

Supplementary Information

Umpolung Coupling of Pyridine-2-carboxaldehydes and Propargylic Carbonates via N-Heterocyclic Carbene/Palladium Synergetic Catalysis

Weiyang Bi,^{a,b} Yunhui Yang,^{a,b,c} Song Ye^{a,b} and Congyang Wang^{*a,b,c}

^aBeijing National Laboratory for Molecular Sciences, CAS Key Laboratory of Molecular Recognition and Function, CAS Research/Education Center for Excellence in Molecular Sciences, Institute of Chemistry, Chinese Academy of Sciences, Beijing, 100190, China

^bUniversity of Chinese Academy of Sciences, Beijing 100049, China

^cPhysical Science Laboratory, Huairou National Comprehensive Science Center, Beijing 101400, China

Email: wangcy@iccas.ac.cn

Table of Contents

1. General Information.....	S3
2. General Procedure for the Preparation of Propargylic Carbonates.....	S4
3. Optimization of Umpolung Coupling of Pyridine-2-carboxaldehydes and Propargylic Carbonates via N-Heterocyclic Carbene/Palladium Synergetic Catalysis.....	S6
4. Experimental Details of Umpolung Coupling of Pyridine-2-carboxaldehydes and Propargylic Carbonates via N-Heterocyclic Carbene/Palladium Synergetic Catalysis.....	S9
5. References	S28
6. NMR Spectra.....	S29

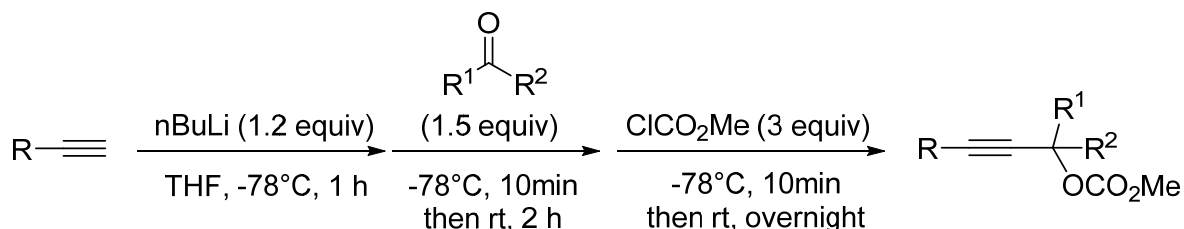
1. General Information

Unless otherwise noted, all reactions were carried out in over-dried reaction vessels with Teflon screw caps under nitrogen. All the chemicals were purchased commercially, and used without further purification. Anhydrous THF were distilled from sodium-benzophenone prior to use. All the pyridine carboxaldehydes **1a-1j**, catalysts and ligands were obtained from chemical suppliers and used as received. Flash column chromatography was performed on silica gel (200 - 300 mesh) with the indicated solvent mixtures. TLC analysis was performed on pre-coated, glass-backed silica gel plates and visualized with UV light.

The ^1H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded on a Bruker 400 AV or 500 AV spectrometers. Chemical shifts (δ) were reported as parts per million (ppm) downfield from tetramethylsilane and the following abbreviations were used to identify the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and all combinations thereof can be explained by their integral parts. The high resolution mass spectra (HRMS) were recorded on a Thermo Scientific Exactive spectrometer or a Bruker APEX IV FTMS mass spectrometer.

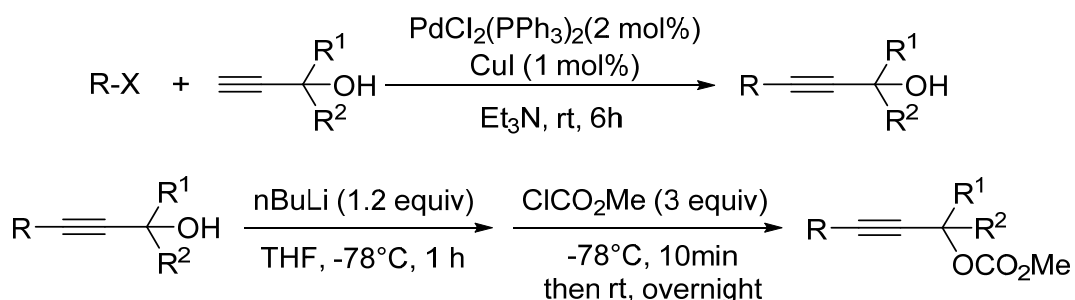
2. General Procedure for the Preparation of Propargylic Carbonates

Propargylic carbonates **2a**, **2c**, **2j**, **2l**, **2m**, **2p** were prepared according to literature procedure¹:



An oven-dried vial equipped with a magnetic stir bar was charged with alkyne (1 equiv.) in anhydrous THF (0.25 M) under nitrogen atmosphere. The solution was chilled to -78°C and *n*-butyllithium (2.5 M in hexane, 1.2 equiv.) was added dropwise. After lithiation for 1 h at -78°C , the solution was warmed to room temperature and stirred for 1 h. The solution was then chilled to -78°C , ketone (1.5 equiv.) was added dropwise, and the solution was warmed to room temperature and stirred for 2 h. The solution was then cooled to -78°C , methyl chloroformate (3 equiv.) was added dropwise, then the solution was warmed to room temperature and stirred overnight as monitored by TLC. The reaction mixture was quenched with saturated aqueous NH_4Cl . The reaction mixture was transferred to a separatory funnel, the organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic phases were washed with brine, dried over Na_2SO_4 , filtered, concentrated under reduced pressure, and purified by silica gel column chromatography to afford the product.

Propargylic carbonates **2b**, **2d-2g**, **2h**, **2i**, **2k**, **2n**, **2o** were prepared according to literature procedure²:



An oven-dried vial equipped with a magnetic stir bar was charged with copper(I) iodide (1 mol %), bis(triphenylphosphine)palladium(II) dichloride (2 mol %) and arylhalide (1.0 equiv.) in triethylamine (0.3 M) under nitrogen atmosphere. 2-methylbut-3-yn-2-ol (1.25 equiv.) was added

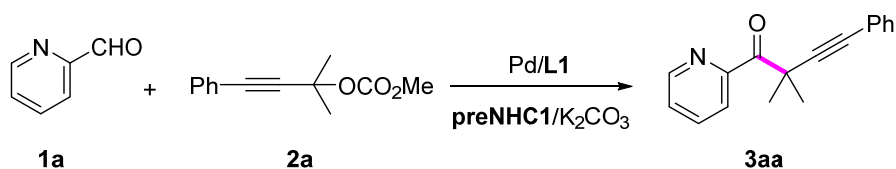
dropwise and the mixture was stirred at room temperature for 6 h. Upon completion as checked by TLC, the reaction mixture was quenched with saturated aqueous NH_4Cl . The reaction mixture was transferred to a separatory funnel, the organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic phases were washed with brine, dried over Na_2SO_4 , filtered, concentrated under reduced pressure, and purified by silica gel column chromatography to afford pure substituted propargylic alcohol product.

An oven-dried vial equipped with a magnetic stir bar was charged with propargylic alcohol (1 equiv.) in anhydrous THF (0.25 M) under nitrogen atmosphere. The solution was chilled to -78°C and n-butyllithium (2.5 M in hexane, 1.2 equiv.) was added dropwise. After 1 h, methyl chloroformate (3 equiv.) was added dropwise at -78°C , and the solution was stirred for 1 h at this temperature. Then the solution was warmed to room temperature and stirred overnight as monitored by TLC. The reaction mixture was quenched with saturated aqueous NH_4Cl . The reaction mixture was transferred to a separatory funnel, the organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic phases were washed with brine, dried over Na_2SO_4 , filtered, concentrated under reduced pressure, and purified by silica gel column chromatography to afford the product.

The analytical data of propargylic carbonates **2a-2p** are consistent with literatures¹⁻⁹.

3. Optimization of Umpolung Coupling of Pyridine-2-carboxaldehydes and Propargylic Carbonates via N-Heterocyclic Carbene/Palladium Synergetic Catalysis

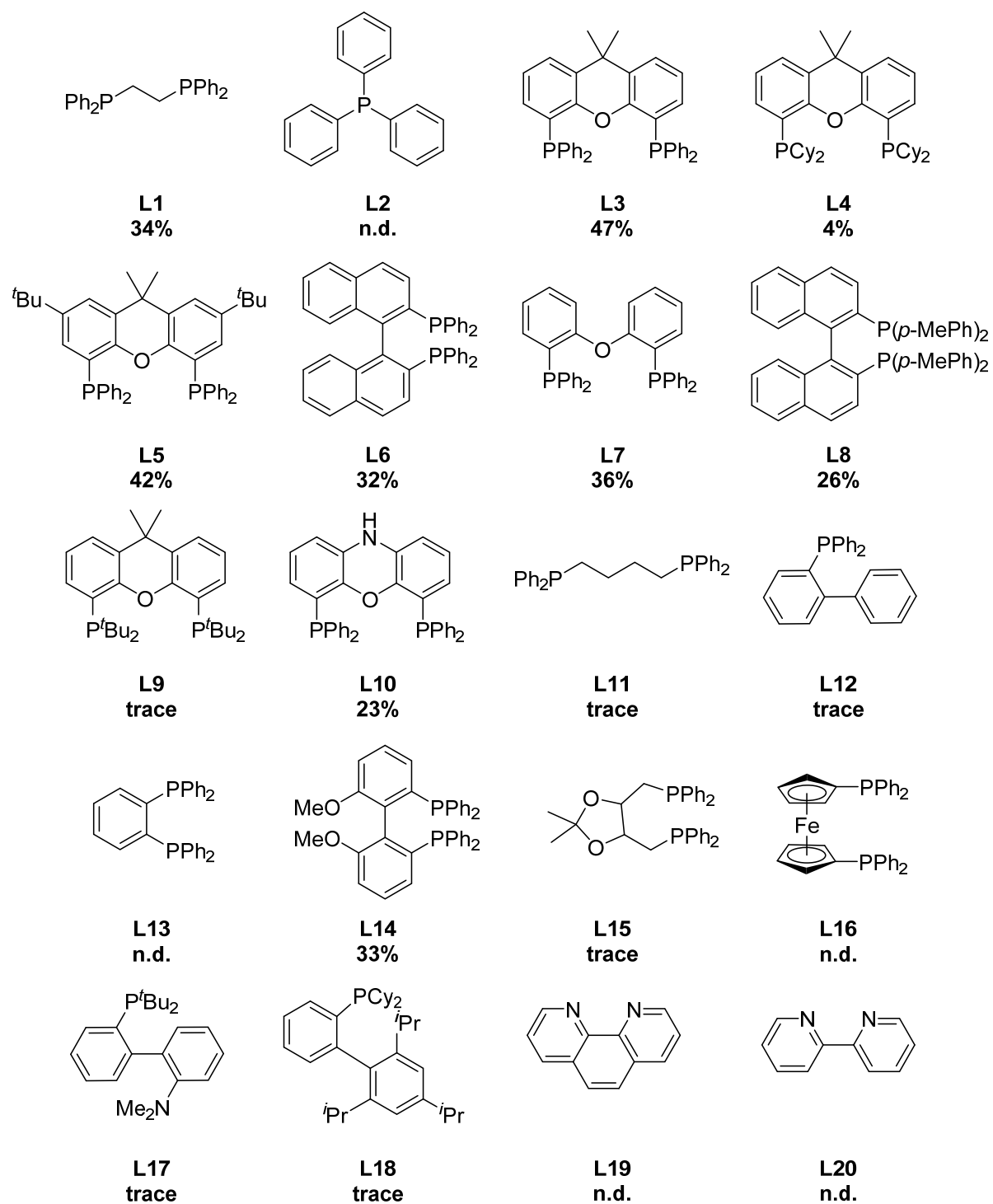
Table S1. Optimization of Pd catalysts^a



Entry	Pd	Yield(%) ^b
1	Pd(dba) ₂	34
2	Pd(TFA) ₂	7
3	PdCl ₂	21
4	Pd(CH ₃ CN) ₂ Cl ₂	15
5	Pd(acac) ₂	28
6	Pd ₂ (dba) ₃	28
7	Pd(OAc) ₂	6
8	Pd(PPh ₃) ₄	29
9	[Pd(π-allyl)Cl ₂] ₂	<1

^a Reaction conditions: **1a** (0.4 mmol, 2 equiv.), **2a** (0.2 mmol, 1 equiv.), Pd catalyst (0.02 mmol, 10 mol%), 1,2-bis(diphenylphosphino)ethane **L1** (0.02 mmol, 10 mol%), preNHC1 (0.04 mmol, 20 mol%), K₂CO₃ (0.4 mmol, 2 equiv.), THF (3.0 mL), 80 °C for 12 h under N₂ atmosphere. ^b Yields determined by ¹H NMR analysis with 1,3,5-trimethoxybenzene as an internal standard.

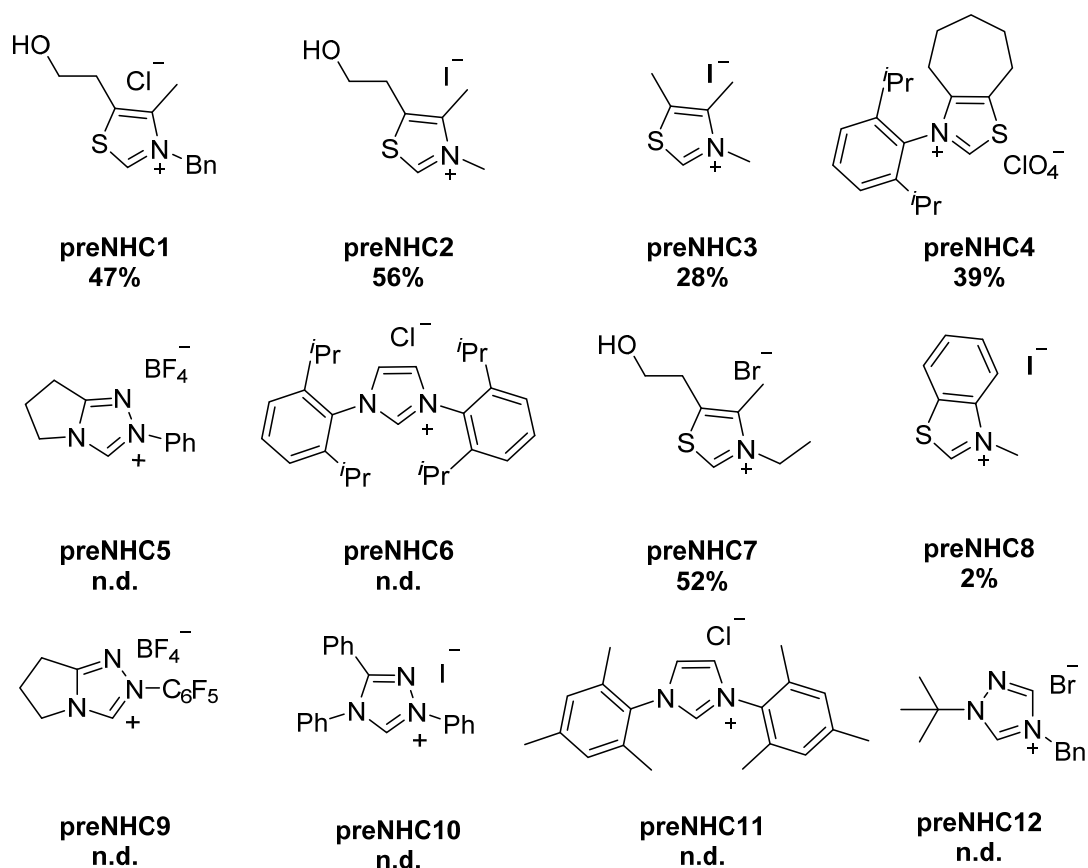
Table S2. Optimization of ligands^{a, b}



^a Reaction conditions: **1a** (0.4 mmol, 2 equiv.), **2a** (0.2 mmol, 1 equiv.), Pd(dba)₂ (0.02 mmol, 10 mol%), ligand (0.02 mmol, 10 mol%), **preNHC2** (0.04 mmol, 20 mol%), K₂CO₃ (0.4 mmol, 2

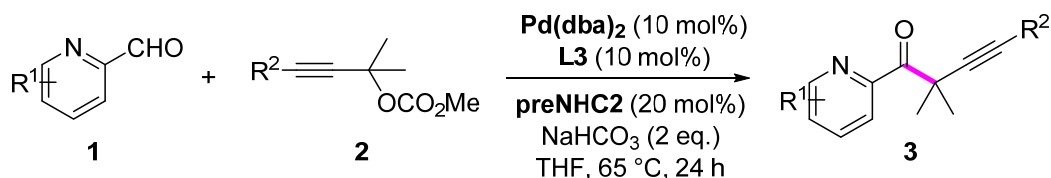
equiv.), THF (3.0 mL), 80 °C for 12 h under N₂ atmosphere. ^b Yields determined by ¹H NMR analysis with 1,3,5-trimethoxybenzene as an internal standard.

Table S3. Optimization of preNHCs^{a,b}



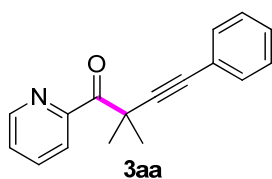
^a Reaction conditions: **1a** (0.4 mmol, 2 equiv.), **2a** (0.2 mmol, 1 equiv.), Pd(dba)₂ (0.02 mmol, 10 mol%), **L3** (0.02 mmol, 10 mol%), preNHC (0.04 mmol, 20 mol%), K₂CO₃ (0.4 mmol, 2 equiv.), THF (3.0 mL), 80 °C for 12 h under N₂ atmosphere. ^b Yields determined by ¹H NMR analysis with 1,3,5-trimethoxybenzene as an internal standard.

4. Experimental Details of Umpolung Coupling of Pyridine-2-carboxaldehydes and Propargylic Carbonates via N-Heterocyclic Carbene/Palladium Synergetic Catalysis



General procedure: To a 25 mL flame-dried Schlenk tube was added bis(dibenzylideneacetone)palladium [$\text{Pd}(\text{dba})_2$] (0.05 mmol, 10.0 mol%, 28.8 mg), 4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene (xantphos) **L3** (0.05 mmol, 10.0 mol%, 28.9 mg), 5-(2-Hydroxyethyl)-3,4-dimethylthiazolium iodide **preNHC2** (0.1 mmol, 20.0 mol%, 28.5 mg), sodium bicarbonate (1.0 mmol, 2 equiv., 84.0 mg) and THF (6 mL) sequentially under N_2 atmosphere. Then the corresponding *o*-azaaryl carboxaldehyde (**1**) (1.0 mmol, 2 equiv.) and propargylic carbonate (**2**) (0.5 mmol, 1 equiv.) were added. The tube was sealed and stirred at 65°C for 24 h. After completion, the reaction mixture was diluted with ethyl acetate (5.0 mL) and filtered through a short pad silica gel washing with ethyl acetate (20 mL). The filtrate was concentrated and purified by silica gel column chromatography to provide the product **3**.

2,2-dimethyl-4-phenyl-1-(pyridin-2-yl)but-3-yn-1-one (**3aa**)



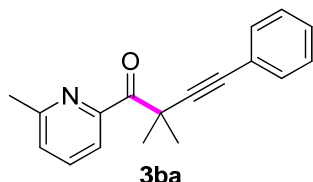
Prepared according to general procedure using pyridine-2-carboxaldehyde (**1a**) (107.0 mg, 1.0 mmol) and methyl (2-methyl-4-phenylbut-3-yn-2-yl) carbonate (**2a**) (109.0 mg, 0.5 mmol); flash column chromatography on silica gel (PE:EA = 50:1) provided **3aa** as a yellow oil (92.2 mg, 0.37 mmol, 74%).

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.72 (d, $J = 5.2$ Hz, 1H), 8.02 (d, $J = 7.6$ Hz, 1H), 7.81 (td, $J = 8.0, 2.0$ Hz, 1H), 7.41 (ddd, $J = 7.6, 4.8, 1.2$ Hz, 1H), 7.32 – 7.17 (m, 5H), 1.79 (s, 6H).

¹³C NMR (101 MHz, Chloroform-*d*) δ 199.9, 153.4, 148.3, 136.6, 131.6, 128.2, 127.8, 126.5, 123.9, 123.8, 93.6, 83.8, 42.9, 27.5.

HRMS (ESI): Calculated for C₁₇H₁₆ON⁺ ([M+H]⁺): 250.12264, Found: 250.12257.

2,2-dimethyl-1-(6-methylpyridin-2-yl)-4-phenylbut-3-yn-1-one (3ba)



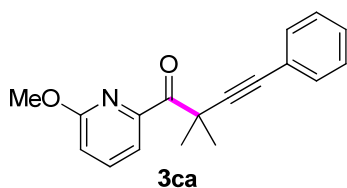
Prepared according to general procedure using 6-methylpicolinaldehyde (**1b**)(121.1 mg, 1.0 mmol) and methyl (2-methyl-4-phenylbut-3-yn-2-yl) carbonate (**2a**)(109.0 mg, 0.5 mmol); flash column chromatography on silica gel (PE:EA = 50:1) provided the **3ba** as a yellow oil (83.2 mg, 0.32 mmol, 63%).

¹H NMR (500 MHz, Chloroform-*d*) δ 7.82 (d, *J* = 8.0 Hz, 1H), 7.67 (t, *J* = 8.0 Hz, 1H), 7.31 – 7.21 (m, 6H), 2.62 (s, 3H), 1.78 (s, 6H).

¹³C NMR (126 MHz, Chloroform-*d*) δ 200.1, 157.2, 152.7, 136.7, 131.5, 128.2, 127.8, 126.1, 124.0, 120.9, 94.0, 83.5, 42.9, 27.6, 24.6.

HRMS (ESI): Calculated for C₁₈H₁₈ON⁺ ([M+H]⁺): 264.13829, Found: 284.13834.

1-(6-methoxypyridin-2-yl)-2,2-dimethyl-4-phenylbut-3-yn-1-one (3ca)



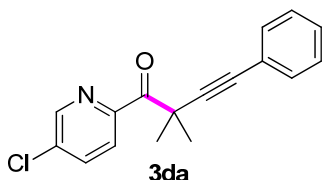
Prepared according to general procedure using 6-methoxypicolinaldehyde (**1c**) (137.1 mg, 1.0 mmol) and methyl (2-methyl-4-phenylbut-3-yn-2-yl) carbonate (**2a**) (109.0 mg, 0.5 mmol); flash column chromatography on silica gel (PE:EA = 30:1) provided the **3ca** as a yellow oil (88.1 mg, 0.32 mmol, 63%).

¹H NMR (500 MHz, Chloroform-*d*) δ 7.73 – 7.60 (m, 2H), 7.32 – 7.19 (m, 5H), 6.91 (dd, *J* = 8.0, 1.0 Hz, 1H), 4.01 (d, *J* = 1.3 Hz, 3H), 1.77 (s, 6H).

¹³C NMR (126 MHz, Chloroform-*d*) δ 199.0, 162.4, 150.1, 139.1, 131.5, 128.3, 127.8, 124.0, 117.3, 115.1, 94.0, 83.1, 54.1, 42.5, 27.4.

