

## Supplementary Information

### **A direct and stereospecific approach to the synthesis of $\alpha$ -glycosyl thiols**

Ravindra T. Dere,<sup>a</sup> Yingxi Wang,<sup>a</sup> and Xiangming Zhu<sup>a,b,\*</sup>

<sup>a</sup> Centre for Synthesis and Chemical Biology, UCD School of Chemistry and Chemical Biology, University College Dublin, Belfield, Dublin 4, Ireland

<sup>b</sup> Zhejiang Key Laboratory for Reactive Chemistry on Solid Surfaces, College of Chemistry and Life Sciences, Zhejiang Normal University, Jinhua 321004, P R China

Tel: +353 17162386; Fax: +353 17162501; Email: [Xiangming.Zhu@ucd.ie](mailto:Xiangming.Zhu@ucd.ie)

### **Table of Contents**

#### **1.0 General Method**

#### **2.0 Synthesis of Glycosyl Thiols: General Procedure**

#### **3.0 Characterization Data for the Products 6 – 10**

#### **4.0 NMR Spectra**

## 1.0 General Method

Reactions were performed in oven-dried glassware under an argon atmosphere using dry solvents. Solvents were evaporated under reduced pressure while maintaining the water bath temperature below 40 °C. All reactions were monitored by thin-layer chromatography (TLC) using silica gel 60 F<sub>254</sub> coated on aluminium sheet and the compounds visualized by UV or by treatment with 8% H<sub>2</sub>SO<sub>4</sub> in methanol followed by heating. Flash chromatography was performed with the appropriate solvent system using 40-60 µm silica gel. Optical rotations were measured at 20 °C. CDCl<sub>3</sub> and tetramethylsilane was used as solvent and internal standard, respectively, for <sup>1</sup>H NMR (400 and 500 MHz) spectra. <sup>13</sup>C NMR spectra were recorded at 100 or 125 MHz by using CDCl<sub>3</sub> as solvent and the signals were assigned with the aid of DEPT, HSQC. Yields refer to chromatographically pure compounds and are calculated based on reagents consumed.

## 2.0 Synthesis of $\alpha$ -Glycosyl Thiols: General Procedure

To a solution of the appropriate 1,6-anhydrosugars (1.0 mmol) and bis(trimethylsilyl)sulfide (1.4 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) was added TMSOTf (0.4 mmol) at 0 °C. The mixture was then stirred at 50 °C until TLC indicated complete consumption of the starting material, then poured into aqueous NaHCO<sub>3</sub>, and extracted with EtOAc. The organic layer was washed successively with water and brine, dried over MgSO<sub>4</sub>, and concentrated in vacuo to give a residue which was purified by flash column chromatography to afford the corresponding  $\alpha$ -glycosyl thiol.

## 3.0 Characterization Data for the Products 6 – 10

**2,3,4-Tri-*O*-benzyl-1-thio- $\alpha$ -D-galactopyranose (6).** [ $\alpha$ ]<sub>D</sub> +93.6 (c 0.8, CHCl<sub>3</sub>); <sup>1</sup>H NMR  $\delta$  (500 MHz, CDCl<sub>3</sub>) 7.38-7.24 (m, 15H, ArH), 5.84 (t, *J* = 5, 4.5 Hz, 1H, H-1),

4.93 and 4.65 (AB peak,  $J = 11.5$  Hz, 2H, PhCH<sub>2</sub>), 4.84 and 4.69 (AB peak,  $J = 12.0$  Hz, 2H, PhCH<sub>2</sub>), 4.72 and 4.69 (AB peak,  $J = 11.0$  Hz, 2H, PhCH<sub>2</sub>), 4.25 (dd,  $J = 5.0, 9.5$  Hz, 1H, H-2), 4.15 (t,  $J = 6.0, 5.5$  Hz, 1H, H-5), 3.89 (br s, 1H, H-4), 3.81 (dd,  $J = 2.5, 9.5$  Hz, 1H, H-3), 3.72 (dd,  $J = 6.5, 11.5$  Hz, 1H, H-6<sub>a</sub>), 3.54-3.49 (m, 1 H, H-6<sub>b</sub>), 1.83 (d,  $J = 4.0$  Hz, 1H, SH); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  138.4, 138.0, 137.8, 128.6, 128.5, 128.44, 128.39, 128.0, 127.9, 127.8, 127.7, 127.6 (aromatic carbons), 79.4 (C-1), 78.6 (C-3), 75.9 (C-2), 74.6 (C-4), 74.4, 73.6, 72.6 (3xPhCH<sub>2</sub>), 71.6 (C-5), 62.0 (C-6). ESI-MS  $m/z$  489.2 [M + Na]<sup>+</sup>. ESI-HRMS calcd for C<sub>27</sub>H<sub>30</sub>NaO<sub>5</sub>S [M + Na]<sup>+</sup> 489.1712, found 489.1712.

