

# Intramolecular Thiol-yne Cyclisation as a Novel Strategy for Thioglycal Synthesis†

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## Supporting Information

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## **Experimental**

### **General Information**

NMR spectra were recorded at room temperature on a Bruker Advance 400 spectrometer,  $^1\text{H}$  (400 MHz) and  $^{13}\text{C}$  (100 MHz). Chemical shifts are reported in parts per million (ppm); coupling constant are reported in units of Hertz (Hz). Mass spectrometry analysis was performed with a Q-Tof Premier Waters Maldi-quadrupole time-of-flight (Q-Tof) mass spectrometer equipped with Z-spray electrospray ionization (ESI) and matrix assisted laser desorption ionisation (MALDI) sources. Optical rotation measurements were recorded using a Rudolf Research Analytical Autopol IV instrument. Unless otherwise stated, all reactions were carried out under a nitrogen atmosphere. All UV reactions were carried out in a Luzchem photoreactor, LZC-EDU (110 V/60 Hz) containing 10 UV lamps (8 watts, UVA blacklight blue 400-315 nm). Analytical thin-layer chromatography was performed using Merck 60 F<sub>254</sub> silica gel and visualised by UV irradiation and molybdenum staining. Purifications were performed by flash column chromatography on silica gel Kieselgel SI60 (40–63  $\mu\text{m}$ ) from Fluka. Dichloromethane and methanol were distilled from calcium hydride under nitrogen prior to use. Tetrahydrofuran was distilled from sodium / benzophenone under nitrogen prior to use. Dimethylformamide was used dry from sure sealed bottles. Reagents were purchased from Sigma and Carbosynth and used without further purification.

### **Experimental Procedures**

#### **(2R,3R,4R)-1,3,4-tris(benzyloxy)hex-5-yn-2-ol (2)**

To a stirred solution of trimethylsilyldiazomethane (3.56 mL, solution 2 M in hexane, 7.13 mmol) in dry THF (60 mL) was added lithium diisopropylamide (14 mL, solution 1.02 M in THF/heptanes/ethylbenzene, 14.25 mmol) at -20 °C. After stirring for 1 hour at this temperature, the mixture was cooled to -78 °C and a solution of 2,3,5-tri-*O*-benzyl-D-arabinofuranose **1** (2.0 g, 4.75 mmol) in dry THF (40 mL) was added via syringe. The resulting mixture was allowed to warm to room temperature over a period of 8 hours. The reaction was quenched by the addition of water (10 mL) and diethyl ether (200 mL) was added. The organic layer was separated and the aqueous layer was extracted with diethyl ether (3x200 mL). The ethereal layers were combined, dried over  $\text{MgSO}_4$ , and evaporated under reduced pressure. The residue was dissolved in MeOH (20 mL) and KF was added (2.76 g, 47.5 mmol). After being stirred for 2 hours at room temperature, the solvent was removed under reduced pressure and the residue was partitioned between dichloromethane (100 mL) and water (100 mL). The organic phase was washed with water (2x50 mL), dried over  $\text{MgSO}_4$  and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexane 10% ethyl acetate) to afford **2** as a colourless oil (1.4 g, 70%).  $[\alpha]_{\text{D}}^{23}$ : -29.8 (c = 1.06,  $\text{CHCl}_3$ ); Rf: 0.35 (hexane 10% ethyl acetate);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.21 – 7.40 (m, 15H, Ph), 4.86 and 4.55 (AB system,  $J = 12$  Hz, 2H,  $\text{PhCH}_2\text{O}$ ), 4.83 and 4.62 (AB system,  $J = 11.6$  Hz, 2H,  $\text{PhCH}_2\text{O}$ ), 4.51 and 4.48 (AB system,  $J = 12$  Hz, 2H,  $\text{PhCH}_2\text{O}$ ), 4.41 (dd,  $J = 2.2$  Hz,  $J = 3.7$  Hz, 1H, H-4), 4.08 – 4.16 (m, 1H, H-2), 3.75 (dd,  $J = 3.8$  Hz,  $J = 7.3$  Hz, 1H, H-3), 3.64 (dd,  $J = 3.3$  Hz,  $J = 9.9$  Hz, 1H, H-1), 3.59 (dd,  $J = 5.1$  Hz,  $J = 9.9$  Hz, 1H, H-1), 2.55 (d,  $J = 2.2$  Hz, 1H, H-6);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  138.1, 137.3, 128.6, 128.5, 128.45, 128.4, 128.3, 128.1, 128.0, 127.9, 127.8 (Ar-C), 80.5 (C-5), 80.1 (C-3), 76.2 (C-6), 74.5 ( $\text{PhCH}_2$ ), 73.5 ( $\text{PhCH}_2$ ), 71.1 ( $\text{PhCH}_2$ ), 70.7 (C-1), 70.3 (C-2), 68.8 (C-4); HRMS (ESI+) for  $\text{C}_{27}\text{H}_{28}\text{NaO}_4$   $[\text{M} + \text{Na}]^+$ : calcd 439.1880; found 439.1880.

### **S-((2S,3S,4R)-1,3,4-tris(benzyloxy)hex-5-yn-2-yl) ethanethioate (3)**

To a stirred solution of **2** (975 mg, 2.43 mmol) in dry dichloromethane (25 mL) was added pyridine (393  $\mu$ L, 4.86 mmol). The reaction mixture was cooled to 0 °C with an ice bath and trifluoromethanesulfonic anhydride (614  $\mu$ L, 3.65 mmol) was added dropwise. The reaction mixture was stirred for 2 hours at room temperature and the solution was filtered over a pad of silica and eluted with dichloromethane. The filtrate was evaporated under reduced pressure and dried under high vacuum. The crude triflate was solubilized in dry DMF (5 mL) and cooled to 0 °C with an ice bath. Potassium thioacetate (554 mg, 4.86 mmol) was added and the reaction mixture was stirred for 2 hours at 0 °C. The reaction mixture was diluted with diethyl ether (50 mL), washed with water (2x25 mL), brine (2x25 mL), dried over MgSO<sub>4</sub> and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexane 10% ethyl acetate) to afford **3** (868 mg, 75%) as pale yellow oil.  $[\alpha]_D^{23}$ : -1.55 (c = 0.1, CHCl<sub>3</sub>); Rf: 0.31 (hexane 20% diethyl ether); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.32-7.40 (m, 15H, Ph), 5.01 and 4.67 (AB system, *J* = 11.45 Hz, 2H, PhCH<sub>2</sub>O), 4.92 and 4.61 (AB system, *J* = 11.45 Hz, 2H, PhCH<sub>2</sub>O), 4.61 and 4.47 (AB system, *J* = 11.45 Hz, 2H, PhCH<sub>2</sub>O), 4.46 (m, 2H, H-4 and H-6), 4.32 (d, *J* = 8.38 Hz, 1H, H-3), 3.74 (t, *J* = 9.69 Hz, 1H, H-1), 3.62 (m, 1H, H-1), 2.65 (s, 1H, H-6), 2.36 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) 194.5 (C=O), 138.4, 137.9, 137.5, 128.3, 128.2, 128.1, 127.8, 127.6, 127.5, 127.4 (Ar-C), 79.6 (C-5), 79.1 (C-3), 76.7 (C-6), 75.4 (PhCH<sub>2</sub>), 73.1 (C-4), 72.5 (PhCH<sub>2</sub>), 71.4 (PhCH<sub>2</sub>), 69.6 (C-1), 45.2 (C-2); HRMS (ESI+) C<sub>29</sub>H<sub>30</sub>NaO<sub>4</sub>S [M + Na]<sup>+</sup>: calcd 497.1763; found 497.1756.

### **1-deoxy-1-methylene-2,3,5-tri-O-benzyl-4-thio-L-xylofuranose (4)**

To a stirred solution of **3** (120 mg, 0.25 mmol) in MeOH (1 mL) was added a freshly prepared solution of sodium methoxide in methanol (1 mL). After being stirred for 1 h, the solution was neutralized with Dowex® H<sup>+</sup> form. The resin was filtered off, washed thoroughly with MeOH and the filtrate was evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexane 5% ethyl acetate) to afford **4** (75 mg, 68%) as a colourless oil.  $[\alpha]_D^{22}$ : -0.83 (c = 0.1, CDCl<sub>3</sub>); Rf: 0.25 (hexane 10% diethyl ether); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.29-7.38 (m, 15H, PhCH), 5.31 (s, 1H, C=CH<sub>2</sub>), 5.27 (s, 1H, C=CH<sub>2</sub>), 4.71 and 4.52 (AB system, *J* = 11.73 Hz, 2H, PhCH<sub>2</sub>O), 4.63 and 4.57 (AB system, *J* = 11.73 Hz, 2H, PhCH<sub>2</sub>O), 4.58 and 4.55 (AB system, *J* = 11.45 Hz, 2H, PhCH<sub>2</sub>O), 4.37 (d, *J* = 3.10 Hz, 1H, H-4), 4.20 (dd, *J* = 11.46 Hz, *J* = 7.03 Hz, 1H, H-2), 4.12 (t, *J* = 3.10 Hz, 1H, H-3), 3.91 (dd, *J* = 9.45 Hz, *J* = 7.03 Hz, 1H, H-1), 3.71 (dd, *J* = 9.45 Hz, *J* = 7.03 Hz, 1H, H-1); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  145.3 (C-5), 137.9, 137.8, 137.6, 128.3, 128.2, 127.8, 127.7, 127.6, 127.5, 127.5, 127.4 (Ar-C), 108.1 (C=CH<sub>2</sub>), 82.2 (C-3), 73.2 (PhCH<sub>2</sub>), 72.3 (PhCH<sub>2</sub>), 70.0 (PhCH<sub>2</sub>), 68.9 (C-1), 50.2 (C-2); HRMS (ESI+) C<sub>27</sub>H<sub>28</sub>NaO<sub>3</sub>S [M + Na]<sup>+</sup>: calcd 455.1651; found 455.1652.

### **(2S,3S,4R)-1,3,4-tris(benzyloxy)hex-5-yn-2-yl 4-nitrobenzoate**

To a stirred solution of **2** (1.3 g, 3.12 mmol) in dry THF (25 mL) was added triphenylphosphine (1.64 g, 6.24 mmol) and 4-nitrobenzoic acid (782.12 mg, 4.68 mmol). The reaction mixture was cooled to 0 °C with an ice bath and diisopropyl azodicarboxylate (1.23 mL, 6.24 mmol) was added dropwise. The reaction mixture was warmed to room temperature and stirred for 16 h. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel (hexane 10% diethyl ether) to afford the nitrobenzoate (1.59 g, 90%) as a colourless viscous oil.  $[\alpha]_D^{23}$ : -31.8 (c = 0.27, CHCl<sub>3</sub>); Rf: 0.24 (hexane 20% diethyl ether); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.22 and 8.09 (AB system, *J* = 8.5 Hz, 4H, PhNO<sub>2</sub>), 7.19 – 7.38 (m, 15H, Ph), 5.66 – 5.76 (m, 1H, H-2), 4.91 and 4.64 (AB system, *J* = 11.5 Hz, 2H, PhCH<sub>2</sub>O), 4.84 and 4.49 (AB system, *J* = 11.6 Hz,

2H, PhCH<sub>2</sub>O), 4.45 and 4.45 (AB system, *J* = 12.1 Hz, 2H, PhCH<sub>2</sub>O), 4.34 (dd, *J* = 2.1 Hz, *J* = 5.9 Hz, 1H, H-4), 4.04 (dd, *J* = 4.6 Hz, *J* = 5.5 Hz, 1H, H-3), 3.72 (dd, *J* = 5.4 Hz, *J* = 10.3 Hz, 1H, H-1), 3.65 (dd, *J* = 5.9 Hz, *J* = 10.3 Hz, 1H, H-1), 2.54 (d, *J* = 2.1 Hz, 1H, H-6) <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 164.1 (C=O), 150.6 (CNO<sub>2</sub>), 138.1, 137.8, 137.2, 135.6, 131.1, 128.6, 128.5, 128.2, 128.1, 127.9, 127.8, 123.6 (Ar-C), 79.5 (C-5), 79.1 (C-3), 76.7 (C-6), 75.3 (PhCH<sub>2</sub>O), 73.7 (C-2), 73.3 (PhCH<sub>2</sub>O), 71.2 (PhCH<sub>2</sub>O), 69.6 (C-4), 67.9 (C-1); HRMS (ESI+) C<sub>34</sub>H<sub>31</sub>NNaO<sub>7</sub> [M + Na]<sup>+</sup> : calcd 588.1998 ; found 588.2000.

