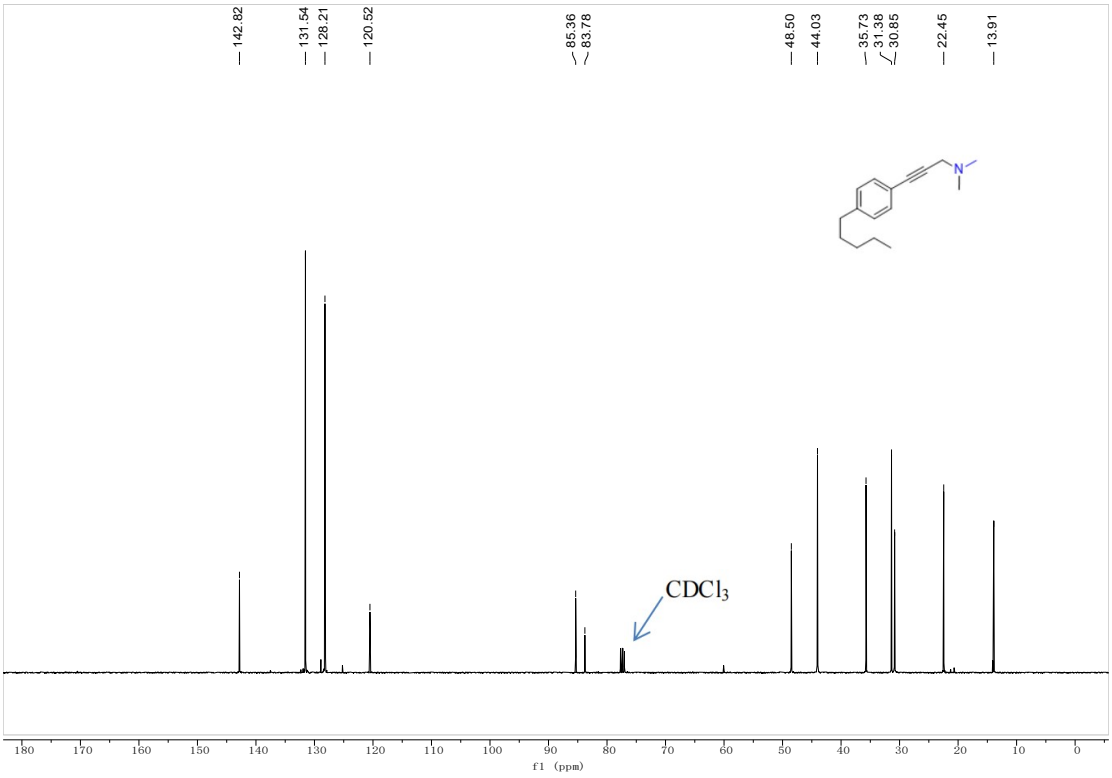
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **1f**



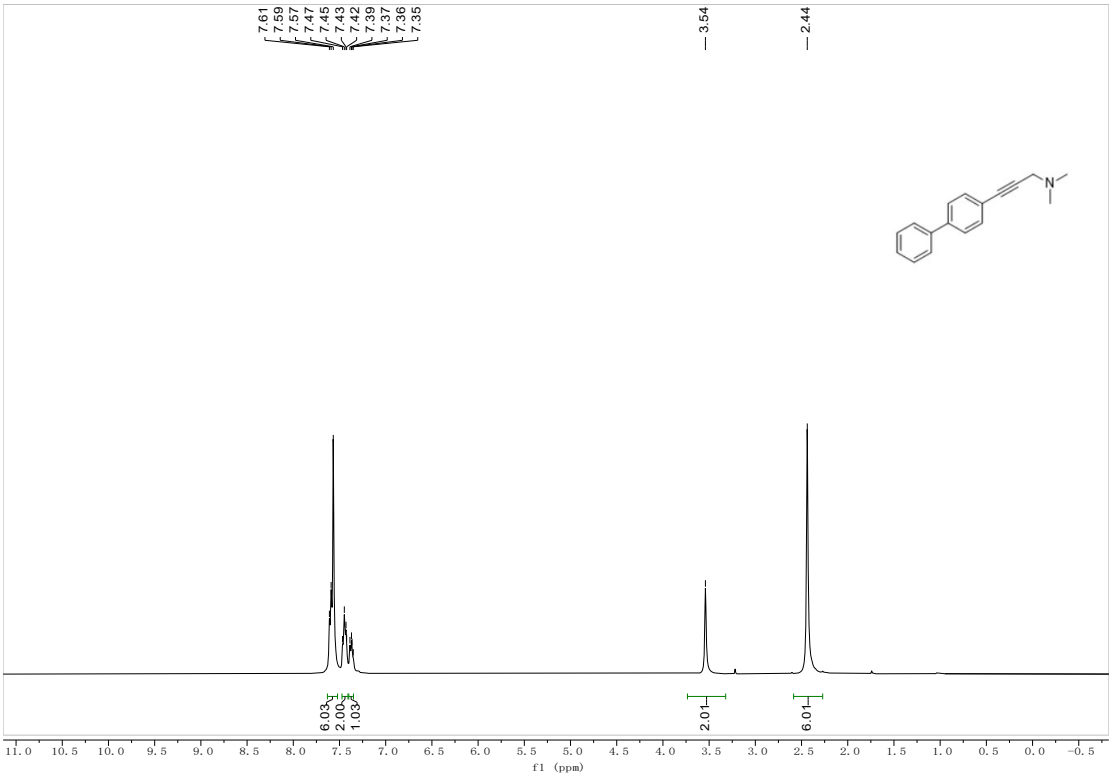
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **1g**



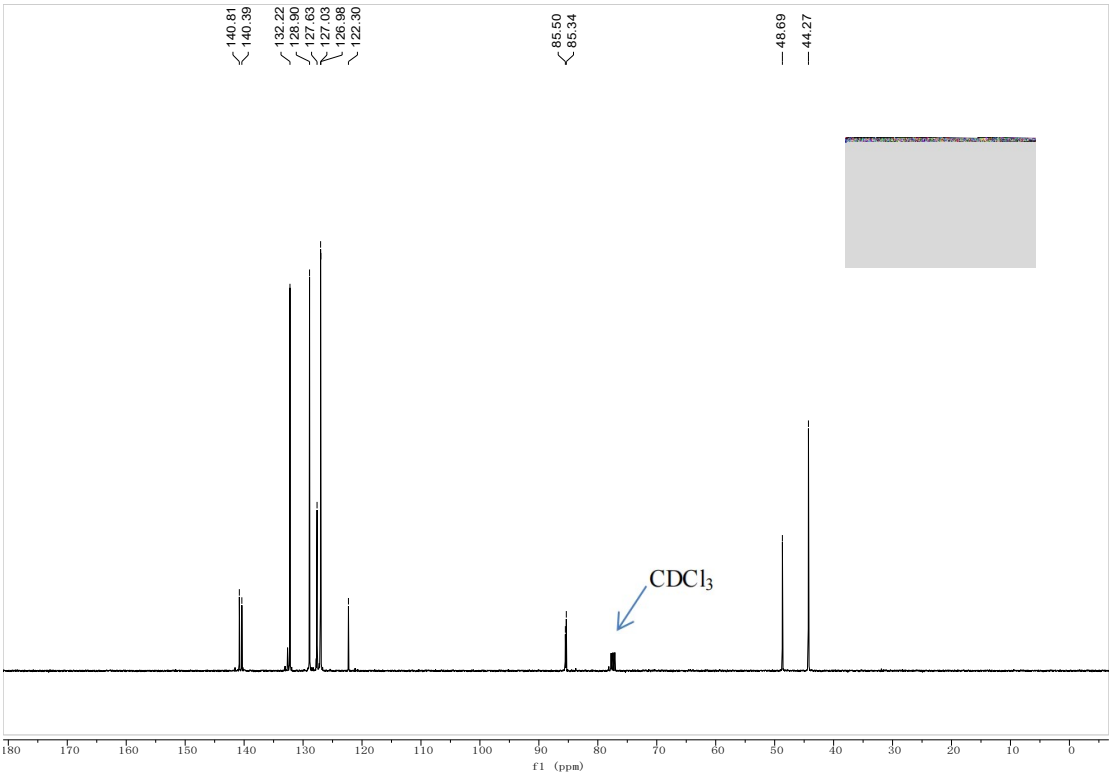
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **1g**



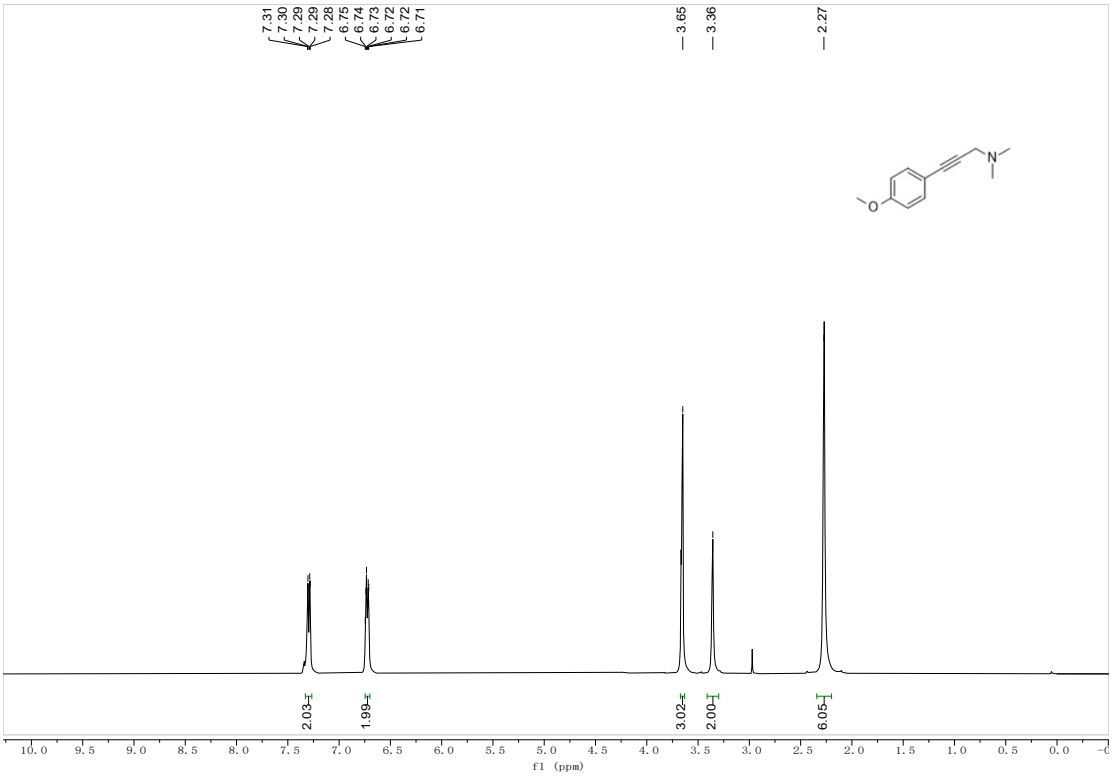
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **1h**



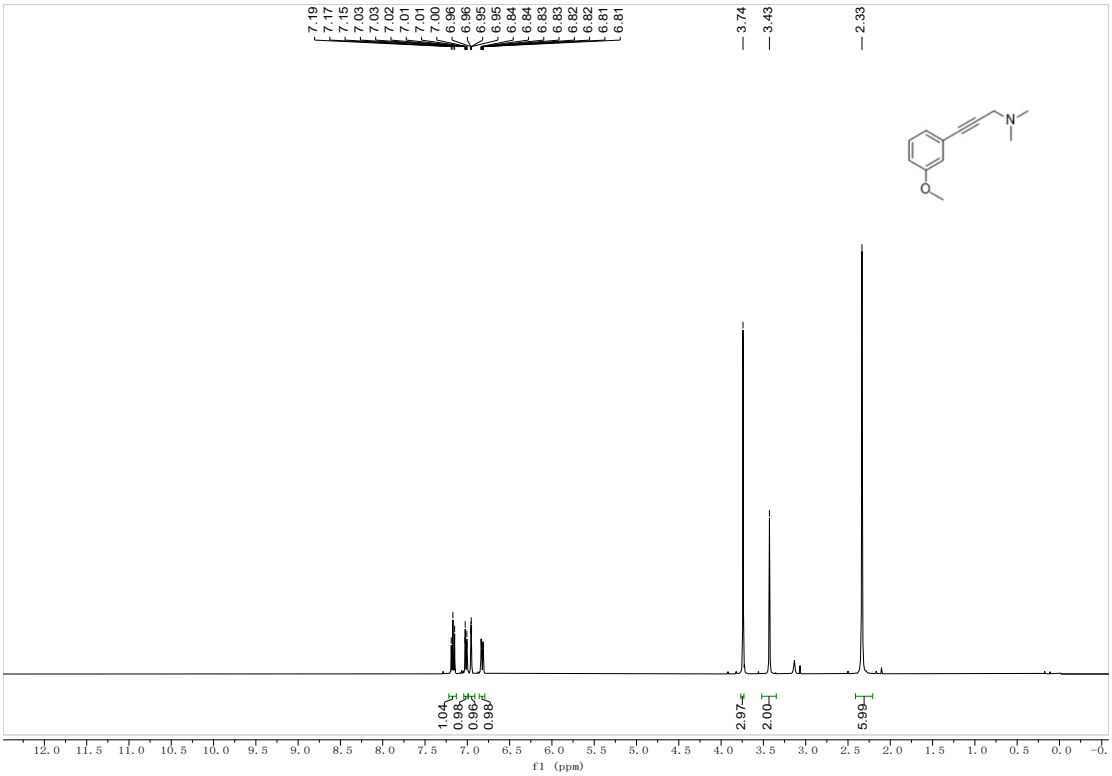
^{13}C NMR (100 MHz, $CDCl_3$)spectrum of compound **1h**



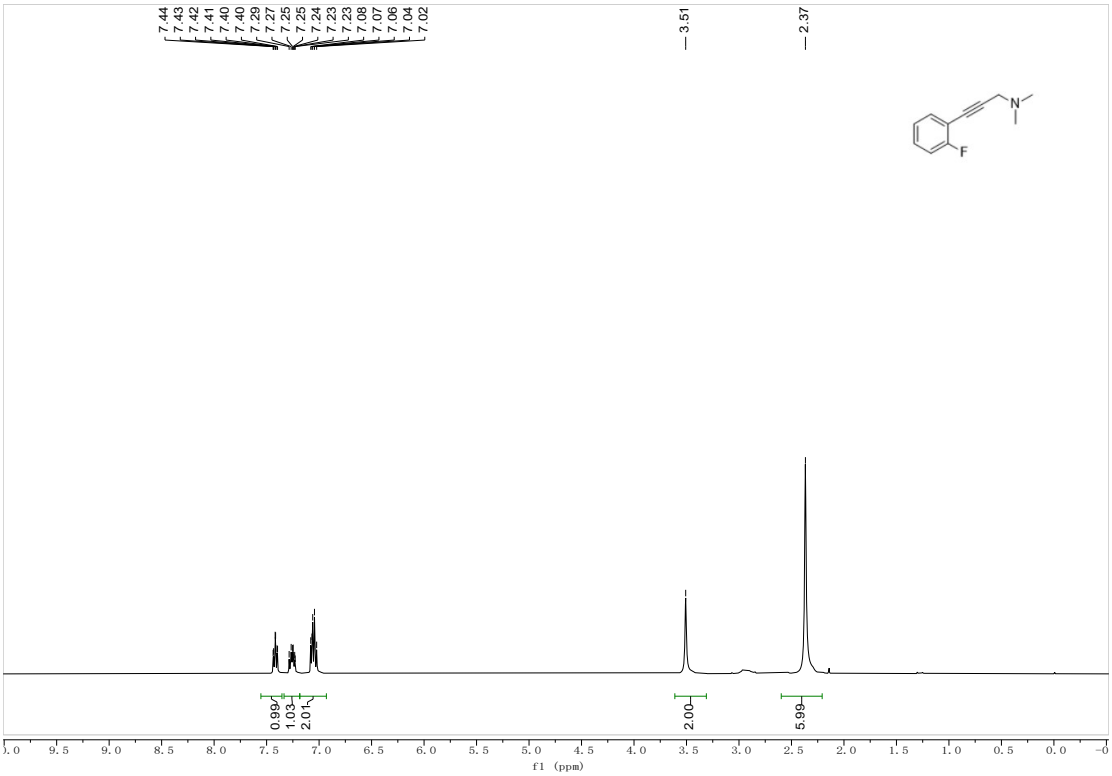
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **1i**



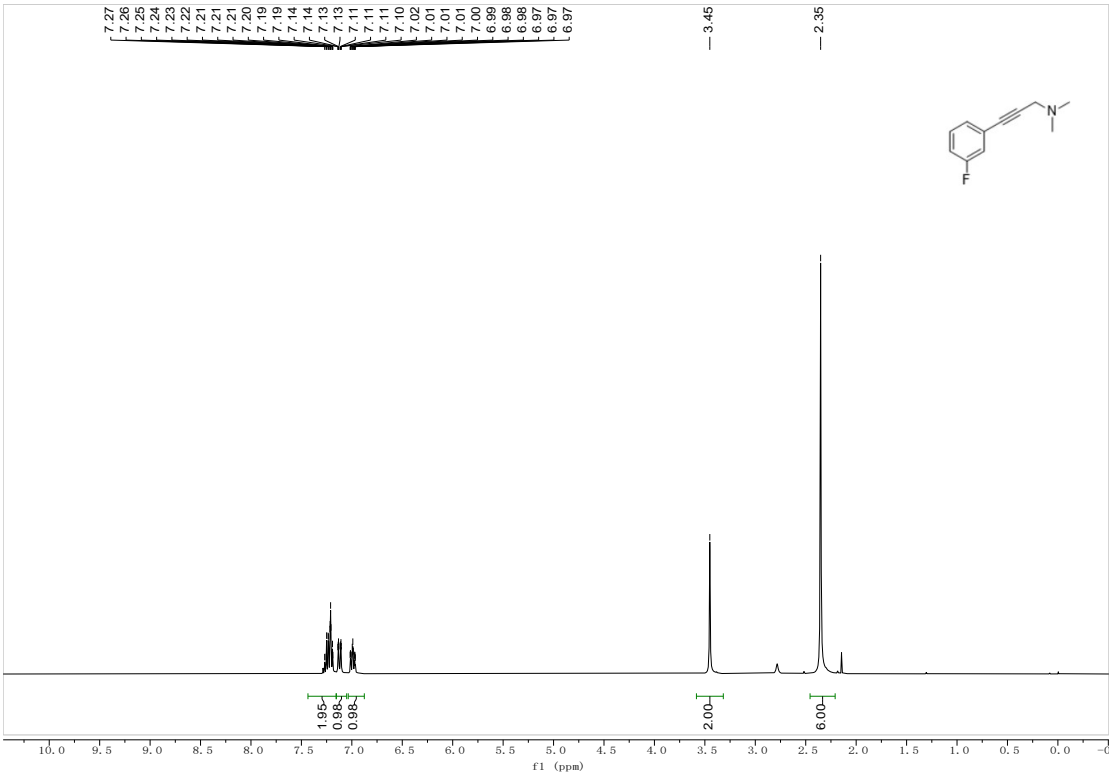
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **1j**



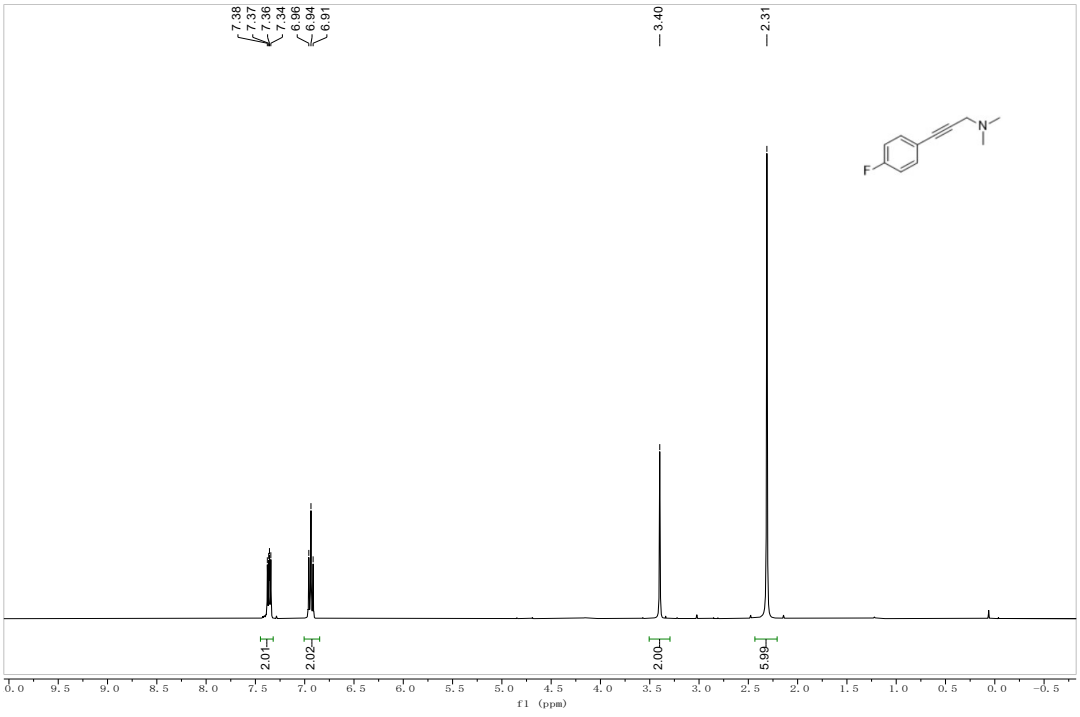
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **1k**



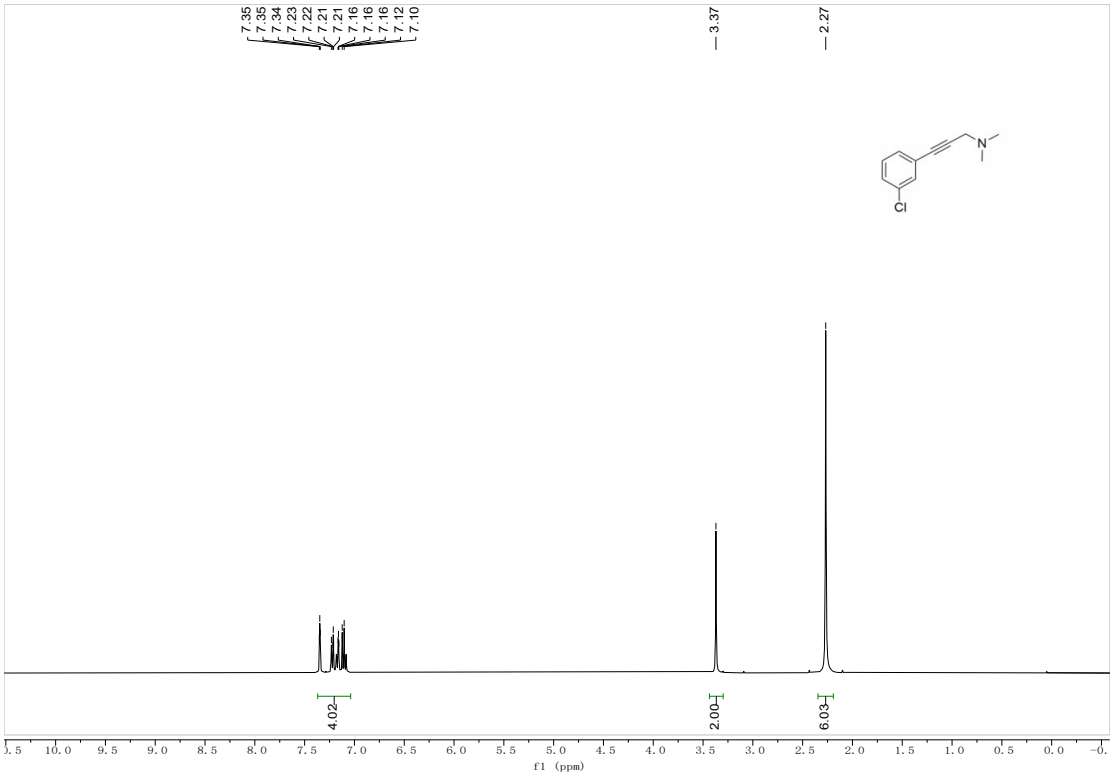
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **1l**



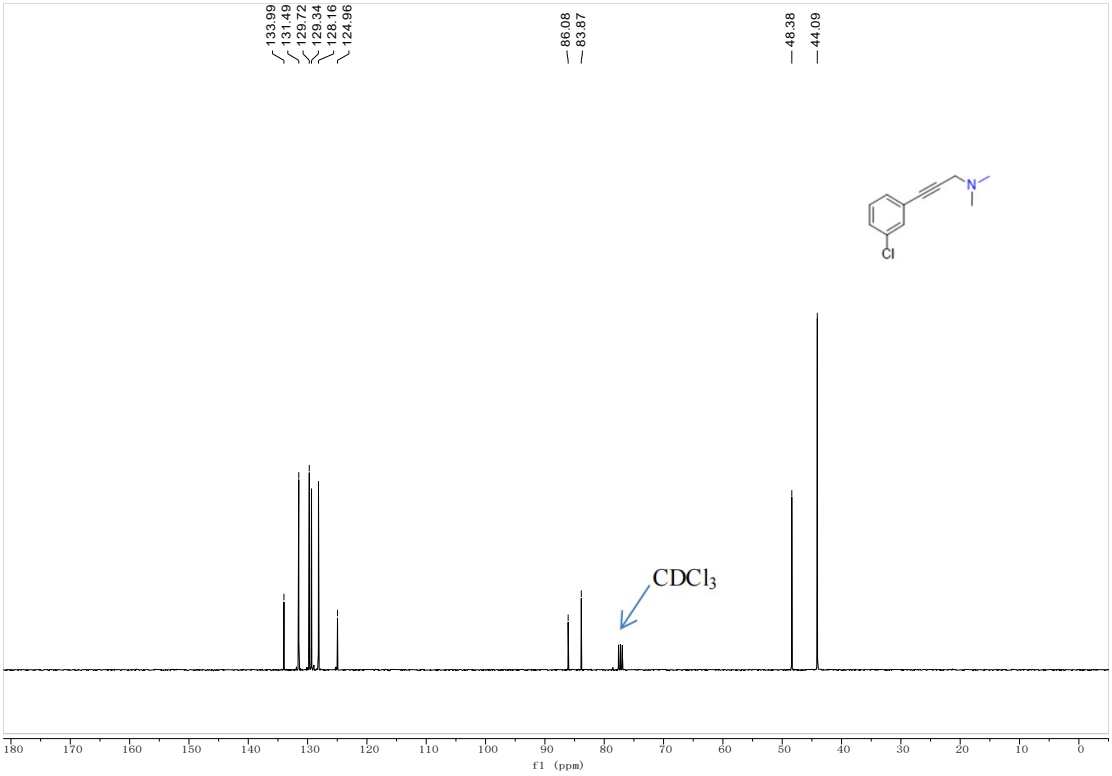
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **1m**



