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Supporting Information

Continuous flow processes for the S-alkynylation of cysteine-containing peptides and thioglycoside under catalyst-free, oxidant-free and mild conditions

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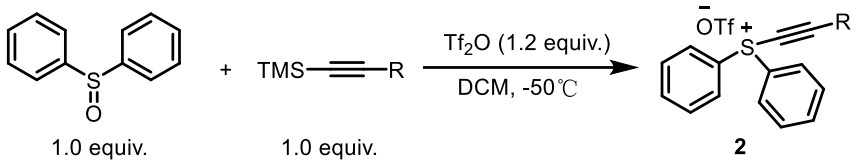
Contents

1. General Information

Unless otherwise stated, all components as well as reagents and solvents were bought from commercial suppliers (Energy Chemical, *J&K* Chemic and TCI) and used without further purification. Product isolation was performed using silica gel 60 (200-300 mesh). TLC analysis was performed using commercially prepared silica gel plates, and visualization was affected at ultraviolet light (254 nm). NMR spectra were recorded on a Bruke Avance operating for ^{1}H NMR at 400 MHz, ^{13}C NMR at 100 MHz, and ^{19}F NMR at 376 MHz. Chemical shifts (δ) were reported in ppm referenced to Tetramethylsilane (TMS) as internal standard. NMR spectra uses the following abbreviations to describe the multiplicity: s = single, d = doublet, t = triplet, q = quartet, m = multiple, dd = double doublet, td = triple doublet. Coupling constants (*J*) were reported in hertz (Hz). NMR data was processed using the MestReNova 9.0.1 software package. High resolution mass spectra were obtained on Agligent Technologies 6520 Accurate Series Q-TOF equipped with ESI.

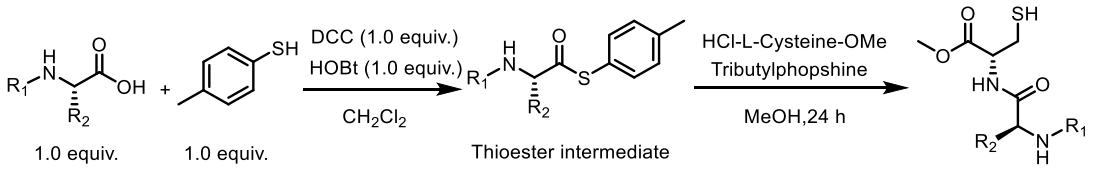
2. General procedure for the synthesis of the substrates

General procedure 1: preparation of transfer reagent



TMS-alkyne reagents were synthesized by the modification of literature procedure[1,2]. Prepared by the modification of a literature procedure[3]. Triflic anhydride (1.2 equiv.) was slowly added at -50 °C to a solution of Phenyl sulfoxide (1.0 equiv.) in DCM. The reaction was stirred for 1 hour at that temperature and then a solution of the desired TMS-alkyne (1.0 equiv.) in DCM (1 mL/mmol) was dropwise added. After this, the reaction mixture was slowly warmed until complete consumption of the starting material (monitored by TLC), the solvent was distilled off under reduced pressure. The resulting crude compound was absorbed on silica gel and purified via column chromatography to obtain corresponding product (DCM/MeOH, varying ratios).

General procedure 2: preparation of peptides



Amino acid derivative (1.0 equiv.) and *p*-toluenethiol (1.0 equiv.) were added to reaction flask under argon atmosphere, then CH_2Cl_2 was added and the flask placed in an ice bath (0^oC). Next, DCC (1.0 equiv.) and HOBt (1.0 equiv.) were added together. The reaction was transferred to room temperature and stirred for overnight. The CH_2Cl_2 was distilled off under reduced pressure and filtered, and the filtered cake was washed with ethyl acetate (3×100 mL) and saturated $NaHCO_3$ (3×30 mL). The obtained filtrate was extracted with ethyl acetate and brine. The organic layer was dried with Na_2SO_4. Depressurization to obtain crude product, then purified by column chromatography (EtOAc/PE, varying ratios) gave the desired intermediates.

L-Cysteine methyl ester HCl (1.0 equiv.) and the thioester derivative obtained from the previous step (1.0 equiv.) were added to MeOH in flask kept under argon atmosphere. Next tributylphopshine (0.6 equiv.) was added and the reaction was stirred at room temperature for 24 hours. The methanol was distilled off under reduced pressure, and then extracted with brine and ethyl acetate (3×100 mL). The organic layer was dried with Na_2SO_4 and concentrated on silica gel under vacuo. Purification by column chromatography (DCM/MeOH, varying ratios) afforded the desired peptides.

General procedure 3: preparation of Boc-Asn-Cys-OMe and Boc-Gln-Cys-OMe

These two dipeptides were prepared according to literature[4].

References

[1] M. Garreau, F. L. Vaillant and J. Waser, *Angew. Int. Ed. Chem*., 2019, **58**, 8182–8186.

[2] R. Frei, M. D. Wondrich. D. P. Hari, P-A. Hari, C. Chauvier and J. Waser, *J. Am. Chem. Soc*., 2014, **136**, 16563–16573.

[3] B. Waldecker, F. Kraft, C. Golz and M. Alcarazo, *Angew. Chem. Int. Ed*., 2018, **57**, 12538–12542.

[4] S. Verhoog, C. W. Kee, Y. Wang, T. Khotavivattana, T. C. Wilson, V. Kersemans, S. Smart, M. Tredwell, B. G. Davis and V. Gouverneur, *J. Am. Chem. Soc*., 2018, 140, **5**, 1572–1575.

3. General procedures for the alkynylation reaction

General Procedure A (GPA): alkynylation of cysteine containing peptides

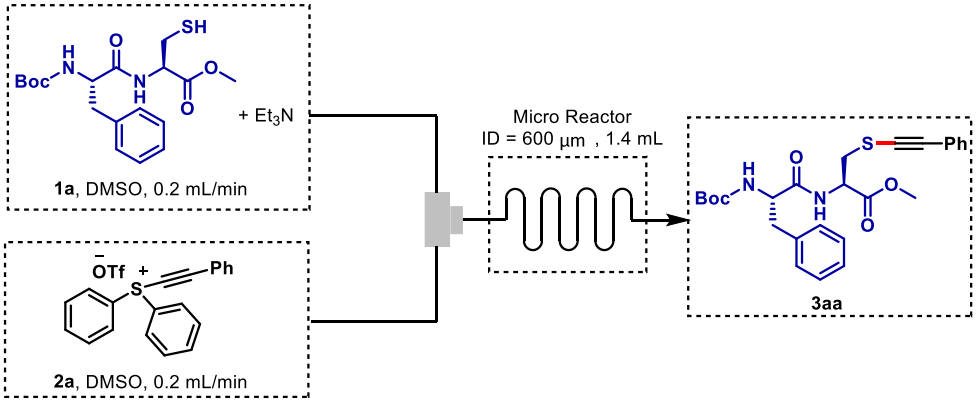


Figure S1 Schematic diagram of a flow set-up for the selective alkynylation of cysteine-containing cysteine dipeptides.

Substrate Boc-Phe-Cys-OMe **1a** (0.0764 g, 0.2 mmol, 1.0 equiv.) was dissolved in 2.0 mL of the solvent DMSO. After sufficient mixing, add 42 μL of Et_3N (0.3 mmol, 1.5 equiv.) to the mixture as reaction solution I. Substrate **2a** was dissolved in 2.0 mL of DMSO as reaction solution II. The two solutions were transferred into two 5 mL BD plastic syringes and introduced into the microreactor (a high purity perfluoroalkoxyalkane, PFA capillary tubing, ID = 600 μm) through syringe pump. The two liquid streams were merged with a Y-Mixer before entering the microreactor. The flow rate was set to 0.4 mL/min (0.2 mL/min per syringe), thus resulting in 3.5 min residence time (volume of reactor = 1.4 mL). After reaching steady state, the reaction sample was collected in a glass vial. Solution remaining in the microreactor was then discharged with DMSO (2.0 mL×2) via syringe pump, and was also collected in the same glass vial. The collected reaction solution was extracted with EtOAc (3×25 mL) and brine, and the organic layer was collected, dried with Na_2SO_4 and evaporated under reduced pressure. The resulting crude compound was absorbed on silica gel and purified via column chromatography (EtOAc/PE, varying ratios). The isolated compound was analyzed by HRMS and NMR.

General Procedure B (GPB): alkynylation of protected thioglycoside

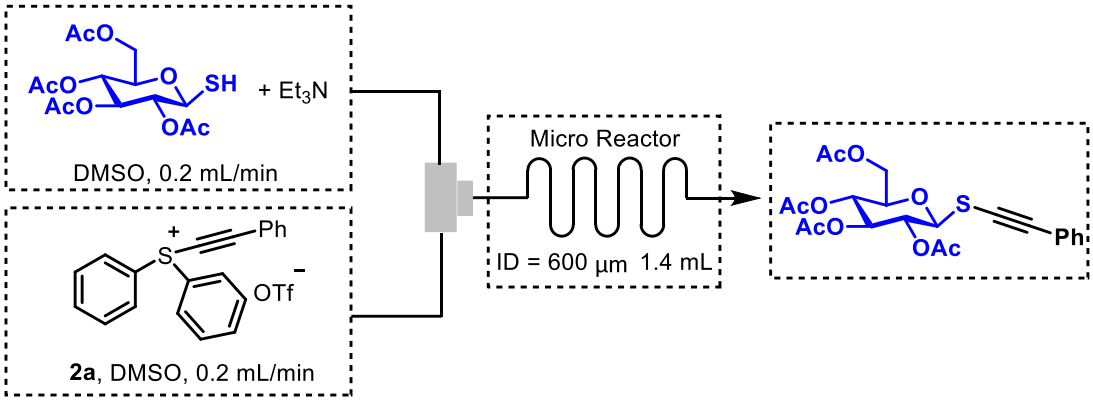


Figure S2 Schematic diagram of a flow set-up for the alkynylation of protected thioglycoside

Substrate thioglycoside (0.0728 g, 0.2 mmol, 1.0 equiv.) was dissolved in DMSO (2.0 mL) and then added 42 μL Et_3N (0.3 mmol, 1.5 equiv.). A second reaction solution was to dissolve the **2a** in DMSO (2.0 mL). The two solutions were transferred into two 5 mL BD plastic syringes and introduced into the microreactor (a high purity perfluoroalkoxyalkane, PFA capillary tubing, ID = 600 μm) through syringe pump. The two liquid streams were merged with a Y-Mixer before entering the reactor. The flow rate was set to 0.4 mL/min (0.2 mL/min per syringe), thus resulting in 3.5 min residence time (volume of reactor = 1.4 mL). After reaching steady state, the reaction sample was collected in a glass vial. Solution remaining in the microreactor was then discharged with DMSO (2.0 mL×2) via syringe pump, and was also collected in the same glass vial. The collected reaction solution was extracted with EtOAc (3×25 mL) and brine, and the organic layer was collected, dried with Na_2SO_4 and evaporated under reduced pressure. The resulting crude compound was absorbed on silica gel and purified via column chromatography (EtOAc/PE, varying ratios). The isolated compound was analyzed by HRMS and NMR.

Figure S3 Details of the microreactor for the alkynylation of cysteine and thioglycoside

4. Gram scale experiment

Boc-Phe-Cys-OMe (**1a**, 1.91 g, 5.0 mmol, 1.0 equiv.) was dissolved in DMSO and then added 1041 μL Et_3N (7.5 mmol, 1.5 equiv.). A second reaction solution was to dissolve the **2a** (3.27 g, 7.5 mmol, 1.5 equiv.) in DMSO (The volume of the two reaction solutions were 10.0 mL). The two solutions were transferred into two 10 mL BD plastic syringes and introduced into the microreactor through syringe pump. The two liquid streams were merged with a Y-Mixer before entering the reactor. The flow rate was set to 0.4 mL/min (0.2 mL/min per syringe), thus resulting in 3.5 min residence time (volume of reactor = 1.4 mL). After reaching steady state, the reaction sample was collected in a glass vial. Solution remaining in the microreactor was then discharged with DMSO (2.5 mL×2) via syringe pump, and was also collected in the same glass vial. The collected reaction solution was extracted with EtOAc (3×100 mL) and brine, and the organic layer was collected, dried with Na_2SO_4 and evaporated under reduced pressure. The resulting crude compound was absorbed on silica gel and purified via column chromatography (EtOAc/PE, varying ratios). The isolated compound was analyzed by HRMS and NMR.

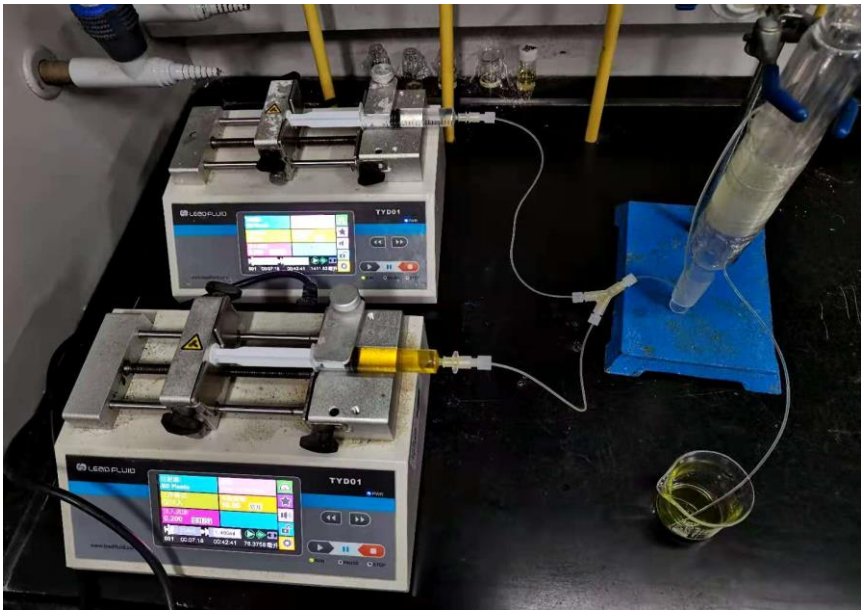


Figure S4 Details of gram scale experiment

5. X-ray crystallography structure of compound 2b

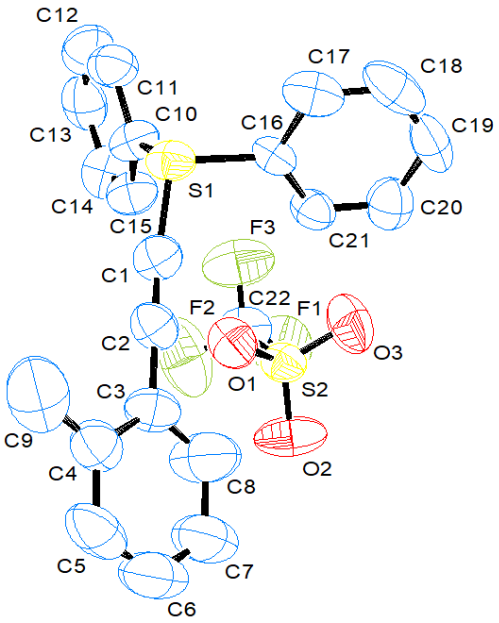
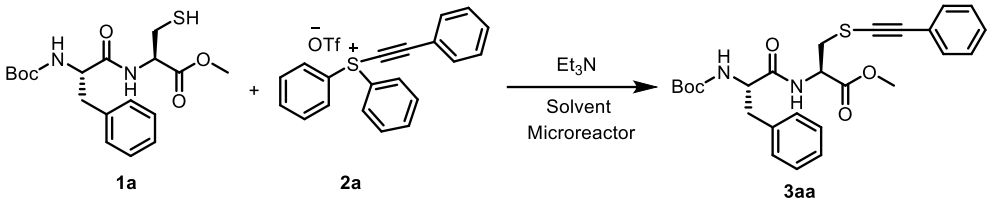


Figure S5 Structure of compound **2b**

The X-ray crystallographic coordinates for structures reported in this article have been deposited at the Cambridge Crystallographic Data Centre (CCDC), under deposition number CCDC 2052127 (**2b**).

6. Optimization of reaction conditions

Table S1. Screening of Solvents.

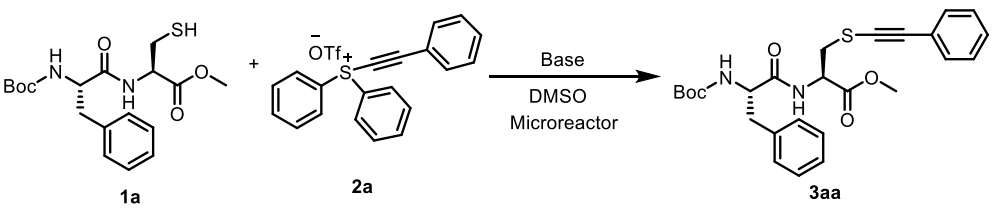


1a 2a 3aa

Entry[a]	Solvent	Residue time (min)	Yield (%)[b]
1	THF	3.5	73
2	DMF	3.5	75
3	DMAC	3.5	81
4	DCM	3.5	62
5	DCE	3.5	64
6	DMSO	3.5	86
7	1,4-dioxane	3.5	53
8	MeCN	3.5	80
9	MeOH	3.5	46
10	Acetone	3.5	55
11	DMSO/H_2O (1:1)	3.5	38
12	DMSO/PBS (1:1)	3.5	35

[a] Reaction conditions: **1a** (0.2 mmol, 1.0 equiv.) and Et_3N (0.3 mmol, 1.5 equiv.) was dissolved in DMSO (2.0 mL); **2a** (0.3 mmol, 1.5 equiv.) was dissolved in DMSO (2.0 mL). The solution was transferred into syringe and introduced into microreactor through syringe pump. The flow rate was set to 0.4 mL/min (0.2 mL/min per syringe). [b] Isolated yield was based on **1a**.

Table S2. Screening of Bases.



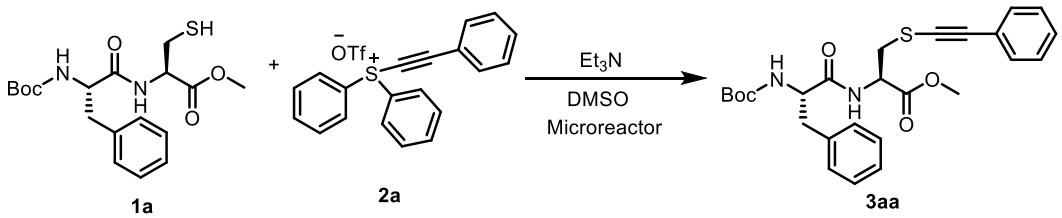
1a 2a 3aa

Entry[a]	Base	Residue time (min)	Yield (%)[b]
1	pyridine	3.5	51

2	2,6-lutidine	3.5	72
3	DIPEA	3.5	57
4	DABCO	3.5	13
5	TMEDA	3.5	57
6	DMAP	3.5	20
7	DBU	3.5	*N.D.*
8	None	3.5	34

[a] Reaction conditions: **1a** (0.2 mmol, 1.0 equiv.) and Base (0.3 mmol, 1.5 equiv.) was dissolved in DMSO (2.0 mL); **2a** (0.3 mmol, 1.5 equiv.) was dissolved in DMSO (2.0 mL). The solution was transferred into syringe and introduced into microreactor through syringe pump. The flow rate was set to 0.4 mL/min (0.2 mL/min per syringe). [b] Isolated yield was based on **1a**. *N.D.* = no detected.

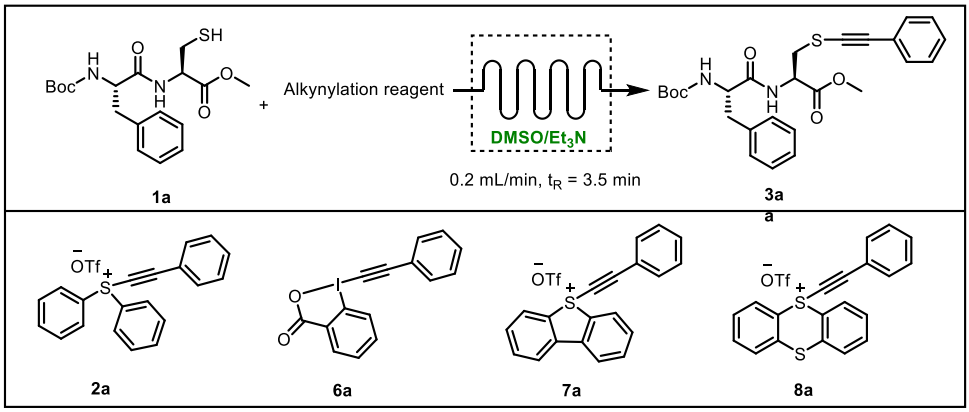
Table S3. Screening of Flow Rate.



Entry[a]	Rate (mL/min)	Residue time (min)	Yield (%)[b]
1	0.2	3.5	86
2	0.15	4.7	86
3	0.3	2.3	80
4[c]	-	-	78

[a] Reaction conditions: **1a** (0.2 mmol, 1.0 equiv.) and Et_3N (0.3 mmol, 1.5 equiv.) was dissolved in DMSO (2.0 mL); **2a** (0.3 mmol, 1.5 equiv.) was dissolved in DMSO (2.0 mL). The solution was transferred into syringe and introduced into microreactor through syringe pump. [b] Isolated yield was based on **1a**. [c] Reaction in batch: Ar atmosphere, rt, 3 h.

Table S4. Screening of Alkynylation Reagents.

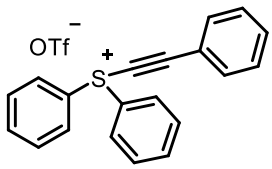


Entry[a]	Reagent	Residue time (min)	Yield (%)[b]
1	**2a**	3.5	86
2	**6a**	3.5	17
3	**7a**	3.5	51
4	**8a**	3.5	56

[a] Reaction conditions: **1a** (0.2 mmol, 1.0 equiv.) and Et_3N (0.3 mmol, 1.5 equiv.) was dissolved in DMSO (2.0 mL); alkynylation reagent (0.3 mmol, 1.5 equiv.) was dissolved in DMSO (2.0 mL). The solution was transferred into syringe and introduced into microreactor through syringe pump. The flow rate was set to 0.4 mL/min (0.2 mL/min per syringe). [b] Isolated yield was based on **1a**.

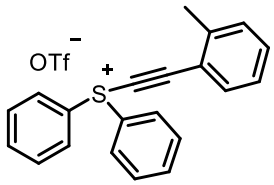
7. Spectra data

((Trifluoromethyl)sulfonyl)-λ^1-oxidane, diphenyl(phenylethynyl)sulfonium salt (**2a**)



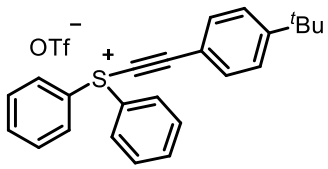
Gray powder (10 mmol scale, 3.48 g, 80%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.25 – 8.14 (m, 4H), 7.83 – 7.78 (m, 2H), 7.74 – 7.68 (m, 6H), 7.64 – 7.60 (m, 1H), 7.49 (t, *J* = 7.7 Hz, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 134.9, 133.7, 133.3, 131.9, 129.6, 129.2, 127.9, 116.9, 111.4, 63.0. ^{19}F NMR (376 MHz, Chloroform-*d*) δ 78.14. HRMS (ESI) m/z: calcd for $C_{20}H_{15}S^+$ [M–OTf]$^+$: 287.0889, found: 287.0892.

((Trifluoromethyl)sulfonyl)-λ^1-oxidane, diphenyl(o-tolylethynyl)sulfonium salt (**2b**)



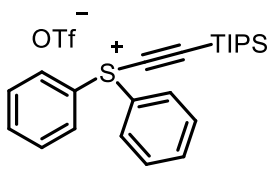
Gray powder (10 mmol scale, 3.23 g, 72%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.25 – 8.17 (m, 4H), 7.79 – 7.69 (m, 7H), 7.50 (t, *J* = 7.3 Hz, 1H), 7.35 – 7.28 (m, 2H), 2.52 (s, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 143.4, 135.0, 134.5, 133.3, 131.9, 130.4, 129.5, 128.0, 126.6, 120.9 (q, *J* = 318.9 Hz, 1C), 116.8, 111.0, 66.0, 20.8. ^{19}F NMR (376 MHz, Chloroform-*d*) δ 78.10. HRMS (ESI) m/z: calcd for $C_{21}H_{17}S^+$ [M–OTf]$^+$: 301.1045, found: 301.1041.

((Trifluoromethyl)sulfonyl)-λ^1-oxidane,((4-(tert-butyl)phenyl)ethynyl)diphenylsulfonium salt (**2c**)



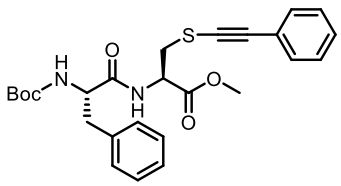
Gray powder (10 mmol scale, 3.64 g, 74%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.27 – 8.14 (m, 4H), 7.78 – 7.67 (m, 8H), 7.51 (d, *J* = 8.5 Hz, 2H), 1.32 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 157.6, 134.9, 133.7, 131.8, 129.5, 128.1, 126.3, 121.0 (q, *J* = 318.6 Hz, 1C), 113.7, 112.4, 62.2, 35.5, 30.9. ^{19}F NMR (376 MHz, Chloroform-*d*) δ 78.09. HRMS (ESI) m/z: calcd for $C_{24}H_{23}S^+$ [M–OTf]$^+$: 343.1515, found: 343.1519.

Diphenyl((triisopropylsilyl)ethynyl)sulfonium (**2d**)



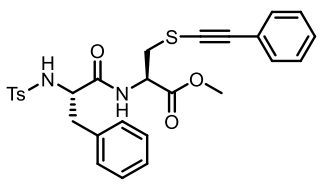
Gray powder (10 mmol scale, 3.72 g, 72%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.17 – 8.12 (m, 4H), 7.77 – 7.69 (m, 6H), 1.32 – 1.25 (m, 3H), 1.14 (d, *J* = 7.2 Hz, 18H). ^{13}C NMR (100 MHz, Chloroform-d) δ 135.1, 131.9, 129.4, 127.5, 122.7, 120.8 (q, *J* = 318.6 Hz, 1C), 18.4, 11.0. ^{19}F NMR (376 MHz, Chloroform-*d*) δ 78.19. HRMS (ESI) m/z: calcd for $C_{23}H_{31}SiS^{+}$ [M–OTf]$^{+}$: 367.1910, found: 367.1910.

Methyl *N*-((tert-butoxycarbonyl)-L-phenylalanyl)-*S*-(phenylethynyl)-L-cysteinate (**3aa**)



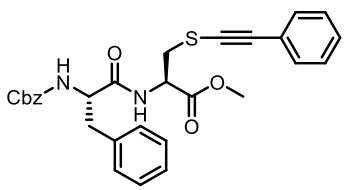
Light yellow solid (82.9 mg, 86%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 (s, 2H), 7.36 – 7.20 (m, 6H), 7.14 – 6.96 (m, 3H), 4.92 (s, 2H), 4.43 (s, 1H), 3.70 (s, 3H), 3.28 (s, 2H), 3.18 – 2.92 (m, 2H), 1.40 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.2, 169.8, 155.4, 136.3, 131.8, 129.2, 128.7, 128.6, 128.5, 127.0, 122.8, 92.8, 80.4, 78.1, 55.7, 52.9, 52.0, 38.1, 37.5, 28.3. HRMS (ESI) m/z: calcd for $C_{26}H_{30}N_2O_5SNa$ [M+Na]$^{+}$: 505.1768, found: 505.1767.

Methyl *S*-(phenylethynyl)-*N*-(tosyl-L-phenylalanyl)-L-cysteinate (**3ab**)



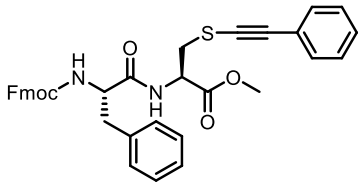
Yellow solid (88.0 mg, 82%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.52 (d, *J* = 8.3 Hz, 2H), 7.44 – 7.38 (m, 2H), 7.34 – 7.26 (m, 4H), 7.18 – 7.09 (m, 5H), 6.88 (d, *J* = 6.4 Hz, 2H), 5.31 (s, 1H), 4.91 – 4.81 (m, 1H), 4.01 (q, *J* = 7.3 Hz, 1H), 3.69 (s, 3H), 3.24 – 3.08 (m, 2H), 3.01 – 2.88 (m, 2H), 2.37 (s, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 170.4, 169.6, 143.7, 136.0, 135.1, 131.8, 129.8, 129.2, 128.8, 128.6, 128.5, 127.1(9), 127.1(5), 122.9, 93.1, 78.1, 57.9, 52.9, 52.1, 38.7, 37.4, 21.6. HRMS (ESI) m/z: calcd for $C_{28}H_{28}N_2O_5S_2Na$ [M+Na]$^{+}$: 559.1332, found: 559.1353.

Methyl *N*-(((benzyloxy)carbonyl)-L-phenylalanyl)-*S*-(phenylethynyl)-L-cysteinate (**3ac**)



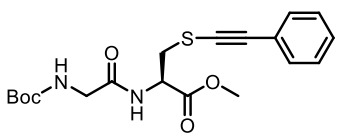
Yellow solid (78.5 mg, 76%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.36 (m, 2H), 7.34 – 7.18 (m, 11H), 7.10 (d, *J* = 5.9 Hz, 2H), 7.02 (s, 1H), 5.36 (s, 1H), 5.11 – 5.00 (s, 2H), 4.96 – 4.84 (m, 1H), 4.53 (s, 1H), 3.67 (s, 3H), 3.23 (d, *J* = 4.0 Hz, 2H), 3.16 – 2.98 (m, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 170.9, 169.8, 156.0, 136.2, 131.7, 129.3, 128.7, 128.6, 128.5, 128.2, 128.1, 127.1, 122.8, 93.1, 78.0, 67.2, 56.1, 52.9, 52.1, 38.4, 37.4. HRMS (ESI) m/z: calcd for $C_{29}H_{28}N_2O_5SNa$ $[M+Na]^+$: 539.1611, found: 539.1649.

Methyl *N*-((((9H-fluoren-9-yl)methoxy)carbonyl)-L-phenylalanyl)-*S*-(phenylethynyl) -L-cysteinate (**3ad**)



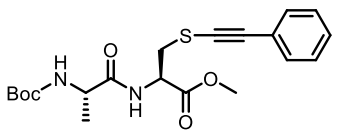
Light yellow solid (51.9 mg, 43%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.76 (d, *J* = 7.5 Hz, 2H), 7.55 – 7.48 (m, 2H), 7.43 – 7.35 (m, 4H), 7.34 – 7.23 (m, 8H), 7.17 – 7.03 (m, 2H), 6.85 (s, 1H), 5.25 (s, 1H), 4.99 – 4.83 (m, 1H), 4.54 – 4.37 (m, 2H), 4.33 (s, 1H), 4.18 (t, *J* = 6.8 Hz, 1H), 3.69 (s, 3H), 3.27 (d, *J* = 4.1 Hz, 2H), 3.15 – 3.00 (m, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 170.6, 169.7, 155.8, 143.8, 143.7, 141.3, 136.1, 131.7, 129.2, 128.8, 128.6, 128.5, 127.7, 127.2, 127.1, 125.0, 122.8, 120.0, 93.1, 77.8, 67.2, 56.1, 52.9, 52.1, 47.1, 38.3, 37.4. HRMS (ESI) m/z: calcd for $C_{36}H_{32}N_2O_5SNa$ $[M+Na]^+$: 627.1924, found: 627.1954.

Methyl *N*-((tert-butoxycarbonyl)glycyl)-*S*-(phenylethynyl)-L-cysteinate (**3ae**)



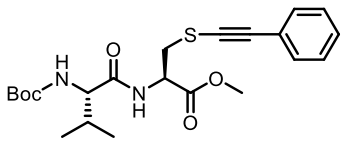
Light yellow oil (62.7 mg, 80%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.47 – 7.36 (m, 2H), 7.35 – 7.25 (m, 3H), 7.21 (s, 1H), 5.23 (s, 1H), 5.05 – 4.90 (m, 1H), 3.92 – 3.79 (m, 2H), 3.73 (s, 3H), 3.40 – 3.22 (m, 2H), 1.46 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 170.1, 169.5, 156.0, 131.6, 128.6, 128.4, 122.8, 92.9, 80.4, 77.9, 53.0, 51.9, 44.2, 37.4, 28.3. HRMS (ESI) m/z: calcd for $C_{19}H_{24}N_2O_5SNa$ $[M+Na]^+$: 415.1298, found: 415.1289.

Methyl *N*-((tert-butoxycarbonyl)-L-alanyl)-*S*-(phenylethynyl)-L-cysteinate (**3af**)



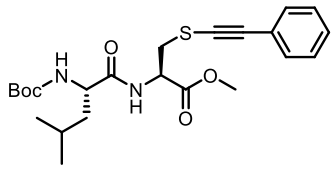
Light yellow oil (66.6 mg, 82%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45 – 7.38 (m, 2H), 7.35 – 7.24 (m, 4H), 5.12 (d, *J* = 7.2 Hz, 1H), 4.99 – 4.90 (m, 1H), 4.25 (s, 1H), 3.72 (s, 3H), 3.32 (d, *J* = 3.5 Hz, 2H), 1.46 (s, 9H), 1.35 (d, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.7, 170.1, 155.4, 131.7, 128.5, 128.4, 122.9, 93.0, 80.2, 78.0, 52.9, 51.9, 50.1, 37.5, 28.33, 18.1. HRMS (ESI) m/z: calcd for $C_{20}H_{26}N_2O_5SNa$ $[M+Na]^+$: 429.1455, found: 429.1446.

Methyl *N*-((tert-butoxycarbonyl)-L-valyl)-*S*-(phenylethynyl)-L-cysteinate (**3ag**)



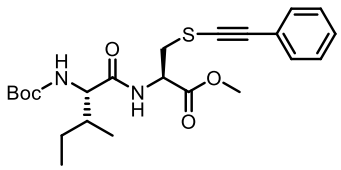
Yellow oil (73.8 mg, 85%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.47 – 7.38 (m, 2H), 7.35 – 7.26 (m, 3H), 7.05 (s, 1H), 5.07 (d, *J* = 7.1 Hz, 1H), 5.00 – 4.93 (m, 1H), 4.04 (s, 1H), 3.72 (s, 3H), 3.39 – 3.24 (m, 2H), 2.26 – 2.14 (m, 1H), 1.46 (s, 9H), 0.97 (d, *J* = 6.7 Hz, 3H), 0.90 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.6, 170.1, 155.8, 131.8, 128.6, 128.4, 122.2, 93.2, 80.1, 77.7, 59.8, 52.9, 51.8, 37.5, 30.8, 28.3, 19.2, 17.5. HRMS (ESI) m/z: calcd for $C_{22}H_{30}N_2O_5SNa$ $[M+Na]^+$: 457.1768, found: 457.1757.

Methyl *N*-((tert-butoxycarbonyl)-L-leucyl)-*S*-(phenylethynyl)-L-cysteinate (**3ah**)



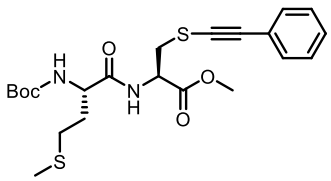
Light yellow oil (71.7 mg, 80%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.46 – 7.40 (m, 2H), 7.34 – 7.28 (m, 3H), 7.17 (s, 1H), 5.00 – 4.91 (m, 1H), 4.80 (s, 1H), 4.16 (s, 1H), 3.73 (s, 3H), 3.31 (d, *J* = 4.6 Hz, 2H), 1.79 – 1.51 (m, 3H), 1.46 (s, 9H), 0.89 (t, *J* = 6.2 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.5, 170.1, 155.6, 131.7, 128.6, 128.4, 122.9, 92.9, 80.3, 78.1, 53.2, 52.9, 52.0, 40.9, 37.5, 28.3, 24.7, 22.9, 21.7. HRMS (ESI) m/z: calcd for $C_{23}H_{32}N_2O_5SNa$ $[M+Na]^+$: 471.1924, found: 471.1934.

Methyl *N*-((tert-butoxycarbonyl)-L-alloisoleucyl)-*S*-(phenylethynyl)-L-cysteinate (**3ai**)



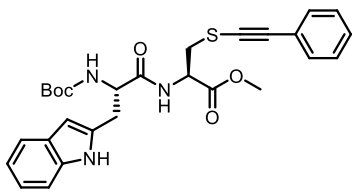
Light yellow solid (75.2 mg, 84%).^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45 – 7.39 (m, 2H), 7.33 – 7.27 (m, 3H), 7.10 (s, 1H), 5.12 (s, 1H), 5.01 – 4.92 (m, 1H), 4.07 (s, 1H), 3.72 (s, 3H), 3.38 – 3.25 (m, 2H), 1.97 – 1.88 (m, 1H), 1.50 – 1.42 (m, 10H), 1.15 – 1.06 (d, *J* = 7.5 Hz, 1H), 0.94 (d, *J* = 6.8 Hz, 3H), 0.89 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.6, 170.1, 155.7, 131.7, 128.5, 128.4, 122.8, 93.2, 80.0, 77.8, 59.3, 52.8, 51.8, 37.5, 37.2, 28.3, 24.7, 15.6, 11.5. HRMS (ESI) m/z: calcd for $C_{23}H_{32}N_2O_5SNa$ $[M+Na]^+$: 471.1924, found: 471.1927.

Methyl *N*-((tert-butoxycarbonyl)-L-methionyl)-*S*-(phenylethynyl)-L-cysteinate (**3aj**)



Light yellow solid (76.4 mg, 82%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45 – 7.39 (m, 2H), 7.34 – 7.25 (m, 4H), 5.24 (s, 1H), 5.00 – 4.93 (m, 1H), 4.35 (s, 1H), 3.73 (s, 3H), 3.37 – 3.26 (m, 2H), 2.56 (t, *J* = 7.2 Hz, 2H), 2.16 – 2.10 (m, 1H), 2.09 (s, 3H), 1.97 – 1.89 (m, 1H), 1.46 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.5, 170.0, 155.5, 131.7, 128.6, 128.4, 122.8, 93.2, 80.3, 77.8, 53.4, 52.9, 51.9, 37.4, 31.5, 30.1, 28.3, 15.2. HRMS (ESI) m/z: calcd for $C_{22}H_{30}N_2O_5S_2Na$ $[M+Na]^+$: 489.1488, found: 489.1498.

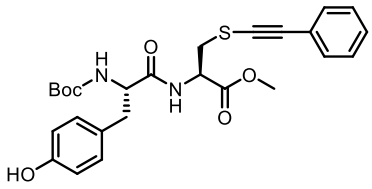
Methyl *N*-((tert-butoxycarbonyl)-L-tryptophyl)-*S*-(phenylethynyl)-L-cysteinate (**3ak**)



Light yellow solid (95.8 mg, 92%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.47 (s, 1H), 7.59 (d, *J* = 7.4 Hz, 1H), 7.42 – 7.23 (m, 6H), 7.20 – 7.13 (m, 1H), 7.12 – 7.05 (m, 1H), 7.04 – 6.87 (m, 2H), 5.20 (s, 1H), 4.83 (s, 1H), 4.51 (s, 1H), 3.61 (s, 3H), 3.38 – 3.03 (m, 4H), 1.42 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.9, 169.8, 155.5, 136.3, 131.7, 128.5, 128.4, 127.5, 123.3, 122.9, 122.2, 119.7, 118.7, 111.4, 110.1, 92.9, 80.3, 78.1, 52.8, 51.8, 37.6, 31.6, 28.3, 22.7,

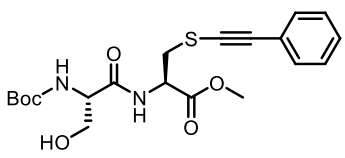
14.2. HRMS (ESI) m/z: calcd for $C_{28}H_{31}N_3O_5SNa$ $[M+Na]^+$: 544.1877, found: 544.1880.

Methyl *N*-((tert-butoxycarbonyl)-L-tyrosyl)-*S*-(phenylethynyl)-L-cysteinate (**3al**)



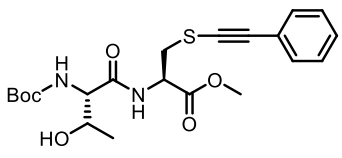
Light yellow solid (85.1 mg, 85%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45 – 7.37 (m, 2H), 7.34 – 7.25 (m, 3H), 7.07 (s, 1H), 6.99 – 6.84 (m, 3H), 6.71 (d, *J* = 7.6 Hz, 2H), 5.14 – 4.99 (m, 1H), 4.91 (s, 1H), 4.37 (s, 1H), 3.69 (s, 3H), 3.31 – 3.19 (m, 2H), 3.07 – 2.86 (m, 2H), 1.42 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.7, 169.9, 155.6, 155.3, 131.7, 130.3, 128.6, 128.5, 127.5, 122.8, 115.7, 93.0, 80.7, 77.9, 55.9, 53.0, 52.0, 37.4, 31.6, 28.3, 22.7, 14.2. HRMS (ESI) m/z: calcd for $C_{26}H_{30}N_2O_6SNa$ $[M+Na]^+$: 521.1717, found: 521.1709.

Methyl *N*-((tert-butoxycarbonyl)-L-seryl)-*S*-(phenylethynyl)-L-cysteinate (**3am**)



Light yellow solid (45.6 mg, 54%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59 (s, 1H), 7.45 – 7.39 (m, 2H), 7.34 – 7.26 (m, 3H), 5.59 (s, 1H), 5.02 – 4.88 (m, 1H), 4.34 – 4.19 (m, 1H), 4.10 – 3.99 (m, 1H), 3.76 – 3.63 (m, 4H), 3.32 (d, *J* = 5.0 Hz, 2H), 2.03 (s, 1H), 1.46 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.4, 170.2, 156.0, 131.7, 128.6, 128.4, 122.8, 93.4, 80.6, 77.5, 62.9, 55.2, 53.0, 52.0, 37.2, 28.3. HRMS (ESI) m/z: calcd for $C_{20}H_{26}N_2O_6SNa$ $[M+Na]^+$: 445.1404, found: 445.1410.

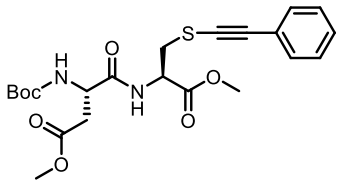
Methyl *N*-((tert-butoxycarbonyl)-L-threonyl)-*S*-(phenylethynyl)-L-cysteinate (**3an**)



Light yellow solid (54.1 mg, 62%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.56 (s, 1H), 7.46 – 7.39 (m, 2H), 7.33 – 7.27 (m, 3H), 5.53 (s, 1H), 5.00 – 4.89 (m, 1H), 4.41 – 4.30 (s, 1H), 4.18 (d, *J* = 6.8 Hz, 1H), 3.73 (s, 3H), 3.31 (d, *J* = 5.1 Hz, 2H), 2.04 – 1.86 (s, 1H), 1.46 (s, 9H), 1.19 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.4, 170.1, 156.3, 131.7, 128.6, 128.4, 122.8, 93.4, 80.5, 77.5,

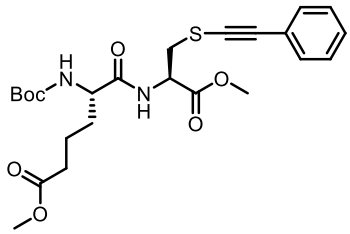
66.9, 58.3, 53.0, 51.8, 37.3, 28.3, 18.1. HRMS (ESI) m/z: calcd for $C_{21}H_{28}N_2O_6SNa$ $[M+Na]^+$: 459.1560, found: 459.1566.

Methyl (*S*)-3-((tert-butoxycarbonyl)amino)-4-(((*R*)-1-methoxy-1-oxo-3-((phenylethynyl)thio) propan-2-yl)amino)-4-oxobutanoate (**3ao**)



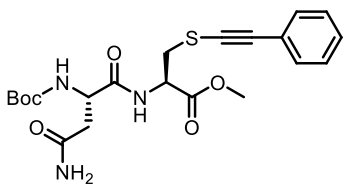
Light yellow solid (73.3 mg, 79%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.52 – 7.37 (m, 3H), 7.34 – 7.24 (m, 3H), 5.66 (s, 1H), 4.98 – 4.85 (m, 1H), 4.59 (s, 1H), 3.71 (d, *J* = 6.6 Hz, 6H), 3.40 – 3.22 (m, 2H), 3.04 – 2.90 (m, 1H), 2.78 – 2.65 (m, 1H), 1.47 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.1, 170.7, 169.9, 155.5, 131.7, 128.5, 128.4, 122.9, 93.1, 80.7, 77.8, 52.9, 52.1, 51.9, 50.6, 37.4, 35.9, 28.3. HRMS (ESI) m/z: calcd for $C_{22}H_{28}N_2O_7SNa$ $[M+Na]^+$: 487.1509, found: 487.1508.

Methyl (*S*)-4-((tert-butoxycarbonyl)amino)-5-(((*R*)-1-methoxy-1-oxo-3-((phenylethynyl)thio)propan-2-yl)amino)-5-oxopentanoate (**3ap**)



Light yellow solid (82.0 mg, 86%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45 – 7.39 (m, 2H), 7.34 – 7.26 (m, 4H), 5.29 (s, 1H), 4.98 – 4.91 (m, 1H), 4.24 (s, 1H), 3.73 (s, 3H), 3.68 (s, 3H), 3.31 (t, *J* = 4.5 Hz, 2H), 2.51 – 2.41 (m, 2H), 2.00 – 1.90 (m, 2H), 1.45 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.7, 171.5, 170.0, 155.6, 131.7, 128.5, 128.4, 122.8, 93.2, 80.3, 77.7, 53.7, 52.9, 51.9, 37.4, 30.2, 28.3, 27.7. HRMS (ESI) m/z: calcd for $C_{23}H_{30}N_2O_7SNa$ $[M+Na]^+$: 501.1666, found: 501.1663.

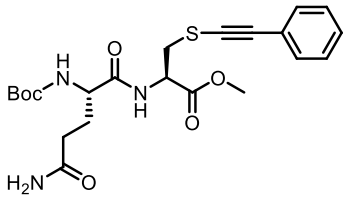
Methyl *N*-((tert-butoxycarbonyl)-L-asparaginyl)-*S*-(phenylethynyl)-L-cysteinate (**3aq**)



Light yellow solid (72.6 mg, 81%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.43 (d, *J* = 7.5 Hz, 1H), 7.49 – 7.42 (m, 2H), 7.41 – 7.35 (m, 3H), 7.30 (s, 1H), 7.05 – 6.84 (m, 2H), 4.71 – 4.60 (m, 1H), 4.38 – 4.23 (m, 1H), 3.63 (s, 3H), 3.31 – 3.24 (m, 1H), 3.21 – 3.10 (m, 1H), 2.48 – 2.32 (m, 2H), 1.38 (s, 9H). ^{13}C

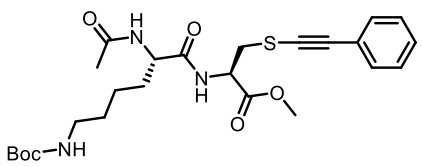
NMR (100 MHz, DMSO-d_6) δ 172.5, 171.8, 170.8, 155.6, 131.7, 129.2, 122.8, 93.5, 79.2, 78.7, 52.8, 51.9, 51.6, 37.6, 36.9, 28.6. HRMS (ESI) m/z: calcd for $C_{21}H_{27}N_3O_6SNa$ $[M+Na]^+$: 472.1513, found: 472.1492.

Methyl *N*-((tert-butoxycarbonyl)-L-glutaminyl)-*S*-(phenylethynyl)-L-cysteinate (**3ar**)



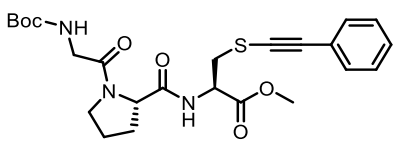
Light yellow solid (74.1 mg, 80%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.95 (s, 1H), 7.47 – 7.37 (m, 2H), 7.34 – 7.24 (m, 3H), 6.55 (s, 1H), 6.17 (s, 1H), 5.74 (s, 1H), 5.01 – 4.86 (m, 1H), 4.34 – 4.22 (m, 1H), 3.72 (s, 3H), 3.38 – 3.18 (m, 2H), 2.43 – 2.33 (m, 2H), 2.11 – 1.96 (m, 2H), 1.43 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 175.7, 172.0, 170.7, 155.9, 131.7, 128.5, 128.4, 122.9, 93.5, 80.2, 77.8, 53.6, 52.9, 51.9, 37.2, 31.7, 29.0, 28.3. HRMS (ESI) m/z: calcd for $C_{22}H_{29}N_3O_6SNa$ $[M+Na]^+$: 486.1669, found: 486.1627.

Methyl *N*-(*N*^{2}-acetyl-*N*^{6}-(tert-butoxycarbonyl)-L-lysyl)-*S*-(phenylethynyl)-L-cystein ate (**3as**)



Light yellow solid (71.7 mg, 71%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45 – 7.36 (m, 3H), 7.33 – 7.27 (m, 3H), 6.48 (s, 1H), 4.97 – 4.86 (m, 1H), 4.82 – 4.70 (m, 1H), 4.58 – 4.50 (m, 1H), 3.74 (s, 3H), 3.30 (d, *J* = 4.7 Hz, 2H), 3.14 – 3.03 (m, 2H), 2.10 – 2.05 (m, 1H), 2.00 (s, 3H), 1.90 – 1.82 (m, 1H), 1.72 – 1.63 (m, 1H), 1.48 – 1.38 (m, 12H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.8, 170.4, 170.1, 156.2, 131.6, 128.5, 128.4, 122.8, 93.4, 79.1, 77.8, 53.0, 52.9, 51.9, 39.9, 37.3, 31.9, 29.6, 28.4, 23.1, 22.3. HRMS (ESI) m/z: calcd for $C_{25}H_{35}N_3O_6SNa$ $[M+Na]^+$: 528.2139, found: 528.2151.

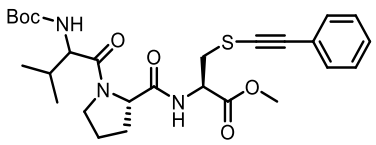
Methyl *N*-(tert-butoxycarbonyl)glycyl-L-prolyl-*S*-(phenylethynyl)-L-cysteinate **(3at**)



Light yellow oil (66.6 mg, 68%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.61 (s, 1H), 7.47 – 7.36 (m, 2H),

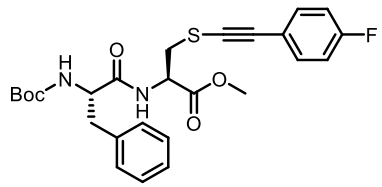
7.34 – 7.24 (m, 3H), 5.46 (s, 1H), 4.96 – 4.78 (m, 1H), 4.64 (d, *J* = 7.4 Hz, 1H), 4.05 – 3.84 (m, 2H), 3.72 (s, 3H), 3.56 – 3.46 (m, 1H), 3.43 – 3.35 (m, 1H), 3.30 (d, *J* = 5.2 Hz, 2H), 2.43 – 2.30 (m, 1H), 2.16 – 1.82 (m, 4H), 1.44 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 170.9, 170.2, 168.8, 155.8, 131.6, 128.4(3), 128.3(7), 93.3, 79.7, 60.1, 52.8, 51.8, 46.2, 43.1, 37.3, 28.3, 27.5, 24.5. HRMS (ESI) m/z: calcd for $C_{24}H_{31}N_3O_6SNa$ $[M+Na]^+$: 512.1826, found: 512.1804.

Methyl *N*-(tert-butoxycarbonyl)valyl-L-prolyl-*S*-(phenylethynyl)-L-cysteinate (**3au**)



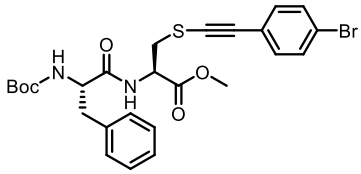
Light yellow oil (84.9 mg, 80%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.60 (s, 1H), 7.43 – 7.37 (m, 2H), 7.32 – 7.26 (m, 3H), 5.30 (s, 1H), 4.91 – 4.83 (m, 1H), 4.70 – 4.60 (m, 1H), 4.37 – 4.24 (m, 1H), 3.75 – 3.67 (m, 4H), 3.62 – 3.56 (m, 1H), 3.36 – 3.22 (m, 2H), 2.34 (d, *J* = 9.6 Hz, 1H), 2.10 – 1.93 (m, 4H), 1.43 (s, 9H), 1.03 (d, *J* = 6.7 Hz, 3H), 0.96 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.7, 171.1, 170.1, 155.9, 131.6, 128.4, 128.3, 123.0, 93.1, 79.6, 77.9, 60.0, 56.8, 52.8, 51.9, 47.6, 37.5, 31.6, 28.3, 27.4, 25.1, 19.7, 17.4. HRMS (ESI) m/z: calcd for $C_{27}H_{37}N_3O_6SNa$ $[M+Na]^+$: 554.2295, found: 554.2247.