#### **(2S,3R,4R)-1,3,4-tris(benzyloxy)hex-5-yn-2-ol (5)**

To a stirred solution of the nitrobenzoate (1.2 g, 2.12 mmol) in MeOH (20 mL) was added a freshly prepared solution of sodium methoxide in methanol (2 mL). After being stirred for 2 h, the solution was neutralized with Dowex® H+ form. The resin was filtered off, washed thoroughly with MeOH and the filtrate was evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexane 30% diethyl ether) to afford **5** (870 mg, 98%), (88% over two steps), as a colourless oil. [ $\alpha$ ]<sub>D</sub><sup>23</sup>: -28.1 (c = 0.18, CHCl<sub>3</sub>); Rf: 0.36 (hexane 50% diethyl ether); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.25 – 7.45 (m, 15H, Ph), 4.95 and 4.60 (AB system, *J* = 11.1 Hz, 2H, PhCH<sub>2</sub>O), 4.89 and 4.57 (AB system, *J* = 11.7 Hz, 2H, PhCH<sub>2</sub>O), 4.51 and 4.46 (AB system, *J* = 11.9 Hz, 2H, PhCH<sub>2</sub>O), 4.46 (dd, *J* = 2.1 Hz, *J* = 7.1 Hz, 1H, H-4), 4.22 (dt, *J* = 2.5 Hz, *J* = 6.1 Hz, 1H, H-2), 3.79 (dd, *J* = 2.5 Hz, *J* = 7.1 Hz, 1H, H-3), 3.50 (dd, *J* = 6.2 Hz, *J* = 9.6 Hz, 1H, H-1), 3.45 (dd, *J* = 6.1 Hz, *J* = 9.6 Hz, 1H, H-1), 2.61 (d, *J* = 2.1 Hz, 1H, H-6) <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 138.2, 138.1, 137.6, 128.6, 128.5, 128.4, 128.2, 128.0, 127.9 (Ar-C), 80.2 (C-5), 79.9 (C-3), 76.4 (C-6), 75.3 (PhCH<sub>2</sub>), 73.4 (PhCH<sub>2</sub>), 71.5 (PhCH<sub>2</sub>), 71.2 (C-1), 71.1 (C-4), 70.2 (C-2); HRMS (ESI+) C<sub>27</sub>H<sub>28</sub>NaO<sub>4</sub> [M + Na]<sup>+</sup> : calcd 439.1885 ; found 439.1883.

#### **S-((2R,3S,4R)-1,3,4-tris(benzyloxy)hex-5-yn-2-yl) ethanethioate (6)**

To a stirred solution of **5** (800 mg, 1.92 mmol) in dry dichloromethane (19 mL) was added pyridine (310 μL, 3.84 mmol). The reaction mixture was cooled to 0 °C with an ice bath and trifluoromethanesulfonic anhydride (485 μL, 2.88 mmol) was added dropwise. The reaction mixture was stirred for 2 hours at room temperature and the solution was filtered over a pad of silica and eluted with dichloromethane. The filtrate was evaporated under reduced pressure and dried under high vacuum. The crude triflate was solubilized in dry DMF (5 mL) and cooled to 0 °C with an ice bath. Potassium thioacetate (438.6 mg, 3.84 mmol) was added and the reaction mixture was stirred for 2 hours at 0 °C. The reaction mixture was diluted with diethyl ether (50 mL), washed with water (2x25 mL), brine (2x25 mL), dried over MgSO<sub>4</sub> and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexane 5% ethyl acetate) to afford **6** (550 mg, 60%) as pale yellow oil. [ $\alpha$ ]<sub>D</sub><sup>23</sup>: -52.8 (c = 0.2, CHCl<sub>3</sub>); Rf: 0.31 (hexane 20% diethyl ether); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.23 – 7.37 (m, 15H, Ph), 4.90 and 4.65 (AB system, *J* = 11.2 Hz, 2H, PhCH<sub>2</sub>O), 4.83 and 4.52 (AB system, *J* = 11.6 Hz, 2H, PhCH<sub>2</sub>O), 4.51 and 4.43 (AB system, *J* = 12.1 Hz, 2H, PhCH<sub>2</sub>O), 4.47 (dd, *J* = 2.1 Hz, *J* = 6 Hz, 1H, H-4), 4.34 – 4.40 (m, 1H, H-2), 3.95 (dd, *J* = 4.5 Hz, *J* = 6 Hz, 1H, H-3), 3.74 (dd, *J* = 6.9 Hz, *J* = 10.2 Hz, 1H, H-1), 3.62 (dd, *J* = 5.5 Hz, *J* = 10.2 Hz, 1H, H-1), 2.61 (d, *J* = 2.1 Hz, 1H, H-6), 2.29 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 194.7 (C=O), 138.3, 138.1, 137.4, 128.4, 128.3, 128.2, 127.9, 127.8, 127.6, 127.55, 127.5 (Ar-C), 81.5 (C-3), 80.3

(C-5), 76.3 (C-6), 75.2 (PhCH<sub>2</sub>), 72.8 (PhCH<sub>2</sub>), 71.1 (PhCH<sub>2</sub>), 70.8 (C-4), 68.8 (C-1), 44.9 (C-2), 30.6 (CH<sub>3</sub>); HRMS (ESI+) C<sub>29</sub>H<sub>30</sub>NaO<sub>4</sub>S [M + Na]<sup>+</sup> : calcd 497.1763 ; found 497.1756.

#### **1-deoxy-1-methylene-2,3,5-tri-*O*-benzyl-4-thio-D-arabinofuranose (7)**

To a stirred solution of **6** (91 mg, 0.21 mmol) in MeOH (1 mL) was added a freshly prepared solution of sodium methoxide in methanol (1 mL). After being stirred for 1 h, the solution was neutralized with Dowex® H<sup>+</sup> form. The resin was filtered off, washed thoroughly with MeOH and the filtrate was evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexane 5% ethyl acetate) to afford **7** (83 mg, 91%) as a colourless oil. [ $\alpha$ ]<sub>D</sub><sup>22</sup>: +16.2 (c = 0.2, CHCl<sub>3</sub>); Rf: 0.25 (hexane 10% diethyl ether); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.24 – 7.42 (m, 15H, Ph), 5.32 (bs, 1H, C=CH<sub>2</sub>), 5.24 (bs, 1H, C=CH<sub>2</sub>), 4.70 (d, PhCH<sub>2</sub>O), 4.65 (s, 2H, PhCH<sub>2</sub>O), 4.48 – 4.57 (m, 3H, PhCH<sub>2</sub>O), 4.39 (d, 1H, *J* = 3.6 Hz, H-2), 4.08 (t, 1H, *J* = 3.2 Hz, H-3), 3.77 – 3.86 (m, 2H, H-5 and H-4), 3.52 – 3.62 (m, 1H, H-5); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  145.0 (C-1), 138.1, 137.8, 137.7, 128.5, 128.4, 127.9, 127.8, 127.75, 127.7, 127.6 (Ar-C), 107.8 (C=CH<sub>2</sub>), 86.9 (C-2), 83.4 (C-3), 73.1 (PhCH<sub>2</sub>O), 72.0 (C-5), 71.9 (PhCH<sub>2</sub>O), 71.6 (PhCH<sub>2</sub>O), 51.3 (C-4); HRMS (ESI+) C<sub>27</sub>H<sub>28</sub>NaO<sub>3</sub>S [M + Na]<sup>+</sup> : calcd 455.1651 ; found 455.1652.

#### **(2R,3S,4R)-1,3,4-tris(benzyloxy)hex-5-yne-2-thiol (8)**

To a stirred solution of **6** (130 mg, 0.274 mmol) in dry THF (3 mL) was added methyllithium (1 ml solution 0.88 M in diethyl ether, 0.877 mmol) at -78 °C. The reaction mixture was warmed to -50 °C and stirred for 3 hours. The reaction was cooled to -78 °C, quenched by addition of aqueous HCl 1 M (3 mL) and diluted with diethyl ether (30 mL). The ethereal layer was washed with water (2x10 mL), dried over MgSO<sub>4</sub> and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexane 5% diethyl ether) to afford **8** (60 mg, 50%) as colourless oil. [ $\alpha$ ]<sub>D</sub><sup>22</sup>: -59 (c = 0.1, CHCl<sub>3</sub>); Rf: 0.25 (hexane 10% diethyl ether); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.24 – 7.43 (m, 15H, Ph), 5.02 and 4.66 (AB system, *J* = 11 Hz, 2H, PhCH<sub>2</sub>O), 4.89 and 4.58 (AB system, *J* = 11.8 Hz, 2H, PhCH<sub>2</sub>O), 4.69 – 4.74 (m, 1H, H-4), 4.52 and 4.49 (AB system, *J* = 11.9 Hz, 2H, PhCH<sub>2</sub>O), 3.79 – 3.89 (m, 2H, H-1 and H-3), 3.69 (dd, *J* = 4.5 Hz, *J* = 9.5 Hz, 1H, H-1), 3.34 – 3.45 (m, 1H, H-2), 2.58 (d, *J* = 2.1 Hz, H-6), 1.86 (d, *J* = 9.84 Hz, 1H, SH); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  138.3, 138.1, 137.4, 128.5, 128.4, 128.3, 128.2, 128.1, 127.9, 127.6 (Ar-C), 83.6 (C-3), 80.9 (C-5), 75.8 (C-6), 75.7 (PhCH<sub>2</sub>), 73.1 (PhCH<sub>2</sub>), 71.1 (C-1), 71.0 (PhCH<sub>2</sub>), 69.5 (C-4), 40.4 (C-2); HRMS (ESI+) C<sub>27</sub>H<sub>28</sub>NaO<sub>3</sub>S [M + Na]<sup>+</sup> : calcd 455.1651 ; found 455.1673.