HRMS (ESI): Calculated for C₁₈H₁₈O₂N⁺ ([M+H]⁺): 280.13321, Found: 280.13339.

1-(5-chloropyridin-2-yl)-2,2-dimethyl-4-phenylbut-3-yn-1-one (**3da**)



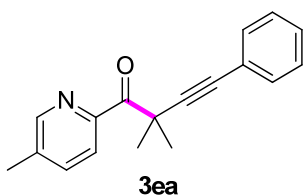
Prepared according to general procedure using 5-chloropicolinaldehyde (**1d**)(141.0 mg, 1.0 mmol) and methyl (2-methyl-4-phenylbut-3-yn-2-yl) carbonate (**2a**)(109.0 mg, 0.5 mmol); flash column chromatography on silica gel (PE:EA = 50:1) provided the **3da** as a yellow oil (101.9 mg, 0.36 mmol, 72%).

¹H NMR (400 MHz, Chloroform-*d*) δ 8.66 (d, *J* = 2.0 Hz, 1H), 8.01 (d, *J* = 8.4 Hz, 1H), 7.80 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.31 – 7.23 (m, 5H), 1.77 (s, 6H).

¹³C NMR (101 MHz, Chloroform-*d*) δ 198.6, 151.0, 147.2, 136.5, 135.4, 131.6, 128.3, 128.0, 125.1, 123.6, 93.2, 83.9, 42.7, 27.4.

HRMS (ESI): Calculated for C₁₇H₁₅ONCl⁺ ([M+H]⁺): 284.08367, Found: 284.08389.

2,2-dimethyl-1-(5-methylpyridin-2-yl)-4-phenylbut-3-yn-1-one (**3ea**)



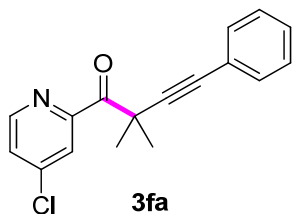
Prepared according to general procedure using 5-methylpicolinaldehyde (**1e**)(121.1 mg, 1.0 mmol) and methyl (2-methyl-4-phenylbut-3-yn-2-yl) carbonate (**2a**)(109.0 mg, 0.5 mmol); flash column chromatography on silica gel (PE:EA = 50:1) provided the **3ea** as a yellow oil (77.4 mg, 0.29 mmol, 59%).

¹H NMR (400 MHz, Chloroform-*d*) δ 8.53 (s, 1H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.59 (d, *J* = 7.6 Hz, 1H), 7.34 – 7.19 (m, 5H), 2.39 (s, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 199.4, 150.7, 148.8, 136.9, 136.9, 131.6, 128.2, 127.8, 123.9, 123.8, 93.8, 83.6, 42.7, 27.5, 18.9.

HRMS (ESI): Calculated for $\text{C}_{18}\text{H}_{18}\text{ON}^+$ ($[\text{M}+\text{H}]^+$): 264.13829, Found: 264.13864.

1-(4-chloropyridin-2-yl)-2,2-dimethyl-4-phenylbut-3-yn-1-one (3fa)



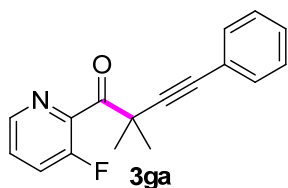
Prepared according to general procedure using 4-chloropicolinaldehyde (**1f**) (141.0 mg, 1.0 mmol) and methyl (2-methyl-4-phenylbut-3-yn-2-yl) carbonate (**2a**) (109.0 mg, 0.5 mmol); flash column chromatography on silica gel (PE:EA = 50:1) provided the **3fa** as a yellow oil (93.2 mg, 0.33 mmol, 66%).

^1H NMR (400 MHz, Chloroform-*d*) δ 8.61 (d, $J = 5.2$ Hz, 1H), 8.02 (d, $J = 2.0$ Hz, 1H), 7.43 (dd, $J = 5.2, 2.4$ Hz, 1H), 7.32 – 7.18 (m, 5H), 1.78 (s, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 198.7, 154.5, 149.2, 145.1, 131.6, 128.2, 128.0, 126.7, 124.4, 123.6, 93.1, 84.1, 42.9, 27.4.

HRMS (ESI): Calculated for $\text{C}_{17}\text{H}_{15}\text{ONCl}^+$ ($[\text{M}+\text{H}]^+$): 284.08367, Found: 284.08392.

1-(3-fluoropyridin-2-yl)-2,2-dimethyl-4-phenylbut-3-yn-1-one (3ga)



Prepared according to general procedure using 3-fluoropicolinaldehyde (**1g**) (125.1 mg, 1.0 mmol) and methyl (2-methyl-4-phenylbut-3-yn-2-yl) carbonate (**2a**) (109.0 mg, 0.5 mmol); flash column chromatography on silica gel (PE:EA = 50:1) provided the **3ga** as a yellow oil (67.8 mg, 0.25 mmol, 51%).

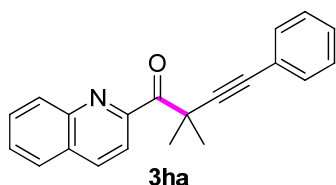
¹H NMR (500 MHz, Chloroform-*d*) δ 8.47 (d, *J* = 4.0 Hz, 1H), 7.54 – 7.47 (m, 1H), 7.43 – 7.39 (m, 1H), 7.26 – 7.15 (m, 5H), 1.75 (s, 6H).

¹⁹F NMR (377 MHz, Chloroform-*d*) δ -121.8.

¹³C NMR (126 MHz, Chloroform-*d*) δ 200.1 (d, *J* = 4.5 Hz), 157.1(d, *J* = 266.1 Hz), 144.6 (d, *J* = 12.9 Hz), 144.2 (d, *J* = 5.0 Hz), 131.5, 128.2, 128.0, 126.8 (d, *J* = 4.3 Hz), 124.4 (d, *J* = 19.0 Hz), 123.3, 92.2, 84.3, 44.3, 27.2.

HRMS (ESI): Calculated for C₁₇H₁₅ONF⁺ ([M+H]⁺): 268.11322, Found: 268.11340.

2,2-dimethyl-4-phenyl-1-(quinolin-2-yl)but-3-yn-1-one (3ha)



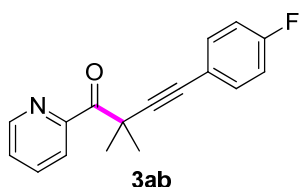
Prepared according to general procedure using quinoline-2-carbaldehyde (**1h**) (157.1 mg, 1.0 mmol) and methyl (2-methyl-4-phenylbut-3-yn-2-yl) carbonate (**2a**) (109.0 mg, 0.5 mmol); flash column chromatography on silica gel (PE:EA = 50:1) provided the **3ha** as a yellow oil (79.4 mg, 0.27 mmol, 53%).

¹H NMR (500 MHz, Chloroform-*d*) δ 8.24 (t, *J* = 8.5 Hz, 2H), 8.09 (d, *J* = 8.5 Hz, 1H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.77 (t, *J* = 8.0 Hz, 1H), 7.64 (t, *J* = 7.5 Hz, 1H), 1.89 (s, 6H).

¹³C NMR (126 MHz, Chloroform-*d*) δ 200.3, 152.5, 146.7, 136.6, 131.6, 130.8, 130.0, 129.2, 128.6, 128.2, 127.7, 127.7, 123.9, 120.1, 93.9, 83.6, 43.1, 27.8.

HRMS (ESI): Calculated for C₂₁H₁₈ON⁺ ([M+H]⁺): 300.13829, Found: 300.13843.

4-(4-fluorophenyl)-2,2-dimethyl-1-(pyridin-2-yl)but-3-yn-1-one (3ab)



Prepared according to general procedure using pyridine-2-carboxaldehyde (**1a**) (107.0 mg, 1.0 mmol) and 4-(4-fluorophenyl)-2-methylbut-3-yn-2-yl methyl carbonate (**2b**) (118.0 mg, 0.5

mmol); flash column chromatography on silica gel (PE:EA = 50:1) provided the **3ab** as a yellow oil (93.4 mg, 0.35 mmol, 70%).

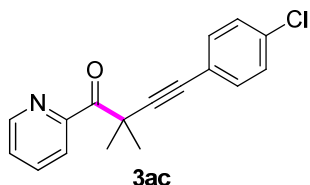
¹H NMR (400 MHz, Chloroform-*d*) δ 8.71 (d, $J = 4.0$ Hz, 1H), 8.02 (d, $J = 7.6$ Hz, 1H), 7.82 (t, $J = 7.6$ Hz, 1H), 7.49 – 7.38 (m, 1H), 7.32 – 7.18 (m, 2H), 6.92 (t, $J = 8.8$ Hz, 2H), 1.78 (s, 6H).

¹⁹F NMR (377 MHz, Chloroform-*d*) δ -112.0.

¹³C NMR (101 MHz, Chloroform-*d*) δ 199.7, 162.3 (d, $J = 249.4$ Hz), 161.1, 153.3, 148.2, 136.7, 133.4 (d, $J = 8.3$ Hz), 126.6, 124.0, 119.9, 115.4 (d, $J = 22.1$ Hz), 93.3, 82.7, 42.8, 27.4.

HRMS (ESI): Calculated for C₁₇H₁₅ONF⁺ ([M+H]⁺): 268.11322, Found: 268.11322.

4-(4-chlorophenyl)-2,2-dimethyl-1-(pyridin-2-yl)but-3-yn-1-one (**3ac**)



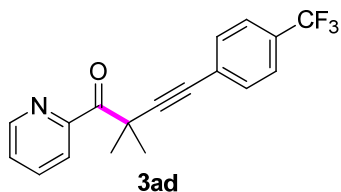
Prepared according to general procedure using pyridine-2-carboxaldehyde (**1a**) (107.0 mg, 1.0 mmol) and 4-(4-chlorophenyl)-2-methylbut-3-yn-2-yl methyl carbonate (**2c**) (126.0 mg, 0.5 mmol); flash column chromatography on silica gel (PE:EA = 50:1) provided the **3ac** as a yellow oil (86.2 mg, 0.30 mmol, 61%).

¹H NMR (400 MHz, Chloroform-*d*) δ 8.71 (s, 1H), 8.02 (d, $J = 7.6$ Hz, 1H), 7.82 (t, $J = 7.6$ Hz, 1H), 7.50 – 7.39 (m, 1H), 7.20 (s, 4H), 1.78 (s, 6H).

¹³C NMR (101 MHz, Chloroform-*d*) δ 199.6, 153.2, 148.2, 136.7, 133.8, 132.8, 128.5, 126.6, 124.0, 122.3, 94.7, 82.7, 42.9, 27.4.

HRMS (ESI): Calculated for C₁₇H₁₅ONCl⁺ ([M+H]⁺): 284.08367, Found: 284.08371.

2,2-dimethyl-1-(pyridin-2-yl)-4-(4-(trifluoromethyl)phenyl)but-3-yn-1-one (**3ad**)



Prepared according to general procedure using pyridine-2-carboxaldehyde (**1a**)(107.0 mg, 1.0 mmol) and methyl (2-methyl-4-(4-(trifluoromethyl)phenyl)but-3-yn-2-yl) carbonate (**2d**)(143.0 mg, 0.5 mmol); flash column chromatography on silica gel (PE:EA = 50:1) provided the **3ad** as a yellow oil (95.5 mg, 0.30 mmol, 60%).

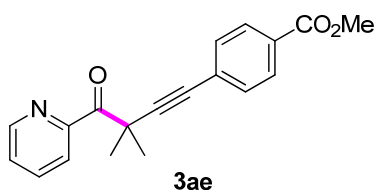
¹H NMR (400 MHz, Chloroform-*d*) δ 8.71 (d, J = 4.4 Hz, 1H), 8.03 (d, J = 7.6 Hz, 1H), 7.83 (td, J = 8.0, 1.6 Hz, 1H), 7.52 – 7.41 (m, 3H), 7.37 (d, J = 8.0 Hz, 2H), 1.80 (s, 6H).

¹⁹F NMR (377 MHz, Chloroform-*d*) δ -62.8.

¹³C NMR (101 MHz, Chloroform-*d*) δ 199.4, 153.1, 148.2, 136.8, 131.8, 127.7, 126.7, 125.5, 125.1 (q, J = 3.7 Hz), 124.0, 96.4, 82.6, 42.9, 27.3.

HRMS (ESI): Calculated for C₁₈H₁₅ONF₃⁺ ([M+H]⁺): 318.11003, Found: 318.10989.

methyl 4-(3,3-dimethyl-4-oxo-4-(pyridin-2-yl)but-1-yn-1-yl)benzoate (3ae**)**



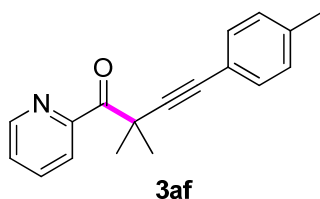
Prepared according to general procedure using pyridine-2-carboxaldehyde (**1a**)(107.0 mg, 1.0 mmol) and methyl 4-(3-((methoxycarbonyl)oxy)-3-methylbut-1-yn-1-yl)benzoate (**2e**)(138.1 mg, 0.5 mmol); flash column chromatography on silica gel (PE:EA = 10:1) provided the **3ae** as a yellow oil (69.1 mg, 0.22 mmol, 44%).

¹H NMR (400 MHz, Chloroform-*d*) δ 8.71 (d, J = 4.4 Hz, 1H), 8.03 (d, J = 7.6 Hz, 1H), 7.90 (d, J = 8.4 Hz, 2H), 7.83 (td, J = 7.6, 1.6 Hz, 1H), 7.45 – 7.42 (m, 1H), 7.33 (d, J = 8.4 Hz, 2H), 3.89 (s, 3H), 1.80 (s, 6H).

¹³C NMR (101 MHz, Chloroform-*d*) δ 199.4, 166.7, 153.1, 148.2, 136.8, 131.5, 129.4, 129.2, 128.6, 126.7, 124.0, 97.0, 83.2, 52.3, 42.9, 27.3.

HRMS (ESI): Calculated for C₁₉H₁₈O₃N⁺ ([M+H]⁺): 308.12812, Found: 308.12817.

2,2-dimethyl-1-(pyridin-2-yl)-4-(p-tolyl)but-3-yn-1-one (3af**)**



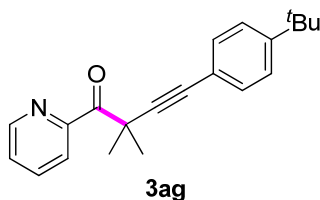
Prepared according to general procedure using pyridine-2-carboxaldehyde (**1a**)(107.0 mg, 1.0 mmol) and methyl (2-methyl-4-(p-tolyl)but-3-yn-2-yl) carbonate (**2f**)(116.1 mg, 0.5 mmol); flash column chromatography on silica gel (PE:EA = 50:1) provided the **3af** as a yellow oil (86.9 mg, 0.33 mmol, 66%).

¹H NMR (400 MHz, Chloroform-*d*) ¹H NMR (400 MHz, Chloroform-*d*) δ 8.70 (d, *J* = 4.4 Hz, 1H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.79 (t, *J* = 8.0 Hz, 1H), 7.44 – 7.35 (m, 1H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.02 (d, *J* = 7.6 Hz, 2H), 2.29 (s, 3H), 1.78 (s, 6H).

¹³C NMR (101 MHz, Chloroform-*d*) δ 199.9, 153.4, 148.2, 137.8, 136.6, 131.4, 128.9, 126.4, 123.9, 120.7, 92.8, 83.9, 42.8, 27.5, 21.5.

HRMS (ESI): Calculated for C₁₈H₁₈ON⁺ ([M+H]⁺): 264.13829, Found: 264.13849.

4-(4-(tert-butyl)phenyl)-2,2-dimethyl-1-(pyridin-2-yl)but-3-yn-1-one (**3ag**)



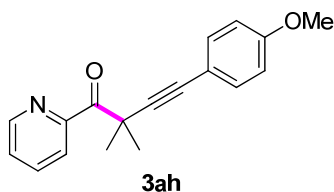
Prepared according to general procedure using pyridine-2-carboxaldehyde (**1a**)(107.0 mg, 1.0 mmol) and 4-(4-(tert-butyl)phenyl)-2-methylbut-3-yn-2-yl methyl carbonate (**2g**)(137.1 mg, 0.5 mmol); flash column chromatography on silica gel (PE:EA = 50:1) provided the **3ag** as a yellow oil (88.0 mg, 0.29 mmol, 58%).

¹H NMR (400 MHz, Chloroform-*d*) δ 8.71 (d, *J* = 4.4 Hz, 1H), 8.02 (d, *J* = 7.6 Hz, 1H), 7.80 (td, *J* = 8.0, 2.0 Hz, 1H), 7.40 (dd, *J* = 7.6, 4.8 Hz, 1H), 7.26 – 7.20 (m, 4H), 1.78 (s, 6H), 1.26 (s, 9H).

¹³C NMR (101 MHz, Chloroform-*d*) δ 200.0, 153.4, 151.0, 148.3, 136.6, 131.3, 126.4, 125.2, 123.9, 120.7, 92.9, 83.9, 42.8, 34.8, 31.3, 27.5.

HRMS (ESI): Calculated for $C_{21}H_{24}ON^+$ ($[M+H]^+$): 306.18524, Found: 306.18539.

4-(4-methoxyphenyl)-2,2-dimethyl-1-(pyridin-2-yl)but-3-yn-1-one (3ah)



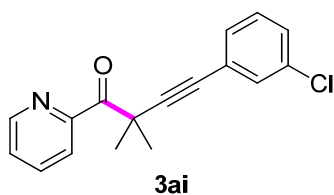
Prepared according to general procedure using pyridine-2-carboxaldehyde (**1a**)(107.0 mg, 1.0 mmol) and 4-(4-methoxyphenyl)-2-methylbut-3-yn-2-yl methyl carbonate (**2h**)(124.1 mg, 0.5 mmol); flash column chromatography on silica gel (PE:EA = 30:1) provided the **3ah** as a yellow oil(98.8 mg, 0.36 mmol, 72%).

1H NMR (400 MHz, Chloroform-*d*) δ 8.72 (d, J = 4.0 Hz, 1H), 8.03 (d, J = 7.6 Hz, 1H), 7.81 (t, J = 7.6 Hz, 1H), 7.48 – 7.34 (m, 1H), 7.21 (d, J = 8.8 Hz, 2H), 6.76 (d, J = 8.8 Hz, 2H), 3.77 (s, 3H), 1.78 (s, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 200.0, 159.3, 153.5, 148.3, 136.6, 133.0, 126.4, 124.0, 116.0, 113.8, 92.0, 83.6, 55.4, 42.8, 27.5.

HRMS (ESI): Calculated for $C_{18}H_{18}O_2N^+$ ($[M+H]^+$): 280.13321, Found: 280.13348.

4-(3-chlorophenyl)-2,2-dimethyl-1-(pyridin-2-yl)but-3-yn-1-one (3ai)



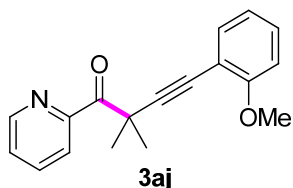
Prepared according to general procedure using pyridine-2-carboxaldehyde (**1a**)(107.0 mg, 1.0 mmol) and 4-(3-chlorophenyl)-2-methylbut-3-yn-2-yl methyl carbonate (**2i**)(126.0 mg, 0.5 mmol); flash column chromatography on silica gel (PE:EA = 50:1) provided the **3ai** as a yellow oil(75.1 mg, 0.27 mmol, 53%).

1H NMR (500 MHz, Chloroform-*d*) δ 8.72 (d, J = 4.0 Hz, 1H), 8.02 (d, J = 8.0 Hz, 1H), 7.83 (t, J = 8.0 Hz, 1H), 7.50 – 7.40 (m, 1H), 7.27 (s, 1H), 7.24 – 7.11 (m, 3H), 1.78 (s, 6H).

¹³C NMR (126 MHz, Chloroform-*d*) δ 199.5, 153.1, 148.3, 136.7, 134.0, 131.5, 129.7, 129.4, 128.1, 126.7, 125.5, 124.0, 95.0, 82.4, 42.8, 27.4.

HRMS (ESI): Calculated for C₁₇H₁₅ONCl⁺ ([M+H]⁺): 284.08367, Found: 284.08380.

4-(2-methoxyphenyl)-2,2-dimethyl-1-(pyridin-2-yl)but-3-yn-1-one (3aj)



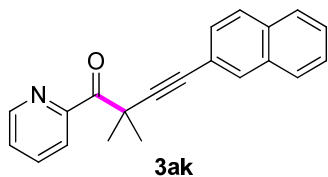
Prepared according to general procedure using pyridine-2-carboxaldehyde (**1a**)(107.0 mg, 1.0 mmol) and 4-(2-methoxyphenyl)-2-methylbut-3-yn-2-yl methyl carbonate (**2j**)(124.1 mg, 0.5 mmol); flash column chromatography on silica gel (PE:EA = 30:1) provided the **3aa** as a yellow oil(102.0 mg, 0.37 mmol, 73%).

¹H NMR (400 MHz, Chloroform-*d*) δ 8.73 (s, 1H), 8.09 (s, 1H), 7.80 (s, 1H), 7.42 (s, 1H), 7.31 – 7.14 (m, 2H), 6.90 – 6.71 (m, 2H), 3.74 (s, 3H), 1.81 (s, 6H).

¹³C NMR (101 MHz, Chloroform-*d*) δ 200.0, 160.1, 153.6, 148.4, 136.6, 133.6, 129.3, 126.3, 124.1, 120.4, 113.0, 110.9, 97.5, 80.2, 55.9, 43.2, 27.5.

HRMS (ESI): Calculated for C₁₈H₁₈O₂N⁺ ([M+H]⁺): 280.13321, Found: 280.13339.

2,2-dimethyl-4-(naphthalen-2-yl)-1-(pyridin-2-yl)but-3-yn-1-one (3ak)



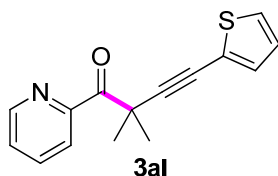
Prepared according to general procedure using pyridine-2-carboxaldehyde (**1a**)(107.0 mg, 1.0 mmol) and methyl (2-methyl-4-(naphthalen-2-yl)but-3-yn-2-yl) carbonate (**2k**)(134.1 mg, 0.5 mmol); flash column chromatography on silica gel (PE:EA = 50:1) provided the **3ak** as a yellow oil (88.2 mg, 0.29 mmol, 59%).

¹H NMR (500 MHz, Chloroform-*d*) δ 8.74 (d, *J* = 4.0 Hz, 1H), 8.06 (d, *J* = 8.0 Hz, 1H), 7.83 – 7.67 (m, 5H), 7.45 – 7.40 (m, 3H), 7.33 (dt, *J* = 8.5, 2.0 Hz, 1H), 1.84 (s, 6H).

¹³C NMR (126 MHz, Chloroform-*d*) δ 199.8, 153.3, 148.3, 136.7, 133.0, 132.6, 131.2, 128.7, 127.8, 126.5, 124.0, 121.1, 94.0, 84.1, 42.9, 27.5.

