Supporting Information

Scalable Synthesis of Highly Stable Cyclopropene Building Blocks: Application for Bioorthogonal Ligation with Tetrazines

Lei Chen,[*b] Yuan Yang,[a] Fei Li,[a] Fei Jin,[b] Bin He,[b] Jun Yang[*a]

[a] *Key laboratory of Macromolecular Science of Shaanxi Province, Key laboratory of Applied Surface and Colloid Chemistry, Ministry of Education, School of Chemistry and Chemical Engineering, Shaanxi Normal University, Xi'an 710119, China*

[b] *State Key Laboratory of Functions and Applications of Medicinal Plants, Engineering Research Center for the Developmentand Application of Ethnic Medicine and TCM (Ministry of Education), Guizhou Provincial Key Laboratory of Pharmaceutics, School of Pharmacy, Guizhou Medical University, Guiyang 550004, China*

∗ Corresponding author.

E-mail address: junyang@snnu.edu.cn

∗ Corresponding author.

E-mail address: leichen@gmc.edu.cn

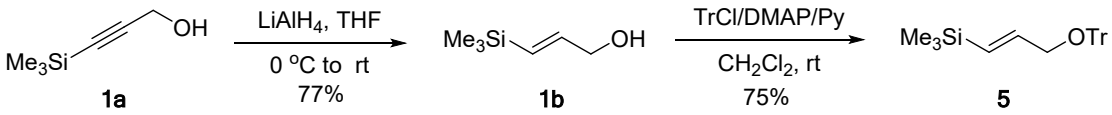
Table of Contents

General Information

All reactions were performed using flame-dried round-bottomed flasks or reaction vessels unless otherwise stated. Where appropriate, reactions were carried out under an inert atmosphere of nitrogen with dry solvents, unless otherwise stated. Yields refer to chromatographically, unless otherwise stated. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Reactions were monitored by thin-layer chromatography carried out on 0.20-0.25 mm Qingdao Marine Chemical Plant silica gel plates (GF254) using ultraviolet light as visualizing agent and an acidic mixture of *p*-anisaldehyde or a basic mixture of potassium permanganate and heat as developing agents. NMR spectra were recorded on a Bruker 600 MHz or 400 MHz spectrometer. High resolution mass spectra (HRMS) dates were recorded on Bruker Apex IV FTMS with ESI source and Bruker Maxis with EI source. Emission spectra were recorded on a Perkin Elmer LS-55 spectrometer.

Synthesis and characterization

Synthesis of compound **5**



1a **1b** **5**

Compound **1b** was synthesized according to literature [1].

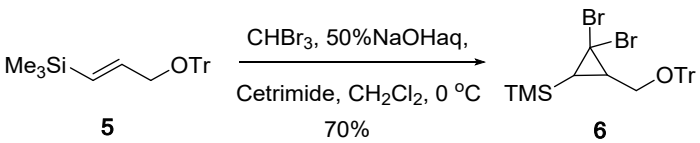
The alcohol **1b** (700 mg, 5.37 mmol) and DMAP (66 mg, 0.537 mmol) was dissolved in DCM (15 mL), added pyridine (0.87 mL, 10.75 mmol) and TrCl (3 g, 10.75 mmol). The reaction was stirred overnight at room temperature. The resulting mixture was diluted with dichloromethane (3×100 mL) and the organic layers was dried over anhydrous sodium sulfate and concentrated *in vacuo*. The crude product was purified by column chromatography on silica to afford compound **5** (1.5 g, 75%) as a white solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.47 (d, *J* = 7.4 Hz, 6H), 7.30 (t, *J* = 7.6 Hz, 6H), 7.24 (t, *J* = 7.3 Hz, 3H), 6.09 (dt, *J* = 18.8, 4.0 Hz, 1H), 6.02 (d, *J* = 18.8 Hz, 1H), 3.65 (dd, *J* = 3.9, 1.1 Hz, 2H), 0.08 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 144.2, 142.6, 129.9, 128.6, 127.8, 126.9, 86.8, 66.9, -1.3.

HRMS (ESI) m/z Calculated for $C_{24}H_{28}OSi$ $[M+Na]^+$: 395.1909, found 395.1907.

Synthesis of compound **6**



5 **6**

To a solution of compoud **5** (19.8 g, 53.1 mmol) in dichloromethane (500 mL) was added bromoform (67 g, 265.1 mmol) and *n*-hexadecyltrimethylammonium bromide (1.93 g, 5.3 mmol), and dropwise to 50% sodium hydroxide (25.6 g, 640 mmol) in water was added, the reaction was

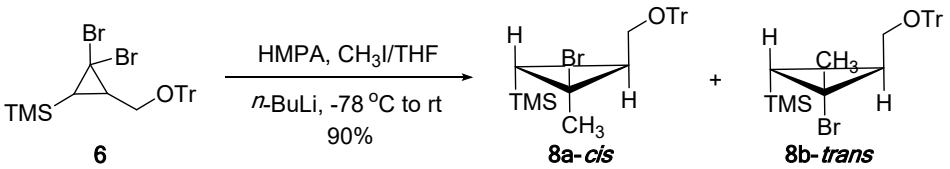
stirred 18 hours vigorously at 0 ℃. The mixture was quenched with water. The mixture was extracted with dichloromethane (3×100 mL). Then the combined organic phases were dried over anhydrous sodium sulfate and concentrated *in vacuo*. The crude product was purified by column chromatography using (PE: DCM = 10: 1) to afford dibromide cyclopropane **6** (34.1 g, 70%) as a sticky faint yellow oil. R_f = 0.3.

^{1}HNMR (600 MHz, $CDCl_3$) δ 7.48 (dd, *J* = 8.4, 1.1 Hz, 6H), 7.35-7.28 (m, 6H), 7.26-7.20 (m, 3H), 3.37 (dd, *J* = 10.2, 6.8 Hz, 1H), 3.23 (dd, *J* = 10.2, 6.3 Hz, 1H), 1.65 (dt, *J* = 10.2, 6.5 Hz, 1H), 0.60 (d, *J* = 10.3 Hz, 1H), 0.16 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 144.0, 128.7, 127.8, 127.0, 86.8, 66.8, 33.7, 32.3, 27.3, -1.3.

HRMS (ESI) m/z Calculated for $C_{26}H_{28}Br_2OSi$ $[M+Na]^+$: 567.0150, found 567.0150.

Synthesis of compound **8a** or **8b**



Methyl iodide (38.3 g, 270 mmol) and hexamethylphosphoramide (39.4 g, 220 mmol) were added to a solution of compound **6** (14.6 g, 27 mmol) in dry tetrahydrofuran (150 mL) at -78 °C under argon atmosphere. The mixture was stirred at the same temperature for 30 min, *n*-butyl lithium (37.8 mL, 94.5 mmol, 2.5 M in hexane) was added dropwise to a stirred mixture of **6**, the reaction was stirred for 2 h and at room temperature. Then the mixture was quenched with saturated aqueous ammonium chloride. The resulting mixture was diluted with ether (3×100 mL) and were washed with saturated sodium chloride, dried over anhydrous sodium sulfate, and concentrated *in vacuo*. The crude product was purified by column chromatography using (PE: DCM = 10: 1) to afford isomer **8** (11.5 g, 90%) as a faint yellow oil. R_f = 0.25 and 0.35.

8b-*trans*: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.50-7.42 (m, 6H), 7.30 (t, *J* = 7.6 Hz, 6H), 7.24 (t, *J* = 7.3 Hz, 3H), 3.16 (dd, *J* = 10.0, 6.4 Hz, 1H), 2.97 (dd, *J* = 10.0, 7.5 Hz, 1H), 1.72 (dt, *J* = 8.7, 7.4 Hz, 1H), 1.67 (s, 3H), 0.13 (s, 9H), -0.30 (d, *J* = 8.9 Hz, 1H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 144.1, 128.6, 127.8, 126.9, 86.4, 64.2, 41.2, 31.3, 27.7, 20.8, -0.9;

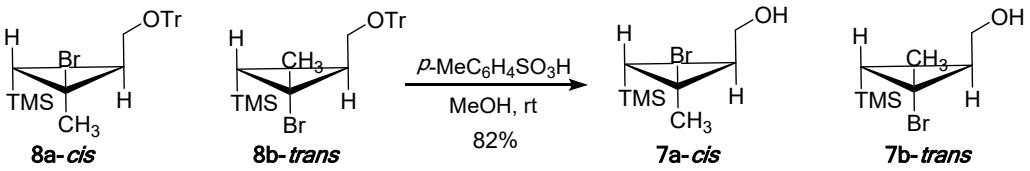
HRMS (ESI) m/z Calculated for $C_{27}H_{31}BrOSi$ $[M+Na]^+$: 501.1224, found 501.1220.

8a-*cis*: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.52-7.38 (m, 6H), 7.30 (t, *J* = 7.6 Hz, 6H), 7.23 (t, *J* = 7.3 Hz, 3H)., 3.34-3.37 (dd, *J* = 9.96, 3.42 Hz, 1H), 3.28-3.31 (dd, *J* = 9.90, 3.42 Hz, 1H), 1.79 (s, 3H), 0.79-0.83 (m, 1H), 0.15-0.17 (d, *J* = 9 Hz, 1H), 0.08 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 144.3, 128.8, 127.7, 126.9, 86.5, 68.3, 41.3, 29.5, 28.9, 22.1, -0.7;

HRMS (ESI) m/z Calculated for $C_{27}H_{31}BrOSi$ $[M+Na]^+$: 501.1222, found 501.1220.

Synthesis of alcohol **7a** or **7b**



Isomer compound **8** (11.5 g, 24 mmol) was dissolved in methol (100 mL) and the mixture was stirred for 10 min, followed by the addition of *p*-toluenesulfonic acid (2.9 g, 17 mmol) were stirred at room temperature. The resulting mixture was concentrated *in vacuo*. The crude product was purified by column chromatography using (PE: EA = 8: 1) to afford isomer **7** (5.85 g, 82%) as a faint yellow oil. R_f = 0.3-0.25.

7a-*cis*: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 3.99-4.02 (m, 1H), 3.59-3.62 (m, 1H), 1.85 (s, 3H), 0.26-0.27 (d, *J* = 8.88 Hz, 1H), 0.07 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 67.6, 42.5, 30.8, 29.5, 21.6, -0.8.

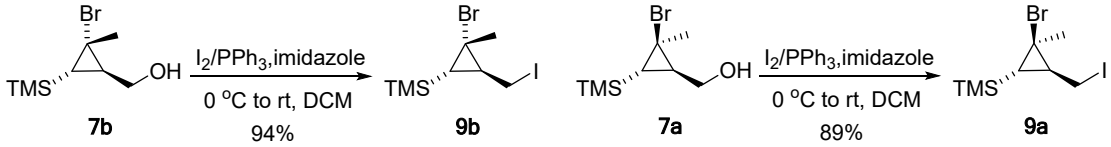
HRMS (ESI) m/z Calculated for $C_8H_{17}BrOSi$ $[M+Na]^+$: 259.0128, found 259.0124.

7b-*trans*: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 3.69-3.71 (dd, *J* = 11.88, 7.02 Hz, 1H), 3.54-3.57 (dd, *J* = 11.94, 3.12 Hz, 1H), 1.88 (s, 3H), 1.73-1.77 (m, 1H), 0.12 (s, 9H), -0.25-0.23 (d, *J* = 8.88 Hz, 1H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 63.5, 40.6, 33.6, 27.4, 20.6, -1.0.

HRMS (ESI) m/z Calculated for $C_8H_{17}BrOSi$ $[M+Na]^+$: 259.0128, found 259.0124.

Synthesis of iodine **9a** and **9b**



Triphenylphosphine (2.65 g, 10.1 mmol) was dissolved in anhydrous dichloromethane (50 mL) and the mixture was stirred at 0 °C, then imidazole (687.6 mg, 10.1 mmol) and iodine (2.56 g, 10.1 mmol) were added to 100 mL round-bottom flask. Compound **7b** (800 mg, 3.37 mmol) or **7a** (200 mg, 0.84 mmol) dissolved in anhydrous dichloromethane (3 mL) was added to the mixture. The resulting mixture was concentrated *in vacuo*. The crude product was purified by column chromatography using (100% PE) to afford **9b** (1.1 g, 94%) or **9a** (1.04 g, 89%) as a brown oil. R_f = 0.8.

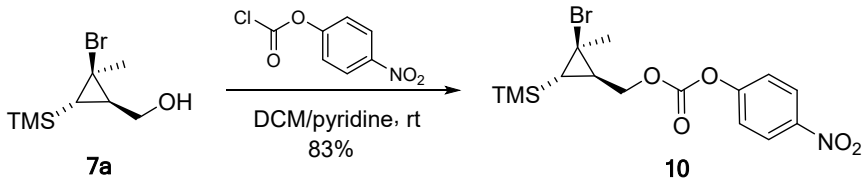
9b: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 3.31 (dd, *J* = 10.0, 7.7 Hz, 1H), 3.15 (dd, *J* = 10.1, 8.5 Hz, 1H), 1.97 (q, *J* = 8.5 Hz, 1H), 1.85 (s, 3H), 0.14 (s, 9H), -0.25 (d, *J* = 8.8 Hz, 1H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 44.3, 35.4, 27.2, 26.5, 6.71, -1.0.

9a: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 3.49 (dd, *J* = 9.8, 7.2 Hz, 1H), 3.39 (dd, *J* = 9.8, 7.9 Hz, 1H), 1.80 (s, 3H), 1.20-1.11(m, 1H), 0.26 (d, *J* = 8.8 Hz, 1H), 0.10 (s, 9H).

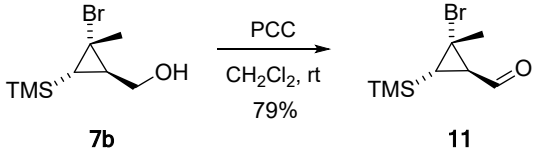
^{13}C NMR (151 MHz, $CDCl_3$) δ 46.6, 32.6, 29.1, 28.4, 11.6, -0.7.

Synthesis of ester **10**



7a (3.3 g, 13.9 mmol) in anhydrous dichloromethane (130 mL) were added to 250 mL round-bottom flask stirred at room temperature, followed by the addition of pyridine (1.35 mL, 16.7 mmol) and *p*-nitrophenyl chloroformate (3.37 g, 16.7 mmol). Then the mixture was quenched with saturated aqueous ammonium chloride. The resulting mixture was diluted with ethyl acetate (3×250 mL) and were washed with saturated sodium chloride, dried over anhydrous sodium sulfate, and concentrated *in vacuo*. The crude product was purified by column chromatography using (PE: EA = 10: 1) to afford compound **10** (4.9 g, 83%) as a white solid. R_f = 0.4.

Synthesis of aldehyde **11**



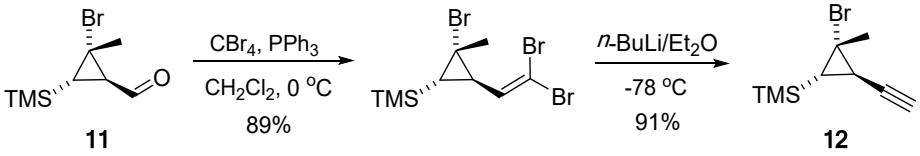
A solution of **7b** (1.8 g, 7.6 mmol) in dichloromethane (25 mL) was treated with Pyridinium chlorochromate (3.3 g, 15.2 mmol). The mixture was stirred at room temperature for 4 h and filtered with kieselguhr. The resulting mixture was concentrated *in vacuo*. The crude product was purified by column chromatography using (PE: EA = 8: 1) to afford **11** (1.4 g, 79%) as a yellow oil. R_f = 0.6.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.47-9.48 (d, *J* = 4.3 Hz, 1H), 2.43-2.46 (dd, *J* = 8.6, 4.3 Hz, 1H), 1.98 (s, 3H), 0.91-0.93 (d, *J* = 8.6 Hz, 1H), 0.16 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 198.5, 42.3, 41.2, 27.7, 25.7, -1.2.

HRMS (ESI) m/z Calculated for $C_8H_{15}BrOSi$ $[M+Na]^+$: 256.9972, found 256.9968.

Synthesis of terminal alkyne **12**



(1) Carbon tetrabromide (3.9 g, 12 mmol) and triphenylphosphine (6.2 g, 24 mmol) in anhydrous dichloromethane (50 mL) were added to 250 mL round-bottom flask stirred at 0 ℃ for 30 mins. Compound **11** (1.4 g, 6 mmol) dissolved in anhydrous dichloromethane (5 mL) was added to the mixture under an argon atmosphere. The resulting mixture was concentrated *in vacuo*. The crude product was purified by column chromatography using (100% PE) to afford compound 2,2-dibromovinyl-methylcyclopropane (2.1 g, 89%) as a faint yellow oil. R_f = 0.95.

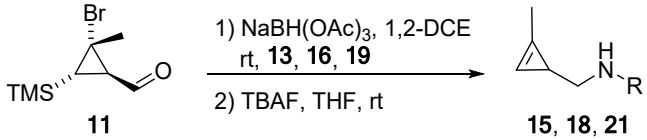
^{1}H NMR (600 MHz, $CDCl_3$) δ 6.06-6.07 (d, *J* = 8.3 Hz, 1H), 2.21-2.24 (t, *J* = 8.5 Hz, 1H), 1.86 (s, 3H), 0.16 (s, 9H), 0.07-0.08 (d, *J* = 8.7 Hz, 1H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 136.4, 89.9, 40.1, 35.1, 28.9, 25.5, -1.1.

(2) Under an argon atmosphere, *n*-Butyl lithium (3.6 mL, 8 mmol, 2.5 M in hexane) was added dropwise to compound 2,2-dibromovinyl-methylcyclopropane (1.6 g, 4 mmol) in dry ether (100 mL) at -78 ℃ stirred for 1 h. The mixture was carefully quenched with saturated aqueous ammonium chloride, diluted with water and ether. The organic layer was extracted with ether (3×150 mL). The combined organics were washed with saturated sodium chloride, dried over anhydrous sodium sulfate, and concentrated *in vacuo*. The crude product was purified by column chromatography using (100% PE) to afford compound **12** (860 mg, 91%) as a faint yellow oil. R_f= 0.9.

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.02 (d, *J* = 2.1 Hz, 1H), 1.94 (s, 3H), 1.88-1.90 (dd, *J* = 8.6, 2.1 Hz, 1H), 0.18 (d, *J* = 8.6 Hz, 1H), 0.15 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 82.9, 68.2, 40.1, 29.1, 26.1, 20.7, -1.2.
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.28 (d, *J* = 9.0 Hz, 2H), 7.40 (d, *J* = 9.0 Hz, 2H), 4.58 (dd, *J* = 11.2, 6.2 Hz, 1H), 4.44 (dd, *J* = 11.3, 8.2 Hz, 1H), 1.86 (s, 3H), 1.10 (dd, *J* = 14.8, 8.3 Hz, 1H), 0.39 (d, *J* = 8.9 Hz, 1H), 0.11 (s, 9H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 155.6, 152.4, 145.4, 125.3, 121.8, 73.6, 40.6, 29.1, 26.8, 22.2, -0.9.
HRMS (ESI) m/z Calculated for $C_{15}H_{20}BrNNaO_5Si$ $[M+Na]^+$: 424.0192, found: 424.0186.

Synthesis of 1-Methylcyclopropene derivatives **15**, **18**, **21**

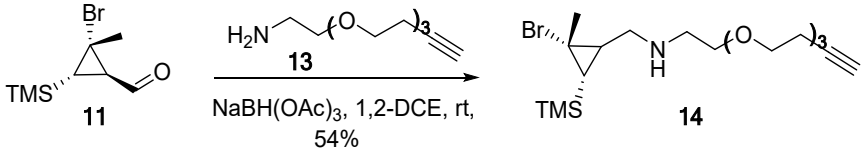


A: General procedure for the synthesis of 15, 18, 21

(1) **13**, **16**, **19** (1.5 equiv) and sodium triacetoxyborohyride (1.5 equiv) in dry dichloroethane, compound **11** (1.0 equiv) was added to round-bottom flask stirred at room temperature for overnight. The mixture was treated with sodium bicarbonate and the organic layer was extracted with dichloromethane (3×50 mL). The combined organic layer was dried and evaporated. The residue was purified by column chromatography to afford compounds **14**, **17**, **20** as a faint yellow oil.

(2) To a solution of compounds **14**, **17**, **20** (1.0 equiv) in dry tetrahydrofuran, TBAF (1M in THF, 2.0 equiv) was added. The reaction mixture was stirred at room temperature overnight. After that the solvent was removed and the residue was purified by column chromatography. The desired products **15**, **18**, **21** were obtained as a yellow oil.

Synthesis of compound **14**



Compound **13** was synthesized according to literature [2].

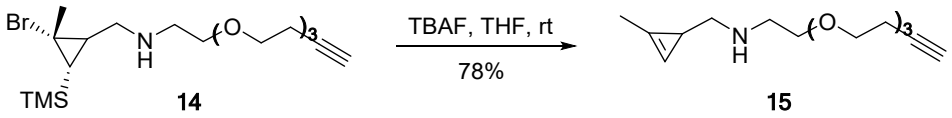
Following the general procedure A(1), cyclopropane **14** was synthesized from compound **11** (15 mg, 1.0 equiv) and **13** (19.3 mg, 1.5 equiv) and $NaBH(OAc)_3$ (20 mg, 1.5 equiv), and purified by thin-layer chromatography (14 mg, 54%). R_f = 0.25 (DCM: MeOH = 30: 1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 4.20 (d, *J* = 2.1 Hz, 2H), 3.79-3.53 (m, 10H), 2.90 (dd, *J* = 12.3, 5.2 Hz, 2H), 2.80 (dd, *J* = 12.7, 7.4 Hz, 1H), 2.73 (dd, *J* = 12.7, 6.4 Hz, 1H), 2.43 (s, 1H), 1.84 (s, 3H), 1.67 (dd, *J* = 15.6, 7.1 Hz, 1H), 0.12 (s, 9H), -0.29 (d, *J* = 9.0 Hz, 1H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 79.6, 74.6, 70.5, 70.4, 70.3, 69.6, 69.1, 58.4, 49.7, 48.3, 40.9, 31.0, 27. 6, 21.2, -0.1.

HRMS (ESI) m/z Calculated for $C_{17}H_{32}BrNO_3Si$ $[M+H]^+$: 406.1408, found 406.1412.

Synthesis of compound **15**



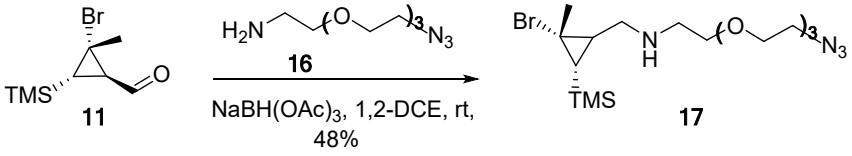
Following the general procedure A(2), cyclopropane **15** was synthesized from compound **14** (12.2 mg, 1.0 equiv) and TBAF (60 μL, 2.0 equiv), purified by thin-layer chromatography (5.7 mg, 78%). R_f = 0.25 (DCM: MeOH = 20: 1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.76 (s, 1H), 4.22 (d, *J* = 2.4 Hz, 2H), 3.92 (t, *J* = 5.1 Hz, 2H), 3.78-3.59 (m, 8H), 3.31-3.18 (m, 2H), 3.09 (dd, *J* = 12.6, 4.7 Hz, 1H), 2.81 (dd, *J* = 12.6, 6.0 Hz, 1H), 2.45 (t, *J* = 2.4 Hz, 1H), 2.18 (d, *J* = 1.1 Hz, 3H), 1.77 (ddd, *J* = 6.2, 4.7, 1.6 Hz, 1H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 119.8, 102.4, 79.5, 74.8, 70.2, 70.2, 70.1, 68.9, 65.9, 58.4, 55.1, 46.6, 14.3, 11.5.

HRMS (ESI) m/z Calculated for $C_{14}H_{23}NO_3$ $[M+H]^+$: 254.1751, found 254.1758.

Synthesis of compound **17**



Compound **16** was synthesized according to literature [3].

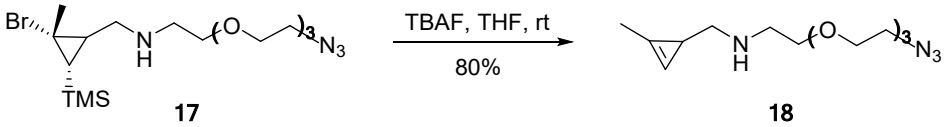
Following the general procedure A(1), cyclopropane **17** was synthesized from compound **11** (15 mg, 1.0 equiv) and **16** (21 mg, 1.5 equiv) and $NaBH(OAc)_3$ (20 mg, 1.5 equiv), and purified by thin-layer chromatography (13.4 mg, 48%). R_f = 0.3 (DCM: MeOH = 35: 1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 3.70-3.61 (m, 12H), 3.39 (t, *J* = 4.8 Hz, 2H), 2.93-2.83 (m, 2H), 2.77 (dd, *J* = 12.6, 7.4 Hz, 1H), 2.72 (dd, *J* = 12.7, 6.4 Hz, 1H), 1.84 (s, 3H), 1.67 (d, *J* = 8.2 Hz, 1H), 0.12 (s, 9H), -0.31 (d, *J* = 9.0 Hz, 1H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 70.7, 70.6, 70.3, 70.0, 69.8, 50.7, 49.8, 48.4, 44.8, 41.0, 31.2, 27.5, 21.2, -1.0.

HRMS (ESI) m/z Calculated for $C_{16}H_{33}BrN_4O_3Si$ $[M+H]^+$: 437.1578, found 437.1591.

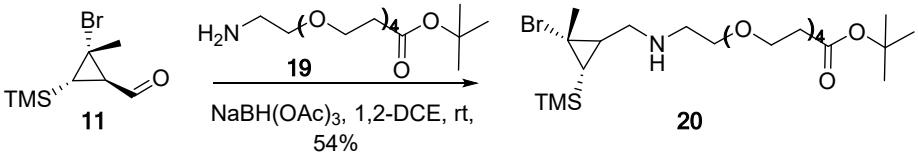
Synthesis of compound **18**



Following the general procedure A(2), cyclopropane **18** was synthesized from compound **17** (13.4 mg, 1.0 equiv) and TBAF (60 μL, 2.0 equiv), purified by thin-layer chromatography (7 mg, 80%). R_f= 0.3 (DCM: MeOH = 15: 1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.75 (s, 1H), 3.90 (t, *J* = 5.0 Hz, 2H), 3.76-3.61 (m, 10H), 3.43 (t, *J* = 5.0 Hz, 2H), 3.20 (dt, *J* = 9.6, 5.1 Hz, 2H), 3.07 (dd, *J* = 12.5, 4.6 Hz, 1H), 2.79 (dd, *J* = 12.5, 6.0 Hz, 1H), 2.18 (d, *J* = 1.2 Hz, 3H), 1.78-1.73 (m, 1H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 119.7, 102.3, 70.5, 70.2, 70.0, 65.8, 55.1, 50.7, 46.5, 29.7, 24.2, 14.3, 11.5.
HRMS (ESI) m/z Calculated for $C_{13}H_{24}N_4O_3$ $[M+H]^+$: 285.1921, found 285.1926.

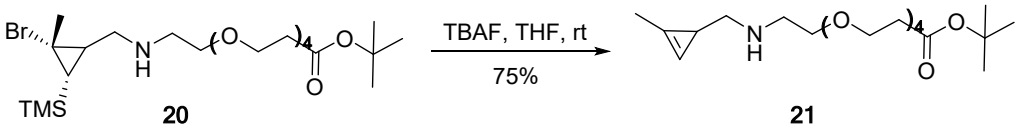
Synthesis of compound **20**



Compound **19** was synthesized according to literature [4].

Following the general procedure A(1), cyclopropane **20** was synthesized from compound **11** (30 mg, 1.0 equiv) and **19** (61 mg, 1.5 equiv) and $NaBH(OAc)_3$ (40 mg, 1.5 equiv), and purified by thick-layer chromatography (36.7 mg, 54%). R_f= 0.3 (DCM: MeOH = 25: 1).
^{1}H NMR (600 MHz, $CDCl_3$) δ 3.79-3.57 (m, 18H), 2.92-2.83 (m,2H), 2.78 (dd, *J* = 12.7, 7.4 Hz, 1H), 2.71 (dd, *J* = 12.7, 6.5 Hz, 1H), 1.82 (s, 3H), 1.66 (dd, *J* = 15.6, 7.1 Hz, 1H), 1.42 (s, 9H), 0.10 (s, 9H), -0.30 (d, *J* = 9.0 Hz, 1H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 170.8, 80.4, 70.5, 70.4, 70.3, 70.2, 69.8, 69.6, 66.8, 49.7, 48.3, 40.9, 39.3, 36.2, 31.0, 28.0, 27.5, 21.1, -1.0.
HRMS (ESI) m/z Calculated for $C_{23}H_{46}BrNO_6Si$ $[M+H]^+$: 540.2351, found 540.2360.

Synthesis of compound **21**



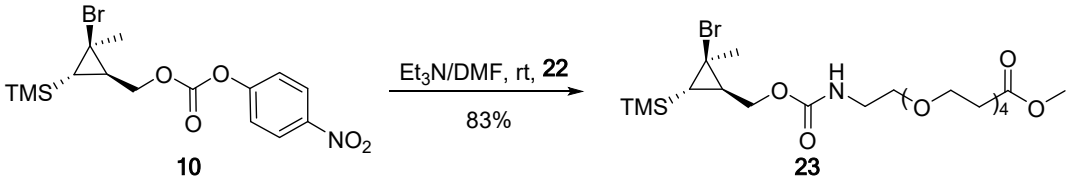
Following the general procedure A(2), cyclopropane **21** was synthesized from compound **20** (40 mg, 1.0 equiv) and TBAF (0.15 mL, 2.0 equiv), purified by thin-layer chromatography (21.5 mg, 75%). R_f = 0.3 (DCM: MeOH = 15: 1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.68 (s, 1H), 3.92 (t, *J* = 5.1 Hz, 2H), 3.76-3.57 (m, 16H), 3.18 (q, *J* = 5.5 Hz, 2H), 3.05 (dd, *J* = 12.5, 4.7 Hz, 1H), 2.78 (dd, *J* = 12.5, 6.1 Hz, 1H), 2.14 (d, *J* = 1.2 Hz, 3H), 1.76 (d, *J* = 1.5 Hz, 1H), 1.44 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 170.8, 103.2, 100.0, 80.6, 70.5, 70.5, 70.4, 70.3, 70.3, 70.2, 68.4, 66.9, 55.7, 47.9, 36.2, 28.1, 16.5, 11.6.

HRMS (ESI) m/z Calculated for $C_{20}H_{37}NO_6$ $[M+H]^+$: 388.2694, found 388.2705.

Synthesis of compound **23**



Compound **22** was synthesized according to literature [5].

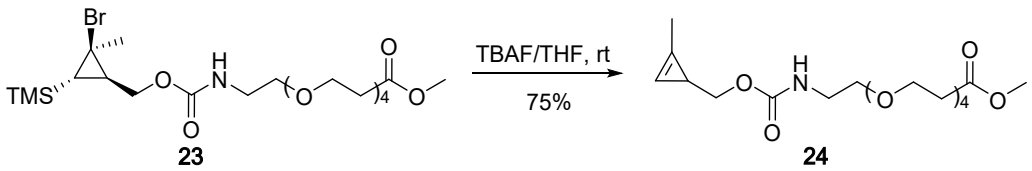
To a dry, argon-flushed schlenk flask charged with triethylamine (2.5 mL, 17.9 mmol) was added **10** (3.6 g, 8.9 mmol) in dry dimethylformamide (20 mL), then **22** (3.0 g, 10.7 mmol) in dry dimethylformamide was added. The reaction mixture was stirred at room temperature for several hours. The reaction mixture was concentrated *in vacuo* and the residue was purified by column chromatography to obtain crude product. After extraction with ethyl acetate (3×150 mL). The combined organic layer was dried and evaporated, and the residue was purified by column chromatography to yield compounds **23** (4.0 g, 83%). R_f = 0.4 (PE: EA= 1: 1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 4.41 (dd, *J* = 11.4, 5.7 Hz, 1H), 4.06 (dd, *J* = 11.1, 8.4 Hz, 1H), 3.74 (t, *J* = 6.5 Hz, 2H), 3.67 (s, 3H), 3.64-3.59 (m, 12H), 3.54 (t, *J* = 5.0 Hz, 2H), 3.36 (d, *J* = 4.8 Hz, 2H), 2.58 (t, *J* = 6.5 Hz, 2H), 2.07 (s, 1H), 1.80 (s, 3H), 0.25 (d, *J* = 8.9 Hz, 1H), 0.05 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ172.0, 156.5, 70.6, 70.5, 70.4, 70.3, 70.1, 68.8, 66.5, 51.6, 40.8, 34.8, 29.2, 27.7, 21.6, 19.1, -0.9.

HRMS (ESI) m/z Calculated for $C_{21}H_{40}BrNNaO_8Si$ $[M+Na]^+$: 564.1599, found: 564.1601.

Synthesis of compound **24**



Compound **23** (4.0 g, 7.4 mmol) in dry tetrahydrofuran (100 mL), TBAF (3.7 mL, 1M in THF, 3.7 mmol) was added. The reaction mixture was stirred at room temperature overnight. After that the

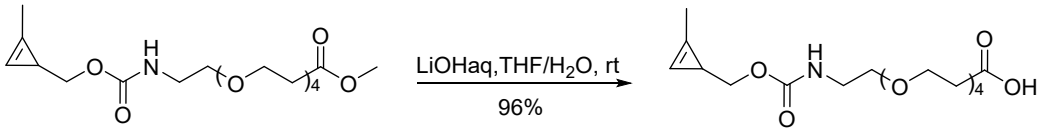
solvent was removed and the residue was purified by column chromatography. The desired product **24** (2.1g, 75%) was obtained as a faint yellow oil. R_f = 0.3 (DCM: MeOH= 15: 1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.56 (s, 1H), 3.91 (d, *J* = 5.0 Hz, 2H), 3.75 (t, *J* = 6.5 Hz, 2H), 3.68 (s, 3H), 3.65-3.60 (m, 12H), 3.55 (t, *J* = 5.1 Hz, 2H), 3.36 (dd, *J* = 10.5, 5.3 Hz, 2H), 2.60 (t, *J* = 6.5 Hz, 2H), 2.12 (s, 3H), 1.63 (dd, *J* = 5.0, 3.8 Hz, 1H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 172.0, 157.0, 120.7, 102. 2, 72.2, 70.6, 70.5, 70.4, 70.3, 70.2, 66.6, 51.6, 40.8, 34.9, 17.3, 11.6.

HRMS (ESI) m/z Calculated for $C_{18}H_{31}NNaO_8$ $[M+Na]^+$: 412.1942, found: 412.1949.

Synthesis of compound **25**



24 **25**

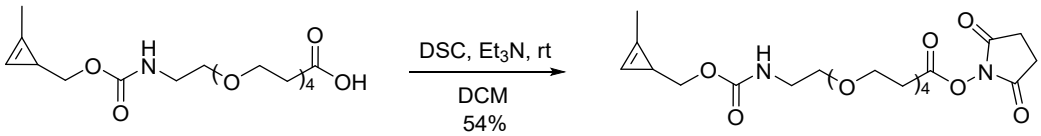
Compound **24** (850 mg, 2.18 mmol) in tetrahydrofuran and methanol (v:v, 1:1), then LiOH solution (183 mg, 4.37 mmol) was added. The reaction mixture was stirred at room temperature 3 h. The mixture was quenched with 1M HCl, extraction with ethyl acetate (3×100 mL). After that the solvent was evaporated. The desired product **25** (790 mg, 96%) was obtained as a white solid without purification.

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.55 (s, 1H), 3.91 (s, 2H), 3.76 (t, *J* = 6.0 Hz, 2H), 3.64 (m, 12H), 3.56 (d, *J* = 4.2 Hz, 2H), 3.36 (s, 2H), 2.60 (d, *J* = 5.4 Hz, 2H), 2.11 (s, 3H), 1.62 (s, 1H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 174.6, 157.1, 120.7, 102.2, 72.3, 70.6, 70.4, 70.2, 66.6, 40.7, 35.0, 17.2, 11.6.

HRMS (ESI) m/z Calculated for $C_{17}H_{29}NNaO_8$ $[M+Na]^+$: 398.1785, found: 398.1785.

Synthesis of compound **26**



25 **26**

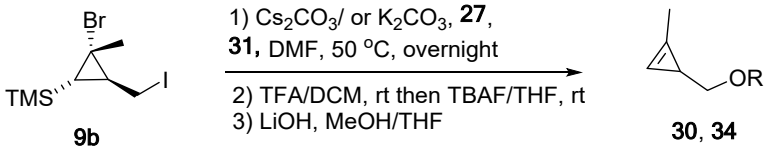
In argon environment, **25** (100 mg, 0.27 mmol) was dissolved in dry DMF (5 mL), triethylamine (55 μL, 0.4 mmol) and *N*, *N*'-disuccinide carbonate (102 mg, 0.4 mmol) were added, and the reaction mixture was stirred at room temperature for several hours. After TLC monitoring, the reaction was washed with water for many times. The organic layer was extracted with DCM (3×50 mL) and each extract was washed with water. The combined organic phases were dried over anhydrous sodium sulfate and concentrated *in vacuo*. The crude product was purified by column chromatography using (PE: EA = 1:1) to afford compound **26** (68 mg, 54%) as a faint yellow oil. R_f = 0.3.

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.54 (s, 1H), 3.89 (d, *J* = 3.4 Hz, 2H), 3.82 (t, *J* = 6.4 Hz, 2H), 3.65-3.56 (m, 12H), 3.53 (t, *J* = 5.0 Hz, 2H), 3.33 (d, *J* = 4.6 Hz, 2H), 2.88 (t, *J* = 6.4 Hz, 2H), 2.81 (s, 4H), 2.10 (s, 3H), 1.61 (s, 1H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 168.9, 166.7, 157.0, 120.6, 102.1, 72.2, 70.6, 70.5, 70.4, 70.2, 70.1, 65.6, 40.7, 32.0, 25.5, 17.2, 11.6.

HRMS (ESI) m/z Calculated for $C_{21}H_{32}N_2NaO_{10}$ $[M+Na]^+$: 495.1949, found: 495.1948.

Synthesis of 1-Methylcyclopropene derivatives **30**, **34**



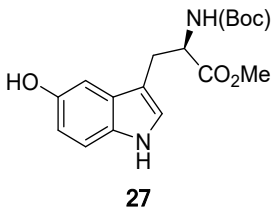
B: General procedure for the synthesis of 30, 34

(1) To a dry, argon-flushed schlenk flask charged with dry potassium carbonate or cesium carbonate (2.0 equiv) was added **9b** (1.5 equiv) and **27**, **31** (1.0 equiv) in dry dimethylformamide. The resulting reaction mixture was stirred at 50 ℃ for overnight. The solvent was removed, and the crude product purified by column chromatography. The product compound **28**, **32** were obtained.

(2) To a solution of compound **28**, **32** (1.0 equiv) in dichloromethane and trifluoroacetic acid (v:v, 3:1) were stirred at room temperature. The reaction mixture was concentrated *in vacuo* to obtain crude product which was used without further purification. The crude product compound (1.0 equiv) in dry tetrahydrofuran, TBAF (1M in THF, 2.0 equiv) was added. The reaction mixture was stirred at room temperature overnight. After that the solvent was removed and the residue was purified by column chromatography. The desired product **29**, **33** was obtained as a faint yellow oil.

(3) Compound **29**, **33** (1.0 equiv) in methanol and tetrahydrofuran (v:v, 1:4) was added lithium hydroxide (2.0 equiv), then the reaction was stirred at room temperature for 4 hours. The reaction mixture was removed methanol *in vacuo*. The reaction mixture was added 1M hydrochloric acid adjust to pH = 6. The organic layer was extracted with ethyl acetate (3×50 mL). The combined organic layer was dried and evaporated. After that the solvent was removed and the residue was purified by column chromatography. The desired product **30**, **34** were obtained.

Synthesis of compound **27**



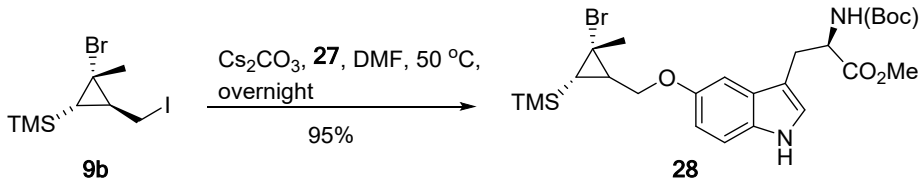
To a solution of 5-hydroxy-L-tryptophan (500 mg, 2.27 mmol) in dry methanol at 0℃ was added thionyl chloride (0.25 mL, 3.41 mmol), then the reaction was transferred to room temperature stirred for overnight. Upon completion the reaction mixture was removed methanol *in vacuo* to obtain crude compound which was used without further purification. Methyl L-tyrosinate (300 mg, 1.28

mmol) in dichloromethane (12 mL) were added to 50 mL round-bottom flask stirred at room temperature, followed by the addition of triethylamine (0.53 mL, 3.84 mmol) and *tert*-butoxycarbonyl anhydride (0.3 mL, 1.28 mmol). The reaction mixture was washed with water. The organic layer was extracted with dichloromethane (3×50 mL). The combined organic layer was dried and evaporated. After that the solvent was removed and the residue was purified by column chromatography. The desired product **27** was obtained. R_f = 0.25 (PE: EA = 3: 1 to PE: EA = 2: 1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.21 (d, *J* = 8.6 Hz, 1H), 7.00-6.90 (m, 1H), 6.77 (d, *J* = 8.7 Hz, 1H), 5.07 (s, 1H), 4.62 (s, 1H), 3.68 (s, 3H), 3.21 (s, 1H), 1.43 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 172.8, 155.3, 149.7, 131.3, 128.3, 123.8, 112.1, 111.8, 109.6, 103.3, 79.7, 54.1, 52.2, 28.3.

Synthesis of compound **28**



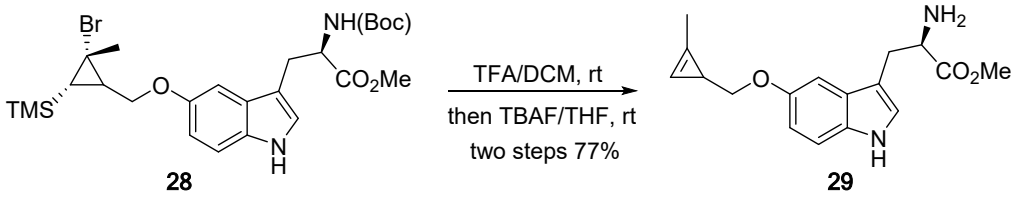
Following the general procedure B(1), cyclopropane **28** was synthesized from compound **9b** (185 mg, 1.5 equiv) and **27** (119 mg, 1.0 equiv) and Cs_2CO_3 (235 mg, 2.0 equiv), and purified by column chromatography (187 mg, 95%). R_f = 0.3 (PE: EA= 5: 1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.26 (d, *J* = 2.1 Hz, 1H), 6.99 (d, *J* = 7.3 Hz, 1H), 6.88 (dd, *J* = 8.7, 2.3 Hz, 1H), 5.08 (d, *J* = 8.2 Hz, 1H), 4.63 (d, *J* = 6.5 Hz, 1H), 4.17-4.06 (m, 1H), 3.90 (ddd, *J* = 10.5, 8.9, 4.7 Hz, 1H), 3.68 (s, 3H), 3.23 (d, *J* = 5.4 Hz, 2H), 2.01-1.90 (m, 1H), 1.89 (s, 3H), 1.42 (s, 9H), 0.14 (s, 9H), -0.10 (d, *J* = 8.9 Hz, 1H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 172.8, 155.3, 153.2, 131.5, 128.0, 123.5, 113.3, 111.8, 109.9, 102.3, 79.8, 69.5, 54.1, 52.2, 40.8, 30.7, 28.3, 27.6, 25.4, 20.7, -1.0.

HRMS (ESI) m/z Calculated for $C_{25}H_{37}BrN_2O_5Si$ $[M+Na]^+$: 575.1547, found 575.1547.

Synthesis of compound **29**



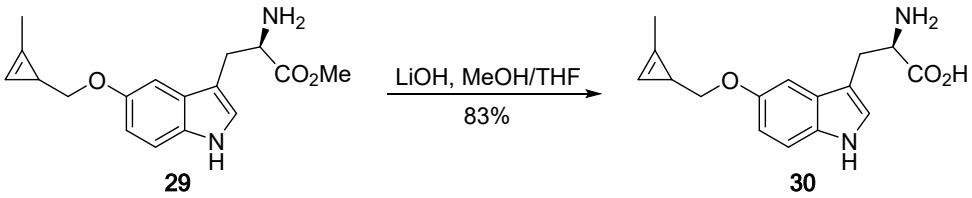
Following the general procedure B(2), cyclopropene **29** was synthesized from compound **28** (68 mg, 1.0 equiv) purified by thin-layer chromatography (11 mg, two steps 77%). R_f = 0.3 (DCM: MeOH = 15: 1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.23 (d, *J* = 8.8 Hz, 1H), 7.03 (dd, *J* = 8.6, 2.4 Hz, 2H), 6.88 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.73-6.55 (m, 1H), 3.98-3.87 (m, 2H), 3.82 (dd, *J* = 7.8, 4.8 Hz, 1H), 3.72 (s, 3H), 3.23 (dd, *J* = 14.4, 4.8 Hz, 1H), 3.01 (dd, *J* = 14.4, 7.7 Hz, 1H), 2.16 (d, *J* = 1.1 Hz, 3H), 1.91-1.81 (m, 1H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 175.7, 153.7, 131.3, 127.9, 123.5, 121.0, 113.2, 111.7, 110.9, 102.8, 102.1, 76.4, 54.9, 52.0, 30.7, 17.7, 11.8.

HRMS (ESI) m/z Calculated for $C_{17}H_{20}N_2O_3$ $[M+Na]^+$: 323.1366, found 323.1363.

Synthesis of compound **30**



29 **30**

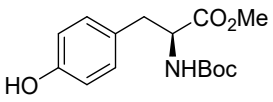
Following the general procedure B(3), cyclopropene **30** was synthesized from compound **29** (11 mg, 1.0 equiv) purified by thin-layer chromatography as a white solid. (8.7 mg, 83%).

^{1}H NMR (600 MHz, MeOD) δ 7.21 (d, *J* = 8.8 Hz, 1H), 7.17 (d, *J* = 2.3 Hz, 1H), 7.10 (s, 1H), 6.75 (dd, *J* = 8.8, 2.3 Hz, 1H), 6.73 (s, 1H), 3.94 (ddd, *J* = 10.0, 4.9, 2.1 Hz, 1H), 3.85 (dd, *J* = 4.9, 1.5 Hz, 1H), 3.62 (d, *J* = 8.5 Hz, 1H), 3.33 (d, *J* = 5.7 Hz, 1H), 2.94-2.80 (m, 1H), 2.11 (d, *J* = 1.1 Hz, 3H), 1.79 (ddd, *J* = 6.6, 4.2, 1.5 Hz, 1H).

^{13}C NMR (151 MHz, MeOD) δ 161.4, 154.5, 133.6, 129.2, 125.4, 122.7, 113.8, 112.9, 111.4, 103.6, 103.3, 77.9, 57.4, 31.6, 18.8, 11.7.

HRMS (ESI) m/z Calculated for $C_{16}H_{18}N_2O_3$ $[M+Na]^+$: 309.1210, found 309.1207.

Synthesis of compound **31**

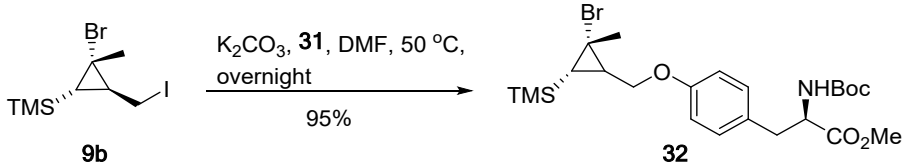


31

Methyl L-tyrosinate (350 mg, 1.54 mmol) in dichloromethane (6 mL) were added to 50 mL round-bottom flask stirred at room temperature, followed by the addition of triethylamine (0.64 mL, 4.62 mmol) and *tert*-butoxycarbonyl anhydride (0.35 mL, 1.54 mmol). The reaction mixture was washed with water. The organic layer was extracted with dichloromethane (3×50 mL). The combined organic layer was dried and evaporated. After that the solvent was removed and the residue was purified by column chromatography. The desired product **31** was obtained. R_f = 0.4 (PE: EA = 3: 1).

Compound **31** was synthesized according to literature [7].

Synthesis of compound **32**



9b **32**

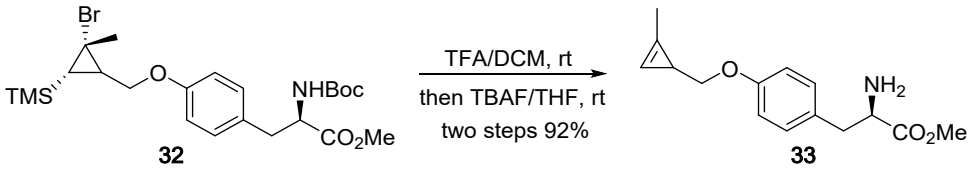
Following the general procedure B(1), cyclopropane **32** was synthesized from compound **9b** (2.66 g, 1.5 equiv) and **31** (1.5 g, 1.0 equiv) and K_2CO_3 (2.1 g, 2.0 equiv), and purified by column chromatography (2.5 g, 95%). R_f = 0.3 (PE: EA= 5: 1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.02 (d, *J* = 8.1 Hz, 2H), 6.82 (d, *J* = 8.5 Hz, 2H), 4.94 (d, *J* = 8.3 Hz, 1H), 4.54 (d, *J* = 7.5 Hz, 1H), 3.99 (dd, *J* = 10.5, 6.1 Hz, 1H), 3.91 (t, *J* = 9.4 Hz, 1H), 3.71 (s, 3H), 3.02 (qd, *J* = 14.0, 5.8 Hz, 2H), 1.93-1.88 (m, 1H), 1.87 (s, 3H), 1.42 (s, 9H), 0.12 (s, 9H), -0.12 (d, *J* = 8.8 Hz, 1H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 172.4, 157.7, 155.1, 130.3, 128.2, 114.8, 79.9, 68.1, 54.5, 52.2, 40.5, 37.4, 30.4, 28.3, 27.6, 20.8, -1.1.

HRMS (ESI) m/z Calculated for $C_{23}H_{36}BrNO_5Si$ $[M+Na]^+$: 536.1444, found 536.1445.

Synthesis of compound **33**



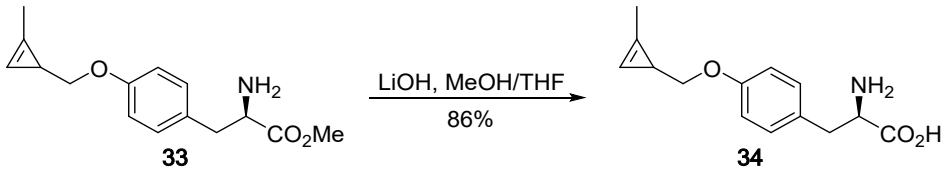
Following the general procedure B(2), cyclopropene **33** was synthesized from compound **32** (2.5 g, 1.0 equiv) purified by column chromatography (1.2 g, two steps 92%). R_f = 0.3 (DCM: MeOH = 15: 1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.13-7.04 (m, 2H), 6.86-6.78 (m, 2H), 3.86 (ddd, *J* = 9.9, 5.0, 3.4 Hz, 1H), 3.81 (ddd, *J* = 9.6, 5.0, 3.8 Hz, 1H), 3.71 (s, 3H), 3.69 (dd, *J* = 7.7, 5.2 Hz, 1H), 3.01 (dd, *J* = 13.7, 5.2 Hz, 1H), 2.81 (dd, *J* = 13.7, 7.7 Hz, 1H), 2.15 (s, 3H), 1.80 (td, *J* = 5.0, 1.6 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 175.5, 158.2, 130.1, 128.6, 120.8, 114.8, 102.5, 75.4, 55.9, 51.9, 40.1, 17.4, 11.7.

HRMS (ESI) m/z Calculated for $C_{15}H_{19}NO_3$ $[M+H]^+$: 262.1443, found 262.1432.

Synthesis of compound **34**



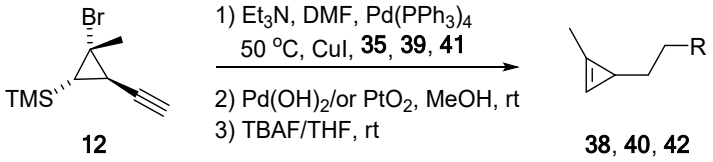
Following the general procedure B(3), cyclopropene **34** was synthesized from compound **33** (1.07 g, 1.0 equiv) purified by column chromatography as a white solid. (876 mg, 86%).

^{1}H NMR (600 MHz, MeOD) δ 7.19-6.98 (m, 2H), 6.80-6.69 (m, 2H), 6.60 (s, 1H), 3.76 (dd, *J* = 10.0, 4.9 Hz, 1H), 3.66 (dd, *J* = 10.1, 5.1 Hz, 1H), 3.59 (dd, *J* = 8.7, 4.3 Hz, 1H), 3.11 (dd, *J* = 14.7, 4.3 Hz, 1H), 2.81 (dd, *J* = 14.7, 8.8 Hz, 1H), 2.02 (d, *J* = 1.2 Hz, 3H), 1.63 (dt, *J* = 5.0, 2.5 Hz, 1H).

^{13}C NMR (151 MHz, MeOD) δ 174.0, 160.2, 131.5, 128.9, 122.5, 116.4, 103.5, 76.7, 57.9, 37.6, 18.6, 11.8.

HRMS (ESI) m/z Calculated for $C_{14}H_{17}NO_3$ $[M+H]^+$: 248.1287, found 248.1275.

Synthesis of 1-Methylcyclopropene derivatives **38**, **40**, **42**



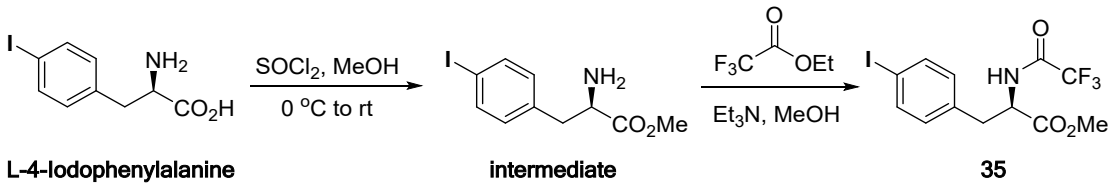
C: General procedure for the synthesis of 38, 40, 42

(1) To a dry, argon-flushed schlenk flask charged with dry trimethylamine (3.0 equiv) was added to this solution copper iodide (0.2 equiv), (beta-4)-platinum (0.1 equiv), and **12** (1.5 equiv) and **35**, **39**, **41** (1.0 equiv) were added in dry dimethylformamide. The resulting reaction mixture was stirred at 50 ℃ overnight. The solvent was removed, and the crude product purified by column chromatography. The product **36**, **49**, **50** was obtained as yellow solid.

(2) To a solution of **36**, **49**, **50** (1.0 equiv) in methanol at room temperature was added 10% palladium hydroxide or platinum dioxide in hydrogen balloon. The resulting reaction mixture was stirred for overnight. Upon completion the reaction mixture was passed through a pad of celite using methanol to remove palladium hydroxide or platinum dioxide. The reaction mixture was concentrated *in vacuo* to obtain crude compound **37**, **51**, **52** which was used without further purification.