#### **(2S,3S,4R)-1,3,4-tris(benzyloxy)hex-5-yne-2-thiol (9)**

To a stirred solution of **3** (200 mg, 0.422 mmol) in dry THF (4 mL) was added methyllithium (1.0 mL solution 0.16 M in diethyl ether, 1.35 mmol) at -78 °C. The reaction mixture was warmed to -50 °C and stirred for 3 hours. The reaction was cooled to -78 °C, quenched by addition of aqueous HCl 1 M (3 mL) and diluted with diethyl ether (30 mL). The ethereal layer was washed with water (2x10 mL), dried over MgSO<sub>4</sub> and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexane 5% diethyl ether) to afford **9** (58 mg, 32%) as a colourless oil. Rf: 0.25 (hexane 10% diethyl ether); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.24-7.36 (m, 15H, Ph), 4.96 and 4.61 (AB system, *J* = 11.45 Hz, 2H, PhCH<sub>2</sub>O), 4.85 and 4.56 (AB system, *J* = 11.45 Hz, 2H, PhCH<sub>2</sub>O), 4.42 (AB system, *J* = 11.45 Hz, 2H, PhCH<sub>2</sub>O), 4.10 (dd, *J* = 8.12 Hz, *J* = 1.95 Hz, 1H, H-3), 3.44-3.55 (m, 3H, H-1, H-2, H-4), 2.57 (d, *J* = 2.24 Hz, 1H, H-6), 1.68 (d, *J* = 10.16 Hz, 1H, SH); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  138.6, 137.9, 137.7, 128.4, 128.3, 128.2, 127.9, 127.8, 127.7, 127.6,

127.5 (Ar-C), 80.2 (C-5), 79.2 (C-3), 76.5 (C-6), 75.3 (PhCH<sub>2</sub>), 73.6 (C-4), 72.8 (PhCH<sub>2</sub>), 72.7 (PhCH<sub>2</sub>), 71.6 (C-1), 40.1 (C-2); HRMS (ESI+) C<sub>27</sub>H<sub>28</sub>NaO<sub>3</sub>S [M + Na]<sup>+</sup> : calcd 455.1651 ; found 455.1673.

### General Procedure for Radical Cyclisation

To a degassed solution of thiol (57.2 mg, 0.132 mmol) in dry DMF (264  $\mu$ L) was added 2,2-dimethoxy-2-phenyl-acetophenone (6.8 mg, 26.4  $\mu$ mol) and 2-methylbenzophenone (4.8  $\mu$ L, 26.4  $\mu$ mol). The solution was placed in a UV oven and irradiated for 1 h without agitation at 20 °C. DMF was removed *in vacuo* and the products were isolated by flash column chromatography on silica gel (hexane 5% ethyl acetate).

### 1-deoxy-1-methylene-2,3,5-tri-O-benzyl-4-thio-D-arabinofuranose (7)

Starting from thiol **8**, general procedure for radical cyclisation was applied. Only **7** and **8** were observed in the product mixture. Results at four different concentrations are tabulated below.

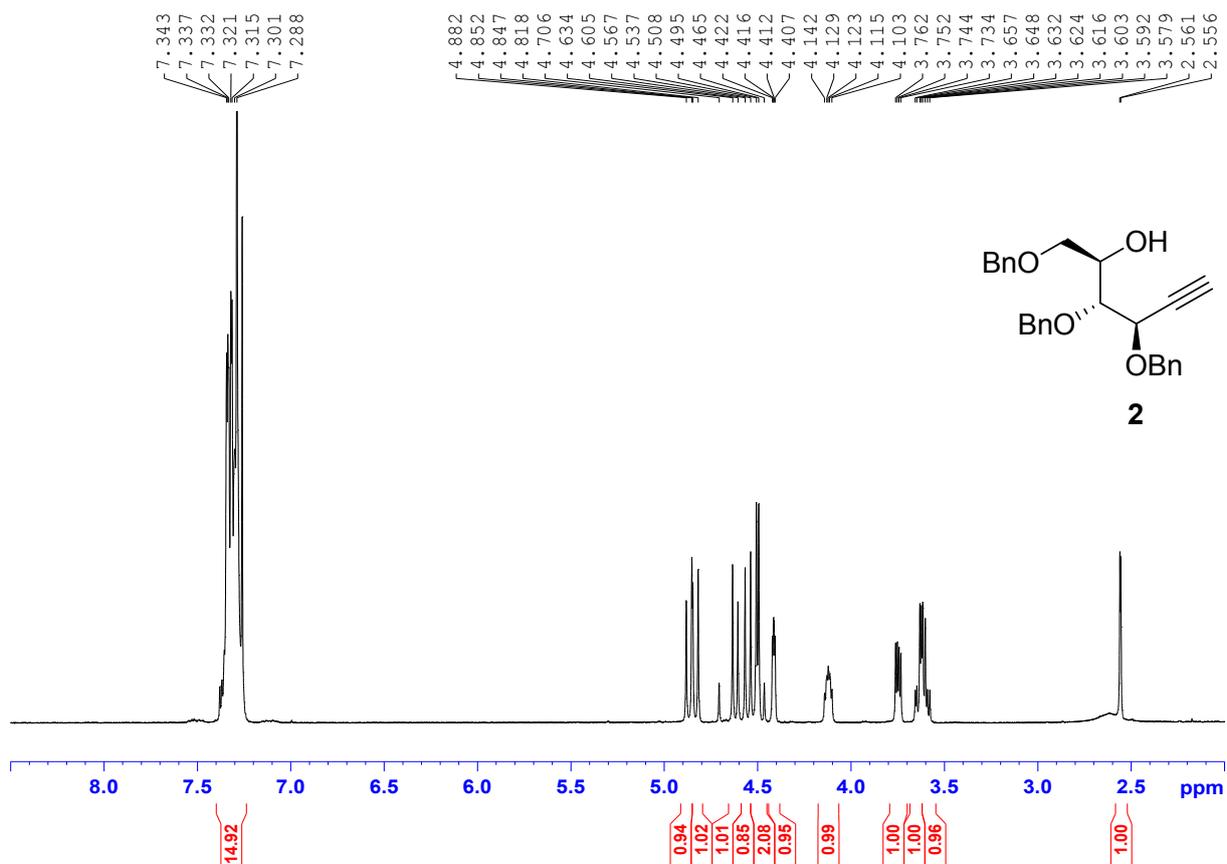
Concentration	DMF volume	% Conversion <sup>a</sup>	% 5-exo	% 6-endo
1 M	0.115 mL	40	100	0
0.5 M	0.23 mL	45	100	0
0.1 M	1.15 mL	58	100	0
0.05 M <sup>b</sup>	2.3 mL	-	-	-

<sup>a</sup> Conversion determined by <sup>1</sup>H-NMR <sup>b</sup>Reaction was incomplete at this concentration, accurate conversion could not be determined.

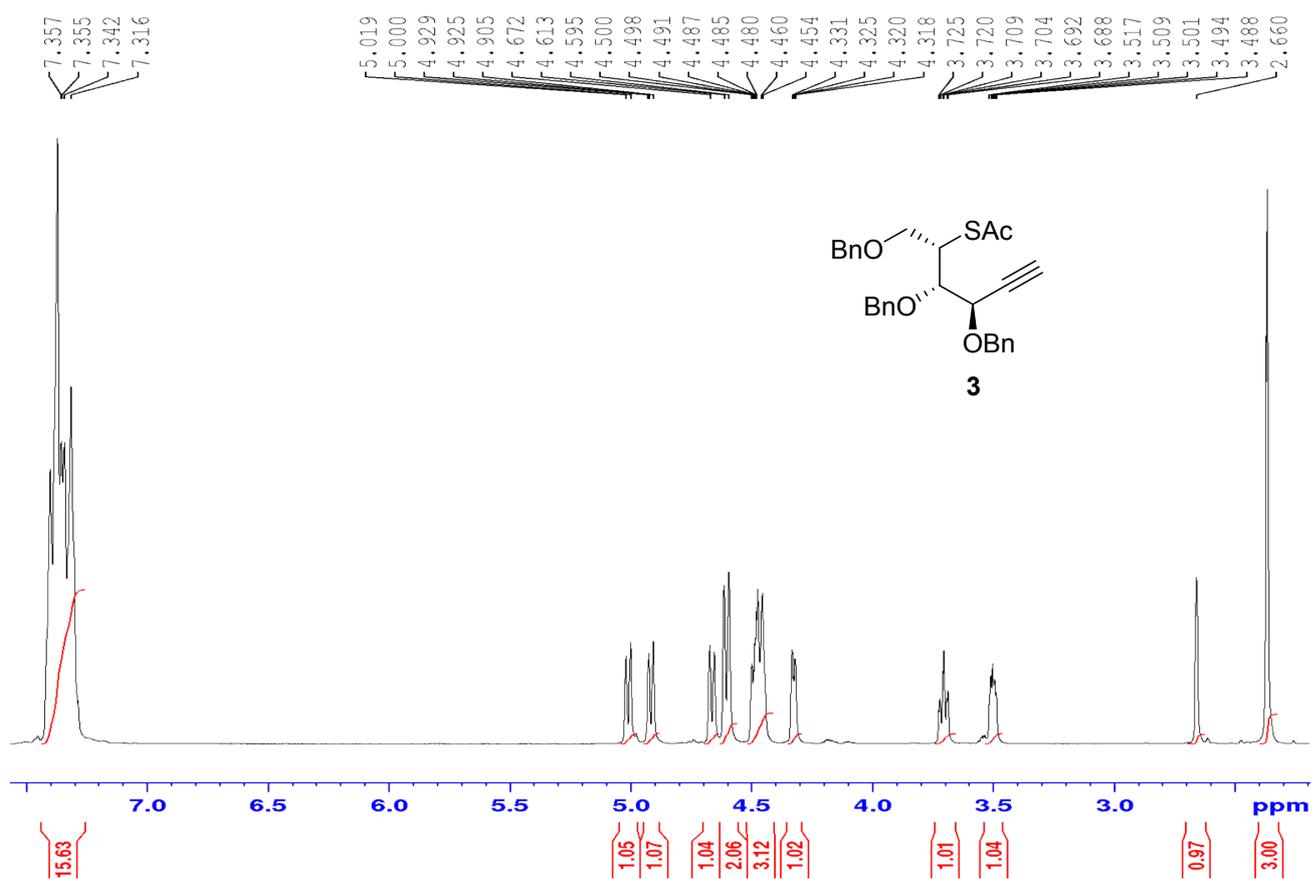
### Tri-O-benzyl-5-thioglucal (**17**)

Starting from thiol **9**, general procedure for radical cyclisation was applied. Following purification by column chromatography, **4** was isolated as a colourless oil (19 mg, 33%), **17** was isolated as a pale yellow oil (12.7 mg, 22%);  $[\alpha]_D^{22}$ : -0.32 (c = 0.1, CDCl<sub>3</sub>) <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.39-7.29 (m, 15H, Ph), 6.37 (d,  $J$  = 10.09 Hz, 1H, H-5), 5.85 (dd,  $J$  = 4.93 Hz,  $J$  = 10.09 Hz, 1H, H-6), 4.71-4.50 (m, 6H, PhCH<sub>2</sub>O), 3.98 (m, 1H, H-3), 3.91 (t,  $J$  = 4.66 Hz, 1H, H-4), 3.76 (dd,  $J$  = 6.31 Hz,  $J$  = 8.99 Hz, 1H, H-1), 3.67 (td,  $J$  = 2.08 Hz,  $J$  = 6.97 Hz, 1H, H-2), 3.63 (t,  $J$  = 8.03, 1H, H-1); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  138.3, 137.8, 128.2, 127.9, 127.7, 127.6 (Ar-C), 124.5 (C-5), 118.3 (C-6), 72.9 (PhCH<sub>2</sub>), 72.4 (C-3), 72.1 (PhCH<sub>2</sub>), 70.8 (PhCH<sub>2</sub>), 70.1 (C-4), 68.7 (C-1), 40.4 (C-2); HRMS (ESI+) C<sub>27</sub>H<sub>28</sub>NaO<sub>3</sub>S [M + Na]<sup>+</sup>: calcd 455.1651 ; found 455.1652.