HRMS (ESI): Calculated for C₂₁H₁₈ON⁺ ([M+H]⁺): 300.13829, Found: 300.13855.

2,2-dimethyl-1-(pyridin-2-yl)-4-(thiophen-2-yl)but-3-yn-1-one (**3al**)



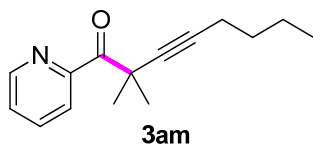
Prepared according to general procedure using pyridine-2-carboxaldehyde (**1a**) (107.0 mg, 1.0 mmol) and methyl (2-methyl-4-(thiophen-2-yl)but-3-yn-2-yl) carbonate (**2l**) (112.0 mg, 0.5 mmol); flash column chromatography on silica gel (PE:EA = 50:1) provided the **3al** as a yellow oil (77.7 mg, 0.30 mmol, 61%).

¹H NMR (400 MHz, Chloroform-*d*) δ 8.73 (d, *J* = 4.0 Hz, 1H), 8.03 (d, *J* = 8.0 Hz, 1H), 7.83 (t, *J* = 7.6 Hz, 1H), 7.50 – 7.40 (m, 1H), 7.15 (d, *J* = 5.2 Hz, 1H), 7.04 (d, *J* = 3.6 Hz, 1H), 6.93 – 6.84 (m, 1H), 1.78 (s, 6H).

¹³C NMR (101 MHz, Chloroform-*d*) δ 199.4, 153.1, 148.2, 136.8, 131.3, 126.8, 126.6, 126.5, 124.0, 97.5, 43.0, 27.3.

HRMS (ESI): Calculated for C₁₅H₁₄ONS⁺ ([M+H]⁺): 256.07906, Found: 256.07925.

2,2-dimethyl-1-(pyridin-2-yl)oct-3-yn-1-one (**3am**)



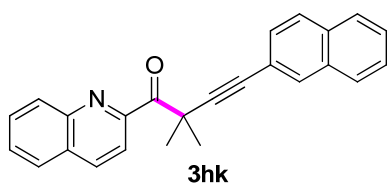
Prepared according to general procedure using pyridine-2-carboxaldehyde (**1a**) (107.0 mg, 1.0 mmol) and methyl (2-methyloct-3-yn-2-yl) carbonate (**2m**) (99.1 mg, 0.5 mmol); flash column chromatography on silica gel (PE:EA = 50:1) provided the **3am** as a yellow oil (47.0 mg, 0.21 mmol, 41%).

^1H NMR (500 MHz, Chloroform-*d*) δ 8.74 – 8.65 (m, 1H), 7.98 (d, J = 8.0 Hz, 1H), 7.85 – 7.69 (m, 1H), 7.42 – 7.37 (m, 1H), 2.10 (td, J = 7.0, 2.5 Hz, 2H), 1.68 (s, 6H), 1.39 – 1.29 (m, 2H), 1.29 – 1.16 (m, 2H), 0.79 (td, J = 7.0, 2.5 Hz, 3H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 200.6, 153.8, 148.2, 136.5, 126.2, 123.9, 84.2, 84.0, 42.4, 30.9, 27.7, 21.8, 18.7, 13.7.

HRMS (ESI): Calculated for $\text{C}_{15}\text{H}_{20}\text{ON}^+$ ($[\text{M}+\text{H}]^+$): 230.15394, Found: 230.15425.

2,2-dimethyl-4-(naphthalen-2-yl)-1-(quinolin-2-yl)but-3-yn-1-one (3hk)

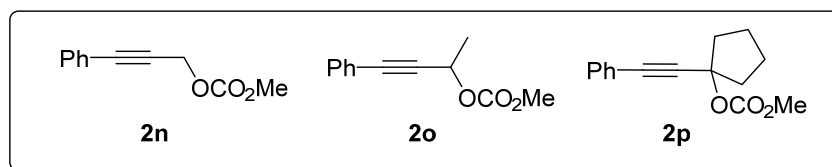


Prepared according to general procedure using quinoline-2-carbaldehyde (**1h**) (157.1 mg, 1.0 mmol) and methyl (2-methyl-4-(naphthalen-2-yl)but-3-yn-2-yl) carbonate (**2k**) (134.1 mg, 0.5 mmol); flash column chromatography on silica gel (PE:EA = 50:1) provided the **3hk** as a yellow solid (134.4 mg, 0.38 mmol, 77%).

^1H NMR (400 MHz, Chloroform-*d*) δ 8.28 (t, J = 8.0 Hz, 2H), 8.11 (d, J = 8.8 Hz, 1H), 7.86 (d, J = 8.4 Hz, 1H), 7.82 – 7.70 (m, 3H), 7.67 – 7.60 (m, 3H), 7.41 (dd, J = 5.6, 3.6 Hz, 2H), 7.30 (d, J = 8.4 Hz, 1H), 1.92 (s, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 200.2, 152.6, 146.7, 136.8, 133.1, 132.6, 131.2, 130.8, 130.1, 129.2, 128.7, 128.6, 127.8, 127.7, 127.7, 126.4, 126.4, 121.2, 120.1, 94.3, 84.1, 43.3, 27.8.

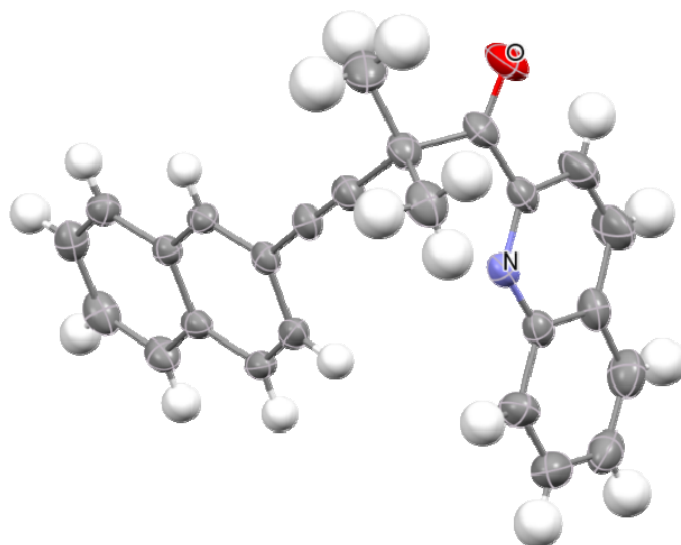
HRMS (ESI): Calculated for $\text{C}_{25}\text{H}_{20}\text{ON}$ ($[\text{M}+\text{H}]^+$): 350.15394, Found: 350.15396.



Scheme S1 Unsuccessful substrates

X-ray Structure and Data of Compound **3hk**

The crystal suitable for X-ray analysis was prepared by slow evaporation of the solvent of the solution of **3hk** in petroleum ether/CH₂Cl₂ at 4°C. The absolute structure of **3hk** was determined with the Flack parameter of 0.001.



Scheme S2 X-ray Crystal Structure of **3hk**

Table S4 Crystal data and structure refinement for **3hk**.

Identification code	MX8850
Empirical formula	C ₂₅ H ₁₉ NO
Formula weight	349.41
Temperature/K	170.00(10)
Crystal system	tetragonal
Space group	P42/n
a/Å	21.9496(3)
b/Å	21.9496(3)
c/Å	7.9389(2)

$\alpha/^\circ$ 90
 $\beta/^\circ$ 90
 $\gamma/^\circ$ 90
 Volume/ \AA^3 3824.84(14)
 Z 8
 $\rho_{\text{calc}}/\text{cm}^3$ 1.214
 μ/mm^{-1} 0.074
 F(000) 1472.0
 Crystal size/ mm^3 $0.41 \times 0.32 \times 0.28$
 Radiation $\text{MoK}\alpha$ ($\lambda = 0.71073$)
 2Θ range for data collection/ $^\circ$ 3.712 to 61.286
 Index ranges $-22 \leq h \leq 31, -30 \leq k \leq 22, -10 \leq l \leq 10$
 Reflections collected 31950
 Independent reflections 5346 [Rint = 0.0176, Rsigma = 0.0136]
 Data/restraints/parameters 5346/0/246
 Goodness-of-fit on F2 1.038
 Final R indexes [$I \geq 2\sigma(I)$] R1 = 0.0438, wR2 = 0.1135
 Final R indexes [all data] R1 = 0.0533, wR2 = 0.1189
 Largest diff. peak/hole / $e \text{\AA}^{-3}$ 0.22/-0.17

Table S5 Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for **3hk**.

Ueq is defined as 1/3 of the trace of the orthogonalised UIJ tensor.

Atom	x	y	z	U(eq)
------	---	---	---	-------

O1	4148.2(5)	6718.8(4)	6845.5(18)	78.9(4)
N1	4183.2(4)	5193.1(4)	8070.8(11)	38.6(2)
C1	2970.4(4)	4706.6(4)	4238.9(12)	31.42(19)
C2	2714.7(4)	4786.1(4)	2676.1(12)	31.23(19)
C3	2732.9(4)	4316.5(4)	1459.8(12)	29.28(18)
C4	2479.7(4)	4392.4(5)	-165.4(13)	36.2(2)
C5	2518.9(5)	3937.3(5)	-1329.2(14)	43.1(2)
C6	2809.7(5)	3388.3(5)	-922.4(15)	46.0(3)
C7	3051.4(5)	3296.6(5)	630.1(15)	40.8(2)
C8	3019.7(4)	3757.9(4)	1870.4(12)	31.15(19)
C9	3269.1(4)	3683.1(4)	3503.6(14)	35.3(2)
C10	3244.2(4)	4140.1(4)	4656.1(13)	34.6(2)
C11	3004.1(4)	5202.5(5)	5408.8(13)	36.7(2)
C12	3092.8(4)	5605.5(5)	6382.6(14)	39.0(2)
C13	3261.3(5)	6125.4(5)	7456.8(16)	43.8(3)
C14	2922.6(7)	6695.4(6)	6861(2)	66.5(4)
C15	3119.0(6)	6004.8(6)	9321.9(17)	55.5(3)
C16	3954.4(5)	6221.6(5)	7212.1(16)	47.2(3)
C17	4385.9(5)	5695.4(5)	7371.8(14)	39.9(2)
C18	4982.7(6)	5759.1(6)	6737(2)	59.1(3)
C19	5361.9(6)	5276.1(7)	6810(2)	67.4(4)
C20	5166.8(5)	4725.7(6)	7532.1(15)	46.1(3)
C21	4568.2(5)	4709.1(5)	8172.8(13)	37.8(2)
C22	4356.2(6)	4170.0(6)	8929.4(18)	54.3(3)

C23	4723.6(7)	3671.3(6)	9020(2)	62.4(4)
C24	5313.2(7)	3681.6(6)	8364.2(19)	60.9(4)
C25	5531.2(6)	4195.6(7)	7640(2)	61.7(4)

Table S6 Anisotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for **3hk**.

The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^2U_{11}+2hka^*b^*U_{12}+\dots]$.

Atom	U11	U22	U33	U23	U13	U12
O1	65.3(6)	37.9(5)	133.6(11)	11.4(5)	-13.7(6)	-19.7(4)
N1	36.2(4)	38.4(4)	41.4(5)	-0.5(4)	1.0(3)	-7.8(3)
C1	23.8(4)	34.1(4)	36.3(5)	-0.1(4)	3.5(3)	-3.6(3)
C2	26.8(4)	27.9(4)	39.1(5)	2.3(3)	1.7(3)	2.1(3)
C3	24.7(4)	29.3(4)	33.8(4)	3.4(3)	3.7(3)	-1.5(3)
C4	35.2(5)	38.0(5)	35.4(5)	5.3(4)	0.2(4)	-1.6(4)
C5	39.9(5)	55.2(6)	34.1(5)	-2.0(4)	2.3(4)	-6.7(5)
C6	39.4(5)	48.9(6)	49.7(6)	-17.1(5)	6.7(5)	-3.0(4)
C7	34.6(5)	32.2(5)	55.7(7)	-6.3(4)	4.1(4)	1.9(4)
C8	24.7(4)	28.2(4)	40.6(5)	2.4(3)	3.9(3)	-2.1(3)
C9	29.9(4)	29.4(4)	46.6(6)	9.0(4)	-1.1(4)	0.7(3)
C10	28.7(4)	39.5(5)	35.7(5)	9.0(4)	-1.9(4)	-4.1(4)
C11	29.3(4)	40.4(5)	40.3(5)	-1.0(4)	1.0(4)	-4.3(4)
C12	33.0(5)	38.4(5)	45.6(6)	-2.1(4)	-0.9(4)	-3.8(4)
C13	43.6(6)	34.0(5)	53.7(6)	-7.9(4)	-3.7(5)	-2.5(4)
C14	63.2(8)	40.8(6)	95.5(12)	-5.6(7)	-13.3(8)	6.1(6)
C15	56.4(7)	55.7(7)	54.3(7)	-18.0(6)	5.3(6)	-0.4(6)
C16	49.1(6)	34.7(5)	57.7(7)	-3.9(5)	-7.4(5)	-12.9(4)

C17 37.8(5)38.7(5)43.3(6)-4.3(4) -3.3(4) -13.5(4)
 C18 44.3(6)50.8(7)82.1(10)9.1(6) 7.1(6) -19.5(5)
 C19 35.0(6)68.8(9)98.5(12)8.5(8) 15.2(7)-11.0(6)
 C20 34.5(5)53.5(6)50.3(6)-5.6(5) -2.5(4) -5.2(5)
 C21 36.6(5)42.0(5)34.9(5)-2.7(4) -4.1(4) -6.8(4)
 C22 50.6(7)49.8(6)62.4(8)13.4(6)1.6(6) -4.3(5)
 C23 69.4(9)47.5(7)70.3(9)11.7(6)-15.7(7)-2.8(6)
 C24 60.4(8)54.0(7)68.2(9)-7.1(6) -22.3(7)10.9(6)
 C25 43.7(6)69.3(9)72.1(9)-9.1(7) -5.5(6) 9.0(6)

Table S7 Bond Lengths for **3hk**

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	C16	1.2069(13)	C11	C12	1.1907(14)
N1	C17	1.3120(13)	C12	C13	1.4719(14)
N1	C21	1.3599(14)	C13	C14	1.5303(17)
C1	C2	1.3729(13)	C13	C15	1.5363(18)
C1	C10	1.4204(13)	C13	C16	1.5482(16)
C1	C11	1.4327(13)	C16	C17	1.4992(16)
C2	C3	1.4130(13)	C17	C18	1.4104(16)
C3	C4	1.4147(13)	C18	C19	1.349(2)
C3	C8	1.4164(12)	C19	C20	1.4042(18)
C4	C5	1.3634(15)	C20	C21	1.4094(15)
C5	C6	1.4015(17)	C20	C25	1.4146(18)
C6	C7	1.3568(17)	C21	C22	1.4062(15)

C7	C8	1.4141(14)	C22	C23	1.3616(18)
C8	C9	1.4169(14)	C23	C24	1.395(2)
C9	C10	1.3587(15)	C24	C25	1.354(2)

Table S8 Bond Angles for **3hk**

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C17	N1	C21	118.08(9)	C14	C13	C15	109.87(11)
C2	C1	C10	119.67(9)	C14	C13	C16	109.09(10)
C2	C1	C11	120.69(9)	C15	C13	C16	110.14(10)
C10	C1	C11	119.48(9)	O1	C16	C13	119.99(11)
C1	C2	C3	120.89(8)	O1	C16	C17	119.64(11)
C2	C3	C4	121.75(8)	C17	C16	C13	120.33(9)
C2	C3	C8	119.13(8)	N1	C17	C16	117.96(10)
C4	C3	C8	119.11(9)	N1	C17	C18	123.33(11)
C5	C4	C3	120.46(9)	C18	C17	C16	118.69(10)
C4	C5	C6	120.18(10)	C19	C18	C17	118.68(11)
C7	C6	C5	120.99(10)	C18	C19	C20	120.36(11)
C6	C7	C8	120.47(10)	C19	C20	C21	116.99(11)
C3	C8	C9	118.85(8)	C19	C20	C25	124.06(12)
C7	C8	C3	118.78(9)	C21	C20	C25	118.94(12)
C7	C8	C9	122.36(9)	N1	C21	C20	122.53(10)
C10	C9	C8	121.01(9)	N1	C21	C22	118.50(10)
C9	C10	C1	120.41(9)	C22	C21	C20	118.97(11)
C12	C11	C1	173.51(10)	C23	C22	C21	120.20(12)

C11	C12	C13	173.30(11)	C22	C23	C24	121.12(13)
C12	C13	C14	109.44(10)	C25	C24	C23	119.99(12)
C12	C13	C15	111.95(10)	C24	C25	C20	120.76(13)
C12	C13	C16	106.27(9)				

Table S9 Hydrogen Atom Coordinates ($\text{\AA}\times 10^4$) and Isotropic Displacement Parameters ($\text{\AA}^2\times 10^3$) **3hk**.

Atom	x	y	z	U(eq)	
H2	2526.93		5153.97	2414.44	37
H4	2285.19		4755.32	-441.99	43
H5	2352.15		3991.32	-2395.69	52
H6	2837.56		3082.17	-1728.76	55
H7	3239.16		2927.7	880.31	49
H9	3452.68		3315.7	3791.01	42
H10	3407.45		4081.46	5724.94	42
H14A	3012.06		6767.41	5694.4	100
H14B	3051.23		7039.74	7516.67	100
H14C	2492.08		6636.76	6999.01	100
H15A	2686.31		5969.88	9470.39	83
H15B	3269.67		6336.26	9991.83	83
H15C	3311.94		5632.93	9668.9	83
H18	5112.2		6126.68	6277.88	71
H19	5754.63		5307.87	6379.04	81
H22	3963.87		4154.13	9369.44	65

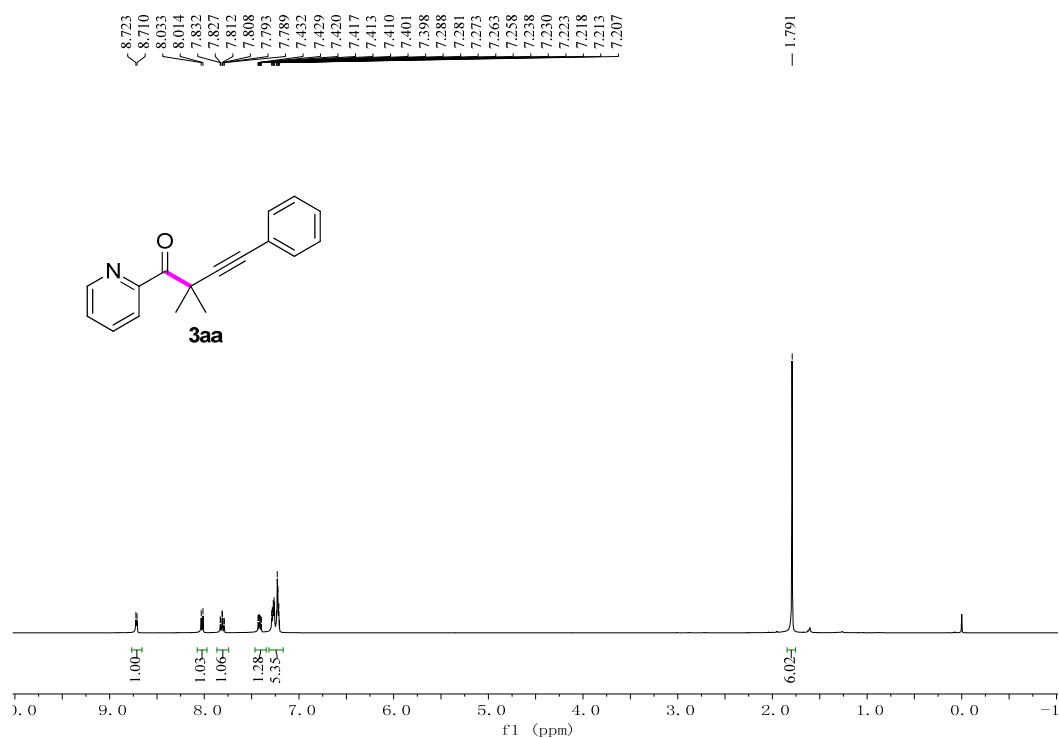
H23	4579.13	3317.84	9527.36	75
H24	5556.36	3335.3	8424.33	73
H25	5925.12	4200.28	7209.04	74

5. References

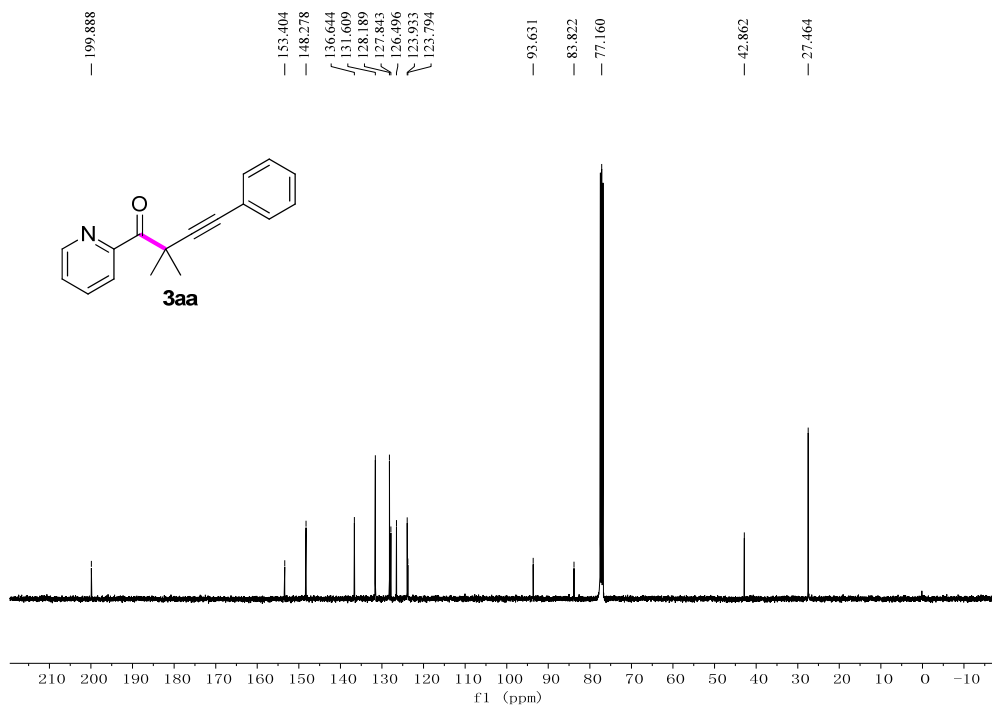
- (1) X. Huang, S. Wu, W. Wu, P. Li, C. Fu and S. Ma, *Nat. Commun.* 2016, **7**, 12382.
- (2) Y. Li, H. Zou, J. Gong, J. Xiang, T. Luo, J. Quan, G. Wang and Z. Yang, *Org. Lett.*, 2007, **9**, 4057.
- (3) M. D. Aparece, W. Hu and J. P. Morken, *ACS. Catal.* 2019, **9**, 11381.
- (4) H. Zou, L. Zhou, Y. Li, Y. Cui, H. Zhong, Z. Pan, Z. Yang and J. Quan, *J. Med. Chem.* 2010, **53**, 994.
- (5) A. E. Nibbs, T. D. Montgomery, Y. Zhu and V. H. Rawal, *J. Org. Chem.* 2015, **80**, 4928.
- (6) H. Ito, Y. Sasaki and M. Sawamura, *J. Am. Chem. Soc.* 2008, **130**, 15774.
- (7) C. K. Hazra and M. Oestreich, *Org. Lett.* 2012, **14**, 4010.
- (8) K. Watanabe, Y. Miyazaki, M. Okubo, B. Zhou, H. Tsuji and M. Kawatsura, *Org. Lett.* 2018, **20**, 5448.
- (9) S. Wu, X. Huang, W. Wu, P. Li, C. Fu and S. Ma, *Nat. Commu.* 2015, **6**, 7946.