(3) To a solution of compound **37**, **51**, **52** (1.0 equiv) in dry tetrahydrofuran, TBAF (1M in THF, 2.0 equiv) was added. The reaction mixture was stirred at room temperature overnight. After that the solvent was removed and the residue was purified by column chromatography. The desired product **38**, **40**, **42** was obtained as a yellow oil.

Synthesis of compound **35**



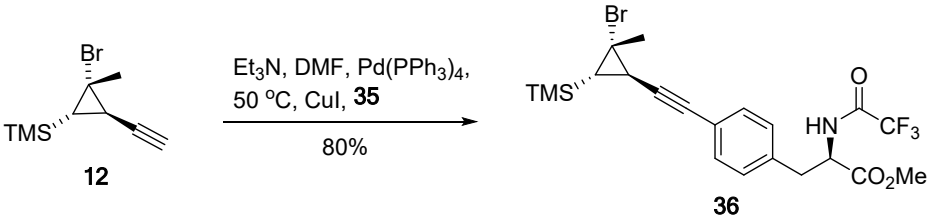
L-4-Iodophenylalanine **intermediate** **35**

To a solution of L-4-Iodophenylalanine (300 mg, 1.03 mmol) in dry methanol at 0 ℃ was added thionyl chloride (0.11 mL, 1.55 mmol), then the reaction was transferred to room temperature stirred for overnight. Upon completion the reaction mixture was removed methanol *in vacuo* to obtain crude compound intermediate which was used without further purification. Methyl ester compound intermediate (320 mg, 1.05 mmol) in methanol (6 mL) were added to 50 mL round-bottom flask stirred at room temperature, followed by the addition of triethylamine (0.22 mL, 1.57 mmol) and ethyl trifluoroacetate (0.19 mL, 1.57 mmol). After that the solvent was removed and the residue was purified by column chromatography. The desired product **35** was obtained. R_f = 0.35 (PE: EA = 5: 1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82-7.46 (m, 2H), 6.92-6.66 (m, 2H), 4.86 (q, *J* = 6.1 Hz, 1H), 3.79 (s, 3H), 3.16 (dd, *J* = 10.7, 5.5 Hz, 2H).

Compound **35** was synthesized according to literature [6].

Synthesis of compound **36**



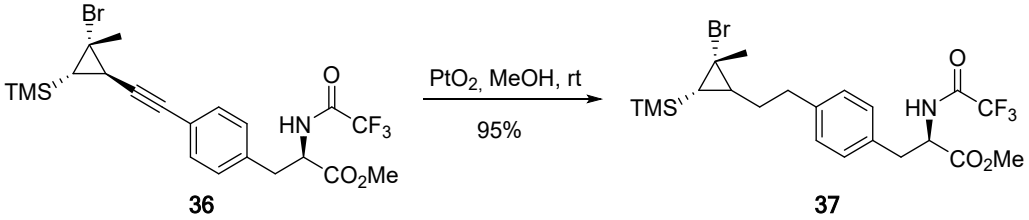
Following the general procedure C(1), cyclopropane **36** was synthesized from compound **12** (86 mg, 1.5 equiv) and **35** (100 mg, 1.0 equiv) and CuI (9.5 mg, 0.2 equiv), Et_3N (0.1 mL, 3.0 equiv), $Pd(PPh_3)_4$ (29 mg, 0.1 equiv) and purified by column chromatography (101 mg, 80%). R_f= 0.3 (PE: EA= 10: 1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32 (d, *J* = 7.9 Hz, 2H), 6.99 (d, *J* = 8.0 Hz, 2H), 6.80 (d, *J* = 7.6 Hz, 1H), 4.85 (dt, *J* = 7.7, 5.6 Hz, 1H), 3.77 (s, 3H), 3.22 (dd, *J* = 14.1, 5.7 Hz, 1H), 3.14 (dd, *J* = 14.1, 5.3 Hz, 1H), 2.09 (d, *J* = 8.5 Hz, 1H), 1.99 (s, 3H), 0.26 (d, *J* = 8.6 Hz, 1H), 0.17 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 170.2, 156.6, 134.3, 131.9, 129.1, 122.8, 116.4, 89.4, 79.8, 53.4, 52.9, 41.2, 37.1, 29.2, 26.8, 21.7, -1.1.

HRMS (ESI) m/z Calculated for $C_{21}H_{25}BrF_3NO_3Si$ $[M+Na]^+$: 526.0631, found 526.0619.

Synthesis of compound **37**



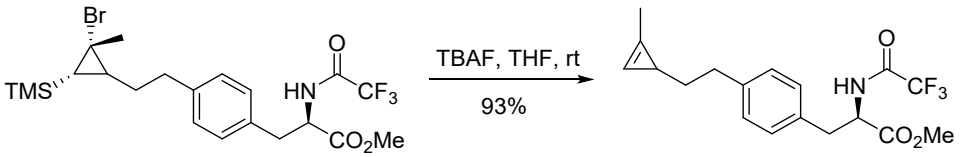
Following the general procedure C(2), cyclopropane **37** was synthesized from compound **36** (98 mg, 1.0 equiv) purified by column chromatography (93.8 mg, 95%). R_f= 0.3 (PE: EA = 8: 1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.14 (d, *J* = 7.8 Hz, 2H), 6.99 (d, *J* = 8.0 Hz, 2H), 6.77 (s, 1H), 4.91-4.81 (m, 1H), 3.79 (d, *J* = 2.4 Hz, 3H), 3.18 (dd, *J* = 13.8, 5.5 Hz, 2H), 2.70 (dd, *J* = 10.2, 3.8 Hz, 1H), 2.67 (dd, *J* = 11.6, 4.4 Hz, 1H), 1.82 (ddd, *J* = 9.1, 7.0, 3.6 Hz, 1H), 1.71 (s, 3H), 1.56-1.50 (m, 1H), 1.39 (dtd, *J* = 9.1, 6.9, 2.1 Hz, 1H), 0.09 (s, 9H), -0.46 (d, *J* = 9.0 Hz, 1H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 170.3, 156.4, 141.1, 132.0, 129.2, 129.0, 116.5, 53.5, 52.8, 42.5, 36.8, 35.3, 32.3, 32.0, 27.5, 22.5, -1.0.

HRMS (ESI) m/z Calculated for $C_{21}H_{29}BrF_3NO_3Si$ $[M+Na]^+$: 530.0944, found 530.0944.

Synthesis of compound **53**



37 **53**

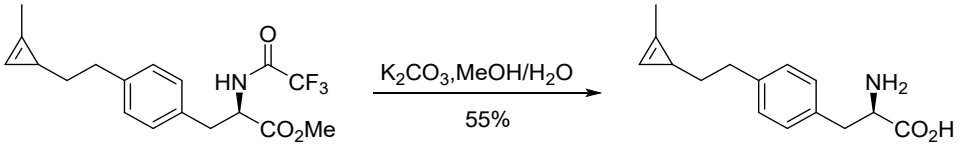
Following the general procedure C(3), cyclopropene **53** was synthesized from compound **37** (90 mg, 1.0 equiv) purified by thick-layer chromatography (58.6 mg, 93%). R_f = 0.3 (PE: EA = 8: 1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.12 (d, *J* = 7.9 Hz, 2H), 6.95 (d, *J* = 7.8 Hz, 2H), 6.73 (s, 1H), 6.57 (s, 1H), 4.93-4.82 (m, 1H), 3.79 (s, 3H), 3.17 (dd, *J* = 13.7, 5.5 Hz, 2H), 2.57 (q, *J* = 7.5, 7.0 Hz, 2H), 1.95 (s, 3H), 1.65-1.54 (m, 2H), 1.42 (td, *J* = 4.8, 1.6 Hz, 1H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 170.4, 156.4, 142.6, 131.3, 129.2, 128.9, 123.9, 116.5, 105.3, 53.5, 52.8, 38.1, 36.8, 34.6, 18.2, 11.6.

HRMS (ESI) m/z Calculated for $C_{18}H_{20}F_3NO_3$ $[M+Na]^+$: 378.1287, found 378.1284.

Synthesis of compound **38**

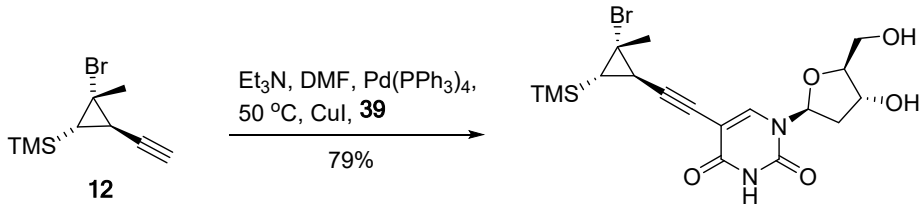


53 **38**

To a solution of compound **53** (3 mg, 0.0084 mmol) in methanol and water (v:v, 4:1) was added potassium hydroxide (9.5 mg, 0.169 mmol), then the reaction was stirred reflux for 4 hours. The reaction mixture was removed methanol *in vacuo*. The reaction mixture was washed with water. The organic layer was extracted with ethyl acetate (3×50 mL). The combined organic layer was dried and evaporated. After that the solvent was removed and the residue was purified by column chromatography. The desired product **38** was obtained.

HRMS (ESI) m/z Calculated for $C_{15}H_{19}NO_2$ $[M+Na]^+$: 268.1308, found 268.1303.

Synthesis of compound **49**



12 **49**

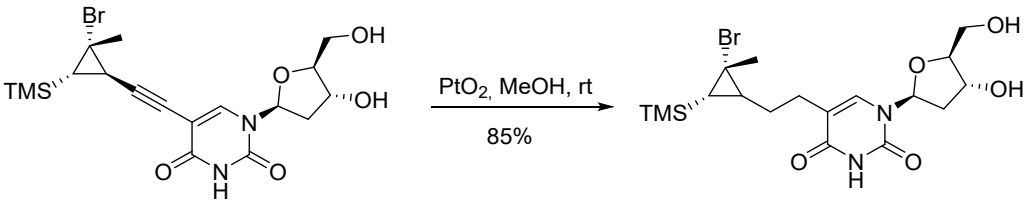
Following the general procedure C(1), cyclopropane **49** was synthesized from compound **12** (98 mg, 1.5 equiv) and **39** (100 mg, 1.0 equiv) and CuI (10.7 mg, 0.2 equiv), Et_3N (0.12 mL, 3.0 equiv), $Pd(PPh_3)_4$ (32 mg, 0.1 equiv) and purified by column chromatography (102 mg, 79%). R_f = 0.56 (DCM: MeOH= 15: 1).

^{1}H NMR (400 MHz, MeOD) δ 8.29 (s, 1H), 6.22-6.26 (t, *J* = 6.5 Hz, 1H), 4.39-4.41 (dd, *J* = 6.5, 3.2 Hz, 1H), 3.92-3.94 (m, 1H), 3.80-3.84 (dd, *J* = 12.0, 3.0 Hz, 1H), 3.72-3.76 (dd, *J* = 12.0, 3.4 Hz, 1H), 2.20-2.30 (m, 2H), 2.09-2.11 (d, *J* = 8.5 Hz, 1H), 1.96 (s, 3H), 0.35-0.38 (dd, *J* = 8.5, 2.2 Hz, 1H), 0.17 (s, 9H).

^{13}C NMR (101 MHz, MeOD) δ 164.3, 151.0, 144.6, 100.4, 93.0, 88.9, 86.7, 72.5, 71.7, 62.3, 42.1, 41.5, 29.6, 27.5, 22.7, -1.3.

HRMS (ESI) m/z Calculated for $C_{18}H_{25}BrN_2O_5Si$ [M+Na]$^+$: 481.0603, found 481.0589.

Synthesis of compound **51**



49 **51**

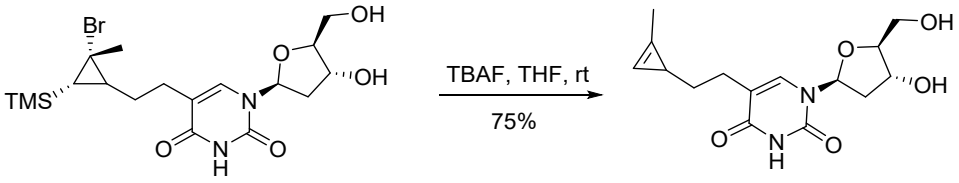
Following the general procedure C(2), cyclopropane **51** was synthesized from compound **49** (100 mg, 1.0 equiv) purified by column chromatography (85 mg, 85%). R_f = 0.6 (100% EtOAc).

^{1}H NMR (600 MHz , MeOD) δ 7.88 -7.91 (m, 1H), 6.27-6.31 (dt, *J* = 10.4, 6.6 Hz, 1H), 4.41-4.44 (dt, *J* = 9.5, 3.9 Hz, 1H), 3.90-3.96 (m, 1H), 3.79-3.83 (dd, *J* = 4.9, 3.3 Hz, 1H), 3.75-3.76 (dd, *J* = 3.4, 1.3 Hz, 1H), 2.40-2.45 (m, 2H), 2.25-2.28 (td, *J* = 6.4, 3.5 Hz, 2H), 1.76-1.81 (d, *J* = 29.2 Hz, 3H), 1.52-1.56 (m, 1H), 1.39-1.41 (dd, *J* = 15.9, 7.1 Hz, 1H), 0.89-0.93 (dd, *J* = 18.2, 6.6 Hz, 1H), 0.10 (s, 9H), -0.37--0.33 (dd, *J* = 19.0, 9.0 Hz, 1H).

^{13}C NMR (151 MHz, MeOD) δ 165.7, 152.1, 138.4, 114.9, 88.7, 86.3, 72.0, 62.5, 41.2, 33.3, 33.1, 27.9, 27.8, 27.6, 23.2, -1.0.

HRMS (ESI) m/z Calculated for $C_{18}H_{29}BrN_2O_5Si$ [M+Na]$^+$:483.0923, found 483.0921.

Synthesis of compound **40**



51 **40**

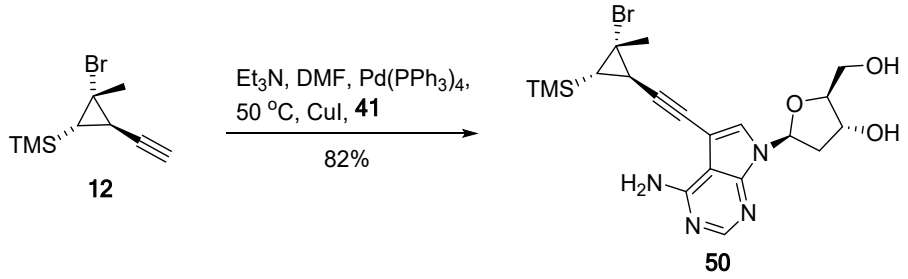
Following the general procedure C(3), cyclopropene **40** was synthesized from compound **51** (85 mg, 1.0 equiv) purified by thick-layer chromatography (64 mg, 75%). R_f = 0.55 (100% EA).

^{1}H NMR (400 MHz, MeOD) δ 7.83 (s, 1H), 6.70 (d, *J* = 3.1 Hz, 1H), 6.29-6.32 (t, *J* = 6.7 Hz, 1H), 4.39-4.42 (dt, *J* = 6.5, 3.5 Hz, 1H), 3.91-3.93 (q, *J* = 3.2 Hz, 1H), 3.71-3.80 (m, 2H), 2.21-2.28 (m, 4H), 2.08 (s, 3H), 1.49-1.50 (d, *J* = 4.1 Hz, 1H), 1.41-1.42 (d, *J* = 4.9 Hz, 1H), 0.89-0.91 (d, *J* = 6.5 Hz, 1H).

^{13}C NMR (101 MHz, MeOD) δ 165.8, 152.1, 138.0, 124.8, 115.9, 105.8, 88.7, 86.1, 72.1, 62.6, 41.1, 35.8, 26.6, 18.7, 11.5.

HRMS (ESI) m/z Calculated for $C_{15}H_{20}N_2O_5$ $[M+Na]^+$: 331.1799, found 331.1799.

Synthesis of compound **50**



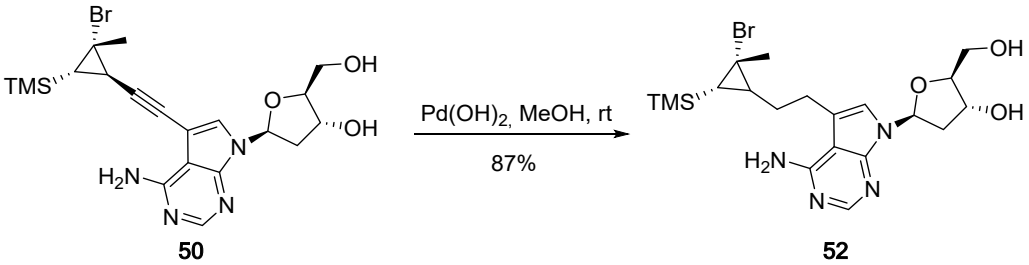
Following the general procedure C(1), cyclopropane **50** was synthesized from compound **12** (46 mg, 1.5 equiv) and **41** (50 mg, 1.0 equiv) and CuI (5.1 mg, 0.2 equiv), Et_3N (55 μL, 3.0 equiv), $Pd(PPh_3)_4$ (15 mg, 0.1 equiv) and purified by thick-layer chromatography (52 mg, 82%). R_f = 0.6 (DCM: MeOH= 15: 1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.18 (s, 1H), 7.14 (s, 1H), 6.19 (dd, *J* = 9.5, 3.7 Hz, 1H), 5.88 (s, 2H), 4.72 (d, *J* = 4.9 Hz, 1H), 4.16 (s, 1H), 3.91 (d, *J* = 12.5 Hz, 1H), 3.77 (d, *J* = 12.1 Hz, 1H), 3.0-2.95 (m, 1H), 2.25-2.23 (dd, *J* = 13.3, 8.0 Hz, 1H), 2.11 (d, *J* = 2.5 Hz, 1H), 1.97 (s, 3H), 0.26 (d, *J* = 8.4 Hz, 1H), 0.17 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 157.8, 152.0, 148.0, 128.2, 105.1, 95.4, 91.4, 89.2, 89.0, 73.0, 72.8, 63.3, 40.8, 40.6, 29.3, 27.0,21.6, -1.2.

HRMS (ESI) m/z Calculated for $C_{20}H_{27}BrN_4O_3Si$ $[M+Na]^+$: 501.0927, found 501.0928.

Synthesis of compound **52**



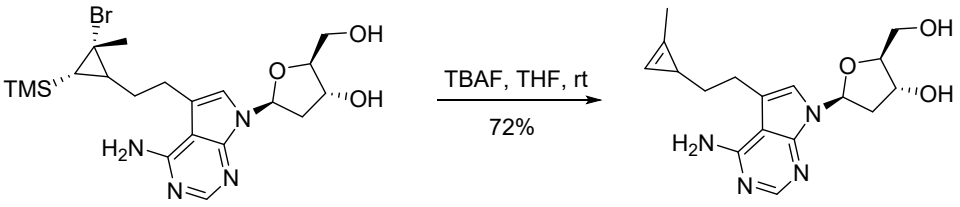
Following the general procedure C(2), cyclopropane **52** was synthesized from compound **50** (45 mg, 1.0 equiv) purified by thin-layer chromatography (39 mg, 87%). R_f = 0.6 (100% EtOAc).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.18 (s, 1H), 6.79 (d, *J* = 8.5 Hz, 1H), 6.18-6.22 (m, 1H), 4.74 (d, *J* = 4.7 Hz, 1H), 4.16 (s, 1H), 3.94 (d, *J* = 12.5 Hz, 1H), 3.77 (d, *J* = 12.5 Hz, 1H), 3.03-3.08 (m, 1H), 2.90 (t, *J* = 6.9 Hz, 2H), 2.21-2.26 (m, 2H), 1.81-1.92 (m, 1H), 1.72 (d, *J* = 54.3 Hz, 3H), 1.56-1.64 (m, 1H), 1.47-1.41 (m, 1H), 1.28-1.22 (m, 1H), 0.10 (s, 9H), -0.44--0.41 (m, 1H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 157.5, 151.0, 149.4, 122.4, 113.7, 104.7, 89.2, 88.9, 73.4, 63.5, 42.2, 40.4, 31.8, 31.4, 27.6, 26.6, 22.6, -0.9.

HRMS (ESI) m/z Calculated for $C_{20}H_{31}BrN_4O_3Si$ $[M+Na]^+$: 505.1240, found 505.1241.

Synthesis of compound **42**



52 **42**

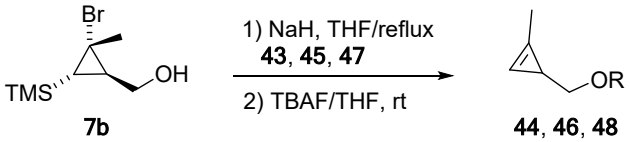
Following the general procedure C(3), cyclopropene **42** was synthesized from compound **52** (42 mg, 1.0 equiv) purified by thin-layer chromatography (30 mg, 72%). R_f = 0.5 (100% EA).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (s, 1H), 6.72 (s, 1H), 6.65 (s,1H), 6.16-6.18 (dd, *J* = 9.4, 5.6 Hz, 1H), 4.75 (d, *J* = 4.9 Hz, 1H), 4.16 (s, 1H), 3.95(d, *J* = 12.5 Hz, 1H), 3.77 (d, *J* = 12.5 Hz, 1H), 3.07-3.11 (m, 1H), 2.65-2.68 (t, *J* = 7.8 Hz, 2H), 2.19-2.21 (dd, *J* = 13.3, 7.9 Hz, 1H),2.06 (d, *J* = 9.4 Hz, 3H), 1.68-1.73 (m, 1H), 1.58-1.62 (m, 1H), 1.49-1.50 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.6, 150.8, 149.2, 123.7, 123.7, 122.1, 114.9, 105.0, 89.4, 88.9, 73.6, 63.6, 40.3, 36.9, 25.7,18.1,11.8.

HRMS (ESI) m/z Calculated for $C_{17}H_{22}N_4O_3$ $[M+Na]^+$: 353.1584, found 353.1584.

Synthesis of 1-Methylcyclopropene derivatives **44**, **46**, **48**



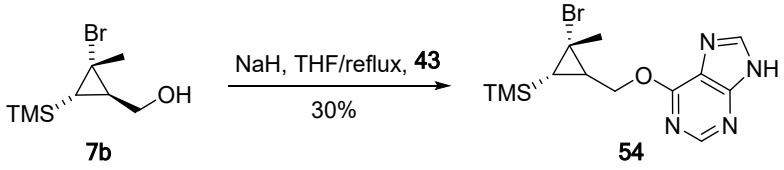
7b **44**, **46**, **48**

D: General procedure for the synthesis of 38, 40, 42

(1) Under an argon atmosphere, **7b** (1.0 equiv) were added to a solution of the sodium hydride (2.0 equiv) in dry tetrahydrofuran, followed by the addition of the corresponding chloro-nucleoside **43**, **45**, **47** (1.5 equiv). The reaction mixture was stirred at reflux. The mixture was quenched with saturated aqueous ammonium chloride. After extraction with ethyl acetate (3×50mL). The combined organic layer was dried and evaporated and the res1idue was purified by column chromatography or thin-layer chromatography to yield compounds **54-56**.

(2) To a solution of compound **54-56** (1.0 equiv) in dry tetrahydrofuran, TBAF (1M in THF, 4.0 equiv) was added. The reaction mixture was stirred at room temperature overnight. After that the solvent was removed and the residue was purified by thin-layer chromatography. The desired product **44**, **46**, **48** were obtained as a yellow oil.

Synthesis of compound **54**



7b **54**

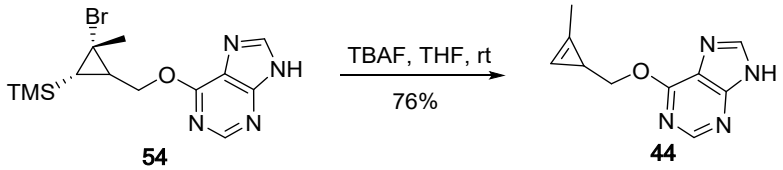
Following the general procedure D(1), cyclopropane **54** was synthesized from compound **7b** (50 mg, 1.0 equiv), **43** (49 mg, 1.5 equiv) and NaH (16.8 mg, 2.0 equiv), and purified by thin-layer chromatography (22.5 mg, 30%). R_f = 0.35 (DCM: MeOH= 20: 1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 12.55 (s, 1H), 8.58 (s, 1H), 8.20 (s, 1H), 4.75 (dd, *J* = 11.3, 6.5 Hz, 1H), 4.67-4.54 (m, 1H), 2.12 (d, *J* = 7.0 Hz, 1H), 2.18-1.81 (s, 3H), 0.08 (d, *J* = 11.8 Hz, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 160.3, 153.3, 151.8, 140.9, 120.1, 69.8, 40.4, 27.7, 24.8, 21.2, -1.0.

HRMS (ESI) m/z Calculated for $C_{13}H_{19}BrN_4OSi$ $[M+Na]^+$: 377.0404, found 377.0399.

Synthesis of compound **44**



54 **44**

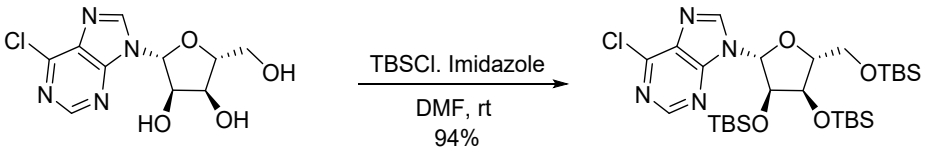
Following the general procedure D(2), cyclopropene **44** was synthesized from compound **54** (7 mg, 1.0 equiv) purified by thin-layer chromatography (3 mg, 76%). R_f = 0.35 (DCM: MeOH = 20: 1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.57 (s, 1H), 8.16 (s, 1H), 6.65 (s, 1H), 4.53 (d, *J* = 5.0 Hz, 2H), 2.16 (s, 3H), 1.93 (t, *J* = 4.7 Hz, 1H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 161.1, 153.1, 151.9, 140.3, 120.5, 112.6, 102.4, 75.2, 29.7, 17.1.

HRMS (ESI) m/z Calculated for $C_{10}H_{10}N_4O$ $[M+Na]^+$: 225.0747, found 225.0745.

Synthesis of compound **45**



6-Chloropurine riboside **45**

6-Chloropurine riboside (500 mg, 1.75 mmol) in dry dimethylformamide (8 mL) were added to 50 mL round-bottom flask stirred at room temperature, followed by the addition of imidazole (1.2 g, 17.5 mmol) and *tert*-Butyldimethylsilyl chloride (1.3 g, 8.72 mmol). The reaction mixture was washed with water. The organic layer was extracted with ethyl acetate (3×50 mL). The combined organic layer was dried and evaporated. The residue was columned on silica to 94% yield **45** (1.02 g). R_f = 0.3 (PE: EA = 20: 1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.75 (s, 1H), 8.55 (s, 1H), 6.13 (d, *J* = 5.0 Hz, 1H), 4.59 (t, *J* = 4.6 Hz, 1H), 4.31 (t, *J* = 4.0 Hz, 1H), 4.16 (td, *J* = 3.6, 2.4 Hz, 1H), 4.02 (dd, *J* = 11.5, 3.5 Hz, 1H), 3.81 (dd, *J* = 11.5, 2.4 Hz, 1H), 0.96 (s, 10H), 0.94 (s, 10H), 0.79 (s, 10H), 0.15 (d, *J* = 6.4 Hz, 6H), 0.10 (d, *J* = 3.0 Hz, 7H), -0.03 (s, 3H), -0.24 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 151.9, 151.5, 150.9, 144.1, 132.1, 88.6, 85.7, 76.4, 71.8, 62.4, 26.1, 25.8, 25.6, 18.6, 18.1, 17.8, 1.0, -4.4, -4.7, -5.1, -5.3, -5.4.

Compound **45** was synthesized according to literature [8].

Synthesis of compound **55**

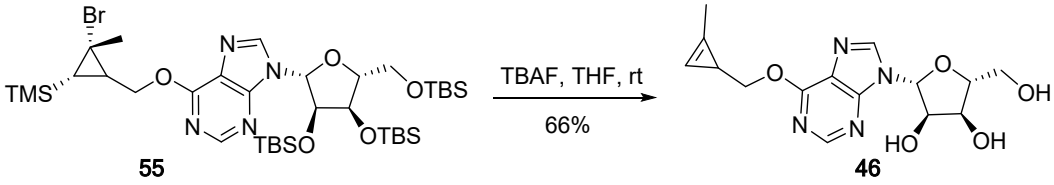
Following the general procedure D(1), cyclopropane **55** was synthesized from compound **7b** (100 mg, 1.0 equiv), **45** (307 mg, 1.5 equiv) and NaH (33.6 mg, 2.0 equiv), and purified by column chromatography (243 mg, 70%). R_f = 0.4 (DCM: PE= 2: 1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.49 (s, 1H), 8.31 (d, *J* = 2.2 Hz, 1H), 6.11-6.09 (m, 1H), 4.72-4.56 (m, 3H), 4.34-4.30 (m, 1H), 4.14 (q, *J* = 3.4 Hz, 1H), 4.02 (ddd, *J* = 11.4, 3.9, 1.5 Hz, 1H), 3.80 (dd, *J* = 11.4, 2.7 Hz, 1H), 2.16-2.09 (m, 1H), 1.96 (s, 3H), 0.96 (s, 9H), 0.94 (s, 9H), 0.80 (s, 9H), 0.14 (d, *J* =6.4 Hz, 6H), 0.10 (d, *J* = 3.7 Hz, 6H), 0.05(s, 9H), -0.02 (dd, *J* = 8.9, 1.7 Hz, 1H), -0.04 (s, 3H), -0.25 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.4, 152.1, 151.8, 141.2, 121.9, 88.3, 85.6, 72.0, 67.0, 62.6, 30.2, 27.8, 26.1, 25.8, 25.7, 21.1, 18.5, 18.1, 17.8, -1.1, -4.4, -4.7, -5.1, -5.4.

HRMS (ESI) m/z Calculated for $C_{36}H_{69}BrN_4O_5Si_4$ $[M+H]^+$: 829.3601, found 829.3591.

Synthesis of compound **46**



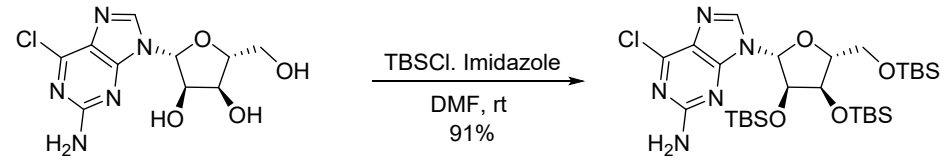
Following the general procedure D(2), cyclopropene **46** was synthesized from compound **55** (243 mg, 1.0 equiv) purified by thick-layer chromatography (65 mg, 66%). R_f = 0.3 (DCM: MeOH = 12: 1).

^{1}H NMR (600 MHz, MeOD) δ 8.50 (s, 1H), 8.44 (s, 1H), 6.72 (s, 1H), 6.06 (d, *J* = 6.0 Hz, 1H), 4.74 (t, *J* = 5.5 Hz, 1H), 4.52 (dd, *J* = 10.9, 4.9 Hz, 1H), 4.46-4.38 (m, 1H), 4.35 (dd, *J* = 5.0, 3.1 Hz, 1H), 4.17 (q, *J* = 2.8 Hz, 1H), 3.89 (dd, *J* = 12.4, 2.7 Hz, 1H), 3.76 (dd, *J* = 12.4, 2.9 Hz, 1H), 2.14 (t, *J* = 1.0 Hz, 3H), 1.85 (td, *J* = 5.2, 1.5 Hz, 1H).

^{13}C NMR (151 MHz, MeOD) δ 160.4, 151.1, 150.4, 141.7, 120.9, 120.1, 120.0, 101.0, 100.9, 89.1, 85.9, 74.1, 73.6, 70.4, 61.2, 22.8, 16.1.

HRMS (ESI) m/z Calculated for $C_{15}H_{18}N_4O_5$ $[M+H]^+$: 335.1350, found 335.1350.

Synthesis of compound **47**



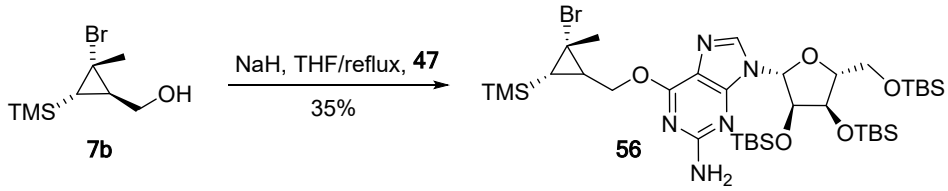
2-Amino-6-chloropurine-9-riboside (500 mg, 1.66 mmol) in dry dimethylformamide (10 mL) were added to 50 mL round-bottom flask stirred at room temperature, followed by the addition of imidazole (1.13 g, 16.6 mmol) and *tert*-Butyldimethylsilyl chloride (1.25 g, 8.29 mmol). The reaction mixture was washed with water. The organic layer was extracted with ethyl acetate (3×50 mL). The combined organic layer was dried and evaporated. The residue was columned on silica to 91% yield **47** (969 mg). R_f = 0.2 (PE: EA = 25: 1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.17 (s, 1H), 5.93 (d, *J* = 5.0 Hz, 1H), 5.02 (s, 2H), 4.47 (d, *J* = 4.7 Hz, 1H), 4.27 (t, *J* = 4.1 Hz, 1H), 4.16-4.08 (m, 1H), 3.97 (dd, *J* = 11.4, 3.4 Hz, 1H), 3.78 (dd, *J* = 11.4, 2.5 Hz, 1H), 0.95 (s, 9H), 0.93 (s, 9H), 0.82 (s, 9H), 0.14 (d, *J* = 4.5 Hz, 6H), 0.10 (d, *J* = 1.9 Hz, 6H), -0.02 (s, 3H), -0.18 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 158.9, 153.6, 151.1, 140.9, 125.6, 87.9, 85.5, 76.3, 71.9, 62.5, 26.1, 25.8, 25.6, 18.6, 18.1, 17.9, 1.0, -4.4, -4.6, -4.7, -5.0, -5.4.

Compound **47** was synthesized according to literature [9].

Synthesis of compound **56**



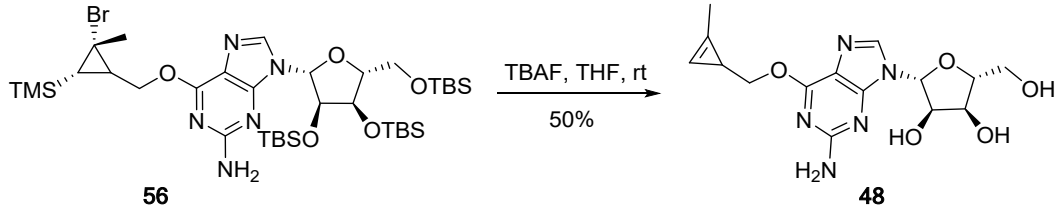
Following the general procedure D(1), cyclopropane **56** was synthesized from compound **7b** (20 mg, 1.0 equiv), **47** (82 mg, 1.5 equiv) and NaH (6.7 mg, 2.0 equiv), and purified by thin-layer chromatography (25 mg, 35%). R_f = 0.25 (PE: EA= 10: 1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.96 (d, *J* = 2.1 Hz, 1H), 5.92 (dd, *J* = 5.2, 1.7 Hz, 1H), 4.89 (d, *J* = 4.3 Hz, 2H), 4.63-4.37 (m, 3H), 4.28 (td, *J* = 4.0, 1.4 Hz, 1H), 4.09 (d, *J* = 3.3 Hz, 1H), 4.01-3.92 (m, 1H), 3.77 (dd, *J* = 11.4, 2.7 Hz, 1H), 2.08 (dt, *J* = 9.1, 7.2 Hz, 1H), 1.93 (s, 3H), 0.95 (s, 9H), 0.93 (s, 9H), 0.81 (s, 9H), 0.12 (d, *J* = 4.5 Hz, 6H), 0.10 (s, 6H), 0.06 (s, 9H), -0.03 (s, 3H), -0.07 (dd, *J* = 8.9, 2.5 Hz, 1H), -0.17 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 160.9, 159.0, 153.9, 138.0, 115.8, 87.8, 85.2, 76.0, 72.0, 66.5, 62.6, 40.8, 30.3, 27.7, 26.1, 25.9, 25.7, 20.9, 18.5, 17.9, -1.1, -4.3, -4.7, -5.0, -5.4.

HRMS (ESI) m/z Calculated for $C_{36}H_{70}BrN_5O_5Si_4$ $[M+H]^+$: 844.3710, found 844.3703.

Synthesis of compound **48**



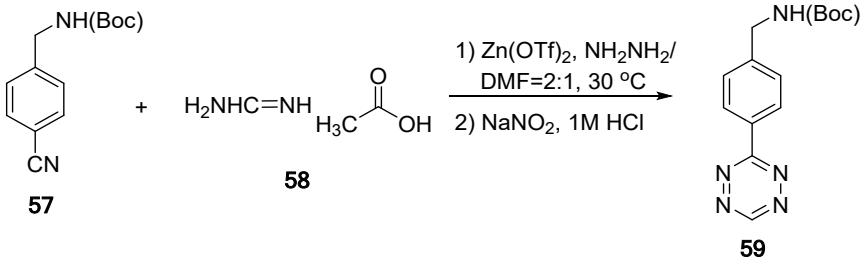
Following the general procedure D(2), cyclopropene **48** was synthesized from compound **56** (25 mg, 1.0 equiv) purified by thin-layer chromatography (5 mg, 50%). R_f = 0.3 (DCM: MeOH = 12: 1 to DCM: Acetone = 3: 1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 (d, *J* = 9.5 Hz, 1H), 6.70 (d, *J* = 13.8 Hz, 1H), 5.66 (d, *J* = 7.5 Hz, 1H), 5.25 (td, *J* = 7.2, 5.0 Hz, 1H), 4.83 (s, 2H), 4.46 (dd, *J* = 5.0, 3.6 Hz, 1H), 4.37-4.21 (m, 3H), 3.93 (d, *J* = 12.6 Hz, 1H), 3.75 (t, *J* = 12.0 Hz, 1H), 2.14 (dd, *J* = 3.5, 1.1 Hz, 3H), 1.94-1.79 (m, 1H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 161.0, 158.6, 138.9, 120.9, 102.9, 102.1, 91.8, 87.6, 75.3, 74.6, 73.2, 72.2, 63.5, 16.7, 11.8.

HRMS (ESI) m/z Calculated for $C_{15}H_{19}N_5O_5$ $[M+H]^+$: 350.1459, found 350.1456.

Synthesis of compound **59**



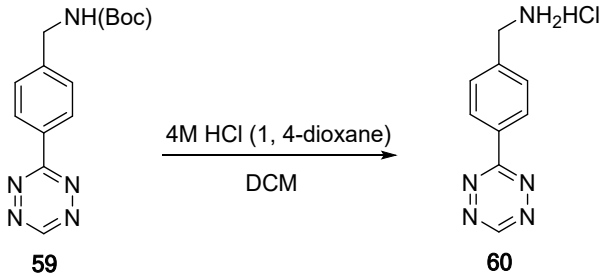
Tert-butyl-(4-cyanobenzene) carbamate **57** (3.0 g, 13 mmol)、formamidine acetate **58** (13.5 g, 130 mmol)、Zinc trifluoromethanesulfonate (2.37 g, 6.5 mmol)、98% anhydrous hydrazine (20.7 mL, 650 mmol) were dissolved in DMF (10 mL), and the reaction mixture was stirred at 30 ℃ for 48 hours. Then, an ice water solution of sodium nitrite (10 equiv) was added, followed by the slow addition of 1 M HCl with vigorous stirring. The reaction mixture turned bright red, and gas production was observed. The addition of HCl was continued until gas production stopped and the pH reached 3.0-4.0. Then, the reaction mixture was extracted with EtOAc (3×200 mL), and the combined organic layers were washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*. The obtained residue was purified by silica gel column chromatography using (PE: EA = 10: 1 to 100% DCM) to afford **59** (980 mg, 40%) as a pink solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 10.21 (s, 1H), 8.60 (d, *J* = 8.2 Hz, 2H), 7.53 (d, *J* = 8.2 Hz, 2H), 4.97 (s, 1H), 4.45 (d, *J* = 6.0 Hz, 2H), 1.49 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 49.4, 142.6, 141.1, 132.1, 120.8, 119.2, 118.8, 51.8, 39.0.

Compound **59** was synthesized according to literature [10].

Synthesis of compound **60**

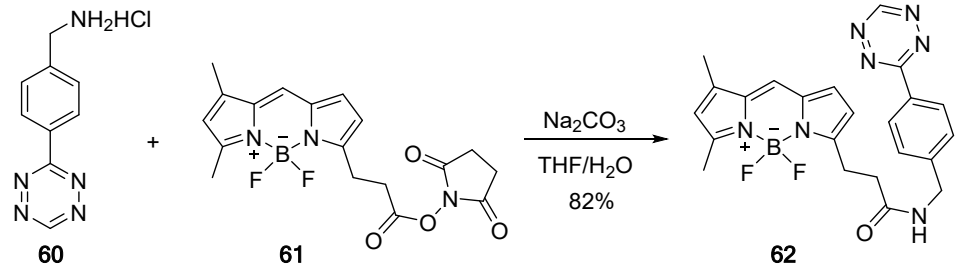


Tetrazine **59** (980 mg, 3.4 mmol) was dissolved in DCM (4 mL) solution, add 4M HCl stored in dioxane (40 mL, 102 mmol) and stir at room temperature for 1 hour. The rection was concentrated *in vacuo*. The obtained residue was afforded **60** (735 mg, 100%), which can be used in the further step.

^{1}H NMR (600 MHz, DMSO-d_6) δ 10.63 (s, 1H), 8.51 (d, J = 8.2 Hz, 2H), 7.81 (d, J = 8.2Hz, 2H), 4.16 (d, J = 4.2 Hz, 2H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 165.3, 158.2, 138.8, 131.9, 129.8, 127.9, 41.8.

Synthesis of compound **62**



60 61 62

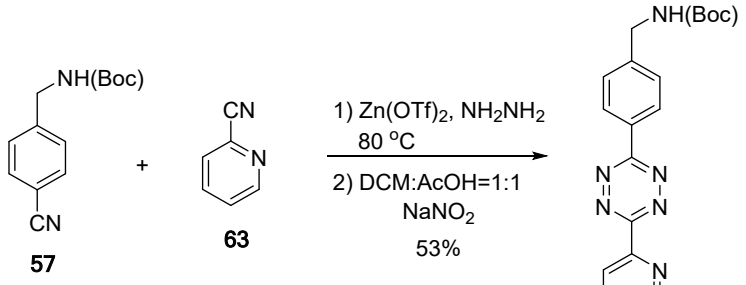
BODIPY-NHS ester **61** (8 mg, 0.02 mmol) and tetrazine amino hydrochloride **60** (5 mg, 0.02 mmol) were dissolved in THF (1 mL), added sodium carbonate solution (7.1 mg, 0.06 mmol), stirred at room temperature for several hours. Then the mixture was quenched with 1M hydrochloric acid. The resulting mixture was diluted with EtOAc (3×15 mL) and were washed with saturated sodium chloride, dried over anhydrous sodium sulfate, and concentrated *in vacuo*. The crude product was purified by thin-layer chromatography to afforded **62** (7.8 mg, 82%) as an orange solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.19 (s, 1H), 8.47 (d, J = 8.3 Hz, 2H), 7.33 (d, J = 8.3 Hz, 2H), 7.09 (s, 1H), 6.89 (d, J = 3.9 Hz, 1H), 6.30 (d, J = 4.0 Hz, 2H), 6.07 (s, 1H), 4.50 (d, J = 5.9 Hz, 2H), 3.31 (t, J = 7.3 Hz, 2H), 2.77 (t, J = 7.3 Hz, 2H), 2.52 (s, 3H), 2.23 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.7, 166.3, 160.5, 157.7, 156.7, 144.2, 144.0, 135.2, 133.3, 130.3, 128.4, 128.3, 128.2, 123.8, 120.5, 117.5, 43.1, 35.9, 24.8, 14.9, 11.3.

HRMS (ESI) m/z Calculated for $C_{23}H_{22}BF_2N_7NaO$ $[M+Na]^+$: 484.1843, found: 484.1845.

Synthesis of compound **64**



57 63 64

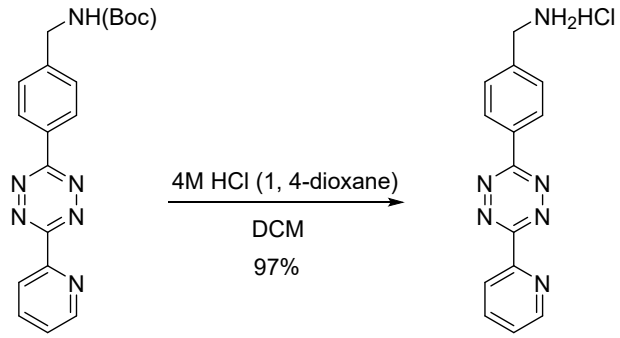
(4-cyanobenzene) *tert*-Butyl carbamate **57** (480 mg, 2 mmol), pyridinonitrile **63** (1.07 g, 10 mmol) and zinc trifluoromethanesulfonate (172 mg, 0.52 mmol) were dissolved in 98% anhydrous hydrazine (3.2 mL, 100 mmol). The reaction solution was heated to 80 ℃ and stirred overnight.

Next, the reaction solution was cooled in an ice-water bath, and an ice water solution of sodium nitrite (44 mmol) was added, followed by the slow addition of DCM: AcOH (20 mL: 20 mL) with vigorous stirring. The reaction mixture turned bright red, and gas production was observed. The addition of HCl was continued until gas production stopped and the pH reached 3.0-4.0. Then, the reaction mixture was extracted with EtOAc (3×100 mL), and the combined organic layers were washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*. The obtained residue was purified by silica gel column chromatography using (DCM: EA = 30: 1) to afford **64** (400 mg, 53%) as a pink solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.97 (d, *J* = 4.4 Hz, 1H), 8.69 (d, *J* = 7.9 Hz, 1H), 8.66 (d, *J* = 8.2 Hz, 2H), 8.00 (td, *J* = 7.8, 1.6 Hz, 1H), 7.57 (dd, *J* = 7.5, 4.8 Hz, 1H), 7.54 (d, *J* = 8.1 Hz, 2H), 5.01 (s, 1H), 4.46 (d, *J* = 5.0 Hz, 2H), 1.49 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 164.2, 163.4, 156.1, 151.0, 150.3, 144.7, 137.5, 130.4, 128.7, 128.1, 126.4, 123.9, 79.8, 44.4, 28.5.

Synthesis of compound **65**



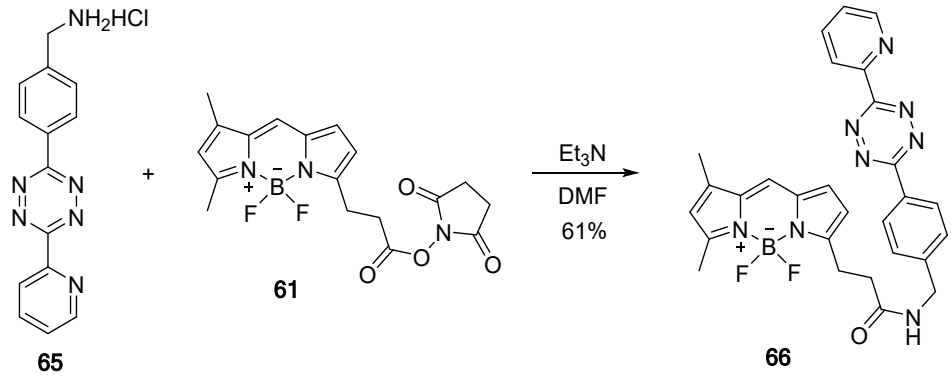
64 **65**

Tetrazine **64** (400 mg, 1.1 mmol) was dissolved in DCM (4 mL) solution, add 4M HCl stored in dioxane (10 mL) and stir at room temperature for 1 hour. Then the mixture was concentrated *in vacuo*. The obtained residue was afforded **65** (320 mg, 97%) as a pink solid, which can be used in the further step.

^{1}H NMR (600 MHz, DMSO-d_6) δ 8.93 (d, *J* = 4.4 Hz, 1H), 8.67 (s, 1H), 8.58 (d, *J* = 8.1 Hz, 2H), 8.17 (td, *J* = 7.8, 1.6 Hz, 1H), 7.82 (d, *J* = 8.2 Hz, 2H), 7.74 (dd, *J* = 7.1, 5.1 Hz, 1H), 4.17 (d, *J* = 5.6 Hz, 2H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 163.3, 163.0, 150.3, 149.8, 139.0, 138.5, 131.6, 130.0, 128.0, 126.8, 124.2, 41.8.

Synthesis of compound **66**



65 61 66

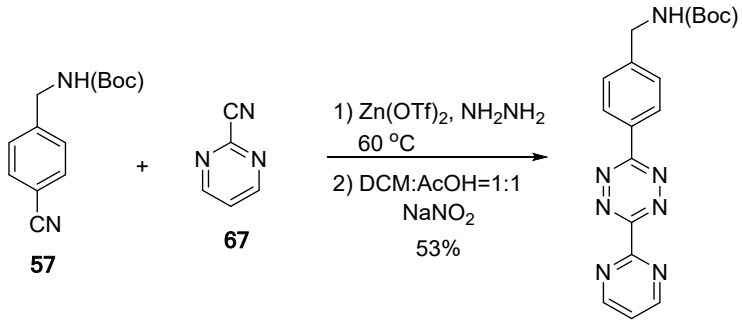
BODIPY-NHS ester **61** (13 mg, 0.03 mmol) and tetrazine amino hydrochloride **65** (10 mg, 0.03 mmol) were dissolved in DMF (1 mL), added triethylamine (10 μL, 0.06 mmol), stirred at room temperature for several hours, Then the mixture was quenched with 1M hydrochloric acid. The resulting mixture was diluted with EtOAc (3×15 mL) and were washed with saturated sodium chloride, dried over anhydrous sodium sulfate, and concentrated *in vacuo*. The crude product was purified by thin-layer chromatography to afforded **66** (11 mg, 61%) as an orange solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.97 (d, *J* = 4.3 Hz, 1H), 8.69 (d, *J* = 7.9 Hz, 1H), 8.54 (d, *J* = 8.3 Hz, 2H), 8.00 (td, *J* = 7.8, 1.6 Hz, 1H), 7.57 (dd, *J* = 7.1, 5.0 Hz, 1H), 7.35 (d, *J* = 8.2 Hz, 2H), 7.10 (s, 1H), 6.89 (d, *J* = 3.9 Hz, 1H), 6.36-6.23 (m, 2H), 6.07 (s, 1H), 4.52 (d, *J* = 5.9 Hz, 2H), 3.32 (t, *J* = 7.3 Hz, 2H), 2.78 (t, *J* = 7.3 Hz, 2H), 2.53 (s, 3H), 2.23 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 171.7, 164.2, 163.4, 160.6, 156.7, 150.9, 150.3, 144.2, 143.9, 137.4, 135.2, 133.4, 130.4, 128.6, 128.4, 128.2, 127.7, 126.3, 123.9, 120.5, 117.6, 43.2, 35.9, 24.8, 14.9, 11.3.

HRMS (ESI) m/z Calculated for $C_{28}H_{25}BF_2N_8NaO$ $[M+Na]^+$: 561.2110, found: 561.2110.

Synthesis of compound **68**



57 67 68

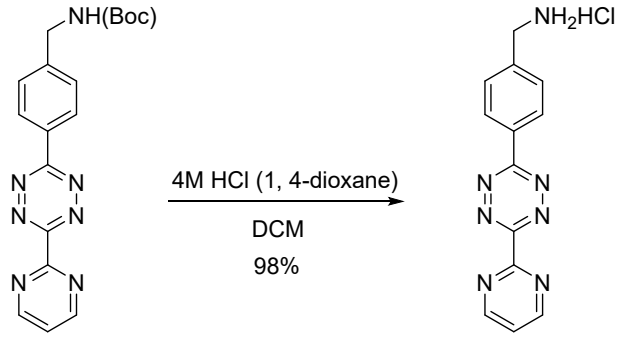
(4-cyanobenzene) *tert*-Butyl carbamate **57** (920 mg, 4 mmol), pyrimidine nitrile **67** (2.04 g, 20 mmol) and zinc trifluoromethanesulfonate (380 mg, 1.04 mmol) were dissolved in 98% anhydrous hydrazine (6.4 mL, 200 mmol). The reaction solution was heated to 60 ℃ and stirred overnight. Next, the reaction solution was cooled in an ice-water bath, and an ice water solution of sodium nitrite (88 mmol) was added, followed by the slow addition of DCM: AcOH (20 mL: 20 mL) with vigorous stirring. The reaction mixture turned bright red, and gas production was observed. The addition of HCl was continued until gas production stopped and the pH reached 3.0-4.0. Then, the reaction mixture was extracted with EtOAc (3×100 mL), and the combined organic layers were

washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*. The obtained residue was purified by silica gel column chromatography using (DCM: EA = 30: 1) to afford **68** (680 mg, 47%) as a purple solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 9.14 (d, *J* = 4.8 Hz, 2H), 8.71 (d, *J* = 8.3 Hz, 2H), 7.59 (t, *J* = 4.8 Hz, 1H), 7.55 (d, *J* = 8.2 Hz, 2H), 4.47 (d, *J* = 5.5 Hz, 2H), 1.49 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 164.4, 163.2, 159.7, 158.5, 156.1, 145.2, 130.3, 129.2, 128.3, 122.6, 80.0, 44.5, 28.5.

Synthesis of compound **69**



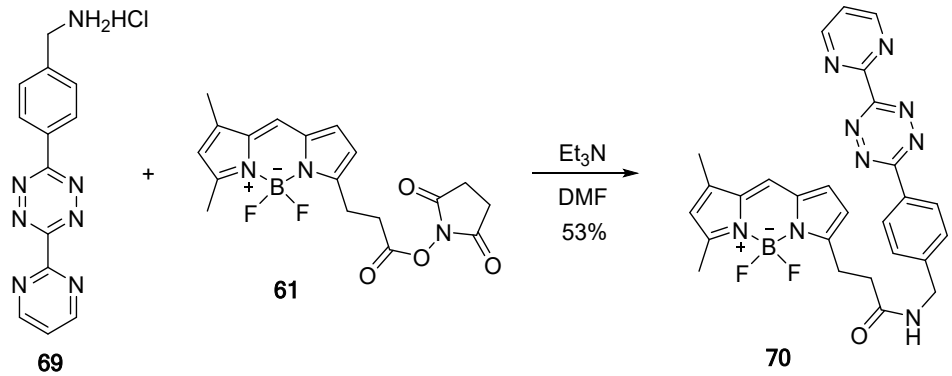
68 **69**

Tetrazine **68** (680 mg, 1.8 mmol) was dissolved in DCM (6 mL) solution, add 4M HCl stored in dioxane (15 mL) and stir at room temperature for 1 hour. Then the mixture was concentrated *in vacuo*. The obtained residue was afforded **69** (550 mg, 98%) as a pink solid, which can be used in the further step.

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.19 (d, *J* = 4.9 Hz, 2H), 8.69 (s, 3H), 8.61 (d, *J* = 8.1 Hz, 2H), 7.92-7.71 (m, 3H), 4.18 (d, *J* = 5.7 Hz, 2H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 163.3, 163.0, 159.1, 158.5, 139.2, 131.5, 123.0, 128.3, 123.0, 41.9.