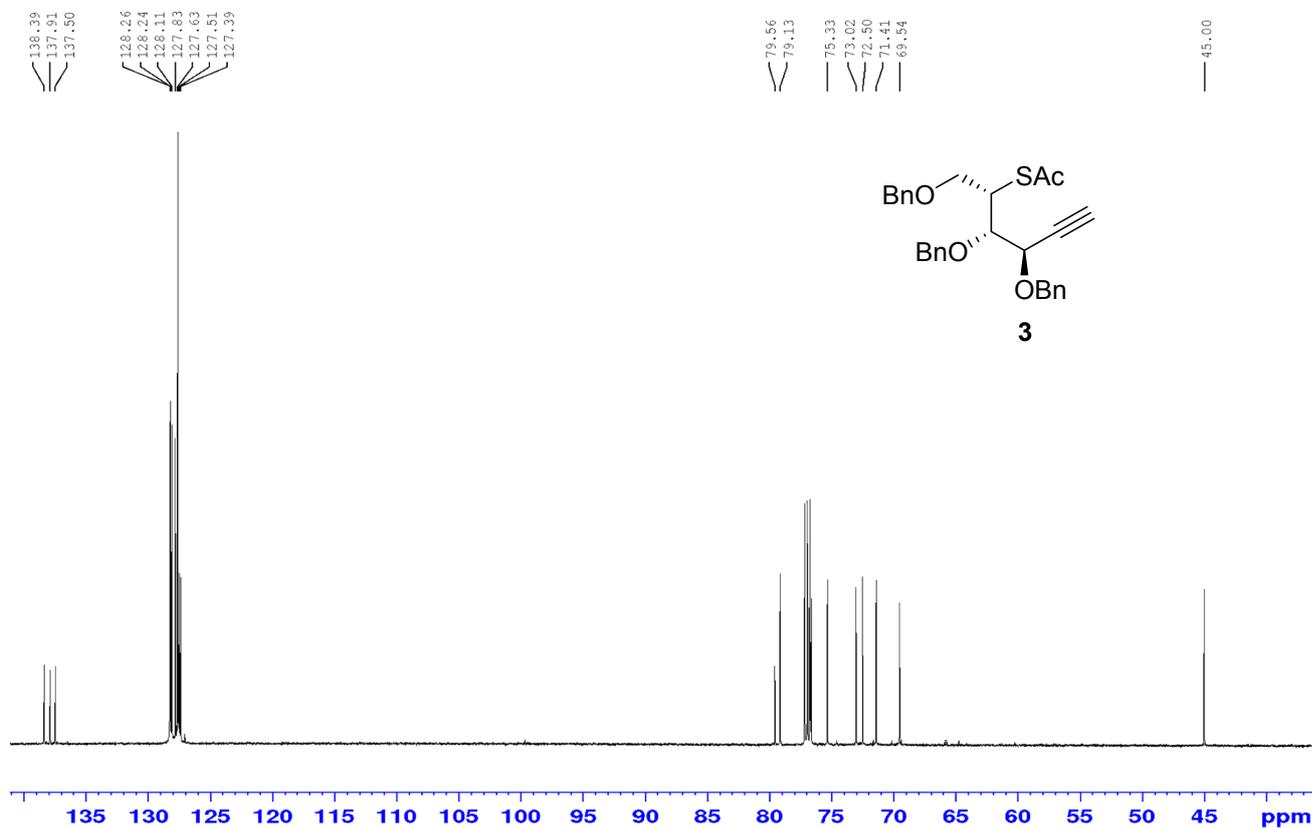
**<sup>1</sup>H NMR spectrum of compound 2 (CDCl<sub>3</sub>, 400 MHz)**



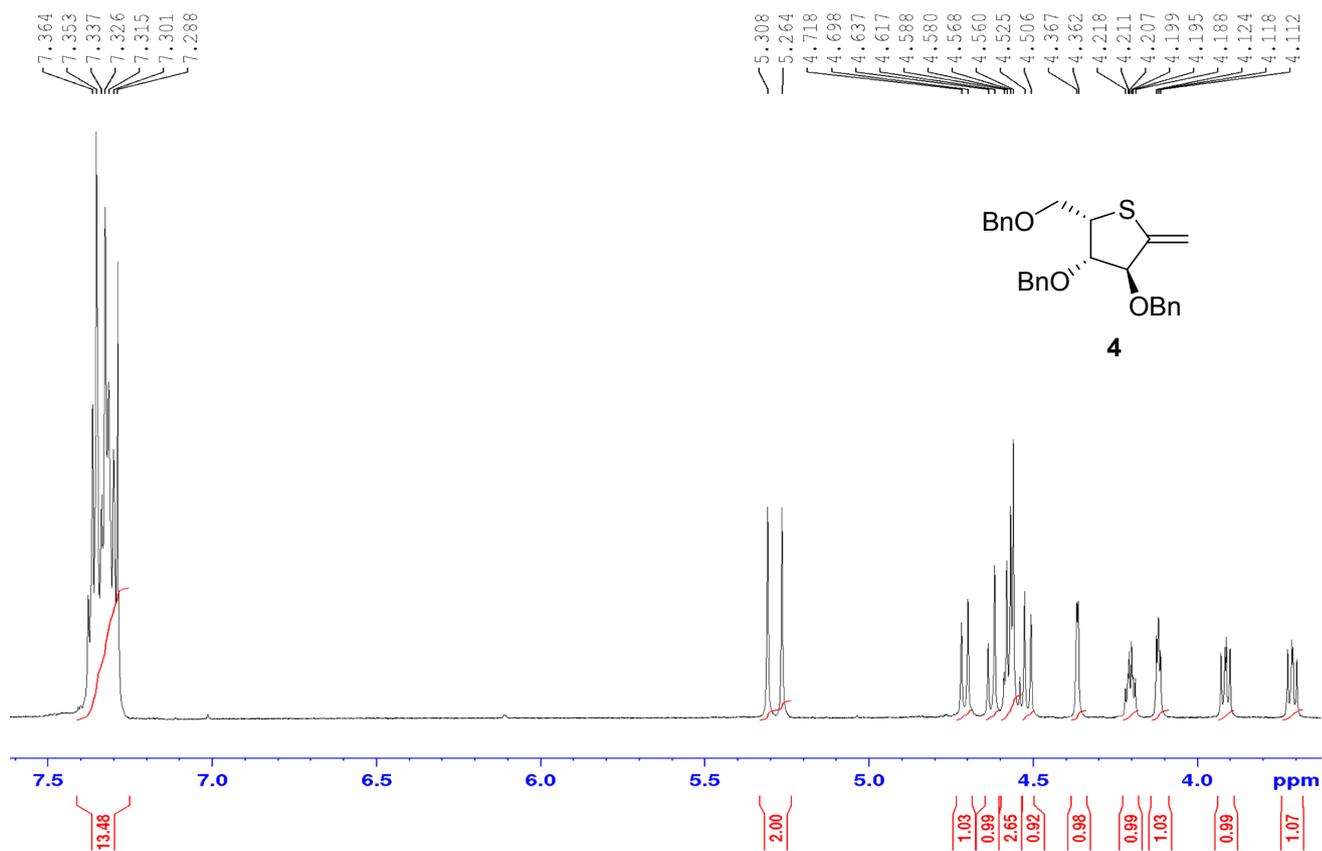
**<sup>1</sup>H NMR spectrum of compound 3 (CDCl<sub>3</sub>, 600 MHz)**



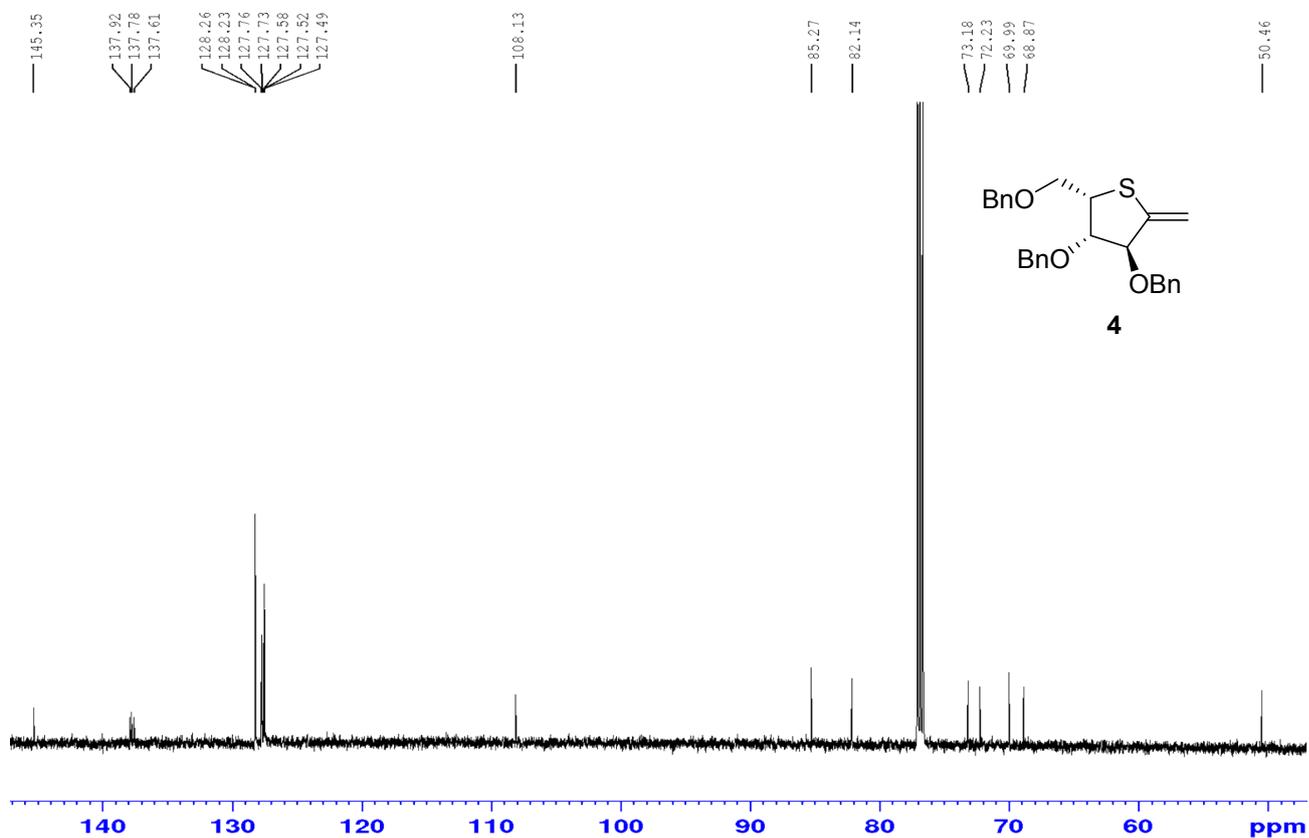
**<sup>13</sup>C NMR spectrum of compound 3 (CDCl<sub>3</sub>, 150 MHz)**