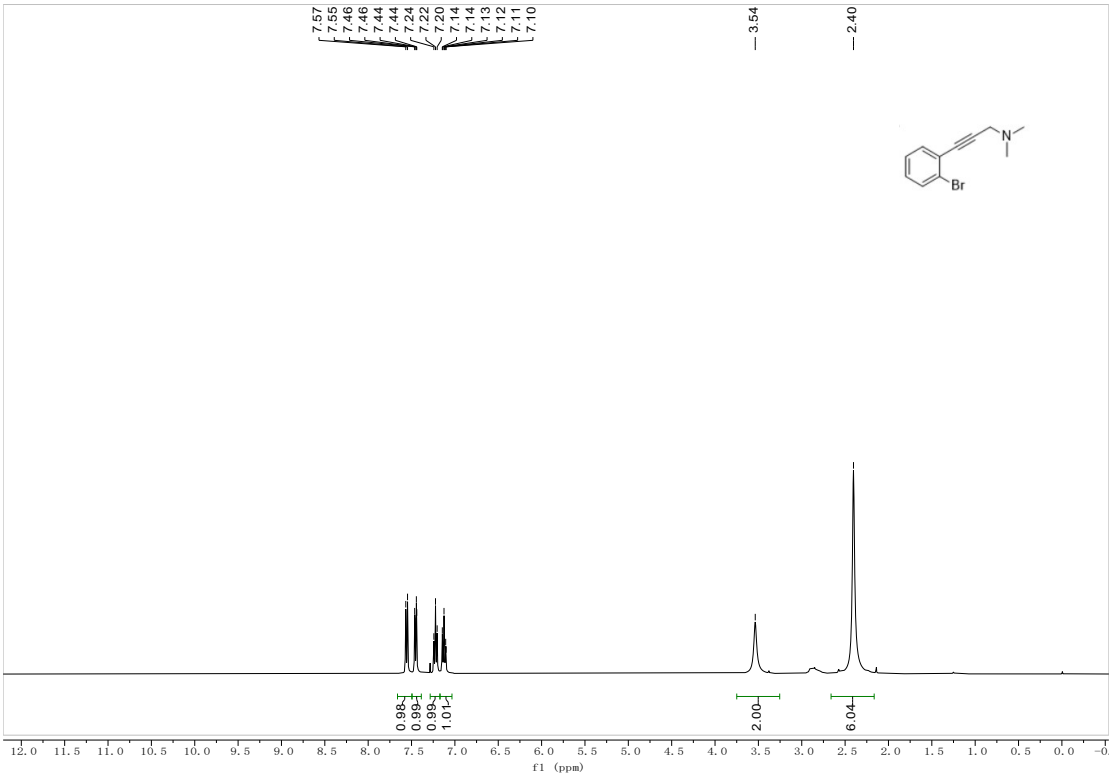
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **1n**



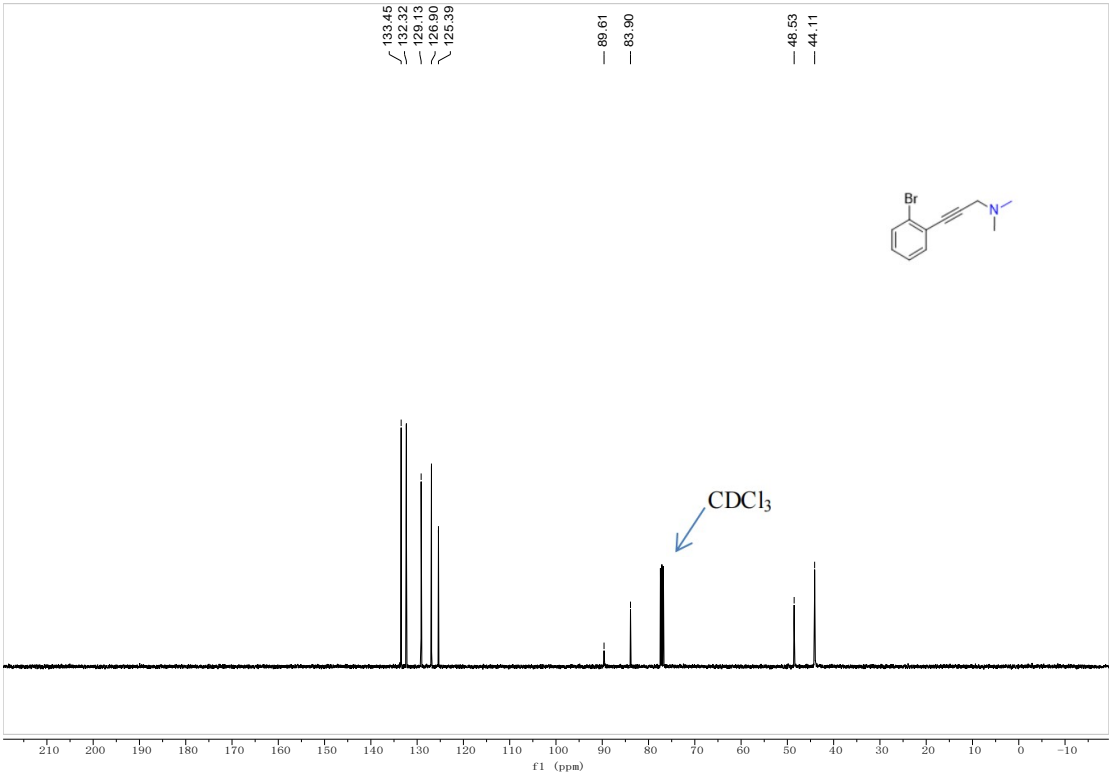
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **1n**



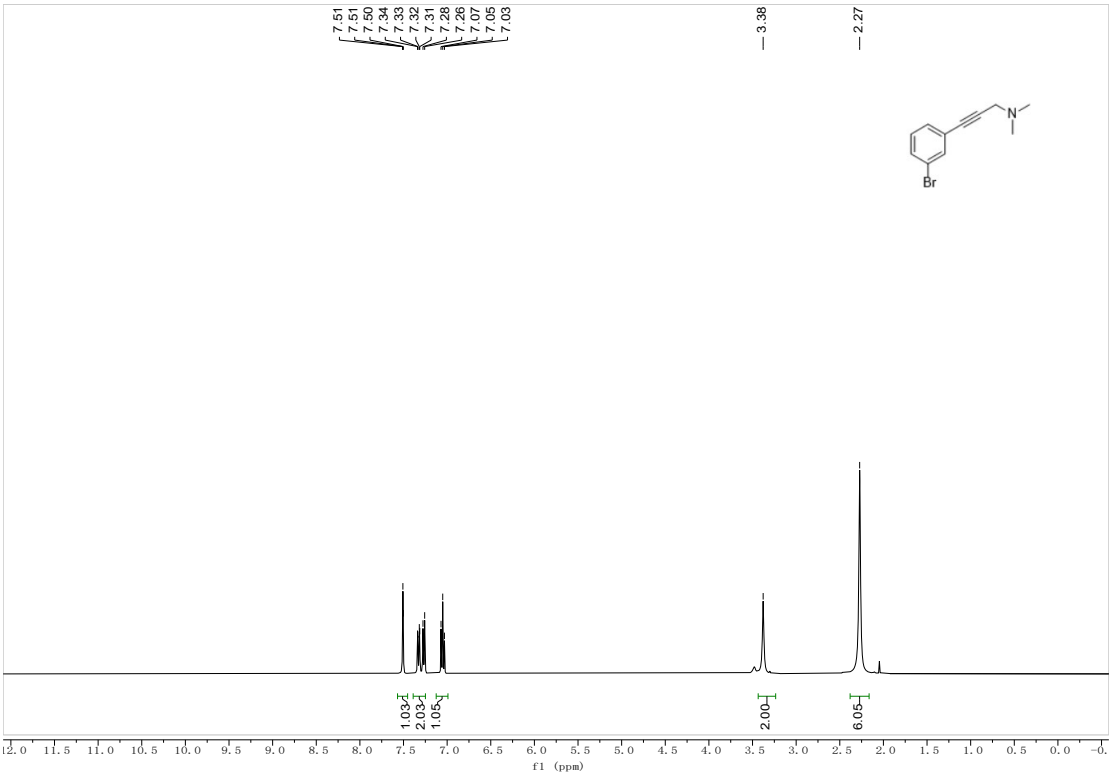
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **1o**



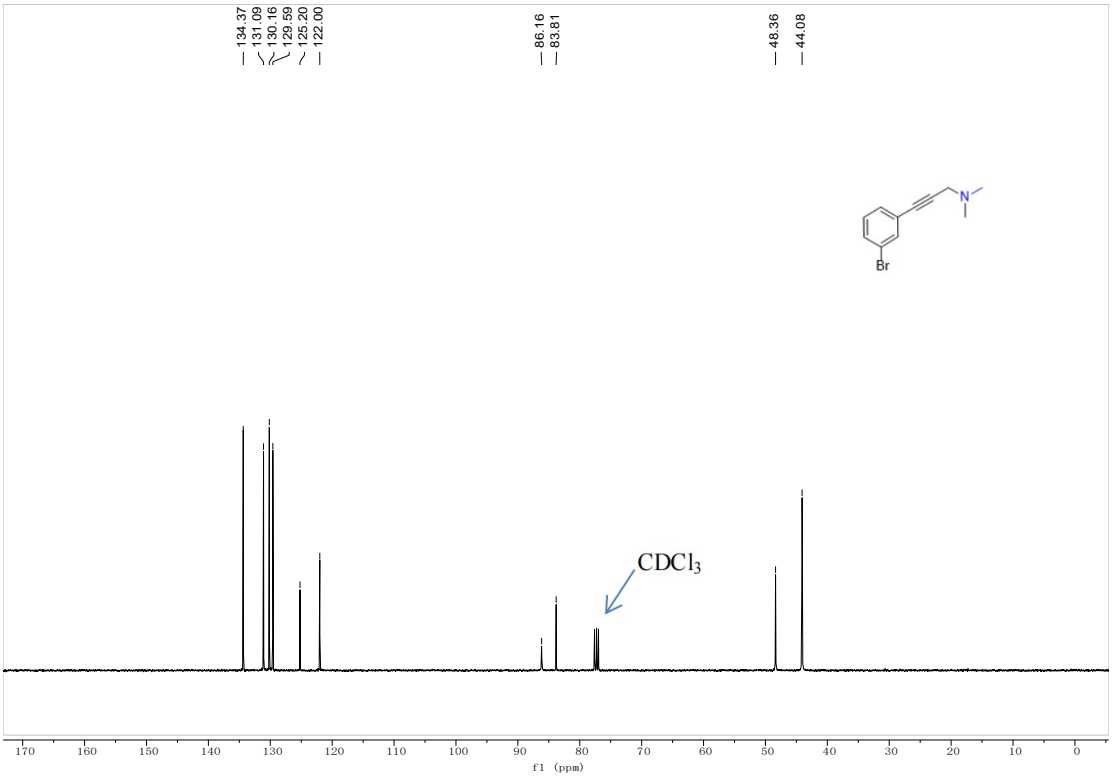
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **1o**



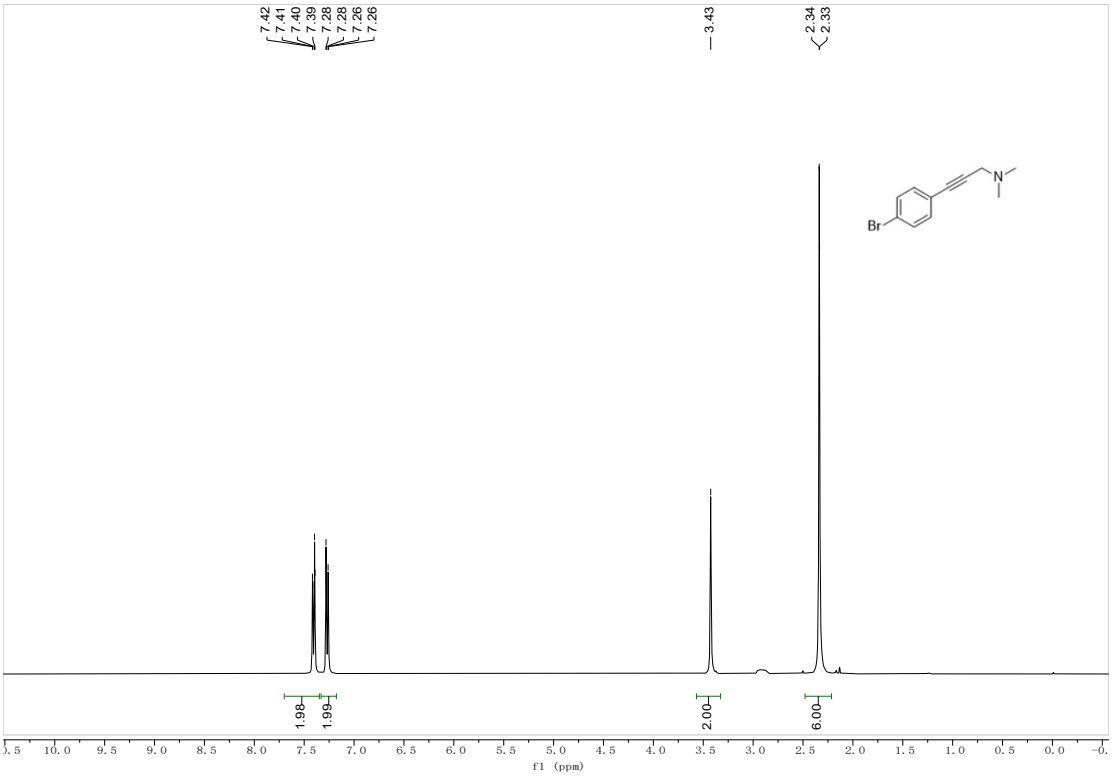
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **1p**



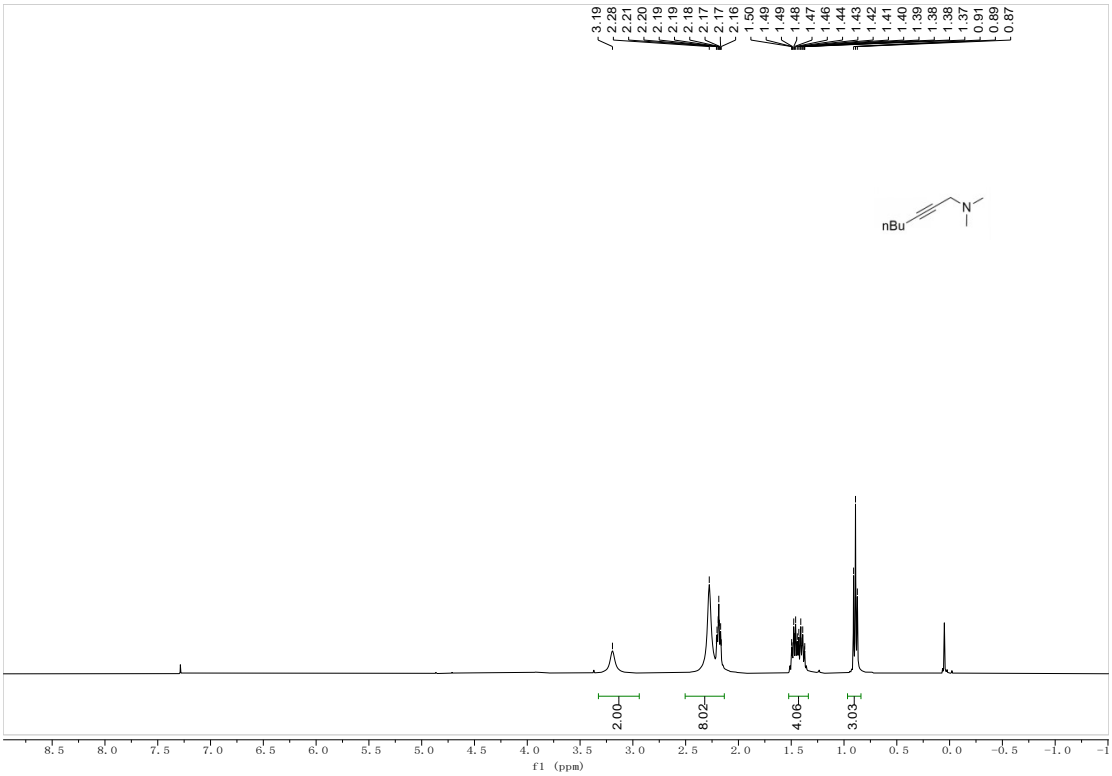
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **1p**



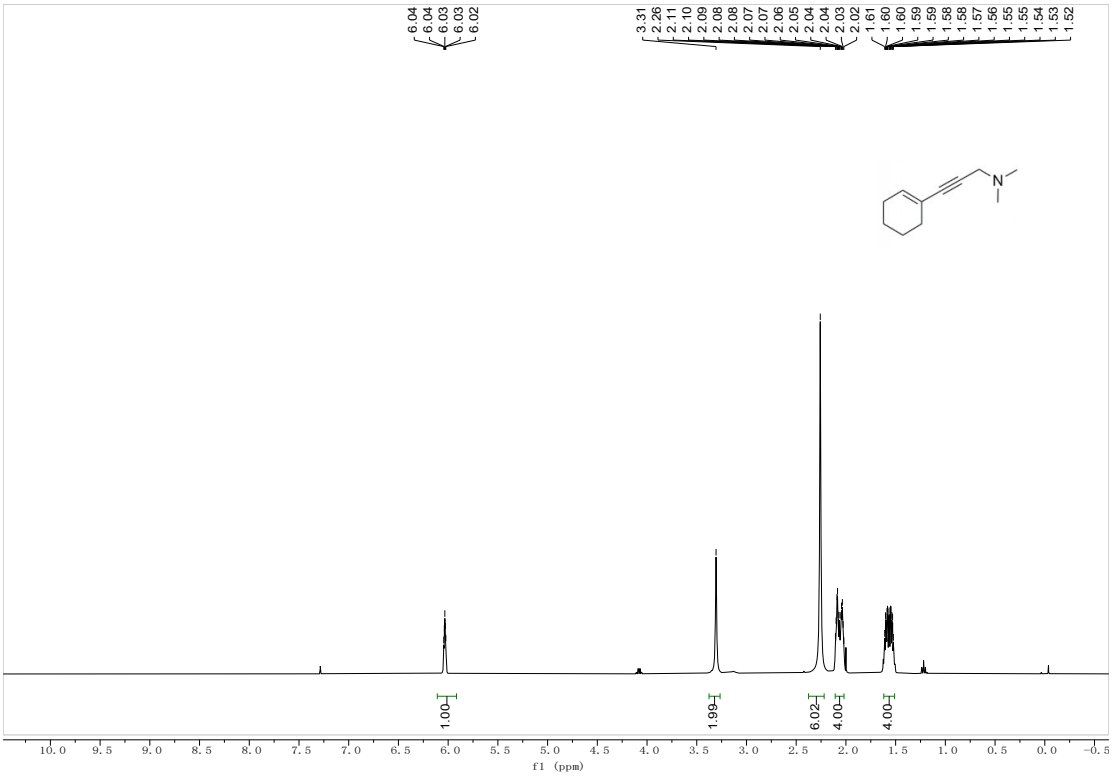
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **1q**



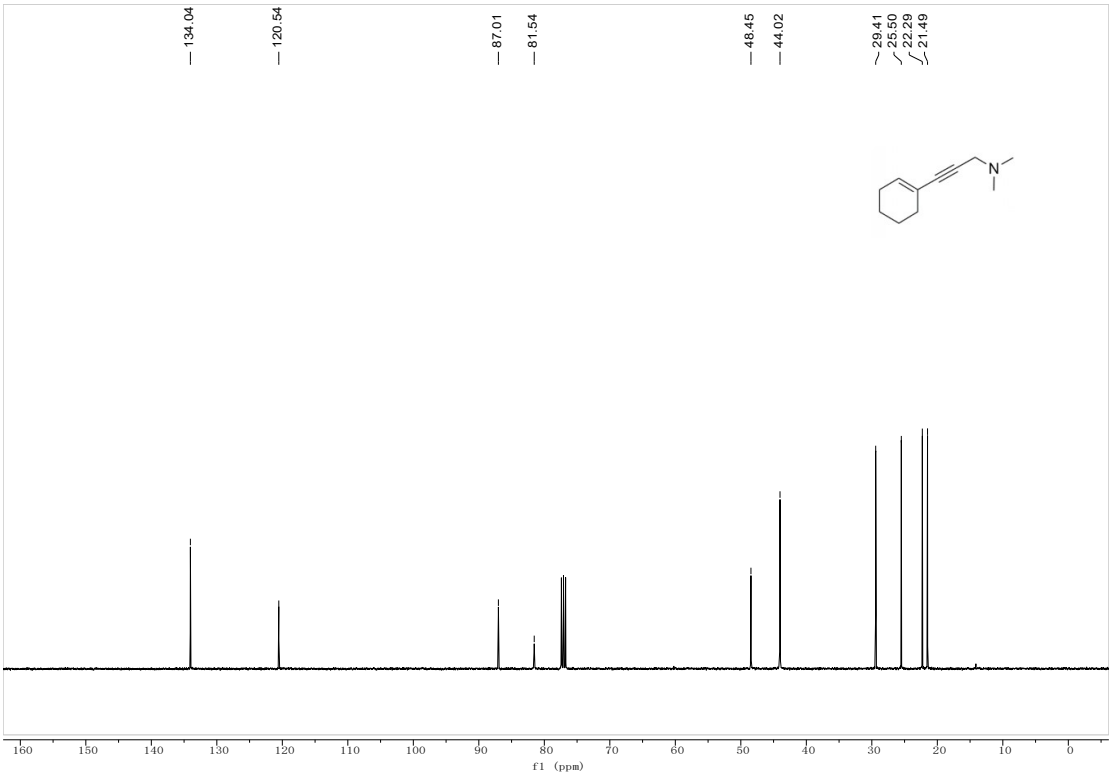
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **1r**



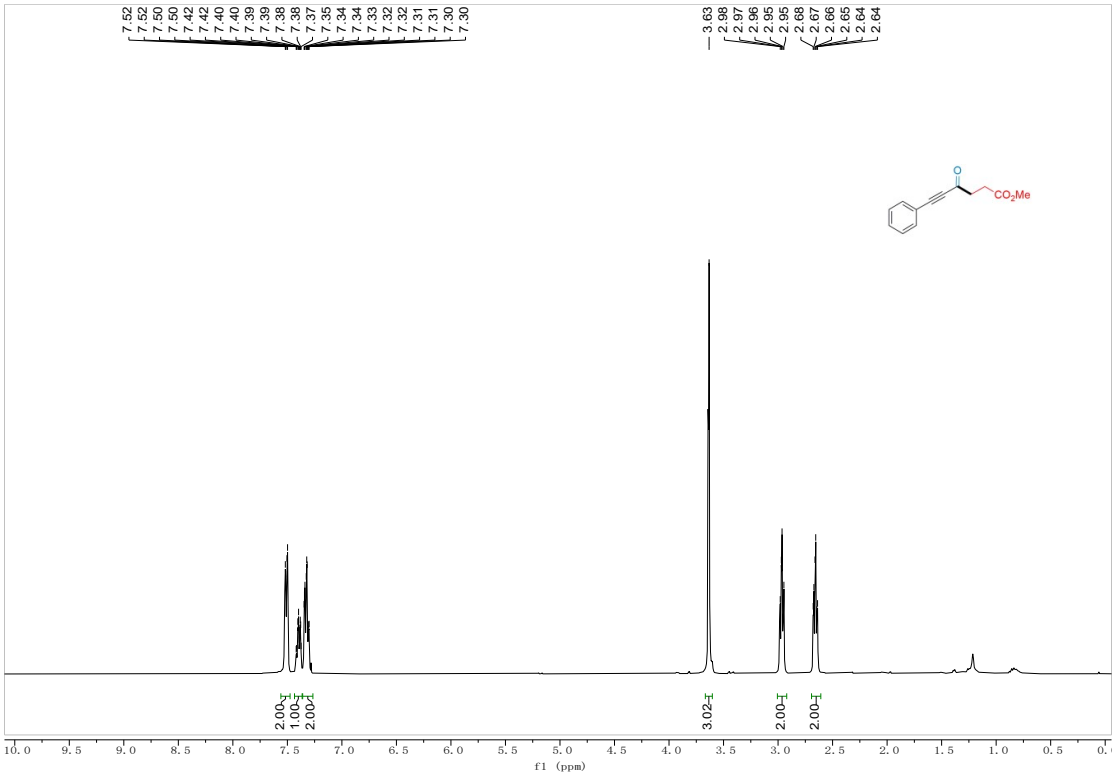
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **1s**



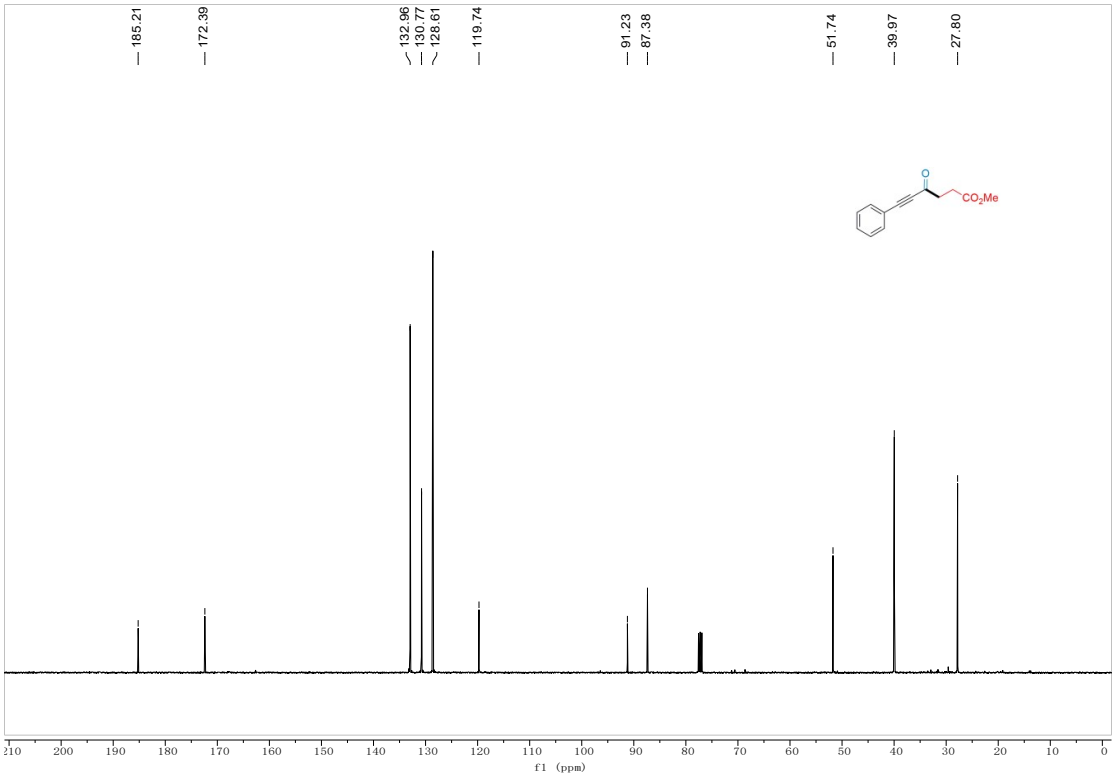
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **1s**