Methyl *N*-((tert-butoxycarbonyl)-L-phenylalanyl)-*S*-((4-fluorophenyl)ethynyl)-L-cysteinate (**3ba**)



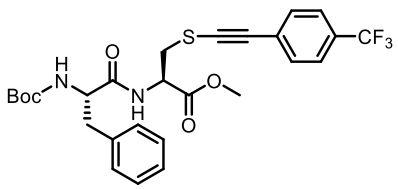
Light yellow solid (80.1 mg, 80%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43 – 7.37 (m, 2H), 7.30 – 7.22 (m, 3H), 7.13 (d, *J* = 7.0 Hz, 2H), 7.05 – 6.96 (m, 3H), 4.99 (s, 1H), 4.94 – 4.89 (m, 1H), 4.44 (s, 1H), 3.69 (s, 3H), 3.26 (d, *J* = 4.8 Hz, 2H), 3.16 – 2.97 (m, 2H), 1.40 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.2, 169.9, 162.6 (d, *J* = 248.8 Hz, 1C), 155.3, 136.4, 133.9, 133.8, 129.3, 128.7, 127.0, 119.0 (d, *J* = 3.3 Hz, 1C), 115.9, 115.7, 91.9, 80.4, 77.8, 55.6, 52.8, 51.9, 38.1, 37.4, 28.2. ^{19}F NMR (376 MHz, Chloroform-*d*) δ 109.97. HRMS (ESI) m/z: calcd for $C_{26}H_{29}FN_2O_5SNa$ $[M+Na]^+$: 523.1673, found: 523.1638.

Methyl *S*-((4-bromophenyl)ethynyl)-*N*-((tert-butoxycarbonyl)-L-phenylalanyl)-L-cysteinate (**3bb**)



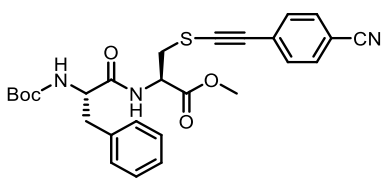
Light yellow solid (72.7 mg, 65%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43 (d, *J* = 8.5 Hz, 2H), 7.30 – 7.22 (m, 5H), 7.12 (d, *J* = 7.0 Hz, 2H), 6.92 (s, 1H), 4.99 – 4.83 (m, 2H), 4.47 – 4.34 (m, 1H), 3.70 (s, 3H), 3.27 (d, *J* = 4.7 Hz, 2H), 3.15 – 2.98 (m, 2H), 1.41 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.2, 169.7, 155.3, 133.3, 133.1, 131.7, 129.2, 128.7, 127.1, 122.8, 121.8, 91.9, 80.5, 79.6, 76.7, 55.7, 52.9, 52.0, 37.5, 34.0, 28.2. HRMS (ESI) m/z: calcd for $C_{26}H_{29}BrN_2O_5SNa$ $[M+Na]^+$: 583.0873, found: 583.0883.

Methyl *N*-((tert-butoxycarbonyl)-L-phenylalanyl)-*S*-((4-(trifluoromethyl)phenyl)ethynyl)-L-cysteinate (**3bc**)



Light yellow solid (90.2 mg, 82%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.55 (d, *J* = 8.3 Hz, 2H), 7.49 (d, *J* = 8.1 Hz, 2H), 7.30 – 7.22 (m, 3H), 7.13 (d, *J* = 6.9 Hz, 2H), 7.02 (s, 1H), 4.95 (d, *J* = 25.7 Hz, 2H), 4.44 (s, 1H), 3.71 (s, 3H), 3.30 (d, *J* = 4.7 Hz, 2H), 3.16 – 3.00 (m, 2H), 1.40 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.3, 169.8, 155.4, 136.3, 131.5, 129.9 (d, *J* = 32.6 Hz, 1C), 129.2, 128.7, 127.0, 126.7, 125.3(8) (d, *J* = 38.5 Hz, 1C), 125.3(7) (q, *J* = 3.8 Hz, 2C), 122.5, 91.8, 81.5, 80.4, 55.7, 52.7, 51.9, 38.1, 37.5, 28.2. ^{19}F NMR (376 MHz, Chloroform-*d*) δ 62.82. HRMS (ESI) m/z: calcd for $C_{27}H_{29}F_3N_2O_5SNa$ $[M+Na]^+$: 573.1641, found: 573.1619.

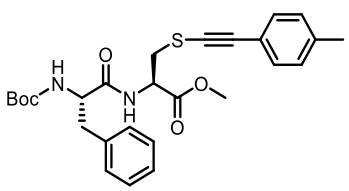
Methyl *N*-((tert-butoxycarbonyl)-L-phenylalanyl)-*S*-((4-cyanophenyl)ethynyl)-L-cysteinate (**3bd**)



Yellow solid (68.6 mg, 68%).^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.58 (d, *J* = 8.3 Hz, 2H), 7.46 (d, *J* = 8.3 Hz, 2H), 7.31 – 7.27 (m, 2H), 7.26 – 7.21 (m, 1H),

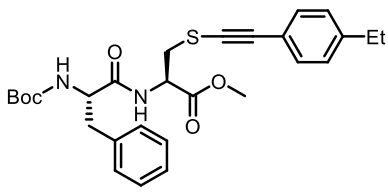
7.15 (d, *J* = 6.9 Hz, 2H), 6.87 (s, 1H), 4.99 – 4.86 (m, 2H), 4.41 (s, 1H), 3.71 (s, 3H), 3.30 (d, *J* = 3.7 Hz, 2H), 3.09 (d, *J* = 6.2 Hz, 2H), 1.41 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.2, 169.7, 155.3, 136.2, 132.1, 131.5, 129.2, 128.8, 127.7, 127.1, 118.4, 111.4, 91.8, 84.1, 80.5, 55.7, 52.9, 51.9, 38.1, 37.6, 28.2. HRMS (ESI) m/z: calcd for $C_{27}H_{29}N_3O_5SNa$ $[M+Na]^+$: 530.1720, found: 530.1686.

Methyl *N*-((tert-butoxycarbonyl)-L-phenylalanyl)-*S*-(p-tolylethynyl)-L-cysteinate (**3be**)



Light yellow solid (79.4 mg, 80%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32 (d, *J* = 8.0 Hz, 2H), 7.27 – 7.20 m, 3H), 7.13 – 7.07 (m, 4H), 7.06 – 7.01 (m, 1H), 4.99 – 4.87 (m, 2H), 4.42 (s, 1H), 3.70 (s, 3H), 3.26 (d, *J* = 4.5 Hz, 2H), 3.17 – 3.11 (m, 1H), 3.00 – 2.90 (m, 1H), 2.35 (s, 3H), 1.40 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.2, 169.8, 155.3, 138.9, 136.4, 131.9, 129.2(6), 129.2(5), 128.7, 127.0, 119.8, 93.0, 80.4, 55.7, 52.9, 52.0, 38.1, 37.5, 28.2, 21.5. HRMS (ESI) m/z: calcd for $C_{27}H_{32}N_2O_5SNa$ $[M+Na]^+$: 519.1924, found: 519.1944

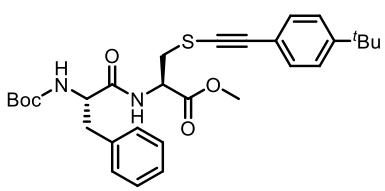
Methyl *N*-((tert-butoxycarbonyl)-L-phenylalanyl)-*S*-((4-ethylphenyl)ethynyl)-L-cysteinate (**3bf**)



Light yellow solid (75.4 mg, 74%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 (d, *J* = 8.0 Hz, 2H), 7.27 – 7.21 (m, 3H), 7.14 (d, *J* = 8.0 Hz, 2H), 7.08 (d, *J* = 6.9 Hz, 2H), 7.03 (s, 1H), 4.98 – 4.83 (m, 2H), 4.42 (s, 1H), 3.70 (s, 3H), 3.27 (d, *J* = 4.5 Hz, 2H), 3.18 – 3.11 (m, 1H), 3.00 – 2.90 (m, 1H), 2.64 (q, *J* = 7.6 Hz, 2H), 1.40 (s, 9H), 1.22 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.2, 169.8, 155.3, 145.2, 136.4, 131.9, 129.2, 128.7, 128.1, 127.0, 120.0, 93.0, 80.4, 55.7, 52.9, 52.1, 38.1, 37.5, 28.8, 28.2, 15.3. HRMS (ESI) m/z: calcd for $C_{28}H_{34}N_2O_5SNa$ $[M+Na]^+$: 533.2081, found: 533.2060.

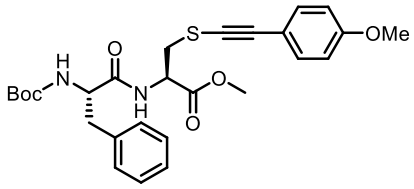
Methyl *N*-((tert-butoxycarbonyl)-L-phenylalanyl)-*S*-((4-(tert-butyl)phenyl)ethynyl)-L-

cysteinate (**3bg**)



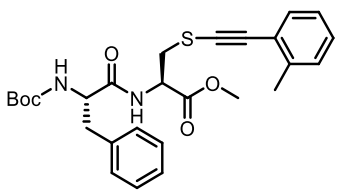
Light yellow solid (84.7 mg, 79%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.30 (m, 4H), 7.28 – 7.20 (m, 3H), 7.13 – 7.02 (m, 3H), 4.92 (s, 2H), 4.43 (s, 1H), 3.71 (s, 3H), 3.27 (d, *J* = 4.3 Hz, 2H), 3.20 – 3.12 (m, 1H), 3.01 – 2.88 (m, 1H), 1.40 (s, 9H), 1.30 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.2, 169.9, 155.3, 152.0, 136.5, 131.7, 129.2, 128.7, 127.0, 125.5, 119.8, 93.3, 80.4, 55.7, 52.9, 52.1, 38.1, 37.5, 34.8, 31.2, 28.2. HRMS (ESI) m/z: calcd for $C_{30}H_{39}N_2O_5SNa$ $[M+Na]^+$: 561.2394, found: 561.2360.

Methyl *N*-((tert-butoxycarbonyl)-L-phenylalanyl)-*S*-((4-methoxyphenyl)ethynyl)-L-cysteinate (**3bh**)



Light yellow solid (58.2 mg, 57%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 (d, *J* = 8.7 Hz, 2H), 7.28 (s, 1H), 7.25 – 7.21 (m, 2H), 7.09 (d, *J* = 7.3 Hz, 2H), 7.00 (d, *J* = 7.3 Hz, 1H), 6.86 – 6.80 (m, 2H), 4.98 – 4.83 (m, 2H), 4.41 (s, 1H), 3.81 (s, 3H), 3.70 (s, 3H), 3.25 (d, *J* = 4.3 Hz, 2H), 3.17 – 3.11 (m, 1H), 3.02 – 2.92 (m, 1H), 1.41 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.1, 169.9, 160.0, 136.4, 133.8, 129.2, 128.7, 127.0, 114.9, 114.1, 92.9, 80.4, 76.2, 55.7, 55.3, 52.8, 52.1, 38.1, 37.5, 28.2. HRMS (ESI) m/z: calcd for $C_{27}H_{32}N_2O_6SNa$ $[M+Na]^+$: 535.1873, found: 535.1835.

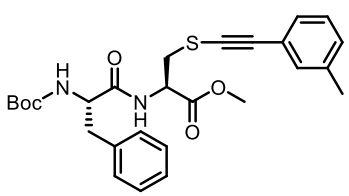
Methyl *N*-((tert-butoxycarbonyl)-L-phenylalanyl)-*S*-(o-tolylethynyl)-L-cysteinate (**3bi**)



Light yellow solid (79.6 mg, 80%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 (d, *J* = 7.5 Hz, 1H), 7.29 – 7.17 (m, 5H), 7.11 (t, *J* = 9.7 Hz, 3H), 7.05 – 6.99 (m, 1H), 5.00 – 4.84 (m, 2H), 4.42 (s, 1H), 3.68 (s, 3H), 3.32 – 3.22 (m, 2H), 3.17 – 3.09 (m, 1H), 3.02 – 2.90 (m, 1H), 2.41 (s, 3H), 1.40 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.2, 169.9, 155.4, 140.6, 136.4, 132.1, 129.6, 129.3,

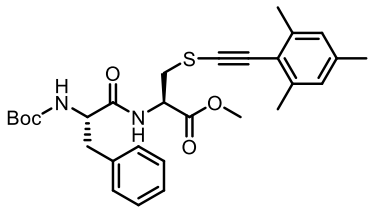
128.7, 128.6, 127.0, 125.7, 122.7, 91.9, 81.5, 80.4, 55.7, 52.8, 52.0, 38.1, 37.8, 28.3, 20.7. HRMS (ESI) m/z: calcd for $C_{27}H_{32}N_2O_5SNa$ $[M+Na]^+$: 519.1924, found: 519.1901.

Methyl *N*-((tert-butoxycarbonyl)-L-phenylalanyl)-*S*-(m-tolylethynyl)-*L*-cysteinate (**3bj**)



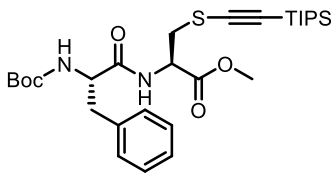
Light yellow solid (85.3 mg, 86%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 – 7.16 (m, 6H), 7.15 – 7.02 (m, 4H), 5.04 – 4.82 (m, 2H), 4.44 (s, 1H), 3.70 (s, 3H), 3.34 – 3.20 (m, 2H), 3.19 – 3.09 (m, 1H), 3.03 – 2.88 (m, 1H), 2.30 (s, 3H), 1.40 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.2, 169.9, 155.4, 138.2, 136.4, 132.3, 129.5, 129.2, 128.9, 128.7, 128.4, 127.0, 93.1, 80.3, 77.7, 55.7, 52.9, 52.1, 38.1, 37.5, 28.2, 21.2. HRMS (ESI) m/z: calcd for $C_{27}H_{32}N_2O_5SNa$ $[M+Na]^+$: 519.1924, found: 519.1899.

Methyl *N*-((tert-butoxycarbonyl)-L-phenylalanyl)-*S*-(mesitylethynyl)-L-cysteinate (**3bk**)



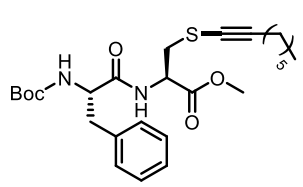
Light yellow solid (84.1 mg, 80%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.29 – 7.21 (m, 3H), 7.06 (d, *J* = 6.9 Hz, 2H), 6.97 (d, *J* = 6.8 Hz, 1H), 6.85 (s, 2H), 4.96 – 4.89 (m, 1H), 4.82 (s, 1H), 4.38 (s, 1H), 3.66 (s, 3H), 3.34 – 3.19 (m, 2H), 3.17 – 3.10 (m, 1H), 2.93 – 2.83 (m, 1H), 2.38 (s, 6H), 2.27 (s, 3H), 1.39 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.4. 169.9, 155.4, 140.8, 138.2, 136.4, 129.2, 128.7, 127.8, 127.0, 119.7, 90.9, 84.4, 80.4, 76.8, 55.8, 52.7, 52.1, 38.1, 28.2, 21.4, 21.0. HRMS (ESI) m/z: calcd for $C_{29}H_{36}N_2O_5SNa$ $[M+Na]^+$: 547.2237, found: 547.2208.

Methyl *N*-((tert-butoxycarbonyl)-L-phenylalanyl)-*S*-((triisopropylsilyl)ethynyl)-L-cysteinate (**3bl**)



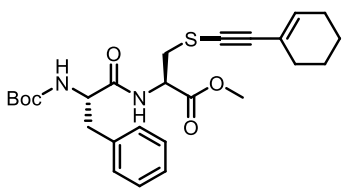
Light yellow solid (94.3 mg, 84%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.30 (t, *J* = 7.2 Hz, 2H), 7.25 (d, *J* = 7.1 Hz, 1H), 7.20 (d, *J* = 7.0 Hz, 2H), 6.76 (s, 1H), 5.02 (s, 1H), 4.84 – 4.76 (m, 1H), 4.48 – 4.32 (m, 1H), 3.75 (s, 3H), 3.28 – 3.11 (m, 1H), 3.15 – 3.06 (m, 3H), 1.41 (s, 9H), 1.07 (s, 21H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.2, 169.9, 155.3, 136.3, 129.3, 128.7, 127.0, 98.2, 94.1, 80.3, 55.5, 52.8, 51.7, 38.1, 28.3, 18.6, 11.3. HRMS (ESI) m/z: calcd for $C_{29}H_{46}SiN_2O_5SNa$ $[M+Na]^+$: 585.2789, found: 585.2757.

Methyl *N*-((tert-butoxycarbonyl)-L-phenylalanyl)-*S*-(oct-1-yn-1-yl)-L-cysteinate (**3bm**)



Colorless oil, (33.3 mg, 34%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32 – 7.28 (m, 2H), 7.26 – 7.19 (m, 3H), 6.70 (s, 1H), 5.00 (s, 1H), 4.81 – 4.74 (m, 1H), 4.40 (s, 1H), 3.74 (s, 3H), 3.25 – 3.15 (m, 2H), 3.14 – 2.99 (m, 4H), 2.23 – 2.16 (m, 2H), 1.54 – 1.47 (m, 2H), 1.41 (s, 9H), 1.37 – 1.30 (m, 4H), 0.90 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.1, 170.8, 155.3, 136.5, 129.4, 128.7, 127.0, 124.8, 84.8, 74.6, 55.6, 52.6, 51.7, 38.2, 33.2, 31.1, 28.4, 28.3, 22.2, 20.4, 18.8, 14.0. HRMS (ESI) m/z: calcd for $C_{26}H_{38}N_2O_5SNa$ $[M+Na]^+$: 513.2394, found: 513.2359.

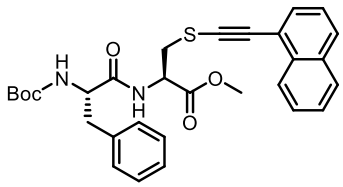
Methyl *N*-((tert-butoxycarbonyl)-L-phenylalanyl)-*S*-(cyclohex-1-en-1-ylethynyl)-L-cysteinate (**3bn**)



Light yellow solid (40.2 mg, 41%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33 – 7.27 (m, 2H), 7.25 (d, *J* = 7.0 Hz, 1H), 7.20 (d, *J* = 7.1 Hz, 2H), 6.91 (s, 1H), 6.12 (s, 1H), 5.05 – 4.91 (m, 1H), 4.90 – 4.84 (m, 1H), 4.43 (s, 1H), 3.75 (s, 3H), 3.20 – 3.01 (m, 4H), 2.12 – 2.05 (m, 4H), 1.63 – 1.53 (m, 4H), 1.41 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.1, 169.9, 155.3, 136.4, 136.2, 129.3, 128.7, 127.0, 124.8, 120.7, 94.9, 80.4, 74.6, 55.6, 52.8, 52.0, 38.2, 37.5, 29.1, 28.2,

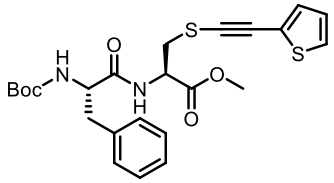
25.7, 22.2, 21.4. HRMS (ESI) m/z: calcd for $C_{26}H_{34}N_2O_5SNa$ $[M+Na]^+$: 509.2081, found: 509.2134.

Methyl *N*-((tert-butoxycarbonyl)-L-phenylalanyl)-S-(naphthalen-1-ylethynyl)-L-cysteinate (**3bo**)



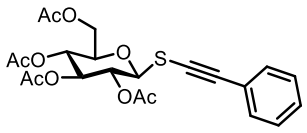
Light yellow solid (82.4 mg, 77%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.27 (d, *J* = 8.2 Hz, 1H), 7.83 (t, *J* = 8.4 Hz, 2H), 7.66 (d, *J* = 6.8 Hz, 1H), 7.62 – 7.56 (m, 1H), 7.55 – 7.49 (m, 1H), 7.40 (t, *J* = 7.7 Hz, 1H), 7.26 – 7.17 (m, 3H), 7.11 – 7.04 (m, 1H), 7.01 (d, *J* = 6.6 Hz, 2H), 5.06 – 4.80 (m, 2H), 4.42 (s, 1H), 3.65 (s, 3H), 3.45 – 3.33 (m, 2H), 3.16 – 3.07 (m, 1H), 2.96 – 2.83 (m, 1H), 1.39 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.2, 169.8, 155.4, 136.3, 133.4, 133.2, 130.9, 129.2, 129.1, 128.7, 128.4, 127.1, 127.0, 126.6, 126.1, 125.3, 120.5, 91.0, 82.9, 80.4, 55.7, 52.9, 52.2, 37.9, 28.2. HRMS (ESI) m/z: calcd for $C_{30}H_{32}N_2O_5SNa$ $[M+Na]^+$: 555.1924, found: 555.1915.

Methyl *N*-((tert-butoxycarbonyl)-L-phenylalanyl)-S-(thiophen-2-ylethynyl)-L-cysteinate (**3bp**)



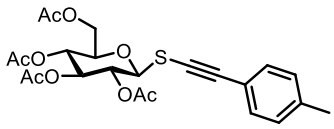
Yellowish brown solid (62.0 mg, 64%).^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 – 7.28 (m, 2H), 7.26 – 7.19 (m, 3H), 7.15 – 7.09 (m, 2H), 7.03 – 6.94 (m, 2H), 4.90 (s, 2H), 4.42 (s, 1H), 3.72 (s, 3H), 3.32 – 3.23 (m, 2H), 3.18 – 3.11 (m, 1H), 3.04 – 2.94 (m, 1H), 1.41 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.1, 169.7, 155.3, 136.3, 133.7, 129.2, 128.7, 128.5, 127.1, 127.0, 123.0, 85.6, 82.7, 80.5, 55.6, 52.9, 52.0, 38.0, 37.6, 28.2. HRMS (ESI) m/z: calcd for $C_{24}H_{28}N_2O_5S_2Na$ $[M+Na]^+$: 511.1332, found: 511.1314.

(2*R*,3*R*,4*S*,5*R*,6*S*)-2-(acetoxymethyl)-6-((phenylethynyl)thio)tetrahydro-2H-pyran-3,4,5-triyl triacetate (**5a**)



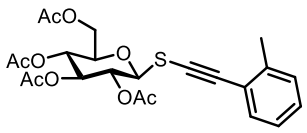
Light yellow solid (61.1 mg, 66%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.53 – 7.47 (m, 2H), 7.37 – 7.29 (m, 3H), 5.36 – 5.25 (m, 2H), 5.15 (t, *J* = 9.6 Hz, 1H), 4.63 (d, *J* = 9.3 Hz, 1H), 4.30 – 4.24 (m, 1H), 4.22 – 4.16 (m, 1H), 3.83 – 3.77 (m, 1H), 2.11 (s, 3H), 2.06 (s, 3H), 2.03 (d, *J* = 5.2 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 170.7, 170.2, 169.4, 169.1, 132.1, 128.9, 128.3, 122.6, 97.1, 84.4, 76.5, 73.9, 72.5, 69.8, 67.8, 62.0, 20.7(3), 20.6(9), 20.6(2), 20.5(9). HRMS (ESI) m/z: calcd for $C_{22}H_{24}O_9SNa$ $[M+Na]^+$: 487.1032, found: 487.1032.

(2*R*,3*R*,4*S*,5*R*,6*S*)-2-(acetoxymethyl)-6-((p-tolylethynyl)thio)tetrahydro-2H-pyran-3,4,5-triyl triacetate (**5b**)



Light yellow solid (53.1 mg, 56%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 (d, *J* = 7.9 Hz, 2H), 7.13 (d, *J* = 7.8 Hz, 2H), 5.35 – 5.24 (m, 2H), 5.14 (t, *J* = 9.5 Hz, 1H), 4.62 (d, *J* = 9.2 Hz, 1H), 4.30 – 4.23 (m, 1H), 4.22 – 4.15 (m, 1H), 3.84 – 3.75 (m, 1H), 2.36 (s, 3H), 2.10 (s, 3H), 2.06 (s, 3H), 2.03 (d, *J* = 5.7 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 170.7, 170.2, 169.4, 169.0, 139.2, 132.2, 129.1, 119.5, 97.3, 84.5, 76.5, 73.9, 71.6, 69.8, 67.9, 62.0, 21.6, 20.7(3), 20.6(8), 20.6(2), 20.5(8). HRMS (ESI) m/z: calcd for $C_{23}H_{26}O_9SNa$ $[M+Na]^+$: 501.1190, found: 501.1143.

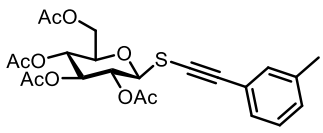
(2*R*,3*R*,4*S*,5*R*,6*S*)-2-(acetoxymethyl)-6-((o-tolylethynyl)thio)tetrahydro-2H-pyran-3,4,5-triyl triacetate (**5c**)



Light yellow solid (69.2 mg, 72%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.46 (d, *J* = 7.5 Hz, 1H), 7.27 – 7.18 (m, 2H), 7.14 (t, *J* = 7.2 Hz, 1H), 5.36 – 5.25 (m, 2H), 5.12 (d, *J* = 9.4 Hz, 1H), 4.62 (d, *J* = 9.3 Hz, 1H), 4.31 – 4.24 (m, 1H), 4.22 – 4.15 (m, 1H), 3.85 – 3.77 (m, 1H), 2.46 (s, 3H), 2.10 (s, 3H), 2.07 – 2.00 (m, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 170.7, 170.2, 169.3, 169.0, 140.7, 132.3, 129.5, 128.8, 125.6, 122.5, 96.0, 84.4, 76.5, 76.1, 73.8, 69.9, 67.8, 62.0, 20.7(3), 20.7(0), 20.6(7), 20.6(2),

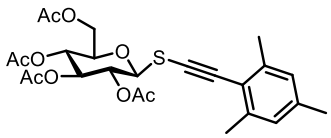
20.5(8). HRMS (ESI) m/z: calcd for $C_{23}H_{26}O_9SNa$ $[M+Na]^+$: 501.1190, found: 501.1167.

(2*R*,3*R*,4*S*,5*R*,6*S*)-2-(acetoxymethyl)-6-((m-tolylethynyl)thio)tetrahydro-2H-pyran-3,4,5-triyl triacetate (**5d**)



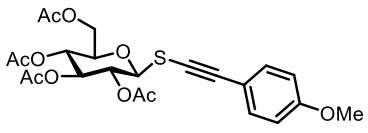
Light yellow solid (70.4 mg, 74%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 (d, *J* = 8.3 Hz, 2H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.15 (d, *J* = 7.4 Hz, 1H), 5.35 – 5.24 (m, 2H), 5.15 (t, *J* = 9.4 Hz, 1H), 4.62 (d, *J* = 9.1 Hz, 1H), 4.30 – 4.23 (m, 1H), 4.22 – 4.15 (m, 1H), 3.84 – 3.76 (m, 1H), 2.34 (s, 3H), 2.10 (s, 3H), 2.06 (s, 3H), 2.03 (d, *J* = 5.1 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 170.7, 170.2, 169.4, 138.0, 132.6, 129.8, 129.2, 128.2, 122.4, 97.2, 84.5, 76.5, 73.9, 72.1, 69.8, 67.9, 62.0, 21.2, 20.7(2), 20.6(8), 20.6(2), 20.5(8). HRMS (ESI) m/z: calcd for $C_{23}H_{26}O_9SNa$ $[M+Na]^+$: 501.1190, found: 501.1162.

(2*R*,3*R*,4*S*,5*R*,6*S*)-2-(acetoxymethyl)-6-((mesitylethynyl)thio)tetrahydro-2H-pyran-3,4,5-triyl triacetate (**5e**)



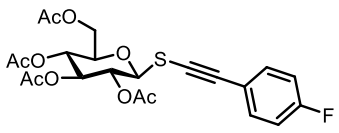
Yellow solid (80.8 mg, 80%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.86 (s, 2H), 5.34 – 5.25 (m, 2H), 5.11 (t, *J* = 9.5 Hz, 1H), 4.60 (d, *J* = 9.3 Hz, 1H), 4.31 – 4.25 (m, 1H), 4.19 – 4.14 (m, 1H), 3.82 – 3.77 (m, 1H), 2.41 (s, 6H), 2.28 (s, 3H), 2.09 (s, 3H), 2.04 (d, *J* = 5.8 Hz, 6H), 2.01 (s, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 170.7, 170.3, 169.3, 169.0, 140.9, 138.4, 131.1, 129.3, 127.6, 124.8, 119.6, 94.9, 84.5, 79.1, 76.4, 73.8, 69.9, 67.8, 62.0, 21.4, 21.0, 20.7(0), 20.6(7), 20.6(2), 20.5(9). HRMS (ESI) m/z: calcd for $C_{25}H_{30}O_9SNa$ $[M+Na]^+$: 529.1503, found: 529.1482.

(2*R*,3*R*,4*S*,5*R*,6*S*)-2-(acetoxymethyl)-6-(((4-methoxyphenyl)ethynyl)thio)tetrahydro-2H-pyran-3,4,5-triyl triacetate (**5f**)



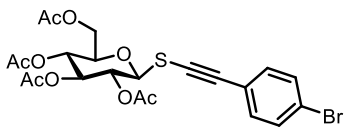
Yellow oil (26.2 mg, 27%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.46 (d, *J* = 8.7 Hz, 2H), 6.85 (d, *J* = 8.7 Hz, 2H), 5.37 – 5.24 (m, 2H), 5.14 (t, *J* = 9.5 Hz, 1H), 4.59 (d, *J* = 9.4 Hz, 1H), 4.29 – 4.23 (m, 1H), 4.21 – 4.15 (m, 1H), 3.82 (s, 3H), 3.80 – 3.76 (m, 1H), 2.11 (s, 3H), 2.06 (s, 3H), 2.03 (d, *J* = 5.7 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 170.7, 170.3, 169.4, 169.1, 160.2, 134.1, 114.7, 114.0, 97.2, 84.5, 73.9, 70.7, 69.7, 67.9, 62.0, 55.3, 20.7(4), 20.7(1), 20.6(2), 20.5(9). HRMS (ESI) m/z: calcd for $C_{23}H_{26}O_{10}SNa$ $[M+Na]^+$: 517.1139, found: 517.1094.

(2*R*,3*R*,4*S*,5*R*,6*S*)-2-(acetoxymethyl)-6-(((4-fluorophenyl)ethynyl)thio)tetrahydro-2H-pyran-3,4,5-triyl triacetate (**5g**)



Light yellow solid (61.8 mg, 64%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54 – 7.46 (m, 2H), 7.03 (t, *J* = 8.7 Hz, 2H), 5.38 – 5.24 (m, 2H), 5.15 (t, *J* = 9.6 Hz, 1H), 4.60 (d, *J* = 9.5 Hz, 1H), 4.30 – 4.23 (m, 1H), 4.22 – 4.16 (m, 1H), 3.84 – 3.77 (m, 1H), 2.11 (s, 3H), 2.06 (s, 3H), 2.03 (d, *J* = 5.6 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 170.6, 170.2, 169.4, 169.0, 164.1, 161.4, 134.4, 134.3, 118.7 (d, *J* = 5.1 Hz, 1C), 115.8, 115.3, 96.1, 84.2, 76.5, 73.9, 72.2, 69.7, 67.8, 62.0, 20.7(1), 20.6(7), 20.6(0), 20.5(7). ^{19}F NMR (376 MHz, Chloroform-*d*) δ 109.49. HRMS (ESI) m/z: calcd for $C_{22}H_{23}FO_9SNa$ $[M+Na]^+$: 505.0939, found: 505.0900.

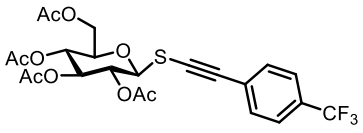
(2*R*,3*R*,4*S*,5*R*,6*S*)-2-(acetoxymethyl)-6-(((4-bromophenyl)ethynyl)thio)tetrahydro-2H-pyran-3,4,5-triyl triacetate (**5h**)



Yellow solid (70.3 mg, 65%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.47 (d, *J* = 8.4 Hz, 2H), 7.36 (d, *J* = 8.4 Hz, 2H), 5.36 – 5.24 (m, 2H), 5.14 (t, *J* = 9.5 Hz, 1H), 4.61 (d, *J* = 9.3 Hz, 1H), 4.30 – 4.23 (m, 1H), 4.21 – 4.15 (m, 1H), 3.84 – 3.77 (m, 1H), 2.10 (s, 3H), 2.06 (s, 3H), 2.03 (d, *J* = 5.7 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 170.7, 170.2, 169.4, 169.0, 133.5, 131.6, 123.3, 121.5, 96.2, 84.3,

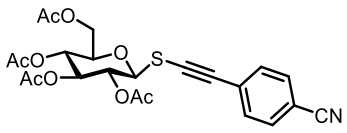
76.6, 74.0, 73.9, 69.7, 67.8, 62.0, 20.7(5), 20.6(8), 20.6(2), 20.5(9). HRMS (ESI) m/z: calcd for $C_{22}H_{23}BrO_9SNa$ $[M+Na]^+$: 565.0138, found: 565.0112.

(2*R*,3*R*,4*S*,5*R*,6*S*)-2-(acetoxymethyl)-6-(((4-(trifluoromethyl)phenyl)ethynyl)thio)tetrahydro-2H-pyran-3,4,5-triyl triacetate (**5i**)



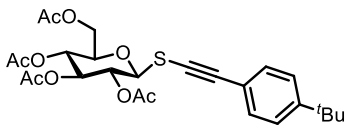
Yellow solid (81.0 mg, 76%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59 (s, 4H), 5.38 – 5.25 (m, 2H), 5.16 (t, *J* = 9.5 Hz, 1H), 4.64 (d, *J* = 9.4 Hz, 1H), 4.31 – 4.24 (m, 1H), 4.19 (d, *J* = 11.4 Hz, 1H), 3.86 – 3.78 (m, 1H), 2.10 (s, 3H), 2.08 – 2.01 (m, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 170.6, 170.2, 169.4, 169.0, 132.0, 130.3 (q, *J* = 32.5 Hz, 1C), 126.4, 125.3 (q, *J* = 3.7 Hz, 2C), 123.8 (q, *J* = 270.8 Hz, 1C), 95.9, 84.2, 76.6, 75.8, 73.8, 69.7, 67.8, 61.9, 20.7, 20.6(3), 20.5(8), 20.5(5). ^{19}F NMR (376 MHz, Chloroform-*d*) δ 62.88. HRMS (ESI) m/z: calcd for $C_{23}H_{23}F_3O_9SNa$ $[M+Na]^+$: 555.0907, found: 555.0876.

(2*R*,3*R*,4*S*,5*R*,6*S*)-2-(acetoxymethyl)-6-(((4-cyanophenyl)ethynyl)thio)tetrahydro-2H-pyran-3,4,5-triyl triacetate (**5j**)



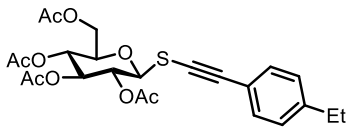
Yellow solid (61.7 mg, 63%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.66 – 7.61 (m, 2H), 7.57 (d, *J* = 8.3 Hz, 2H), 5.38 – 5.25 (m, 2H), 5.16 (t, *J* = 9.6 Hz, 1H), 4.63 (d, *J* = 9.5 Hz, 1H), 4.30 – 4.24 (m, 1H), 4.22 – 4.15 (m, 1H), 3.85 – 3.78 (m, 1H), 2.10 (s, 3H), 2.08 – 2.01 (m, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 170.6, 170.2, 169.4, 169.0, 132.0(9), 132.0(6), 127.4, 118.5, 111.9, 95.9, 84.1, 78.2, 76.7, 73.8, 69.6, 67.8, 61.9, 20.7, 20.6(4), 20.6(0), 20.5(8). HRMS (ESI) m/z: calcd for $C_{23}H_{23}O_9SNa$ $[M+Na]^+$: 512.0986, found: 512.0937.

(2*R*,3*R*,4*S*,5*R*,6*S*)-2-(acetoxymethyl)-6-(((4-(tert-butyl)phenyl)ethynyl)thio)tetrahydro-2H-pyran-3,4,5-triyl triacetate (**5k**)



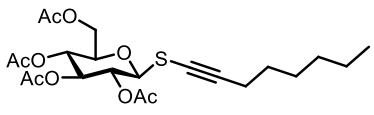
Light yellow solid (72.9 mg, 70%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45 (d, *J* = 8.3 Hz, 2H), 7.35 (d, *J* = 8.3 Hz, 2H), 5.36 – 5.24 (m, 2H), 5.13 (t, *J* = 9.5 Hz, 1H), 4.62 (d, *J* = 9.3 Hz, 1H), 4.29 – 4.23 (m, 1H), 4.21 – 4.15 (m, 1H), 3.83 – 3.76 (m, 1H), 2.11 (s, 3H), 2.06 (s, 3H), 2.03 (d, *J* = 5.9 Hz, 6H), 1.31 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 170.7, 170.2, 169.3, 169.0, 152.4, 132.1, 125.4, 119.6, 97.3, 84.5, 76.5, 73.9, 71.6, 69.8, 67.9, 62.0, 34.9, 31.1, 20.7(4), 20.6(9), 20.6(2), 20.5(8). HRMS (ESI) m/z: calcd for $C_{26}H_{32}O_9SNa$ $[M+Na]^+$: 543.1659, found: 543.1628.

(2*R*,3*R*,4*S*,5*R*,6*S*)-2-(acetoxymethyl)-6-(((4-ethylphenyl)ethynyl)thio)tetrahydro-2H-pyran-3,4,5-triyl triacetate (**5l**)



Light yellow solid (57.0 mg, 58%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43 (d, *J* = 8.1 Hz, 2H), 7.16 (d, *J* = 8.1 Hz, 2H), 5.35 – 5.24 (m, 2H), 5.14 (t, *J* = 9.6 Hz, 1H), 4.61 (d, *J* = 9.3 Hz, 1H), 4.29 – 4.23 (m, 1H), 4.22 – 4.15 (m, 1H), 3.84 – 3.75 (m, 1H), 2.65 (q, *J* = 7.6 Hz, 2H), 2.11 (s, 3H), 2.06 (s, 3H), 2.03 (d, *J* = 5.7 Hz, 6H), 1.23 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 170.7, 170.3, 169.4, 169.1, 145.6, 132.3, 127.9, 119.8, 97.3, 84.5, 76.5, 73.9, 71.6, 69.8, 67.9, 62.0, 28.9, 20.7(5), 20.7(0), 20.6(3), 20.5(9), 15.4. HRMS (ESI) m/z: calcd for $C_{24}H_{28}O_9SNa$ $[M+Na]^+$: 515.1346, found: 515.1324.

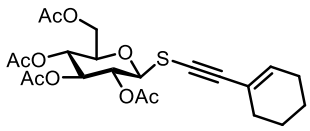
(2*R*,3*R*,4*S*,5*R*,6*S*)-2-(acetoxymethyl)-6-(oct-1-yn-1-ylthio)tetrahydro-2H-pyran-3,4,5-triyl triacetate (**5m**)



Colorless oil (32.2 mg, 34%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.29 – 5.23 (m, 1H), 5.14 – 5.05 (m, 2H), 4.76 (d, *J* = 10.2 Hz, 1H), 4.30 – 4.25 (m, 1H), 4.17 – 4.12 (m, 1H), 3.74 – 3.69 (m, 1H), 3.56 (dt, *J* = 16.0, 2.3 Hz, 1H), 3.31 (dt, *J* = 16.1, 2.4 Hz, 1H), 2.23 – 2.18 (m, 2H), 2.09 (s, 3H), 2.07 (s, 3H), 2.03 (s, 3H), 2.02 (s, 3H), 1.54 – 1.48 (q, *J* = 7.1 Hz, 2H), 1.39 – 1.31 (m, 4H), 0.92 (t, *J* = 7.1 Hz, 3H). ^{13}C

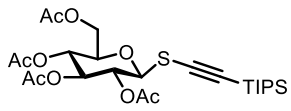
NMR (100 MHz, Chloroform-*d*) δ 170.7, 170.3, 169.5, 169.4, 84.6, 82.2, 75.9, 74.3, 73.9, 69.8, 68.3, 62.0, 31.1, 28.4, 22.2, 20.7(8), 20.7(3), 20.6(6), 20.6(2), 18.8, 18.4, 14.0. HRMS (ESI) m/z: calcd for $C_{22}H_{32}O_9SNa$ $[M+Na]^+$: 495.1659, found: 495.1629.

(2*R*,3*R*,4*S*,5*R*,6*S*)-2-(acetoxymethyl)-6-((cyclohex-1-en-1-ylethynyl)thio)tetrahydro-2H-pyran-3,4,5-triyl triacetate (**5n**)



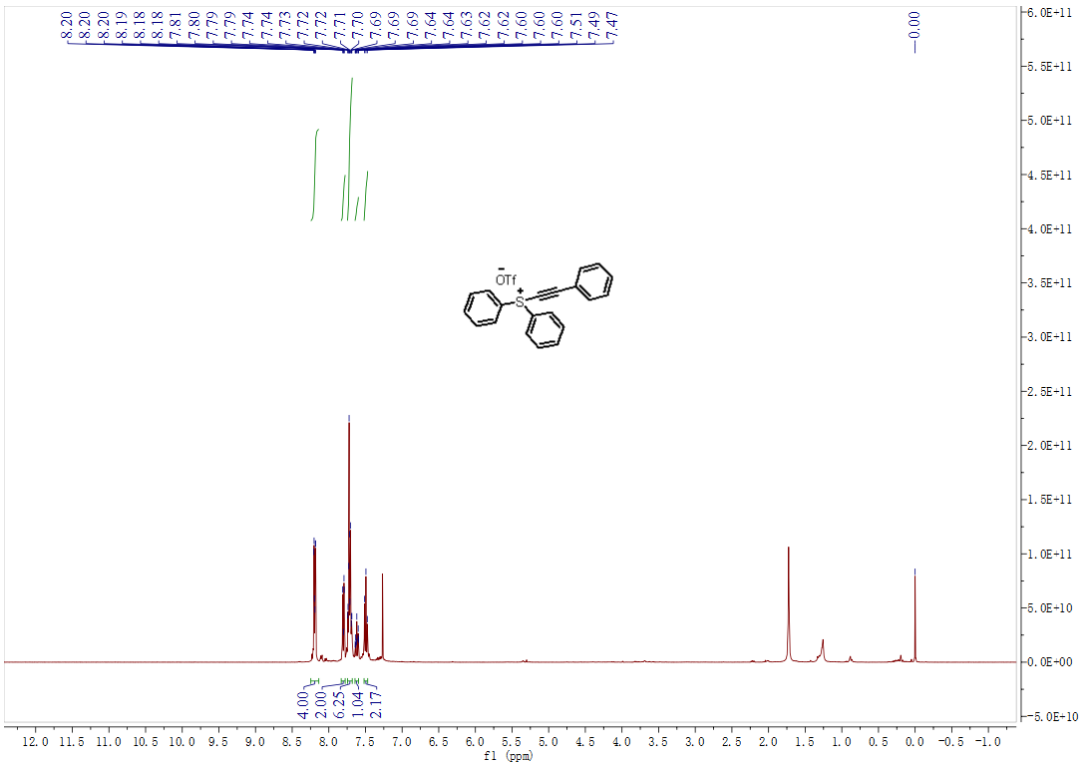
Light yellow solid (21.5 mg, 23%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.26 – 6.19 (m, 1H), 5.28 – 5.22 (m, 2H), 5.16 – 5.11 (m, 1H), 4.55 – 4.50 (m, 1H), 4.28 – 4.23 (m, 1H), 4.19 – 4.15 (m, 1H), 3.79 – 3.74 (m, 1H), 2.18 – 2.11 (m, 4H), 2.09 (s, 3H), 2.08 (s, 3H), 2.04 (s, 3H), 2.02 (s, 3H), 1.69 – 1.59 (m, 4H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 170.7, 170.3, 169.4, 169.0, 137.3, 120.6, 99.1, 84.5, 76.4, 73.9, 69.7, 69.0, 67.9, 62.0, 28.9, 25.8, 22.2, 21.4, 20.8, 20.7, 20.6(5), 20.6(2). HRMS (ESI) m/z: calcd for $C_{22}H_{28}O_9SNa$ $[M+Na]^+$: 491.1346, found: 491.1348.

(2*R*,3*R*,4*S*,5*R*,6*S*)-2-(acetoxymethyl)-6-(((triisopropylsilyl)ethynyl)thio)tetrahydro-2H-pyran-3,4,5-triyl triacetate (**5o**)

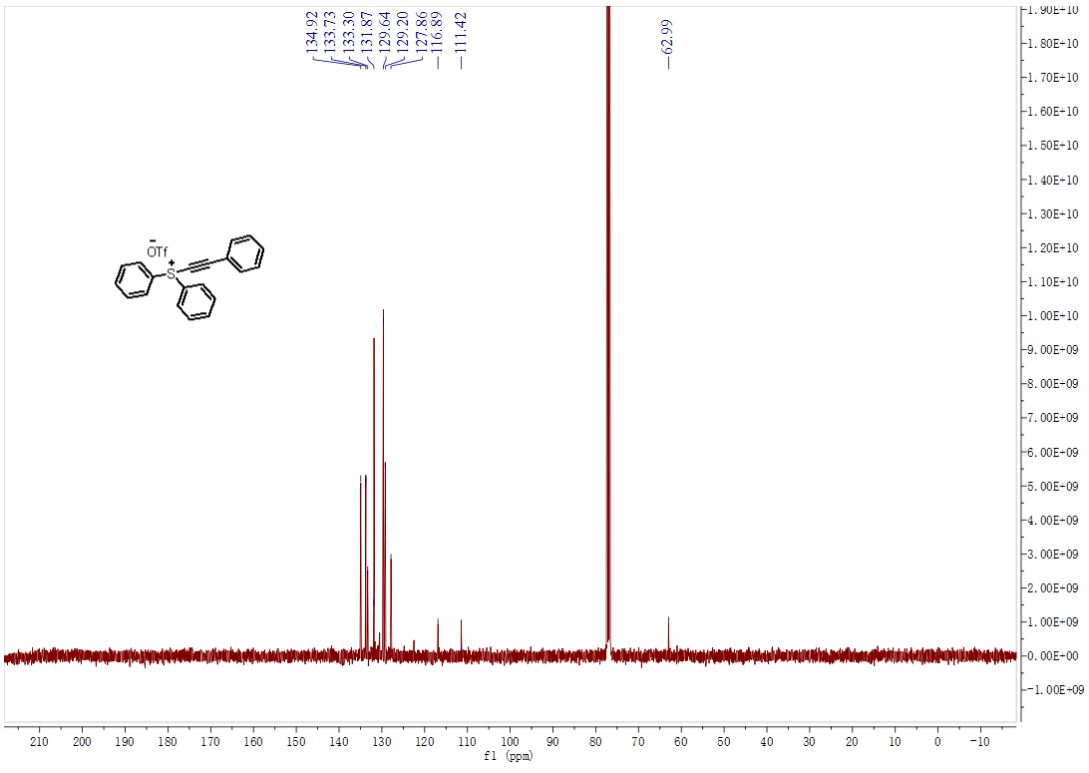


Light yellow solid (77.4 mg, 71%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.26 (d, *J* = 4.1 Hz, 2H), 5.10 (d, *J* = 8.3 Hz, 1H), 4.62 – 4.51 (m, 1H), 4.31 – 4.22 (m, 1H), 4.13 (d, *J* = 12.1 Hz, 1H), 3.76 (d, *J* = 6.1 Hz, 1H), 2.08 (s, 6H), 2.02 (d, *J* = 6.8 Hz, 6H), 1.10 (s, 21H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 170.7, 170.3, 169.3, 168.9, 102.3, 88.8, 84.9, 76.5, 73.8, 69.9, 67.8, 62.0, 20.7, 20.6(2), 20.6(1), 20.5(7), 18.5(9), 18.5(8), 11.3. HRMS (ESI) m/z: calcd for $C_{25}H_{40}SiO_9SNa$ $[M+Na]^+$: 567.2055, found: 567.2023.

