Supporting Information

1,3-Butadiynyl sulfide-based compact trialkyne platform molecule for sequential assembly of three azides

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Contents

General Remarks

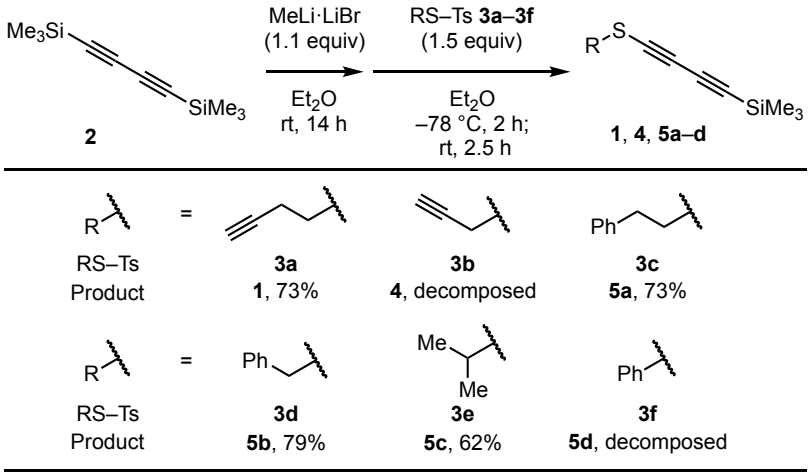
All reactions were performed with dry glassware under atmosphere of argon unless otherwise noted. Analytical thin-layer chromatography (TLC) was performed on precoated (0.25 mm) silica-gel plates (Merck Chemicals Ltd., Silica Gel 60 F_{254}, Cat. No. 1.05715). Column chromatography was conducted using silica-gel (Kanto Chemical Co., Inc., Silica Gel 60, spherical, particle size 40–50 μm, Cat. No. 37562-85). Preparative TLC using methanol as eluent was performed on Silica Gel 60 PF_{254} (Merck Chemicals Ltd., Cat. No. 1.07747); otherwise, Wakogel® B-5F (FUJIFILM Wako Pure Chemical Corporation, Cat. No. 230-00043) was used. Melting points (Mp) were measured on a YANACO MP-J3 instrument or an OptiMelt MPA100 (Stanford Research Systems), and are uncorrected. ^{1}H NMR spectra were obtained with a Bruker AVANCE 400 spectrometer at 400 MHz, a Bruker AVANCE 500 spectrometer at 500 MHz, or a JEOL ECA-500 spectrometer at 500 MHz. ^{19}F NMR spectra were obtained with a Bruker AVANCE 400 spectrometer at 376 MHz. ^{13}C NMR spectra were obtained with a JEOL ECA-500 spectrometer or a Bruker AVANCE 500 spectrometer at 126 MHz. All NMR measurements were carried out at 25 ºC unless otherwise noted. $CDCl_3$ (Kanto

Chemical Co. Inc., Cat. No. 07663-23) was used as a solvent for obtaining NMR spectra. Chemical shifts (δ) are given in parts per million (ppm) downfield from $(CH_3)_4Si$ (δ 0.00 ppm for ^1H NMR in $CDCl_3$), the solvent peak (δ 77.0 ppm for ^{13}C NMR in $CDCl_3$), or α,α,α-trifluorotoluene (δ −63.0 ppm for ^{19}F NMR in $CDCl_3$) as an internal reference with coupling constants (*J*) in hertz (Hz). The abbreviations s, d, t, q, sept, m, and br signify singlet, doublet, triplet, quartet, septet, multiplet, and broad, respectively. IR spectra were measured at room temperature by diffuse reflectance method on a Shimadzu IRPrestige-21 spectrometer attached with DRS-8000A or by attenuated total reflection (ATR) method on a Shimadzu IRSpirit-T spectrometer equipped with a QATR^{TM}-S single reflection ATR optical attachment and a diamond crystal plate with the absorption band given in cm^{-1}. High-resolution mass spectra (HRMS) were measured on a Bruker micrOTOF mass spectrometer or a Thermo Fisher Scientific ExactiveTM Plus Orbitrap mass spectrometer under positive electrospray ionization (ESI^+) conditions.

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Potassium 4-toluenethiosulfonate (Cat. No. T1185), dichloro(*p*-cymene)-ruthenium(II) dimer (Cat. No. D2751), tetrakis(acetonitrille)copper(I) tetrafluoroborate ($[Cu(MeCN)_4]BF_4$) (Cat. No. T2666), 11-azido-3,6,9-trioxaundecan-1-amine (Cat. No. A2363), azido-PEO_{11}-amine (Cat. No. A3007), and azido-PEO_3-biotin (**15**$_{\mathbf{short}}$) (Cat. No. A2523) were purchased from Tokyo Chemical Industry Co., Ltd. MeLi·LiBr complex (1.5 M solution in diethyl ether) (Cat. No. 186201), chloro(pentamethylcyclopentadienyl)(cycloocta-diene)ruthenium(II) (Cp*RuCl(cod)) (Cat. No. 667234), di-μ-chlorotetracarbonyldirhodium(I) ($[RhCl(CO)_2]_2$) (Cat. No. 209031), chloro(pentamethylcyclopentadienyl)bis(triphenylphos-phine)ruthenium(II) (Cp*RuCl$(PPh_3)_2$) (Cat. No. 673293), 1-azidoadamantane (**6d**) (Cat. No. 276219), tetra-*n*-butylammonium fluoride (TBAF) (1.0 M solution in THF) (Cat. No. 216143), (*R*)-2-(azidomethyl)-1-Boc-pyrrolidine (**6i**) (Cat. No. 670006), and triphenylphosphine (polymer-bound, 100–200 mesh, *ca.* 3.0 mmol/g loading, 2% cross-linked with divinylbenzene) (Cat. No. 366455) were purchased from Sigma–Aldrich Japan. 1,4-Bis(trimethylsilyl)-1,3-butadiyne (**2**) (Cat. No. 320-49913), diethyl ether (Super Dehydrated, Cat. No. 045-31645), 3-bromo-1-propyne (Cat. No. 167-07122), *N,N*-dimethylformamide (Super Dehydrated, Cat. No. 045-32365), di-μ-chlorobis[(η-cycloocta-1,5-diene)iridium(I)] ($[IrCl(cod)]_2$) (Cat. No. 047-31443), benzyl azide (**6a**) (Cat. No. 355-40762), dichloromethane (Super Dehydrated, Cat. No. 044-31235), 1,4-dioxane (Super Dehydrated, Cat. No. 042-31655), toluene (Super Deydrated, Cat. No. 204-17915), *tert*-butyl alcohol (Cat. No. 028-03386), (+)-sodium L-ascorbate (Cat. No. 196-01252), copper(II) sulfate pentahydrate ($CuSO_4·5H_2O$) (Cat. No. 030-04425), triethylamine (Cat. No. 202-02646), and ethyl azidoacetate (**6h**) (Cat. No. 326-44312) were purchased from FUJIFILM Wako Pure Chemical Corporation.

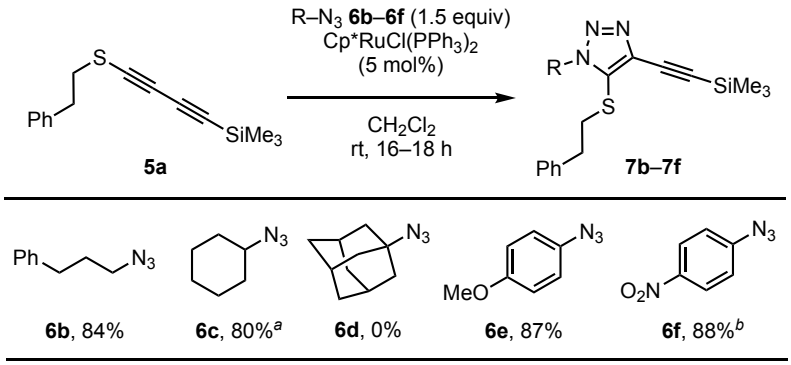
Thiosulfonates **3c**,[S1] **3d**,[S2] **3e**,[S3] **3f**,[S2] (3-azidopropyl)benzene (**6b**),[S4] azidocyclohexane (**6c**),[S5] 1-azido-4-methoxybenzene (**6e**),[S6] 1-azido-4-nitrobenzene (**6f**),[S6] 1-(azidomethyl)-4-fluorobenzene (**6g**),[S7] tris((1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl)amine (TBTA),[S8] *N*-(2-(2-((6-chlorohexyl)oxy)ethoxy)ethyl)-4-ethynylbenzamide (**S4**),[S9] succinimido 4-(azidomethyl)-benzoate,[S10] biotin succinimidyl ester (**S6**),[S11] 4-(azidomethyl)-*N*-(2-(2-(6-chlorohexyloxy)-ethoxy)ethyl)benzamide (**13**$_{\mathbf{short}}$),[S12] and TESRA-PEO_3-azide (**14**)[S12] were prepared according to the reported methods.

CAUTION! ***Azido-containing compounds are presumed to be potentially explosive. Although we have never experienced such an explosion with azido compounds used in this study, all manipulations should be carefully carried out behind a safety shield in a hood.***



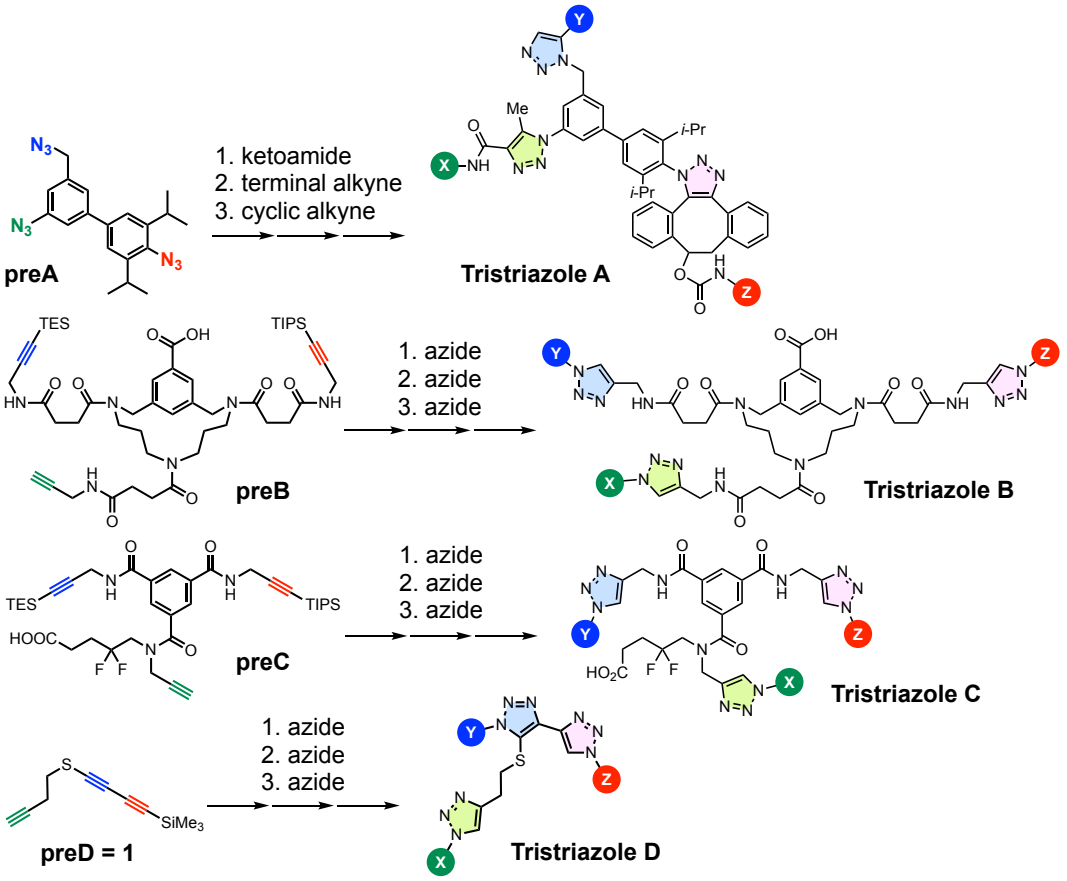
Scheme S1 Synthesis of 1,3-butadiynyl sulfides.

Simple alkyl 1,3-butadiynyl sulfides such as **5a**–**5c** was also prepared according to the method for preparation of trialkyne **1**, whereas phenyl sulfide **5d** could not be obtained. It should be mentioned that isolation of the desilylprotonated derivatives was difficult; although the presence of the desired products was observed by ^{1}H NMR analysis after treatment of **1** and **5a**–**5c** with tetrabutylammonium fluoride (TBAF) (THF, rt), insoluble black solids were obtained after concentration of their solutions under reduced pressure. These results indicated that unprotected 1,3-butadiynyl sulfides are unstable; therefore, we conducted the following studies using silyl-protected 1,3-butadiynyl sulfides to achieve a chemoselective click reaction.



Scheme S2 Substrate scope of azides in RuAtAC using 1,3-butadiynyl sulfide **5a**. [a]10 mol% of Cp*RuCl(PPh$_3$)$_2$ was used. [b]20 mol% of Cp*RuCl(PPh$_3$)$_2$ was used.

The optimized conditions for RuAtAC of 1,3-butadiynyl sulfide **5a** (Table 1, Entry 5) was applicable to the reactions with various azides. The reactions with primary and secondary azides **6b** and **6c** efficiently gave the corresponding triazoles **7b** and **7c**, respectively, although 10 mol% of catalyst was required in the latter case. Unfortunately, the reaction with sterically hindered 1-adamantyl azide (**6d**) did not proceed even under heating at 50 ºC. Aromatic azides also participated in this reaction; the reaction with *p*-anisyl azide (**6e**) afforded triazole **7e** in 87% yield, while electron-deficient aromatic azides such as **6f** required an increased amount of catalyst to furnish the desired product **7f** in satisfactory yield.



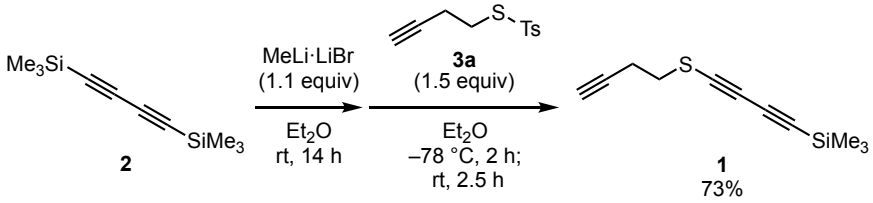
	A	B	C	D (This work)
Steps for platform synthesis	8	18	10	3 (two-pot)
Total yield for platform synthesis (%)	62	8	8	64
Molecular weight of platform molecule	375.4	959.4	728.0	206.4
Molecular weight of tristriazole core	744.8	814.8	583.5	260.3

Scheme S3 Comparison of the properties of distinguishable homo-triclickable platform molecules.

Our method outperformed previously reported strategies in terms of the ease of the synthesis of trialkyne platform molecule **1**, which was prepared in 64% overall yield in three steps, including the step for the preparation of thiosulfonate **3a** (see below for details). This contrasts with the 8 to 18 steps required for the platform synthesis in previous methods. Furthermore, the core structure of the resulting tristriazole **D** is more compact than those of previously reported tristriazoles **A**–**C** derived from triazido platform **preA**[S9] and trialkyne platform **preB**[S13] and **preC**,[S14] respectively. This enabled the synthesis of tristriazoles with lower molecular weight, which are favorable for drug discovery purposes.

Chemical Experiments

A typical procedure for the preparation of 1,3-butadiynyl sulfides (Schemes 2 and S1)

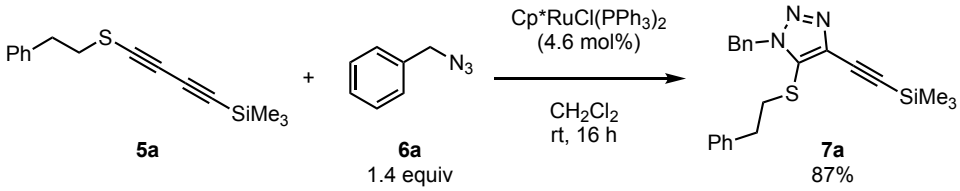


To a solution of 1,4-bis(trimethylsilyl)-1,3-butadiyne (**2**) (1.94 g, 9.98 mmol) dissolved in diethyl ether (20 mL) was slowly added MeLi·LiBr complex (1.5 M solution in diethyl ether, 7.40 mL, 11 mmol, 1.1 equiv) at room temperature. After stirring for 14 h at the same temperature, the resulting dark green solution was cooled to −78 °C. To the mixture was slowly added a solution of **3a** (3.68 g, 15.3 mmol, 1.5 equiv) dissolved in diethyl ether (5.0 mL). The resulting yellow suspension was stirred at −78 °C for 2 h, then allowed to warm to room temperature. After stirring for 2.5 h at the same temperature, to the suspension were added MeOH (5 mL) and an aqueous saturated solution of ammonium chloride (5 mL). The mixture was extracted with EtOAc (10 mL × 3), and the combined organic extract was washed with brine (10 mL), dried (Na_2SO_4), and after filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography (silica-gel 125 g, *n*-hexane only) to give ((but-3-yn-1-ylthio)buta-1,3-diyn-1-yl)trimethylsilane (**1**) (1.51 g, 7.32 mmol, 73.3 %) as a yellow oil. Triyne **1** is an air- and moisture-stable oil that can be stored under an argon atmosphere in a freezer (–20 °C) for over a year.

*Synthesis of S-(but-3-yn-1-yl) 4-methylbenzenesulfonothioate (**3a**)*

To a suspension of potassium 4-toluenethiosulfonate (11.4 g, 50.4 mmol) dissolved in DMF (100 mL) was added 4-bromo-1-butyne (13.3 g, 100 mmol, 2.0 equiv) at room temperature. After stirring for 16 h at the same temperature, the reaction mixture was concentrated under reduced pressure. The residue was diluted with water (20 mL), extracted with EtOAc (50 mL × 3), and the combined organic extract was washed with water (50 mL) and brine (50 mL), dried (Na_2SO_4), and after filtration, the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography (silica-gel 200 g, *n*-hexane/EtOAc = 100/0 to 90/10) to give *S*-(but-3-yn-1-yl) 4-methylbenzenesulfonothioate (**3a**) (10.5 g, 43.7 mmol, 86.7%) as a colorless oil. The spectral data were consistent with those reported in the literature.[S2]

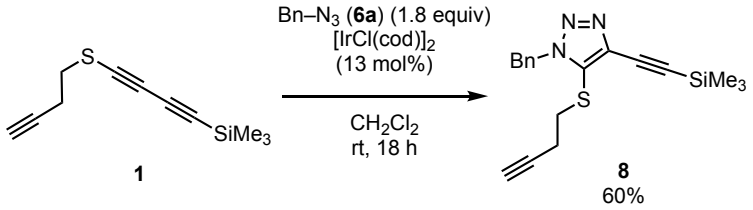
*A typical procedure for RuAtAC between 1,3-butadiyne **5a** and azides **6** (Table 1 and Scheme S2)*



To a solution of ((phenethylthio)buta-1,3-diyn-1-yl)trimethylsilane (**5a**) (30.6 mg, 0.118 mmol) and benzyl azide (**6a**) (22.8 mg, 0.171 mmol, 1.4 equiv) dissolved in dichloromethane

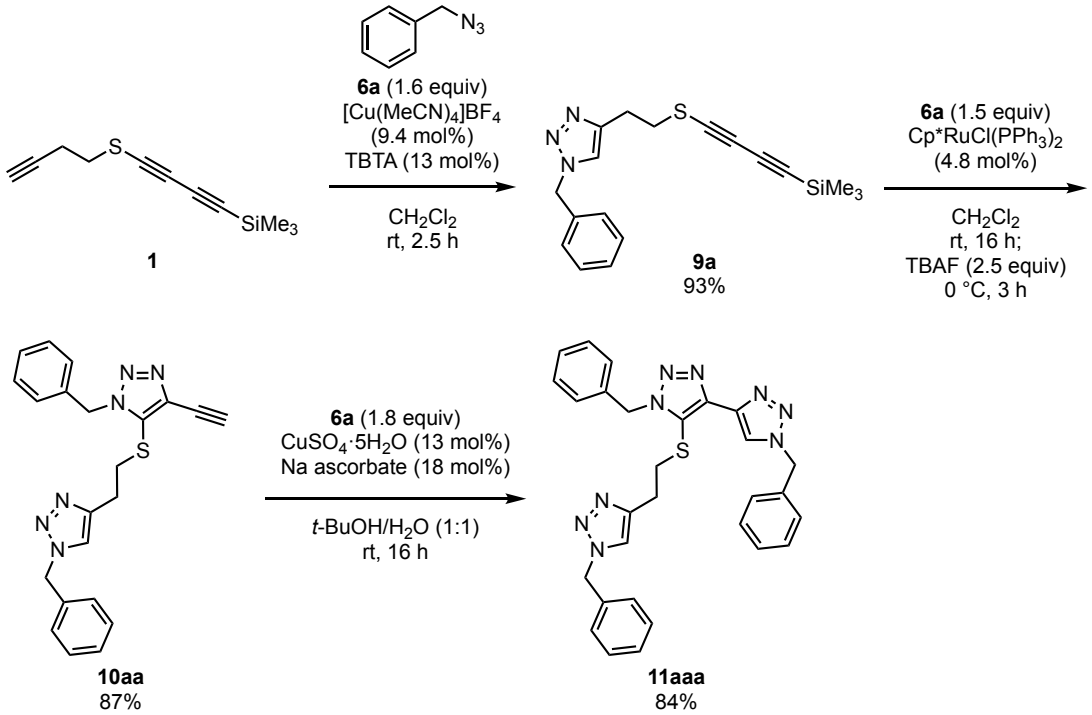
(1.0 mL) was added Cp*RuCl(PPh$_3$)$_2$ (4.3 mg, 5.4 μmol, 4.6 mol%) at room temperature. After stirring for 16 h at the same temperature, the mixture was concentrated under reduced pressure. The residue was purified by preparative PTLC (*n*-hexane/EtOAc = 80/20) to give 1-benzyl-5-(phenethylthio)-4-((trimethylsilyl)ethynyl)-1*H*-1,2,3-triazole (**7a**) (40.3 mg, 0.103 mmol, 86.9%) as a colorless oil.

*IrAtAC between **1** and benzyl azide (**6a**) (Scheme 3A)*



To a solution of **1** (21.4 mg, 0.104 mmol) and **6a** (24.6 mg, 0.185 mmol, 1.8 equiv) dissolved in dichloromethane (1.0 mL) were added [IrCl(cod)]$_2$ (9.4 mg, 14 μmol, 13 mol%) at room temperature. After stirring for 18 h at the same temperature, the mixture was concentrated under reduced pressure. The residue was purified by preparative PTLC (*n*-hexane/EtOAc = 80/20) to give 1-benzyl-5-(but-3-yn-1-ylthio)-4-((trimethylsilyl)ethynyl)-1*H*-1,2,3-triazole (**8**) (21.0 mg, 61.9 μmol, 59.6%) as a colorless oil.

*Typical procedures for the three sequential cycloadditions of trialkyne **1** with three azides: 1) CuAAC at the terminal alkyne, 2) RuAtAC at the thioalkyne moiety followed by desilylprotonation, and 3) CuAAC at the resulting alkyne moiety (Schemes 3B and 4)*



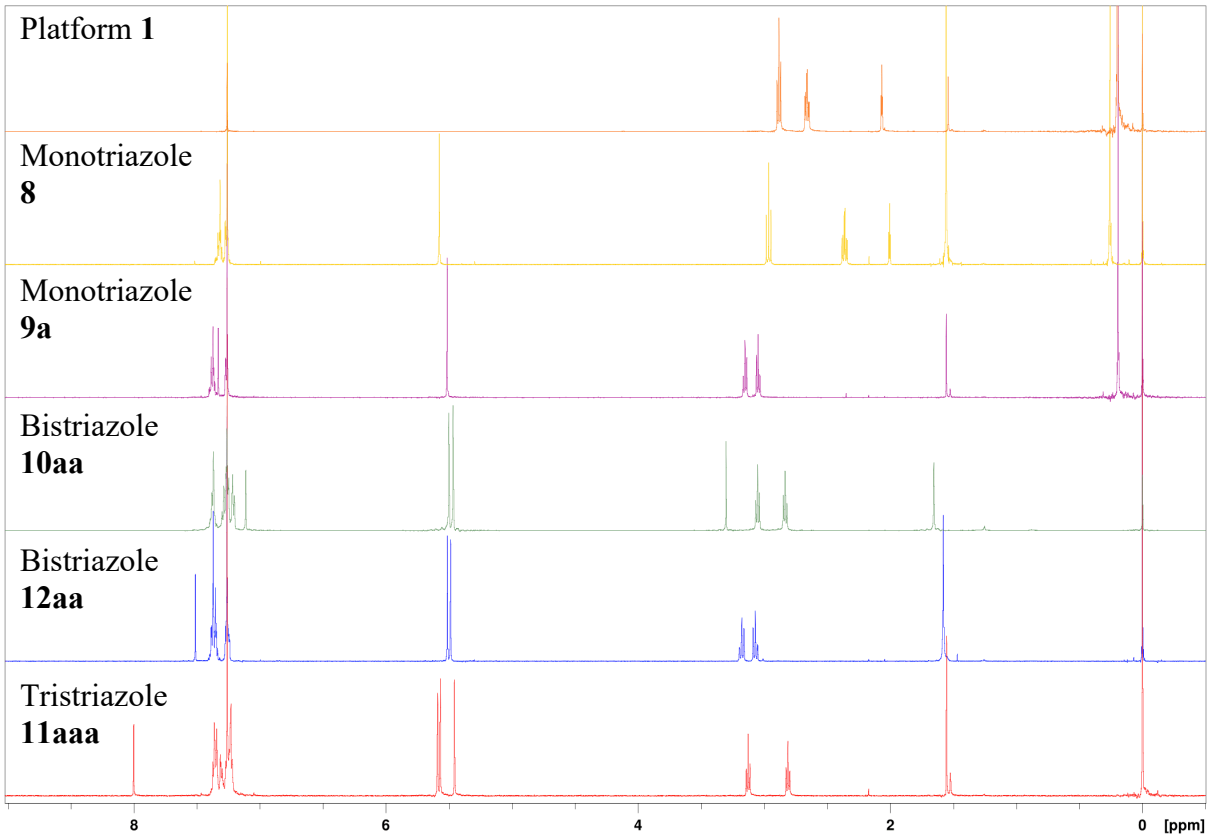
To a solution of **1** (37.0 mg, 0.179 mmol) and **6a** (37.3 mg, 0.280 mmol, 1.6 equiv) dissolved in dichloromethane (1.0 mL) were added [Cu(MeCN)$_4$]BF$_4$ (5.3 mg, 17 μmol, 9.4 mol%) and TBTA (12.4 mg, 23.4 μmol, 13 mol%) at room temperature. After stirring for 2.5 h at the same temperature, to the mixture was added water (10 mL). The mixture was extracted with EtOAc (10 mL × 3), and the combined organic extract was washed with brine (10 mL), dried (Na$_2$SO$_4$), and after filtration, the filtrate was concentrated under reduced pressure. The

residue was purified by preparative PTLC (*n*-hexane/EtOAc = 80/20) to give 1-benzyl-4-(2-(((trimethylsilyl)buta-1,3-diyn-1-yl)thio)ethyl)-1*H*-1,2,3-triazole (**9a**) (56.8 mg, 0.167 mmol, 93.3%) as a colorless solid.

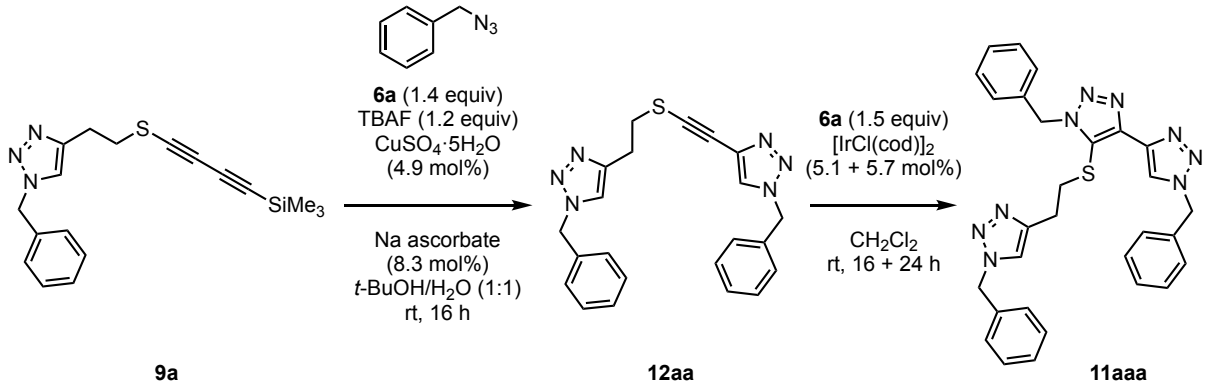
To a solution of triazole **9a** (61.7 mg, 0.182 mmol) and **6a** (37.2 mg, 0.279 mmol, 1.5 equiv) dissolved in dichloromethane (1.5 mL) was added Cp*RuCl(PPh_3)$_2$ (6.9 mg, 8.7 μmol, 4.8 mol%) at room temperature. After stirring for 16 h at the same temperature, to the mixture was added TBAF (1.0 M solution in THF, 0.450 mL, 0.45 mmol, 2.5 equiv) at 0 ºC and the reaction mixture was continued stirring for 3 h at the same temperature. The mixture was quenched with an aqueous saturated solution of ammonium chloride (10 mL) and extracted with EtOAc (10 mL × 3). The combined organic extract was washed with brine (10 mL), dried (Na_2SO_4), and after filtration, the filtrate was concentrated under reduced pressure. The residue was purified by preparative PTLC (*n*-hexane/EtOAc = 60/40) to give 1-benzyl-5-((2-(1-benzyl-1*H*-1,2,3-triazol-4-yl)ethyl)thio)-4-ethynyl-1*H*-1,2,3-triazole (**10aa**) (63.1 mg, 0.158 mmol, 86.7%) as a colorless solid.

To a solution of bistriazole **10aa** (63.1 mg, 0.158 mmol) and **6a** (37.5 mg, 0.282 mmol, 1.8 equiv) suspended in a 1:1 mixture of water and *tert*-butyl alcohol (400 μL) were added sodium ascorbate (5.6 mg, 28 μmol, 18 mol%) and $CuSO_4 \cdot 5H_2O$ (5.3 mg, 21 μmol, 13 mol%) at room temperature. After stirring for 16 h at the same temperature, the reaction mixture was diluted with water (1 mL), extracted with EtOAc (10 mL × 3), and the combined organic extract was washed with brine (10 mL), dried (Na_2SO_4), and after filtration, the filtrate was concentrated under reduced pressure. The residue was purified by preparative PTLC (*n*-hexane/EtOAc = 20/80) to give 1,1′-dibenzyl-5-((2-(1-benzyl-1*H*-1,2,3-triazol-4-yl)ethyl)-thio)-1*H*,1′*H*-4,4′-bi(1,2,3-triazole) (**11aaa**) (70.3 mg, 0.132 mmol, 83.6%) as a colorless solid.

*Stacked ^{1}H NMR spectra of **1**, **8**, **9a**, **10aa**, **12aa**, and **11aaa** ($CDCl_3$)*



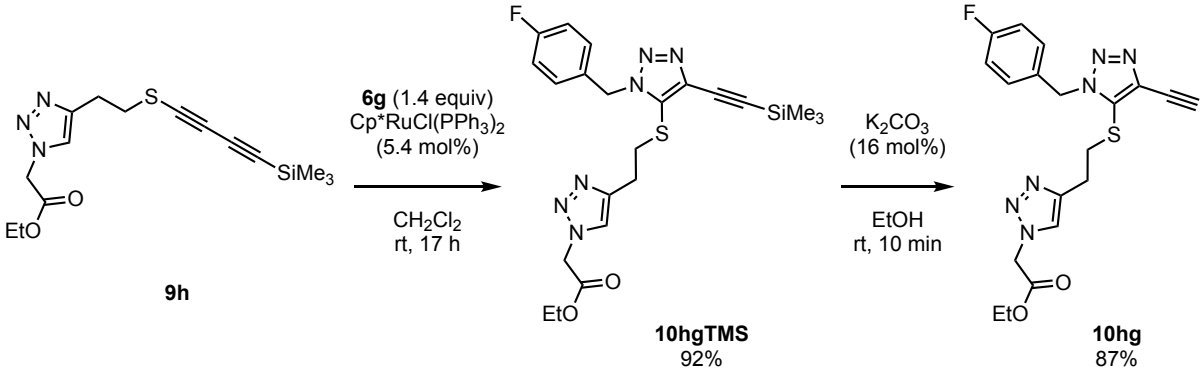
*Sequential cycloadditions of 1,3-butadiyne **9a** with two azides*:
1) CuAAC at the TMS-protected alkyne moiety and 2) RuAtAC at the thioalkyne moiety (Scheme 3B)



To a solution of triazole **9a** (66.4 mg, 0.196 mmol) and **6a** (35.4 mg, 0.266 mmol, 1.4 equiv) suspended in a 1:1 mixture of water and *tert*-butyl alcohol (640 μL) were added sodium ascorbate (3.2 mg, 16 μmol, 8.3 mol%), TBAF (1.0 M solution in THF, 240 μL, 0.24 mmol, 1.2 equiv), and $CuSO_4·5H_2O$ (2.4 mg, 9.6 μmol, 4.9 mol%) at room temperature. After stirring for 16 h at the same temperature, the reaction was diluted with water, extracted with EtOAc (10 mL × 3), and the combined organic extract was washed with brine (10 mL), dried (Na_2SO_4) and after filtration, the filtrate was concentrated under reduced pressure. The residue was purified by preparative PTLC (*n*-hexane/EtOAc = 3/2) to give 1-benzyl-4-(((2-(1-benzyl-1*H*-1,2,3-triazol-4-yl)ethyl)thio)ethynyl)-1*H*-1,2,3-triazole (**12aa**) (67.3 mg, 0.168 mmol, 85.9%) as a colorless solid.

To a solution of bistriazole **12aa** (20.0 mg, 49.9 μmol) and **6a** (9.7 mg, 72.9 μmol, 1.5 equiv) dissolved in dichloromethane (500 μL) was added $[IrCl(cod)]_2$ (1.7 mg, 2.5 μmol, 5.1 mol%) at room temperature. After stirring for 16 h at the same temperature, to the mixture was added $[IrCl(cod)]_2$ (1.9 mg, 2.8 μmol, 5.7 mol%) at room temperature. After stirring for 24 h at the same temperature, the mixture was concentrated under reduced pressure. The residue was purified by preparative PTLC (*n*-hexane/EtOAc = 40/60) to give 1,1′-dibenzyl-5-((2-(1-benzyl-1*H*-1,2,3-triazol-4-yl)ethyl)thio)-1*H*,1′*H*-4,4′-bi(1,2,3-triazole) (**11aaa**) (21.1 mg, 39.5 μmol, 79.2%) as a colorless solid.

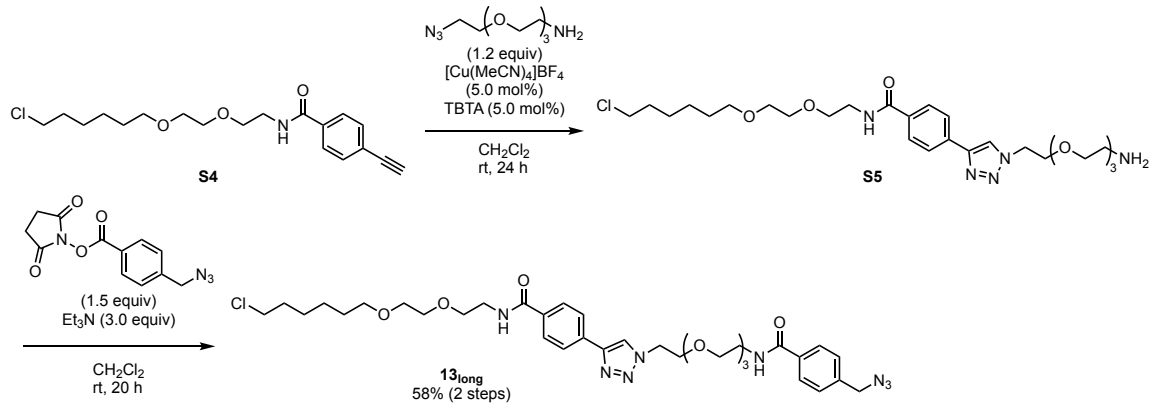
*RuAtAC of **9h** and subsequent desilylprotonation using K_2CO_3 in ethanol (Scheme 4)*



To a solution of triazole **9h** (53.3 mg, 0.159 mmol) and **6g** (34.2 mg, 0.226 mmol, 1.4 equiv) dissolved in dichloromethane (1.5 mL) was added Cp*RuCl(PPh_3)$_2$ (6.8 mg, 8.5 μmol, 5.4 mol%) at room temperature. After stirring for 17 h at the same temperature, the reaction mixture was concentrated under reduced pressure. The residue was purified by preparative PTLC (*n*-hexane/EtOAc = 50/50) to give ethyl 2-(4-(2-((1-(4-fluorobenzyl)-4-((trimethylsilyl)ethynyl)-1*H*-1,2,3-triazol-5-yl)thio)ethyl)-1*H*-1,2,3-triazol-1-yl)acetate (**10hgTMS**) (71.1 mg, 0.146 mmol, 92.0%) as a yellow oil.

To a solution of triazole **10hgTMS** (26.1 mg, 53.6 μmol) dissolved in ethanol (50 μL) was added potassium carbonate (1.2 mg, 8.7 μmol, 16 mol%) at room temperature. After stirring for 10 min at the same temperature, the reaction mixture was filtered through a pad of silica-gel, and then concentrated under reduced pressure. The residue was purified by preparative PTLC (*n*-hexane/EtOAc = 40/60) to give ethyl 2-(4-(2-((4-ethynyl-1-(4-fluorobenzyl)-1*H*-1,2,3-triazol-5-yl)thio)ethyl)-1*H*-1,2,3-triazol-1-yl)acetate (**10hg**) (19.4 mg, 46.8 μmol, 87.3%) as a yellow oil.

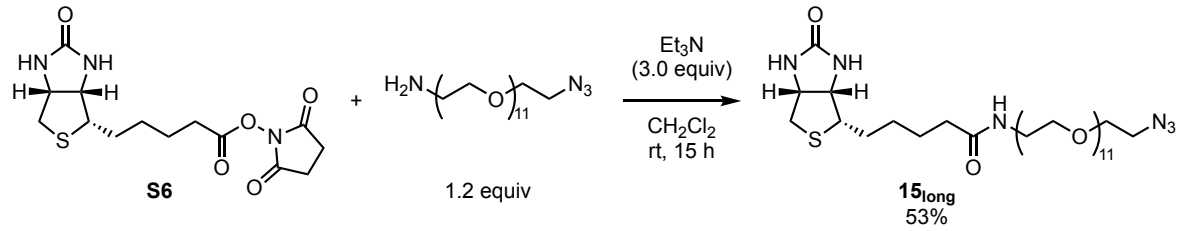
*Preparation of azido-HaloTag ligand **13$_{long}$***



To a solution of **S4** (361 mg, 1.03 mmol) and 11-azido-3,6,9-trioxaundecan-1-amine (271 mg, 1.24 mmol, 1.2 equiv) dissolved in dichloromethane (10 mL) were added [Cu(MeCN)$_4$]BF$_4$ (16.0 mg, 50.9 μmol, 5.0 mol%) and TBTA (27.0 mg, 50.9 μmol, 5.0 mol%) at room temperature. After stirring for 24 h at the same temperature, to the mixture was added water (10 mL). The mixture was extracted with dichloromethane (10 mL × 3), and the combined organic extract was washed with brine (10 mL), dried (Na_2SO_4), and after filtration, the filtrate was concentrated under reduced pressure to give 4-(1-(2-(2-(2-(2-aminoethoxy)-ethoxy)ethoxy)ethyl)-1*H*-1,2,3-triazol-4-yl)-*N*-(2-(2-((6-chlorohexyl)oxy)ethoxy)ethyl)benzamide (**S5**) as a sticky yellow oil, which was used in the next step without further purification.