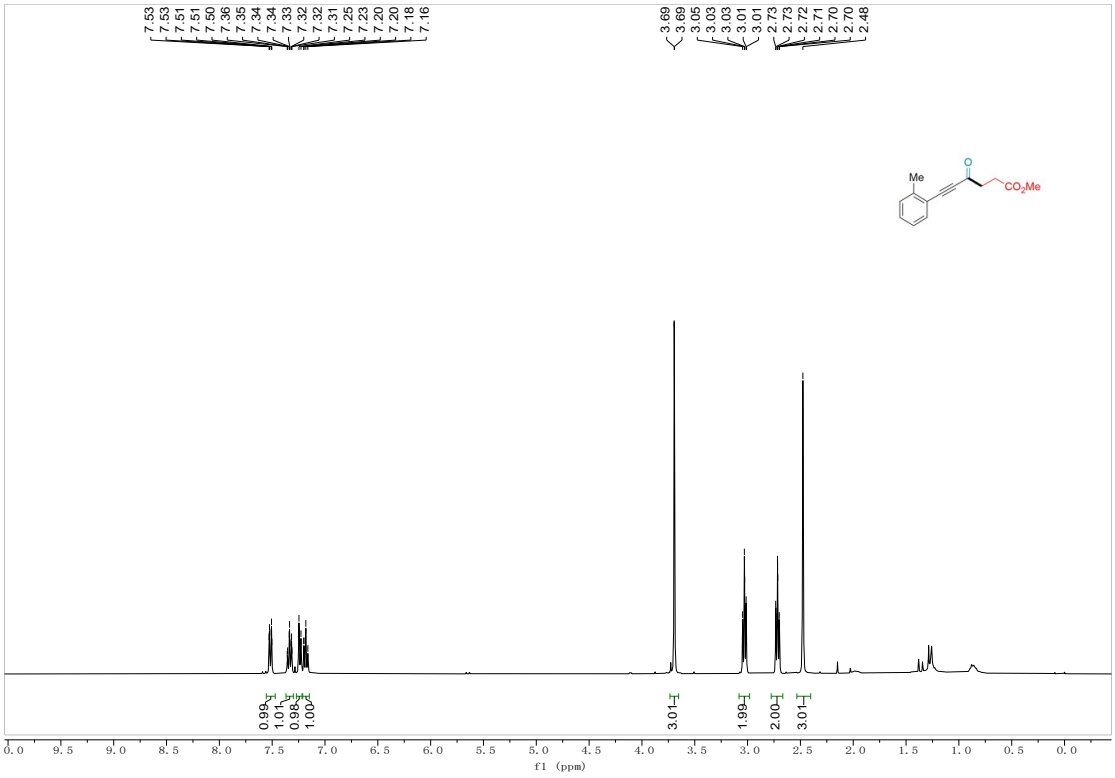
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3a**



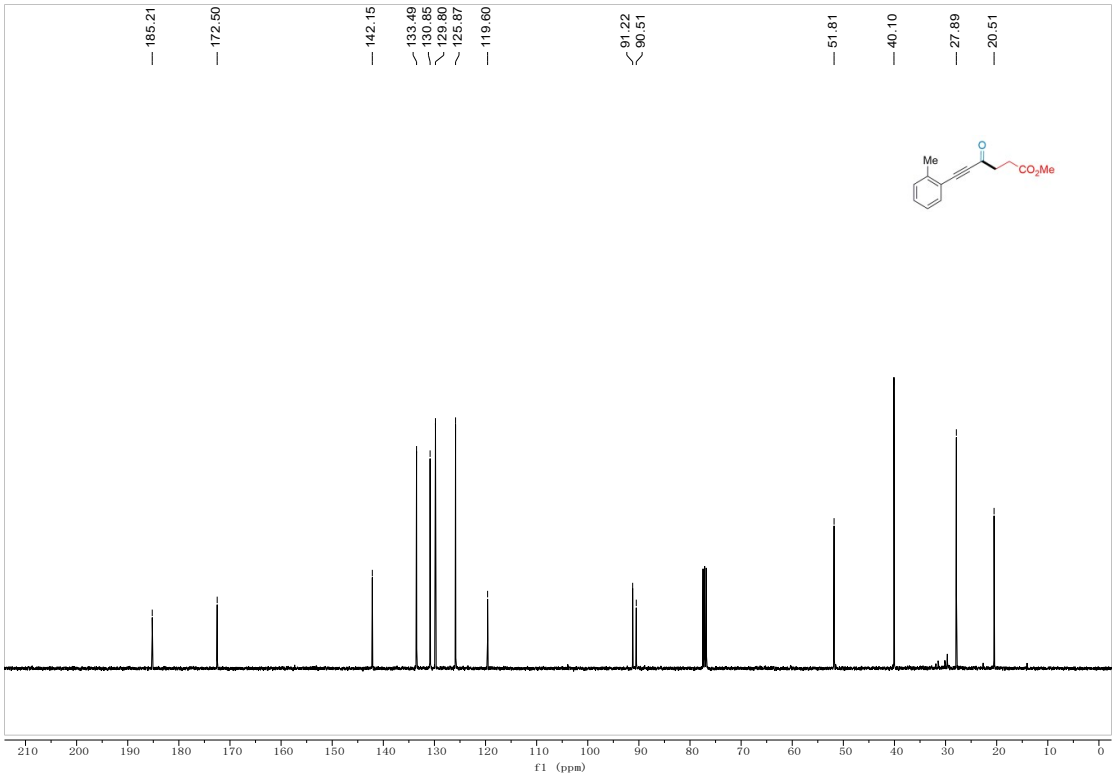
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **3a**



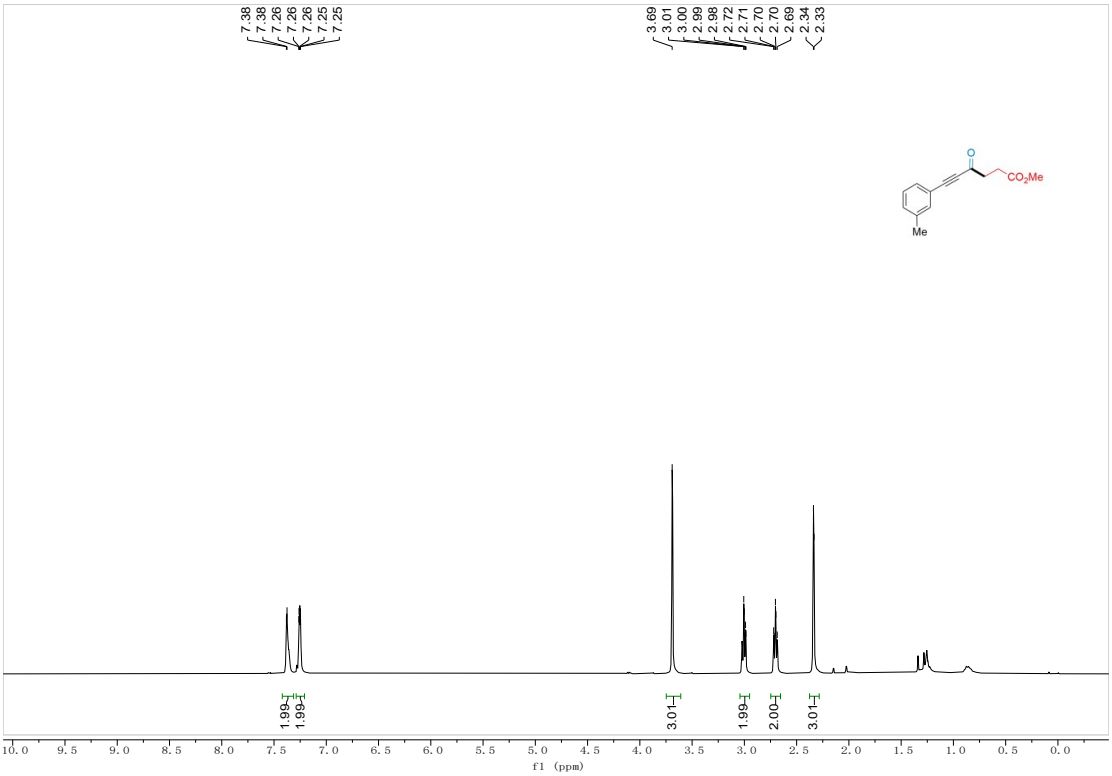
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3b**



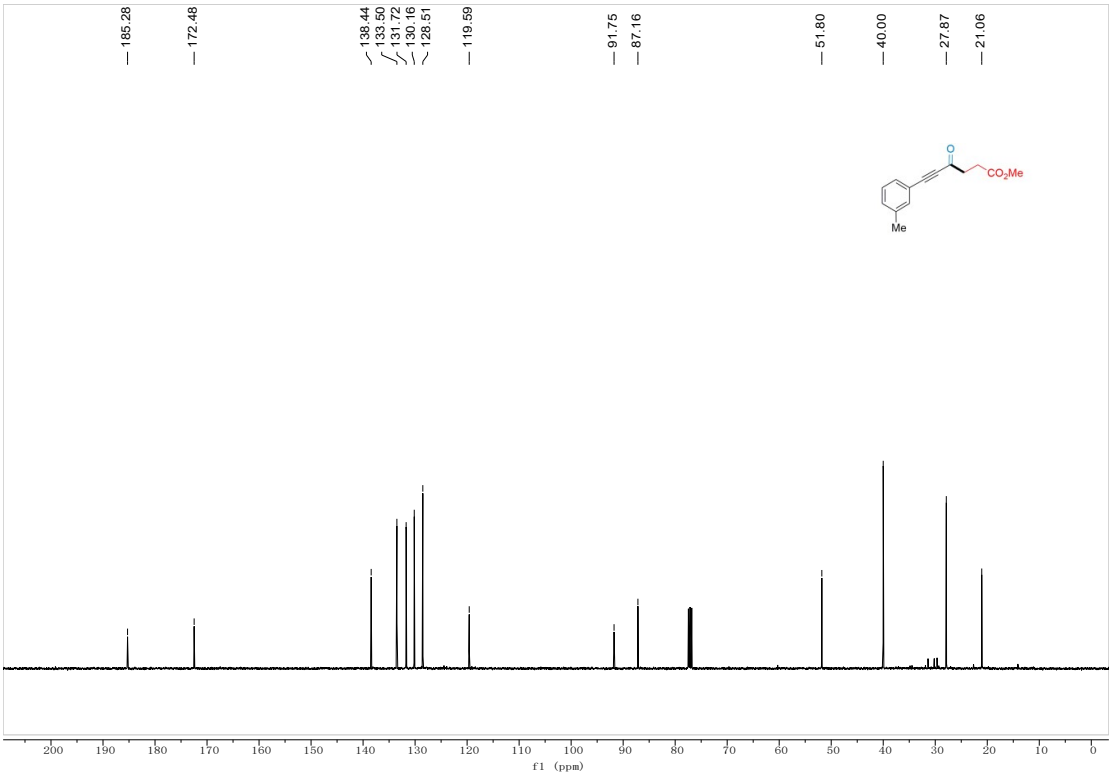
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **3b**



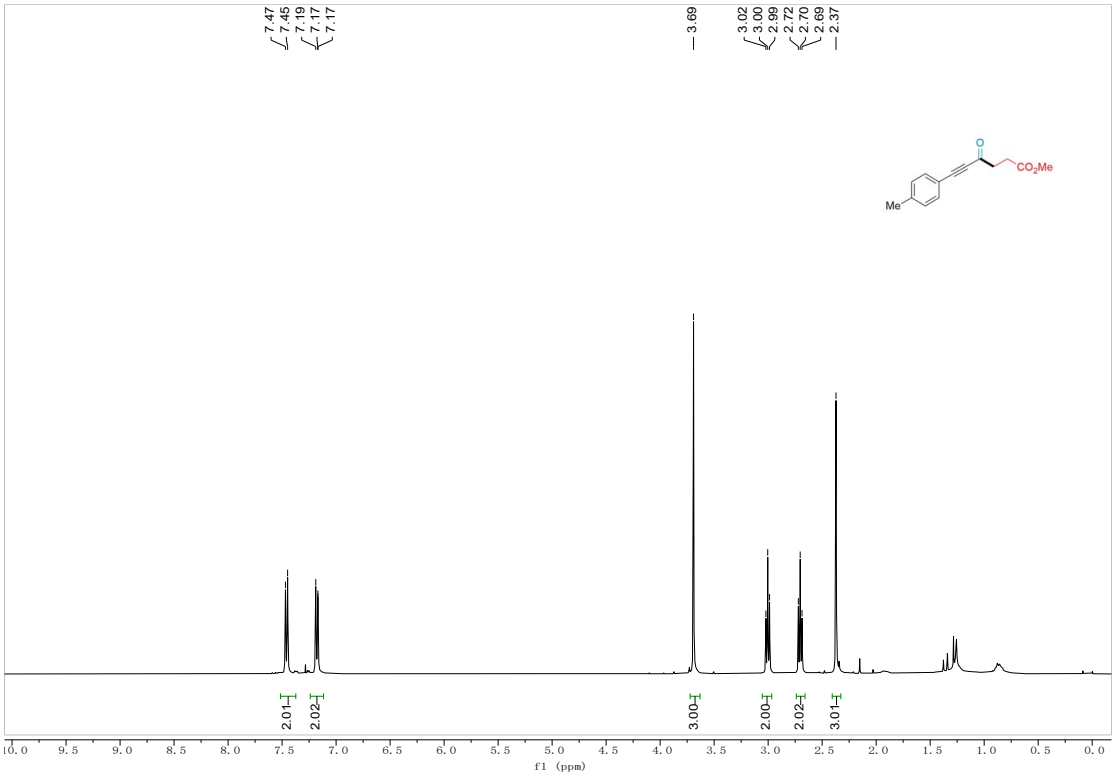
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3c**



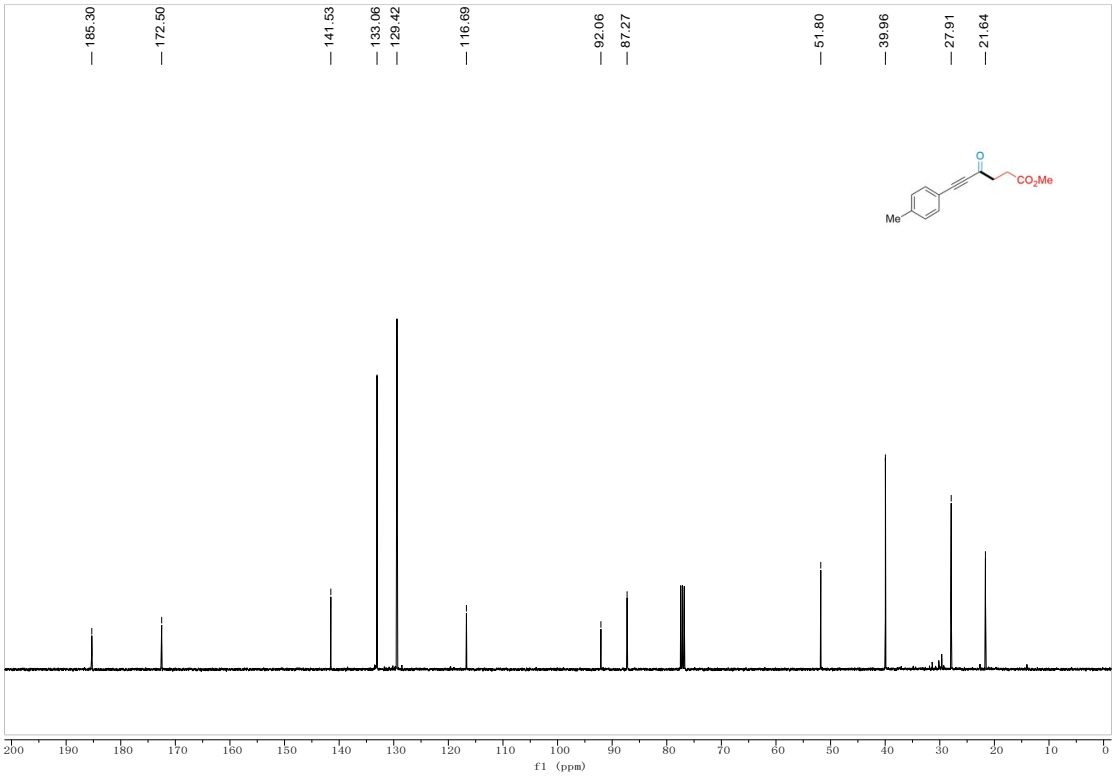
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **3c**



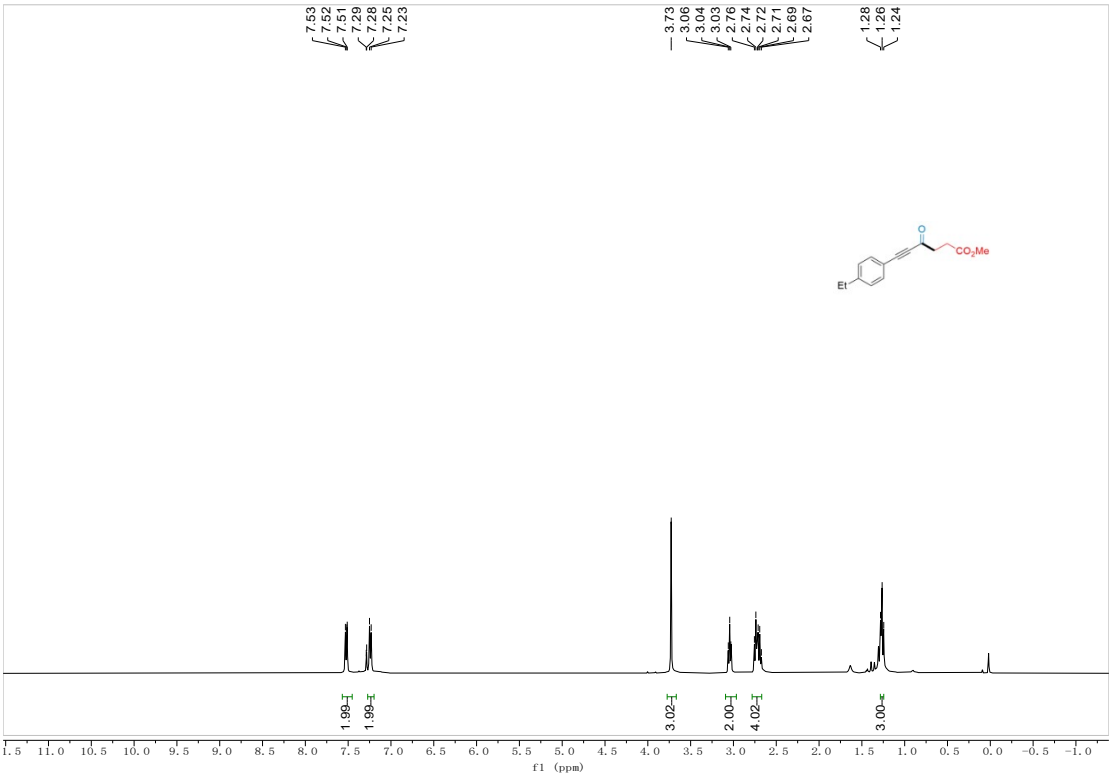
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3d**



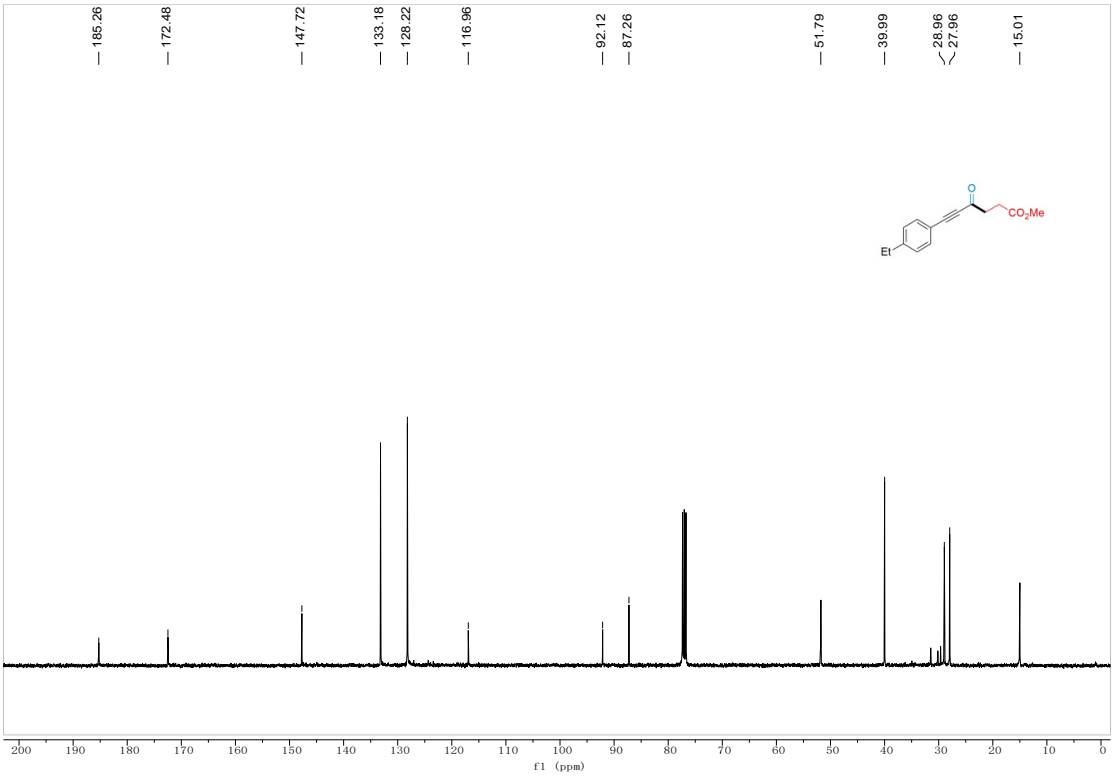
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **3d**



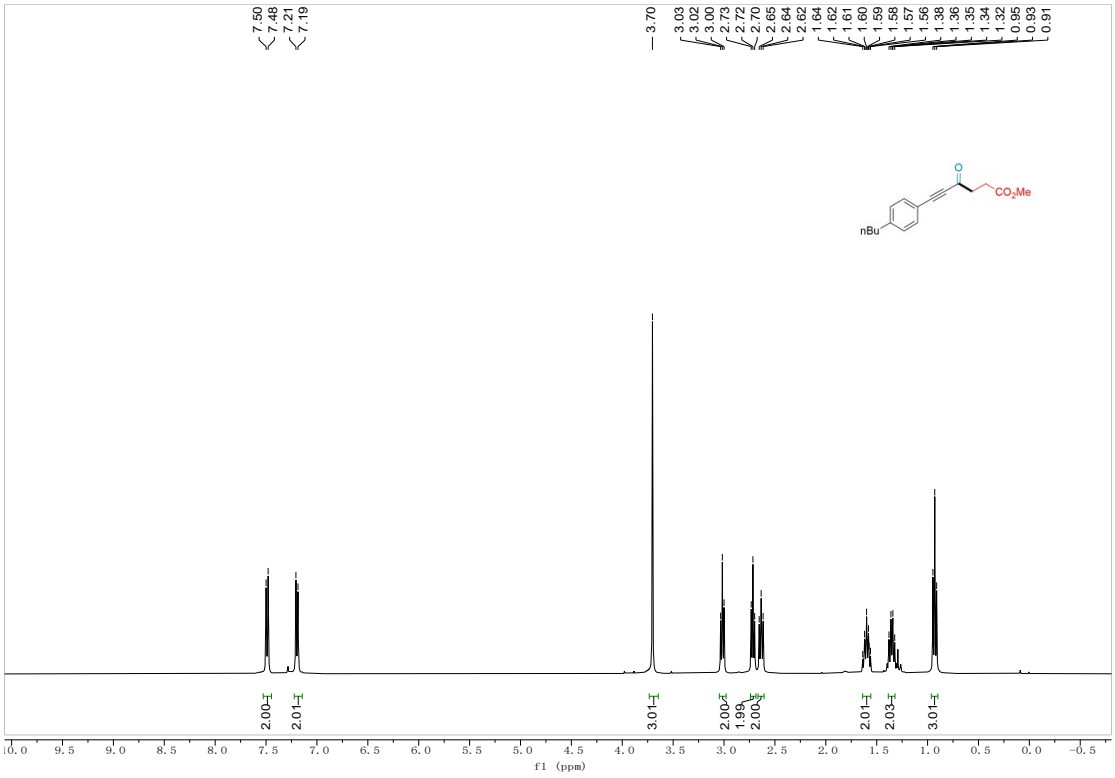
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3e**