**2,3,4-Tri-*O*-benzyl-1-thio- $\alpha$ -D-glucopyranose (7).** [ $\alpha$ ]<sub>D</sub> +95.1 (c 1.0 CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.31-7.22 (m, 15H, ArH), 5.62 (t,  $J = 5.2, 4.8$  Hz, 1H, H-1), 4.88 and 4.74 (AB peak,  $J = 10.8$  Hz, 2H, PhCH<sub>2</sub>), 4.81 and 4.58 (AB peak,  $J = 11.0$  Hz, 2H, PhCH<sub>2</sub>), 4.66 and 4.57 (AB peak,  $J = 11.8$  Hz, 2H, PhCH<sub>2</sub>), 4.02 (m, 1H, H-5), 3.82 (t,  $J = 9.2, 8.8$  Hz, 1H, H-3), 3.68 (m, 3 H, H-2, H-6<sub>a</sub>, H-6<sub>b</sub>), 3.48 (t,  $J = 10.0, 9.2$  Hz, 1H, H-4), 1.84 (d,  $J = 4.8$  Hz, 1H, SH); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) 138.7, 138.2, 137.7, 128.66, 128.65, 128.6, 128.22, 128.20, 128.17, 128.13, 128.09, 127.8 (aromatic carbons), 81.8 (C-3), 79.5 (C-2), 78.9 (C-1), 77.1 (C-4), 75.9, 75.2, 72.6 (3xPhCH<sub>2</sub>), 72.0 (C-5), 61.9 (C-6). ESI-MS  $m/z$  489.2 [M + Na]<sup>+</sup>. ESI-HRMS calcd for C<sub>27</sub>H<sub>30</sub>NaO<sub>5</sub>S [M + Na]<sup>+</sup> 489.1712, found 489.1698.

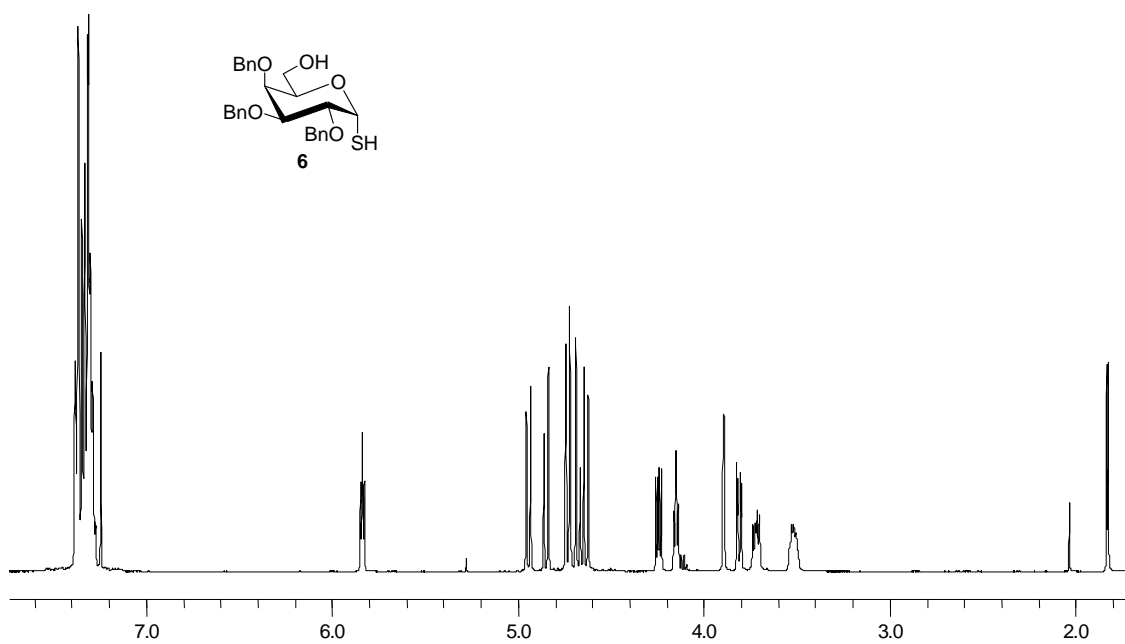
**2,3,4-Tri-*O*-allyl-1-thio- $\alpha$ -D-glucopyranose (8).** [ $\alpha$ ]<sub>D</sub> +173.1 (c 2.0, CHCl<sub>3</sub>); <sup>1</sup>H NMR  $\delta$  (500 MHz, CDCl<sub>3</sub>) 5.99-5.87 (m, 3H, 3xCH<sub>2</sub>CHCH<sub>2</sub>), 5.70 (t,  $J = 5.0$  Hz, 1H, H-1), 5.29 (m, 3H, 3xCH<sub>2</sub>CHCH<sub>a</sub>H<sub>b</sub>), 5.18 (m, 3H, 3xCH<sub>2</sub>CHCH<sub>a</sub>H<sub>b</sub>), 4.37-4.08 (m, 6H, 3xCH<sub>2</sub>CHCH<sub>2</sub>), 4.01 (dt,  $J = 3.5, 10.0$  Hz, 1H, H-5), 3.82 (dd,  $J = 2.0, 12.0$  Hz, 1H, H-6<sub>a</sub>), 3.75 (d,  $J = 11.5$  Hz, 1H, H-6<sub>b</sub>), 3.58 (overlapped m, 2H, H-2, H-3), 3.35 (t,  $J = 9.0, 9.5$  Hz, 1H, H-4), 1.88 (d,  $J = 5.0$  Hz, 1H, SH); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  135.1, 134.6, 134.3 (3xCH<sub>2</sub>CHCH<sub>2</sub>), 117.5, 117.1, 116.6 (3xCH<sub>2</sub>CHCH<sub>2</sub>), 81.0 (C-3), 78.96 (C-1), 78.80 (C-2), 77.0 (C-4), 74.3, 73.8 (2xCH<sub>2</sub>CHCH<sub>2</sub>), 71.8 (C-5), 71.5 (CH<sub>2</sub>CHCH<sub>2</sub>), 61.7 (C-6). ESI-MS  $m/z$  339.1 [M + Na]<sup>+</sup>. ESI-HRMS calcd for C<sub>15</sub>H<sub>25</sub>O<sub>5</sub>S [M + H]<sup>+</sup> 317.1423, found 317.1436.