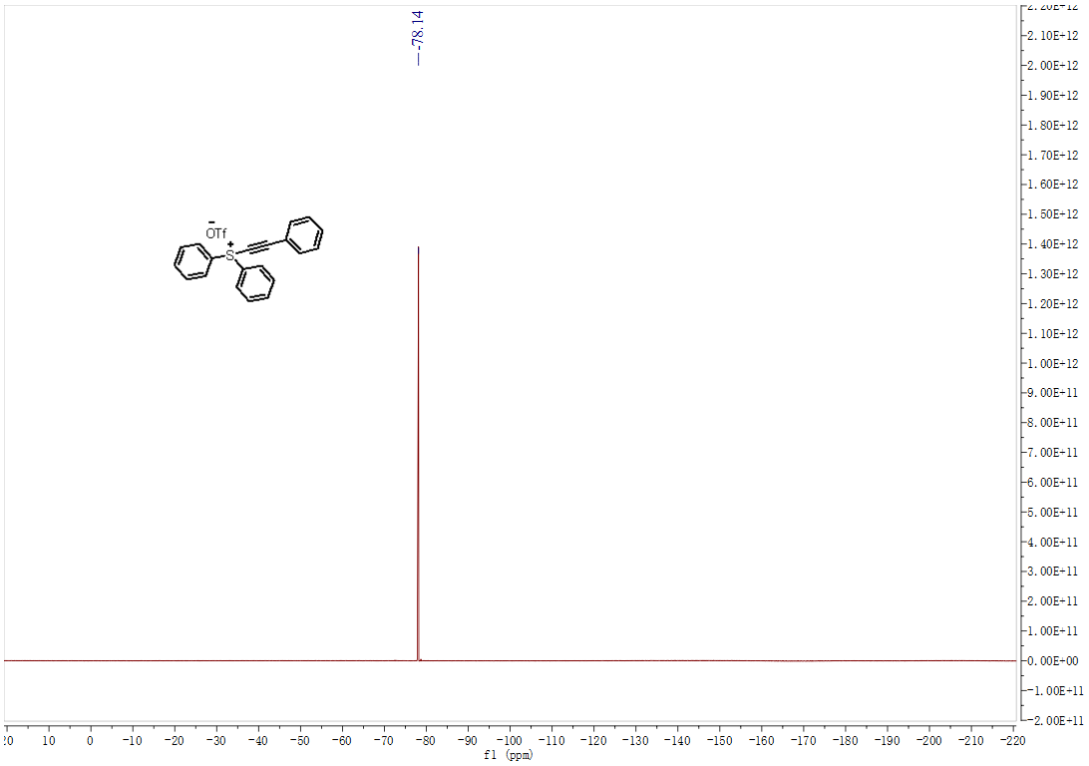
8. Spectra



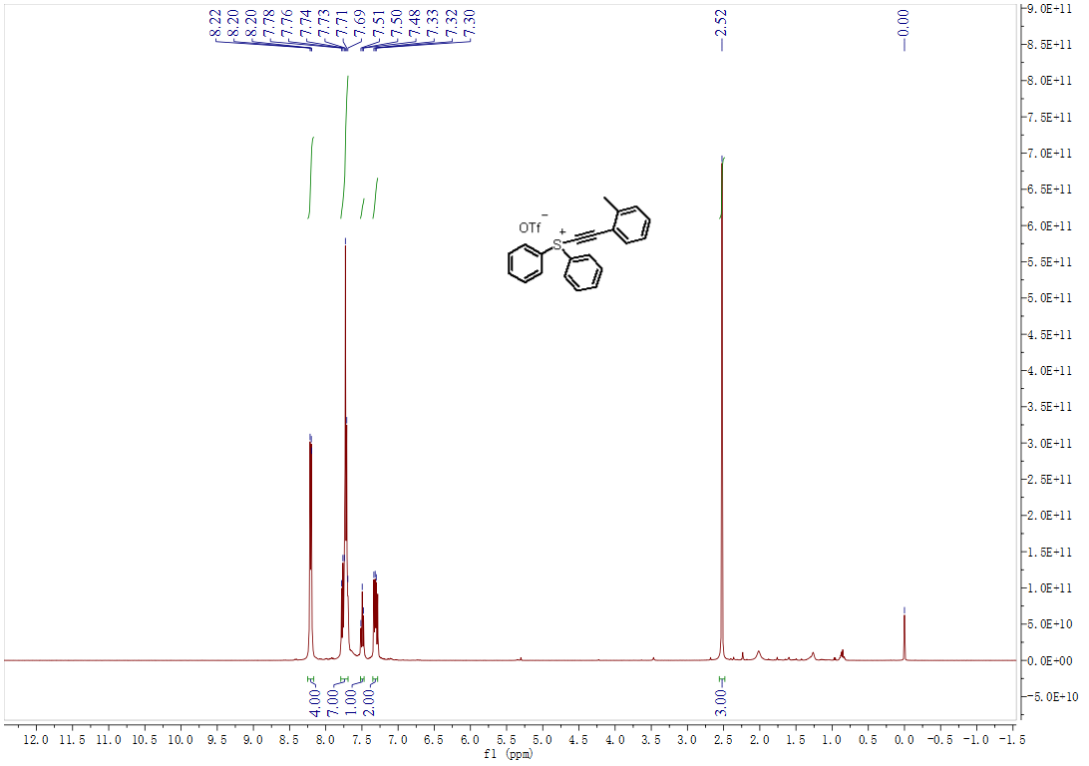
^{1}H NMR of **2a** (400 MHz, $CDCl_3$)



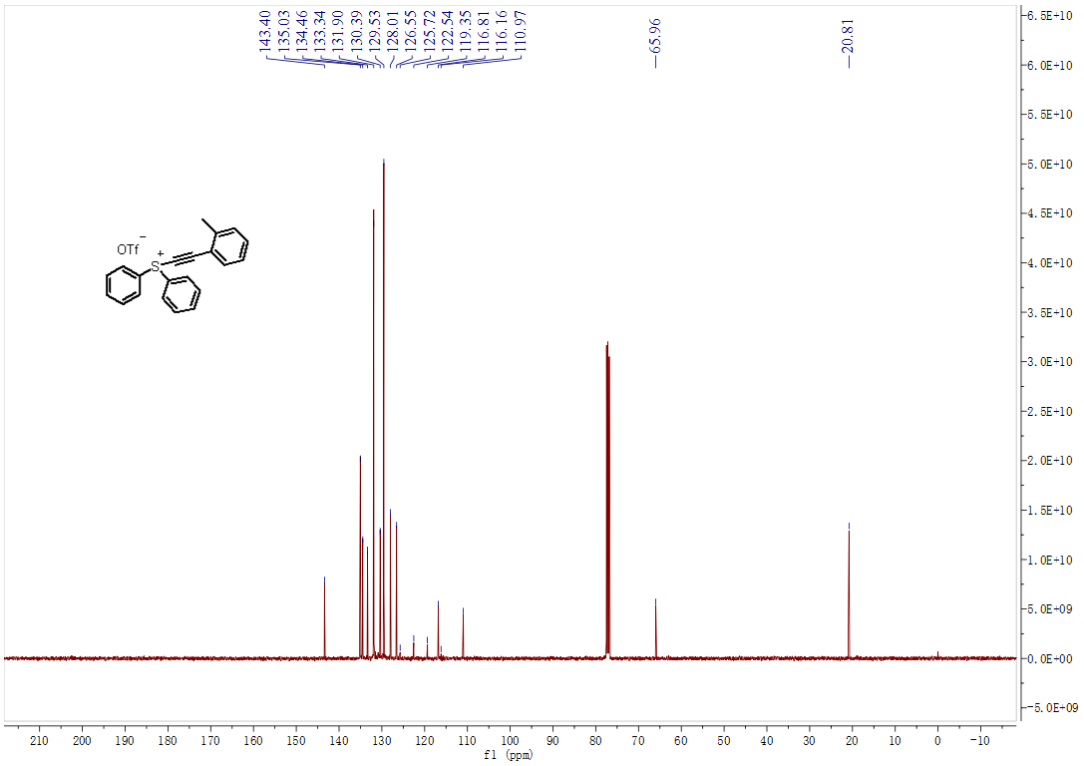
^{13}C NMR of **2a** (100 MHz, $CDCl_3$)



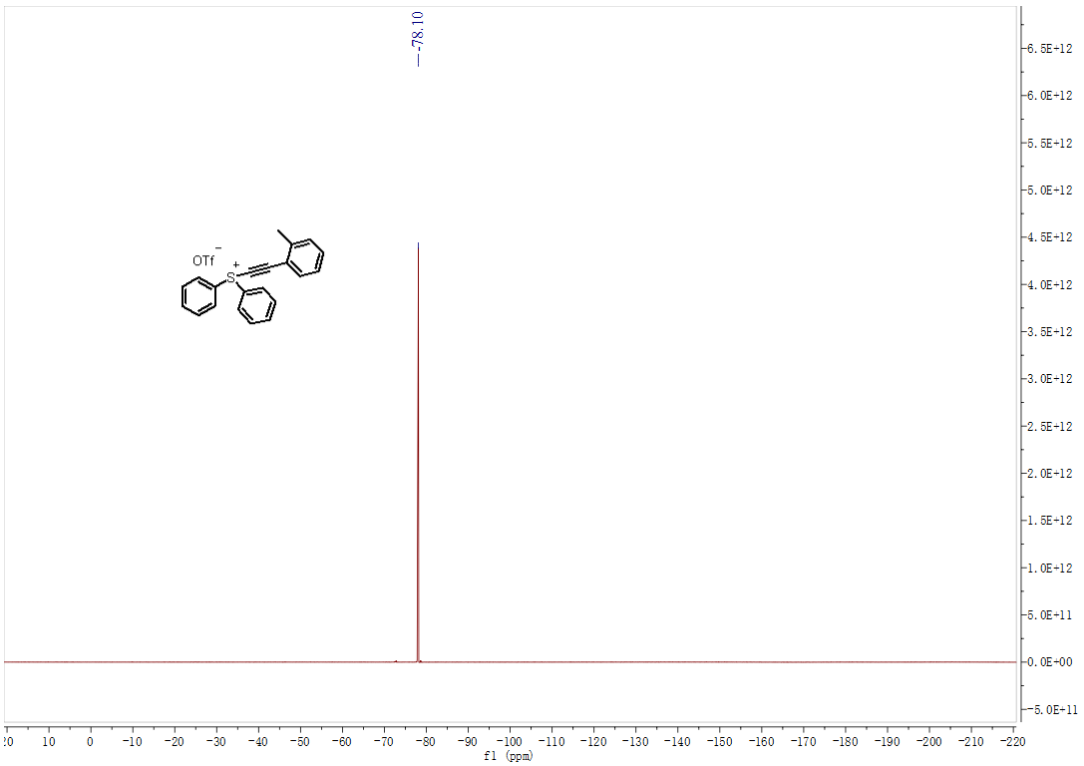
^{19}F NMR of **2a** (376 MHz, $CDCl_3$)



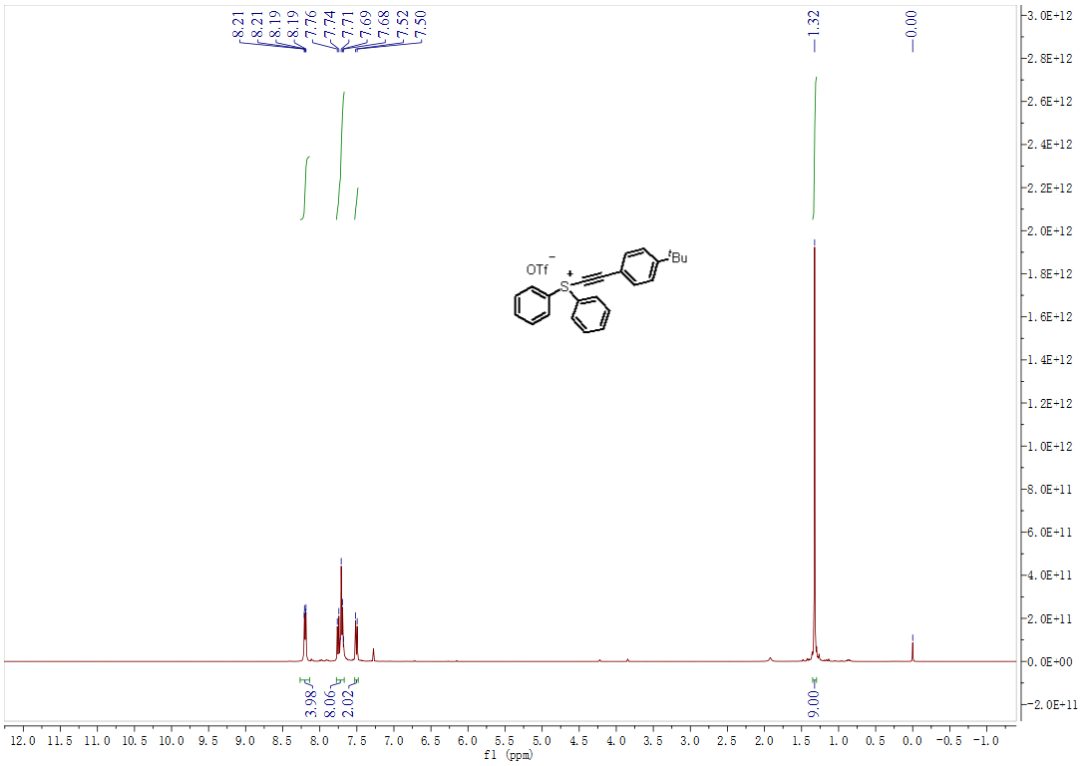
^{1}H NMR of **2b** (400 MHz, $CDCl_3$)



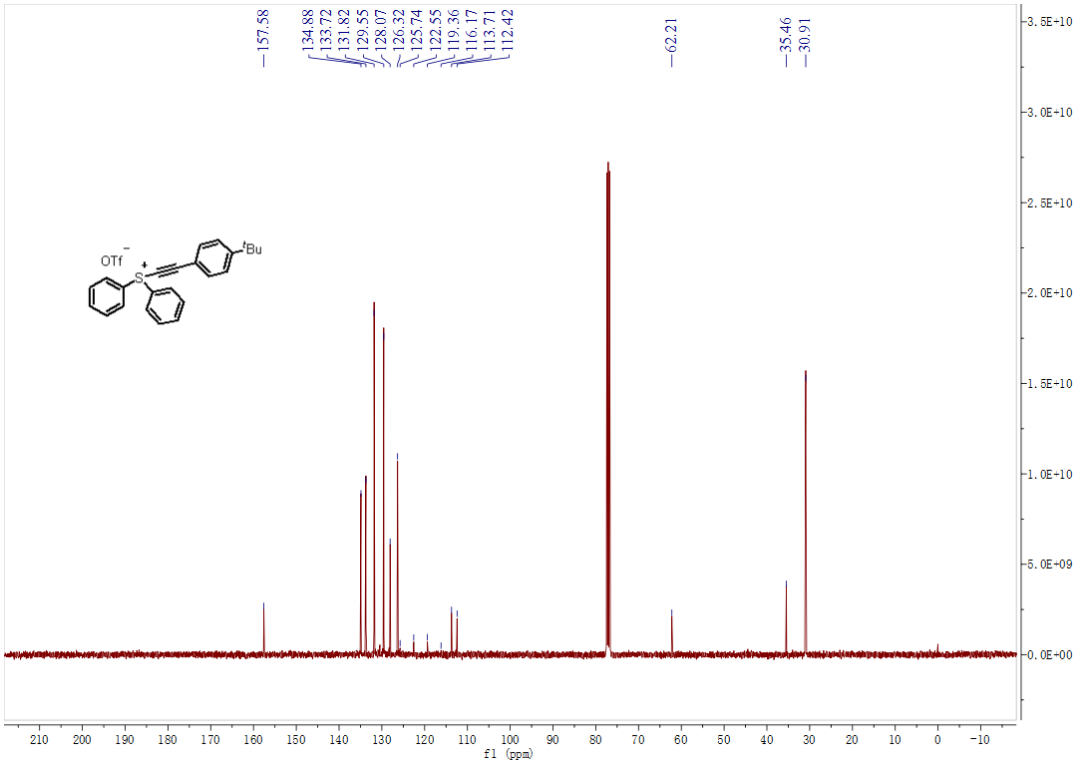
^{13}C NMR of **2b** (100 MHz, $CDCl_3$)



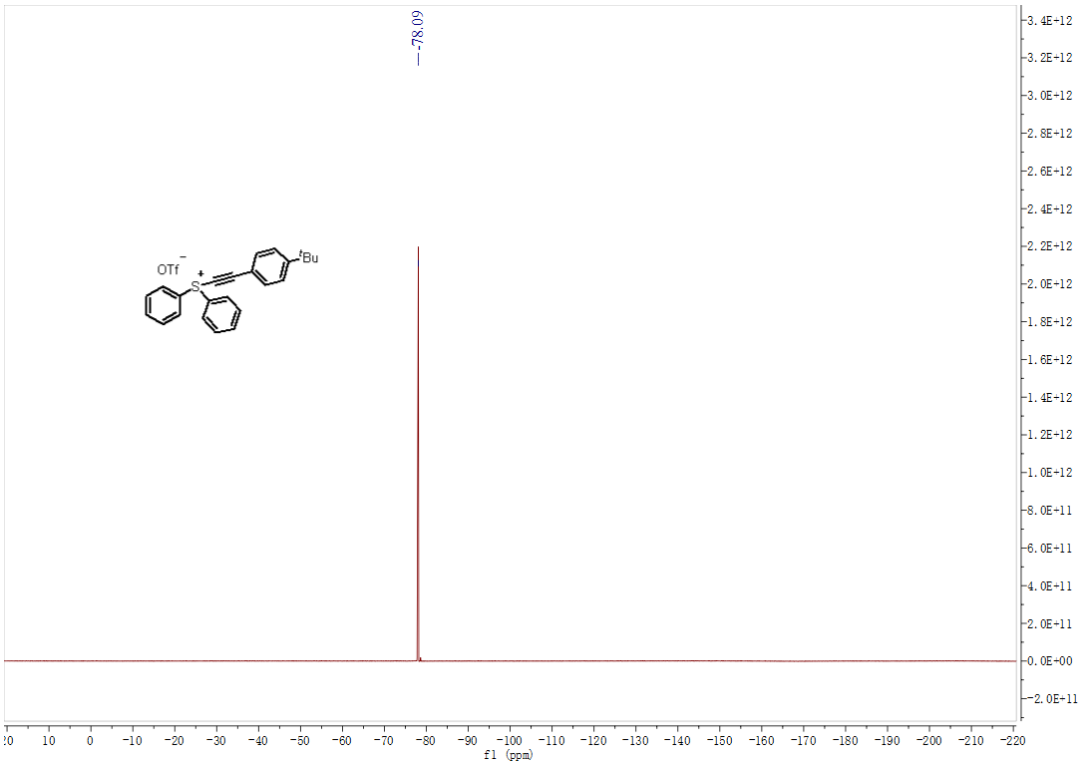
^{19}F NMR of **2b** (376 MHz, $CDCl_3$)



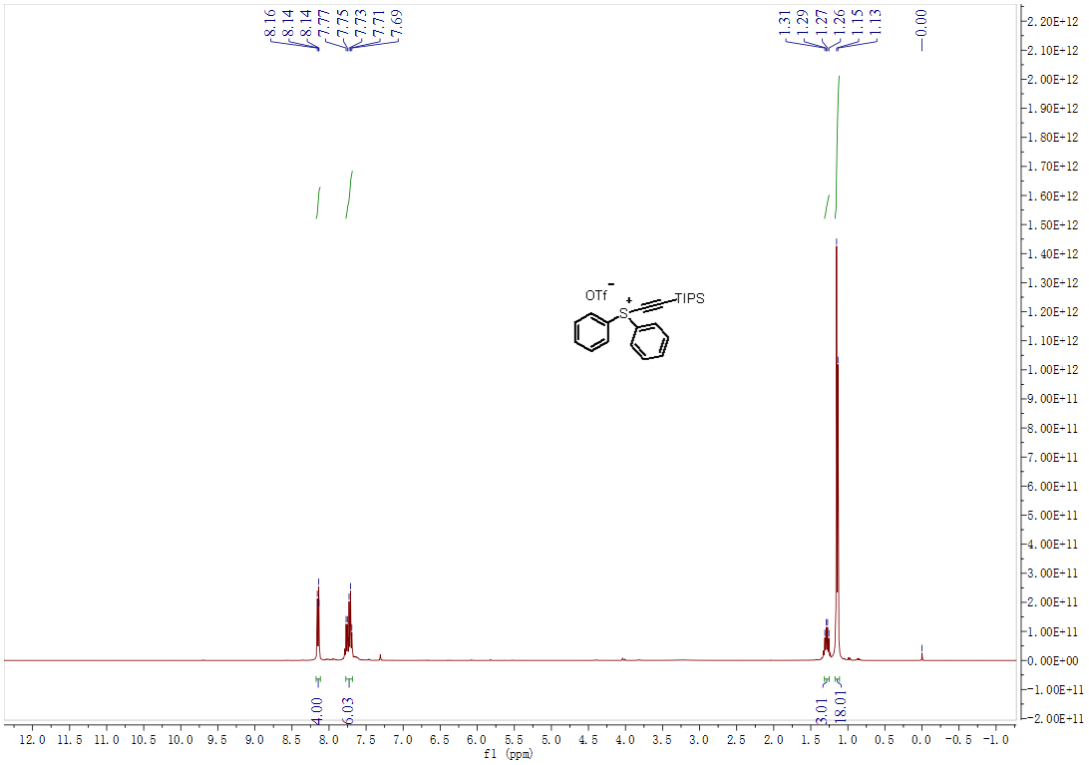
^{1}H NMR of **2c** (400 MHz, $CDCl_3$)



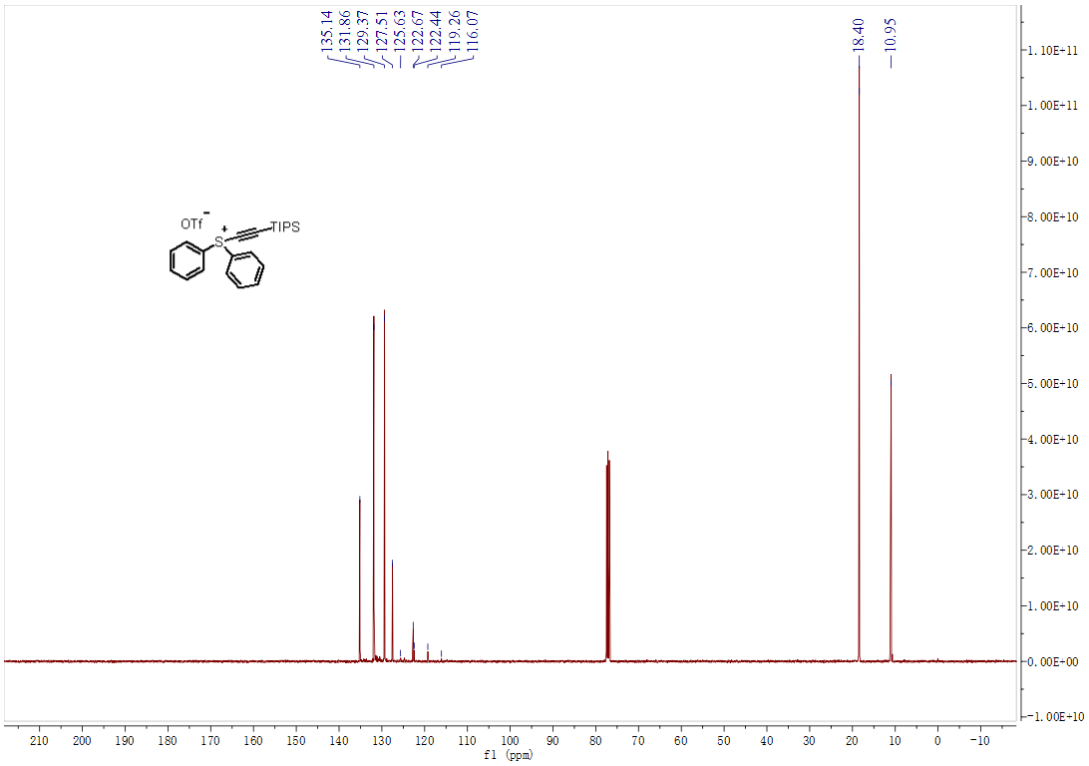
^{13}C NMR of **2c** (100 MHz, $CDCl_3$)



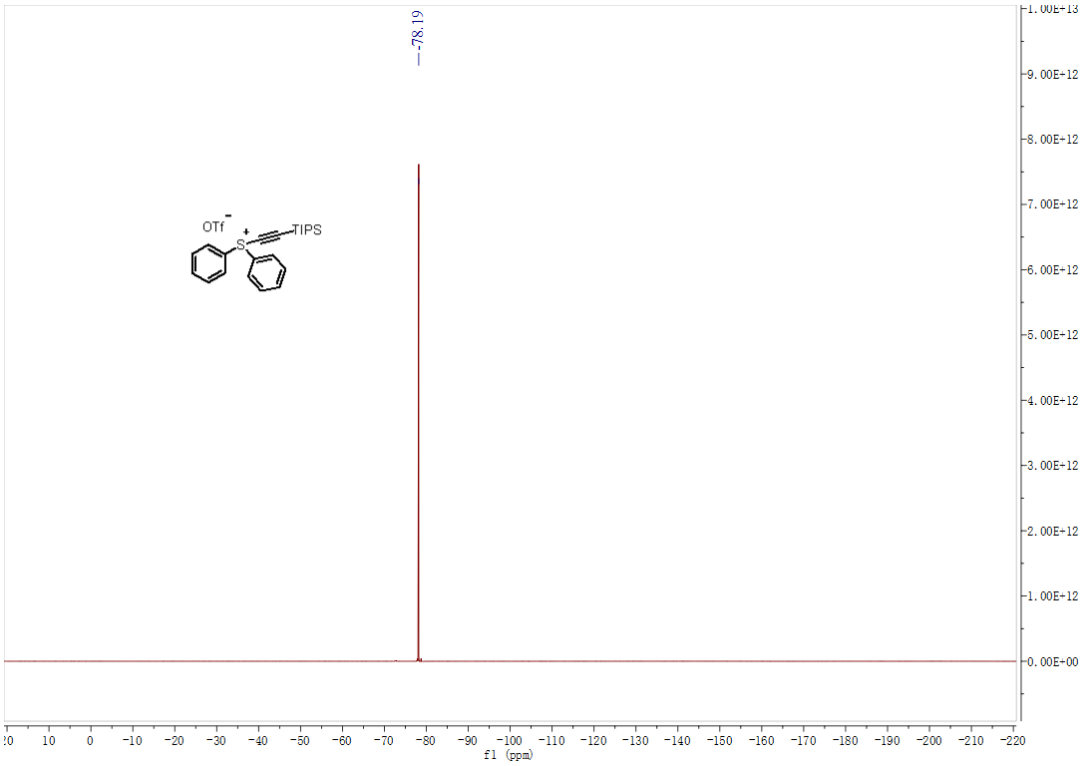
^{19}F NMR of **2c** (376 MHz, $CDCl_3$)



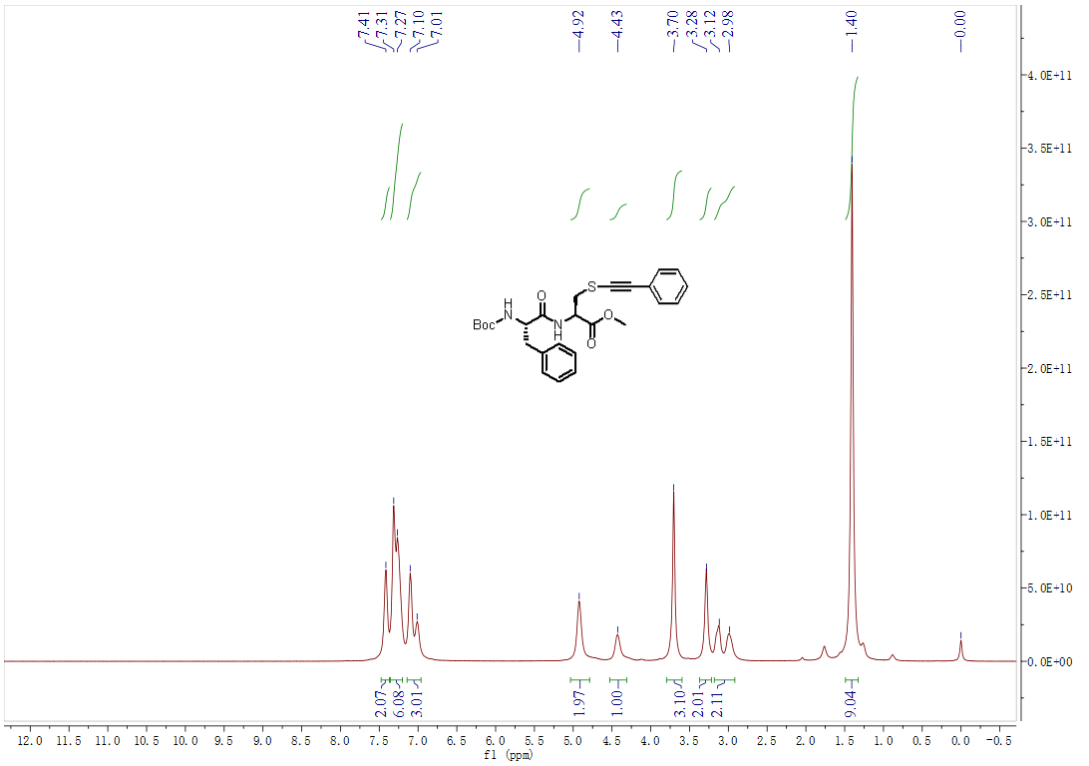
^{1}H NMR of **2d** (400 MHz, $CDCl_3$)



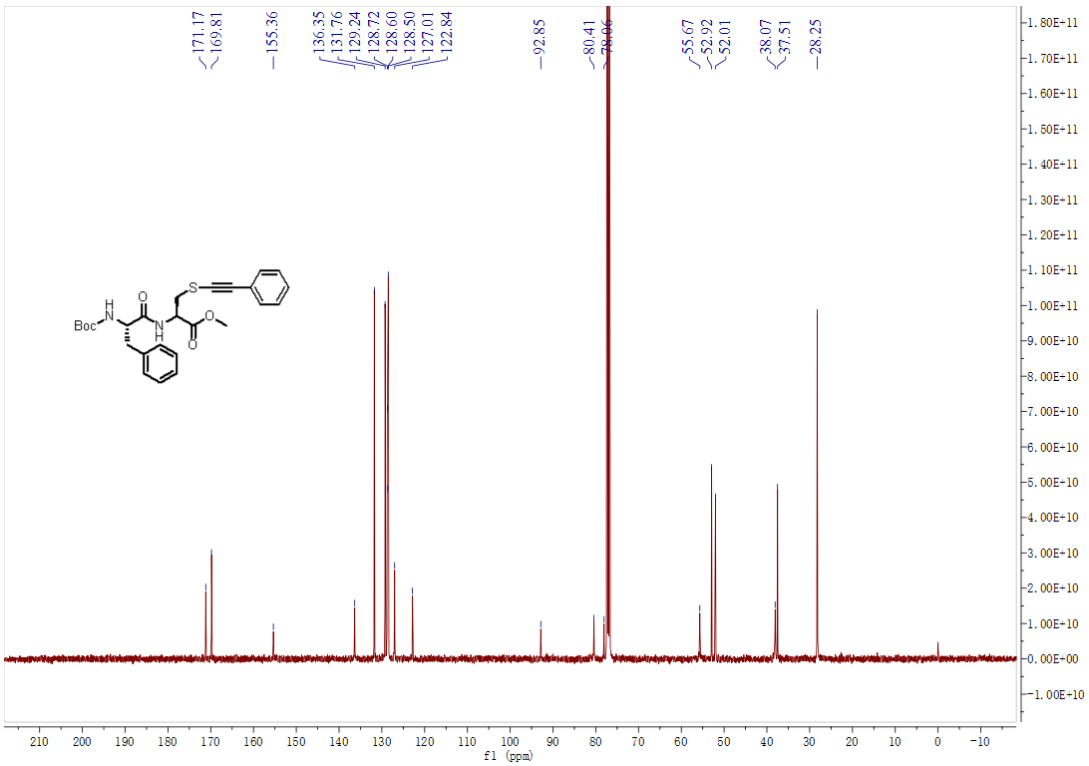
^{13}C NMR of **2d** (100 MHz, $CDCl_3$)



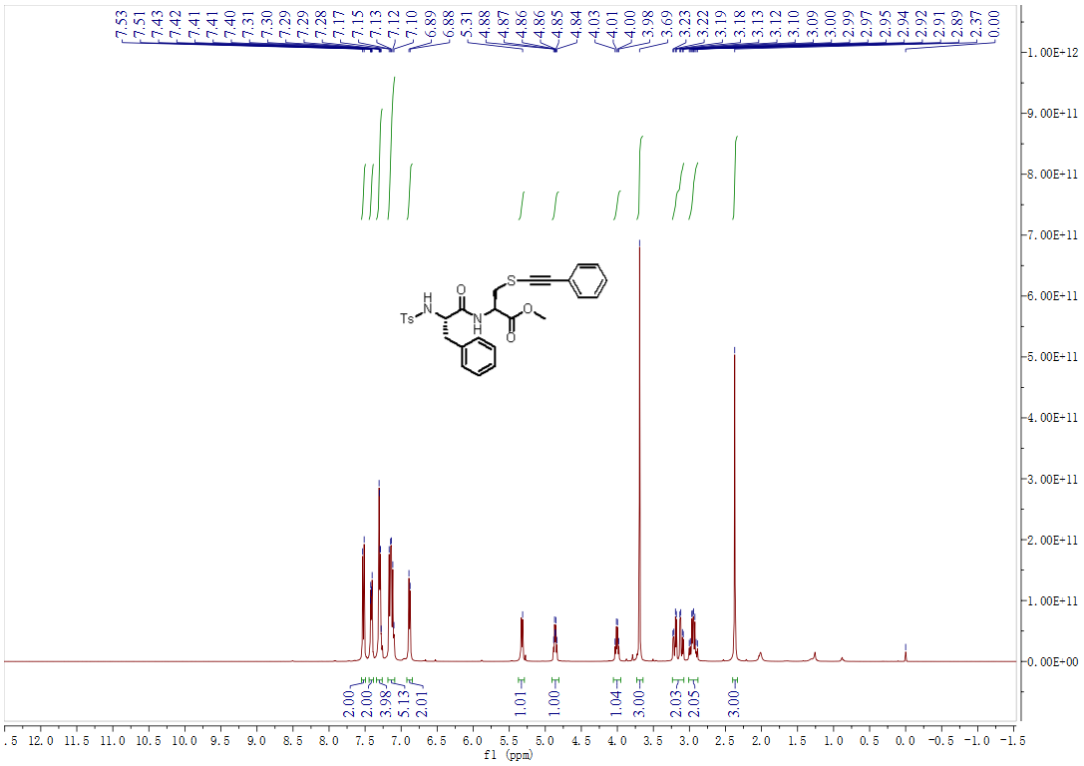
^{19}F NMR of **2d** (376 MHz, $CDCl_3$)



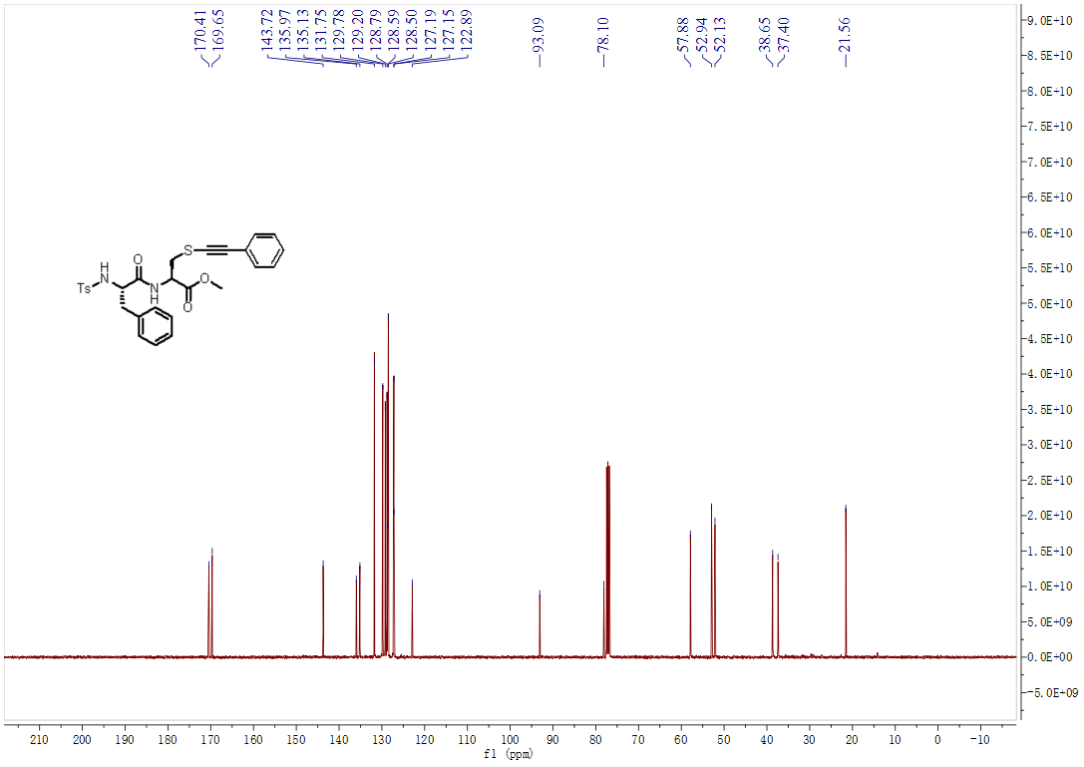
^{1}H NMR of **3aa** (400 MHz, $CDCl_3$)



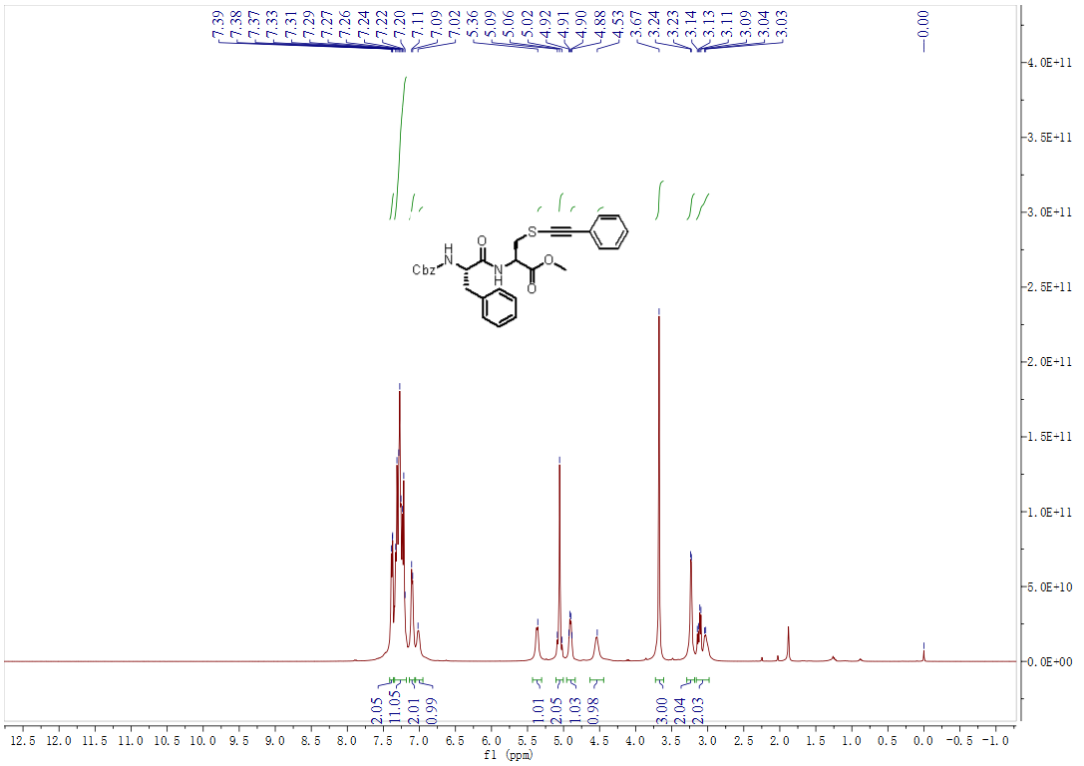
^{13}C NMR of **3aa** (100 MHz, $CDCl_3$)



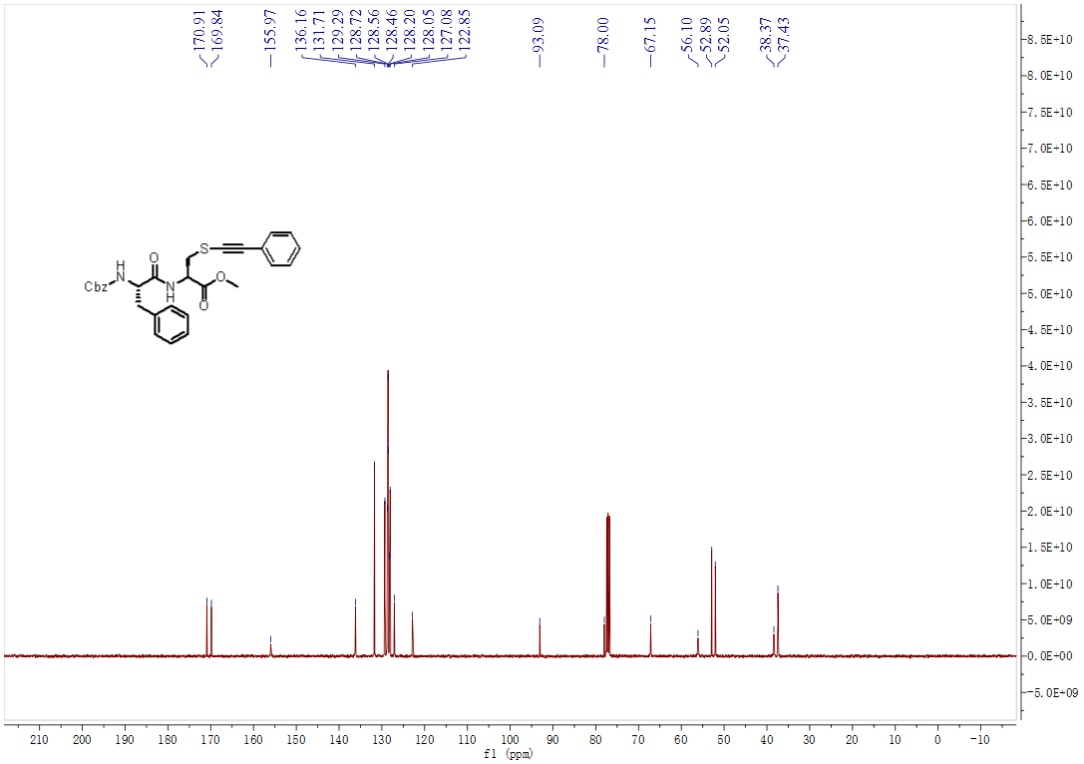
^{1}H NMR of **3ab** (400 MHz, $CDCl_3$)



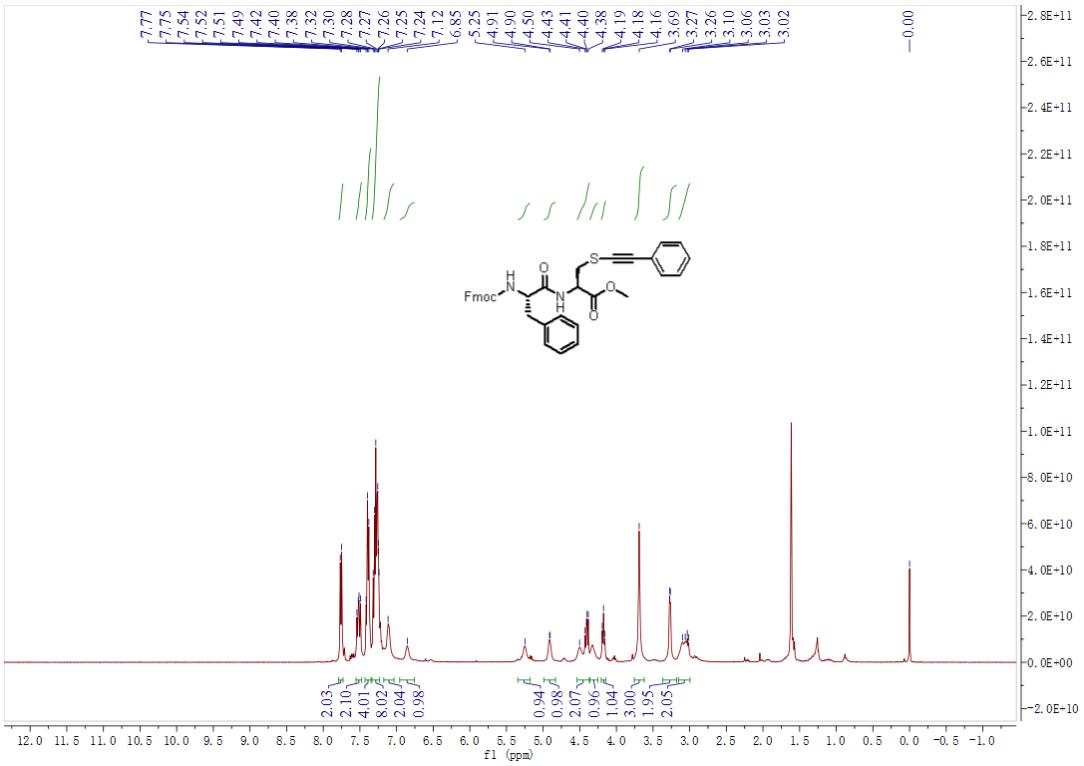
^{13}C NMR of **3ab** (100 MHz, $CDCl_3$)



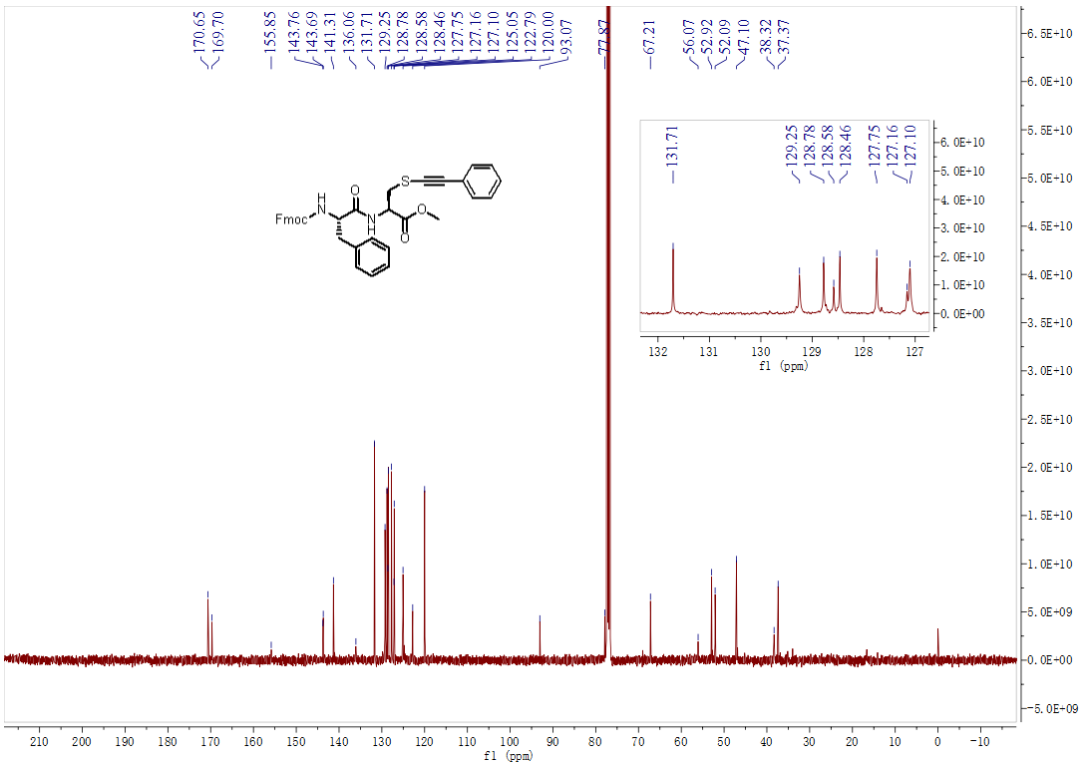
^{1}H NMR of **3ac** (400 MHz, $CDCl_3$)



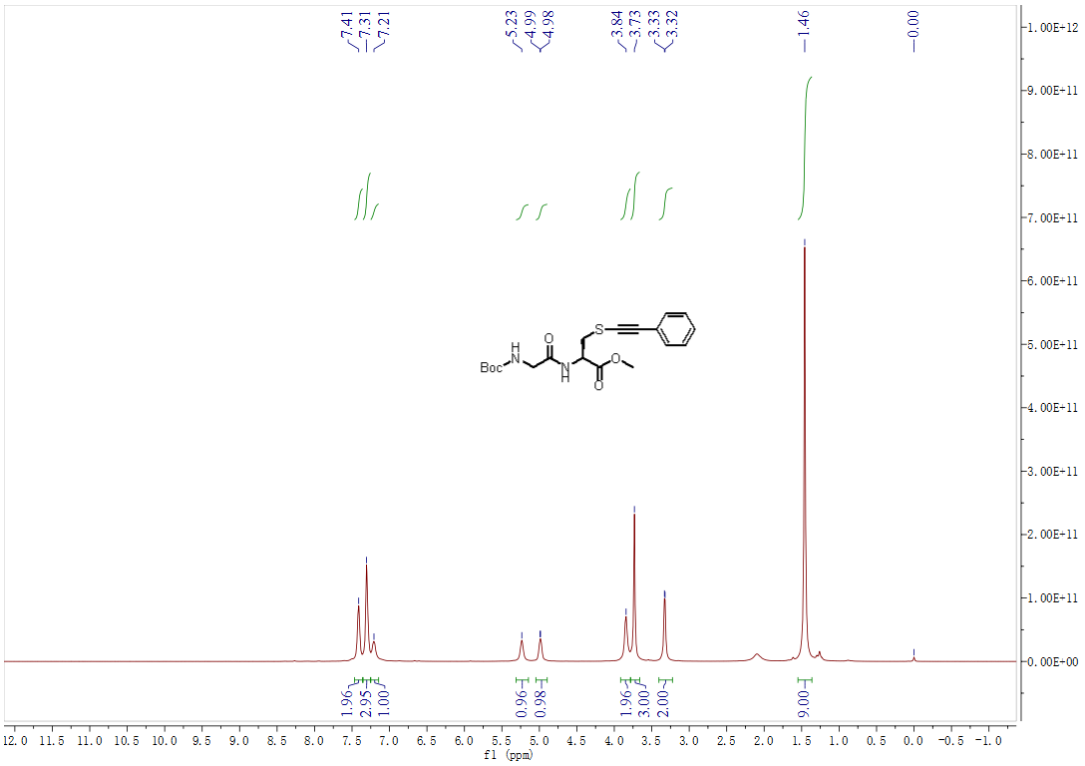
^{13}C NMR of **3ac** (100 MHz, $CDCl_3$)



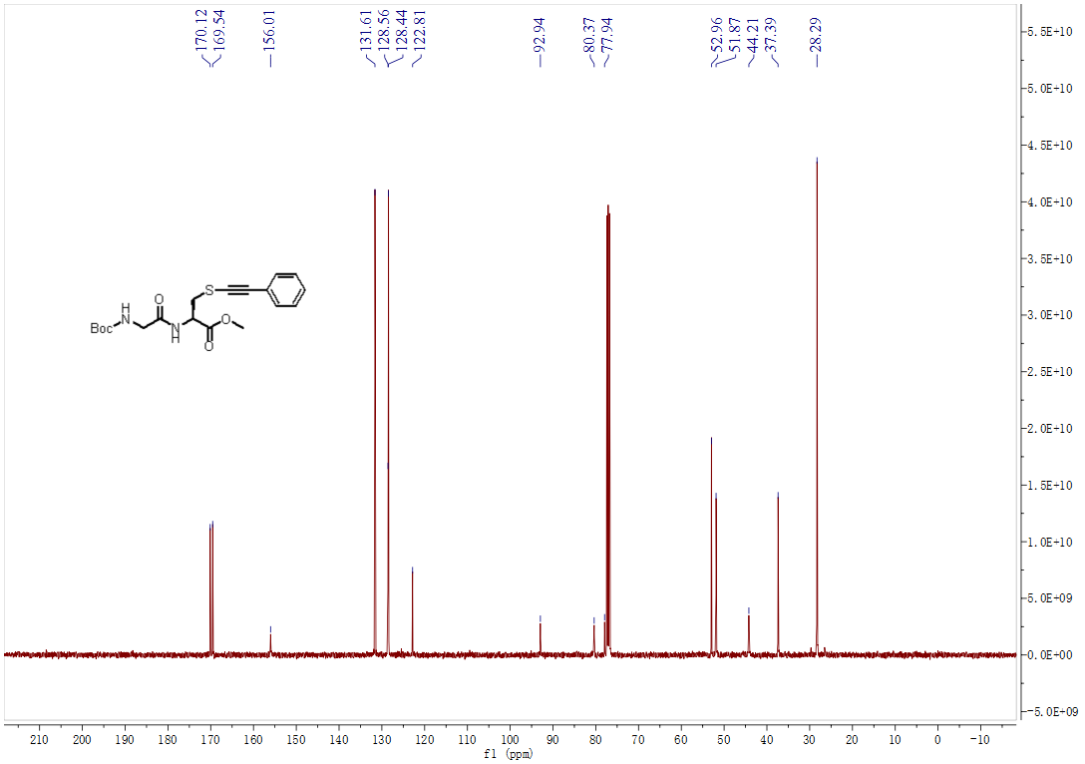
^{1}H NMR of **3ad** (400 MHz, $CDCl_3$)



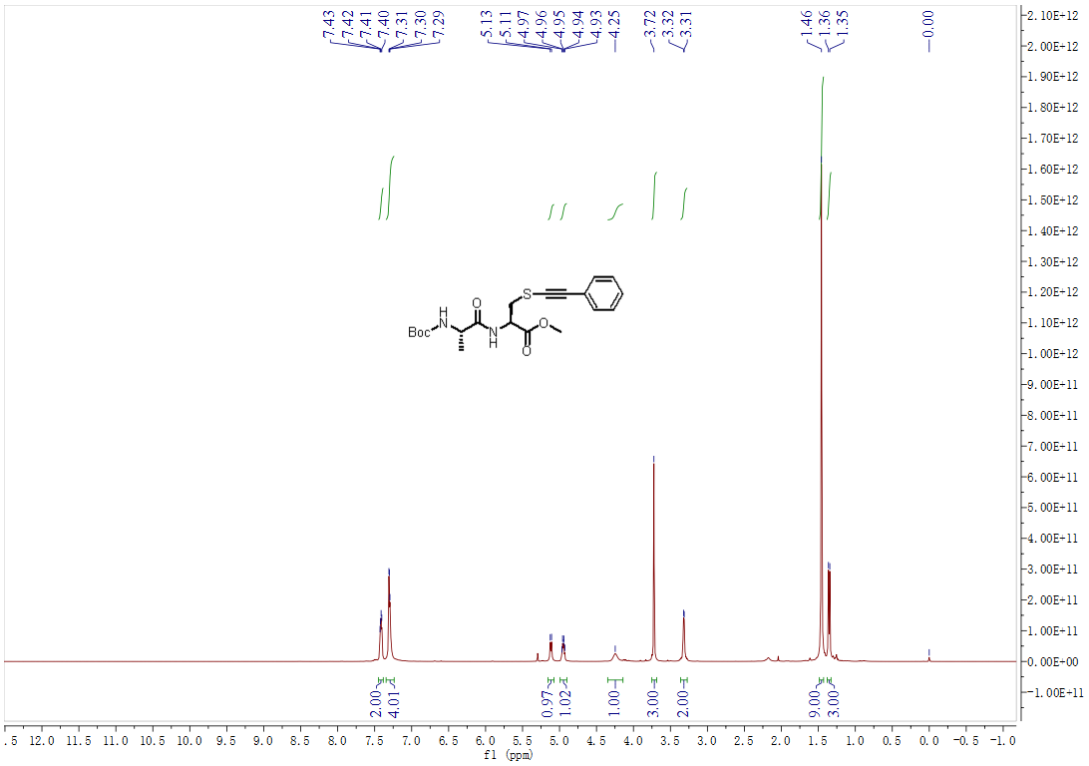
^{13}C NMR of **3ad** (100 MHz, $CDCl_3$)