Synthesis of compound **70**



69 **61** **70**

BODIPY-NHS ester **61** (13 mg, 0.03 mmol) and tetrazine amino hydrochloride **69** (10 mg, 0.03 mmol) were dissolved in DMF (1 mL), added triethylamine (9.5μL, 0.06 mmol), stirred at room temperature for several hours. Then the mixture was quenched with 1M hydrochloric acid. The resulting mixture was diluted with EtOAc (3×15 mL) and dried over anhydrous sodium sulfate and

concentrated *in vacuo*. The crude product was purified by thin-layer chromatography to afforded **70** (9.5 mg, 53%) as an orange solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 9.13 (d, *J* = 4.8 Hz, 1H), 8.58 (d, *J* = 8.3 Hz, 2H), 7.59 (s, 1H), 7.36 (d, *J* = 8.3 Hz, 2H), 7.10 (s, 1H), 6.89 (d, *J* = 3.9 Hz, 1H), 6.31 (d, *J* = 3.9 Hz, 2H), 6.06 (s, 1H), 4.52 (d, *J* = 5.9 Hz, 2H), 3.32 (t, *J* = 7.3 Hz, 2H), 2.78 (t, *J* = 7.3 Hz, 2H), 2.52 (s, 3H), 2.23 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 171.6, 164.3, 163.1, 160.6, 159.6, 158.4, 156.7, 144.3, 144.2, 135.2, 133.4, 130.1, 129.0, 128.4, 128.2, 125.4, 123.8, 122.4, 120.5, 117.6, 43.1, 35.9, 24.8, 14.9, 11.3.

HRMS (ESI) m/z Calculated for $C_{27}H_{24}BF_2N_9NaO$ $[M+Na]^+$: 562.2062, found: 562.2060.

The stability of compounds 40 and 46

A stock solution of cyclopropene derivative **40** (40 mM) and **46** (25 mM) in DMSO were diluted with 10-fold to a final concentration of **40** (4 mM) and **46** (2.5 mM) and incubated at room temperature or 37 ℃ in DMSO-d_6: D_2O = 4: 1 (0.4 mL: 0.1 mL). The NMR was taken over a period of one week at the following time points: 0 min, 90 min, 6 h, 30 h, 1 week. The results showed that the compounds **46** were very stable at 37 ℃ for a week or even a long time.

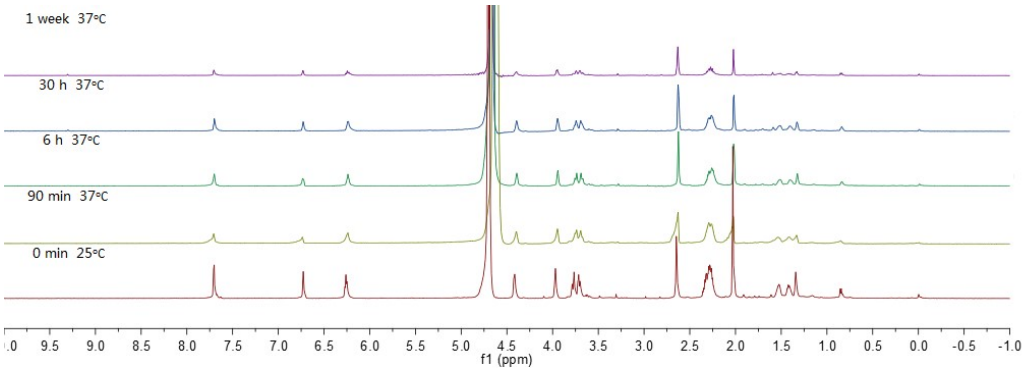


Figure S1. Stability of compound **40**

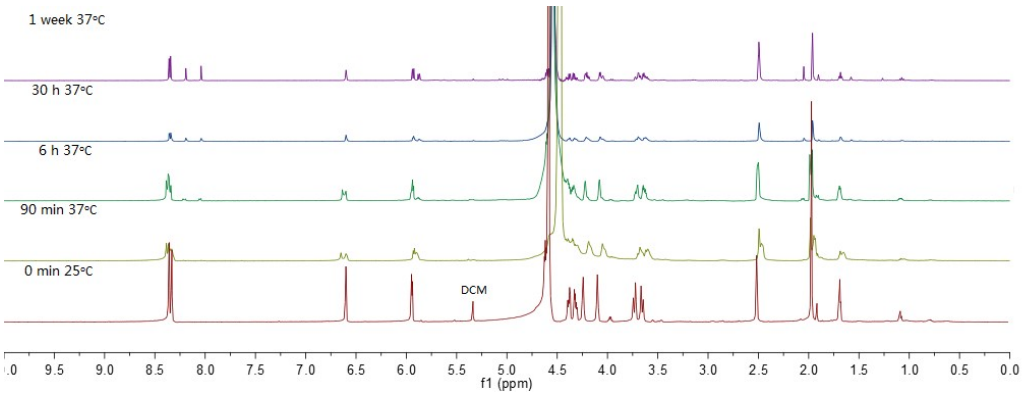


Figure S2. Stability of compound **46**

The bioorthogonal reaction kinetic measurements

1-MCP derivatives **18**, **40** and **46** reacted with *S*-tetrazine-BODIPYs **62**, **66**, **70** respectively, and the reaction rate was measured by fluorescence spectrophotometer. Reaction rates were obtained by

fitting the exponential increase of 1-MCP derivatives **18**, **40** and **46** as a pseudo first order reaction. According to the time and peak height can obtain the $\mathbf{t_{1/2}}$ (k = 1/[CYC.]* $t_{1/2}$), then get the observed reaction rates (K_{obs}), next Plotted K_{obs} *vs.* 1-MCP concentrations yielded a line, the slope of the resulting line was used to determine the second-order rate constant. All substances to be tested and *S*-tetrazine-BODIPY were freshly prepared. The reactants were configured as DMF storage solution, *S*-tetrazine-BODIPY was quantified (10 mM), 1-MCP derivatives require significant excess and stored in dark at 4 ℃ for standby. A 100 mM stock solution of compounds **18**, **40**, **46** was prepared in DMF was used for the kinetic measurement, and the change of the probe absorption intensity was measured over time. Measurements were immediately started upon the addition of excess 1-MCP derivatives **18**, **40**, **46** (final concentrations of 0.2, 0.4, 0.6, 0.8, 1.0 mM) to reaction solution. *S*-tetrazine-BODIPYs **62**, **66**, **70** solutions at 20 μM final concentration in DMF/PBS (V/V 1:1). The peak height of the compound **62**, **66**, **70** reacted with 1-MCPs **18**, **40**, **46** at 521 nm was tracked over the reaction timeframe by measuring the emission spectra every 5 min for 1-MCP.

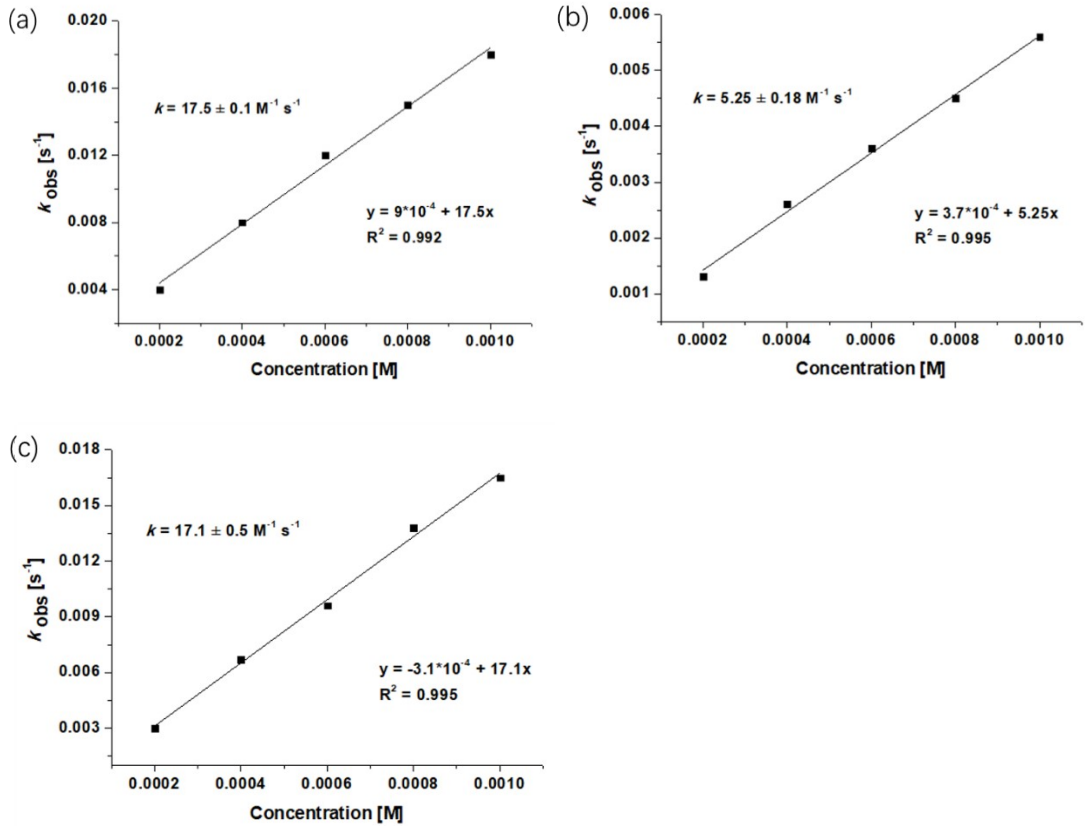


Figure S3. The bioorthogonal reaction kinetic measurements of 1-MCP **40** with *S*-tetrazine-BODIPYs **62**, **66**, **70**. (a) *S*-tetrazine-BODIPY **62** with 1-MCP **40**; (b) *S*-tetrazine-BODIPY **66** with 1-MCP **40**; (c) *S*-tetrazine-BODIPY **70** with 1-MCP **40**.

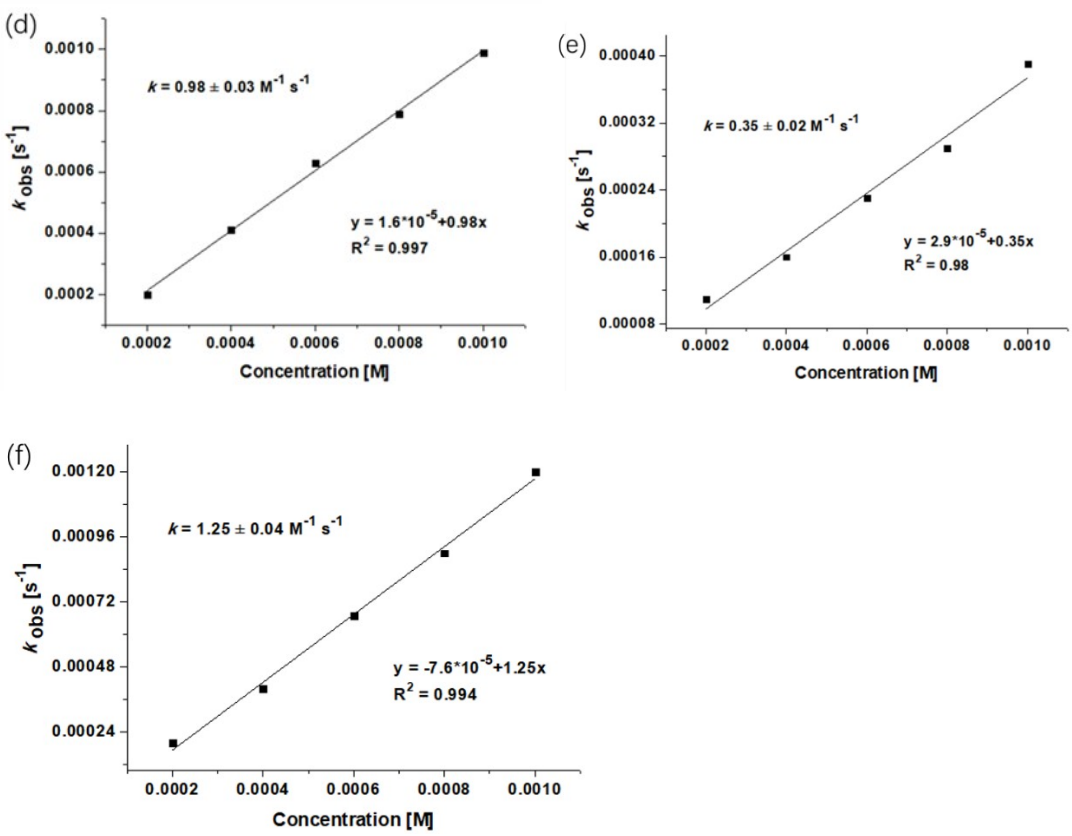


Figure S4. The bioorthogonal reaction kinetic measurements of 1-MCP **46** with *S*-tetrazine-BODIPYs **62**, **66**, **70**. (d) *S*-tetrazine-BODIPY **62** with 1-MCP **46**; (e) *S*-tetrazine-BODIPY **66** with 1-MCP **46**; (f) *S*-tetrazine-BODIPY **70** with 1-MCP **46**.

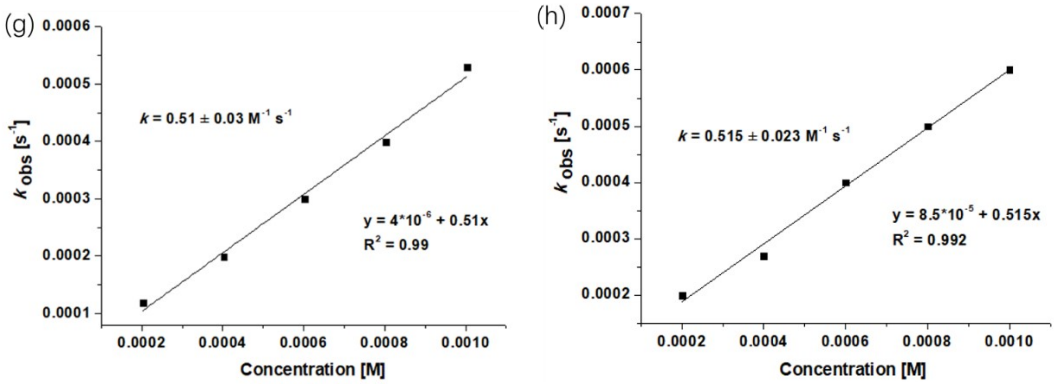


Figure S5. The bioorthogonal reaction kinetic measurements of 1-MCP **18** with *S*-tetrazine-BODIPY **62**, **70**. (g) *S*-tetrazine-BODIPY **62** with 1-MCP **18**; (h) *S*-tetrazine-BODIPY **70** with 1-MCP **18**.

Fluorescence spectrum measurement of compounds

Fluorescence quantum yields were measured by creating 2 mM stocks of freshly purified *S*-tetrazine-BODIPY dyes in DMF and reacted with 10-fold excess 1-MCPs **18**, **40**, **46** at the final concentrations of 20 μM *S*-tetrazine-BODIPY **62**, **66**, **70** and 0.2 mM 1-MCPs **18**, **40**, **46** in

DMF/PBS (V/V 1:1) solution, the reaction mixture was kept at 37 °C. The solution of *S*-tetrazine-BODIPY dye were excited at 488 nm (4.0 nm slit width) and emission signal were tracked over the 500-600 nm range (4.0 nm slit width). Absorbance spectra were recorded on a TU-1901 spectrometer. Emission spectra were recorded on a Perkin Elmer LS-55 spectrometer. Measurements were made in 1 cm x 1 cm quartz cuvettes with a total sample volume of 2.0 mL.

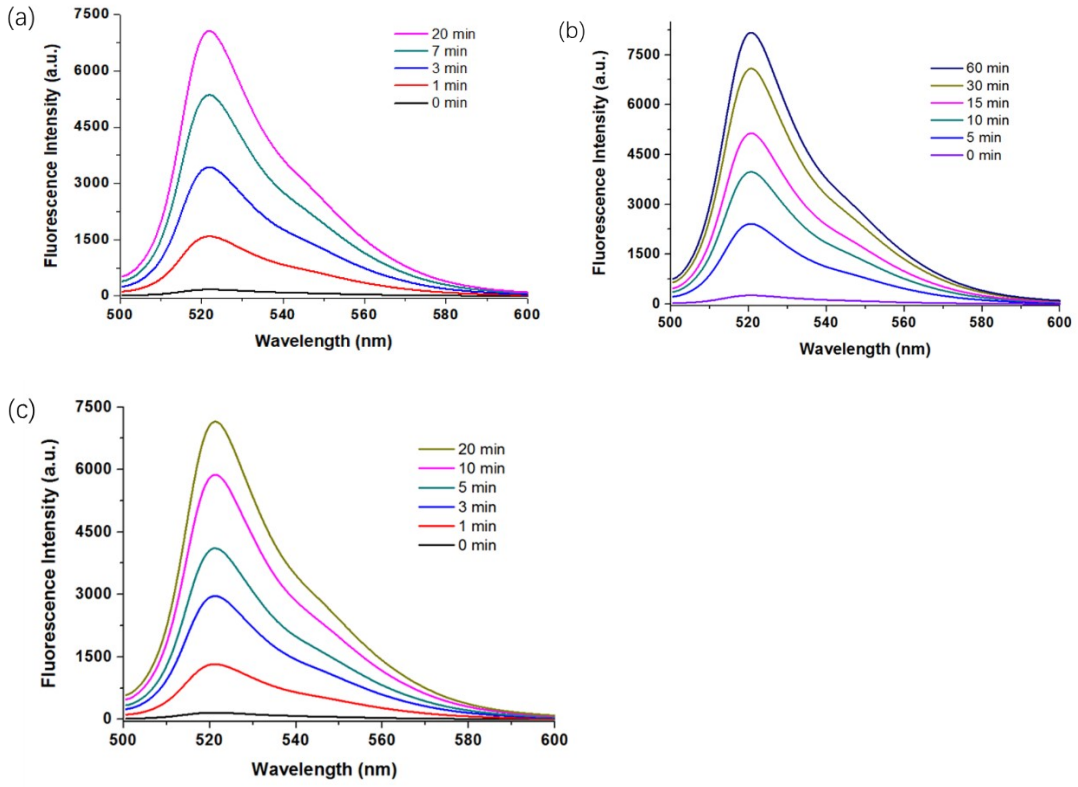
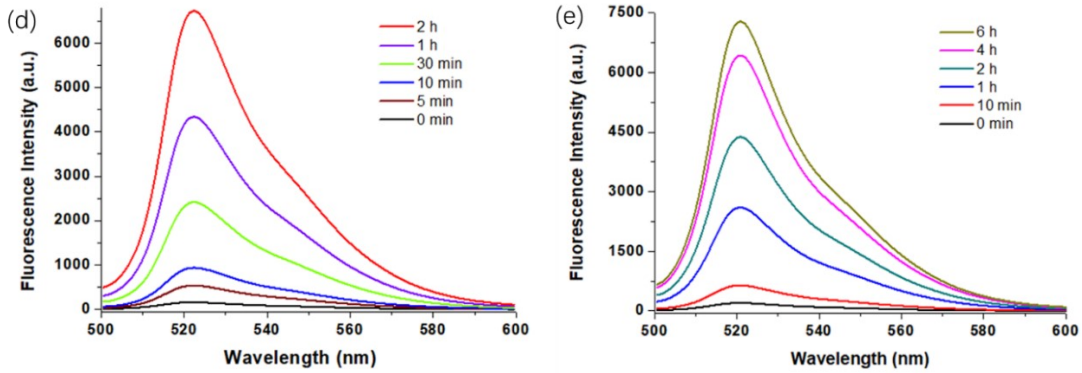


Figure S6. Measurement of fluorescence spectra of time-dependent compound **40** (0.2 mM) with *S*-tetrazine-BODIPY **62**, **66**, **70** (20 μM), respectively. (a) *S*-tetrazine-BODIPY **62** with 1-MCP **40**; (b) *S*-tetrazine-BODIPY **66** with 1-MCP **40**; (c) *S*-tetrazine-BODIPY **70** with 1-MCP **40**.



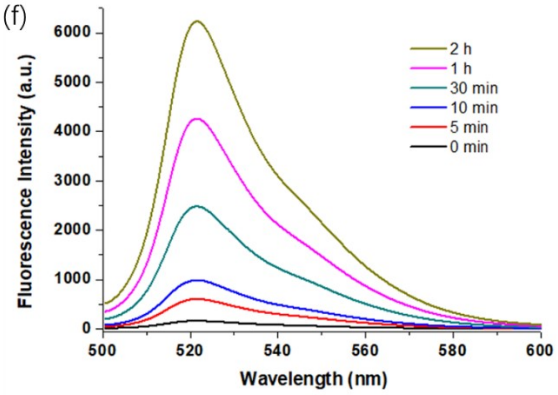


Figure S7. Measurement of fluorescence spectra of time-dependent compound **46** (0.2 mM) with *S*-tetrazine-BODIPY **62**, **66**, **70** (20 μM), respectively. (d) *S*-tetrazine-BODIPY **62** with 1-MCP **46**; (e) *S*-tetrazine-BODIPY **66** with 1-MCP **46**; (f) *S*-tetrazine-BODIPY **70** with 1-MCP **46**.

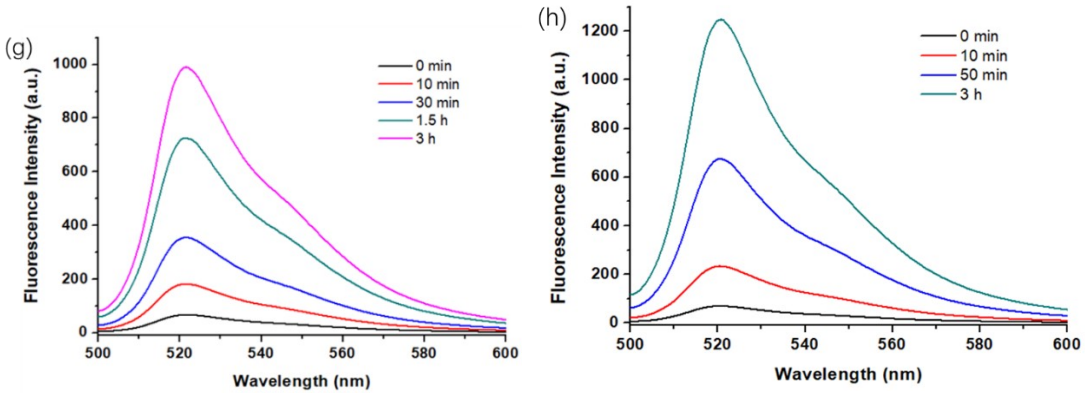
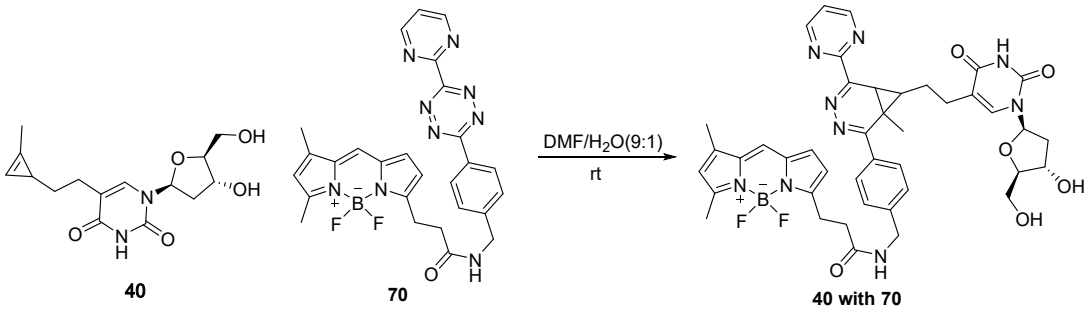


Figure S8. Measurement of fluorescence spectra of time-dependent compounds **18** (0.2 mM) with *S*-tetrazine-BODIPY **62**, **66**, **70** (20 μM), respectively. (g) *S*-tetrazine-BODIPY **62** with 1-MCP **18**; (h) *S*-tetrazine-BODIPY **70** with 1-MCP **18**.

HPLC characterization of the bioorthogonal reaction between 1-MCP 40 and 46 with tetrazines 70



40 **70** **40 with 70**

Chemical Formula: $C_{42}H_{44}BF_2N_9O_6$
Exact Mass: 819.3476

Compound **40** (100 mM) and *S*-tetrazine-BODIPY **70** (10 mM) were combined in at a final concentration of 5 mM compound **70** and 10 mM **39**. The reaction solution was at room temperature for 10 min in DMF/H_2O = 9: 1, then analyzed by LC-MS in order to identify the molecular mass corresponding to adducts **40 with 70** (m/z 820$[M+1]^+$, Figure S10)

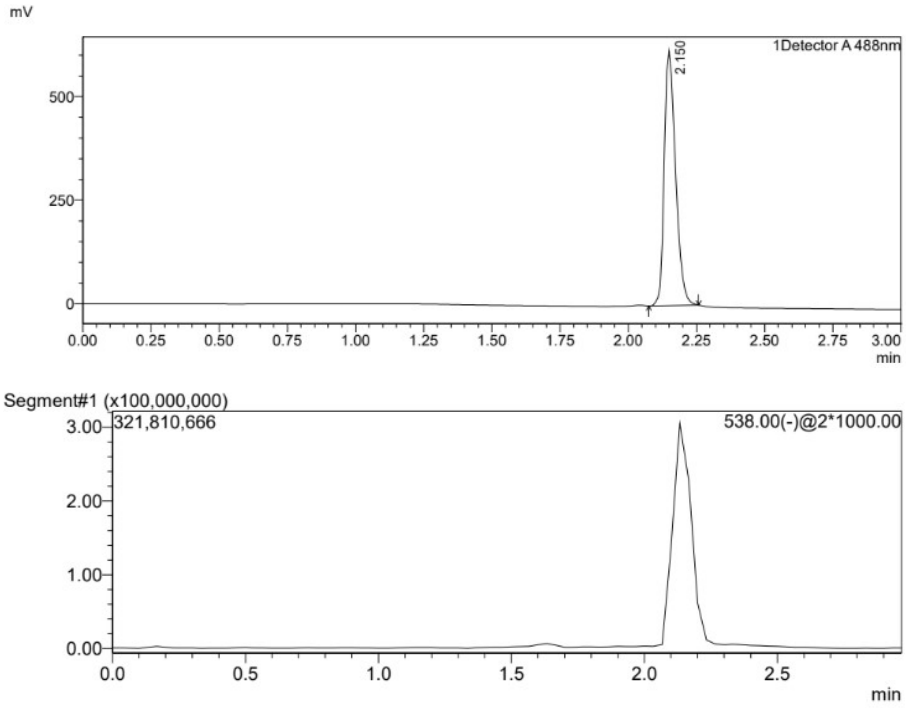


Figure S9. LC-MS of *S*-tetrazine-BODIPY **70** ($t_{1/2}$ = 2.15 min, 2-100% ACN/H_2O/0.01%FA, 0.7 min/mL, Ex = 488 nm, Shimpack)

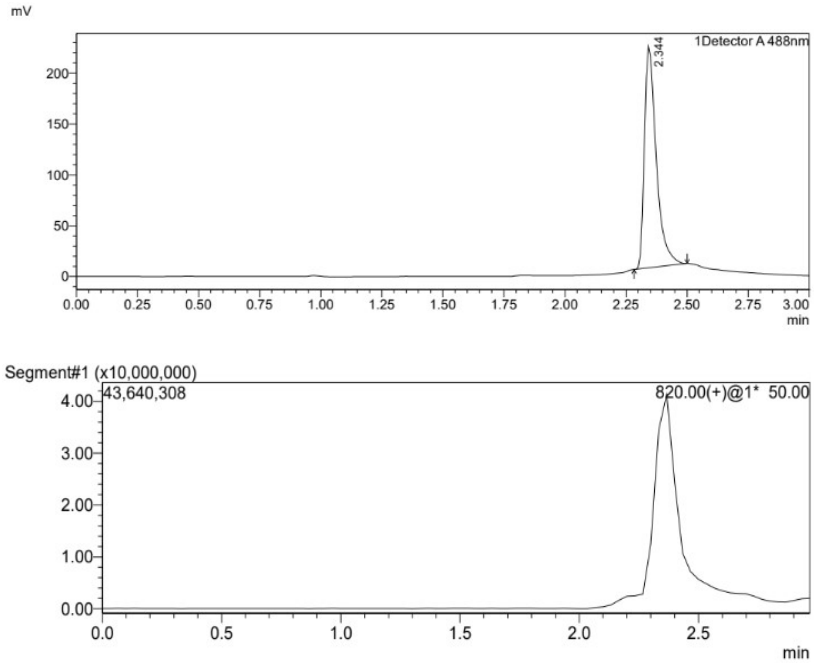
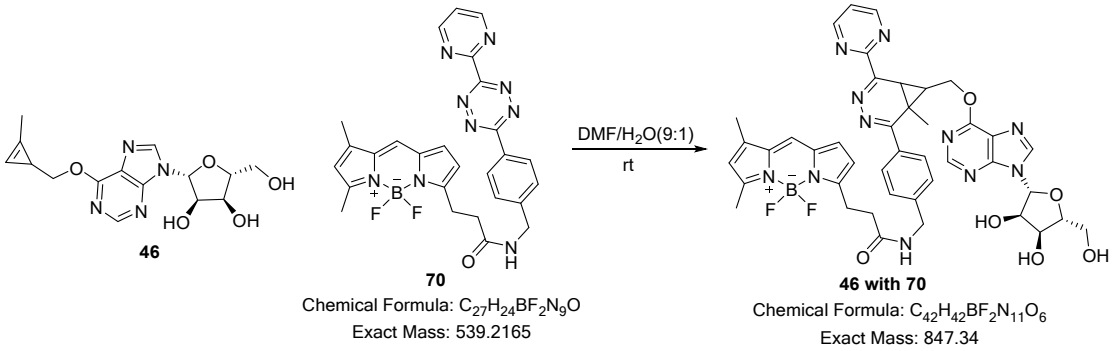


Figure S10. LC-MS of reaction **40** and **70** ($t_{1/2}$ = 2.344 min, 2-100% ACN/H_2O/0.01%FA, 0.7 min/mL, Ex = 488 nm, Shimpack)



Compound **46** (100 mM) and *S*-tetrazine-BODIPY **70** (10 mM) were combined in at a final concentration of 5 mM compound **70** and 10 mM **46**. The reaction solution was at room temperature for 10 min in DMF/H_2O = 9: 1, then analyzed by LC-MS in order to identify the molecular mass corresponding to adducts **46 with 70** (m/z 846[M-1]$^+$, Figure S10)

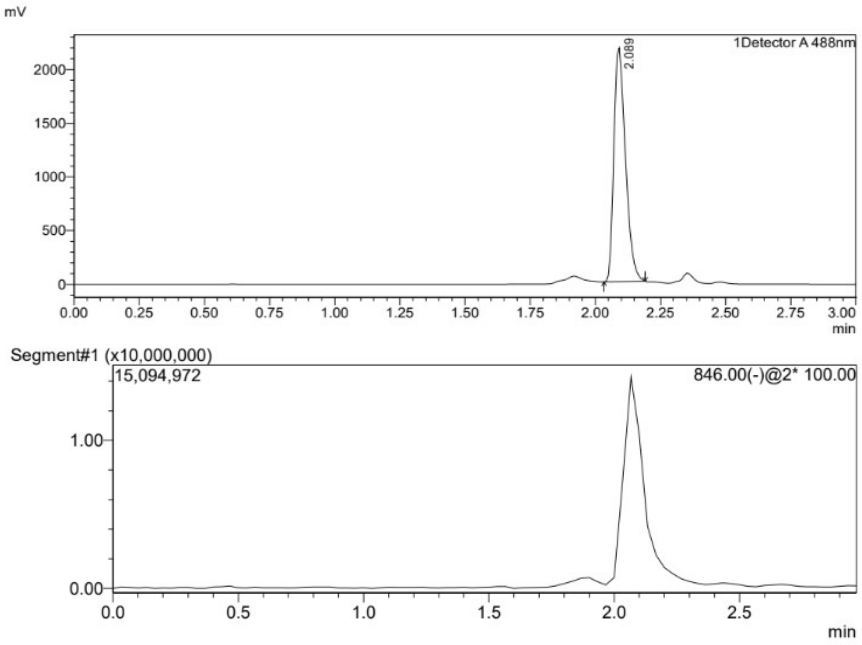


Figure S11. LC-MS of reaction **46** with **70** ($t_{1/2}$ = 2.089 min, 2-100% ACN/H_2O/0.01%FA, 0.7 min/mL, Ex = 488 nm, Shimpack)

Measurement kinetic and bioorthogonal reaction of 1-MCP nucleoside probe 40 with 5-TAMRA-Tz

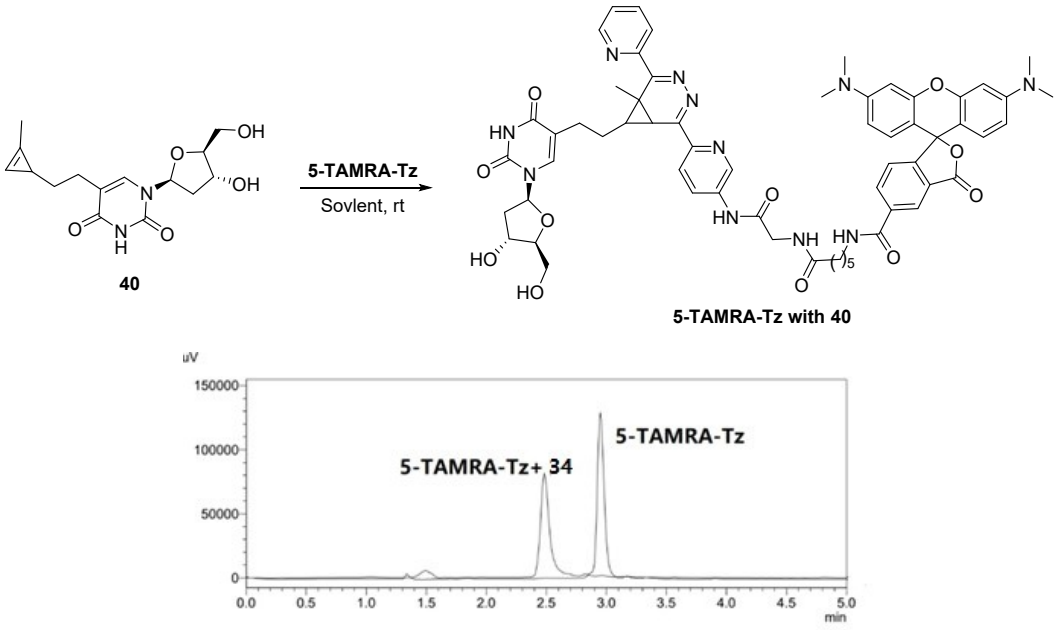


Figure S12. LC-MS of reaction **40** (0.2 mM) and **5-TAMRA-Tz** (0.02 mM) ($t_{1/2}$ = 2.5 min, 2-100% ACN/H_2O/0.01%FA, 0.7 min/mL, Ex = 546 nm, Shimpack)

Table S1. Kinetic of the reaction of 1-MCP nucleoside **40** with 5-TAMRA-Tz in different solvents

Entry	Sovlent	$t_{1/2}$ [s]	k_2 [M^{-1} s^{-1}]
1	DMF/PBS[1](v:v/1:1)	597	4.45 ± 0.16
2	DMSO/PBS[2] (v:v/1:1)	301	5.25 ± 0.24
3	PBS[3]	37	56.6 ± 1.94
4	EtOH/H_2O[1] (v:v/1:1)	546	4.85 ± 0.20
5	MeOH/H_2O[1] (v:v/1:1)	437	5.95 ± 0.08

[1] 0.02 mM 5-TAMRA-Tz, 0.2 mM **40**, 25 ℃; [2] 0.04 mM 5-TAMRA-Tz, 0.4 mM **40**, 25 ℃; [3] 0.01 mM 5-TAMRA-Tz, 0.1 mM **40**, 25 ℃, pH 7.4.

Measurement of cytotoxicity

Firstly, we evaluated the viability of HeLa cells by tetrazolium salt MTT assay and analyzed the effect of its cytotoxicity on the growth of HeLa cells. As shown in Figure S13, after HeLa cells were incubated with 1-MCP nucleoside **40** and **46** for 12 hours at 37 ℃, 1-MCP nucleoside **46** had a survival rate of more than 85% in the concentration range of 0-100 μM, while 1-MCP nucleoside **40** was almost 100%.

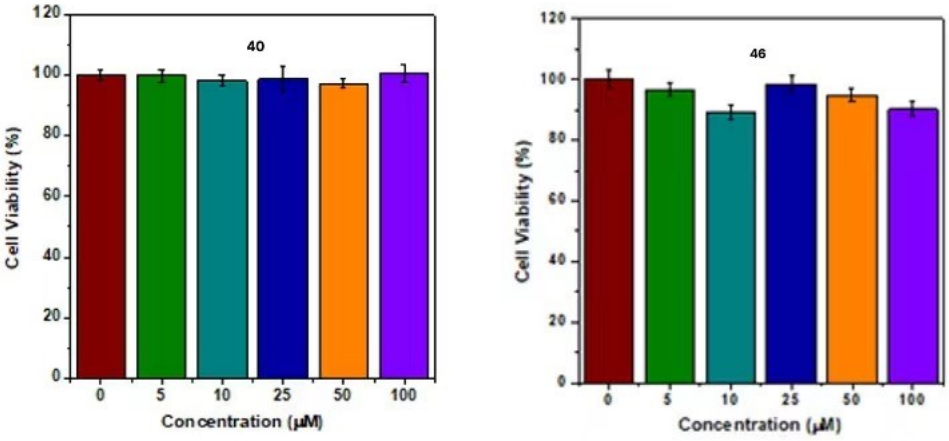


Figure S13. Survival rates of 1-MCPs **40** and **46** in HeLa cells at different concentrations.

NOEDS analysis 7a and 7b

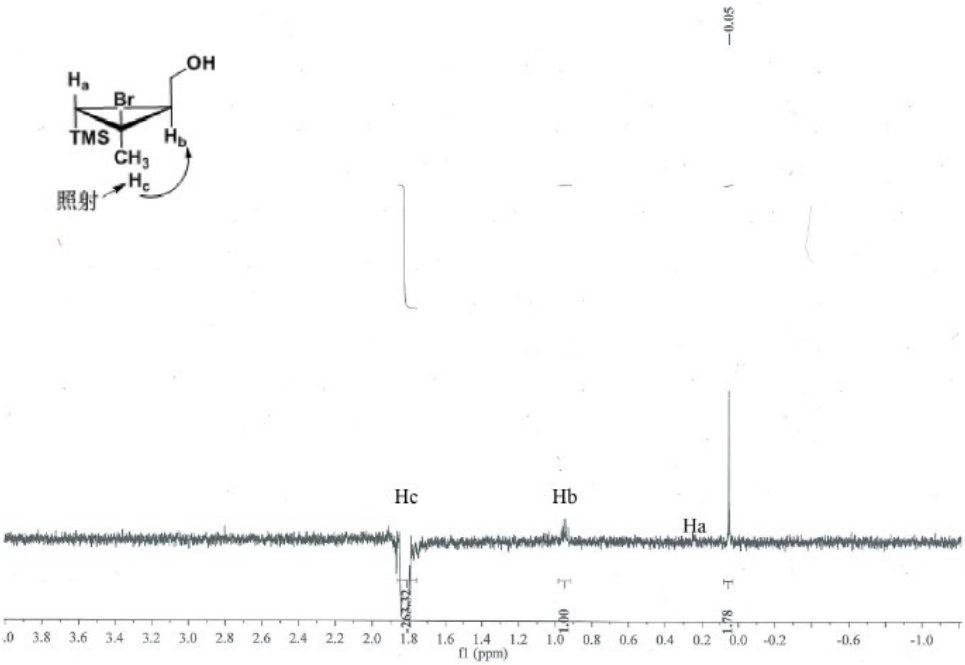


Figure S14. Identified structure of **7a**.

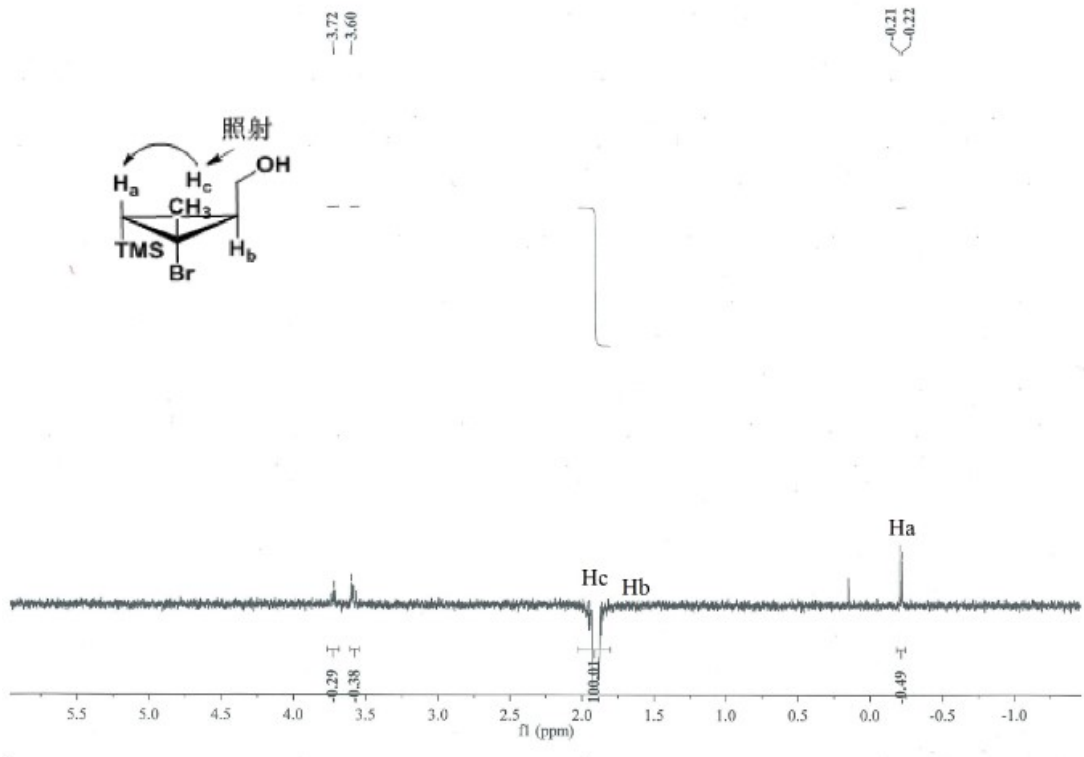
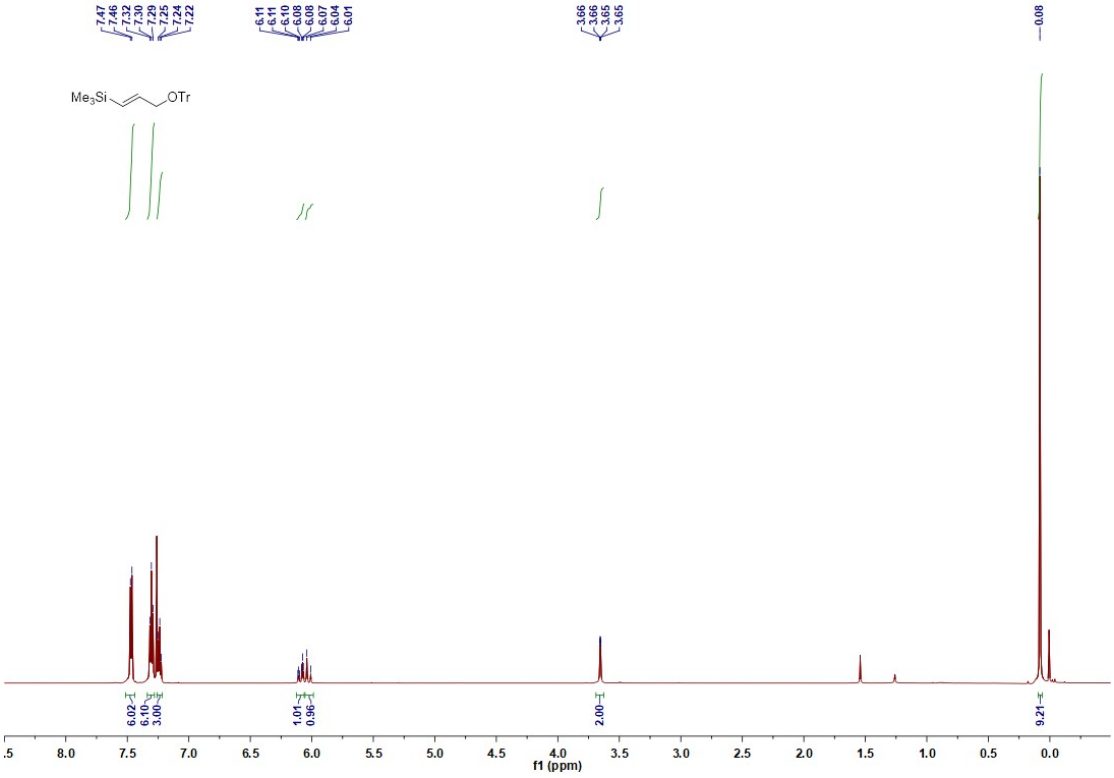


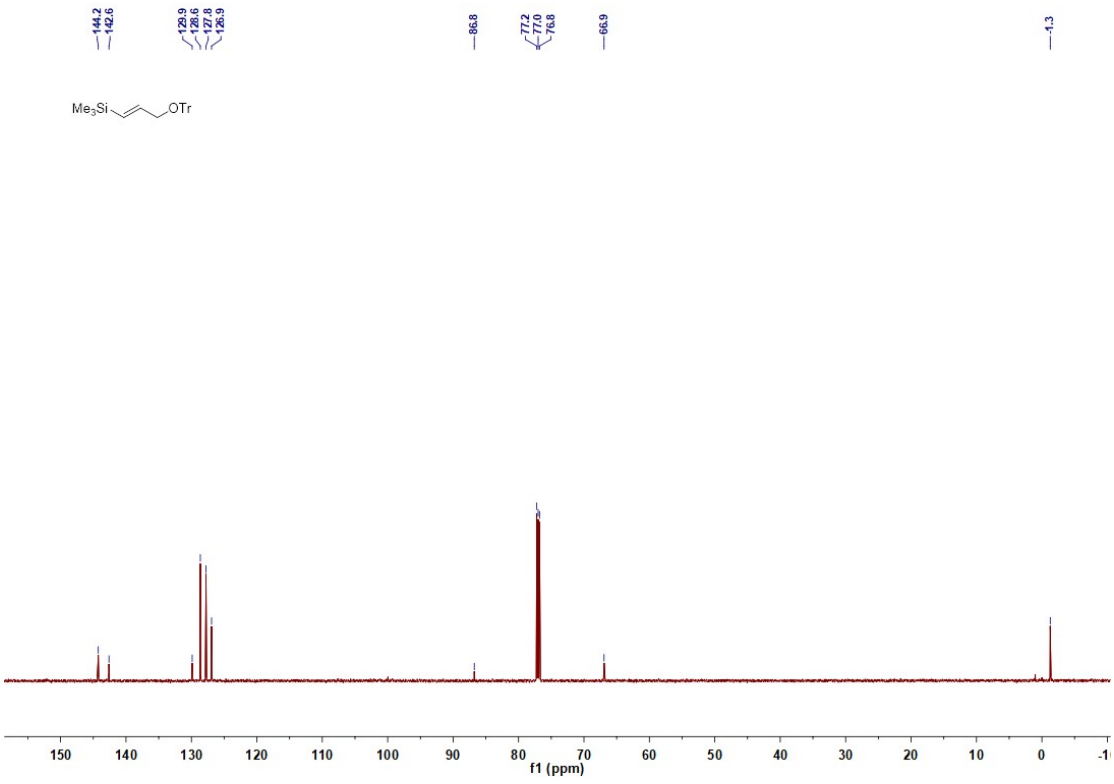
Figure S15. Identified structure of **7b**.