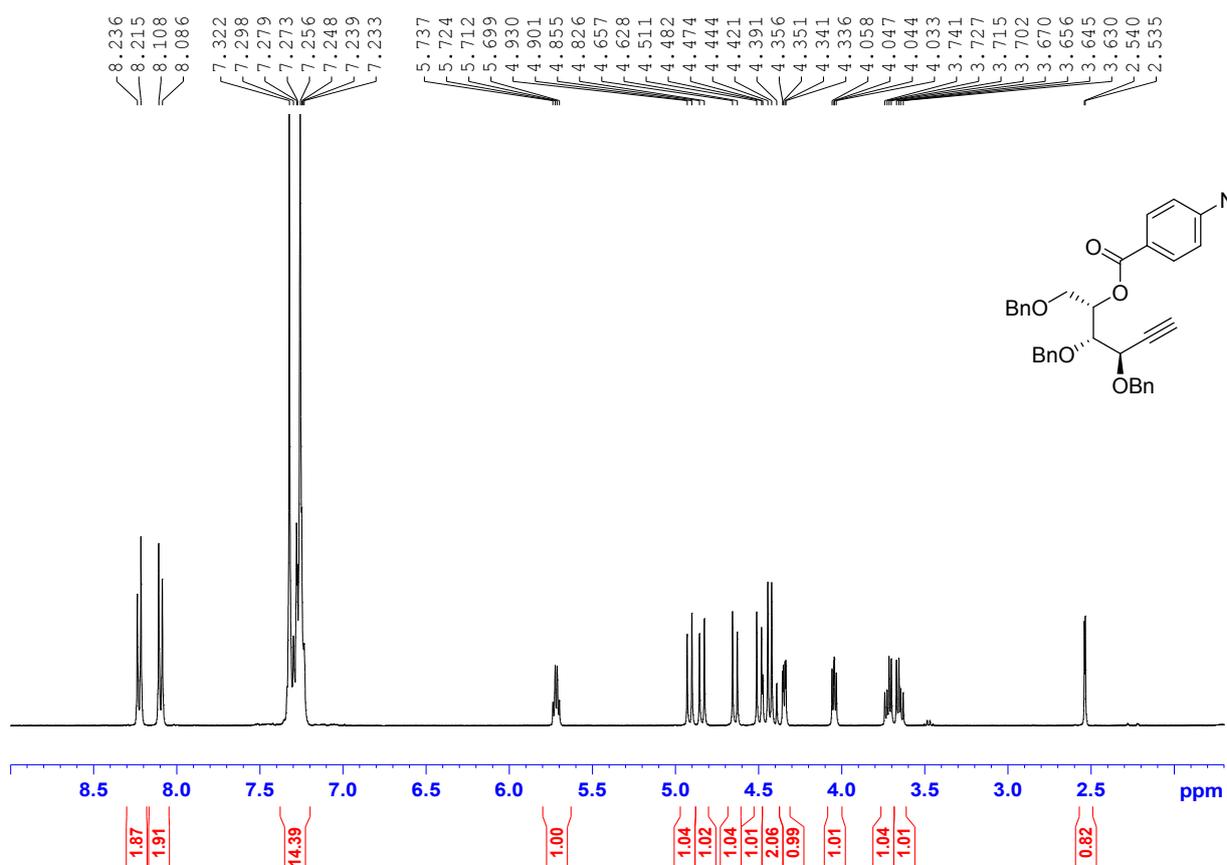
**<sup>1</sup>H NMR spectrum of compound 4 (CDCl<sub>3</sub>, 600 MHz)**



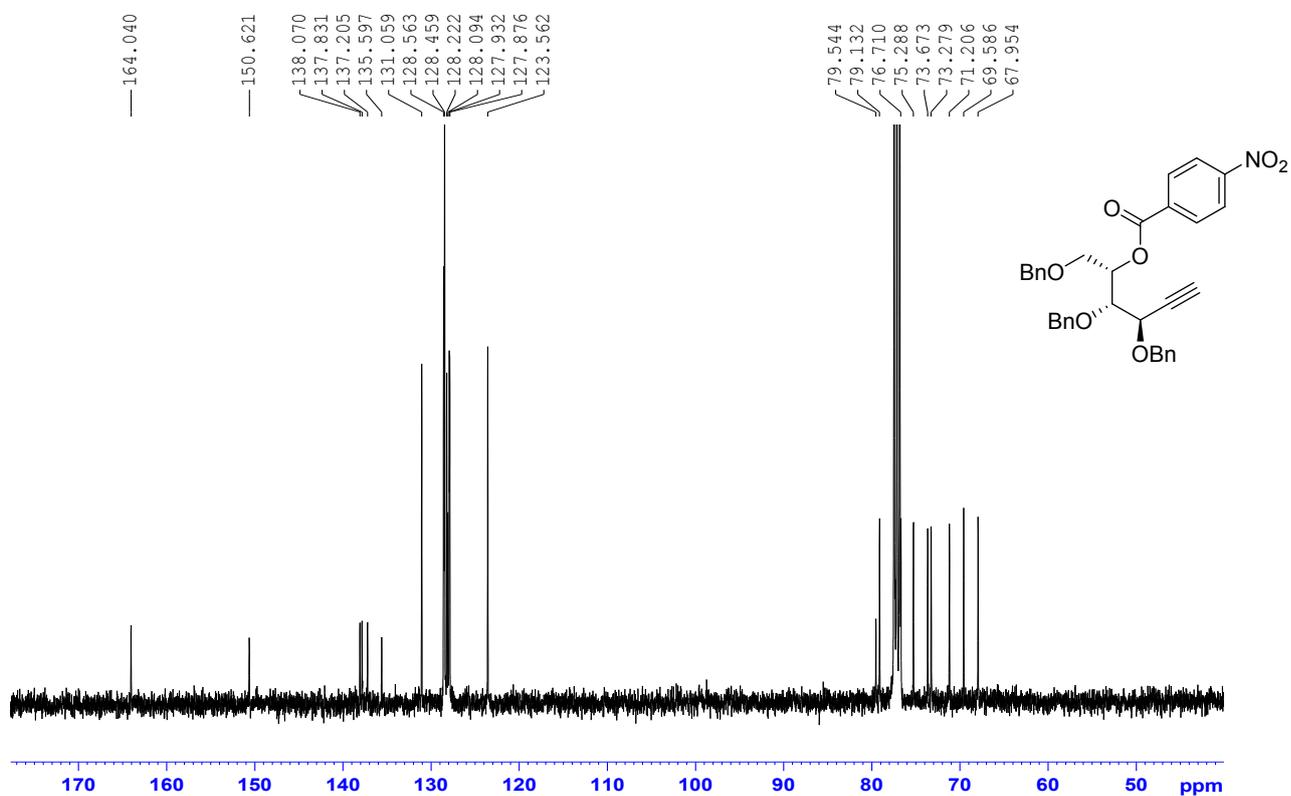
**<sup>13</sup>C NMR spectrum of compound 4 (CDCl<sub>3</sub>, 150 MHz)**



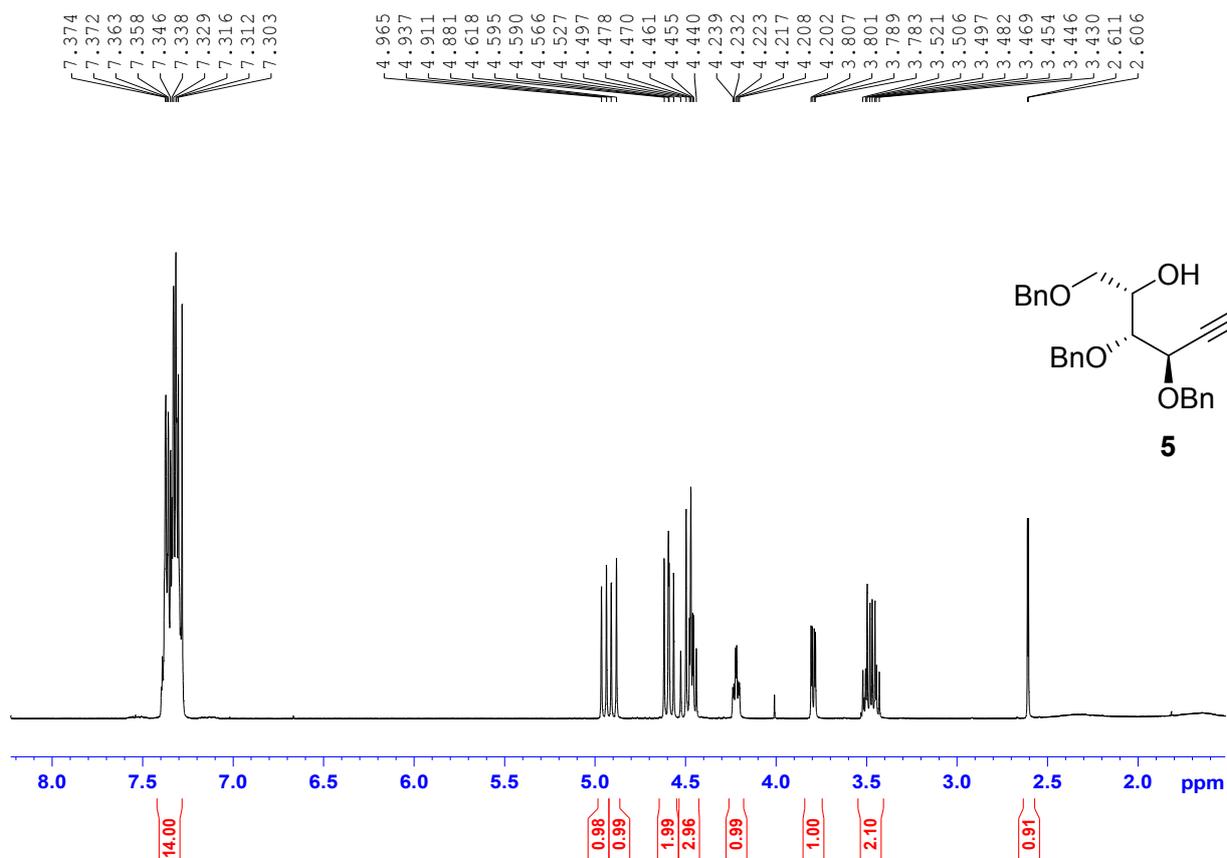
**<sup>1</sup>H NMR spectrum of nitrobenzoate (CDCl<sub>3</sub>, 400 MHz)**



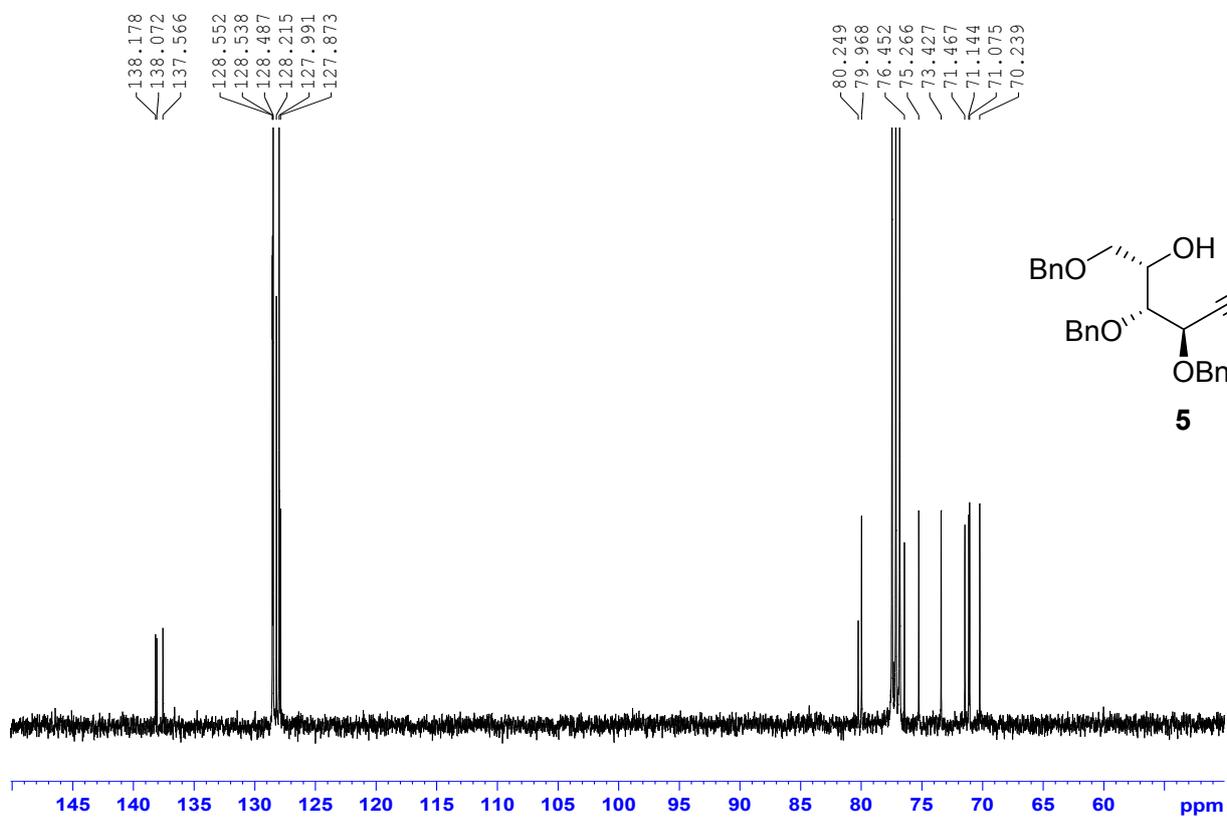
**<sup>13</sup>C NMR spectrum of compound nitrobenzoate (CDCl<sub>3</sub>, 100 MHz)**