**2,3-Di-O-allyl-4-O-benzyl-1-thio- $\alpha$ -D-glucopyranose (9).**  $[\alpha]_D +117$  (c 0.2,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR  $\delta$  (500 MHz,  $\text{CDCl}_3$ ) 7.35-7.25 (m, 5H, ArH), 6.00-5.88 (m, 2H,  $2\times\text{CH}_2\text{CHCH}_2$ ), 5.71 (t,  $J = 5.5$  Hz, 1H, H-1), 5.31 (m, 2H,  $\text{CH}_2\text{CHCH}_2$ ), 5.19 (m, 2H,  $\text{CH}_2\text{CHCH}_2$ ), 4.88 and 4.66 (AB peak,  $J = 10.5, 11.0$  Hz, 2H,  $\text{PhCH}_2$ ), 4.40 (dd,  $J = 5.5, 12.0$  Hz, 1H,  $\text{CH}_2\text{CHCH}_2$ ), 4.28 (dd,  $J = 5.5, 12.0$  Hz, 1H,  $\text{CH}_2\text{CHCH}_2$ ), 4.17 (dd,  $J = 5.5, 12.5$  Hz, 1H,  $\text{CH}_2\text{CHCH}_2$ ), 4.10 (dd,  $J = 5.5, 12.5$  Hz, 1H,  $\text{CH}_2\text{CHCH}_2$ ), 4.05 (dt,  $J = 3.5, 10.0$  Hz, 1H, H-5), 3.79-3.68 (overlapped m, 3H, H-3, H-4, H-6<sub>a</sub>), 3.62 (dd,  $J = 5.5, 9.5$  Hz, 1H, H-2), 3.49 (t,  $J = 9.5$  Hz, 1H, H-6<sub>b</sub>), 1.87 (d,  $J = 4.5$  Hz, 1H, SH);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  138.1, 135.1, 134.3, ( $2\times\text{CH}_2\text{CHCH}_2$ ) 128.50, 128.45, 128.1, 127.9, 127.8 (aromatic carbons), 117.6, 116.7 ( $2\times\text{CH}_2\text{CHCH}_2$ ), 81.3 (C-1), 79.1 (C-3), 78.8 (C-2), 77.0 (C-4), 75.1 ( $\text{PhCH}_2$ ), 74.4, 71.8 ( $2\times\text{CH}_2\text{CHCH}_2$ ), 71.5 (C-5), 61.8 (C-6). ESI-MS  $m/z$  389.1  $[\text{M} + \text{Na}]^+$ . ESI-HRMS calcd for  $\text{C}_{19}\text{H}_{26}\text{O}_5\text{NaS}$   $[\text{M} + \text{Na}]^+$  389.1399, found 389.1418.