NMR spectra

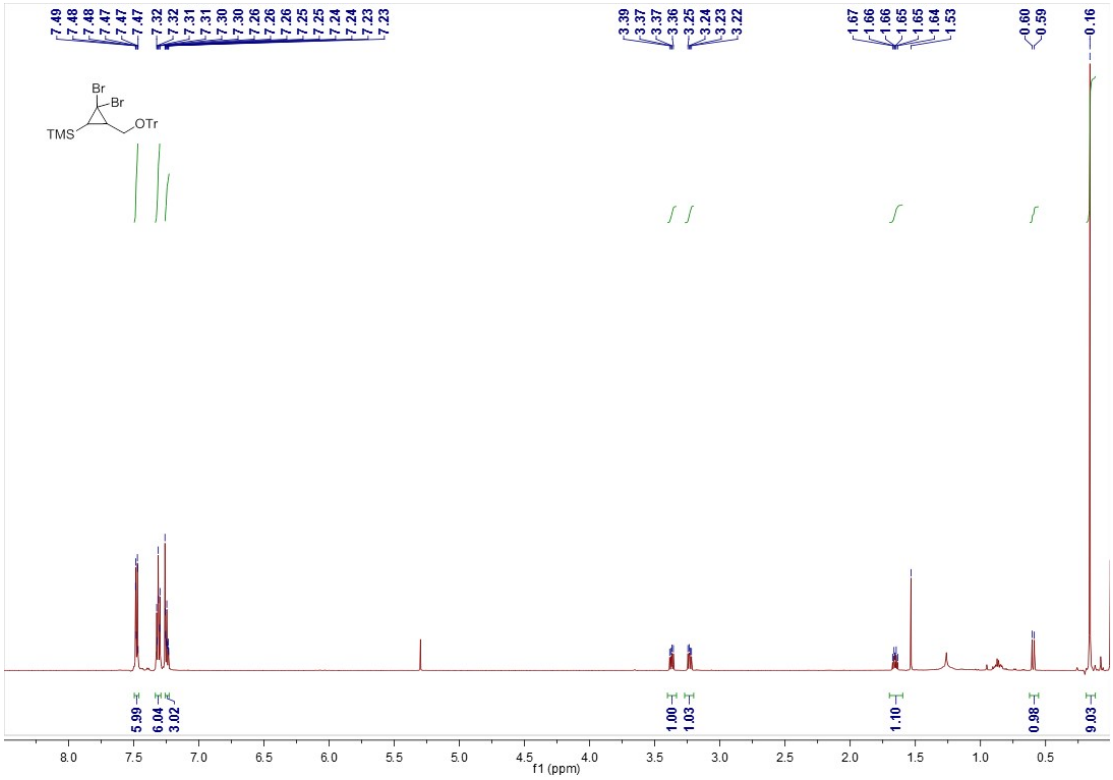
Compound 5 ^{1}H NMR



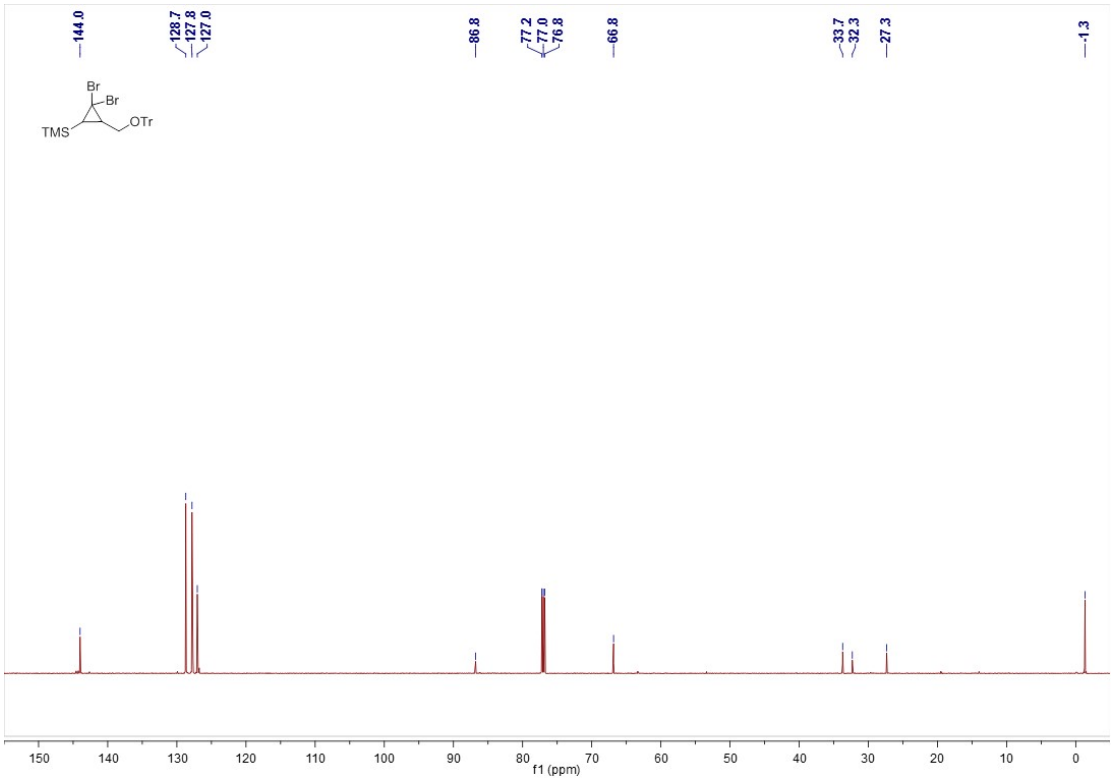
Compound 5 ^{13}C NMR



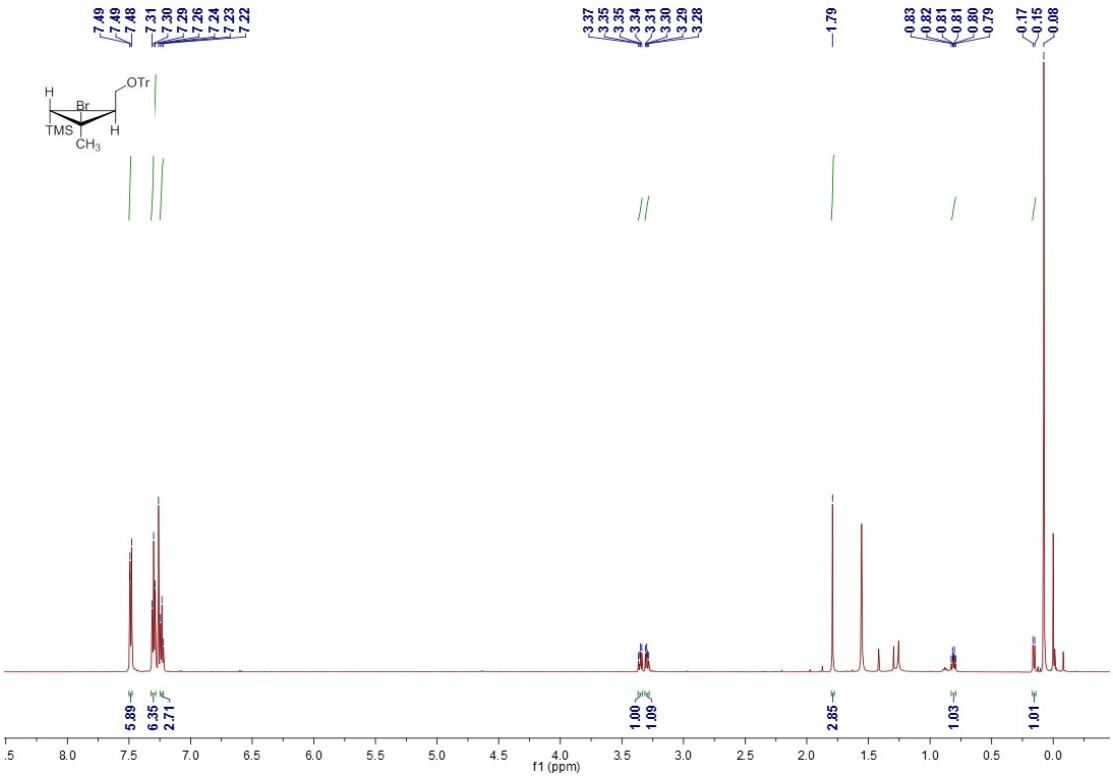
Compound 6 ^{1}H NMR



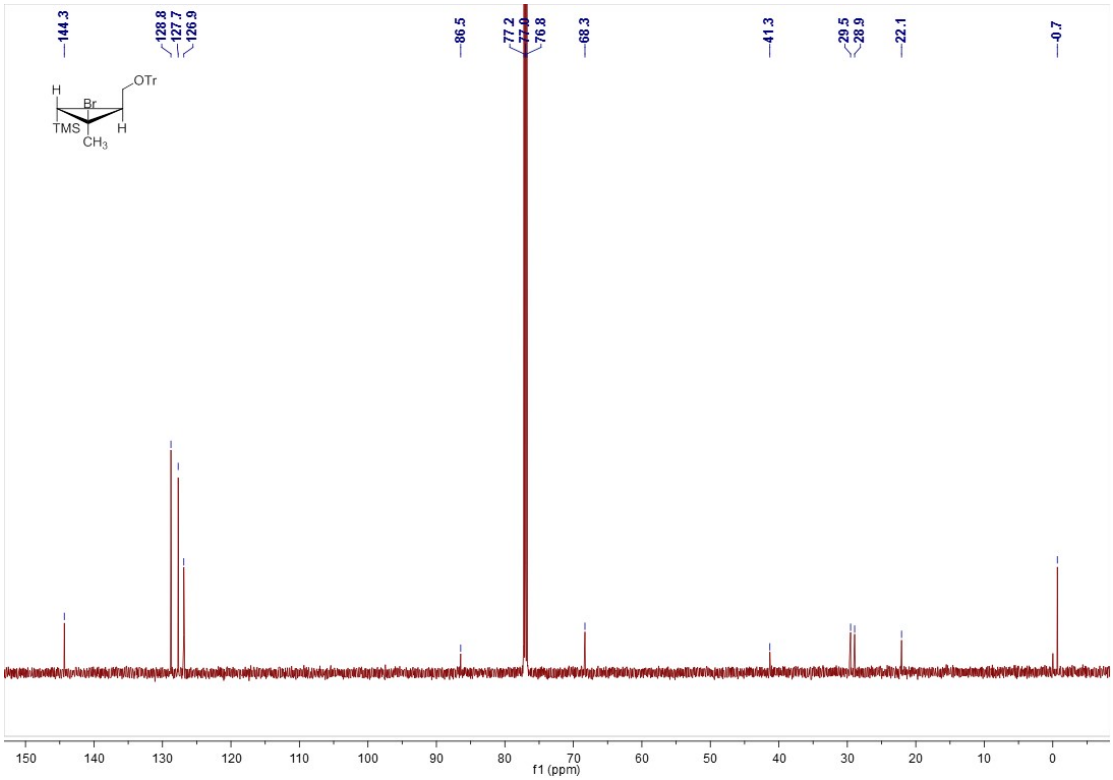
Compound 6 ^{13}C NMR



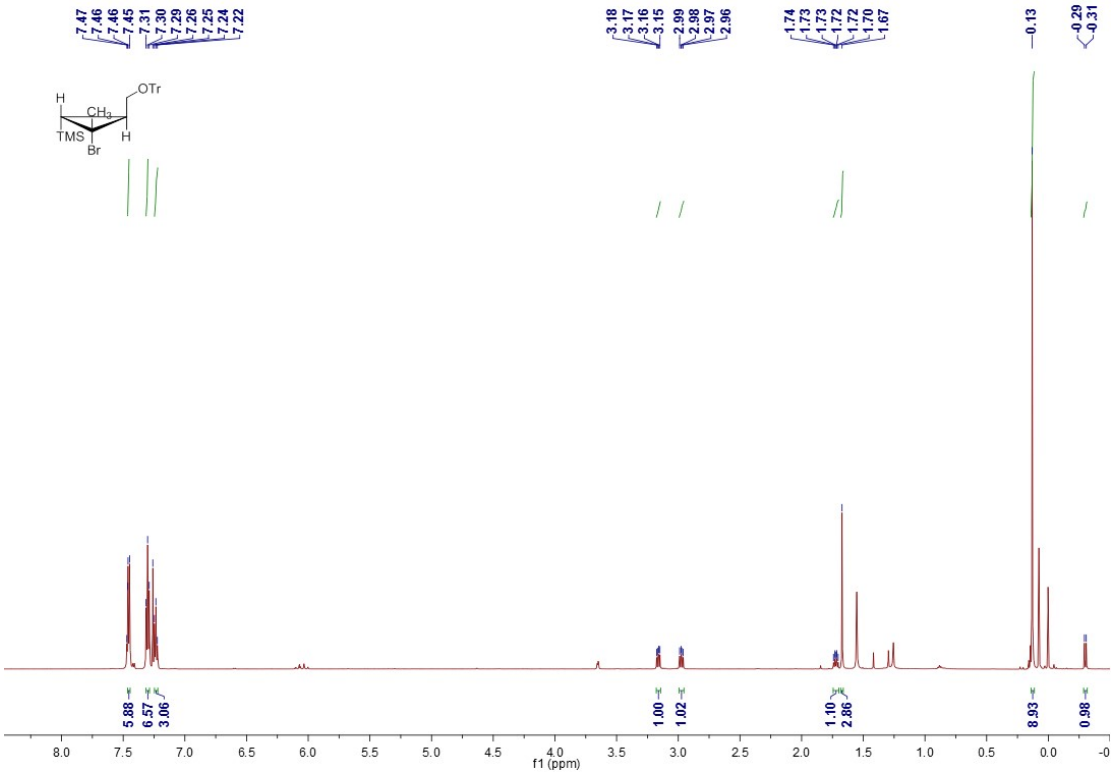
Compound 8a ^{1}H NMR



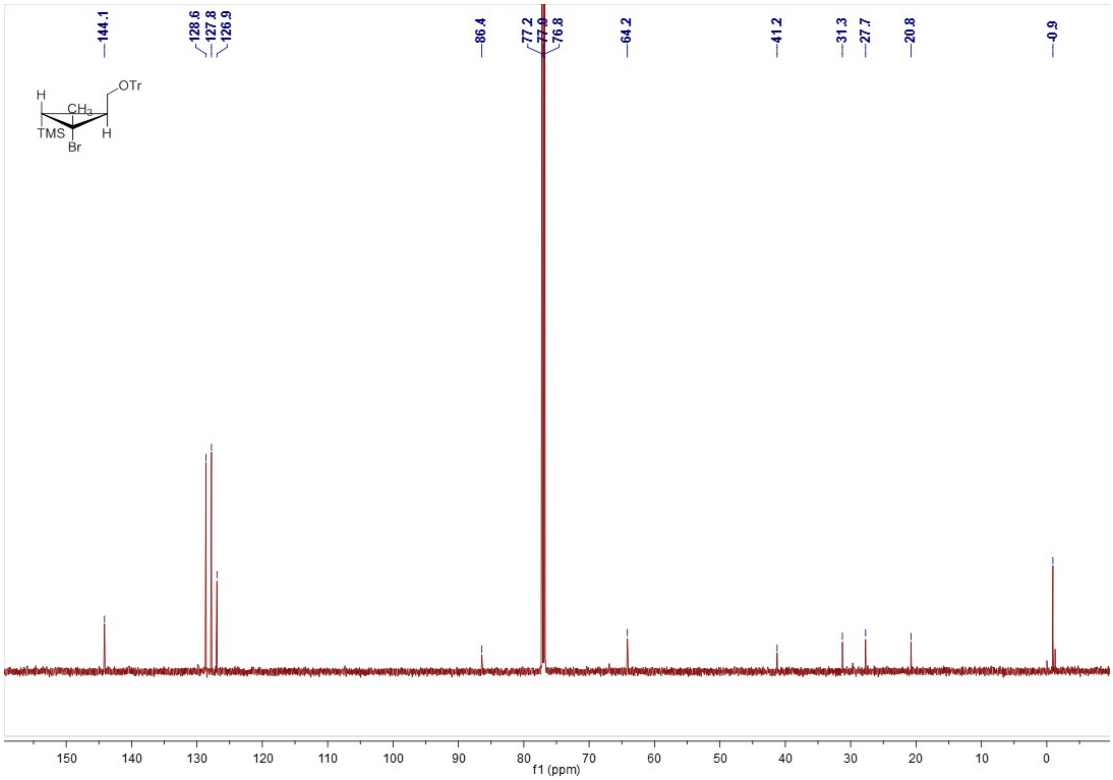
Compound 8a ^{13}C NMR



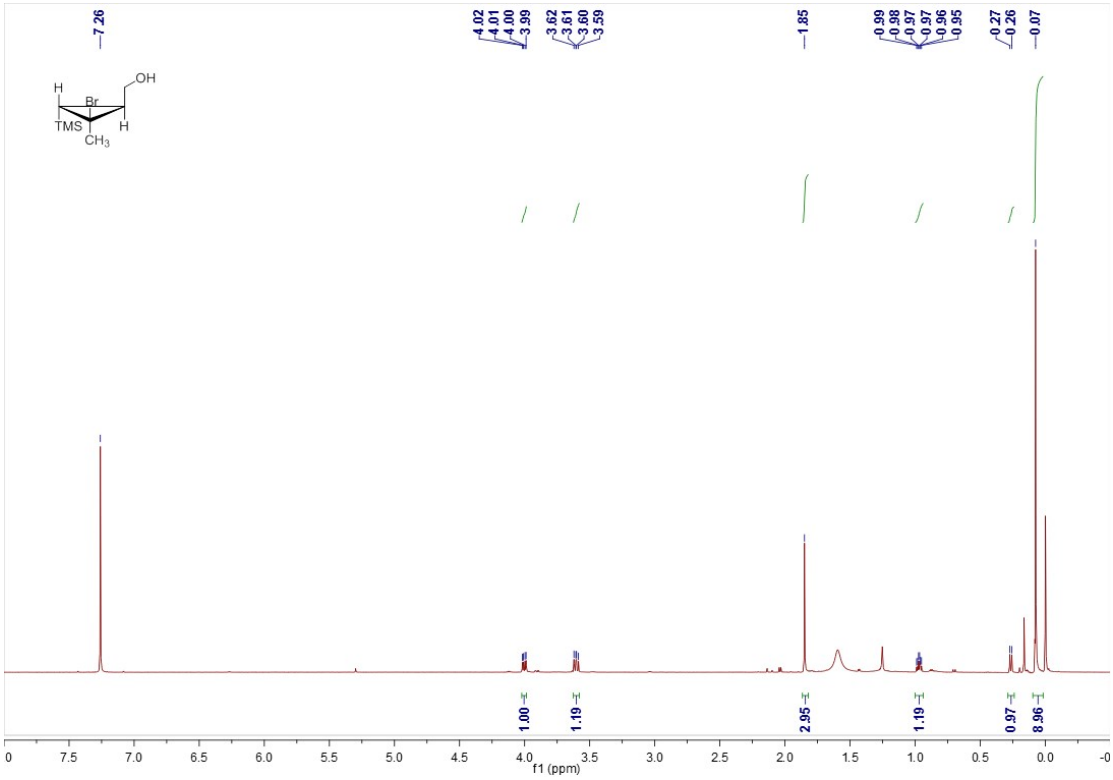
Compound 8b ^{1}H NMR



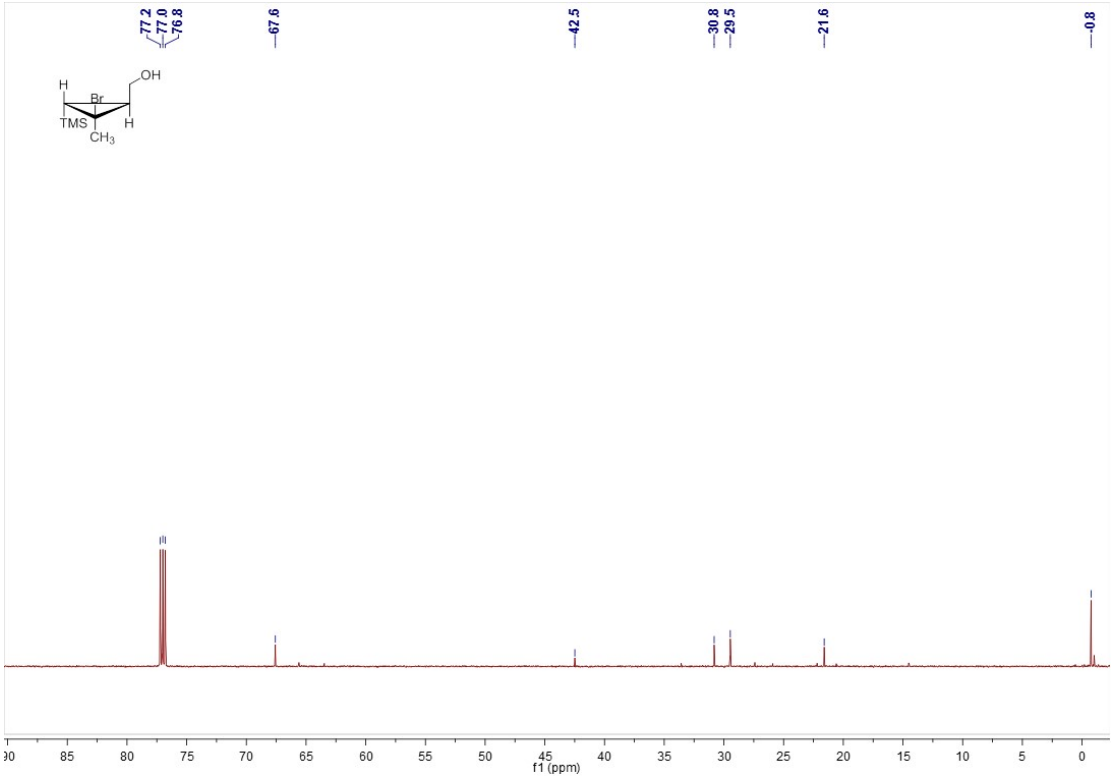
Compound 8b ^{13}C NMR



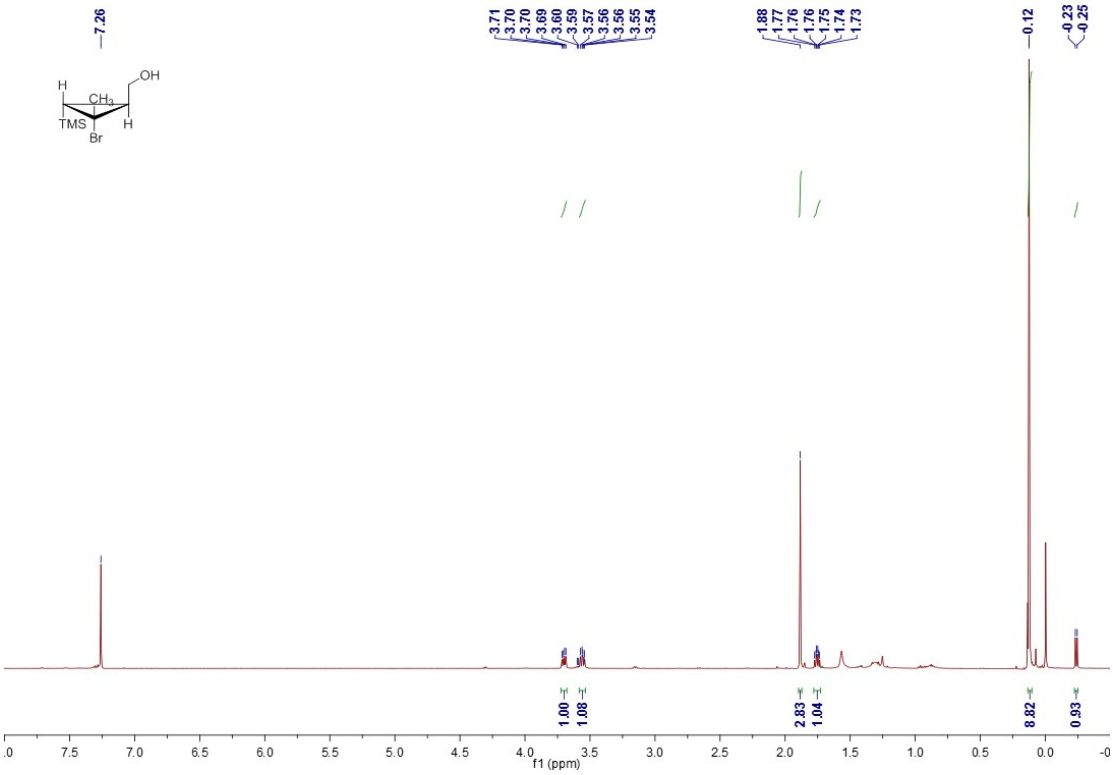
Compound 7a ^{1}H NMR



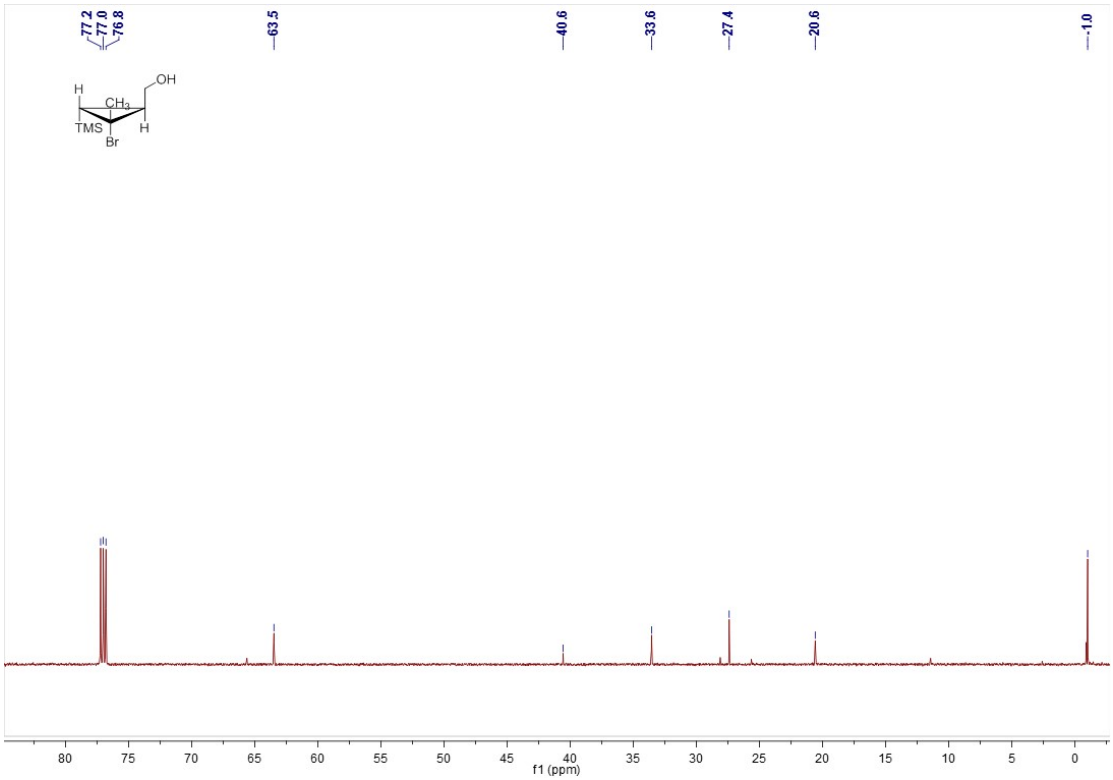
Compound 7a ^{13}C NMR



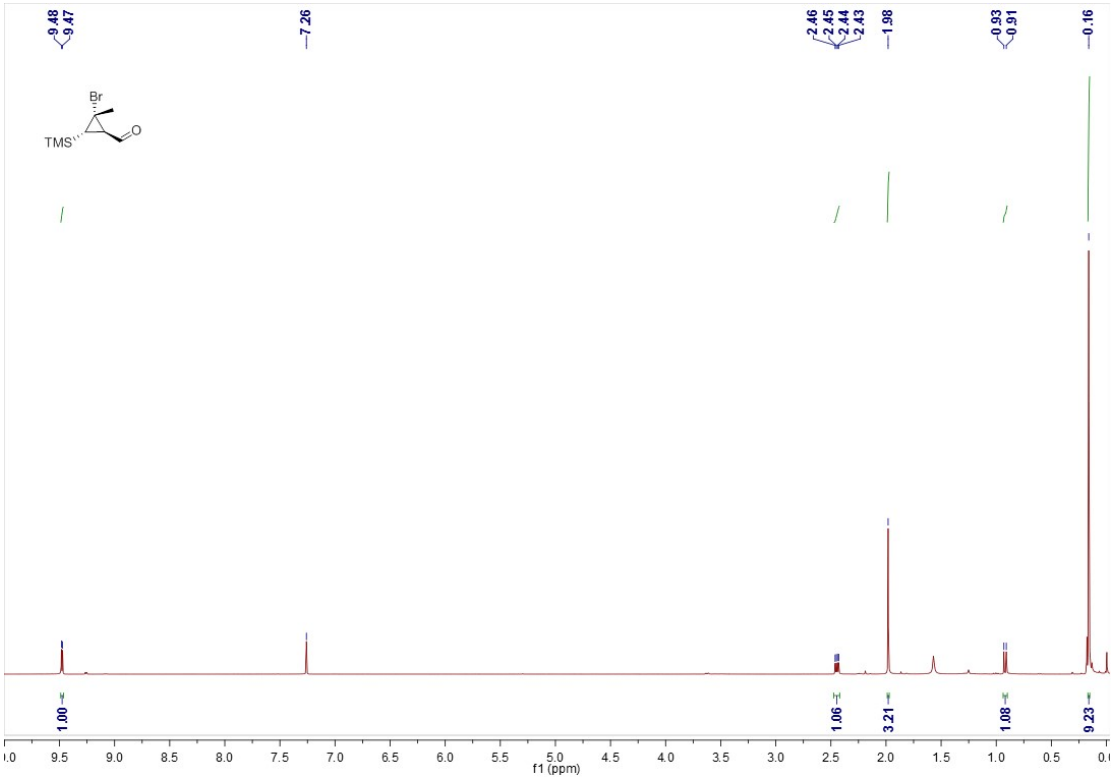
Compound 7b ^{1}H NMR



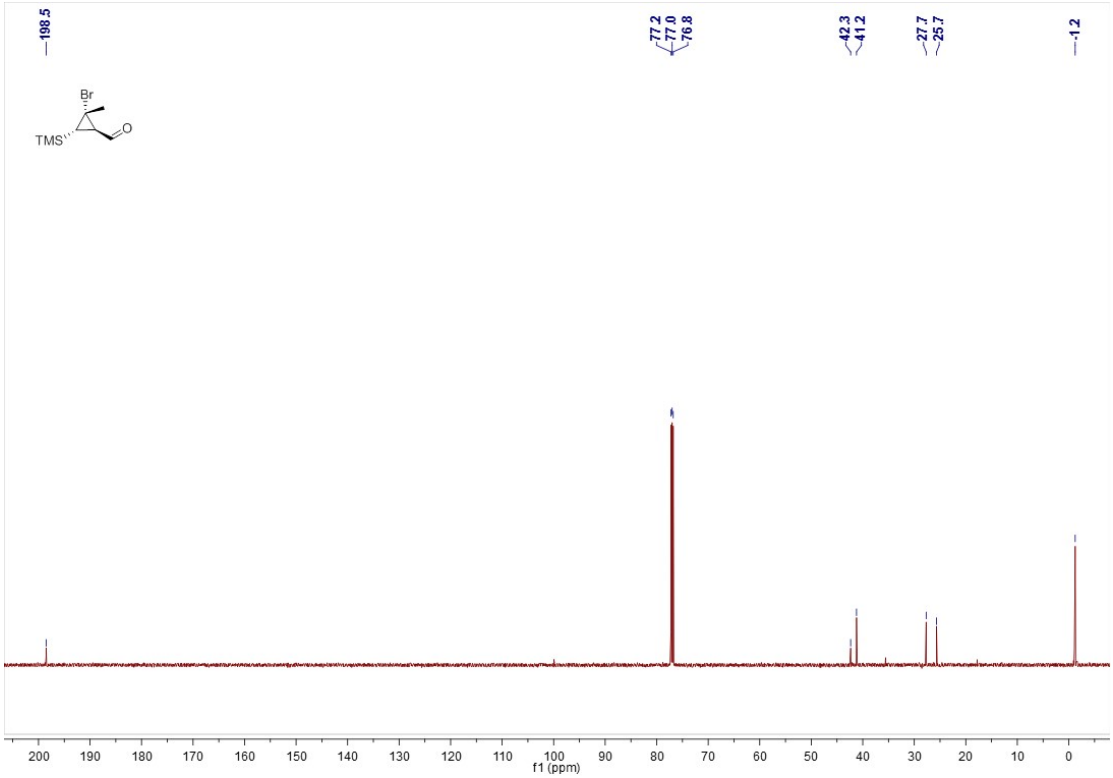
Compound 7b ^{13}C NMR



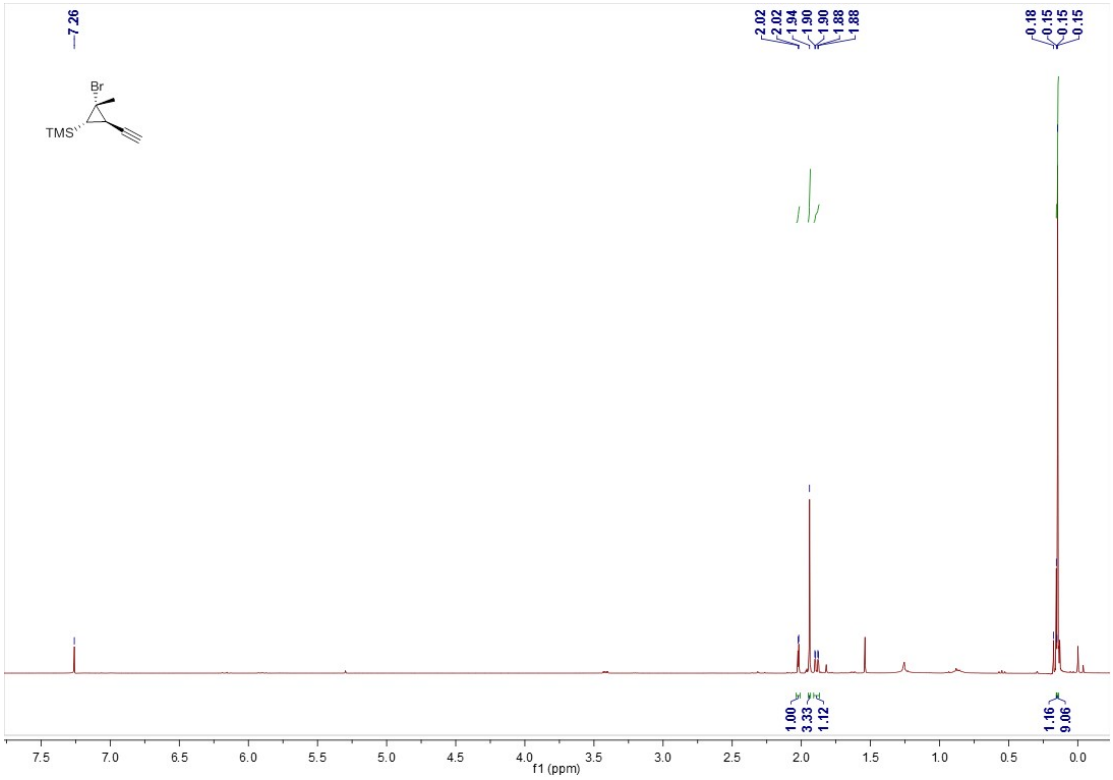
Compound 11 ^{1}H NMR



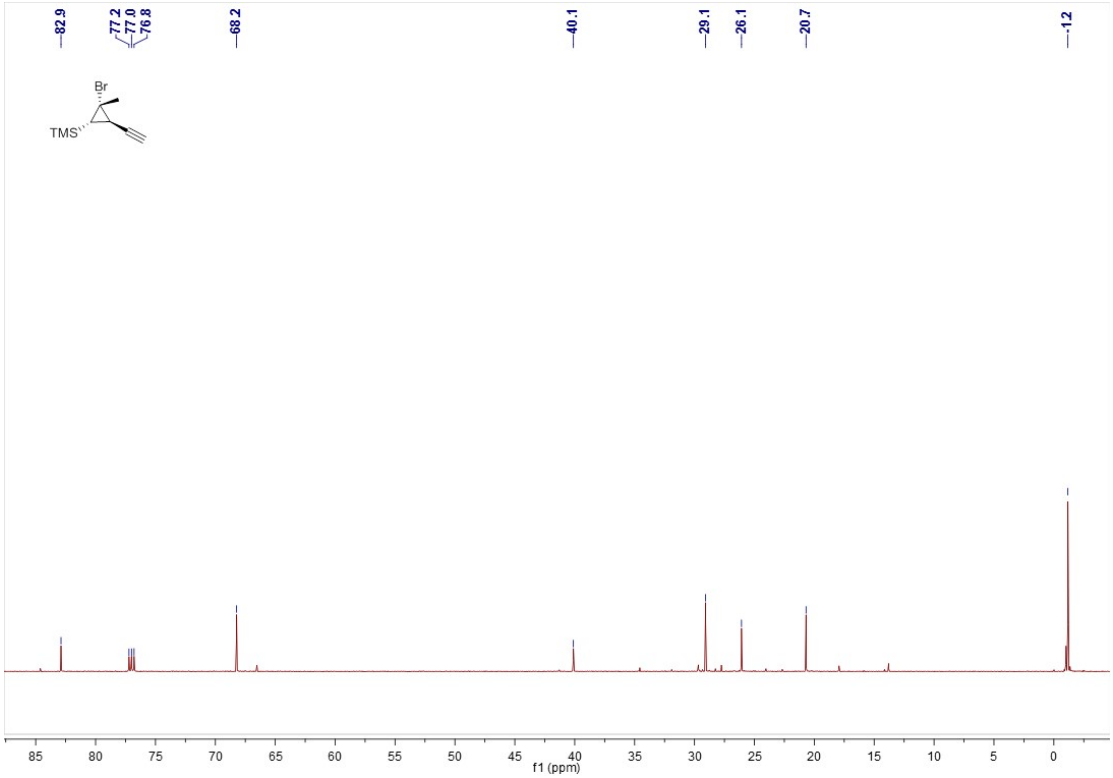
Compound 11 ^{13}C NMR



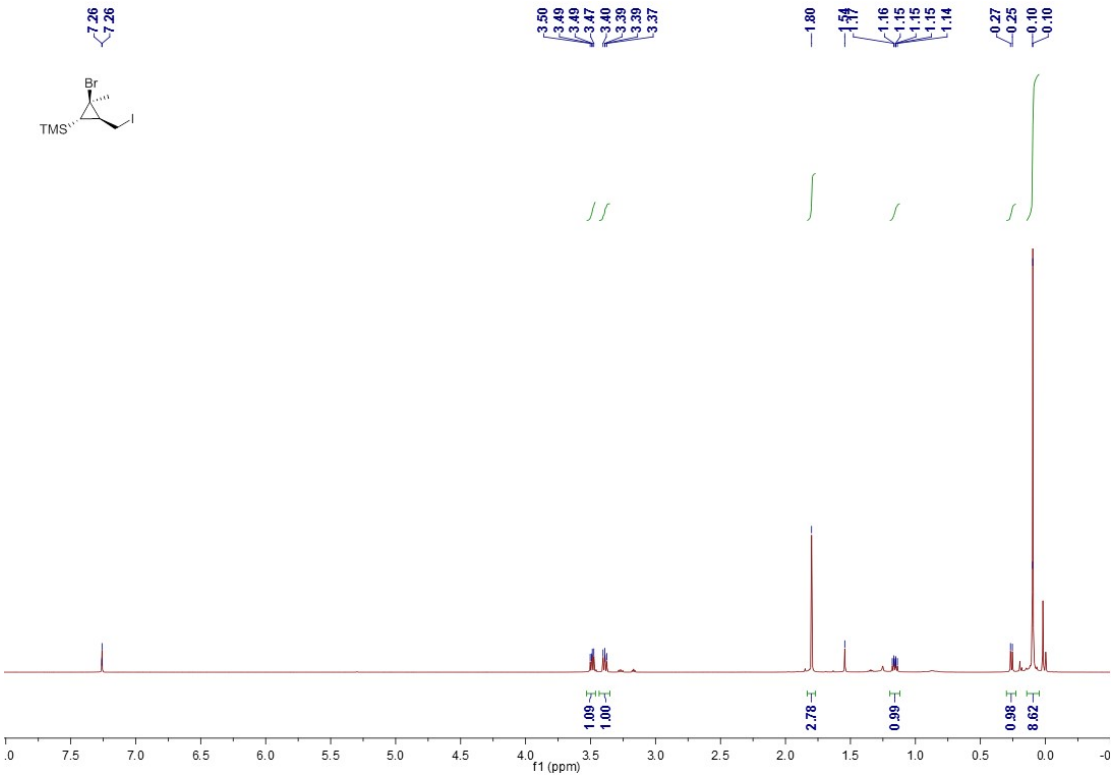
Compound 12 ^{1}H NMR



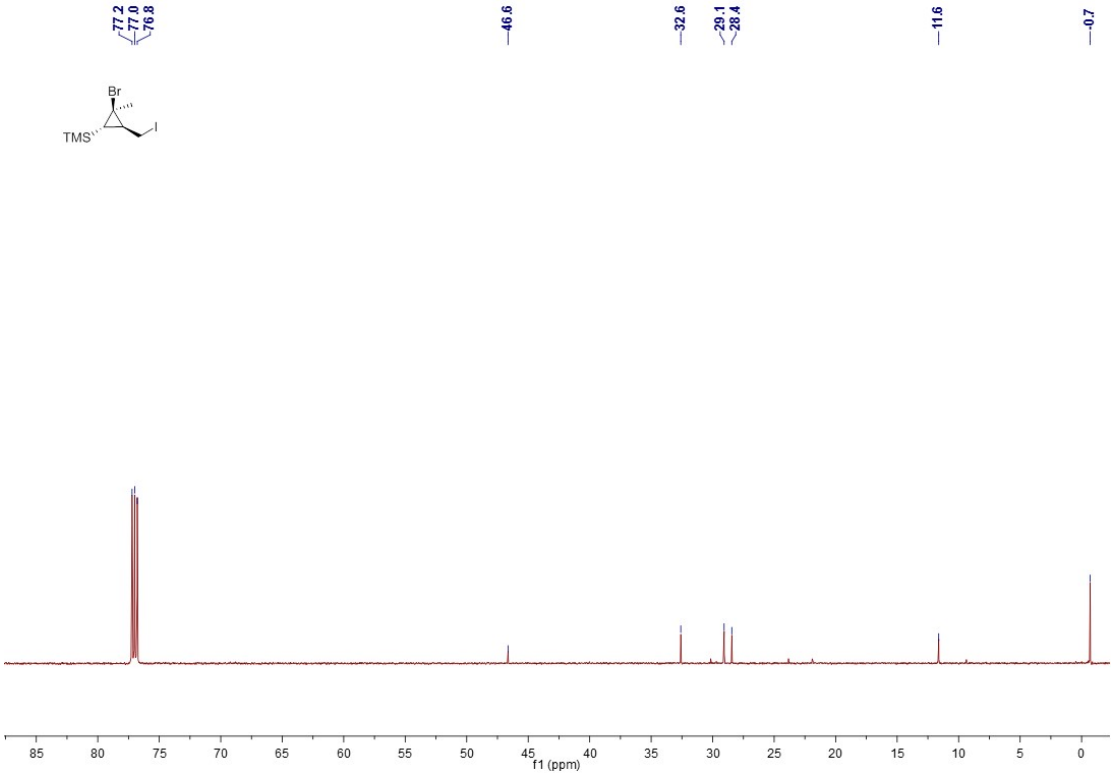
Compound 12 ^{13}C NMR



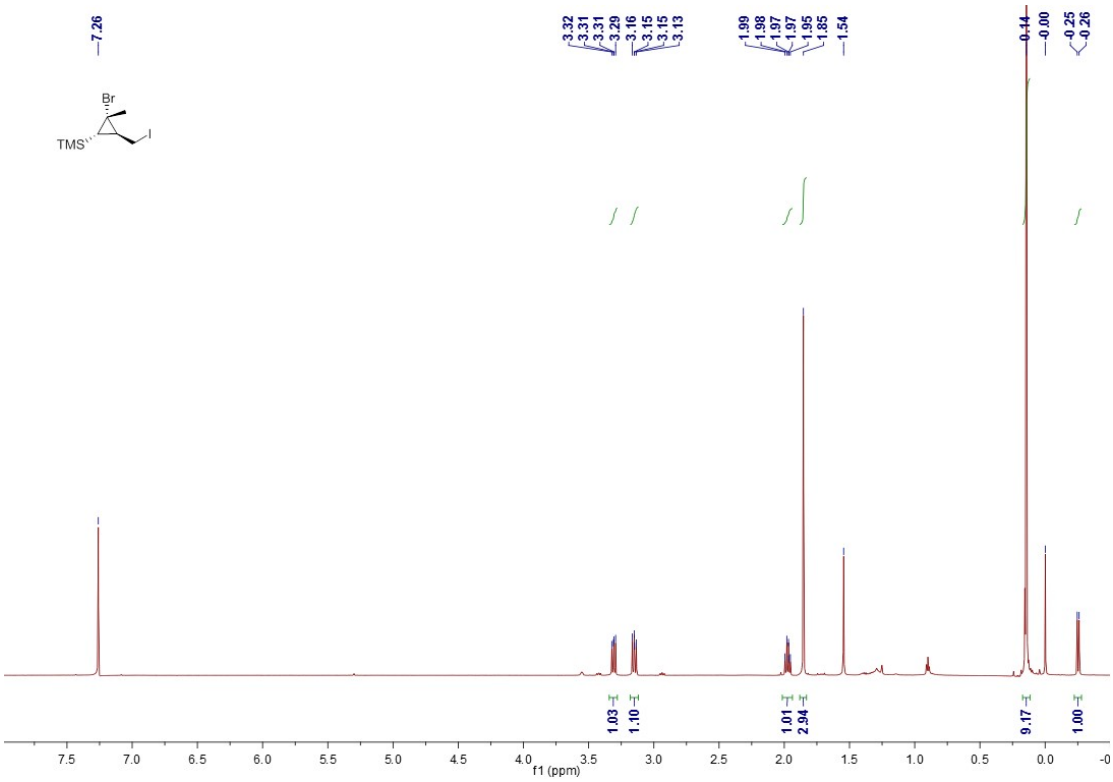
Compound 9a ^{1}H NMR



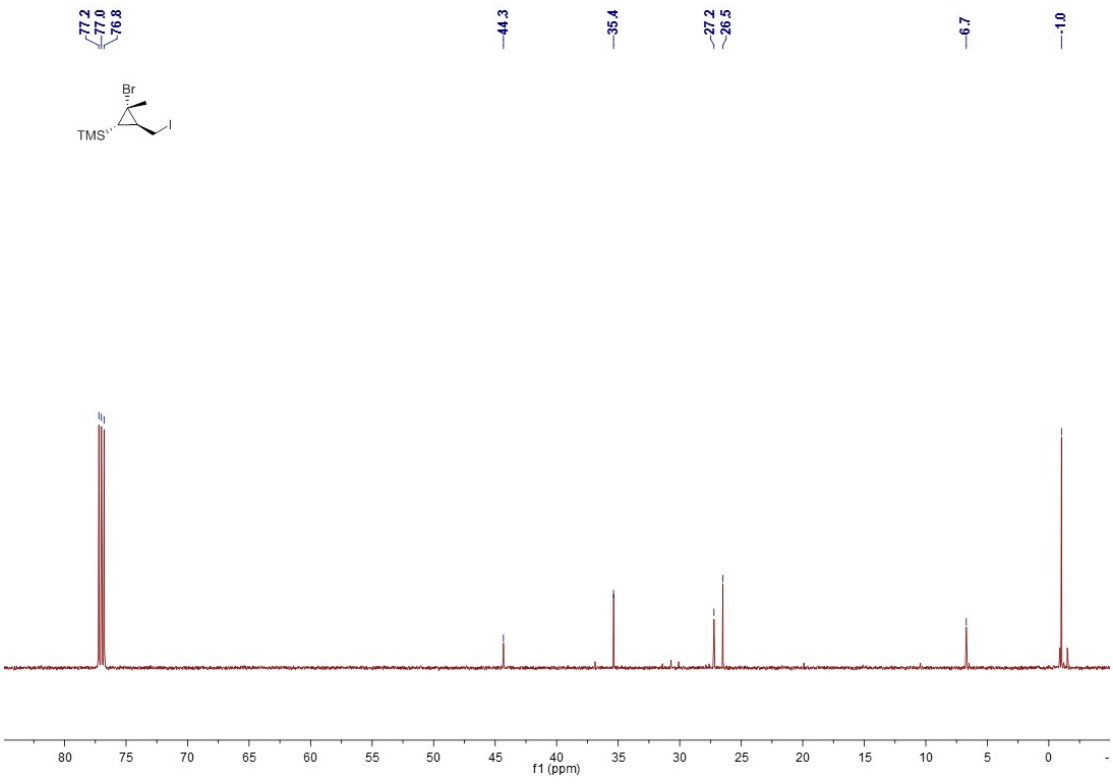
Compound 9a ^{13}C NMR



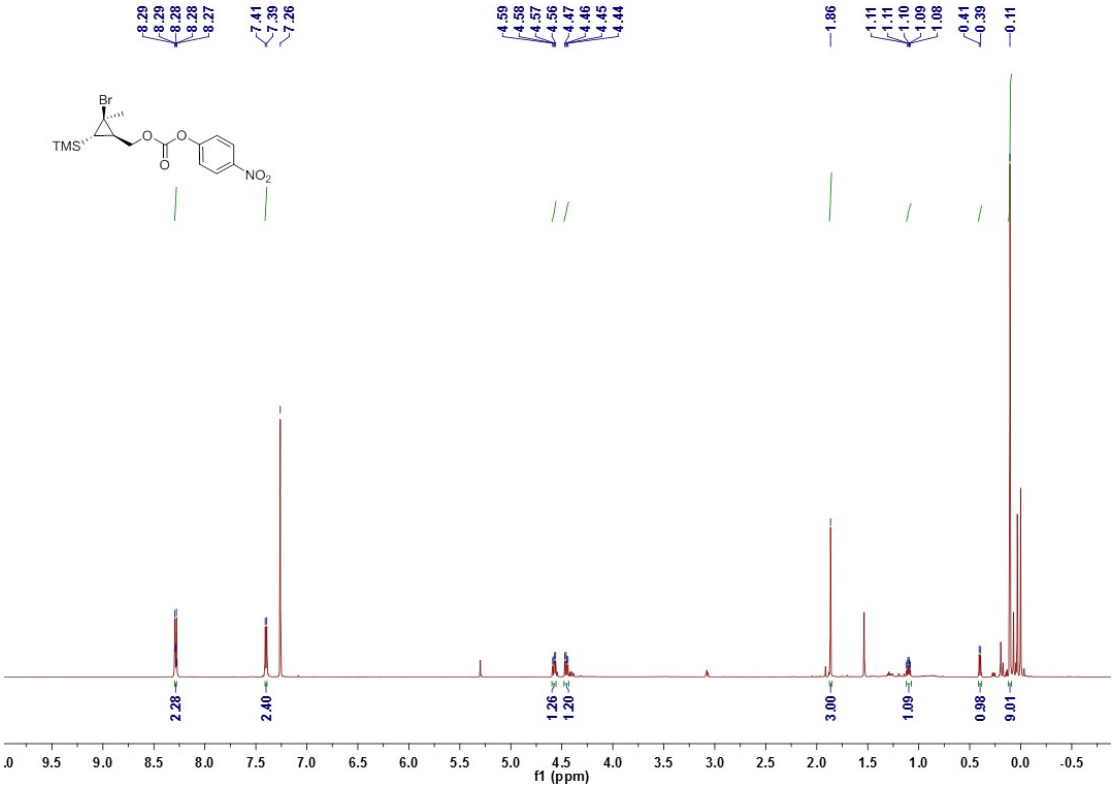
Compound 9b ^{1}H NMR



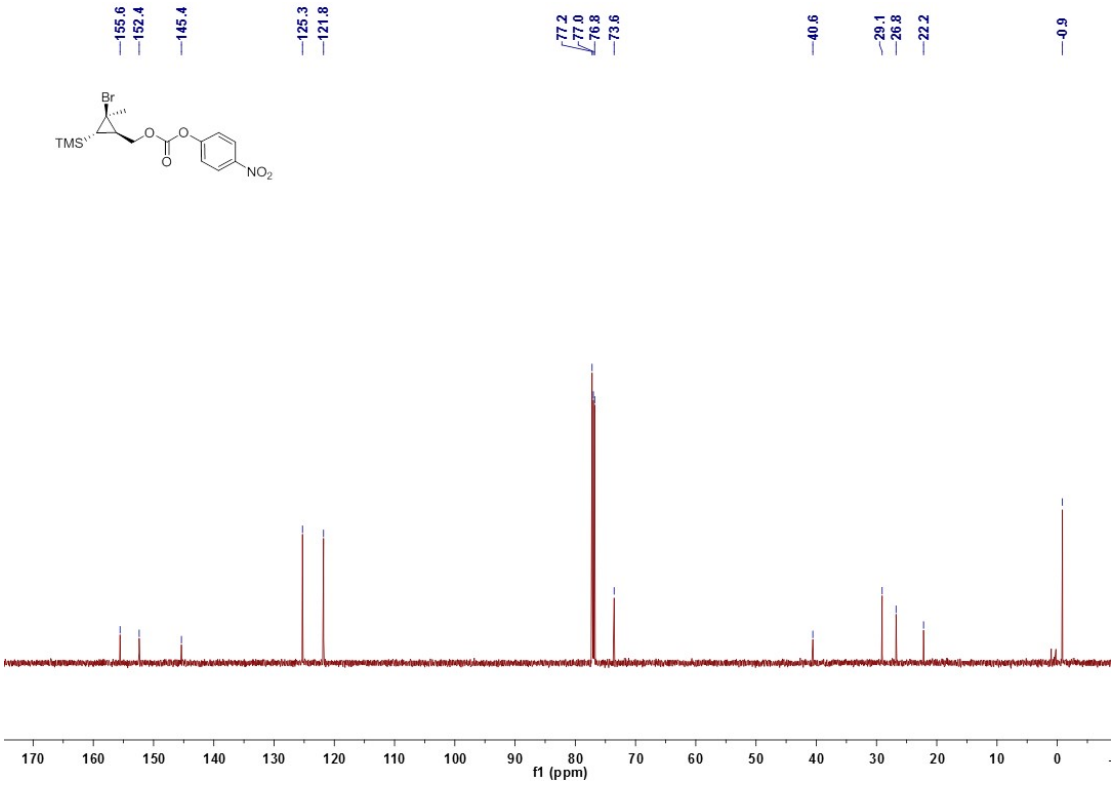
Compound 9b ^{13}C NMR



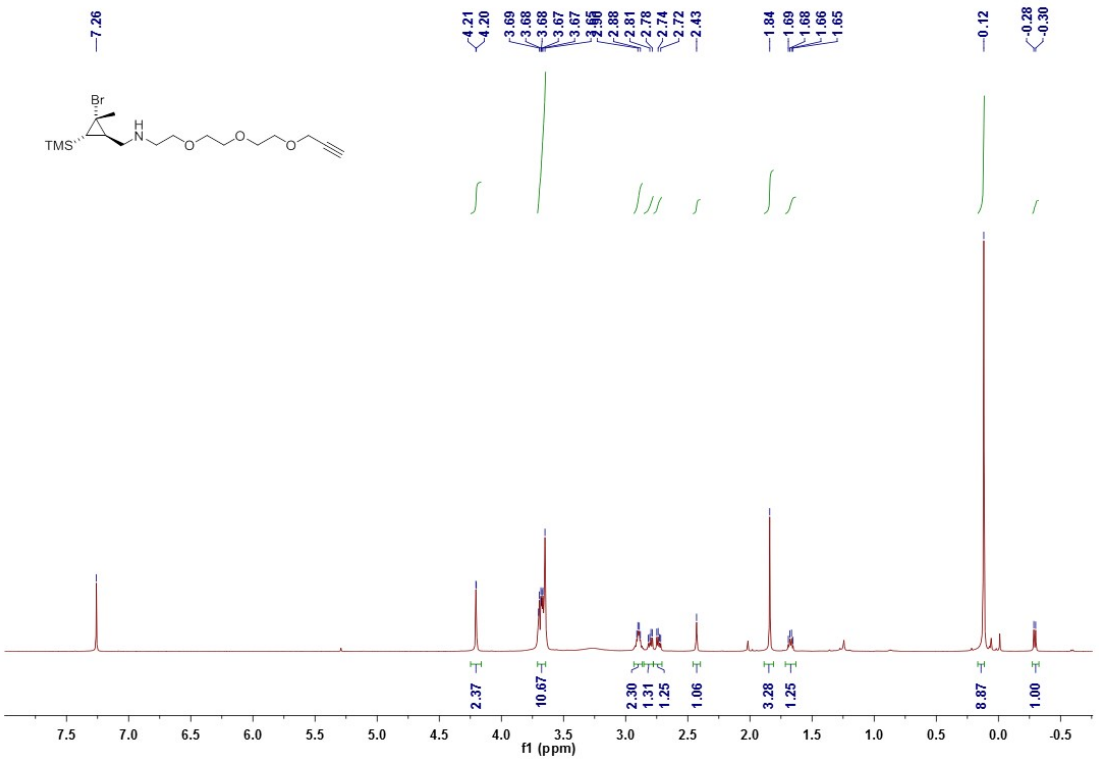
Compound 10 ^{1}H NMR



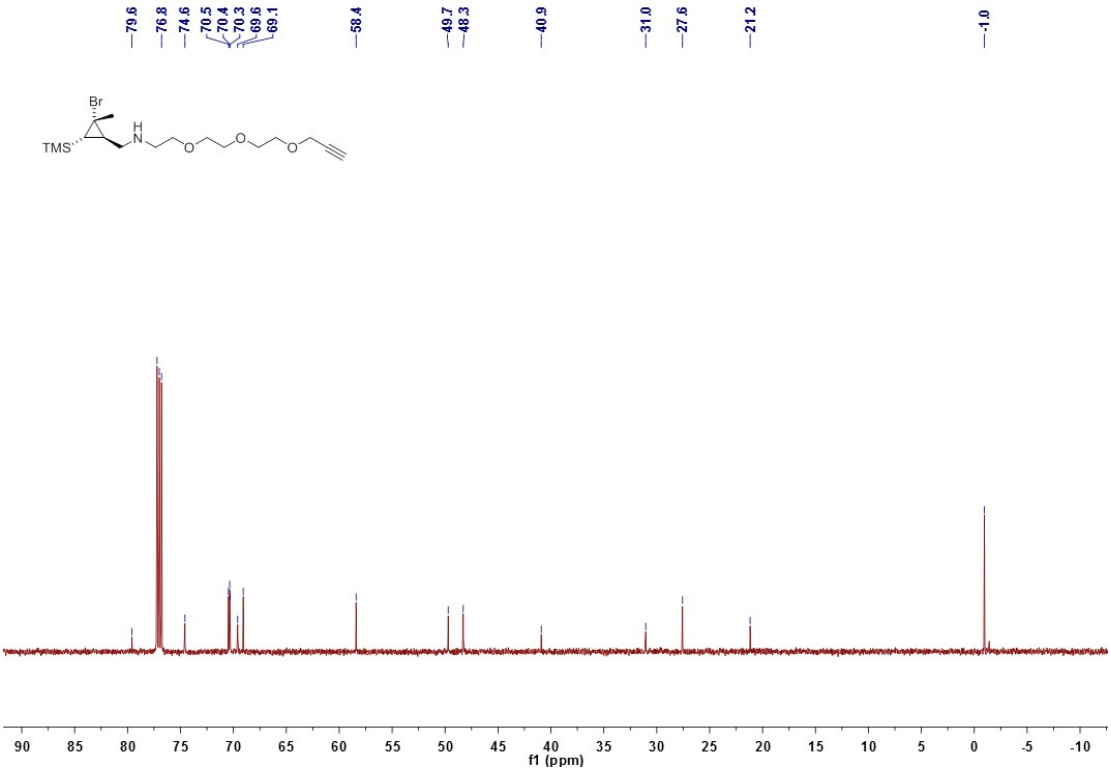
Compound 10 ^{13}C NMR



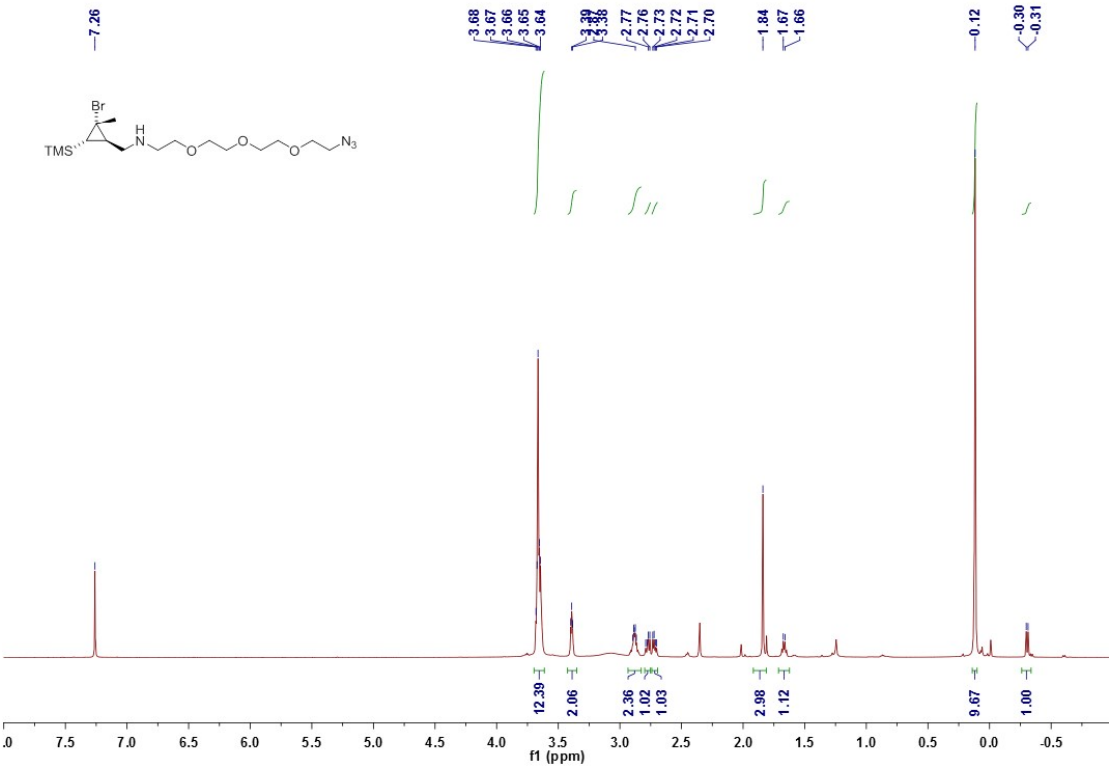
Compound 14 ^{1}H NMR



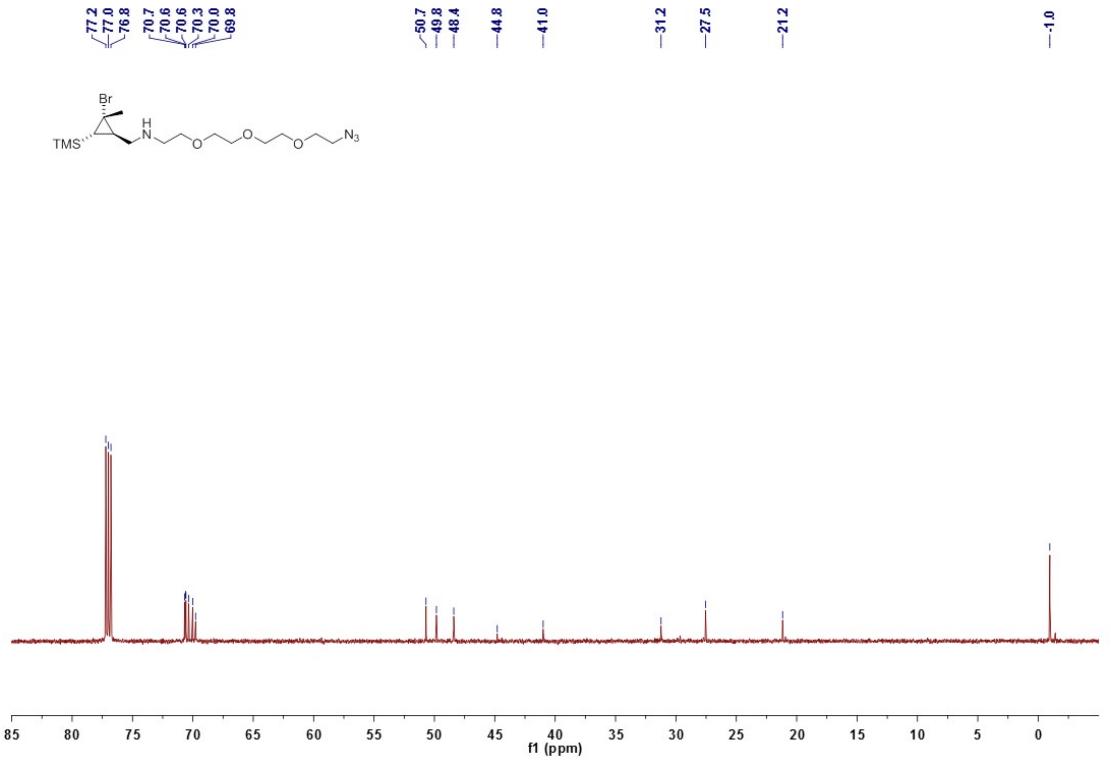