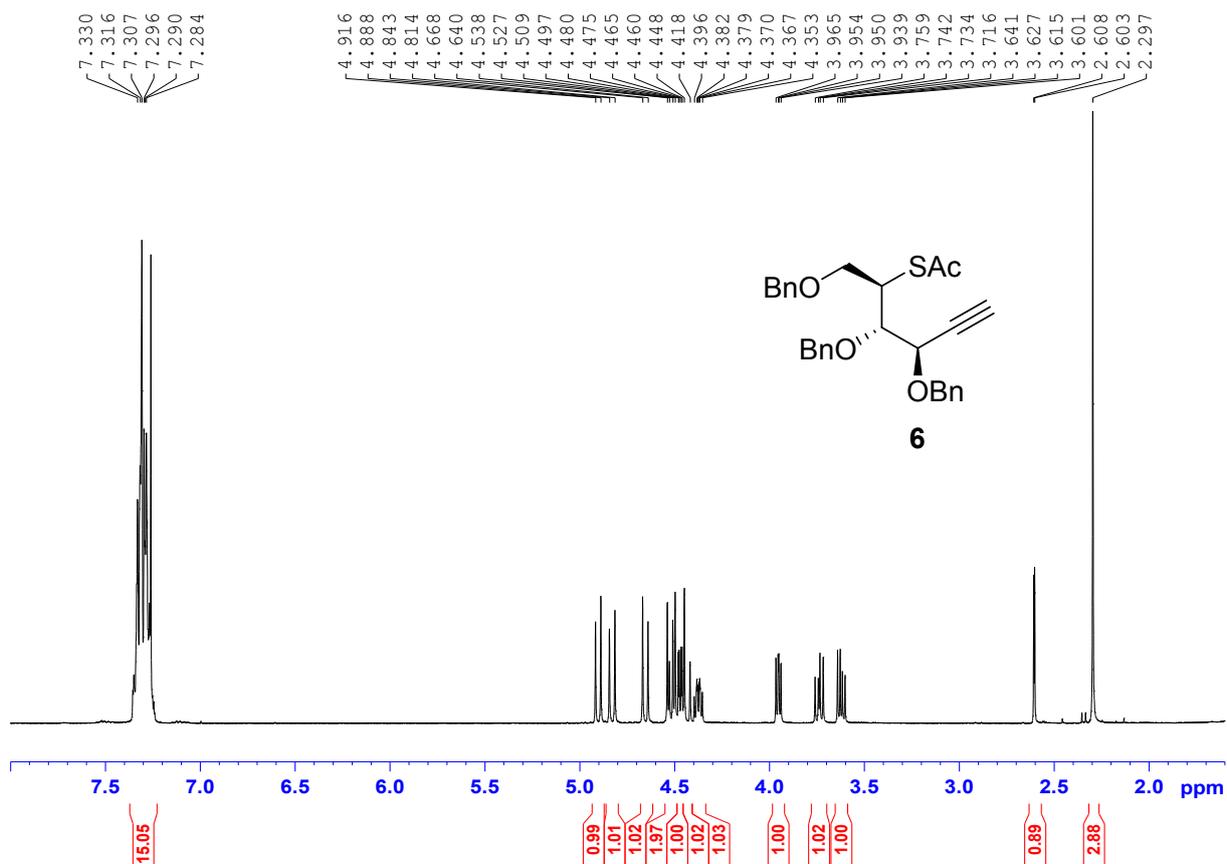
**<sup>1</sup>H NMR spectrum of compound 5 (CDCl<sub>3</sub>, 400 MHz)**



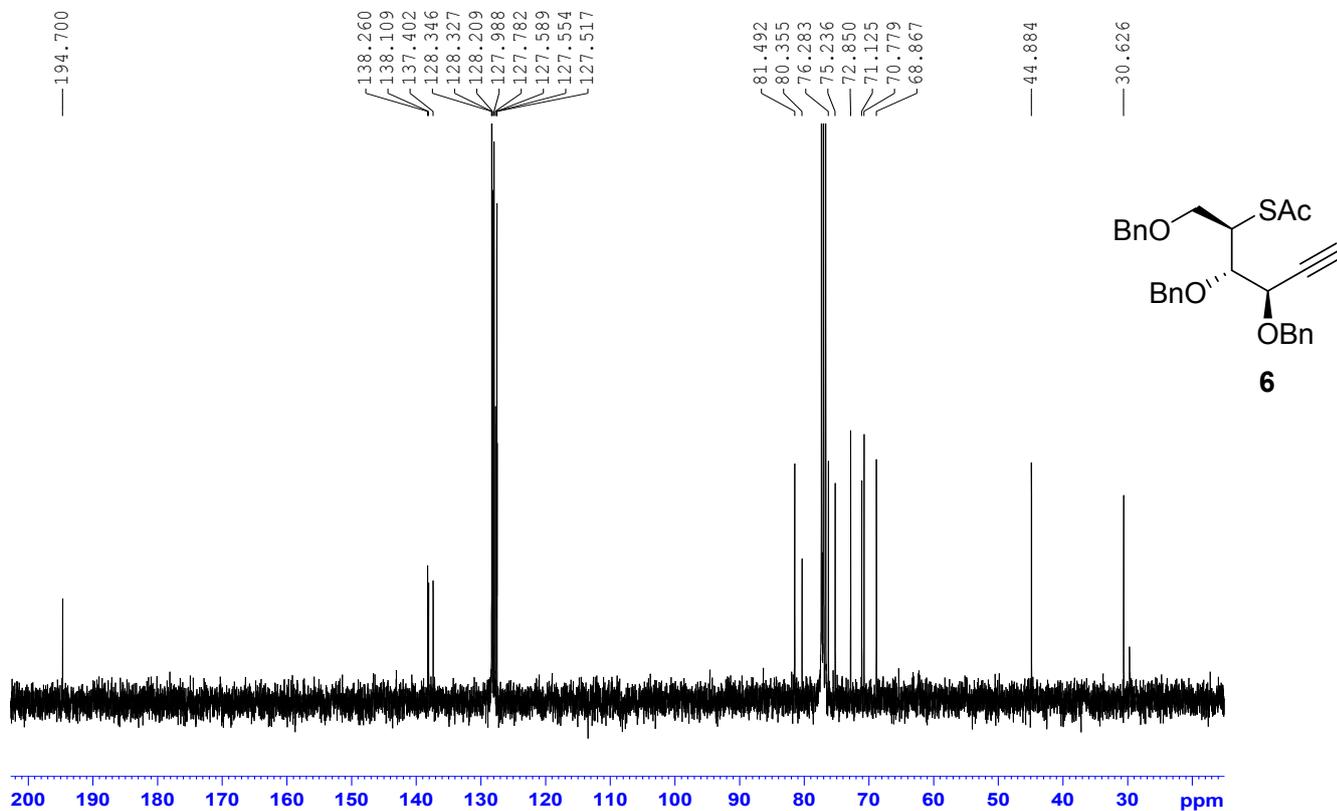
**<sup>13</sup>C NMR spectrum of compound 5 (CDCl<sub>3</sub>, 100 MHz)**



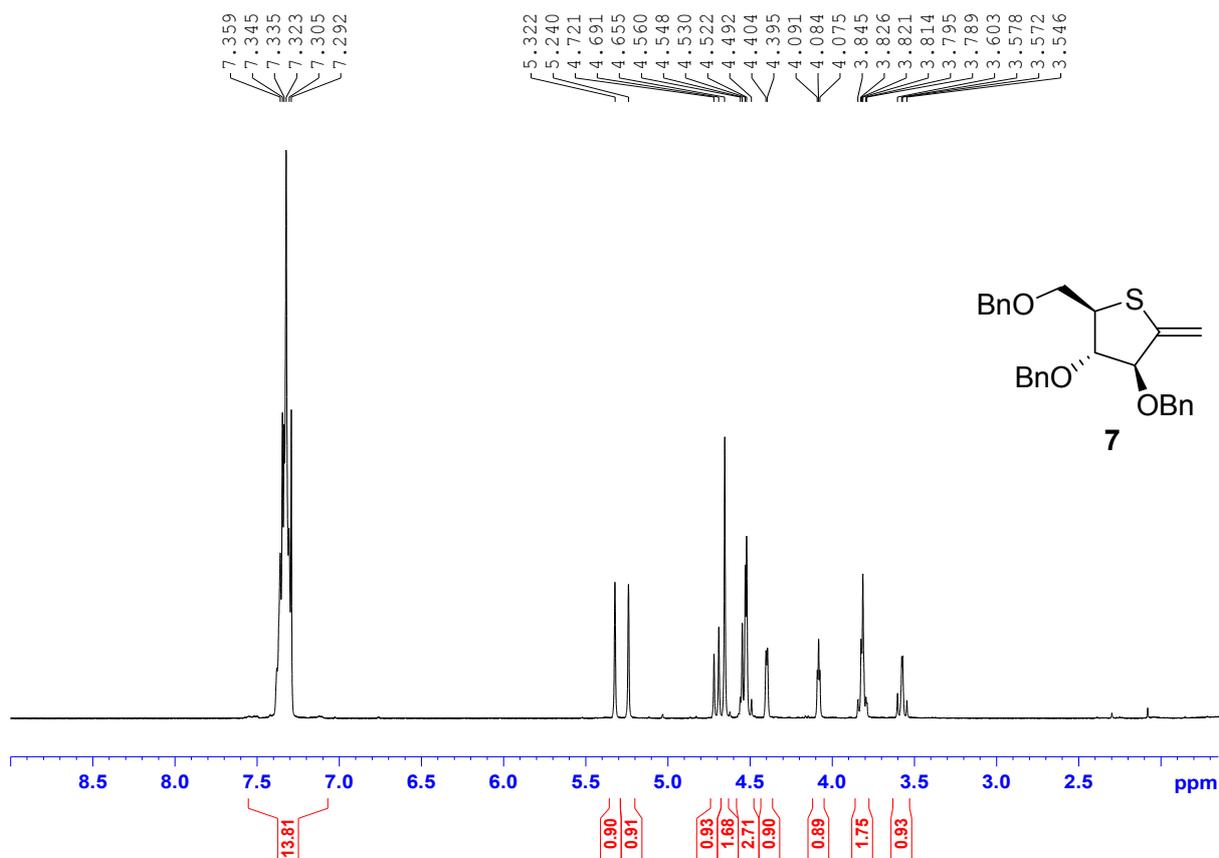
**<sup>1</sup>H NMR spectrum of compound 6 (CDCl<sub>3</sub>, 400 MHz)**