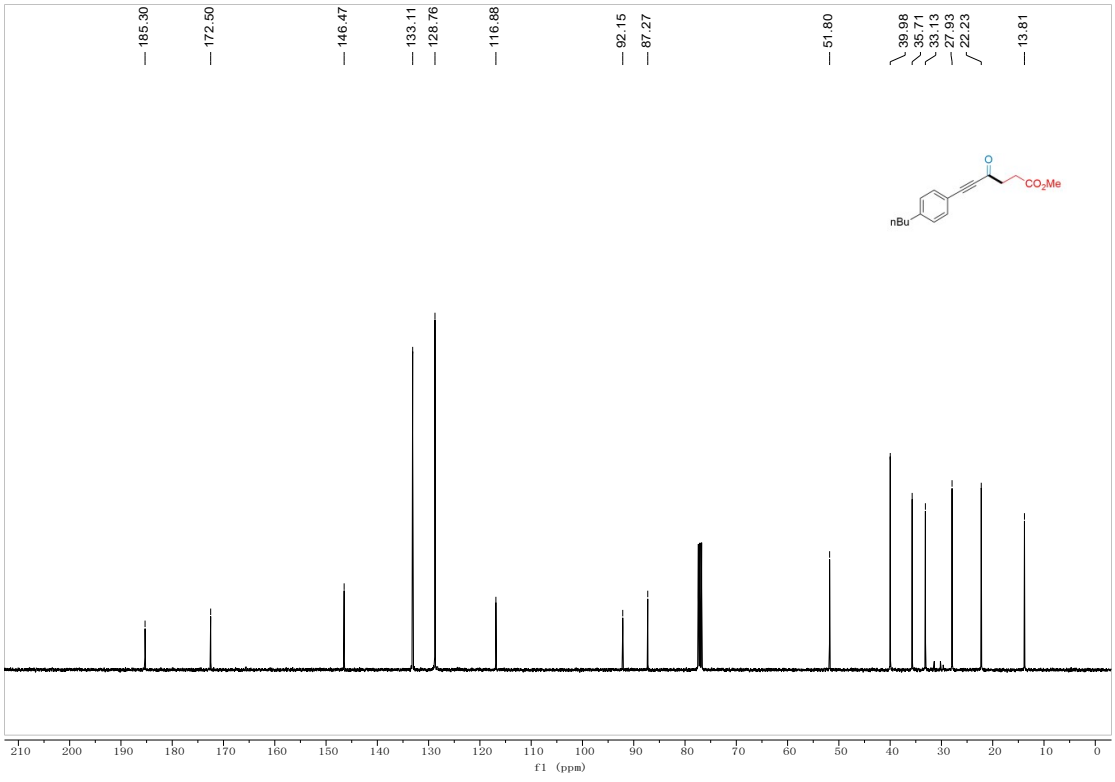
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **3e**



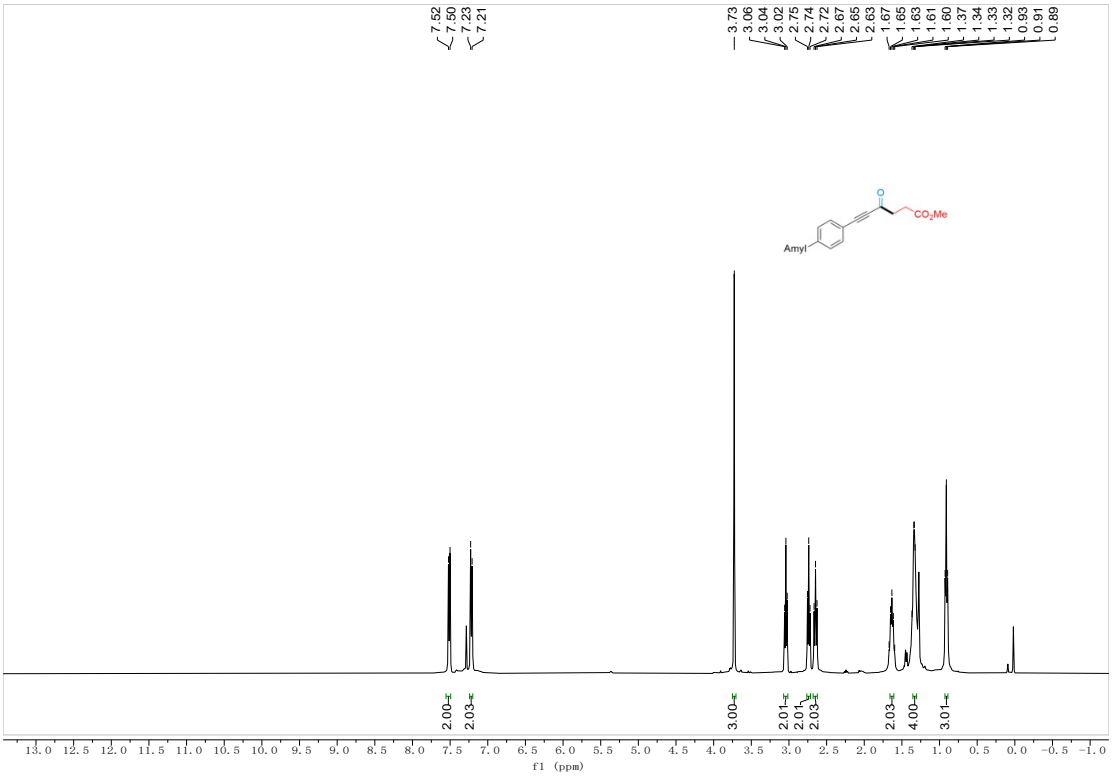
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3f**



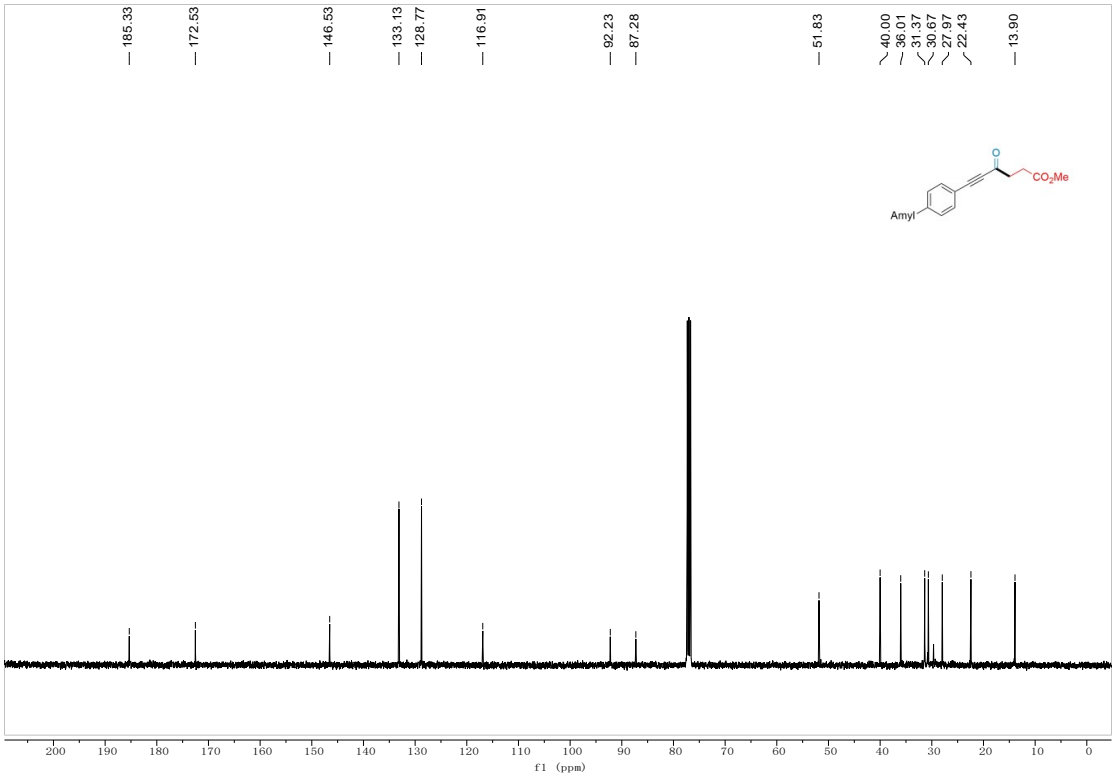
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **3f**



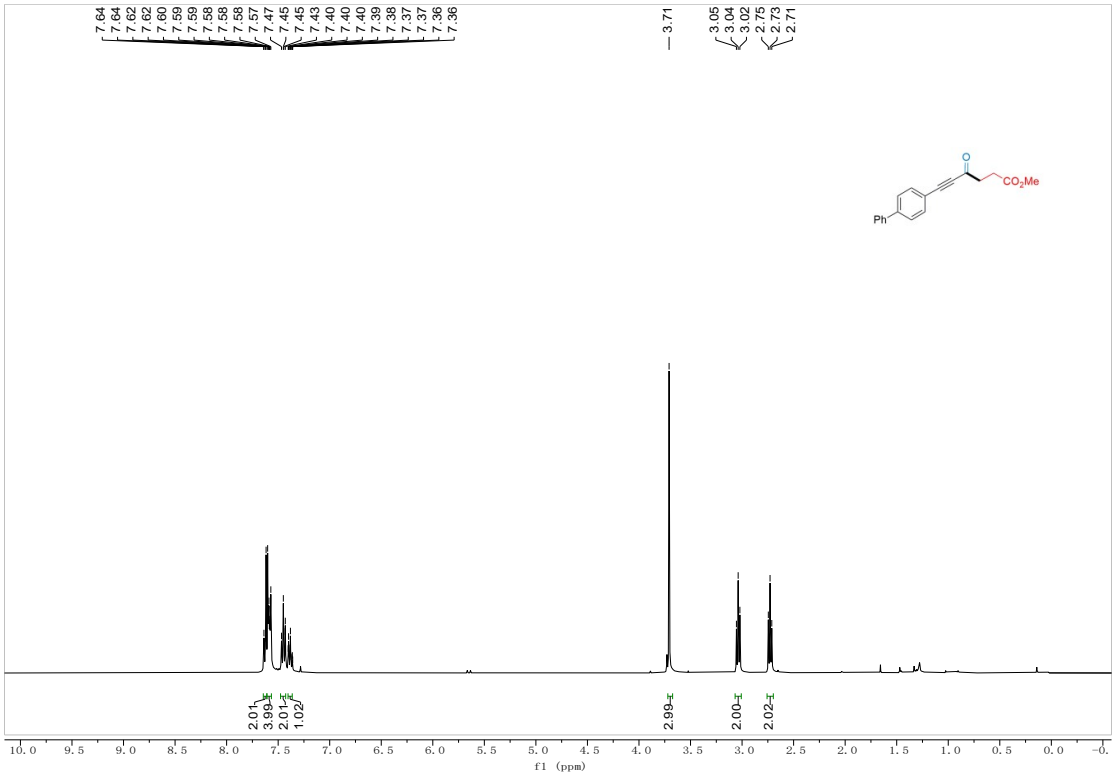
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3g**



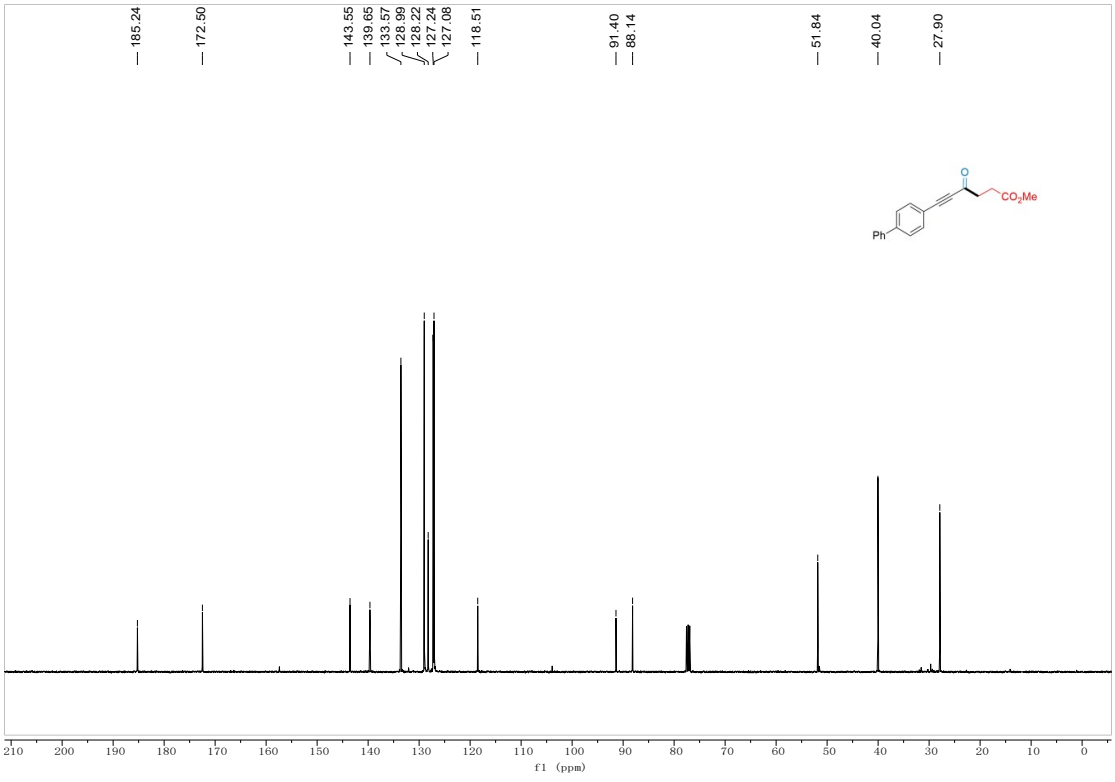
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **3g**



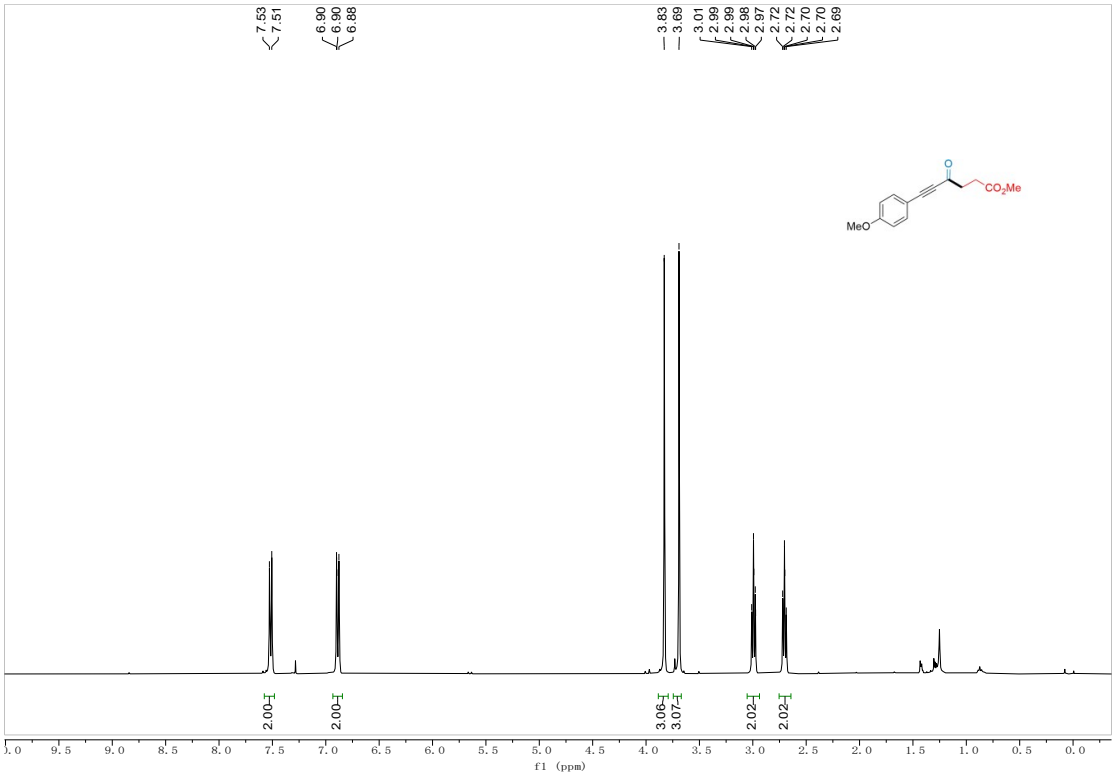
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3h**



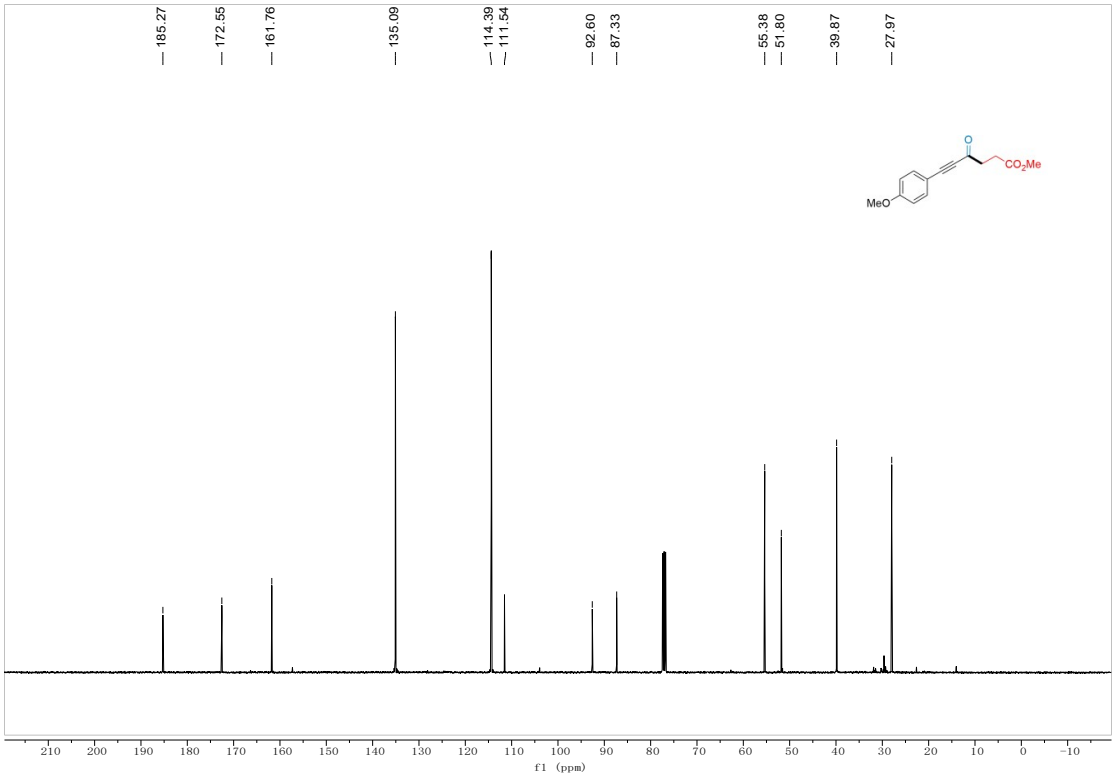
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **3h**



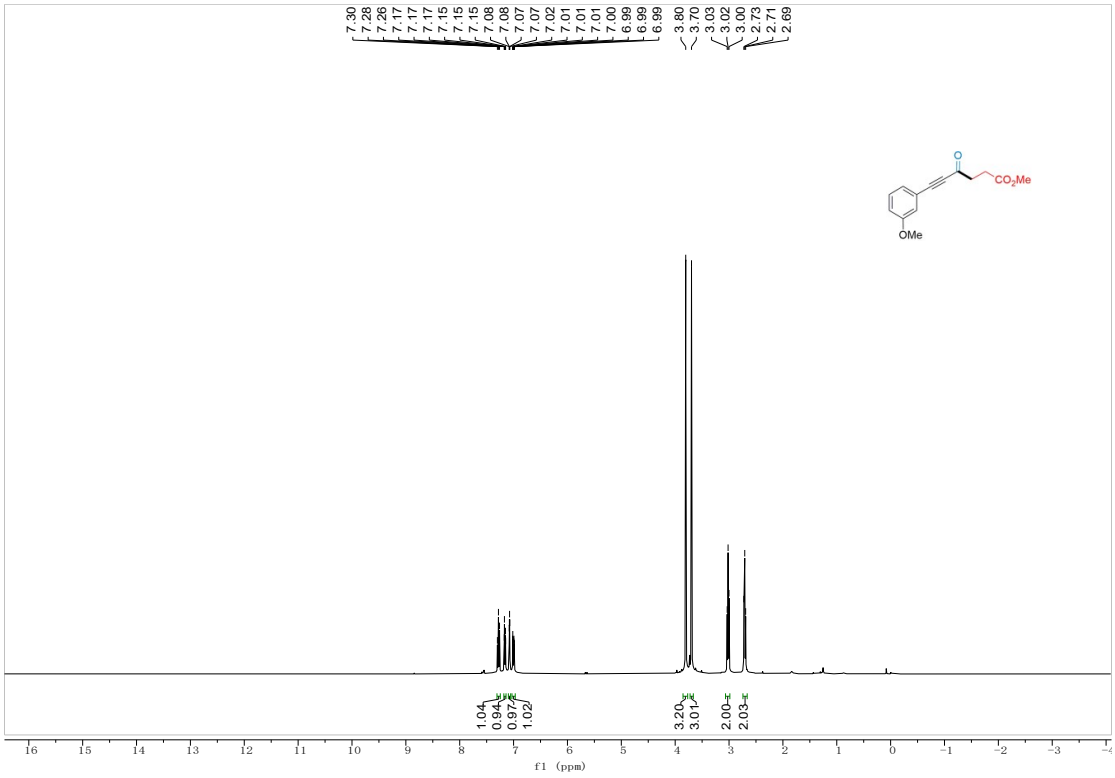
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3i**



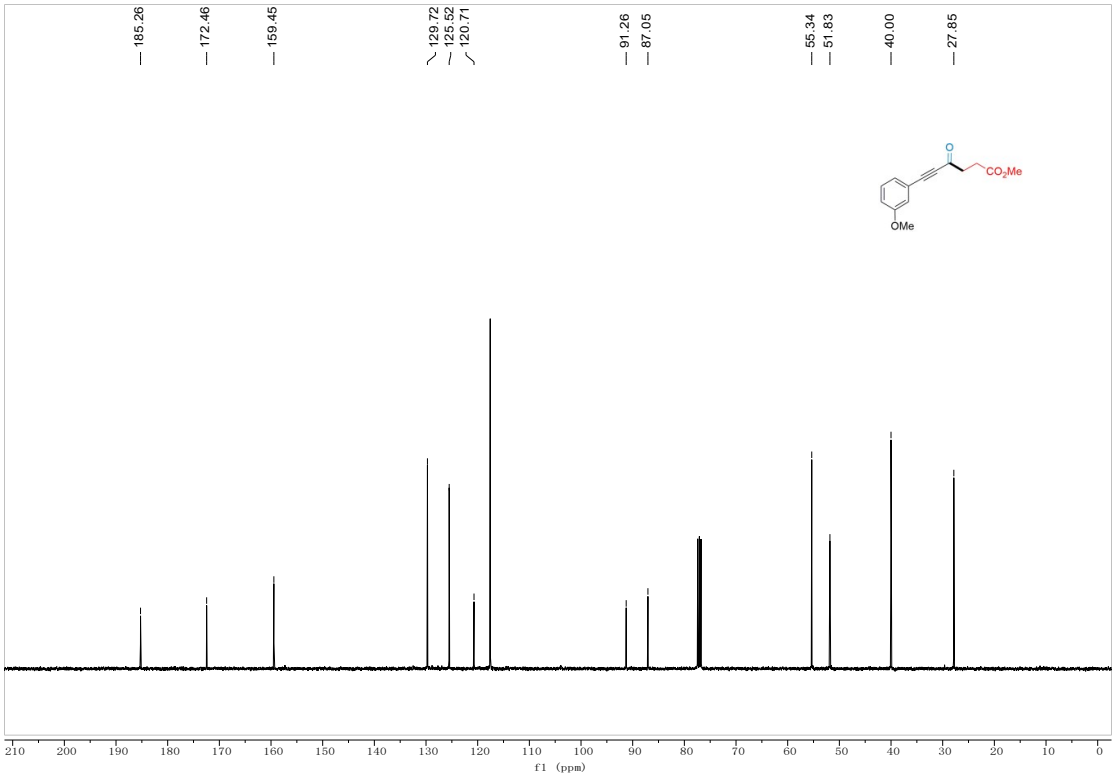
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **3i**



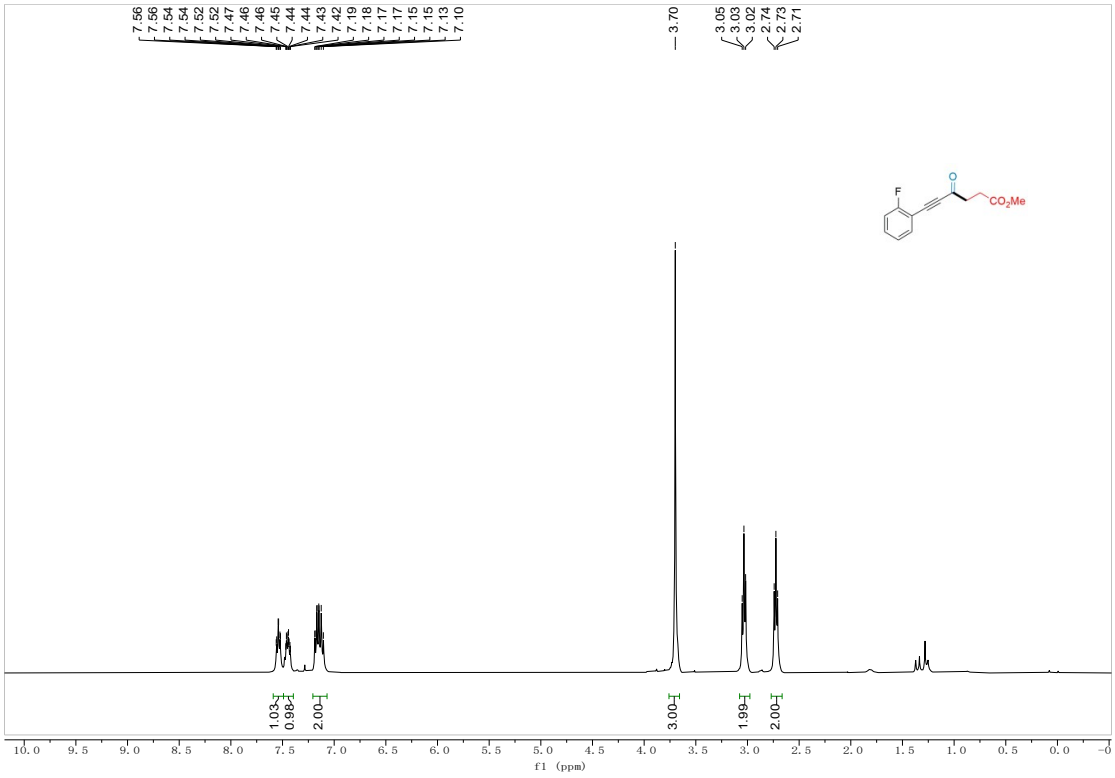
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3j**