Compound 14 ^{13}C NMR



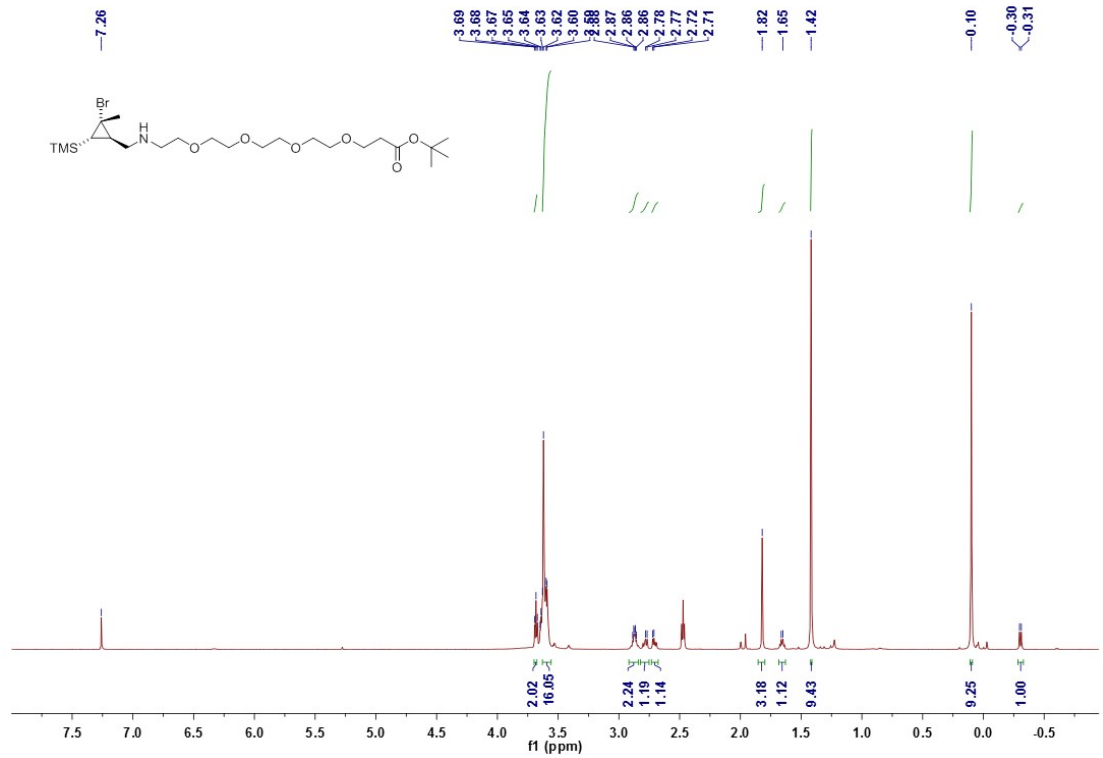
Compound 17 ^{1}H NMR



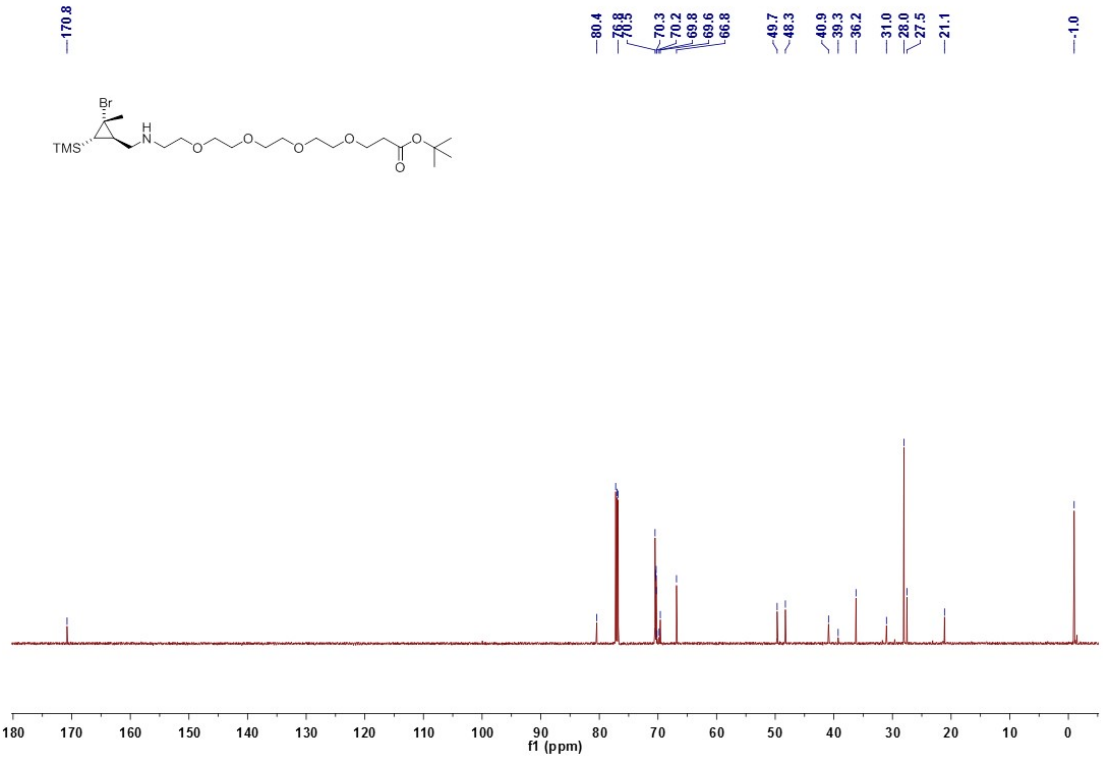
Compound 17 ^{13}C NMR



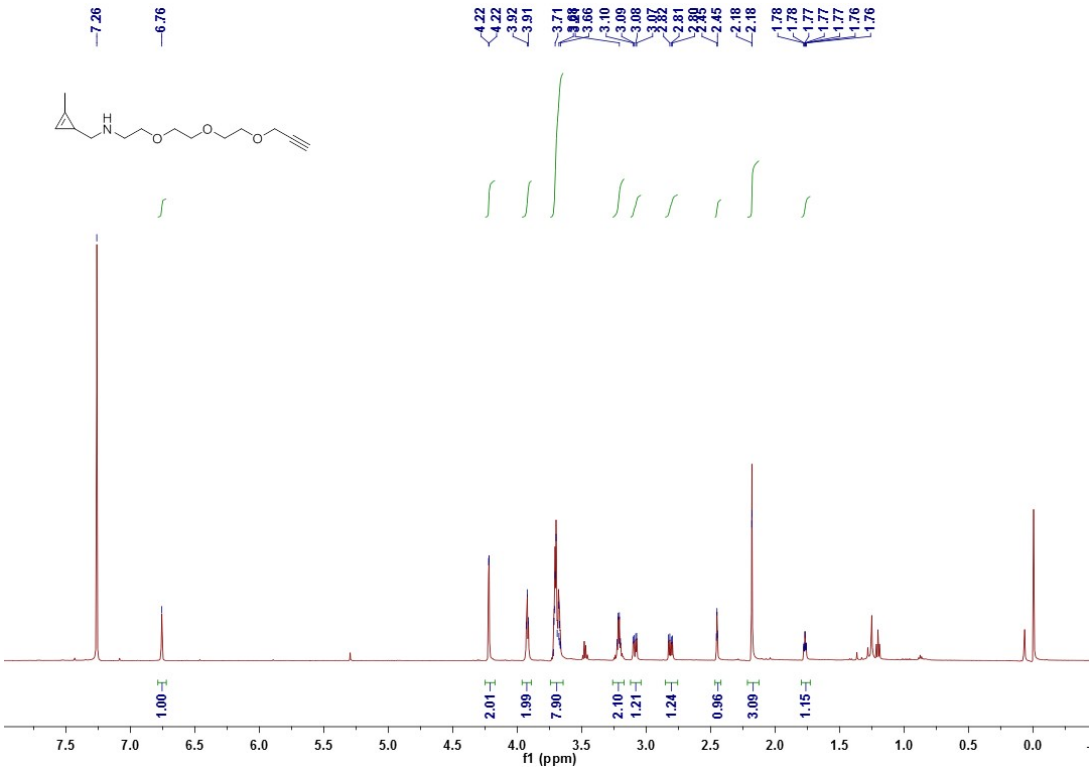
Compound 20 ^{1}H NMR



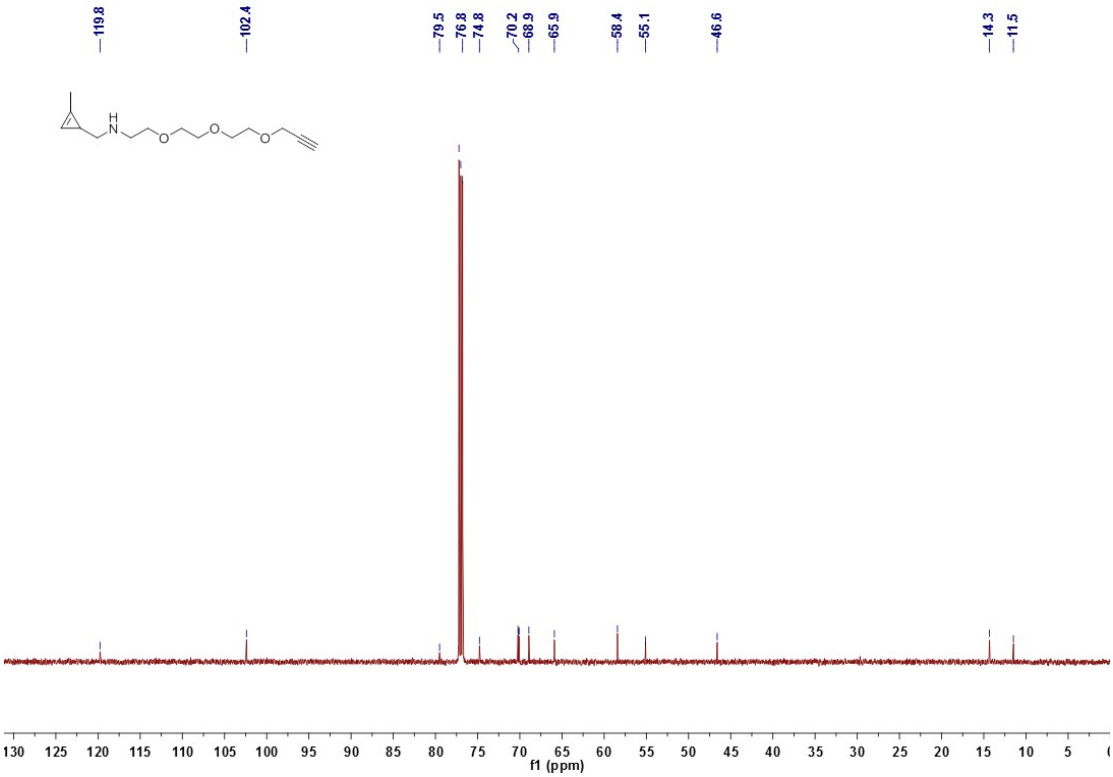
Compound 20 ^{13}C NMR



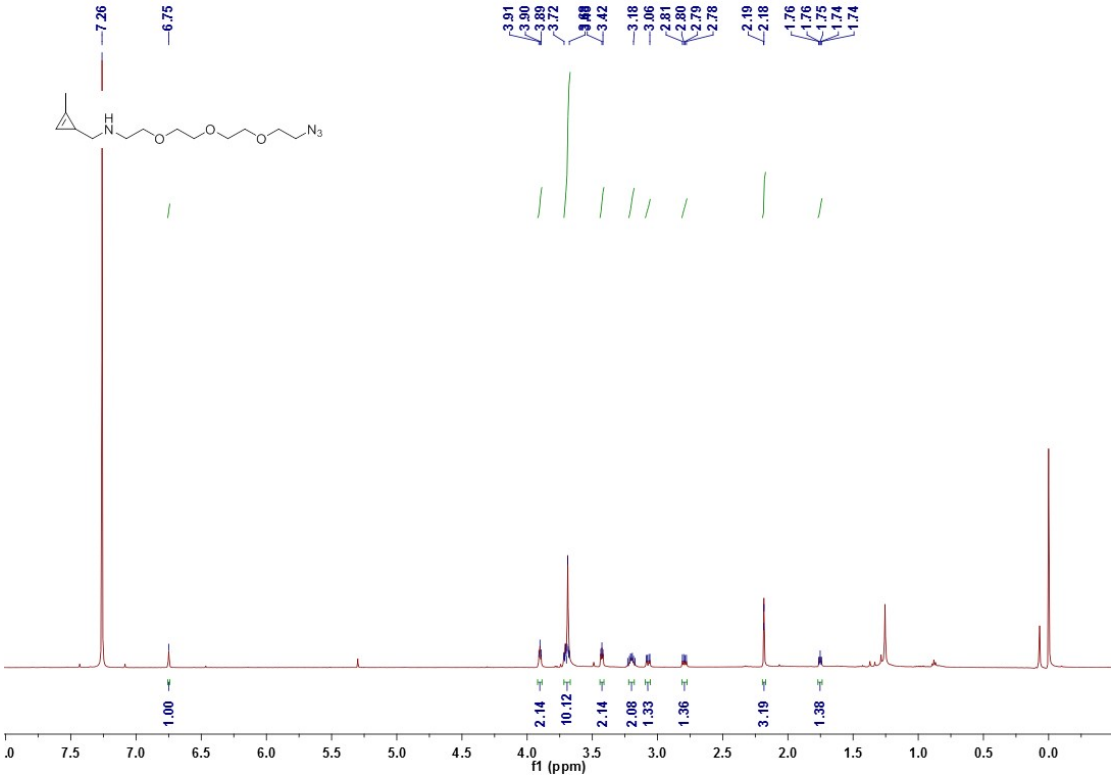
Compound 15 ^{1}H NMR



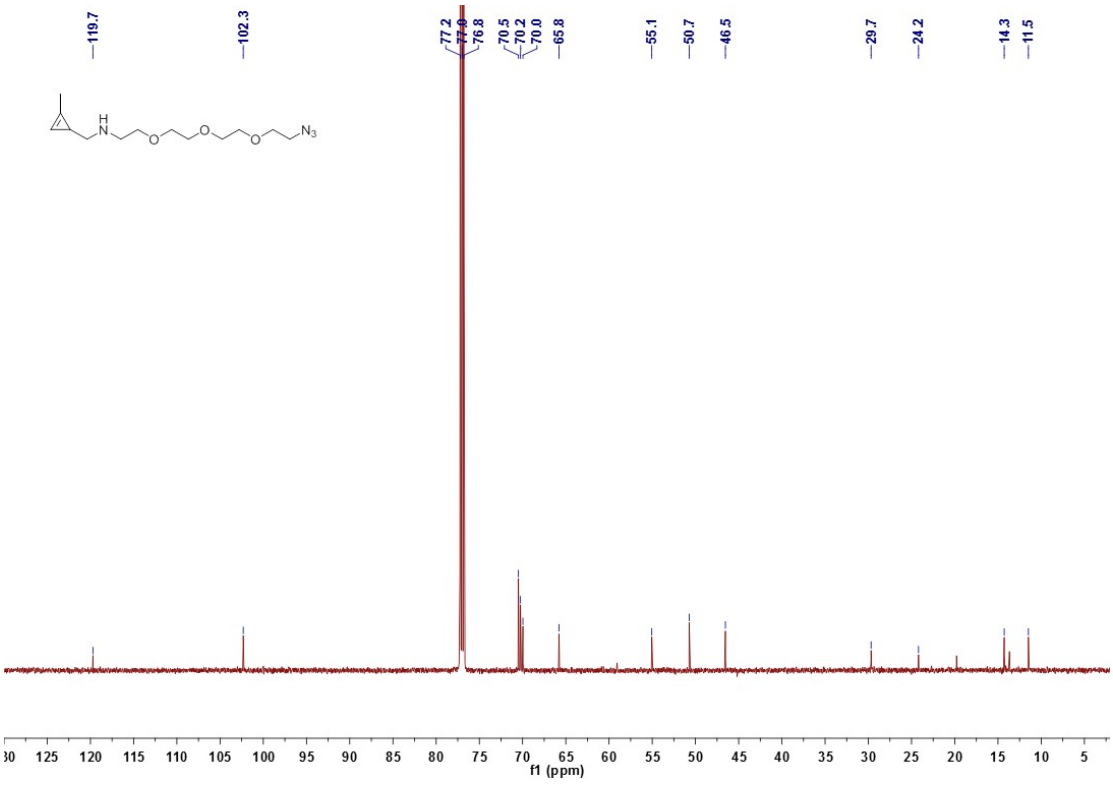
Compound 15 ^{13}C NMR



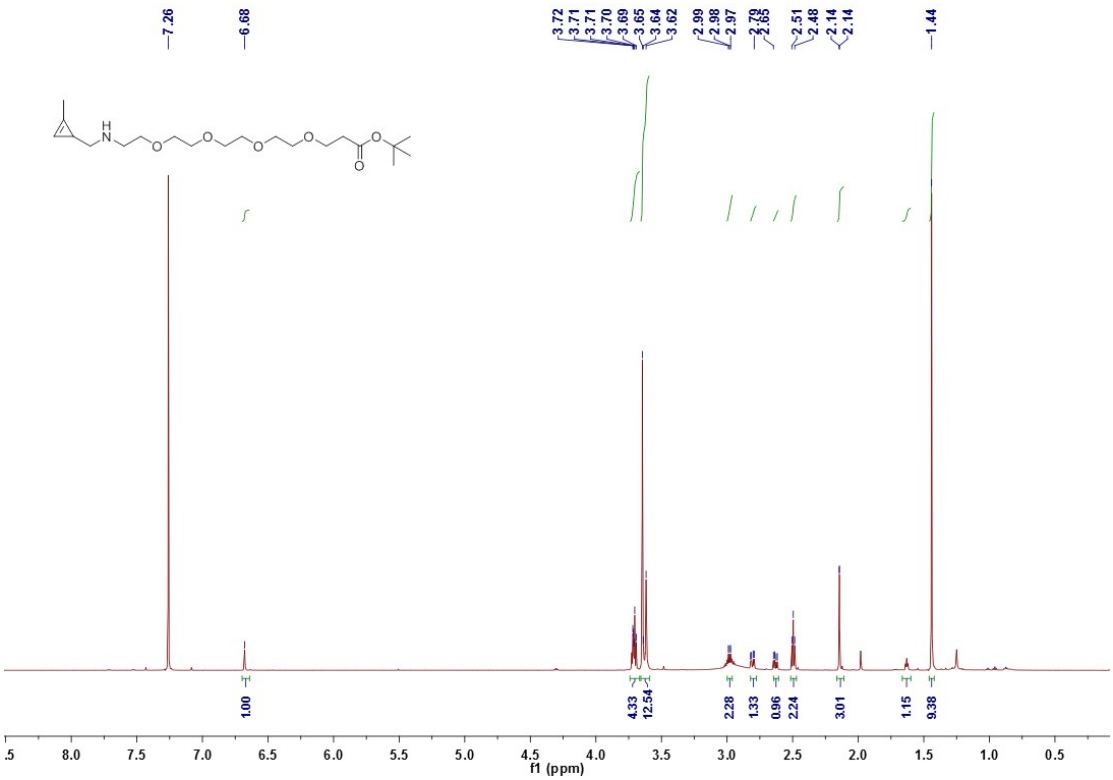
Compound 18 ^{1}H NMR



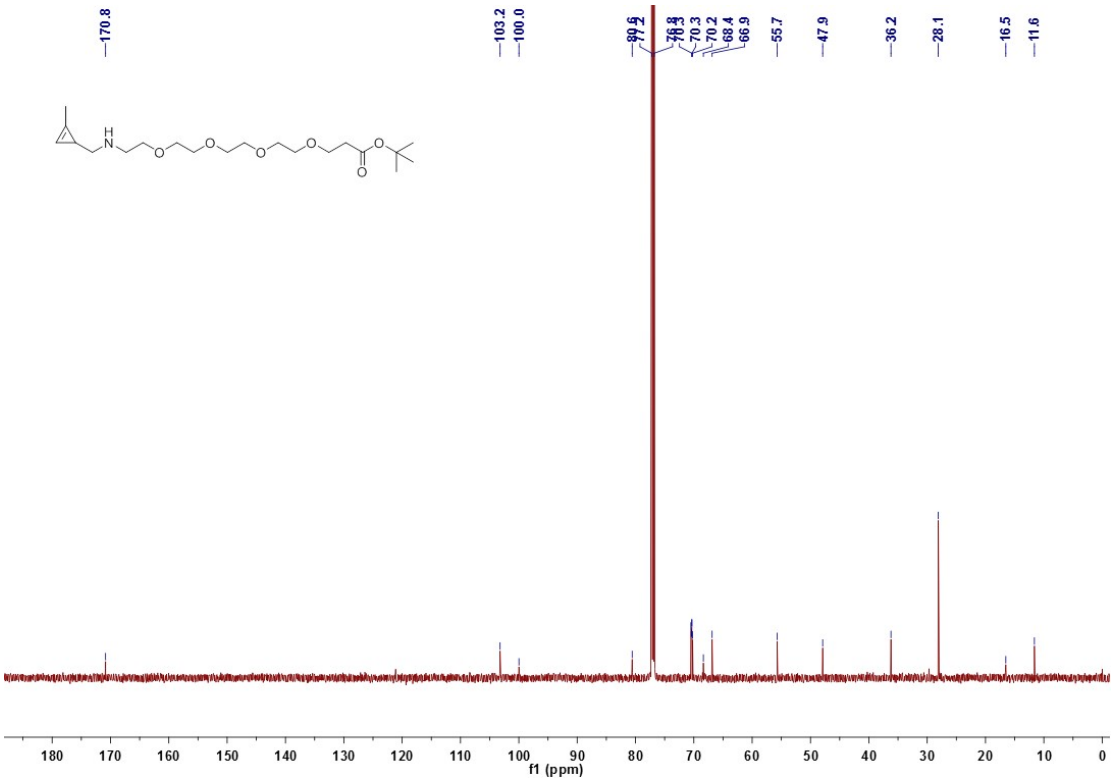
Compound 18 ^{13}C NMR



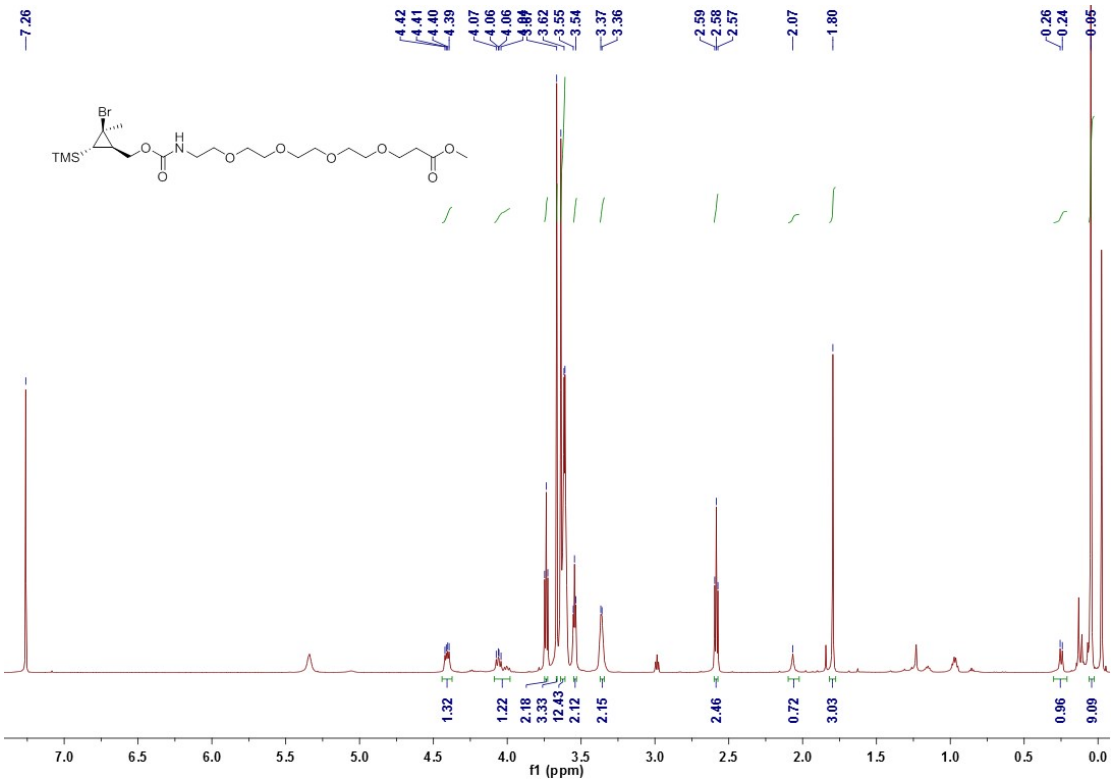
Compound 21 ^{1}H NMR



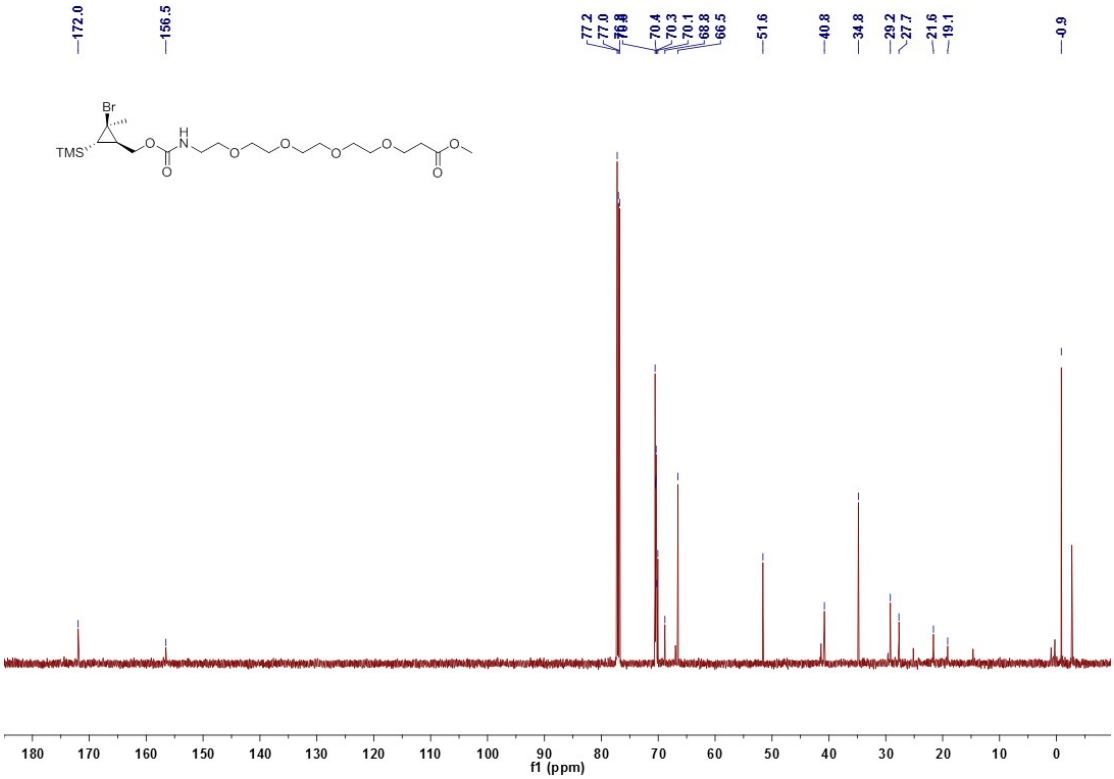
Compound 21 ^{13}C NMR



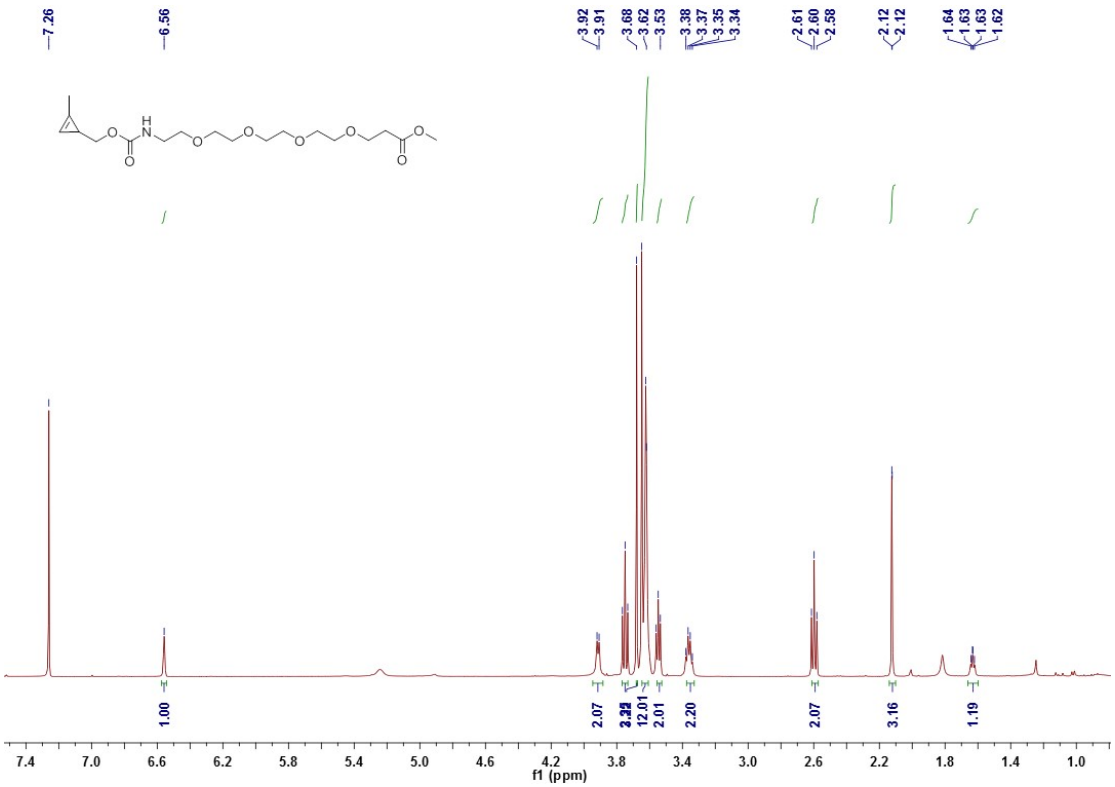
Compound 23 ^{1}H NMR



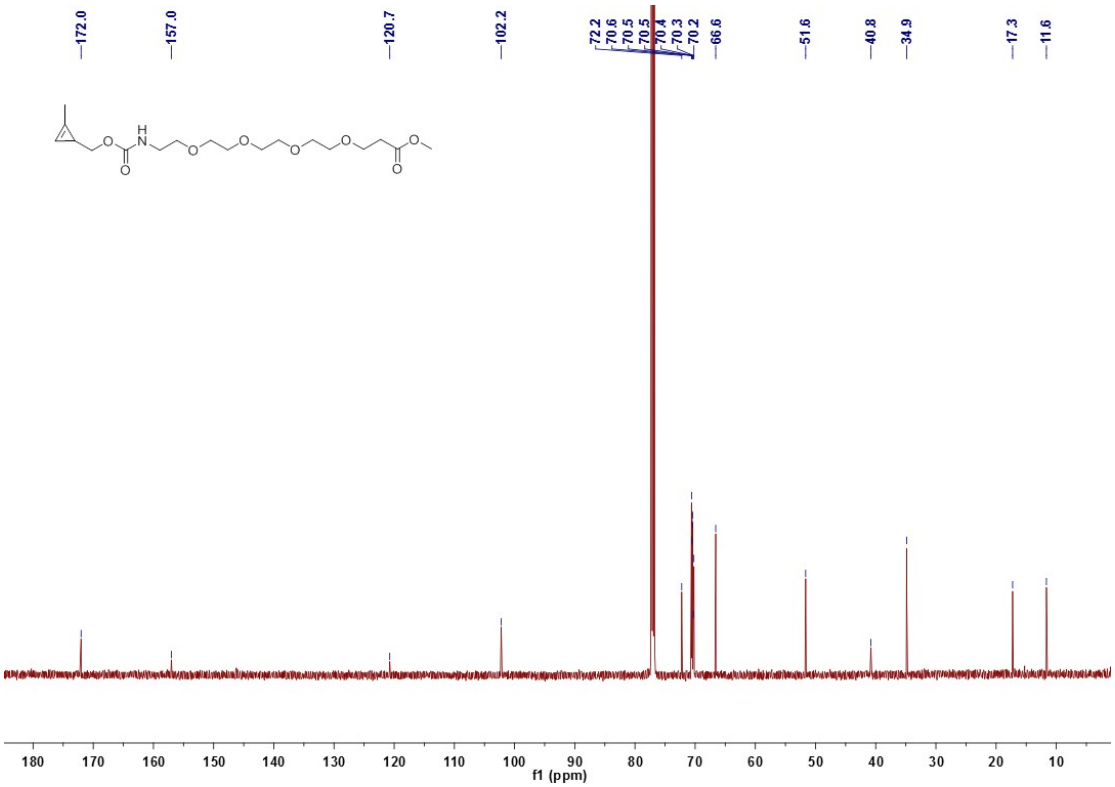
Compound 23 ^{13}C NMR



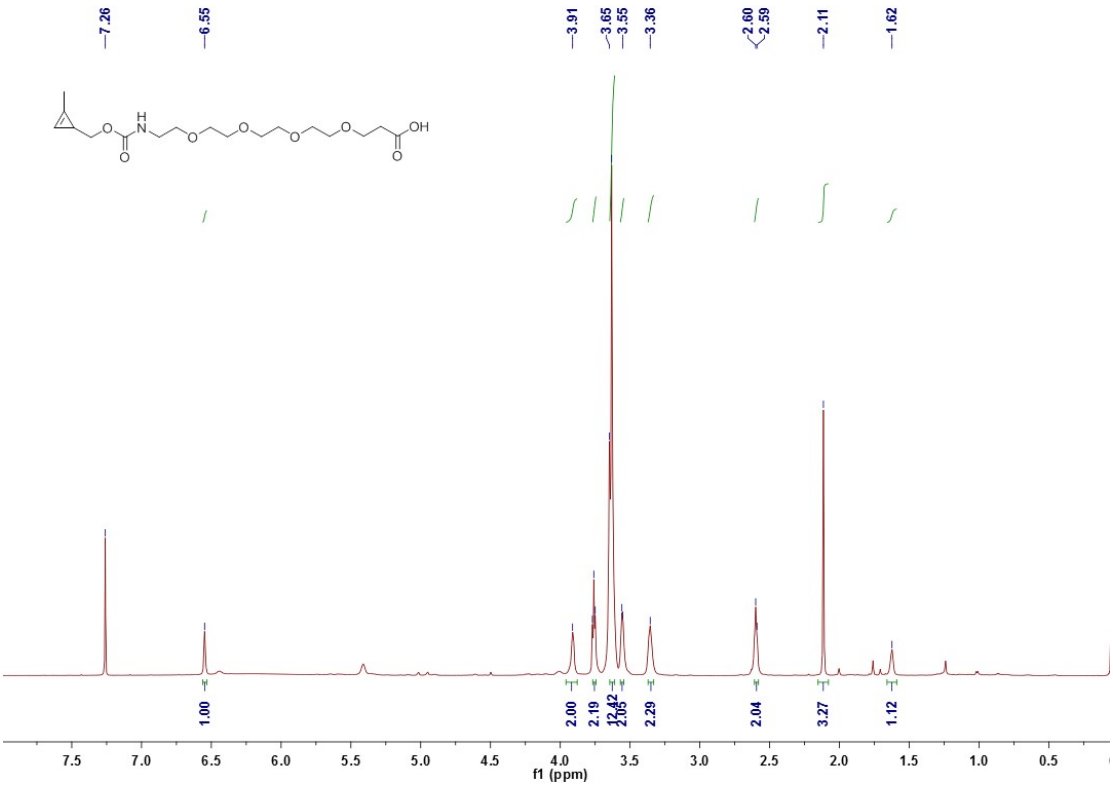
Compound 24 ^{1}H NMR



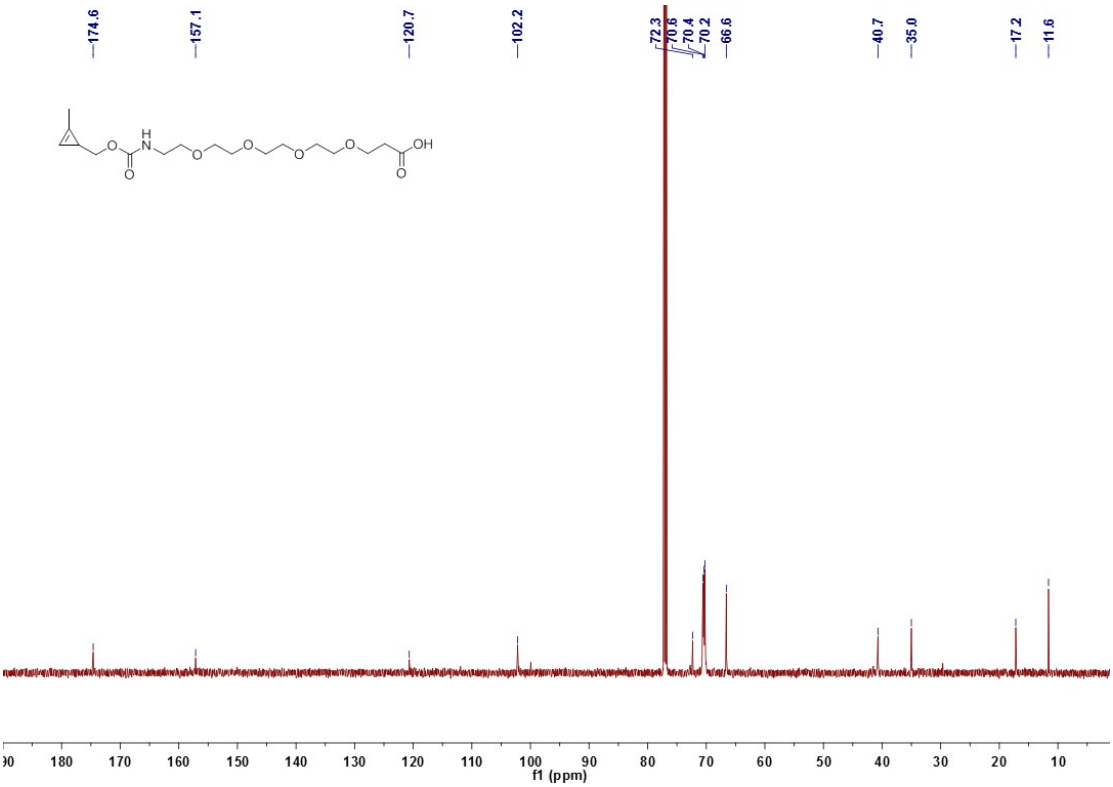
Compound 24 ^{13}C NMR



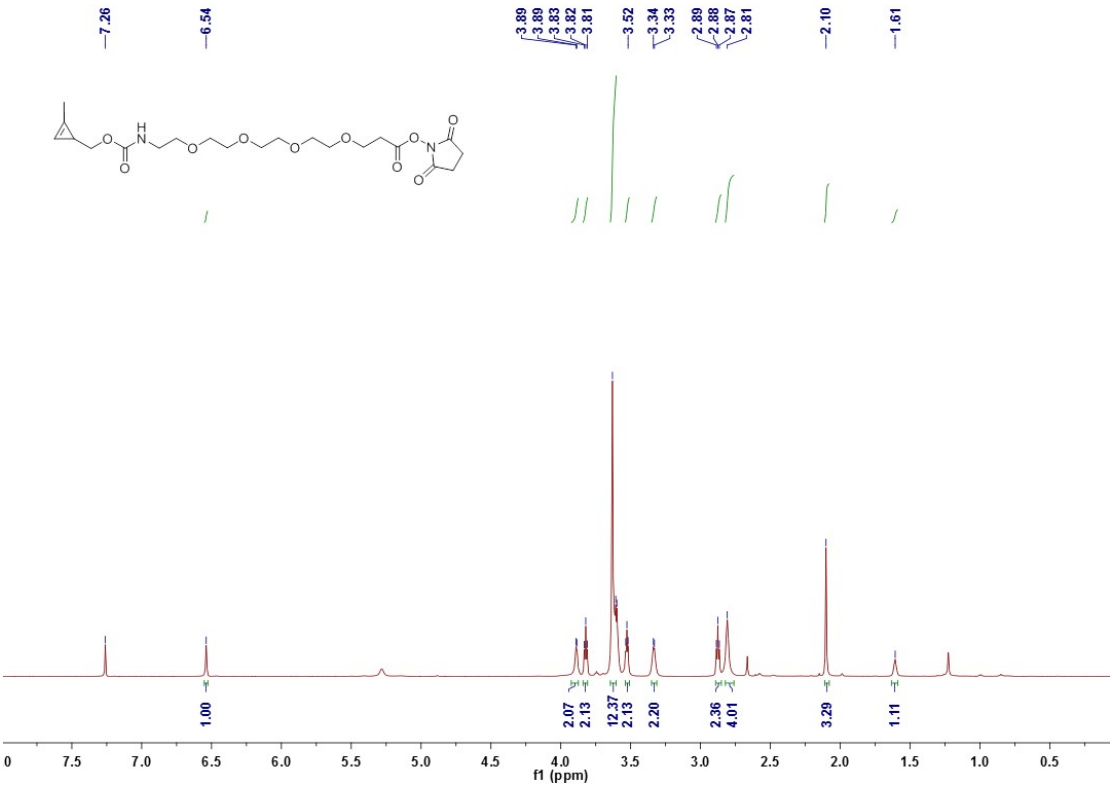
Compound 25 ^{1}H NMR



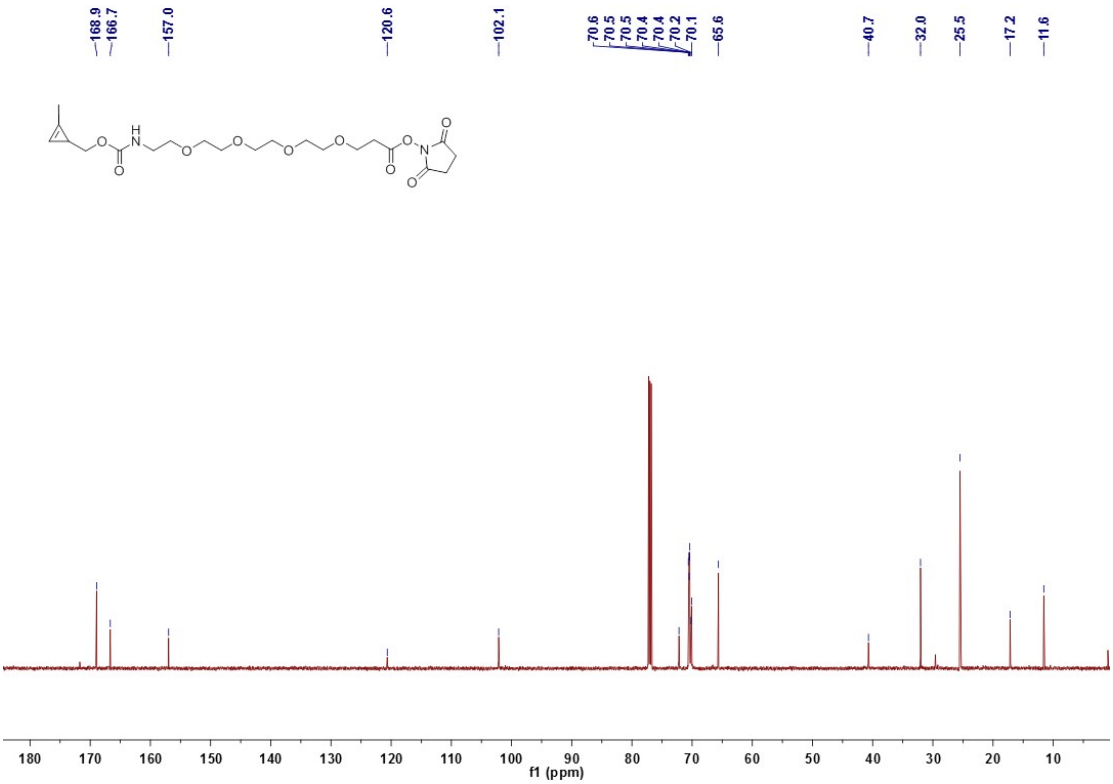
Compound 25 ^{13}C NMR



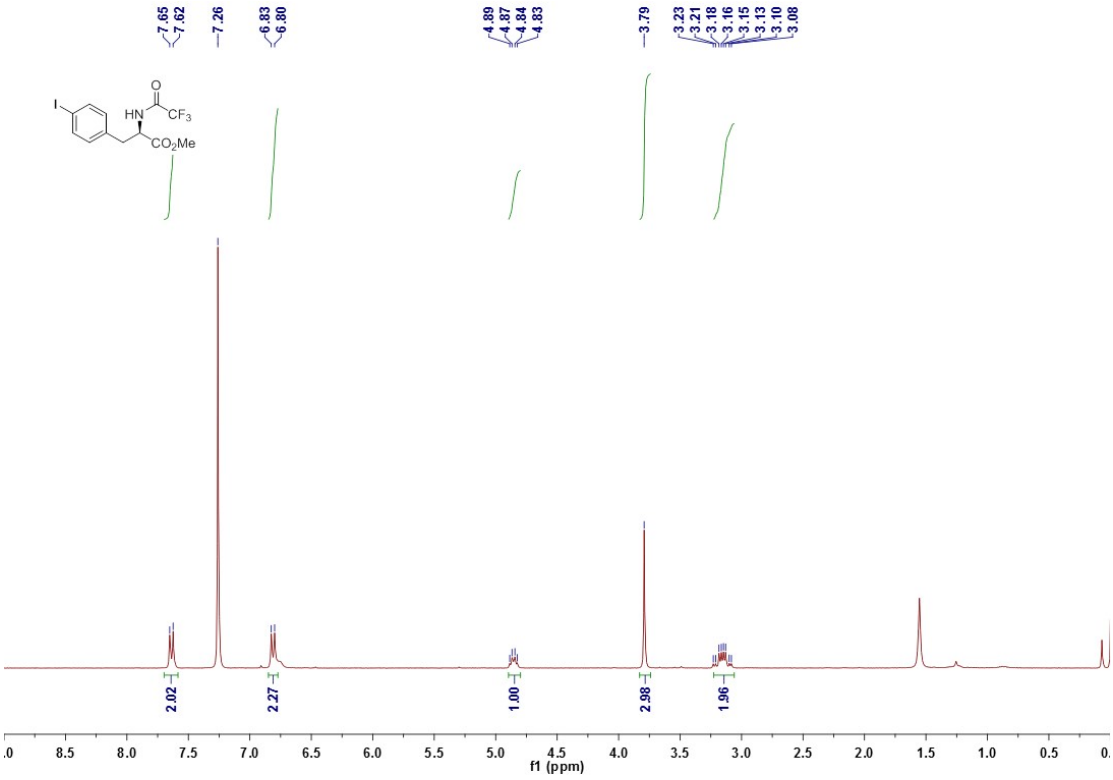
Compound 26 ^{1}H NMR



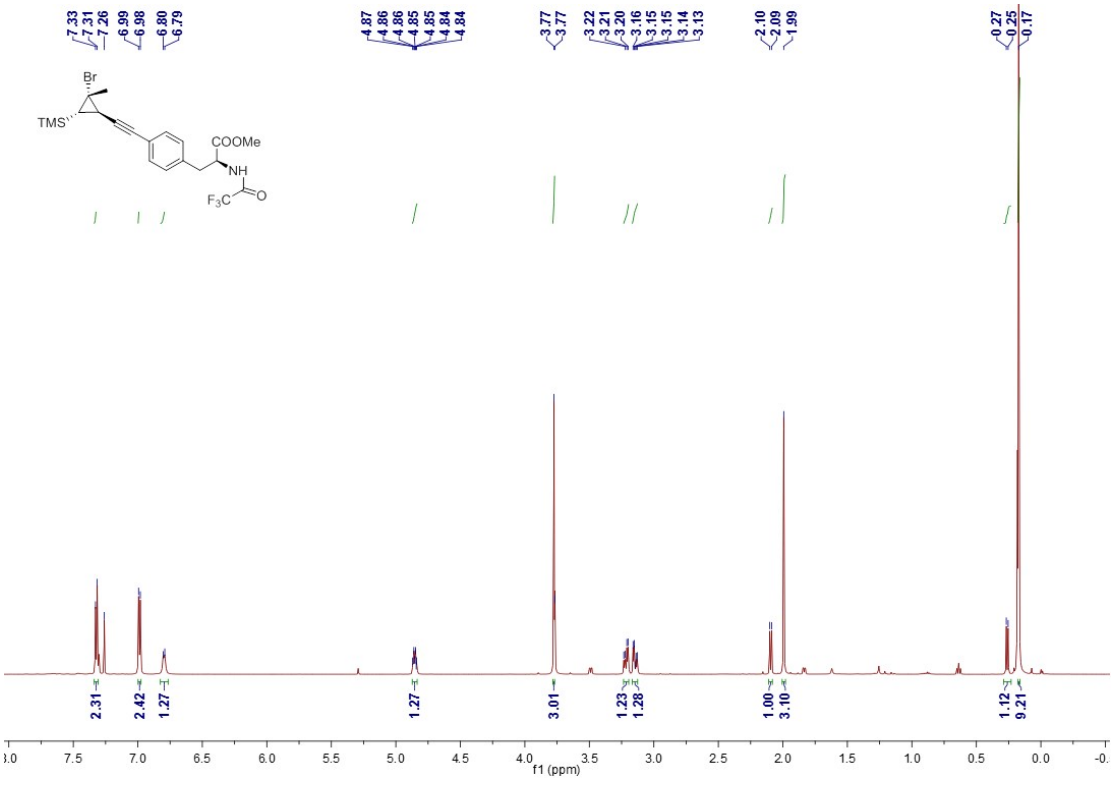
Compound 26 ^{13}C NMR



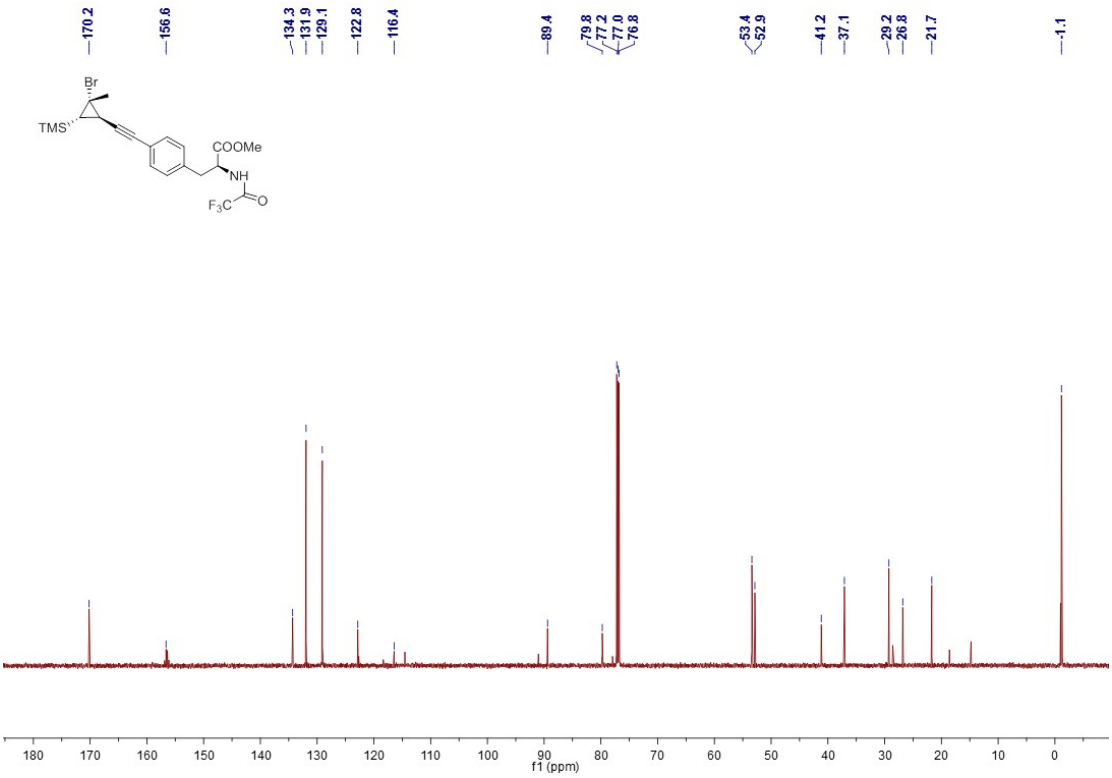
Compound 35 ^{1}H NMR



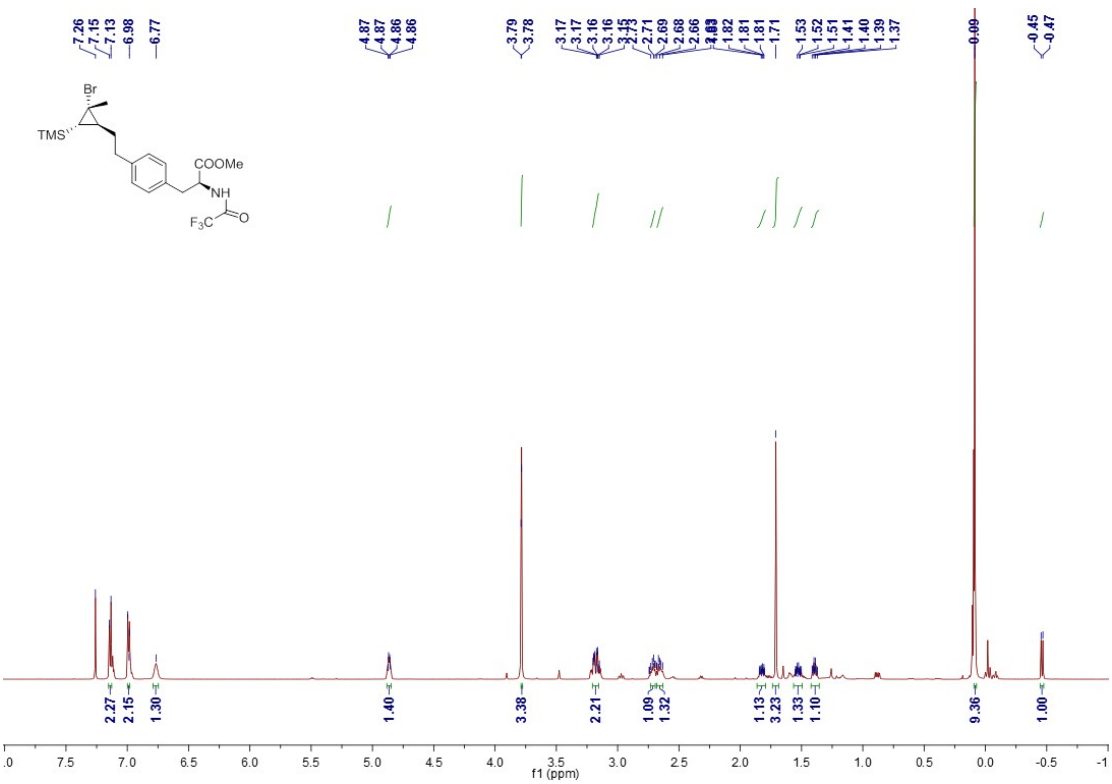
Compound 36 ^{1}H NMR



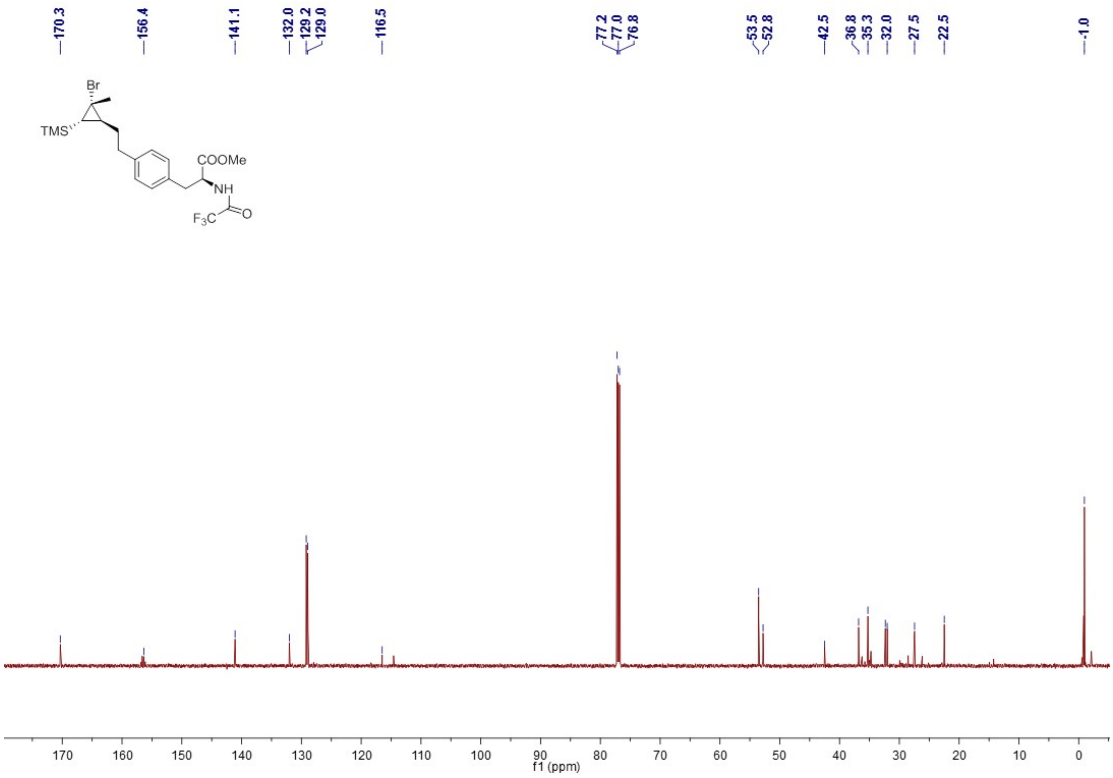
Compound 36 ^{13}C NMR



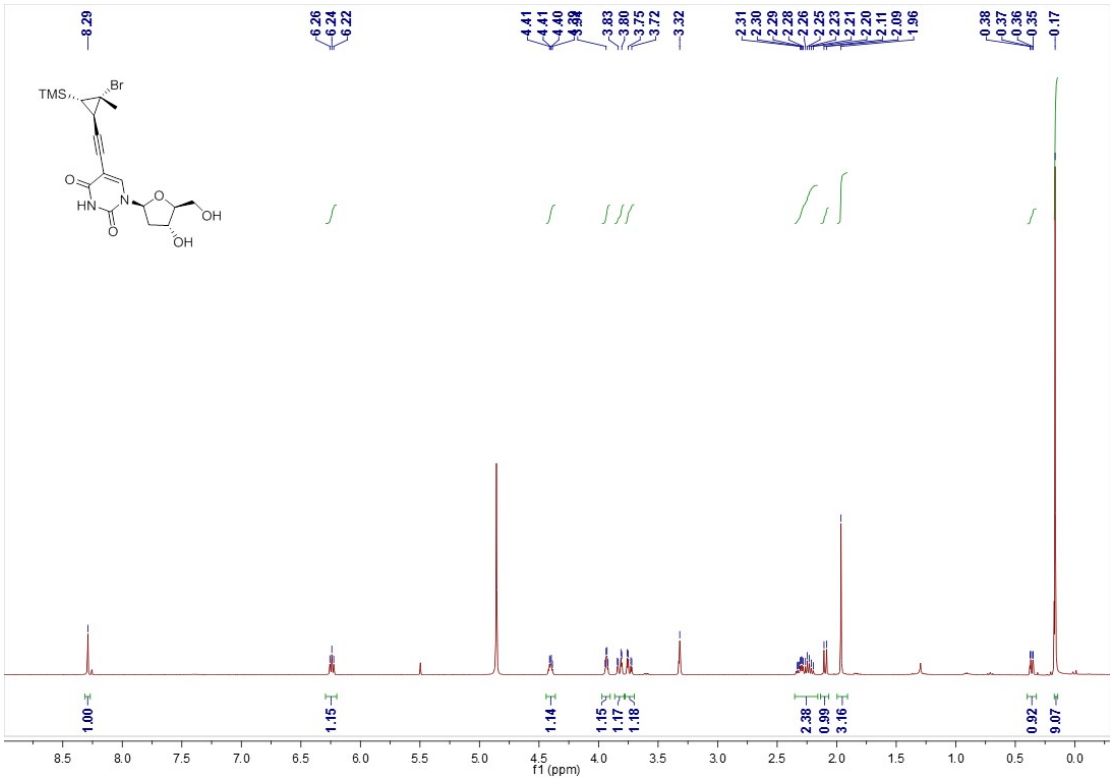
Compound 37 ^{1}H NMR



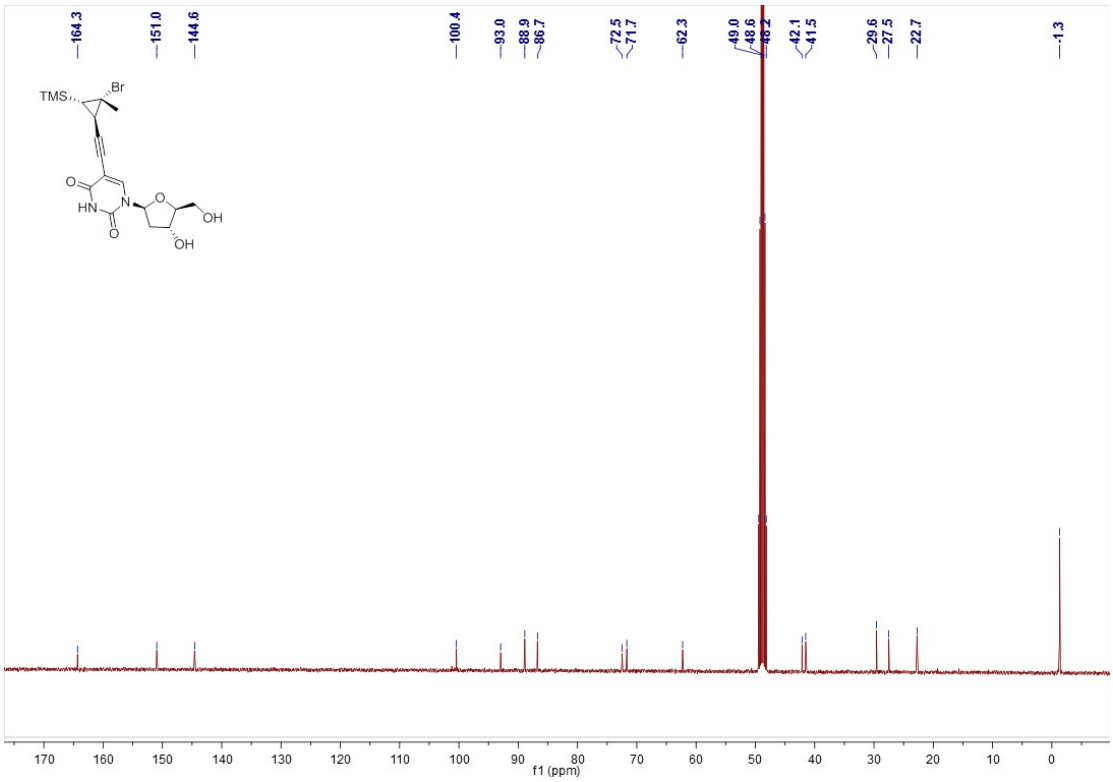
Compound 37 ^{13}C NMR



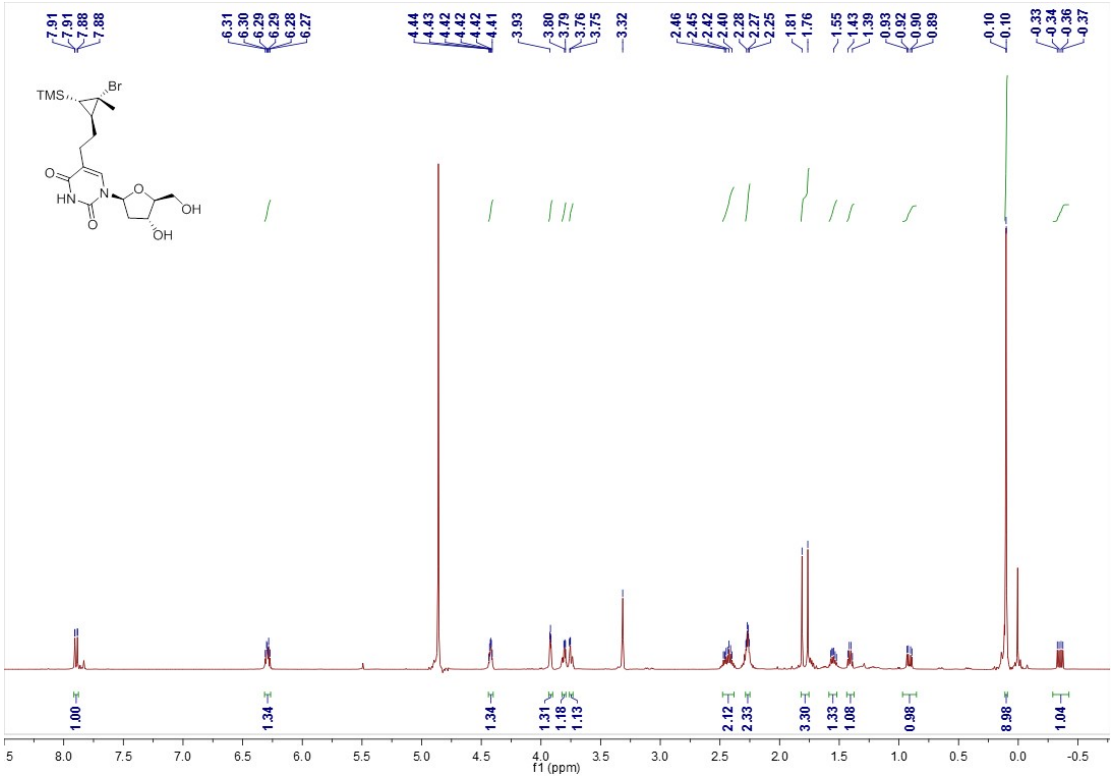