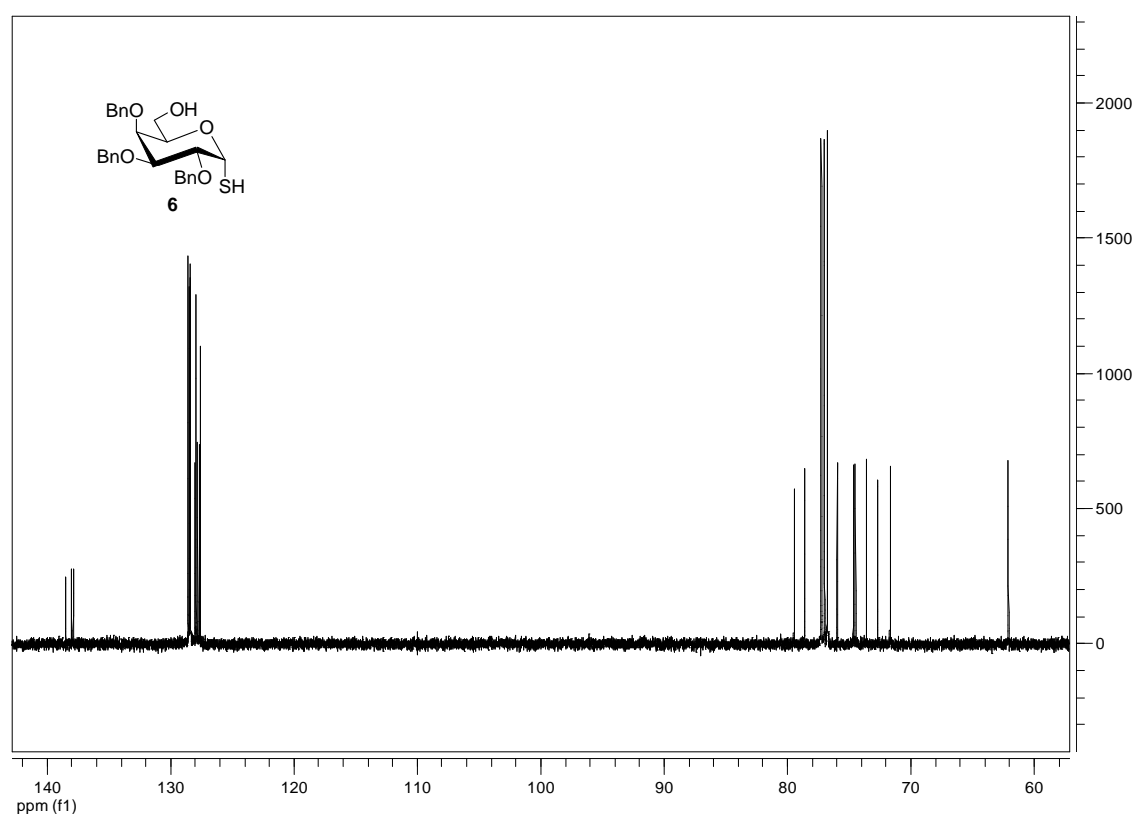
**2,3-Di-O-allyl-4-O-benzyl-1-thio- $\alpha$ -D-galactopyranose (10).**  $[\alpha]_D +76.2$  (c 2.0,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.39-7.32 (m, 5H, ArH), 6.02-5.91 (m, 2H,  $2\times\text{CH}_2\text{CHCH}_2$ ), 5.87 (t,  $J = 4.5$  Hz, 1H, H-1), 5.36 (m, 2H,  $\text{CH}_2\text{CHCH}_2$ ), 5.22 (m, 2H,  $\text{CH}_2\text{CHCH}_2$ ), 4.98 and 4.96 (AB peak,  $J = 11.5$  Hz, 2H,  $\text{PhCH}_2$ ), 4.33-4.17 (m, 4H,  $2\times\text{CH}_2\text{CHCH}_2$ ), 4.20 (overlapped m, 1H, H-5), 4.12 (dd,  $J = 5.5, 10.0$  Hz, 1H, H-2), 3.91 (br s, 1H, H-4), 3.76 (dd,  $J = 6.5, 11.5$  Hz, 1H, H-6<sub>a</sub>), 3.68 (dd,  $J = 2.5, 9.5$  Hz, 1H, H-3), 3.56 (m, 1H, H-6<sub>b</sub>), 1.83 (d,  $J = 4.0$  Hz, 1H, SH);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  138.1, 134.9, 134.5 ( $2\times\text{CH}_2\text{CHCH}_2$ ), 128.6, 128.51, 128.0 (aromatic carbons), 117.3, 116.6 ( $2\times\text{CH}_2\text{CHCH}_2$ ), 79.5 (C-1), 78.3 (C-3), 75.6 (C-2), 74.49 (C-4), 74.45 ( $\text{PhCH}_2$ ), 72.2, 71.7 ( $2\times\text{CH}_2\text{CHCH}_2$ ), 71.6 (C-5), 62.1 (C-6). ESI-MS  $m/z$  389.1  $[\text{M} + \text{Na}]^+$ . ESI-HRMS calcd for  $\text{C}_{19}\text{H}_{27}\text{O}_5\text{S}$   $[\text{M} + \text{H}]^+$  367.1579, found 367.1562.