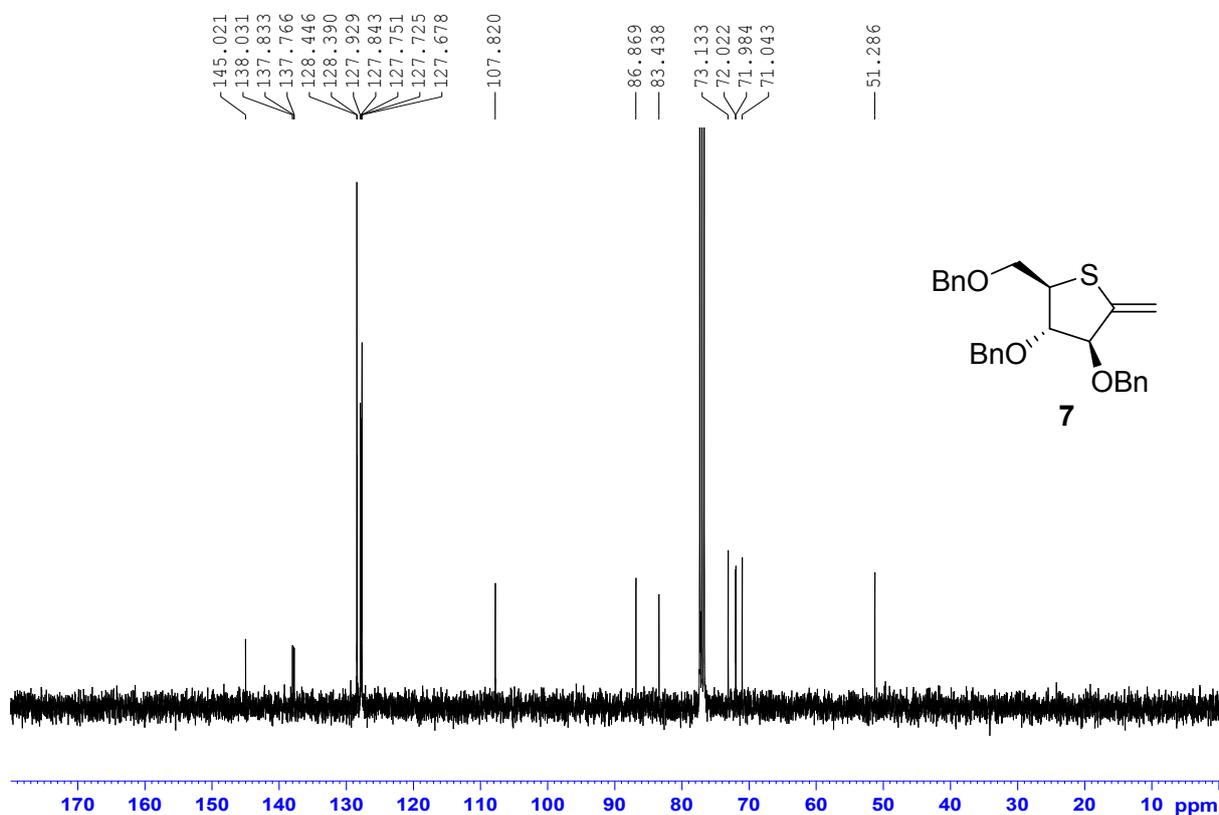
**<sup>13</sup>C NMR spectrum of compound 6 (CDCl<sub>3</sub>, 100 MHz)**



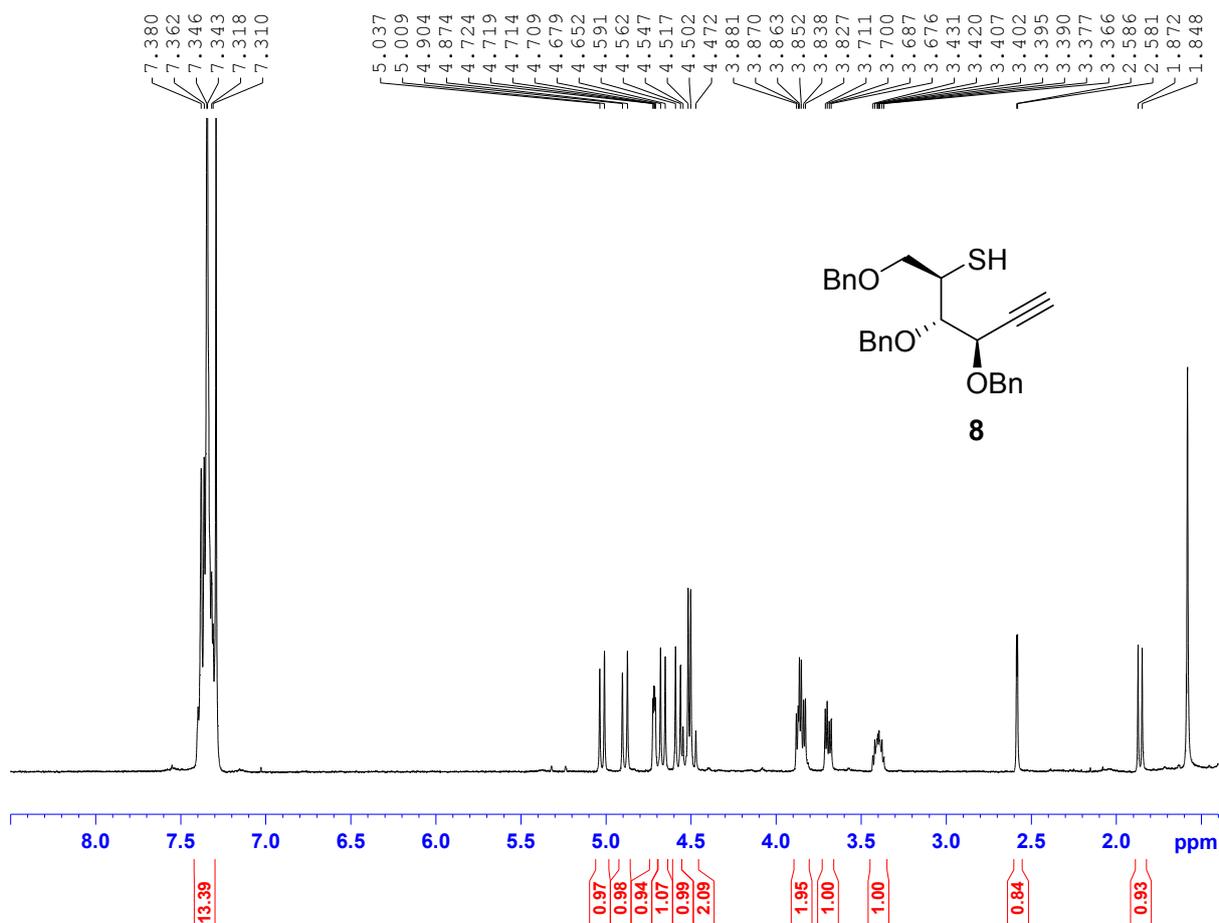
**<sup>1</sup>H NMR spectrum of compound 7 (CDCl<sub>3</sub>, 400 MHz)**



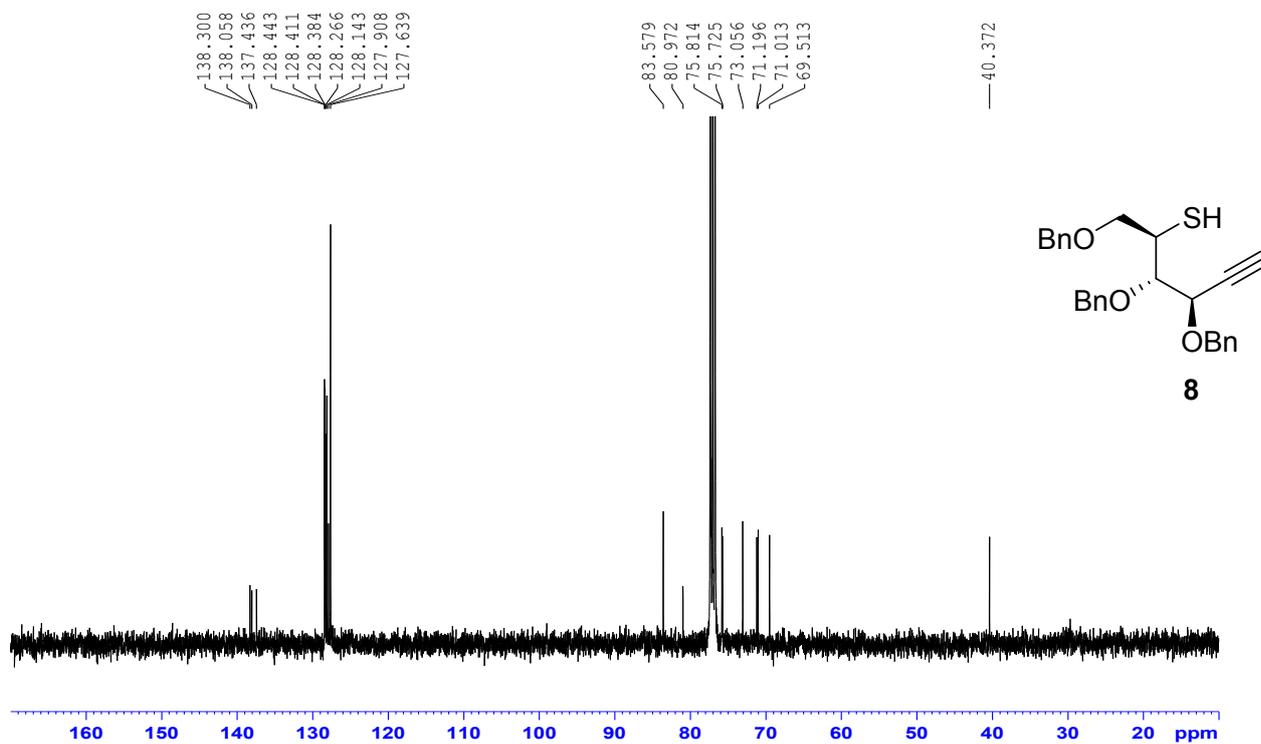
**<sup>13</sup>C NMR spectrum of compound 7 (CDCl<sub>3</sub>, 100 MHz)**