6. NMR spectra

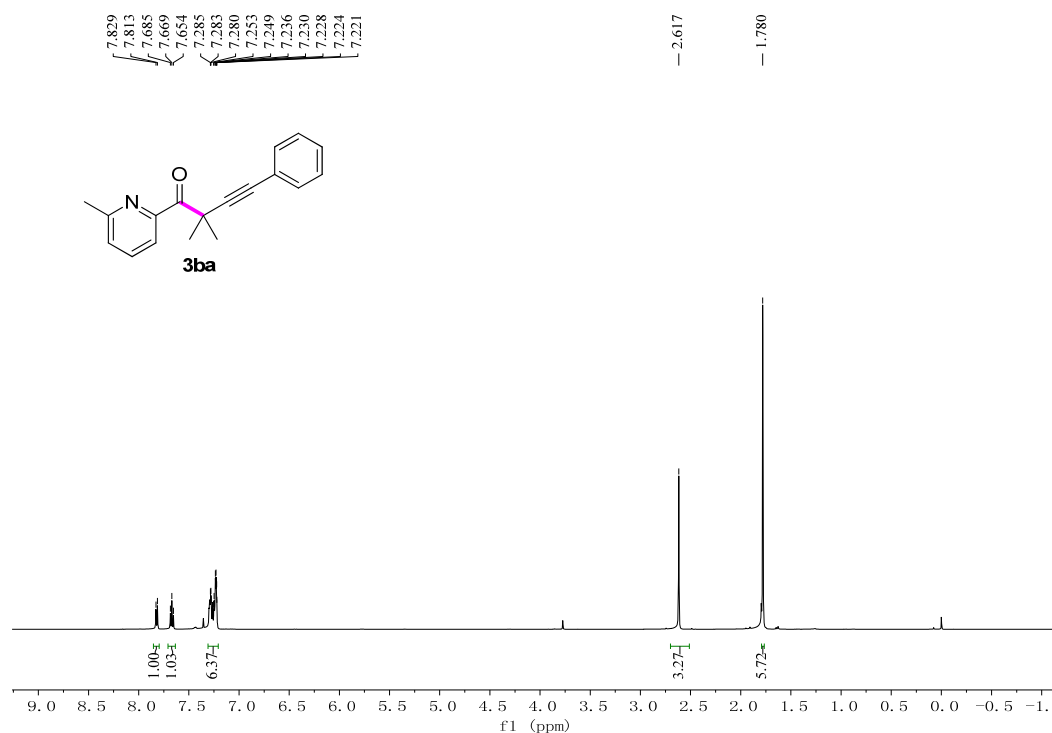
^1H NMR spectrum of compound **3aa**



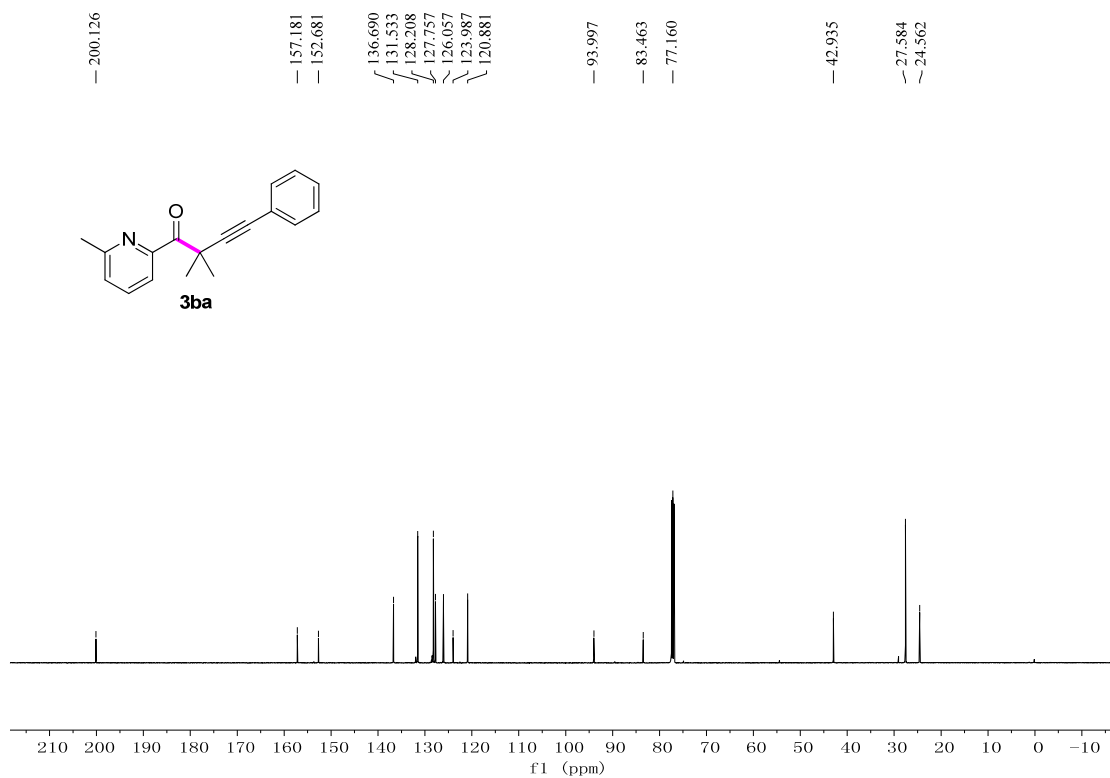
^{13}C NMR spectrum of compound **3aa**



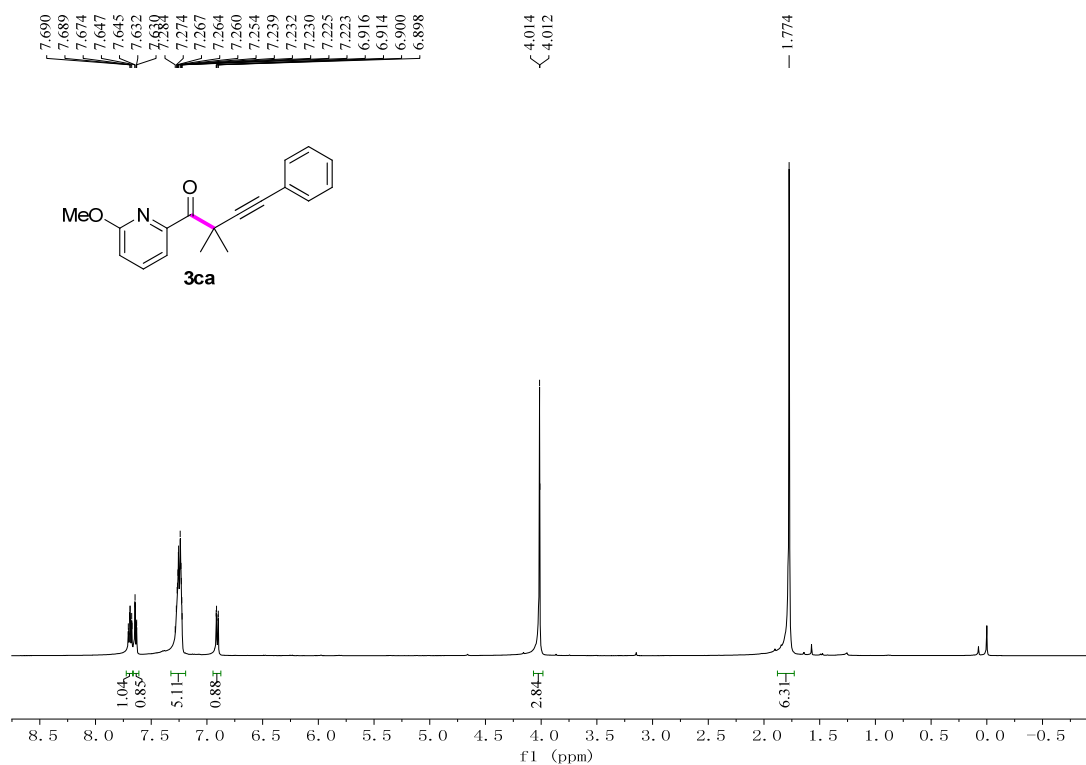
¹H NMR spectrum of compound **3ba**



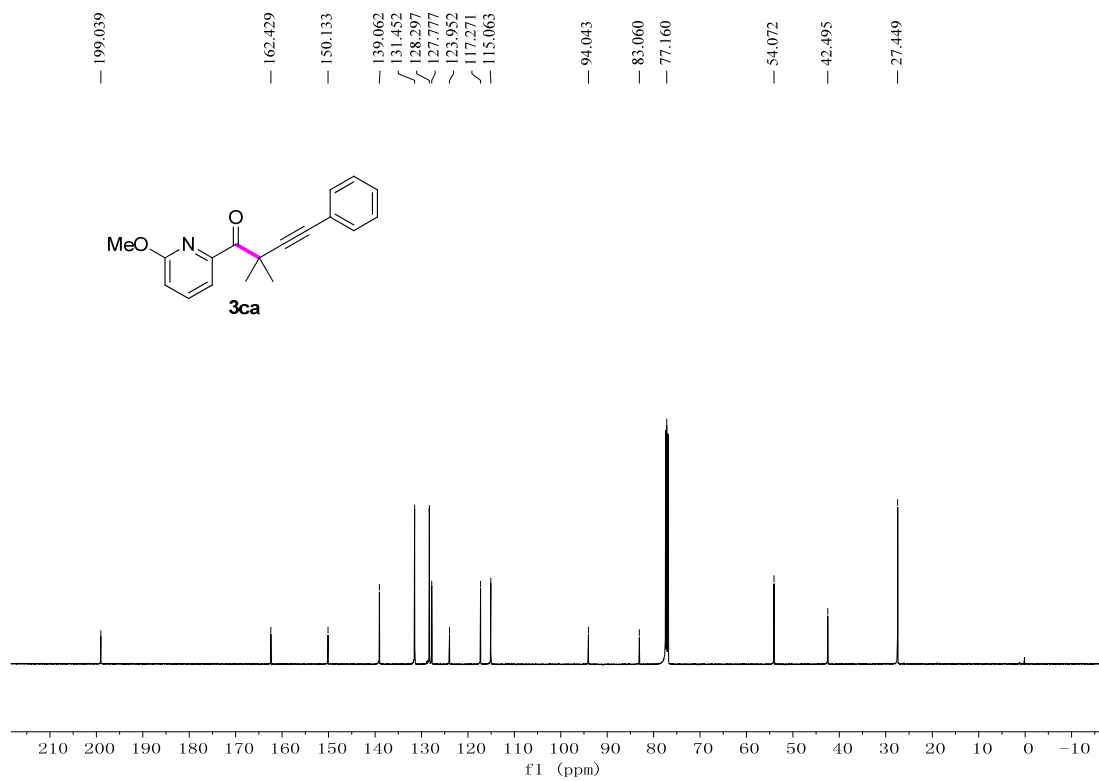
¹³C NMR spectrum of compound **3ba**



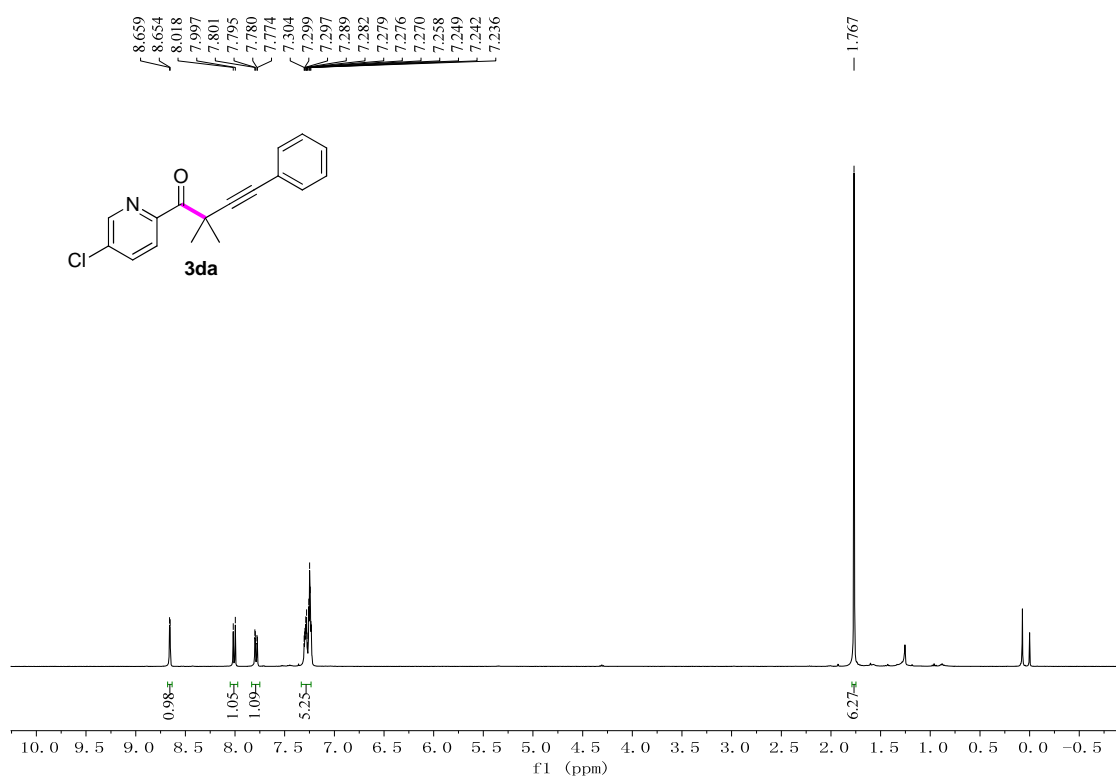
¹H NMR spectrum of compound **3ca**



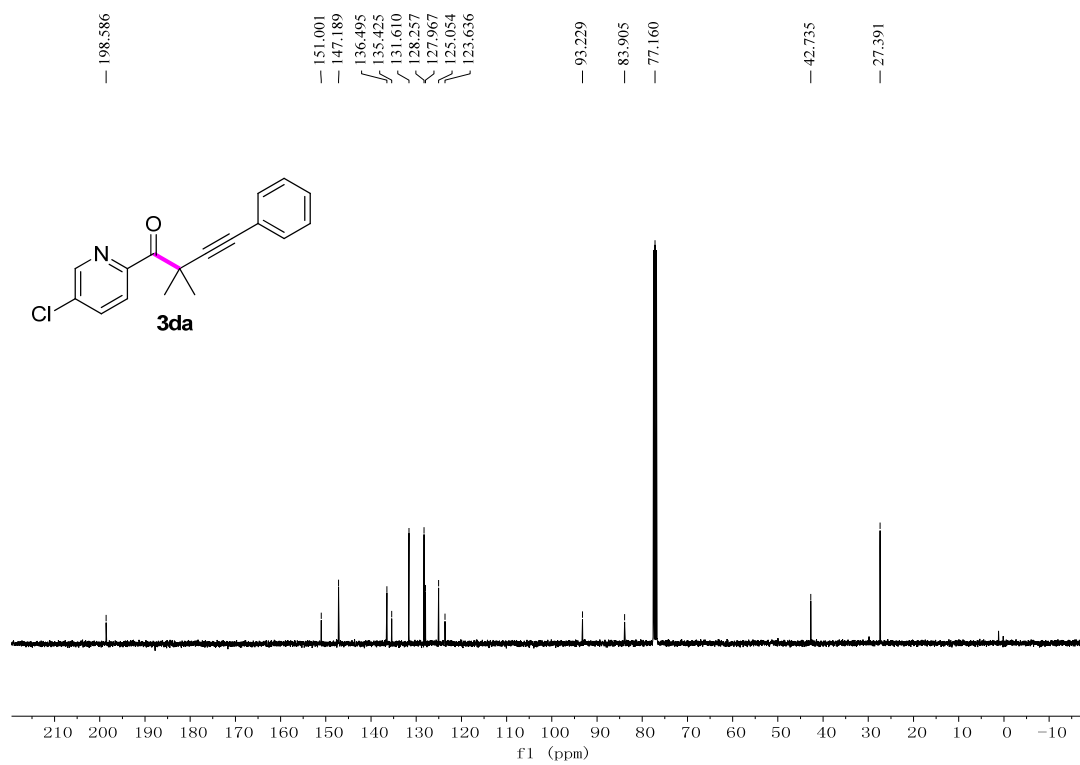
¹³C NMR spectrum of compound **3ca**



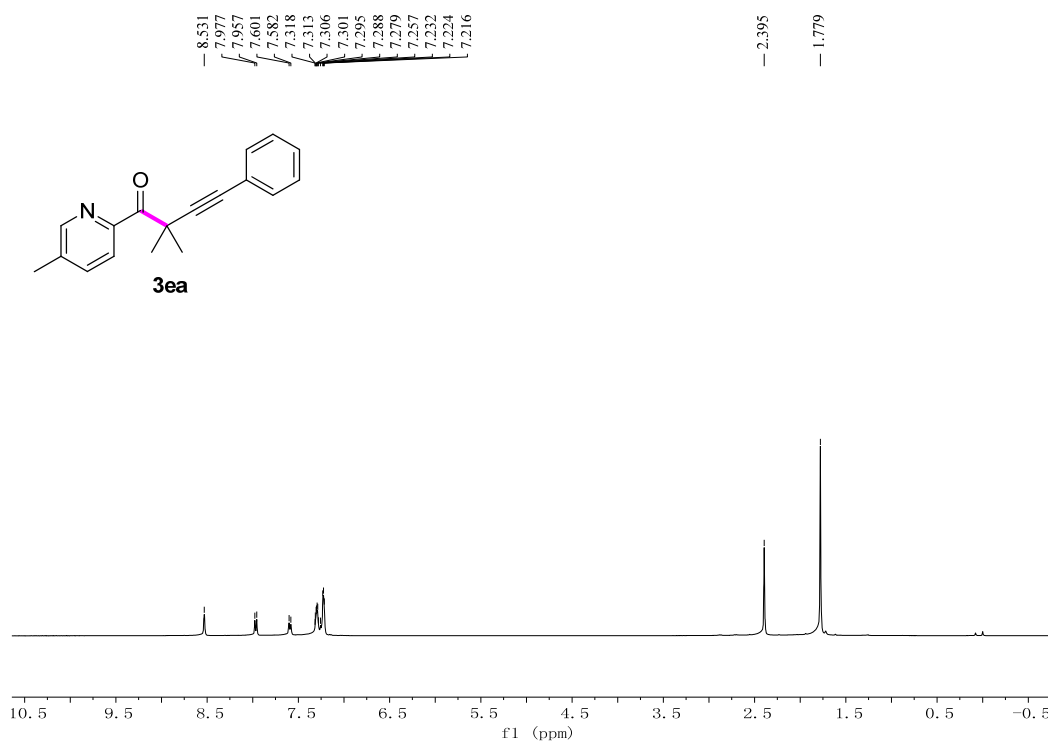