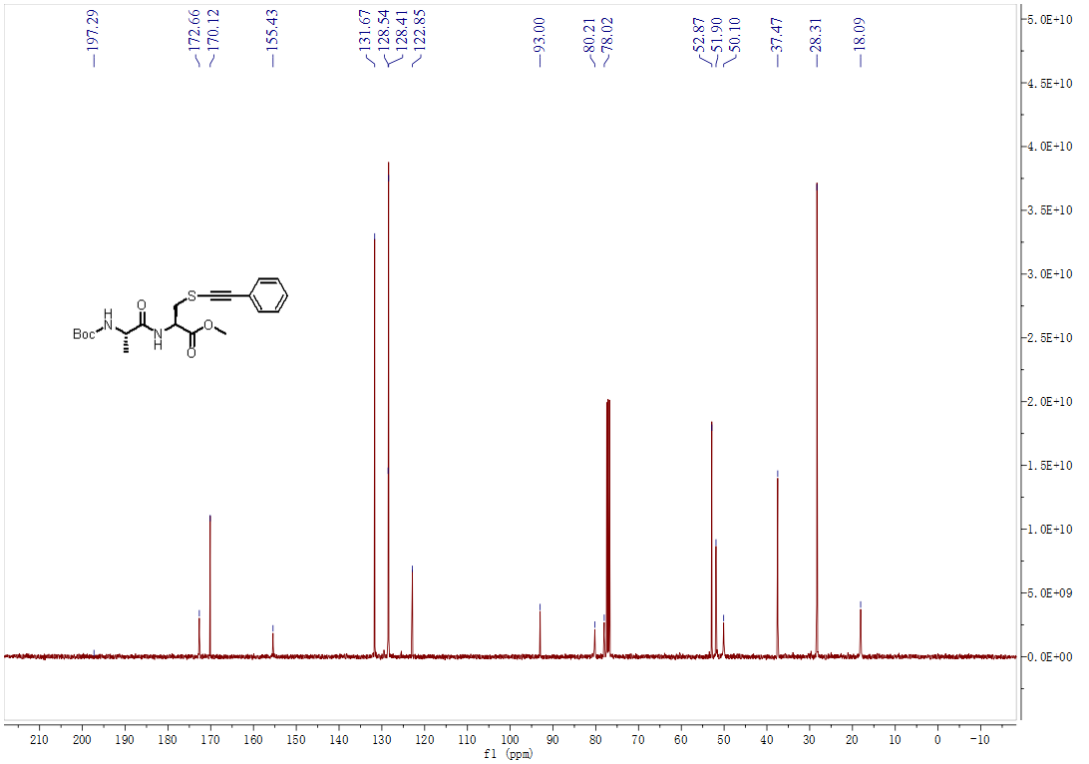
^{1}H NMR of **3ae** (400 MHz, $CDCl_3$)



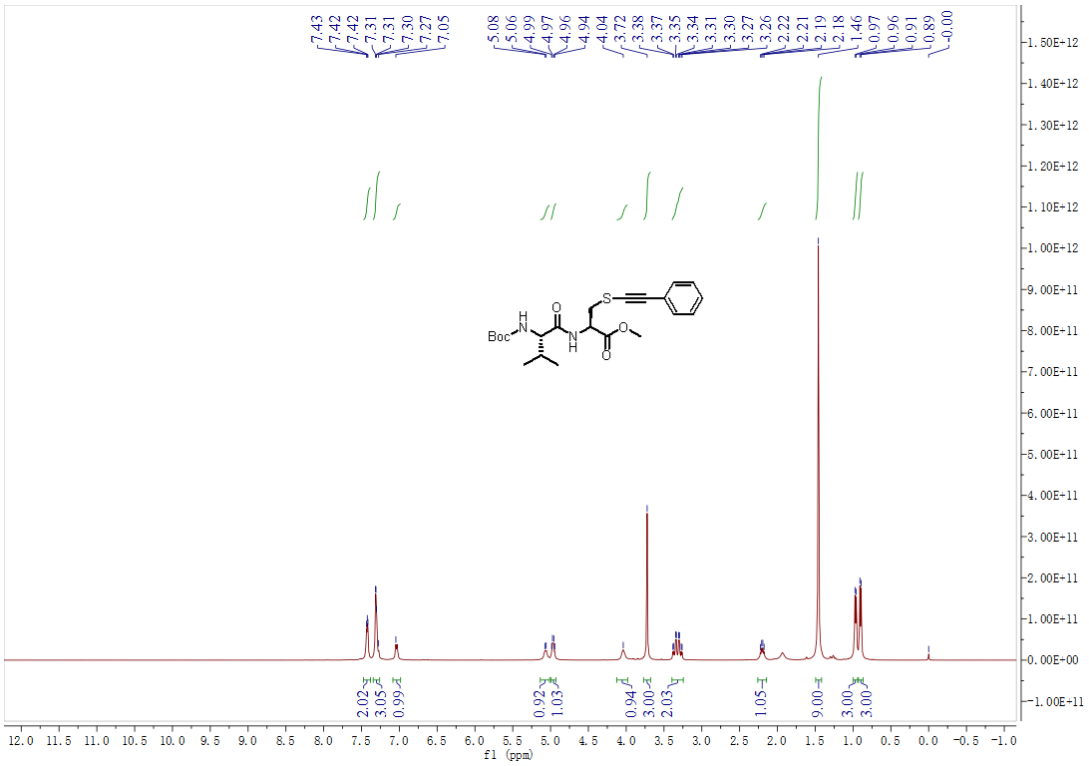
^{13}C NMR of **3ae** (100 MHz, $CDCl_3$)



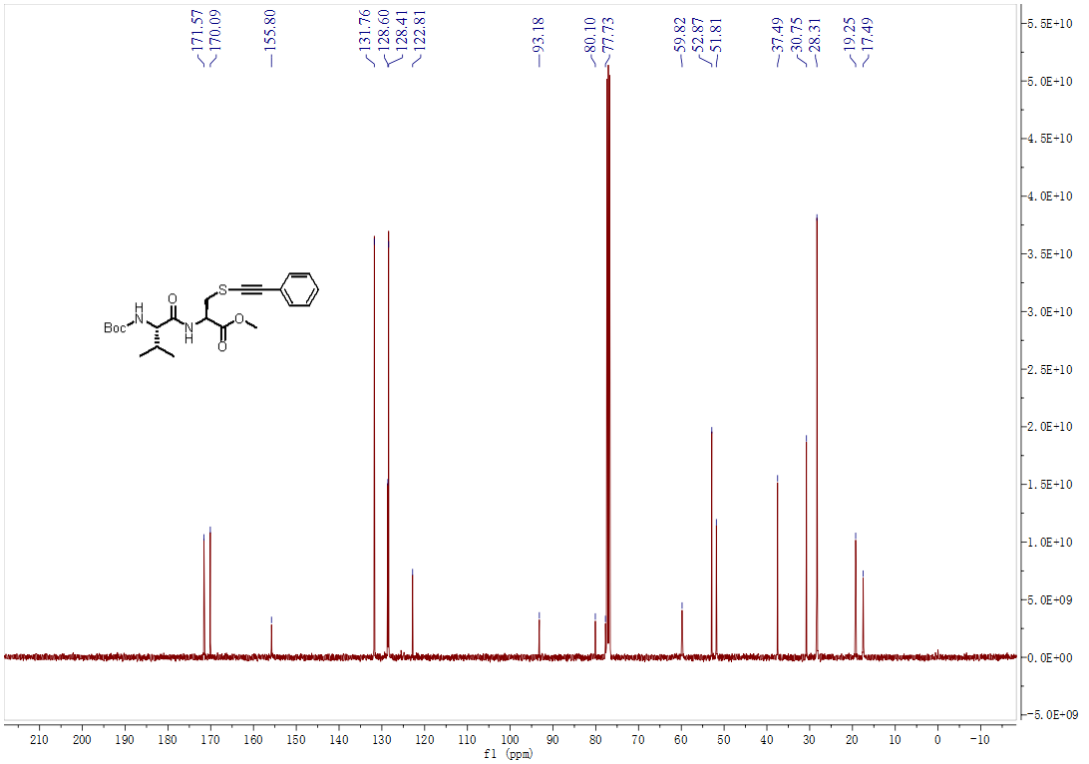
^{1}H NMR of **3af** (400 MHz, $CDCl_3$)



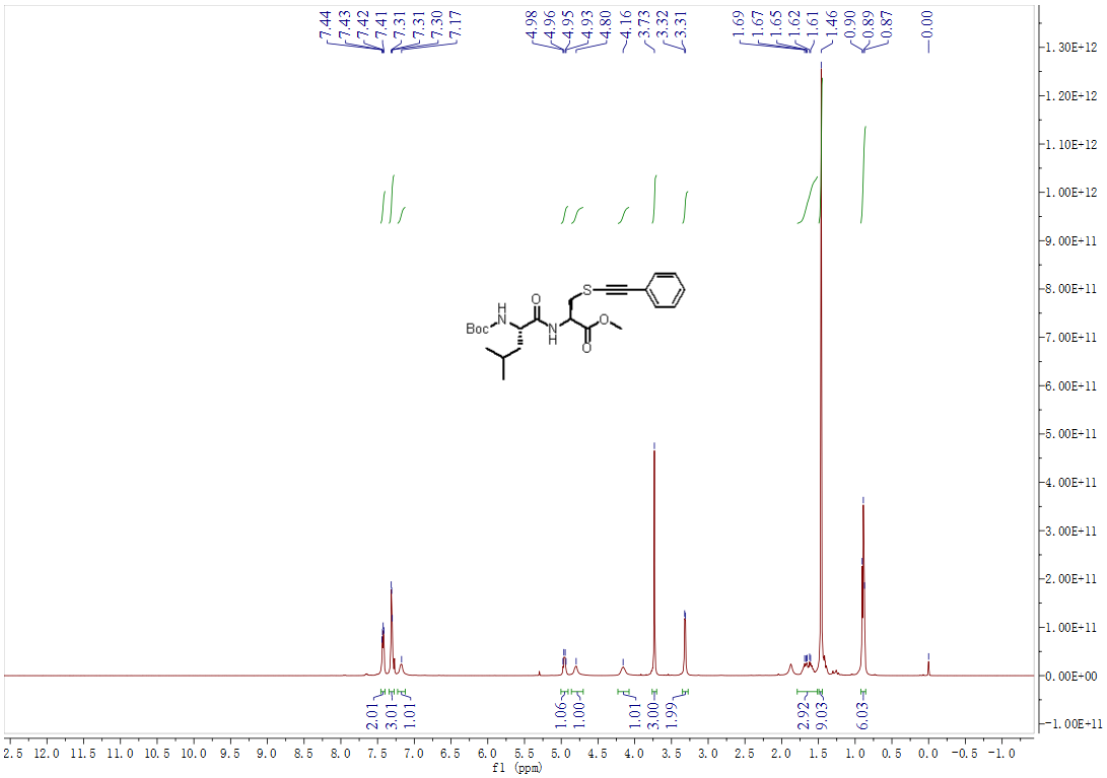
^{13}C NMR of **3af** (100 MHz, $CDCl_3$)



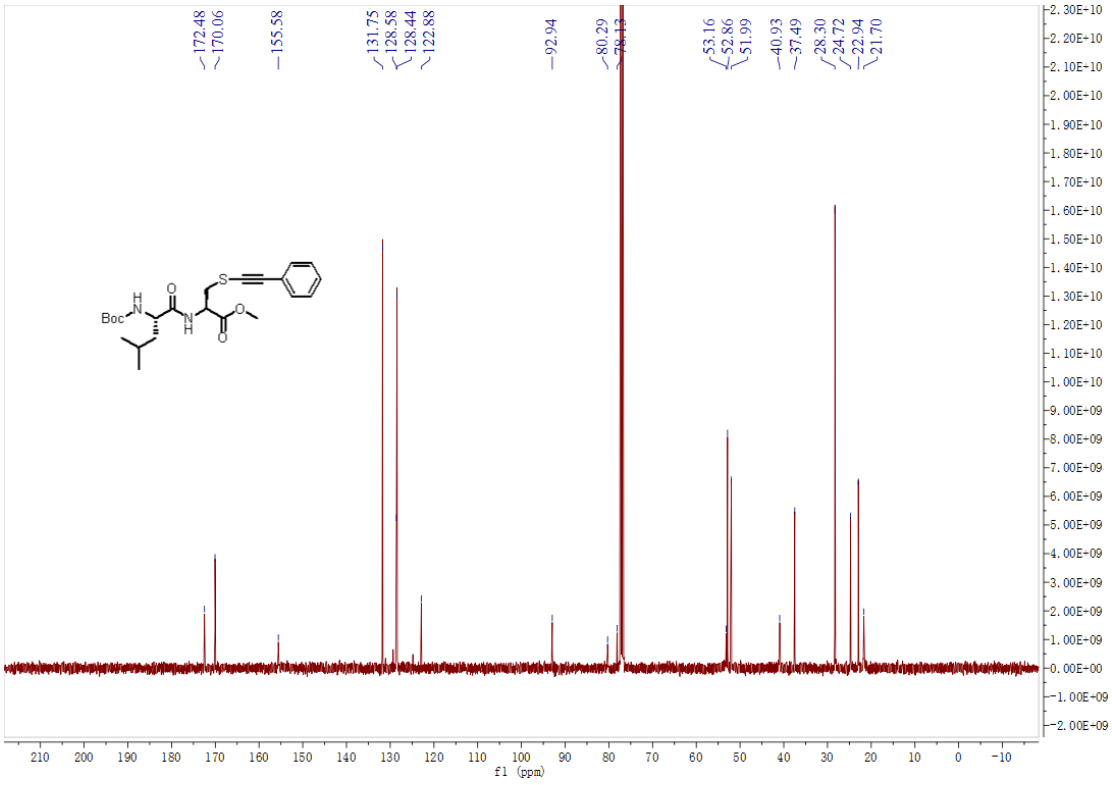
^{1}H NMR of **3ag** (400 MHz, $CDCl_3$)



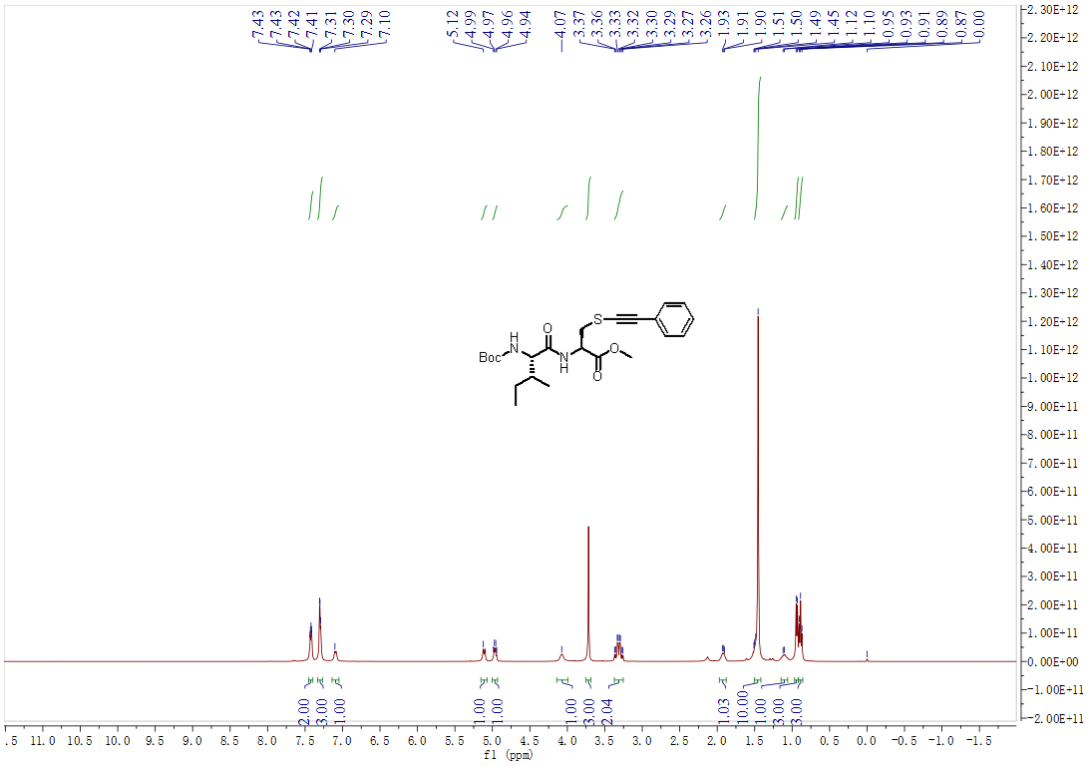
^{13}C NMR of **3ag** (100 MHz, $CDCl_3$)



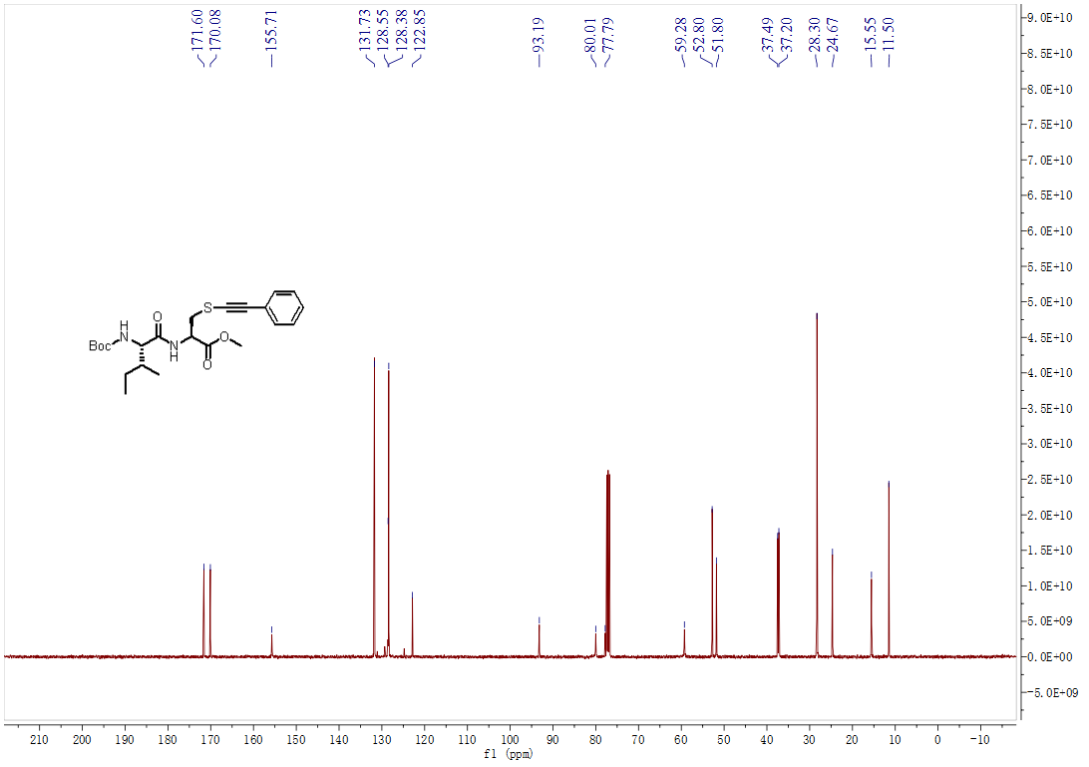
^{1}H NMR of **3ah** (400 MHz, $CDCl_3$)



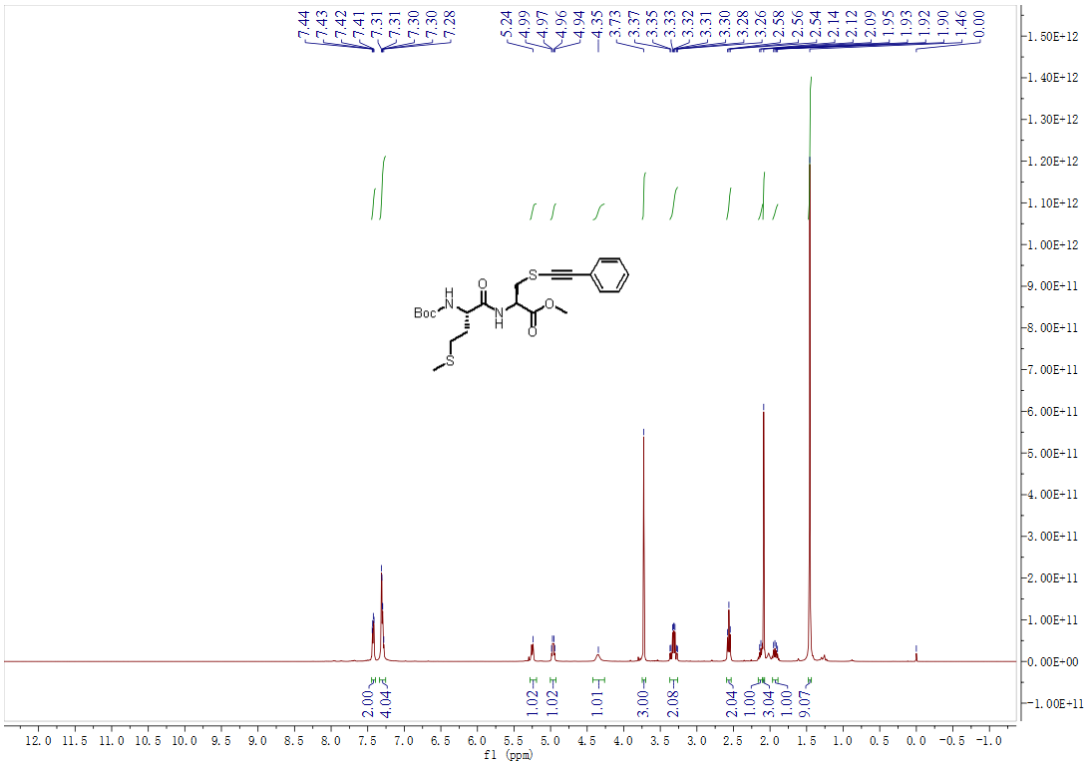
^{13}C NMR of **3ah** (100 MHz, $CDCl_3$)



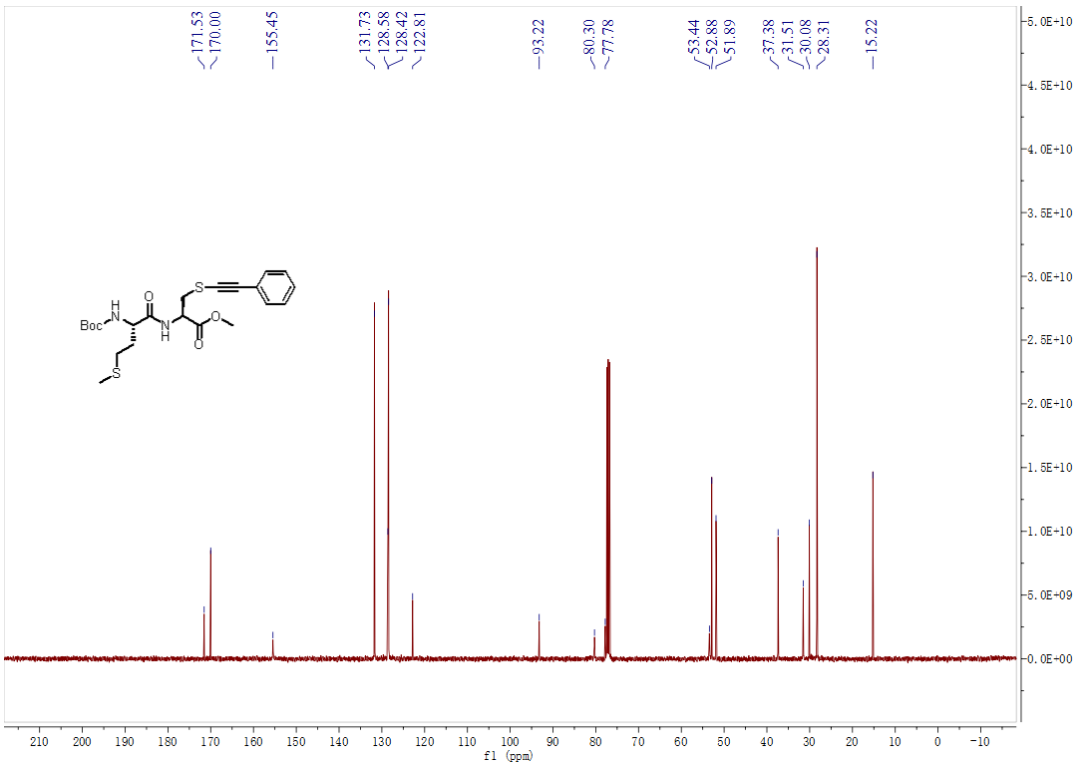
^{1}H NMR of **3ai** (400 MHz, $CDCl_3$)



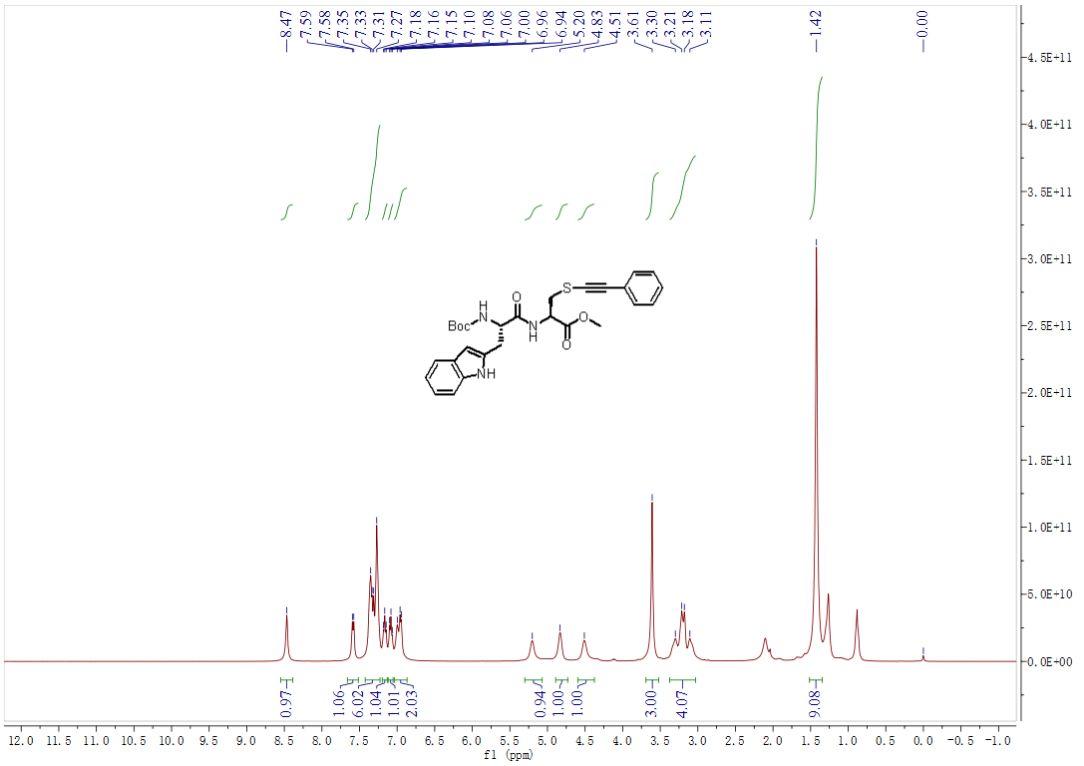
^{13}C NMR of **3ai** (100 MHz, $CDCl_3$)



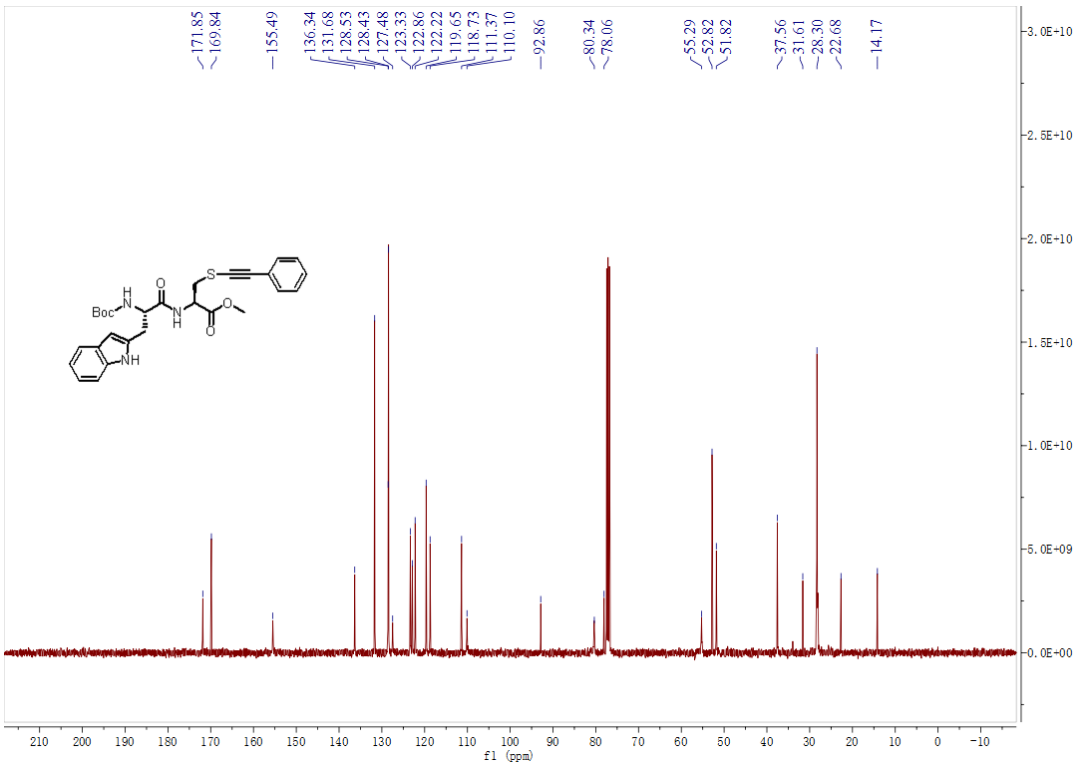
^{1}H NMR of **3aj** (400 MHz, $CDCl_3$)



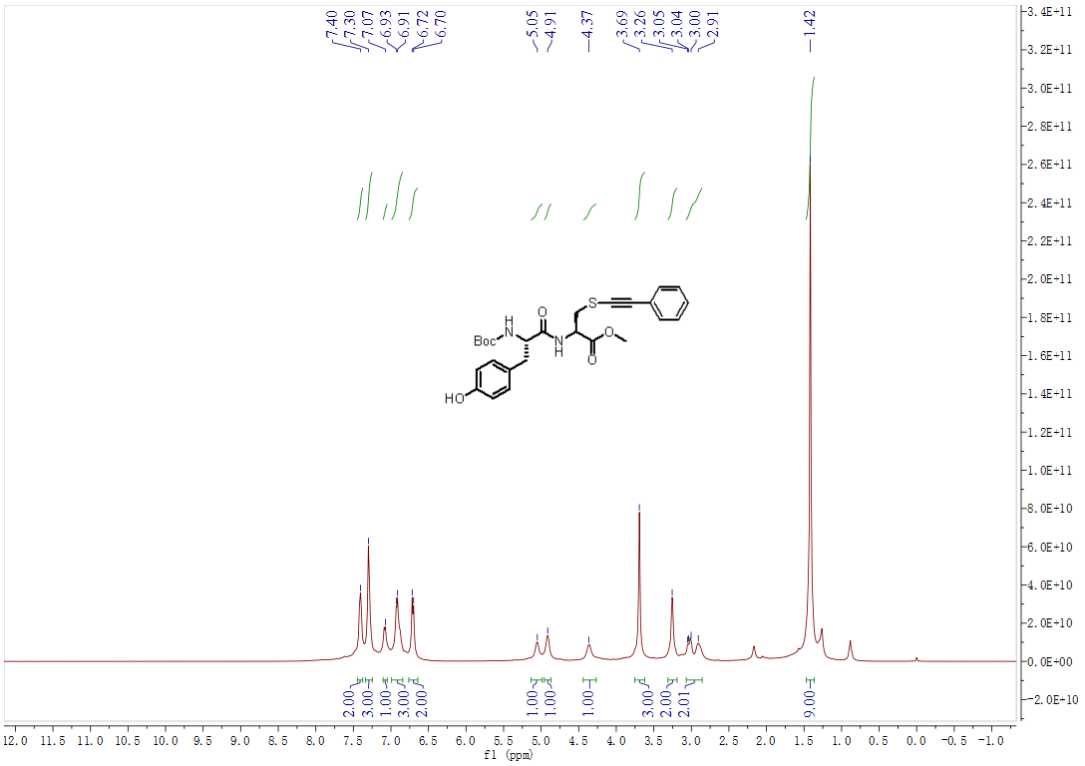
^{13}C NMR of **3aj** (100 MHz, $CDCl_3$)



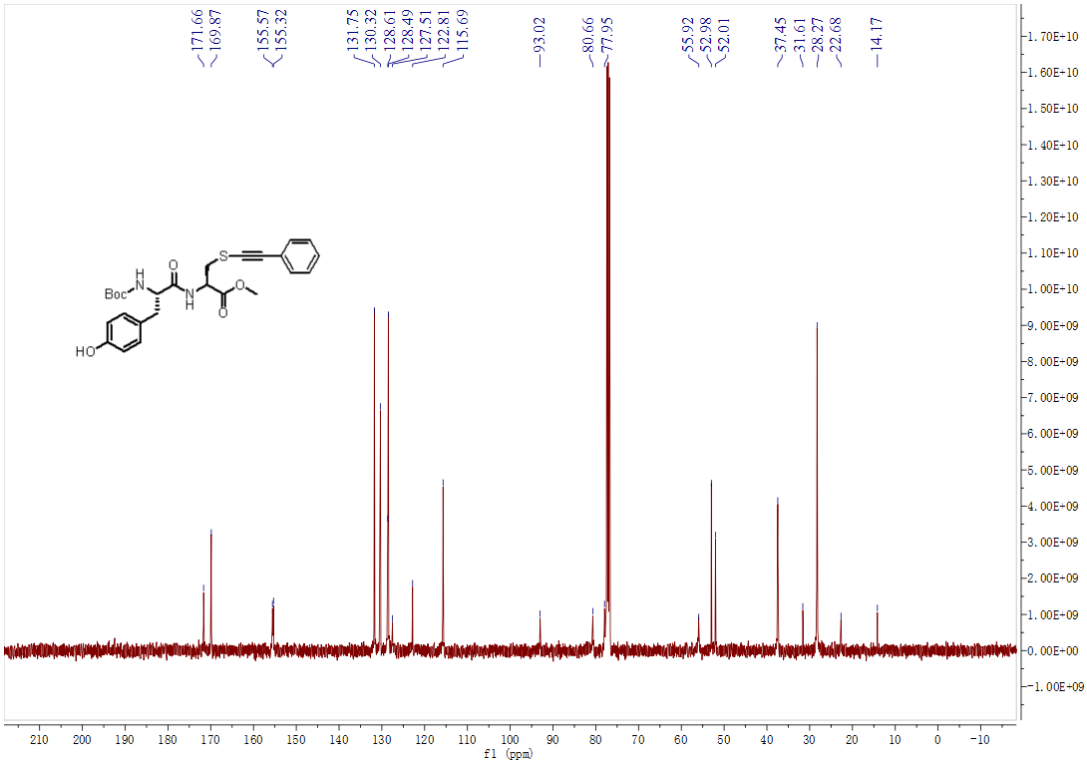
^{1}H NMR of **3ak** (400 MHz, $CDCl_3$)



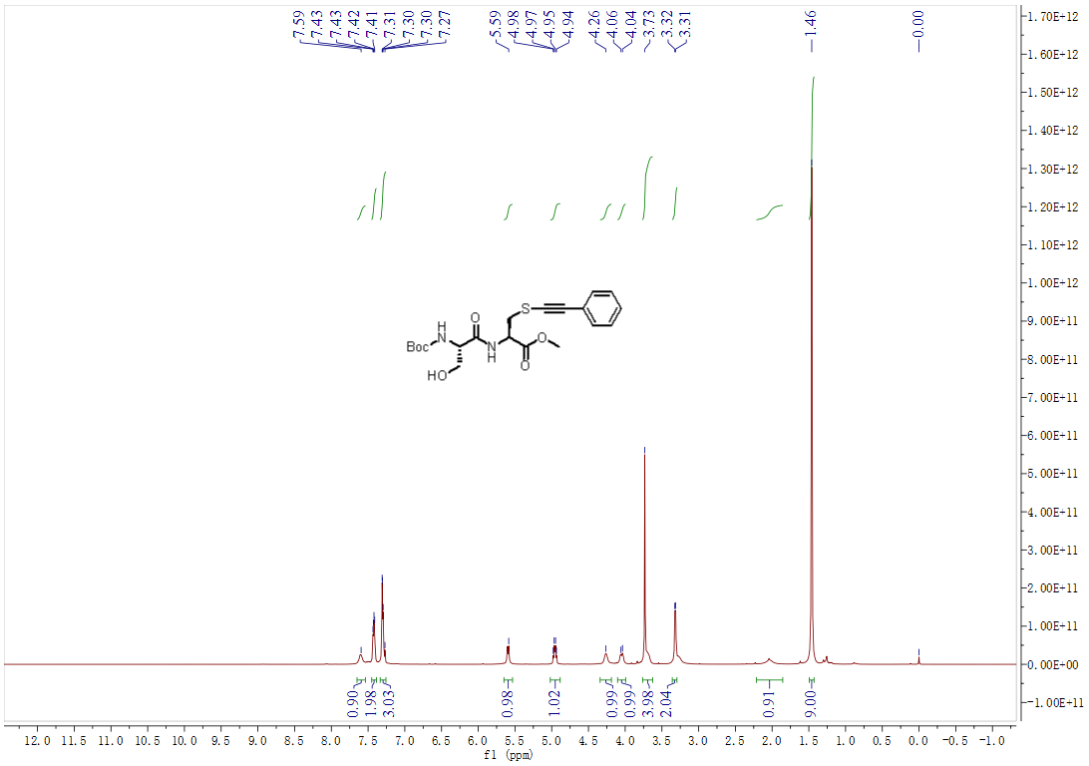
^{13}C NMR of **3ak** (100 MHz, $CDCl_3$)



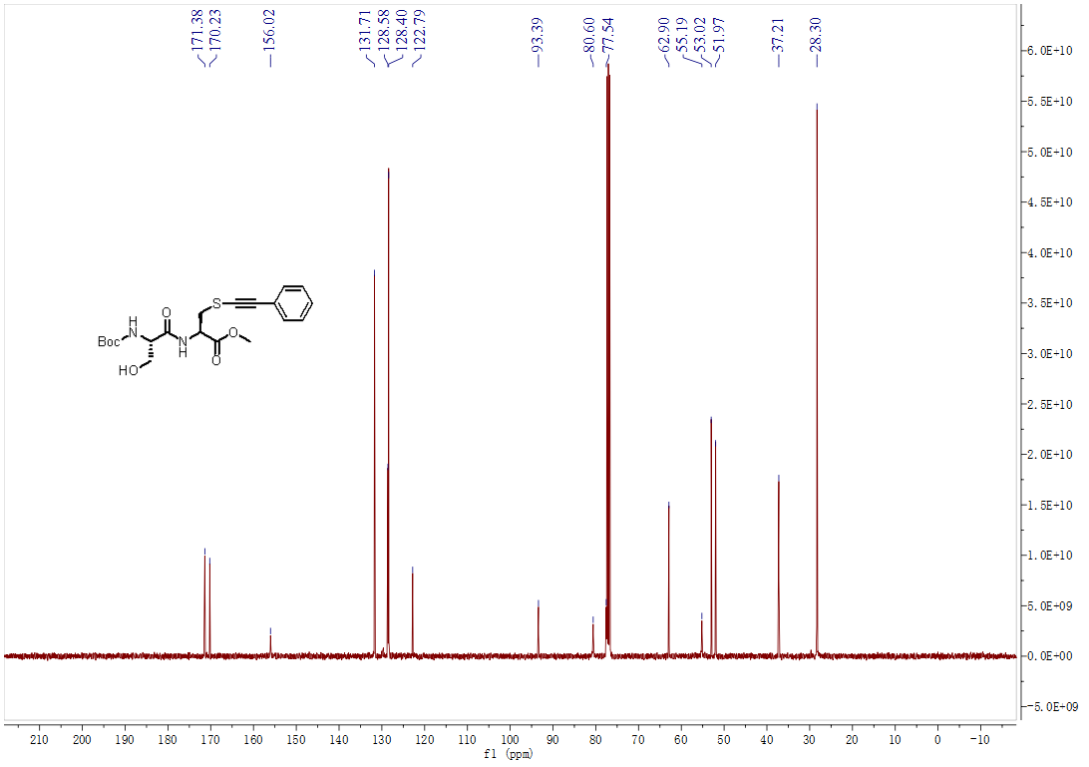
^{1}H NMR of **3al** (400 MHz, $CDCl_3$)



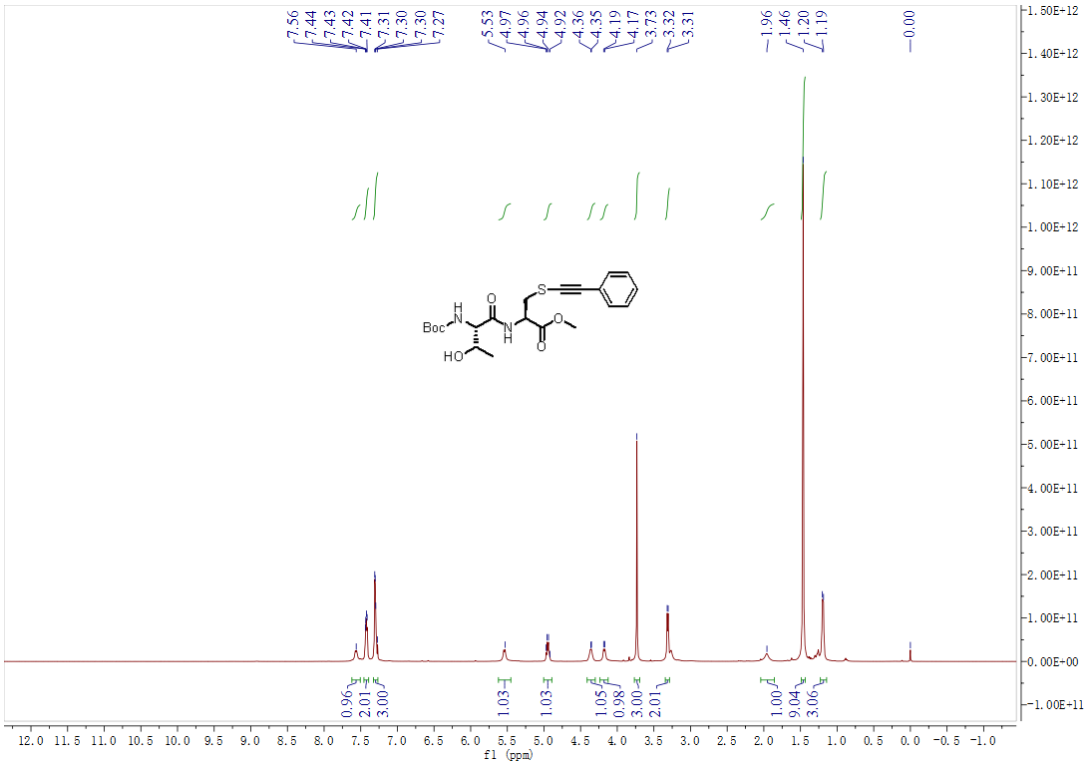
^{13}C NMR of **3al** (100 MHz, $CDCl_3$)



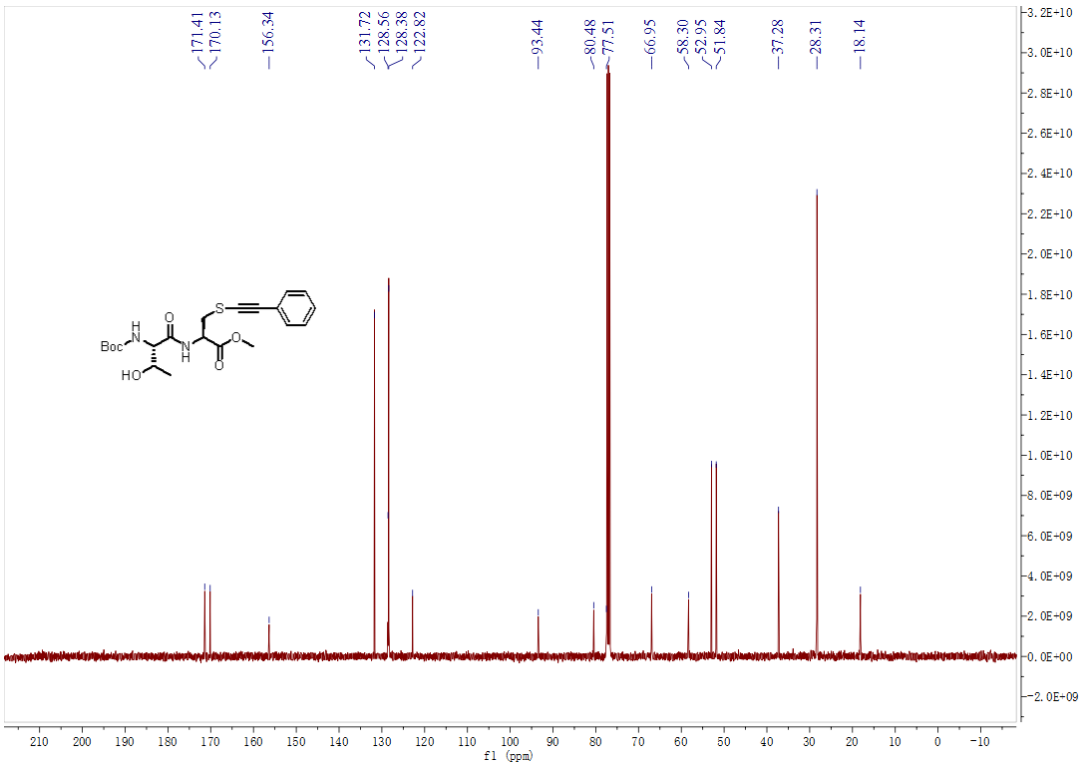
^{1}H NMR of **3am** (400 MHz, $CDCl_3$)



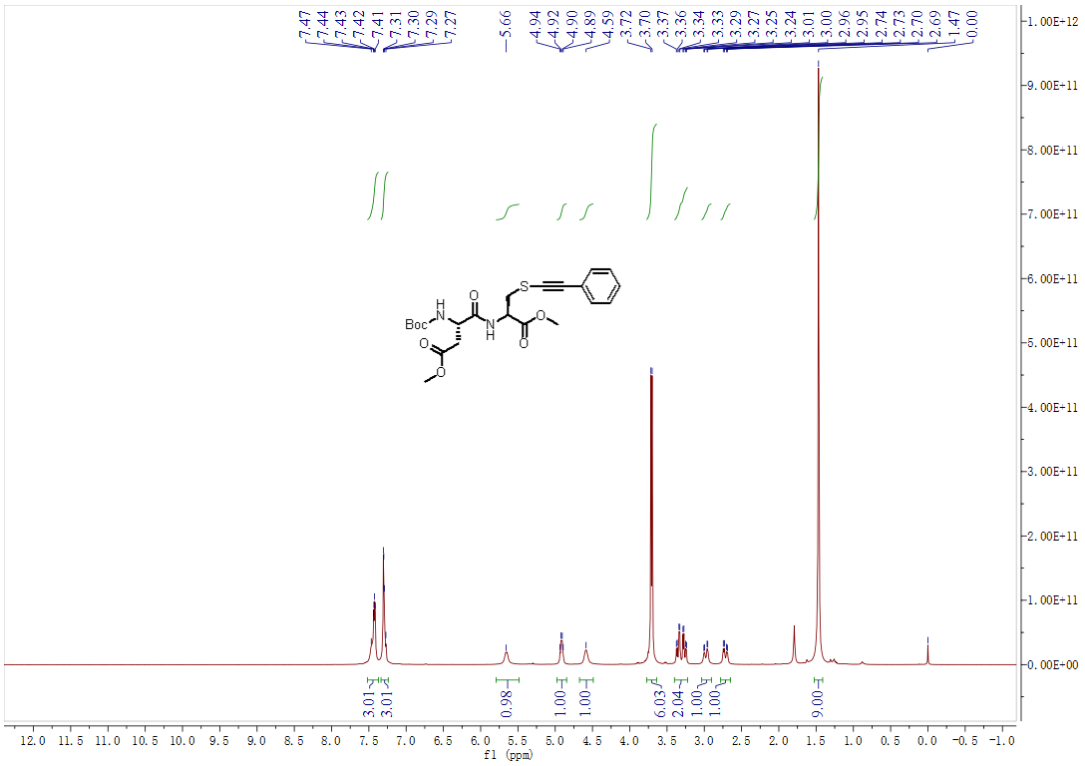
^{13}C NMR of **3am** (100 MHz, $CDCl_3$)



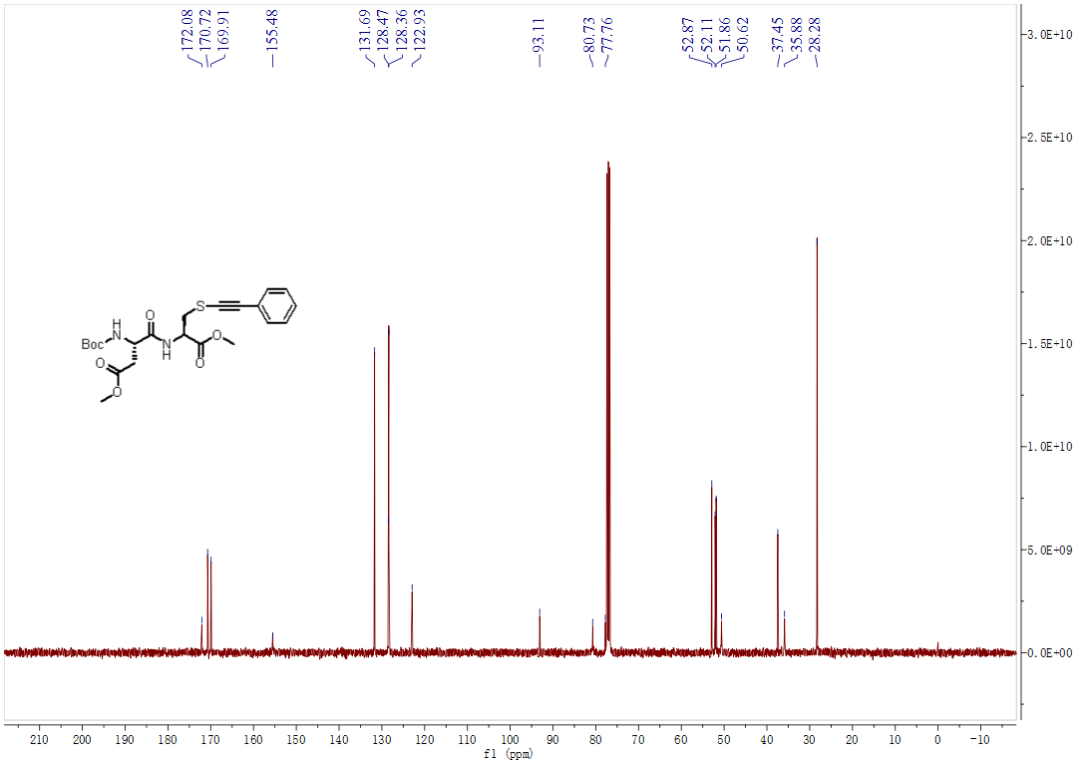
^{1}H NMR of **3an** (400 MHz, $CDCl_3$)