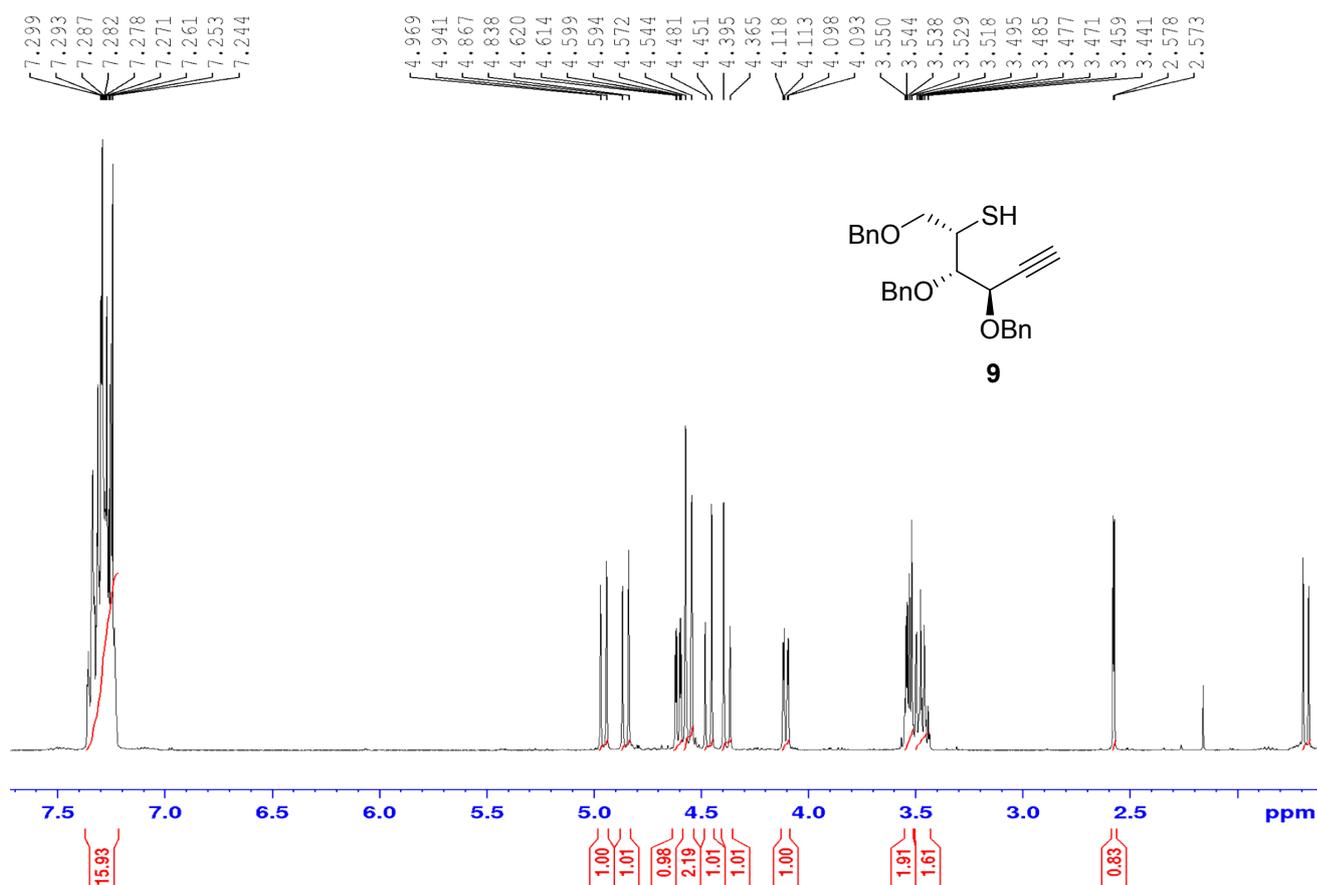
**<sup>1</sup>H NMR spectrum of compound 8 (CDCl<sub>3</sub>, 400 MHz)**



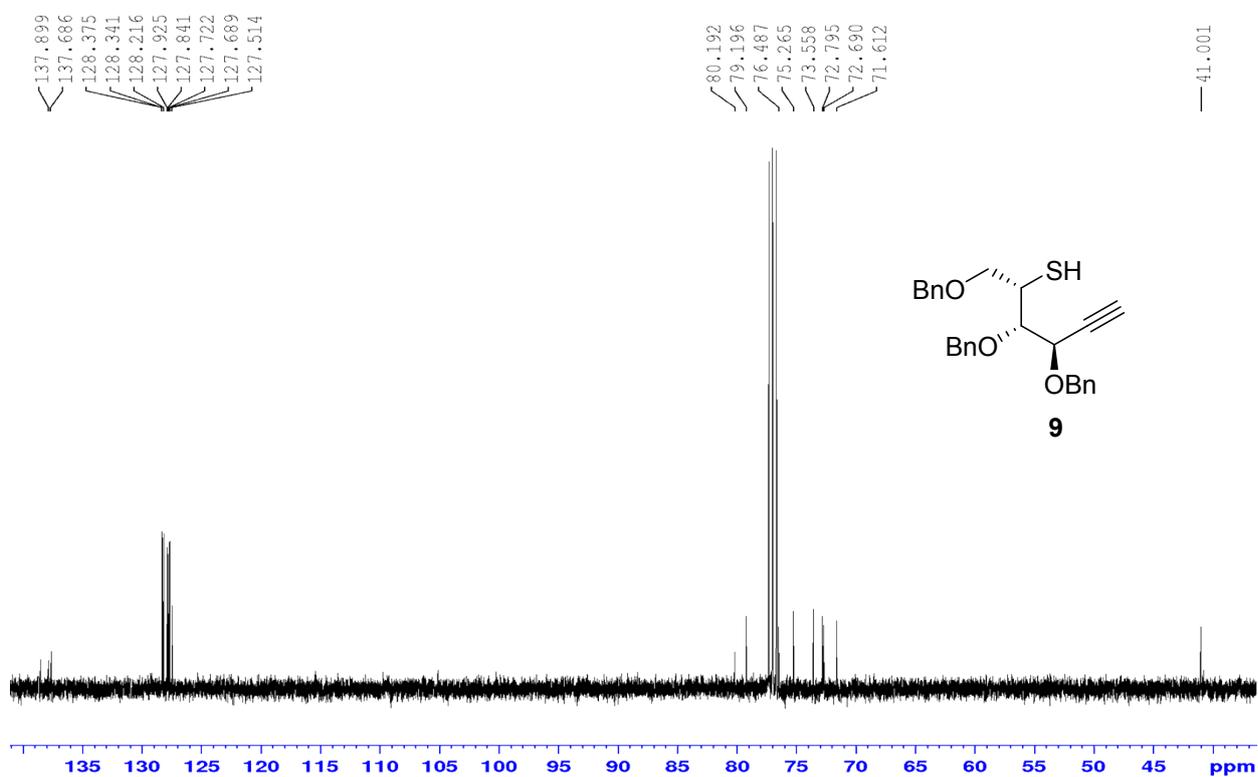
**<sup>13</sup>C NMR spectrum of compound 8 (CDCl<sub>3</sub>, 100 MHz)**



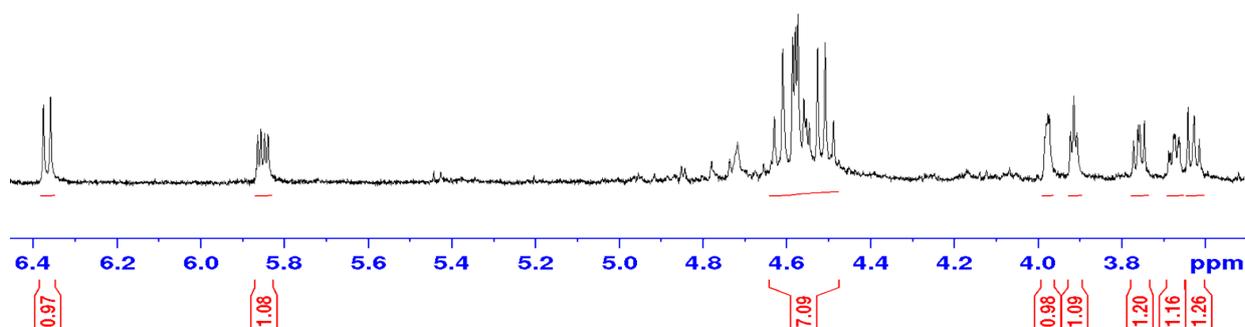
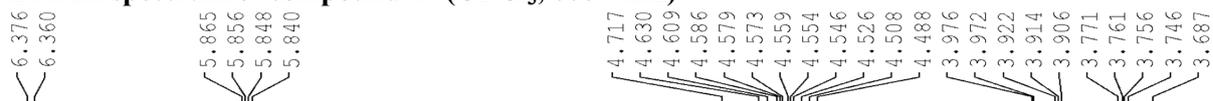
**<sup>1</sup>H NMR spectrum of compound 9 (CDCl<sub>3</sub>, 400 MHz)**



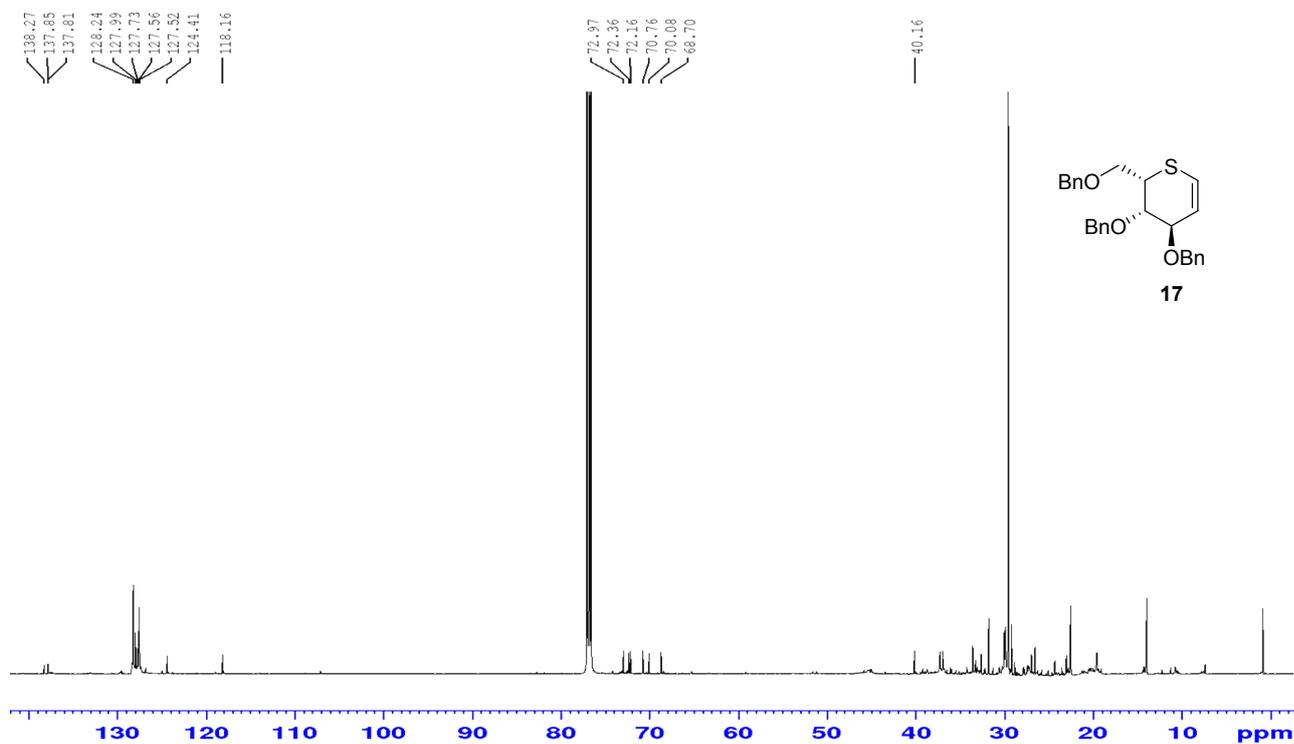
**<sup>13</sup>C NMR spectrum of compound 9 (CDCl<sub>3</sub>, 100 MHz)**



**<sup>1</sup>H NMR spectrum of compound 17 (CDCl<sub>3</sub>, 600 MHz)**



**<sup>13</sup>C NMR spectrum of compound 17 (CDCl<sub>3</sub>, 150 MHz)**



HSQC spectrum of compound 17 (CDCl<sub>3</sub>, 150 MHz)