#### 4.0 NMR Spectra

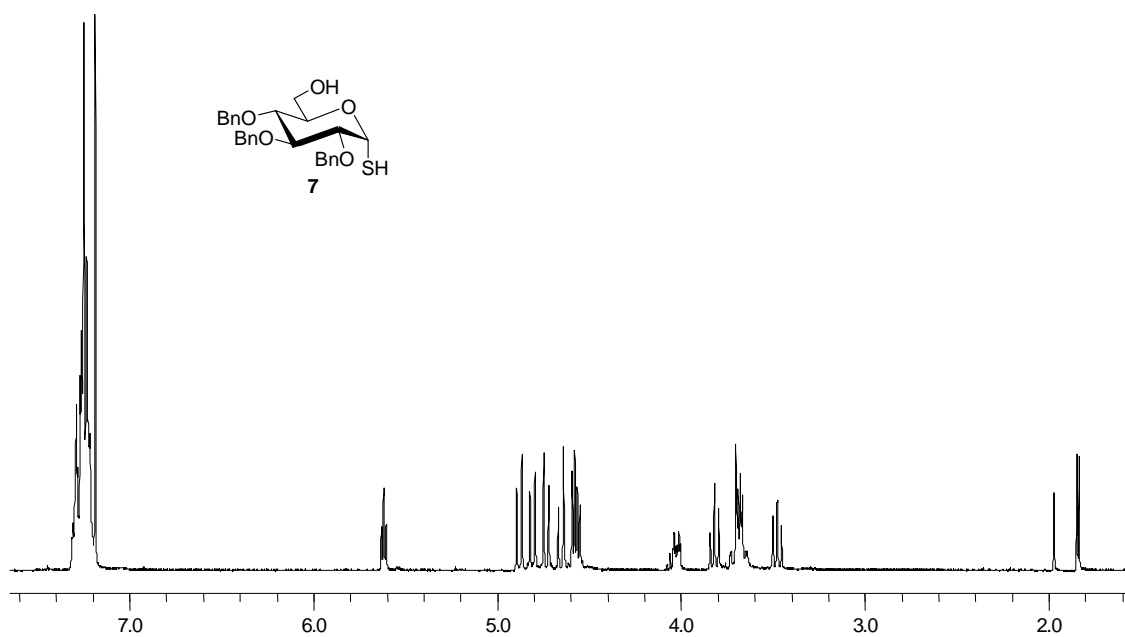
**$^1\text{H}$  NMR spectrum of compound 6**



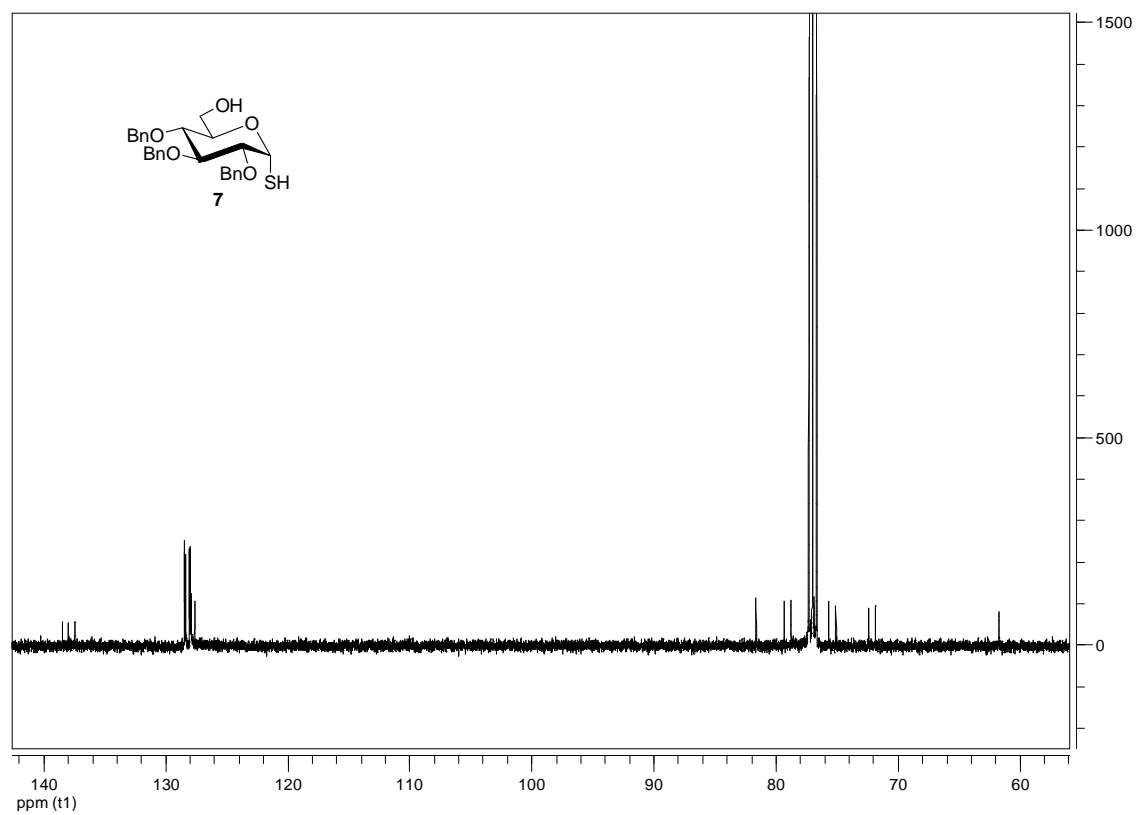
**$^{13}\text{C}$  NMR spectrum of compound 6**