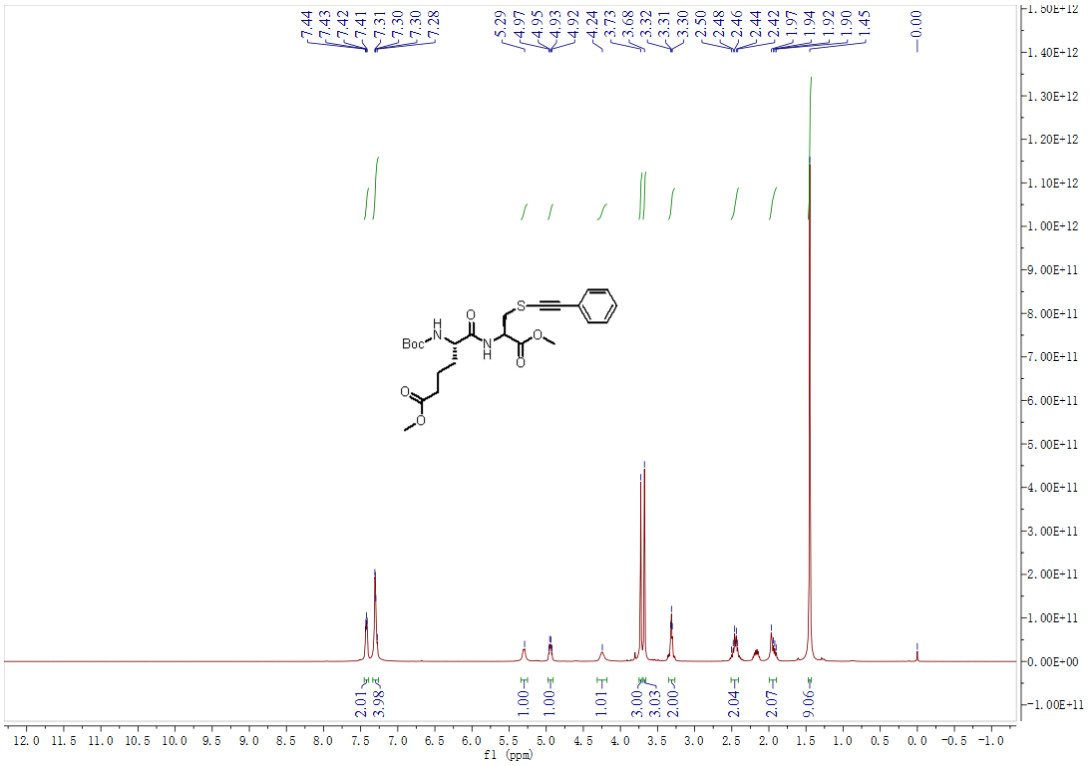
^{13}C NMR of **3an** (100 MHz, $CDCl_3$)



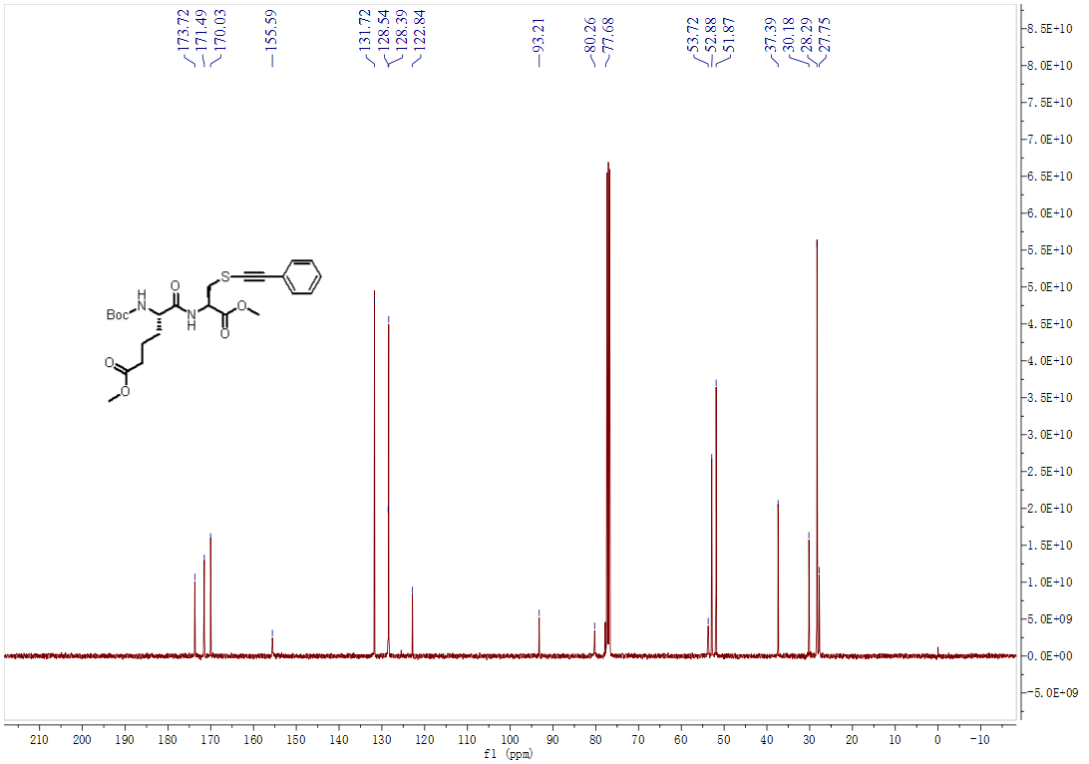
^{1}H NMR of **3ao** (400 MHz, $CDCl_3$)



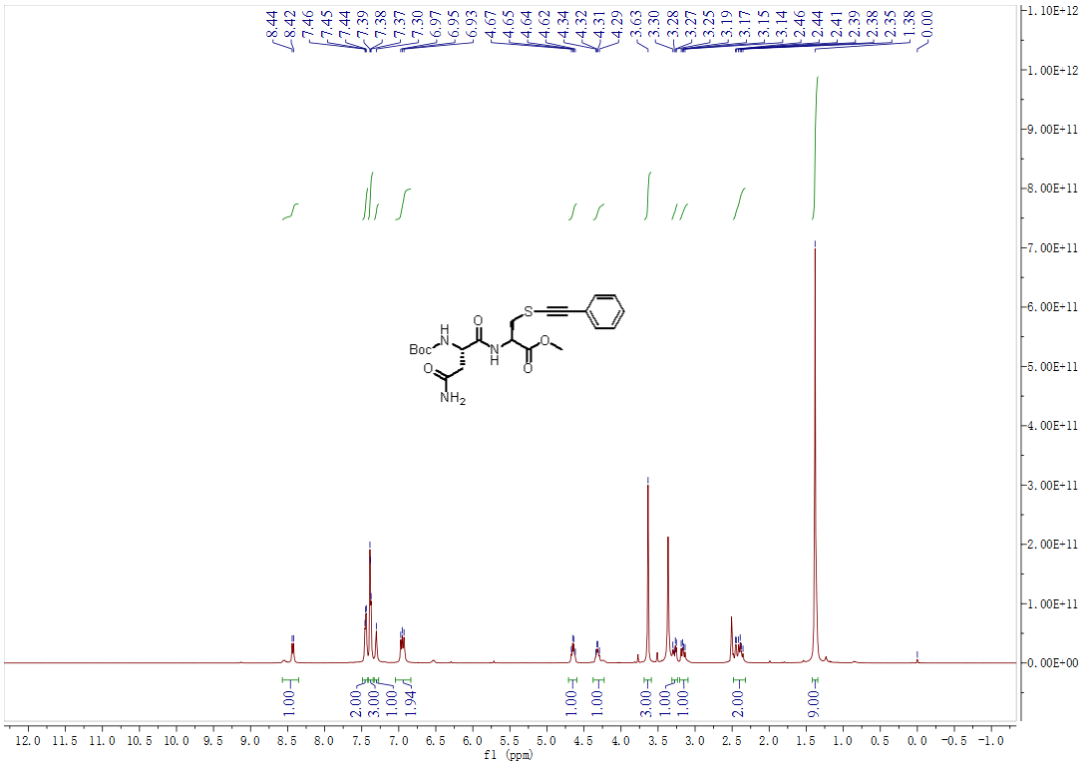
^{13}C NMR of **3ao** (100 MHz, $CDCl_3$)



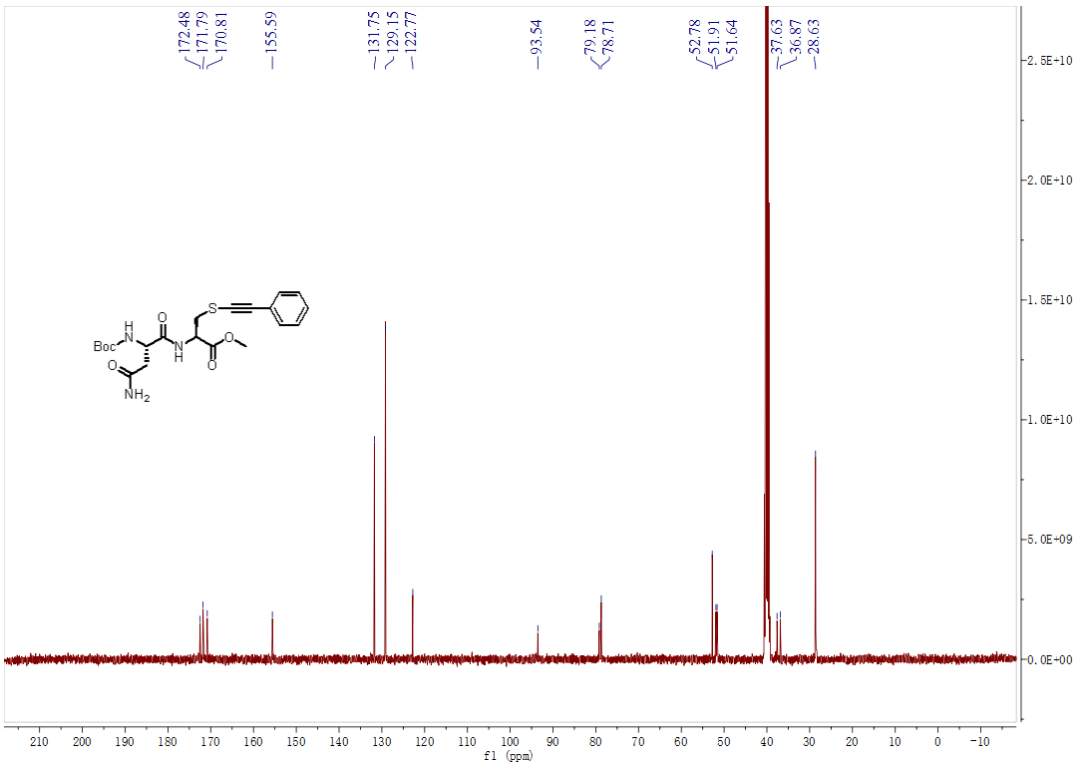
^{1}H NMR of **3ap** (400 MHz, $CDCl_3$)



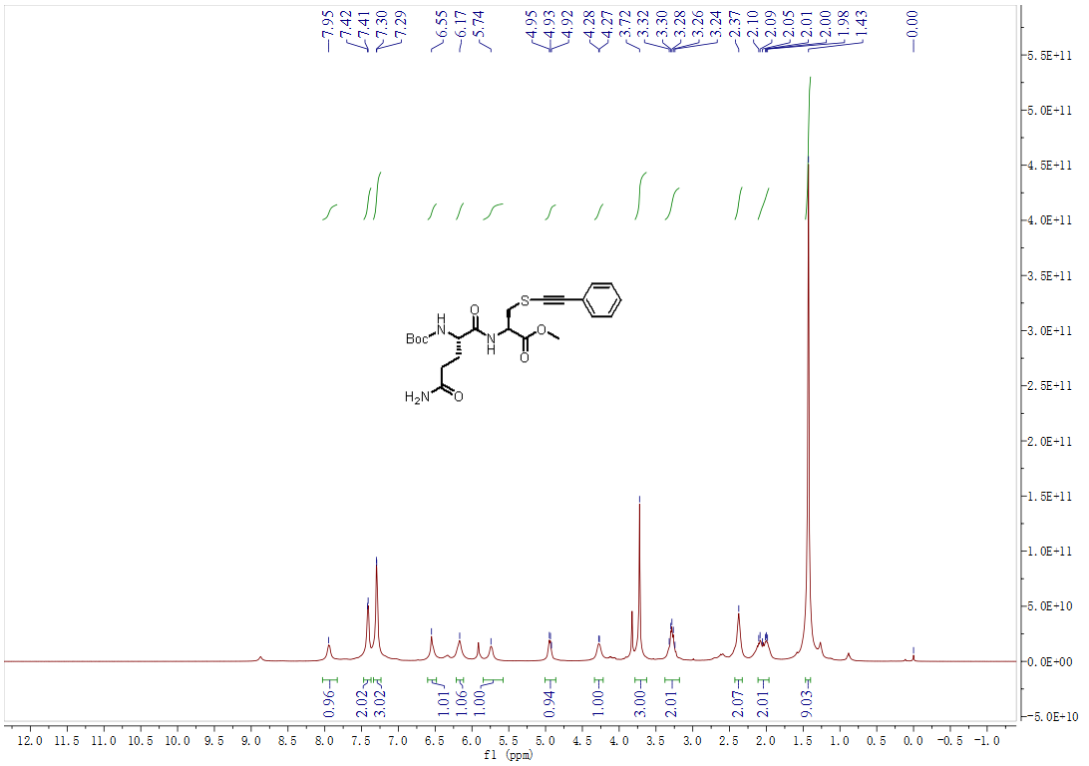
^{13}C NMR of **3ap** (100 MHz, $CDCl_3$)



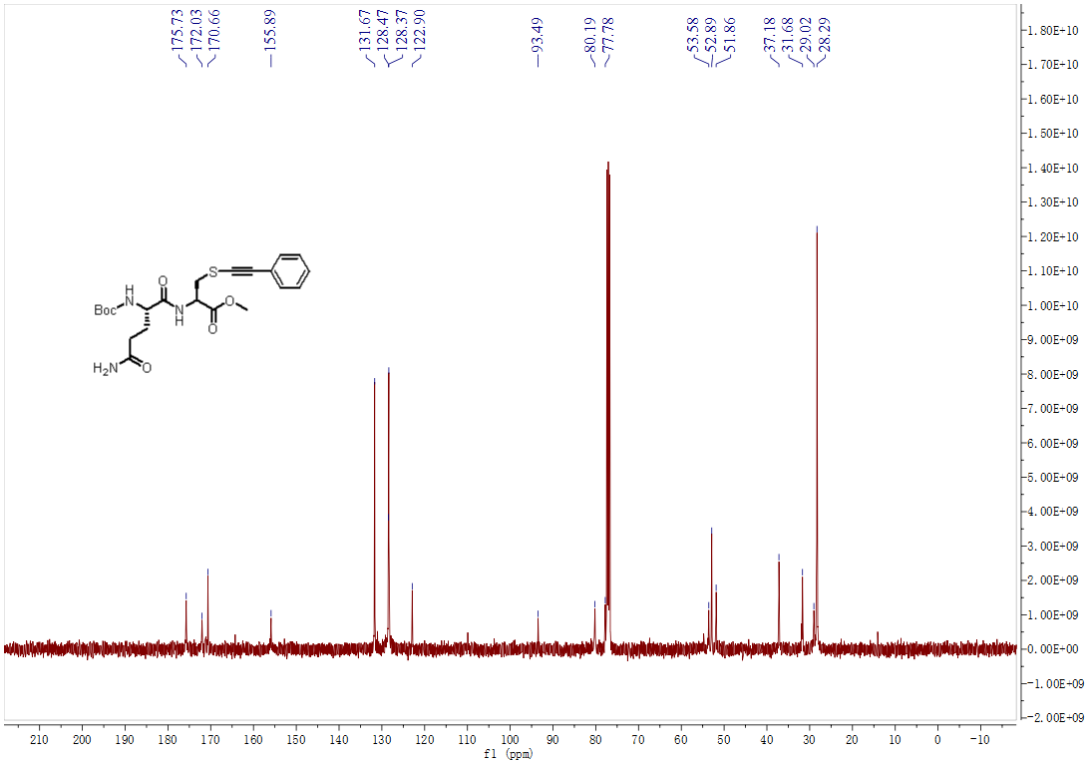
^{1}H NMR of **3aq** (400 MHz, DMSO-d_6)



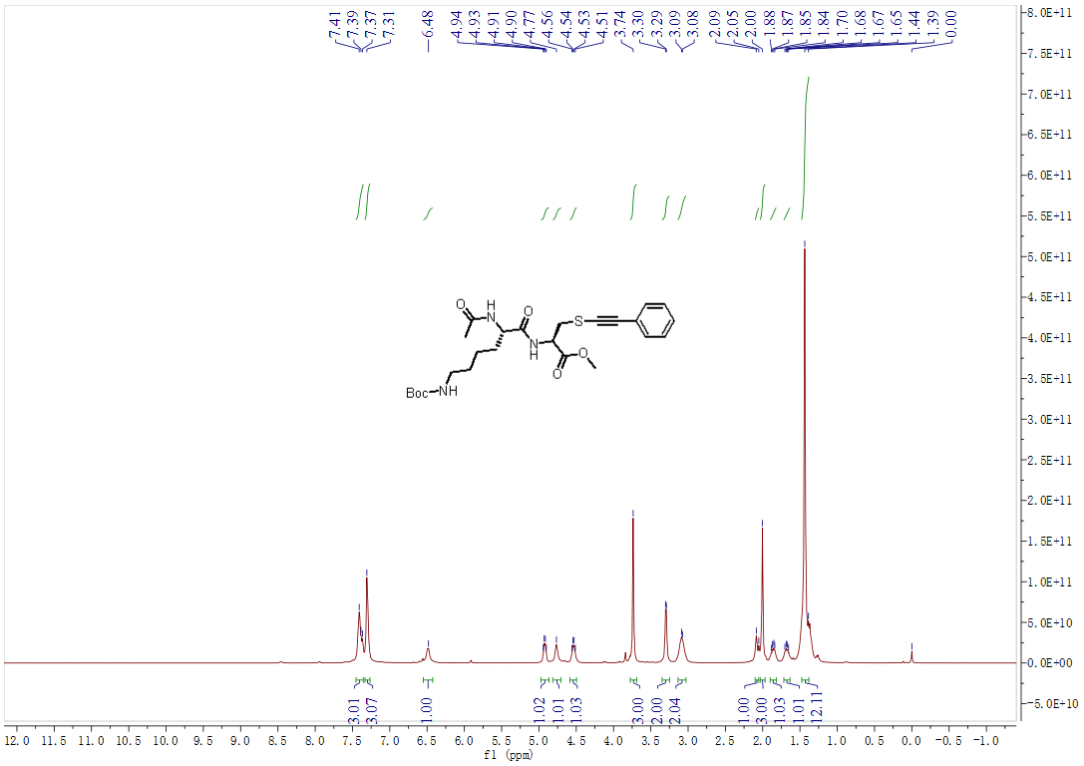
^{13}C NMR of **3aq** (100 MHz, DMSO-d_6)



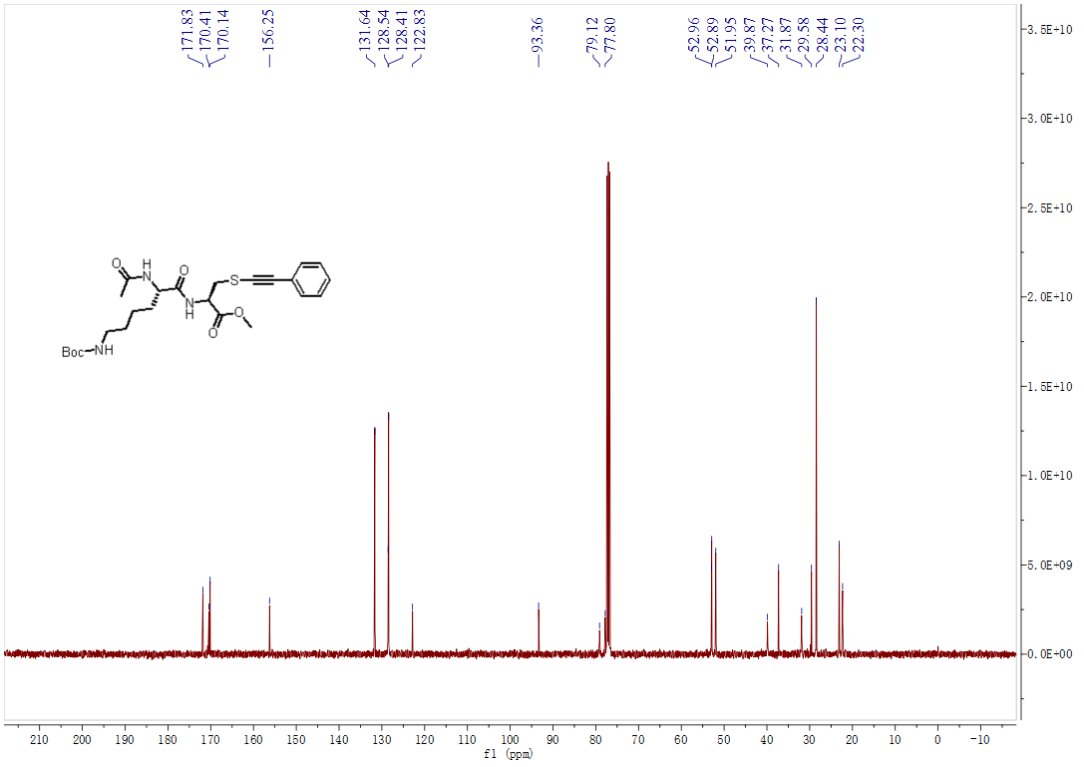
^{1}H NMR of **3ar** (400 MHz, $CDCl_3$)



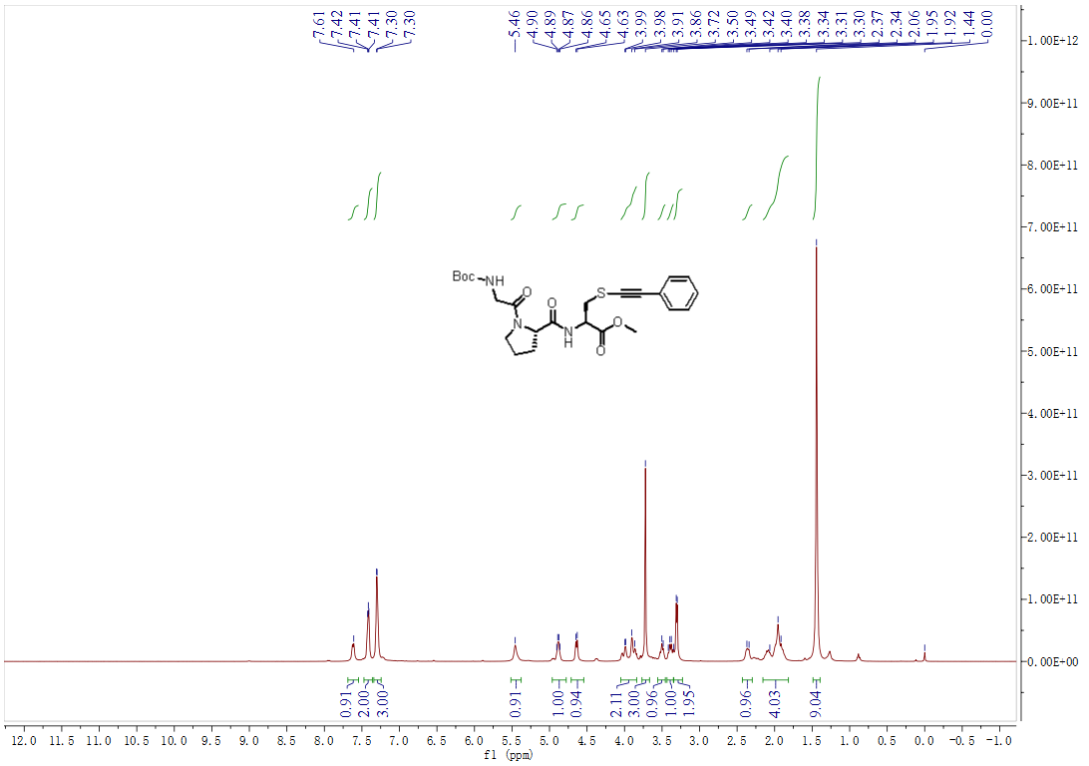
^{13}C NMR of **3ar** (100 MHz, $CDCl_3$)



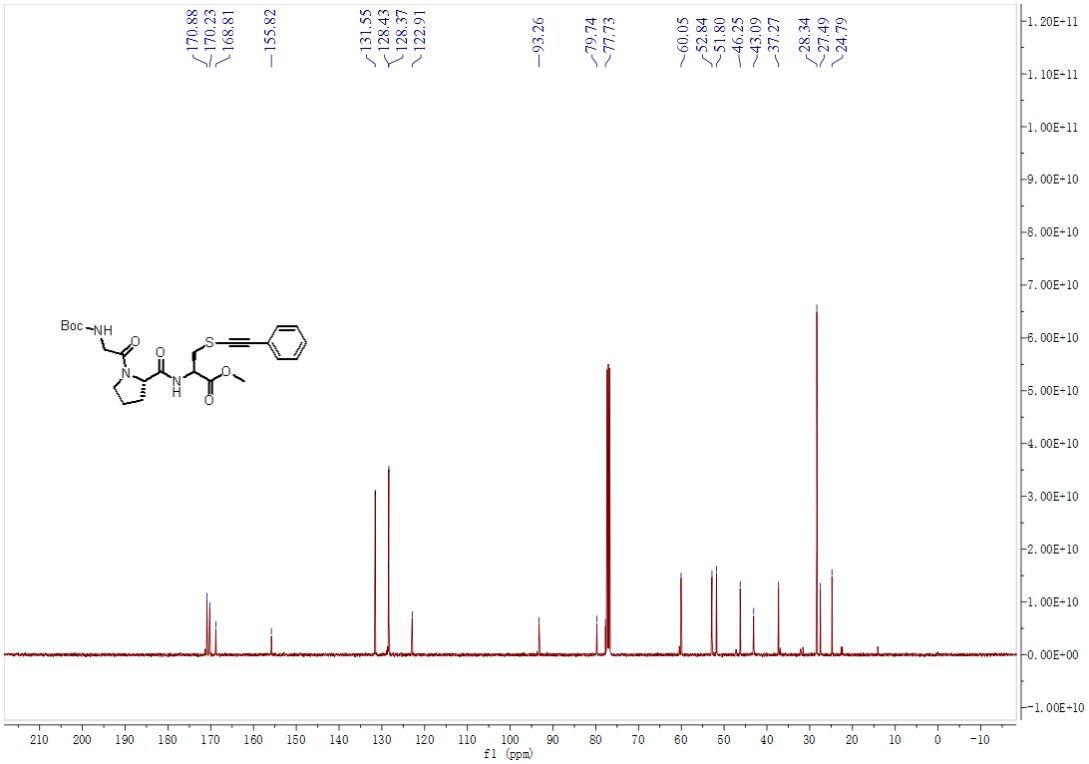
^{1}H NMR of **3as** (400 MHz, $CDCl_3$)



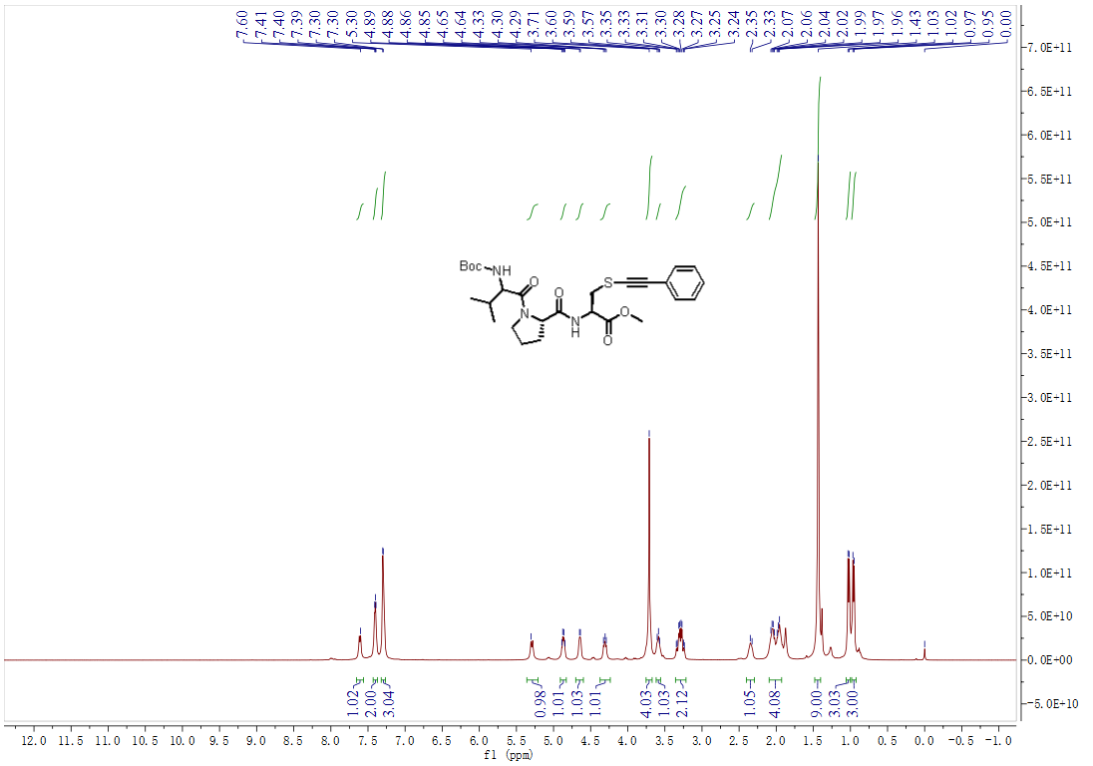
^{13}C NMR of **3as** (100 MHz, $CDCl_3$)



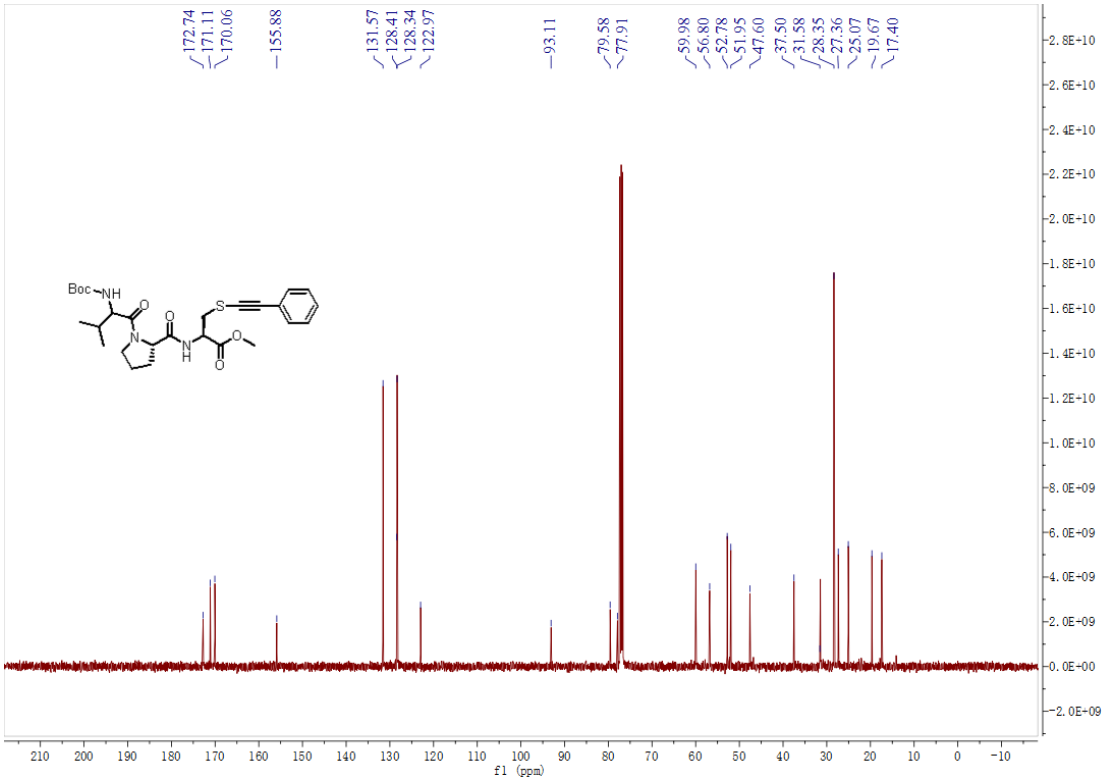
^{1}H NMR of **3at** (400 MHz, $CDCl_3$)



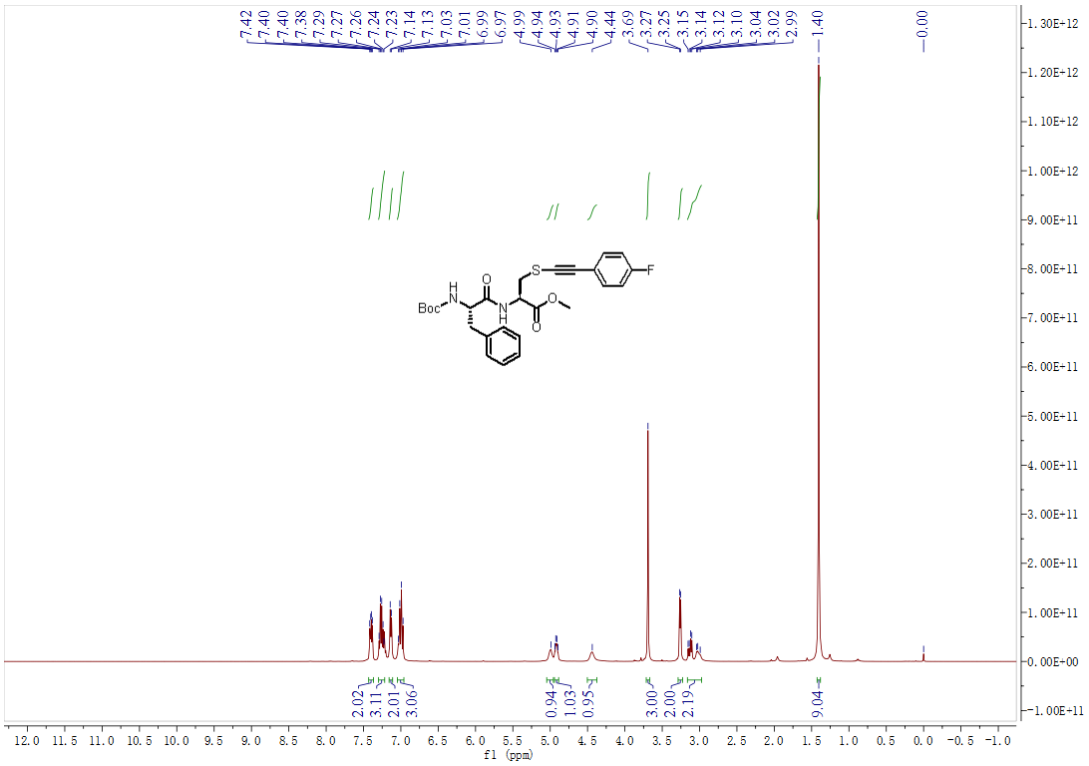
^{13}C NMR of **3at** (100 MHz, $CDCl_3$)



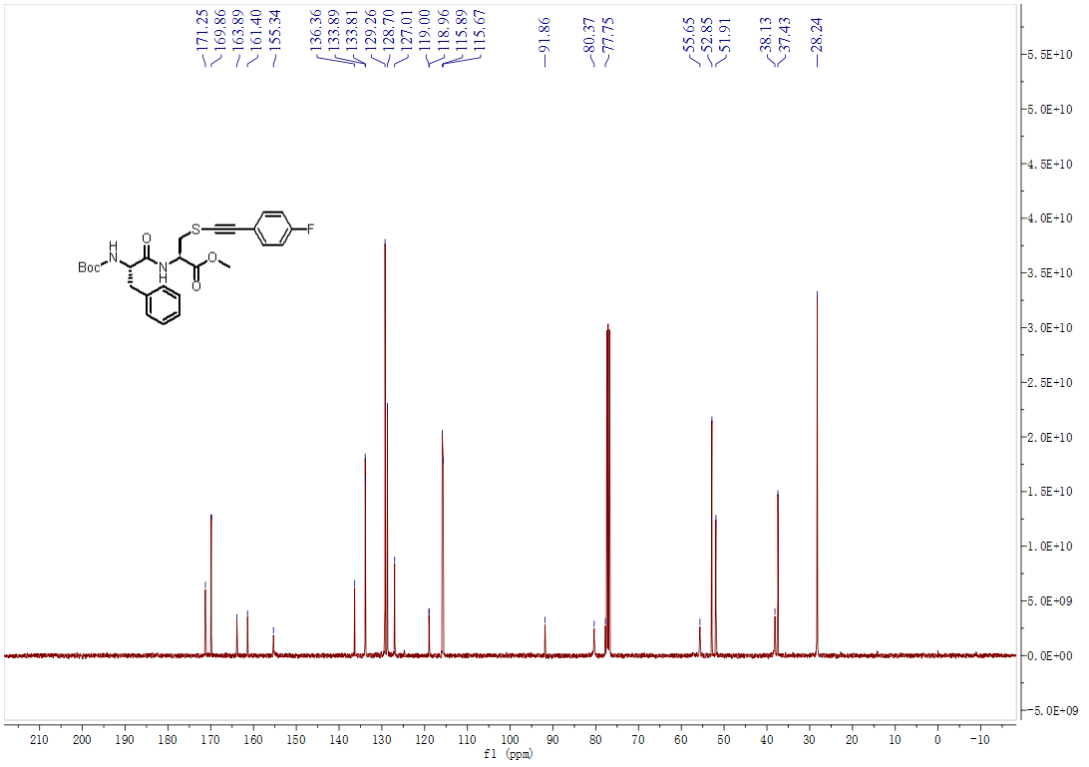
^{1}H NMR of **3au** (400 MHz, $CDCl_3$)



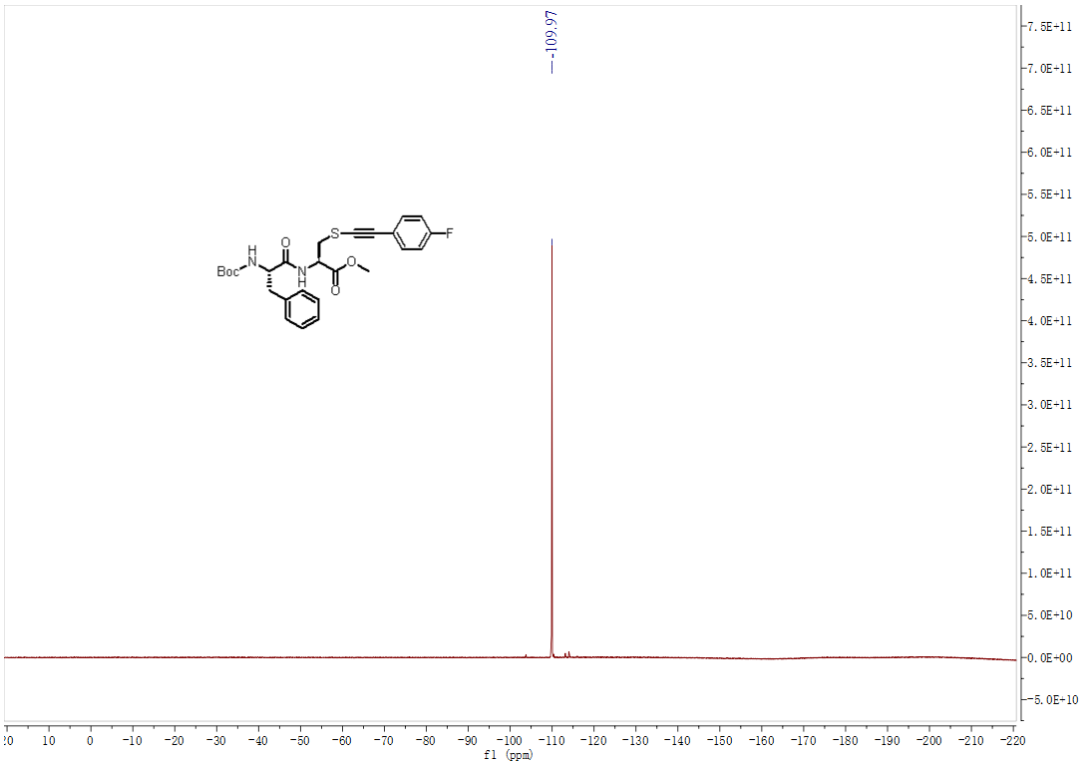
^{13}C NMR of **3au** (100 MHz, $CDCl_3$)



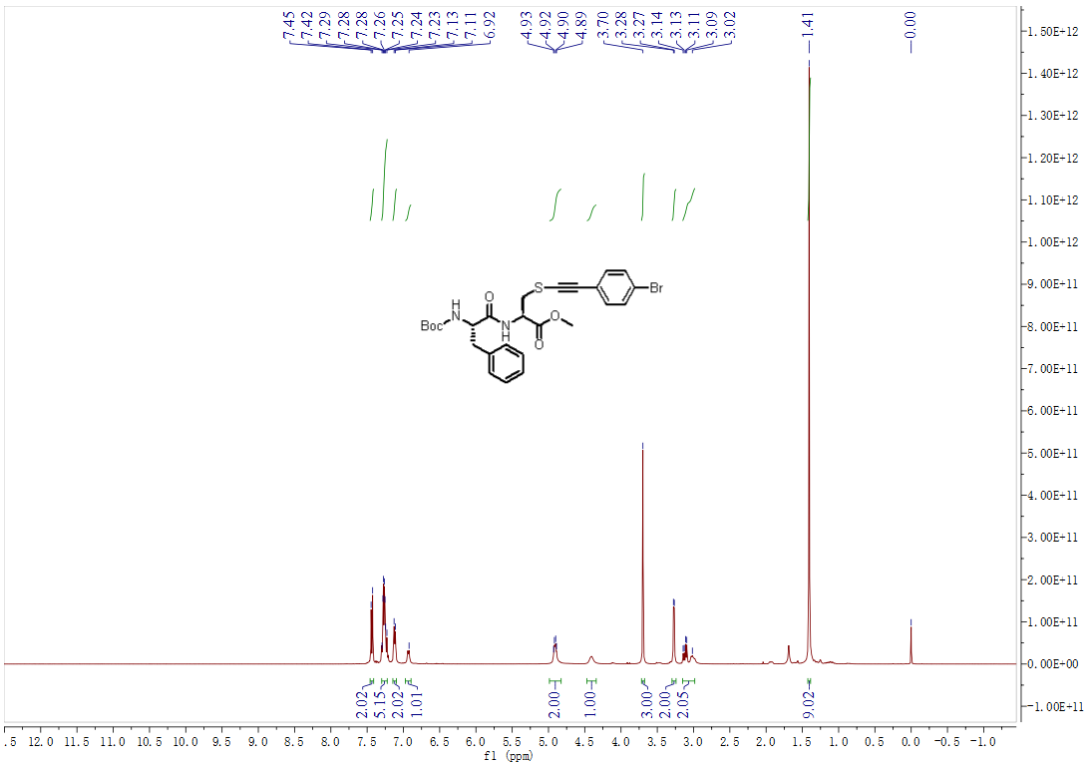
^{1}H NMR of **3ba** (400 MHz, $CDCl_3$)



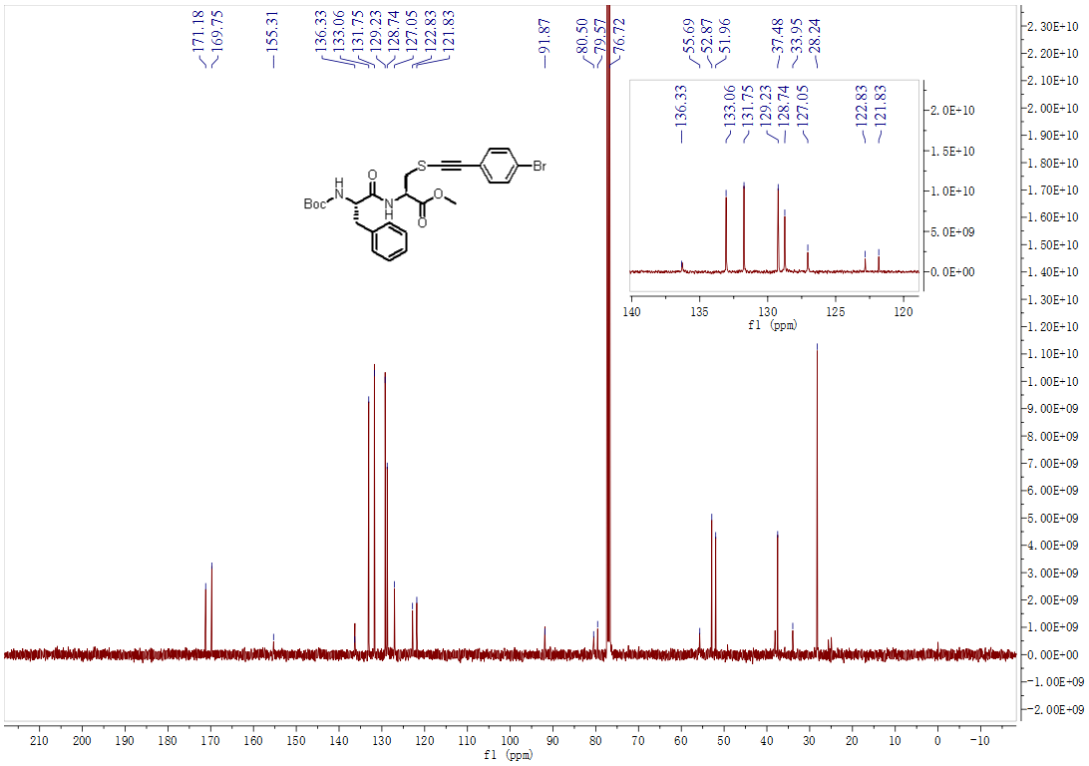
^{13}C NMR of **3ba** (100 MHz, $CDCl_3$)



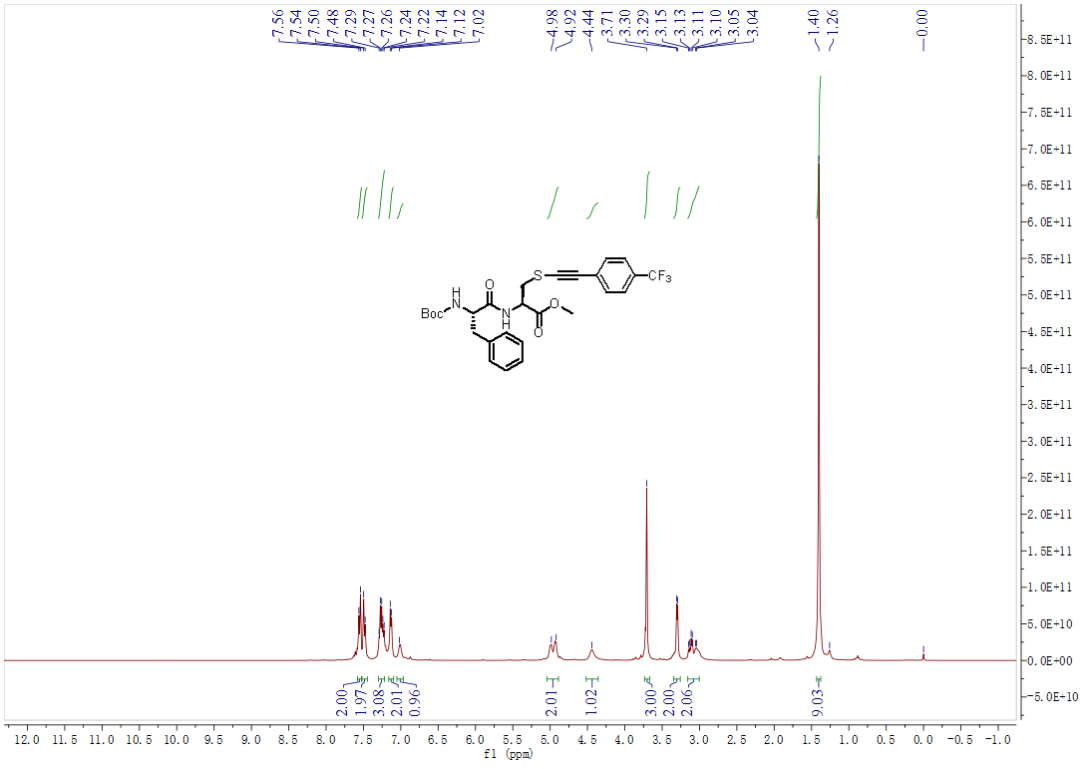
^{19}F NMR of **3ba** (376 MHz, $CDCl_3$)



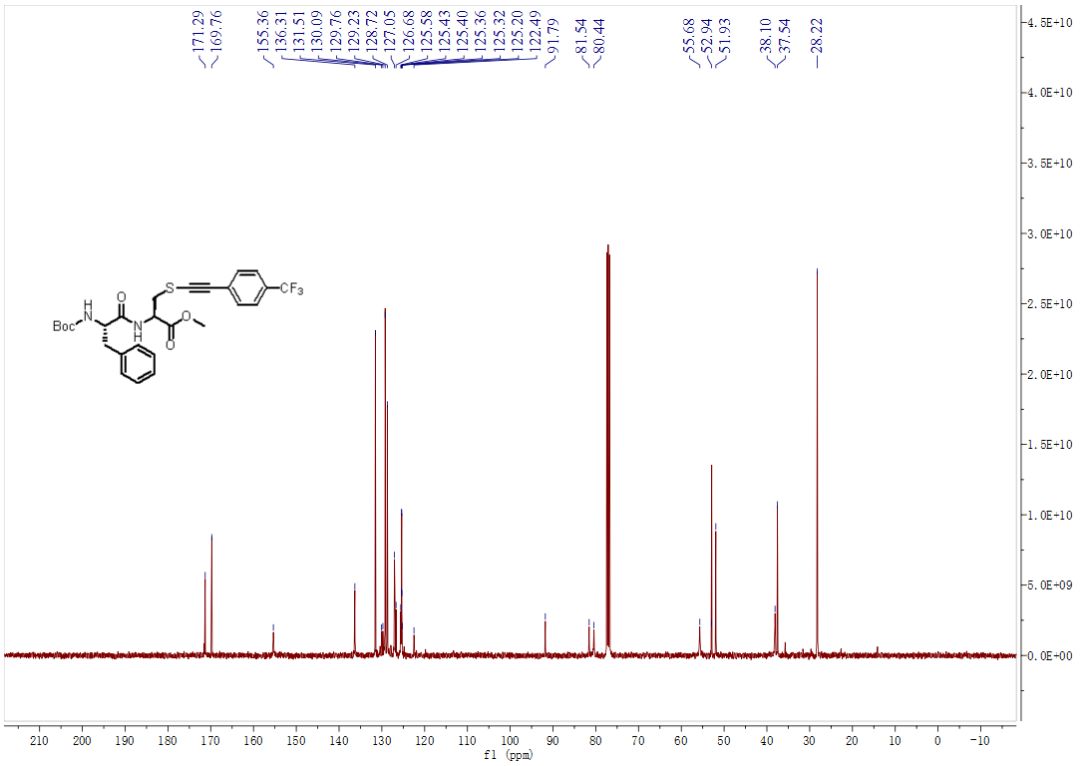
^{1}H NMR of **3bb** (400 MHz, $CDCl_3$)



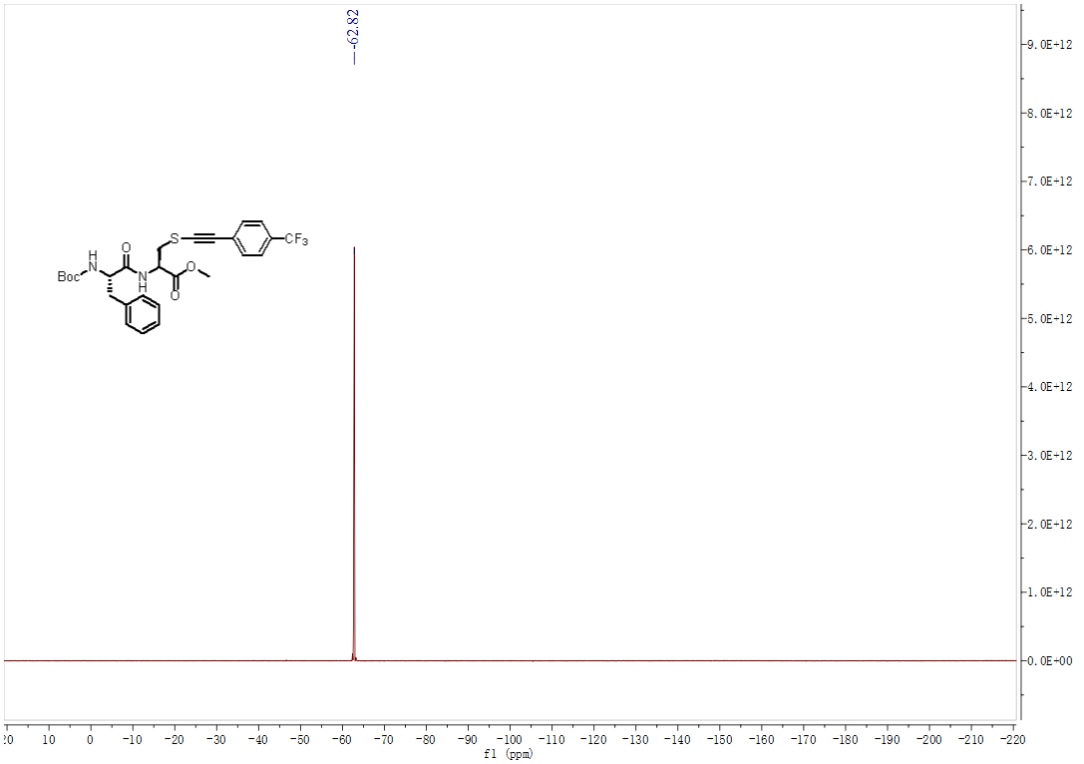
^{13}C NMR of **3bb** (100 MHz, $CDCl_3$)