¹H NMR spectrum of compound **3da**



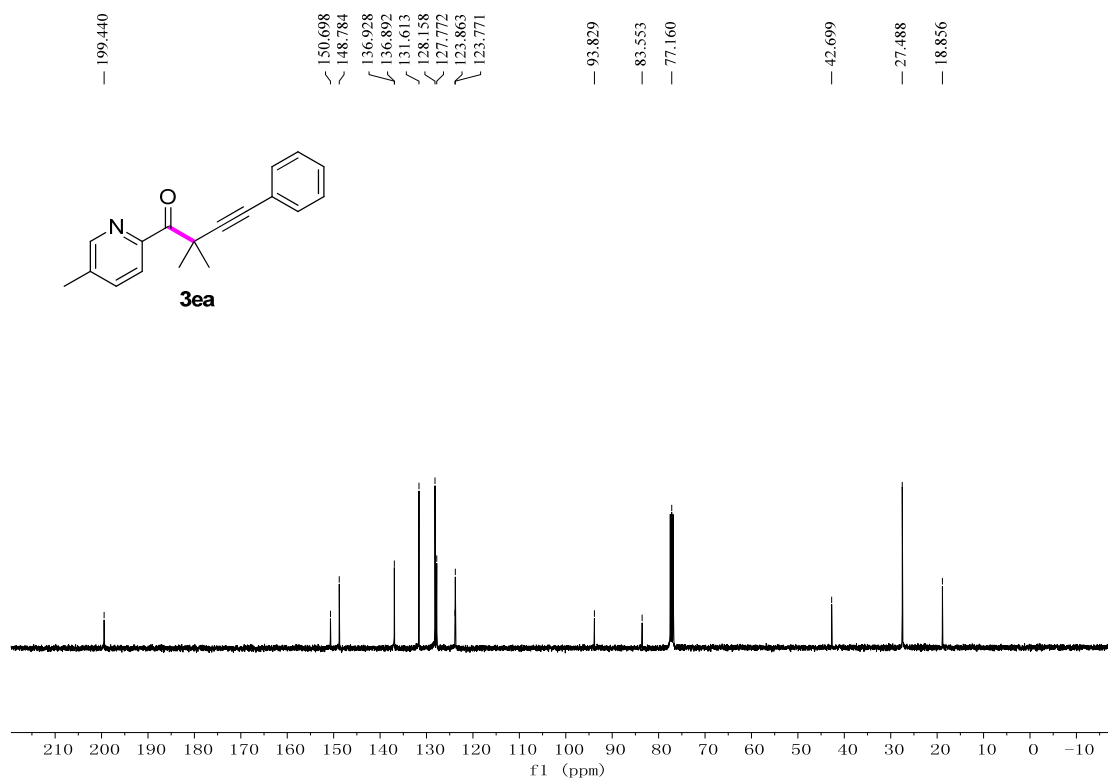
¹³C NMR spectrum of compound **3da**



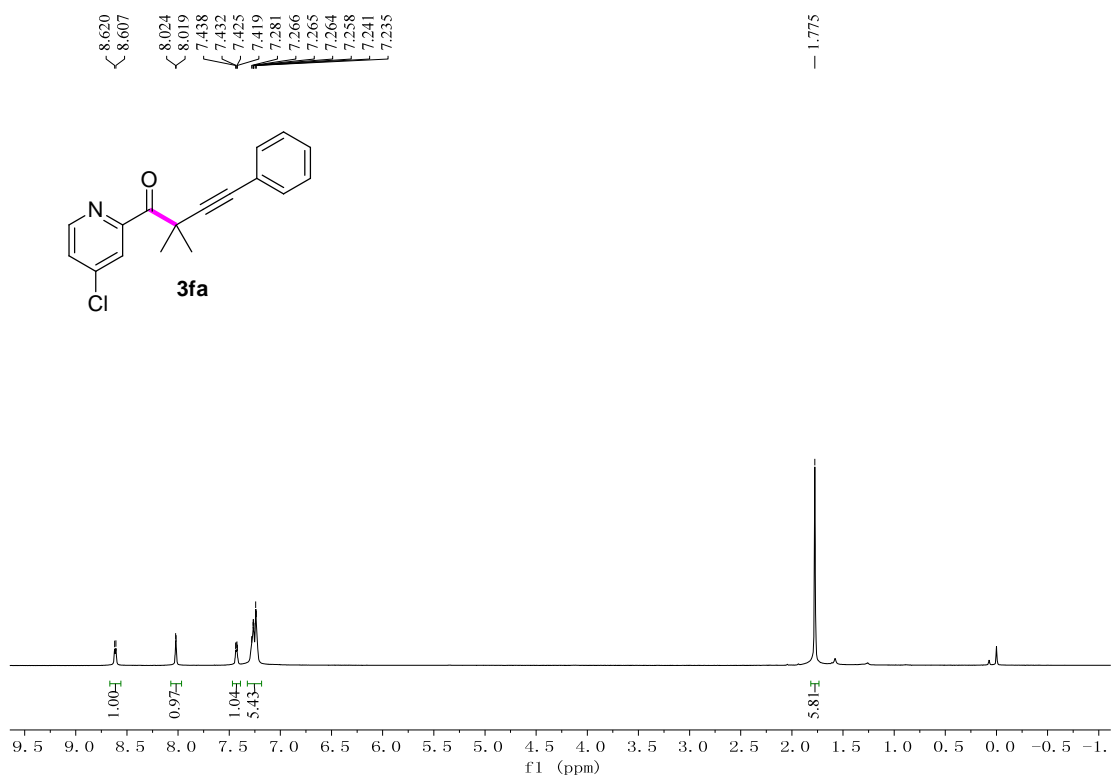
¹H NMR spectrum of compound **3ea**



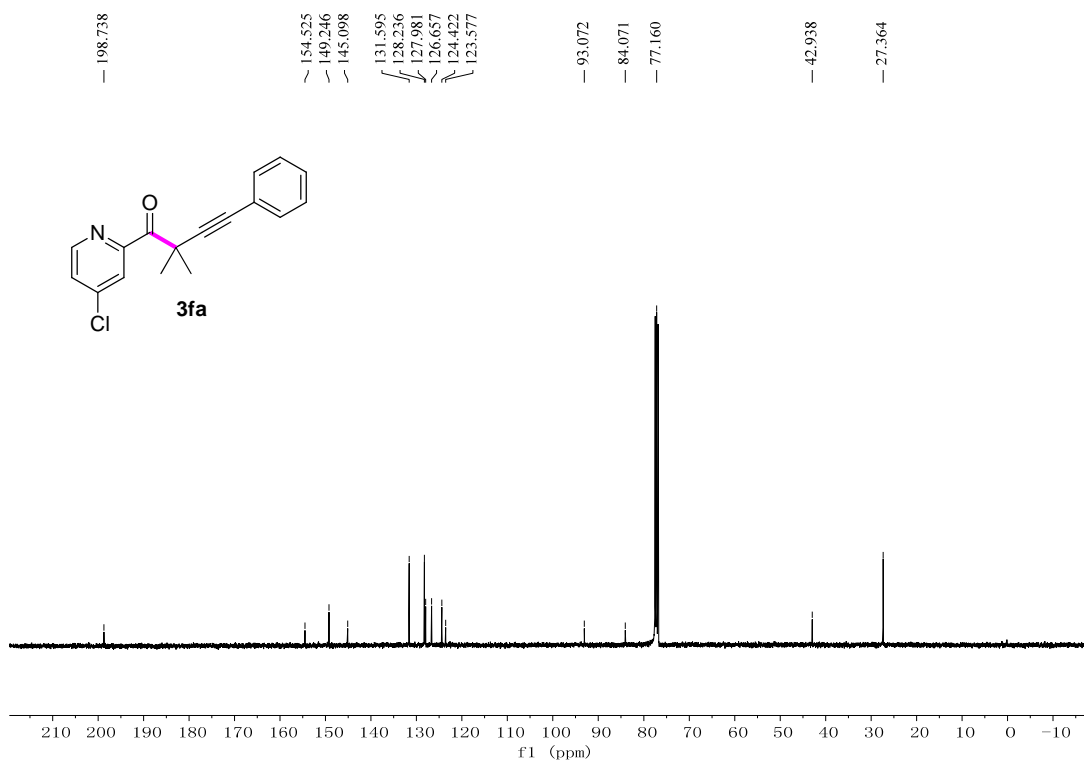
¹³C NMR spectrum of compound **3ea**



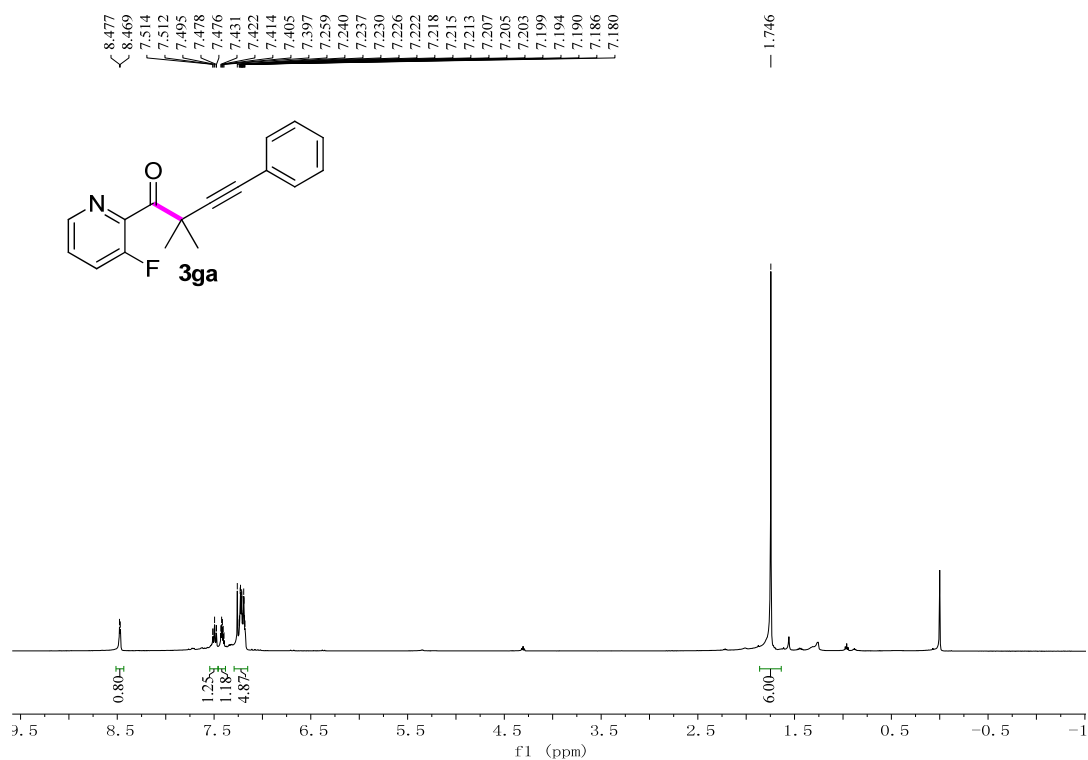
¹H NMR spectrum of compound **3fa**



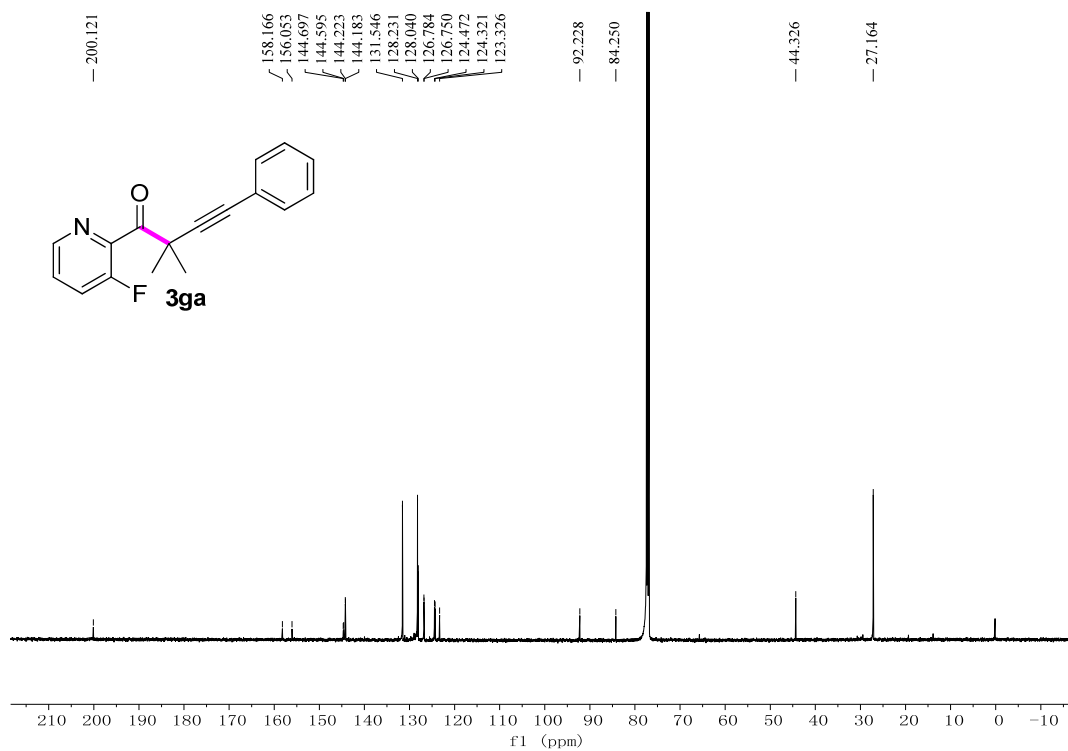
¹³C NMR spectrum of compound **3fa**



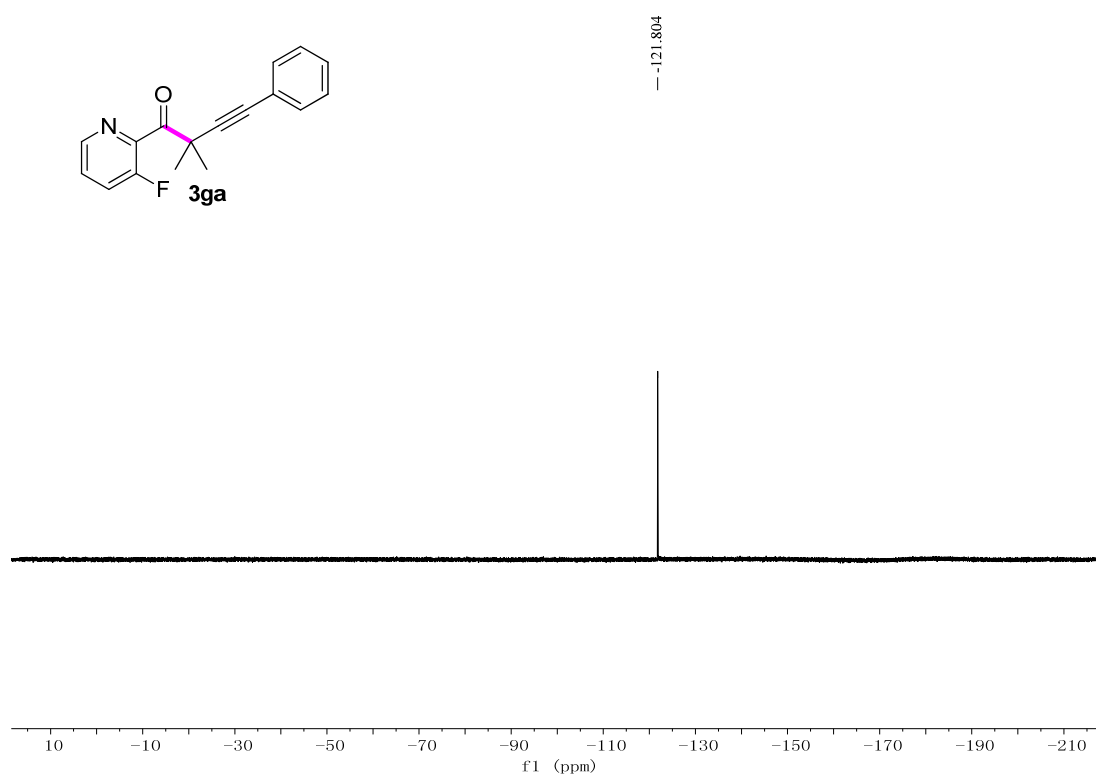
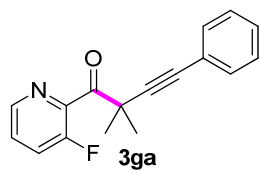
¹H NMR spectrum of compound **3ga**