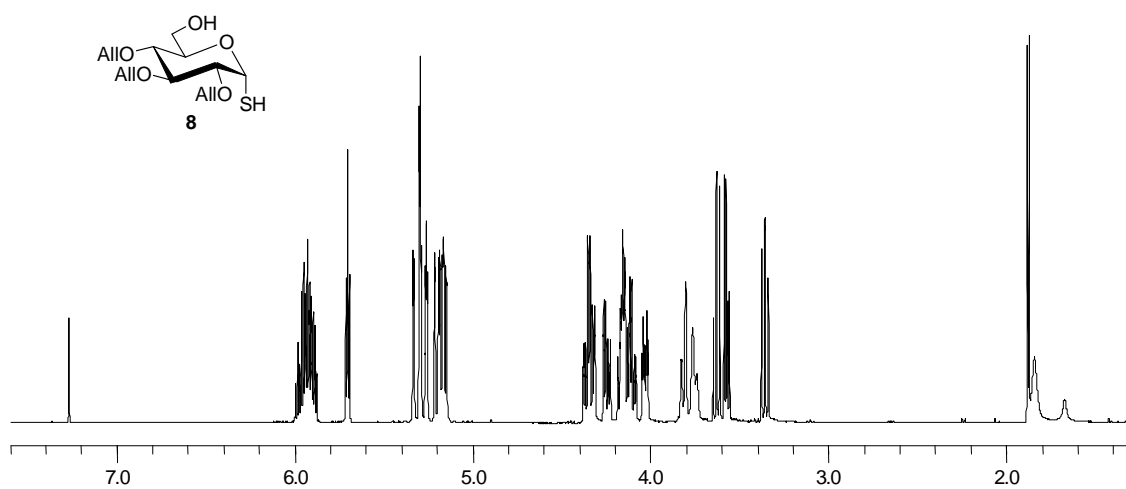
**$^1\text{H}$  NMR spectrum of compound 7**



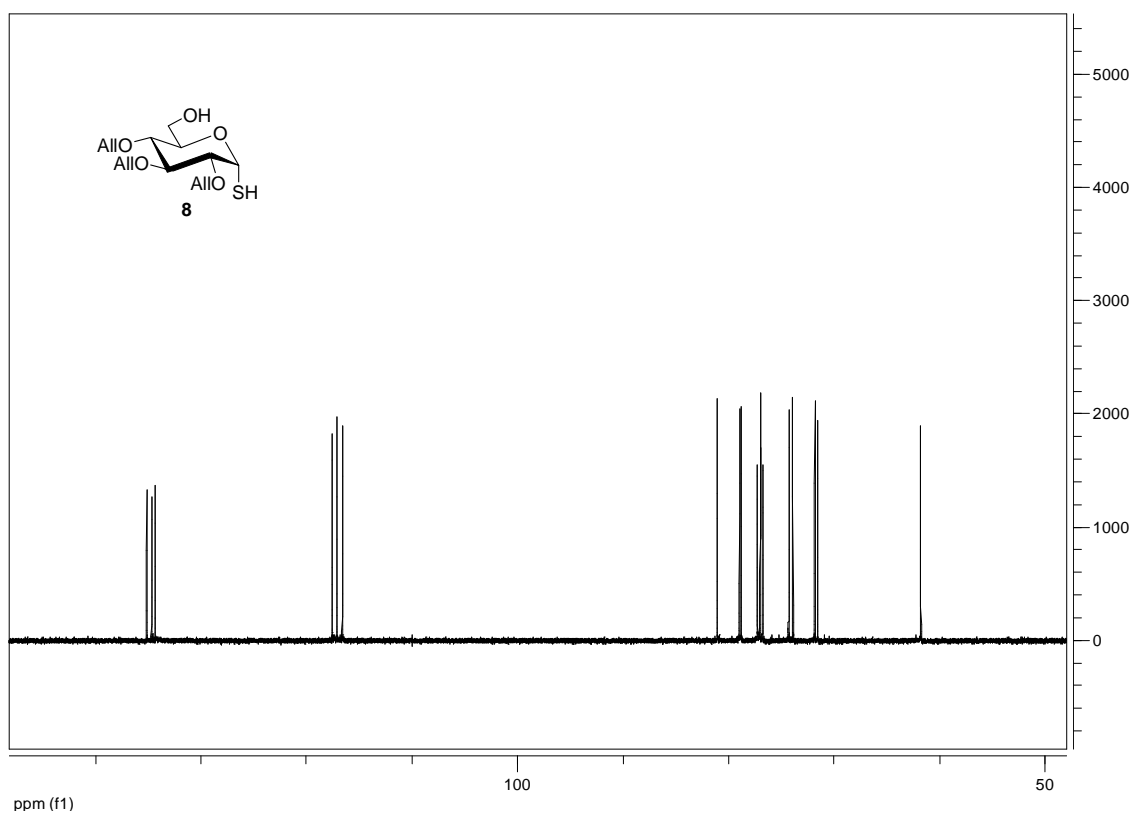
**$^{13}\text{C}$  NMR spectrum of compound 7**