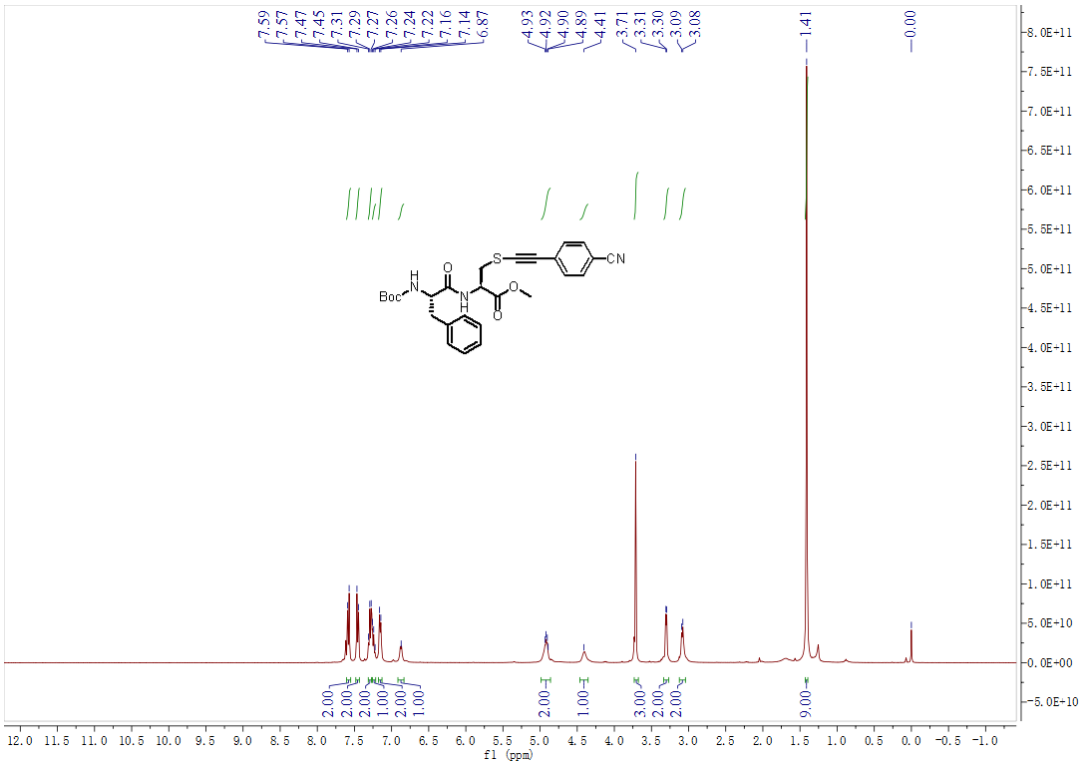
^{1}H NMR of **3bc** (400 MHz, $CDCl_3$)



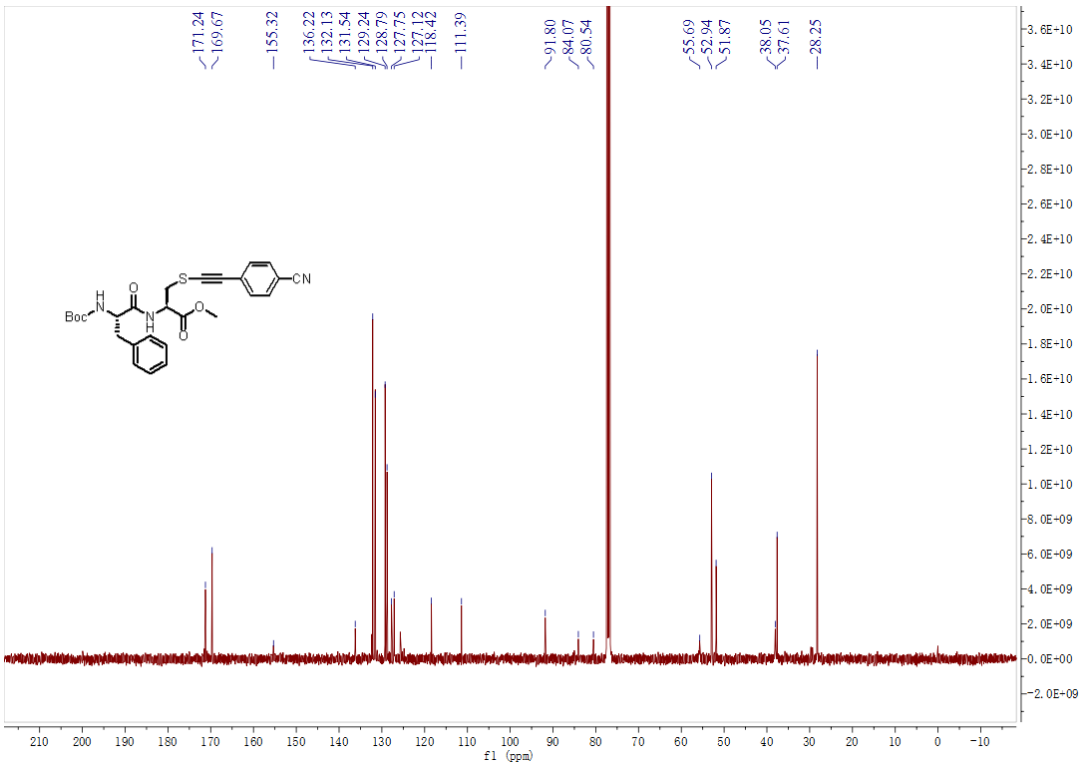
^{13}C NMR of **3bc** (100 MHz, $CDCl_3$)



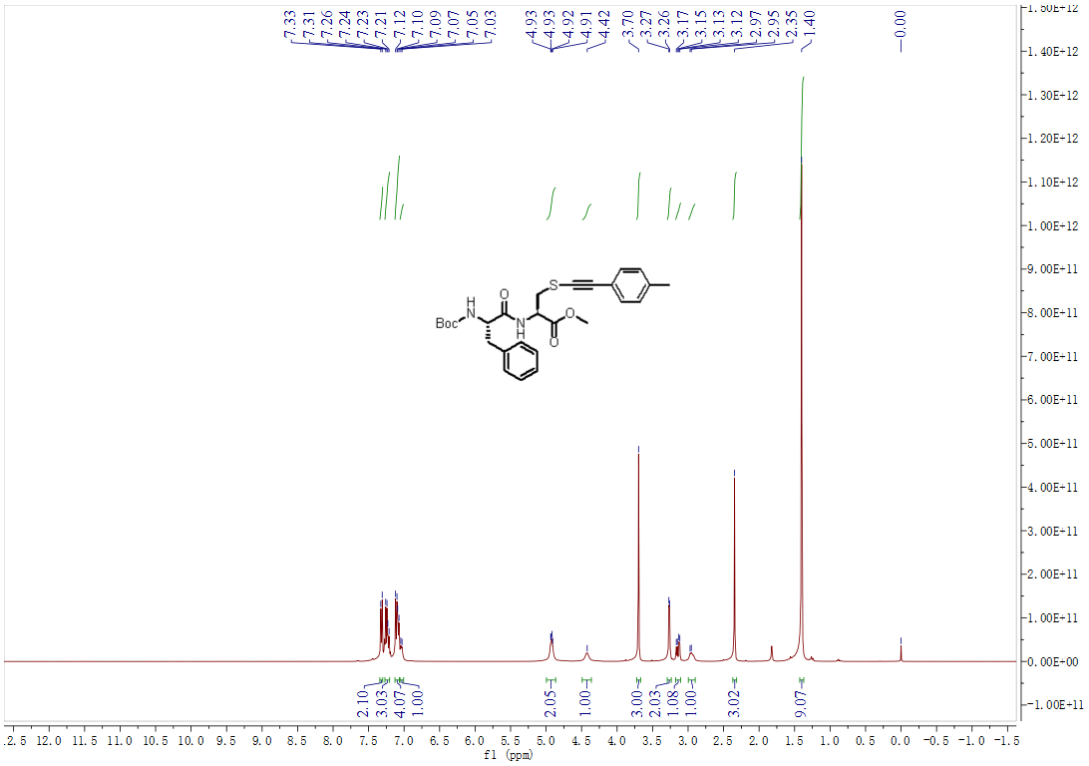
^{19}F NMR of **3bc** (376 MHz, $CDCl_3$)



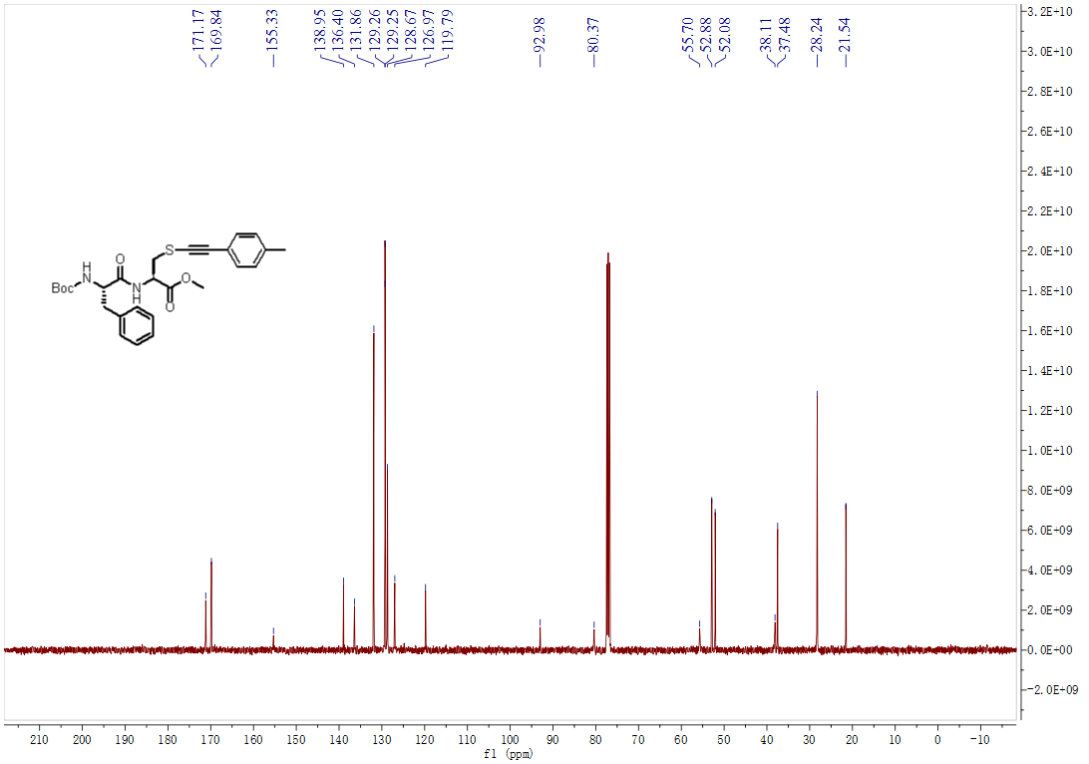
^{1}H NMR of **3bd** (400 MHz, $CDCl_3$)



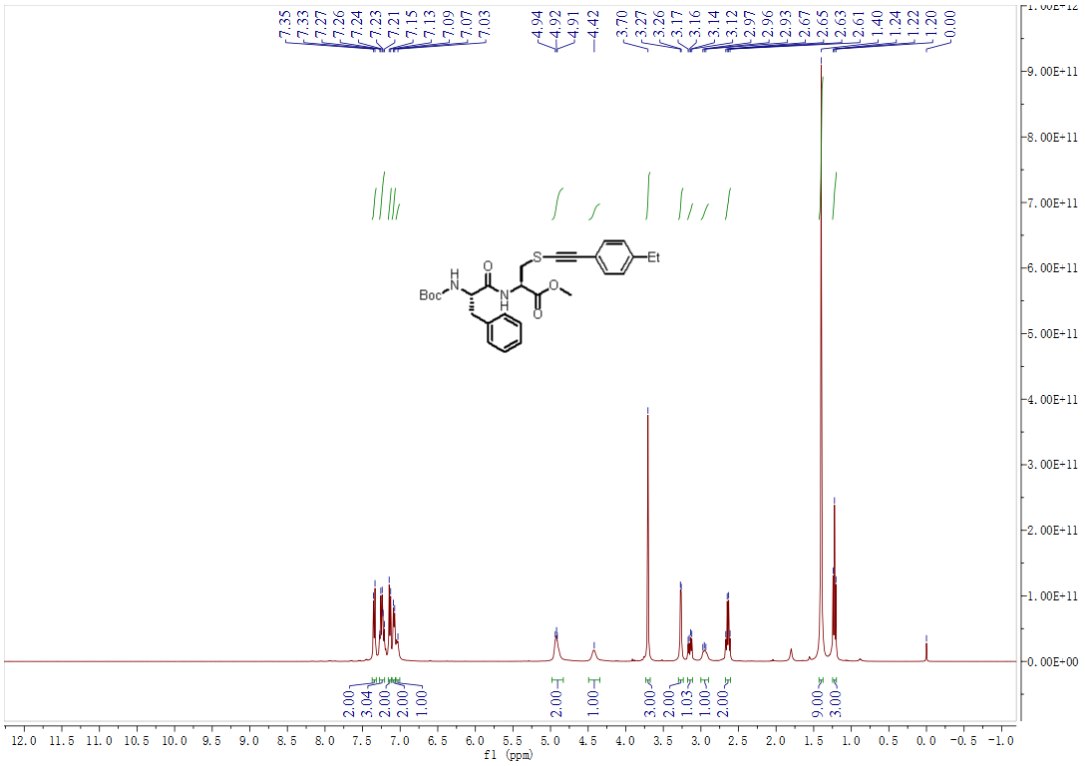
^{13}C NMR of **3bd** (100 MHz, $CDCl_3$)



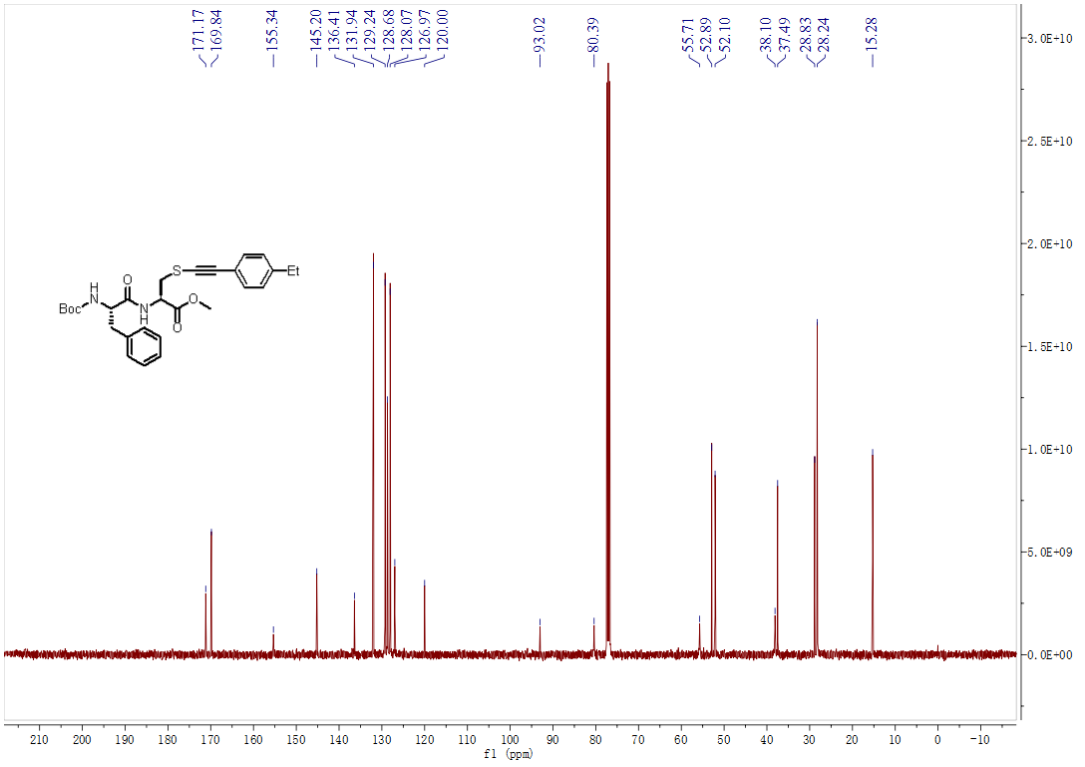
^{1}H NMR of **3be** (400 MHz, $CDCl_3$)



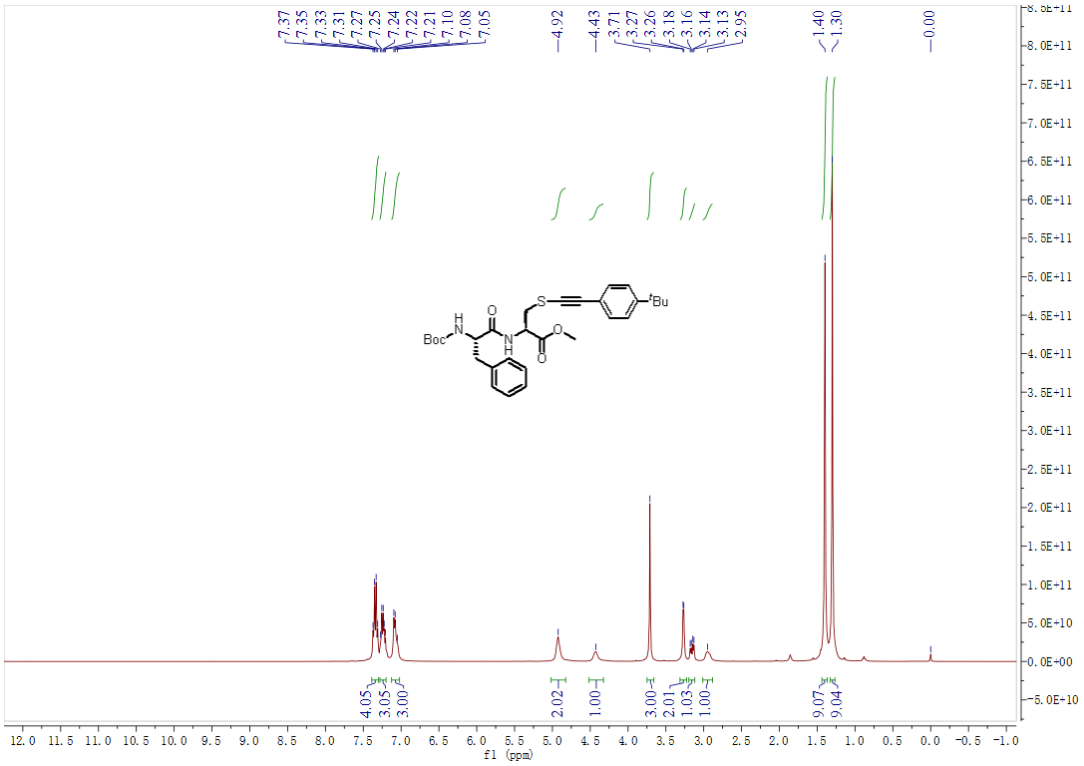
^{13}C NMR of **3be** (100 MHz, $CDCl_3$)



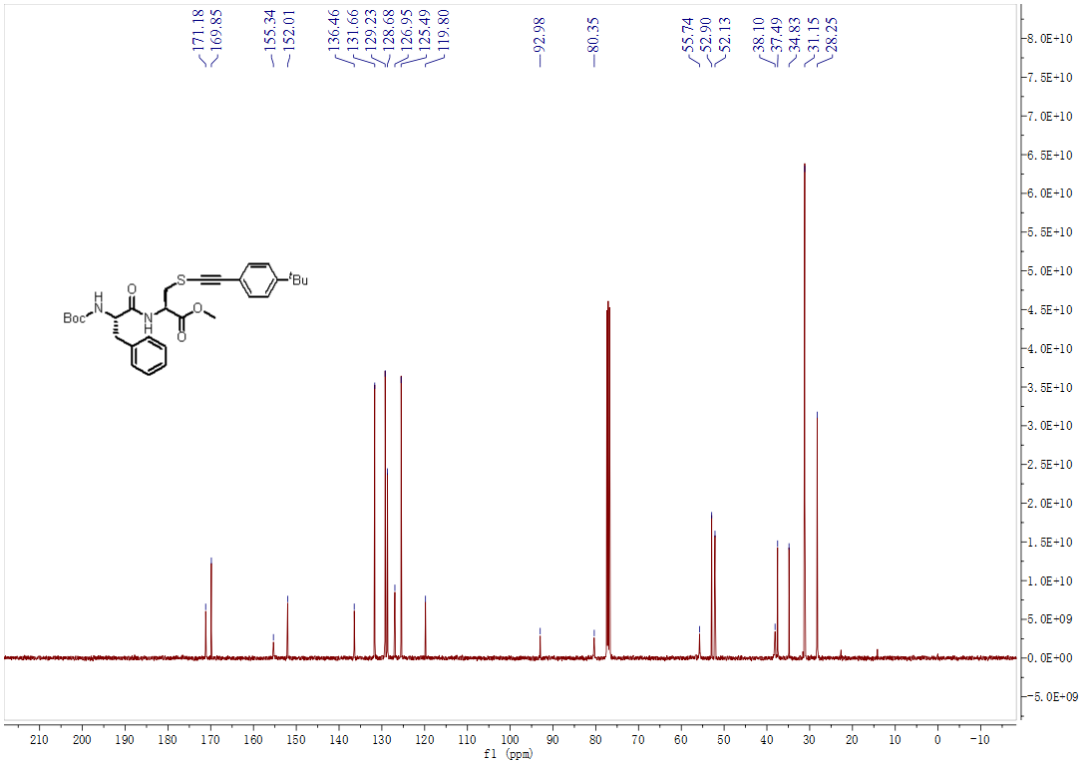
^{1}H NMR of **3bf** (400 MHz, $CDCl_3$)



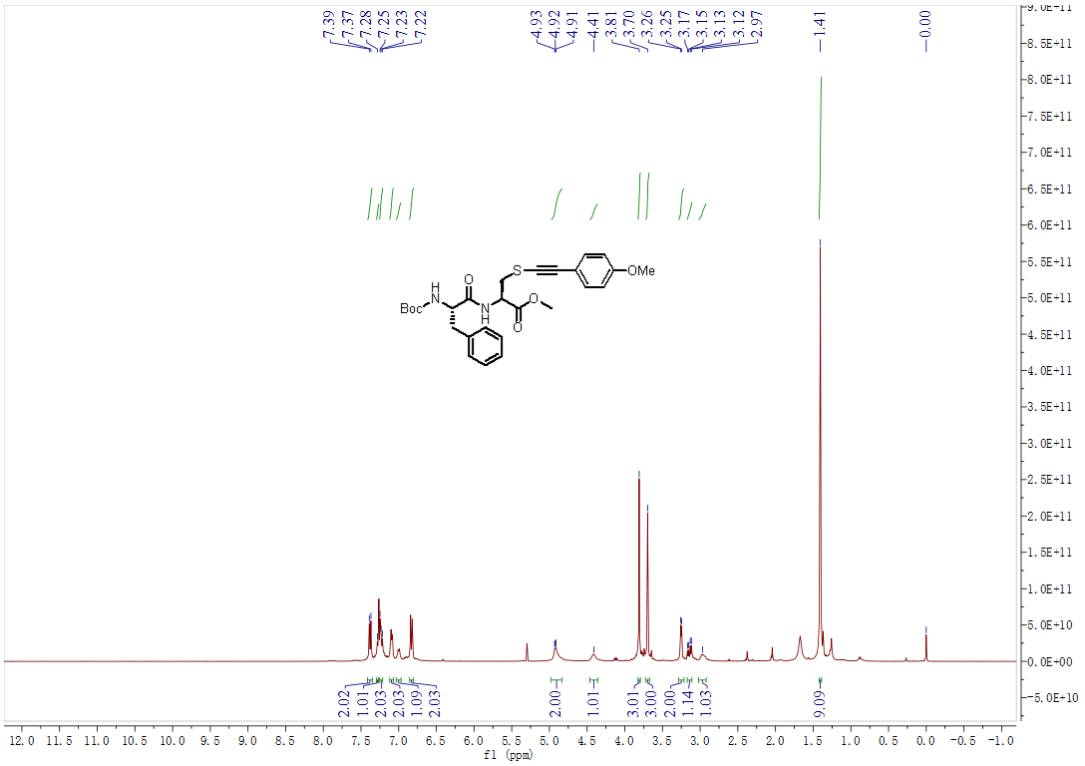
^{13}C NMR of **3bf** (100 MHz, $CDCl_3$)



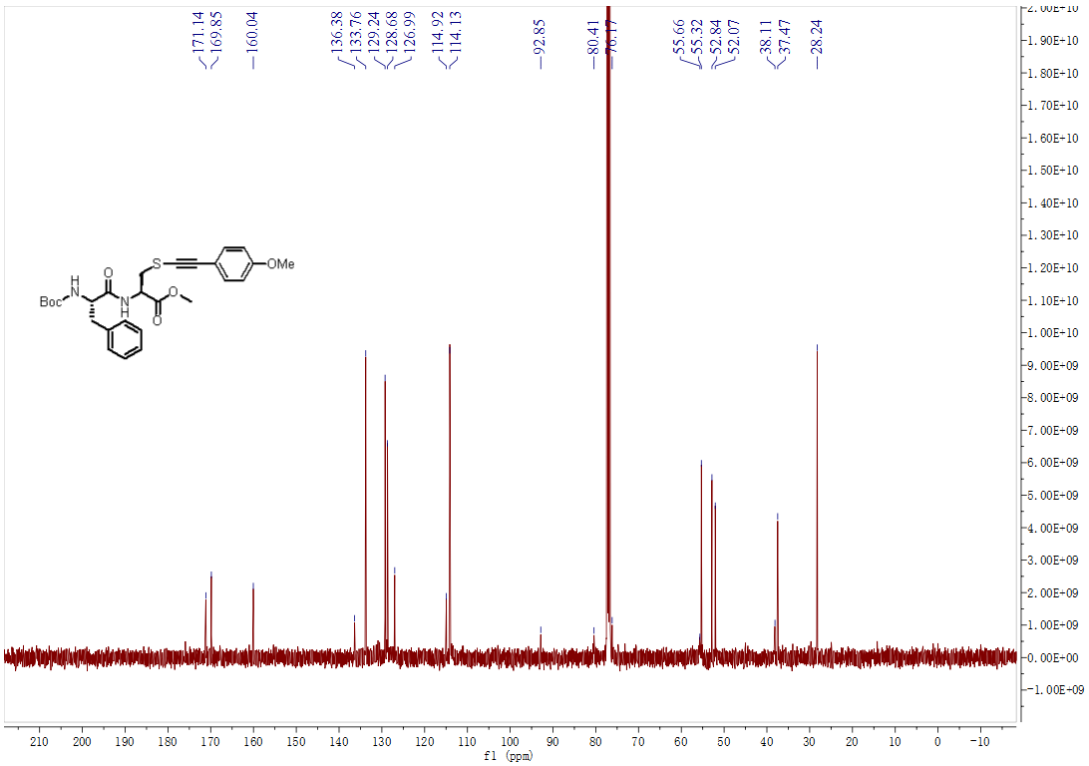
^{1}H NMR of **3bg** (400 MHz, $CDCl_3$)



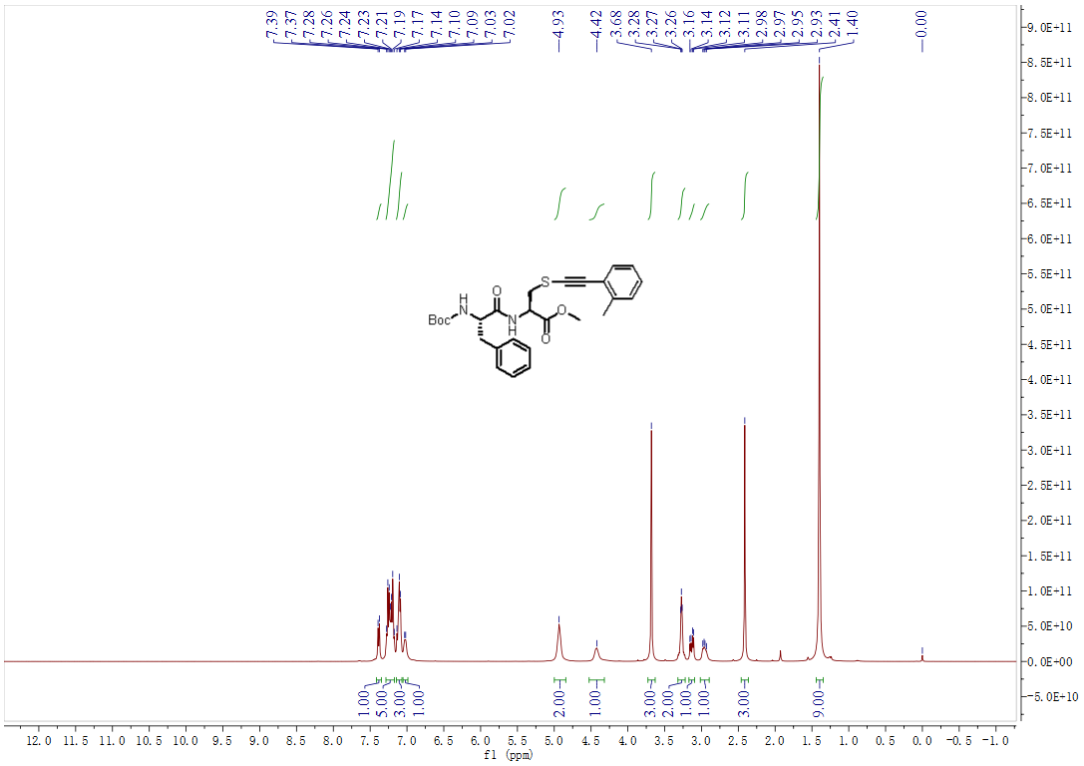
^{13}C NMR of **3bg** (100 MHz, $CDCl_3$)



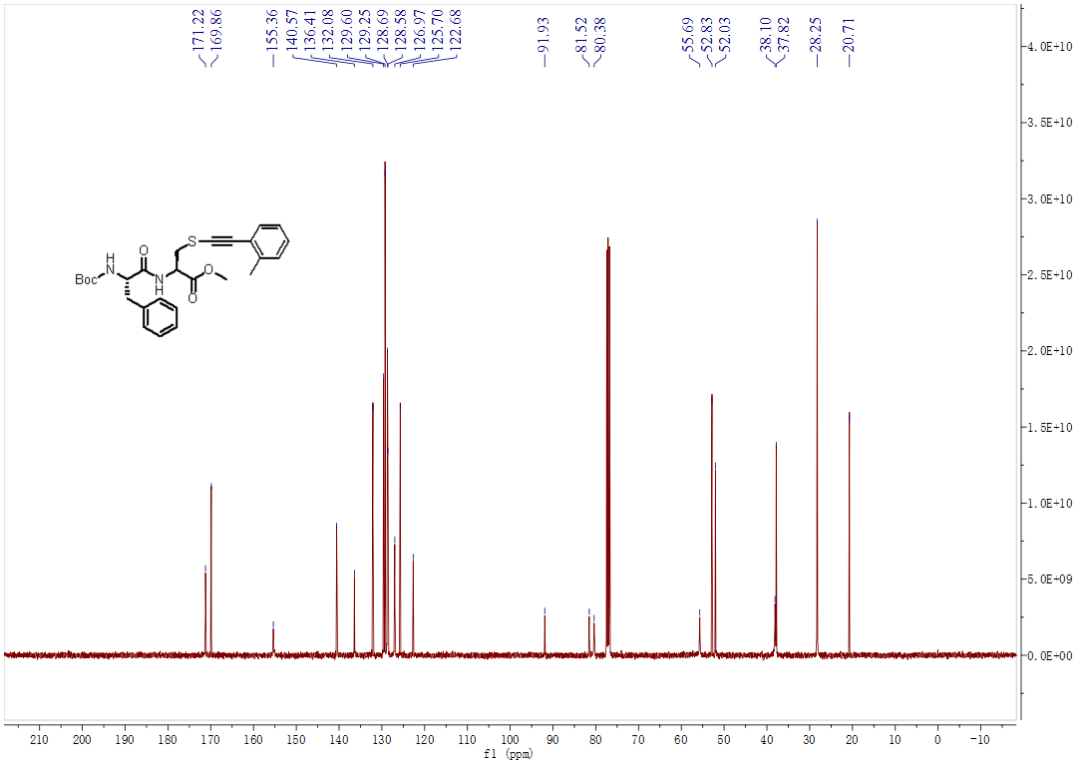
^{1}H NMR of **3bh** (400 MHz, $CDCl_3$)



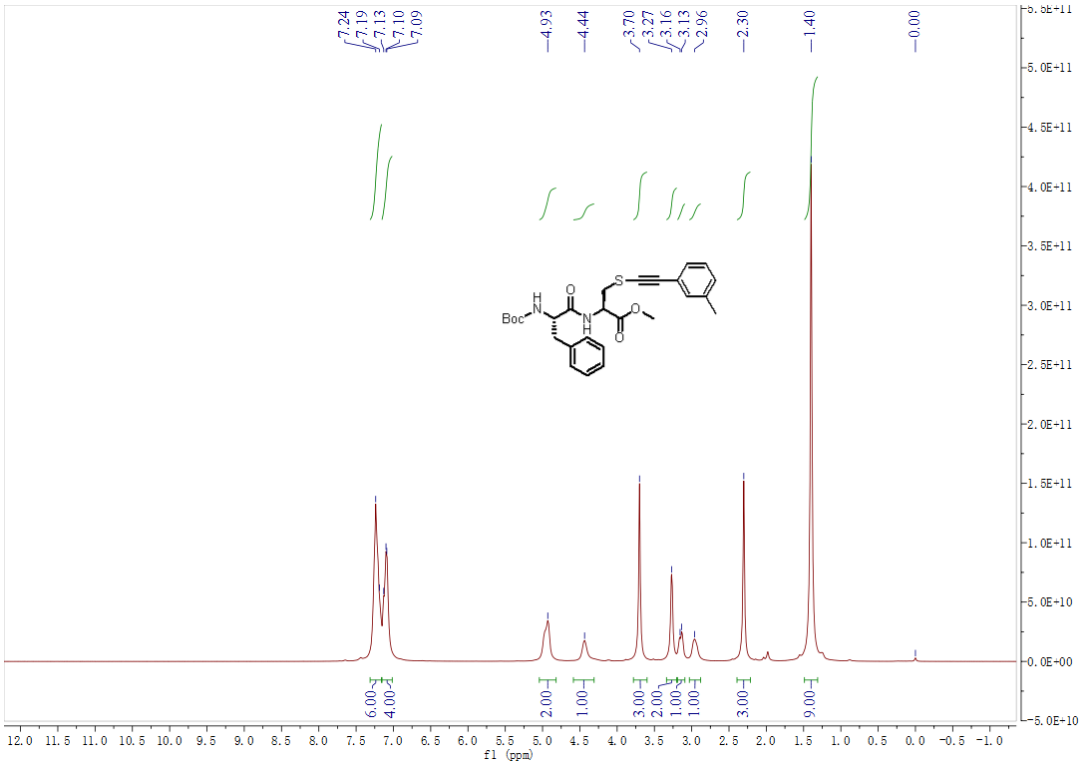
^{13}C NMR of **3bh** (100 MHz, $CDCl_3$)



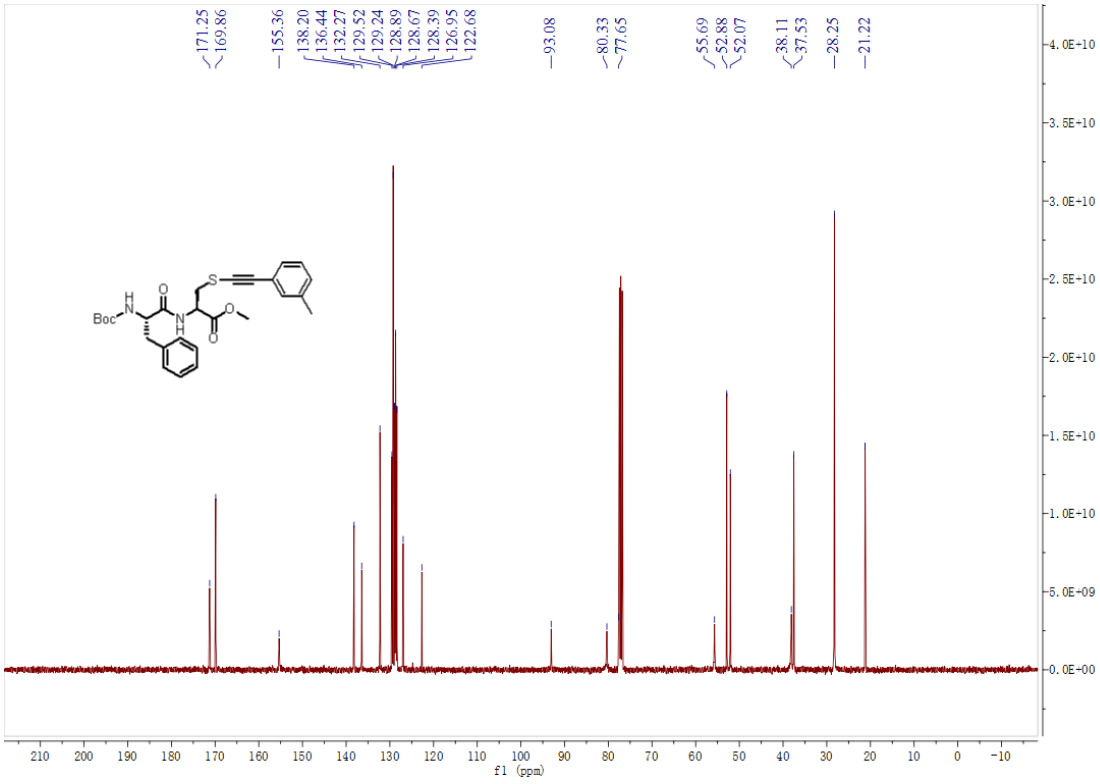
^{1}H NMR of **3bi** (400 MHz, $CDCl_3$)



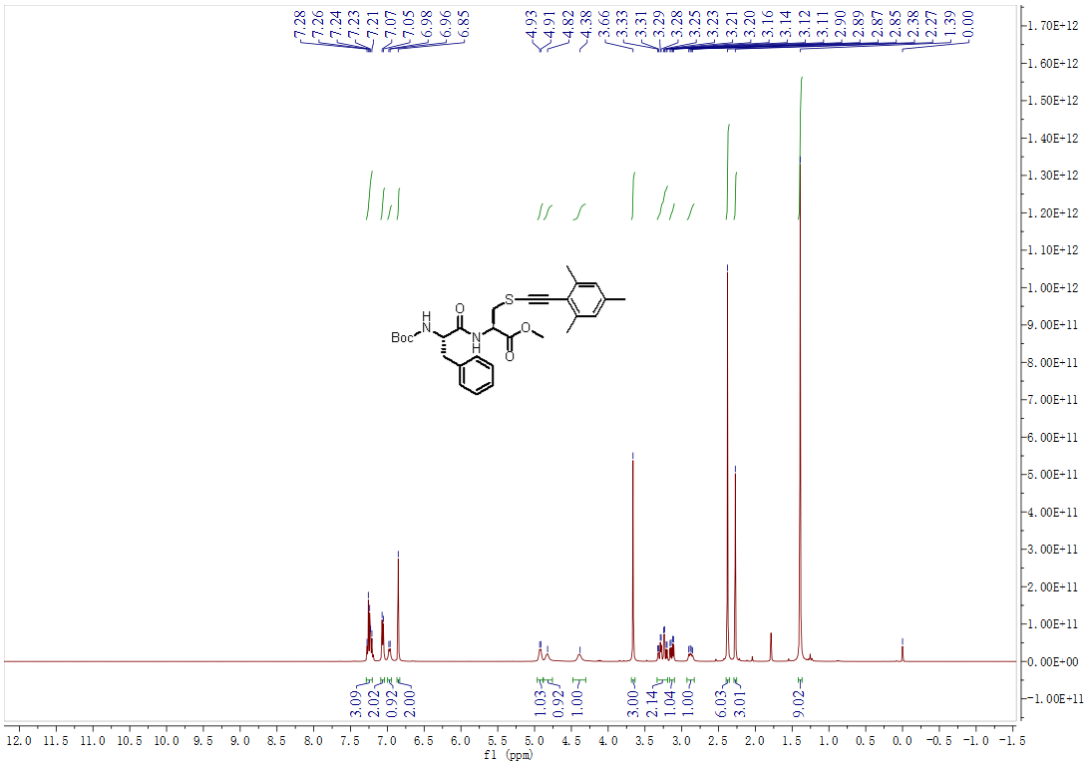
^{13}C NMR of **3bi** (100 MHz, $CDCl_3$)



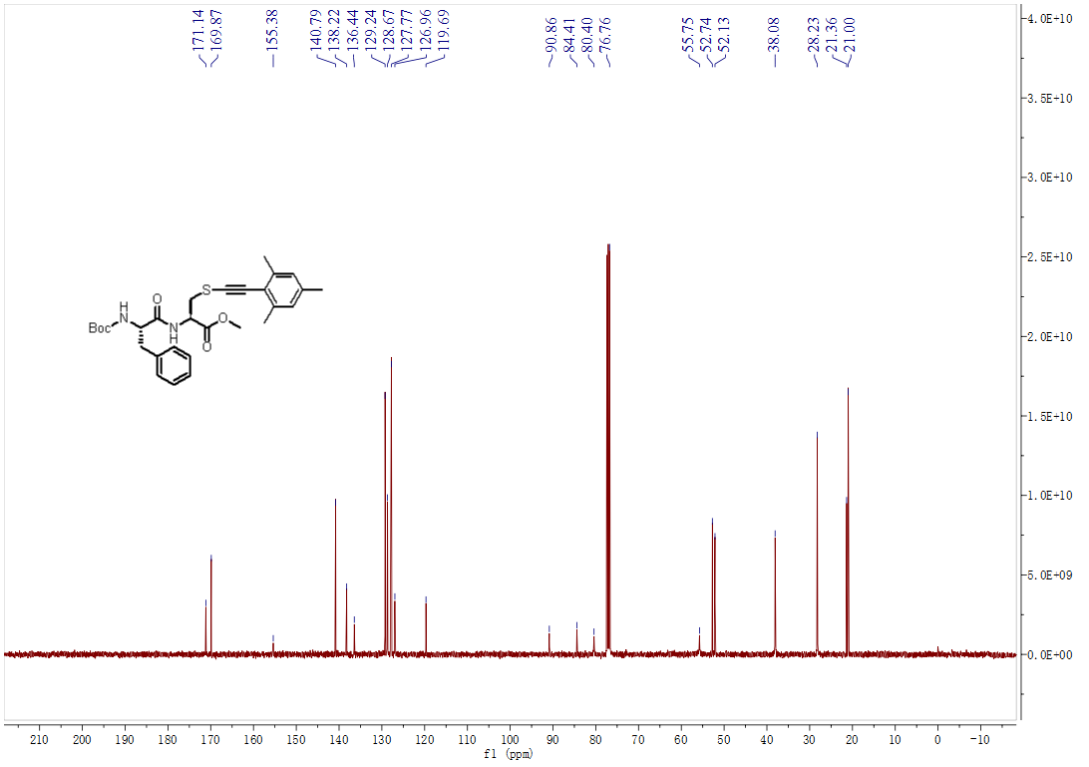
^{1}H NMR of **3bj** (400 MHz, $CDCl_3$)



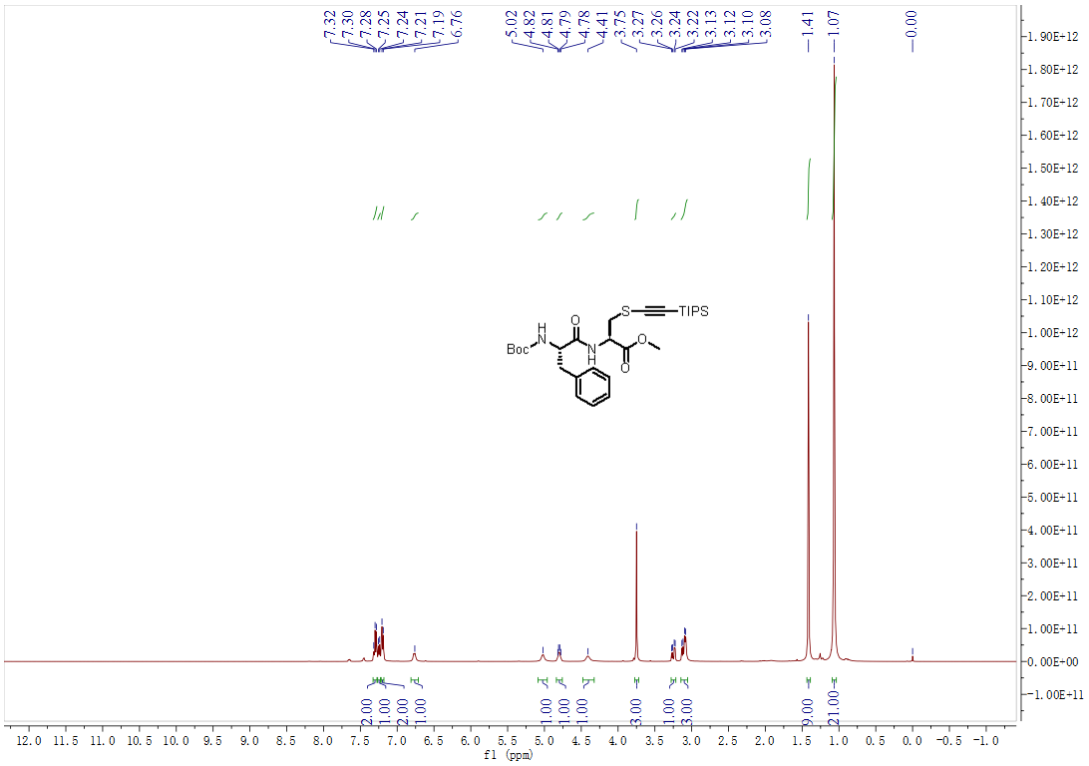
^{13}C NMR of **3bj** (100 MHz, $CDCl_3$)



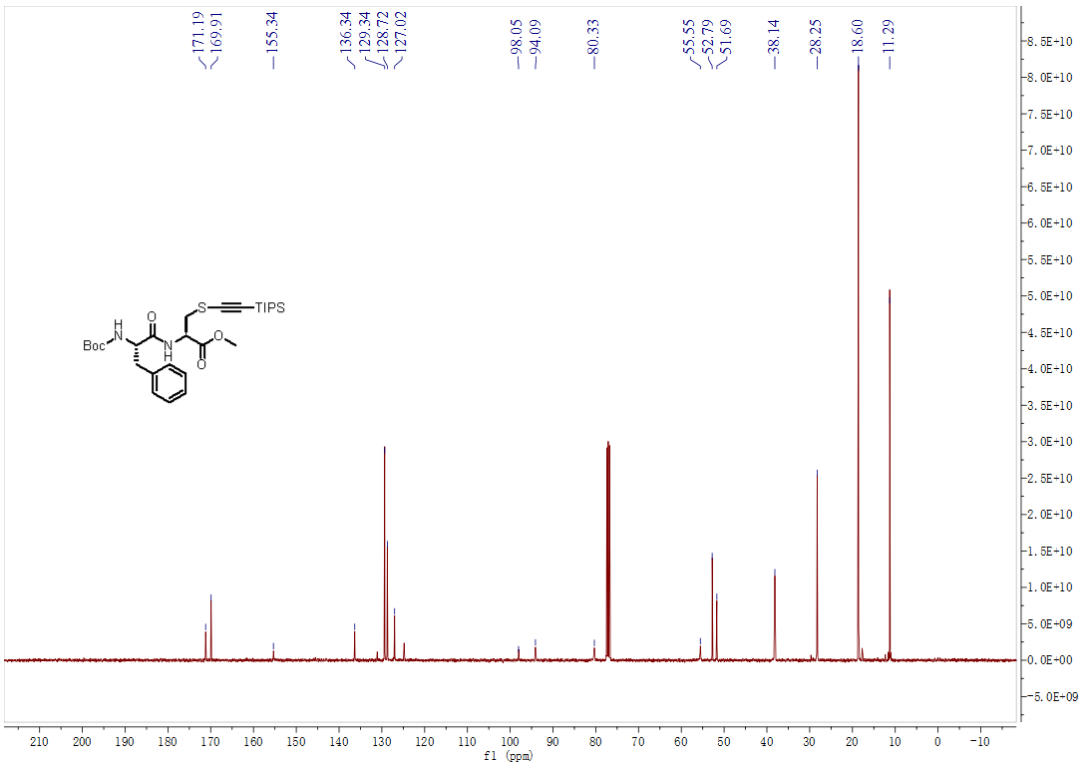
^{1}H NMR of **3bk** (400 MHz, $CDCl_3$)



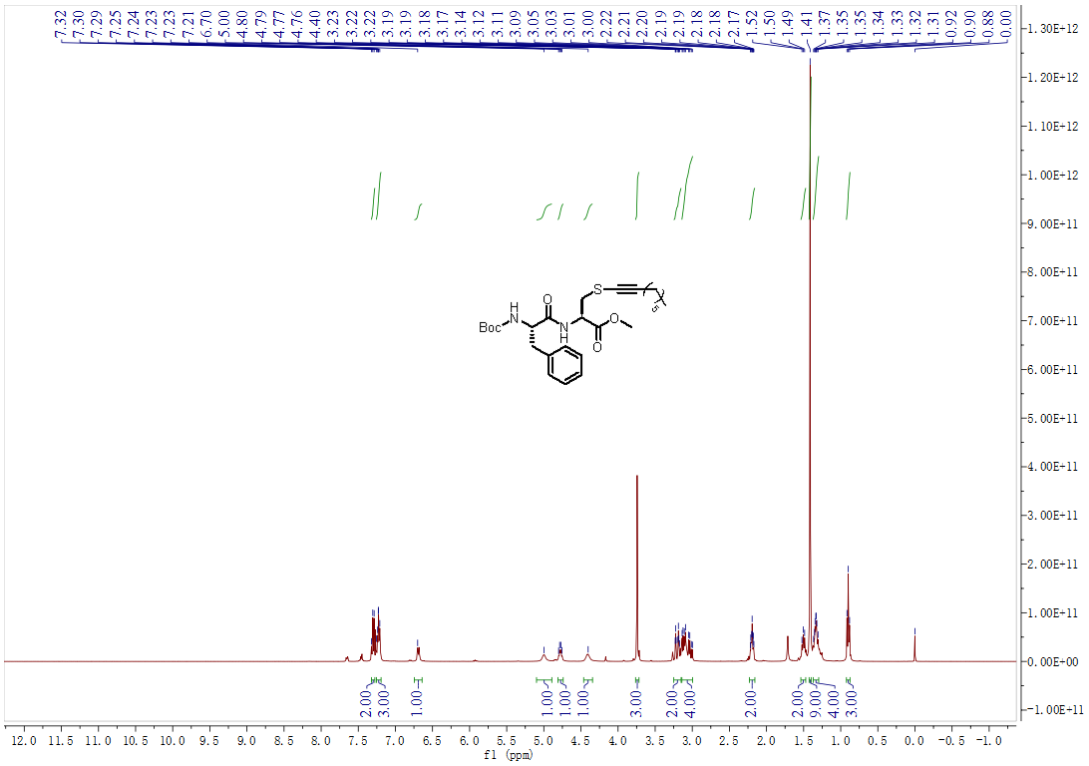
^{13}C NMR of **3bk** (100 MHz, $CDCl_3$)