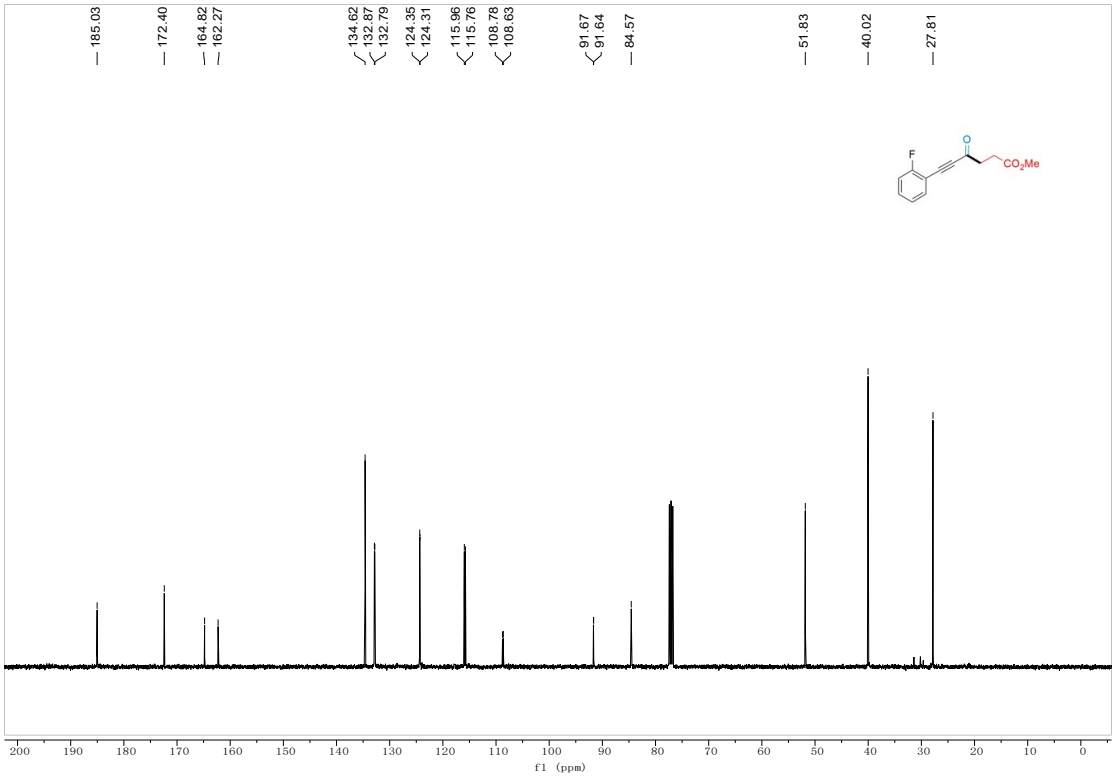
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **3j**



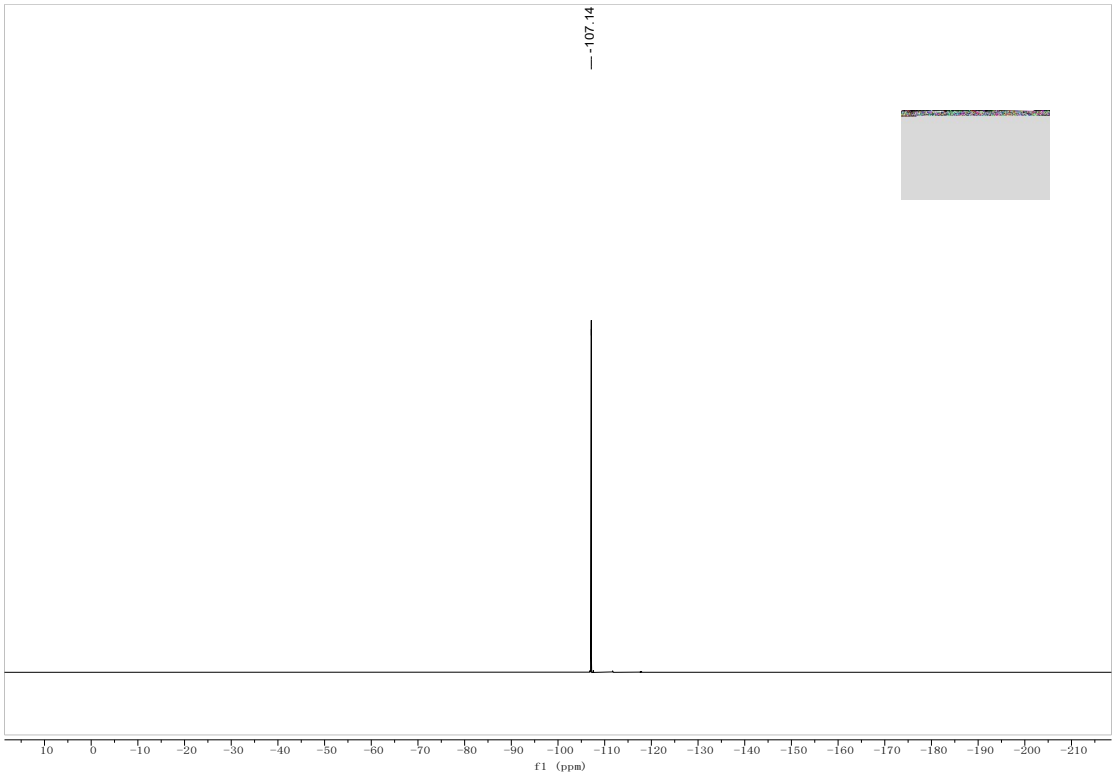
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3k**



^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **3k**



^{19}F NMR (376 MHz, $CDCl_3$) spectrum of compound **3k**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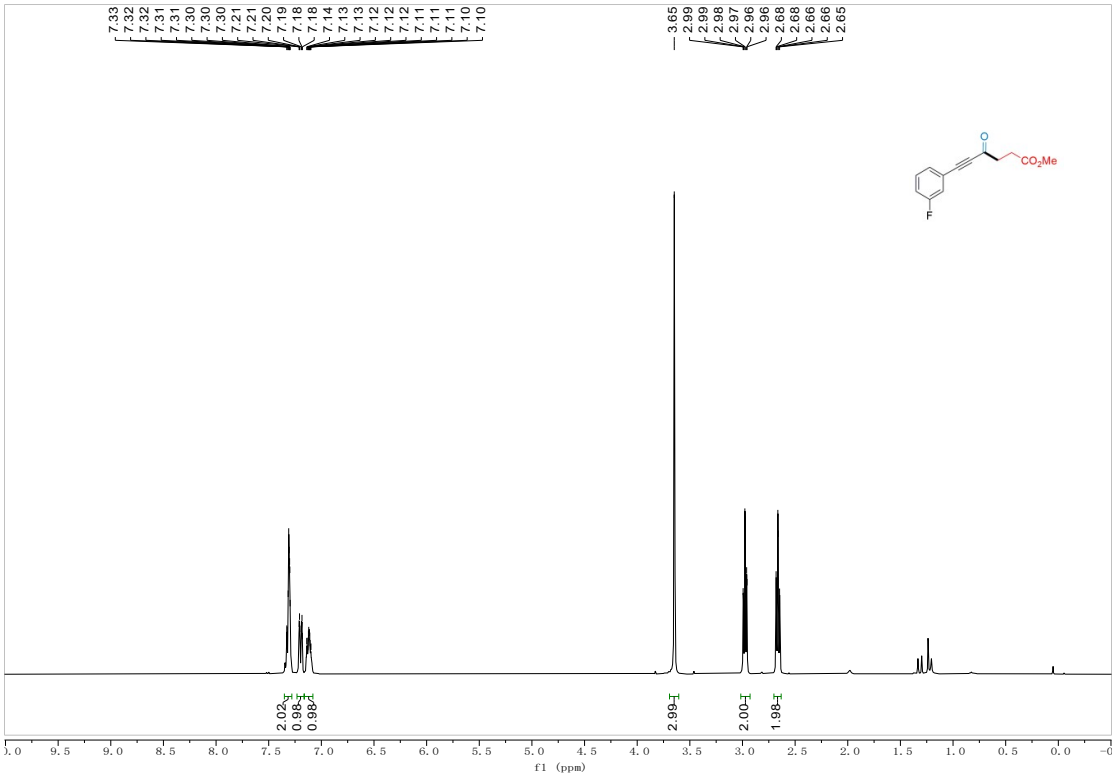
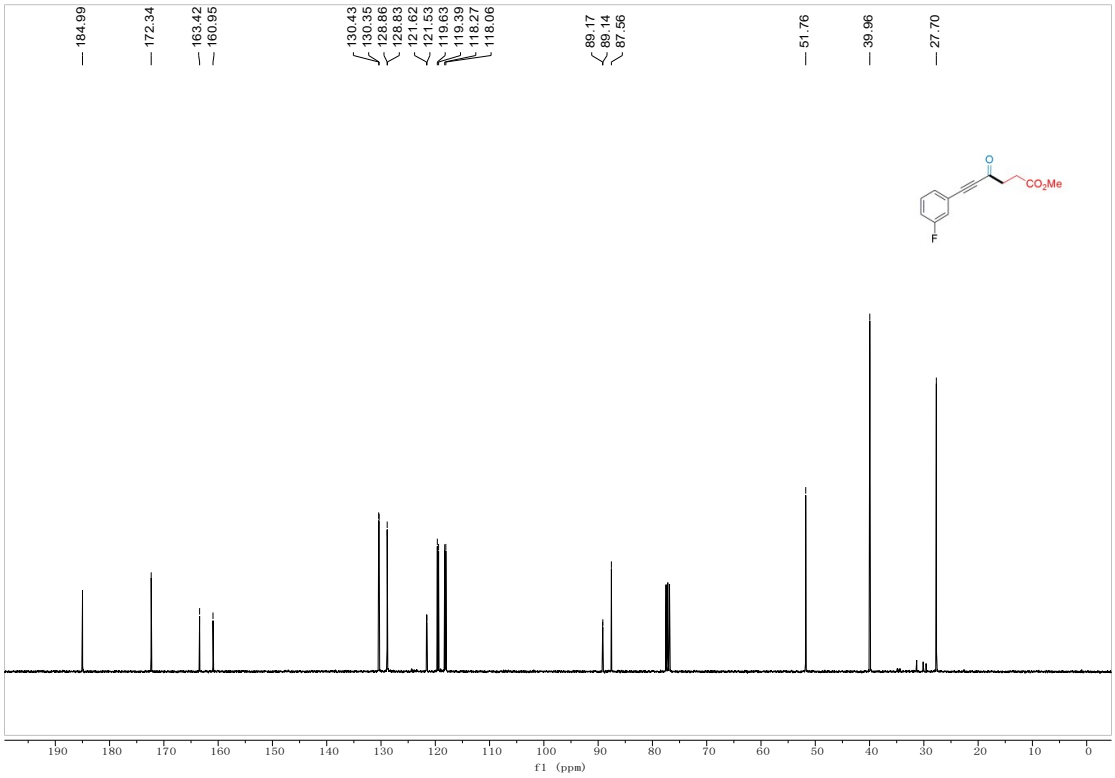
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

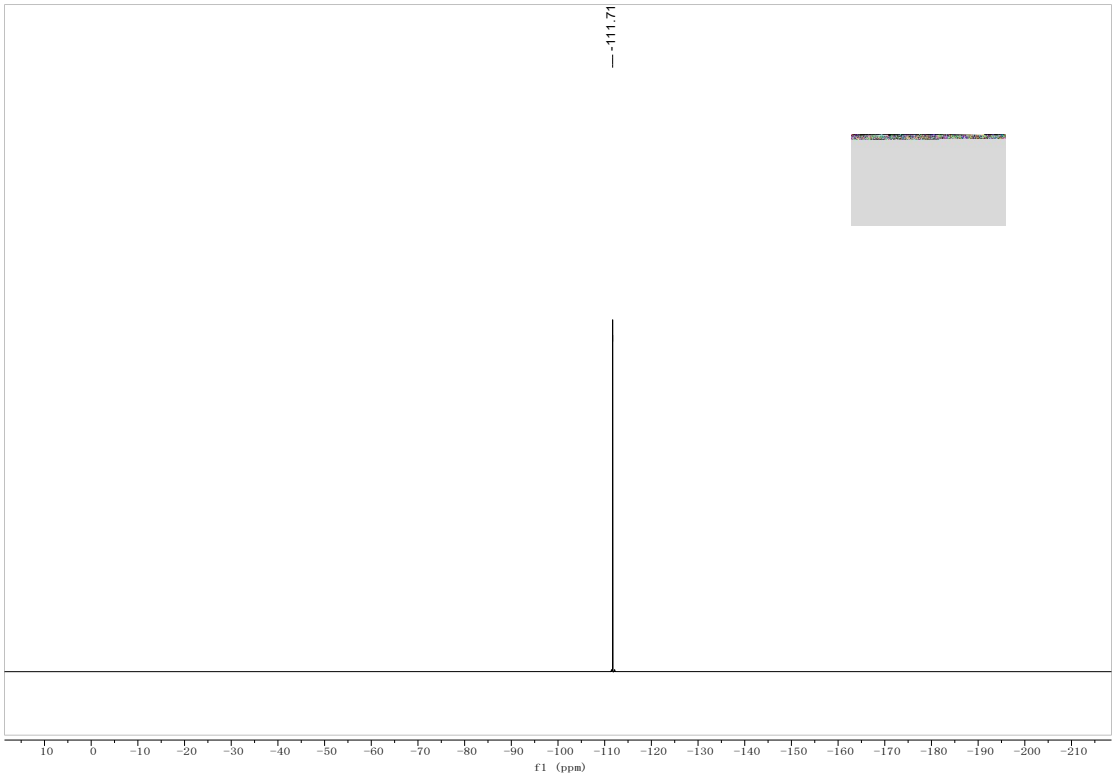
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3l**



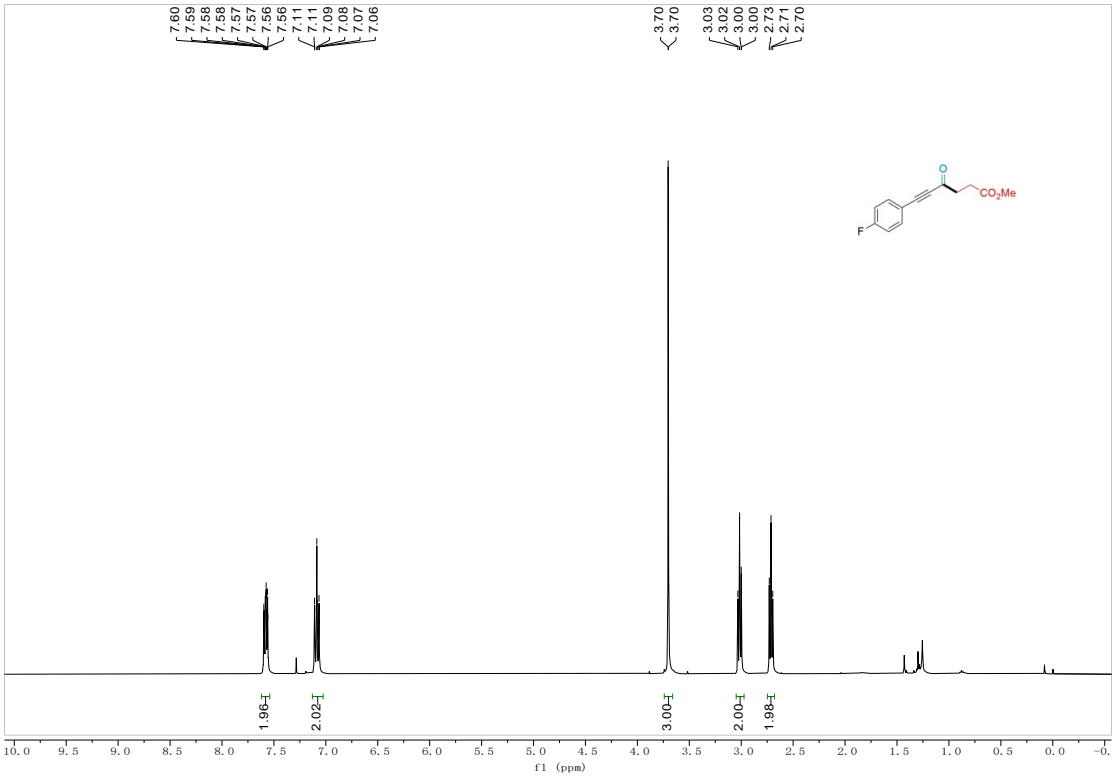
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **3l**



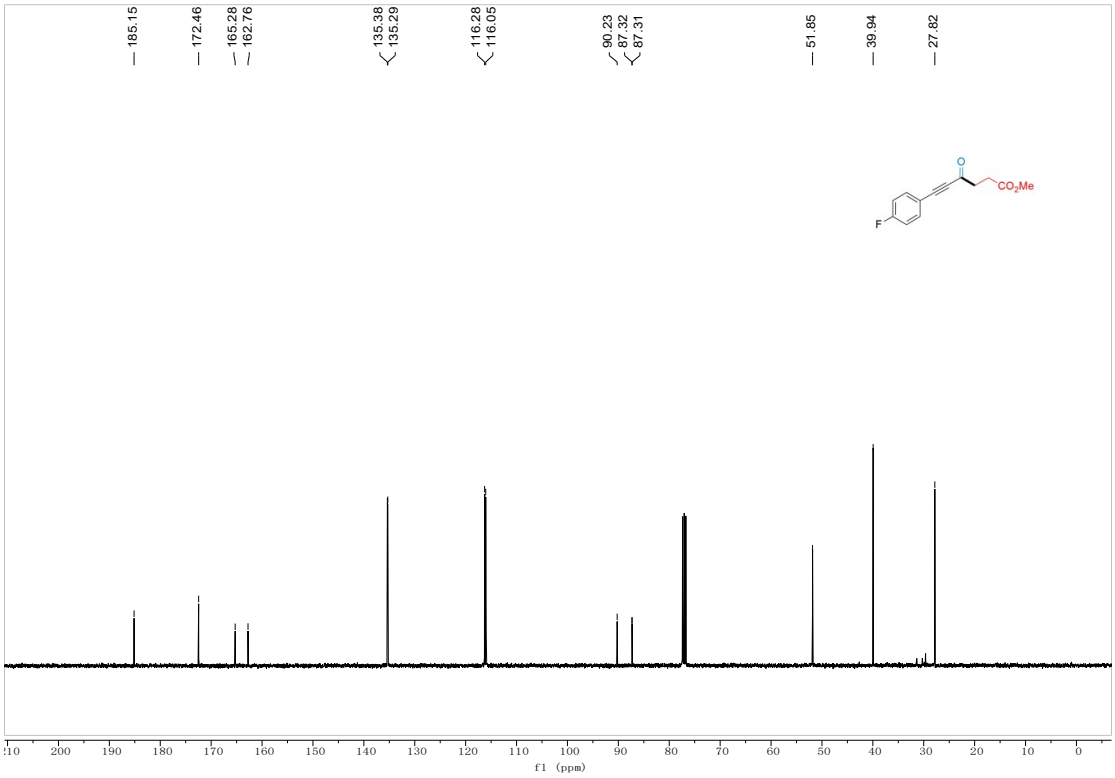
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of compound **3l**



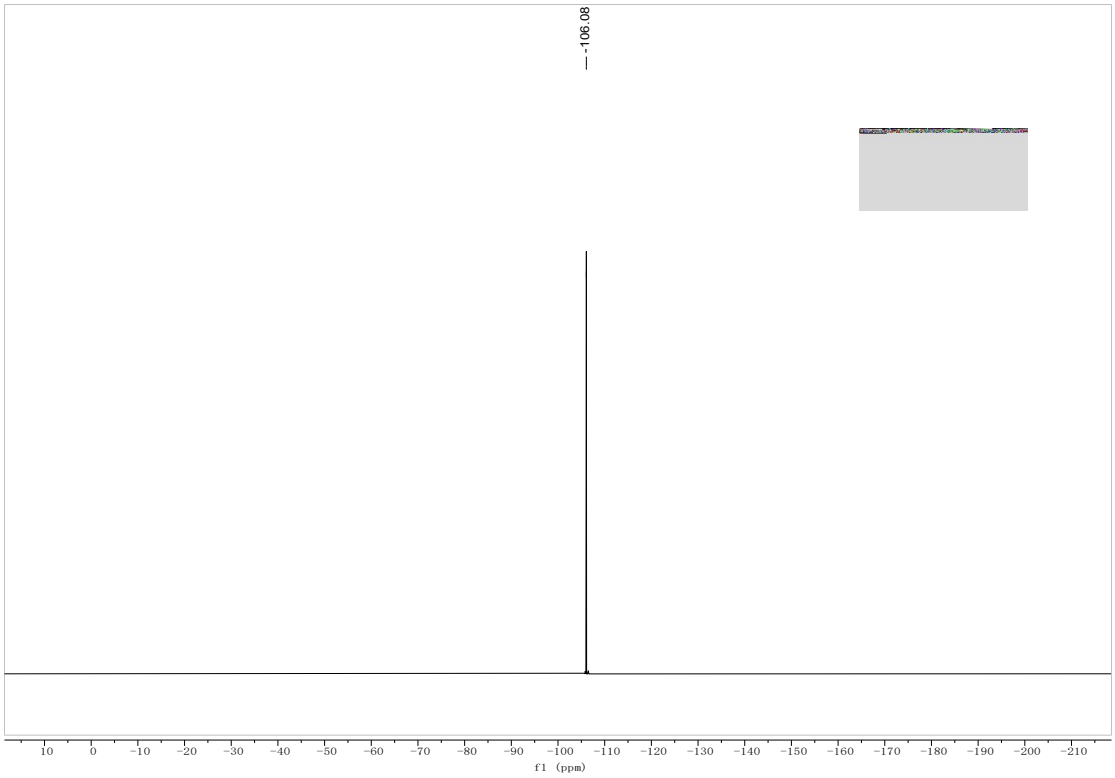
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3m**



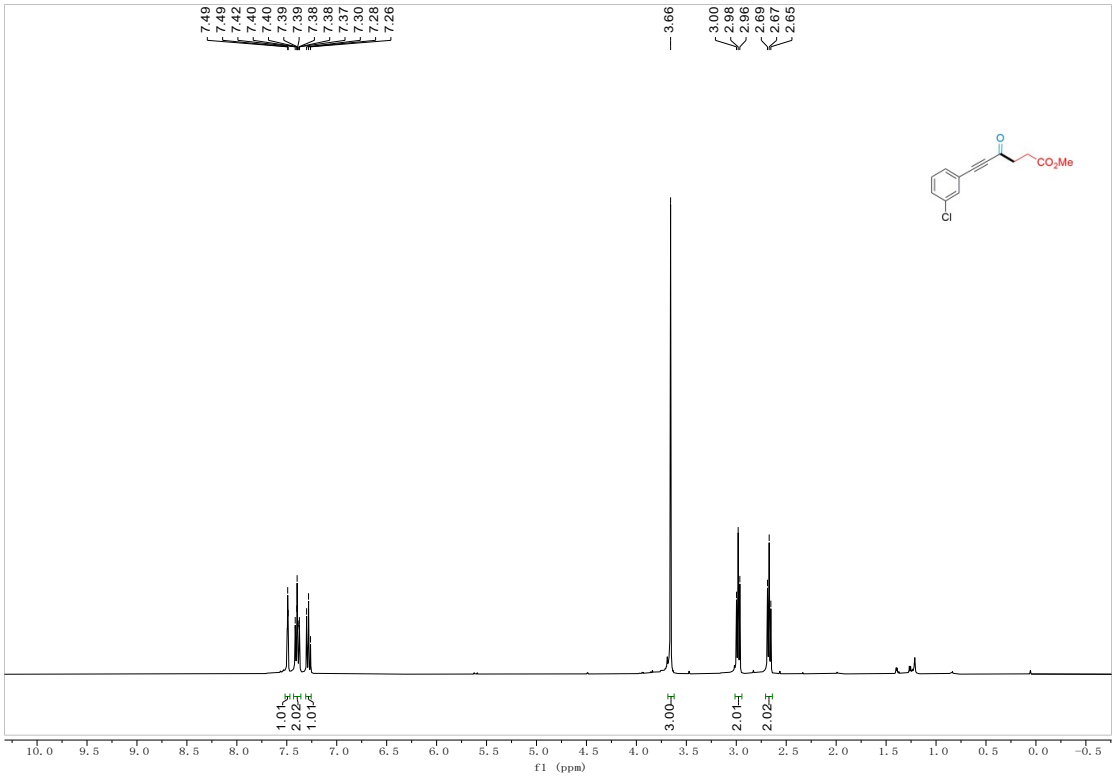
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **3m**



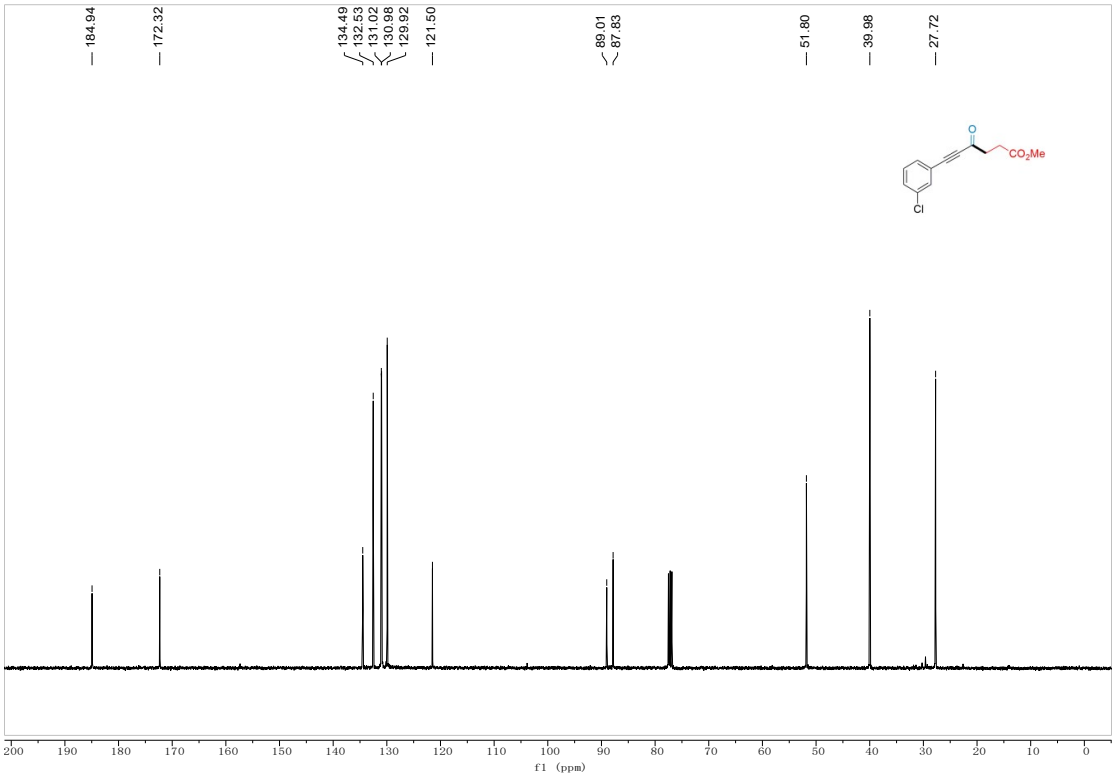
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of compound **3m**