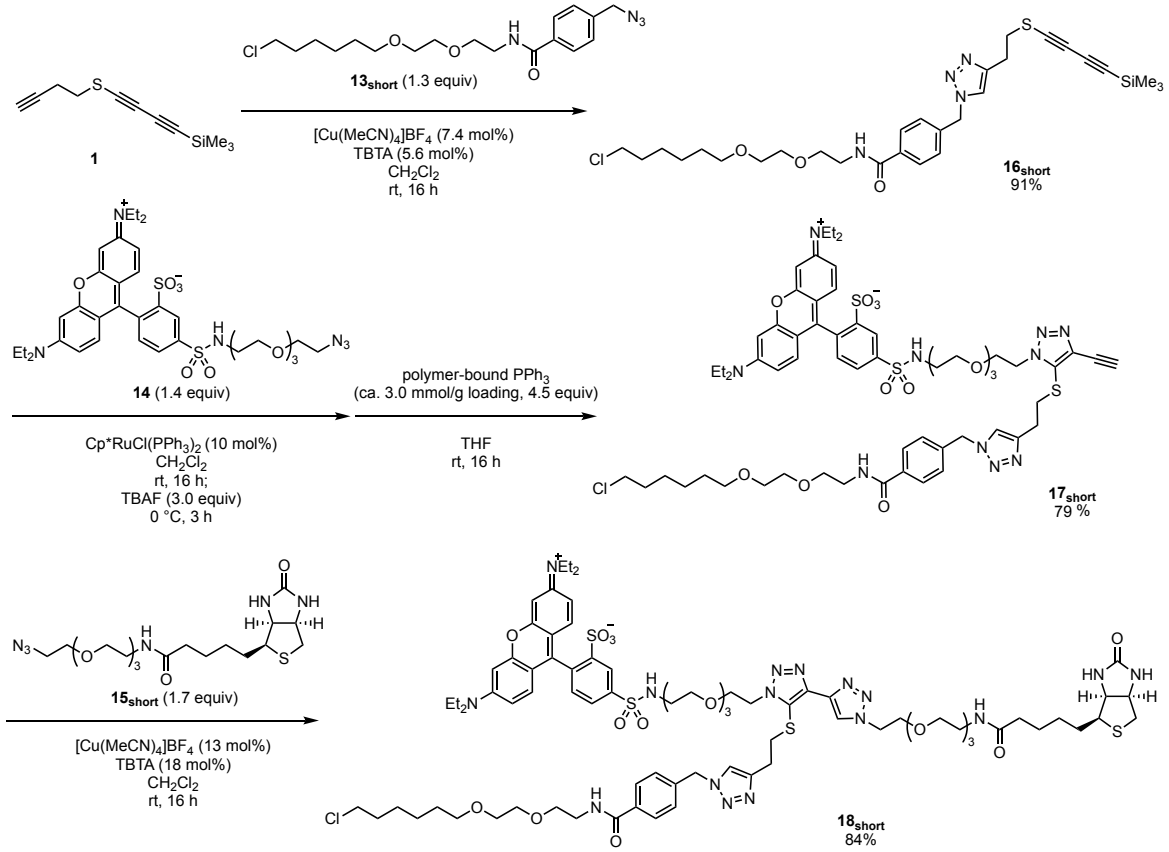
To a solution of a crude mixture containing **S5** in dichloromethane (10 mL) were successively added triethylamine (428 μL, 3.08 mmol, 3.0 equiv) and succinimido 4-(azidomethyl)benzoate (420 mg, 1.53 mmol, 1.5 equiv) at room temperature. After stirring for 20 h at the same temperature, to the mixture was added water (15 mL). The mixture was extracted with dichloromethane (10 mL × 3), and the combined organic extract was washed with brine (10 mL), dried (Na_2SO_4), and after filtration, the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography (silica-gel 40 g, dichloromethane/MeOH = 100/0 to 90/10) to give 4-(azidomethyl)-*N*-(2-(2-(2-(2-(4-(4-((2-(2-((6-chlorohexyl)oxy)ethoxy)ethyl)carbamoyl)phenyl)-1*H*-1,2,3-triazol-1-yl)ethoxy)ethoxy)-ethoxy)ethyl)benzamide (**13_{long}**) (432 mg, 0.592 mmol, 57.7% in 2 steps from **S4**) as a colorless solid.

Synthesis of azido-PEO_{11}-biotin ***15_{long}***



To a solution of biotin succinimidyl ester (**S6**) (123 mg, 0.360 mmol) dissolved in dichloromethane (5.0 mL) were successively added triethylamine (1.50 mL, 1.08 mmol, 3.0 equiv) and azido-PEO_{11}-amine (250 mg, 0.438 mmol, 1.2 equiv) at room temperature. After stirring for 15 h at the same temperature, to the mixture was added water (15 mL). The mixture was extracted with dichloromethane (10 mL × 3), and the combined organic extract was washed with brine (10 mL), and dried (Na_2SO_4), and after filtration, the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography (silica-gel 12 g, dichloromethane/MeOH = 100/0 to 90/10) to give 4-(azidomethyl)-*N*-(2-(2-(2-(2-(4-(4-((2-(2-((6-chlorohexyl)oxy)ethoxy)ethyl)carbamoyl)phenyl)-1*H*-1,2,3-triazol-1-yl)ethoxy)ethoxy)ethoxy)ethyl)benzamide (**15_{long}**) (152 mg, 0.191 mmol, 52.9%) as a sticky colorless solid.

*Synthesis of trifunctional probe **18**$_{short}$ from trialkyne **1** via the three sequential cycloadditions with three functional azides (Scheme 5)*

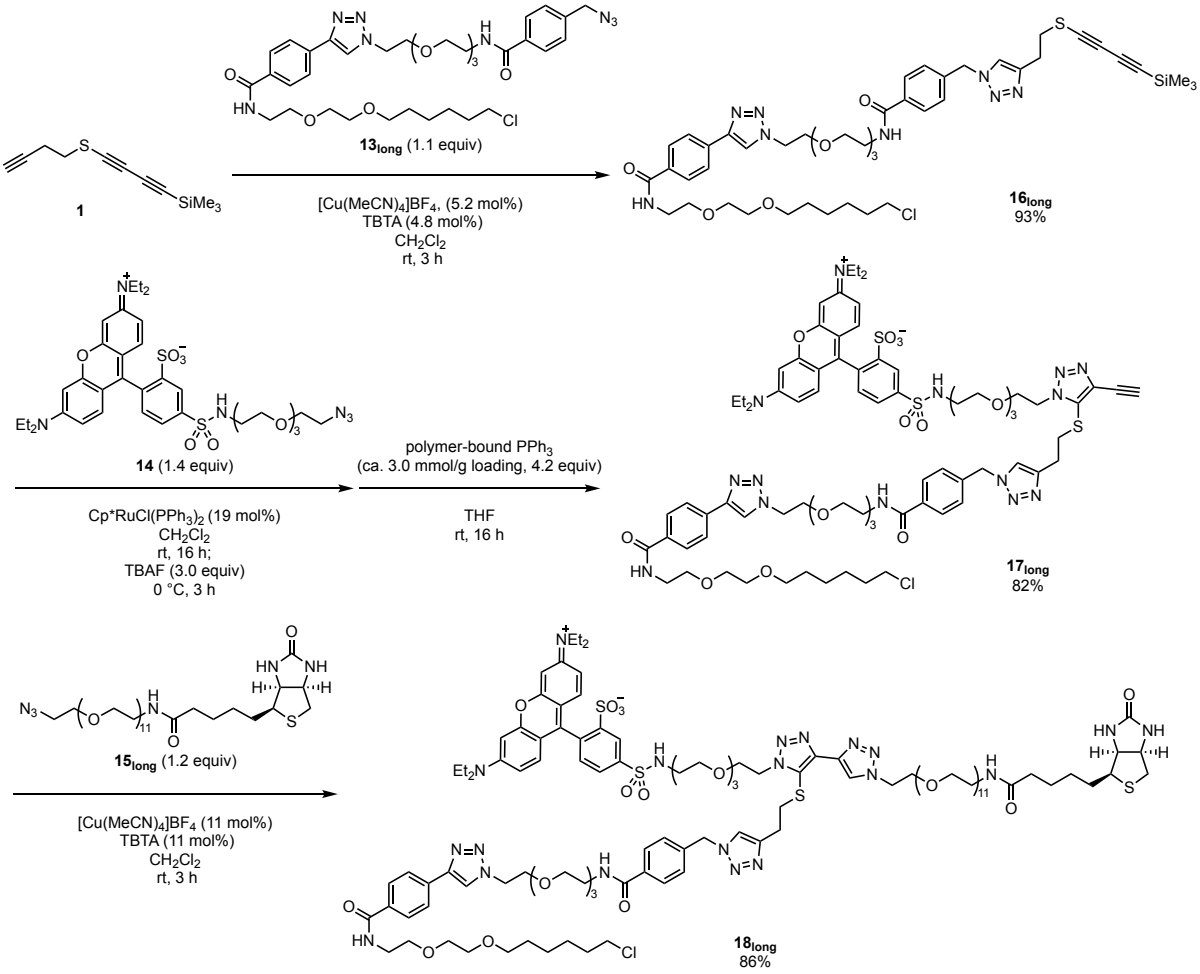


To a solution of **1** (37.1 mg, 0.180 mmol) and 4-(azidomethyl)-*N*-(2-(2-(6-chlorohexyl-oxy)ethoxy)ethyl)benzamide (**13**$_{short}$) (86.7 mg, 0.226 mmol, 1.3 equiv) dissolved in dichloro-methane (2.0 mL) were added $[Cu(MeCN)_4]BF_4$ (4.2 mg, 13 μmol, 7.4 mol%) and TBTA (5.3 mg, 10 μmol, 5.6 mol%) at room temperature. After stirring for 16 h at the same temperature, to the mixture was added water (10 mL). The mixture was extracted with EtOAc (10 mL × 3), and the combined organic extract was washed with brine (10 mL), dried (Na_2SO_4) and after filtration, the filtrate was concentrated under reduced pressure. The residue was purified by preparative PTLC (dichloromethane/MeOH = 90/10) to give triazole **16**$_{short}$ (96.6 mg, 0.164 mmol, 91.2%) as a colorless solid.

To a solution of triazole **16**$_{short}$ (26.8 mg, 45.5 μmol) and TESRA-PEO_3-azide **14** (49.1 mg, 64.7 μmol, 1.4 equiv) dissolved in dichloromethane (2.0 mL) was added $Cp^*RuCl(PPh_3)_2$ (3.8 mg, 4.8 μmol, 10 mol%) at room temperature. After stirring for 16 h at the same temperature, to the mixture was added TBAF (1.0 M solution in THF, 0.136 mL, 0.14 mmol, 3.0 equiv) at 0 ºC and the reaction mixture was continued stirring for 3 h at the same temperature. The mixture was quenched with an aqueous saturated solution of ammonium chloride (10 mL) and extracted with EtOAc (10 mL × 3). The combined organic extract was washed with brine (10 mL), dried (Na_2SO_4), and after filtration, the filtrate was concentrated under reduced pressure. To the solution of the residue dissolved in THF (2.0 mL) was added polymer-bound triphenylphosphine (ca. 3.0 mmol/g loading, 68.1 mg, 0.20 mmol, 4.5 equiv) at room temperature to reduce the remaining azide. After stirring for 16 h at the same temperature, the resulting suspension was filtrated using a Kiriyama funnel (washed with dichloromethane) and the filtrate was concentrated under reduced pressure. The residue was purified by preparative PTLC (dichloromethane/MeOH = 90/10) to give bistriazole **17**$_{short}$ (45.8 mg, 35.9 μmol, 78.9%) as a red solid.

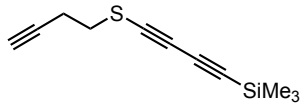
To a solution of bistriazole **17$_{short}$** (22.5 mg, 17.6 μmol) and azido-PEO$_3$-biotin **15$_{short}$** (13.5 mg, 30.4 μmol, 1.7 equiv) dissolved in dichloromethane (500 μL) were added [Cu(MeCN)$_4$]BF$_4$ (0.7 mg, 2 μmol, 13 mol%) and TBTA (1.7 mg, 3.2 μmol, 18 mol%) at room temperature. After stirring for 16 h at the same temperature, to the mixture was added water (5 mL). The mixture was extracted with EtOAc (5 mL × 3), and the combined organic extract was washed with brine (5 mL), dried (Na_2SO_4) and after filtration, the filtrate was concentrated under reduced pressure. The residue was purified by preparative PTLC (dichloromethane/ MeOH = 90/10) to give tristriazole **18$_{short}$** (25.4 mg, 14.8 μmol, 83.7%) as a red solid. As a result, trifunctional probe **18$_{short}$** was prepared from the trialkyne platform **1** in 60.3% overall yield in 3 steps.

Similarly, trifunctional probe **18$_{long}$** was prepared from the trialkyne platform **1** in 65.1% overall yield in 3 steps (Scheme 5).



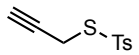
Characterization Data of New Compounds

((But-3-yn-1-ylthio)buta-1,3-diyn-1-yl)trimethylsilane (**1**)



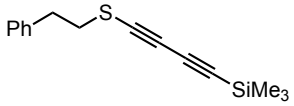
Yellow oil; TLC R_f 0.55 (*n*-hexane only); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.89 (t, 2H, J = 7.3 Hz), 2.66 (td, 2H, J = 7.3, 2.6 Hz), 2.07 (t, 1H, J = 2.6 Hz), 0.20 (s, 9H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 89.0 (1C), 88.0 (1C), 81.1 (1C), 80.6 (1C), 70.3 (1C), 68.2 (1C), 34.0 (1C), 19.5 (1C), −0.4 (3C); IR (KBr, cm^{-1}) 648, 760, 847, 1130, 1250, 1420, 2075, 2162, 2264, 2959, 3298; HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{11}H_{14}NaSSi^+$, 229.0478; Found, 229.0473.

S-(Prop-2-yn-1-yl) 4-methylbenzenesulfonothioate (**3b**)



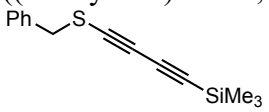
The title compound was obtained in 87.7% (1.00 g, 4.42 mmol) from potassium 4-toluenethiosulfonate (1.14 g, 5.04 mmol) following the procedure for the synthesis of **3a**. Colorless solid; Mp 45–47 ºC (decomp.); TLC R_f 0.58 (*n*-hexane/EtOAc = 80/20); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.87–7.82 (AA'BB', 2H), 7.37–7.33 (AA'BB', 2H), 3.79 (d, 2H, J = 2.9 Hz), 2.46 (s, 3H), 2.14 (t, 1H, J = 2.9 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 145.2 (1C), 141.7 (1C), 129.8 (2C), 127.3 (2C), 76.3 (1C), 73.4 (1C), 24.2 (1C), 21.7 (1C); IR (KBr, cm^{-1}) 461, 518, 583, 652, 699, 811, 1072, 1134, 1296, 1312, 1401, 1593, 3272; HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{10}H_{10}NaO_2S_2^+$, 249.0014; Found, 249.0013.

((Phenethylthio)buta-1,3-diyn-1-yl)trimethylsilane (**5a**)



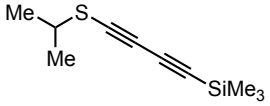
The title compound was obtained in 72.9% (1.89 g, 7.31 mmol) from **2** (1.95 g, 10.0 mmol). Yellow oil; TLC R_f 0.40 (*n*-hexane only); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.34–7.19 (AA'BB'C, 5H), 3.08–3.02 (m, 2H), 3.00–2.94 (m, 2H), 0.21 (s, 9H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 139.0 (1C), 128.7 (2C), 128.6 (2C), 126.8 (1C), 88.5 (1C), 88.2 (1C), 80.1 (1C), 69.4 (1C), 36.7 (1C), 35.7 (1C), −0.4 (3C); IR (KBr, cm^{-1}) 770, 847, 1130, 1250, 1454, 1497, 2160, 2959, 3028, 3289; HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{15}H_{18}NaSSi^+$, 281.0791; Found, 281.0786.

((Benzylthio)buta-1,3-diyn-1-yl)trimethylsilane (**5b**)



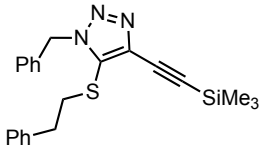
The title compound was obtained in 78.7% (966 mg, 3.95 mmol) from **2** (976 mg, 5.02 mmol). Orange oil; TLC R_f 0.54 (*n*-hexane only); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.38–7.29 (AA'BB'C, 5H), 3.99 (s, 2H), 0.19 (s, 9H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 135.8 (1C), 129.0 (2C), 128.7 (2C), 128.0 (1C), 89.1 (1C), 88.1 (1C), 80.9 (1C), 69.4 (1C), 40.4 (1C), −0.4 (3C); IR (KBr, cm^{-1}) 648, 696, 760, 847, 1130, 1250, 1454, 1495, 2073, 2160, 2264, 2959, 3030; HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{14}H_{16}NaSSi^+$, 267.0634; Found, 267.0632.

((Isopropylthio)buta-1,3-diyn-1-yl)trimethylsilane (**5c**)



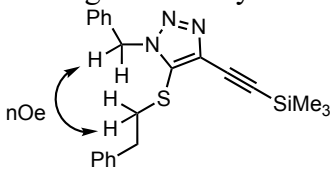
The title compound was obtained in 62.2% (127 mg, 0.647 mmol) from **2** (202 mg, 1.04 mmol). Yellow oil; TLC R_f 0.63 (*n*-hexane only); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.22 (sept, 1H, J = 6.7 Hz), 1.39 (d, 6H, J = 6.7 Hz), 0.20 (s, 9H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 88.5 (1C), 88.3 (1C), 81.3 (1C), 69.0 (1C), 40.4 (1C), 23.0 (2C), −0.4 (3C); IR (KBr, cm^{-1}) 760, 845, 1130, 1250, 1462, 2160,2926, 2963; HRMS (ESI) *m*/*z*: [M + H]$^+$ Calcd for $C_{10}H_{17}SSi^+$, 197.0815; Found, 197.0810.

1-Benzyl-5-(phenethylthio)-4-((trimethylsilyl)ethynyl)-1*H*-1,2,3-triazole (**7a**)

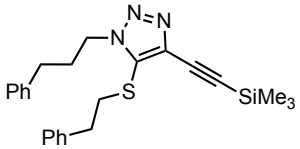


Colorless oil; TLC R_f 0.61 (*n*-hexane/EtOAc = 80/20); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.34–7.19 (m, 8H), 7.08–7.04 (m, 2H), 5.48 (s, 2H), 3.10 (t, 2H, J = 7.9 Hz), 2.72 (t, 2H, J = 7.9 Hz), 0.23 (s, 9H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 139.0 (1C), 134.62 (1C), 134.57 (1C), 133.1 (1C), 128.9 (2C), 128.53 (2C), 128.46 (1C), 128.4 (2C), 127.8 (2C), 126.7 (1C), 102.1 (1C), 93.8 (1C), 52.3 (1C), 36.0 (1C), 35.2 (1C), −0.4 (3C); IR (KBr, cm^{-1}) 712, 760, 845, 1250, 1325, 1454, 1497, 2166, 2957, 3028; HRMS (ESI) *m*/*z*: [M + Na]$^+$ Calcd for $C_{22}H_{25}N_3NaSSi^+$, 414.1431; Found, 414.1430.

The regiochemistry of **7a** was determined by NOE NMR method.

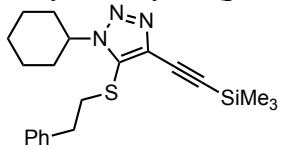


5-(Phenethylthio)-1-(3-phenylpropyl)-4-((trimethylsilyl)ethynyl)-1*H*-1,2,3-triazole (**7b**)



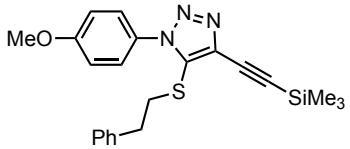
The title compound was obtained in 84.1% (38.1 mg, 90.8 μmol) from **5a** (27.9 mg, 0.108 mmol). Yellow oil; TLC R_f 0.56 (*n*-hexane/EtOAc = 75/25); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.33–7.09 (m, 10H), 4.28 (t, 2H, J = 7.2 Hz), 3.29 (t, 2H, J = 7.8 Hz), 2.85 (t, 2H, J = 7.8 Hz), 2.62 (t, 2H, J = 7.7 Hz), 2.21–2.11 (m, 2H), 0.24 (s, 9H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 140.1 (1C), 138.9 (1C), 133.9 (1C), 132.8 (1C), 128.6 (2C), 128.54 (2C), 128.48 (2C), 128.4 (2C), 126.8 (1C), 126.3 (1C), 102.0 (1C), 93.9 (1C), 48.0 (1C), 36.1 (1C), 35.2 (1C), 32.5 (1C), 31.4 (1C), −0.4 (3C); IR (KBr, cm^{-1}) 698, 760, 845, 1250, 1327, 1454, 1497, 2166, 2955, 3026; HRMS (ESI) *m*/*z*: [M + Na]$^+$ Calcd for $C_{24}H_{29}N_3NaSSi^+$, 442.1744; Found, 442.1748.

1-Cyclohexyl-5-(phenethylthio)-4-((trimethylsilyl)ethynyl)-1*H*-1,2,3-triazole (**7c**)



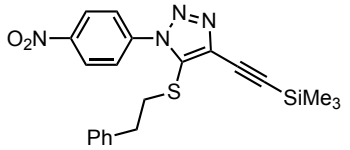
The title compound was obtained in 79.9% (29.4 mg, 76.6 μmol) from **5a** (24.8 mg, 96.0 μmol) using 10 mol% catalyst. Yellow oil; TLC R_f 0.60 (*n*-hexane/EtOAc = 80/20); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.32–7.20 (m, 3H), 7.18–7.13 (m, 2H), 4.34 (tt, 1H, *J* = 11.6, 3.9 Hz), 3.28 (t, 2H, *J* = 7.8 Hz), 2.86 (t, 2H, *J* = 7.8 Hz), 2.10–1.88 (m, 6H), 1.78–1.69 (m, 1H), 1.48–1.23 (m, 3H), 0.24 (s, 9H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 139.0 (1C), 133.7 (1C), 131.9 (1C), 128.6 (2C), 128.5 (2C), 126.7 (1C), 101.7 (1C), 94.1 (1C), 58.6 (1C), 36.1 (1C), 35.5 (1C), 32.8 (2C), 25.4 (2C), 25.0 (1C), −0.3 (3C); IR (KBr, cm^{-1}) 698, 760, 845, 1250, 1323, 1452, 1497, 2166, 2857, 2934; HRMS (ESI) *m*/*z*: [M + Na]$^+$ Calcd for $C_{21}H_{29}N_3NaSSi^+$, 406.1744; Found, 406.1750.

1-(4-Methoxyphenyl)-5-(phenethylthio)-4-((trimethylsilyl)ethynyl)-1*H*-1,2,3-triazole (**7e**)



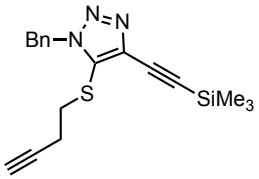
The title compound was obtained in 87.3% (39.1 mg, 95.9 μmol) from **5a** (28.4 mg, 0.110 mmol). Colorless solid; Mp 110–112 ºC; TLC R_f 0.45 (*n*-hexane/EtOAc = 80/20); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.44–7.37 (AA'BB', 2H), 7.29–7.17 (AA'BB'C, 3H), 7.11–7.05 (AA'BB'C, 2H), 7.04–6.98 (AA'BB', 2H), 3.88 (s, 3H), 3.24 (t, 2H, *J* = 7.8 Hz), 2.78 (t, 2H, *J* = 7.8 Hz), 0.26 (s, 9H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 160.5 (1C), 138.9 (1C), 133.9 (1C), 133.7 (1C), 128.53 (1C), 128.50 (2C), 128.48 (2C), 126.7 (3C), 114.4 (2C), 102.3 (1C), 93.7 (1C), 55.6 (1C), 36.0 (1C), 34.9 (1C), −0.4 (3C); IR (KBr, cm^{-1}) 760, 843, 1252, 1514, 2166, 2849, 2922, 2957; HRMS (ESI) *m*/*z*: [M + Na]$^+$ Calcd for $C_{22}H_{25}N_3NaOSSi^+$, 430.1380; Found, 430.1386.

1-(4-Nitrophenyl)-5-(phenethylthio)-4-((trimethylsilyl)ethynyl)-1*H*-1,2,3-triazole (**7f**)



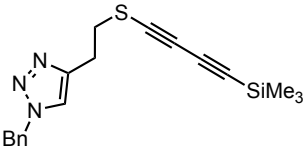
The title compound was obtained in 88.3% (18.2 mg, 43.1 μmol) from **5a** (12.6 mg, 48.8 μmol) using 20 mol% catalyst. Colorless solid; Mp 110–112 ºC; TLC R_f 0.53 (*n*-hexane/EtOAc = 80/20); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.40–8.35 (AA'BB', 2H), 7.78–7.43 (AA'BB', 2H), 7.28–7.18 (AA'BB'C, 3H), 7.09–7.02 (AA'BB'C, 2H), 3.37 (t, 2H, *J* = 7.6 Hz), 2.83 (t, 2H, *J* = 7.6 Hz), 0.28 (s, 9H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 147.8 (1C), 140.3 (1C), 138.4 (1C), 134.8 (1C), 134.0 (1C), 128.6 (2C), 128.4 (2C), 126.9 (1C), 125.6 (2C), 124.7 (2C), 103.8 (1C), 93.0 (1C), 35.7 (1C), 35.1 (1C), −0.4 (3C); IR (KBr, cm^{-1}); 704, 750, 853, 1252, 1522, 1593, 1609, 2164, 2959, 3026, 3063, 3119, 3439; HRMS (ESI) *m*/*z*: [M + H]$^+$ Calcd for $C_{21}H_{23}N_4O_2SSi^+$, 423.1306; Found, 423.1300.

1-Benzyl-5-(but-3-yn-1-ylthio)-4-((trimethylsilyl)ethynyl)-1*H*-1,2,3-triazole (**8**)



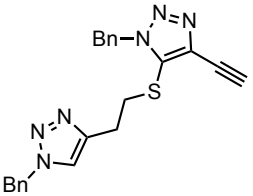
Colorless oil; TLC R_f 0.52 (*n*-hexane/EtOAc = 80/20); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.36–7.29 (AA'BB'C, 3H), 7.29–7.24 (AA'BB'C, 2H), 5.58 (s, 2H), 2.97 (t, 2H, *J* = 7.1 Hz), 2.36 (td, 2H, *J* = 7.1, 2.6 Hz), 2.01 (t, 1H, *J* = 2.6 Hz), 0.26 (s, 9H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 134.8 (1C), 134.5 (1C), 132.4 (1C), 128.9 (2C), 128.5 (1C), 127.8 (2C), 102.2 (1C), 93.4 (1C), 81.0 (1C), 70.3 (1C), 52.4 (1C), 33.1 (1C), 19.9 (1C), −0.4 (3C); IR (Diamond, cm^{-1}); 710, 841, 1250, 1325, 1497, 2167, 2959, 3293; HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{18}H_{21}N_3NaSSi^+$, 362.1118; Found, 362.1115.

1-Benzyl-4-(2-(((trimethylsilyl)buta-1,3-diyn-1-yl)thio)ethyl)-1*H*-1,2,3-triazole (**9a**)



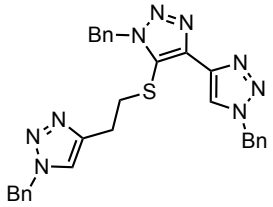
Colorless solid; Mp 71–73 ºC; TLC R_f 0.47 (*n*-hexane/EtOAc = 70/30); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.41–7.35 (AA'BB'C, 3H), 7.33 (s, 1H), 7.28–7.25 (AA'BB'C, 2H), 5.52 (s, 2H), 3.15 (t, 2H, *J* = 7.1 Hz), 3.04 (t, 2H, *J* = 7.1 Hz), 0.19 (s, 9H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 145.0 (1C), 134.6 (1C), 129.0 (2C), 128.6 (1C), 127.9 (2C), 121.7 (1C), 88.5 (1C), 88.0 (1C), 80.1 (1C), 68.9 (1C), 54.0 (1C), 34.6 (1C), 25.6 (1C), −0.5 (3C); IR (KBr, cm^{-1}) 725, 847, 1049, 1130, 1250, 1497, 2160, 2957, 3429; HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{18}H_{21}N_3NaSSi^+$, 362.1118; Found, 362.1118.

1-Benzyl-5-((2-(1-benzyl-1*H*-1,2,3-triazol-4-yl)ethyl)thio)-4-ethynyl-1*H*-1,2,3-triazole (**10aa**)



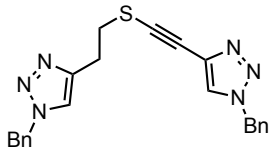
Colorless solid; Mp 74–76 ºC; TLC R_f 0.48 (*n*-hexane/EtOAc = 60/40); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.44–7.33 (m, 3H), 7.31–7.19 (m, 7H), 7.11 (s, 1H), 5.50 (s, 2H), 5.47 (s, 2H), 3.30 (s, 1H), 3.05 (t, 2H, *J* = 7.2 Hz), 2.84 (t, 2H, *J* = 7.2 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 145.2 (1C), 134.6 (1C), 134.5 (1C), 134.4 (1C), 133.0 (1C), 129.1 (2C), 128.9 (2C), 128.8 (1C), 128.5 (1C), 128.1 (2C), 127.8 (2C), 121.2 (1C), 83.9 (1C), 73.2 (1C), 54.1 (1C), 52.4 (1C), 34.2 (1C), 26.1 (1C); IR (KBr, cm^{-1}) 731, 1049, 1221, 1437, 1549, 1605, 2938, 3032, 3136, 3285, 3433; HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{22}H_{20}N_6NaS^+$, 423.1362; Found, 423.1362.

1,1′-Dibenzyl-5-((2-(1-benzyl-1*H*-1,2,3-triazol-4-yl)ethyl)thio)-1*H*,1′*H*-4,4′-bi(1,2,3-triazole) (**11aaa**)



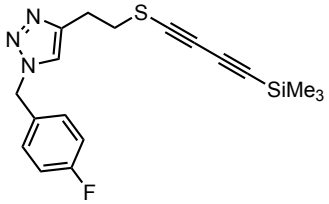
Colorless solid; Mp 131–133 ºC; TLC R_f 0.55 (CH_2Cl_2/MeOH = 95/5); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.00 (s, 1H), 7.39–7.21 (m, 16H), 5.59 (s, 2H), 5.57 (s, 2H), 5.46 (s, 2H), 3.13 (t, 2H, J = 7.2 Hz), 2.81 (t, 2H, J =7.2 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ145.5 (1C), 142.7 (1C), 139.9 (1C), 135.1 (1C), 134.7 (1C), 134.2 (1C), 129.1 (2C), 129.0 (2C), 128.8 (1C), 128.7 (2C), 128.6 (1C), 128.2 (1C), 128.1 (2C), 128.0 (2C), 127.6 (2C), 126.3 (1C), 121.9 (1C), 121.3 (1C), 54.2 (1C), 53.9 (1C), 51.9 (1C), 35.1 (1C), 25.7 (1C); IR (KBr, cm^{-1}) 721, 810, 1051, 1225, 1456, 1497, 1605, 2938, 3032, 3134, 3449; HRMS (ESI) *m*/*z*: [M + H]$^+$ Calcd for $C_{29}H_{28}N_9S^+$, 534.2183; Found, 534.2188.

1-Benzyl-4-(2-(((1-benzyl-1*H*-1,2,3-triazol-4-yl)ethyl)thio)ethynyl)-1*H*-1,2,3-triazole (**12aa**)



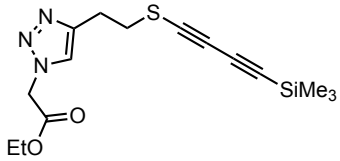
Colorless solid; Mp 83–85 ºC; TLC R_f 0.43 (CH_2Cl_2/MeOH = 95/5); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.51 (s, 1H), 7.40–7.33 (m, 7H), 7.28–7.24 (m, 4H), 5.51 (s, 2H), 5.49 (s, 2H), 3.18 (t, 2H, J = 6.9 Hz), 3.07 (t, 2H, J = 6.9 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 145.4 (1C), 134.7 (1C), 134.0 (1C), 131.3 (1C), 129.2 (2C), 129.1 (2C), 129.0 (1C), 128.6 (1C), 128.1 (2C), 128.0 (2C), 126.4 (1C), 121.8 (1C), 83.2 (1C), 82.5 (1C), 54.3 (1C), 54.0 (1C), 34.7 (1C), 25.8 (1C); IR (KBr, cm^{-1}) 723, 806, 1049, 1221, 1456, 1497, 2181, 2930, 3032, 3134, 3447; HRMS (ESI) *m*/*z*: [M + H]$^+$ Calcd for $C_{22}H_{21}N_6S^+$, 401.1543; Found, 401.1543.

1-(4-Fluorobenzyl)-4-(2-(((trimethylsilyl)buta-1,3-diyn-1-yl)thio)ethyl)-1*H*-1,2,3-triazole (**9g**)



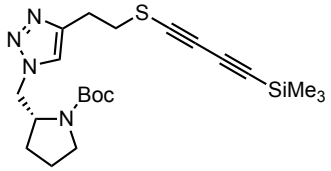
The title compound was obtained in 92.4% (63.2 mg, 0.177 mmol) from **1** (39.5 mg, 0.191 mmol). Colorless solid; Mp 65–67 ºC; TLC R_f 0.48 (*n*-hexane/EtOAc = 60/40); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.33 (s, 1H), 7.28–7.23 (AA'BB', 2H), 7.11–7.04 (AA'BB', 2H), 5.49 (s, 2H), 3.16 (t, 2H, J = 6.9 Hz), 3.05 (t, 2H, J = 6.9 Hz), 0.20 (s, 9H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 162.7 (d, 1C, $J_{C–F}$ = 248.8 Hz), 145.2 (1C), 130.5 (d, 1C, $J_{C–F}$ = 3.6 Hz), 129.8 (d, 2C, $J_{C–F}$ = 8.4 Hz), 121.6 (1C), 116.1 (d, 2C, $J_{C–F}$ = 21.6 Hz), 88.6 (1C), 88.0 (1C), 80.1 (1C), 68.8 (1C), 53.3 (1C), 34.6 (1C), 25.6 (1C), −0.5 (3C); ^{19}F NMR ($CDCl_3$, 376 MHz): δ −113.0 (m); IR (KBr, cm^{-1}) 760, 849, 1049, 1130, 1225, 1250, 1510, 1605, 2160, 2959; HRMS (ESI) *m*/*z*: [M + Na]$^+$ Calcd for $C_{18}H_{20}FN_3NaSSi^+$, 380.1023; Found, 380.1030.

Ethyl 2-(4-(2-(((trimethylsilyl)buta-1,3-diyn-1-yl)thio)ethyl)-1*H*-1,2,3-triazol-1-yl)acetate (**9h**)



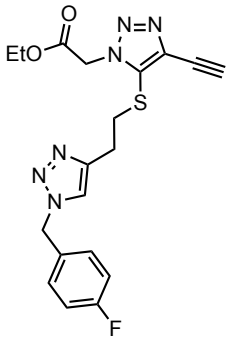
The title compound was obtained in 91.2% (65.7 mg, 0.196 mmol) from **1** (44.3 mg, 0.215 mmol). Colorless solid; Mp 74–76 ºC; TLC R_f 0.41 (*n*-hexane/EtOAc = 60/40); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.58 (s, 1H), 5.15 (s, 2H), 4.28 (q, 2H, J = 7.1 Hz), 3.22 (t, 2H, J = 7.0 Hz), 3.08 (t, 2H, J = 7.0 Hz), 1.31 (t, 3H, J = 7.1 Hz), 0.21 (s, 9H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 166.2 (1C), 145.0 (1C), 123.2 (1C), 88.6 (1C), 88.0 (1C), 80.1 (1C), 68.8 (1C), 62.3 (1C), 50.7 (1C), 34.5 (1C), 25.5 (1C), 14.0 (1C), −0.5 (3C); IR (KBr, cm^{-1}) 760, 849, 1022, 1051, 1130, 1215, 1250, 1751, 2160, 2959; HRMS (ESI) *m*/*z*: [M + H]$^+$ Calcd for $C_{15}H_{22}N_3O_2SSi^+$, 336.1197; Found, 336.1192.

(*R*)-1-((1-Boc-pyrrolidin-2-yl)methyl)-4-(2-(((trimethylsilyl)buta-1,3-diyn-1-yl)thio)ethyl)-1*H*-1,2,3-triazole (**9i**)



The title compound was obtained in 93.4% (171 mg, 0.395 mmol) from **1** (87.3 mg, 0.423 mmol). Yellow oil; TLC R_f 0.43 (*n*-hexane/EtOAc = 60/40); ^{1}H NMR ($CDCl_3$, 500 MHz, * indicates signals of the minor rotamer): δ 7.39 (s, 1H), 7.27 (s, 1H)*, 4.73–4.32 (m, 2H), 4.18–4.06 (m, 1H), 3.46–2.97 (m, 6H), 2.03–1.85 (m, 2H), 1.82–1.64 (m, 1H), 1.59–1.24 (m, 10H), 0.20 (s, 9H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 154.7 (1C), 154.1 (1C)*, 144.8 (1C)*, 144.6 (1C), 122.7 (1C), 122.3 (1C)*, 88.5 (1C), 88.0 (1C), 80.1 (1C), 79.8 (1C), 68.7 (1C), 57.0 (1C), 52.4 (1C)*, 51.3 (1C), 47.0 (1C), 46.6 (1C)*, 34.8 (1C), 34.7 (1C)*, 28.8 (1C)*, 28.4 (3C), 28.0 (1C), 25.5 (1C)*, 25.3 (1C), 23.2 (1C), 22.5 (1C)*, −0.5 (3C); IR (KBr, cm^{-1}) 762, 847, 1022, 1159, 1223, 1323, 1510, 1751, 2168, 2959; HRMS (ESI) *m*/*z*: [M + H]$^+$ Calcd for $C_{21}H_{33}N_4O_2SSi^+$, 433.2088; Found, 433.2082.

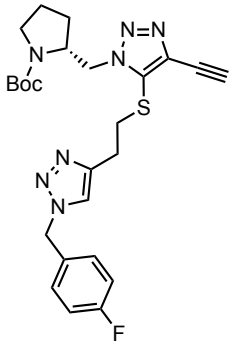
Ethyl 2-(4-ethynyl-5-((2-(1-(4-fluorobenzyl)-1*H*-1,2,3-triazol-4-yl)ethyl)thio)-1*H*-1,2,3-triazol-1-yl)acetate (**10gh**)



The title compound was obtained in 91.1% (59.7 mg, 0.144 mmol) from **9g** (56.5 mg, 0.158 mmol). Yellow oil; TLC R_f 0.41 (CH_2Cl_2/MeOH = 95/5); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.31–7.21 (AA'BB', 2H), 7.23 (s, 1H), 7.11–7.03 (AA'BB', 2H), 5.44 (s, 2H), 5.14 (s, 2H), 4.23 (q, 2H, J = 7.1 Hz), 3.38 (s, 1H), 3.27 (t, 2H, J = 7.2 Hz), 2.98 (t, 2H, J = 7.2 Hz), 1.28 (t, 3H, J = 7.1 Hz); ^{13}C{^{1}H}NMR ($CDCl_3$, 126 MHz): 165.9 (1C) 162.8 (d, 1C, $J_{C–F}$ = 249.0 Hz), 145.2 (1C), 134.4 (1C), 134.1 (1C), 130.4 (d, 1C, $J_{C–F}$ = 3.5 Hz), 130.0 (d, 2C, $J_{C–F}$ = 8.3 Hz), 121.2 (1C), 116.1 (d, 2C, $J_{C–F}$ = 22.0Hz), 84.1 (1C), 73.0 (1C), 62.5(1C), 53.3(1C), 49.4 (1C), 34.3

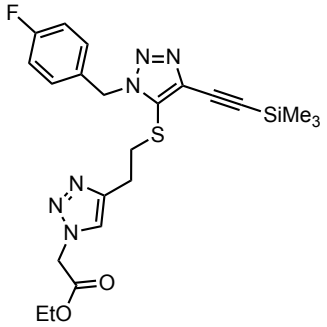
(1C), 26.4 (1C), 14.0 (1C); ^{19}F NMR ($CDCl_3$, 376 MHz): δ −112.8 (m); IR (KBr, cm^{-1}): 492, 527, 773, 1020, 1051, 1223, 1329, 1435, 1510, 1607, 1749, 2124, 2988, 3289, 3431; HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{19}H_{19}FN_6NaO_2S^+$, 437.1166; Found, 437.1177.