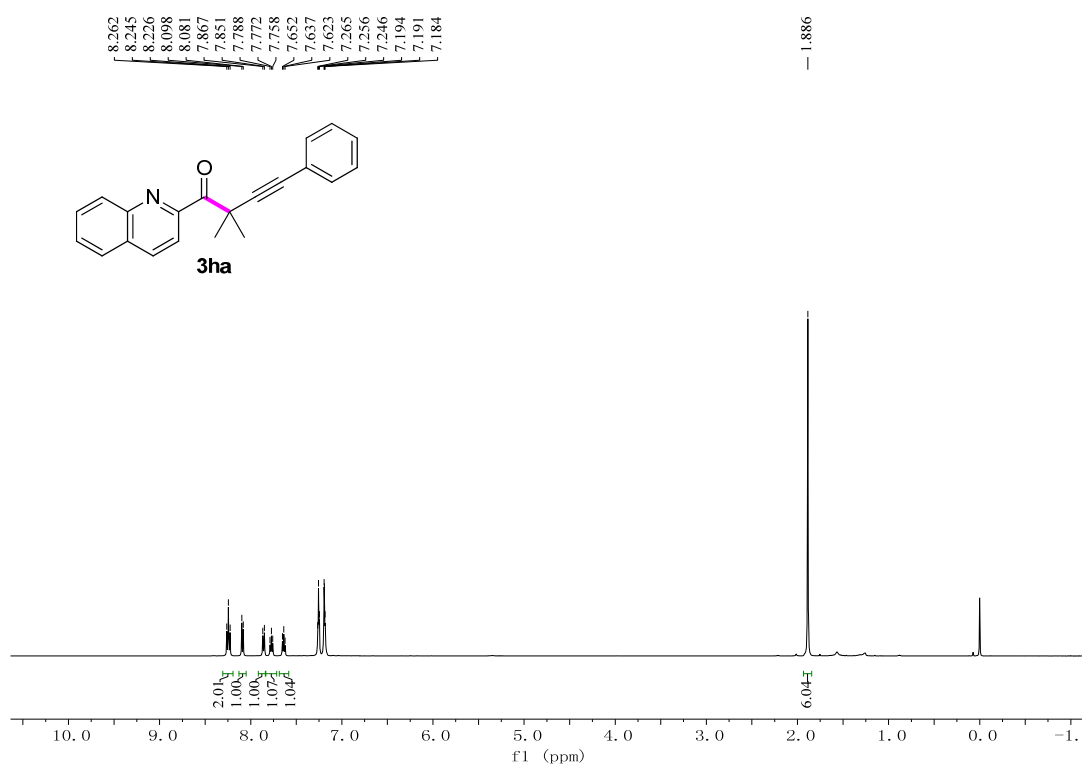
¹³C NMR spectrum of compound **3ga**



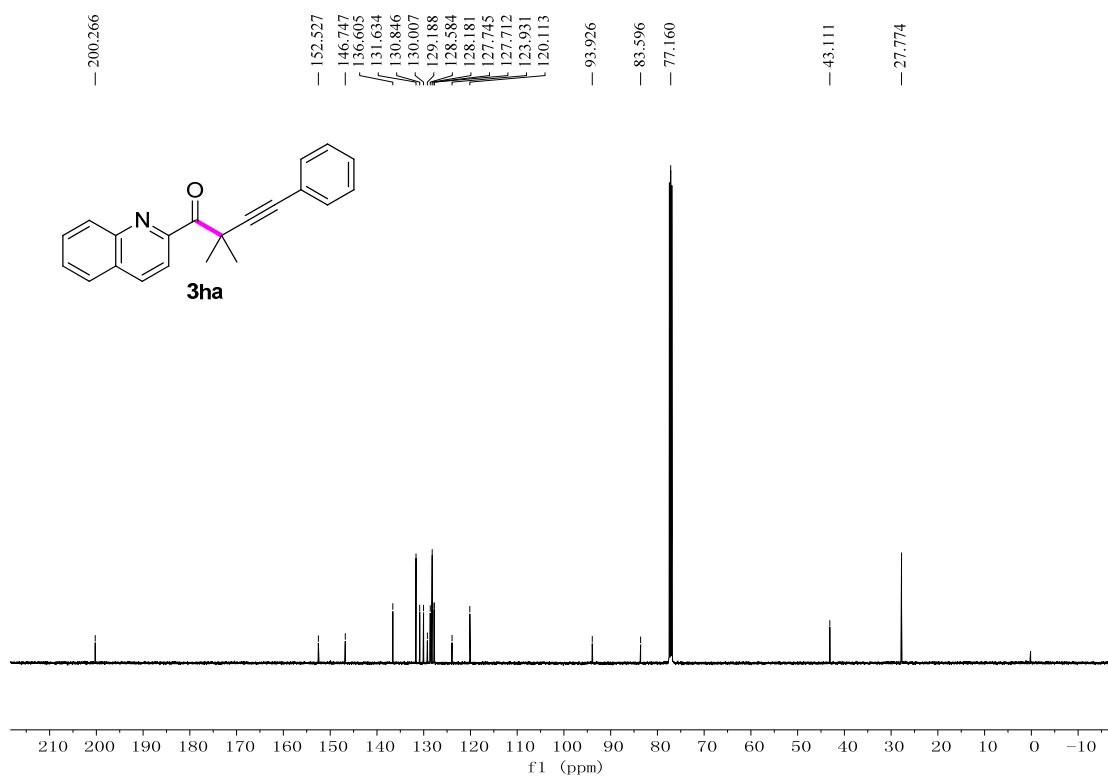
¹⁹F NMR spectrum of compound **3ga**



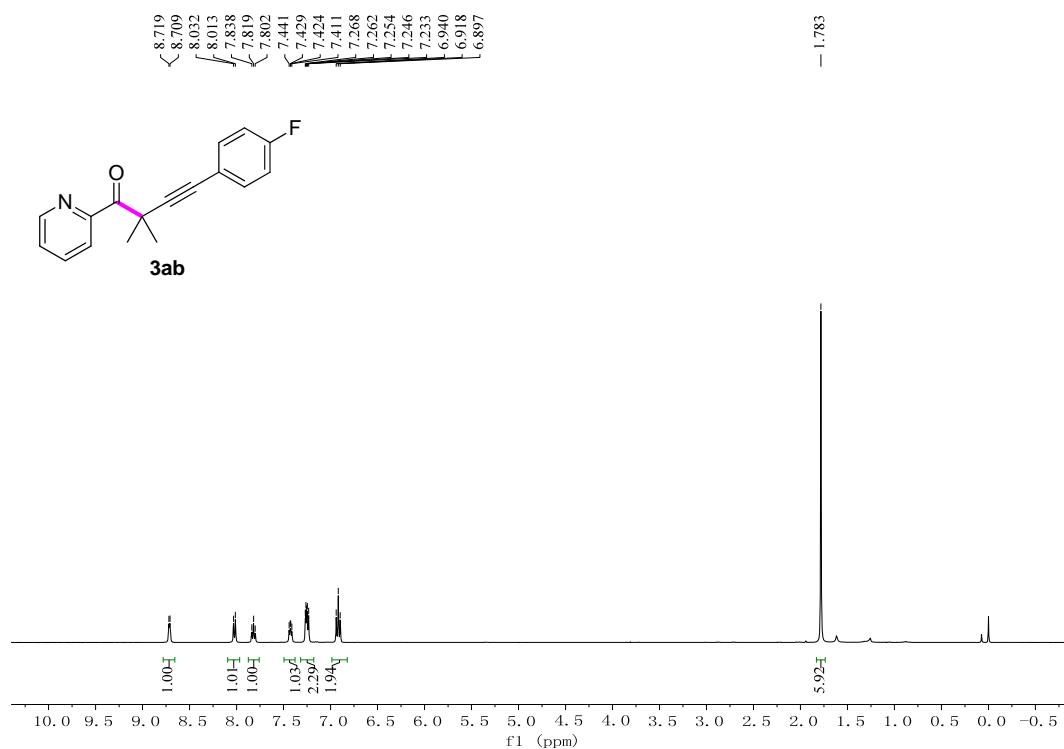
¹H NMR spectrum of compound **3ha**



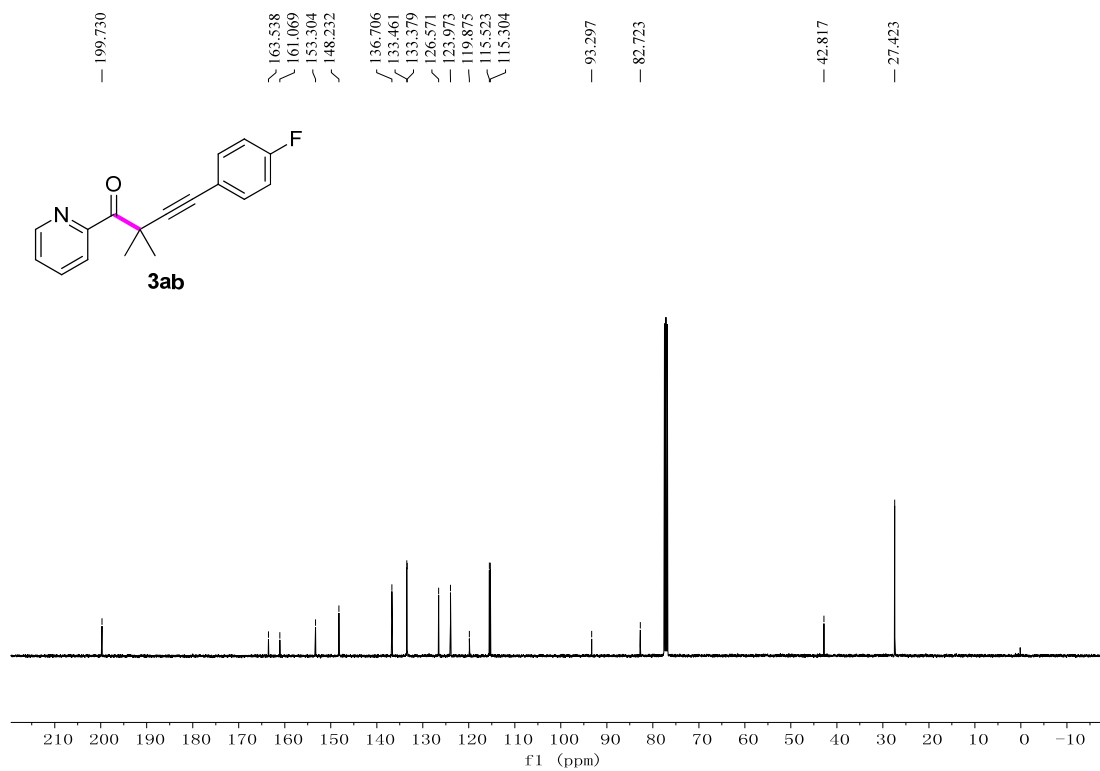
¹³C NMR spectrum of compound **3ha**



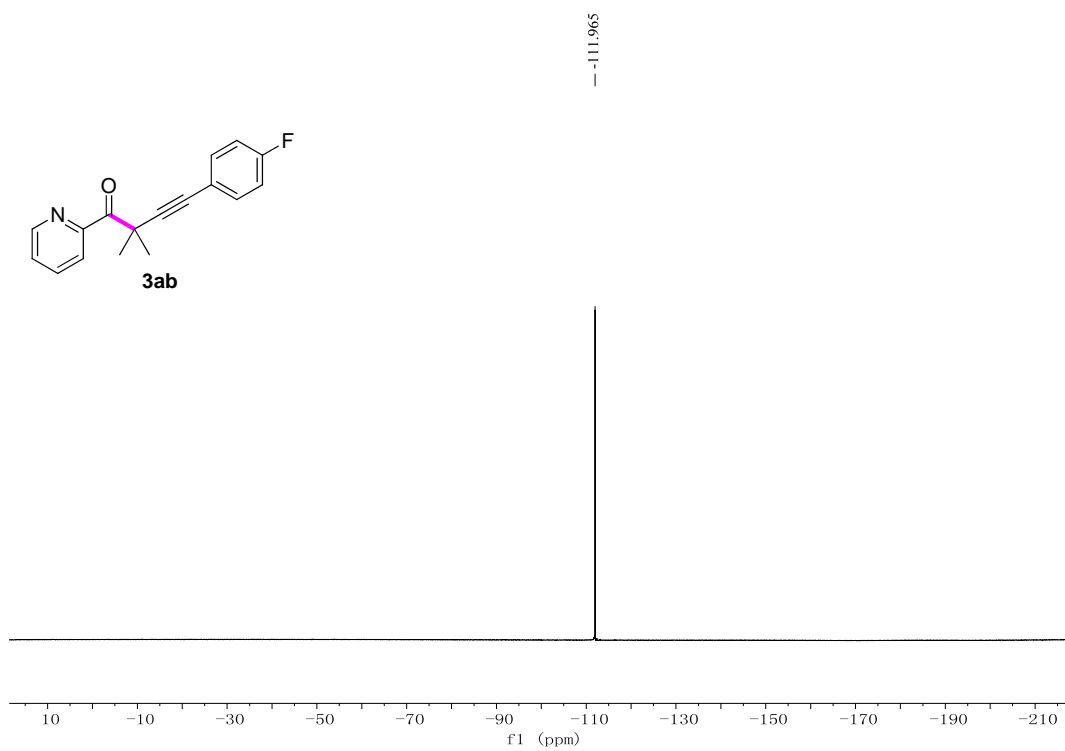
¹H NMR spectrum of compound **3ab**



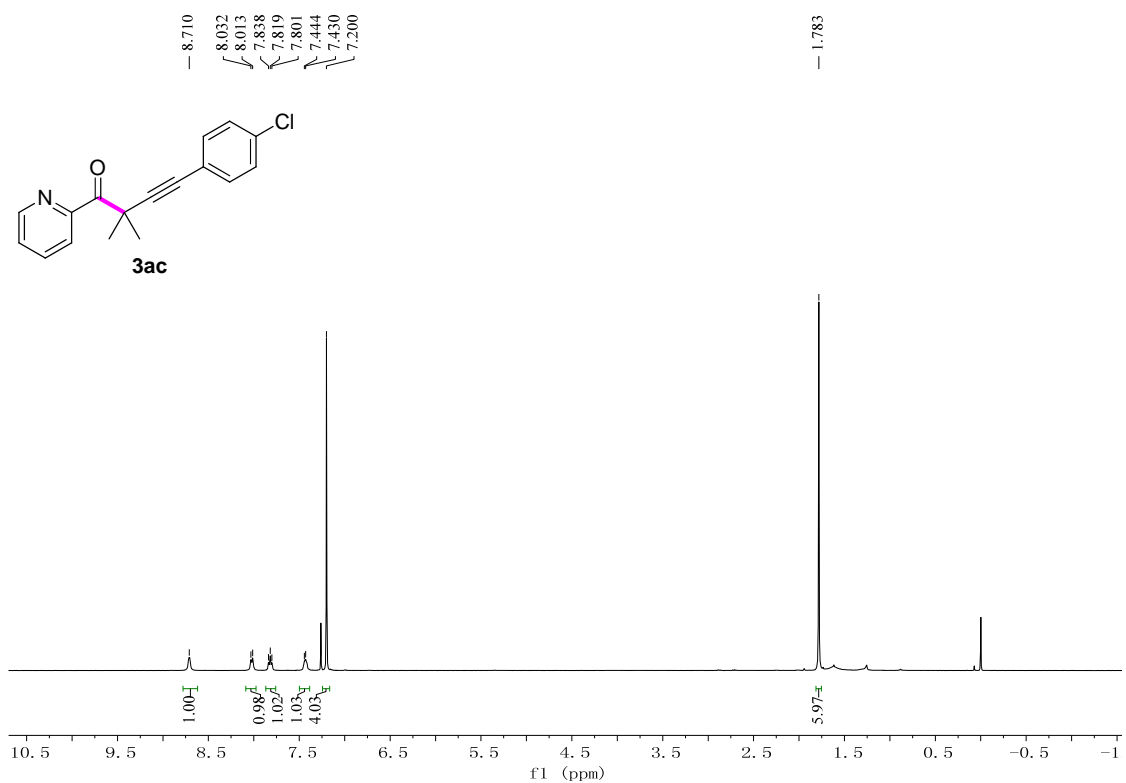
¹³C NMR spectrum of compound **3ab**



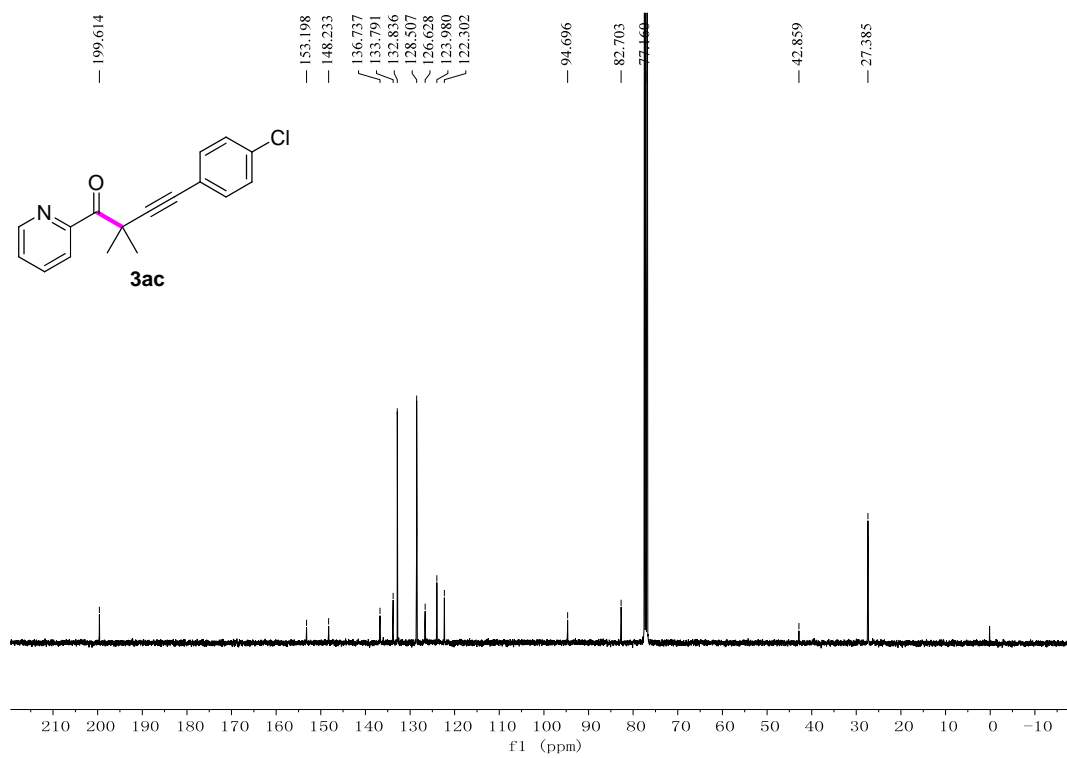
^{19}F NMR spectrum of compound **3ab**



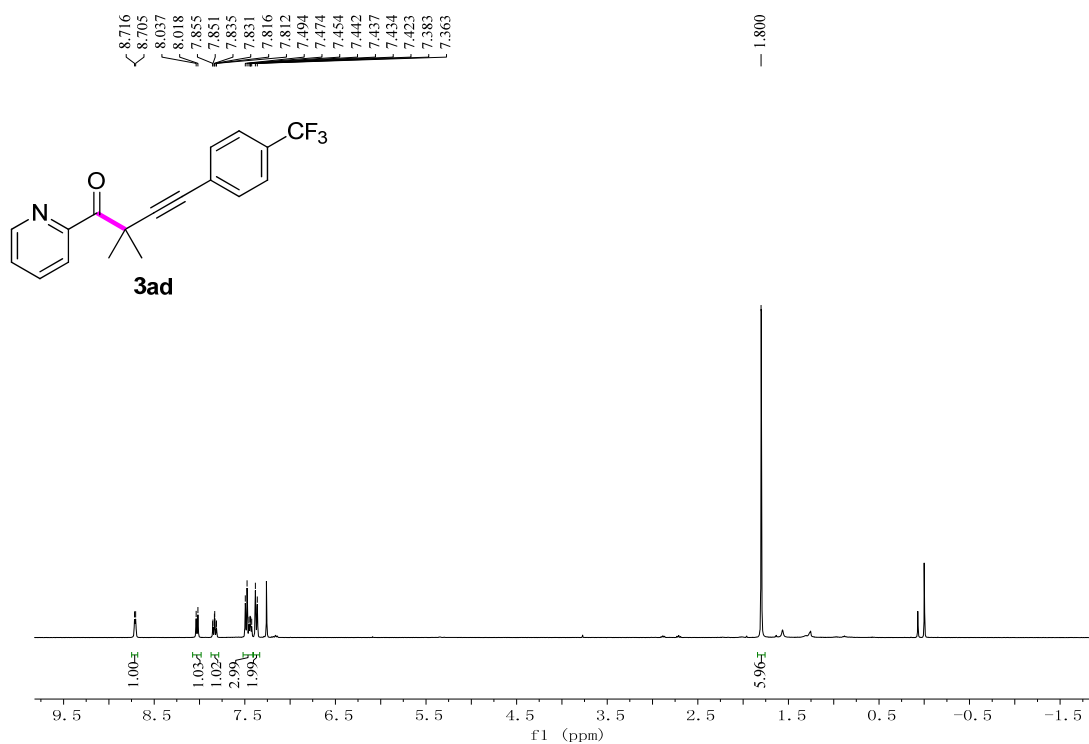
¹H NMR spectrum of compound **3ac**



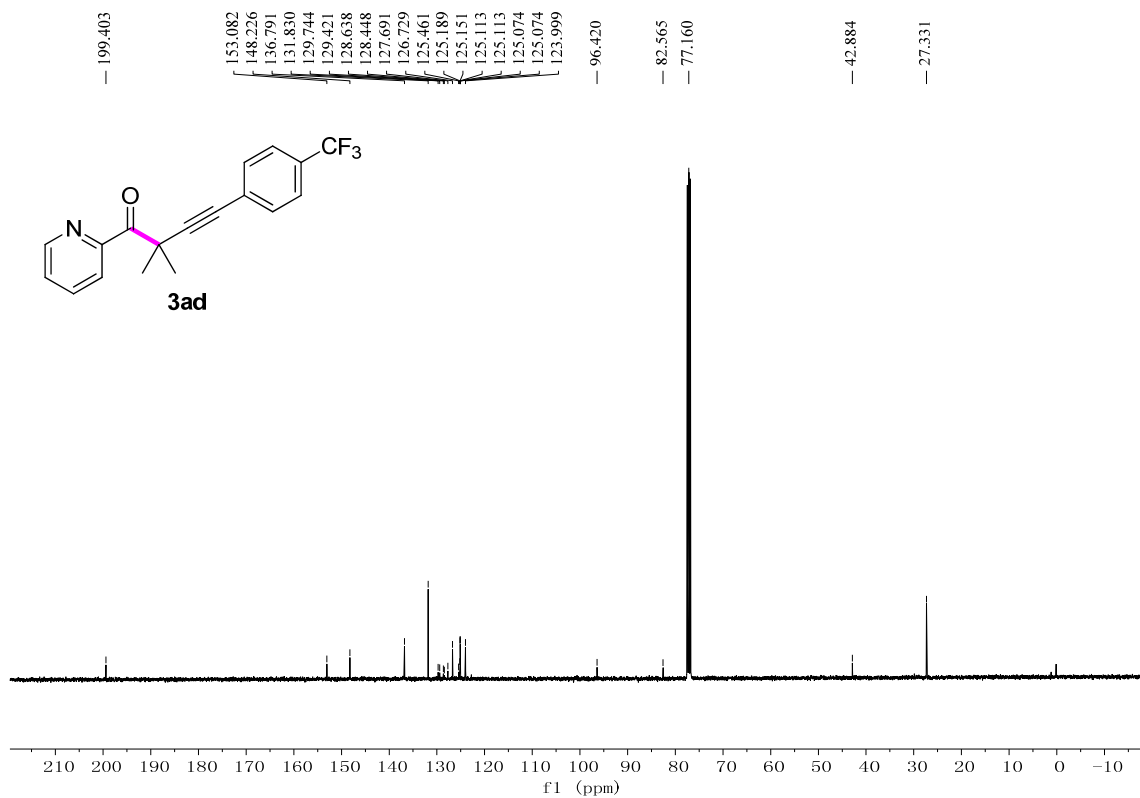
¹³C NMR spectrum of compound **3ac**



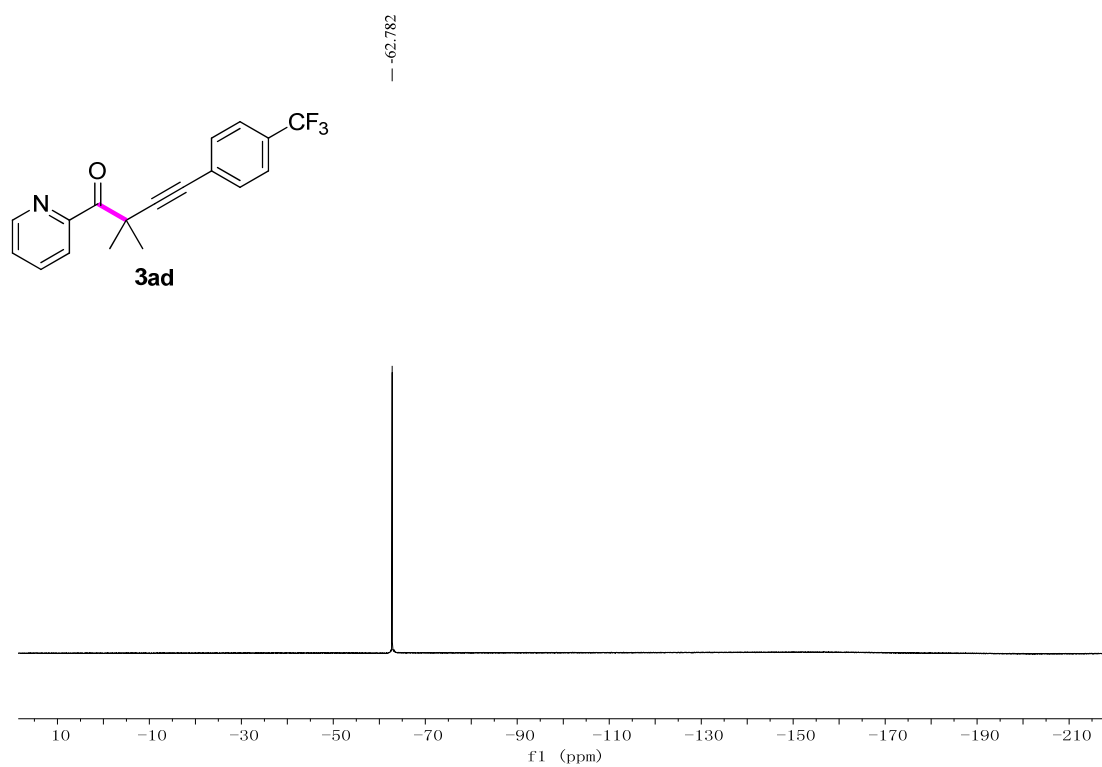
^1H NMR spectrum of compound **3ad**