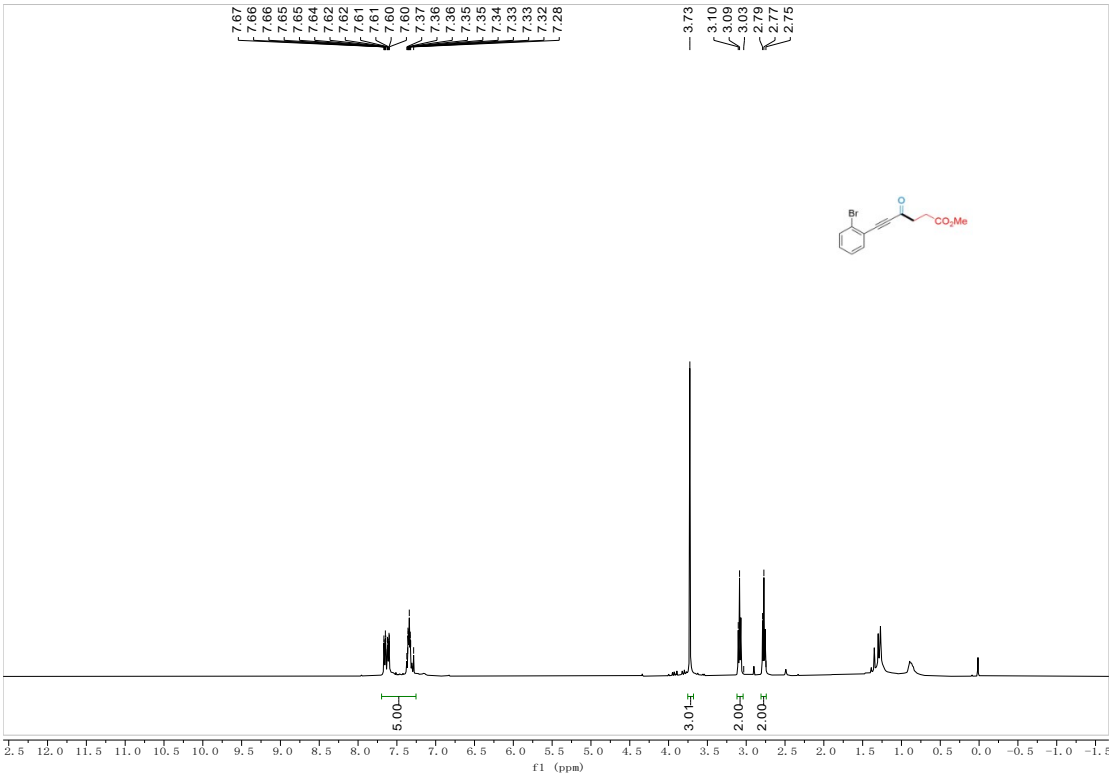
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3n**



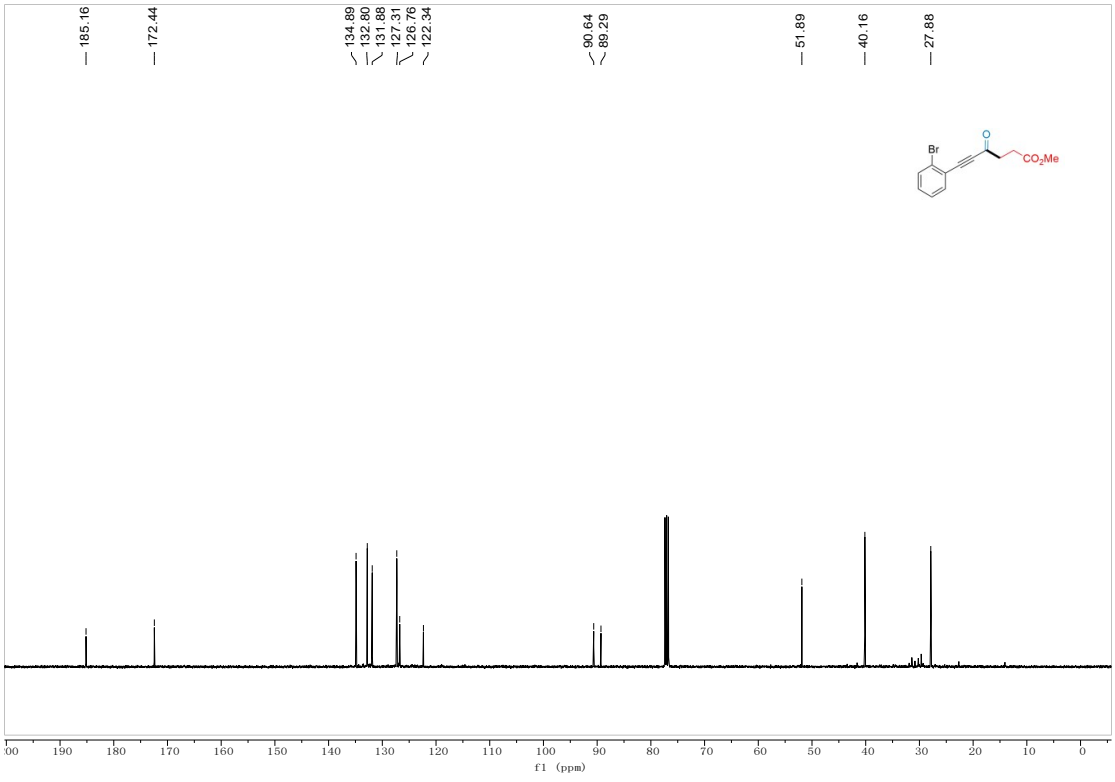
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **3n**



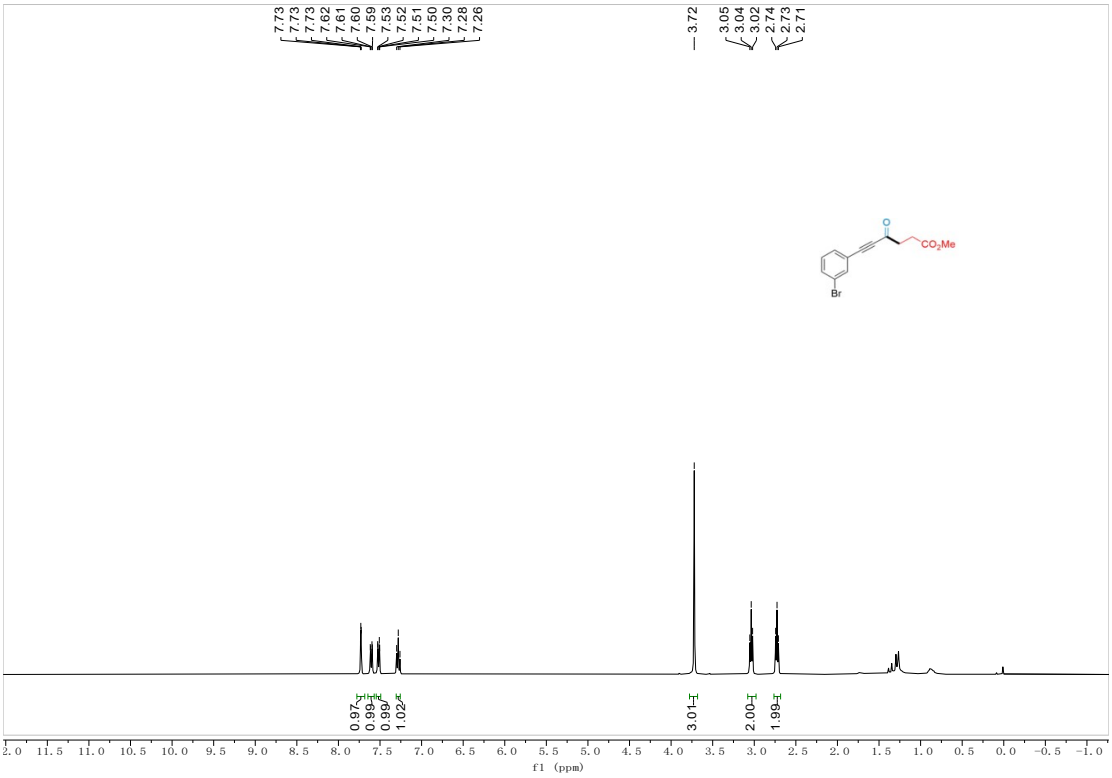
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3o**



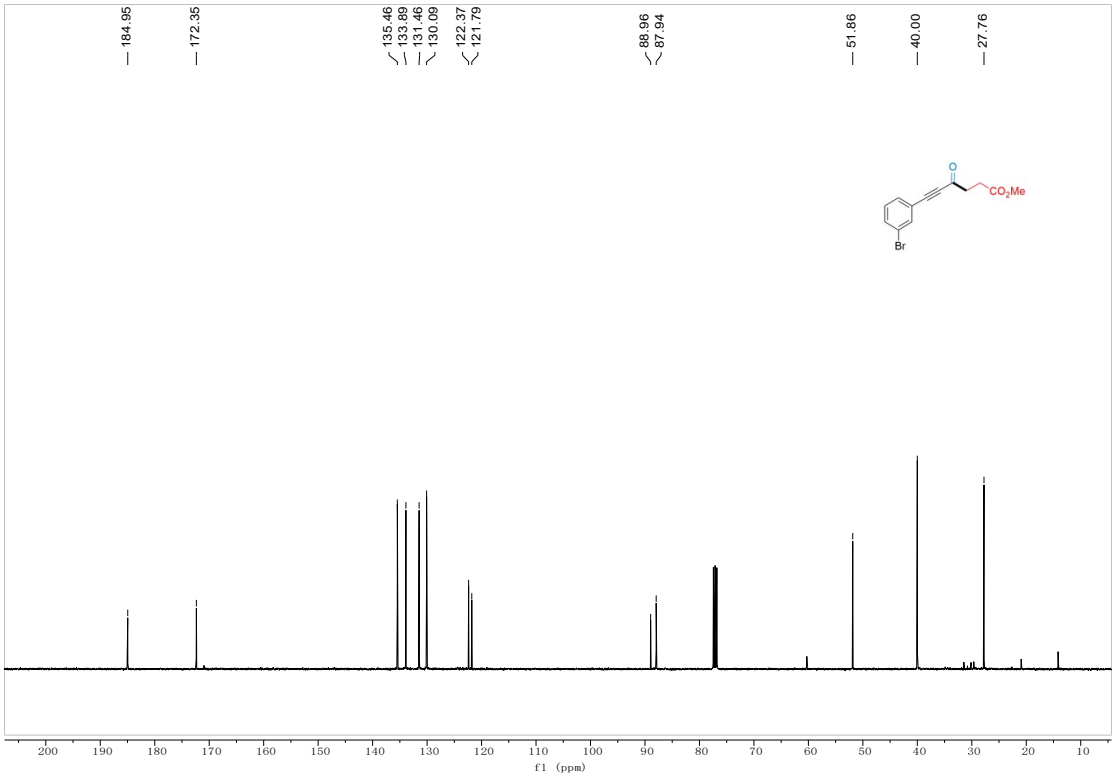
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **3o**



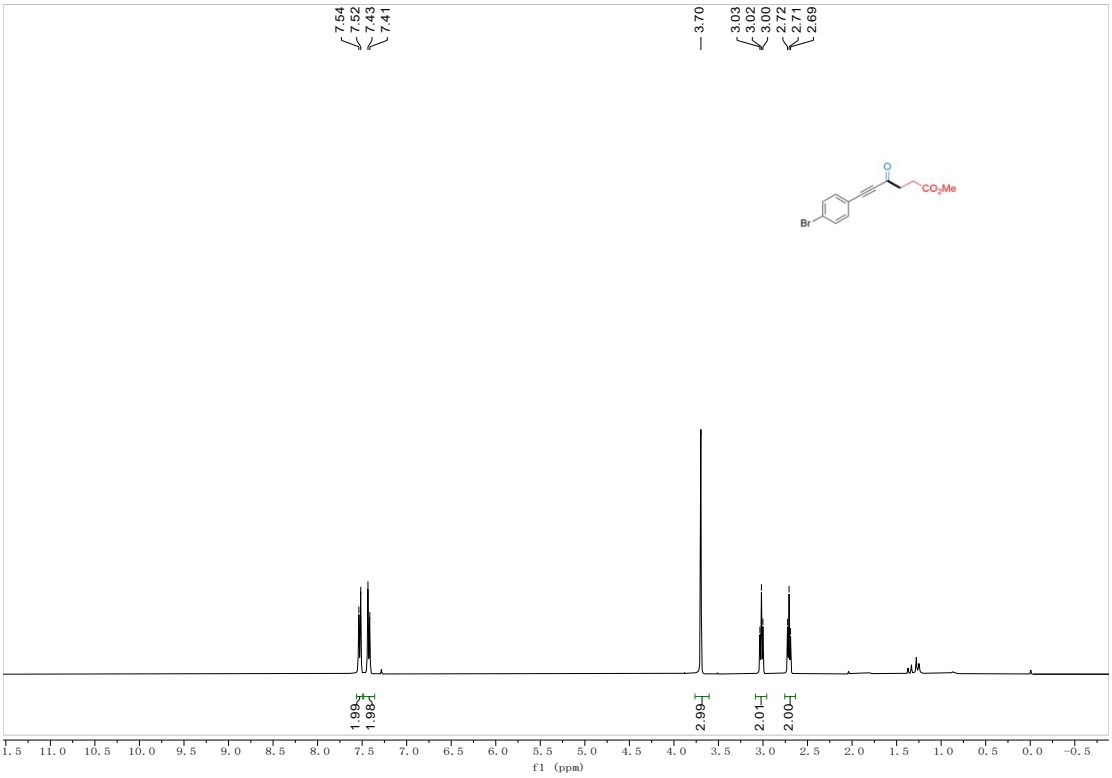
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3p**



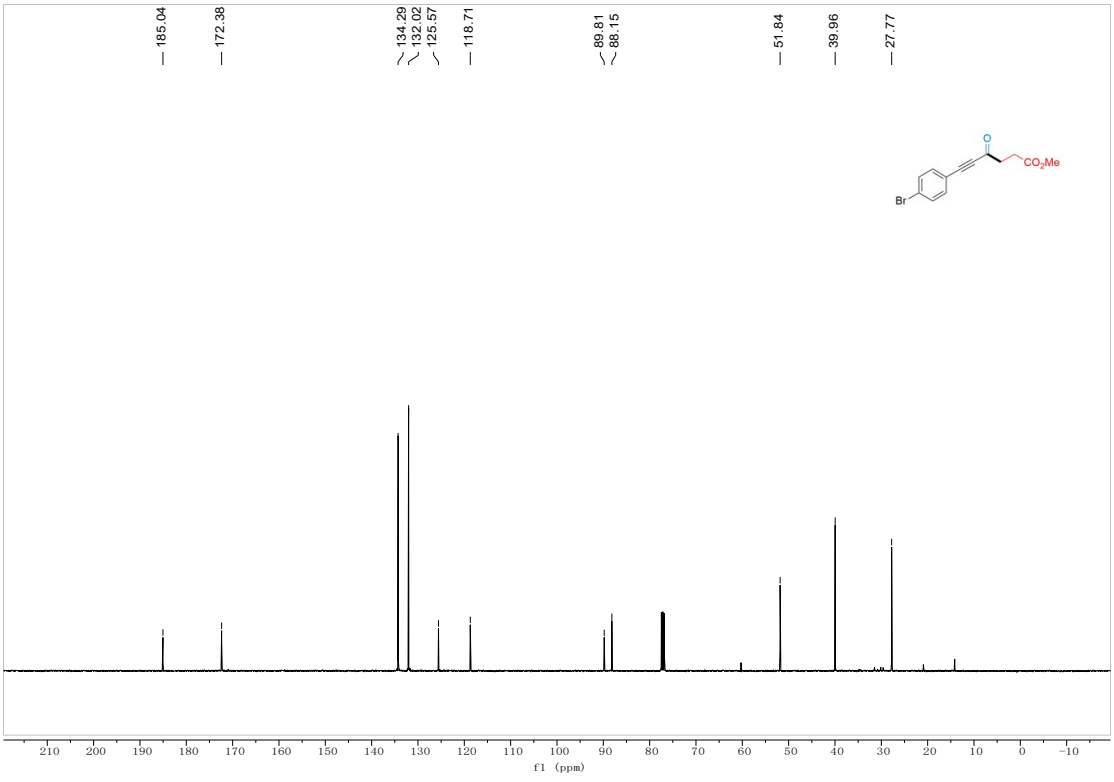
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **3p**



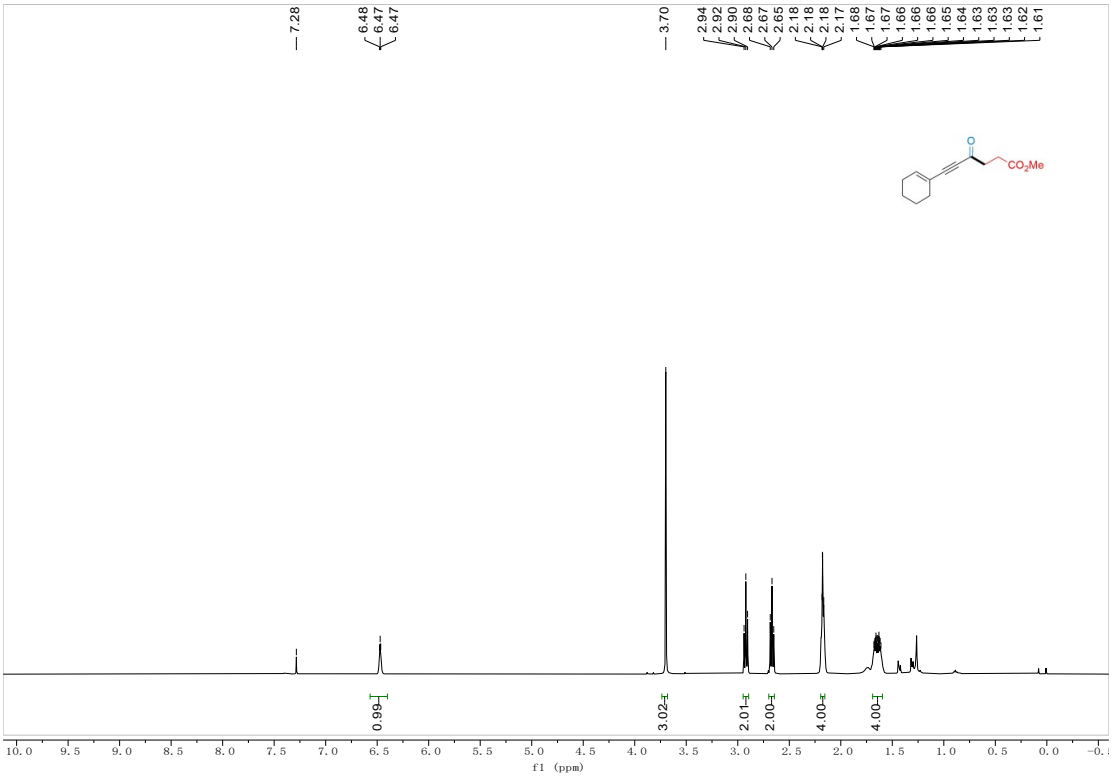
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3q**



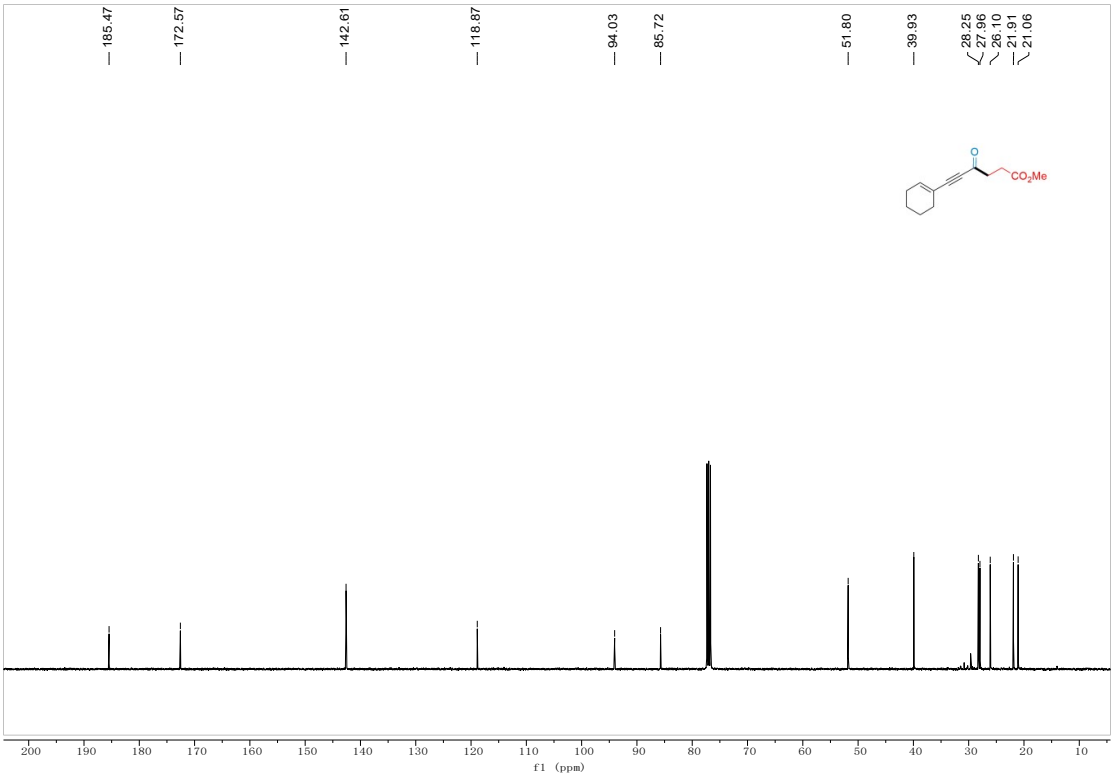
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **3q**



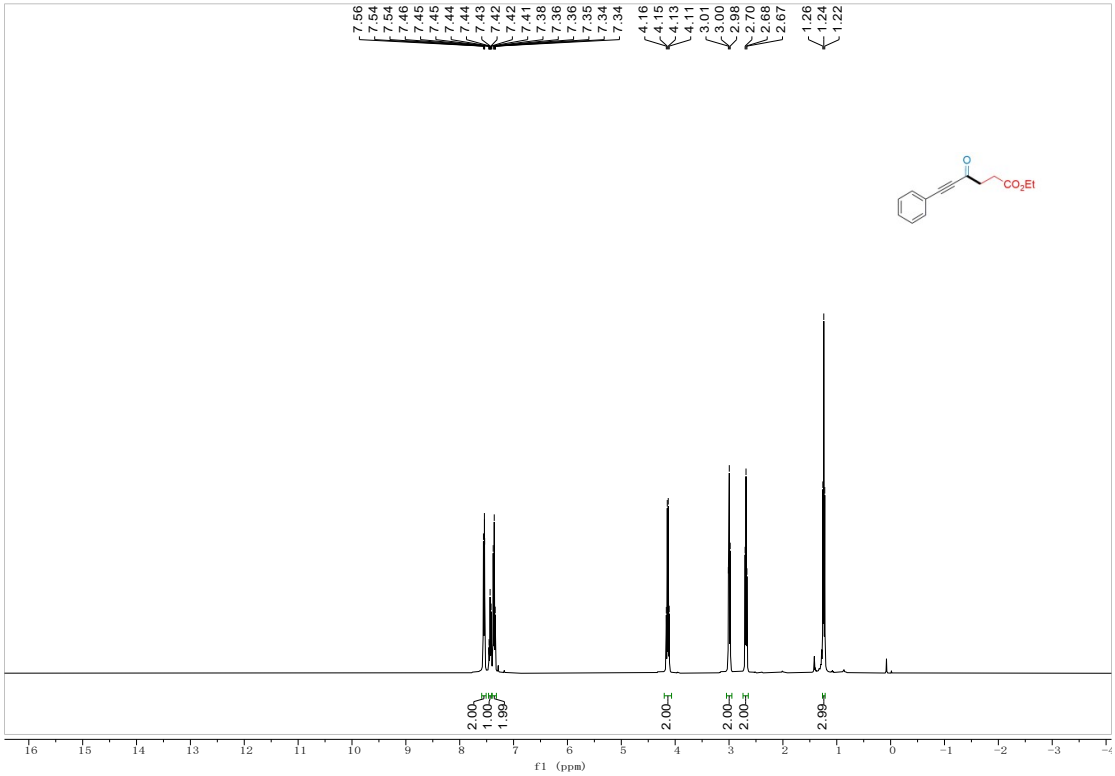
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3s**



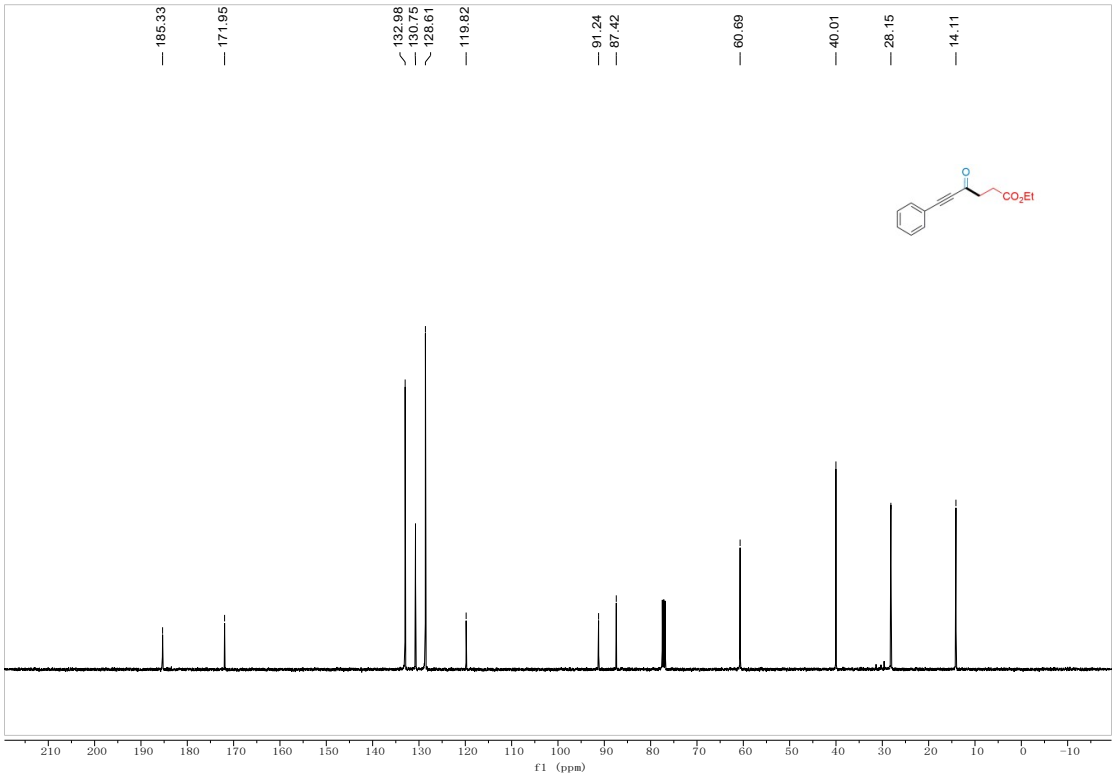
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **3s**