(*R*)-1-((1-Boc-pyrrolidin-2-yl)methyl)-4-ethynyl-5-((2-(1-(4-fluorobenzyl)-1*H*-1,2,3-triazol-4-yl)ethyl)thio)-1*H*-1,2,3-triazole (**10gi**)



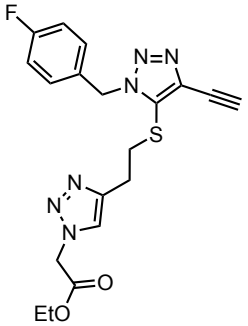
The title compound was obtained in 93.5% (67.7 mg, 0.132 mmol) from **9g** (50.6 mg, 0.142 mmol). Yellow oil; TLC R_f 0.45 (CH_2Cl_2/MeOH = 95/5); ^{1}H NMR ($CDCl_3$, 500 MHz, * indicates signals of the minor rotamer): δ 7.32 (s, 1H), 7.30–7.23 (AA'BB', 2H), 7.21 (s, 1H)*, 7.11–7.03 (AA'BB', 2H), 5.45 (s, 2H), 4.53–4.18 (m, 3H), 3.46–3.17 (m, 5H), 3.02–2.92 (m, 1H), 1.94–1.70 (m, 3H), 1.44 (s, 9H), 1.40 (s, 9H)*, 1.51–1.20 (m, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 162.6 (d, 1C, $J_{C–F}$ = 247.7 Hz), 154.4 (1C)*, 154.0 (1C), 145.1 (1C)*, 145.0 (1C), 134.0 (1C), 133.1 (1C)*, 132.8 (1C), 130.4 (d, 1C, $J_{C–F}$ = 8.8 Hz), 129.8 (d, 2C, $J_{C–F}$ = 6.3 Hz), 121.3 (1C), 121.1 (1C)*, 115.8 (d, 2C, $J_{C–F}$ = 22.6 Hz), 84.0 (1C)*, 83.8 (1C), 80.0 (1C), 79.5 (1C)*, 73.2 (1C), 56.7 (1C)*, 56.1 (1C), 53.0 (1C), 50.6 (1C)*, 50.1 (1C), 46.5 (1C), 46.1 (1C)*, 34.0 (1C), 33.8 (1C)*, 28.4 (1C), 28.21 (3C)*, 28.15 (3C), 27.5 (1C)*, 26.2 (1C), 23.2 (1C), 22.3 (1C)*; ^{19}F NMR ($CDCl_3$, 376 MHz): δ −112.9 (s)*, −113.0 (s); IR (KBr, cm^{-1}) 773, 961, 1051, 1111, 1165, 1223, 1393, 1510, 1607, 1686, 2122, 2974, 3287; HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{25}H_{30}FN_7NaO_2S^+$, 534.2058; Found, 534.2070.

Ethyl 2-(4-(2-((1-(4-fluorobenzyl)-4-((trimethylsilyl)ethynyl)-1*H*-1,2,3-triazol-5-yl)thio)ethyl)-1*H*-1,2,3-triazol-1-yl)acetate (**10hgTMS**)



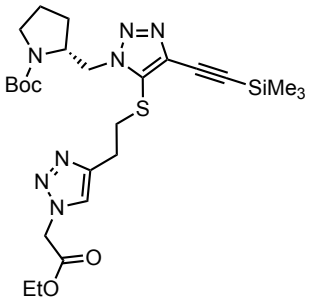
Yellow oil; TLC R_f 0.47 (CH_2Cl_2/MeOH = 95/5); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.37 (s, 1H), 7.28–7.21 (AA'BB', 2H), 7.04–6.96 (AA'BB', 2H), 5.49 (s, 2H), 5.11 (s, 2H), 4.27 (q, 2H, *J* = 7.1 Hz), 3.25 (t, 2H, *J* = 7.1 Hz), 2.96 (t, 2H, *J* = 7.1 Hz), 1.31 (t, 3H, *J* = 7.1 Hz), 0.24 (s, 9H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 166.2 (1C), 162.6 (d, 1C, $J_{C–F}$ = 248.3 Hz), 145.1 (1C), 134.7 (1C), 132.7 (1C), 130.4 (d, 1C, $J_{C–F}$ = 3.6 Hz), 129.8 (d, 2C, $J_{C–F}$ = 8.4 Hz), 122.7 (1C), 115.8 (d, 2C, $J_{C–F}$ = 21.6 Hz), 102.2 (1C), 93.5 (1C), 62.4 (1C), 51.6 (1C), 50.7 (1C), 33.7 (1C), 26.2 (1C), 14.0 (1C), −0.4 (3C); ^{19}F NMR ($CDCl_3$, 376 MHz): δ −113.3 (s); IR (KBr, cm^{-1}) 741, 847, 912, 1022, 1051, 1221, 1510, 1605, 1751, 2168, 2959, 3142, 3464; HRMS (ESI) *m*/*z*: $[M + H]^+$ Calcd for $C_{22}H_{28}FN_6O_2SSi^+$, 487.1742; Found, 487.1732.

Ethyl 2-(4-(2-((4-ethynyl-1-(4-fluorobenzyl)-1*H*-1,2,3-triazol-5-yl)thio)ethyl)-1*H*-1,2,3-triazol-1-yl)acetate (**10hg**)



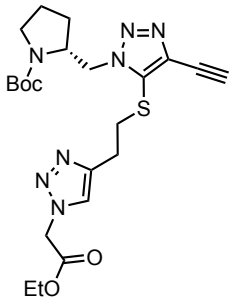
Yellow oil; TLC R_f 0.47 (CH_2Cl_2/MeOH = 95/5); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.42 (s, 1H), 7.29–7.25 (AA'BB', 2H), 7.04–6.98 (AA'BB', 2H), 5.52 (s, 2H), 5.12 (s, 2H), 4.27 (q, 2H, J = 7.1 Hz), 3.45 (s, 1H), 3.19 (t, 2H, J = 7.2 Hz), 2.95 (t, 2H, J = 7.2 Hz), 1.31 (t, 3H, J = 7.1 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 166.3 (1C), 162.7 (d, 1C, $J_{C–F}$ = 249.0 Hz), 145.1 (1C), 134.2 (1C), 133.0 (1C), 130.4 (1C), 129.9 (d, 2C, $J_{C–F}$ = 8.3 Hz), 122.7 (1C), 115.9 (d, 2C, $J_{C–F}$ = 21.9 Hz), 84.1 (1C), 73.1 (1C), 62.4 (1C), 51.7 (1C), 50.7 (1C), 34.1 (1C), 26.1 (1C), 14.0 (1C); ^{19}F NMR ($CDCl_3$, 376 MHz): δ −113.1 (m); IR (KBr, cm^{-1}) 762, 845, 1022, 1169, 1213, 1250, 1391, 1686, 1751, 2168, 2963, 3368; HRMS (ESI) *m*/*z*: [M + Na]$^+$ Calcd for $C_{19}H_{19}FN_6NaO_2S^+$, 437.1166; Found, 437.1176.

Ethyl (*R*)-2-(4-(2-((1-((1-butylpyrrolidin-2-yl)methyl)-4-((trimethylsilyl)ethynyl)-1*H*-1,2,3-triazol-5-yl)thio)ethyl)-1*H*-1,2,3-triazol-1-yl)acetate (**10hiTMS**)



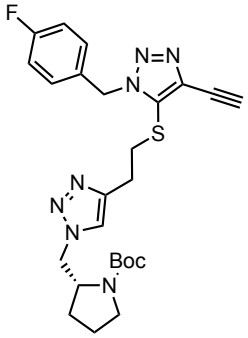
The title compound was obtained in 90.7% (87.6 mg, 0.156 mmol) from **9h** (57.7 mg, 0.172 mmol). Colorless amorphous solid; Mp 80–82 ºC; TLC R_f 0.44 (CH_2Cl_2/MeOH = 95/5); ^{1}H NMR ($CDCl_3$, 400 MHz, * indicates signals of the minor rotamer): δ 7.58 (s, 1H)*, 7.43 (s, 1H), 5.11 (s, 2H), 4.54–4.31 (m, 2H), 4.26 (q, 2H, J = 7.1 Hz), 4.23–4.19 (m, 1H), 3.48–3.07 (m, 2H), 3.02 (d, 2H, J = 7.0 Hz), 1.94–1.52 (m, 4H), 1.45 (s, 9H)*, 1.41 (s, 9H), 1.31 (t, 3H, J = 7.1 Hz), 0.25 (s, 9H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 166.2 (1C), 154.6 (1C), 154.3 (1C)*, 145.3 (1C)*, 145.1 (1C), 133.7 (1C), 122.9 (1C), 122.7 (1C)*, 102.0 (1C), 93.8 (1C), 80.2 (1C), 79.7 (1C)*, 62.4 (1C), 56.8 (1C), 56.4 (1C)*, 50.7 (1C), 50.2 (1C), 46.8 (1C), 46.3 (1C)*, 33.8 (1C), 33.4 (1C)*, 28.42 (1C), 28.35 (1C), 27.6 (1C), 26.4 (1C), 23.4 (1C), 22.5 (1C)*, 14.0 (3C), −0.4 (3C); IR (KBr, cm^{-1}) 743, 912, 1020, 1051, 1223, 1510, 1607, 1749, 2124, 2986, 3287; HRMS (ESI) *m*/*z*: [M + H]$^+$ Calcd for $C_{25}H_{40}N_7O_4SSi^+$, 562.2626; Found, 562.2625.

Ethyl (*R*)-2-(4-(2-((1-((1-Boc-pyrrolidin-2-yl)methyl)-4-ethynyl-1*H*-1,2,3-triazol-5-yl)thio)ethyl)-1*H*-1,2,3-triazol-1-yl)acetate (**10hi**)



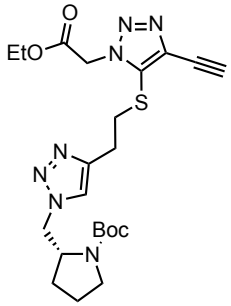
The title compound was obtained in 77.4% (19.3 mg, 39.4 μmol) from **10hiTMS** (28.6 mg, 50.9 μmol). Colorless oil; TLC R_f 0.41 (CH_2Cl_2/MeOH = 95/5); ^{1}H NMR ($CDCl_3$, 400 MHz, * indicates signals of the minor rotamer): δ 7.61 (s, 1H)*, 7.49 (s, 1H), 5.13 (s, 2H), 4.58–4.20 (m, 3H), 4.27 (q, 2H, J = 7.2 Hz), 3.48 (s, 1H), 3.45–3.18 (m, 4H), 3.02 (t, 2H, J = 7.0 Hz), 2.02–1.50 (m, 4H), 1.44 (s, 9H), 1.40 (s, 9H)*, 1.31 (t, 3H, J = 7.2 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 166.3 (1C), 154.6 (1C)*, 154.2 (1C), 145.1 (1C)*, 145.0 (1C), 134.0 (1C), 133.3 (1C)*, 132.9 (1C), 123.0 (1C)*, 122.8 (1C), 84.1 (1C), 84.0 (1C)*, 80.2 (1C)*, 79.6 (1C), 73.3 (1C), 62.3 (1C), 56.8 (1C), 56.3 (1C)*, 50.75 (1C), 50.67 (1C), 50.3 (1C)*, 46.7 (1C), 46.2 (1C)*, 34.1 (1C)*, 33.7 (1C), 28.5 (1C), 28.35 (1C), 28.29 (1C)*, 27.6 (1C)*, 26.2 (1C), 23.3 (1C)*, 22.5 (1C), 14.0 (3C); IR (KBr, cm^{-1}) 773, 912, 1022, 1051, 1219, 1395, 1680, 1751, 2124, 2243, 2978, 3254; HRMS (ESI) *m*/*z*: [M + H]$^+$ Calcd for $C_{22}H_{32}N_7O_4S^+$, 490.2231; Found, 490.2231.

(*R*)-5-((2-(1-((1-Boc-pyrrolidin-2-yl)methyl)-1*H*-1,2,3-triazol-4-yl)ethyl)thio)-4-ethynyl-1-(4-fluorobenzyl)-1*H*-1,2,3-triazole (**10ig**)



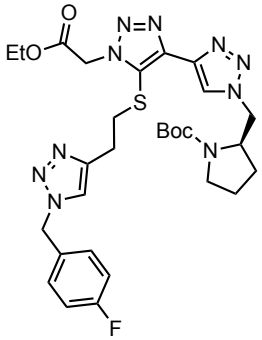
The title compound was obtained in 91.2% (55.0 mg, 0.108 mmol) from **9i** (51.0 mg, 0.118 mmol). Yellow oil; TLC R_f 0.45 (CH_2Cl_2/MeOH = 95/5); ^{1}H NMR ($CDCl_3$, 400 MHz, * indicates signals of the minor rotamer): δ 7.35 (s, 1H), 7.31–7.24 (AA'BB', 2H), 7.21 (s, 1H)*, 7.06–6.98 (AA'BB', 2H), 5.55 (s, 2H), 4.57–4.37 (m, 2H), 4.12–4.02 (m, 1H), 3.52 (s, 1H)*, 3.49 (s, 1H), 3.44–3.21 (m, 1H), 3.21–3.05 (m, 3H), 2.91 (t, 2H, J = 7.2 Hz), 2.03–1.80 (m, 2H), 1.80–1.67 (m, 1H), 1.49 (s, 9H), 1.56–1.23 (m, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 162.5 (d, 1C, $J_{C–F}$ = 247.7 Hz), 154.6 (1C), 154.0 (1C)*, 144.7 (1C)*, 144.6 (1C), 134.1 (1C), 132.9 (1C), 130.2 (d, 1C, $J_{C–F}$ = 3.8 Hz), 129.7 (d, 2C, $J_{C–F}$ = 8.8 Hz), 122.1 (1C), 122.0 (1C)*, 115.8 (d, 2C, $J_{C–F}$ = 3.8 Hz), 84.2 (1C)*, 84.1 (1C), 80.2 (1C)*, 79.8 (1C), 73.1 (1C), 57.1 (1C), 56.9 (1C)*, 52.4 (1C), 51.51 (1C), 51.47 (1C)*, 46.9 (1C), 46.6 (1C)*, 34.4 (1C), 34.3 (1C)*, 28.7 (1C)*, 28.3 (3C), 28.0 (1C), 26.0 (1C), 23.2 (1C), 22.4 (1C)*; ^{19}F NMR ($CDCl_3$, 376 MHz): δ −113.0 (s); IR (KBr, cm^{-1}) 773, 1051, 1119, 1161, 1225, 1398, 1508, 1676, 2122, 2976, 3292; HRMS (ESI) *m*/*z*: [M + Na]$^+$ Calcd for $C_{25}H_{30}FN_7NaO_2S^+$, 534.2058; Found, 534.2056.

Ethyl (*R*)-2-(5-((2-(1-((1-Boc-pyrrolidin-2-yl)methyl)-1*H*-1,2,3-triazol-4-yl)ethyl)thio)-4-ethynyl-1*H*-1,2,3-triazol-1-yl)acetate (**10ih**)



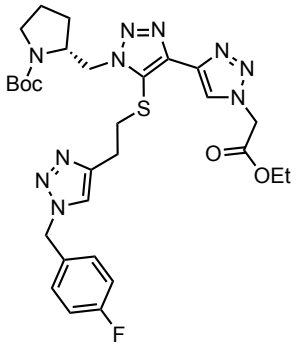
The title compound was obtained in 93.9% (72.8 mg, 0.149 mmol) from **9i** (68.5 mg, 0.158 mmol). Yellow oil; TLC R_f 0.48 (CH_2Cl_2/MeOH = 95/5); ^{1}H NMR ($CDCl_3$, 400 MHz, * indicates signals of the minor rotamer): δ 7.41 (s, 1H)*, 7.28 (s, 1H), 5.20 (s, 2H), 4.60–4.37 (m, 2H), 4.25 (q, 2H, *J* = 7.2 Hz), 4.13–4.04 (m, 1H), 3.58–3.50 (m, 1H), 3.43–3.11 (m, 4H), 3.01 (t, 2H, *J* = 7.0 Hz), 2.02–1.82 (m, 2H), 1.80–1.69 (m, 2H), 1.49 (s, 9H), 1.29 (t, 3H, *J* = 7.2 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 165.8 (1C), 154.7 (1C), 154.2 (1C)*, 145.0 (1C)*, 144.9 (1C), 134.3 (1C), 134.2 (1C), 122.3 (1C), 122.1 (1C)*, 84.3 (1C)*, 84.2 (1C), 80.3 (1C)*, 80.0 (1C), 73.1 (1C), 62.5 (1C), 57.2 (1C), 57.0 (1C)*, 52.5 (1C)*, 51.6 (1C), 49.5 (1C), 47.0 (1C), 46.7 (1C)*, 34.6 (1C), 28.8 (1C)*, 28.5 (1C), 28.1 (1C), 26.3 (1C)*, 26.2 (1C), 23.3 (1C), 22.6 (1C)*, 14.0 (3C); IR (KBr, cm^{-1}) 542, 723, 773, 876, 1022, 1117, 1167, 1217, 1396, 1686, 1749, 2976, 3237, 3460; HRMS (ESI) *m*/*z*: [M + Na]$^+$ Calcd for $C_{22}H_{31}N_7NaO_4S^+$, 512.2050; Found, 512.2040.

Ethyl (*R*)-2-(1′-((1-Boc-pyrrolidin-2-yl)methyl)-5-((2-(1-(4-fluorobenzyl)-1*H*-1,2,3-triazol-4-yl)ethyl)thio)-1*H*,1′*H*-[4,4′-bi(1,2,3-triazol)]-1-yl)acetate (**11ghi**)



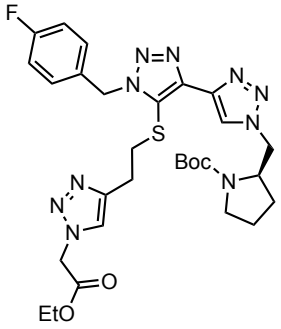
The title compound was obtained in 87.7% (80.9 mg, 0.126 mmol) from **10gh** (59.7 mg, 0.144 mmol). Colorless solid; Mp 66–67 ºC; TLC R_f 0.50 (CH_2Cl_2/MeOH = 92/8); ^{1}H NMR ($CDCl_3$, 500 MHz, * indicates signals of the minor rotamer): δ 8.08 (s, 1H), 7.37 (s, 1H), 7.30–7.22 (AA'BB', 2H), 7.09–7.01 (AA'BB', 2H), 5.44 (s, 2H), 5.24 (s, 2H), 4.80–4.54 (m, 2H), 4.54–4.34 (m, 2H)*, 4.24 (q, 2H, *J* = 7.1 Hz), 4.30–4.12 (m, 1H), 3.48–3.11 (m, 4H), 2.96 (t, 2H, *J* = 7.0 Hz), 2.03–1.35 (m, 4H), 1.51 (s, 9H), 1.28 (t, 3H, *J* = 7.1 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 166.3 (1C), 162.7 (d, 1C, J_{C-F} = 247.7 Hz), 154.8 (1C), 154.1 (1C)*, 145.7 (1C), 142.3 (1C), 139.8 (1C)*, 139.7 (1C), 130.6 (d, 1C, *J* = 3.8 Hz), 129.9 (d, 2C, *J* = 7.5 Hz), 127.6 (1C)*, 127.4 (1C), 122.9 (1C), 122.5 (1C)*, 121.4 (1C), 116.0 (d, 2C, *J* = 21.4 Hz), 80.4 (1C)*, 80.1 (1C), 62.4 (1C), 57.0 (1C), 53.2 (1C), 52.7 (1C)*, 51.7 (1C), 49.3 (1C), 47.1 (1C), 46.6 (1C)*, 35.2 (1C), 28.9 (1C)*, 28.4 (1C), 28.1 (1C), 25.9 (1C), 23.4 (1C), 22.6 (1C)*, 14.0 (3C); ^{19}F NMR ($CDCl_3$, 376 MHz): δ −113.2 (s); IR (KBr, cm^{-1}) 773, 1051, 1119, 1163, 1223, 1395, 1686, 1751, 2924; HRMS (ESI) *m*/*z*: [M + H]$^+$ Calcd for $C_{29}H_{38}FN_{10}O_4S^+$, 641.2777; Found, 641.2776.

Ethyl (*R*)-2-(1′-((1-Boc-pyrrolidin-2-yl)methyl)-5′-((2-(1-(4-fluorobenzyl)-1*H*-1,2,3-triazol-4-yl)ethyl)thio)-1*H*,1′*H*-[4,4'-bi(1,2,3-triazol)]-1-yl)acetate (**11gih**)



The title compound was obtained in 77.7% (54.7 mg, 85.4 μmol) from **10gi** (56.2 mg, 0.110 mmol). Colorless solid; Mp 48–53 ºC; TLC R_f 0.47 (CH_2Cl_2/MeOH = 92/8); ^{1}H NMR ($CDCl_3$, 400 MHz, * indicates signals of the minor rotamer): δ 8.25 (s, 1H), 7.46 (s, 1H), 7.31 (s, 1H)*, 7.30–7.21 (AA'BB', 2H), 7.09–6.99 (AA'BB', 2H), 5.44 (s, 2H), 5.24 (s, 2H), 4.68–4.34 (m, 2H), 4.28 (q, 2H, J = 7.1 Hz), 4.34–4.24 (m, 1H), 3.49–3.19 (m, 4H), 2.99–2.88 (m, 2H), 1.93–1.64 (m, 4H), 1.43 (s, 9H), 1.31 (t, 3H, J = 7.2 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 166.0 (1C), 162.7 (d, 1C, $J_{C–F}$ = 247.7 Hz), 154.6 (1C), 154.2 (1C)*, 145.7 (1C), 145.5 (1C)*, 141.6 (1C), 140.1 (d, 1C, J = 5.0 Hz), 129.9 (d, 2C, J = 7.5 Hz), 130.7 (1C), 130.5 (1C)*, 129.9 (d, 2C, J = 8.8 Hz), 127.3 (1C), 127.2 (1C)*, 123.3 (1C), 121.6 (1C), 121.4 (1C)*, 115.9 (d, 2C, J = 21.4 Hz), 80.0 (1C)*, 79.5 (1C), 62.4 (1C), 56.8 (1C)*, 56.5 (1C), 53.1 (1C), 50.9 (1C), 50.2(1C)*, 49.8 (1C), 46.7 (1C), 46.3 (1C)*, 35.0 (1C), 28.5 (1C), 28.4 (1C), 27.6 (1C)*, 25.9 (1C), 23.3 (1C), 22.5 (1C), 14.0 (3C); ^{19}F NMR ($CDCl_3$, 376 MHz): δ −113.2 (s)*, −113.4 (s); IR (KBr, cm^{-1}) 542, 773, 912, 1051, 1223, 1395, 1510, 1605, 1686, 1751, 2243, 2976, 3134, 3412; HRMS (ESI) *m*/*z*: [M + H]$^+$ Calcd for $C_{29}H_{38}FN_{10}O_4S^+$, 641.2777; Found, 641.2783.

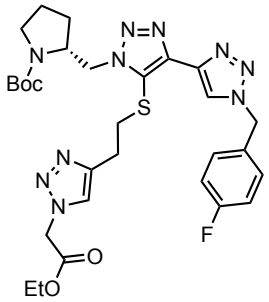
Ethyl (*R*)-2-(4-(2-((1′-((1-Boc-pyrrolidin-2-yl)methyl)-1-(4-fluorobenzyl)-1*H*,1′*H*-[4,4′-bi(1,2,3-triazol)]-5-yl)thio)ethyl)-1*H*-1,2,3-triazol-1-yl)acetate (**11hgi**)



The title compound was obtained in 86.5% (23.8 mg, 37.1 μmol) from **10hg** (17.8 mg, 42.9 μmol). Colorless solid; Mp 38–43 ºC; TLC R_f 0.53 (CH_2Cl_2/MeOH = 92/8); ^{1}H NMR ($CDCl_3$, 400 MHz, * indicates signals of the minor rotamer): δ 8.07 (s, 1H), 7.49 (s, 1H), 7.36–7.27 (AA'BB', 2H), 7.05–6.96 (AA'BB', 2H), 5.62 (s, 2H), 5.12 (s, 2H), 4.77–4.53 (m, 2H)*, 4.53–4.40 (m, 2H), 4.26 (q, 2H, J = 7.2 Hz), 4.21–4.11 (m, 1H), 3.48–3.10 (m, 2H), 3.24 (t, 2H, J = 6.9 Hz), 2.91 (t, 2H, J = 6.9 Hz), 2.02–1.86 (m, 2H), 1.86–1.63 (m, 1H), 1.50 (s, 9H), 1.55–1.36 (m, 1H), 1.30 (t, 3H, J = 7.2 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 166.3 (1C), 162.5 (d, 1C, $J_{C–F}$ = 247.7 Hz), 154.7 (1C), 154.1 (1C)*, 145.4 (1C), 142.7 (1C), 142.6 (1C)*, 139.7 (1C)*, 139.6 (1C), 130.9 (d, 1C, J = 3.8 Hz), 129.8 (d, 2C, J = 8.8 Hz), 126.2 (1C)*, 126.1 (1C), 122.9 (1C), 122.7 (1C), 122.5 (1C)*, 115.7 (d, 2C, J = 21.4 Hz), 80.3 (1C)*, 80.0 (1C), 62.2 (1C), 57.0 (1C), 52.6 (1C)*, 51.6 (1C), 51.3 (1C), 50.7 (1C), 47.0 (1C), 46.6 (1C)*, 35.1 (1C), 28.8 (1C)*, 28.4 (1C), 28.0 (1C), 25.6 (1C), 23.3 (1C), 22.5 (1C)*, 14.0 (3C); ^{19}F NMR ($CDCl_3$, 376 MHz): δ −113.5 (s); IR (KBr, cm^{-1}) 775, 908, 1051, 1223, 1396, 1508, 1676,

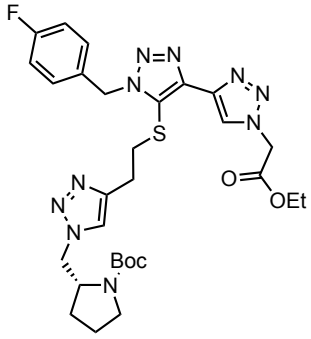
1751, 2052, 2243, 2978, 3248; HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{29}H_{37}FN_{10}NaO_4S^+$, 663.2596; Found, 663.2602.

Ethyl (*R*)-2-(4-(2-((1-((1-Boc-pyrrolidin-2-yl)methyl)-1′-(4-fluorobenzyl)-1*H*,1′*H*-[4,4′-bi(1,2,3-triazol)]-5-yl)thio)ethyl)-1*H*-1,2,3-triazol-1-yl)acetate (**11hig**)



The title compound was obtained in 83.3% (25.3 mg, 39.5 μmol) from **10hi** (23.2 mg, 47.4 μmol). Colorless solid; Mp 39–44 ºC; TLC R_f 0.47 (CH_2Cl_2/MeOH = 92/8); ^{1}H NMR ($CDCl_3$, 400 MHz, * indicates signals of the minor rotamer): δ 8.03 (s, 1H), 7.69 (s, 1H), 7.52 (s, 1H)*, 7.37–7.30 (AA'BB', 2H), 7.12–7.04 (AA'BB', 2H), 5.57 (s, 2H), 5.12 (s, 2H), 5.10 (s, 2H)*, 4.66–4.36 (m, 2H), 4.26 (q, 2H, J = 7.2 Hz), 4.33–4.21 (m, 1H), 3.47–3.17 (m, 2H), 3.39 (t, 2H, J = 7.1 Hz), 2.97 (t, 2H, J = 7.1 Hz), 1.91–1.55 (m, 4H), 1.44 (s, 9H), 1.42 (s, 9H)*, 1.30 (t, 3H, J = 7.2 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 166.3 (1C), 162.7 (d, 1C, $J_{C–F}$ = 247.7 Hz), 154.5 (1C), 154.1 (1C)*, 145.5 (1C), 145.3 (1C)*, 141.7 (1C), 140.1 (1C), 130.2 (d, 1C, J = 2.5 Hz), 130.0 (d, 2C, J = 8.8 Hz), 127.1 (1C), 126.9 (1C)*, 123.1 (1C), 122.9 (1C)*, 121.8 (1C), 116.0 (d, 2C, J = 21.4 Hz), 79.9 (1C)*, 79.4 (1C), 62.2 (1C)*, 62.1 (1C), 56.8 (1C)*, 56.4 (1C), 53.4 (1C), 50.6 (1C), 50.1 (1C)*, 49.7 (1C), 46.6 (1C), 46.2 (1C)*, 35.1 (1C), 35.0 (1C)*, 28.3 (1C), 27.5 (1C), 25.7 (1C), 23.2 (1C), 22.4 (1C)*, 13.9 (3C); ^{19}F NMR ($CDCl_3$, 376 MHz): δ −112.7 (s)*, −112.8 (s); IR (KBr, cm^{-1}) 772, 1051, 1119, 1169, 1223, 1395, 1510, 1676, 1751, 2058, 2978, 3312; HRMS (ESI) *m*/*z*: $[M + H]^+$ Calcd for $C_{29}H_{38}FN_{10}O_4S^+$, 641.2777; Found, 641.2778.

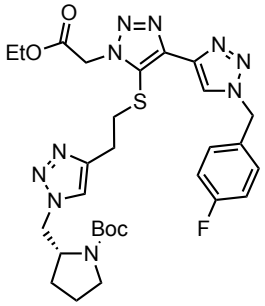
Ethyl (*R*)-2-(5′-((2-(1-((1-Boc-pyrrolidin-2-yl)methyl)-1*H*-1,2,3-triazol-4-yl)ethyl)thio)-1′-(4-fluorobenzyl)-1*H*,1′*H*-[4,4'-bi(1,2,3-triazol)]-1-yl)acetate (**11igh**)



The title compound was obtained in 81.0% (48.5 mg, 75.7 μmol) from **10ig** (47.8 mg, 93.4 μmol). Colorless amorphous solid; Mp 31–33 ºC; TLC R_f 0.47 (CH_2Cl_2/MeOH = 92/8); ^{1}H NMR ($CDCl_3$, 400 MHz, * indicates signals of the minor rotamer): δ 8.27 (s, 1H), 7.36–7.27 (m, 3H), 7.06–6.97 (AA'BB', 2H), 5.66 (s, 2H), 5.24 (s, 2H), 4.80–4.32 (m, 2H), 4.28 (q, 2H, J = 7.1 Hz), 4.15–4.02 (m, 1H), 3.46–3.12 (m, 2H), 3.18 (t, 2H, J = 6.8 Hz), 2.88 (t, 2H, J = 6.8 Hz), 1.97–1.65 (m, 4H), 1.48 (s, 9H), 1.31 (t, 3H, J = 7.1 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 166.0 (1C), 162.5 (d, 1C, $J_{C–F}$ = 247.7 Hz), 154.7 (1C), 154.1 (1C)*, 145.2 (1C)*, 145.1 (1C), 142.5 (1C), 139.9 (1C), 130.9 (d, 1C, J = 3.8 Hz), 129.8 (d, 2C, J = 8.8 Hz), 126.4 (1C), 123.4 (1C), 122.1 (1C), 115.8 (d, 2C, J = 21.4 Hz), 80.2 (1C)*, 79.8 (1C), 62.4 (1C), 57.0 (1C), 52.4 (1C), 51.5 (1C)*, 51.3 (1C), 50.9 (1C), 46.9 (1C), 46.6 (1C)*, 35.4 (1C), 28.8 (1C)*,

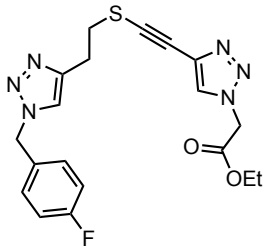
28.4 (1C), 28.1 (1C), 25.8 (1C), 23.3 (1C), 22.5 (1C)*, 14.0 (3C); ^{19}F NMR ($CDCl_3$, 376 MHz): δ −113.5 (s); IR (KBr, cm^{-1}) 773, 1161, 1221, 1395, 1510, 1690, 1751, 2928, 2976, 3453; HRMS (ESI) *m*/*z*: $[M + H]^+$ Calcd for $C_{29}H_{38}FN_{10}O_4S^+$, 641.2777; Found, 641.2780.

Ethyl (*R*)-2-(5-((2-(1-((1-Boc-pyrrolidin-2-yl)methyl)-1*H*-1,2,3-triazol-4-yl)ethyl)thio)-1′-(4-fluorobenzyl)-1*H*,1′*H*-[4,4′-bi(1,2,3-triazol)]-1-yl)acetate (**11ihg**)



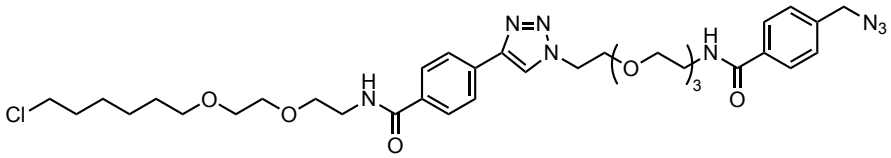
The title compound was obtained in 82.6% (73.5 mg, 0.115 mmol) from **10ih** (68.0 mg, 0.139 mmol). Colorless solid; Mp 35–37 ºC; TLC R_f 0.53 (CH_2Cl_2/MeOH = 92/8); ^{1}H NMR ($CDCl_3$, 400 MHz, * indicates signals of the minor rotamer): δ 8.08 (s, 1H), 7.36 (s, 1H), 7.39–7.31 (AA'BB', 2H), 7.12–7.04 (AA'BB', 2H), 5.59 (s, 2H), 5.28 (s, 2H), 4.56–4.41 (m, 2H), 4.41–4.28 (m, 2H)*, 4.24 (q, 2H, *J* = 7.1 Hz), 4.13–4.04 (m, 1H), 3.40 (t, 2H, *J* = 7.2 Hz), 3.32–3.11 (m, 2H), 3.03–2.92 (m, 2H), 1.99–1.61 (m, 4H), 1.48 (s, 9H), 1.28 (t, 3H, *J* = 7.1 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 166.2 (1C), 162.8 (d, 1C, $J_{C–F}$ = 247.7 Hz), 154.6 (1C), 154.1 (1C), 145.3 (d, 1C, *J* = 8.8 Hz), 142.2 (1C), 140.0 (1C), 130.1 (d, 2C, *J* = 8.8 Hz), 127.5 (1C), 122.1 (1C), 121.9 (1C), 116.1 (d, 2C, *J* = 22.6 Hz), 80.1 (1C)*, 79.8 (1C), 62.3 (1C), 57.0 (1C), 53.4 (1C), 52.4 (1C)*, 51.5 (1C), 49.3 (1C), 46.9 (1C), 46.5 (1C)*, 35.4 (1C), 28.7 (1C)*, 28.4 (1C), 28.0 (1C), 25.8 (1C), 23.2 (1C), 22.5 (1C)*, 14.0 (3C); ^{19}F NMR ($CDCl_3$, 376 MHz): δ −112.8 (m); IR (KBr, cm^{-1}) 775, 1051, 1163, 1223, 1396, 1512, 1694, 1746, 2014, 2978, 3339; HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{29}H_{37}FN_{10}NaO_4S^+$, 663.2596; Found, 663.2602.

Ethyl 2-(4-(((2-(1-(4-fluorobenzyl)-1*H*-1,2,3-triazol-4-yl)ethyl)thio)ethynyl)-1*H*-1,2,3-triazol-1-yl)acetate (**12gh**)



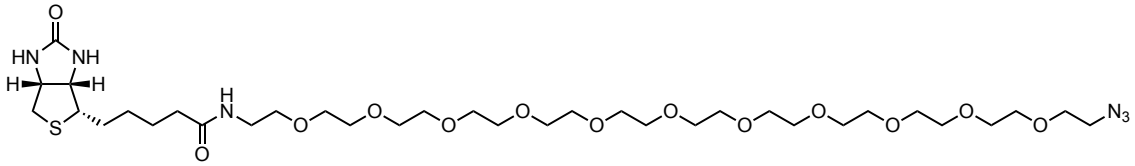
The title compound was obtained in 91.7% (76.4 mg, 0.184 mmol) from **9g** (71.9 mg, 0.201 mmol). Colorless solid; Mp 96–98 ºC; TLC R_f 0.47 (CH_2Cl_2/MeOH = 95/5); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.76 (s, 1H), 7.41 (s, 1H), 7.29–7.23 (AA'BB', 2H), 7.09–7.02 (AA'BB', 2H), 5.48 (s, 2H), 5.14 (s, 2H), 4.28 (q, 2H, *J* = 7.1 Hz), 3.21 (t, 2H, *J* = 6.7 Hz), 3.11 (t, 2H, *J* = 6.7 Hz), 1.31 (t, 3H, *J* = 7.1 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 165.8 (1C), 162.6 (d, 1C, $J_{C–F}$ = 248.2 Hz), 145.3 (1C), 131.2 (1C), 130.6 (d, 1C, $J_{C–F}$ = 3.0 Hz), 129.8 (d, 2C, $J_{C–F}$ = 8.3 Hz), 127.9 (1C), 121.8 (1C), 115.9 (d, 2C, $J_{C–F}$ = 21.9 Hz), 83.3 (1C), 82.3 (1C), 62.5 (1C), 53.1 (1C), 50.8 (1C), 34.6 (1C), 25.6 (1C), 13.9 (1C); ^{19}F NMR ($CDCl_3$, 376 MHz): δ −113.2 (s); IR (Diamond, cm^{-1}) 498, 538, 772, 822, 1061, 1096, 1508, 1603, 1751, 3126; HRMS (ESI) *m*/*z*: $[M + H]^+$ Calcd for $C_{19}H_{20}FN_6O_2S^+$, 415.1347; Found, 415.1344.

4-(Azidomethyl)-*N*-(2-(2-(2-(2-(4-(4-((2-(2-((6-chlorohexyl)oxy)ethoxy)ethyl)carbamoyl)phenyl)-1*H*-1,2,3-triazol-1-yl)ethoxy)ethoxy)ethoxy)ethyl)benzamide (**13$_{long}$**)



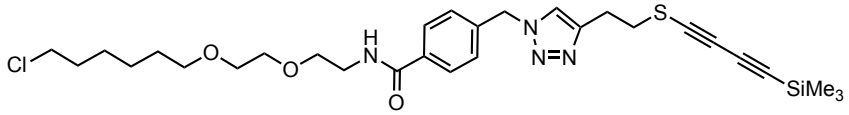
Colorless solid; Mp 69–71 ºC; TLC R_f 0.61 (CH_2Cl_2/MeOH = 90/10); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.03 (s, 1H), 7.92–7.78 (m, 6H), 7.40–7.33 (AA'BB', 2H), 6.83 (brs, 2H), 4.55 (t, 2H, *J* = 5.0 Hz), 4.39 (s, 2H), 3.88 (t, 2H, *J* = 5.0 Hz), 3.73–3.58 (m, 20H), 3.49 (t, 2H, *J* = 6.7 Hz), 3.46 (t, 2H, *J* = 6.7 Hz), 1.72 (tt, 2H, *J* = 7.0, 7.0 Hz), 1.67–1.53 (m, 2H), 1.46–1.28 (m, 4H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 167.0 (1C), 166.9 (1C), 146.5 (1C), 138.7 (1C), 134.3 (1C), 133.8 (1C), 133.6 (1C), 128.1 (2C), 127.6 (2C), 127.5 (2C), 125.5 (2C), 121.6 (1C), 71.2 (1C), 70.4 (1C), 70.33 (1C), 70.27 (1C), 70.1 (1C), 70.0 (1C), 69.9 (1C), 69.6 (1C), 69.5 (1C), 69.2 (1C), 54.1 (1C), 50.3 (1C), 45.0 (1C), 39.6 (2C), 32.4 (1C), 29.3 (1C), 26.6 (1C), 25.3 (1C); IR (KBr, cm^{-1}) 714, 858, 1117, 1302, 1458, 1541, 1639, 1713, 2100, 2866, 2932, 3343; HRMS (ESI) *m*/*z*: [M + Na]$^+$ Calcd for $C_{35}H_{49}ClN_8NaO_7^+$, 751.3305; Found, 751.3330.