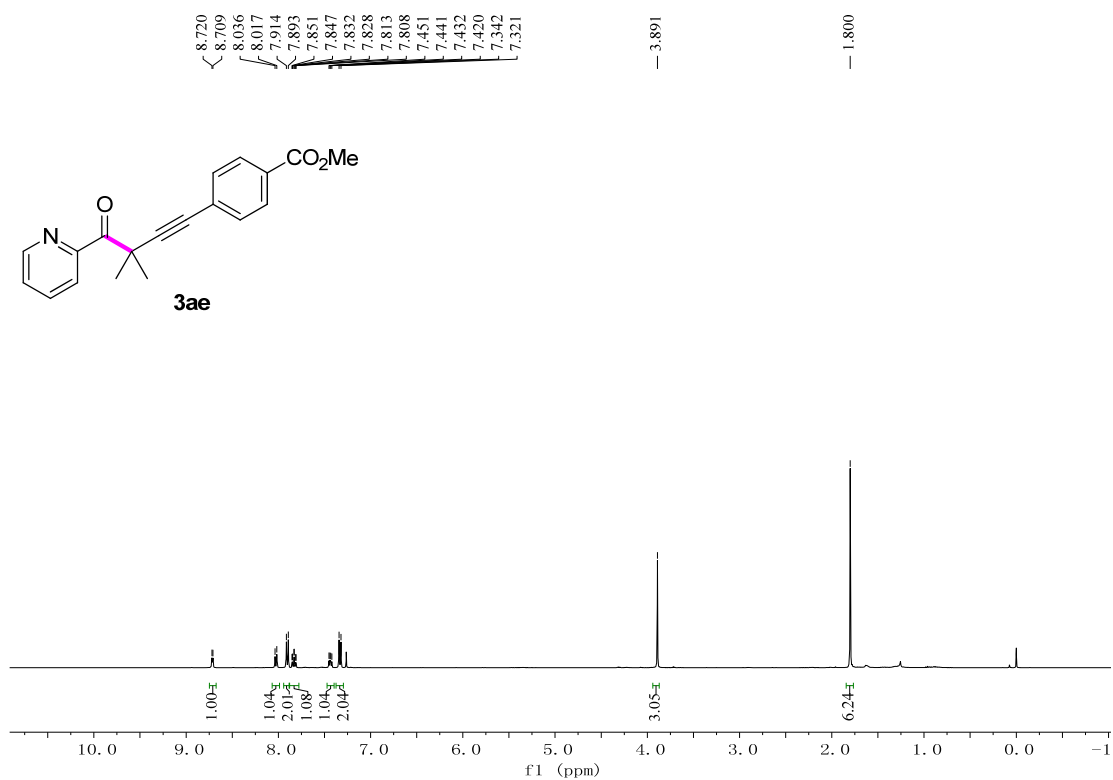
^{13}C NMR spectrum of compound **3ad**



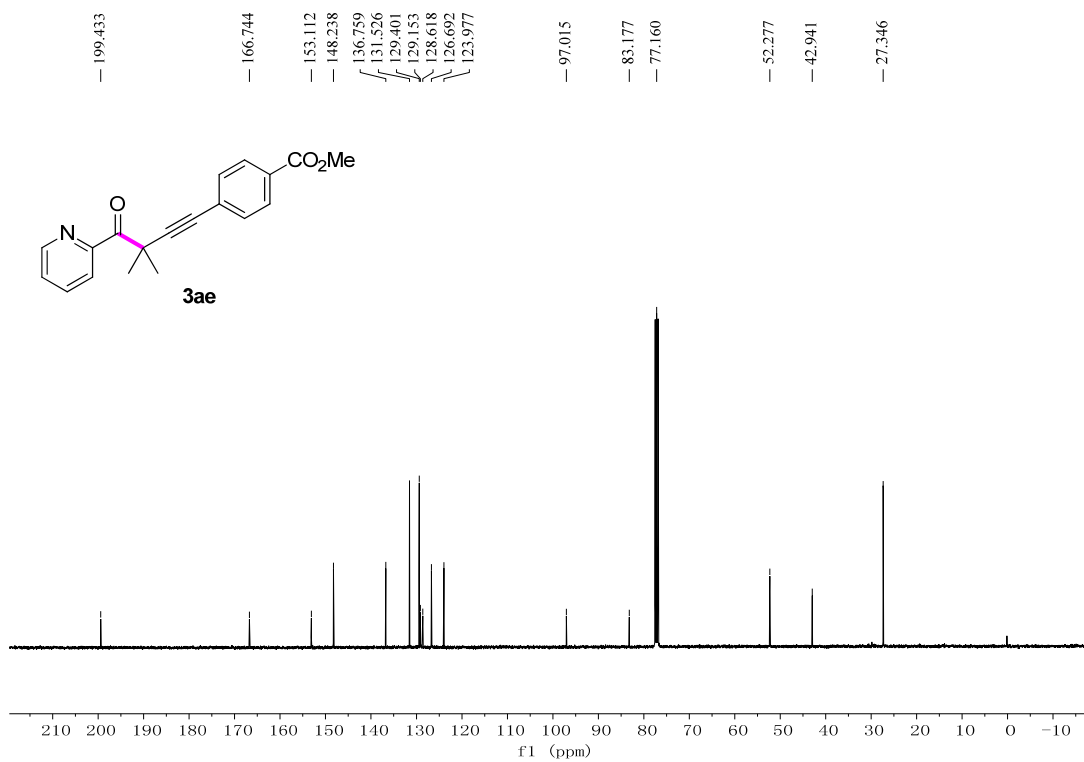
^{19}F NMR spectrum of compound **3ad**



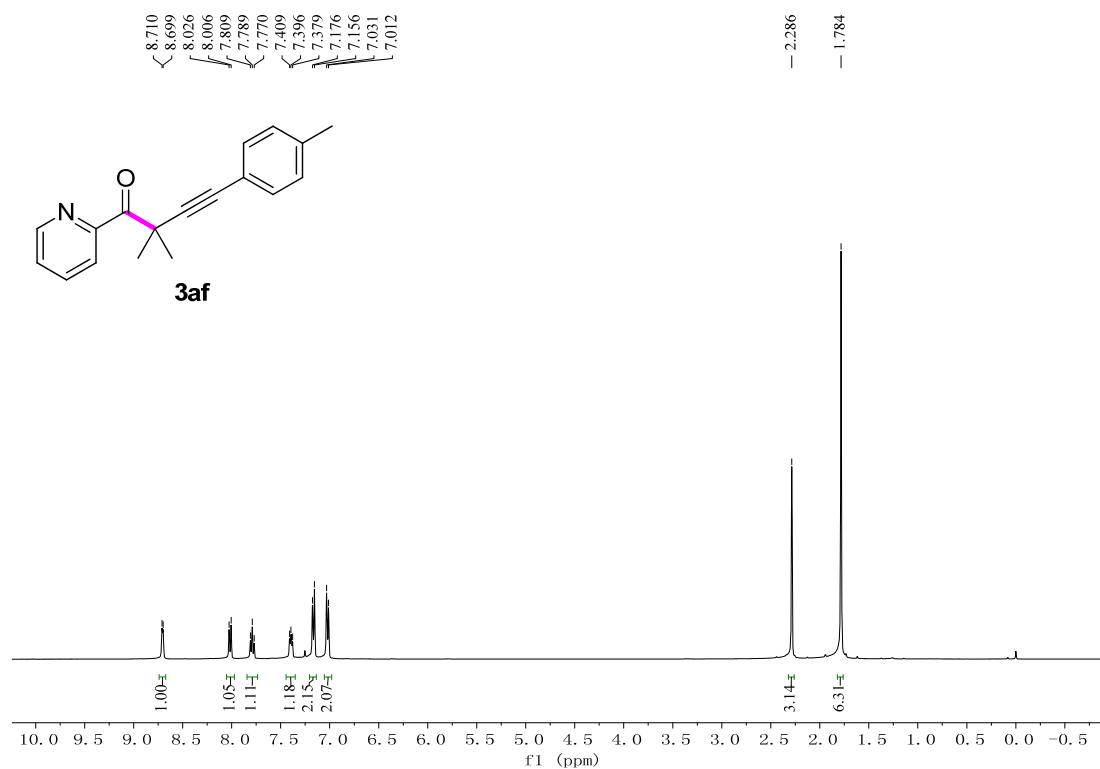
¹H NMR spectrum of compound **3ae**



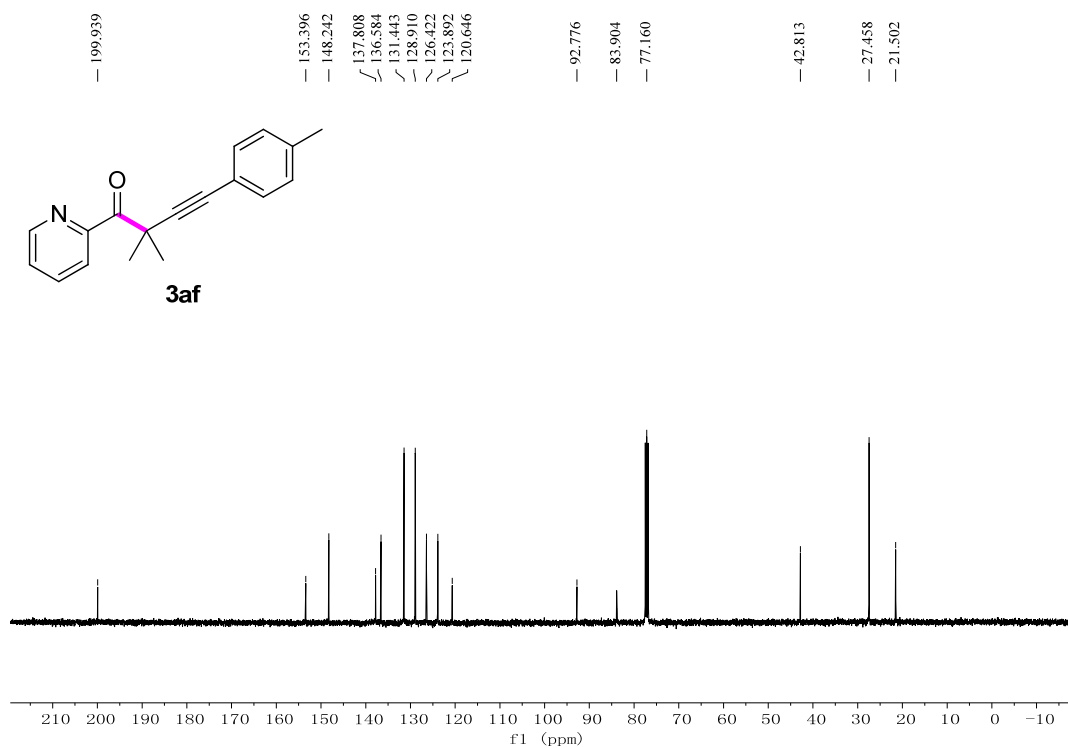
¹³C NMR spectrum of compound **3ae**



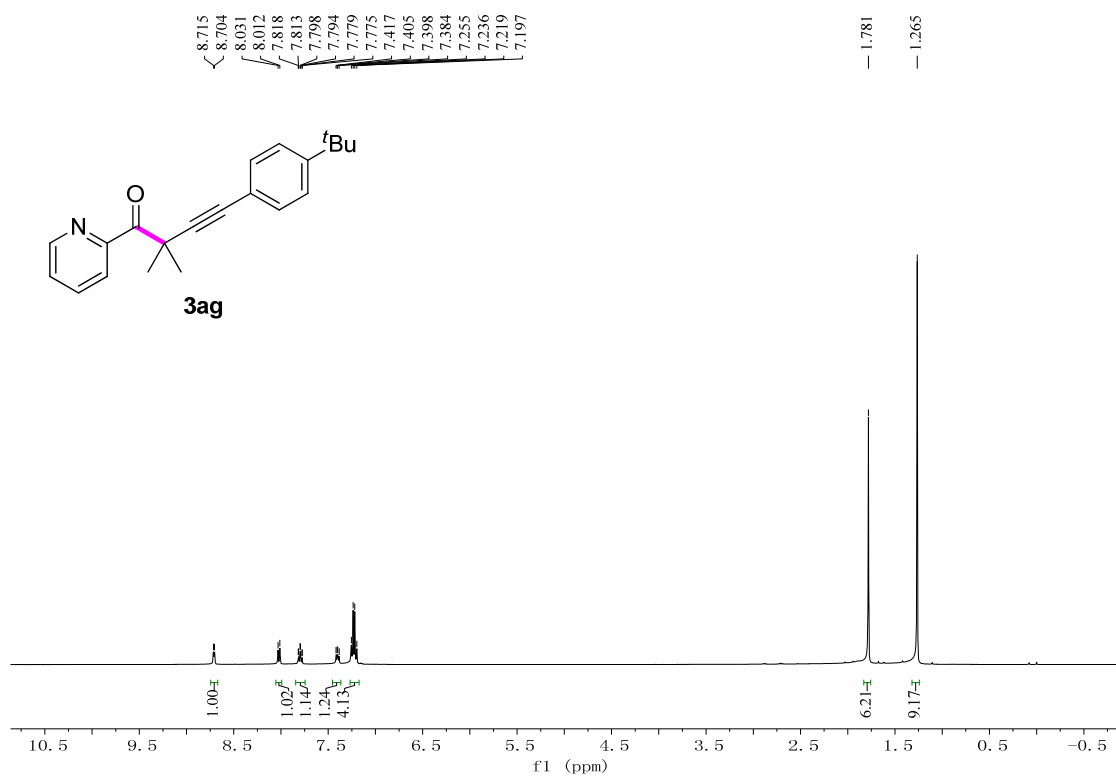
^1H NMR spectrum of compound **3af**



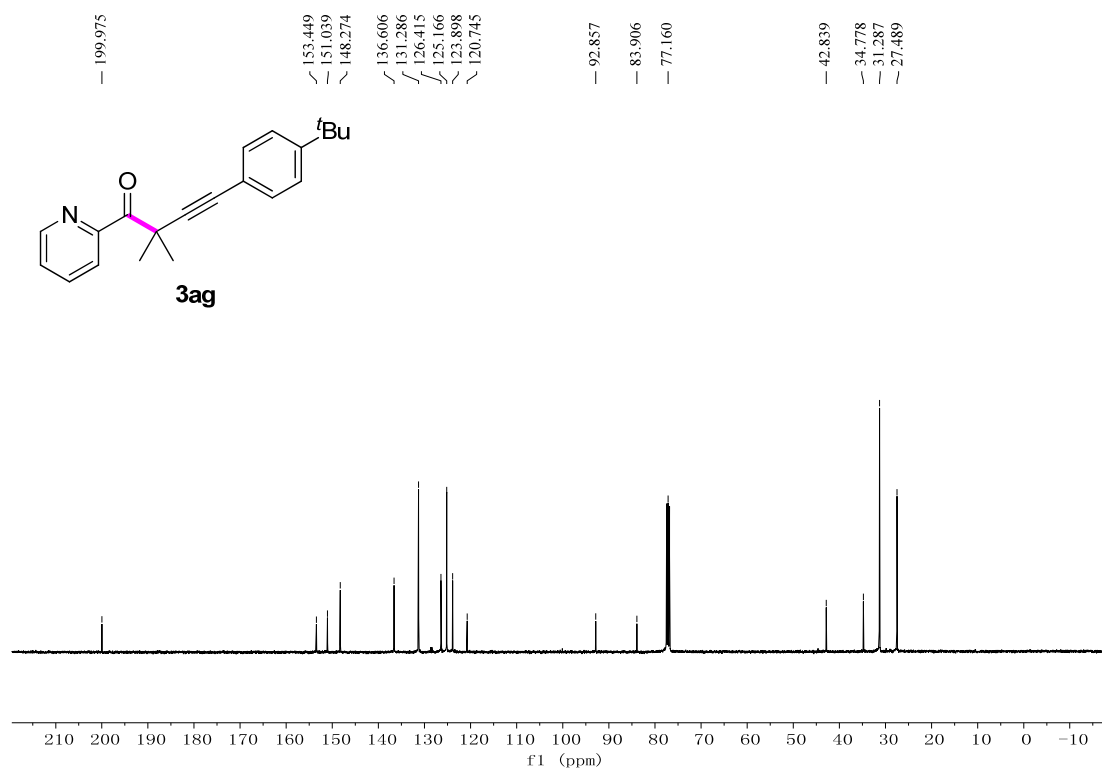
^{13}C NMR spectrum of compound **3af**



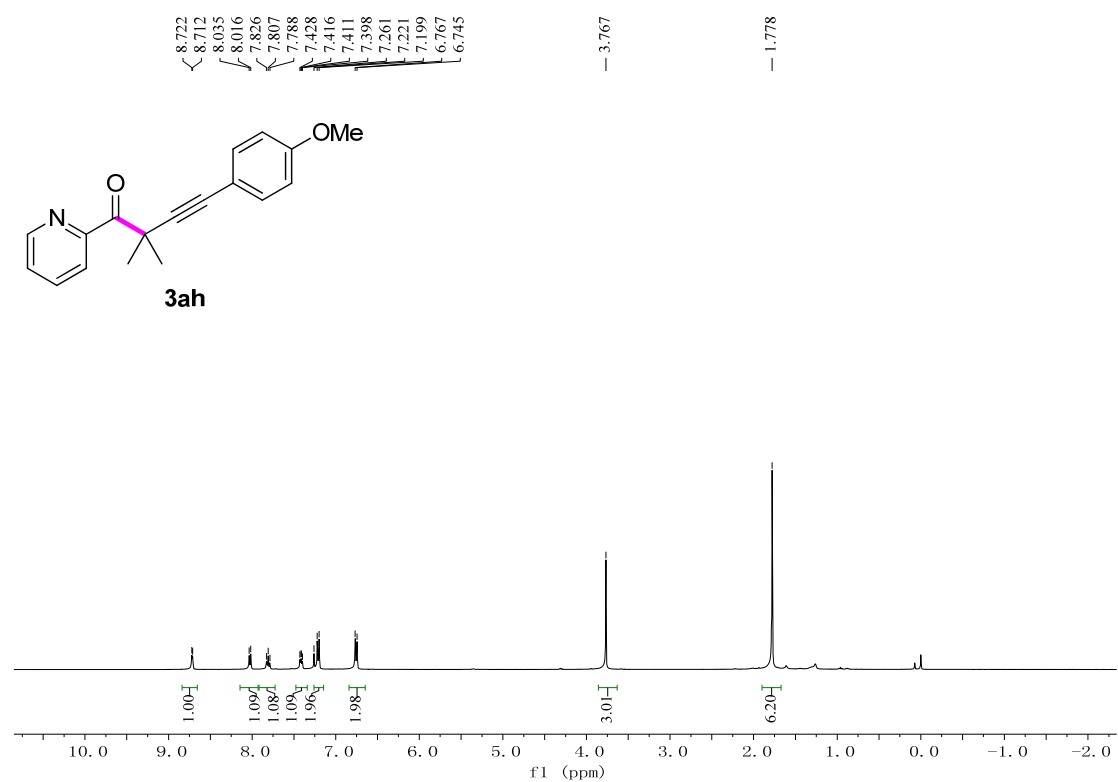
¹H NMR spectrum of compound **3ag**



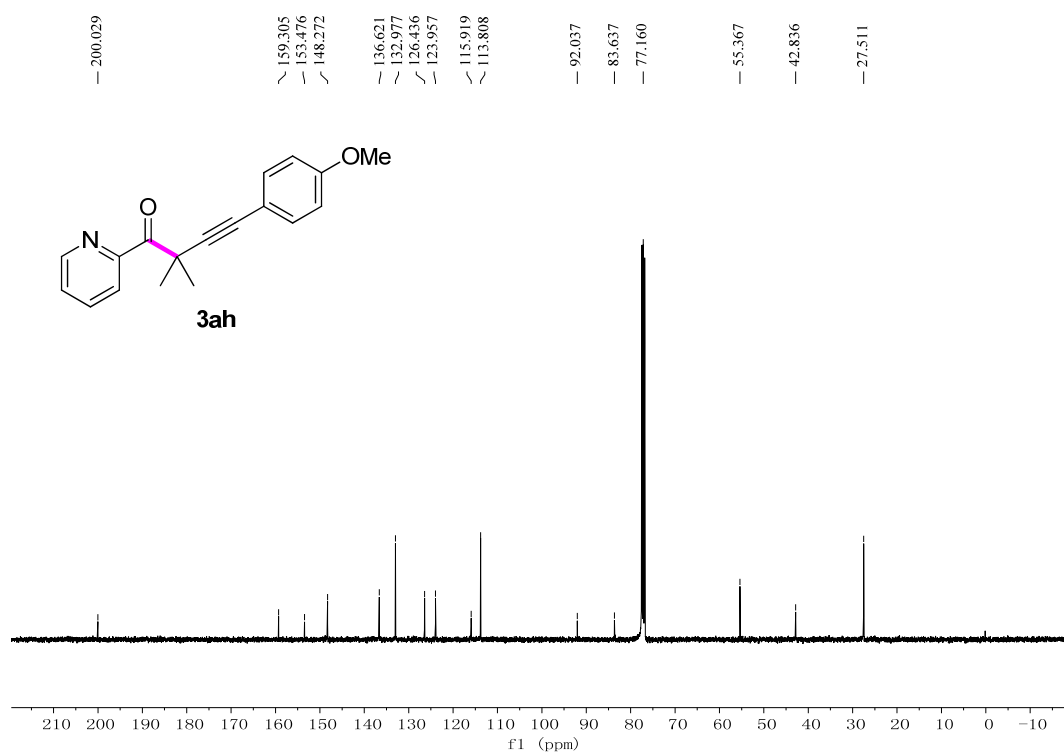
¹³C NMR spectrum of compound **3ag**



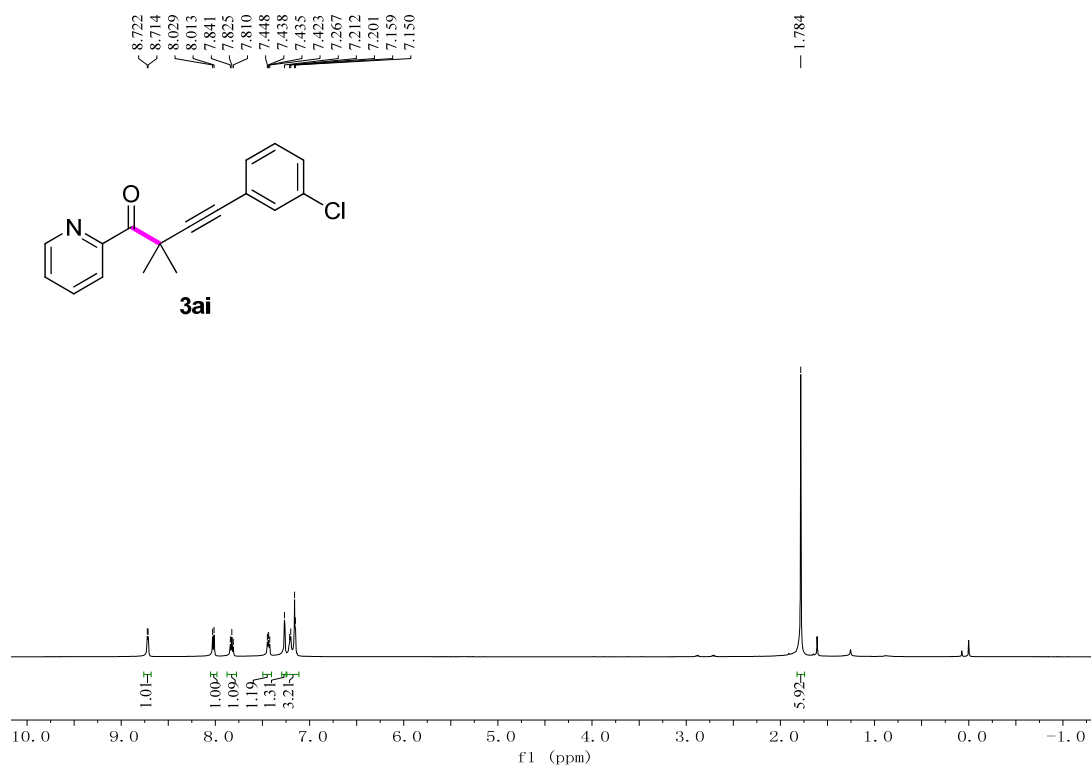
¹H NMR spectrum of compound **3ah**



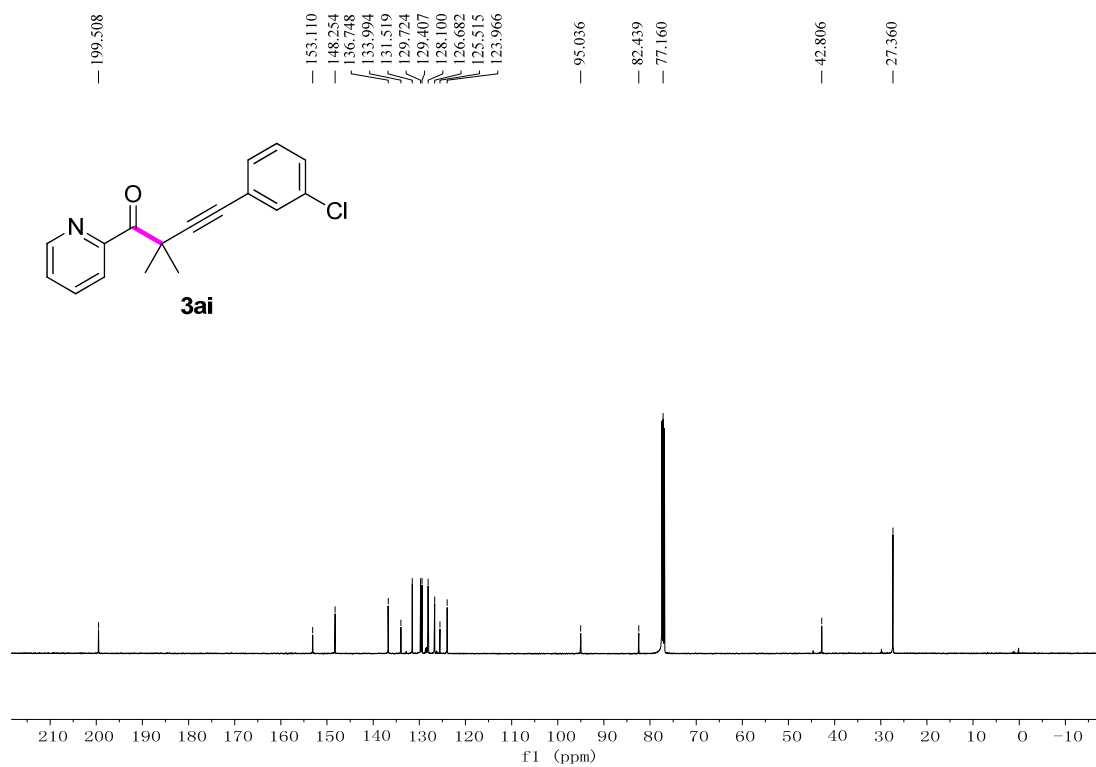
¹³C NMR spectrum of compound **3ah**



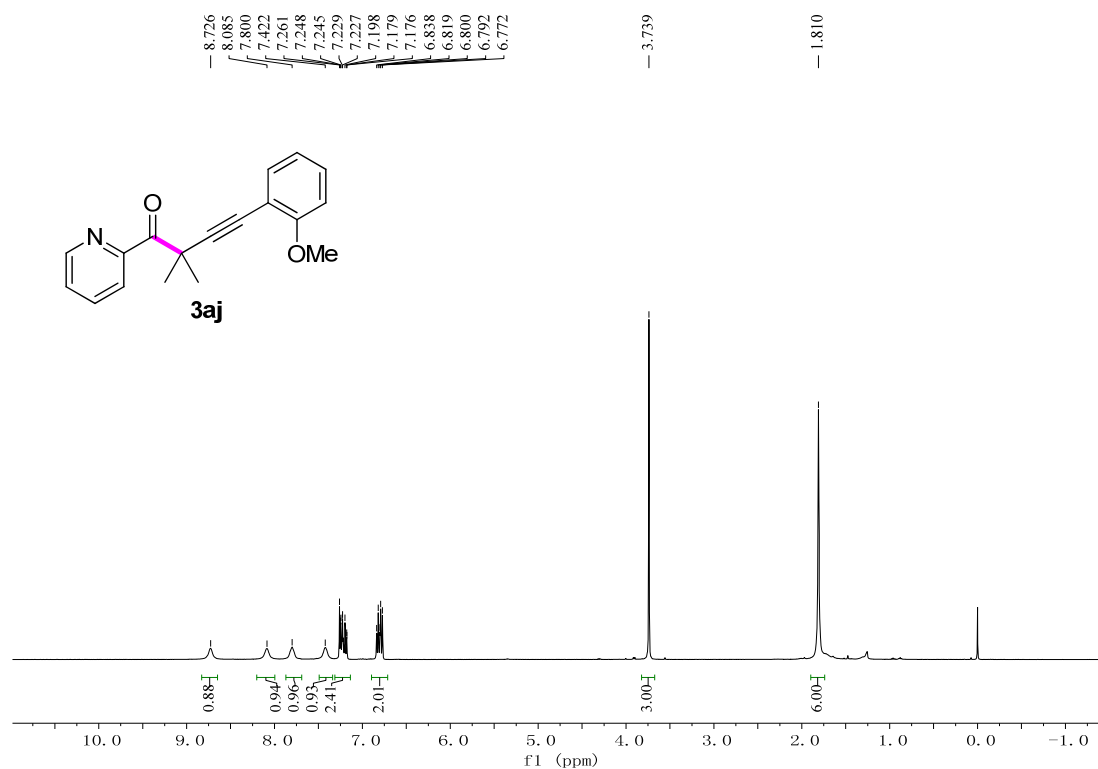