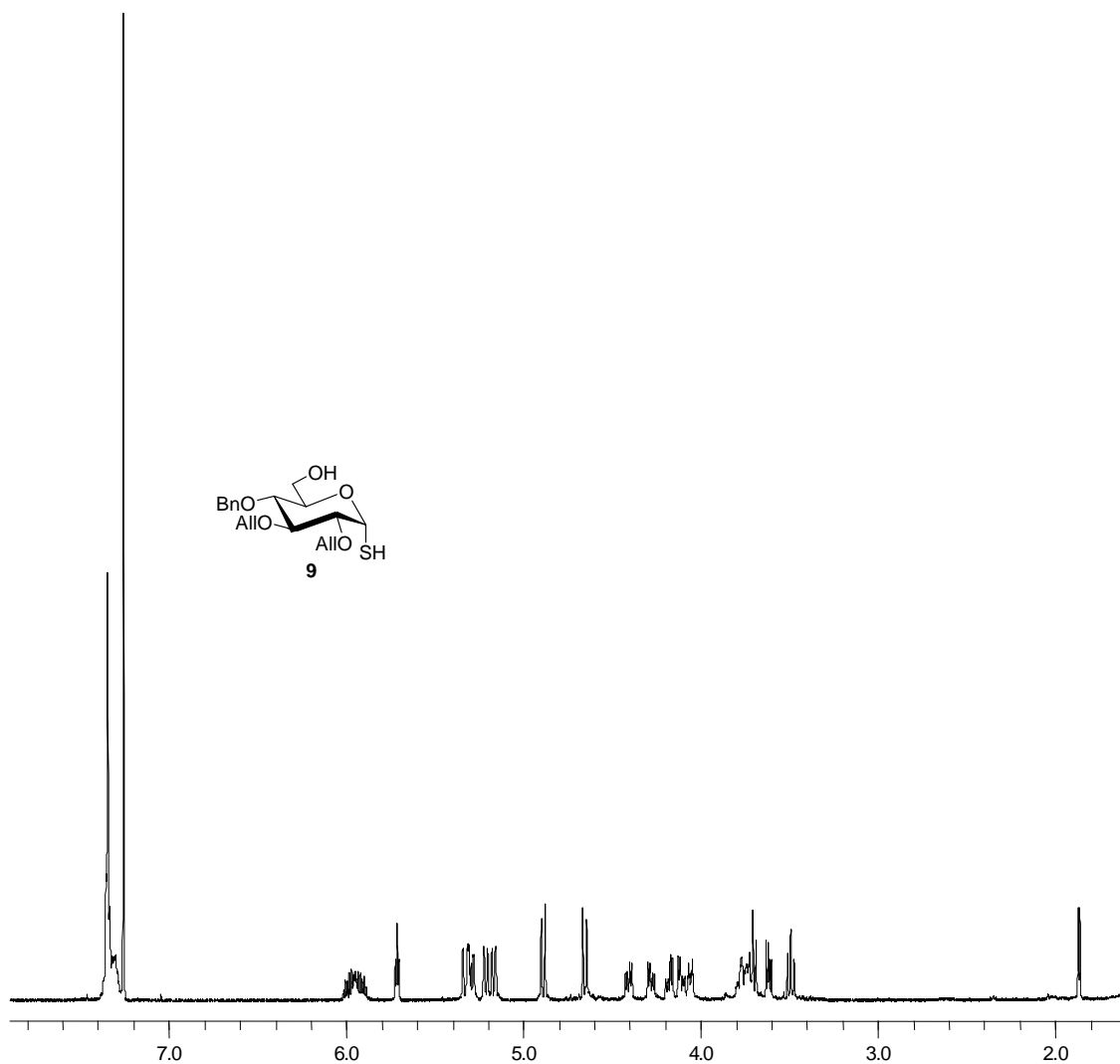
### $^1\text{H}$ NMR spectrum of compound 8