N-(35-Azido-3,6,9,12,15,18,21,24,27,30,33-undecaoxapentatriacontyl)-5-((3a*S*,4*S*,6a*R*)-2-oxohexahydro-1*H*-thieno(3,4-*d*)imidazol-4-yl)pentanamide (**15$_{long}$**)



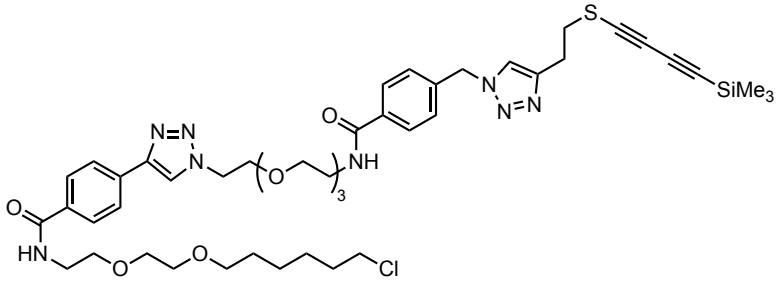
Sticky colorless solid; Mp 86–88 ºC; TLC R_f 0.59 (CH_2Cl_2/MeOH = 90/10); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.85 (t, 1H, *J* = 5.4 Hz), 6.15 (brs, 1H), 5.25 (brs, 1H), 4.32 (dd, 1H, *J* = 7.2, 4.8 Hz), 4.32 (dd, 1H, *J* = 7.2, 5.2 Hz), 3.77–3.59 (m, 42H), 3.56 (t, 2H, *J* = 4.8 Hz), 3.51–3.41 (m, 2H), 3.39 (t, 2H, *J* = 5.2 Hz), 3.14 (td, 1H, *J* = 7.3, 5.2 Hz), 2.91 (dd, 1H, *J* = 12.8, 4.8 Hz), 2.74 (d, 1H, *J* = 12.8 Hz), 2.28–2.18 (m, 2H), 1.82–1.60 (m, 4H), 1.45 (tt, 2H, *J* = 7.6, 7.6 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 173.1 (1C), 164.0 (1C), 70.33 (1C), 70.31 (1C), 70.28 (1C), 70.2 (14C), 70.1 (1C), 70.0 (1C), 69.72 (1C), 69.69 (1C), 69.6 (1C), 61.4 (1C), 59.9 (1C), 55.5 (1C), 50.3 (1C), 40.2 (1C), 38.8 (1C), 35.6 (1C), 28.0 (1C), 27.8 (1C), 25.3 (1C); IR (KBr, cm^{-1}) 642, 839, 951, 1105, 1250, 1350, 1458, 1545, 1690, 2106, 2918, 3080, 3285; HRMS (ESI) *m*/*z*: [M + Na]$^+$ Calcd for $C_{34}H_{64}N_6NaO_{13}S^+$, 819.4144; Found, 819.4145.

Platform–HTL conjugate **16$_{short}$**



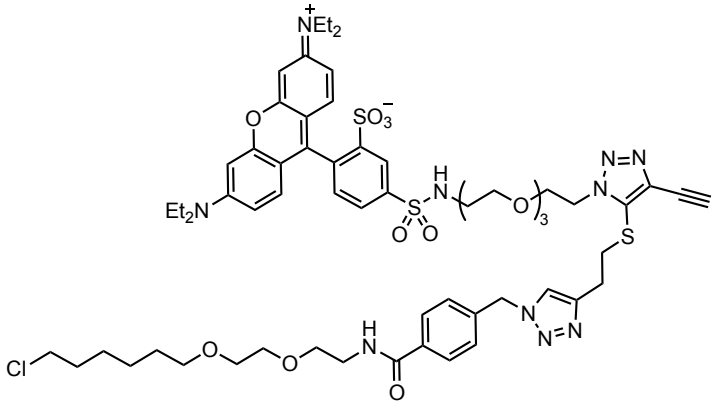
Colorless solid; Mp 40–42 ºC; TLC R_f 0.55 (CH_2Cl_2/MeOH = 92/8); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.83–7.77 (AA'BB', 2H), 7.37 (s, 1H), 7.33–7.29 (AA'BB', 2H), 6.71 (brs, 1H), 5.56 (s, 2H), 3.70–3.63 (m, 6H), 3.61–3.57 (m, 2H), 3.52 (t, 2H, J = 6.6 Hz), 3.46 (t, 2H, J = 6.6 Hz), 3.17 (t, 2H, 6.8 Hz), 3.06 (t, 2H, J = 6.8 Hz), 1.74 (tt, 2H, J = 7.0, 7.0 Hz), 1.57 (tt, 2H, J = 7.0, 7.0 Hz), 1.47–1.29 (m, 4H), 0.19 (s, 9H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 166.6 (1C), 145.3 (1C), 138.0 (1C), 134.9 (1C), 127.9 (2C), 127.8 (2C), 121.9 (1C), 88.6 (1C), 88.0 (1C), 80.1 (1C), 71.2 (1C), 70.2 (1C), 70.0 (1C), 69.6 (1C), 68.8 (1C), 53.5 (1C), 45.0 (1C), 39.7 (1C), 34.6 (1C), 32.4 (1C), 29.4 (1C), 26.6 (1C), 25.6 (1C), 25.3 (1C), −0.4 (3C); IR (Br, cm^{-1}) 845, 1051, 1128, 1250, 1431, 1541, 1616, 2073, 2160, 2864, 2938, 3528; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{29}H_{42}ClN_4O_3SSi^+$, 589.2430; Found, 589.2430.

Platform–HTL conjugate **16$_{long}$**



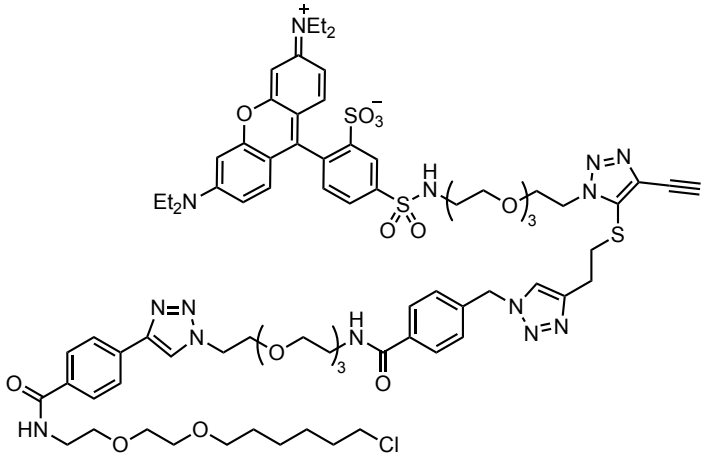
The title compound was obtained in 93.1% (48.1 mg, 51.4 μmol) from **1** (11.4 mg, 55.2 μmol). Colorless solid; Mp 77–79 ºC; TLC R_f 0.47 (CH_2Cl_2/MeOH = 92/8); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.05 (s, 1H), 7.90–7.82 (m, 4H), 7.81–7.77 (AA'BB', 2H), 7.42 (s, 1H), 7.29–7.24 (AA'BB', 2H), 6.91 (brs, 1H), 6.88 (brs, 1H), 5.45 (s, 2H), 4.54 (t, 2H, J = 4.9 Hz), 3.87 (t, 2H, J = 4.9 Hz), 3.72–3.65 (m, 6H), 3.63–3.57 (m, 14H), 3.49 (t, 2H, J = 6.7 Hz), 3.46 (t, 2H, J = 6.7 Hz), 3.16 (t, 2H, J = 6.8 Hz), 3.05 (t, 2H, J = 6.8 Hz), 1.72 (tt, 2H, J = 7.1, 7.1 Hz), 1.57 (tt, 2H, J = 7.1, 7.1 Hz), 1.46–1.28 (m, 4H), 0.19 (s, 9H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 167.0 (1C), 166.7 (1C), 146.6 (1C), 145.3 (1C), 138.0 (1C), 134.8 (1C), 133.8 (1C), 133.6 (1C), 127.81 (2C), 127.78 (2C), 127.6 (2C), 125.5 (2C), 122.0 (1C), 121.6 (1C), 88.6 (1C), 88.0 (1C), 80.1 (1C), 71.2 (1C), 70.41 (1C), 70.37 (1C), 70.3 (1C), 70.2 (1C), 70.1 (1C), 69.9 (1C), 69.61 (1C), 69.56 (1C), 69.3 (1C), 68.8 (1C), 53.5 (1C), 50.3 (1C), 45.0 (1C), 39.7 (2C), 34.6 (1C), 32.4 (1C), 29.4 (1C), 26.6 (1C), 25.6 (1C), 25.3 (1C), −0.5 (3C); IR (KBr, cm^{-1}) 654, 849, 1128, 1249, 1304, 1352, 1458, 1537, 1643, 2160, 2864, 2934, 3343; HRMS (ESI) m/z: [M + Na]$^+$ Calcd for $C_{46}H_{63}ClN_8NaO_7SSi^+$, 957.3890; Found, 957.3863.

Platform–HTL–Rhodamine conjugate **17$_{short}$**



Red solid; Mp >250 ºC; TLC R_f 0.42 (CH_2Cl_2/MeOH = 92/8); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.83 (d, 1H, J = 1.8 Hz), 7.99 (dd, 1H, J = 7.9, 1.8 Hz), 7.84–7.79 (AA'BB', 2H), 7.66 (s, 1H), 7.37–7.32 (AA'BB', 2H), 7.28–7.17 (m, 4H), 6.77 (dd, 2H, J = 9.5, 2.4 Hz), 6.64 (d, 2H, J = 2.4 Hz), 6.47 (brs, 1H), 5.51 (s, 2H), 4.51 (t, 2H, J = 5.2 Hz), 3.87 (t, 2H, J = 5.2 Hz), 3.63–3.41 (m, 31H), 3.33–3.23 (m, 4H), 2.94 (t, 2H, J = 7.1 Hz), 1.74 (tt, 2H, J = 7.1, 7.1 Hz), 1.55 (tt, 2H, J = 7.1, 7.1 Hz), 1.47–1.22 (m, 16H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 166.7 (1C), 158.8 (1C), 157.8 (2C), 155.4 (2C), 148.1 (1C), 145.3 (1C), 142.0 (1C), 138.2 (1C), 134.5 (1C), 134.1 (1C), 133.8 (1C), 133.5 (1C), 133.3 (2C), 129.8 (1C), 128.2 (2C), 127.8 (2C), 127.2 (1C), 127.1 (1C), 122.5 (1C), 114.2 (2C), 113.5 (2C), 95.6 (2C), 84.1 (1C), 73.4 (1C), 71.1 (1C), 70.5 (1C), 70.4 (1C), 70.23 (1C), 70.22 (1C), 70.1 (1C), 70.0 (1C), 69.5 (1C), 69.4 (1C), 69.1 (1C), 53.3 (1C), 48.4 (1C), 45.8 (4C), 45.1 (1C), 43.2 (1C), 39.5 (1C), 34.5 (1C), 32.5 (1C), 29.4 (1C), 26.6 (1C), 26.1 (1C), 25.3 (1C), 12.6 (4C); IR (KBr, cm^{-1}) 735, 822, 1076, 1134, 1180, 1246, 1339, 1466, 1591, 1649, 2868, 2932, 3219; HRMS (ESI) m/z: [M + Na]$^+$ Calcd for $C_{61}H_{79}ClN_{10}NaO_{12}S_3^+$, 1297.4622; Found, 1297.4630.

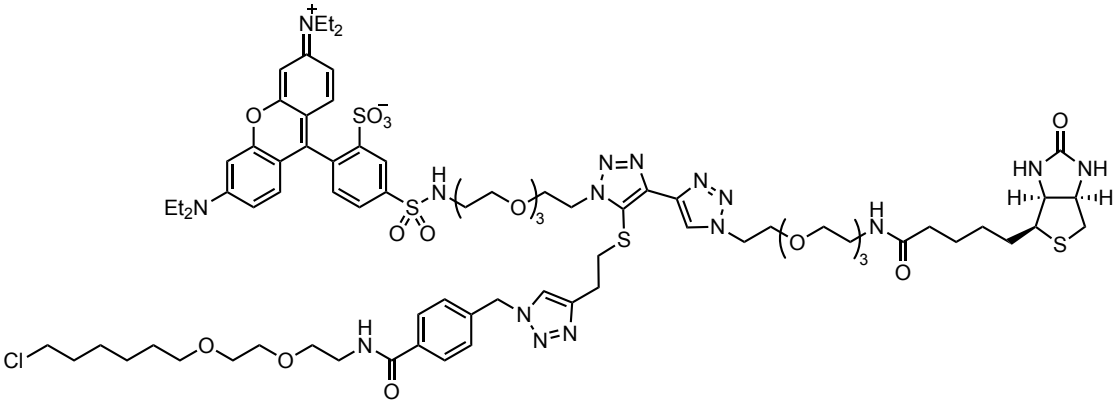
Platform–HTL–Rhodamine conjugate **17$_{long}$**



The title compound was obtained in 81.5% (61.2 mg, 37.7 μmol) from **16$_{long}$** (43.3 mg, 46.3 μmol). Red solid; Mp >250 ºC (decomp.); TLC R_f 0.41 (CH_2Cl_2/MeOH = 92/8); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.86 (d, 1H, J = 1.7 Hz), 8.19 (s, 1H), 7.98 (dd, 1H, J = 7.9, 1.7 Hz), 7.87–7.73 (m, 6H), 7.65 (s, 1H), 7.56 (t, 1H, J = 5.2 Hz), 7.31 (d, 2H, J = 8.2 Hz), 7.19 (d, 1H, J = 7.9 Hz), 7.17–7.10 (m, 3H), 6.71 (dd, 2H, J = 9.5, 2.3 Hz), 6.52 (d, 3H, J = 2.3 Hz), 5.51 (s, 2H), 4.50 (t, 2H, J = 5.1 Hz), 4.44 (t, 2H, J = 4.9 Hz), 3.88 (t, 2H, J = 5.1 Hz), 3.82 (t, 2H, J = 5.0 Hz), 3.71–3.39 (m, 41H), 3.29 (t, 2H, J = 7.1 Hz), 3.26–3.20 (m, 2H), 2.95 (t, 2H, J = 7.1 Hz), 1.72 (tt, 2H, J = 7.1, 7.1 Hz), 1.56 (tt, 2H, J = 7.1, 7.1 Hz), 1.45–1.29 (m, 4H), 1.24 (t, 14H, J = 7.1 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 167.0 (1C), 166.8 (1C), 158.2 (1C),

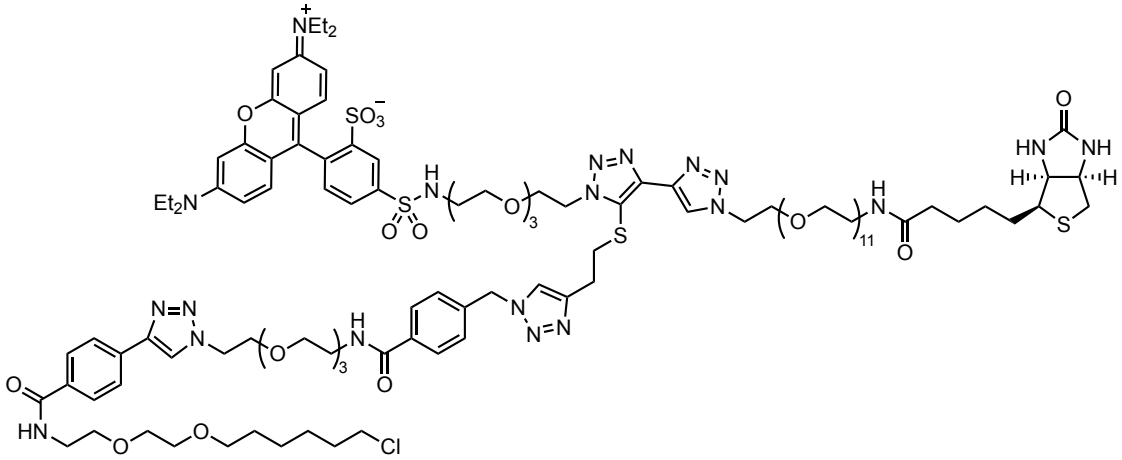
157.6 (2C), 155.3 (2C), 147.8 (1C), 146.4 (1C), 145.3 (2C), 142.1 (1C), 138.1 (1C), 134.5 (1C), 134.1 (1C), 133.8 (1C), 133.7 (1C), 133.6 (1C), 133.5 (1C), 133.0 (2C), 130.0 (1C), 128.1 (2C), 127.9 (2C), 127.6 (2C), 127.2 (1C), 127.1 (1C), 125.3 (2C), 122.5 (1C), 122.2 (1C), 114.1 (2C), 113.4 (2C), 95.5 (1C), 84.2 (1C), 73.4 (1C), 71.2 (2C), 70.5 (1C), 70.3 (3C), 70.19 (1C), 70.15 (1C), 70.14 (2C), 70.06 (1C), 69.9 (2C), 69.5 (1C), 69.4 (1C), 69.3 (1C), 69.0 (1C), 53.3 (1C), 50.0 (1C), 48.3 (1C), 45.8 (4C), 45.0 (1C), 43.1 (1C), 39.5 (1C), 34.5 (1C), 32.4 (1C), 29.4 (1C), 26.6 (1C), 26.1 (1C), 25.3 (1C), 12.5 (4C); IR (KBr, cm^{-1}) 733, 822, 922, 1076, 1246, 1416, 1591, 1647, 2868, 2932, 3132, 3296; HRMS (ESI) *m*/*z*: $[M + 2Na]^{2+}$ Calcd for $C_{78}H_{101}ClN_{14}Na_2O_{16}S_3^{2+}$, 833.3078; Found, 833.3071.

Platform–HTL–Rhodamine–biotin conjugate **18$_{short}$**



Red solid; Mp >250 ºC (decomp.); TLC R_f 0.46 (CH_2Cl_2/MeOH = 90/10); ^1H NMR ($CDCl_3$, 500 MHz): δ 8.87 (d, 1H, *J* = 2.0 Hz), 8.47 (s, 1H), 8.00 (dd, 1H, *J* = 7.8, 2.0 Hz), 7.84–7.77 (AA'BB', 2H), 7.68 (s, 1H), 7.39–7.32 (AA'BB', 2H), 7.30 (t, 1H, *J* = 5.5 Hz), 7.26–7.17 (m, 3H), 7.10 (t, 1H, *J* = 5.3 Hz), 6.81 (td, 2H, *J* = 9.5, 2.5 Hz), 6.66 (d, 2H, *J* = 1.5 Hz), 5.84 (s, 1H), 5.52 (s, 2H), 5.50 (s, 1H), 4.65 (t, 2H, *J* = 5.0 Hz), 4.62 (t, 2H, *J* = 5.3 Hz), 4.45–4.39 (m, 1H), 4.28–4.22 (m, 1H), 3.99–3.88 (m, 4H), 3.73–3.41 (m, 39H), 3.38–3.29 (m, 4H), 3.19 (t, 2H, *J* = 5.0 Hz), 3.10–3.04 (m, 1H), 2.93 (t, 2H, *J* = 7.0 Hz), 2.82 (dd, 1H, *J* = 12.5, 5.0 Hz), 2.70 (d, 1H, *J* = 12.5 Hz), 2.12 (t, 2H, *J* = 7.5 Hz), 1.78–1.47 (m, 8H), 1.46–1.22 (m, 20H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 126 MHz): δ 173.6 (1C), 166.9 (1C), 163.6 (1C), 158.7 (1C), 157.8 (1C), 155.51 (1C), 155.46 (1C), 147.8 (1C), 145.8 (1C), 142.2 (1C), 139.2 (1C), 138.4 (1C), 134.6 (1C), 133.4 (1C), 133.3 (1C), 129.7 (2C), 128.2 (2C), 127.8 (2C), 127.3 (2C), 127.2 (2C), 123.6 (2C), 122.5 (2C), 114.3 (2C), 113.65 (1C), 113.56 (1C), 95.6 (1C), 71.2 (1C), 70.6 (1C), 70.5 (1C), 70.39 (1C), 70.38 (1C), 70.3 (1C), 70.24 (1C), 70.21 (1C), 70.15 (1C), 70.09 (1C), 70.0 (1C), 69.8 (1C), 69.7 (1C), 69.6 (1C), 69.42 (1C), 69.38 (1C), 63.7 (1C), 61.8 (1C), 60.1 (1C), 55.6 (1C), 53.4 (1C), 50.3 (1C), 48.0 (1C), 45.8 (2C), 45.1 (2C), 43.1 (1C), 40.5 (1C), 39.6 (1C), 39.1 (1C), 35.7 (1C), 35.2 (1C), 32.5 (1C), 29.4 (1C), 28.1 (1C), 27.9 (1C), 26.6 (1C), 25.8 (1C), 25.6 (1C), 25.3 (1C), 12.6 (4C); IR (KBr, cm^{-1}) 419, 683, 1076, 1134, 1180, 1341, 1591, 1628, 2066, 2932, 3311; HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{79}H_{111}ClN_{16}NaO_{17}S_4^+$, 1741.6777; Found, 1741.6798.

Platform–HTL–Rhodamine–biotin conjugate **18$_{long}$**



The title compound was obtained in 85.8% (47.1 mg, 19.5 μmol) from **17$_{long}$** (36.8 mg, 22.7 μmol). Red solid; Mp >250 ºC; (decomp.); TLC R_f 0.45 (CH_2Cl_2/MeOH = 90/10); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.87 (d, 1H, J = 1.6 Hz), 8.36 (s, 1H), 8.19 (s, 1H), 8.00 (dd, 1H, J = 7.9, 1.6 Hz), 7.89–7.83 (AA'BB', 2H), 7.83–7.77 (m, 4H), 7.69 (s, 1H), 7.67 (t, 1H, J = 5.4 Hz), 7.35–7.30 (AA'BB', 2H), 7.23–7.17 (AA'BB', 2H), 7.17–7.12 (m, 3H), 6.95 (t, 1H, J = 5.3 Hz), 6.72 (d, 2H, J = 9.5 Hz), 6.54 (d, 2H, J = 2.0 Hz), 5.78 (s, 1H), 5.51 (s, 2H), 5.31 (s, 1H), 4.63 (t, 2H, J = 2.5 Hz), 4.58 (t, 2H, J = 5.2 Hz), 4.50–4.46 (m, 1H), 4.44 (t, 2H, J = 5.1 Hz), 4.32–4.26 (m, 1H), 3.94–3.88 (m, 4H), 3.82 (t, 2H, J = 4.9 Hz), 3.70–3.37 (m, 84H), 3.34 (t, 2H, J = 7.0 Hz), 3.22 (t, 2H, J = 4.3 Hz), 3.15–3.08 (m, 1H), 2.91 (t, 2H, J = 7.1 Hz), 2.87 (dd, 1H, J = 12.9, 5.1 Hz), 2.72 (d, 1H, J = 12.9 Hz), 2.19 (t, 2H, J = 7.4 Hz), 1.78–1.51 (m, 8H), 1.47–1.29 (m, 8H), 1.25 (t, 12H, J = 7.0 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 173.4 (1C), 167.1 (1C), 166.9 (1C), 163.4 (1C), 158.2 (1C), 157.6 (2C), 155.4 (2C), 147.7 (1C), 146.5 (1C), 145.7 (1C), 142.25 (2C), 142.21 (1C), 139.3 (1C), 138.3 (1C), 134.5 (1C), 133.7 (1C), 133.6 (1C), 133.5 (1C), 133.1 (1C), 130.0 (1C), 128.1 (2C), 128.0 (2C), 127.6 (2C), 127.3 (1C), 127.2 (1C), 127.1 (2C), 125.4 (2C), 123.3 (1C), 122.6 (1C), 122.3 (1C), 114.1 (2C), 113.5 (2C), 95.6 (1C), 71.2 (1C), 70.52 (1C), 70.49 (1C), 70.46 (1C), 70.41 (17C), 70.37 (8C), 70.2 (1C), 70.1 (1C), 70.00 (1C), 69.99 (1C), 69.9 (1C), 69.6 (1C), 69.5 (1C), 69.39 (1C), 69.35 (1C), 61.7 (1C), 60.1 (1C), 55.4 (1C), 53.4 (1C), 50.3 (1C), 50.1 (1C), 47.9 (1C), 45.9 (4C), 45.1 (1C), 43.1 (1C), 40.5 (1C), 39.6 (1C), 39.0 (1C), 35.7 (1C), 35.2 (1C), 32.5 (1C), 29.7 (1C), 29.4 (1C), 28.1 (1C), 28.0 (1C), 26.6 (1C), 25.8 (1C), 25.5 (1C), 25.4 (1C), 12.6 (4C); IR (KBr, cm^{-1}) 826, 922, 1132, 1275, 1466, 1647, 1692, 2870, 2918, 3406; HRMS (ESI) *m*/*z*: [M + 2Na]$^{2+}$ Calcd for $^{12}C_{111}{}^{13}CH_{165}ClN_{20}Na_2O_{29}S_4{}^{2+}$, 1232.0220; Found, 1232.0238.

Biological Experiments

Production of recombinant GST-HaloTag protein in *E. coli*.

Escherichia coli strain Rosetta (DE3) pLysS cells (Merck Chemicals Ltd., Nottingham, England) were transformed with pGEX6P-1-HaloTag vector,[S12] and cultured in LB media containing 50 mg L^{-1} Carbenicillin (Nacalai Tesque, Kyoto, Japan) and 34 mg L^{-1} chloramphenicol (Nacalai Tesque). After induction with isopropyl β-D-thiogalactopyranoside (final concentration at 2 mM) (Nacalai Tesque) for 16 h at 30 °C, the cells were collected by centrifugation at 4,500 g for 20 min, and frozen in liquid N_2. After thawing, the cells were suspended in cell lysis buffer containing 20 mM HEPES-KOH pH 8.0, 200 mM NaCl, 2 mM tris(2-carboxyethyl)phosphine hydrochloride (TCEP; Nacalai Tesque), 10% glycerol (Nacalai Tesque), and 1% Triton X-100, and then lysozyme (Nacalai Tesque) was added to the cell lysate, which were incubated on ice for 30 min. $MgCl_2$ (final concentration at 10 mM) and DNase I (final concentration of approximately 20 μg mL^{-1}) were added into the cell lysate, and incubation was continued for 1 h at 4 °C. Cell debris and larger particles were removed by centrifugation at 8,000 g for 20 min at 4 °C, and the supernatant was then filtered through a 0.45-μm filter. The supernatant of the cell lysate containing GST-HaloTag protein was applied onto a COSMOGEL GST-Accept resin (Nacalai Tesque), which had been pre-equilibrated with PBS. After excessive washing of the resin with PBS, the bound HaloTag-GST protein was subjected to the next chemical modification.

Chemical modification of GST-HaloTag

GST-HaloTag (total 0.7 nmol) bound on the resin (bed volume; 10 μL) was incubated with 100 μM of the indicated compounds in PBS overnight at 4 °C. For SDS-PAGE analysis, the labeled GST-HaloTag proteins were eluted by incubation for 5 min at 95 °C with LDS sample loading buffer (58 mM Tris-HCl pH 6.8, 1.7% lithium dodecyl sulfate (LDS), 5% glycerol, 100 mM dithiothreitol, 5% 2-mercaptoethanol).

Sodium dodecylsulfate-polyacrylamide gel electrophoresis (SDS-PAGE)

SDS-PAGE analysis was carried out under reducing conditions using a 5–20% polyacrylamide gel (ATTO, Tokyo, Japan). The gel was fluorescently visualized by FUSION SOLO. 7S. EDGE (Vilber-Lourmat, France) and imported into Inkscape (version 1.0.1) for cropping. The gel was also stained with CBB Stain One Super (Nacalai Tesque) according to the manufacturer's instruction (Figure S1).

The separated proteins in the gels were electrically transferred onto PVDF membranes in Mini Trans-Blot Cell (Bio-Rad Laboratories, Inc.). The membranes were immersed in Blocking One solution (Nacalai Tesque), and then incubated with horseradish peroxidase-conjugated streptavidin (HRP-streptavidin) (Kirkegaard & Perry Laboratories, Inc., Meryland, USA) diluted in 1% Blocking One /Tris-based saline containing 0.1% Tween 20 (TBST) at 4 °C for 16 h. The membranes were extensively washed with TBST, and then reacted with ImmunoStar Zeta (FUJIFILM Wako Pure Chemical Corporation, Osaka, Japan). Luminescence signals were imaged on FUSION SOLO. 7S. EDGE and imported into Inkscape (version 1.0.1) for cropping.

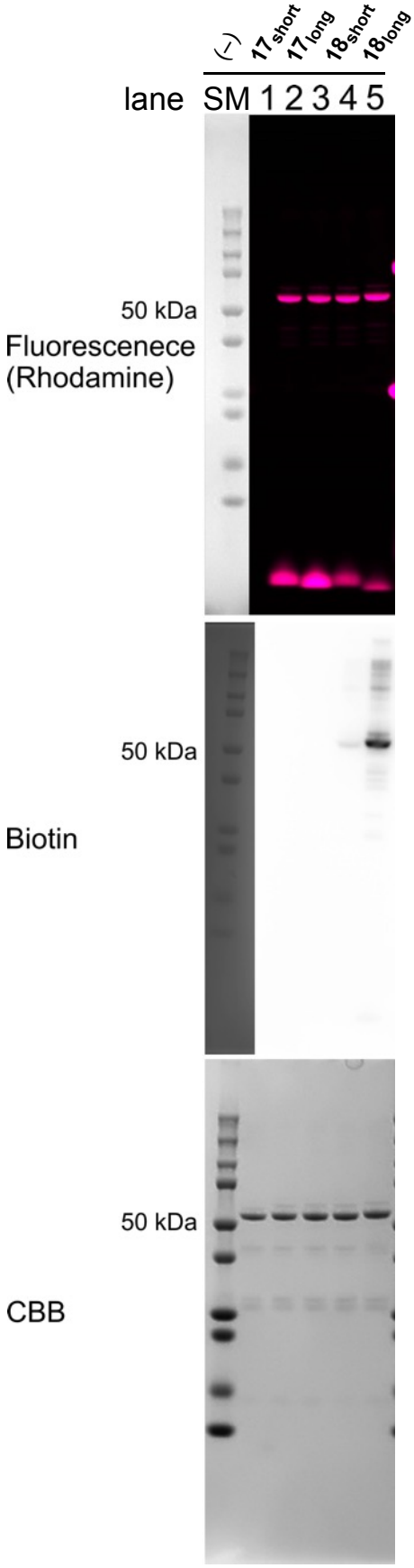


Figure S1 Chemical modification of the GST-fused HaloTag protein by multifunctional probes**17** and **18**. SM indicates size marker. See Figure S2 for the original full images.

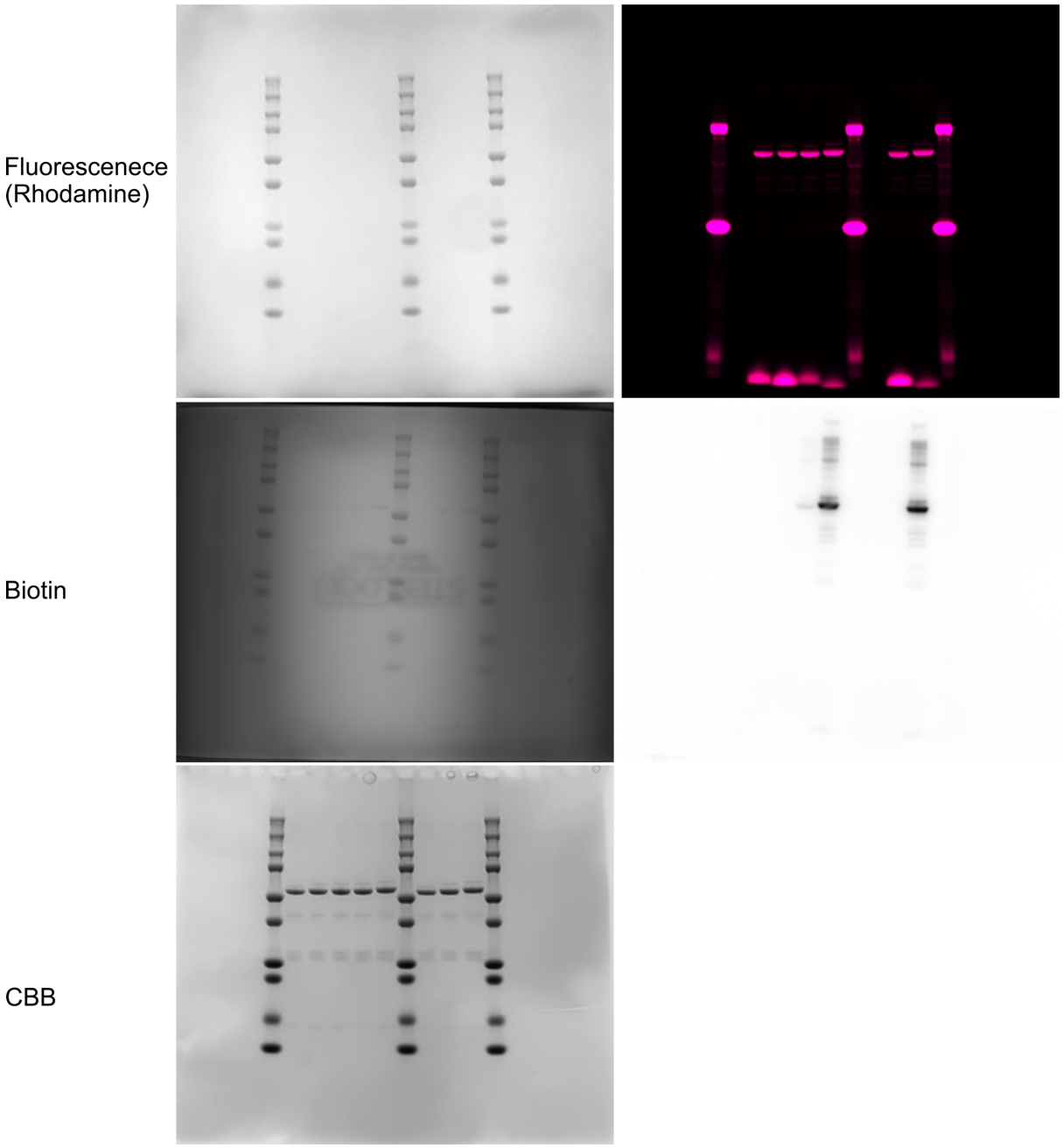


Figure S2 The original full images of the gels shown in Scheme 5B and Figure S1.

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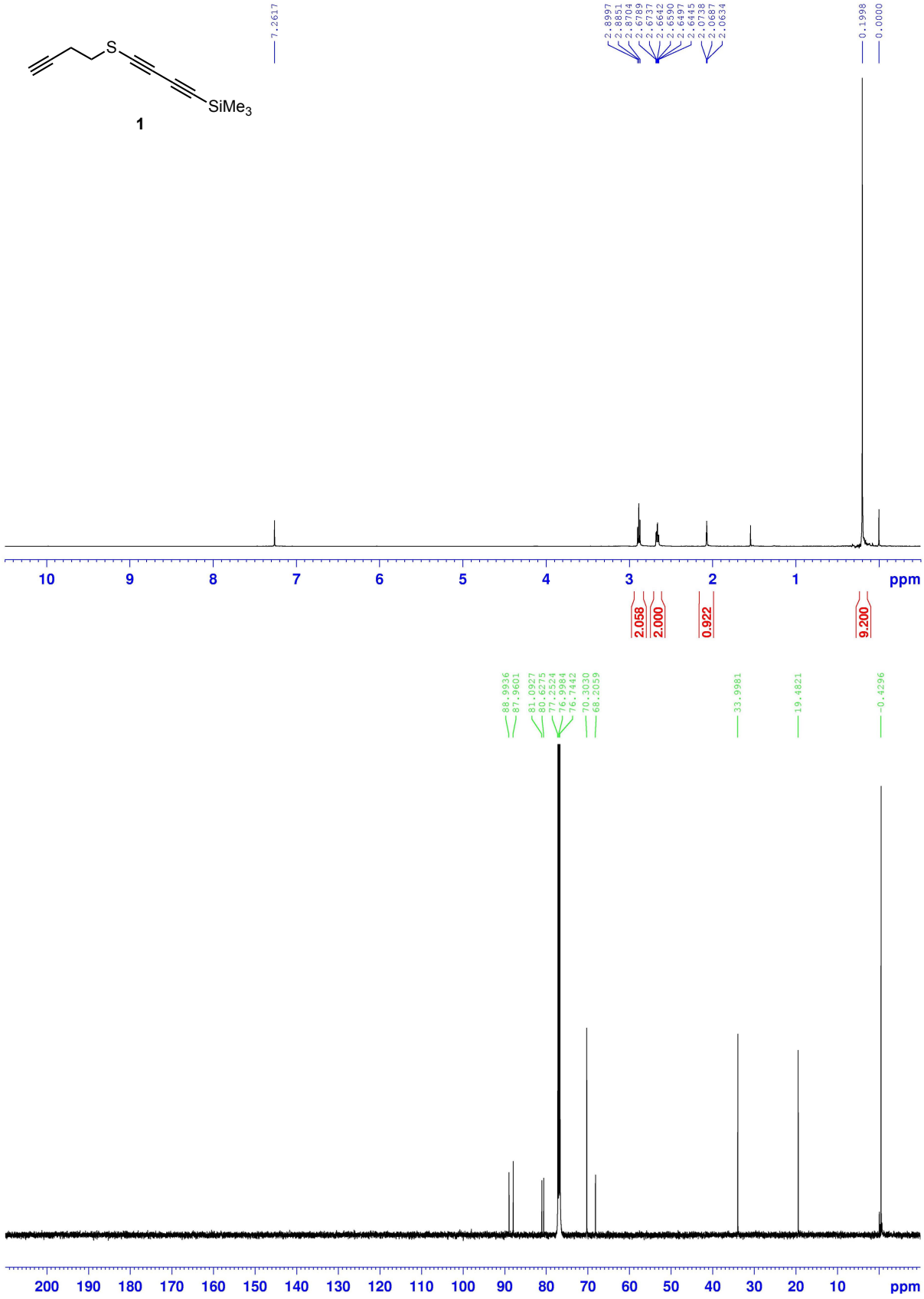
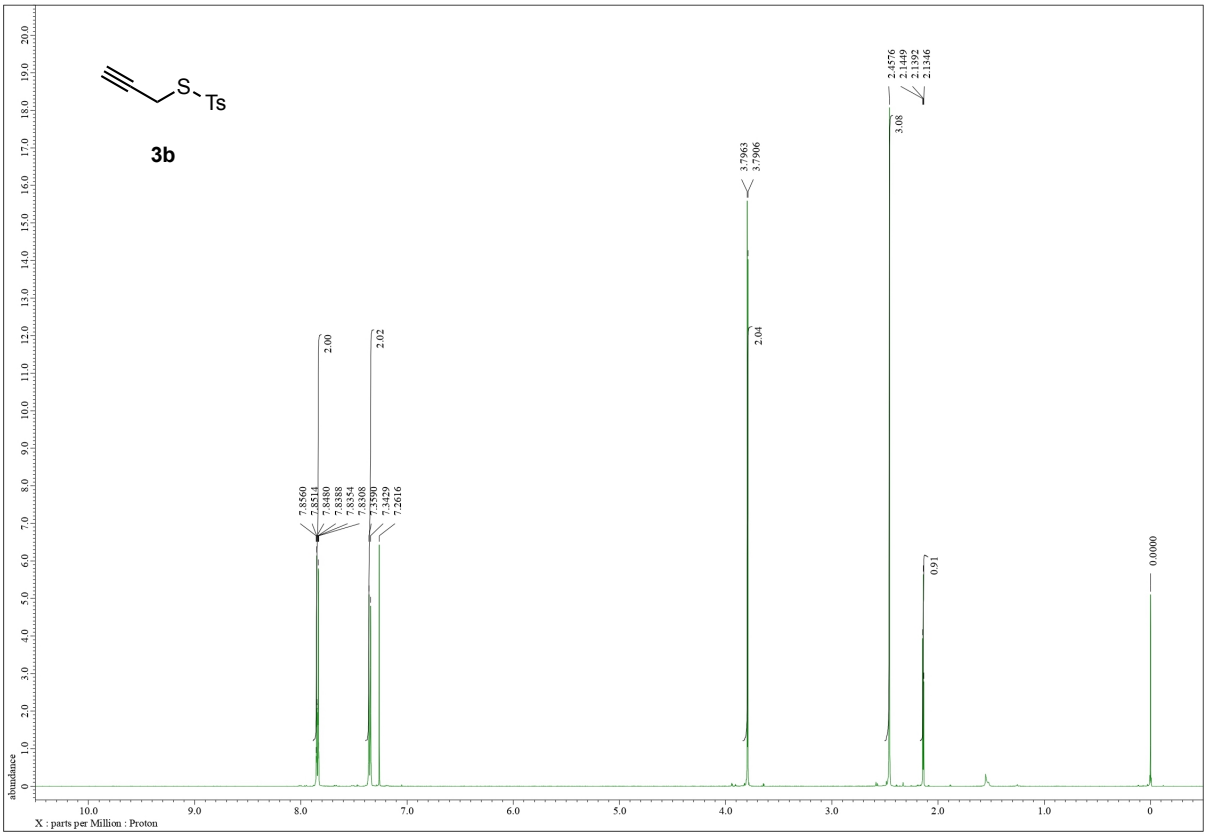
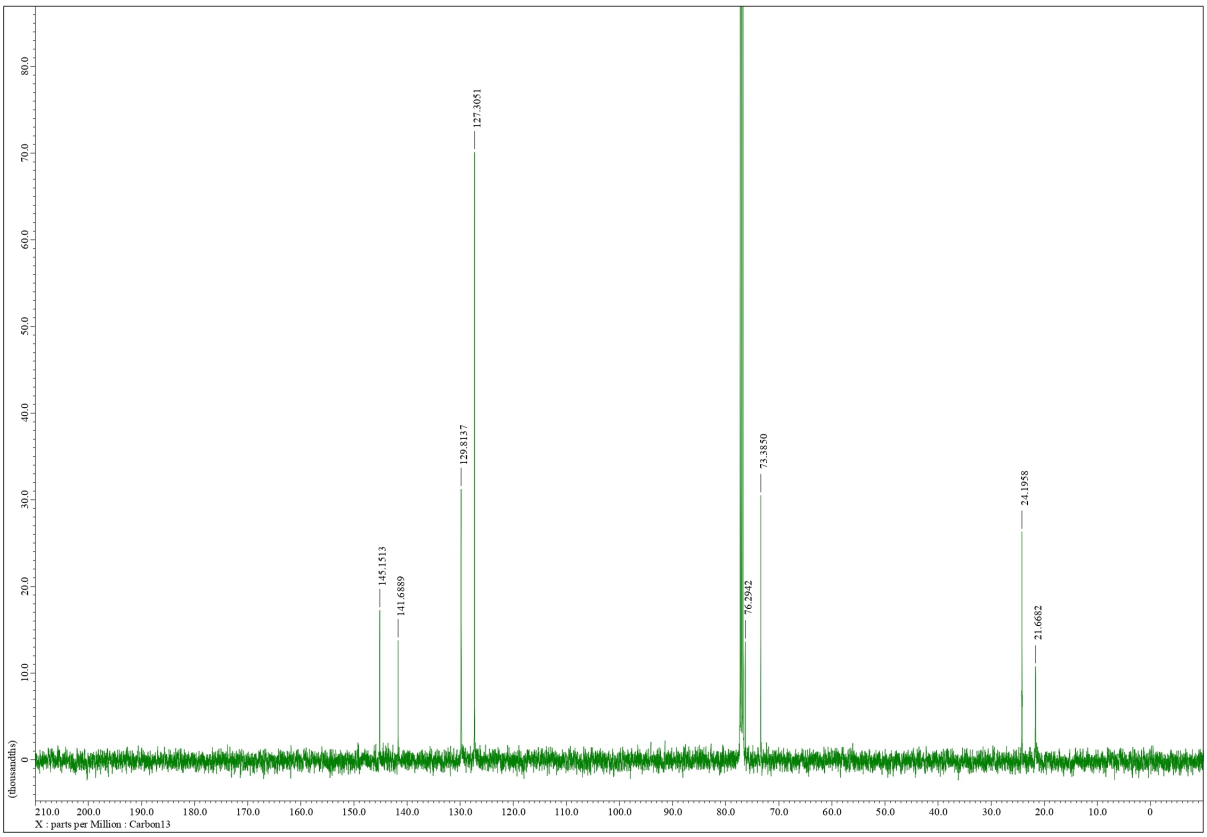
^{1}H and ^{13}C NMR Spectra of Compounds