Compound 49 ^{1}H NMR



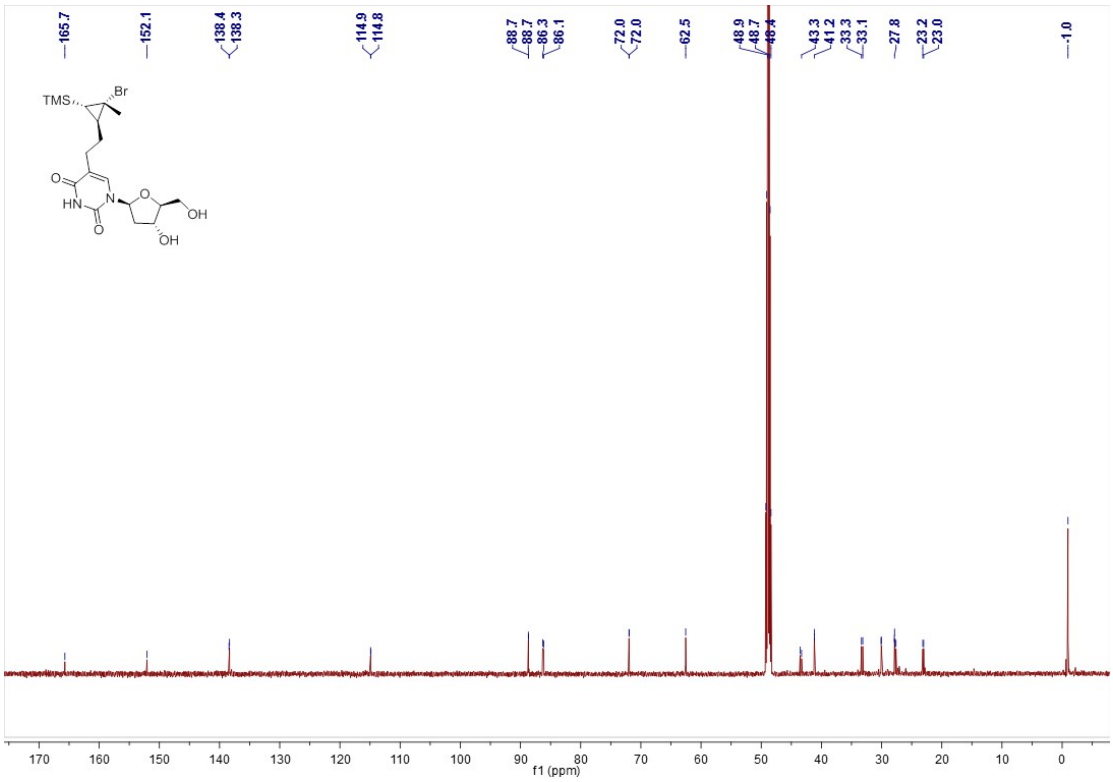
Compound 49 ^{13}C NMR



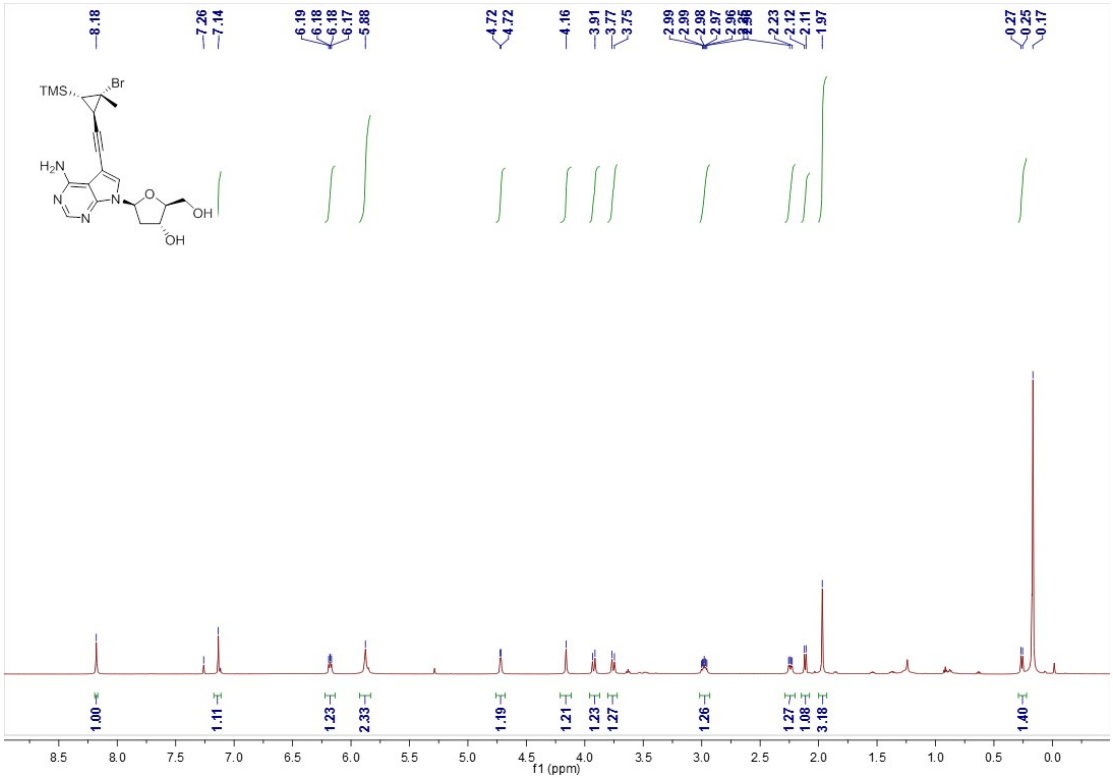
Compound 51 ^{1}H NMR



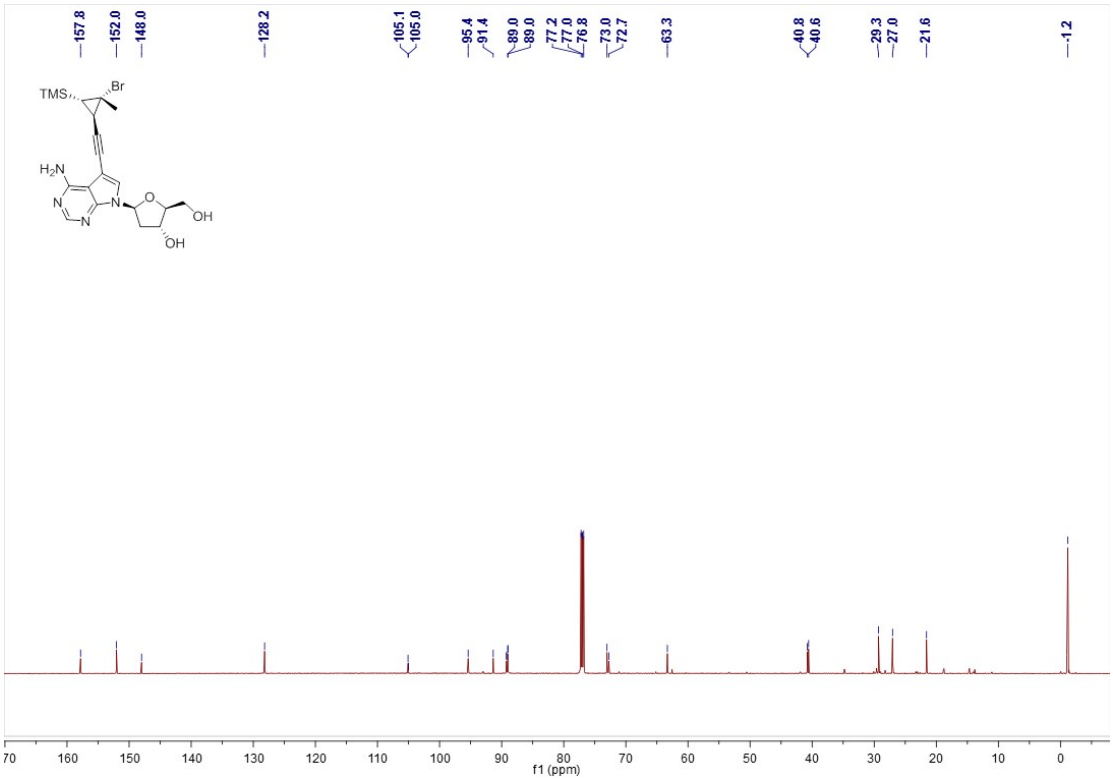
Compound 51 ^{13}C NMR



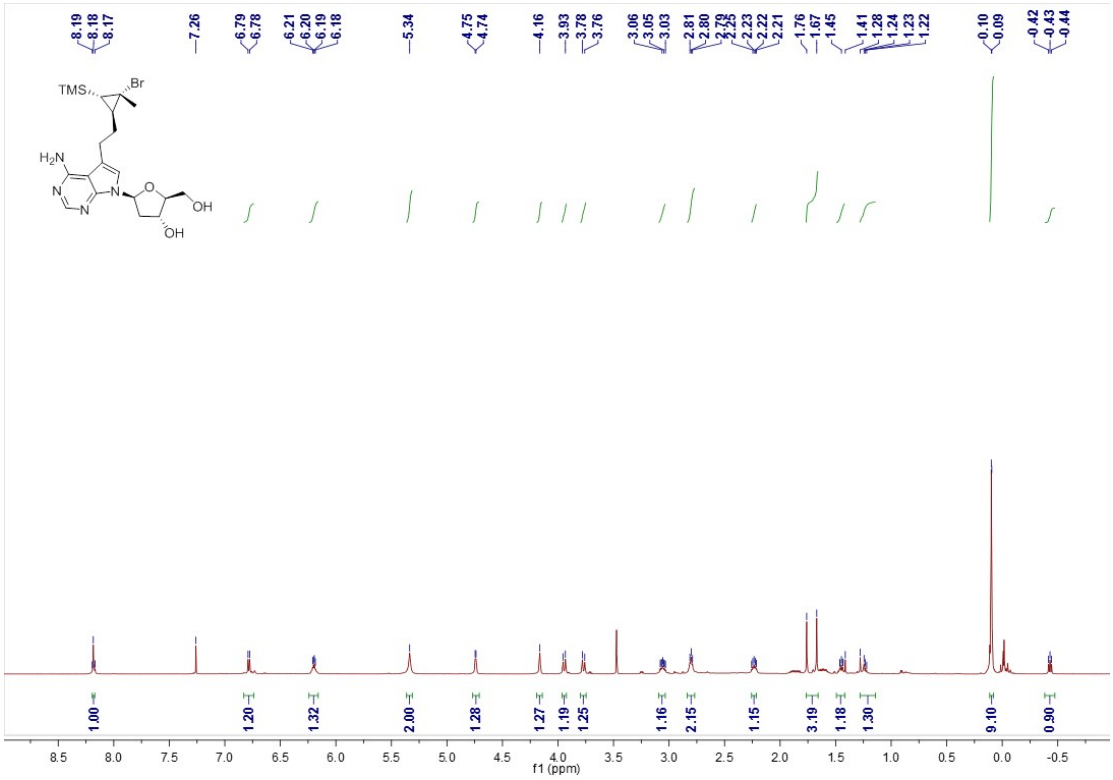
Compound 50 ^{1}H NMR



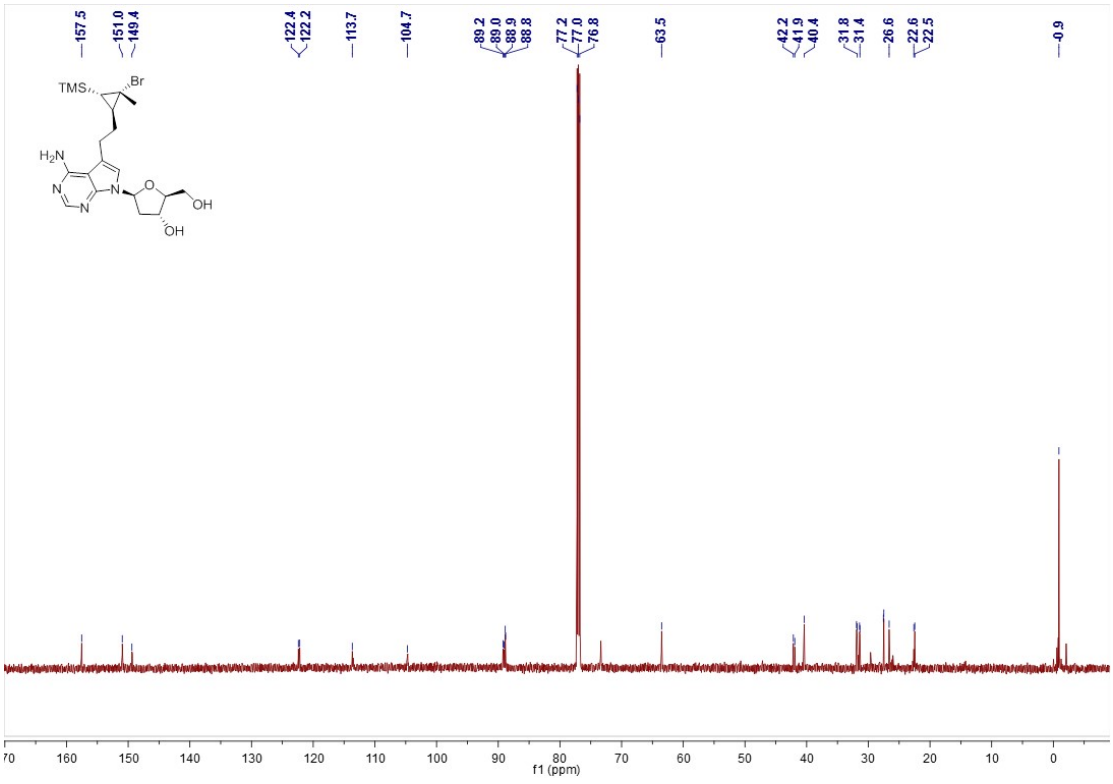
Compound 50 ^{13}C NMR



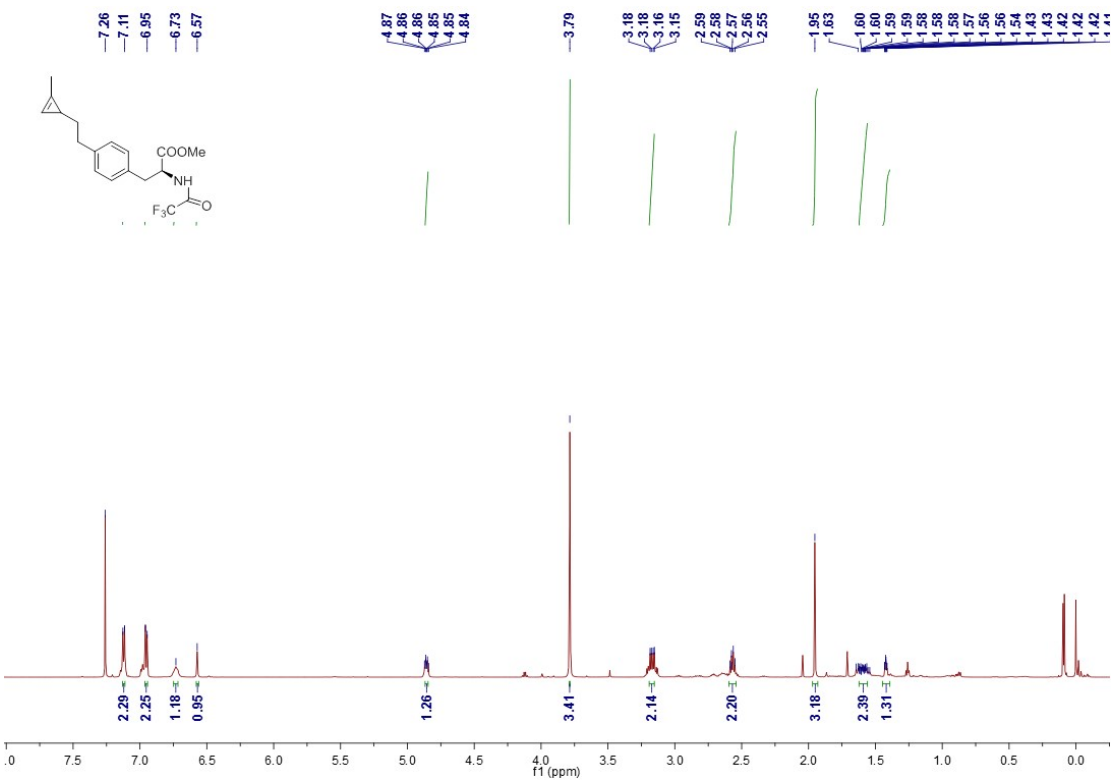
Compound 52 ^{1}H NMR



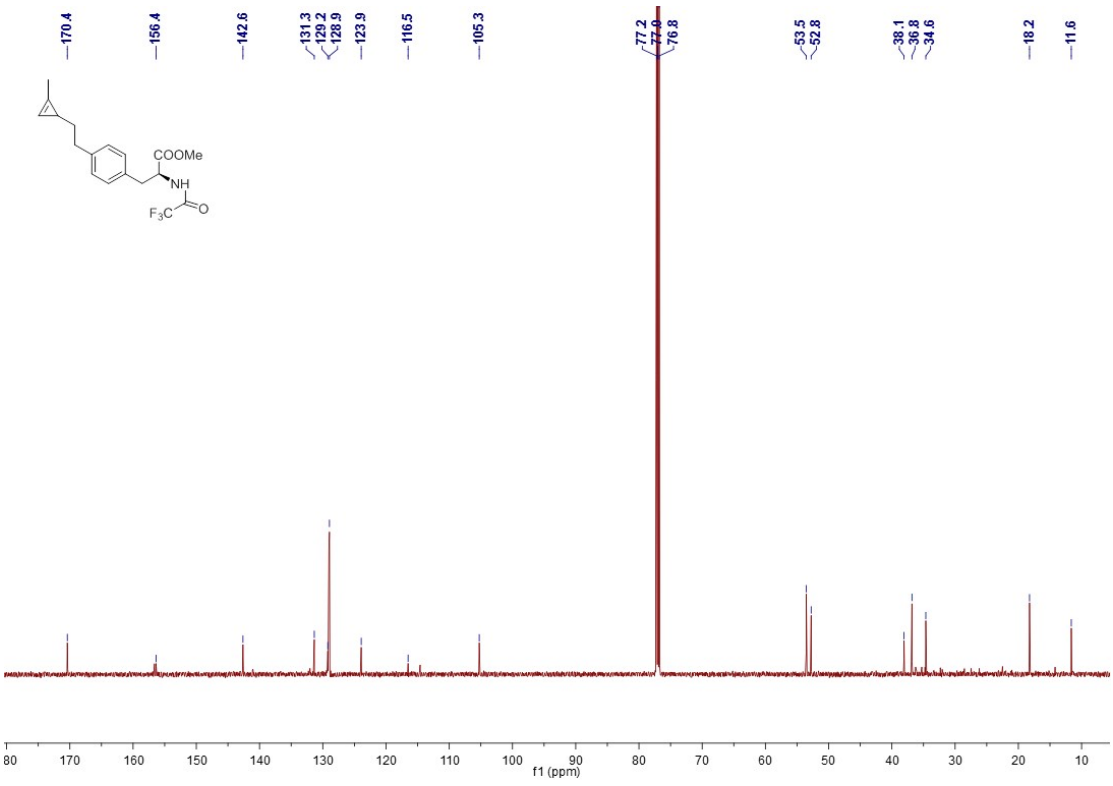
Compound 52 ^{13}C NMR



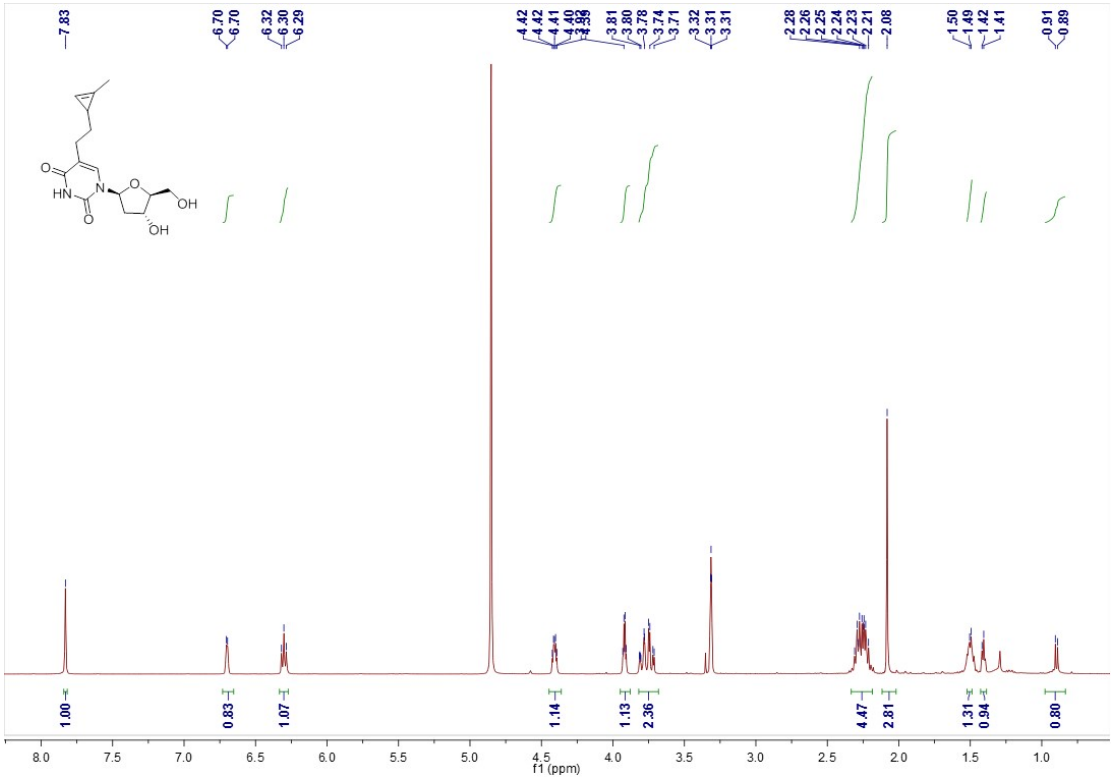
Compound 53 ^{1}H NMR



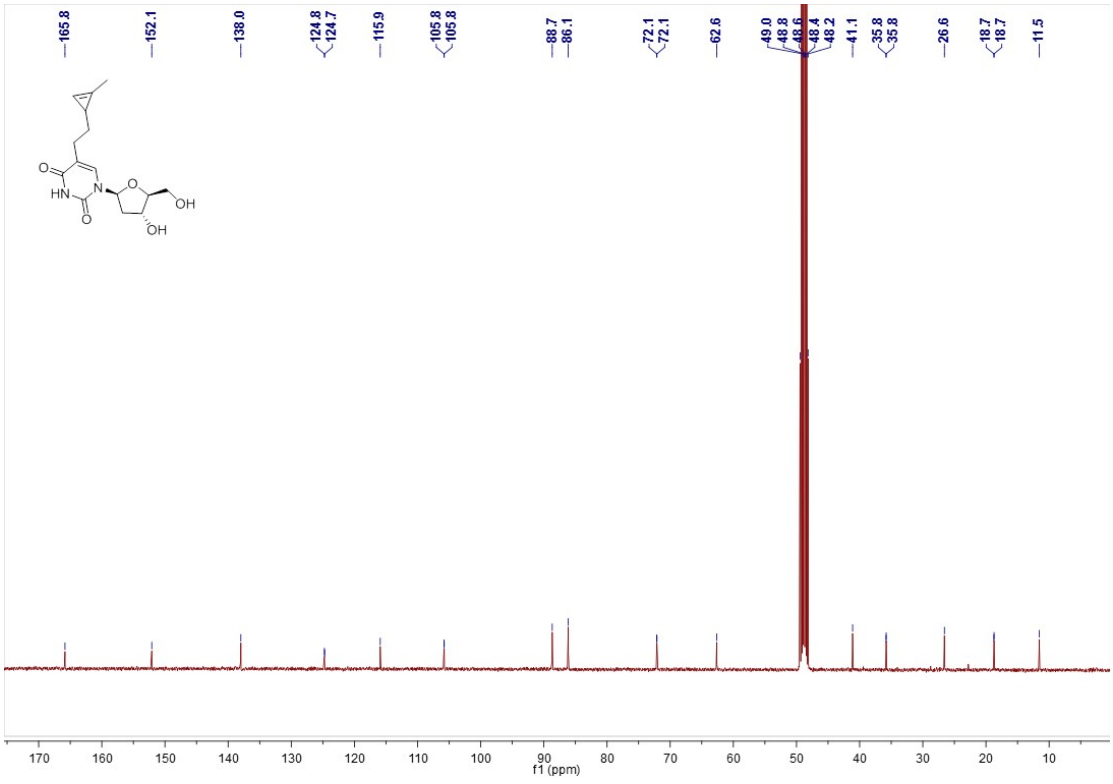
Compound 53 ^{13}C NMR



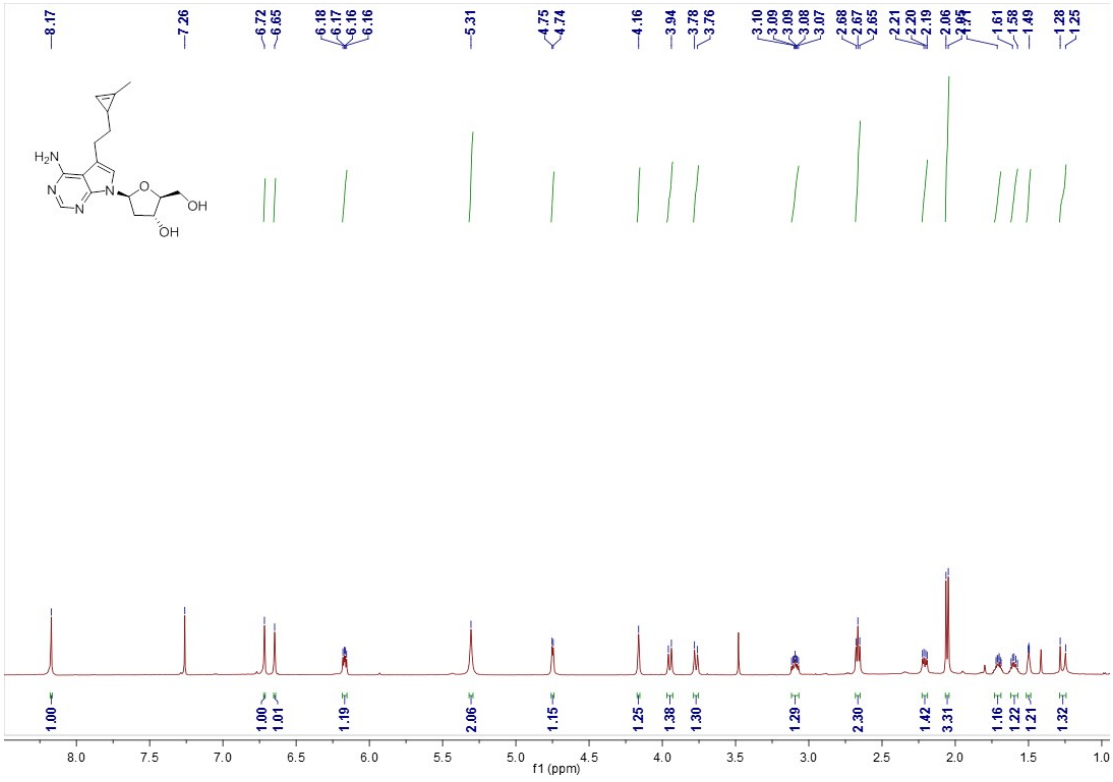
Compound 40 ^{1}H NMR



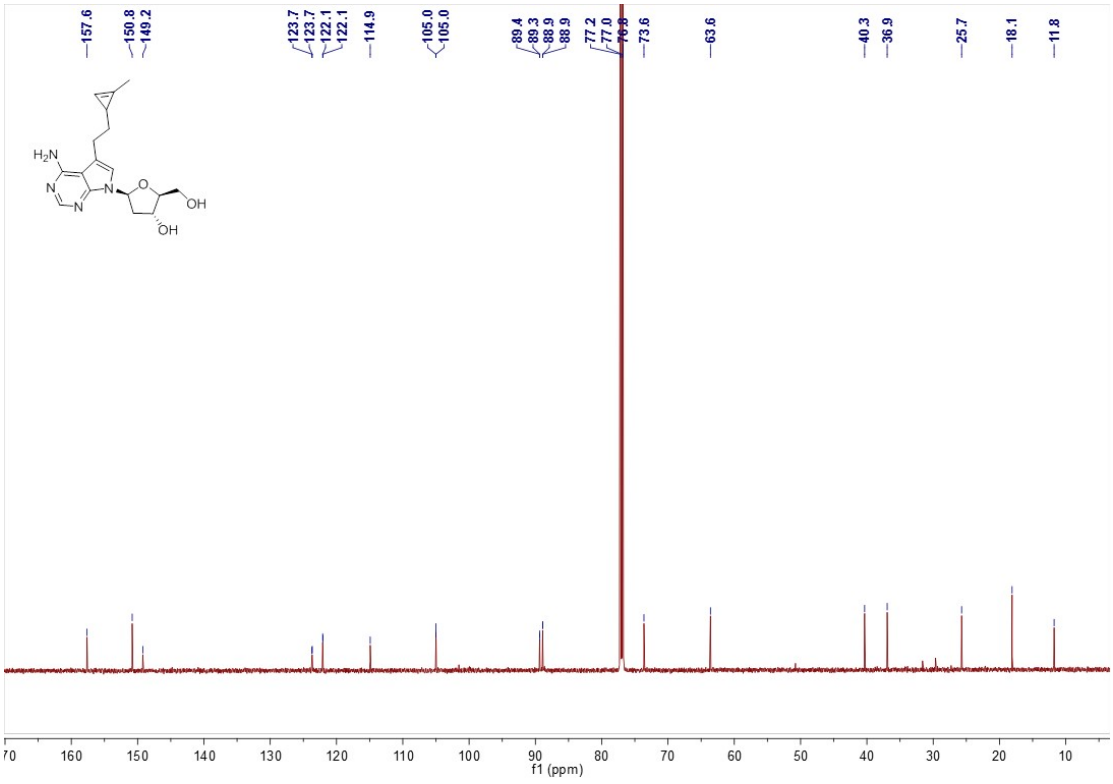
Compound 40 ^{13}C NMR



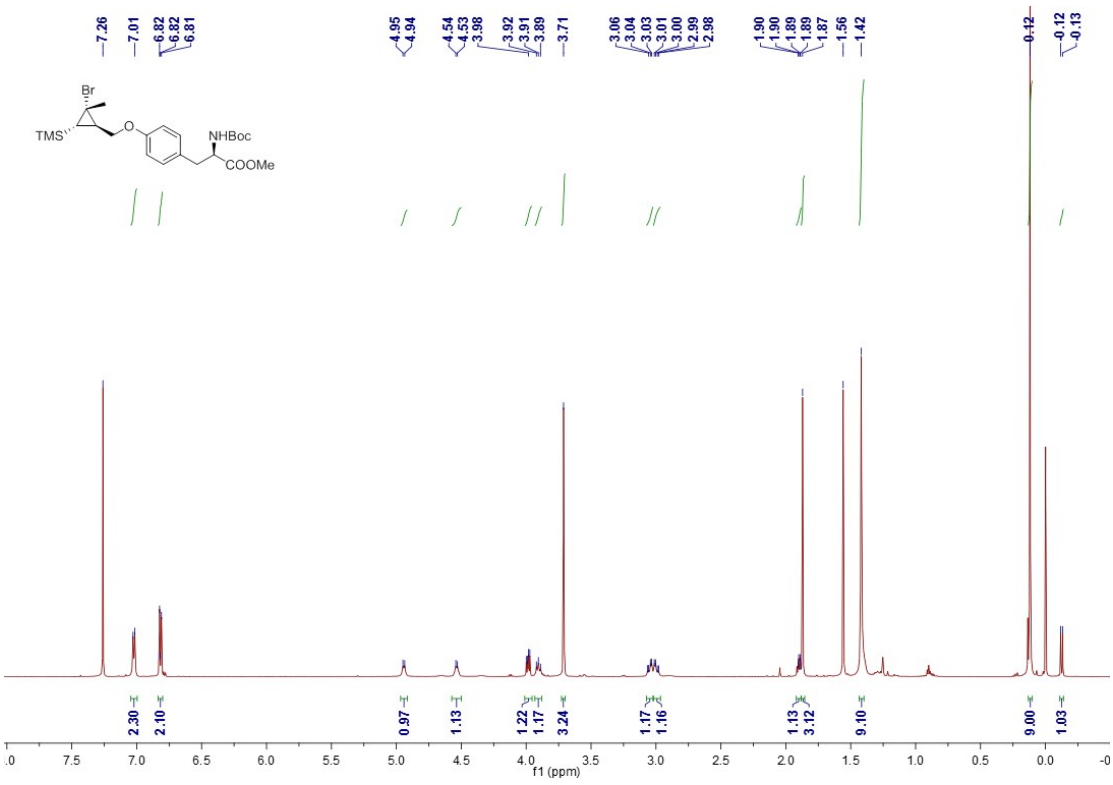
Compound 42 ^{1}H NMR



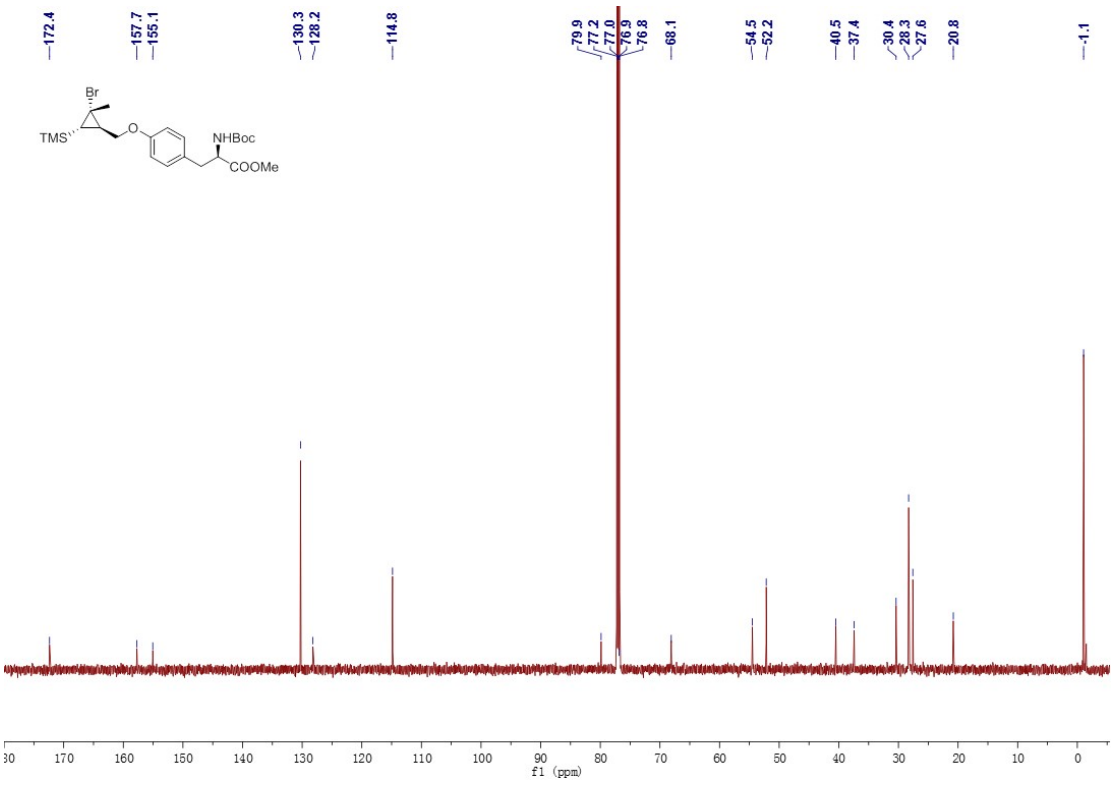
Compound 42 ^{13}C NMR



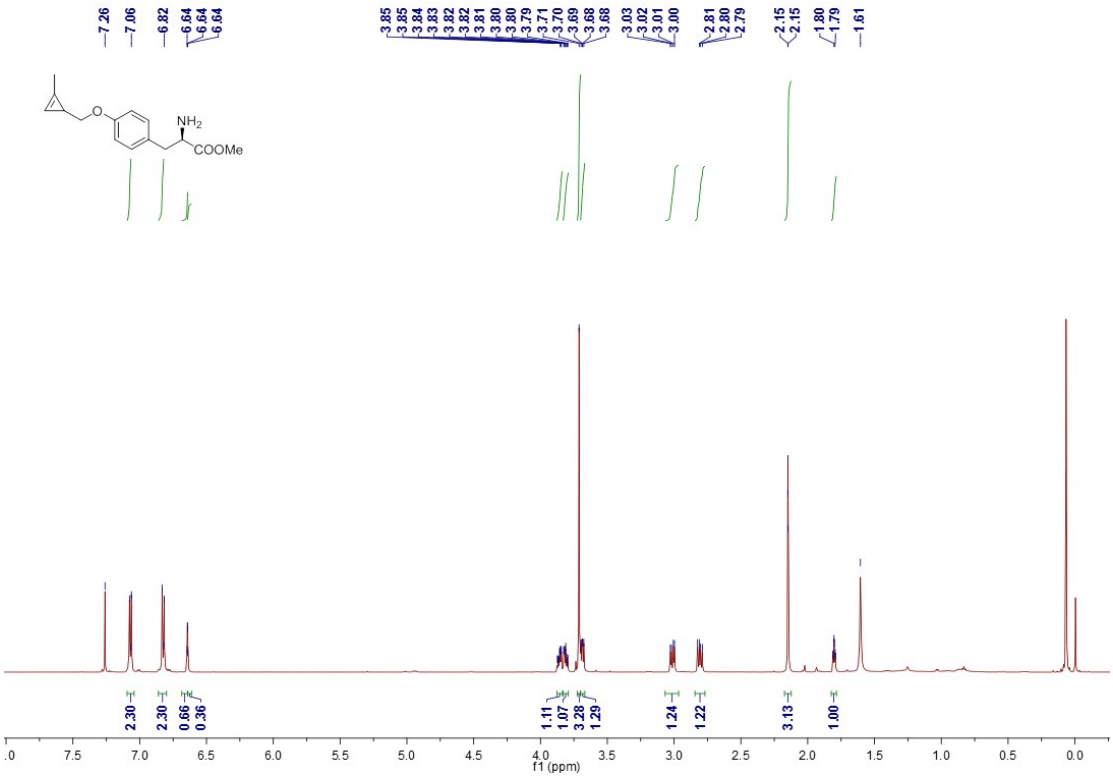
Compound 32 ^{1}H NMR



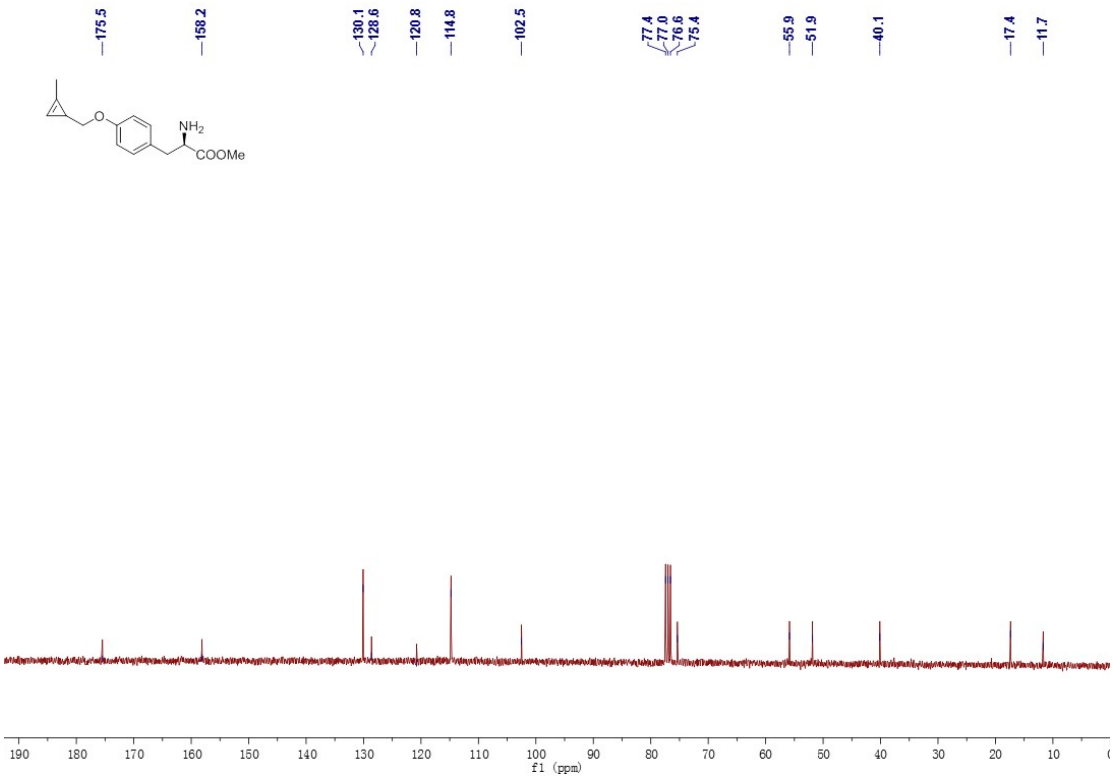
Compound 32 ^{13}C NMR



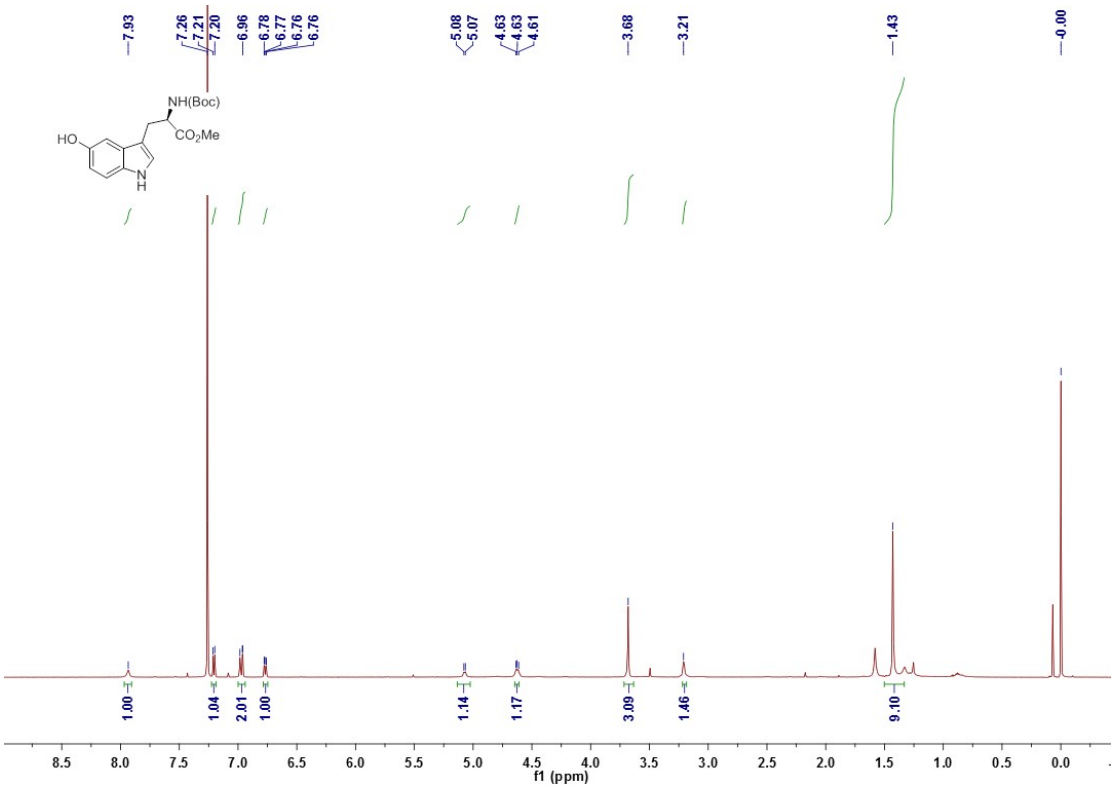
Compound 33 ^{1}H NMR



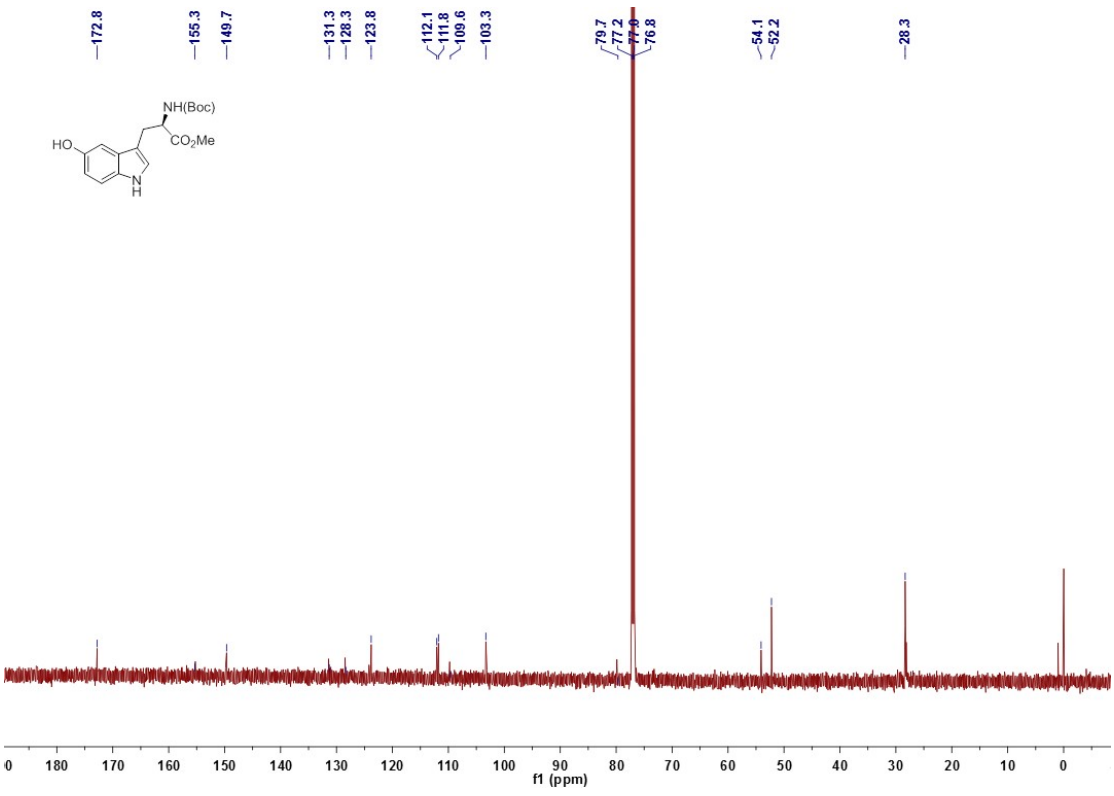
Compound 33 ^{13}C NMR



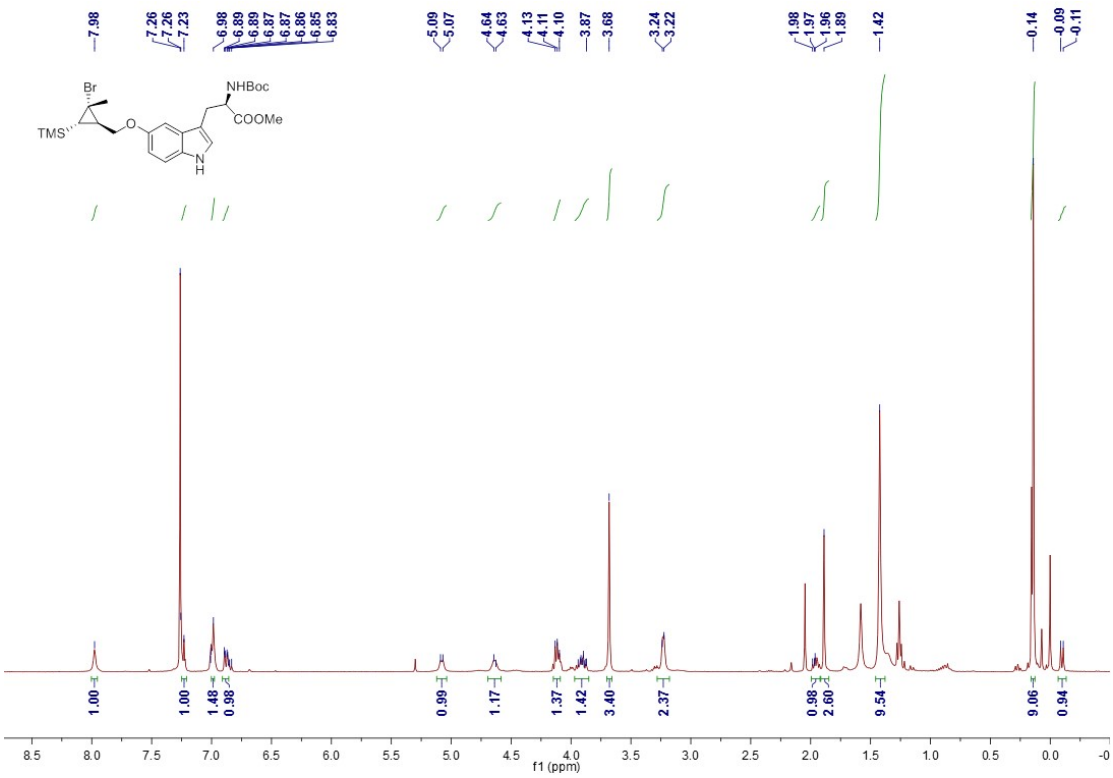
Compound 27 ^{1}H NMR



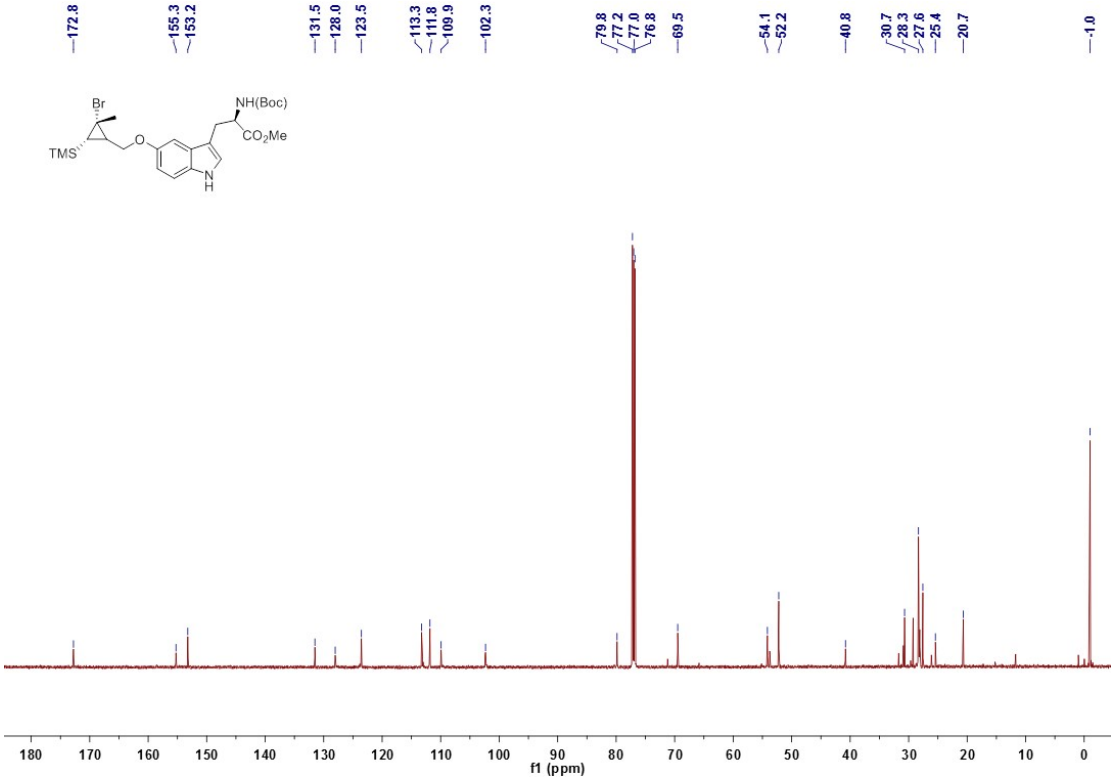
Compound 27 ^{13}C NMR



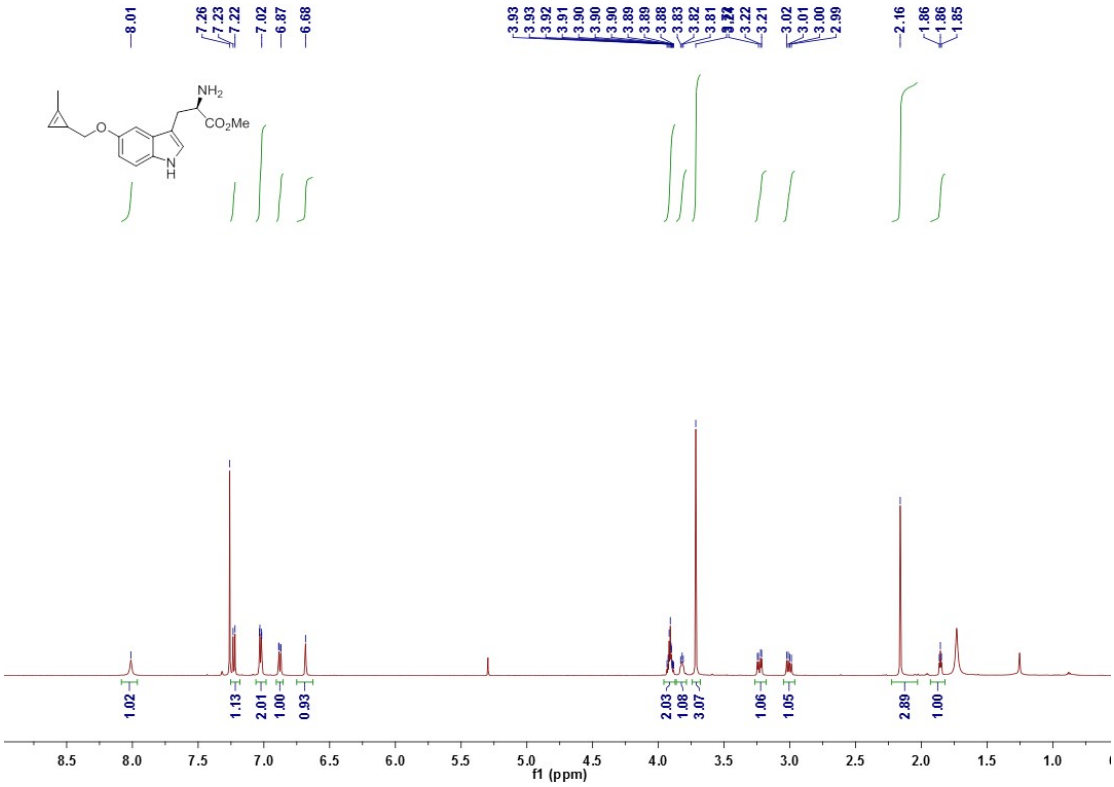
Compound 28 ^{1}H NMR



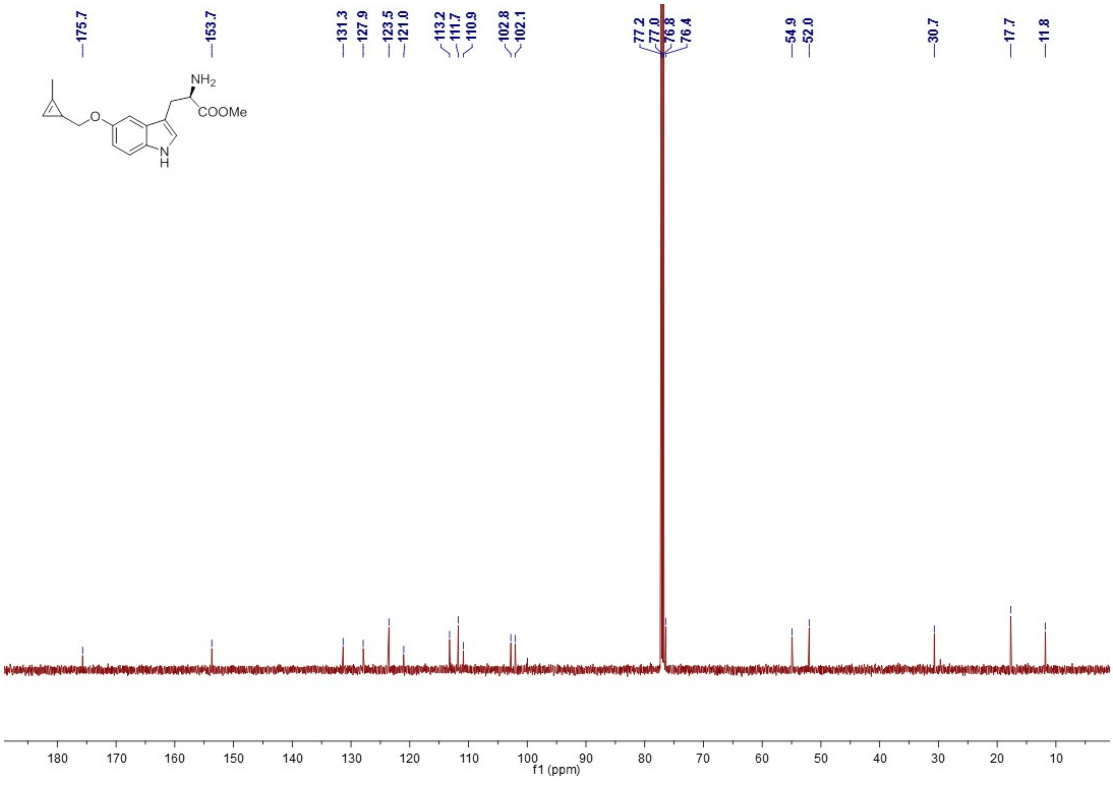
Compound 28 ^{13}C NMR



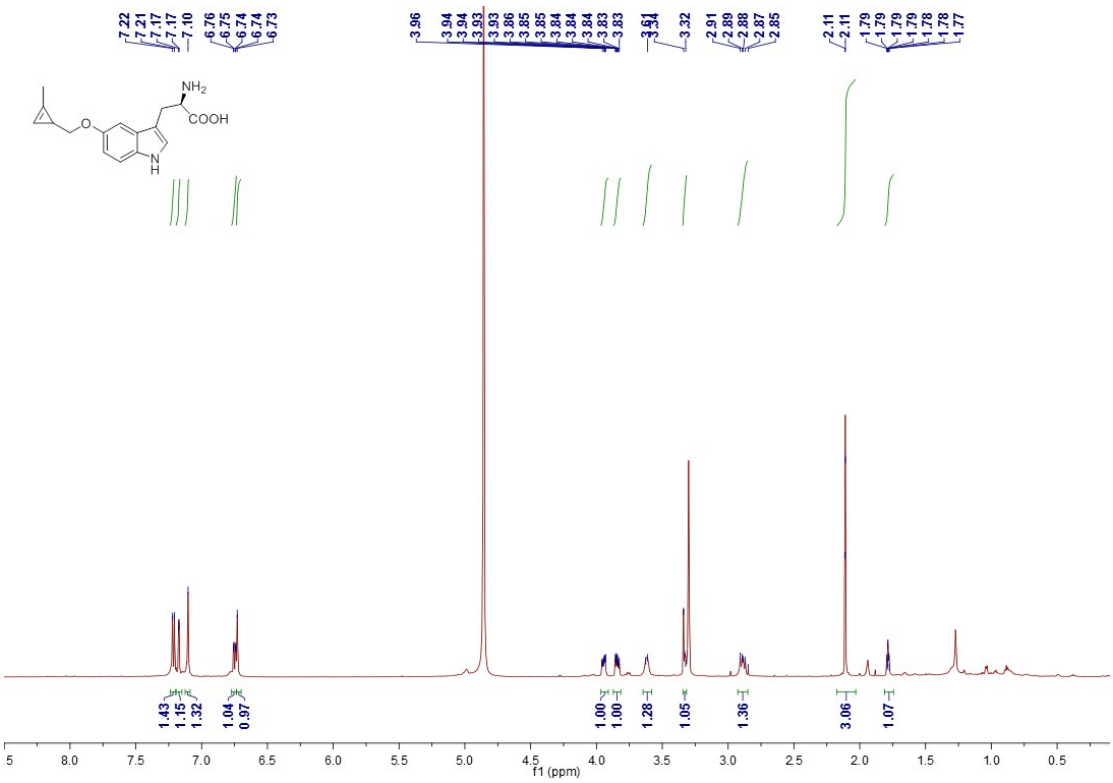
Compound 29 ^{1}H NMR



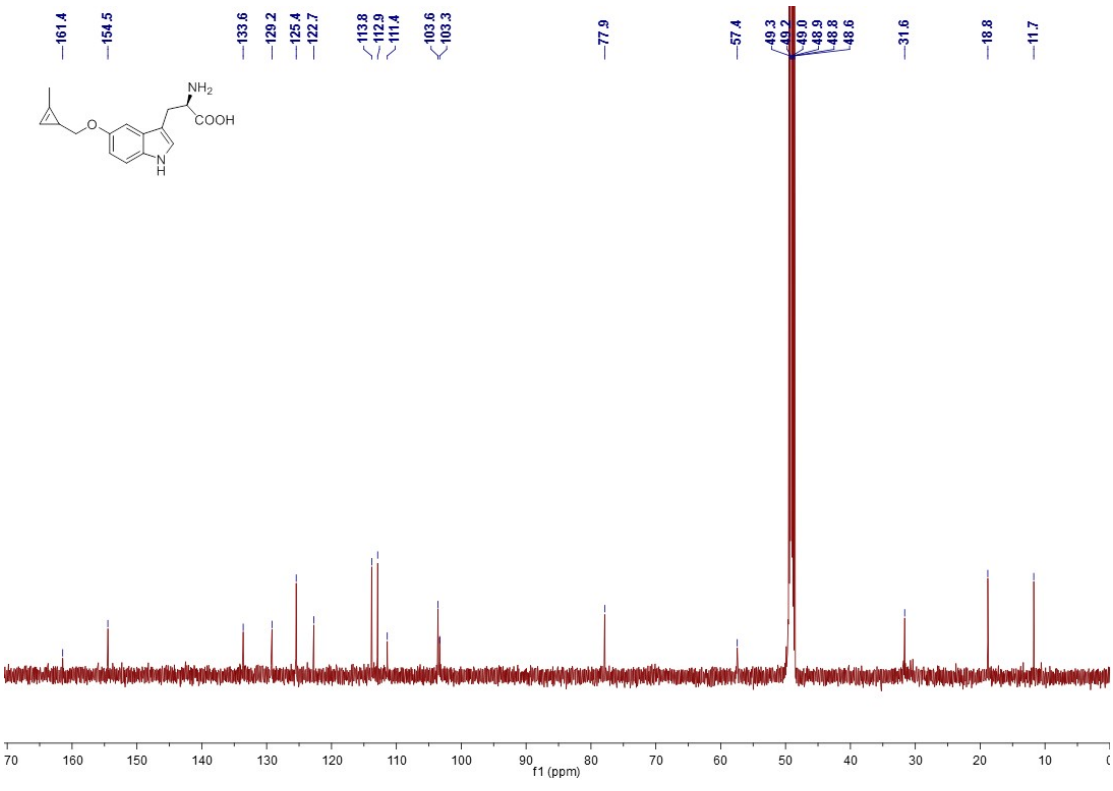
Compound 29 ^{13}C NMR



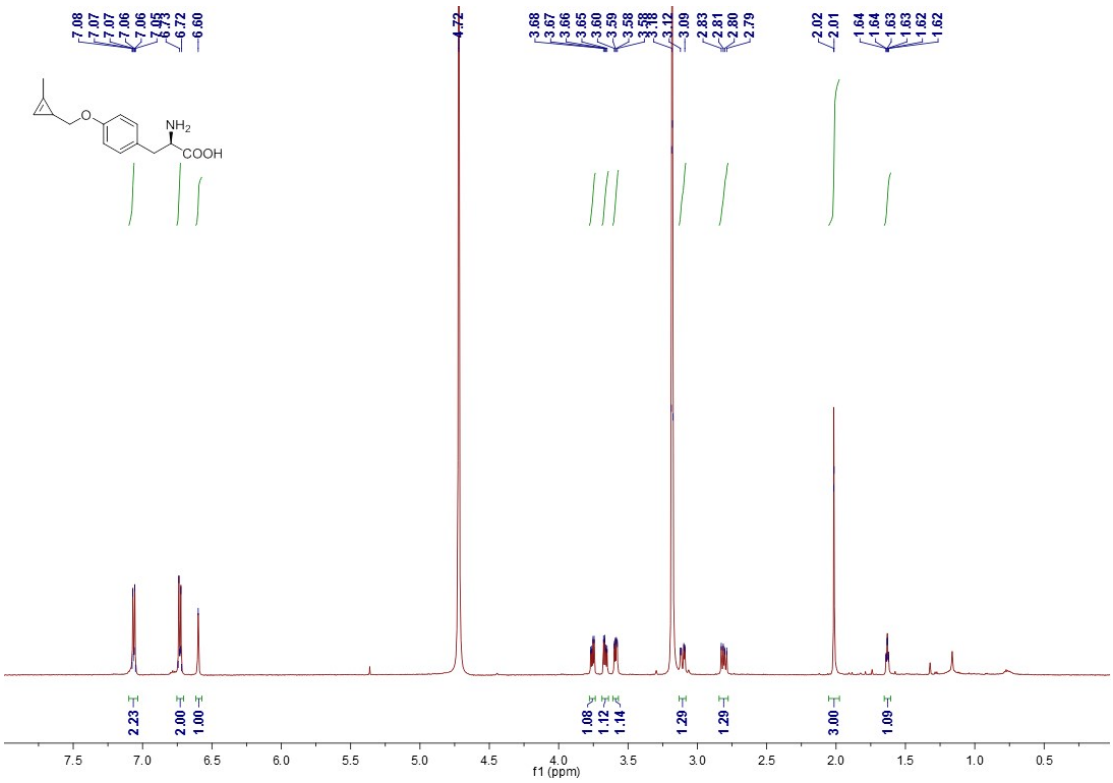