### $^{13}\text{C}$ NMR spectrum of compound 8

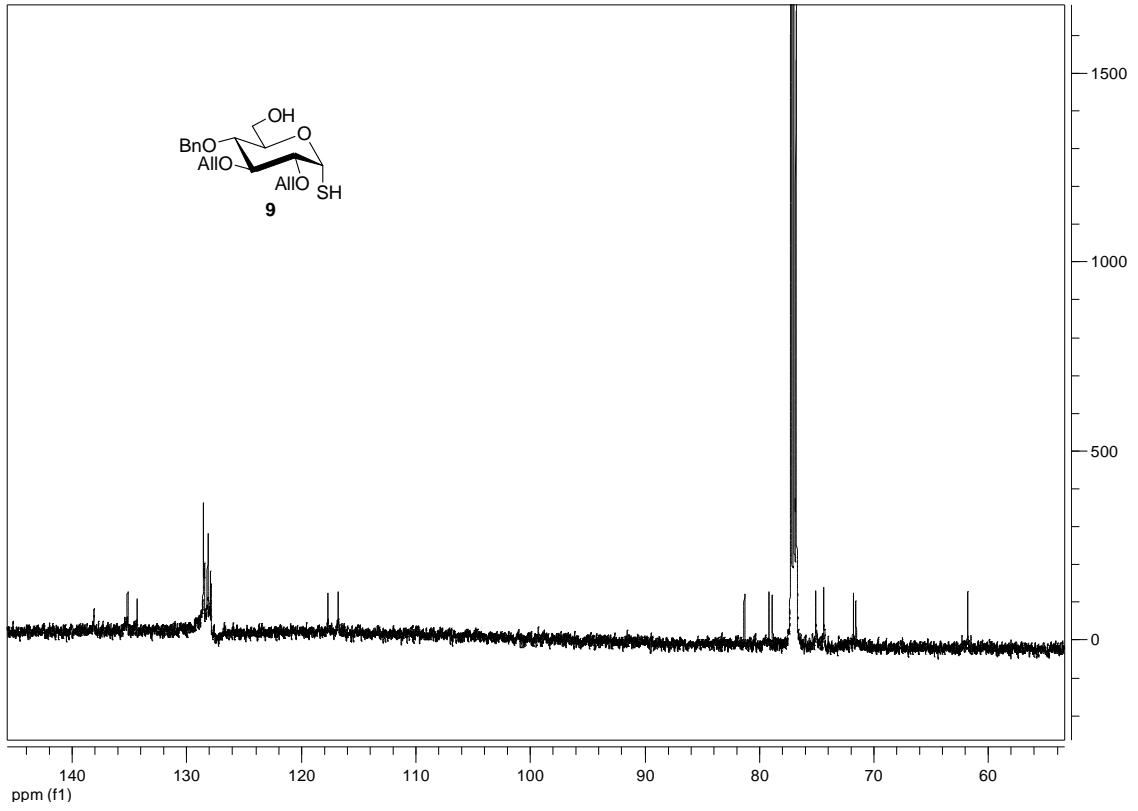


**$^1\text{H}$  NMR spectrum of compound 9**

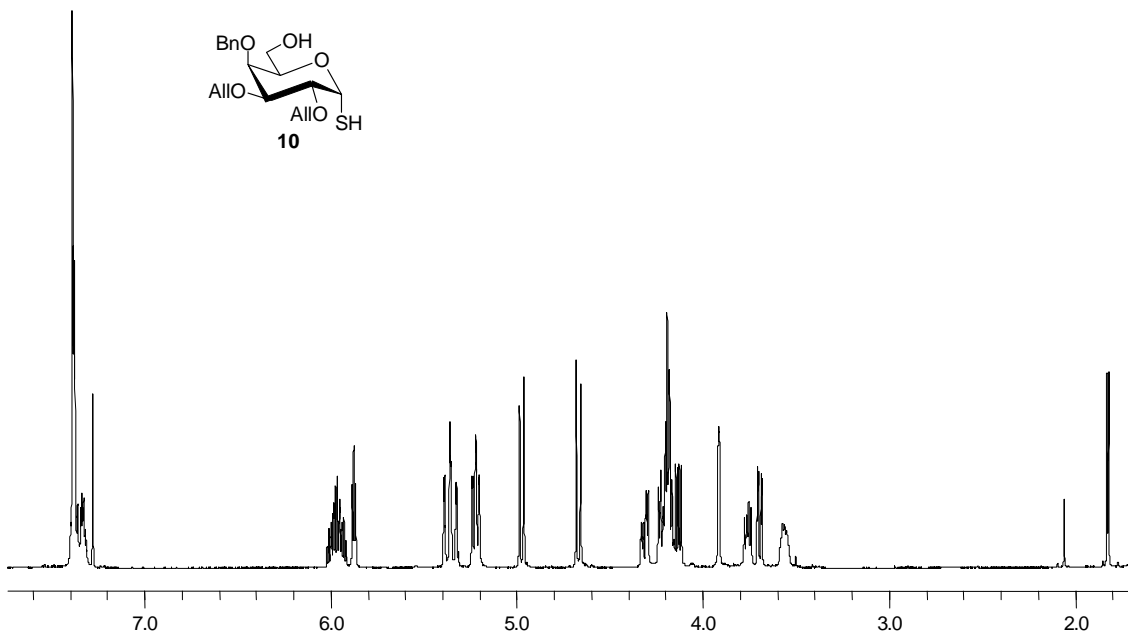


**$^{13}\text{C}$  NMR spectrum of compound 9**





**<sup>1</sup>H NMR spectrum of compound 10**



**<sup>13</sup>C NMR spectrum of compound 10**