^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **1** ($CDCl_3$)

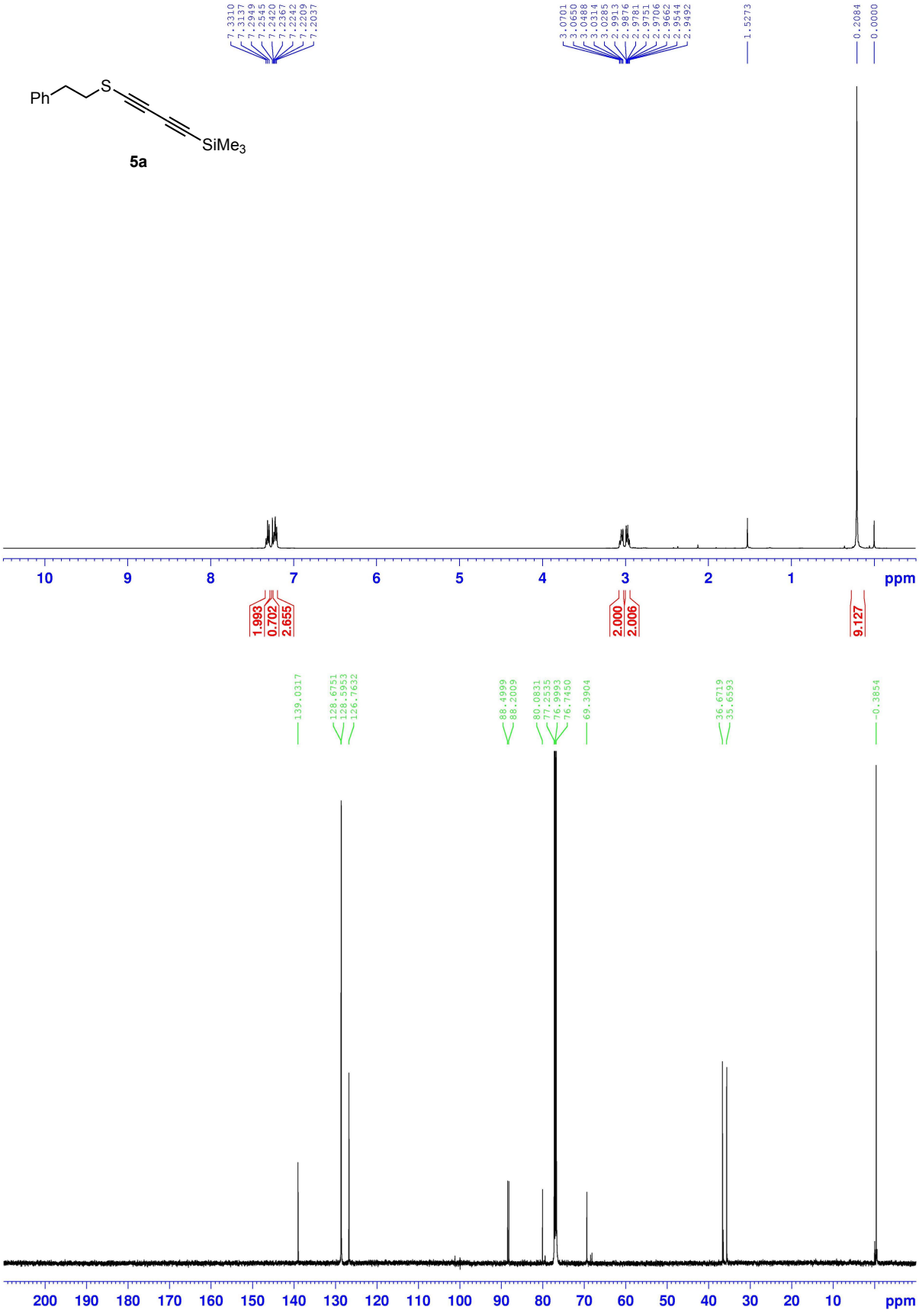


^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **3b** ($CDCl_3$)

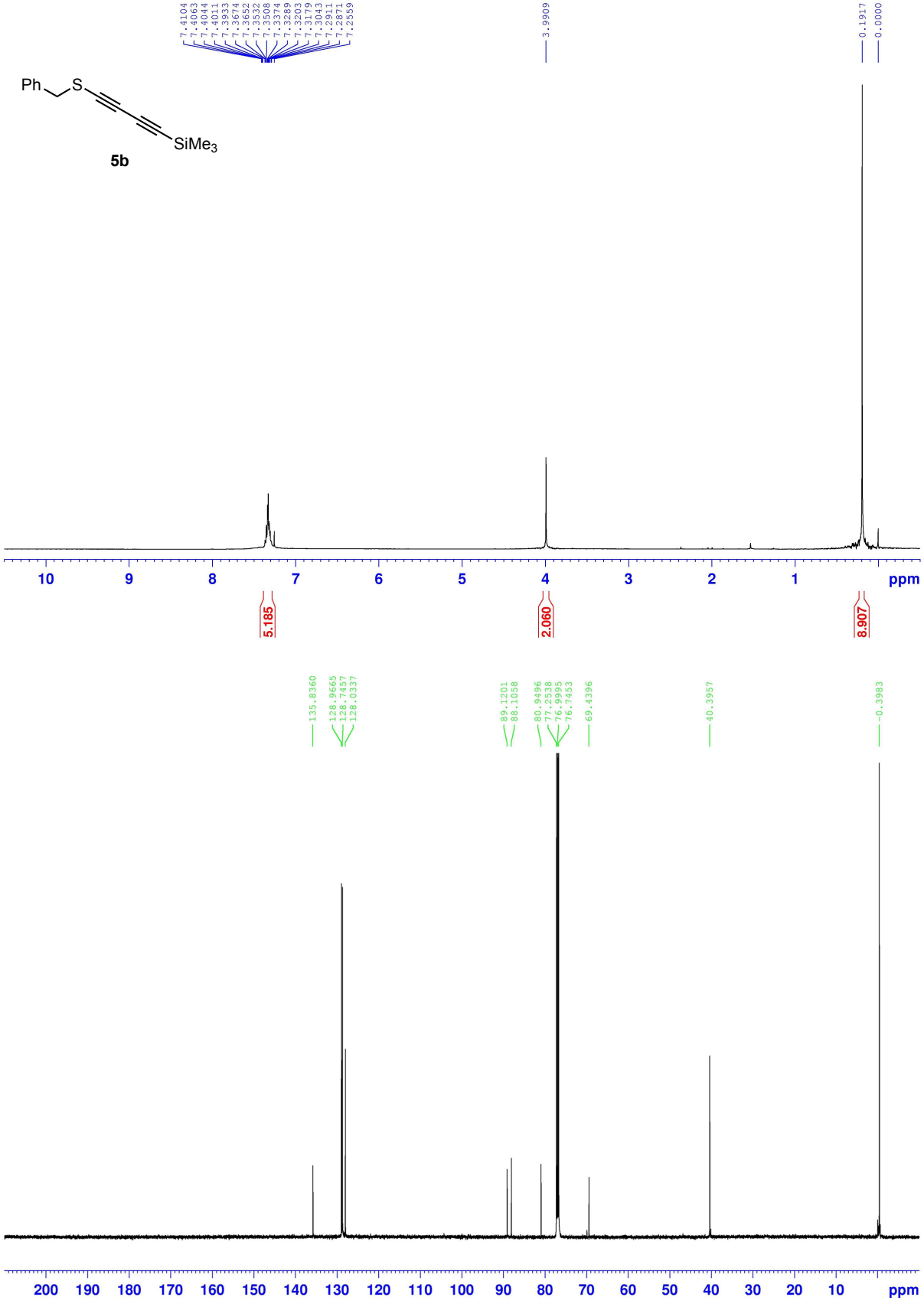




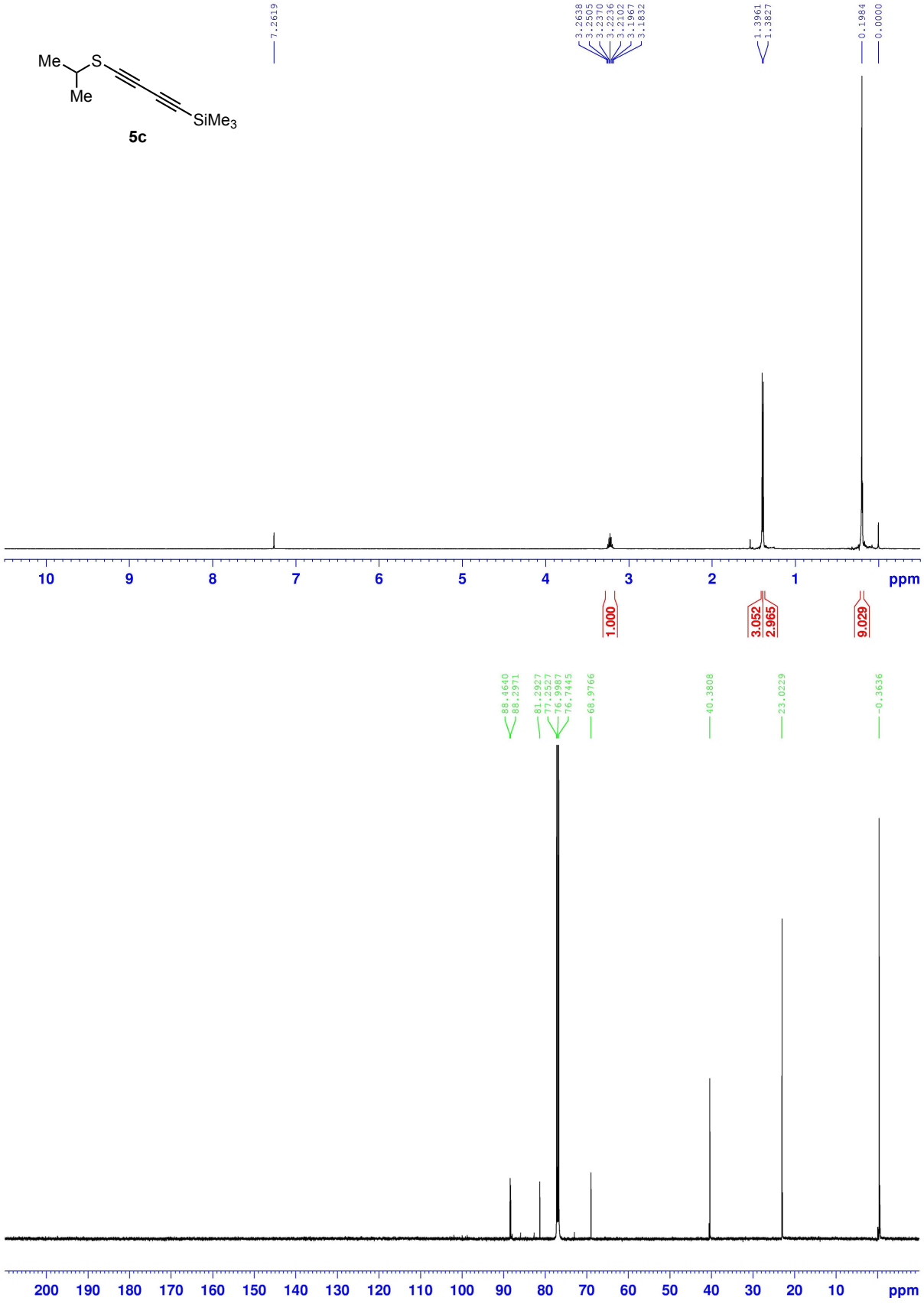
^{1}H NMR (400 MHz) and ^{13}C NMR (126 MHz) spectra of **5a** ($CDCl_3$)



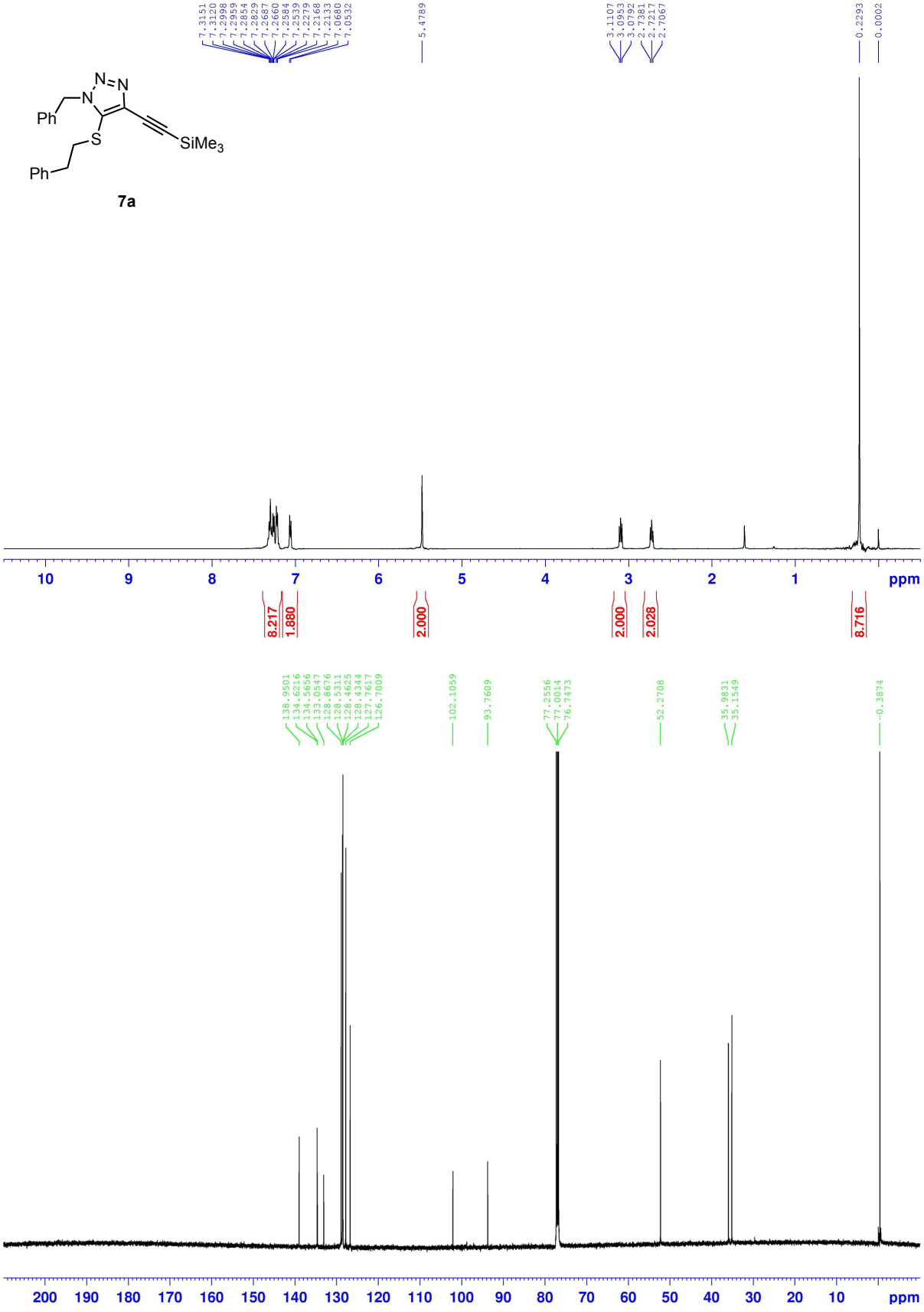
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **5b** ($CDCl_3$)



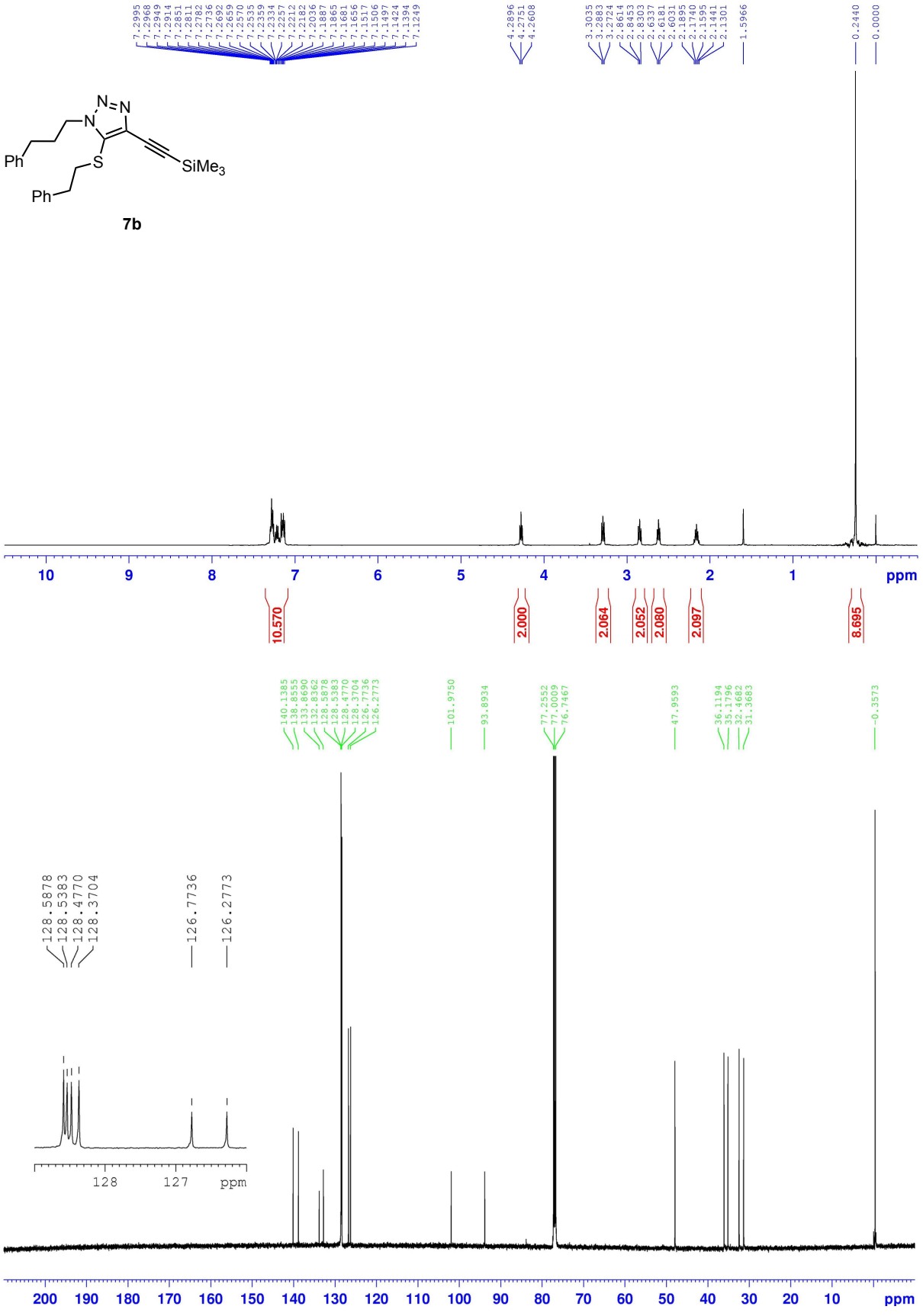
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **5c** ($CDCl_3$)



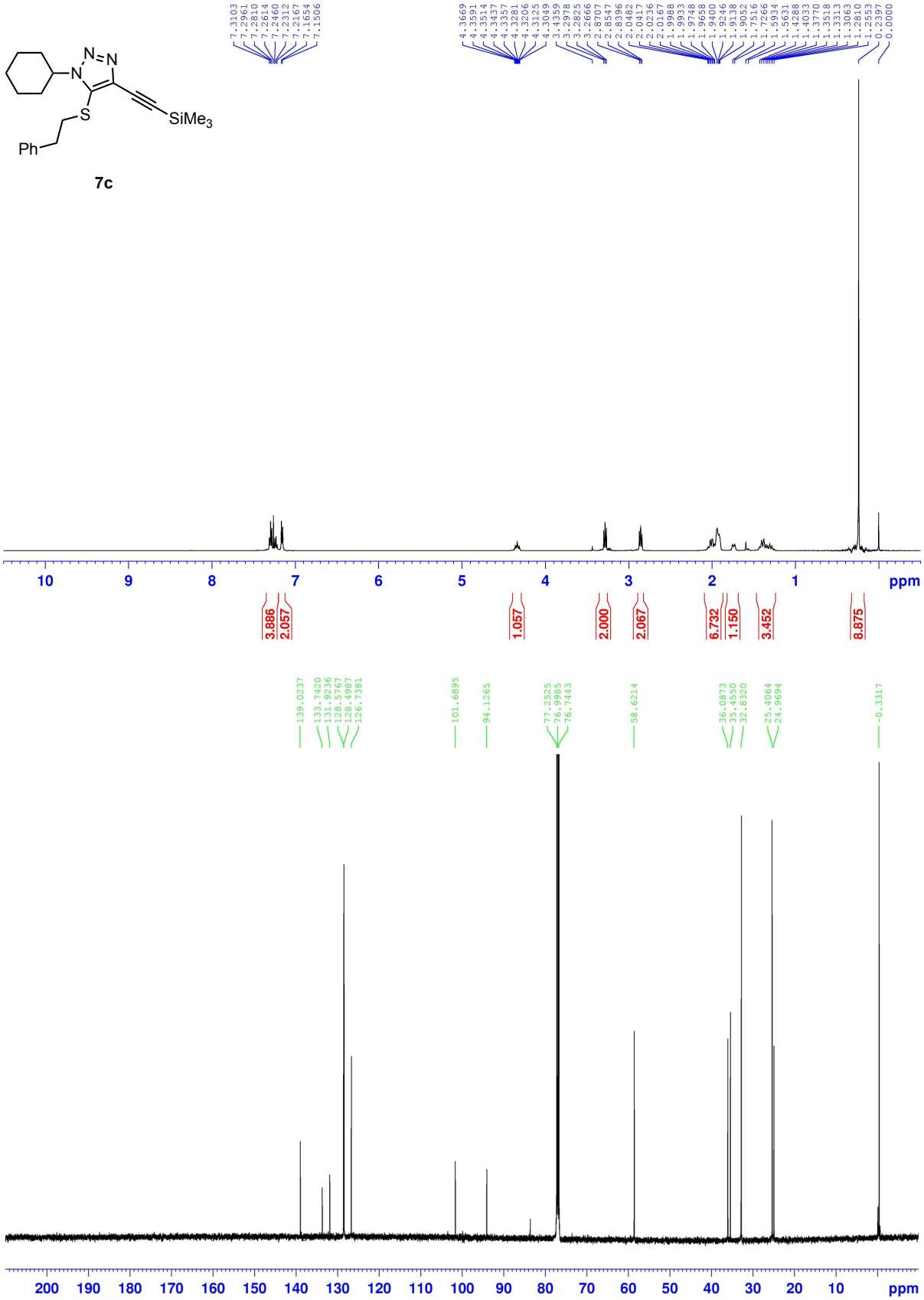
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **7a** ($CDCl_3$)



^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **7b** ($CDCl_3$)

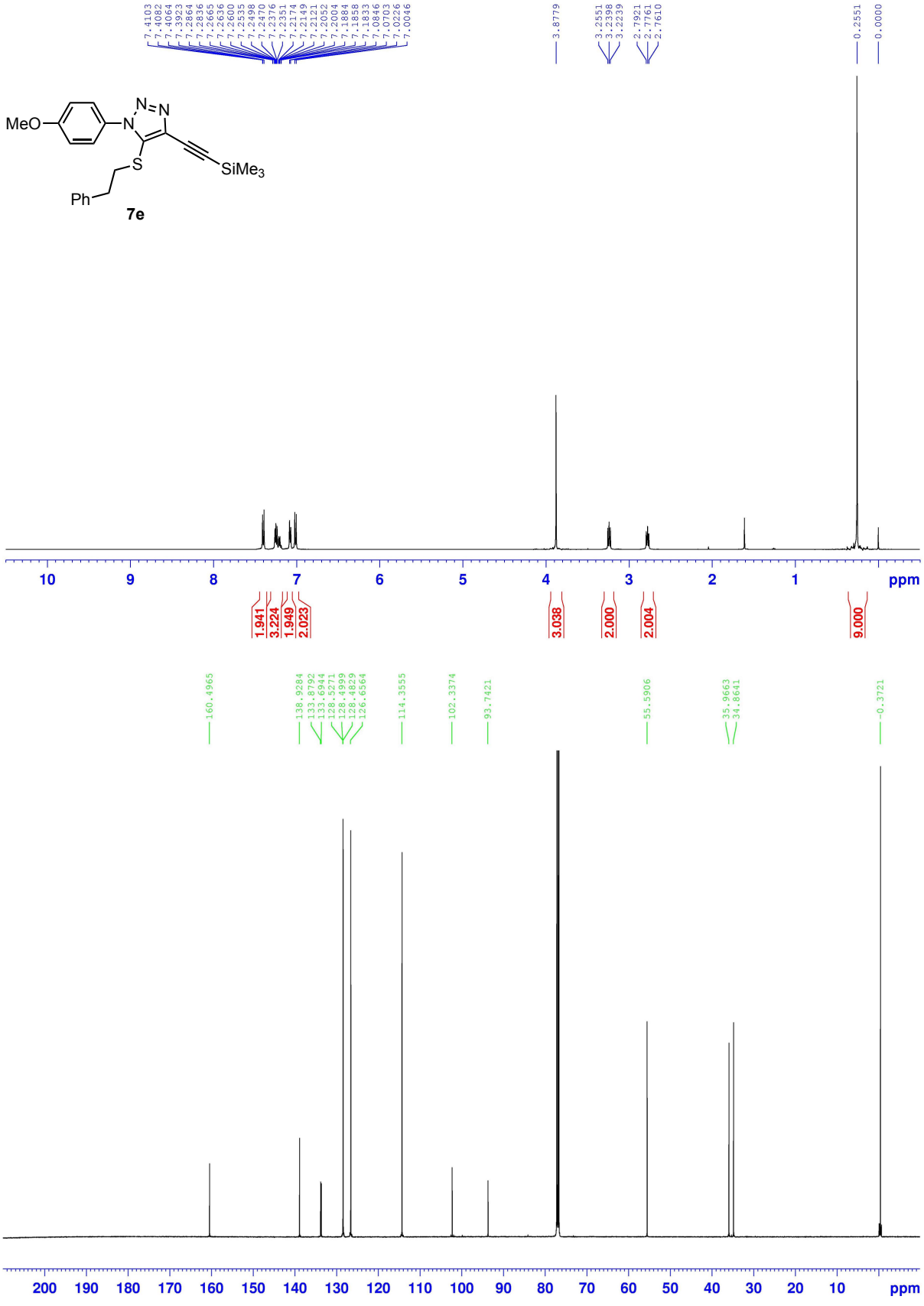


^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **7c** ($CDCl_3$)

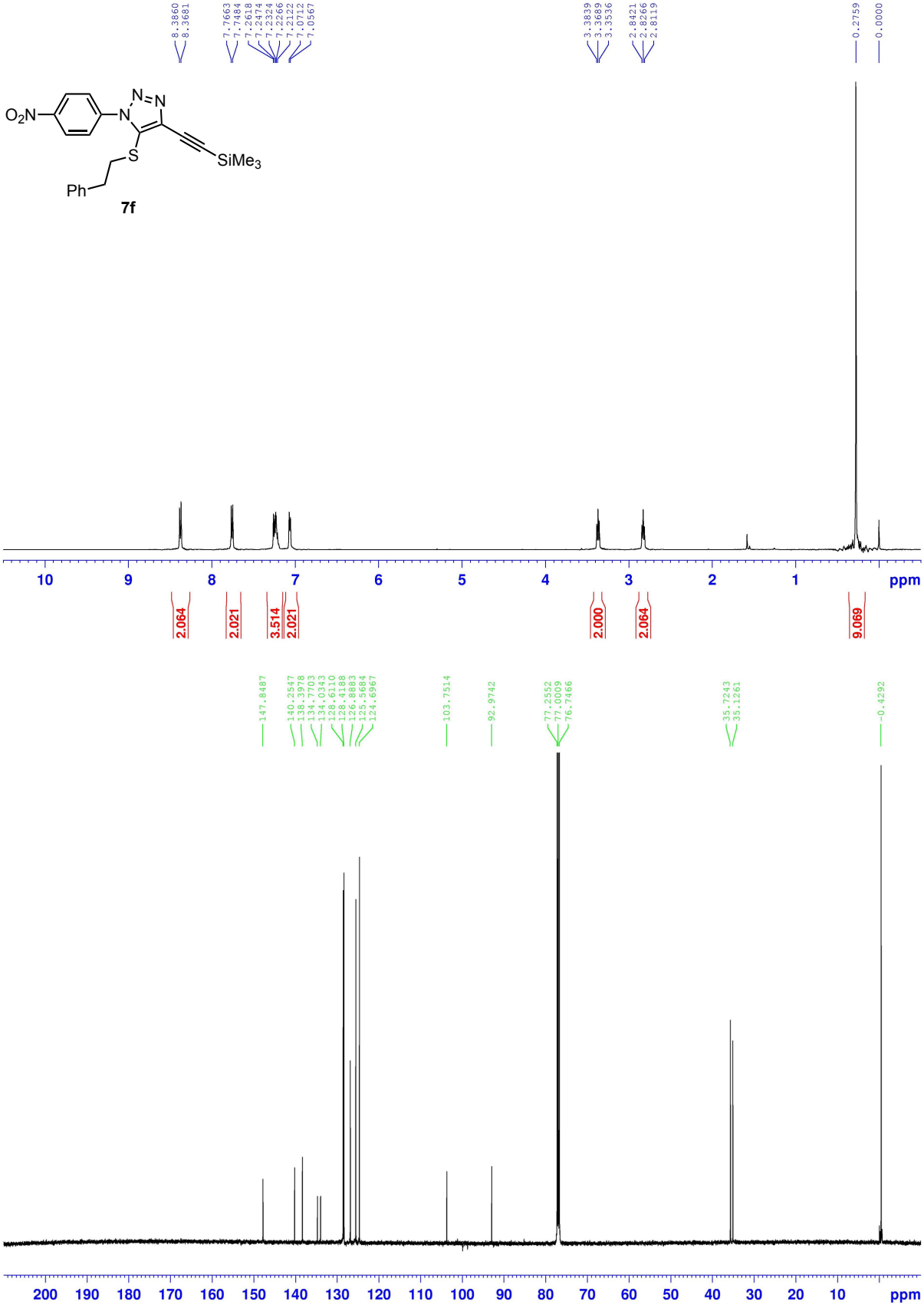


7c

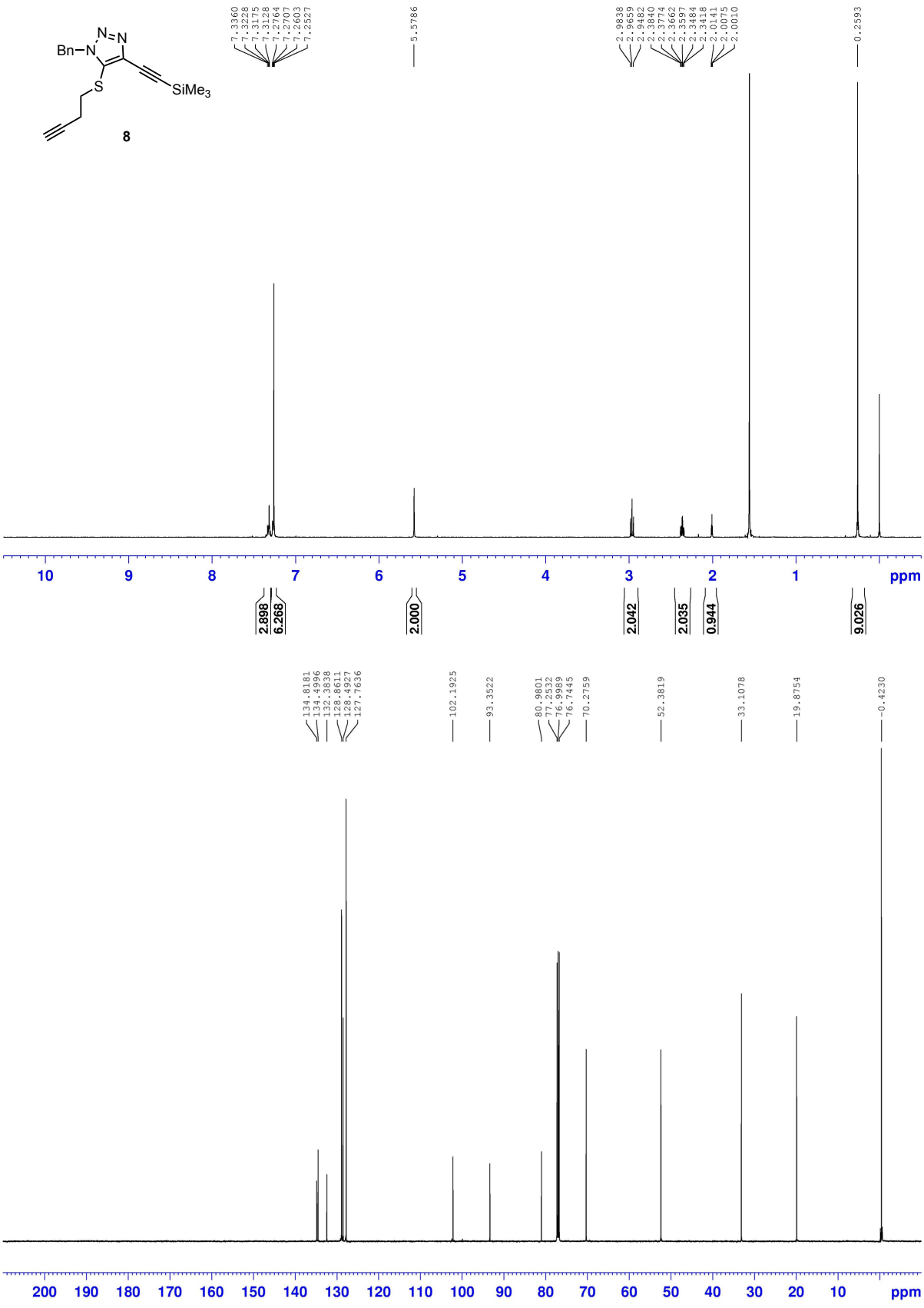
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **7e** ($CDCl_3$)



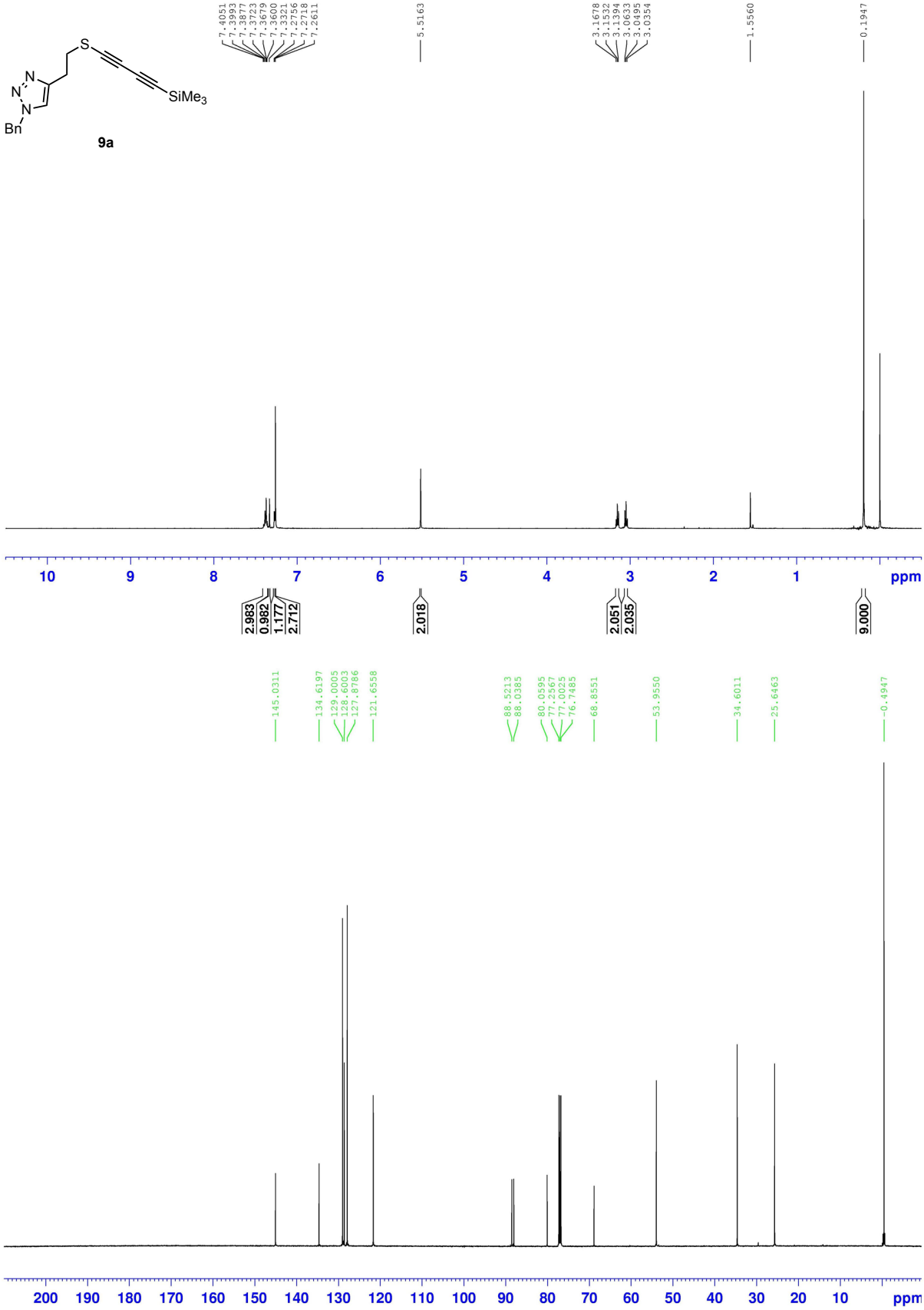
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **7f** ($CDCl_3$)