Compound 30 ^{1}H NMR



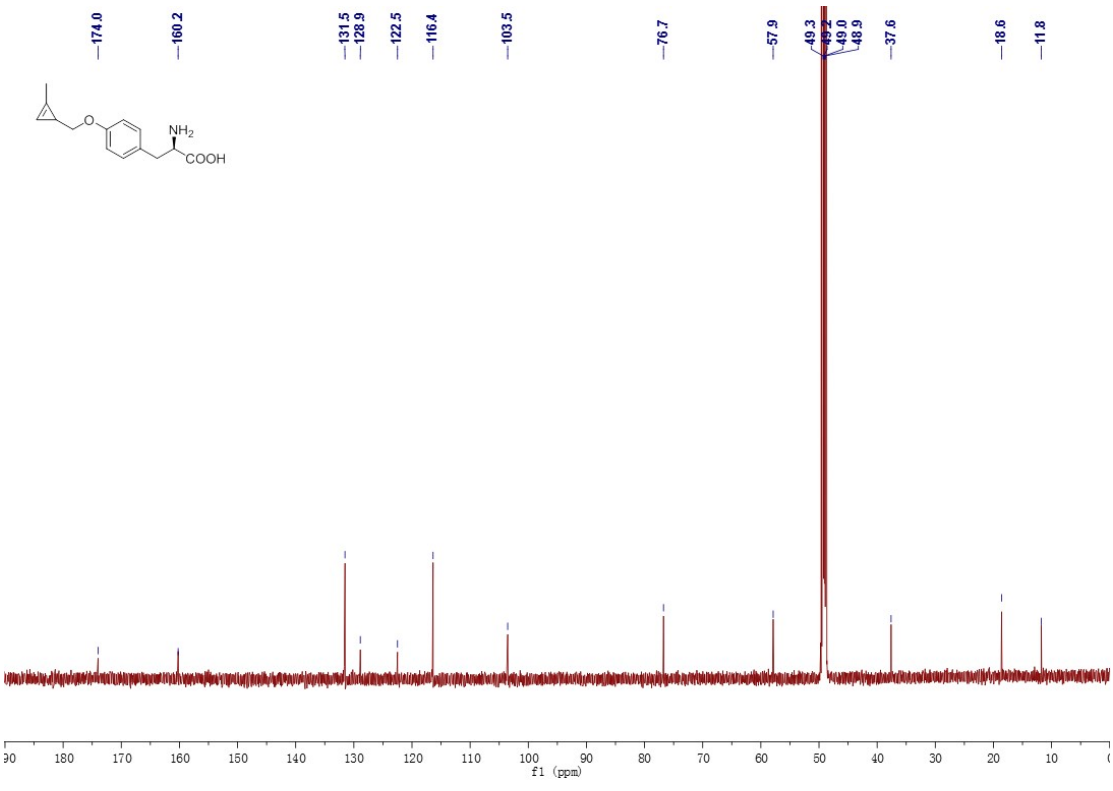
Compound 30 ^{13}C NMR



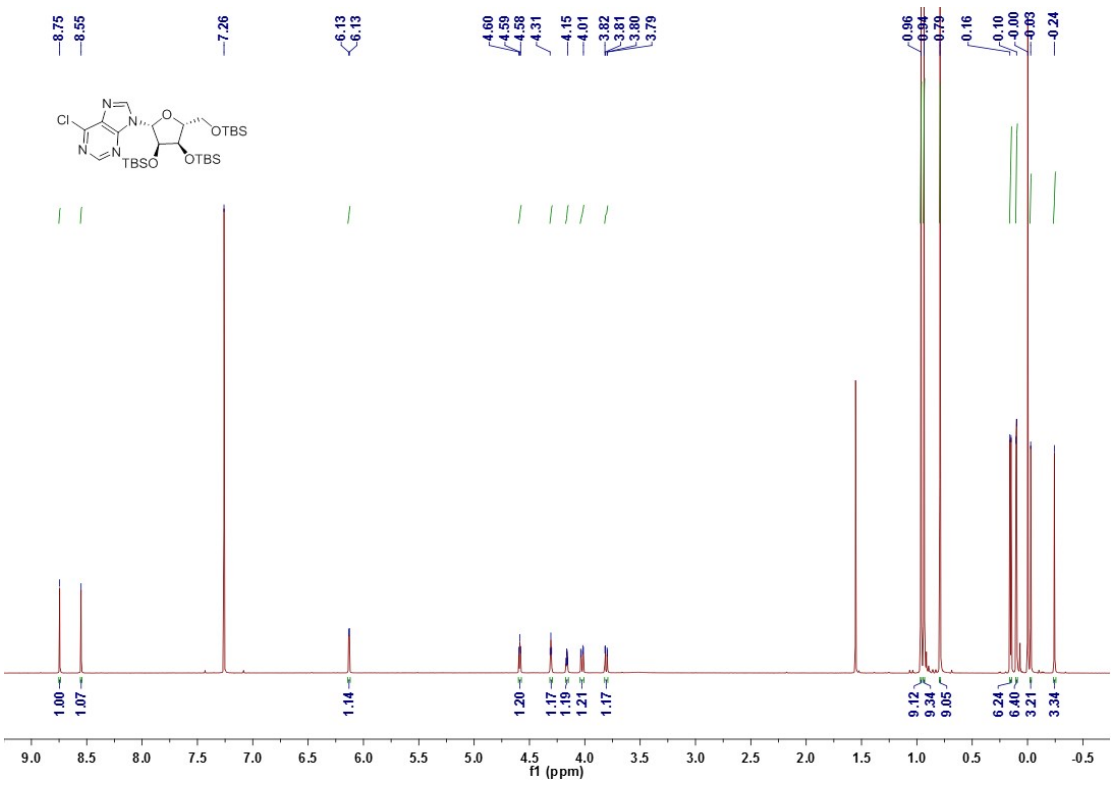
Compound 34 ^{1}H NMR



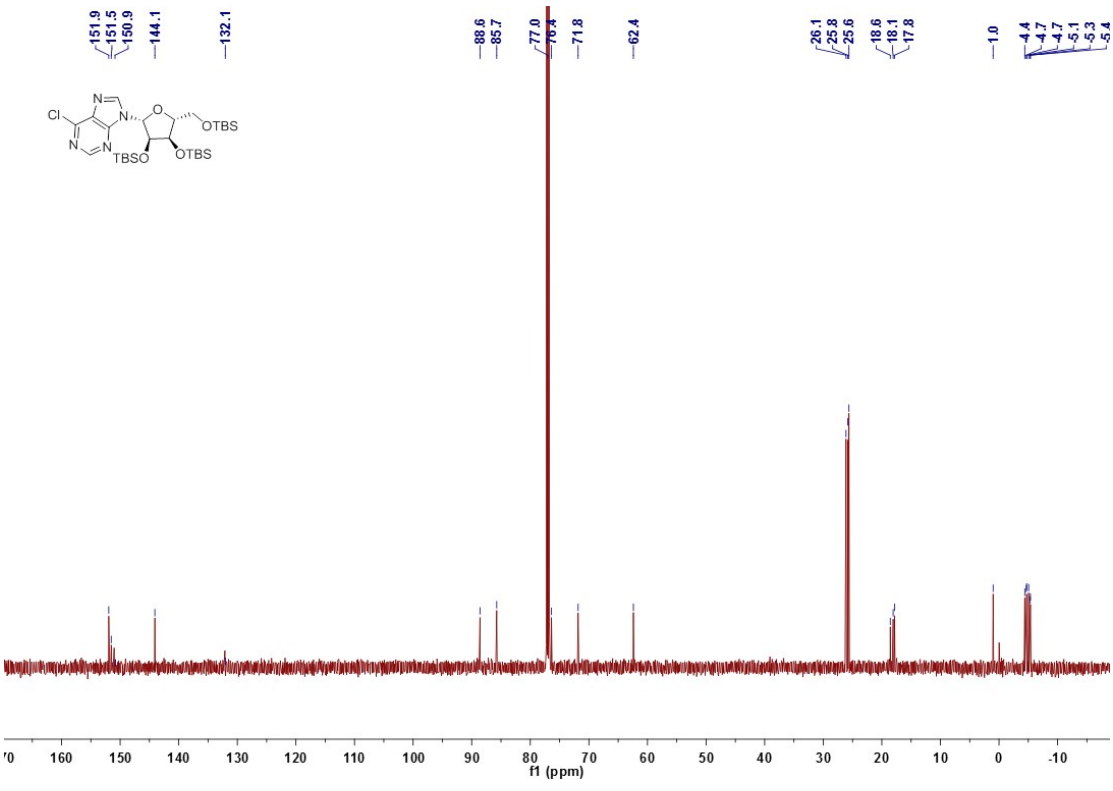
Compound 34 ^{13}C NMR



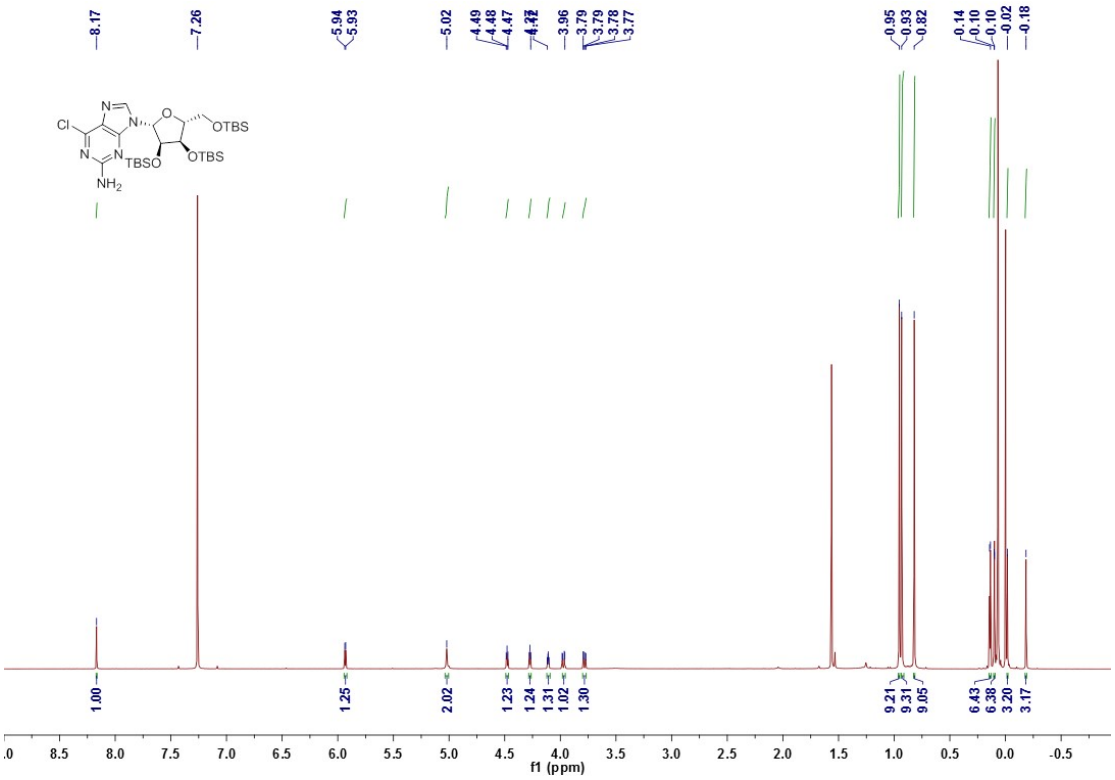
Compound 45 ^{1}H NMR



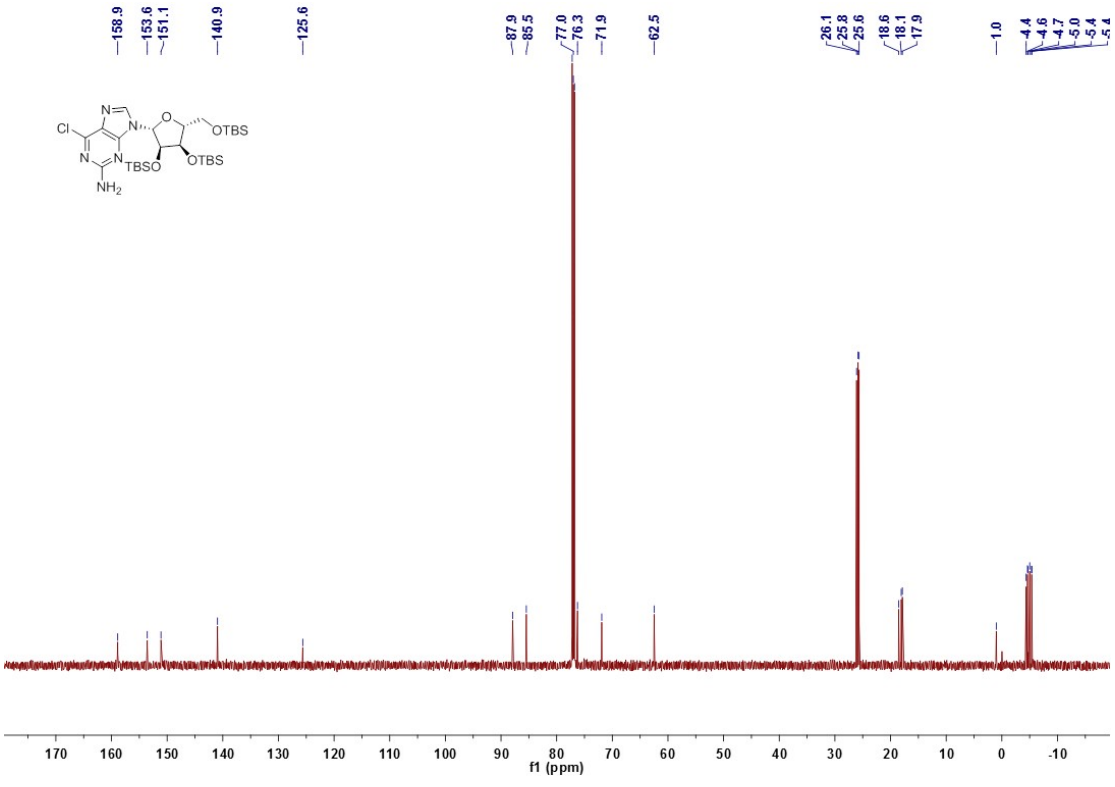
Compound 45 ^{13}C NMR



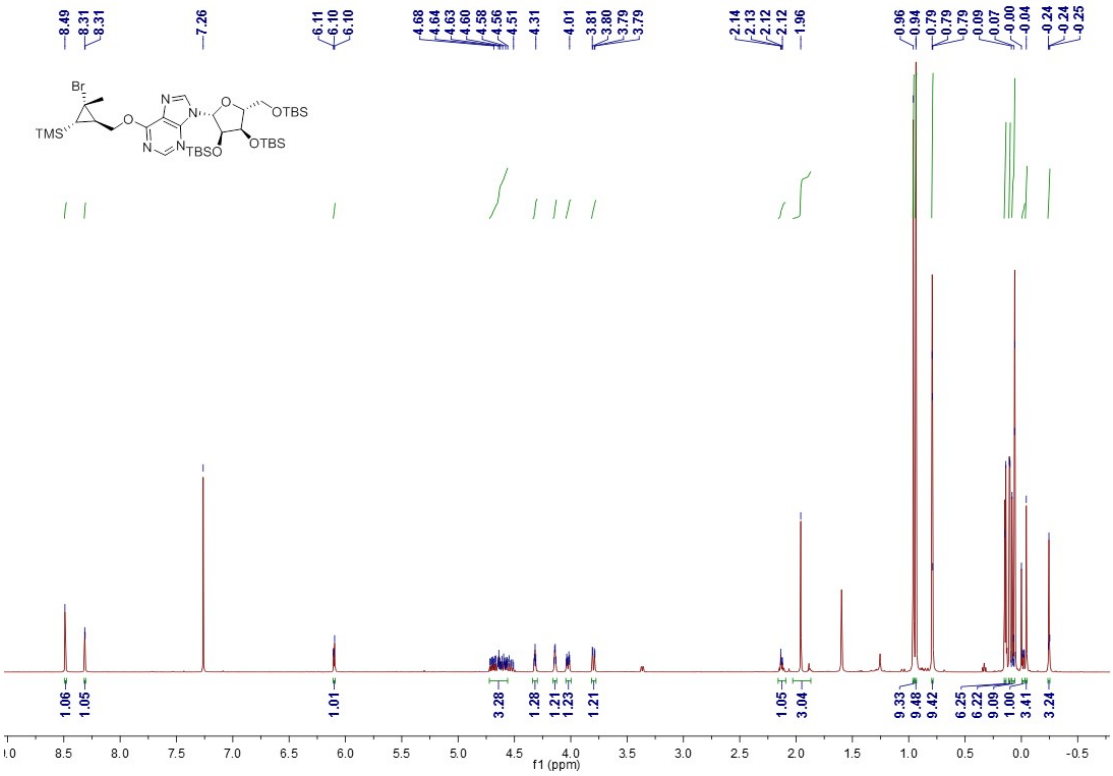
Compound 47 ^{1}H NMR



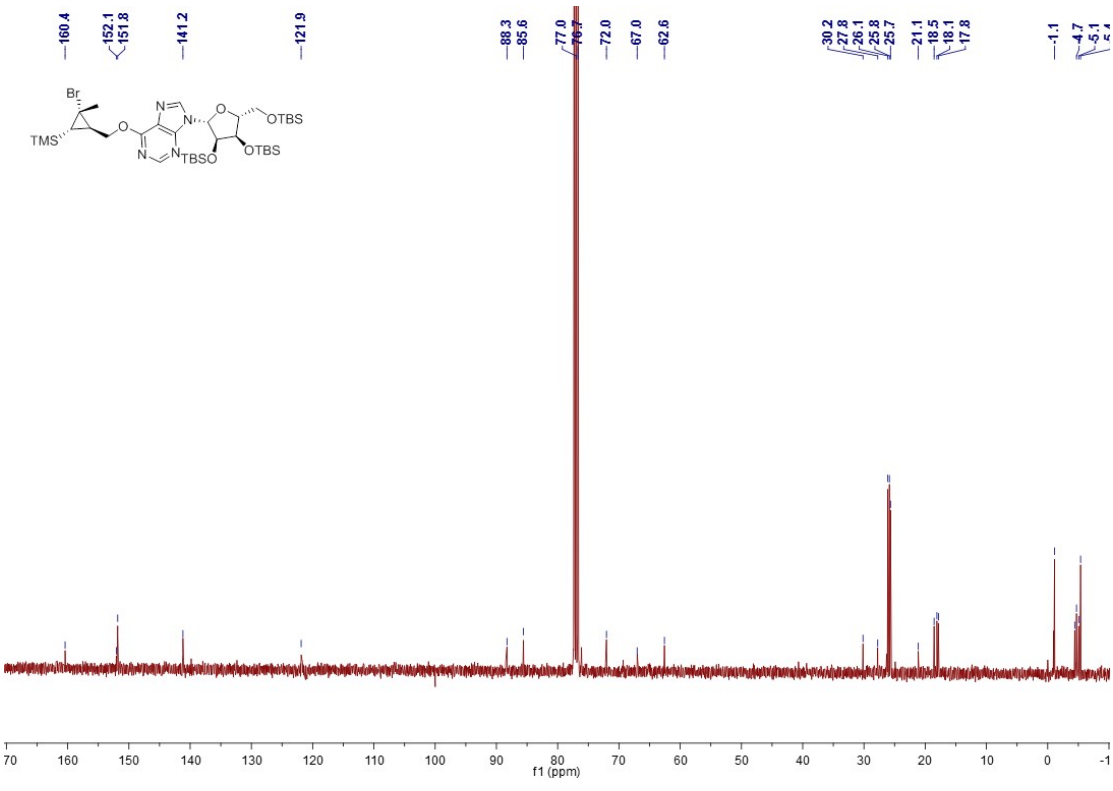
Compound 47 ^{13}C NMR



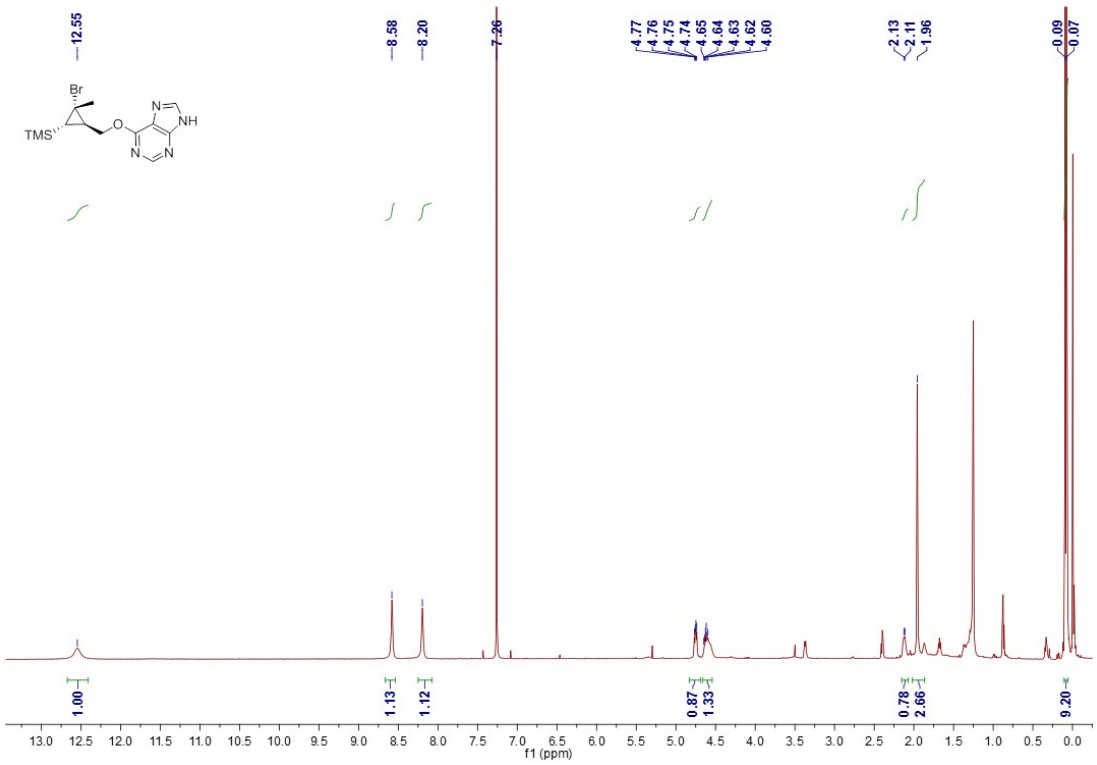
Compound 55 ^{1}H NMR



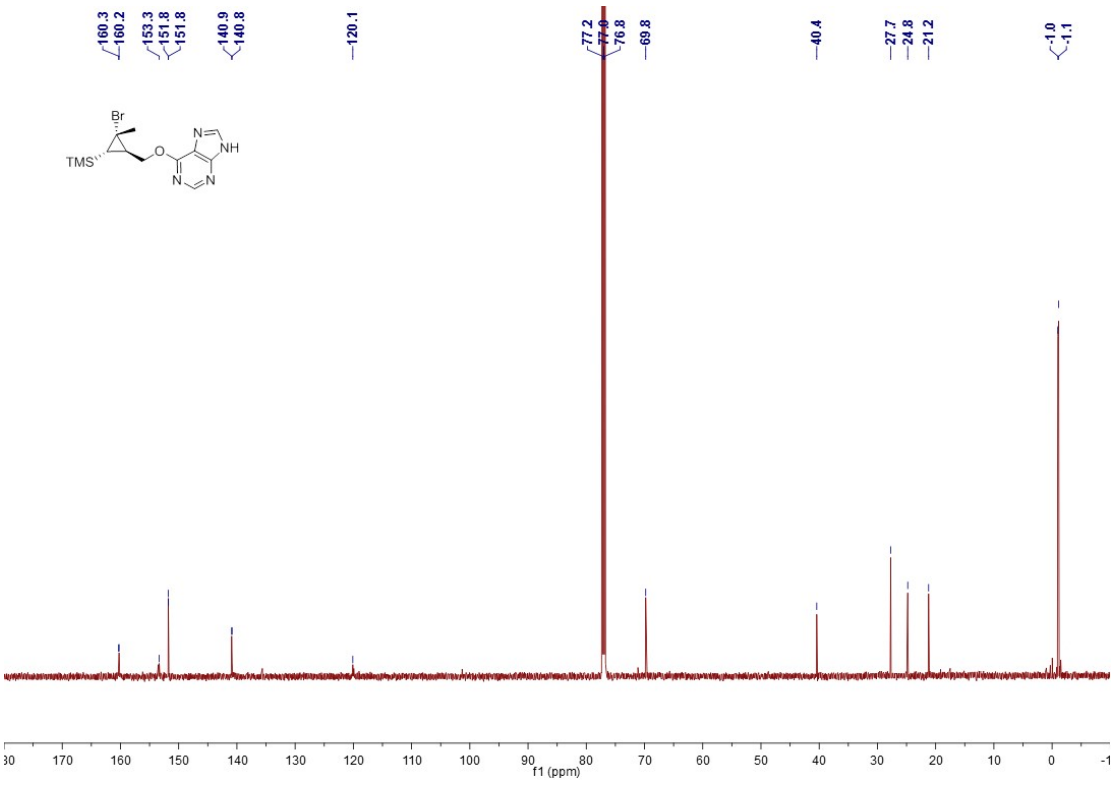
Compound 55 ^{13}C NMR



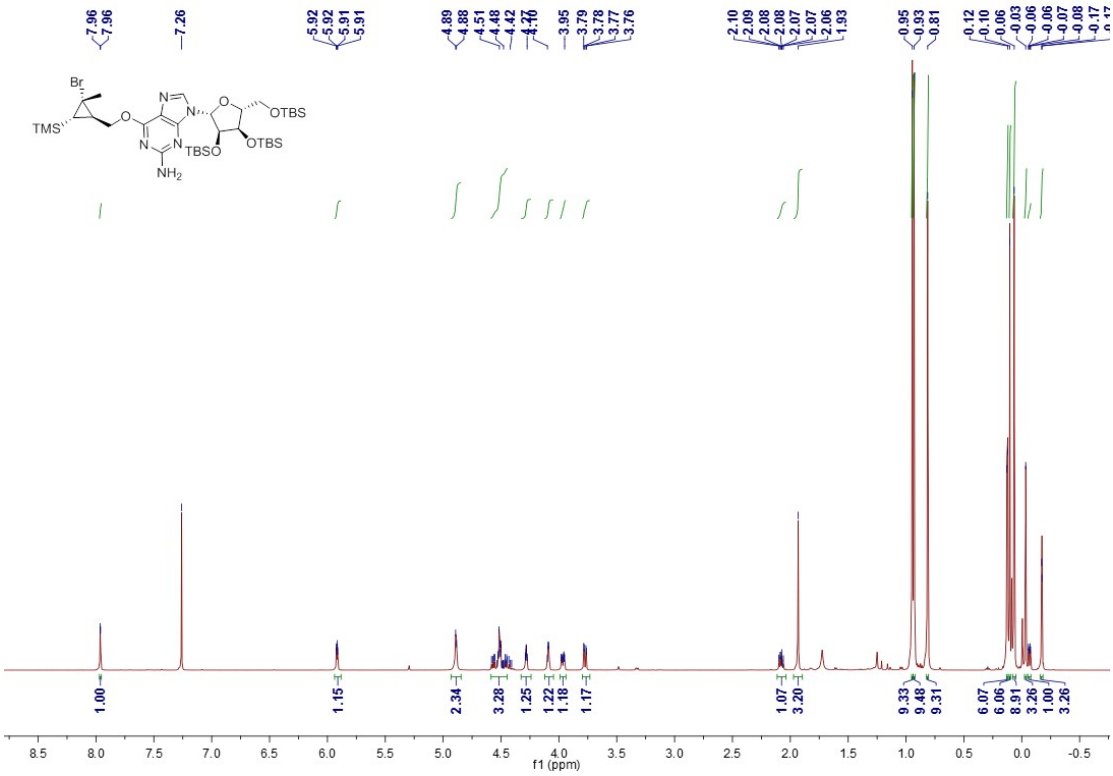
Compound 54 ^{1}H NMR



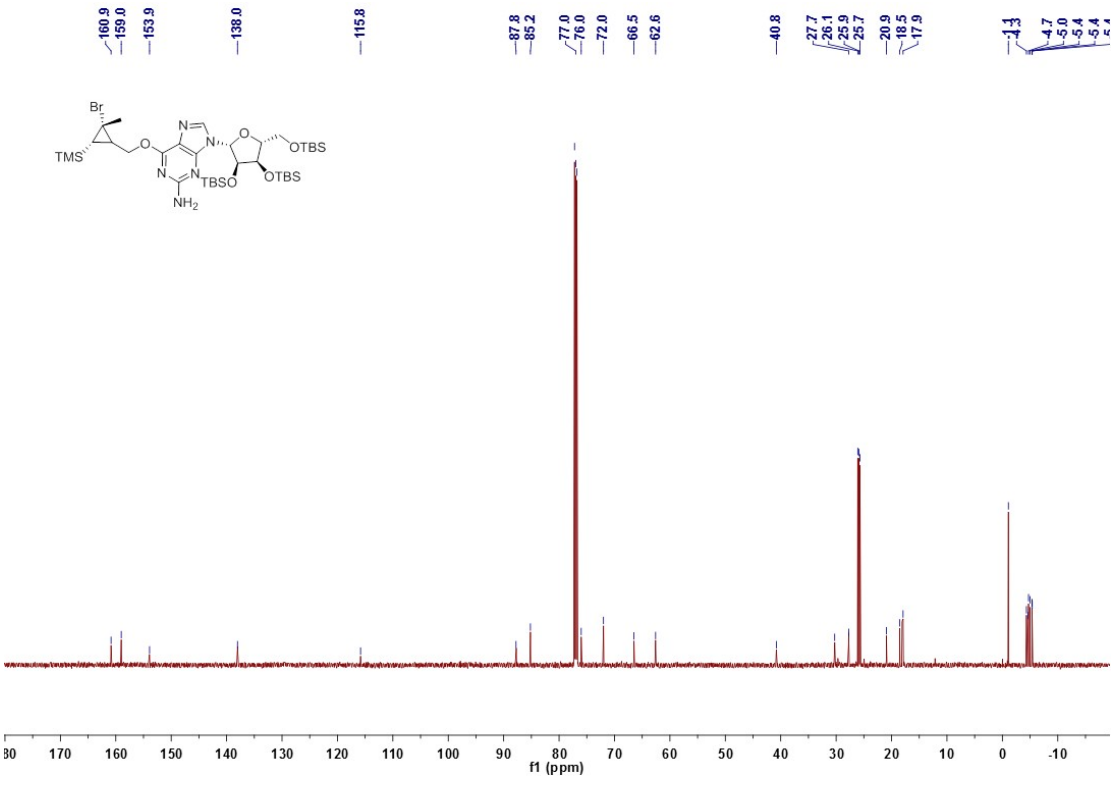
Compound 54 ^{13}C NMR



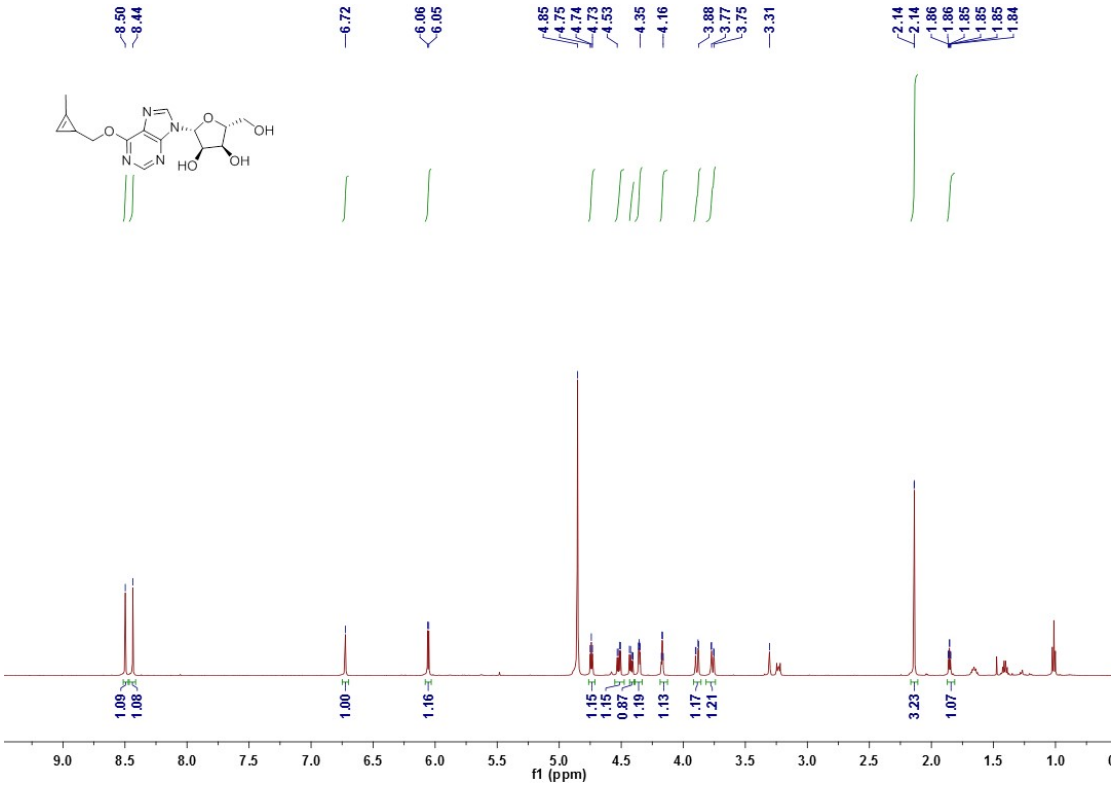
Compound 56 ^{1}H NMR



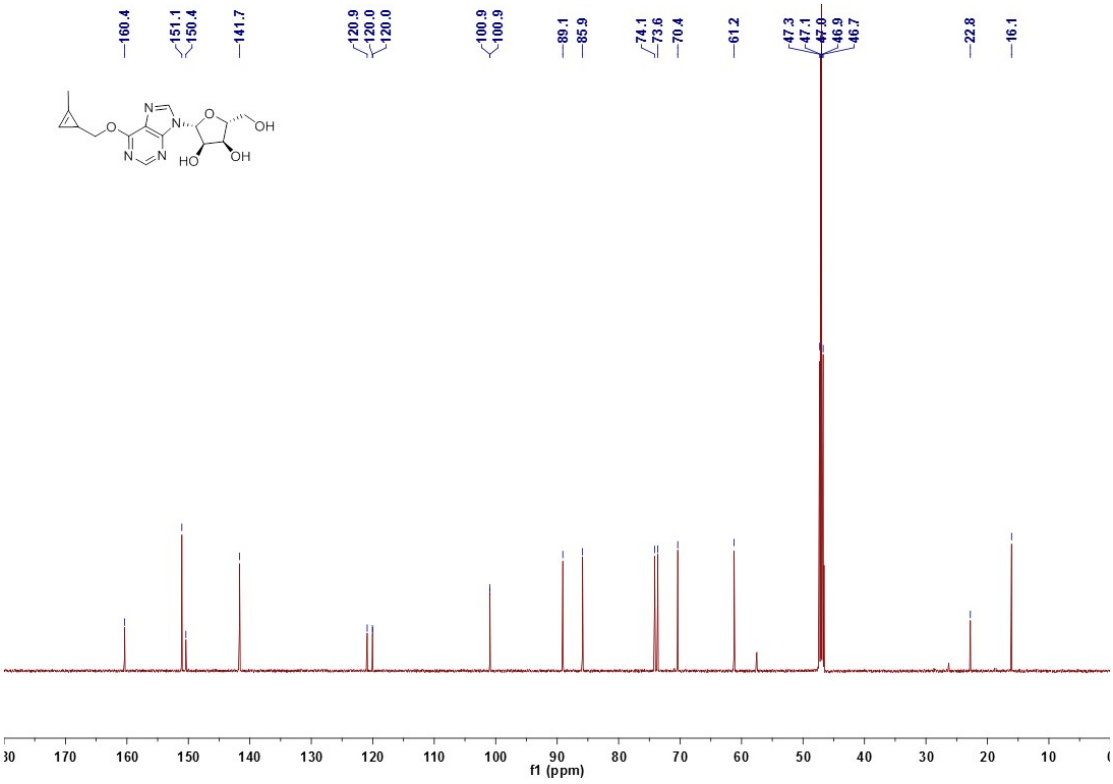
Compound 56 ^{13}C NMR



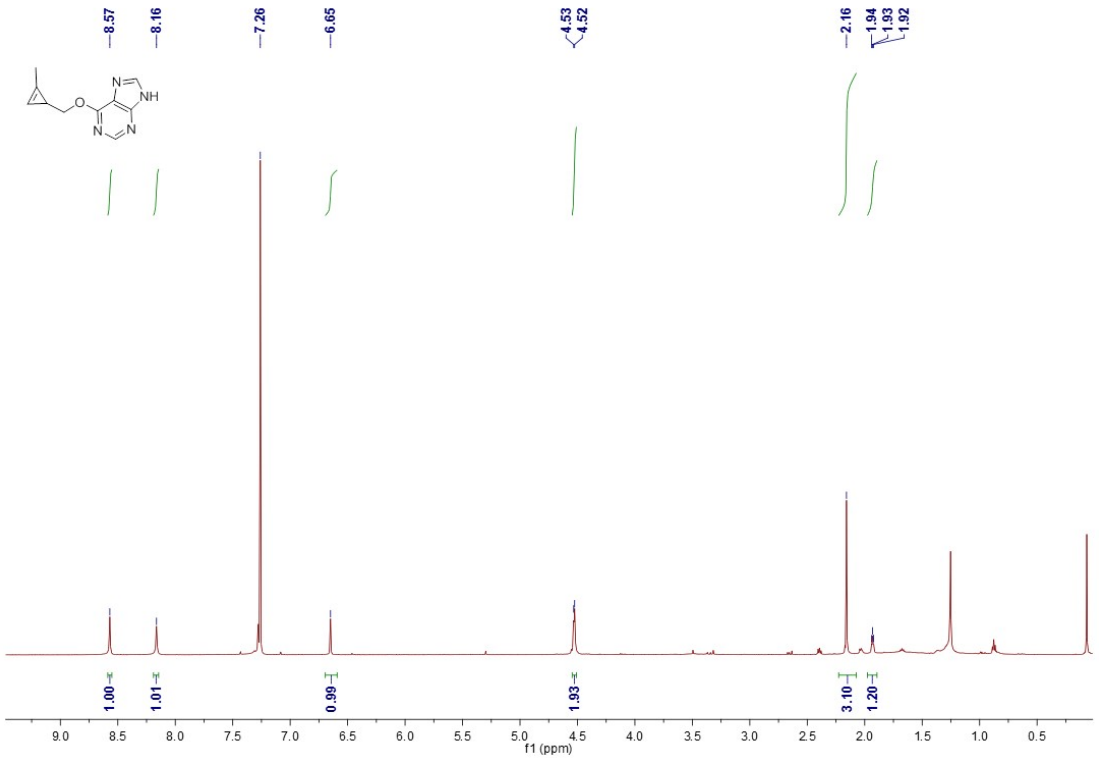
Compound 46 ^{1}H NMR



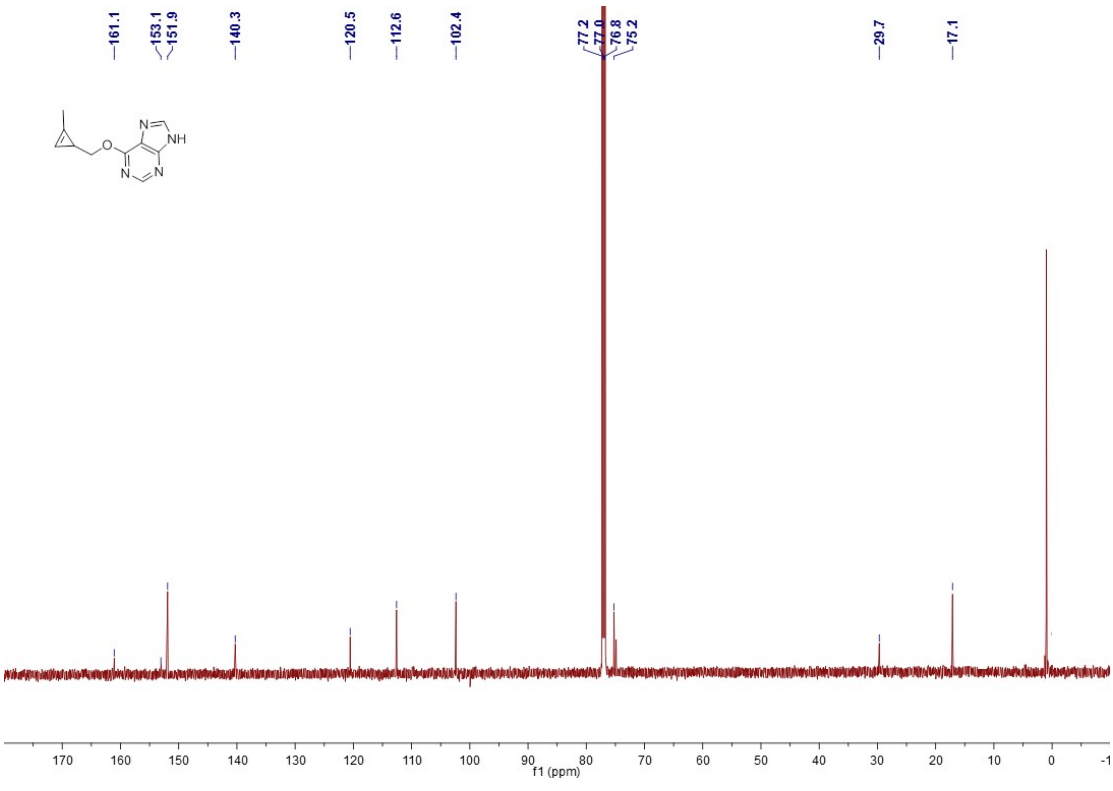
Compound 46 ^{13}C NMR



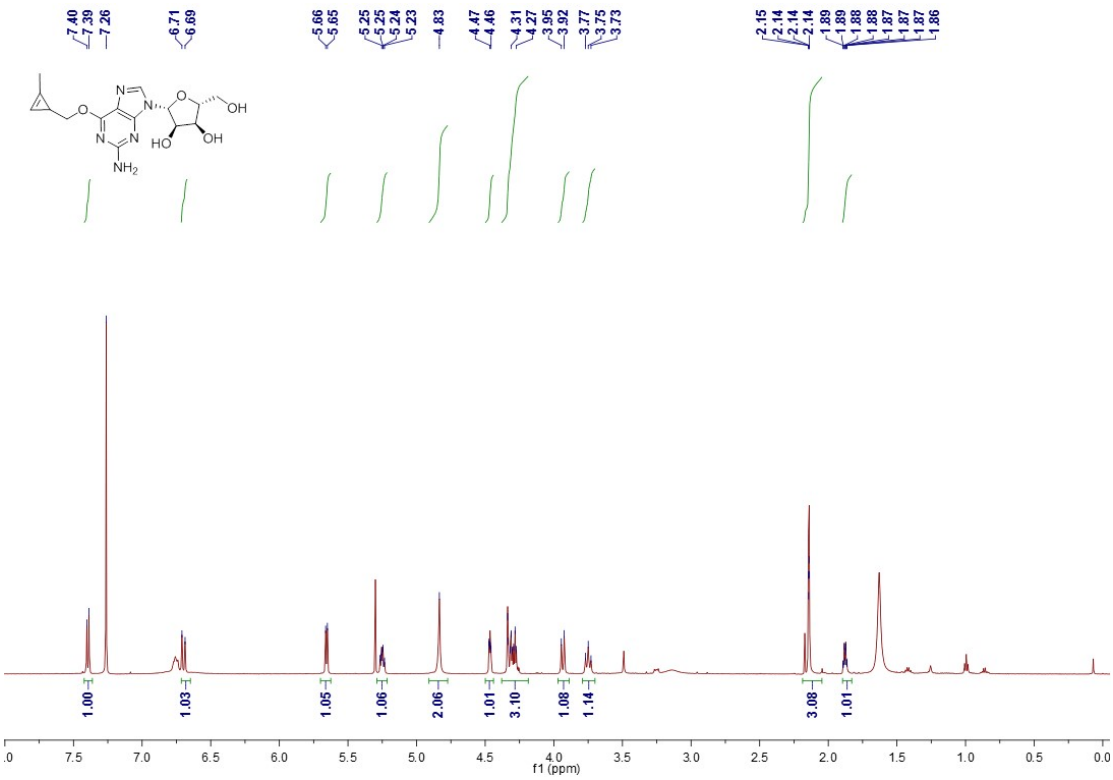
Compound 44 ^{1}H NMR



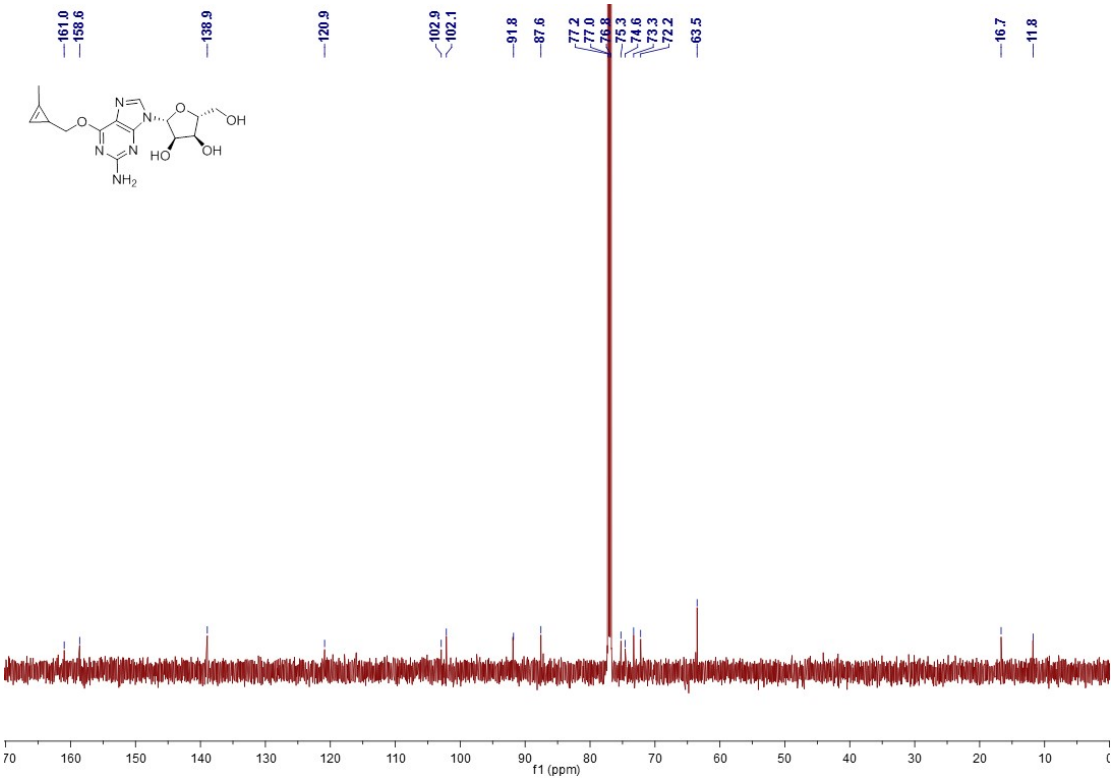
Compound 44 ^{13}C NMR



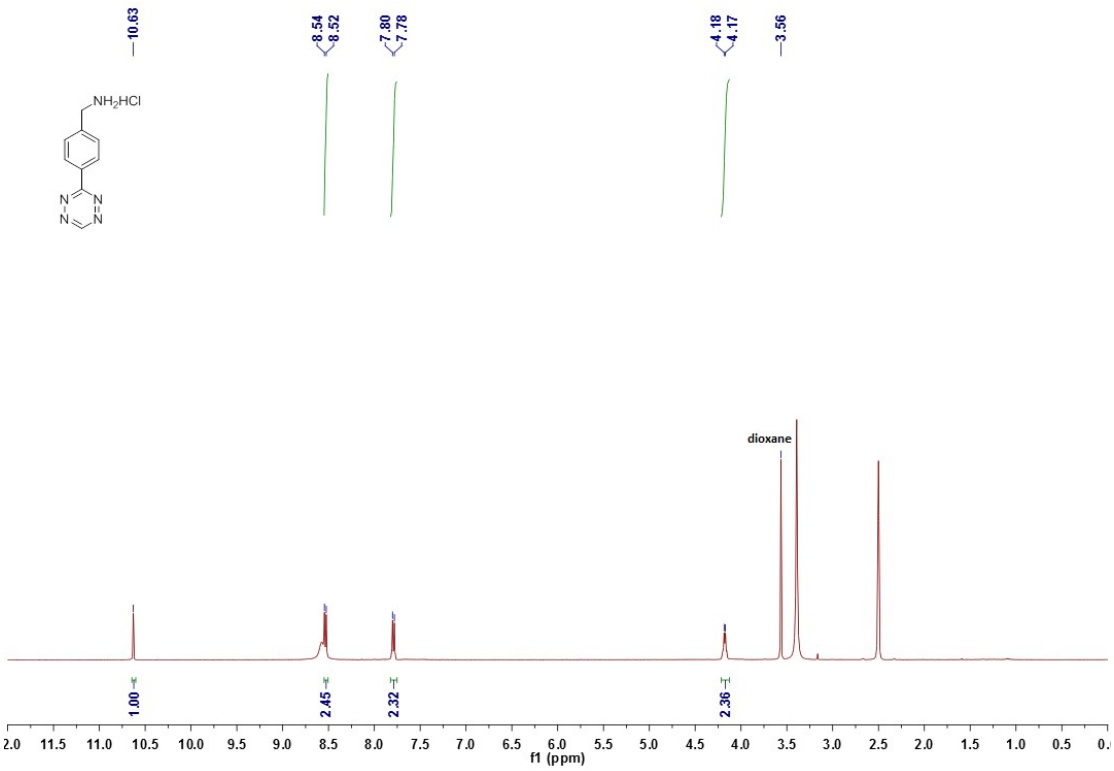
Compound 48 ^{1}H NMR



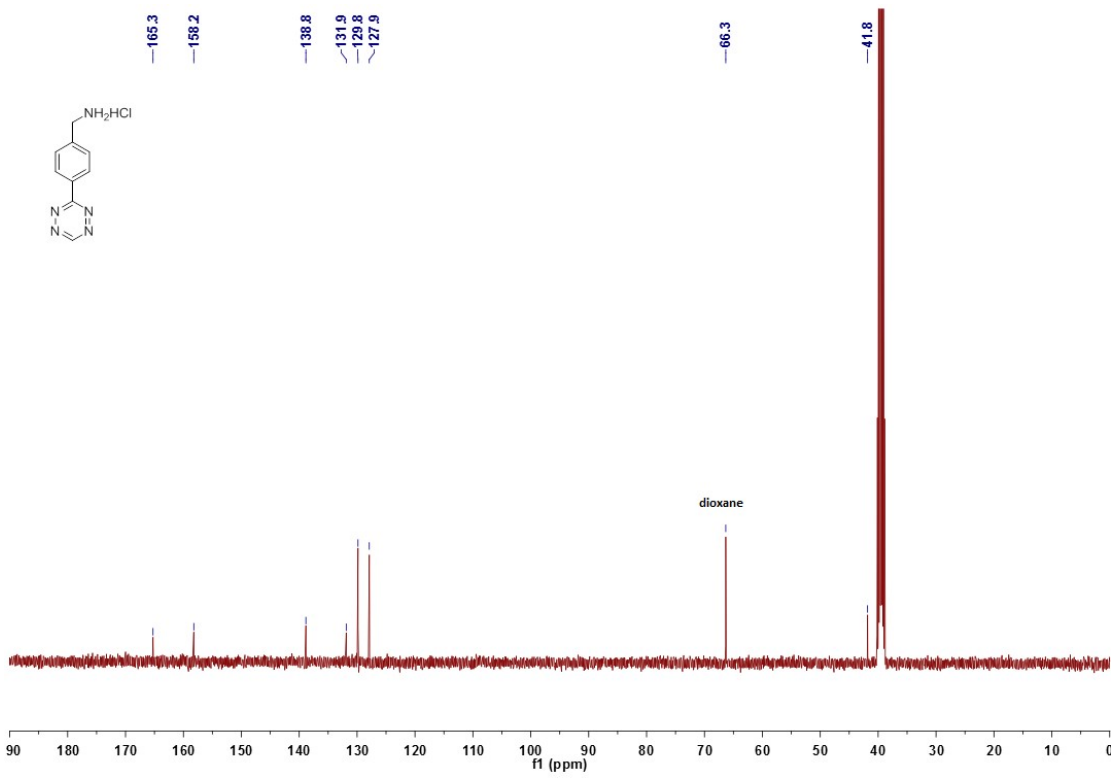
Compound 48 ^{13}C NMR



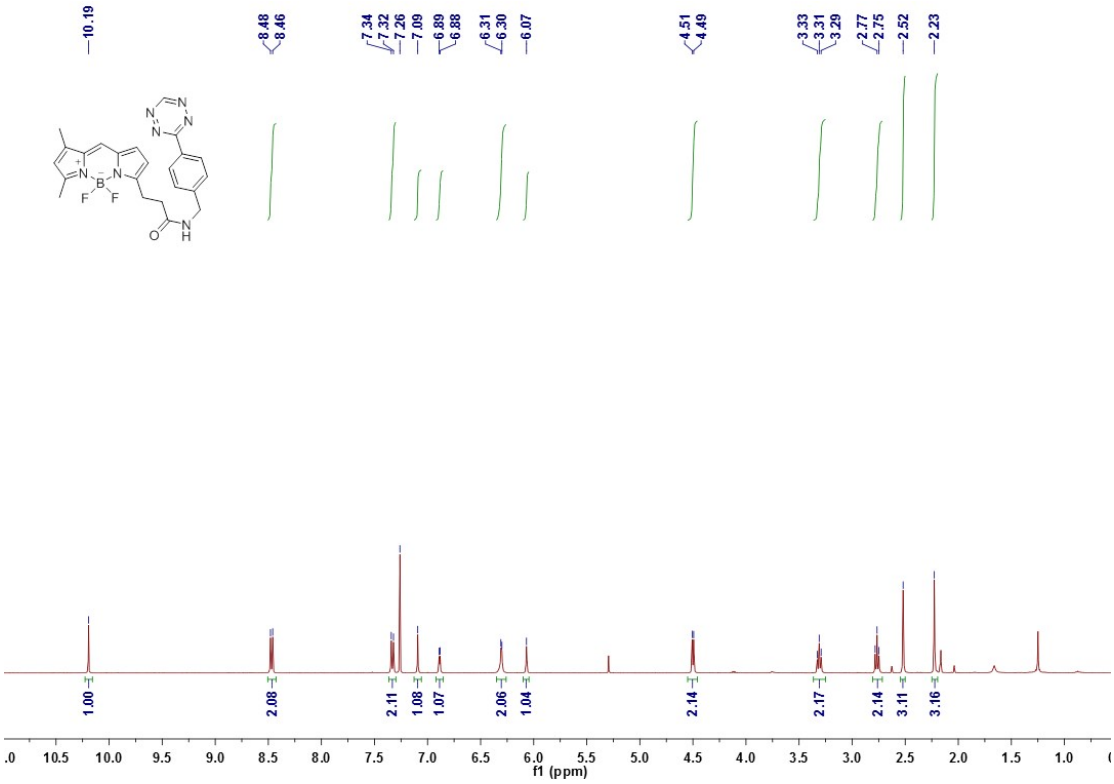
Compound 60 ^{1}H NMR



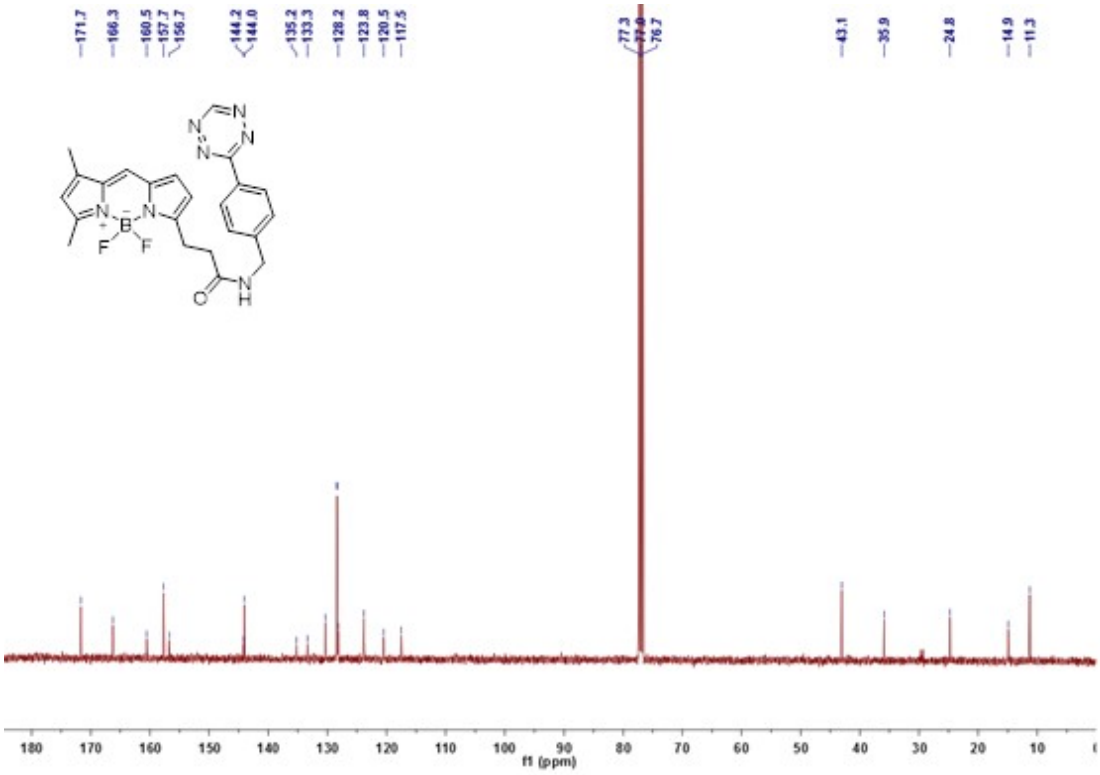
Compound 60 ^{13}C NMR



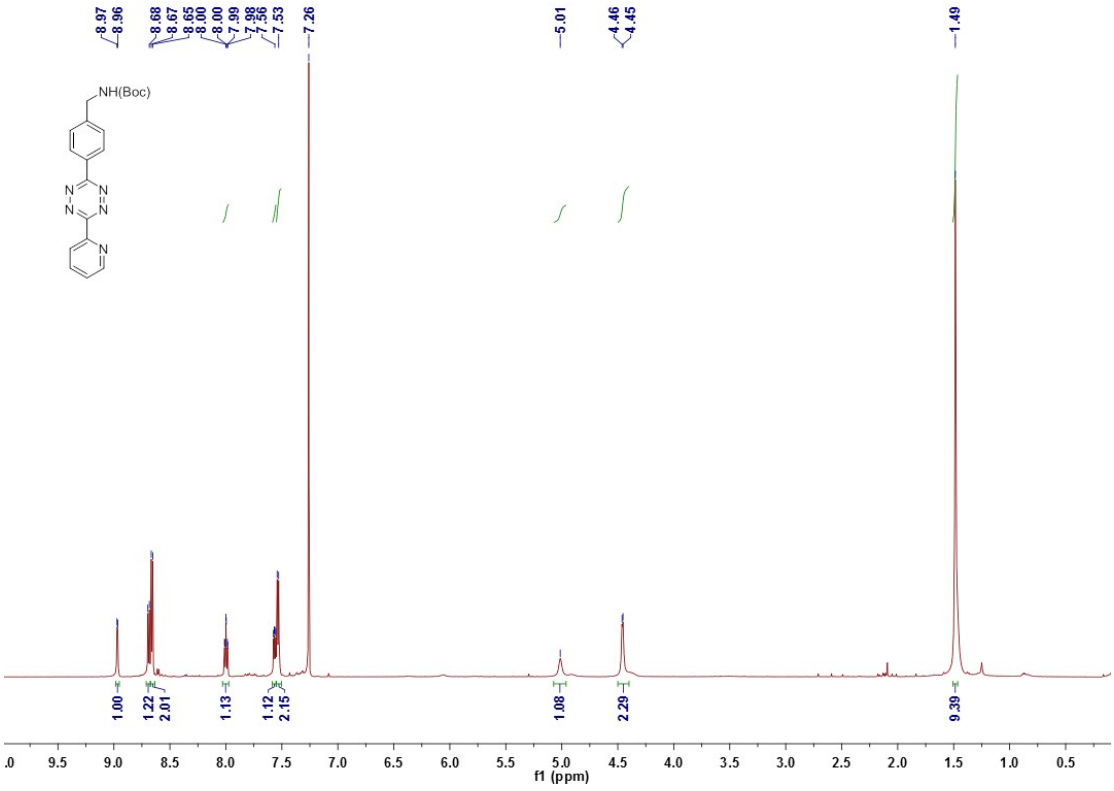
Compound 62 ^{1}H NMR



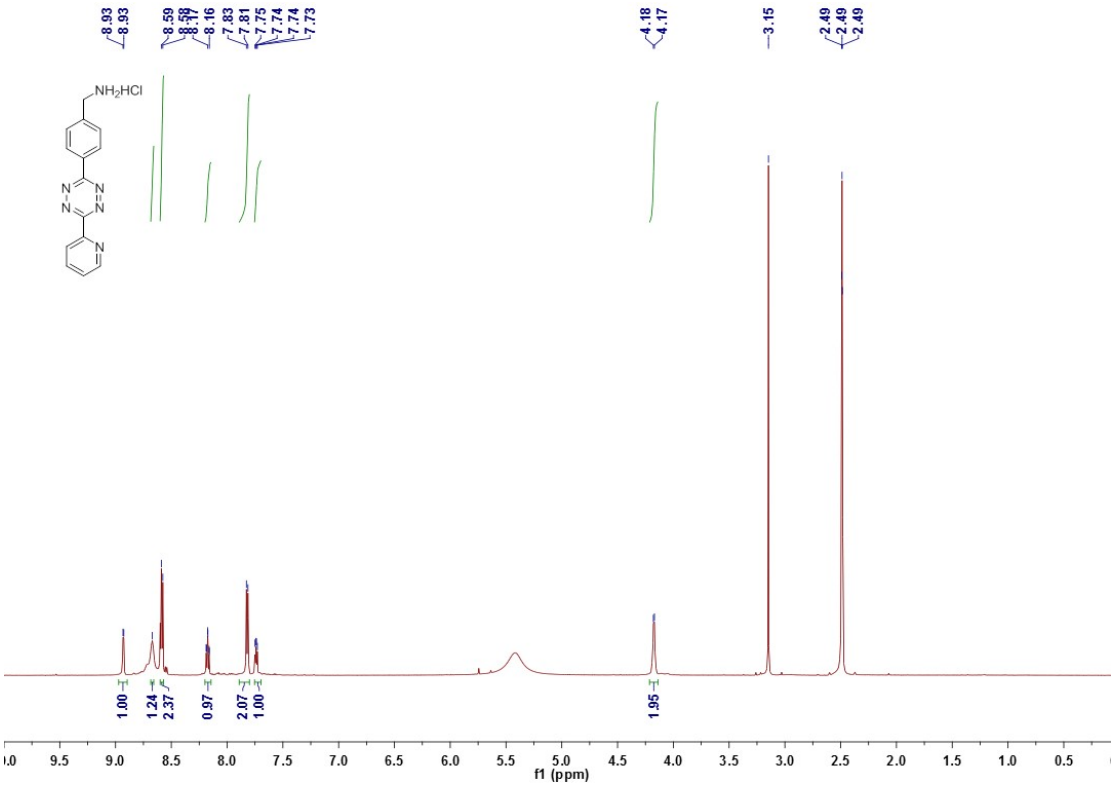
Compound 62 ^{13}C NMR