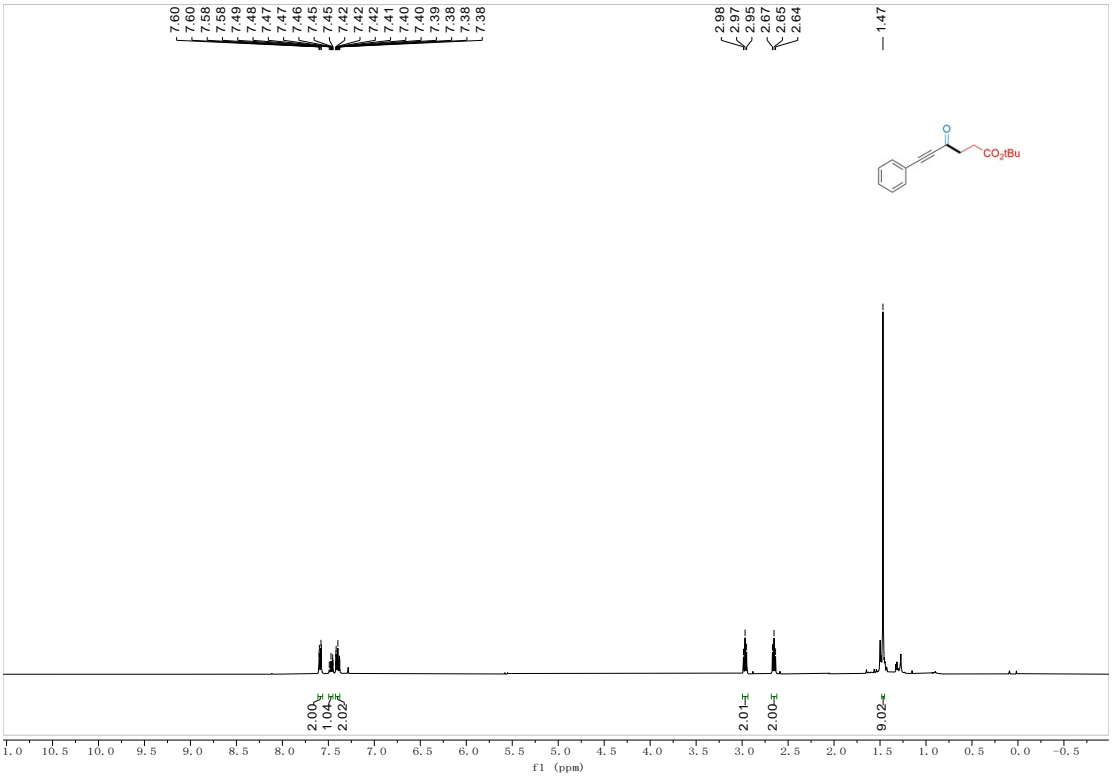
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3t**



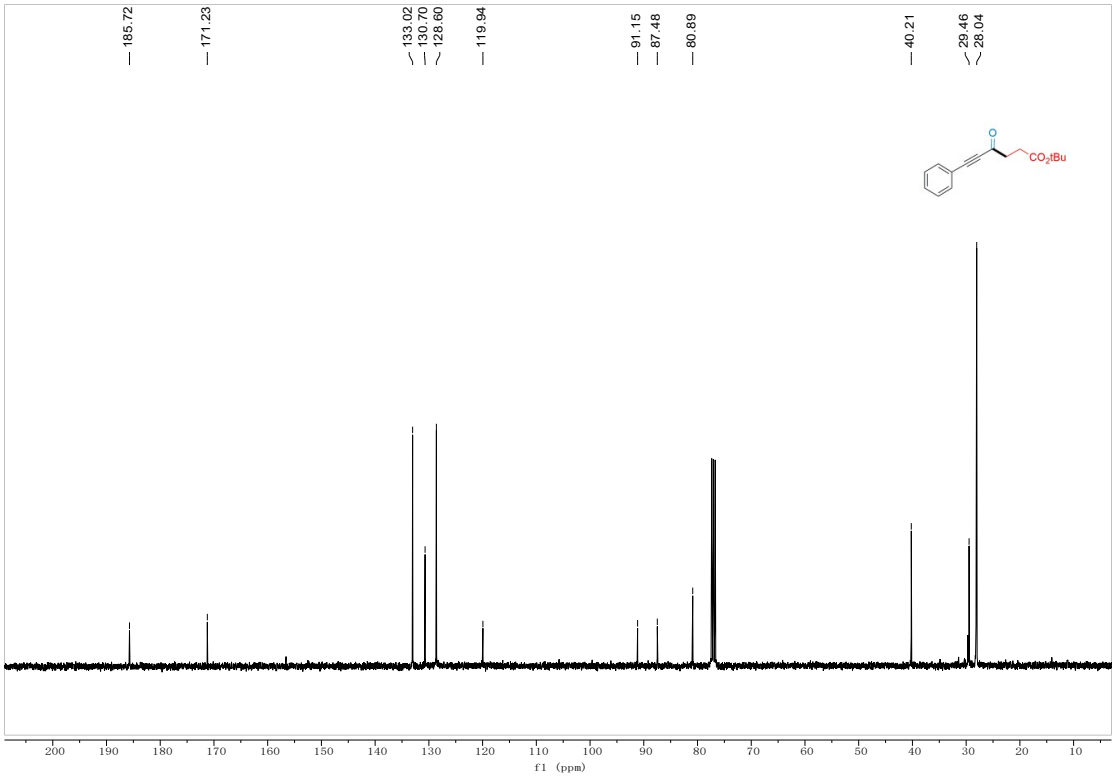
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **3t**



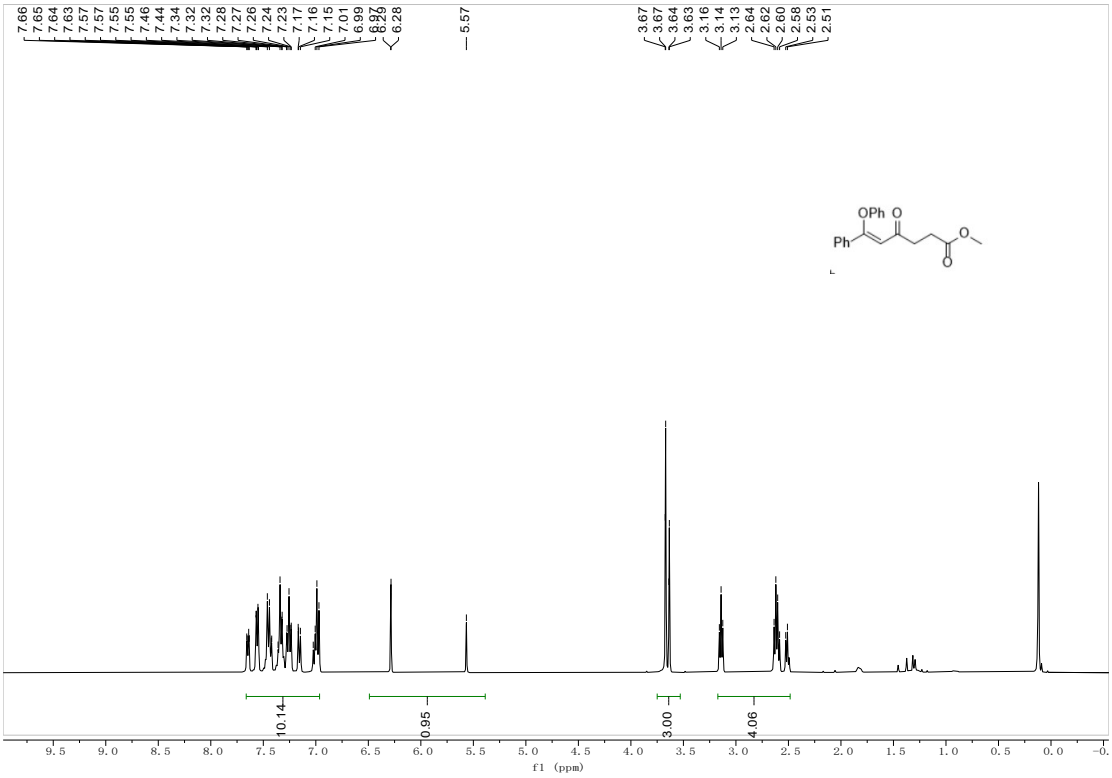
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3u**



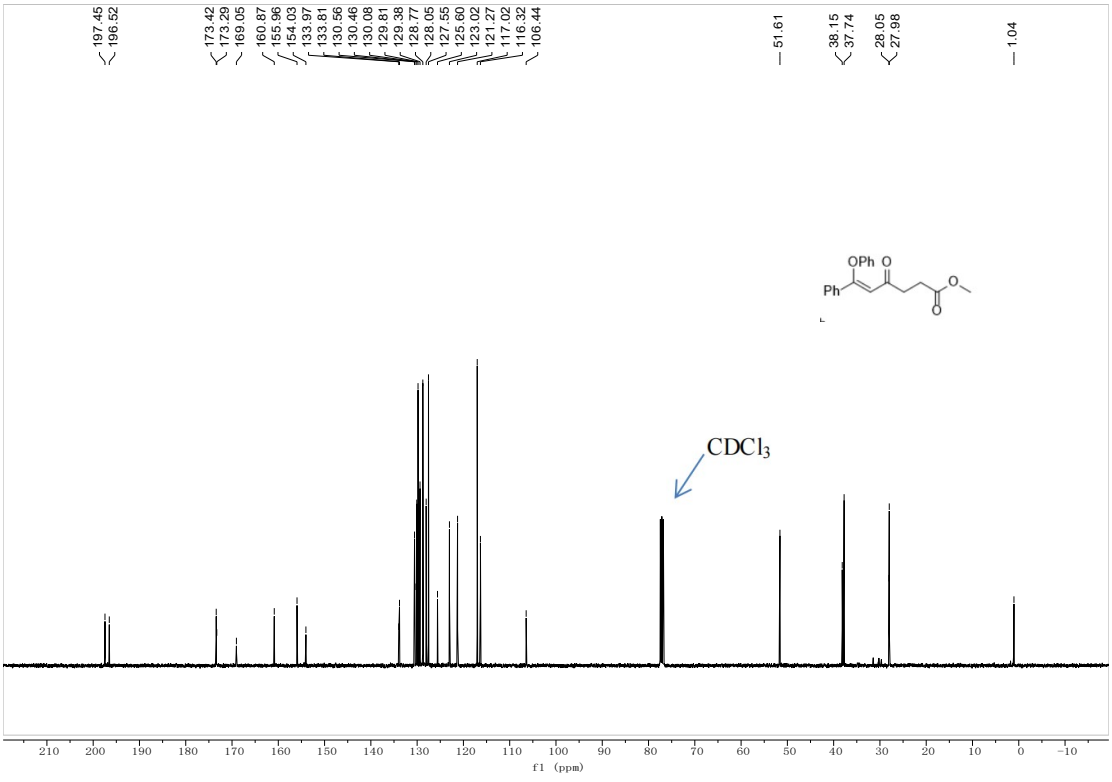
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **3u**



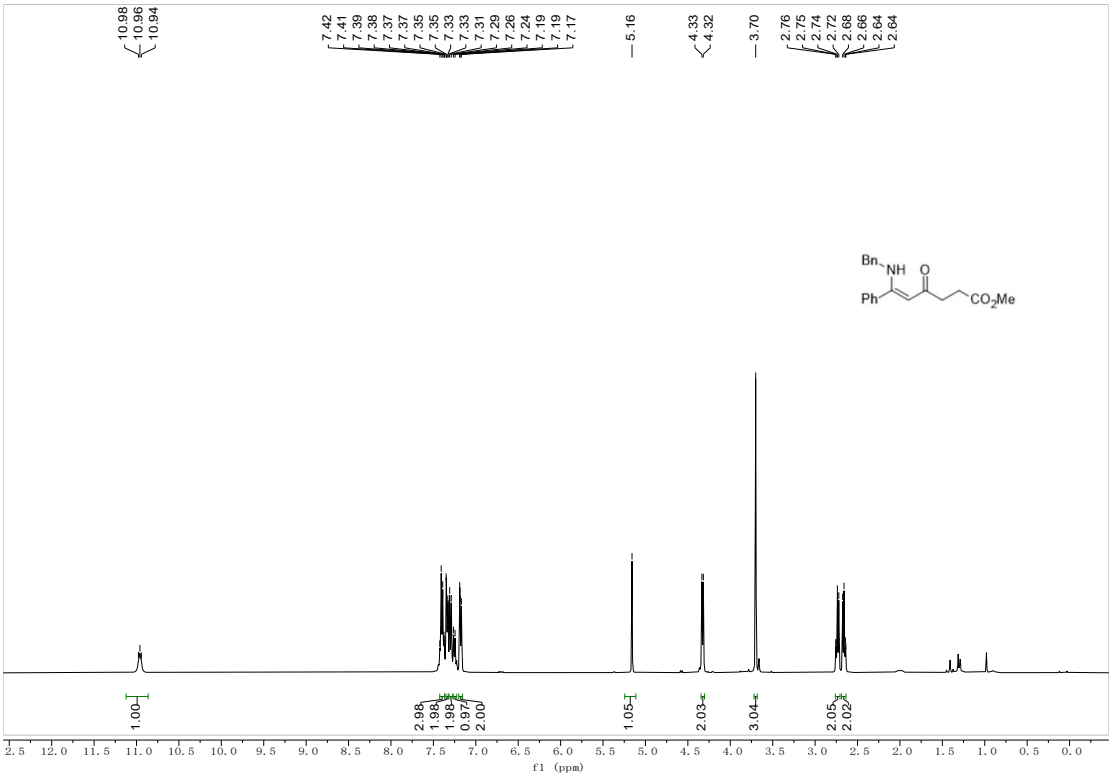
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **4**



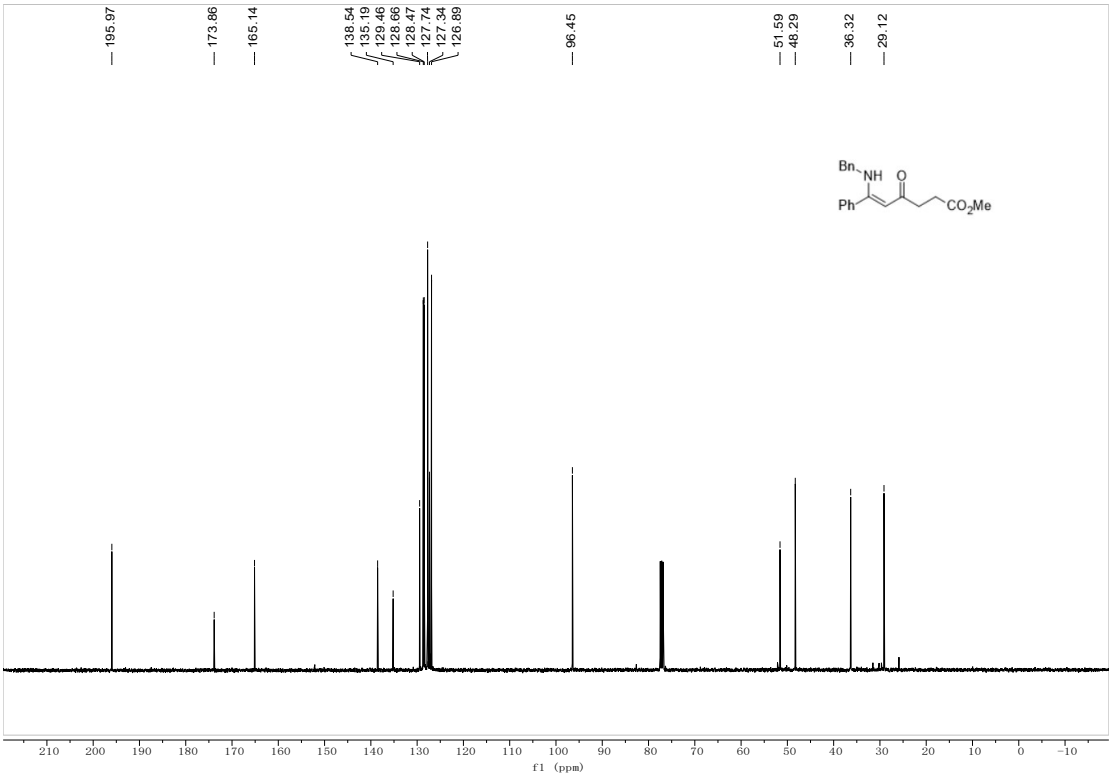
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **4**



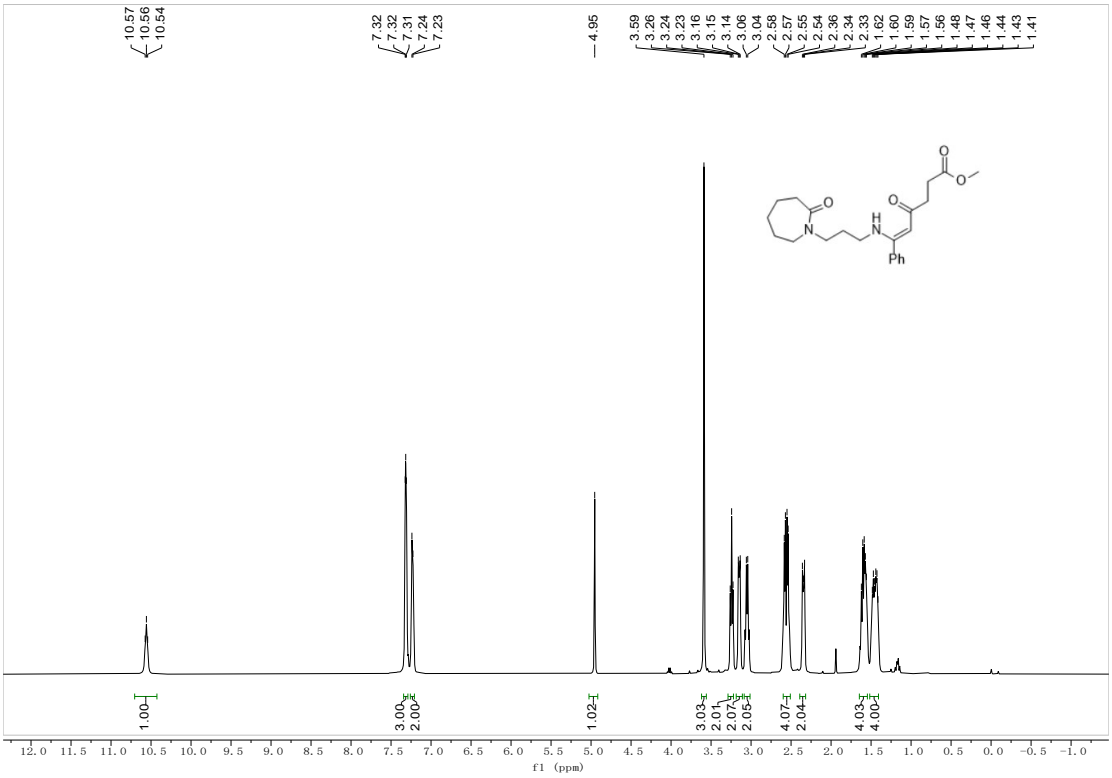
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **5**



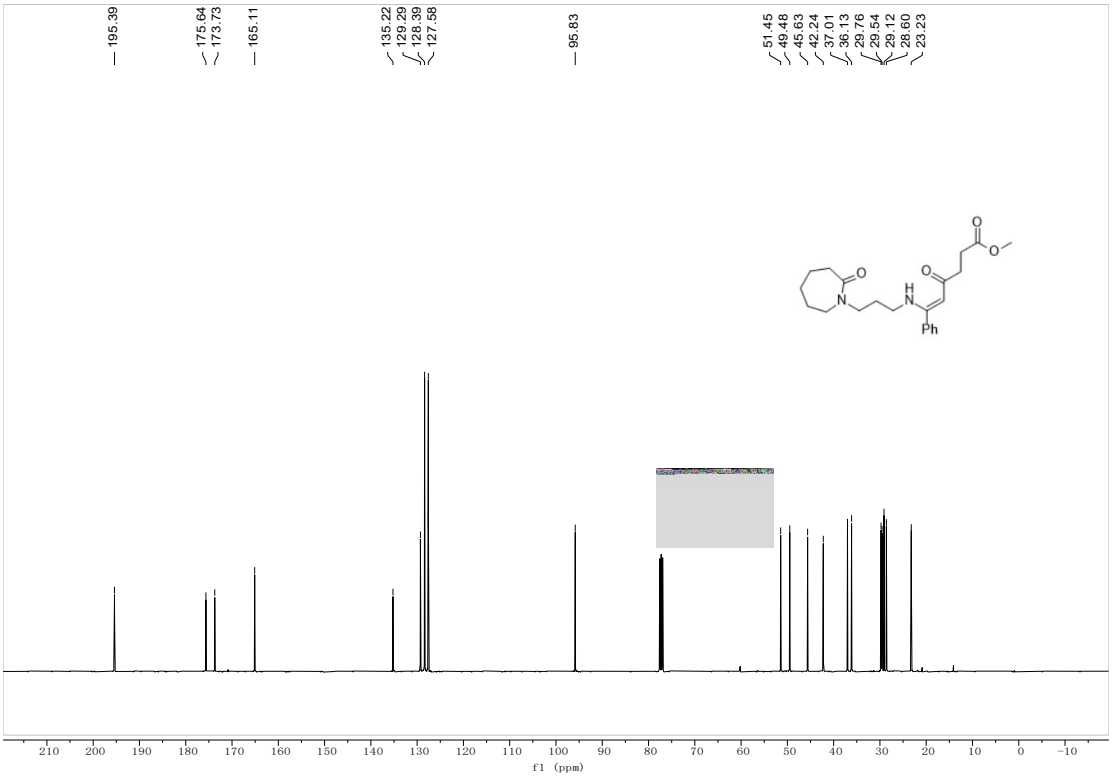
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **5**



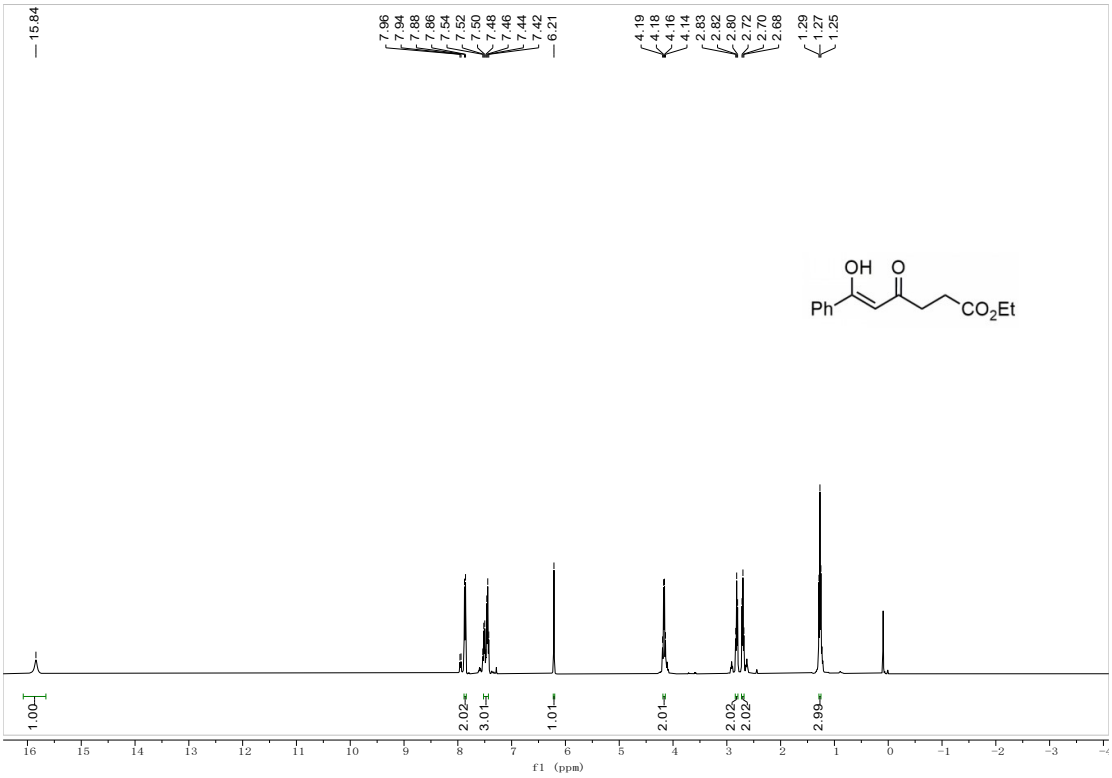
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **6**