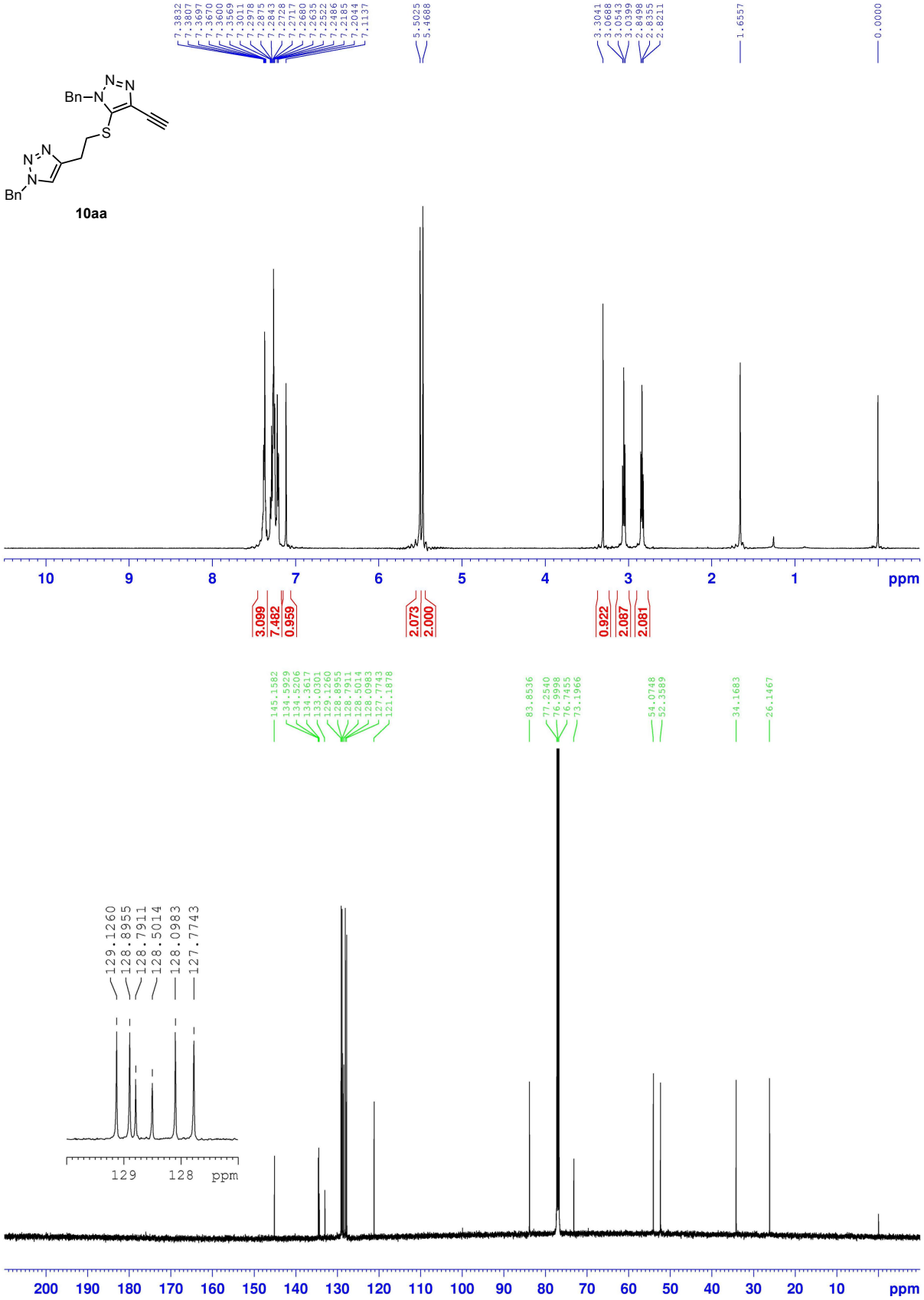
^{1}H NMR (400 MHz) and ^{13}C NMR (126 MHz) spectra of **8** ($CDCl_3$)



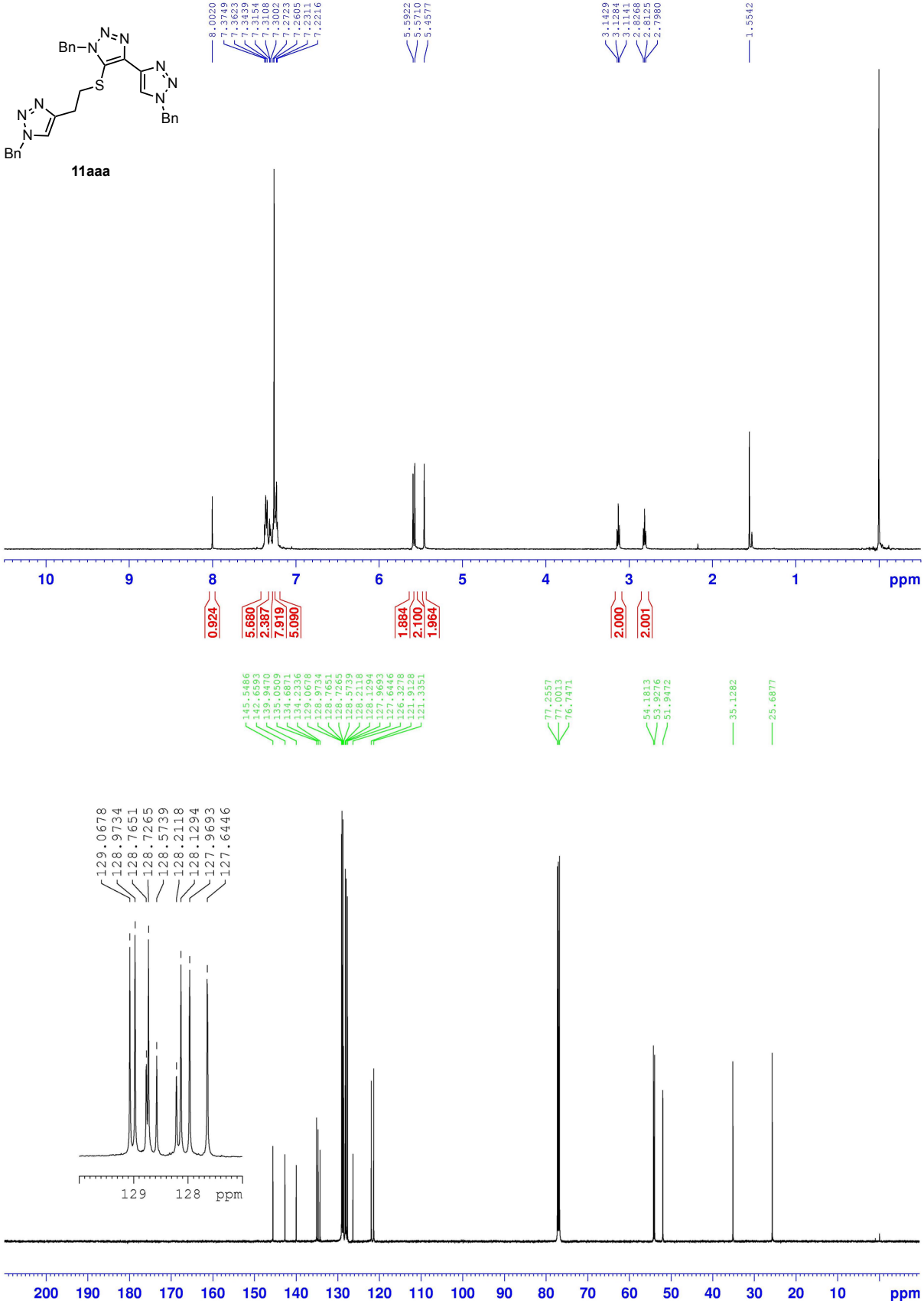
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **9a** ($CDCl_3$)



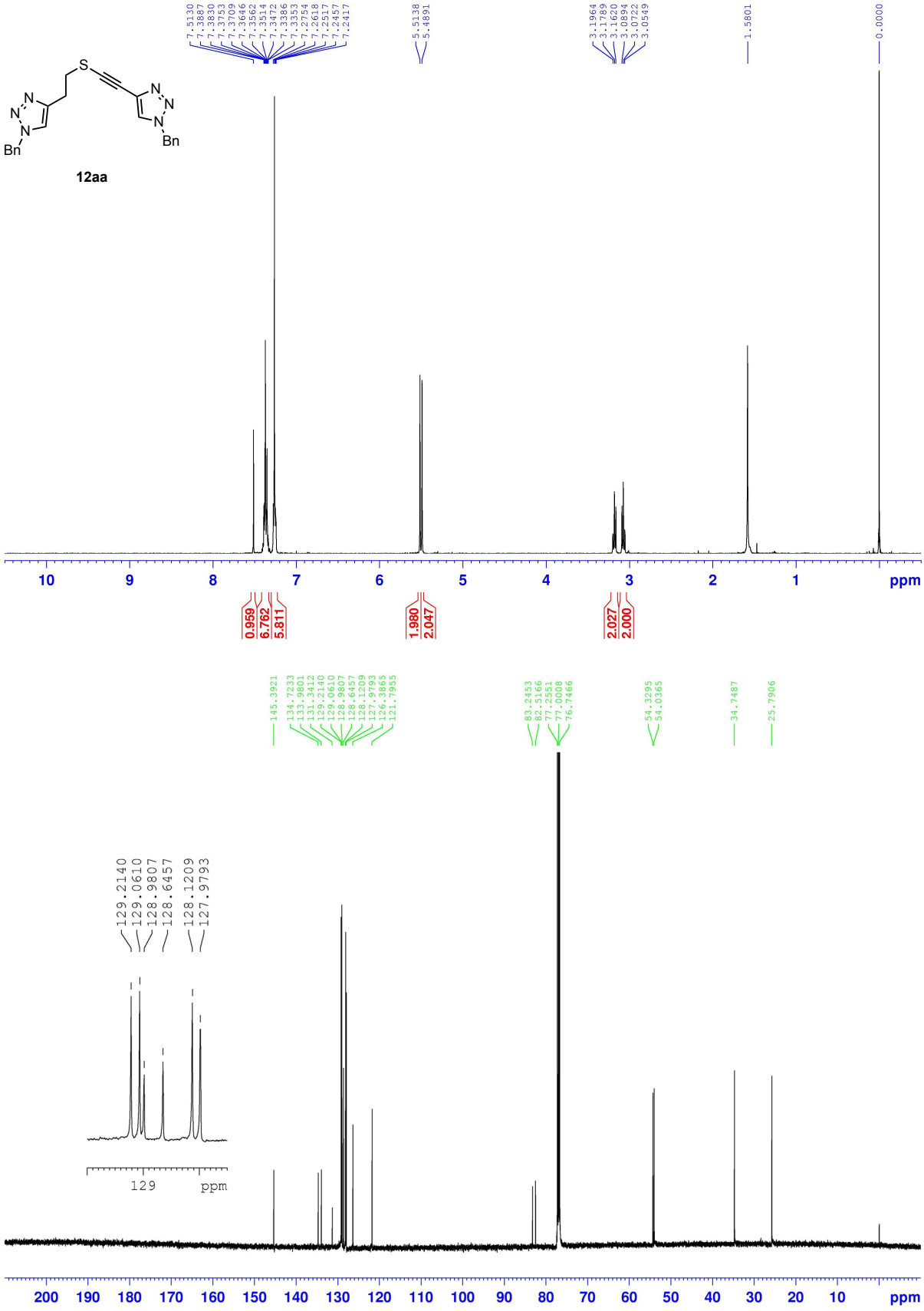
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **10aa** ($CDCl_3$)



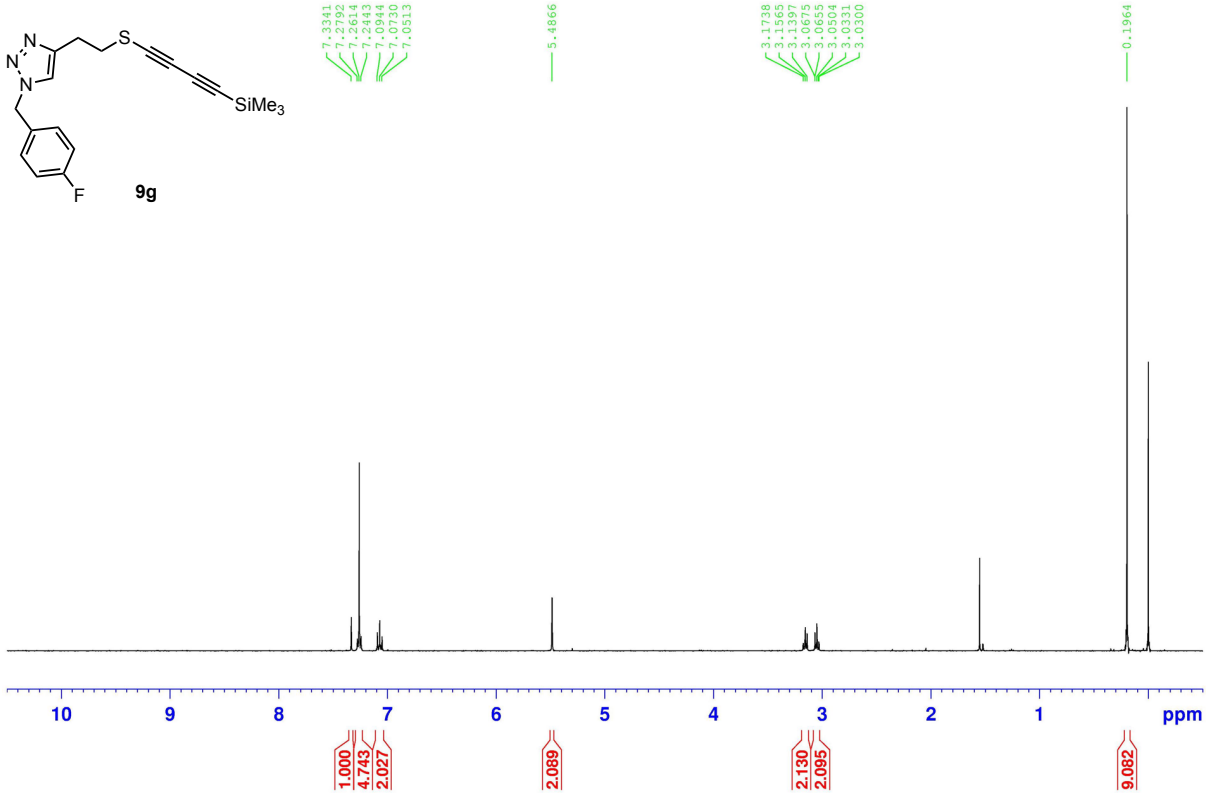
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **11aaa** ($CDCl_3$)

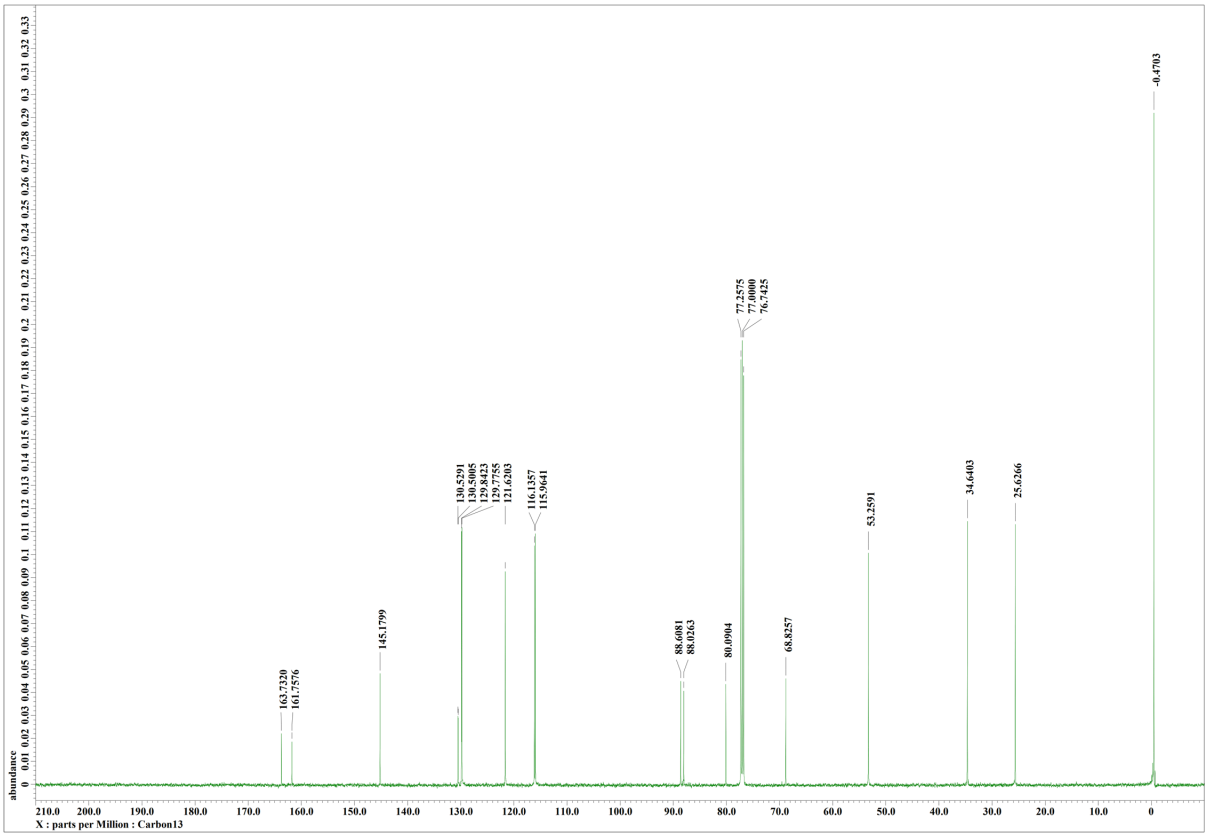


^{1}H NMR (400 MHz) and ^{13}C NMR (126 MHz) spectra of **12aa** ($CDCl_3$)

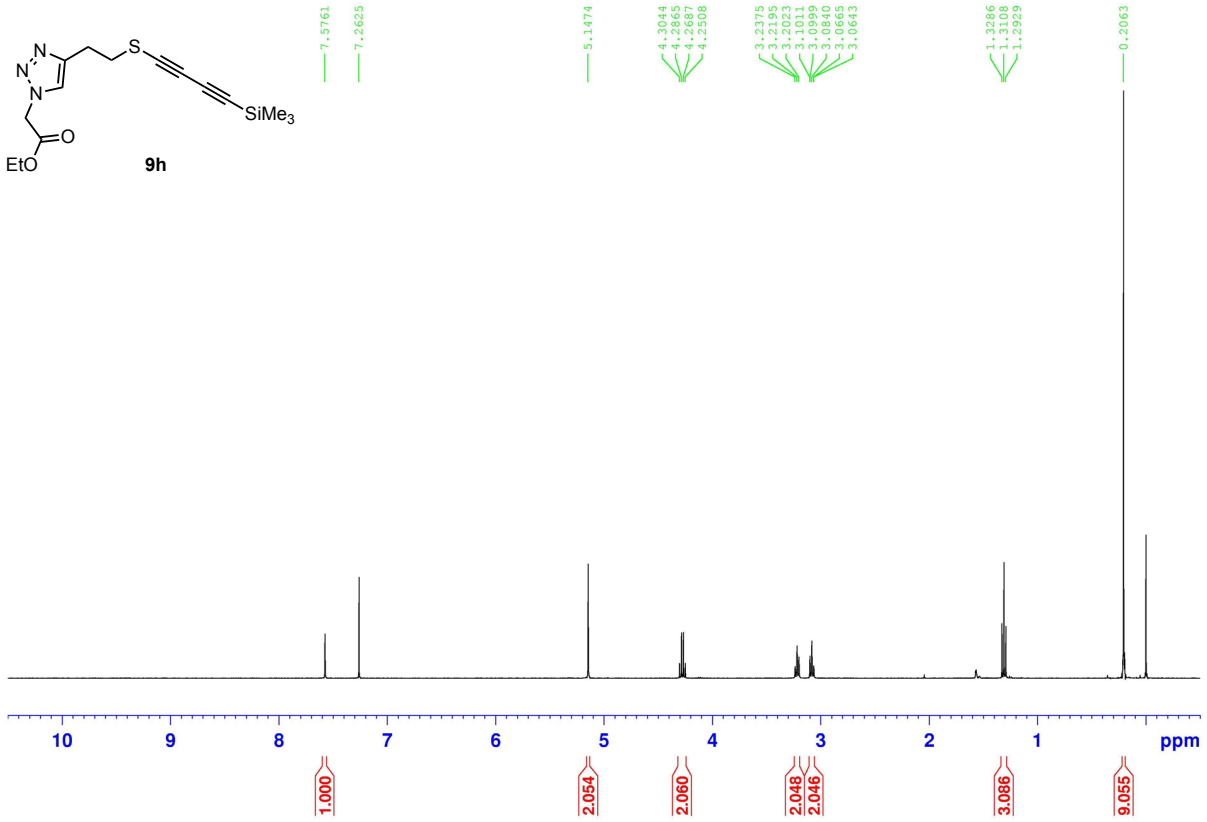


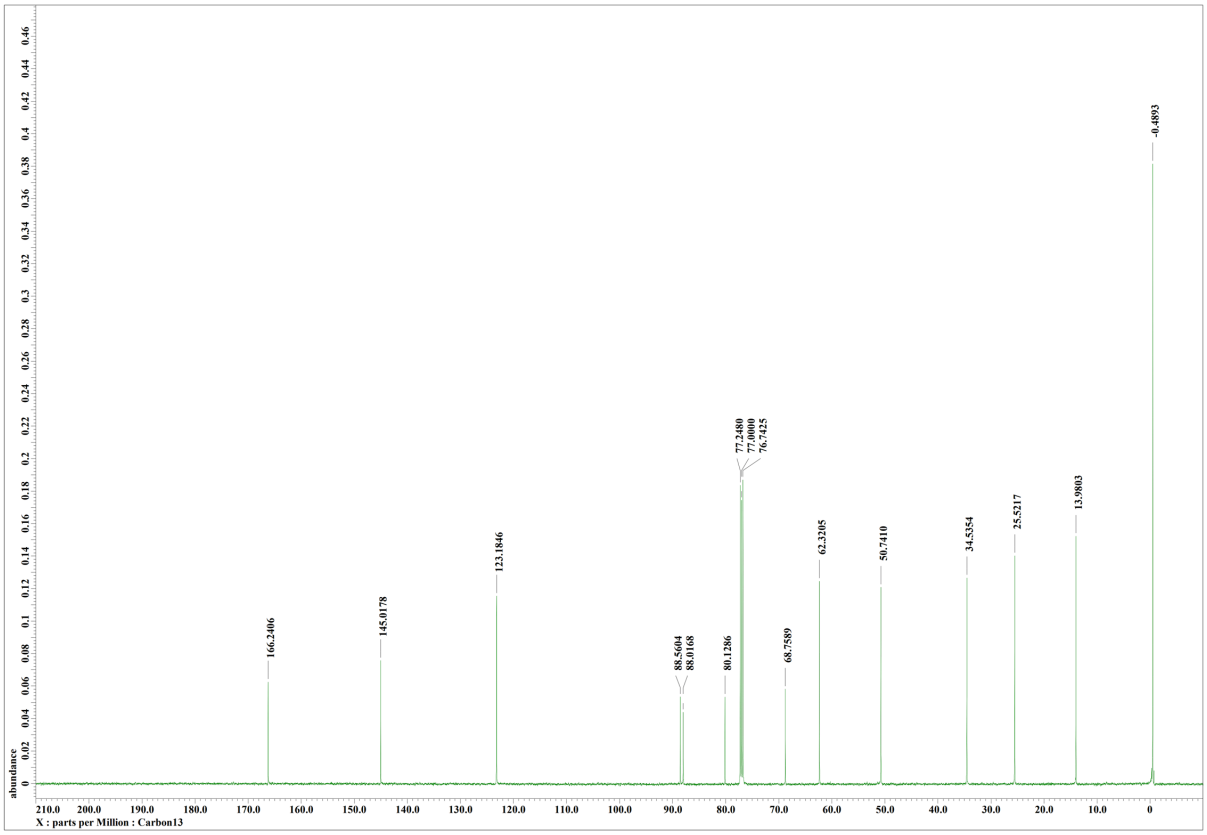
^{1}H NMR (400 MHz) and ^{13}C NMR (126 MHz) spectra of **9g** ($CDCl_3$)



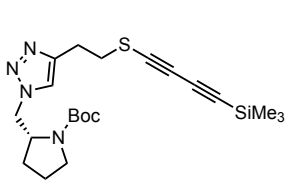


^{1}H NMR (400 MHz) and ^{13}C NMR (126 MHz) spectra of **9h** ($CDCl_3$)



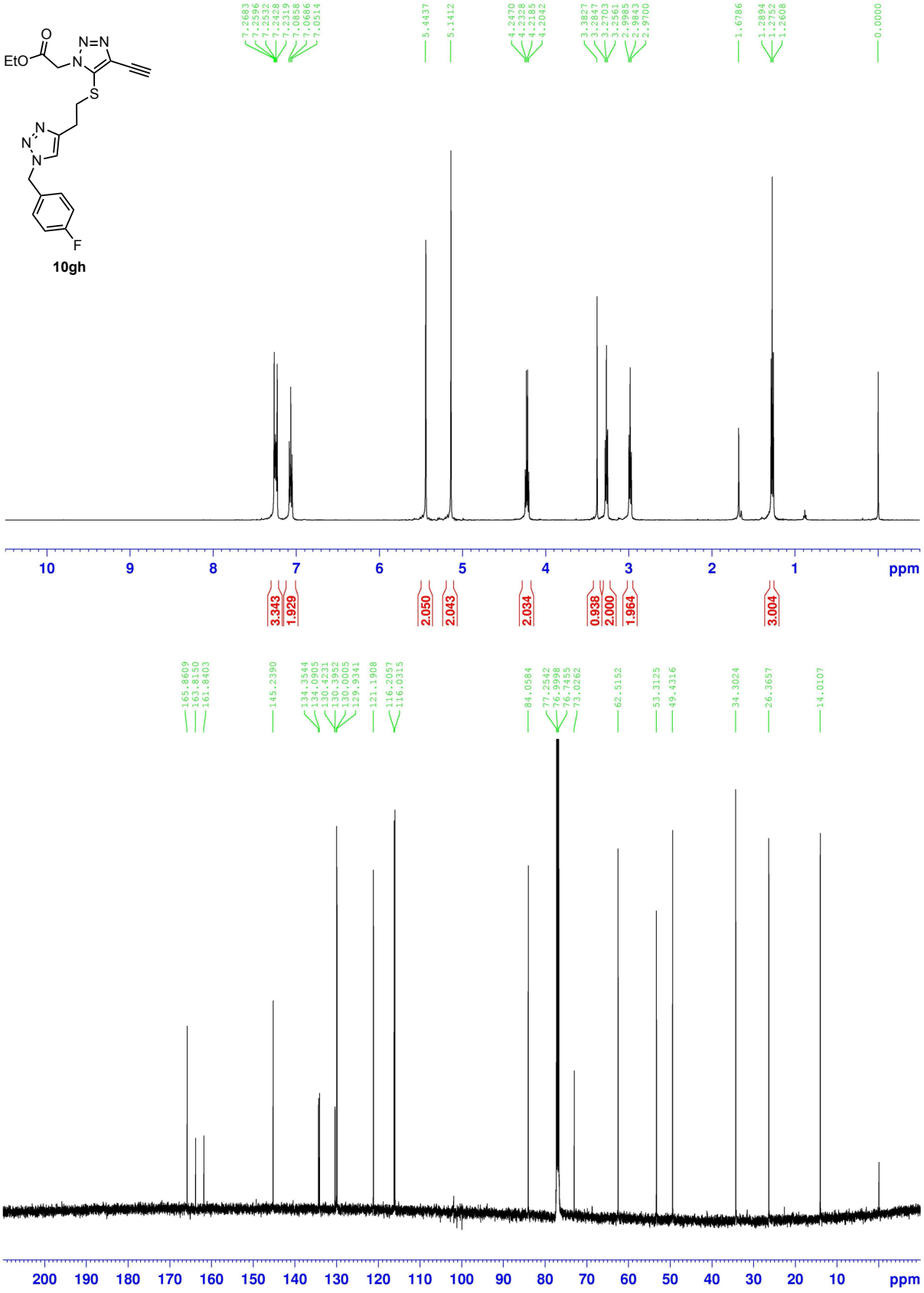


^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **9i** ($CDCl_3$)

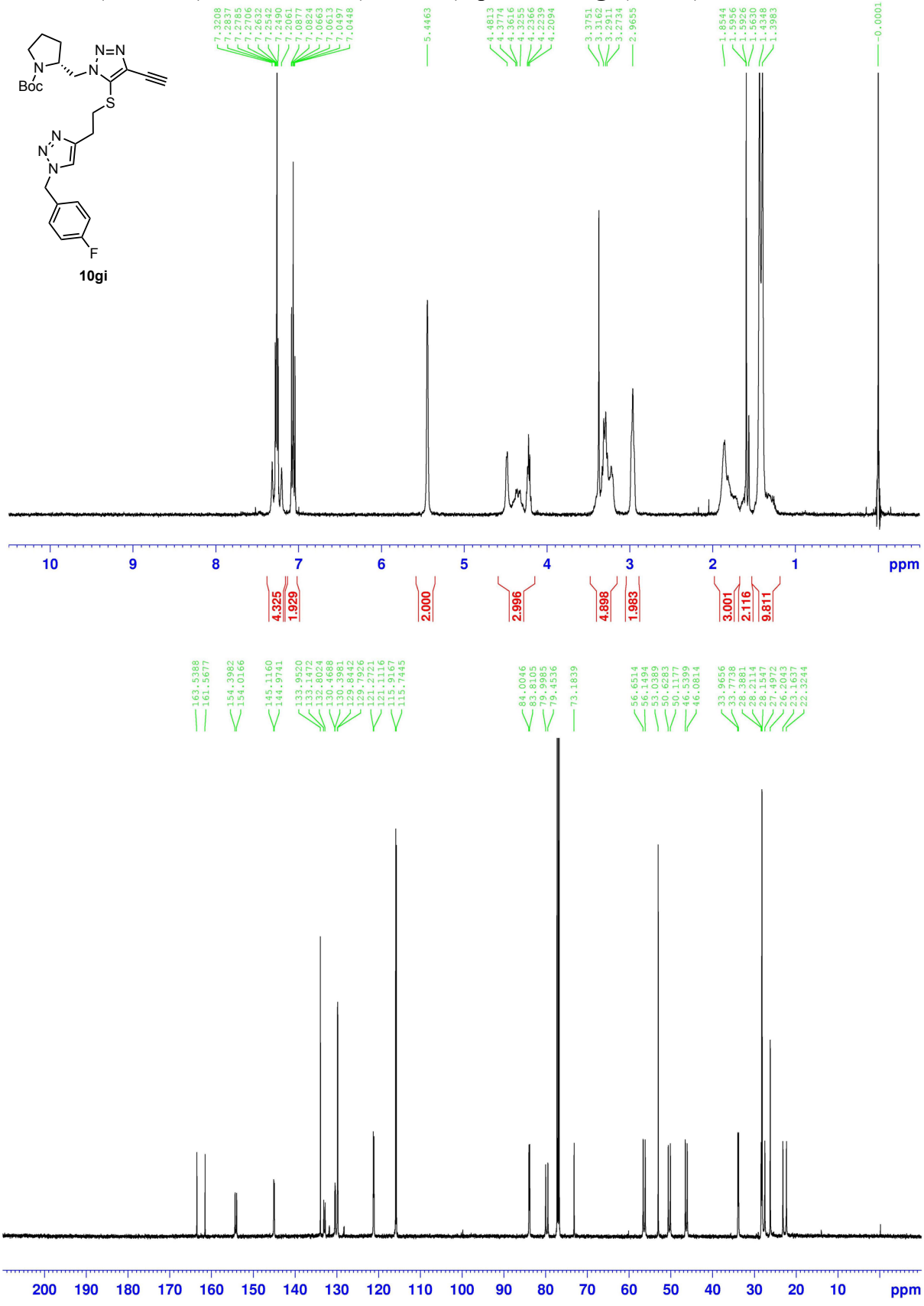


9i

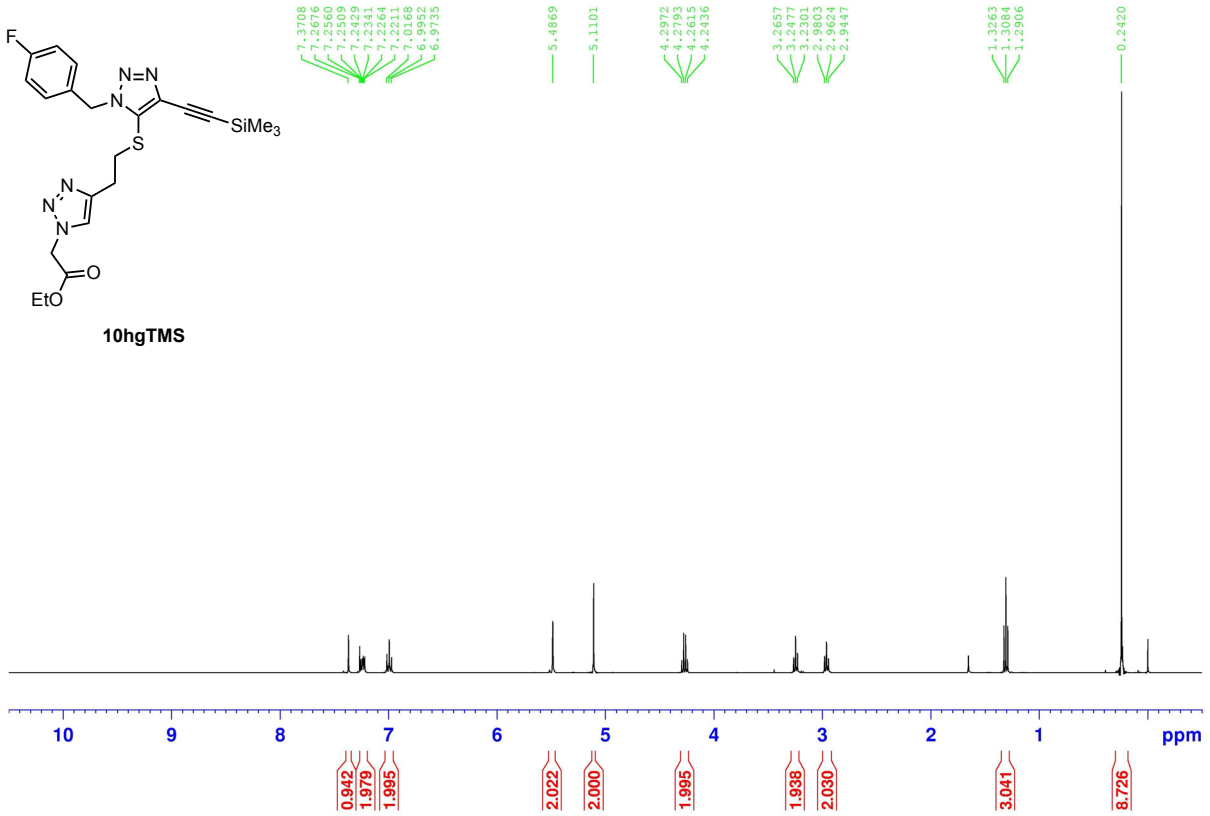
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **10gh** ($CDCl_3$)

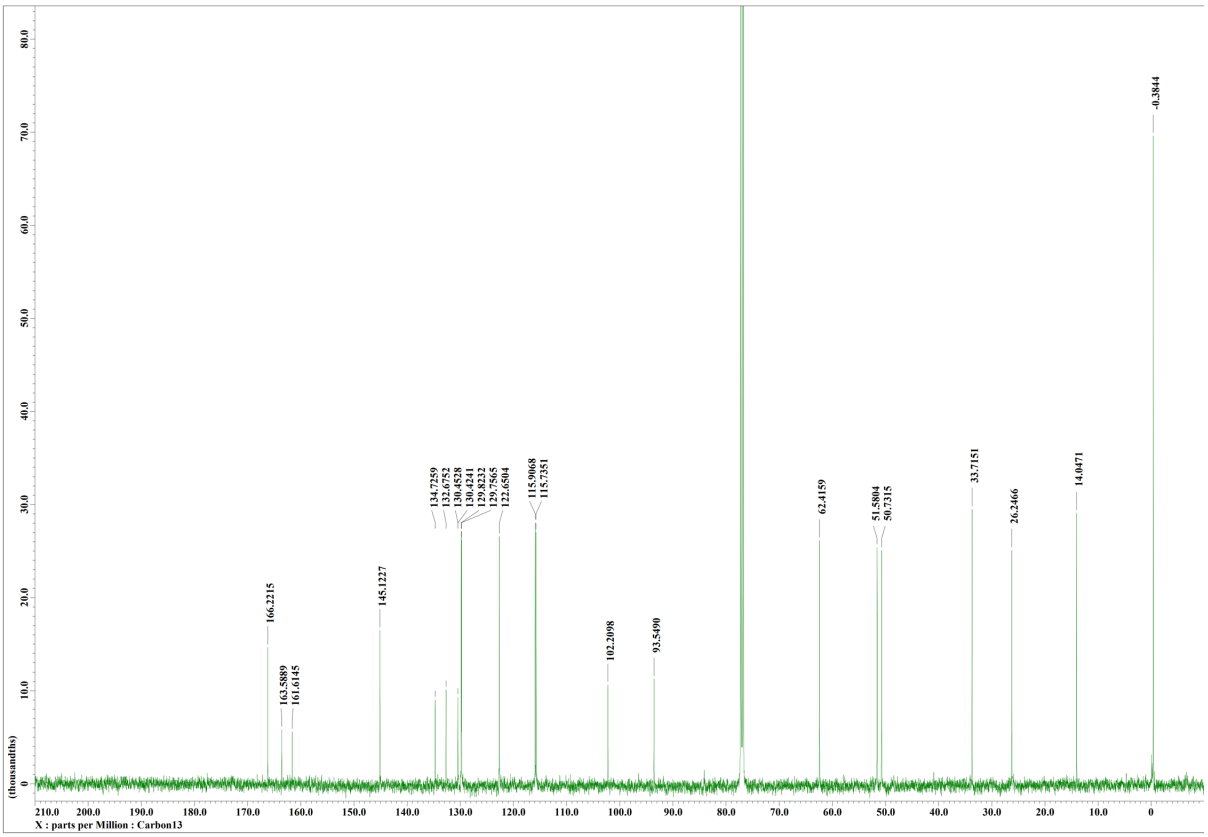


^{1}H NMR (400 MHz) and ^{13}C NMR (126 MHz) spectra of **10gi** ($CDCl_3$)