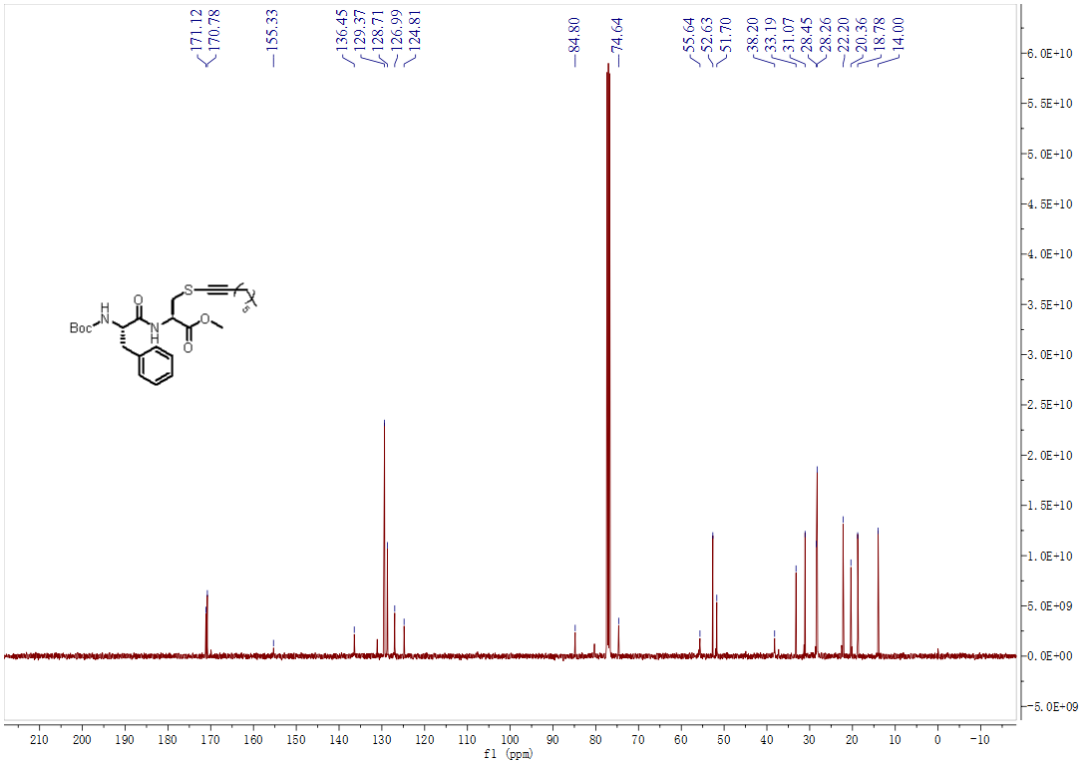
^{1}H NMR of **3bl** (400 MHz, $CDCl_3$)



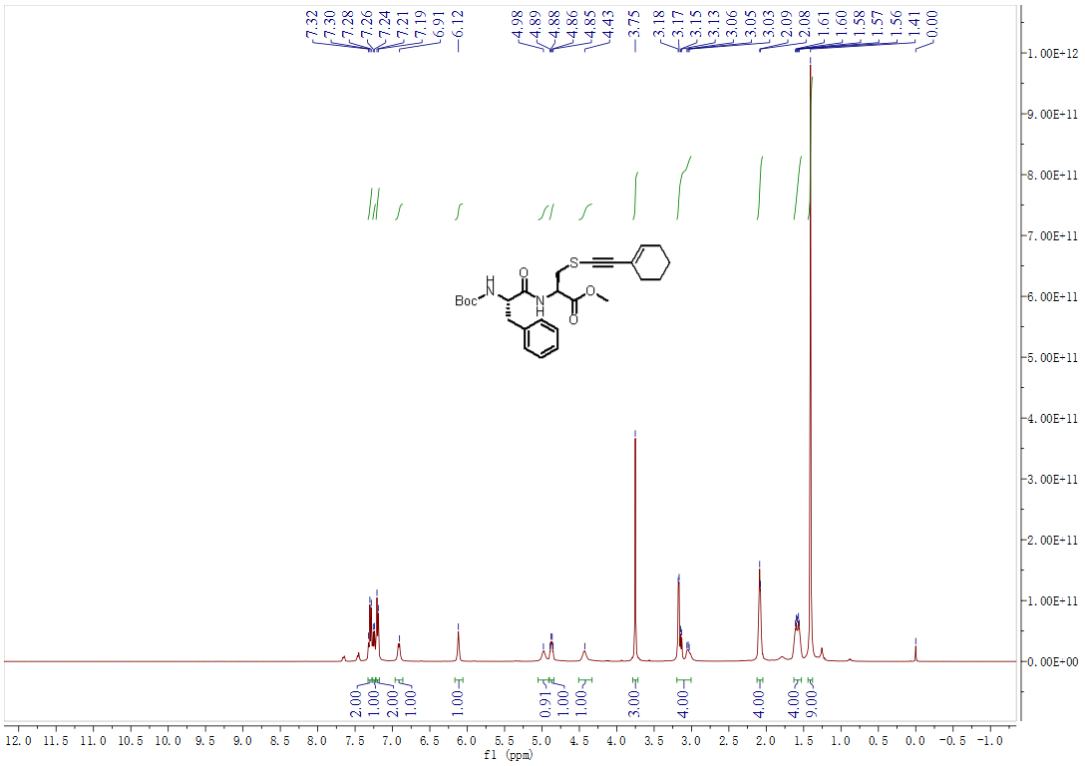
^{13}C NMR of **3bl** (100 MHz, $CDCl_3$)



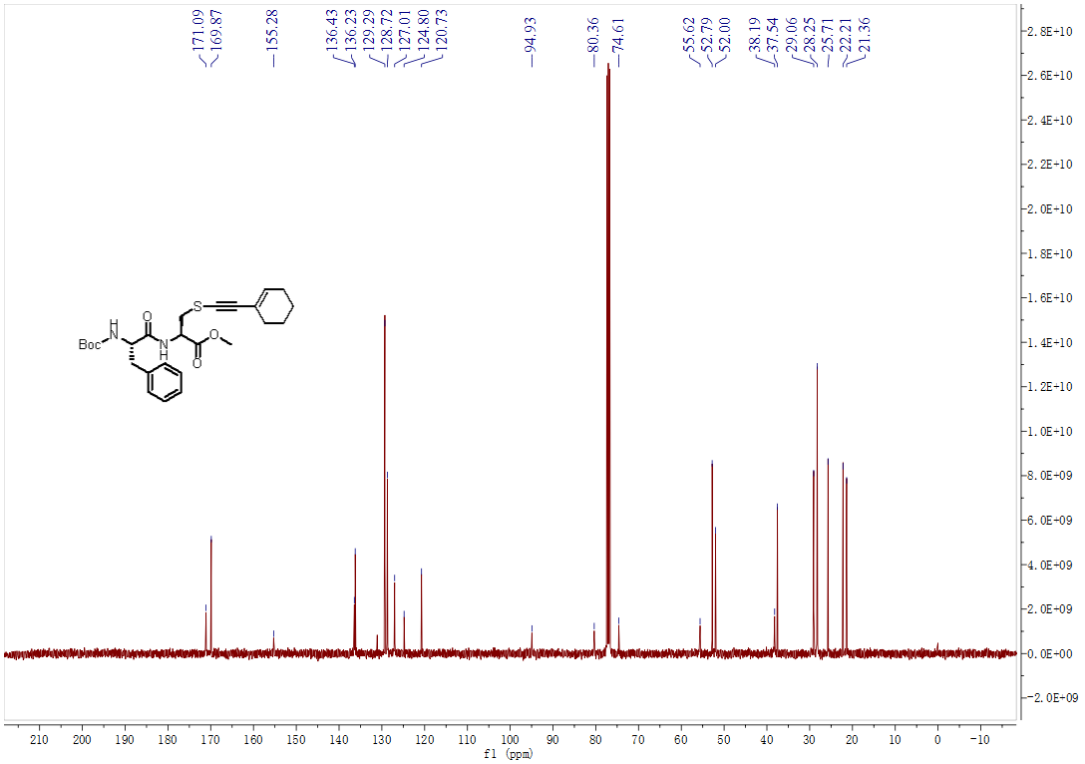
^{1}H NMR of **3bm** (400 MHz, $CDCl_3$)



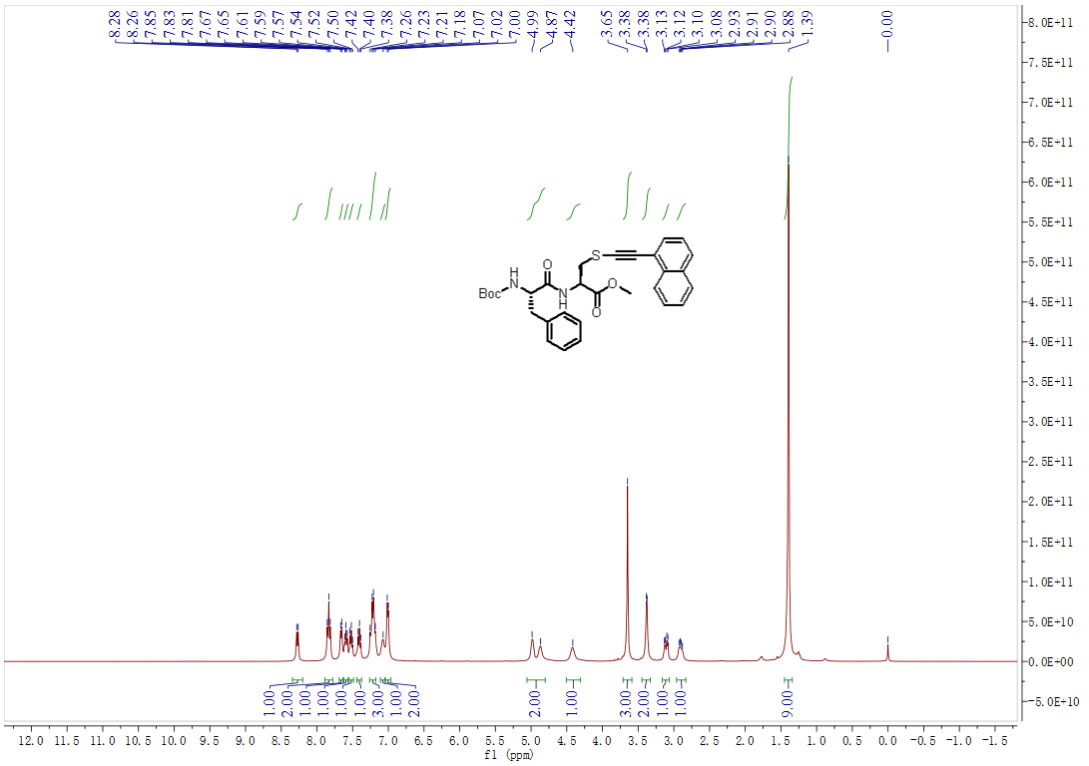
^{13}C NMR of **3bm** (100 MHz, $CDCl_3$)



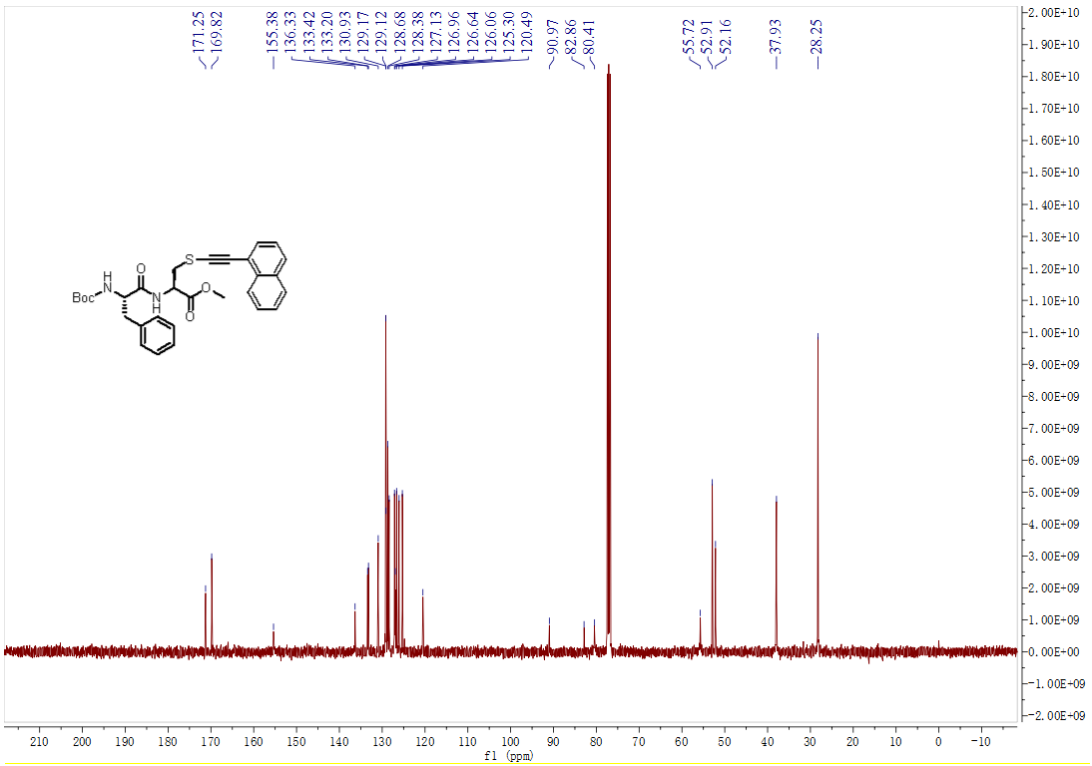
^{1}H NMR of **3bn** (400 MHz, $CDCl_3$)



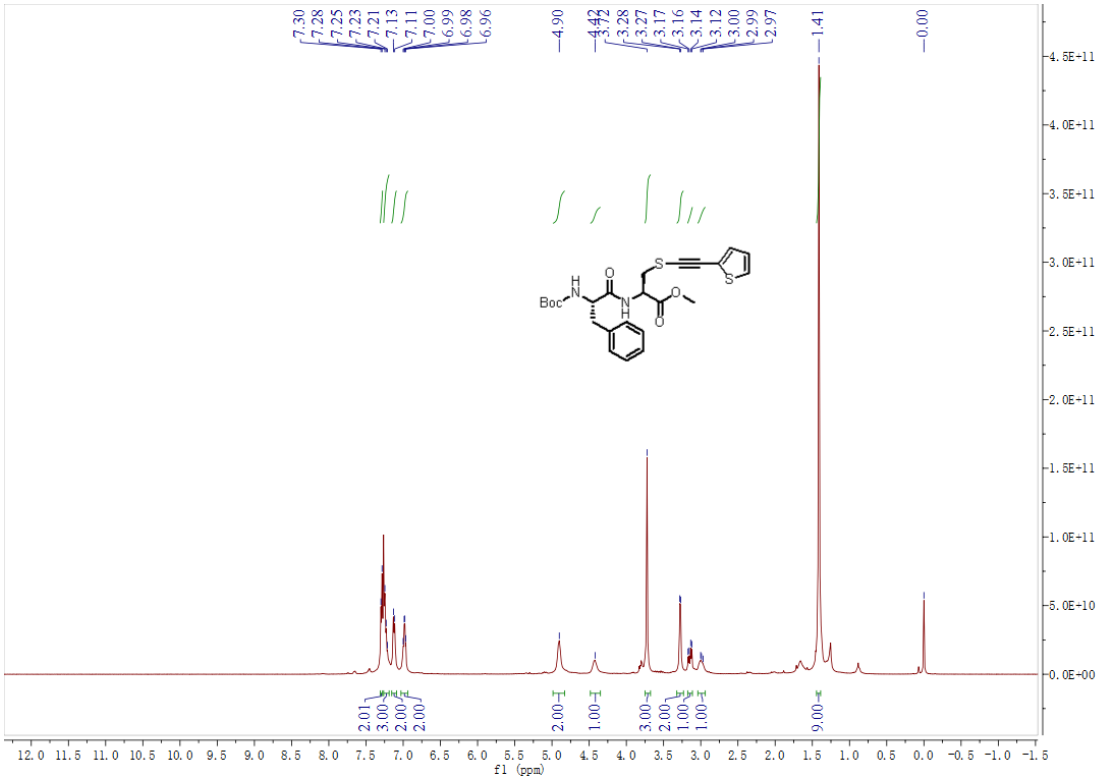
^{13}C NMR of **3bn** (100 MHz, $CDCl_3$)



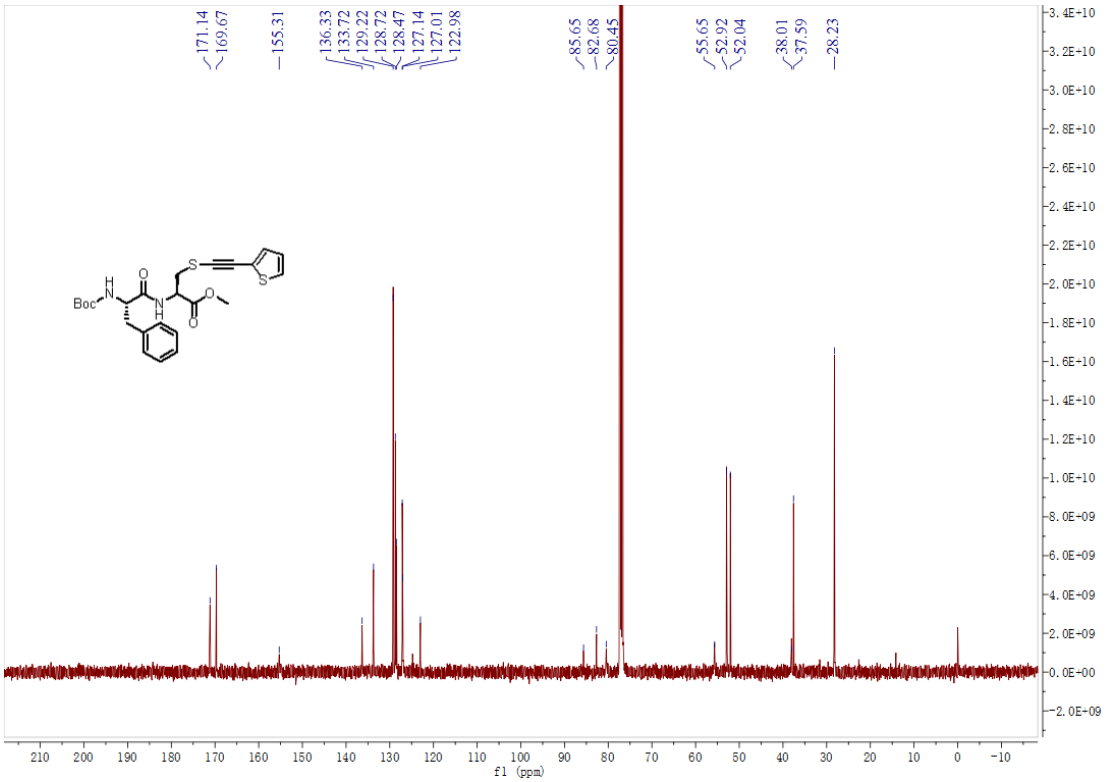
^{1}H NMR of **3bo** (400 MHz, $CDCl_3$)



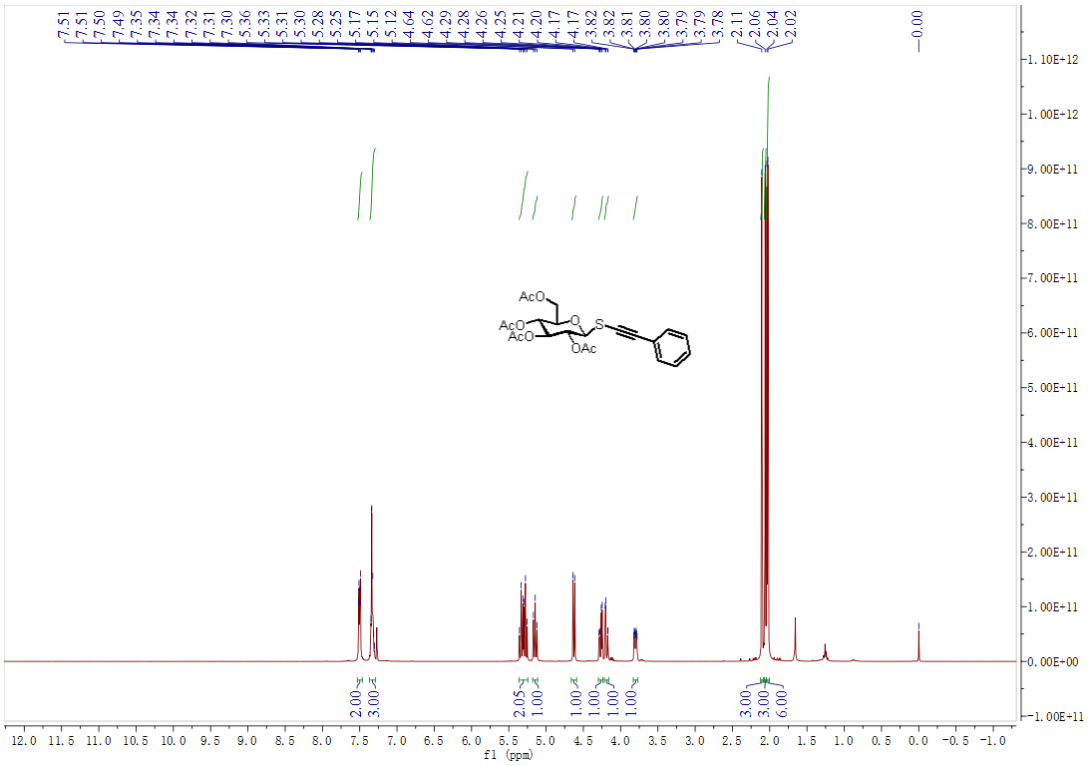
^{13}C NMR of **3bo** (100 MHz, $CDCl_3$)



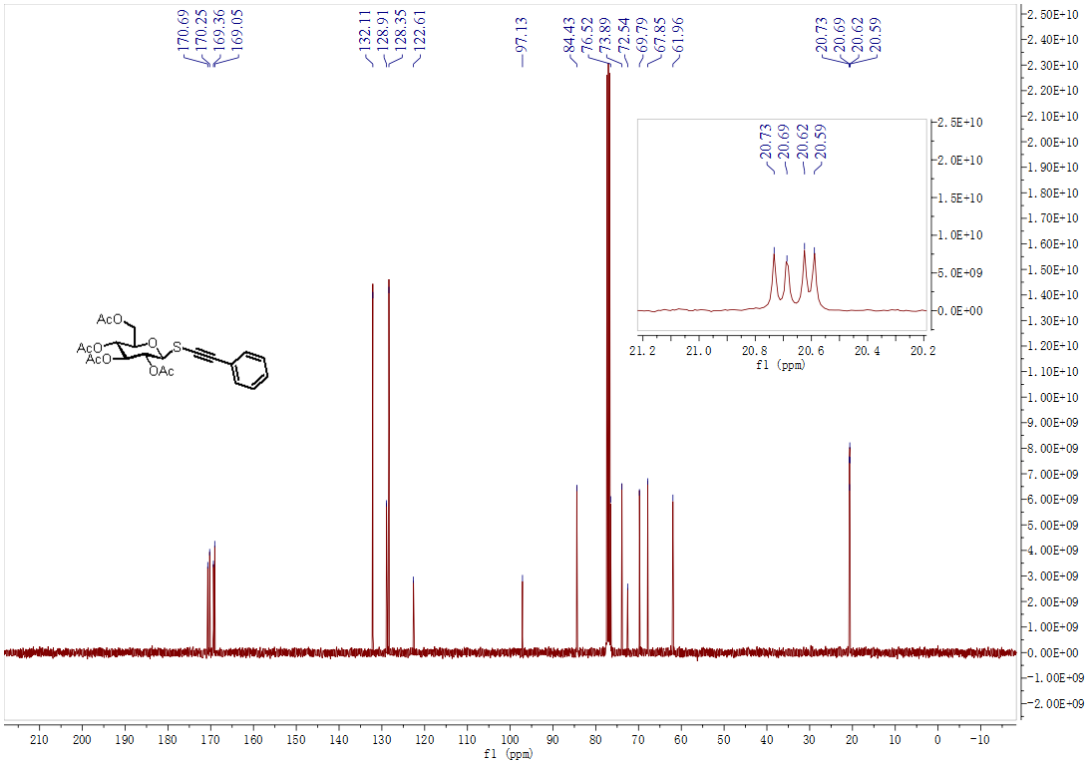
^{1}H NMR of **3bp** (400 MHz, $CDCl_3$)



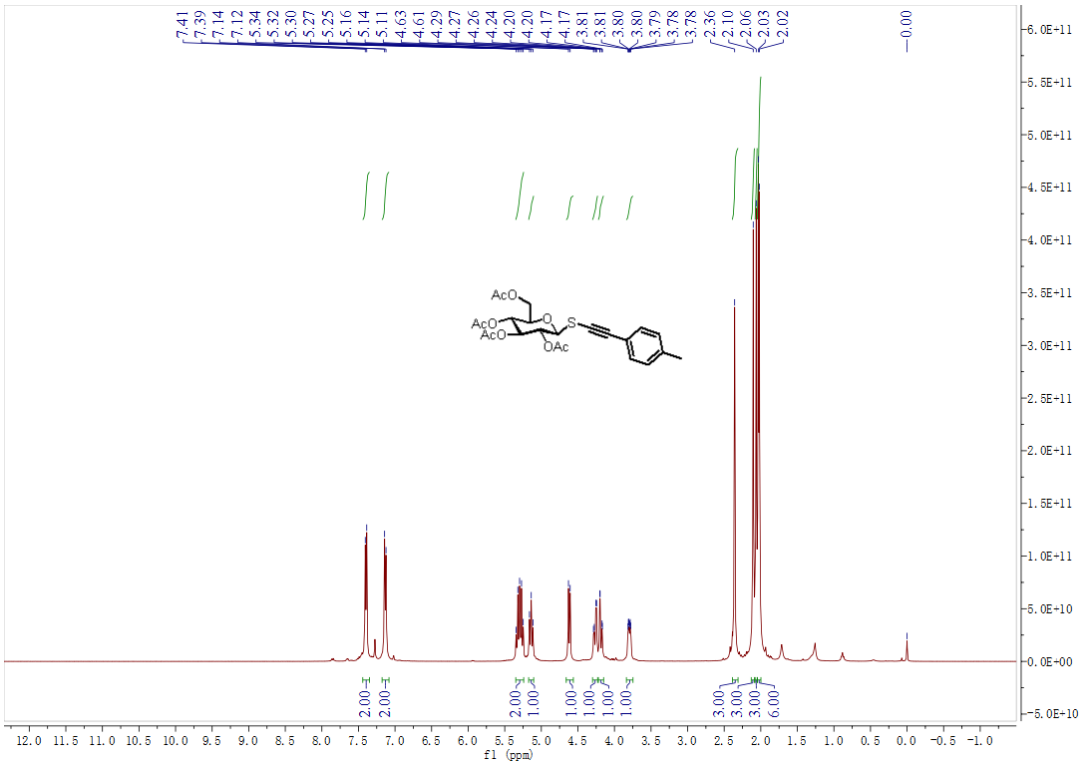
^{13}C NMR of **3bp** (100 MHz, $CDCl_3$)



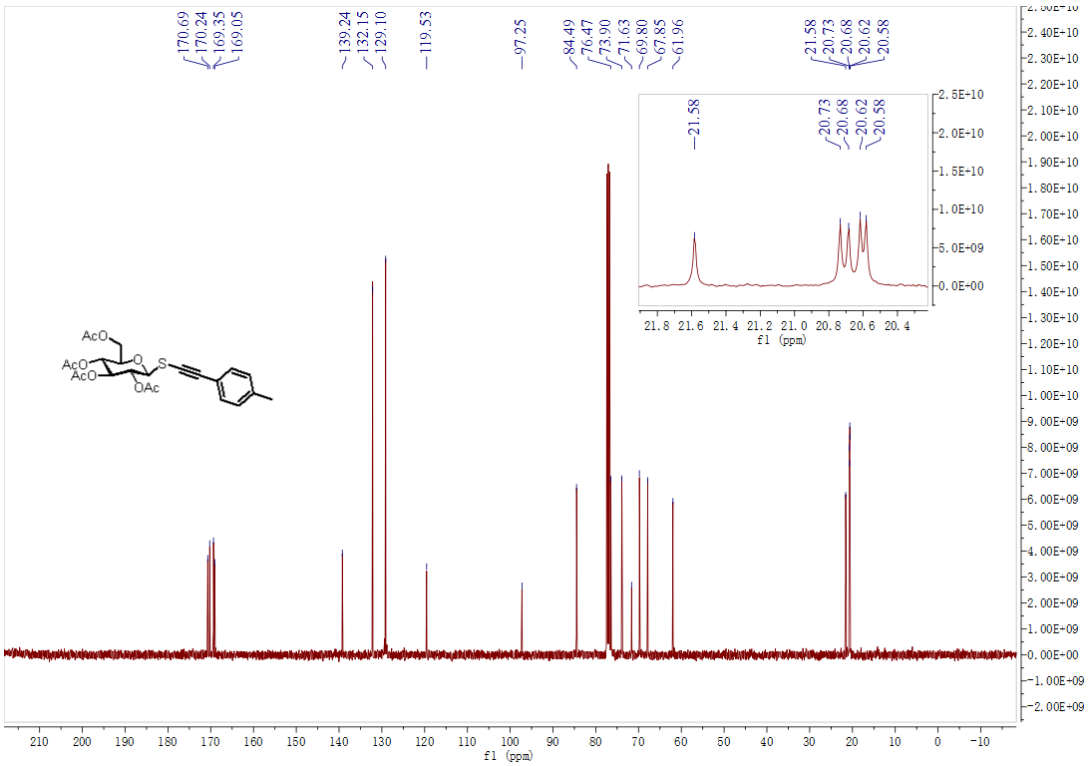
^{1}H NMR of **5a** (400 MHz, $CDCl_3$)



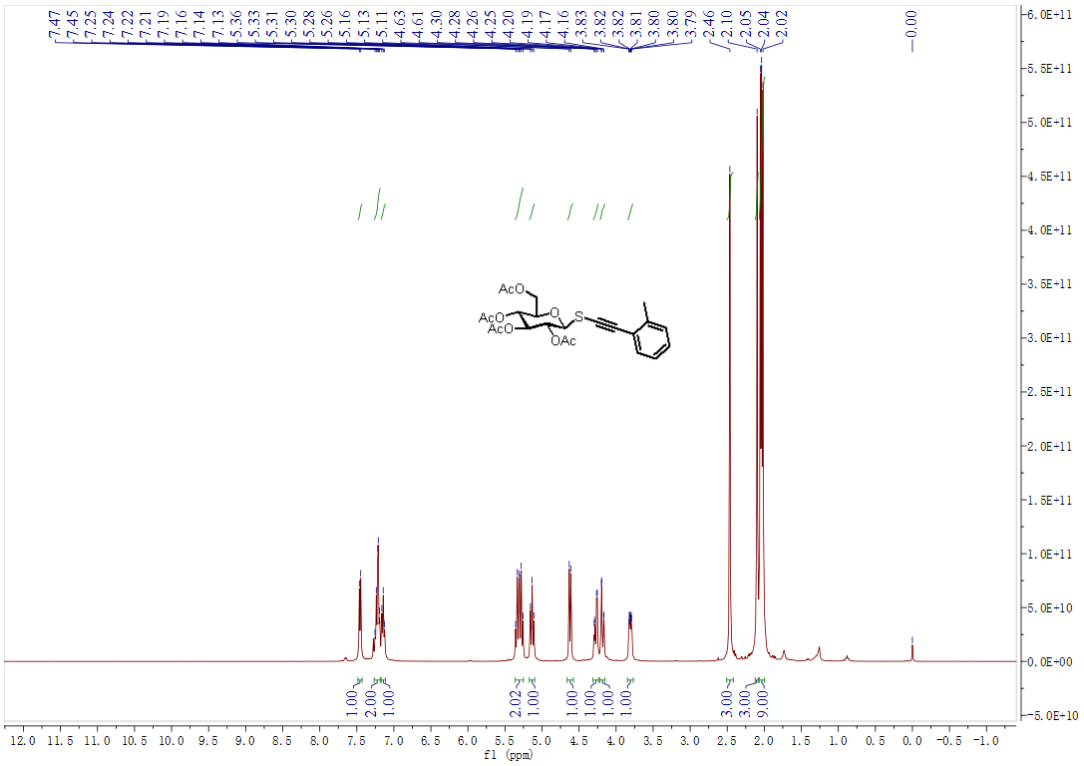
^{13}C NMR of **5a** (100 MHz, $CDCl_3$)



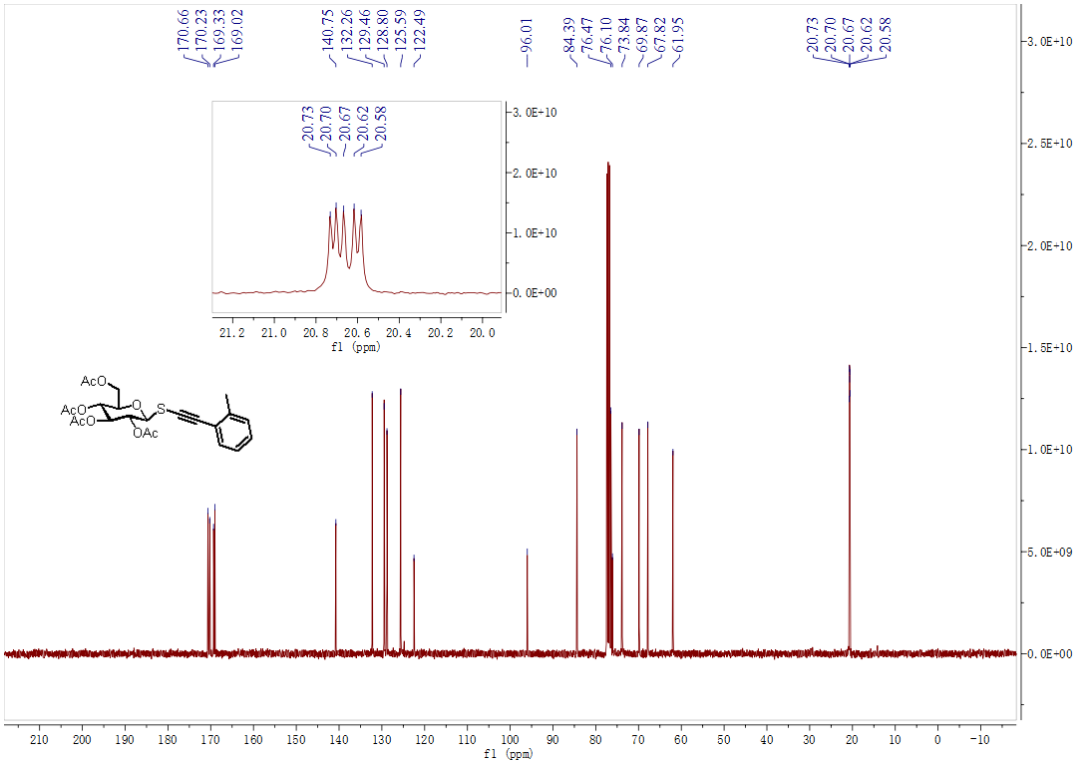
^{1}H NMR of **5b** (400 MHz, $CDCl_3$)



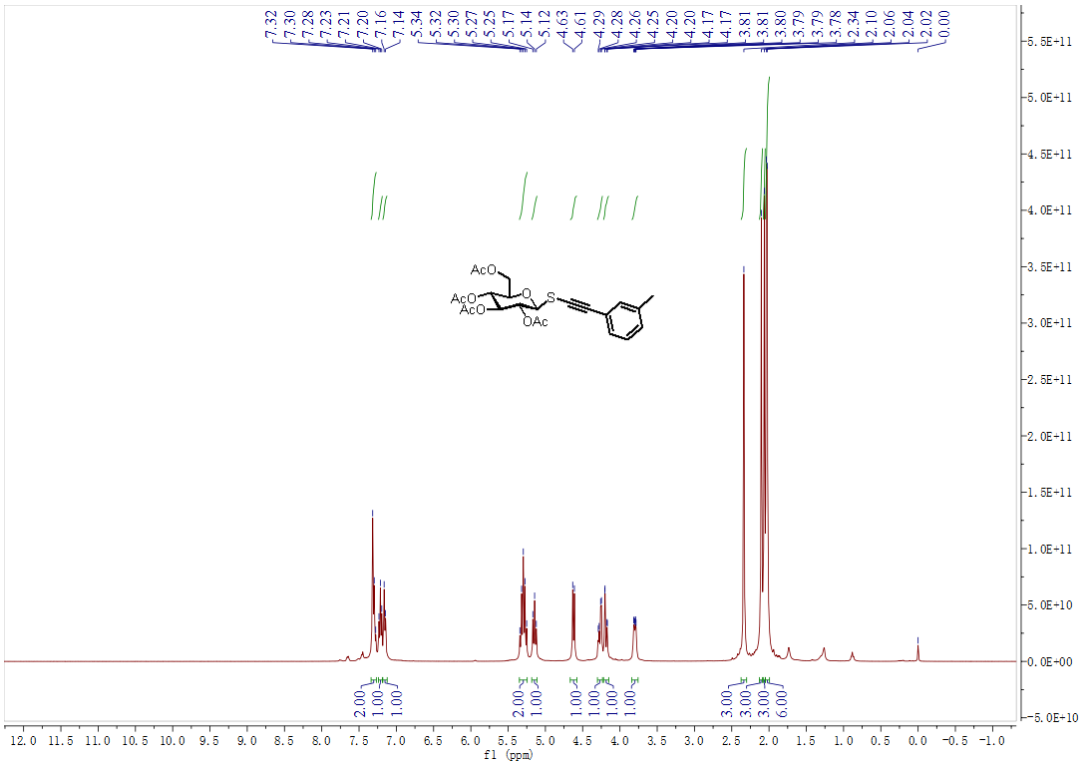
^{13}C NMR of **5b** (100 MHz, $CDCl_3$)



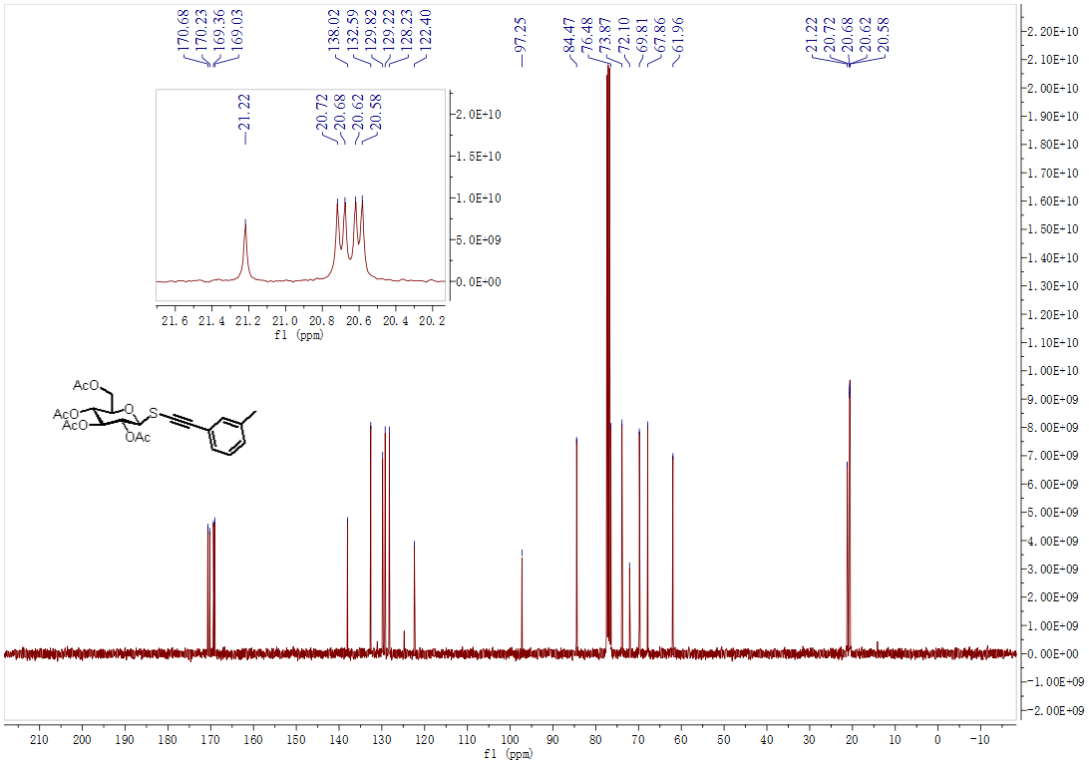
^{1}H NMR of **5c** (400 MHz, $CDCl_3$)



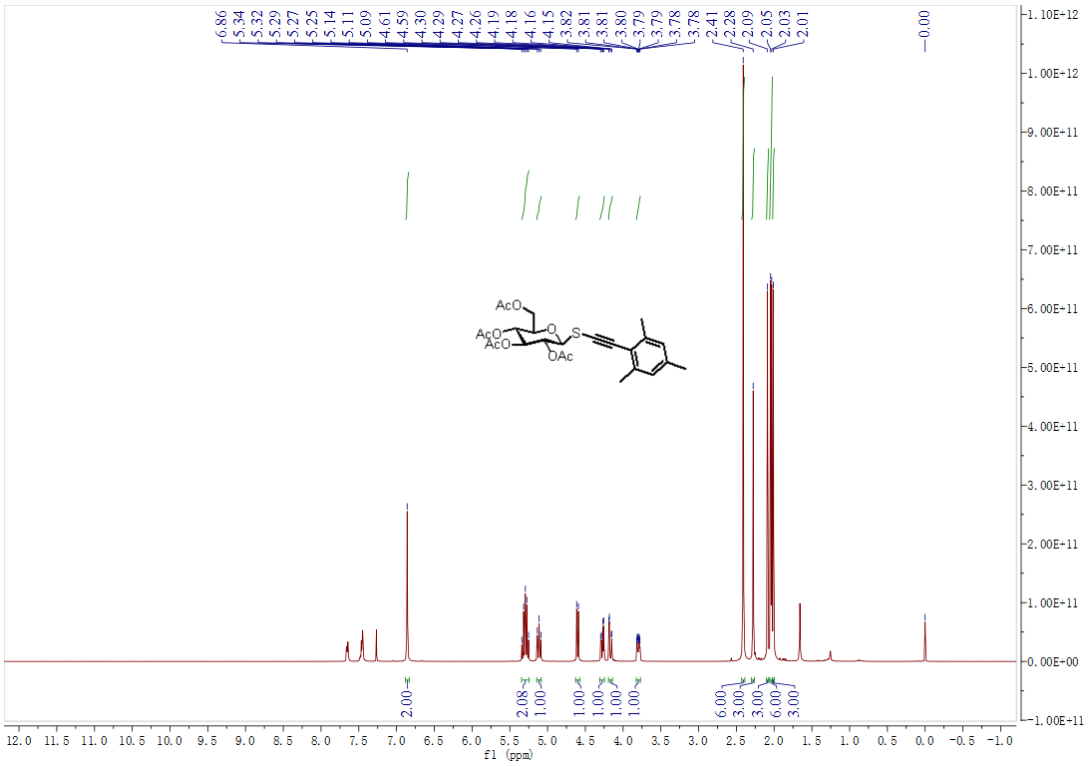
^{13}C NMR of **5c** (100 MHz, $CDCl_3$)



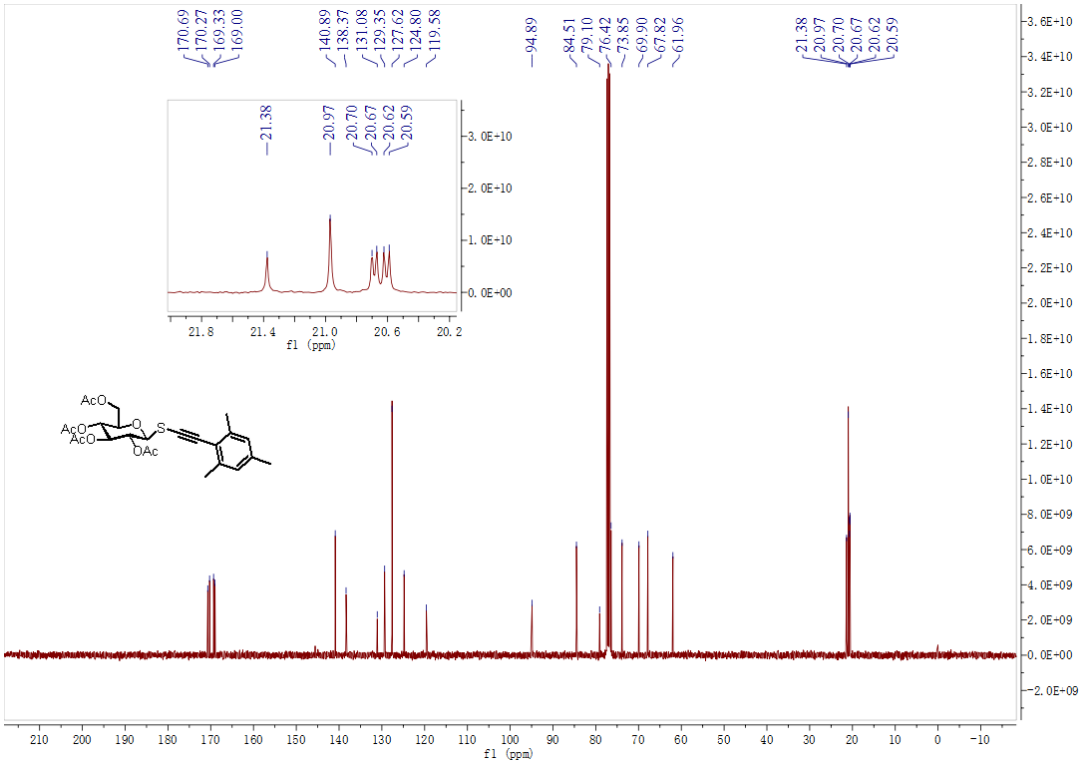
^{1}H NMR of **5d** (400 MHz, $CDCl_3$)



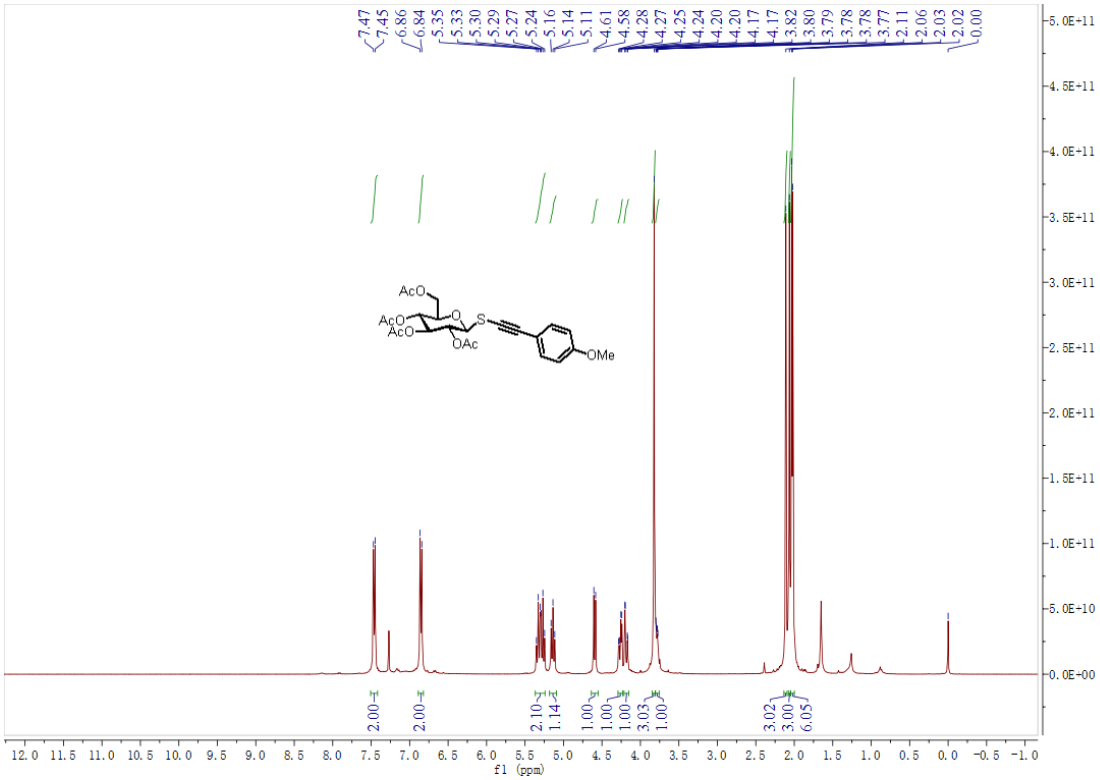
^{13}C NMR of **5d** (100 MHz, $CDCl_3$)



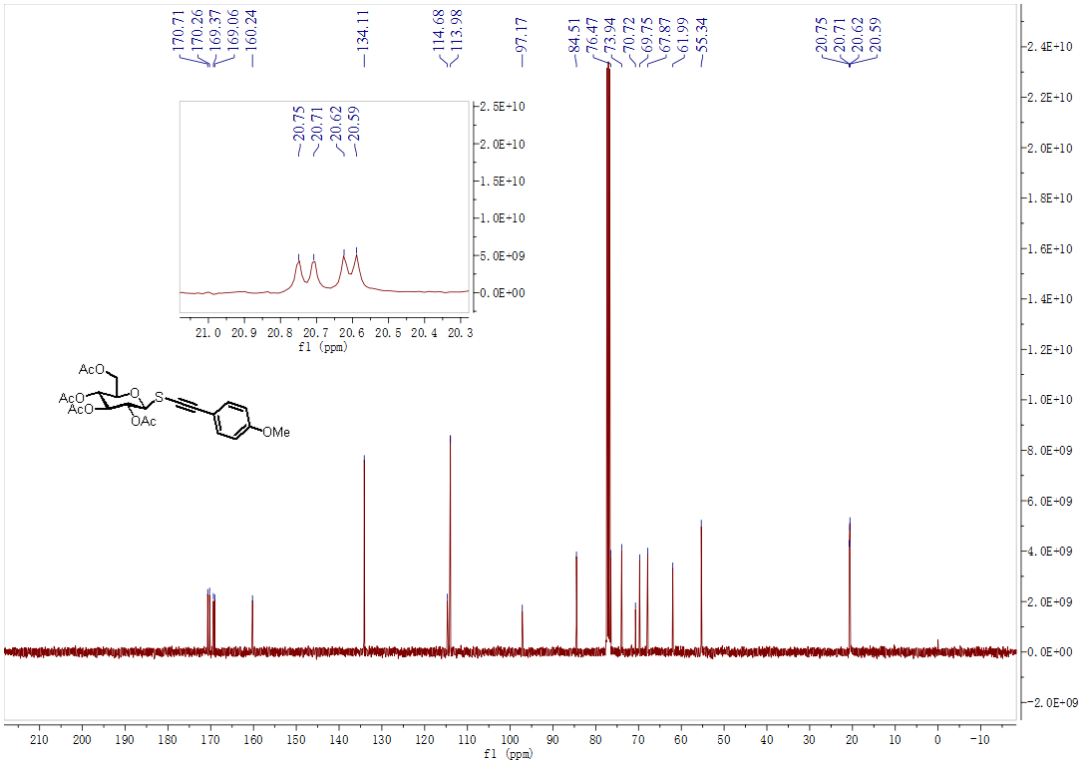
^{1}H NMR of **5e** (400 MHz, $CDCl_3$)



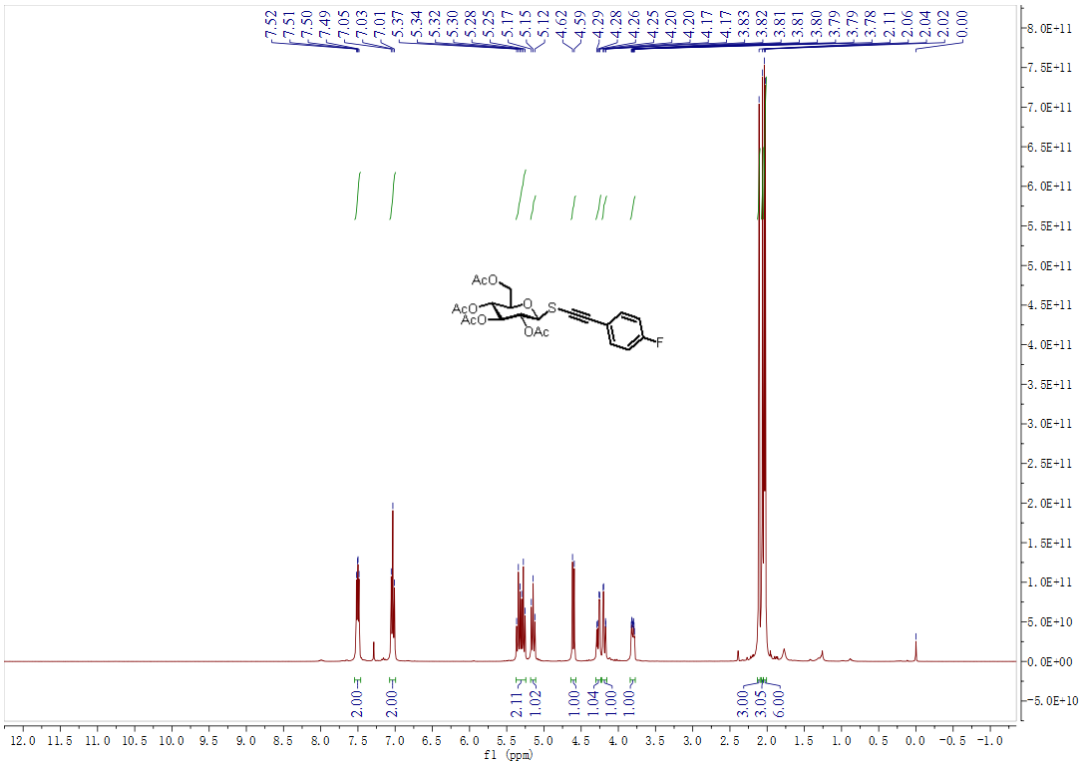
^{13}C NMR of **5e** (100 MHz, $CDCl_3$)