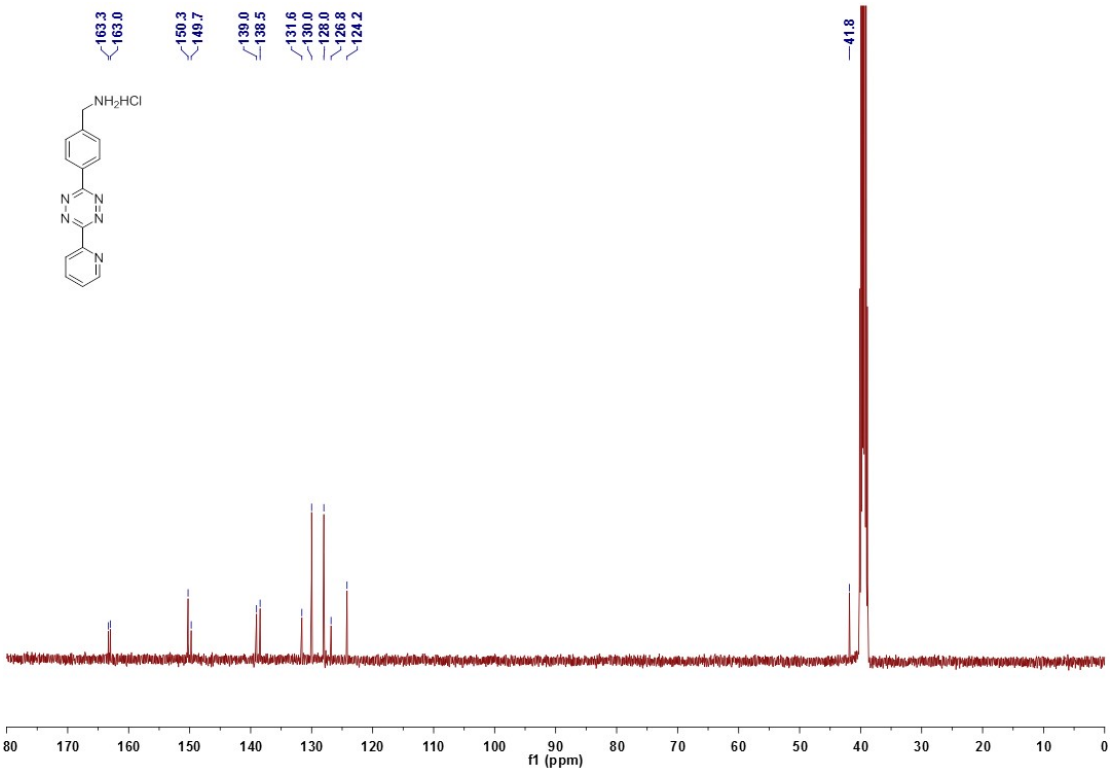
Compound 64 ^{1}H NMR



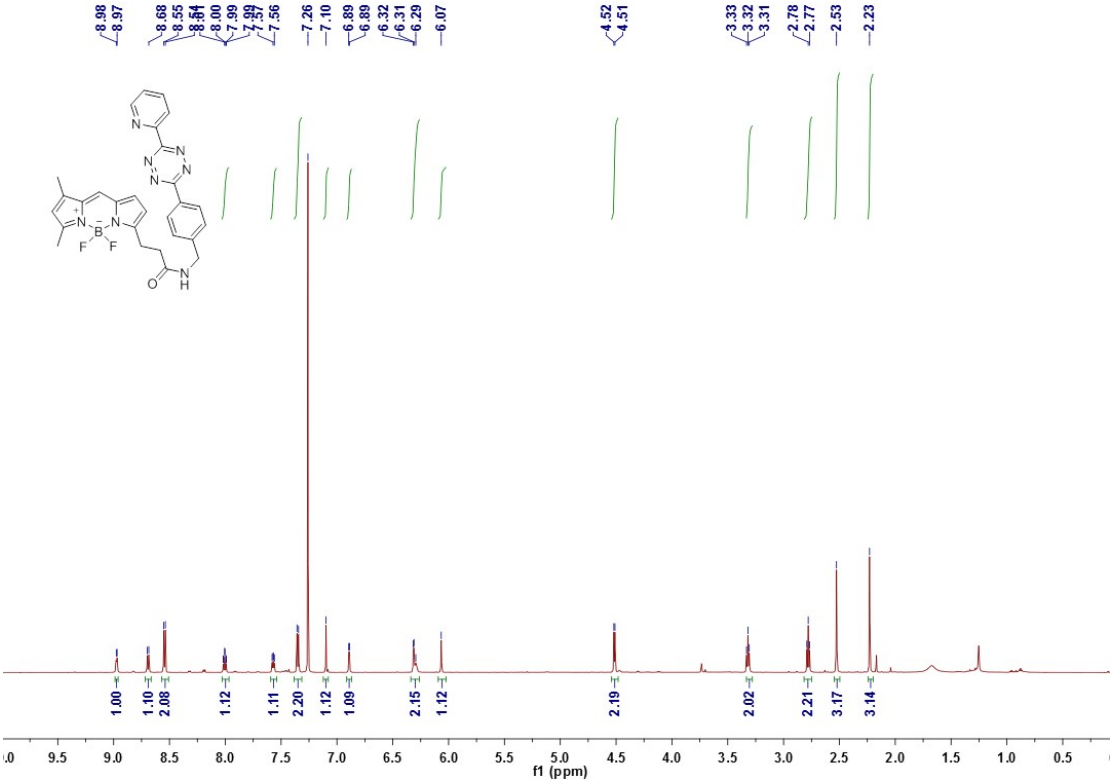
Compound 65 ^{1}H NMR



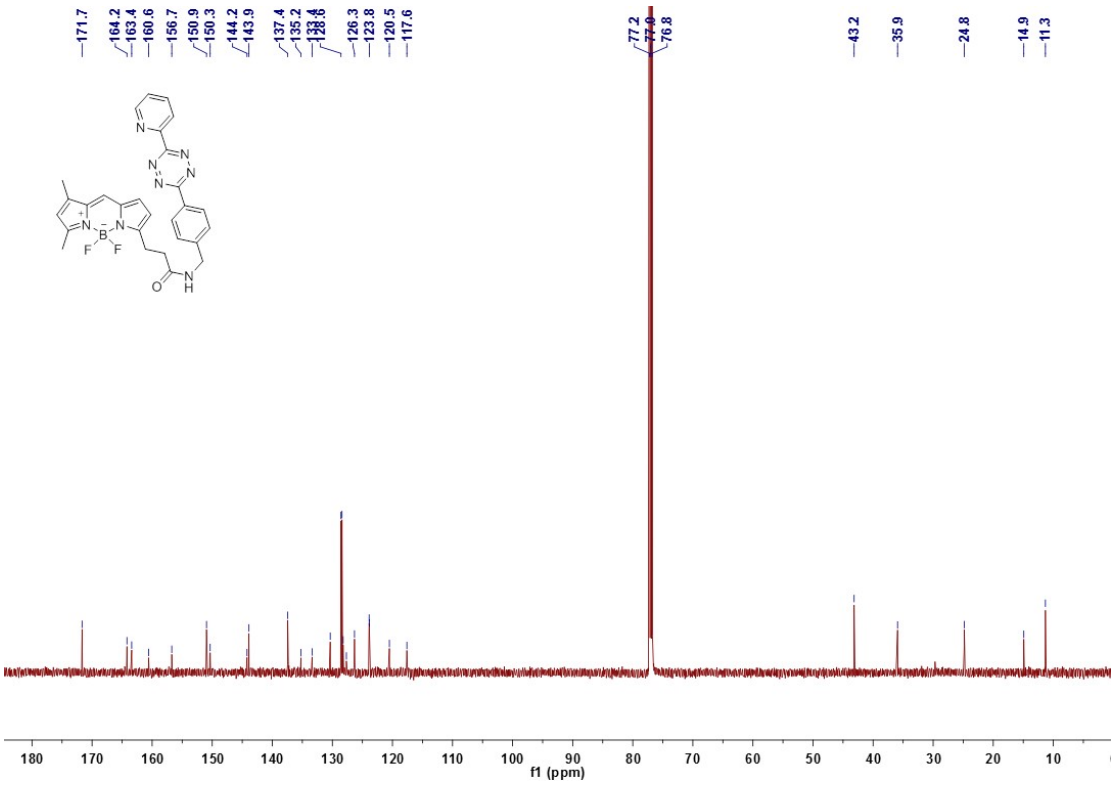
Compound 65 ^{13}C NMR



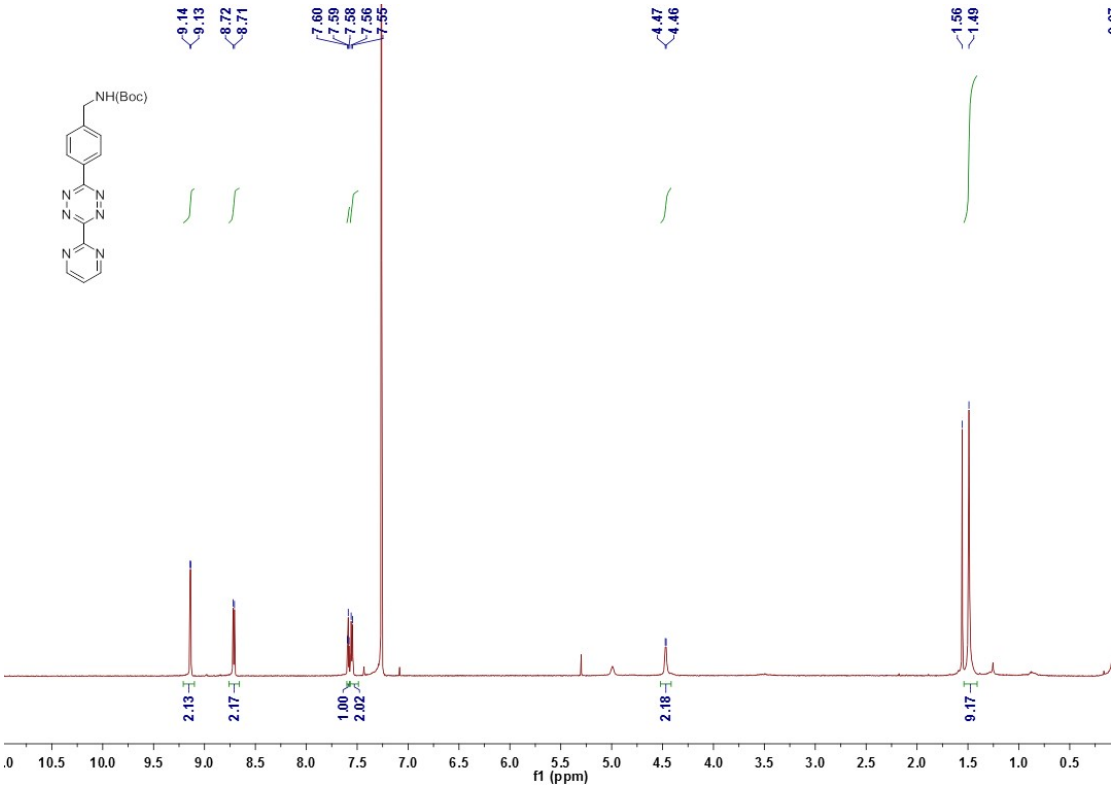
Compound 66 ^{1}H NMR



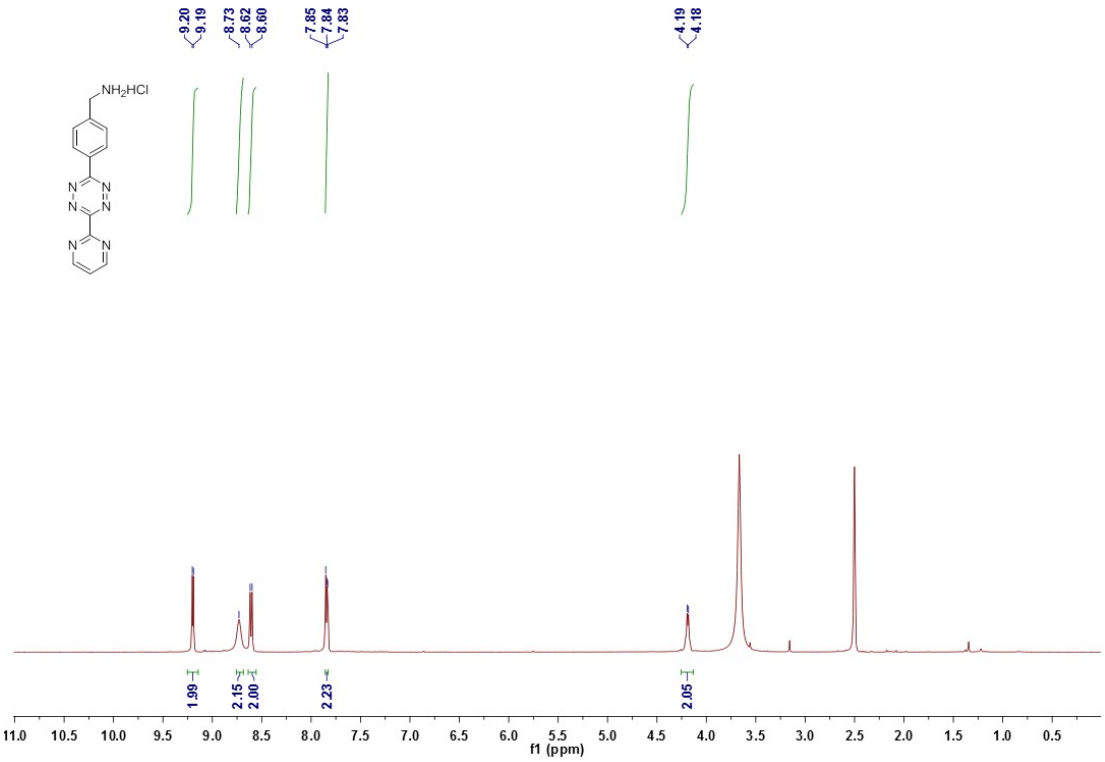
Compound 66 ^{13}C NMR



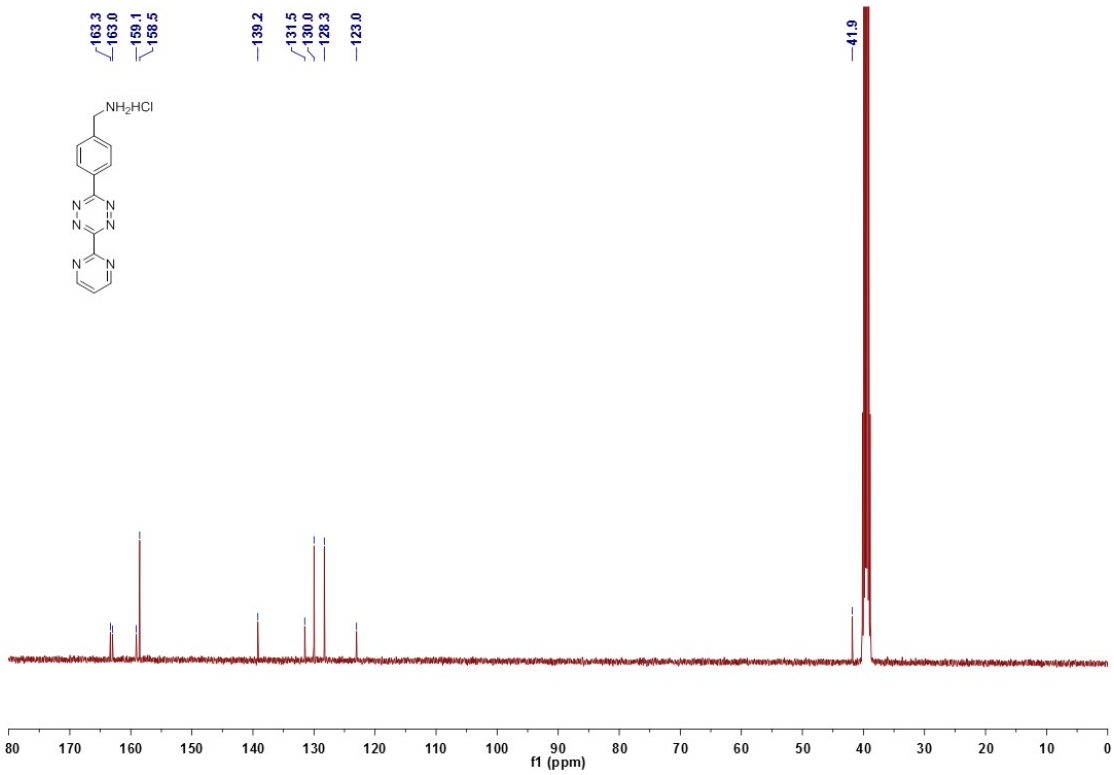
Compound 68 ^{1}H NMR



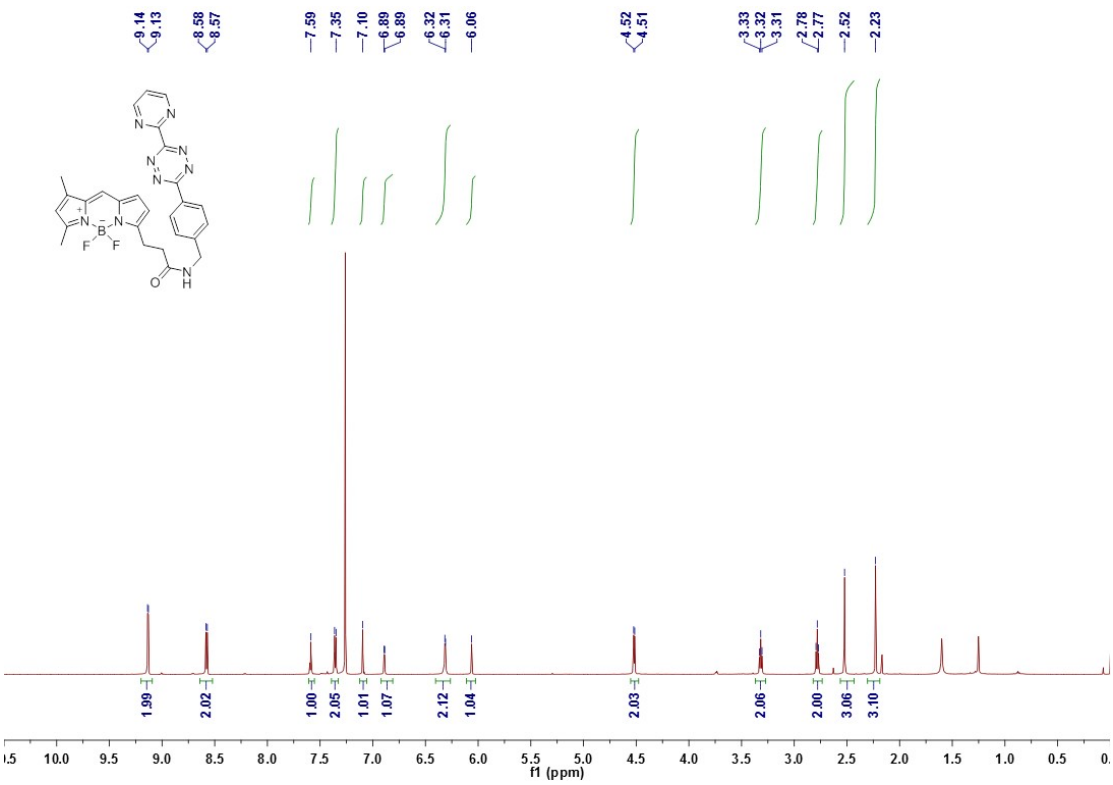
Compound 69 ^{1}H NMR



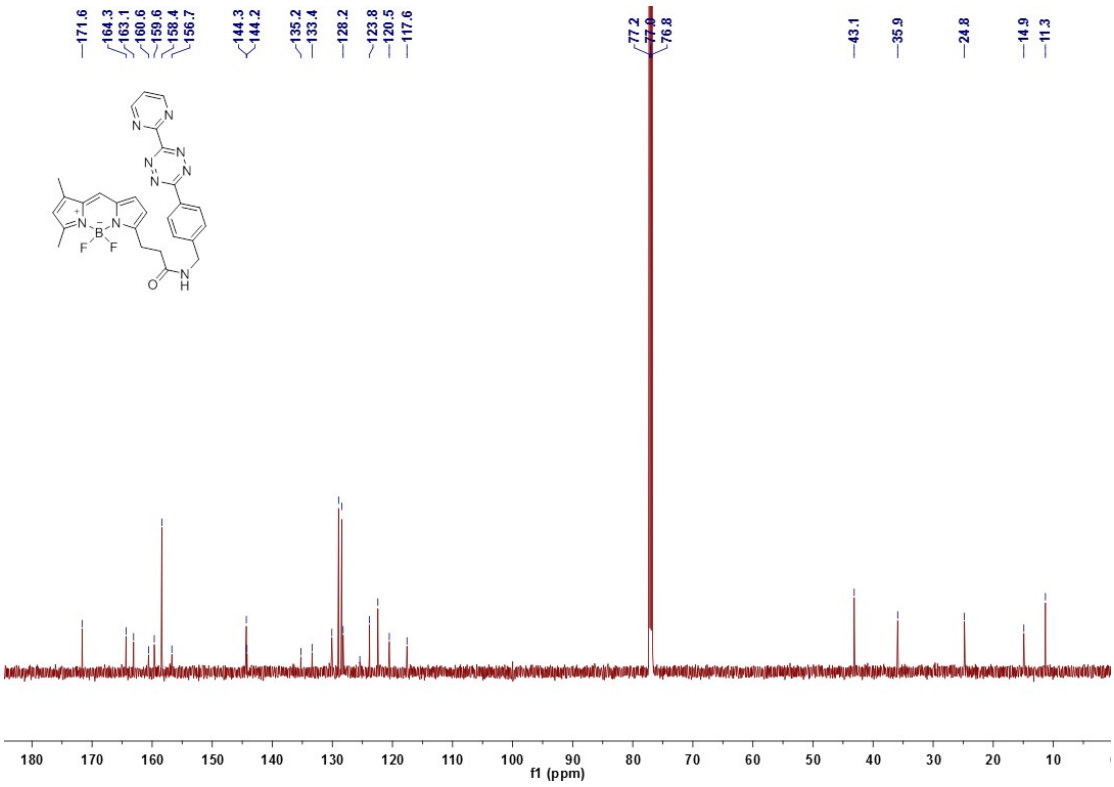
Compound 69 ^{13}C NMR



Compound 70 ^{1}H NMR



Compound 70 ^{13}C NMR



References

[1] Birkofer, Leonhard, Kittler, Juergen, *Chemische Berichte*, **1982**, *115*, 3737-3746.

[2] J. N. N. Eildal, A. Bach, J. Dogan, F. Ye, M. J. Zhang, P Jemth, *Chembiochem*., **2015**, *16*, 64-49.
[3] C. D. Spicer, M. A. Booth, D. Mawad, A. Armgarth, C. B. Nielsen, M. M. Stevens, *Chem*, **2017**, *2*, 125-138.
[4] X. Wu, X. Zong, M. Ji, *J. Chem. Res*., **2016**, *40*, 368-370.
[5] X. Wu, X. Zong, M. Ji, *J. Chem. Res*., **2016**, *6*, 368-370.
[6] H. Chen, R. Y. Mao, M. Brzozowski, N. H. Nguyen, B. E. Sleebs, *Org. Lett*., **2021**, *23*, 4244-4249.
[7] Z. Huang, O. Kwon, H. Y. Huang, A. Fadli, X. Marat, M. Moreau, J. P. Lumb, *Angew. Chem. Int. Ed*., **2018**, *57*, 11963-11967.
[8] S. N. Geigle, L. A. Wyss, S. J. Sturla, D. G. Gillingham, *Chem. Sci*., **2017**, *8*, 499-506.
[9] T. Maruyama, N. Moriwaka, Y. Demizu, M. Ohtsuka, *Tetrahedron Lett*., **2005**, *46*, 8225-8228.
[10] J. Yang, M. R. Karver, W. L. Li, S. Sahu, N. K. Devaraj, *Angew. Chem. Int. Ed*., **2012**, *51*, 5222-5225.