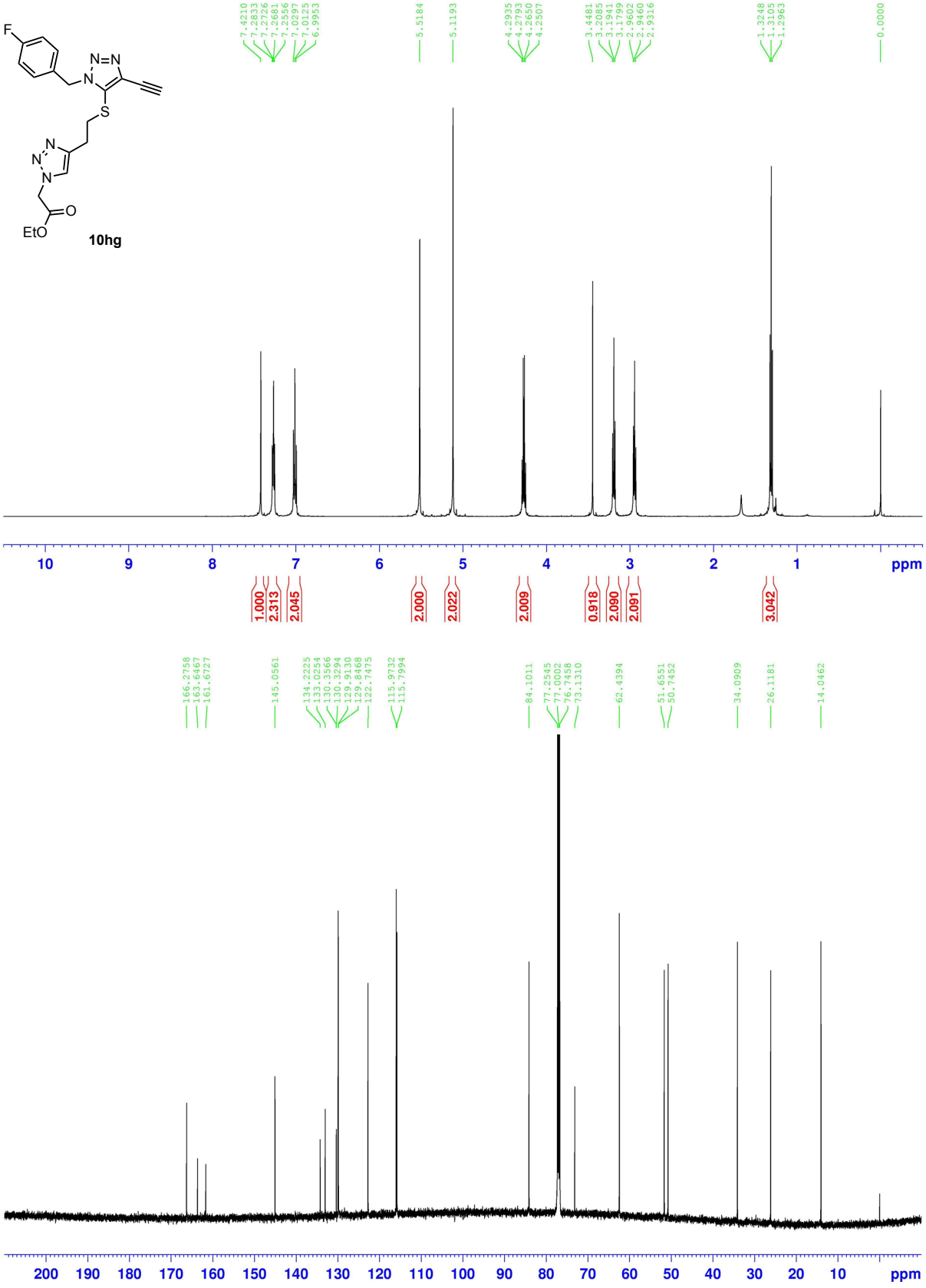


^{1}H NMR (400 MHz) and ^{13}C NMR (126 MHz) spectra of **10hgTMS** ($CDCl_3$)

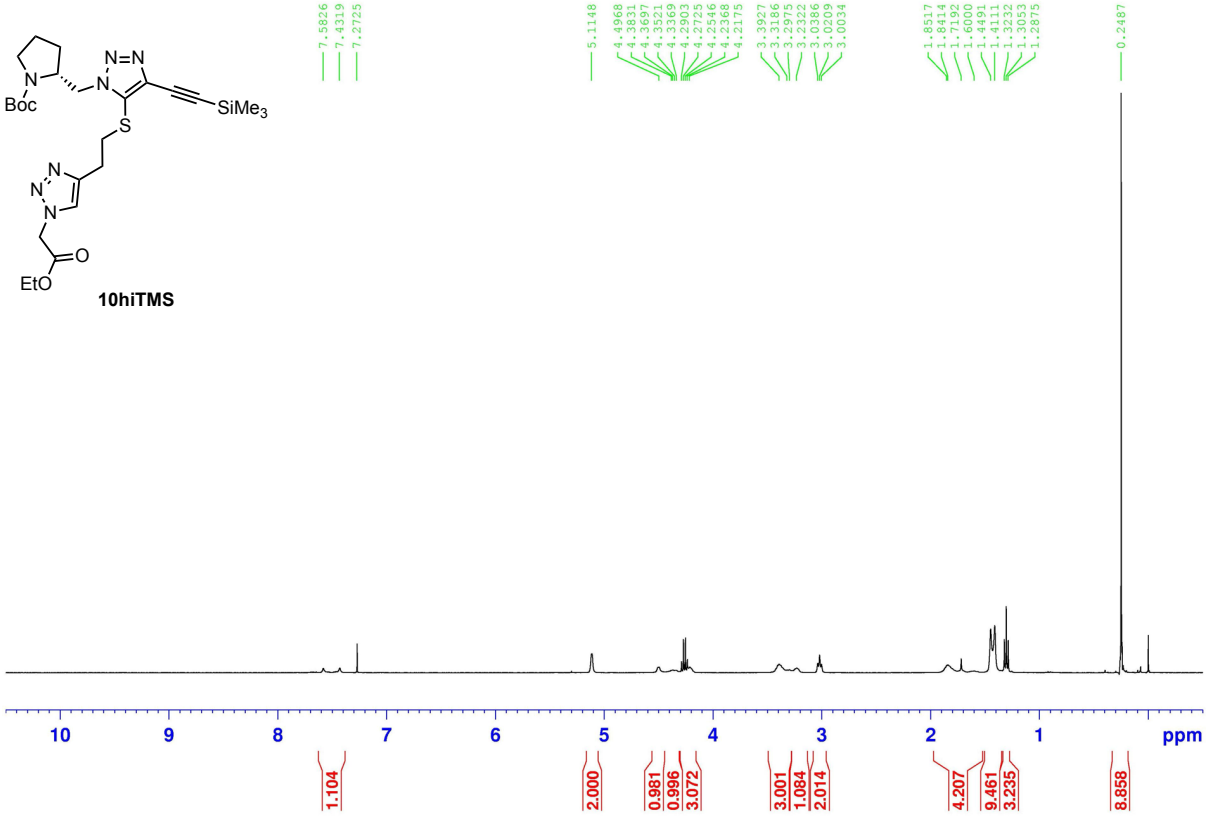


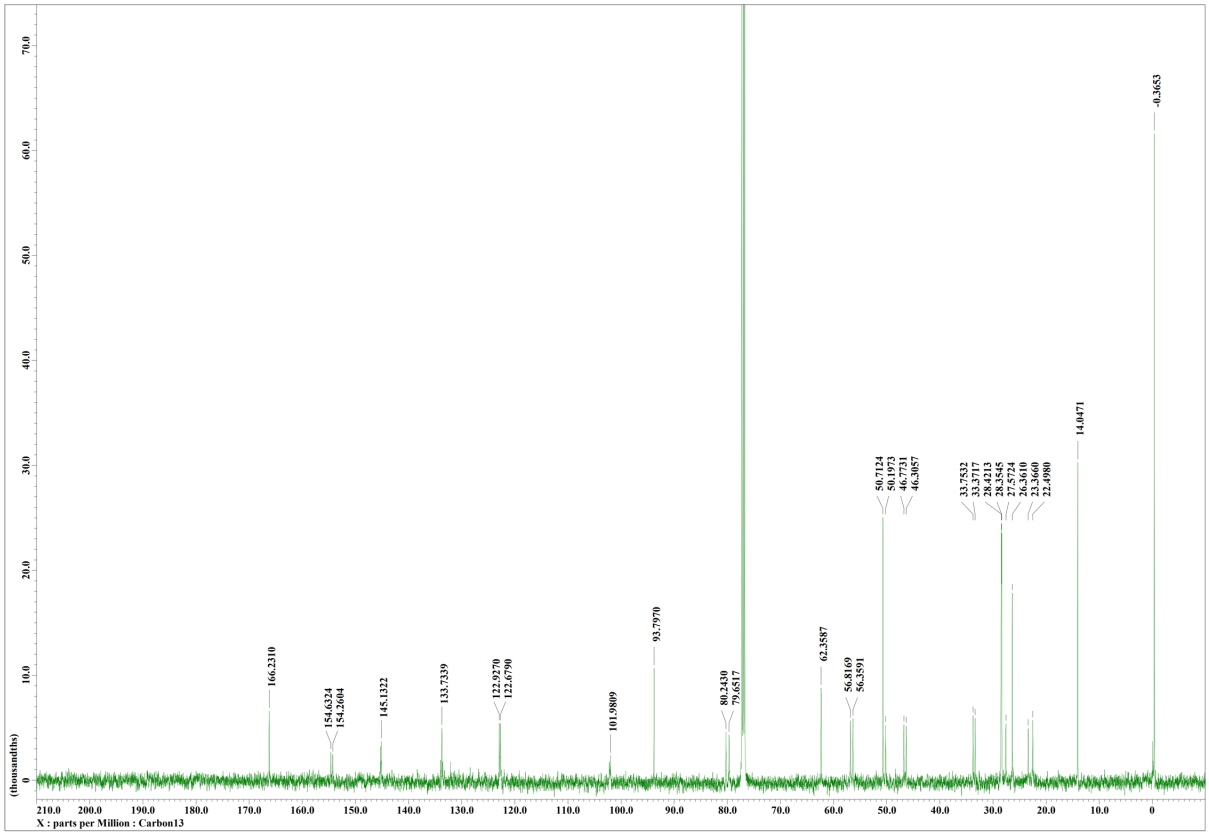


^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **10hg** ($CDCl_3$)

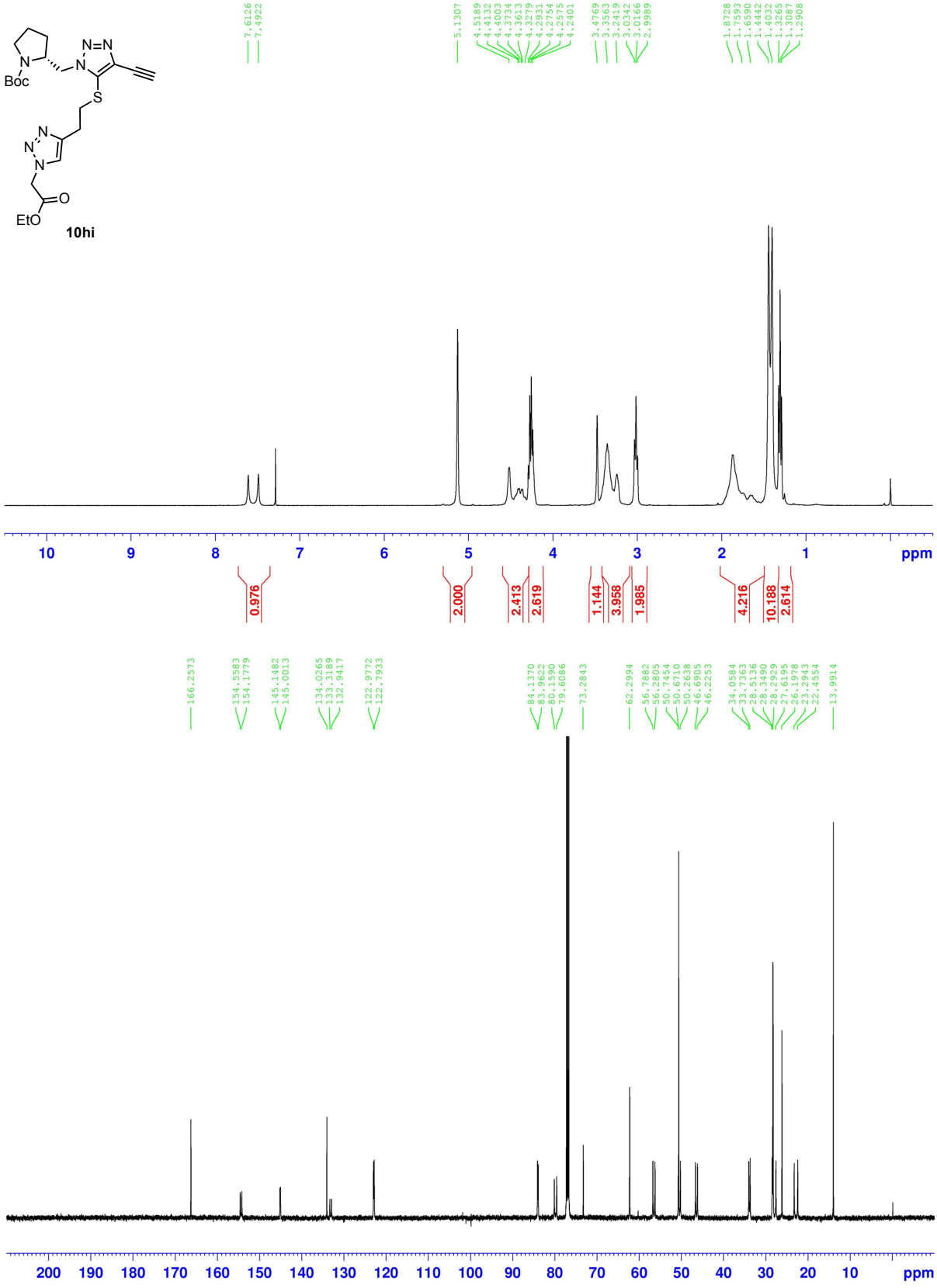


^{1}H NMR (400 MHz) and ^{13}C NMR (126 MHz) spectra of **10hiTMS** ($CDCl_3$)

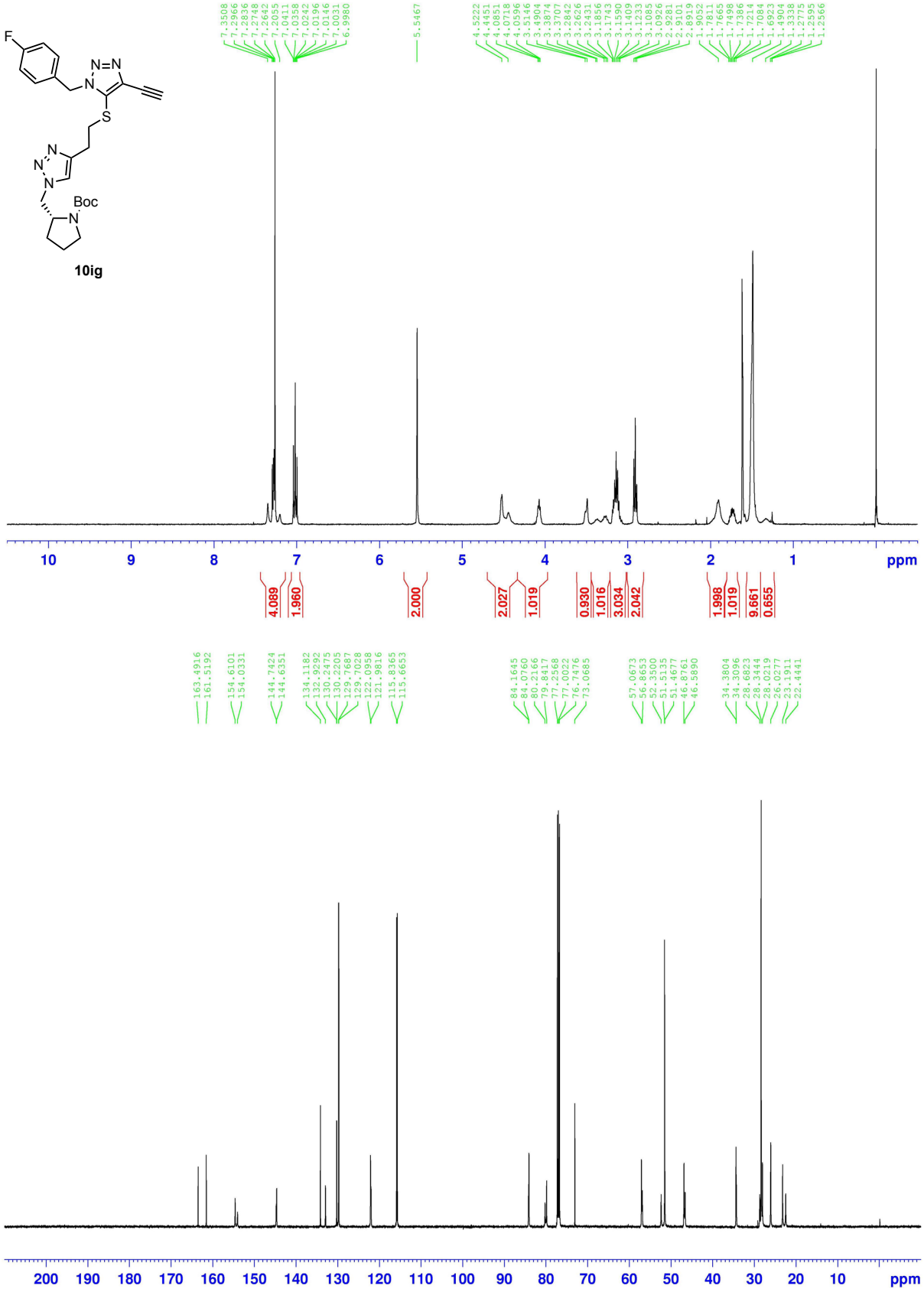




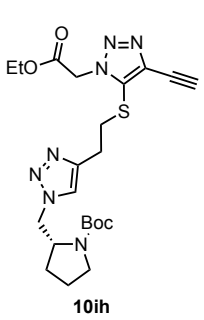
^{1}H NMR (400 MHz) and ^{13}C NMR (126 MHz) spectra of **10hi** ($CDCl_3$)



^{1}H NMR (400 MHz) and ^{13}C NMR (126 MHz) spectra of **10ig** ($CDCl_3$)

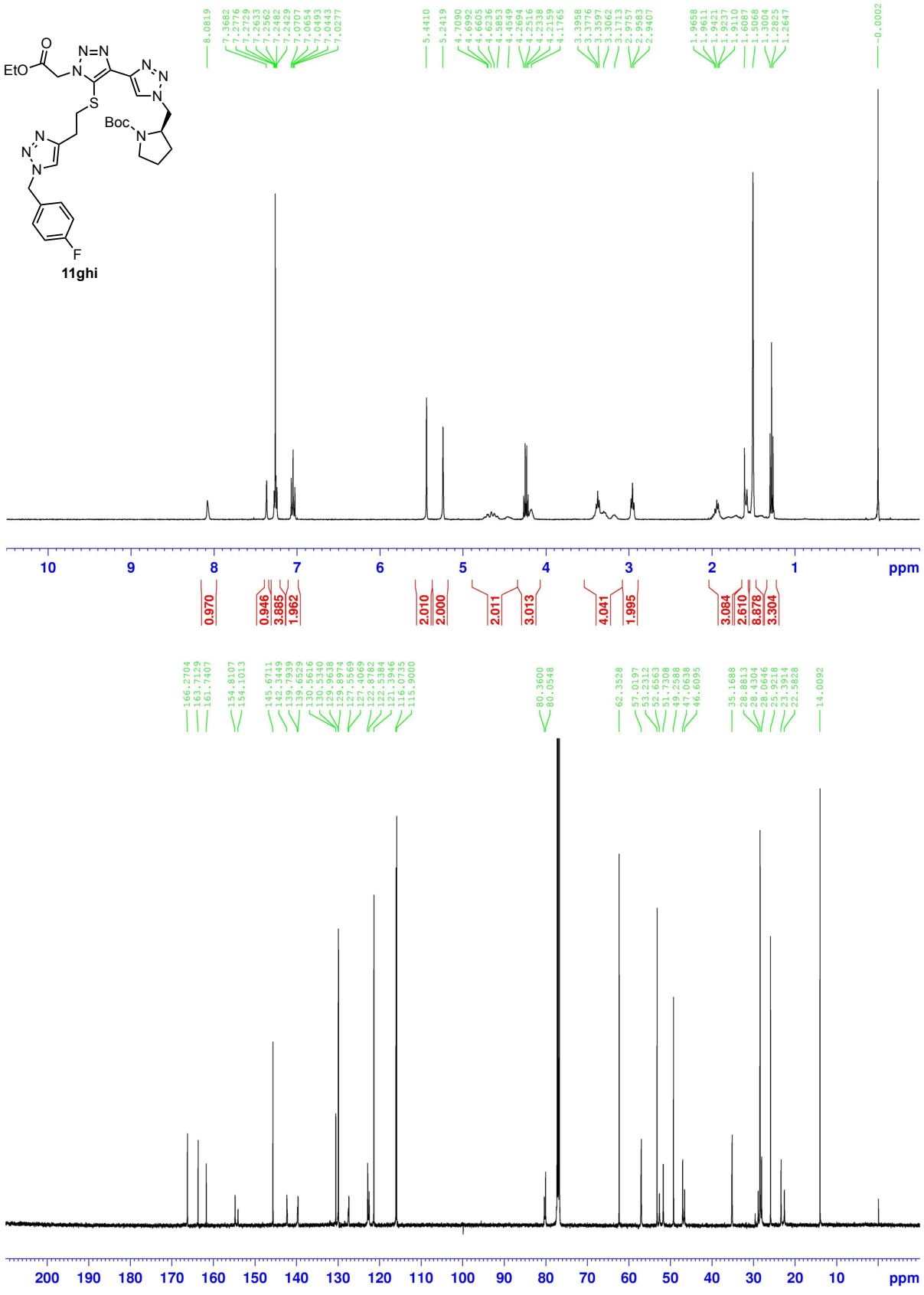


^{1}H NMR (400 MHz) and ^{13}C NMR (126 MHz) spectra of **10ih** ($CDCl_3$)

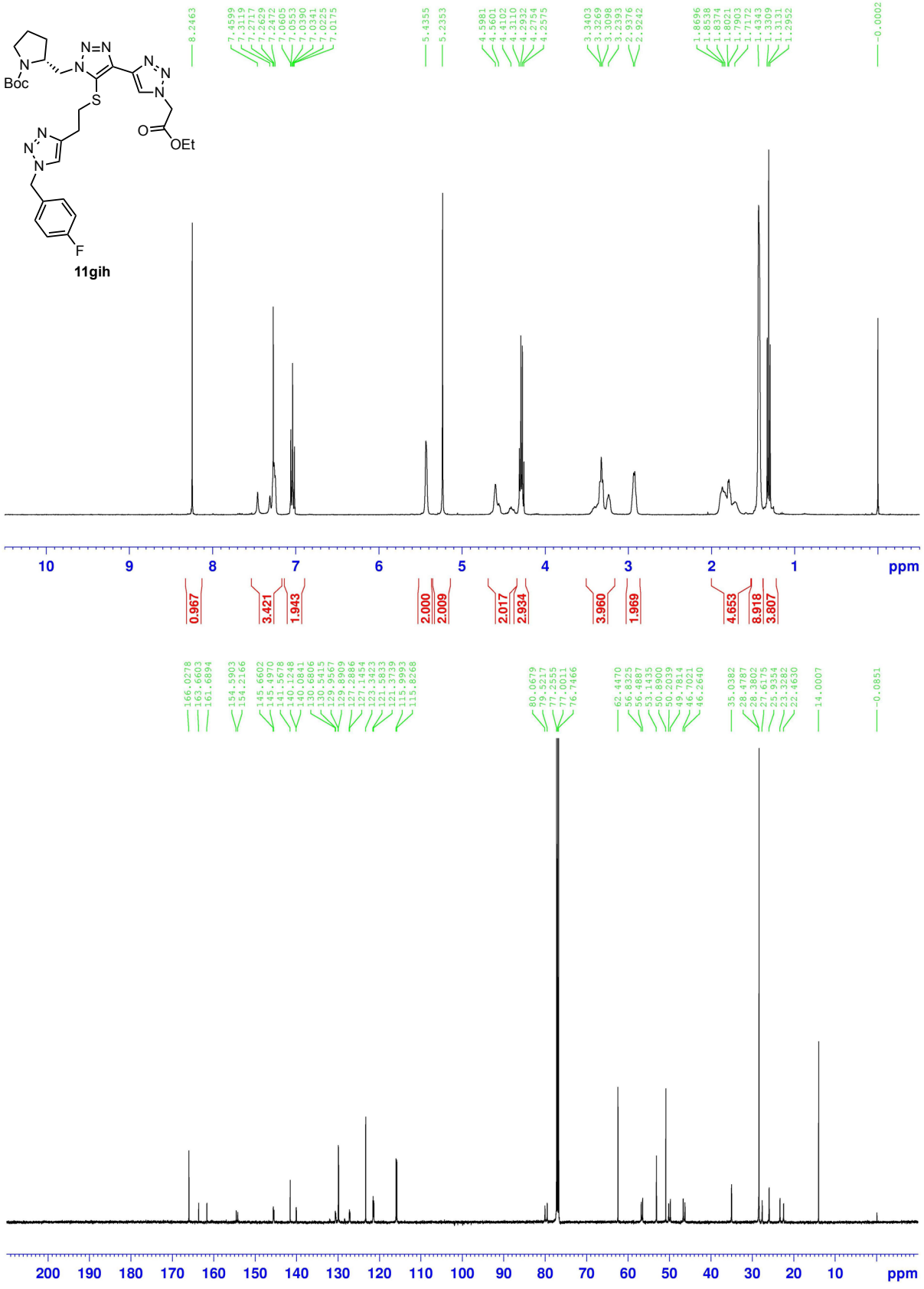


10ih

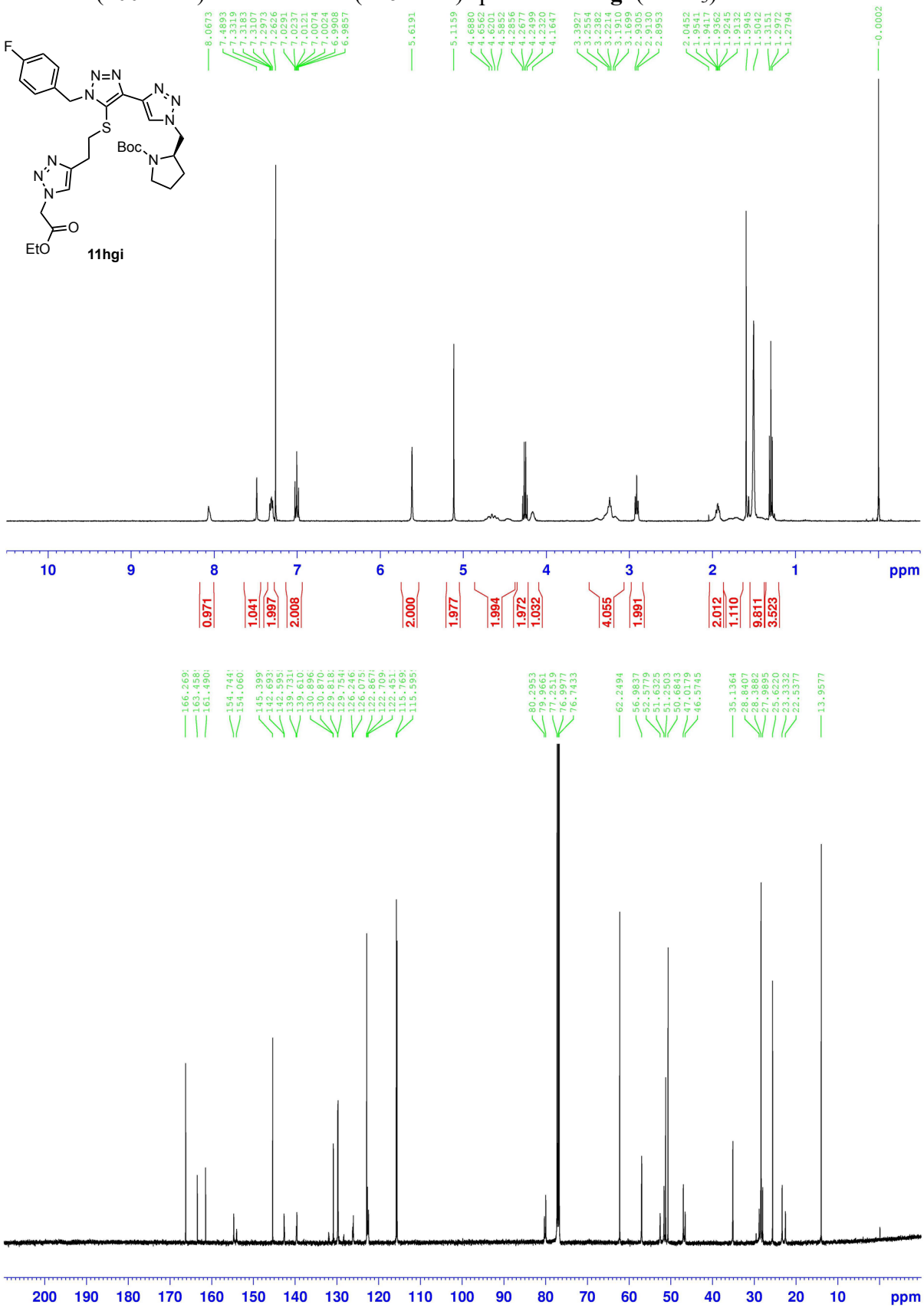
^{1}H NMR (400 MHz) and ^{13}C NMR (126 MHz) spectra of **11ghi** ($CDCl_3$)



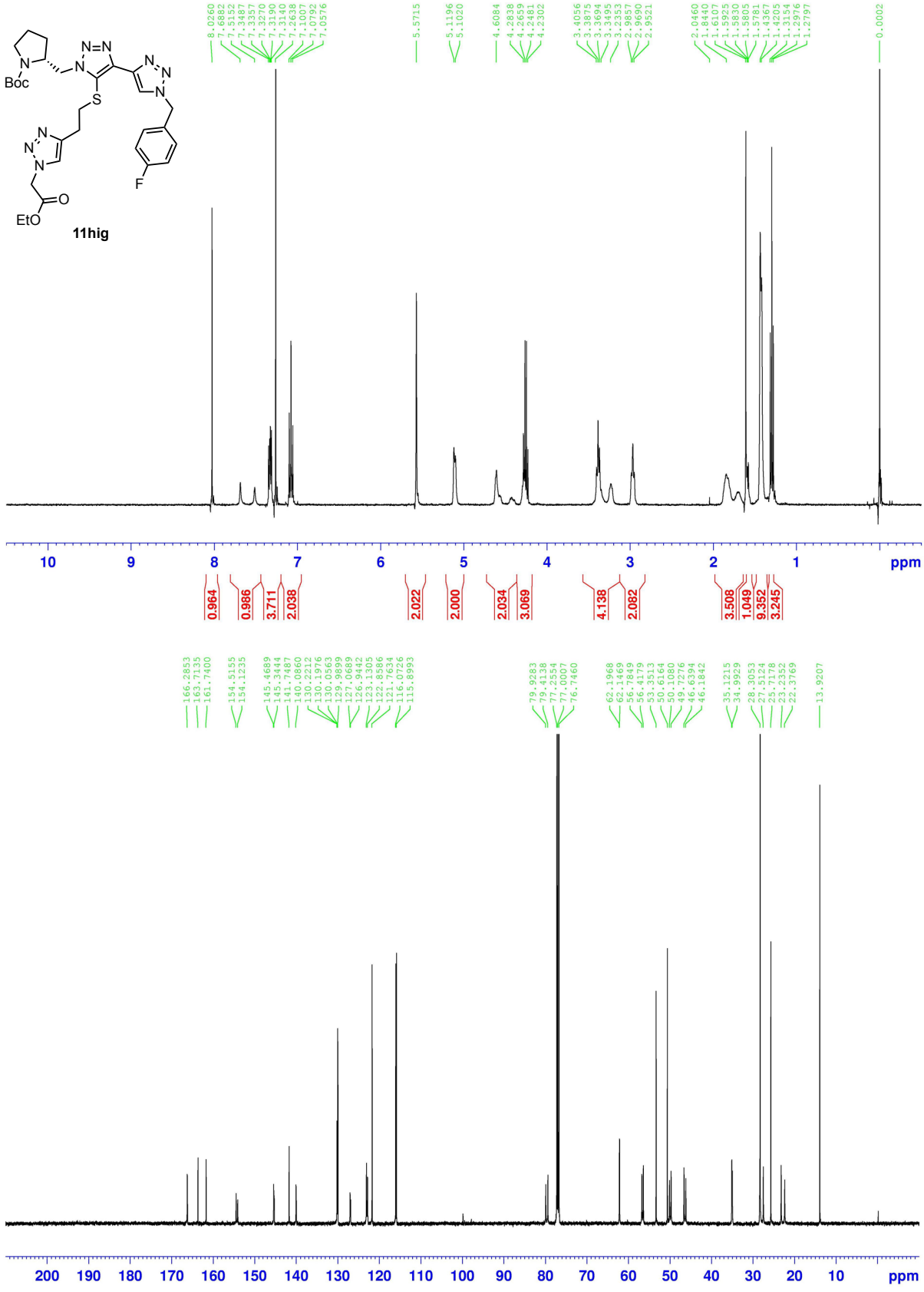
^{1}H NMR (400 MHz) and ^{13}C NMR (126 MHz) spectra of **11gih** ($CDCl_3$)



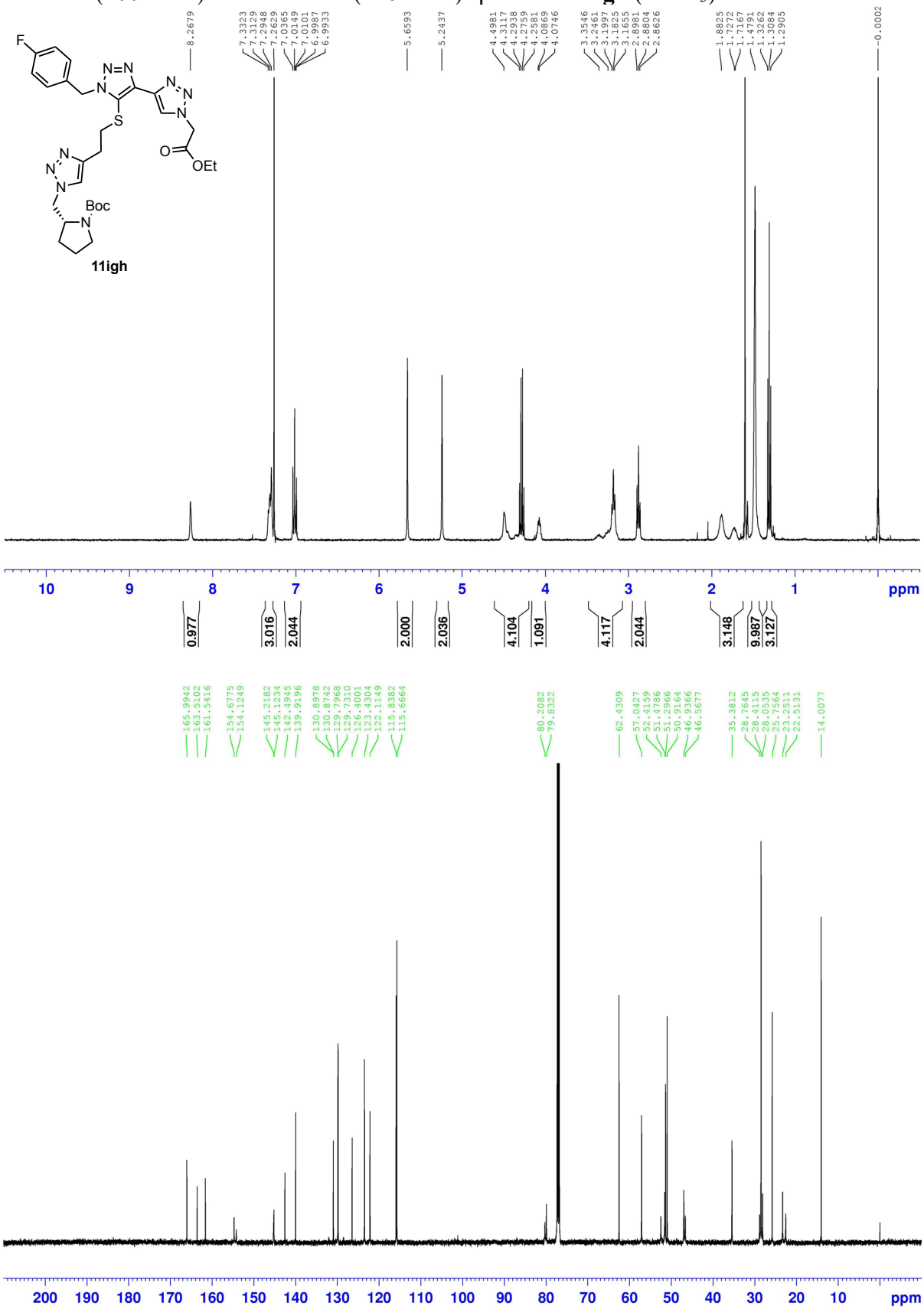
^{1}H NMR (400 MHz) and ^{13}C NMR (126 MHz) spectra of **11hgi** ($CDCl_3$)



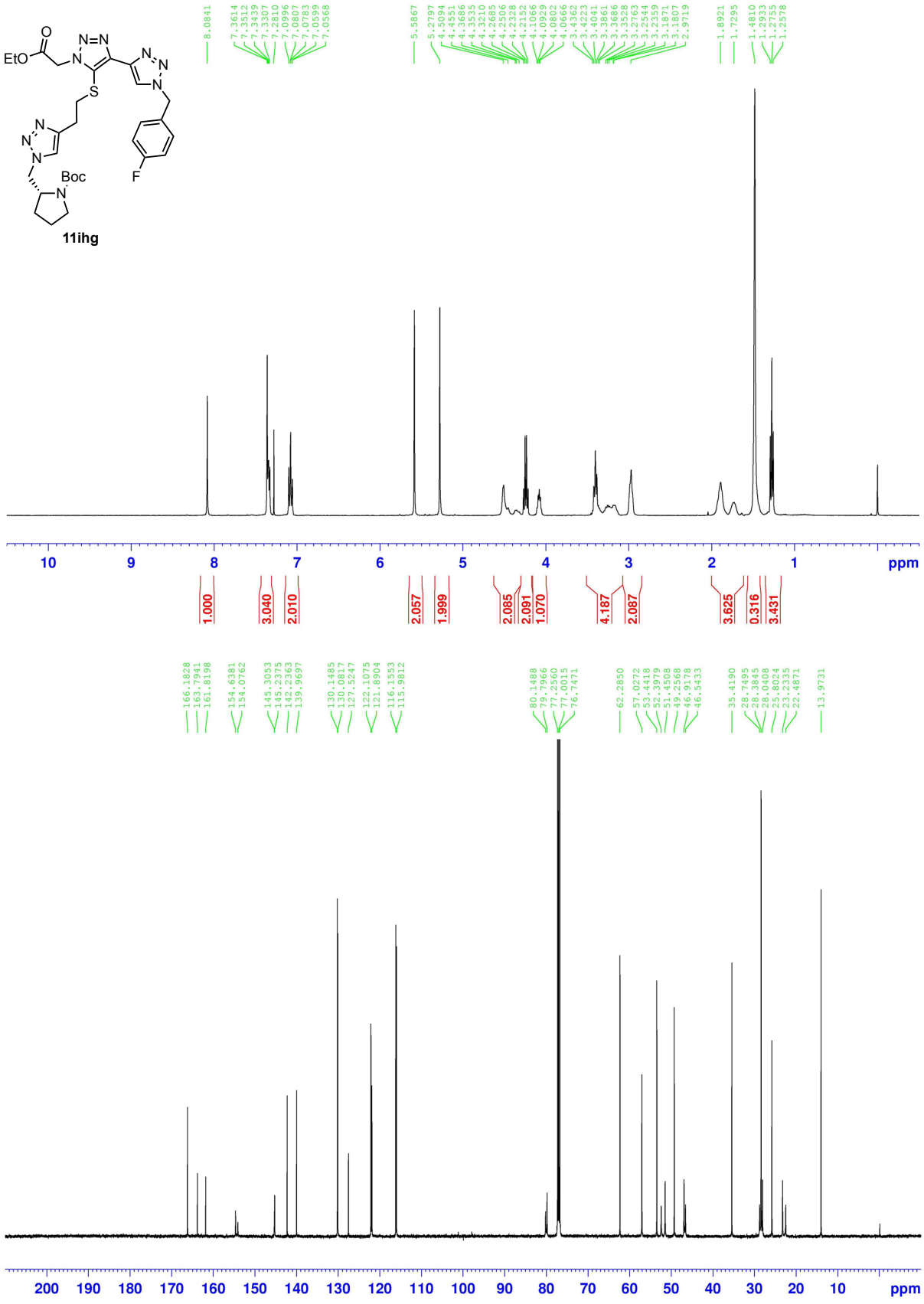
^{1}H NMR (400 MHz) and ^{13}C NMR (126 MHz) spectra of **11hig** ($CDCl_3$)