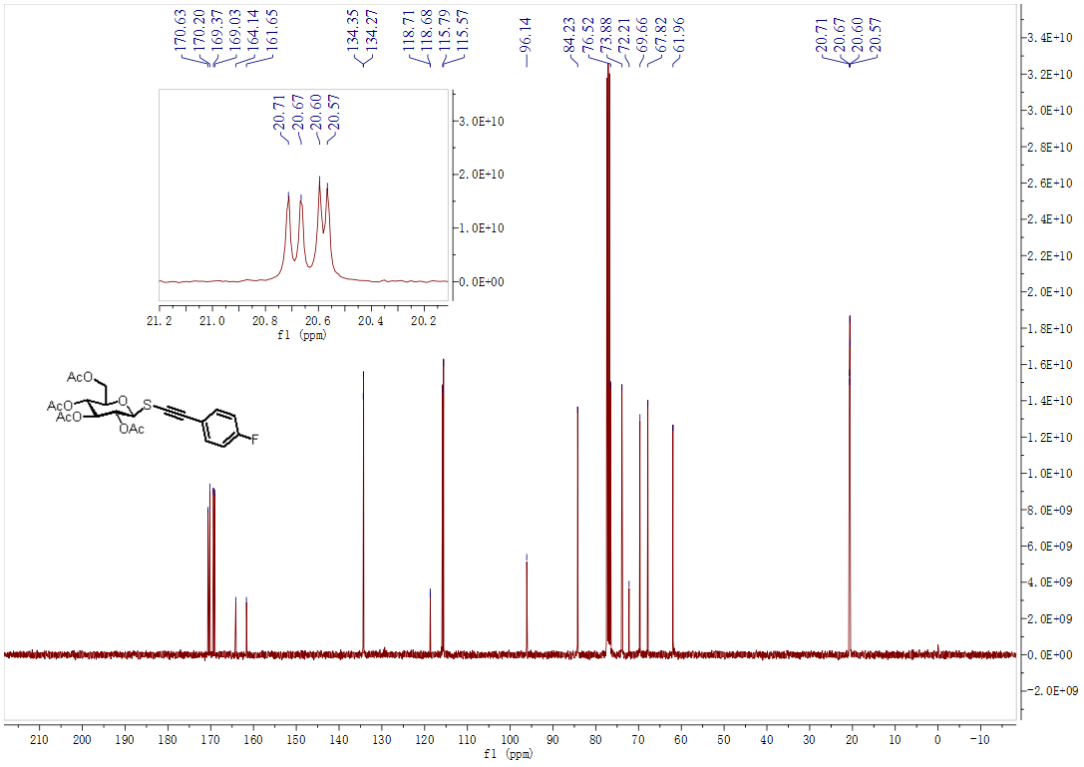
^{1}H NMR of **5f** (400 MHz, $CDCl_3$)



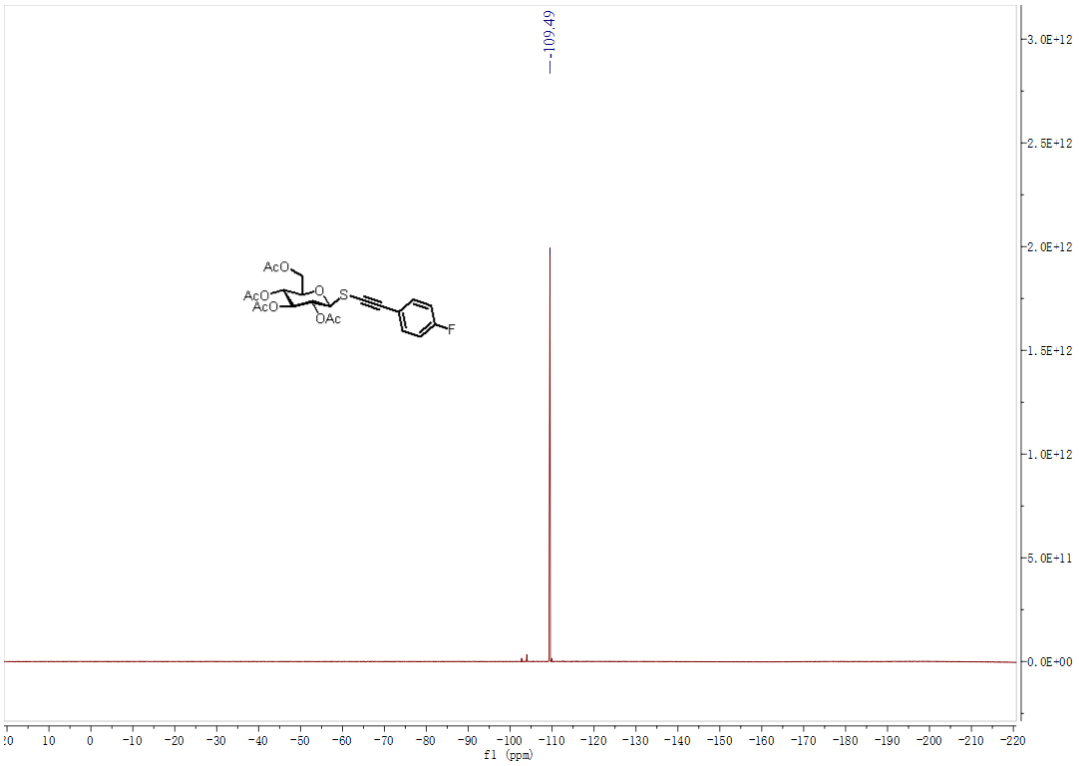
^{13}C NMR of **5f** (100 MHz, $CDCl_3$)



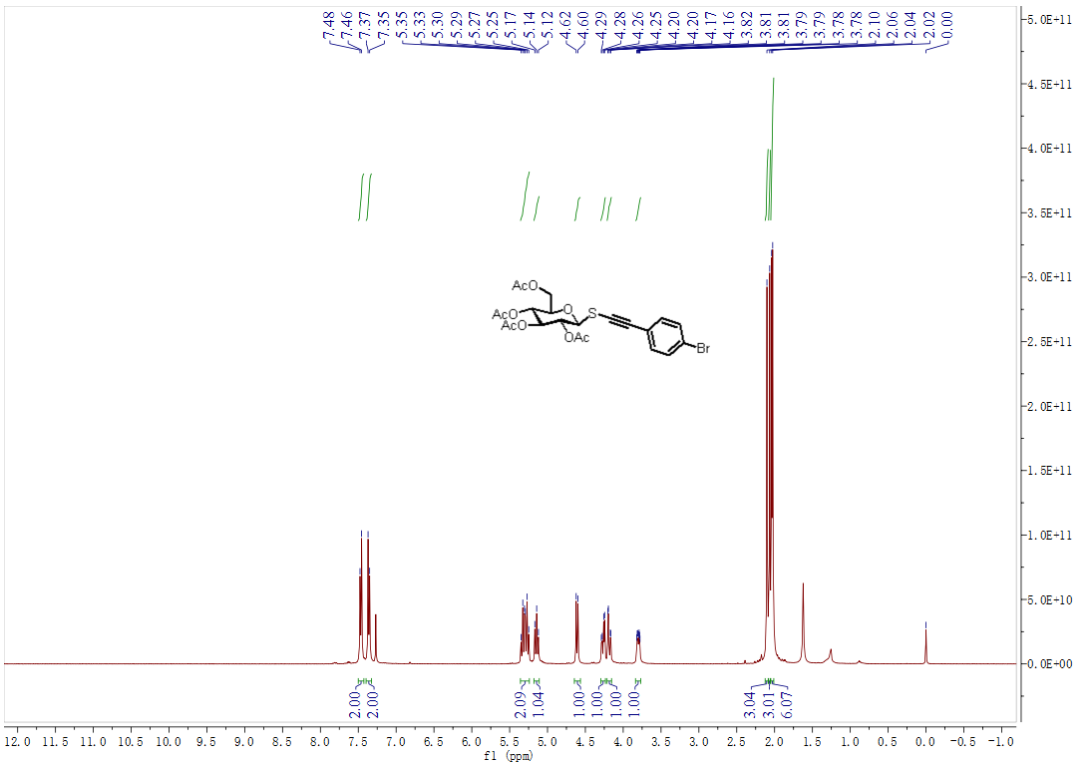
^{1}H NMR of **5g** (400 MHz, $CDCl_3$)



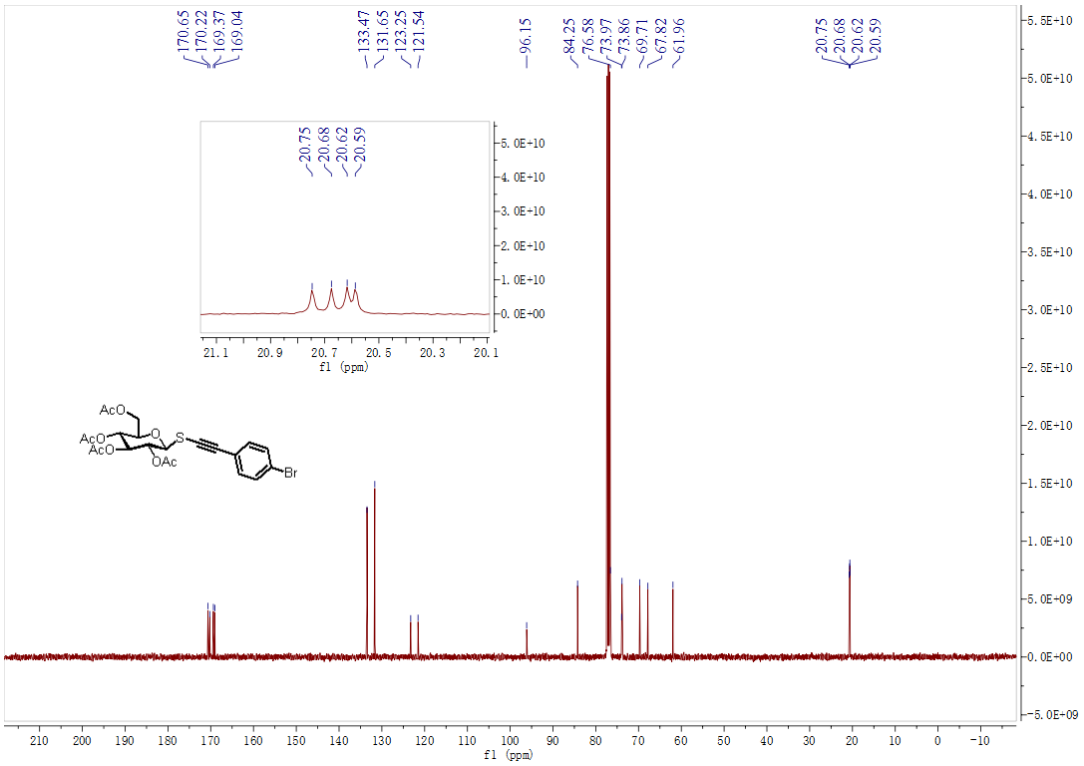
^{13}C NMR of **5g** (100 MHz, $CDCl_3$)



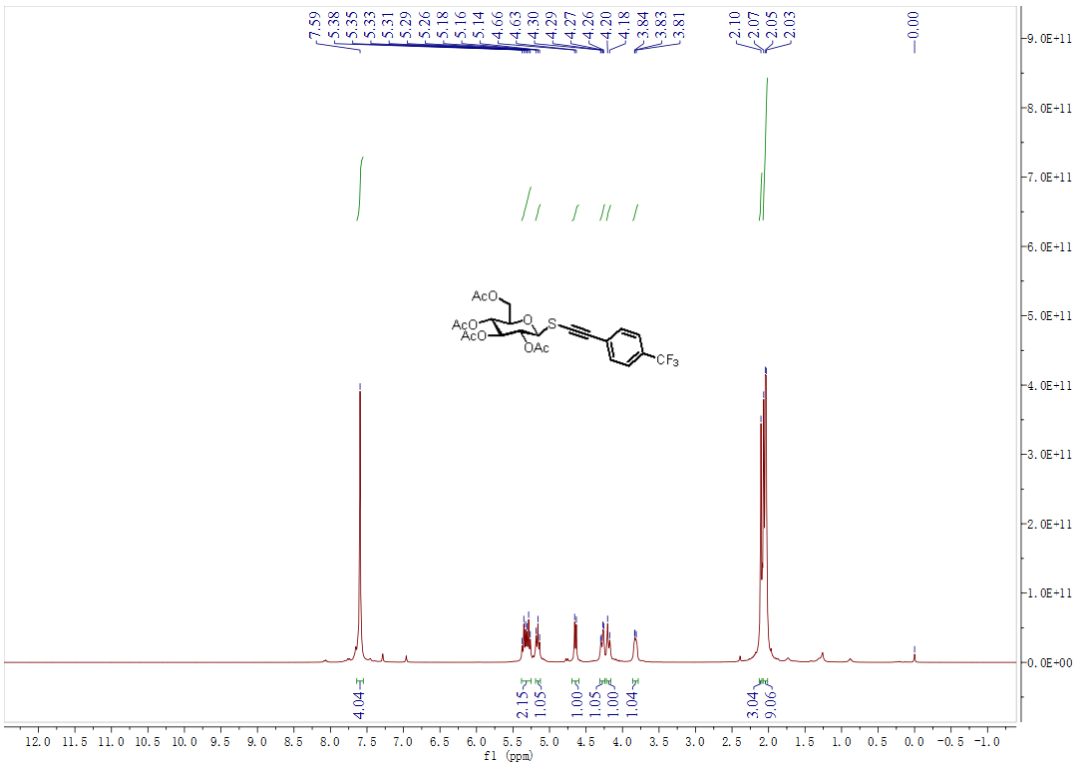
^{19}F NMR of **5g** (376 MHz, $CDCl_3$)



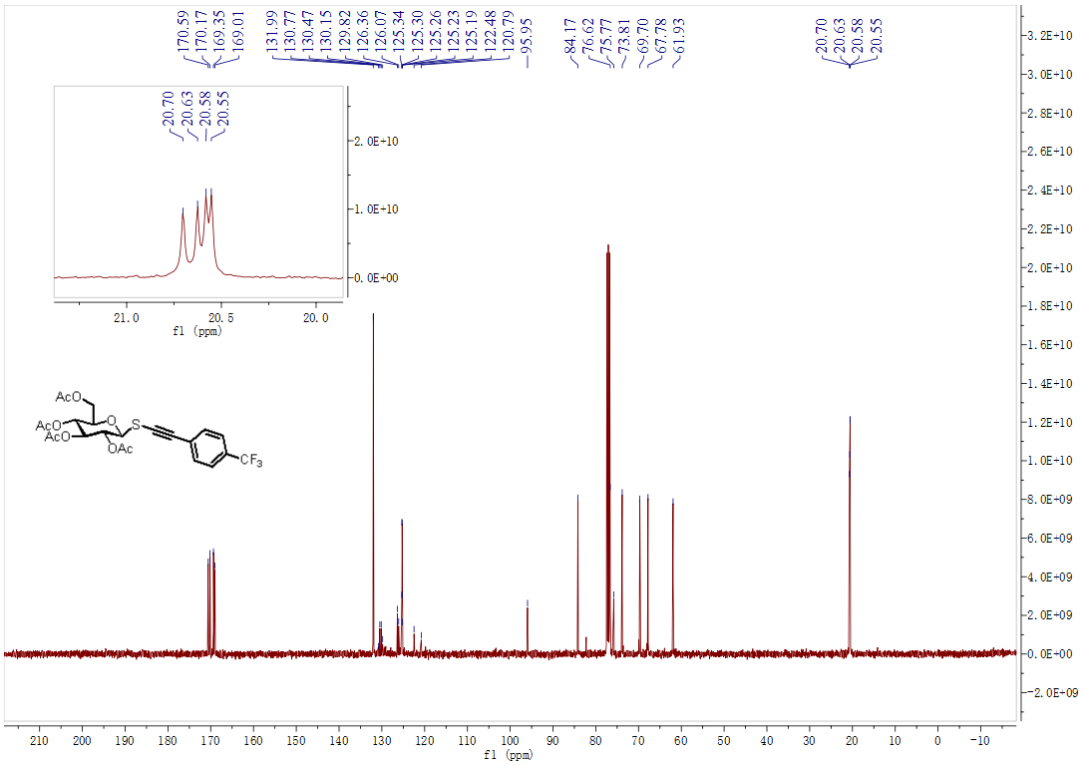
^{1}H NMR of **5h** (400 MHz, $CDCl_3$)



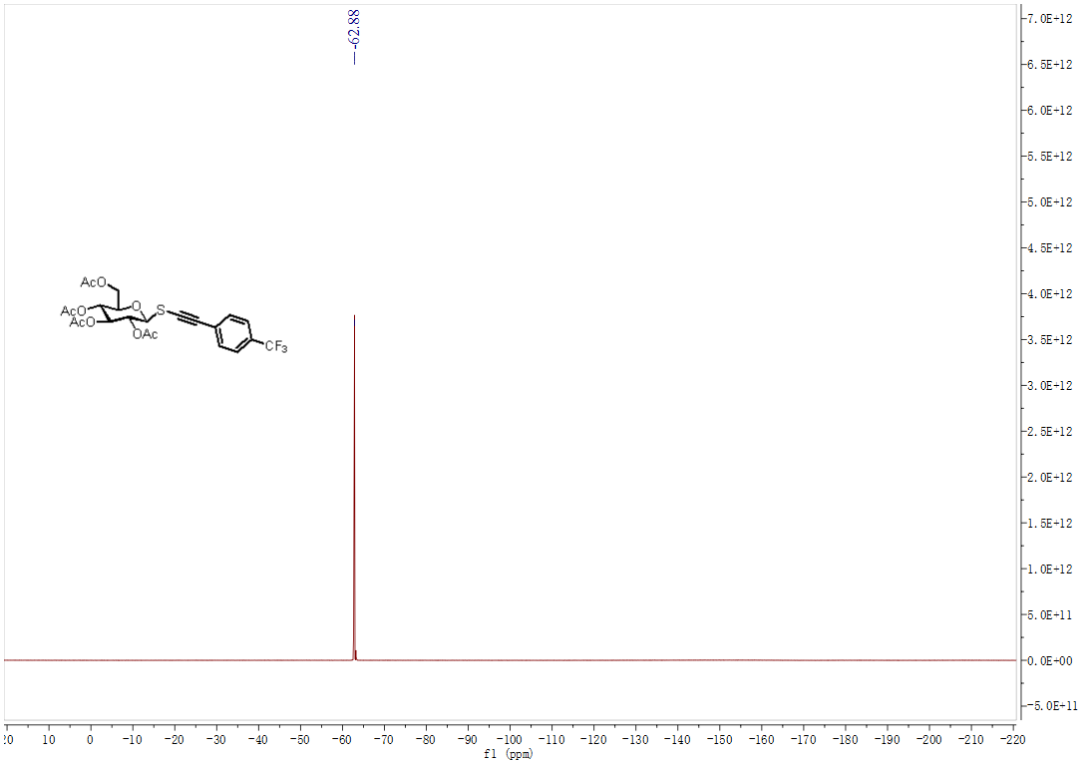
^{13}C NMR of **5h** (100 MHz, $CDCl_3$)



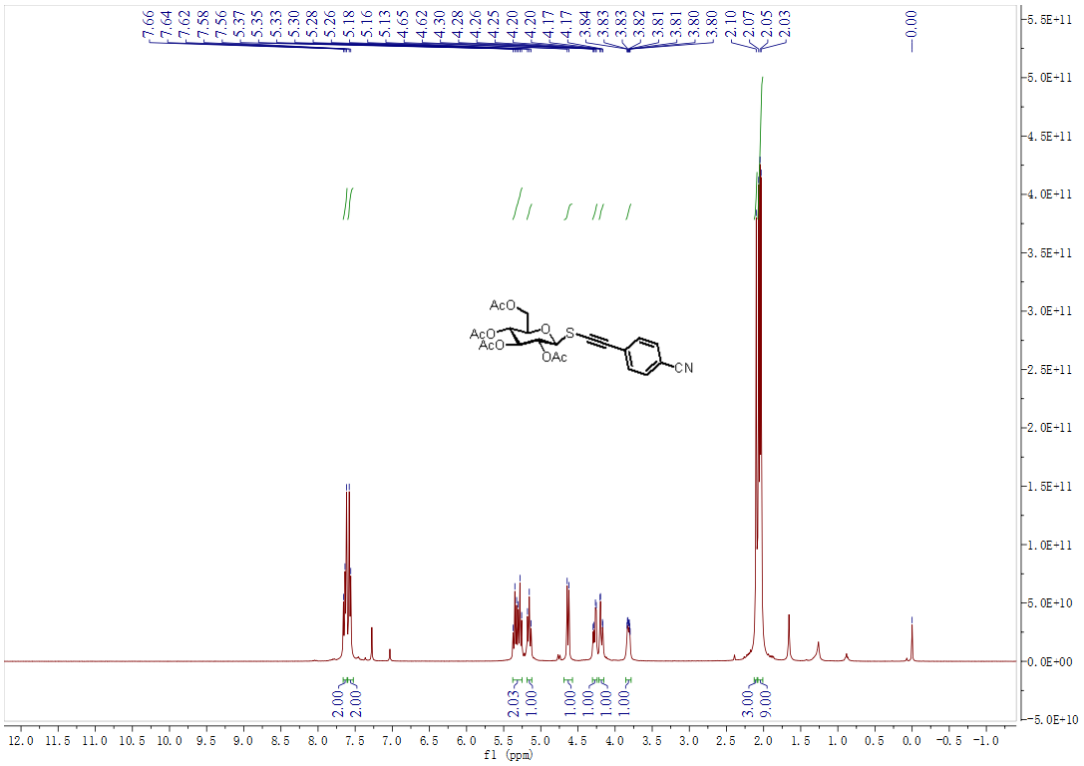
^{1}H NMR of **5i** (400 MHz, $CDCl_3$)



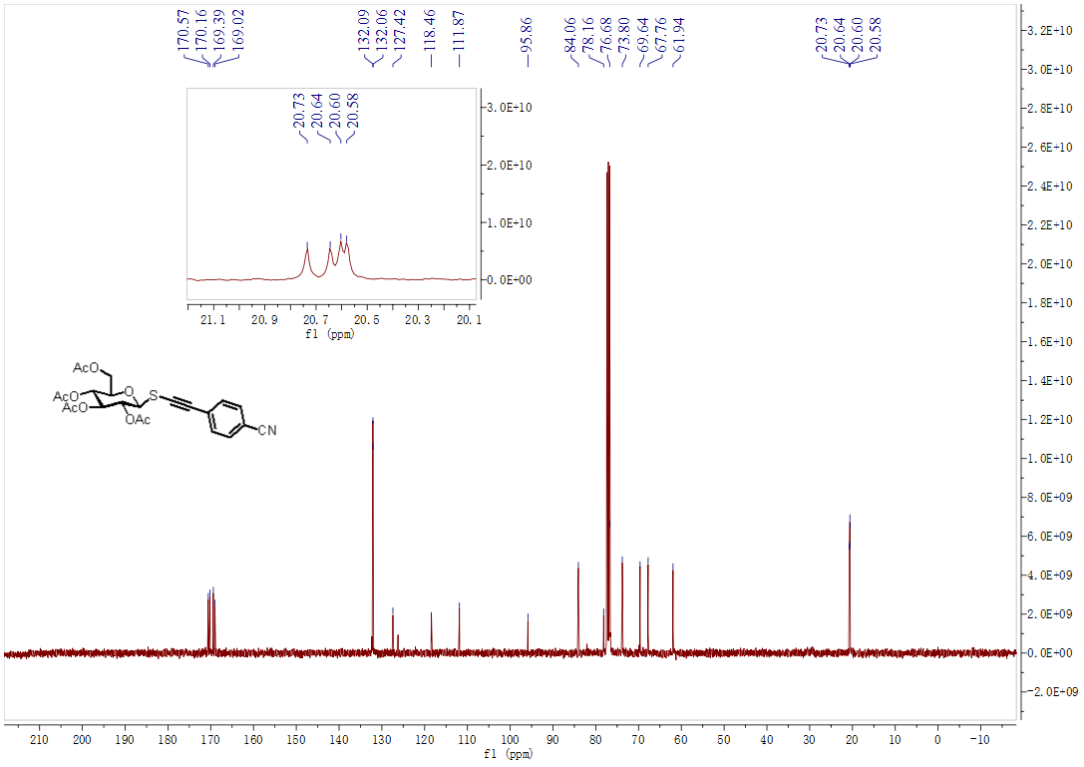
^{13}C NMR of **5i** (100 MHz, $CDCl_3$)



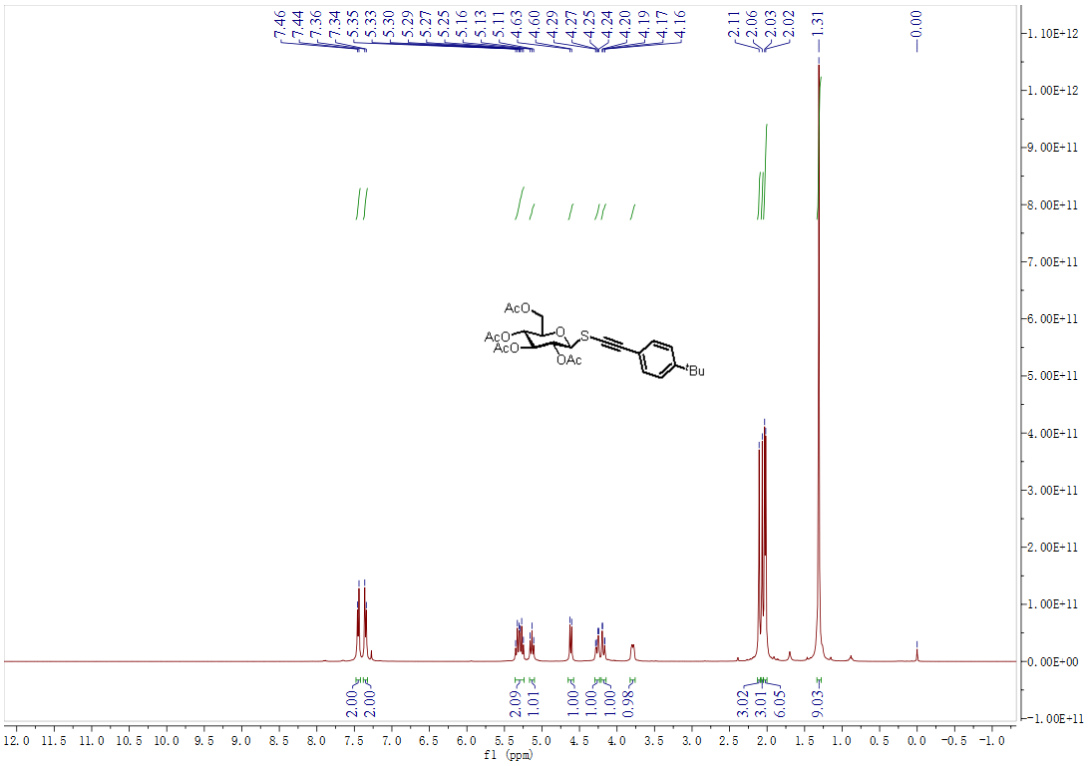
^{19}F NMR of **5i** (376 MHz, $CDCl_3$)



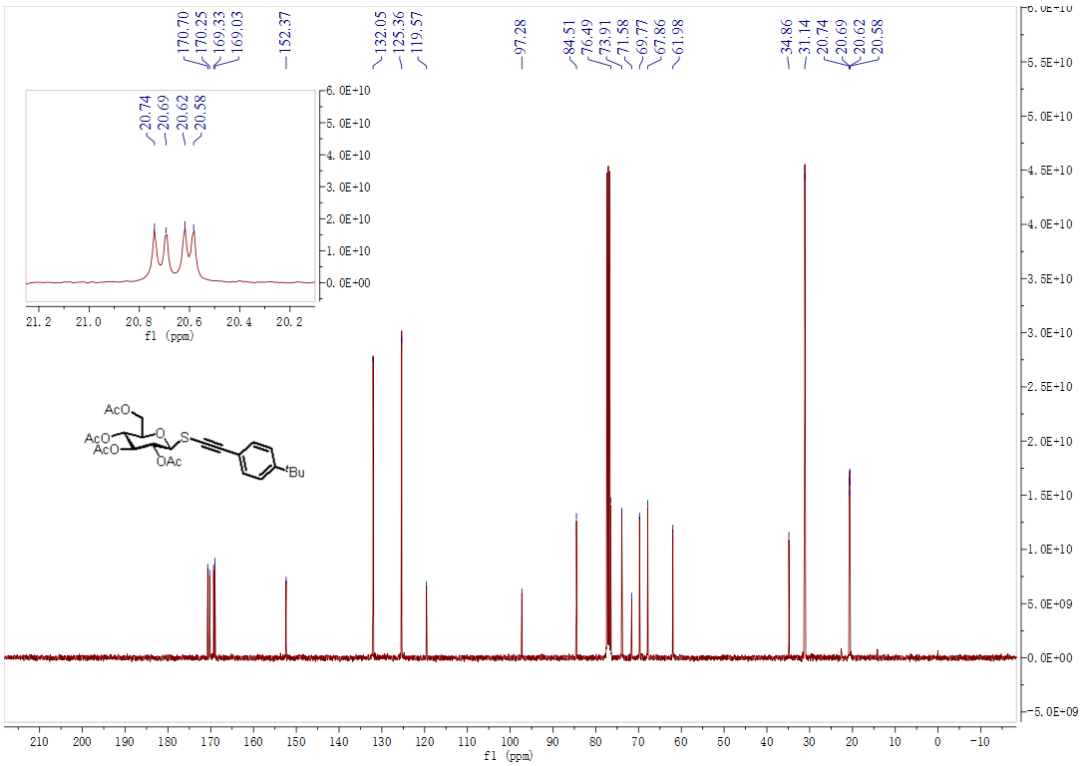
^{1}H NMR of **5j** (400 MHz, $CDCl_3$)



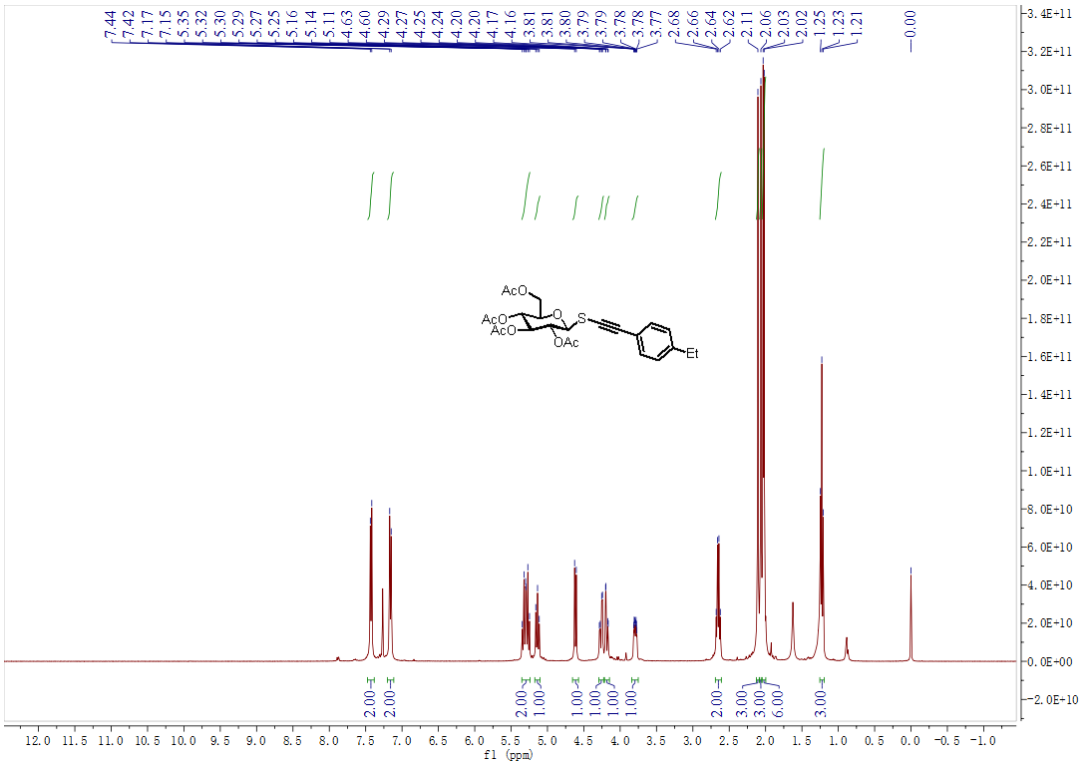
^{13}C NMR of **5j** (100 MHz, $CDCl_3$)



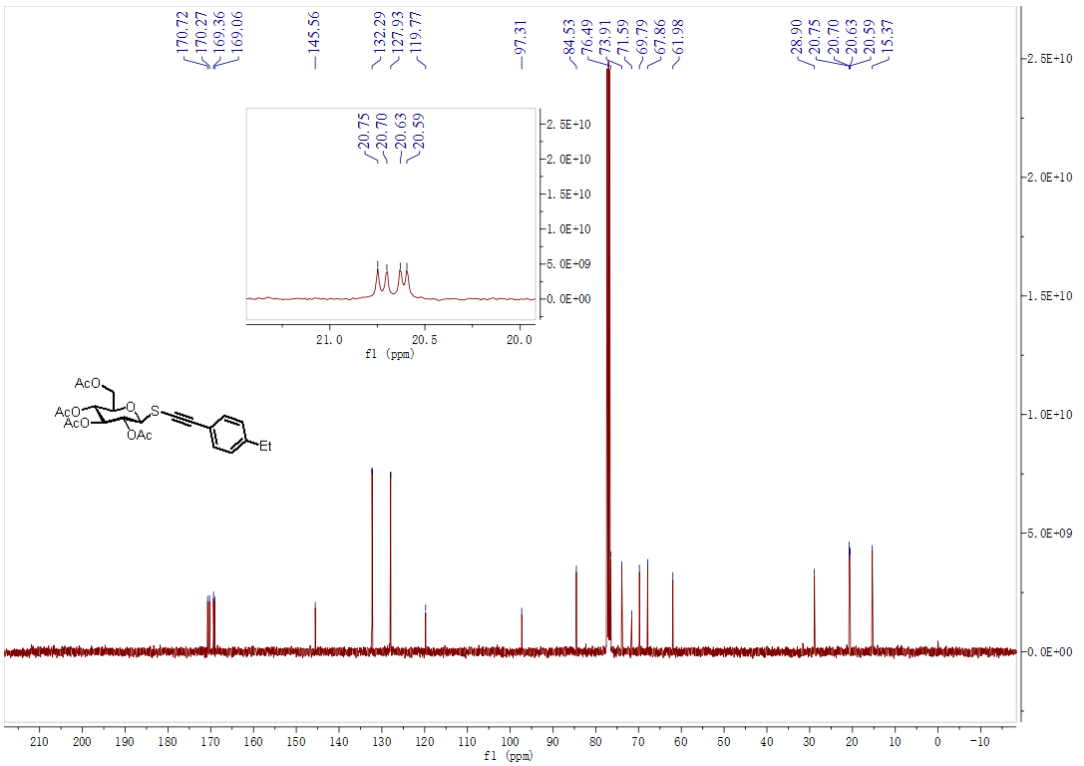
^{1}H NMR of **5k** (400 MHz, $CDCl_3$)



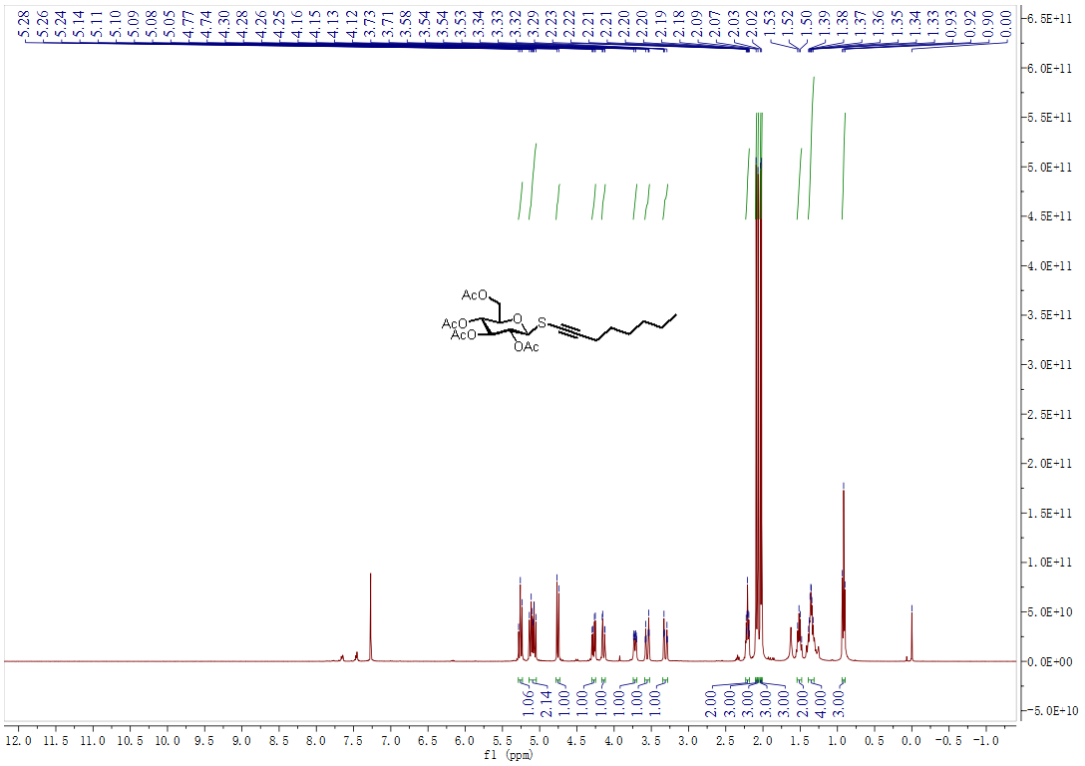
^{13}C NMR of **5k** (100 MHz, $CDCl_3$)



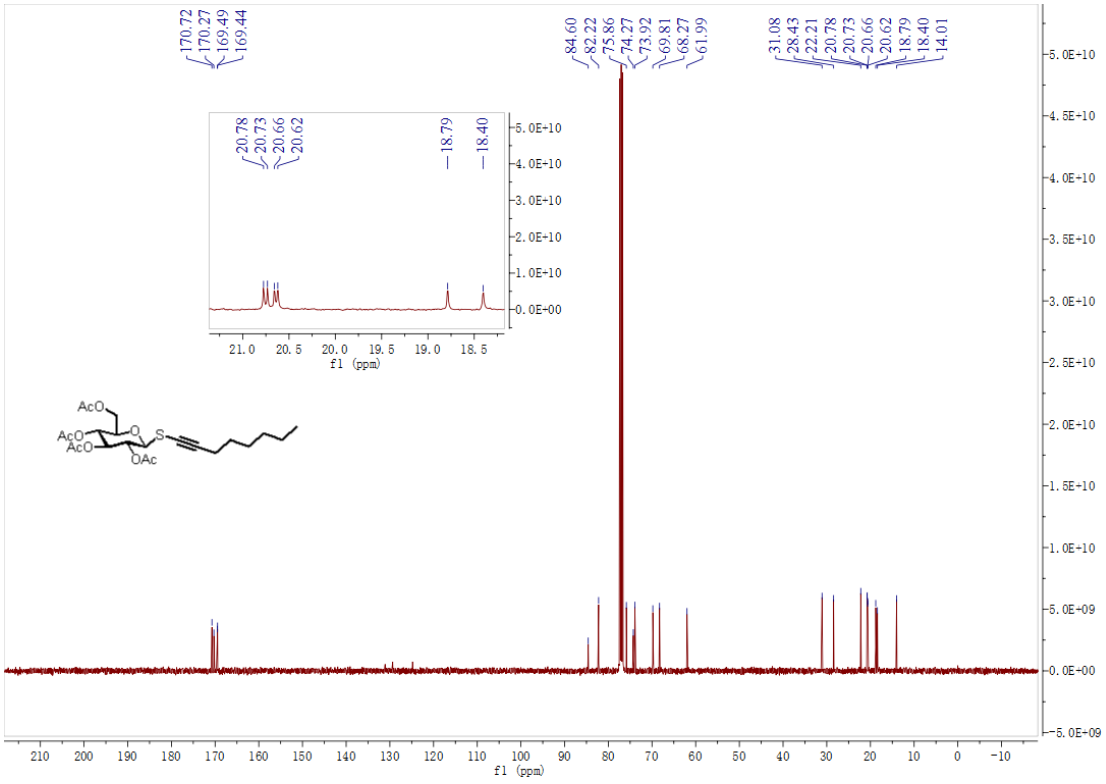
^{1}H NMR of **5l** (400 MHz, $CDCl_3$)



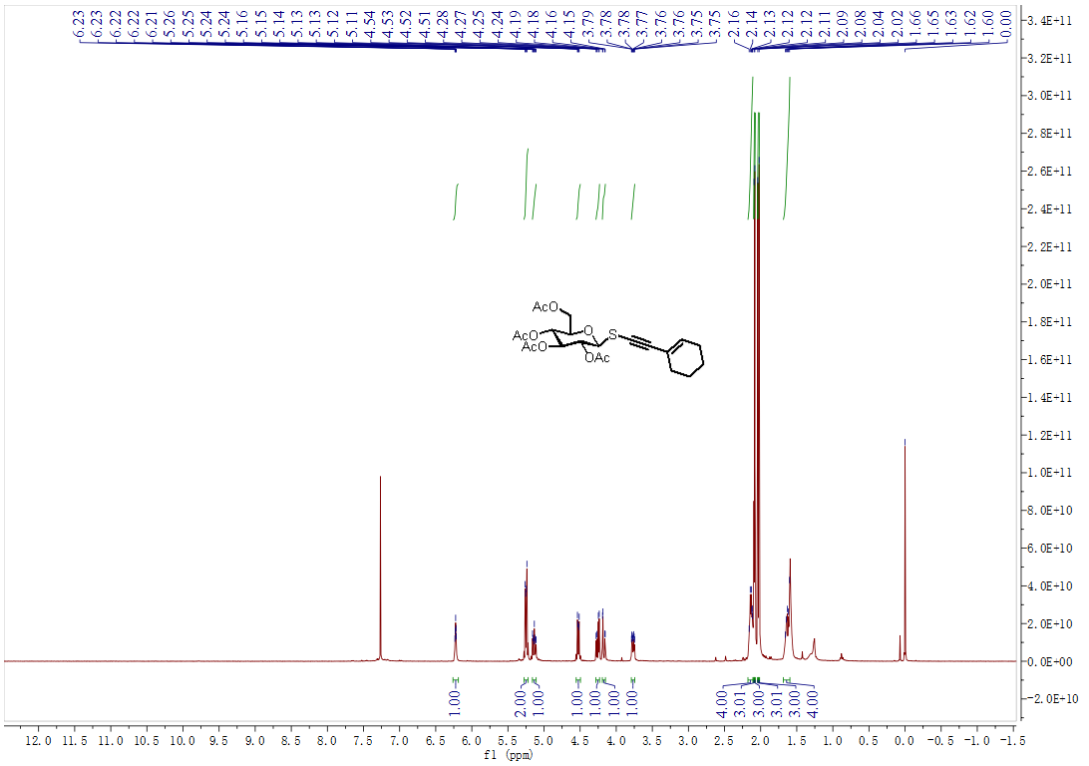
^{13}C NMR of **5l** (100 MHz, $CDCl_3$)



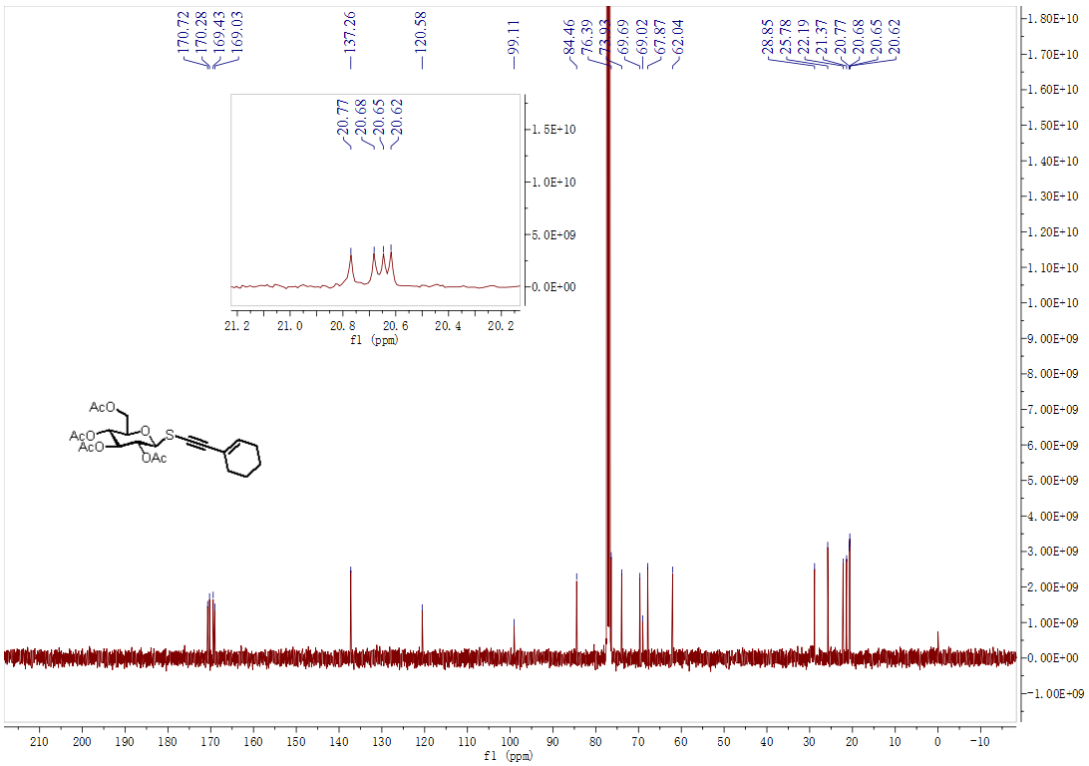
^{1}H NMR of **5m** (400 MHz, $CDCl_3$)



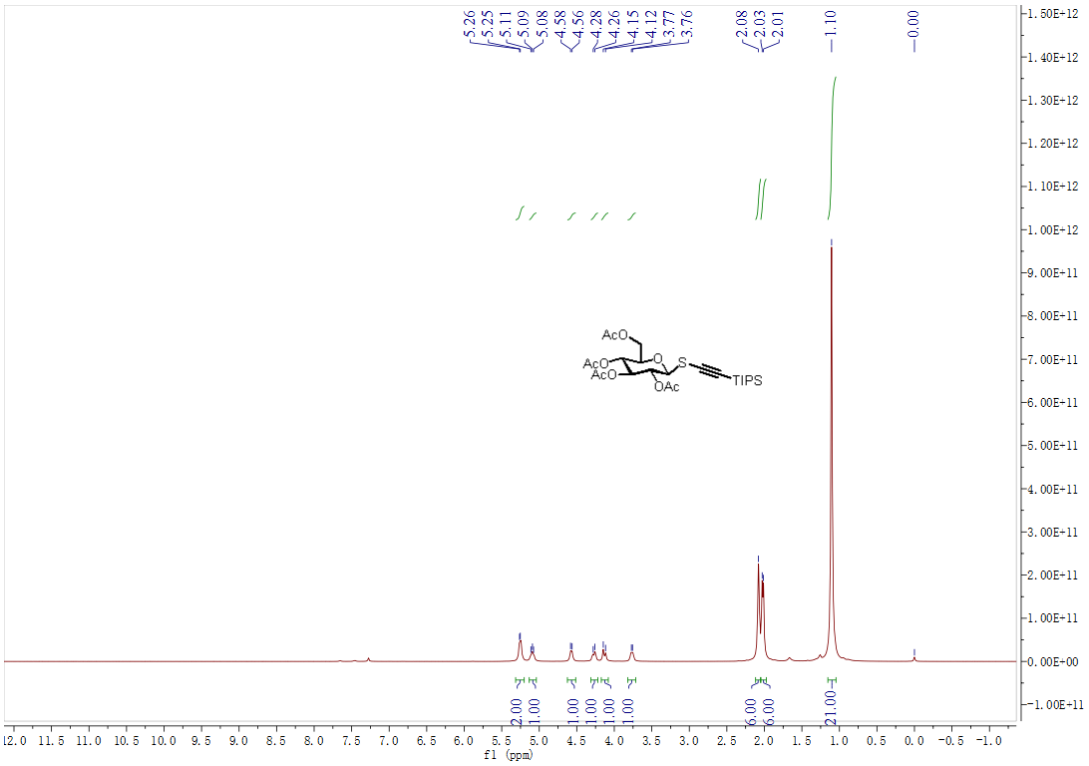
^{13}C NMR of **5m** (100 MHz, $CDCl_3$)



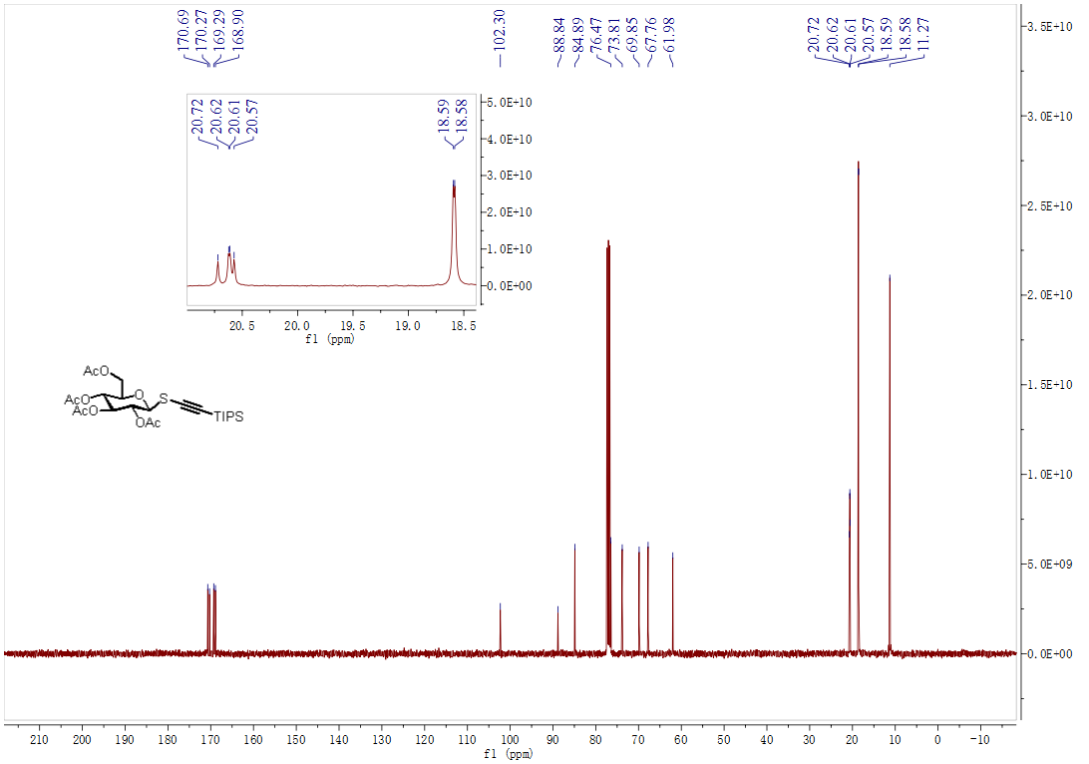
^{1}H NMR of **5n** (400 MHz, $CDCl_3$)



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



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



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