^1H NMR spectrum of compound **3ai**



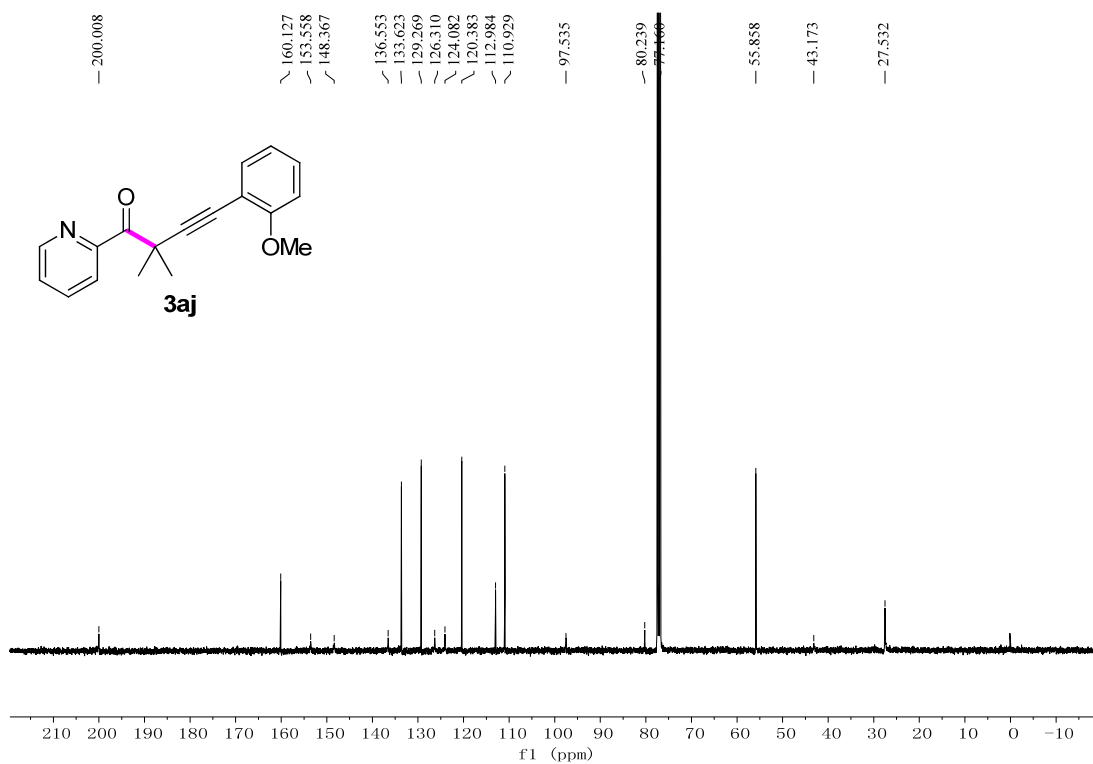
^{13}C NMR spectrum of compound **3ai**



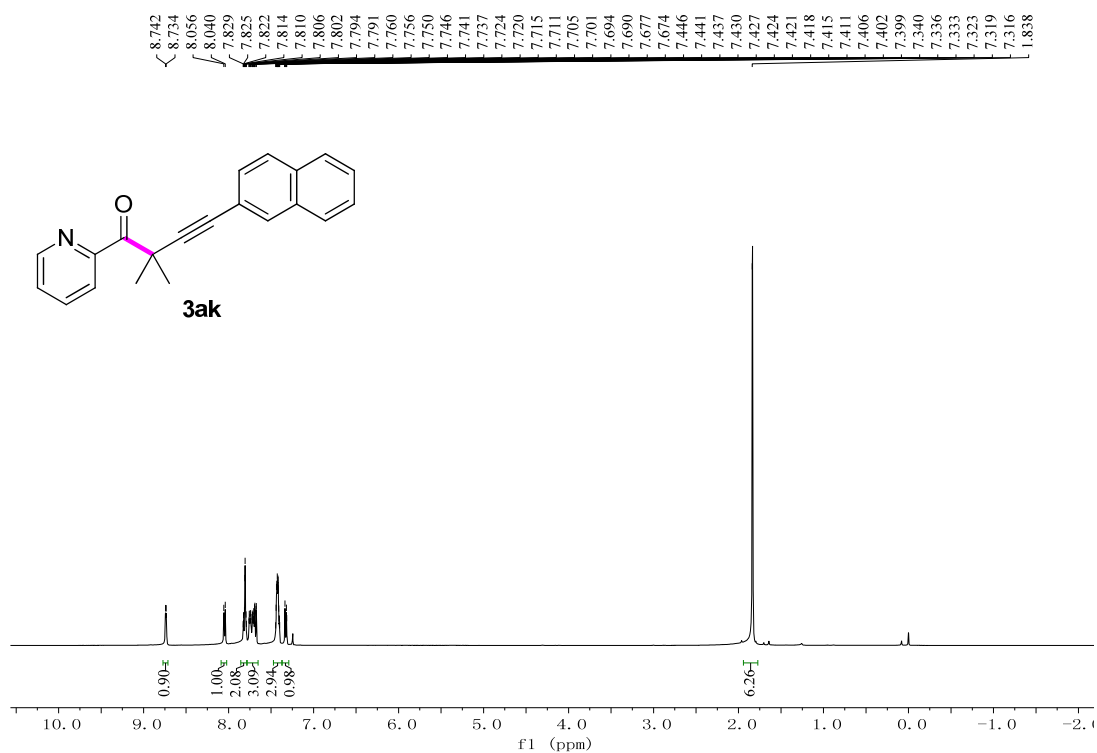
^1H NMR spectrum of compound **3aj**



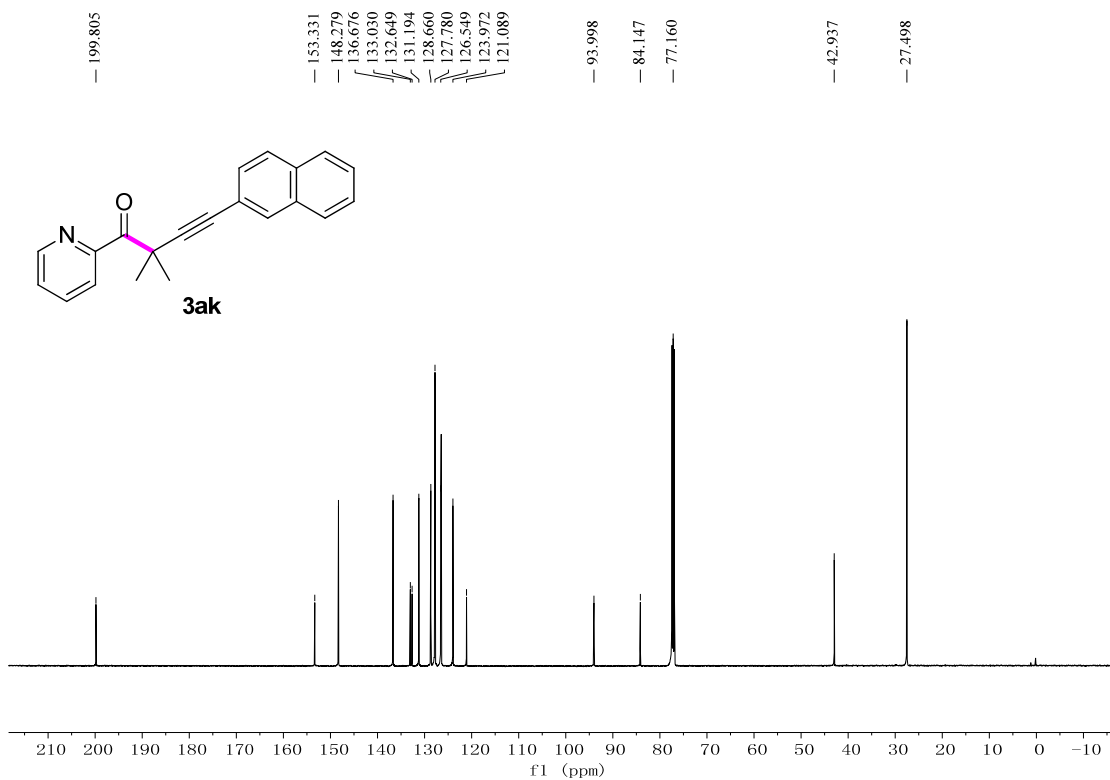
^{13}C NMR spectrum of compound **3aj**



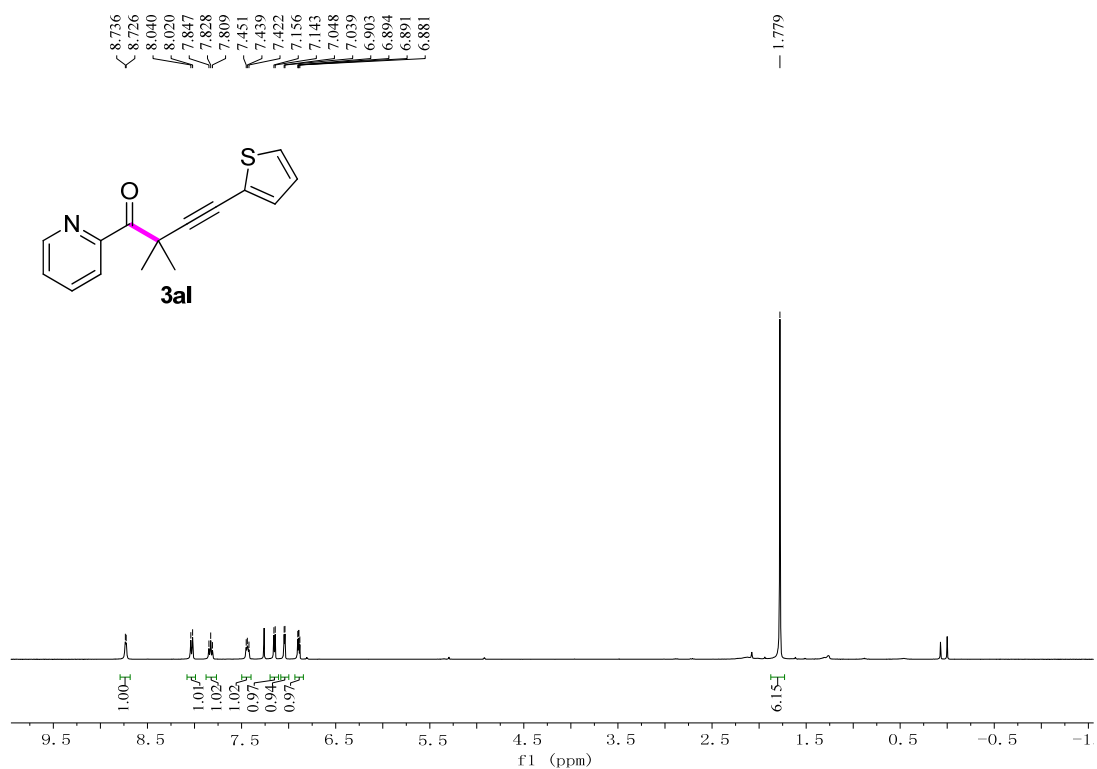
¹H NMR spectrum of compound **3ak**



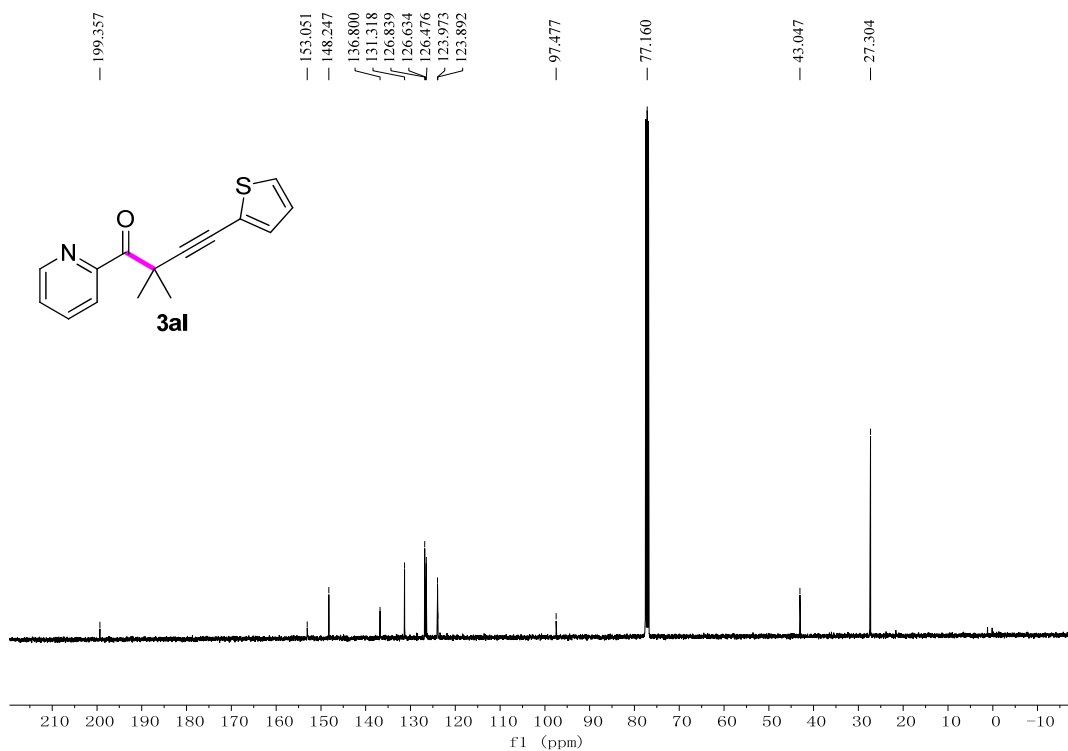
¹³C NMR spectrum of compound **3ak**



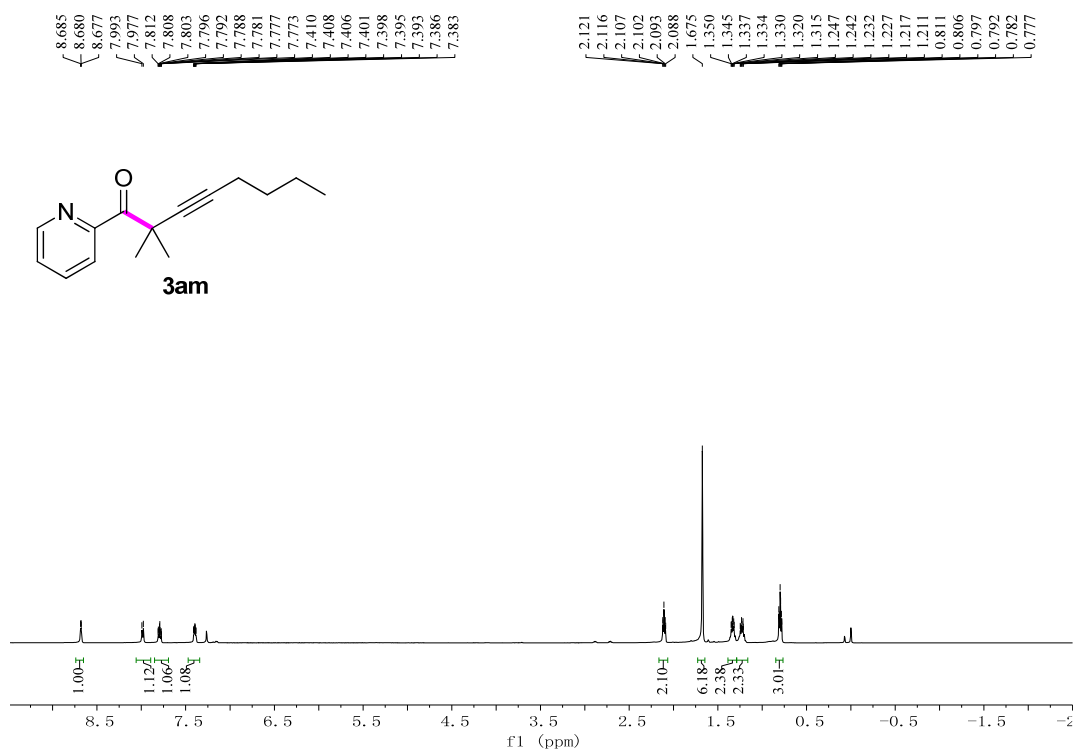
¹H NMR spectrum of compound **3al**



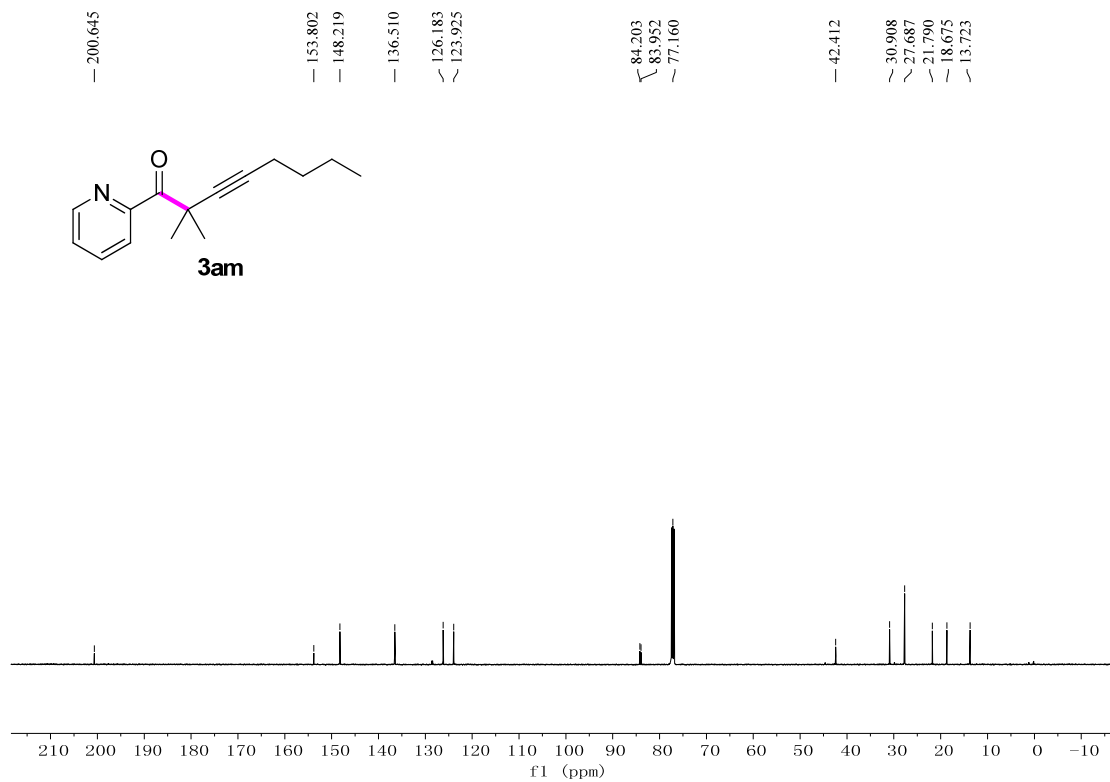
¹³C NMR spectrum of compound **3al**



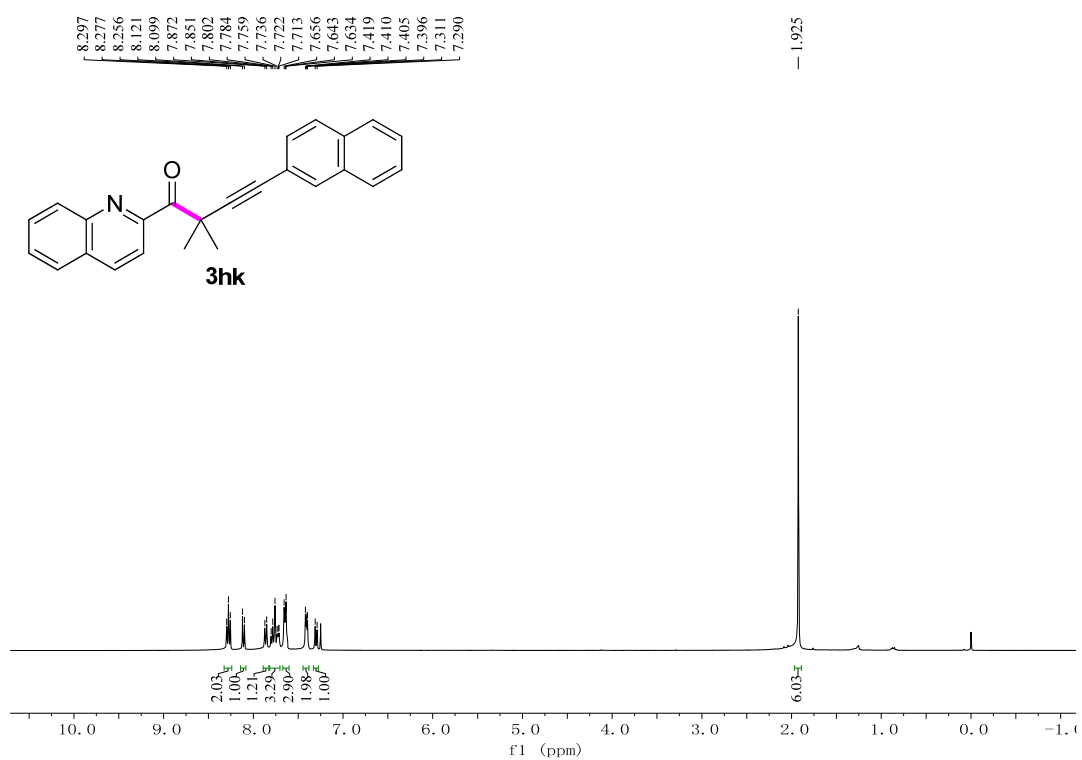
¹H NMR spectrum of compound **3am**



¹³C NMR spectrum of compound **3am**



¹H NMR spectrum of compound **3hk**



¹³C NMR spectrum of compound **3hk**