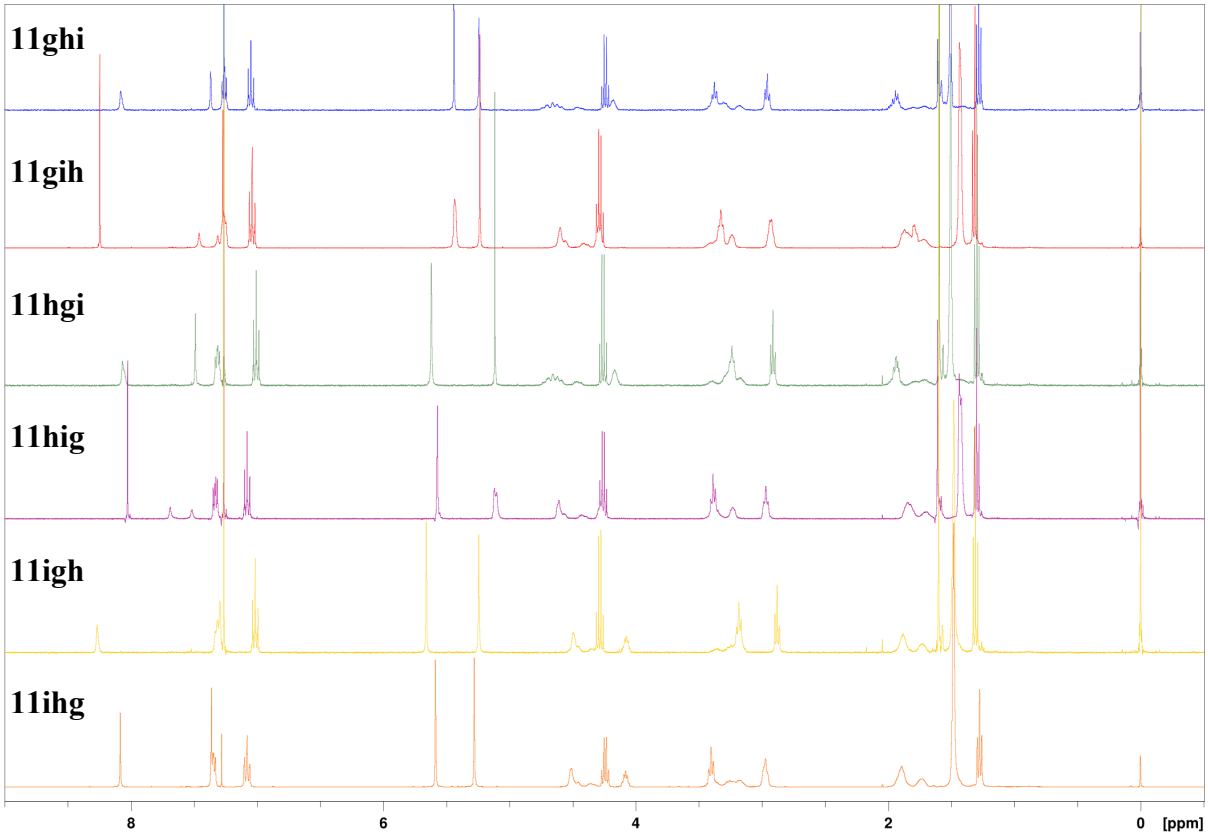
^{1}H NMR (400 MHz) and ^{13}C NMR (126 MHz) spectra of **11igh** ($CDCl_3$)



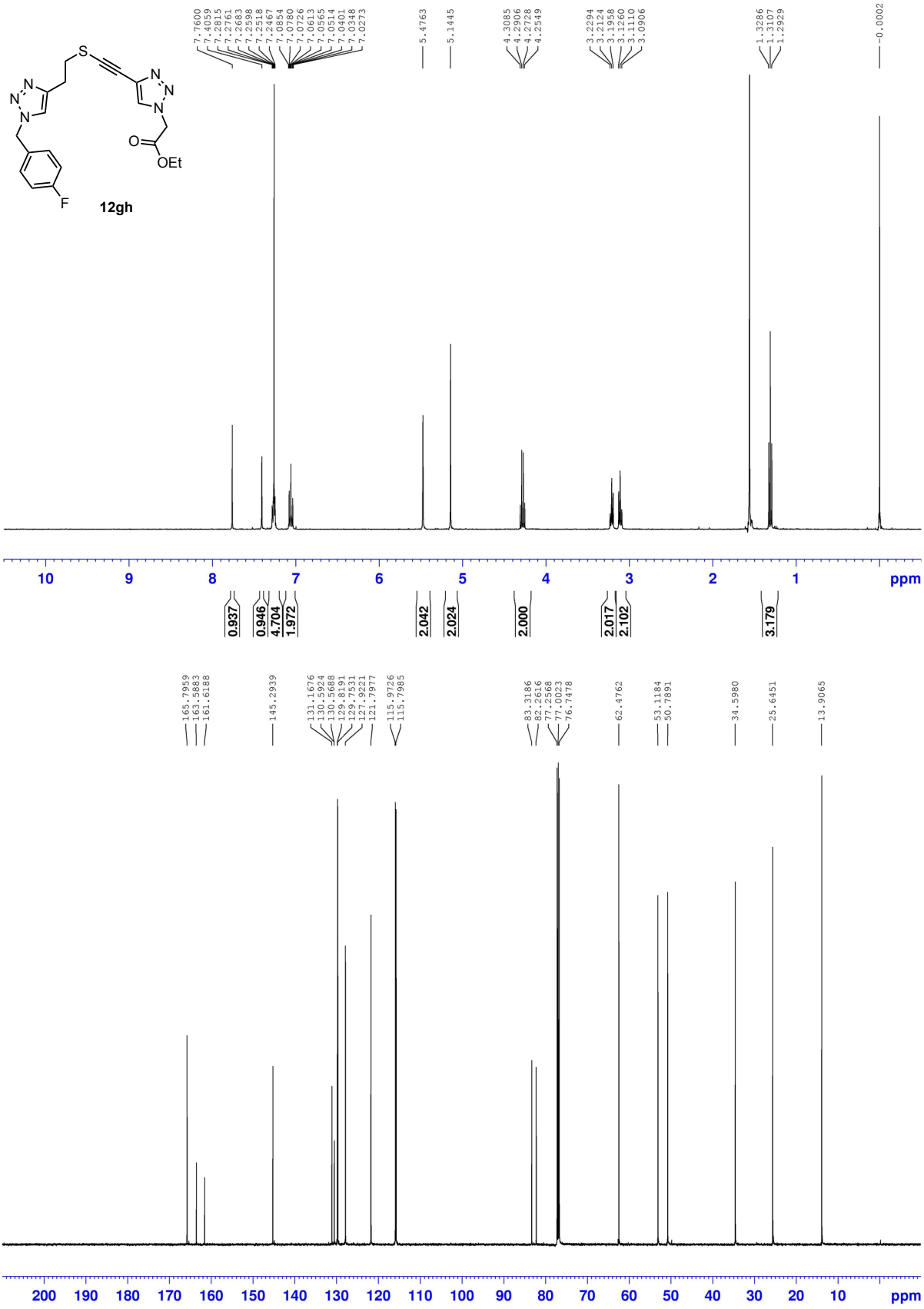
^{1}H NMR (400 MHz) and ^{13}C NMR (126 MHz) spectra of **11ihg** ($CDCl_3$)



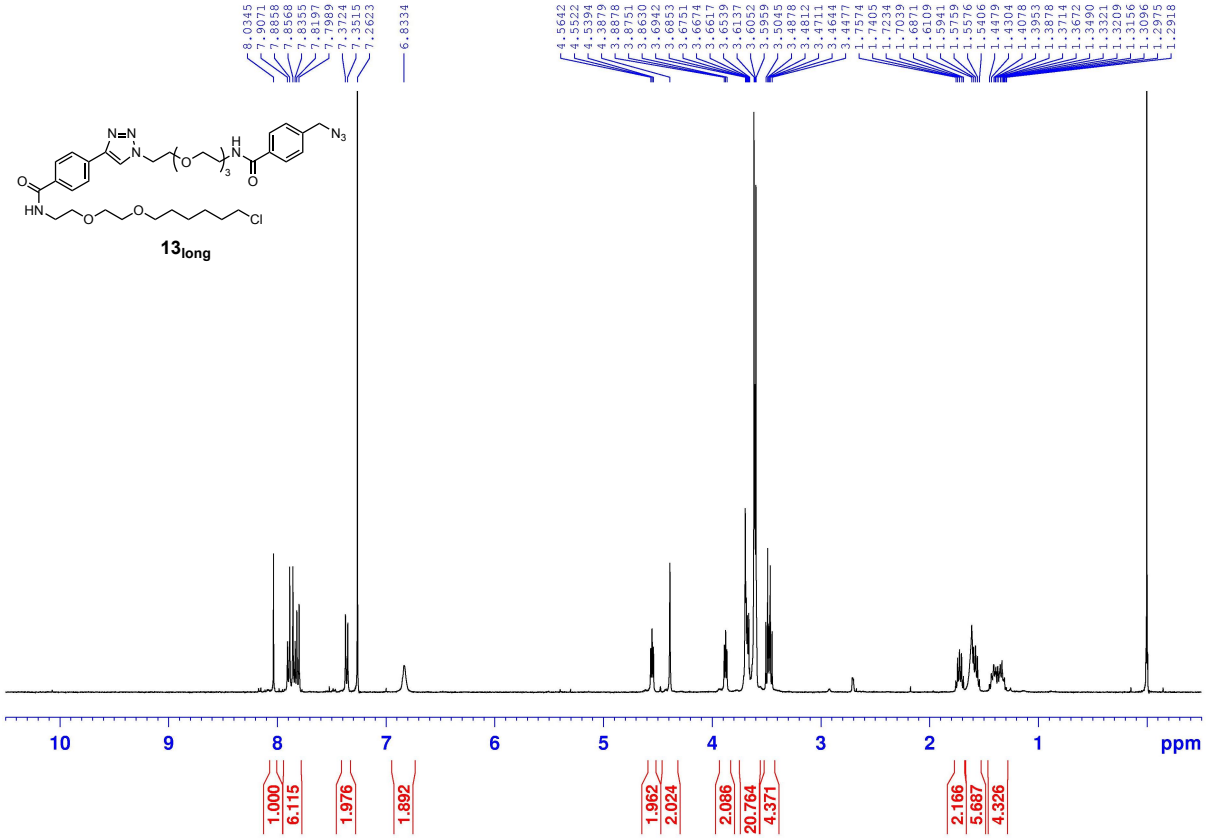
Stacked ^{1}H NMR spectra of tristriazoles **11ghi**, **11gih**, **11hgi**, **11hig**, **11igh**, and **11ihg** ($CDCl_3$)

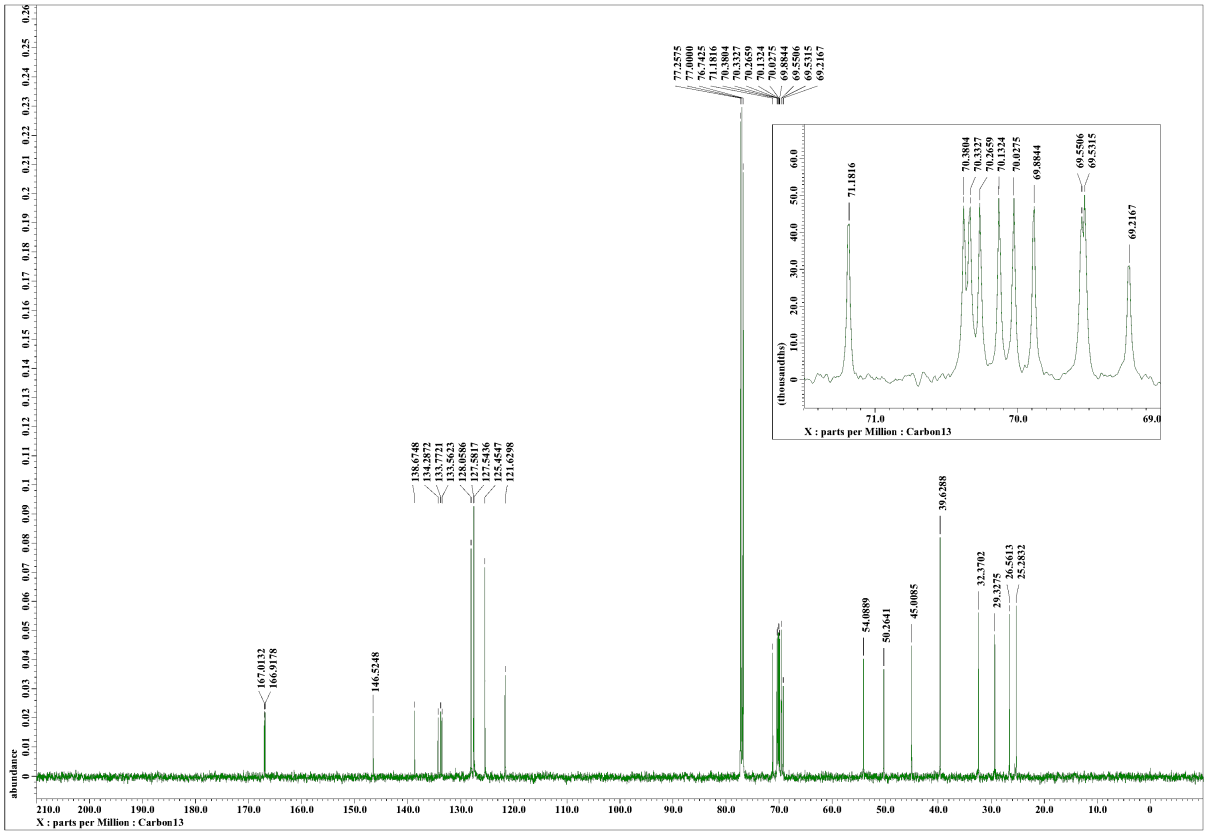


^{1}H NMR (400 MHz) and ^{13}C NMR (126 MHz) spectra of **12gh** ($CDCl_3$)

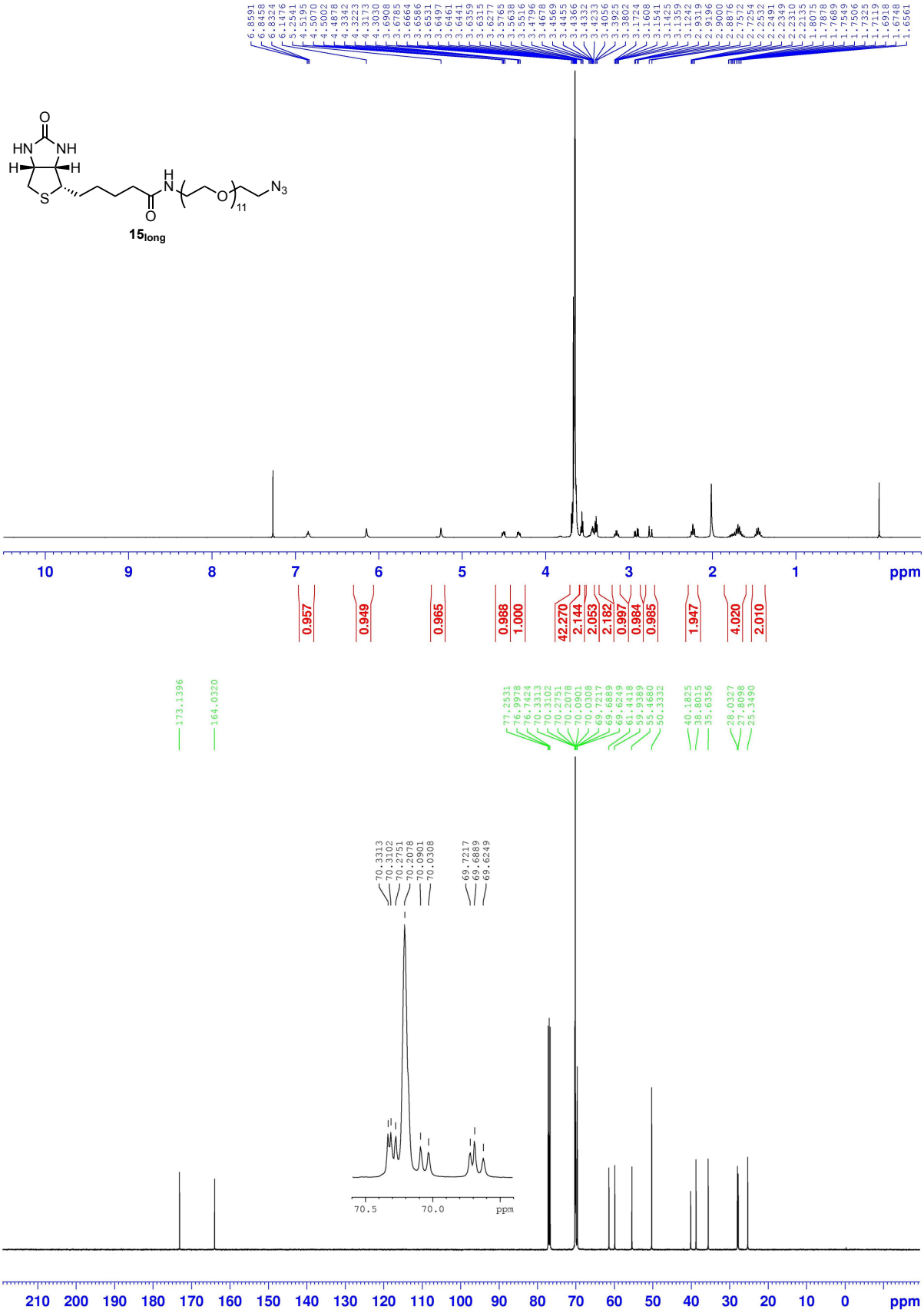


^{1}H NMR (400 MHz) and ^{13}C NMR (126 MHz) spectra of **13_{long}** ($CDCl_3$)

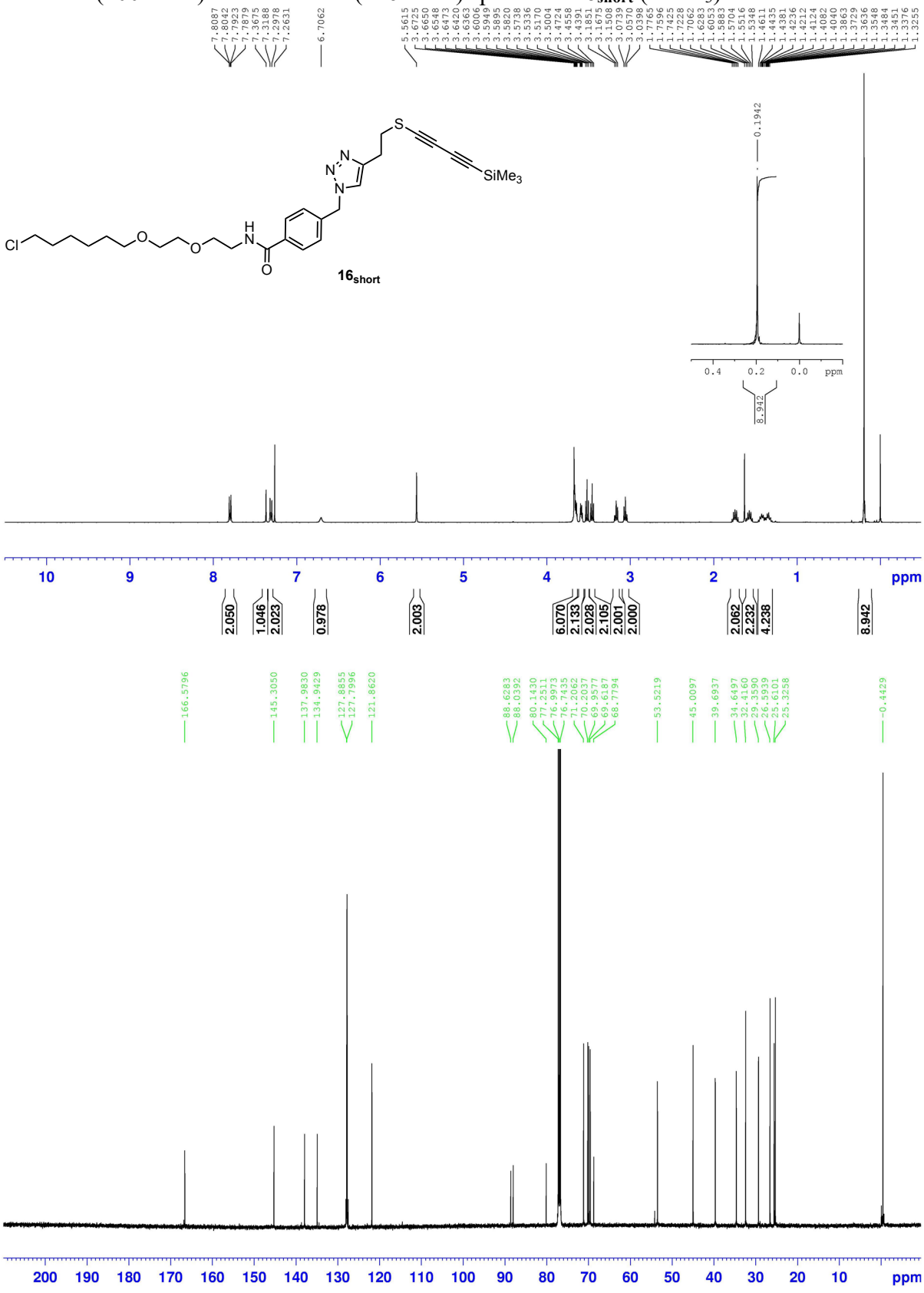




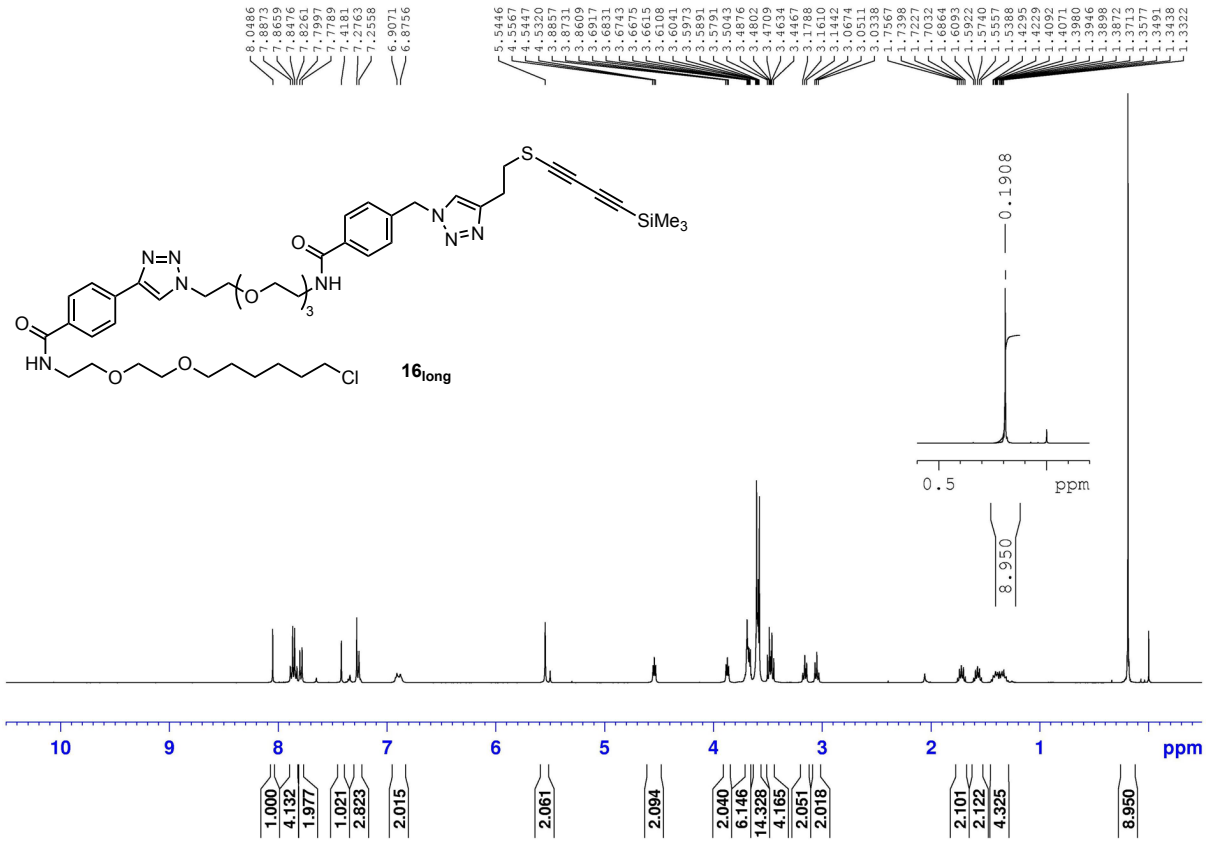
^{1}H NMR (400 MHz) and ^{13}C NMR (126 MHz) spectra of **15$_{long}$** ($CDCl_3$)

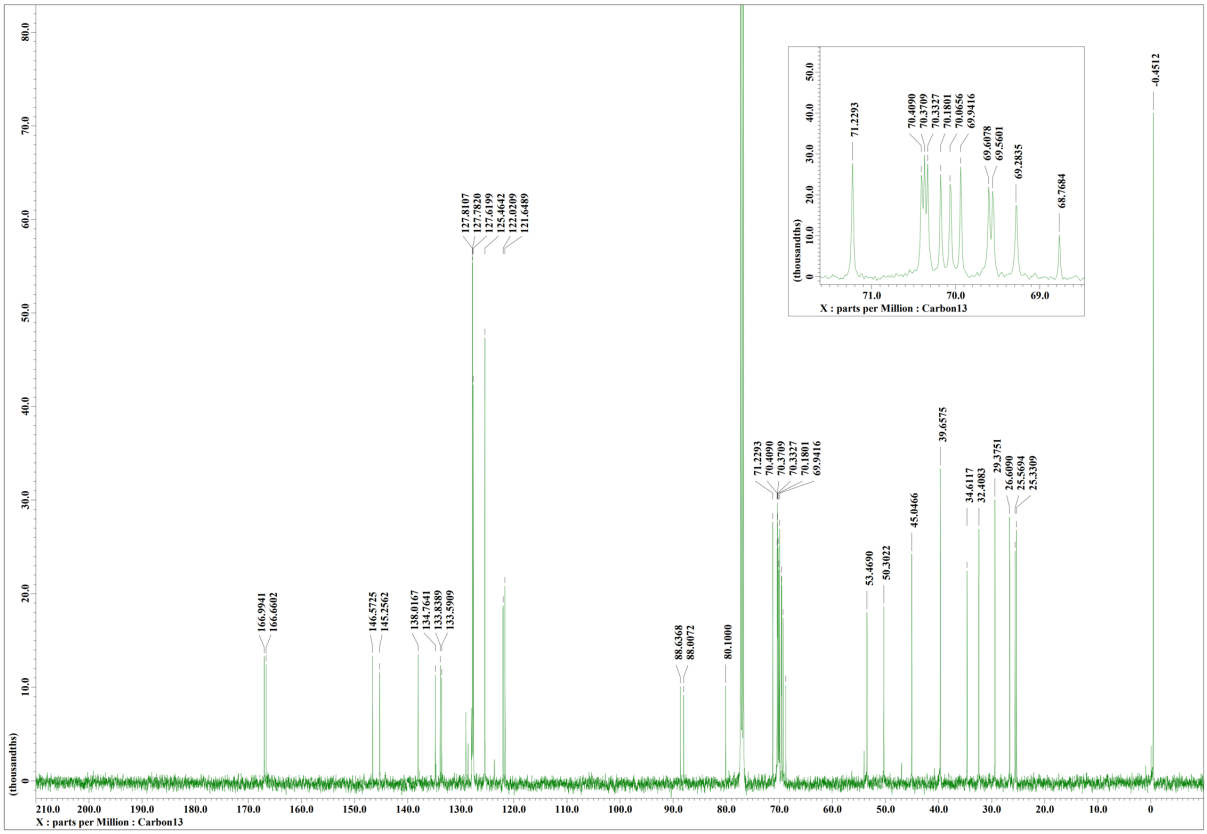


^{1}H NMR (400 MHz) and ^{13}C NMR (126 MHz) spectra of **16$_{short}$** ($CDCl_3$)

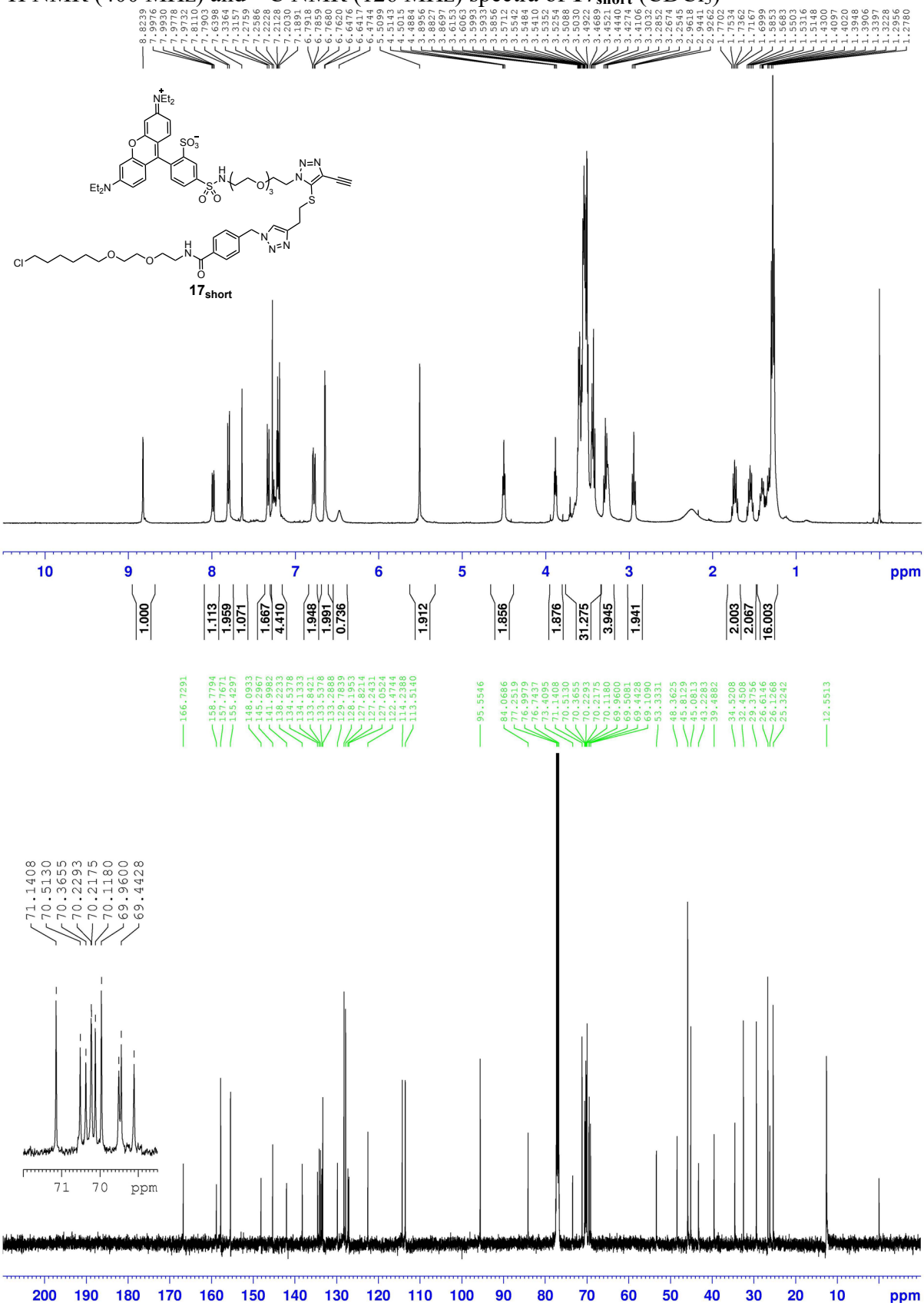


^{1}H NMR (400 MHz) and ^{13}C NMR (126 MHz) spectra of **16$_{long}$** ($CDCl_3$)

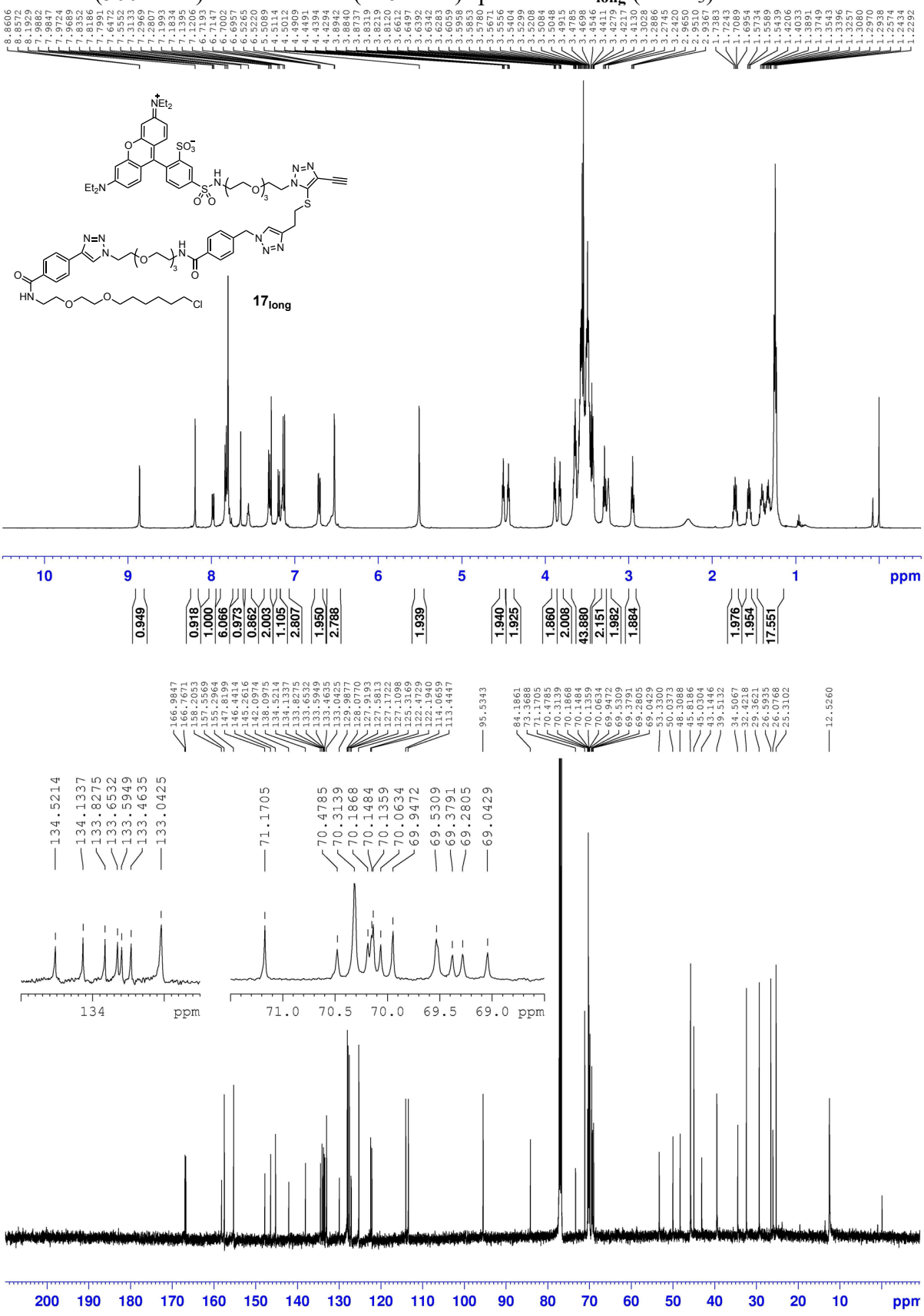




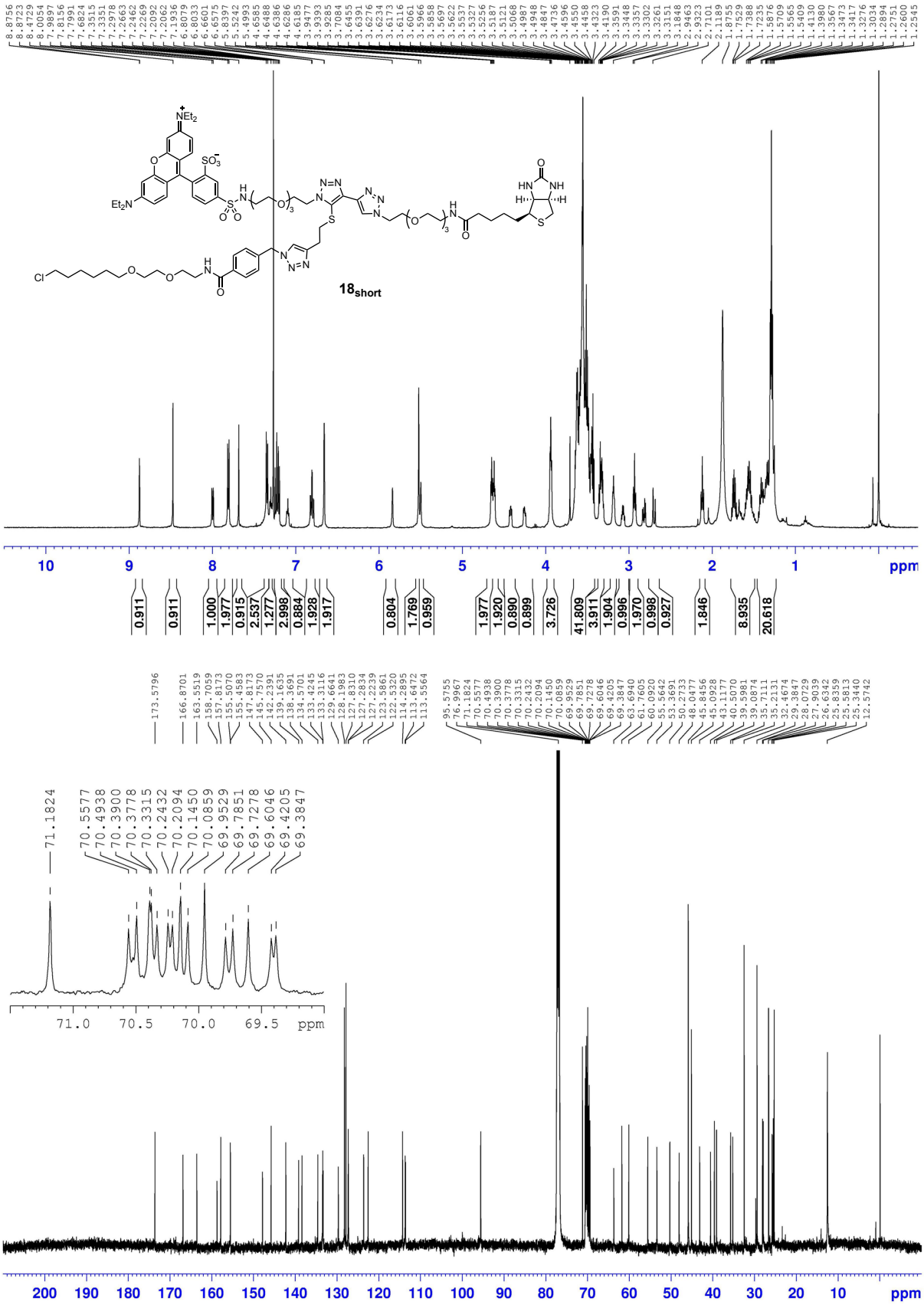
^{1}H NMR (400 MHz) and ^{13}C NMR (126 MHz) spectra of **17$_{short}$** ($CDCl_3$)



^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **17$_{long}$** ($CDCl_3$)



^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **18$_{short}$** ($CDCl_3$)



^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **18$_{long}$** ($CDCl_3$)