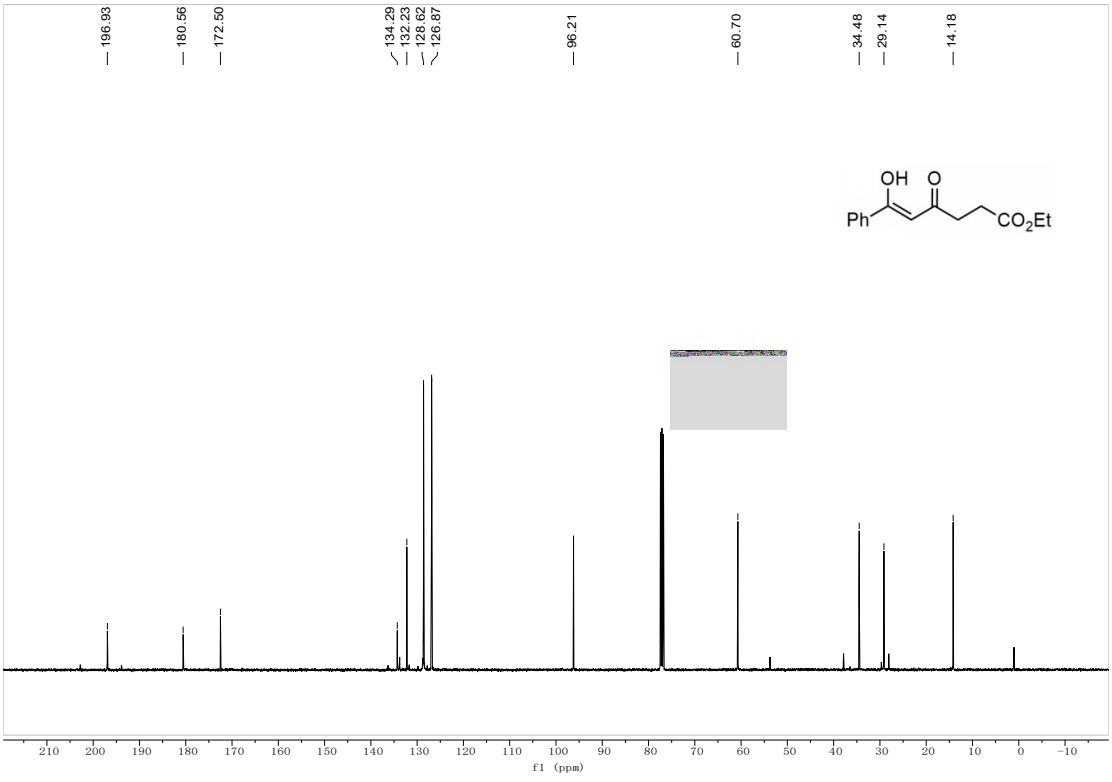
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **6**



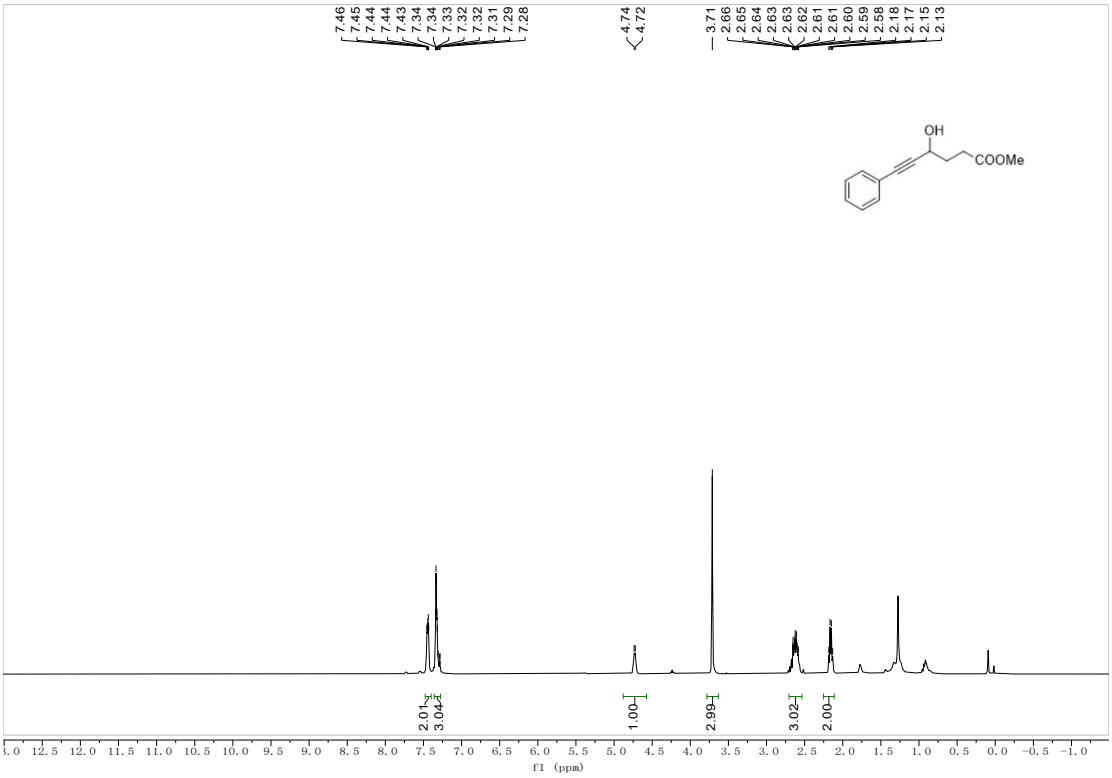
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **7**



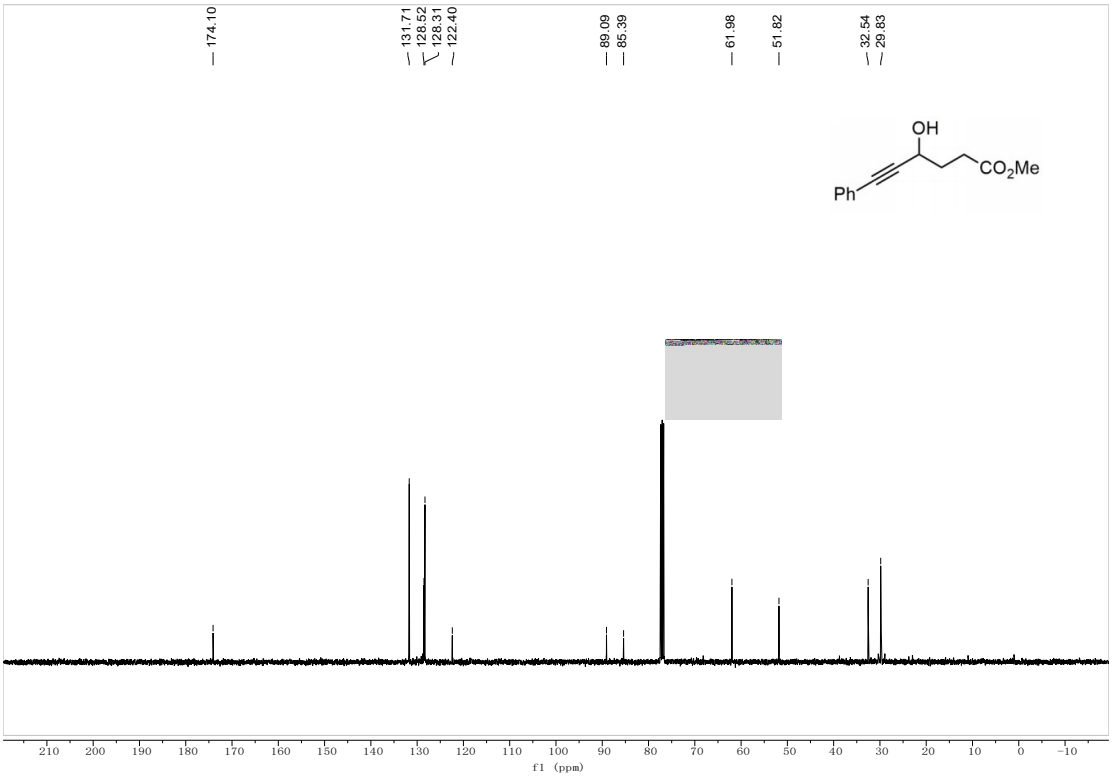
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **7**



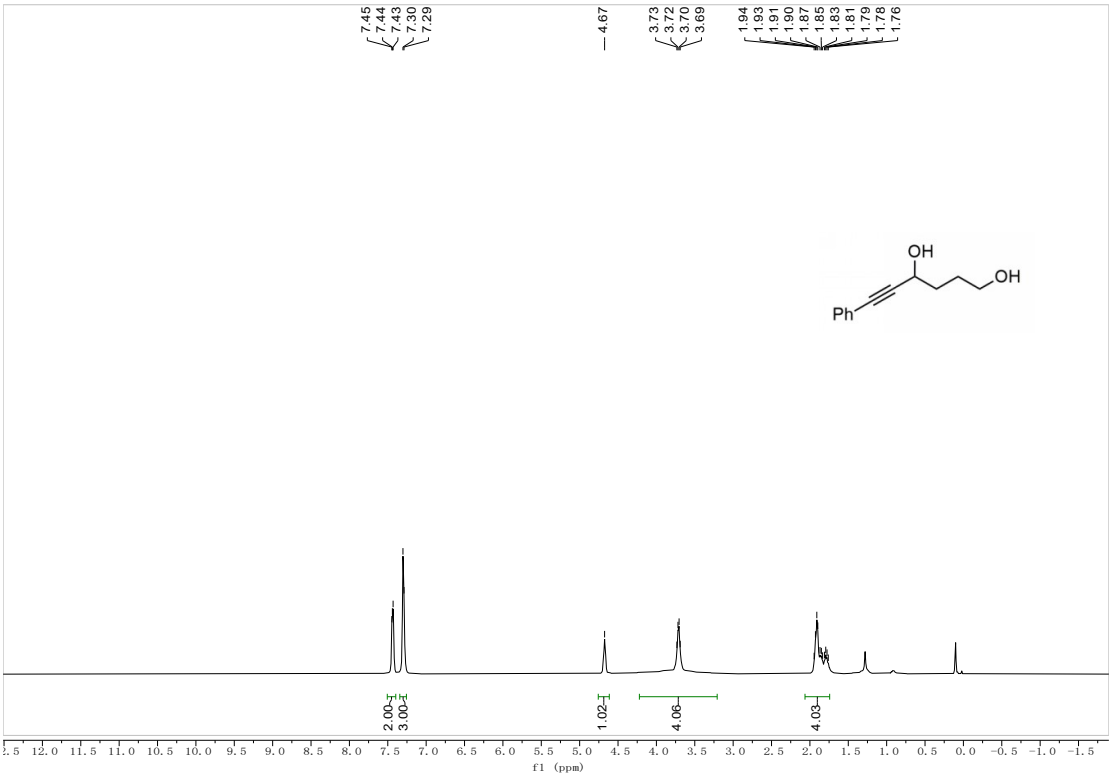
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **8**



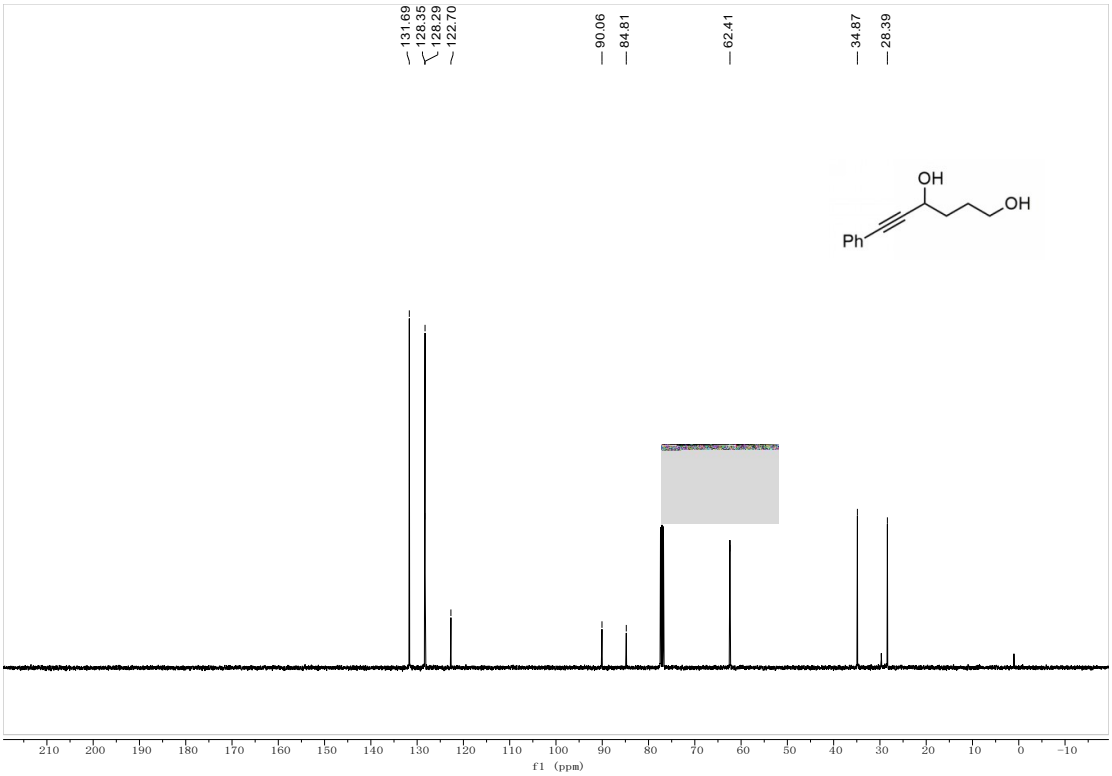
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **8**



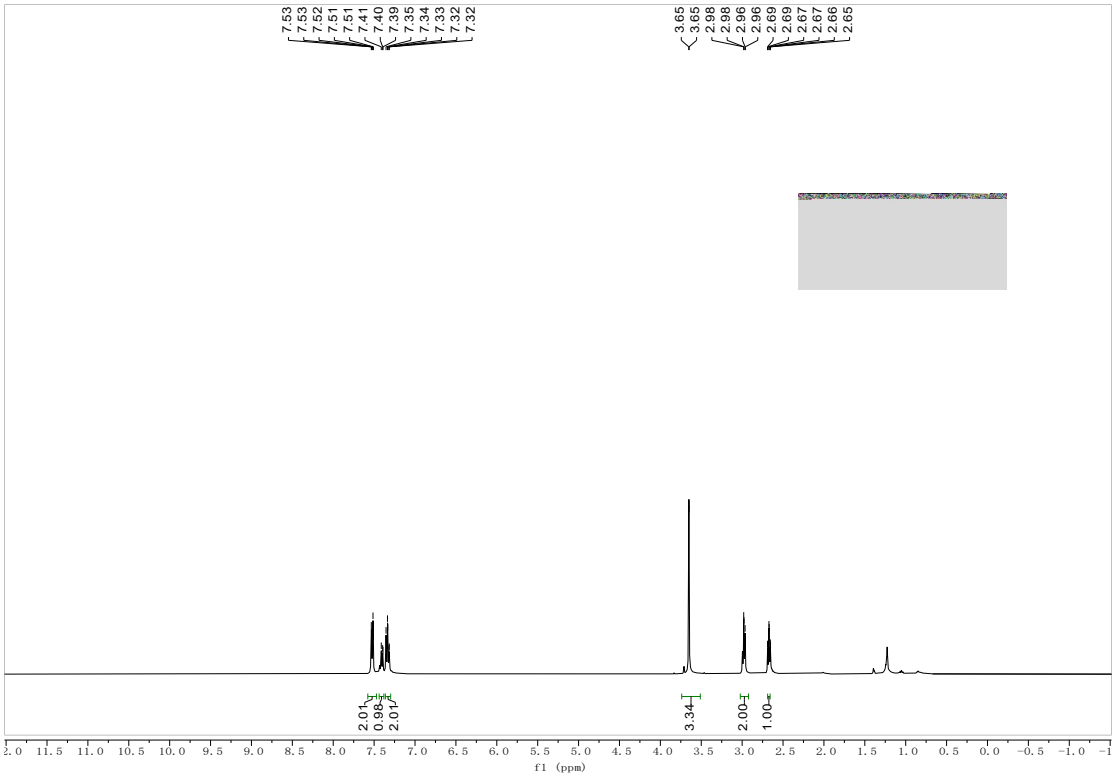
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **9**



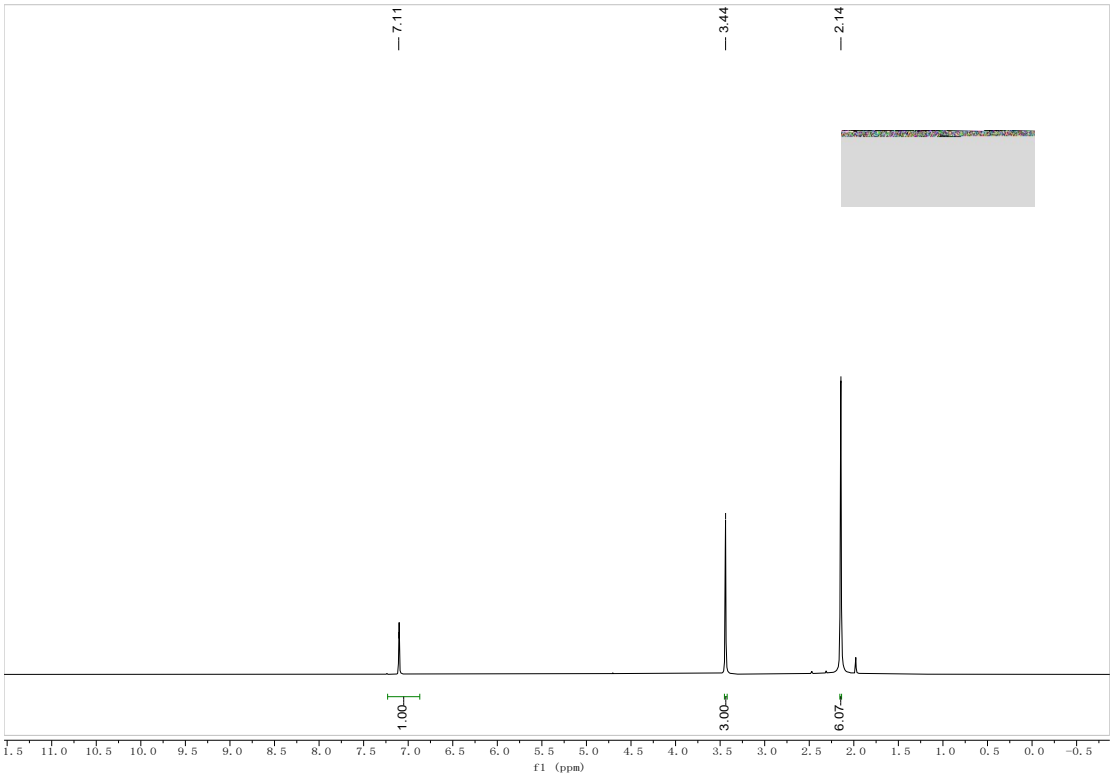
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **9**



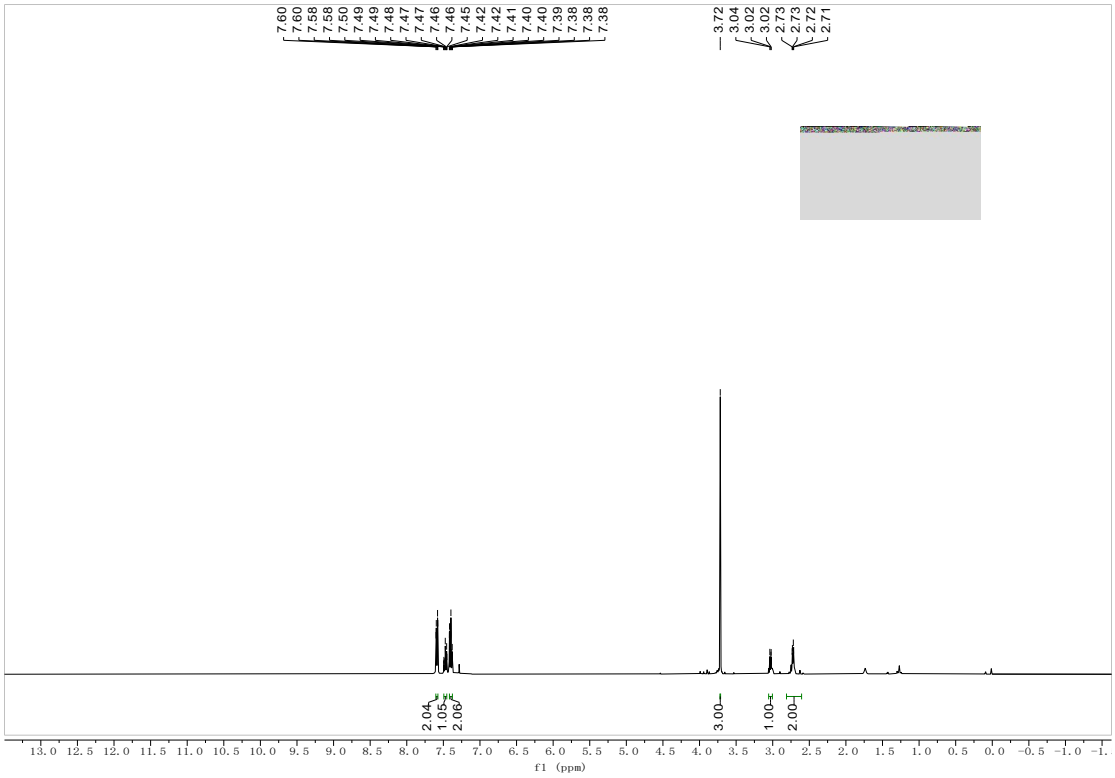
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **10**



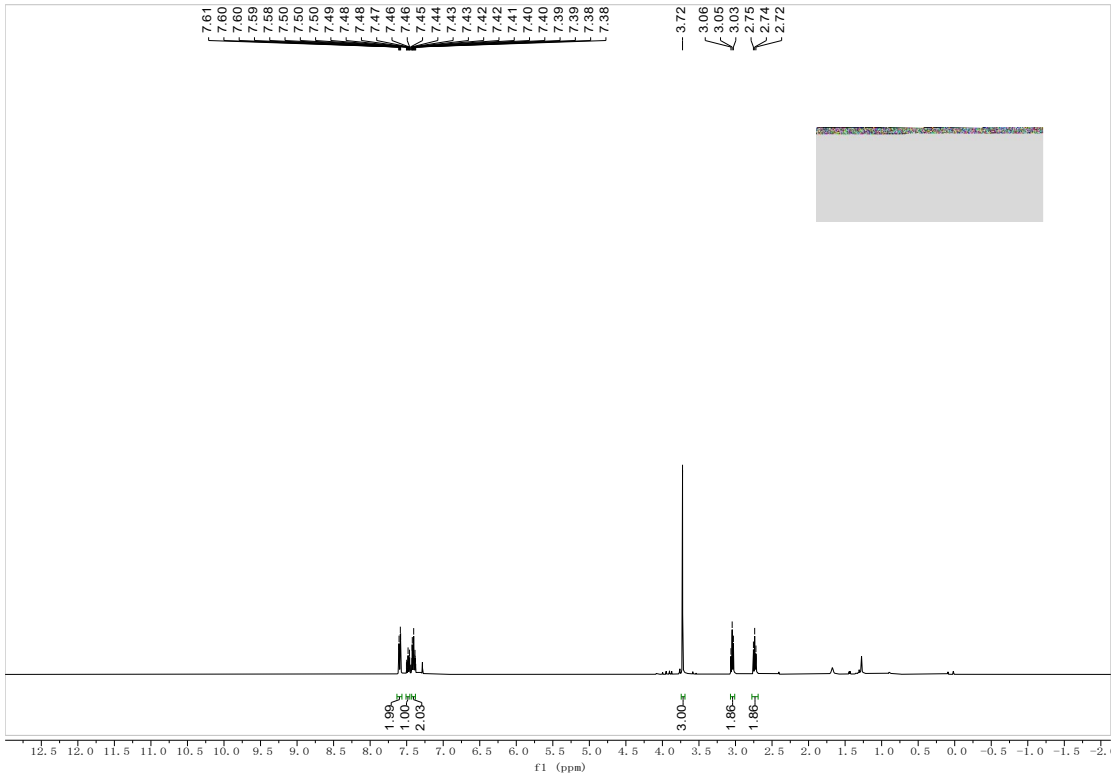
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **11**



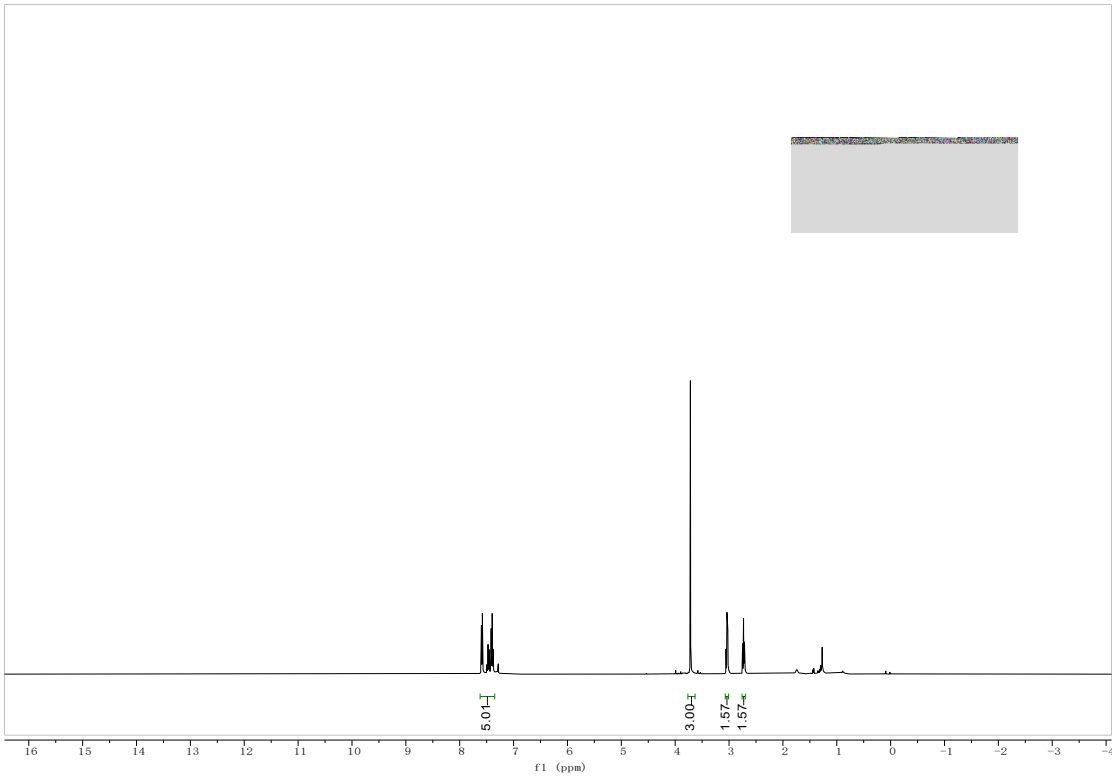
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **12**



^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **13**



^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **14**



^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **15**